VERTEX PHARMACEUTICALS INC / MA
Form 10-K
February 17, 2009

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

ý **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the Fiscal Year Ended December 31, 2008

or

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from _____ to _____
Commission file number 000-19319

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 No.)
130 Waverly Street **Cambridge, Massachusetts**	**02139-4242**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code **(617) 444-6100**

Securities registered pursuant to Section 12(b) of the Exchange Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, $0.01 Par Value Per Share	The Nasdaq Global Select Market
Rights to Purchase Series A Junior Participating Preferred Stock	

Securities registered pursuant to Section 12(g) of the Exchange Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ý No o

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes o No ý

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ý No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ý

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

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes o No ý

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) based on the last reported sale price of the common stock on June 30, 2008 (the last trading day of the registrant's second fiscal quarter of 2008) was $3.1 billion.

As of February 10, 2009, the registrant had 152,189,782 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive Proxy Statement for the 2009 Annual Meeting of Stockholders to be held on May 14, 2009 are incorporated by reference into Part III of this Annual Report on Form 10-K.

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VERTEX PHARMACEUTICALS INCORPORATED

ANNUAL REPORT ON FORM 10-K

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"We," "us," "Vertex" and the "Company" as used in this Annual Report on Form 10-K, refer to Vertex Pharmaceuticals Incorporated, a Massachusetts corporation, and its subsidiaries.

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PART I

ITEM 1. 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.

HCV infection is a life-threatening disease that affects approximately 3.2 million people in the United States and causes inflammation of the liver, significantly increasing the risk that a patient will develop liver failure or liver cancer. Genotype 1 HCV is the most prevalent HCV genotype in North America, the European Union and Japan. Our Phase 3 clinical trial ADVANCE is designed to evaluate telaprevir in treatment-naïve patients with genotype 1 HCV, with the goal of supporting registration of telaprevir by establishing that telaprevir-based treatment regimens can significantly improve sustained viral response, or SVR, rates while decreasing the total treatment duration for most patients from 48 weeks to 24 weeks. Our Phase 3 clinical trial REALIZE is designed to evaluate a telaprevir-based treatment regimen in each major category of patients with genotype 1 HCV who have failed to achieve an SVR with prior treatment with pegylated-interferon, or peg-IFN, and ribavirin, or RBV. We designed our registration program based on data from our Phase 2b clinical trials, including data from our PROVE 1 and PROVE 2 clinical trials in treatment-naïve patients, in which the SVR rates in the 24-week telaprevir-based treatment arms were 61% and 69% compared to 41% and 46% in the control arms, respectively. Our registration program also is based on promising interim data from our Phase 2b clinical trial in treatment-experienced patients. Safety data from our Phase 2 clinical trials indicated that the most common adverse events, regardless of treatment assignment, were fatigue, rash, headache and nausea. Gastrointestinal disorders, skin adverse events, including rash and pruritus, and anemia were more frequent, and the rash more frequently severe, in the telaprevir arms than in the control arms over the dosing period. We are collaborating on the global clinical development program for telaprevir with Janssen Pharmaceutica, N.V., a Johnson & Johnson company, and Mitsubishi Tanabe Pharma Corporation. We have retained exclusive commercial rights to telaprevir in North America.

Cystic fibrosis is an inherited disorder that results in a progressive decline in lung function and a significant decrease in the life expectancy of patients with CF. The drug candidates that we are developing for CF are designed to address the underlying cause of CF by partially restoring the function of defective cystic fibrosis transmembrane conductance regulator, or CFTR, proteins in CF patients. In October 2008, we completed a Phase 2a clinical trial of VX-770 in 39 patients with CF who had the G551D mutation that involved dosing VX-770 over 14-day and 28-day periods. The primary endpoint for this clinical trial was safety, and no serious adverse events attributable to VX-770 were observed. Based on the promising lung function data from this clinical trial, as measured by improvements in FEV_1, the lung function test most commonly used to monitor CF disease progression, and based also on observed changes in biomarkers that seek to measure the activity of the CFTR protein, we are working with regulatory authorities in North America and Europe to finalize the design of a registration program for VX-770.

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

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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.

OUR STRATEGY

Our goal is to become a fully integrated biotechnology company with industry-leading capabilities in research, development and commercialization of innovative drugs that provide substantial benefits to patients with serious diseases. The key elements of our strategy are:

Complete development of and successfully commercialize telaprevir. We are investing significant resources in our registration program for telaprevir, which is designed to support registration of telaprevir for treatment-naïve and treatment-experienced patients infected with genotype 1 HCV. We are focused on 24-week response-guided telaprevir-based treatment regimens for treatment-naïve patients and on treating all categories of treatment-experienced patients, including null responders to peg-IFN and RBV, who are the most difficult category of HCV patients to treat successfully. In preparation for the planned launch of telaprevir, we are investing in our marketing organization and beginning a dialogue with commercial health insurers and government organizations regarding the public health risk posed by HCV and the potential for specifically targeted antiviral agents to provide substantial benefits to patients, thereby reducing the burden of HCV infection on the health care system.

Establish a leadership position in the treatment of HCV infection. We believe that if telaprevir is launched on the timeline that is currently anticipated, our most substantial initial competition will be from combination treatment regimens involving protease inhibitors, if any, that are approved on a similar timeline to telaprevir. Over the longer term, we believe that treatment of HCV infection will continue to require combination drug therapies in order to achieve optimal SVR rates, including potentially all-oral drug combinations that would not require or would reduce reliance on interferons, which require weekly injections. We are pursuing business development activities with potentially complimentary therapies including polymerase inhibitors, other direct acting antivirals, and novel interferons, which could be developed in combination with telaprevir or our earlier-stage protease inhibitors.

Develop our CF drug candidates. We believe that we have the potential to develop and commercialize drug candidates that could be used to treat a range of patients with CF. In the first half of 2009, we intend to commence a registration program for VX-770 that will focus on adult and pediatric patients with the G551D mutation. In the first half of 2009 we also are planning to commence a Phase 2a clinical trial of VX-809, a drug candidate targeted at a broader group of patients with CF that have mutations resulting in different defects in the CFTR protein. We believe that drugs that address the underlying causes of CF can provide meaningful benefits to patients.

Invest in research and early development. We intend to continue to invest significant resources in research and early development across a relatively broad array of therapeutic areas due to the relatively high potential for failure of any specific effort. We believe this diversified strategy is essential to the strength of our business as we seek to identify additional promising drug candidates that could populate our future drug development pipeline. We direct our research activities toward therapies designed to address serious diseases because these therapies have the potential to deliver the greatest value for patients, physicians and the health care system.

Capitalize on collaboration arrangements and business development opportunities. Collaborations provide us with financial support and other valuable resources for our development and research programs. We plan to continue to rely on collaborators to support, develop and commercialize some of our drug candidates either worldwide or in markets in which we are not concentrating our resources. We also seek opportunistically to license and acquire technologies, resources and drugs or drug candidates that have the potential to strengthen our drug discovery platform, pipeline and/or commercial opportunities.

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PIPELINE

Our pipeline is described in the following table. In addition to those listed below, we are engaging in preclinical activities with respect to several additional drug candidates.

Drug or Drug Candidate	Clinical Indication(s)	Phase	Marketing Rights (Region)
Infectious Diseases			
Lexiva/Telzir	HIV infection	Marketed	GlaxoSmithKline (Worldwide)*
Telaprevir (VX-950)	Chronic HCV infection	Phase 3	Vertex (North America) Mitsubishi Tanabe (Far East) Janssen (Rest of World)
VX-813	Chronic HCV infection	Phase 1a	Vertex (Worldwide)
VX-985	Chronic HCV infection	Preclinical	Vertex (Worldwide)
Cystic Fibrosis			
VX-770	Cystic fibrosis	Phase 2a	Vertex (Worldwide)
VX-809	Cystic fibrosis	Phase 1b	Vertex (Worldwide)
IMID			
VX-509	IMID	Phase 1a	Vertex (Worldwide)
Cancer			
MK-5108 (VX-689)	Cancer	Phase 1	Merck & Co., Inc. (Worldwide)
AVN-944 (VX-944)	Cancer	Phase 2	Avalon Pharmaceuticals, Inc. (Worldwide)

* We sold our rights to future royalties from sales of Lexiva/Telzir in May 2008.

Telaprevir (VX-950) (investigational oral HCV protease inhibitor for the treatment of chronic HCV infection)

Telaprevir, our lead drug candidate, is an orally-administered hepatitis C protease inhibitor. Telaprevir is designed to inhibit the NS3-4A serine protease, an enzyme necessary for HCV replication. The United States Food and Drug Administration, or FDA, has granted "Fast Track" designation to telaprevir. Telaprevir is being investigated in several concurrent late-stage clinical trials, including ADVANCE, a Phase 3 clinical trial in treatment-naïve patients, ILLUMINATE, a clinical trial in treatment-naïve patients, and REALIZE, a Phase 3 clinical trial in treatment-experienced patients. Enrollment in ADVANCE, ILLUMINATE and REALIZE was completed in October 2008, December 2008 and February 2009, respectively. We are planning on submitting an NDA for telaprevir in the second half of 2010, assuming the successful completion of our ongoing registration program.

Under our agreement with Janssen, we have retained exclusive commercial rights to telaprevir in North America and are leading the clinical development program of telaprevir in North America and the Janssen territories. Janssen has the right to market telaprevir in the rest of the world except for Japan and certain Far East countries, where we are collaborating with Mitsubishi Tanabe. Janssen has agreed to be responsible for 50% of drug development costs under the development program for the Vertex and Janssen territories and to make contingent milestone payments based on the successful development, approval and launch of telaprevir. Janssen will be responsible for the commercialization of telaprevir, including the manufacture of its own commercial supply of telaprevir, outside of North America and the Far East. Telaprevir was discovered in our collaboration, now ended, with Eli Lilly and Company. We expect to pay Eli Lilly certain royalties on future sales of telaprevir, if approved.

Background: Prevalence and Treatment of Chronic Hepatitis C Virus Infection

HCV infection causes an inflammation of the liver called chronic hepatitis. This condition can progress to scarring of the liver, called fibrosis, or more advanced scarring, called cirrhosis. Patients with cirrhosis may go on to develop liver failure or the complications of cirrhosis, including liver cancer. The World Health Organization has reported that HCV is responsible for more than 50% of all liver cancer cases and two-thirds of all liver transplants in the developed world.

The World Health Organization has estimated that about 170 million people are chronically infected with HCV worldwide and that an additional 3 million to 4 million people are infected each year. The Centers for Disease Control and Prevention have estimated that approximately 3.2 million people in the United States are chronically infected with HCV.

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Our clinical development activities related to telaprevir are focused on genotype 1 HCV, which is the most prevalent form of HCV in the United States, the European Union and Japan. We believe that approximately 2.6 million patients in the United States have genotype 1 HCV. We believe that these patients include approximately 750,000 patients who have already been diagnosed with genotype 1 HCV and 1.8 million patients who remain undiagnosed.

In addition to being the most prevalent form of HCV, genotype 1 HCV is currently the most difficult to treat of the primary HCV genotypes. The current standard treatment for infection by genotype 1 HCV, which was first approved in 2001, is a combination of peg-IFN and RBV, generally administered for 48 weeks. This treatment regimen is associated with significant side effects, including fatigue, flu-like symptoms, rash, depression and anemia. Among patients who begin treatment, a significant percentage of patients infected with genotype 1 HCV fail to show a long-term sustained response to therapy. For example, on an intent-to-treat basis, 41% and 46%, respectively, of genotype 1 HCV patients in the control arms of our Phase 2b clinical trials known as PROVE 1 and PROVE 2 achieved an SVR. In another recent clinical trial conducting by another company involving approximately 3,070 treatment-naïve patients in the United States with genotype 1 HCV, between 38% and 41% of patients receiving peg-IFN and RBV achieved an SVR. We believe that over 250,000 patients with genotype 1 HCV in the United States have undergone prior therapy with peg-IFN and RBV, but have failed to achieve an SVR.

Telaprevir Clinical Development

In October 2008, we completed enrollment of ADVANCE, a Phase 3 clinical trial of telaprevir-based treatment regimens in treatment-naïve patients with genotype 1 HCV. The ADVANCE trial is an international 3-arm double-blinded placebo-controlled clinical trial that enrolled approximately 1,050 patients. The clinical trial contains two telaprevir-based treatment arms, one in which patients receive 12 weeks of telaprevir-based triple combination therapy and one in which patients receive 8 weeks of telaprevir-based triple combination therapy, in each case taking peg-IFN and RBV for a subsequent period of time after telaprevir. Patients in both of the telaprevir-based treatment arms who meet extended rapid viral response criteria, or eRVR, will complete all treatment after 24 weeks, while patients who are responding to treatment but do not meet the eRVR criteria will continue receiving peg-IFN and RBV for a total of 48 weeks of therapy. To achieve an eRVR a patient must have undetectable HCV RNA levels at week 4 and week 12 after the start of treatment. In February 2009, we announced that dosing of telaprevir or placebo, 8 or 12 weeks, depending on treatment arm assignment, as part of the combination regimen, is complete in all patients enrolled in the ADVANCE trial. We expect to have SVR data from this clinical trial in the first half of 2010.

ADVANCE Clinical Trial Design

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In February 2009, our collaborator Tibotec Pharmaceuticals Ltd., which is a Johnson & Johnson company and an affiliate of Janssen, completed enrollment of approximately 650 patients in the Phase 3 clinical trial referred to as the REALIZE trial. The REALIZE trial is an international 3-arm clinical trial of telaprevir-based treatment regimens in patients with genotype 1 HCV who failed to achieve an SVR with previous treatment with peg-IFN and RBV. The REALIZE includes the following patient groups:

null responders those patients who achieved less than a 2 log reduction in HCV RNA levels at week 12 of prior therapy;

partial responders those patients who achieved at least a 2 log reduction in HCV RNA levels at week 12, but failed to achieve undetectable HCV RNA levels by week 24 of prior therapy; and

relapsers those patients who achieved undetectable HCV RNA levels at the completion of at least 42 weeks of prior treatment, but relapsed after treatment ended.

REALIZE Clinical Trial Design

In December 2008, we completed enrollment of patients in a clinical trial, referred to as the ILLUMINATE clinical trial, which includes evaluation of 24-week and 48-week total treatment durations in treatment-naïve patients infected with genotype 1 HCV who achieve eRVR in response to telaprevir-based treatment regimens. This clinical trial is a randomized, open-label trial that enrolled approximately 500 patients. ILLUMINATE is designed to supplement SVR data obtained from the ADVANCE trial to evaluate the benefit/risk, for patients who achieve an eRVR, of extending treatment with peg-IFN and RBV from 24 to 48 weeks. We expect to have SVR data from this trial in the first half of 2010.

ILLUMINATE Clinical Trial Design

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Telaprevir Clinical Data

Treatment-Naïve Patients

We have completed two Phase 2b clinical trials of telaprevir-based combination therapy in patients with genotype 1 HCV, which enrolled an aggregate of approximately 580 treatment-naïve patients and are referred to as PROVE 1 and PROVE 2. On an intent-to-treat basis, in the 24-week telaprevir-based treatment arms of PROVE 1 and PROVE 2, 61% and 69%, respectively, of patients achieved an SVR. The criteria for SVR in PROVE 1 and PROVE 2 required that the patients have undetectable HCV RNA levels less than 10 IU/mL as measured by the Roche TaqMan® assay 24 weeks post-treatment. On an intent-to-treat basis, 41% and 46%, respectively, of patients in the control arms of PROVE 1 and PROVE 2 achieved an SVR.

An undetectable HCV RNA level measured 24 weeks following completion of therapy is the current method for determining whether a patient has achieved an SVR. For PROVE 1 and PROVE 2, we have SVR data for all of the clinical trial arms. For some of our other clinical trials of telaprevir, we do not yet have final SVR data for all patients in one or more of the clinical trial arms. If SVR data is not available, we may occasionally present information, if we have it, concerning undetectable HCV RNA levels at 12 weeks post-treatment, HCV RNA levels at the end-of-treatment and/or on-treatment HCV RNA levels after patients have completed 4, 12, 24 or 36 weeks of treatment.

SVR has become the accepted measure of response because prior clinical trials and observational studies by third parties suggest that most viral relapse occurs in the first 24 weeks after completion of therapy, with very low rates of relapse more than 24 weeks after completion of treatment. In PROVE 2, we had approximately 118 patients in the telaprevir-based treatment arms who achieved an SVR undetectable HCV RNA 24 weeks after the end-of-treatment and who were followed out to 48 weeks after the end-of-treatment. Of these, two patients experienced viral relapse after the 24-week post-treatment SVR assessment. Each of these two late relapsing patients had discontinued treatment after approximately 60 days, and one of them was in the PROVE 2 treatment arm that excluded RBV. In the REALIZE, ADVANCE and ILLUMINATE clinical trials, SVR rates will be measured in each of the telaprevir-based treatment arms and the control arms 72 weeks after treatment commences regardless of the planned duration or actual duration of therapy.

Patients Who Did Not Respond To Prior Therapy

We also have reported results of an interim analysis from PROVE 3, a randomized, double-blind, placebo-controlled Phase 2b clinical trial of telaprevir-based combination therapy in patients with genotype 1 HCV who did not achieve an SVR with a previous treatment with peg-IFN and RBV. The interim analysis included 115 patients who received treatment with a 24-week telaprevir-based regimen 12 weeks of telaprevir-based triple-combination therapy followed by an additional 12 weeks of peg-IFN and RBV treatment. Of the 115 patients in this treatment arm, 66 were prior non-responders, which includes null responders and partial responders; 40 were prior relapsers; and 9 were prior breakthroughs patients who had viral rebound during prior treatment. The following table summarizes the results of this interim analysis performed 12 weeks after completion of therapy for the patients in this 24-week telaprevir-based treatment arm of PROVE 3. SVR rates for patients in this clinical trial arm are not yet available.

Patient Group	Total Number of Patients	Number of Patients with Undetectable HCV RNA 12 weeks post-treatment	Percentage of Patients with Undetectable HCV RNA 12 weeks post-treatment
Non-responders (includes null and partial responders)	66	27	41%
Relapsers	40	29	73%
Breakthroughs	9	4	44%
Total	115	60	52%

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In the control arm of PROVE 3, which is evaluating 48 weeks of peg-IFN and RBV only, data indicated that on an intent-to-treat basis 8% of the 114 patients in the control arm had undetectable HCV RNA at week 12 on-treatment, and 30% had undetectable HCV RNA at week 36. In prior third-party studies of peg-IFN and RBV in treatment-failure patients, the proportion of patients who had undetectable HCV RNA at week 36 on-treatment has been significantly higher than the proportion who ultimately achieved SVR. End-of-treatment and post-treatment data including SVR rates are not yet available for the control arm of PROVE 3. Patient dosing has been completed in all arms of PROVE 3 and all patients are now being followed post-treatment.

In addition to the 24-week telaprevir-based regimen that includes RBV described above and the 48-week control arm described above, two other treatment regimens are being evaluated in PROVE 3: a 24-week telaprevir-based treatment arm without RBV, and a 48-week treatment arm that includes 24 weeks of telaprevir dosing in combination with peg-IFN and RBV followed by 24 weeks of peg-IFN and RBV alone. The interim PROVE 3 analysis supports the inclusion of RBV in future clinical trials of telaprevir-based regimens in treatment-failure patients, similar to earlier observations in our clinical trials with treatment-naïve subjects. Available on-treatment results from the PROVE 3 treatment arm in which patients received 24 weeks of treatment with telaprevir suggest that additional dosing of telaprevir beyond 12 weeks does not confer additional benefit to patients.

We also are conducting a clinical trial, referred to as the 107 Study, in patients who did not achieve an SVR in the control arms of the PROVE 1, PROVE 2 or PROVE 3 clinical trials. In this clinical trial, these treatment-experienced patients are being treated with telaprevir triple combination therapy for 12 weeks followed by 12 or 36 weeks of treatment with peg-IFN and RBV alone depending on their prior response to treatment and their response to treatment in the 107 Study. The following table summarizes data from an interim analysis of results from the 107 Study. The interim results include data for patients who have reached the applicable measurement date or would have reached the applicable measurement date, but who discontinued treatment or whose HCV RNA levels became detectable prior to that date.

Patient Group	Total Number of Patients	Percentage of Patients with Undetectable HCV RNA 4 weeks on-treatment	Percentage of Patients with Undetectable HCV RNA 12 weeks on-treatment	Percentage of Patients with Undetectable HCV RNA 24 weeks on-treatment
Null Responders	48	40% (19 of 48)	61% (28 of 46)	43% (18 of 42)
Partial Responders	33	85% (28 of 33)	90% (26 of 29)	82% (18 of 22)
Relapsers	22	91% (20 of 22)	94% (16 of 17)	83% (5 of 6)
Breakthroughs	1	100% (1 of 1)	100% (1 of 1)	0% (0 of 1)

Safety

Our Phase 2 clinical trials enrolled more than 1,000 patients with genotype 1 HCV. The adverse event profile has been generally consistent across these clinical trials. Safety data from our Phase 2 clinical trials indicated that the most common adverse events, regardless of treatment assignment, were fatigue, rash, headache and nausea. The most common adverse events reported more frequently in patients receiving telaprevir have been gastrointestinal events, skin events rash and pruritus and anemia. There have been reports of severe rashes in clinical trials involving telaprevir-based treatments. In our Phase 2 clinical trials, the most common adverse event leading to discontinuation among patients receiving a telaprevir-based treatment regimen was rash. In PROVE 1 and PROVE 2 rash resulted in treatment discontinuations in approximately 7% of patients in the telaprevir-based treatment arms. Other adverse events reported in our Phase 2 clinical trials were similar in type and frequency to those seen with peg-IFN and RBV treatment.

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Additional Telaprevir Trials

In the PROVE, ADVANCE, REALIZE and ILLUMINATE clinical trials, the patients in the telaprevir-based treatment arms are being dosed with 750 mg of telaprevir three-times daily every eight hours. In order to explore the safety and antiviral activity of a twice-daily every twelve hours dosing regimen of telaprevir, Tibotec is conducting the C208 clinical trial, which enrolled approximately 160 treatment-naïve patients infected with genotype 1 HCV. The purpose of the C208 trial is to compare twice-daily dosing regimens of telaprevir 1,125 mg every 12 hours in combination with peg-IFN and RBV, with three-times daily dosing regimens 750 mg every 8 hours in combination with peg-IFN and RBV. Two different types of peg-IFN, known as alfa-2a and alfa-2b, are being used in this clinical trial. The following table summarizes the week 4 and week 12 interim data from the C208 trial.

Telaprevir Dosing	Combination Therapy	Total Number of Patients	Percentage of Patients with Undetectable HCV RNA 4 weeks on-treatment	Percentage of Patients with Undetectable HCV RNA 12 weeks on-treatment
750 mg every 8 hours	alfa-2a (PEGASYS)/RBV	40	80%	93%
750 mg every 8 hours	alfa-2b (PEGINTRON)/RBV	42	69%	93%
1,125 mg every 12 hours	alfa-2a (PEGASYS)/RBV	40	83%	83%
1,125 mg every 12 hours	alfa-2b (PEGINTRON)/RBV	39	67%	85%

In this analysis, in the three-times daily alfa-2a treatment arm and the three-times daily alfa-2b treatment arm four patients and two patients, respectively, discontinued treatment due to adverse events and one patient and three patients, respectively, experienced viral breakthrough. In the twice-daily alfa-2a and twice-daily alfa-2b arms, four patients and three patients, respectively, discontinued treatment due to adverse events, and two patients and three patients, respectively, experienced viral breakthrough. We believe that this interim data support the potential for further evaluation of twice-daily dosing of telaprevir.

Tibotec also is conducting two clinical trials of telaprevir in patients with different HCV genotypes. Tibotec has completed an interim analysis of one of these trials, which we refer to as the C209 clinical trial. C209 is a clinical trial exploring the viral kinetics of telaprevir in approximately 50 patients with genotype 2 or genotype 3 HCV infection. The interim analysis was conducted after all subjects had completed 2 weeks of telaprevir dosing in combination with peg-IFN and RBV. Preliminary viral kinetic results at the end of week 2 of dosing suggest that telaprevir has substantial antiviral activity against genotype 2 HCV. Analyses of viral dynamics are underway to further characterize the antiviral activity of telaprevir against genotype 2 HCV. Preliminary viral kinetic results at the end of week 2 do not support further investigation of telaprevir in patients with genotype 3 HCV infection. In the other of these clinical trials, Tibotec is evaluating telaprevir-based treatment regimens in patients infected with genotype 4 HCV.

We are planning to initiate with Tibotec a Phase 2 clinical trial of telaprevir in patients with HIV/HCV co-infection in the second half 2009.

Mitsubishi Tanabe Clinical Program

Mitsubishi Tanabe has initiated registration trials of telaprevir in Japan focused on evaluation of 24-week telaprevir-based regimens in approximately 300 patients with genotype 1 HCV. These trials include both treatment-naïve patients and treatment-experienced patients. In these clinical trials, telaprevir is being dosed for 12 weeks in combination with peg-IFN and RBV. Mitsubishi Tanabe expects to have SVR data from its Phase 3 clinical trials of telaprevir in mid-2011.

VX-813 and VX-985 (investigational oral HCV protease inhibitors for the treatment of chronic HCV infection)

VX-813 and VX-985 are novel, investigational HCV protease inhibitors we discovered. We have initiated a Phase 1a clinical trial of VX-813 in healthy volunteers and VX-985 is in pre-clinical development. In the first quarter of 2009, we terminated development of VX-500, another protease inhibitor, based on interim results from a Phase 1b clinical trial. We have worldwide development and commercialization rights to VX-813 and VX-985.

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Cystic Fibrosis

Cystic fibrosis is a recessive genetic disorder that affects about 30,000 people in the United States and 70,000 worldwide. While CF is a systemic disease, progressive loss of lung function is the primary cause of increased mortality in patients with CF. Abnormally thick mucus in the lungs of patients with CF leads to chronic lung infections, lung inflammation and ultimately progressive decline in lung function. Some patients with CF also experience problems with digestion, due to a lack of CFTR function in the pancreas, resulting in the need for enzyme replacement therapy. According to the Cystic Fibrosis Foundation in 2006, the predicted median age of survival for patients with cystic fibrosis is 37 years. The underlying cause of CF is a genetically inherited deficiency in the production or activity of the CFTR protein. The CFTR protein is involved in controlling the movement of chloride ions into and out of cells in the lung, sweat glands, pancreas and other organs.

CF develops when neither of the two copies of the *CFTR* gene, referred to as alleles, produce sufficient functional CFTR protein. There are numerous mutations in the *CFTR* gene that result in CF, including the G551D mutation and the F508del mutation. The G551D mutation, which is present in approximately 4% of the CF population in the United States, results in a gating defect where the defective CFTR protein reaches the cell surface but does not efficiently transport chloride ions across the cell membrane. The F508del mutation, which is present in approximately 90% of the patients with CF in the United States, results in a trafficking defect where the CFTR protein does not reach the cell surface in sufficient quantities. In addition to the primary trafficking defect, we believe based on *in vitro* studies that the F508del CFTR protein may also have a gating defect that affects the function of any F508del CFTR proteins that do reach the cell surface.

There currently is no available therapy that improves the function of defective CFTR proteins. Instead, available treatments for CF pulmonary disease focus on improving mucus clearance from the lungs as well as treating lung infections and inflammation. Improved mucus clearance is sought through physical therapy, inhalation of a mucus thinning drug such as Pulmozyme, or inhalation of hypertonic saline. Lung infections are treated with inhaled and systemic antibiotics while inflammation is treated with anti-inflammatory agents like ibuprofen. In addition, the majority of CF patients take pancreatic enzyme supplements to assist with food absorption in digestion. FEV_1, a test of the amount of air that an individual can exhale in one second is the lung function test most commonly used to monitor CF disease progression, which is characterized by progressive decreases in FEV_1 values compared to FEV_1 values observed in healthy individuals. In addition to being used to monitor disease progression, the FEV_1 test has been used as an efficacy end-point for the currently approved pulmonary drugs for the treatment of CF. Since CF is a chronic disease, pivotal clinical trials of CF drug candidates have involved the measurement of FEV_1 values over a number of months. Mean increases in predicted FEV_1 of between 5% and 10% over 24-week periods have been observed in the pivotal clinical trials of the mucus thinning drugs and antibiotics most widely used for the management of CF.

We are conducting clinical trials of two drug candidates, VX-770 and VX-809, that were designed to improve the function of defective CFTR proteins in patients with CF. We discovered VX-770 and VX-809 in our research collaboration with Cystic Fibrosis Foundation Therapeutics Incorporated, or CFFT, and with the support and participation of the Cystic Fibrosis Foundation. We hold worldwide development and commercialization rights to VX-770 and VX-809, but we would be required to pay CFFT royalties on any future sales of VX-770 or VX-809, if approved.

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VX-770 (investigational oral CFTR potentiator for the treatment of cystic fibrosis)

VX-770 is an investigational drug candidate designed to increase chloride ion transport across cell membranes by partially restoring the activity of defective CFTR proteins. We are working with regulatory authorities in North America and Europe on the design of a registration program for VX-770 and expect to begin this registration program in the first half of 2009. The VX-770 registration program will focus on CF patients who carry the G551D mutation on at least one allele, including both adult and pediatric patients.

Registration Program

The registration program for VX-770 is expected to include three separate clinical trials:

The first clinical trial in the VX-770 registration program will be an international clinical trial that will enroll patients with CF ages 12 and older with the G551D mutation on at least one of the two alleles. The trial is expected to evaluate VX-770 administered orally twice daily compared to placebo over a period of at least six months. We expect to initiate this trial in the first half of 2009.

The second clinical trial is expected to be an international clinical trial that will enroll patients with CF ages 6 to 11 with the G551D mutation on at least one allele. This trial is expected to evaluate VX-770 administered orally twice daily compared to placebo. We expect that this clinical trial will involve a smaller group of patients than the first clinical trial.

The third clinical trial is expected to enroll CF patients with the F508del mutation on both of the two alleles. The trial is expected to evaluate VX-770 when administered orally twice daily. This trial is expected to provide additional safety data for the VX-770 registration program and will be the first clinical trial to evaluate the clinical activity of VX-770 in patients with the F508del mutation on both alleles.

The primary efficacy endpoint of all trials in the VX-770 registration program will be based on FEV_1 measurements, which were used for the currently approved CF pulmonary drugs. Additional secondary endpoints, including sweat chloride, which is described below, will also be measured to determine the effect of VX-770 in helping to restore the function of defective CFTR proteins.

Phase 2a Clinical Trial of VX-770

The Phase 2a clinical trial of VX-770 enrolled 39 patients with the G551D mutation on at least one allele, 20 of whom were enrolled in Part 1 of the clinical trial and 19 of whom were enrolled in Part 2 of the clinical trial. Patients in Part 1 of this clinical trial were dosed with VX-770 or placebo over 14 day periods. In Part 2 of this Phase 2a clinical trial, patients were dosed over 28 days in the following three arms: eight patients received 150 mg of VX-770 twice-daily; seven patients received 250 mg of VX-770 twice-daily; and four patients received a placebo twice-daily.

Safety (primary endpoint)

The primary endpoint of the VX-770 Phase 2a clinical trial was safety. In Part 1, observed adverse events were similar between VX-770 and placebo treatment over the dosing period. Two serious adverse events were observed in one patient in Part 1, but were not attributed to VX-770. In Part 2 of this clinical trial, no serious adverse events were reported and no patients discontinued treatment over the 28-day dosing periods. Also in Part 2, all reported adverse advents were mild or moderate in severity. A detailed safety analysis is ongoing.

Lung Function and CFTR Protein Function (secondary endpoints)

In the VX-770 Phase 2a clinical trial, we measured secondary endpoints of lung function and CFTR protein function. We measured changes in lung function using FEV_1. CFTR activity was

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evaluated through measurements of sweat chloride and nasal potential difference, or NPD. Elevated sweat chloride levels high levels of salt in sweat occur in CF patients and result directly from defective CFTR activity in epithelial cells in the sweat duct. Patients with CF typically have elevated sweat chloride levels that are in excess of 60 mmol/L, compared to normal values of less than 40 mmol/L. NPD assesses several aspects of ion channel activity by measuring voltage changes across the nasal epithelia and is used as a direct measure of CFTR activity and chloride ion movement in upper airway epithelial cells. Typical assessments of patient NPD show very low CFTR-mediated chloride ion transport in the nasal passage of patients with CF.

In Part 1 of the Phase 2a clinical trial of VX-770, the eight patients who received 150 mg twice-daily over 14 days had a 10.1% improvement in lung function as measured by an increase in FEV_1. In these patients, sweat chloride levels had a mean decrease of 42.3 mmol/L from a mean baseline of 95.5 mmol/L over the 14-day dosing period. The NPD component decreased by 5.4 mV, indicating increased CFTR function. There were no statistically significant changes in any of the efficacy measures in the placebo arms of Part 1. The four patients receiving placebo in Part 1 showed a slight decrease in FEV_1, no notable change in sweat chloride levels and a -1.74 mV change in NPD.

A summary of data regarding lung function and biomarkers of the CFTR protein function, including "p-values" from Part 2 of this Phase 2a clinical trial is set forth in the table below. The result of statistical testing is often defined in terms of a "p-value," with a p-value of 0.05 or less generally considered to represent a statistically significant difference.

Number of Patients	Treatment Arm	FEV_1 Mean Increase from Baseline at day 28 (p-value)	Sweat Chloride Mean Decrease from Baseline at day 28 (p-value)	Sweat Chloride Baseline	NPD Mean Decrease from Baseline at day 28 (p-value)
8	150 mg	11.6% (p<0.01)	-52.8 mmol/L(p<0.01)	102 mmol/L	-4.3 mV (p<0.05)
7	250 mg	7.4% (p<0.05)	-32.4 mmol/L (p<0.05)	94.9 mmol/L	-10.1 mV (p<0.05)
4	Placebo	7.0% (p=0.13)	+4.8 mmol/L (p=0.38)	98.3 mmol/L	+0.3 mV (p=0.88)

The pattern of FEV_1 response in the VX-770 arms was characterized by a rapid and sustained increase in FEV_1 through 28 days. The increase in FEV_1 in the placebo arm was not considered statistically significant.

VX-809 (investigational oral CFTR corrector compound for the treatment of CF)

We are evaluating VX-809, an investigational corrector compound designed to increase the concentration of CFTR proteins on the cell surface in patients with CFTR mutations that result in trafficking defects. We have completed two Phase 1 clinical trials of VX-809 in healthy volunteers. The first clinical trial was a single and multiple-dose trial. The second was a single-dose clinical trial examining the pharmacokinetics and safety of a solid dosage form of VX-809. We have completed an escalating dose pharmacokinetics and safety Phase 1 trial of VX-809 in patients with CF who carry the F508del mutation on at least one of the two alleles. We plan to initiate a Phase 2a, 28-day clinical trial of VX-809 in the first half of 2009. *In vitro*, correctors have shown the ability to restore function of defective F508del CFTR protein, with increased trafficking of F508del CFTR protein to the cell surface and enhanced gating activity of F508del CFTR protein on the cell surface.

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Immune-Mediated Inflammatory Disease

VX-509 (oral JAK3 inhibitor for the treatment of IMID)

We believe that JAK3 is a promising target for the design of immunosuppressant drugs. We have completed a Phase 1 clinical trial of VX-509, and anticipate it will be investigated for the treatment of multiple IMID. The Phase 1 clinical trial enrolled three groups of healthy volunteers dosed for 14 days with ascending doses of VX-509. We anticipate that a Phase 2 clinical trial in rheumatoid arthritis will commence in the second half of 2009. Based on *in vitro* data, VX-509 appears to be a potent and selective inhibitor of JAK3. We hold worldwide development and commercial rights to VX-509 and may seek to out-license VX-509.

Cancer

MK-5108 (VX-689): Aurora kinase inhibition for the treatment of cancer (Merck & Co., Inc.)

We are collaborating with Merck & Co., Inc. in the area of Aurora kinase inhibitors, including MK-5108 (VX-689). Aurora kinases are enzymes thought to play multiple roles in the development and progression of cancer, acting as regulators of cell proliferation, transforming normal cells into cancer cells and downregulating p53, one of the body's natural tumor suppressors. We believe that inhibitors of Aurora kinases may be useful as highly targeted treatments for a range of cancer indications. Merck holds worldwide development and commercialization rights to MK-5108 (VX-689) and certain additional compounds identified during our research program with Merck, which has ended. In the second quarter of 2008, Merck initiated a Phase 1 clinical trial of MK-5108 (VX-689), alone and in combination with docetaxel, in patients with advanced and/or refractory tumors. In the third quarter of 2008, Merck selected additional Aurora kinase inhibitors for possible development.

AVN-944 (VX-944): IMPDH inhibition for the treatment of cancer (Avalon Pharmaceuticals, Inc.)

Our collaborator Avalon Pharmaceuticals, Inc. has the right to develop AVN-944 (VX-944), an IMPDH inhibitor, for the treatment of advanced hematological malignancies, such as leukemia, lymphoma or myeloma. Inosine 5-monophosphate dehydrogenase, or IMPDH, is an enzyme thought to be critical for the synthesis of guanosine triphosphate, a molecule required for DNA synthesis and cellular signaling. IMPDH is over-expressed in many cancer cells, especially in hemotological malignancies. Reports in medical literature and presentations at scientific conferences provide a clinical rationale for the development of IMPDH inhibitors for the treatment of hematologic malignancies. Results from certain preclinical studies of AVN-944 (VX-944) indicated that AVN-944 (VX-944) inhibited the *in vitro* proliferation of lymphoid and myeloid cells, the principal cells involved in the most common types of human leukemias. AVN-944 (VX-944) is currently in Phase 2 clinical development. In August 2008, Avalon restructured its operations and indicated that it was evaluating the clinical data from our AVN-944 (VX-944) development program to assess strategies for further development of AVN-944 (VX-944). Avalon holds worldwide development and commercialization rights to AVN-944 (VX-944) in oncology.

RESEARCH PROGRAMS

We believe that our integrated drug design approach has significantly enhanced our ability to discover and develop small molecule drug candidates directed at biologically complex targets associated with serious diseases. Our drug design platform integrates biology, pharmacology, drug metabolism and pharmacokinetics, toxicology, material sciences, biophysics, medicinal chemistry and process chemistry, automation and information technologies in a coordinated and simultaneous fashion throughout the discovery process. We believe that our approach has been validated through our success in moving drug candidates into clinical trials. We recently have decided to focus on several core therapeutic areas, in order to expand and develop our expertise in specific therapeutic areas and to permit a framework for portfolio planning and execution. Currently, the four therapeutic areas of highest priority to us are: infectious diseases, including viral and bacterial infections; IMIDs; cancer; and neurological diseases and disorders, including pain. Driven by the complexity of the therapeutic areas selected, we are

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attempting to identify multiple targets within each indication that, either as a stand-alone or in combination, could provide treatment options that are transformational in nature. The objective of this approach is to enable us to eventually provide multiple drugs in each of these therapeutic areas. We selected these therapeutic areas by mapping our research strengths, including expertise in kinases, proteases and membrane proteins, onto therapeutic areas with high unmet need, with an emphasis on indications where we believe we, independently or in collaboration with other pharmaceutical companies, will be able to discover, develop, and commercialize important medicines for serious diseases. Within each therapeutic area, we intend to focus initially on specific indications.

Our past drug discovery efforts have produced a variety of drug candidates that have been commercialized or are currently in preclinical or clinical development. We believe our ongoing research programs continue to create potential value for us by generating new drug candidates in areas of significant unmet medical need. We have commenced preclinical activities for a number of additional investigational compounds one or more of which may enter clinical development in 2009.

In order to obtain advice regarding our research programs, we have invited respected individuals with industry, medical and/or research expertise to participate in advisory boards focused on specific therapeutic areas and discovery approaches. Each of our scientific advisory boards is comprised of individuals with experience in the relevant area who provide input through interaction with our senior executives focused on drug innovation and technologies. The members of our scientific advisory boards are not employees and only are expected to devote a small portion of their time to us.

To augment our internal research programs, we seek to collaborate with leading academic research institutions, government laboratories, foundations and other organizations in order to advance research in our areas of therapeutic interest as well as in areas of basic technological enablement. We have established relationships with organizations and organized consortia of organizations from around the world with expertise in areas of interest to us, and intend to leverage that experience to further our research efforts. For example, in 2008, we entered into a collaboration with CHDI Foundation, Inc., a non-profit foundation committed to accelerating the discovery and development of new drugs that delay the onset or slow the progression of Huntington's disease. This collaboration is aimed at developing assays for use in discovering novel compounds for the treatment of Huntington's disease.

CORPORATE COLLABORATIONS

We have entered into corporate collaborations with pharmaceutical and other companies and organizations that provide financial and other resources, including capabilities in research, development, manufacturing, and sales and marketing, to support our research and development programs.

Janssen Pharmaceutica, N.V.

In June 2006, we entered into a license, development, manufacturing and commercialization agreement with Janssen. Under the collaboration agreement, we will collaborate with Janssen to develop and commercialize telaprevir. Under the terms of the collaboration agreement, we retain exclusive commercial rights to telaprevir in North America and will continue to lead the development plan for telaprevir in North America and the Janssen territories. Janssen received exclusive rights to commercialize telaprevir outside of North America and the Far East. In connection with the execution of the collaboration agreement, we received an up-front payment of $165.0 million in July 2006. In addition, the agreement provided for contingent milestone payments to us, which could total up to $380.0 million if telaprevir is successfully developed, approved and launched. As of December 31, 2008, we had received $100.0 million of these contingent milestone payments. Janssen has agreed to be responsible for 50% of drug development costs under the development program for North America and the Janssen territories. Each of the parties to the collaboration agreement will be responsible for drug supply in their respective territories. The collaboration agreement also includes a tiered royalty averaging in the mid-20% range, as a percentage of net sales in the Janssen territories, depending upon successful commercialization. In addition, Janssen will be responsible for certain third-party royalties in its territories. Janssen may terminate the collaboration agreement upon six months' notice to us. In

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such an event, all manufacturing, commercialization and intellectual property rights to telaprevir under the collaboration agreement will revert to us.

As part of the collaboration agreement, following regulatory approval and commercialization of telaprevir in both North America and Janssen's territory, we have agreed to establish a global health initiative with Tibotec, with the goals of advancing the prevention, diagnosis, treatment and cure of HCV infection, which will be principally directed toward developing countries.

Mitsubishi Tanabe Pharma Corporation

In June 2004, we entered into a license, development and commercialization agreement with Mitsubishi Tanabe for the development and commercialization of telaprevir in Japan and certain other Far East countries. Under the terms of the agreement, Mitsubishi Tanabe has the right to develop and commercialize telaprevir in its territory. Under the agreement, we have received payments from Mitsubishi Tanabe for Phase 2 clinical development, including an up-front license fee, development milestone payments and contributions to certain drug development costs incurred by us for telaprevir. We recognized $9.9 million, $4.4 million and $8.6 million in revenues under this agreement in 2008, 2007 and 2006, respectively. Mitsubishi Tanabe has commenced Phase 3 clinical development of telaprevir. We currently are negotiating the extent of Mitsubishi Tanabe's future sharing of our costs beyond Phase 2 clinical development as provided in the agreement. We will also be entitled to royalties on sales of telaprevir, if approved, in Mitsubishi Tanabe's territory. Mitsubishi Tanabe may terminate the agreement at any time without cause upon 60 days' prior written notice.

Cystic Fibrosis Foundation Therapeutics Incorporated

In May 2004, we entered into a collaboration agreement with CFFT pursuant to which CFFT provided us with funding for our CF research and development programs, which funding was completed in 2008. We recognized $0.8 million, $15.9 million and $12.6 million in revenues under this agreement in 2008, 2007 and 2006, respectively. Two drug candidates currently in clinical development, VX-770 and VX-809, were discovered by us under this research collaboration. We retain the right to develop and commercialize any compounds discovered in the course of the research collaboration, including VX-770 and VX-809, and we will pay a royalty to CFFT on the net sales of any approved drugs discovered in the collaboration.

Merck & Co., Inc.

In June 2004, we entered into a global collaboration with Merck to discover, develop and commercialize Aurora kinase inhibitors. Merck made an up-front license payment to us of $20 million in June 2004, and provided research funding of $15.8 million between June 2004 and September 2006. In addition, the agreement provided for as much as $350 million in milestone payments to us. Currently, Merck is developing MK-5108 (VX-689) in a Phase 1 clinical trial involving patients with advanced and/or refractory tumors. In the third quarter of 2008, Merck selected additional Aurora kinase inhibitors for possible development.

Under the agreement, we recognized two milestone payments totaling $19.5 million in 2005, three milestone payments totaling $36.3 million in 2006, one milestone payment of $9.0 million in 2007 and one milestone payment of $6.0 million in 2008. Under the agreement, Merck is responsible for developing and commercializing the drug candidates that result from our collaboration worldwide and will pay us royalties on any product sales. Merck may terminate the agreement at any time without cause upon 90 days' advance written notice, except that a longer notice period is required in certain circumstances.

Avalon Pharmaceuticals, Inc.

In February 2005, we entered into a license agreement with Avalon for the development and commercialization of the IMPDH inhibitor AVN-944 (VX-944) for the treatment of cancer. Under the agreement, Avalon has the exclusive worldwide right and responsibility to develop and commercialize

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AVN-944 (VX-944) for the treatment of cancer. Avalon made a $5.0 million up-front license payment to us and has agreed to make additional milestone payments to us for the successful development of AVN-944 (VX-944) in multiple cancer indications. Avalon will pay us royalties on any product sales. The agreement provides us with certain rights to co-promote AVN-944 (VX-944). Neither party has the right to terminate the agreement other than for cause. If the agreement is terminated, we will regain development and commercialization rights to AVN-944 (VX-944).

GlaxoSmithKline plc

In 1993, we entered into a collaboration with GlaxoSmithKline covering the research, development and commercialization of HIV protease inhibitors, including Agenerase (amprenavir) and Lexiva/Telzir (fosamprenavir calcium). The agreement provides that GlaxoSmithKline will pay us a royalty on all net sales of the HIV protease inhibitors covered by the agreement. We began earning a royalty from GlaxoSmithKline in 1999 on net sales of Agenerase, in the fourth quarter of 2003 on net sales of Lexiva, and in the third quarter of 2004 on net sales of Telzir. Lexiva and Telzir have replaced Agenerase in worldwide markets. In May 2008, we sold our right to receive future royalties from GlaxoSmithKline with respect to these HIV protease inhibitors, excluding the amount necessary to pay a third party a subroyalty on these net sales, for a one-time cash payment of $160.0 million.

INTELLECTUAL PROPERTY

We actively seek protection for our products and proprietary information by means of United States and foreign patents, trademarks, and copyrights, as appropriate. In addition, we rely upon trade secret protection and contractual arrangements to protect certain of our proprietary information and products. We have patents and pending patent applications that relate to potential drug targets, compounds we are developing to modulate those targets, methods of making or using those compounds and proprietary elements of our drug discovery platform.

Much of our technology and many of our processes depend upon the knowledge, experience and skills of key scientific and technical personnel. To protect our rights to our proprietary know-how and technology, we require all employees, as well as our consultants and advisors when feasible, to enter into confidentiality agreements that require disclosure and assignment to us of ideas, developments, discoveries and inventions made by these employees, consultants and advisors in the course of their service to us.

We hold issued patents and pending patent applications in the United States, and in foreign countries we deem appropriate, covering intellectual property developed as part of each of our significant research, development and commercial programs. Our intellectual property holdings include but are not limited to:

United States and foreign patents and patent applications covering telaprevir, VX-813, VX-985 and many other HCV protease inhibitors.

United States and foreign patent applications covering potentiators and correctors of the CFTR protein, including VX-770 and VX-809 and many other related compounds, and the use of those potentiators and correctors to treat CF.

United States and foreign patents and patent applications covering inhibitors of a variety of kinase proteins, including VX-509, a JAK3 inhibitor.

United States and foreign patent applications covering the manufacture, pharmaceutical compositions, related solid forms, formulations, dosing regimens and methods of use of these compounds, including telaprevir and VX-770.

From time to time we enter into non-exclusive license agreements for proprietary third-party technology used in connection with our research activities. These license agreements typically provide for the payment by us of a license fee, but may also include terms providing for milestone payments or royalties for the development and/or commercialization of our drug products arising from the related research.

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MANUFACTURING

As we advance our proprietary drug candidates through clinical development toward commercialization, we will continue to build our supply chain resources and maintain our quality assurance resources. We rely on a worldwide network of third parties 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 those drugs, if they are approved for sale.

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 to 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.

We require for our own use, and are responsible to Janssen for, a supply of telaprevir for clinical trials in North America and the European Union, respectively. We will require a supply of telaprevir for sale in North America if we are successful in obtaining marketing approval. We have completed the technical development work for our commercial formulation of telaprevir and we are manufacturing telaprevir, through our third-party manufacturer network, to meet our, Janssen and Mitsubishi Tanabe's clinical supply needs. We have established relationships with multiple third-party manufacturers for the manufacture of telaprevir commercial supply and have completed contracts for our primary supply of drug substance and most raw materials. We believe our past and continuing efforts to expand our relationships with third-party manufacturers and oversee their activities will be important to support a timely and effective commercial launch of telaprevir and its consistent supply in subsequent years.

We are completing the transfer of 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 that supply of materials that cannot be second-sourced can be managed with inventory planning, there is always a risk that we may underestimate demand, and that our manufacturing capacity through third-party manufacturers may not be sufficient. 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 require 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 obtain marketing approval. We obtain VX-770 to meet our clinical supply needs through a third-party manufacturer network and are focused on completing the technical development work and commercial formulation of VX-770. Over the next several years, we expect to expand our existing relationships with our third-party manufacturers 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.

We are focusing resources on the development of systems and processes to track, monitor and oversee our third-party manufacturers' activities. We regularly evaluate the performance of our third-party manufacturers with the objective of confirming their continuing capabilities to meet our needs efficiently and economically. Manufacturing facilities, both foreign and domestic, are subject to inspections by or under the authority of the FDA and by or under the authority of other federal, state, local or foreign authorities. A failure by any of our third-party manufacturers to pass an inspection could adversely affect our ability to launch telaprevir or VX-770 in a timely manner, if we obtain marketing approval, or adversely affect our ability to continue to distribute telaprevir or VX-770 after launch.

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We have established a quality assurance program intended to ensure that our third-party manufacturers and service providers produce materials and provide services, when applicable, in accordance with the FDA's current Good Manufacturing Practices, or cGMP, and other applicable regulations.

COMPETITION

The pharmaceutical industry is characterized by extensive research efforts, rapid technological progress and intense competition. There are many public and private companies, including pharmaceutical companies, chemical companies and biotechnology companies, engaged in developing products for the same human therapeutic areas that we are targeting. Many of our competitors have substantially greater financial, technical and human resources than we do and are more experienced in the development of new drugs than we are. In order for us to compete successfully, we may need to demonstrate improved safety, efficacy, ease of manufacturing and market acceptance of our products relative to our competitor's products that have received or will receive regulatory approval for marketing.

We face competition based on the safety and efficacy of our drug candidates, the timing and scope of regulatory approvals, the availability and cost of supply, marketing and sales capabilities, reimbursement coverage, price, patent protection and other factors. Our competitors may develop or commercialize more effective, safer or more affordable products than we are able to develop or commercialize or obtain more effective patent protection. As a result, our competitors may commercialize products more rapidly or effectively than we do, which would adversely affect our competitive position, the likelihood that our drug candidates, if approved, would achieve initial market acceptance and our ability to generate meaningful revenues from those drugs. Even if our drug candidates are approved and achieve initial market acceptance, competitive products may render our drugs obsolete or noncompetitive. If any such drug is rendered obsolete, we may not be able to recover the expenses of developing and commercializing that drug. With respect to all of our drugs and drug candidates, we are aware of existing treatments and numerous drug candidates in development by our competitors.

HCV Infection

A combination of peg-IFN, which requires weekly injections, and RBV administered for 48 weeks is the current standard treatment for genotype 1 HCV infection. This treatment regimen is associated with significant side effects, including fatigue, flu-like symptoms, rash, depression and anemia. A significant portion of patients who begin treatment do not achieve an SVR. Based on discussions with physicians who treat patients with HCV, we believe that there are a significant number of patients with HCV who are waiting to receive treatment until new therapies are developed that are more effective or involve less difficult treatment regimens. In addition, we believe that there are a significant number of patients with HCV who have not achieved SVR with previous interferon-based treatments.

While we are aware of numerous companies that are developing potentially competitive drug candidates, Schering-Plough's protease inhibitor, boceprevir, is the only protease inhibitor that is being developed on a timeline comparable to telaprevir. In November 2008, Schering-Plough completed enrollment in a Phase 3 clinical trial that included approximately 375 treatment-experienced patients but excluded null responders to prior treatment. In January 2009, Schering-Plough completed enrollment of a Phase 3 clinical trial involving approximately 1,080 treatment-naïve patients with genotype 1 HCV. We believe that Schering-Plough may obtain SVR data from these Phase 3 clinical trials in 2010 and, if favorable, that Schering-Plough could file an NDA with the FDA on a timeline comparable to telaprevir. If telaprevir and boceprevir are both approved on a comparable timeline, we believe that the drugs would compete in the marketplace based on, among other things, safety and efficacy data from their respective clinical trials, breadth of approved use, cost, cost of co-therapies and side-effect profile. In addition to boceprevir, we are aware of a number of other companies developing protease inhibitors that are in earlier stages of development. We believe that these earlier-stage drug

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candidates, if approved, would be launched several years after telaprevir based on telaprevir's current developmental timeline.

There also are companies developing HCV polymerase inhibitors, a class of compounds distinct from protease inhibitors, for the treatment of HCV infection. The HCV polymerase is responsible for synthesizing viral RNA during HCV replication. We expect that polymerase inhibitors, if successfully developed, may be a component of a combination therapy that includes a protease inhibitor, such as telaprevir, and thus likely would be complementary to and not competitive with our HCV protease inhibitors.

We are aware of numerous other compounds in clinical trials that target HCV through other mechanisms of action that are in clinical trials, and we believe that there are many additional potential HCV treatments in research or early development. We believe that there is a potential for new oral drug candidates, if approved, to be administered together with or without peg-IFN and/or RBV. We expect to explore the potential for other combination therapies, including combinations where all the component drugs would be administered orally. Future competition in the HCV treatment market may result from the administration of a combination of new oral therapies. Oral therapies that previously have been tested in combination with peg-IFN and RBV may have a competitive advantage over those that have not been previously tested in combination.

CF

Several companies are engaged in the process of developing treatments for CF, including a limited number of drug candidates that are designed to improve the function of CFTR proteins, and a number of antibiotics and anti-inflammatories. PTC Therapeutics, Inc. is investigating ataluren, which was formerly known as PTC124, a drug candidate designed to improve the production of CFTR proteins in patients with nonsense genetic mutations that halt the production of CFTR proteins before the protein is fully formed. Inspire Pharmaceuticals Inc. is conducting Phase 3 clinical trials of denufosol tetrasodium, an inhaled molecule designed to stimulate chloride and liquid secretions in the airways of patients with CF.

GOVERNMENT REGULATION

The research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record keeping, promotion, advertising, distribution and marketing of the drug candidates that we are developing are subject to extensive regulation by United States and foreign governmental authorities. In particular, pharmaceutical products are subject to rigorous preclinical, nonclinical and clinical testing and other approval requirements by the FDA in the United States under the Federal Food, Drug and Cosmetic Act, and by comparable agencies in most foreign countries. In addition to prohibiting the sale and distribution of pharmaceutical products prior to regulatory approval, the FDA and comparable agencies in most foreign countries prohibit the pre-approval promotion of investigational drugs. We have summarized the FDA process below, but other countries may have different approval processes with which we or our collaborators will need to comply if we seek to conduct clinical trials or obtain marketing approval in those countries. In addition, even if we ultimately intend to seek initial marketing approval in the United States, we may conduct early clinical trials in other countries, for a variety of reasons, and therefore the submission of our initial investigational new drug, or IND, application in the United States may not occur until after one or more foreign-sited clinical trials have been initiated.

FDA Approval Process

As an initial step in the FDA regulatory review process, toxicity studies in animals and other nonclinical studies typically are conducted to help identify potential safety problems that might be associated with administration of the drug candidate being tested. For certain diseases, animal models exist that are believed to be predictive of efficacy in humans. For such diseases, a drug candidate

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typically is tested for efficacy in that animal model. The results of these initial animal safety and disease model studies are submitted to the FDA as a part of the IND submission, prior to commencement of human clinical trials in the United States. For several of our drug candidates, no appropriately predictive animal model exists. As a result, no *in vivo* evidence of efficacy will be available until those drug candidates progress to human clinical trials. A variety of nonclinical studies in a number of animal species, and other nonclinical studies, ordinarily are conducted while human clinical trials are underway, to provide supplemental toxicology and other information. This information as well as the results from the early clinical trials provide a foundation for the design of broader and more lengthy human clinical trials.

Clinical trials typically are conducted in three sequential phases, although the phases may overlap. Phase 1 frequently begins with the initial introduction of the drug candidate into healthy human subjects prior to introduction into patients. The drug candidate may then be tested in a relatively small number of patients for preliminary information, dosage tolerance, absorption, metabolism, excretion, clinical pharmacology and, if possible, for early information on efficacy. Phase 2 typically involves trials in a small sample of the intended patient population to assess the efficacy of the drug for a specific indication, to determine dose tolerance and the optimal dose range and to gather additional information relating to safety and potential adverse effects. Phase 3 trials are undertaken to further evaluate clinical safety and efficacy in an expanded patient population at geographically dispersed trial sites, to obtain information on the overall risk-benefit ratio of the drug candidate and to provide an adequate basis for proposed labeling. Each trial is conducted in accordance with standards set forth in a protocol that details the design and objectives of the trial, the parameters to be used to monitor safety and the efficacy criteria to be evaluated. For clinical trials in the United States, each protocol must be submitted to the FDA to supplement the original IND submission. Further, each clinical trial must be evaluated by an independent Institutional Review Board, or IRB, which evaluates clinical research at or for each institution at which the trial will be conducted. The IRBs will consider, among other things, ethical factors and the safety of human subjects in the proposed trials.

Data from nonclinical testing and all clinical trials, along with descriptions of the manufacturing process, analytical tests, proposed labeling and other relevant information, are submitted to the FDA as part of requesting approval to market the drug in the NDA. The process of completing nonclinical and clinical testing, submitting the NDA and obtaining FDA approval for a new drug is likely to take a number of years and require the expenditure of substantial resources. Preparing an NDA involves extensive data collection, verification, analysis and expense, and there can be no assurance that approval of the drug candidate that is the subject of a particular NDA will be granted on a timely basis, if at all. The FDA reviews all NDAs to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The approval process is affected by a number of factors, including the severity of the targeted disease, the availability of alternative treatments and the risks and benefits demonstrated in clinical trials. The FDA may deny an NDA if applicable regulatory criteria are not satisfied or may require additional testing or information. Among the conditions for marketing approval is the requirement that the prospective manufacturer's quality control and manufacturing procedures conform to the FDA's cGMP regulations, which must be followed at all times. In complying with standards set forth in these regulations, manufacturers must continue to expend time, money and effort in the area of production and quality control to ensure full compliance. Manufacturing facilities, both foreign and domestic, also are subject to inspections by the FDA and by other federal, state, local agencies or foreign authorities.

Under the FDA Modernization Act of 1997, the FDA may grant "Fast Track" designation to facilitate the development of a drug intended for the treatment of a serious or life-threatening condition if the drug demonstrates, among other things, the potential to address an unmet medical need. The benefits of Fast Track designation include scheduled meetings with the FDA to receive input on development plans, the option of submitting an NDA in sections (rather than submitting all sections simultaneously), and the option of requesting evaluation of trials using surrogate endpoints. Fast Track

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designation does not necessarily lead to a priority review or accelerated approval of a drug candidate by the FDA. Telaprevir and VX-770 have received Fast Track designation by the FDA.

Timing to Approval

We estimate that it generally takes 10 to 15 years, or possibly longer, to discover, develop and bring to market a new pharmaceutical product in the United States as outlined below:

Phase:	Objective:	Estimated Duration:
Discovery	Lead identification and target validation	2 to 4 years
Preclinical	Initial toxicology for preliminary identification of risks for humans; gather early pharmacokinetic data	1 to 2 years
Phase 1	Initial evaluation of safety in humans; study how the drug candidate works and is metabolized	1 to 2 years
Phase 2	Gather data on the effectiveness of the drug candidate and its optimal dosage; continue safety evaluation	2 to 4 years
Phase 3	Confirm efficacy, dosage regime and safety profile of the drug candidate; submit NDA	2 to 4 years
FDA approval	Approval by the FDA to sell and market the drug for the approved indication	6 months to 2 years

A drug candidate may fail to progress at any point during this process. Animal and other nonclinical studies typically are conducted during each phase of human clinical trials.

Patent Term Restoration

Pursuant to the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, some of our patents, under certain conditions, may be eligible for limited patent term extension for a period of up to five years as compensation for patent term lost during drug development and the FDA regulatory review process. However, this extension period cannot be extended beyond 14 years from the drug's approval date. The patent term restoration period is generally one-half the period of time elapsed between the effective date of an IND application and the submission date of an NDA, plus the period of time between the submission date of the NDA and FDA approval. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves applications for any patent term extension or restoration. We intend to seek the benefits of this statute, but there can be no assurance that we will be able to obtain any such benefits.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a "rare disease or condition" that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. If a drug that has an orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the product is entitled to orphan exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Nevertheless, competitors may receive approval of different drugs or biologics for the indications for which the orphan product has exclusivity. VX-770 has been granted orphan drug designation.

Post-approval Studies

Even after FDA approval has been obtained, further studies, including post-approval trials, may be required to provide additional data on safety and will be required to gain approval for the sale of a

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drug as a treatment for clinical indications other than those for which the drug initially was approved. Also, the FDA will require post-approval reporting to monitor the side-effects of the drug. Results of post-approval programs may limit or expand the indications for which the drug may be marketed. Further, if there are any requests for modifications to the initial FDA approval for the drug, including changes in indication, manufacturing process, labeling or manufacturing facilities, submission of a supplemental NDA to the FDA may be required.

Reimbursement

Sales of drugs depend in significant part on the availability of third-party reimbursement. Third-party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. We anticipate third-party payors will provide reimbursement for our drugs if we are successful in obtaining marketing approval. However, third-party payors are increasingly challenging pricing, and in some cases, examining the cost-effectiveness of drugs. In the future, we may need to conduct expensive pharmacoeconomic studies for some of our drug candidates in order to demonstrate their cost-effectiveness, if we successfully obtain marketing approval. The process of seeking reimbursement from third-party payors in the future may be time consuming and expensive.

The Medicare Prescription Drug Improvement and Modernization Act of 2003, or the MMA, extended a prescription drug benefit to Medicare beneficiaries and imposed requirements for the distribution and pricing of prescription drugs under Medicare Part D. Unlike other Medicare benefits, the drug benefit available under Part D is not standardized and there is no guarantee that any drug for which we obtain approval will be covered under Part D.

We expect that there may continue to be a number of federal and state proposals to implement governmental pricing controls and limit the growth of health care costs, including the cost of prescription drugs. At the present time, Medicare is prohibited from negotiating directly with pharmaceutical companies for drugs. However, Congress is considering passing legislation that would lift the ban on federal negotiations.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be marketed lawfully. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market.

Foreign Regulation

In addition to regulations in the United States, we and our collaborators will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of drugs. Whether or not we obtain FDA approval for a drug, approval of a drug candidate by the comparable regulatory authorities of foreign countries must be obtained before we or our collaborators can commence clinical trials or marketing of the drug in those countries. The approval process varies from country to country and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

Under European Union regulatory systems, marketing authorization applications may be submitted either under a centralized or decentralized procedure. The centralized procedure, which is compulsory for medicines produced by certain biotechnological processes and optional for those that are highly innovative, provides for the grant of a single marketing authorization that is valid for all European Union member states. For drugs without approval in any European Union member state, the decentralized procedure provides for assessment of a marketing application by one member state,

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known as the reference member state, and review and possible approval of that assessment by one or more other, or concerned, member states. Under this procedure, an applicant submits an application, or dossier, and related materials draft summary of product characteristics, draft labeling and package leaflet to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points may eventually be referred to the European Commission, whose decision is binding on all member states of the European Union.

Other Regulations

Pharmaceutical companies also are subject to various federal and state laws pertaining to health care "fraud and abuse," including anti-kickback laws and false claims laws. Anti-kickback laws make it illegal for any entity or person to solicit, offer, receive, or pay any remuneration in exchange for or to induce the referral of business, including the purchase or prescription of a particular drug. False claims laws prohibit anyone from knowingly and willingly presenting to third-party payors including Medicare and Medicaid, or causing to be presented, for payment claims for reimbursed drugs or services that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services.

In addition to the statutes and regulations described above, we also are subject to regulation under the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act and other federal, state, local and foreign regulations, now or hereafter in effect.

OTHER MATTERS

Employees

As of December 31, 2008, we had 1,333 employees (1,310 full-time, 23 part-time). The number of our full-time employees increased by 16% during 2008, from 1,132 on December 31, 2007. We may further increase our headcount in 2009 as we invest in expanding our drug development and commercialization capabilities. Of our employees, 1,043 were based in Cambridge, Massachusetts, 99 were located in Europe and 176 were located at our facility in San Diego, California. Our scientific staff members have diversified experience and expertise in molecular and cell biology, biochemistry, synthetic organic chemistry, protein X-ray crystallography, protein nuclear magnetic resonance spectroscopy, microbiology, computational chemistry, biophysical chemistry, medicinal chemistry, clinical pharmacology and clinical medicine. Our clinical development personnel have extensive expertise in designing and executing clinical trials, and we are building our commercialization organization. Our employees are not covered by a collective bargaining agreement, and we consider our relations with our employees to be good.

Information Available on the Internet

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 available to you free of charge through the "Finances/Investor Info-SEC Filings" 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.

Corporate Information

Vertex was incorporated in Massachusetts in 1989, and our principal executive offices are located at 130 Waverly Street, Cambridge, Massachusetts 02139. We have research sites located in San Diego, California, Coralville, Iowa and Milton Park, U.K.

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EXECUTIVE OFFICERS AND DIRECTORS

The names, ages and positions held by our executive officers and directors are as follows:

Name	Age	Position
Joshua S. Boger, Ph.D.	57	Chief Executive Officer and Director
Matthew W. Emmens	57	President and Director
Kurt C. Graves	41	Executive Vice President, Chief Commercial Officer and Head, Strategic Development
Freda C. Lewis-Hall, M.D., FAPA	53	Executive Vice President, Medicines Development
Peter Mueller, Ph.D.	52	Executive Vice President, Drug Innovation and Realization, and Chief Scientific Officer
Ian F. Smith, C.P.A., A.C.A.	43	Executive Vice President and Chief Financial Officer
Kenneth S. Boger, M.B.A., J.D.	62	Senior Vice President and General Counsel
Richard C. Garrison	60	Senior Vice President and Catalyst
Lisa Kelly-Croswell	42	Senior Vice President, Human Resources
Amit K. Sachdev, J.D.	41	Senior Vice President, Corporate Affairs and Public Policy
Paul M. Silva	42	Vice President and Corporate Controller
Charles A. Sanders, M.D.	77	Chairman of the Board
Eric K. Brandt	46	Director
Roger W. Brimblecombe, Ph.D., D.Sc.	79	Director
Stuart J.M. Collinson, Ph.D.	49	Director
Eugene H. Cordes, Ph.D.	72	Director
Bruce I. Sachs	49	Director
Elaine S. Ullian	61	Director

Dr. Joshua Boger is the founder of Vertex. He has been our Chief Executive Officer since 1992, and is expected to step down as our Chief Executive Officer in May 2009. He was our Chairman of the Board from 1997 until May 2006 and our President from our inception in 1989 until December 2000, and again from May 2005 through February 2009. He was our Chief Scientific Officer from 1989 until May 1992. Dr. Boger has been a director since Vertex's inception. Prior to founding Vertex in 1989, Dr. Boger held the position of Senior Director of Basic Chemistry at Merck Sharp & Dohme Research Laboratories in Rahway, New Jersey, where he headed both the Department of Medicinal Chemistry of Immunology & Inflammation and the Department of Biophysical Chemistry. Dr. Boger is the current chairman of the Biotechnology Industry Organization (BIO). Dr. Boger holds a B.A. in chemistry and philosophy from Wesleyan University and M.S. and Ph.D. degrees in chemistry from Harvard University. Dr. Boger is the brother of Mr. Kenneth Boger, our Senior Vice President and General Counsel.

Mr. Emmens became our President in February 2009 and has been a member of our Board of Directors since 2004. We have agreed that Mr. Emmens will become our Chairman and Chief Executive Officer on May 23, 2009. Mr. Emmens is the Chairman of the Board of Directors of Shire Pharmaceuticals Group plc. and has been a member of Shire's board since March 2003. From March 2003 to June 2008, Mr. Emmens was also the Chief Executive Officer of Shire Pharmaceuticals Group plc. Before joining Shire in 2003, Mr. Emmens served as president of Merck KGaA's global prescription pharmaceuticals business in Darmstadt, Germany. In 1999, he joined Merck KGaA and established EMD Pharmaceuticals, its United States prescription pharmaceutical business. Mr. Emmens

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held the position of President and Chief Executive Officer at EMD Pharmaceuticals from 1999 to 2001. Prior to this, Mr. Emmens held various positions, including Chief Executive Officer, at Astra Merck, Inc. as well as several positions at Merck & Co., Inc.. Mr. Emmens received a B.S. degree in business management from Farleigh Dickinson University.

Mr. Graves is our Executive Vice President, Chief Commercial Officer and Head, Strategic Development, a position he has held since joining us in July 2007. From 1999 through June 2007, Mr. Graves held various executive positions at Novartis Pharmaceuticals, including Global Head of General Medicines Business Unit & Chief Marketing Officer, Pharmaceuticals from September 2003 through June 2007. Prior to that, Mr. Graves served as Senior Vice President & General Manager US Pharma & Commercial Operations; Vice President, Head of US Marketing & Primary Care Franchises; and Vice President & Business Unit Head: Respiratory, GI, Dermatology and Bone Franchises. Prior to joining Novartis, Mr. Graves was GI Business Unit Head US Gastrointestinal Franchise, at Astra Pharmaceuticals, LP from 1997 to 1998. From 1993 to 1997, Mr. Graves served in a variety of roles at Astra Merck Pharmaceuticals including Executive Director, Business Unit Commercialization Leader. He has extensive training in marketing & sales and general management, including training at the University of Michigan Business School, Wharton School of Business and Harvard Business School. Mr. Graves holds a B.S. in Biology from Hillsdale College.

Dr. Lewis-Hall is our Executive Vice President, Medicines Development, a position she has held since June 2008. From 2003 through May 2008, Dr. Lewis-Hall was a Senior Vice President, U.S. Pharmaceuticals, Medical Affairs for Bristol-Myers Squibb Company. Prior to Bristol-Myers Squibb, Dr. Lewis-Hall was Vice President, Research and Development, Product Development for Pharmacia Corporation and served in a number of positions for Eli Lilly and Company from 1994 through 2002. Dr. Lewis-Hall was Vice Chairperson and an Associate Professor in Howard University College of Medicine's Department of Psychiatry from 1988 through 1994. Dr. Lewis-Hall holds a B.A. in natural sciences from Johns Hopkins University and an M.D. from Howard University Hospital and College of Medicine.

Dr. Mueller is our Executive Vice President, Drug Innovation and Realization, and Chief Scientific Officer, a position he has held since February 2006. In this role, Dr. Mueller is responsible for our global research initiatives, pharmaceutical development, pharmaceutical operations as well as quality assurance and control. From July 2003 to February 2006, Dr. Mueller was our Chief Scientific Officer and Senior Vice President, Drug Discovery and Innovation. Prior to joining Vertex, Dr. Mueller was the Senior Vice President, Research and Development, of Boehringer Ingelheim Pharmaceuticals, Inc., with responsibility for the development of all drug candidates in the company's worldwide portfolio in North America. He led research programs in the areas of immunology, inflammatory cardiovascular disease and gene therapy on a global basis. During his time with Boehringer Ingelheim, Dr. Mueller oversaw the discovery of numerous development candidates and held several positions in basic research, medicinal chemistry and management. Dr. Mueller received both an undergraduate degree and a Ph.D. in chemistry at the Albert Einstein University of Ulm, Germany, where he also holds a Professorship in Theoretic Organic Chemistry. He completed fellowships in quantum pharmacology at Oxford University and in biophysics at Rochester University.

Mr. Smith is our Executive Vice President and Chief Financial Officer, a position he has held since February 2006. From November 2003 to February 2006, he was our Senior Vice President and Chief Financial Officer, and from October 2001 to November 2003, he served as our Vice President and Chief Financial Officer. Prior to joining Vertex, Mr. Smith served as a partner in the Life Science and Technology Practice Group of Ernst & Young LLP, an accounting firm, from 1999 to 2001. Mr. Smith initially joined Ernst & Young's U.K. firm in 1987, and then joined its Boston office in 1995. Mr. Smith currently is a member of the Boards of Directors of Acorda Therapeutics, Inc., Epix Pharmaceuticals, Inc., Infinity Pharmaceuticals, Inc. and TolerRx Inc. Mr. Smith holds a B.A. in accounting and finance from Manchester Metropolitan University, U.K., is a member of the American Institute of Certified Public Accountants and is a Chartered Accountant of England and Wales.

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Mr. Kenneth Boger is our Senior Vice President and General Counsel, a position he has held since joining us in 2001. He came to Vertex from the law firm of Kirkpatrick & Lockhart LLP, now known as K&L Gates, where he was a partner specializing in business and corporate law and was a member of the firm's Management Committee. Prior to the merger of Kirkpatrick & Lockhart with the Boston law firm of Warner & Stackpole LLP in 1999, Mr. Boger was a partner at Warner & Stackpole, where he served on its Executive Committee from 1988 to 1997. Mr. Boger holds an A.B. in history from Duke University, an M.B.A. from the Graduate School of Business at the University of Chicago, and a J.D. from Boston College Law School. Mr. Boger is the brother of Dr. Joshua Boger, our Chief Executive Officer.

Mr. Garrison is our Senior Vice President and Catalyst, a position he has held since joining us in December 2005. From June 2001 to December 2005, Mr. Garrison was the founder and President of Bink Inc., a strategic consulting firm. Prior to that, Mr. Garrison was, for 18 years, the Chairman and Chief Executive Officer of Ingalls, Quinn & Johnson, one of New England's largest advertising agencies. Mr. Garrison holds a B.A. in English from Princeton University.

Ms. Kelly-Croswell is our Senior Vice President, Human Resources, a position she has held since July 2007. Ms. Kelly-Croswell served as our Vice President, Human Resources from July 2006 to June 2007. From November 2005 through June 2006, Ms. Kelly-Croswell served as Vice President of Human Resources of NitroMed, Inc., a pharmaceutical company. From February 2004 to November 2005, Ms. Kelly-Croswell served as Senior Vice President, Human Resources at CIGNA, an employee benefits company, for the Health Care Division and Service Operations. From September 2001 to February 2004, Ms. Kelly-Croswell served as Vice President of Human Resources for Global Research and Development for the Monsanto Company, an agricultural products and solutions company that she joined in 1998. Ms. Kelly-Croswell holds a B.S. in Finance and an M.A. in Labor and Industrial Relations from the University of Illinois at Urbana-Champaign.

Mr. Sachdev is our Senior Vice President, Corporate Affairs and Public Policy, a position he has held since he joined us in July 2007. Mr. Sachdev served as Executive Vice President, Health of the Biotechnology Industry Organization (BIO) from April 2005 through June 2007. At BIO, he was the senior executive responsible for managing BIO's Health Section, its Governing Board, and for directing all health care policy and execution. Mr. Sachdev was the Deputy Commissioner for Policy at the FDA from April 2004 through April 2005, and held several other senior positions within the FDA from September 2002 through April 2004. From 1998 to 2002, Mr. Sachdev served as Majority Counsel to the Committee on Energy and Commerce in the U.S. House of Representatives, where he was responsible for bioterrorism, food safety and environmental issues. From 1993 to 1997, Mr. Sachdev practiced law, first at the Chemical Manufacturers Association, and then with the law firm of Ropes & Gray. Mr. Sachdev holds a B.S from Carnegie Mellon University, and a J.D. from the Emory University School of Law.

Mr. Silva is our Vice President and Corporate Controller, a position he has held since September 2008. Mr. Silva joined us in August 2007 as Senior Director, Accounting Operations. Prior to joining us, he was the Vice President, Internal Reporting at Iron Mountain Incorporated from July 2006 until August 2007 and a consultant to Iron Mountain's financing department from April 2005 until July 2006. He was the Finance Director of the Bioscience Technologies Division of Thermo Electron Corporation from 2002 to April 2005. Mr. Silva holds a B.S. in accounting from Assumption College.

Dr. Sanders has been a member of our Board of Directors since 1996, served as our lead outside director from 2003 until 2006 and has served as our Chairman since May 2006. In May 2009, he will resume his role as lead outside director upon Mr. Emmen's planned election as Chairman. He retired in 1994 as Chief Executive Officer and in 1995 as Chairman of Glaxo Inc. From 1990 to 1995, he served as a member of the board of Glaxo plc. From 1981 to 1989, Dr. Sanders held a number of positions at Squibb Corporation, including that of Vice Chairman. Dr. Sanders has served in the past on the boards of Merrill Lynch, Reynolds Metals Co., Morton International Inc. and Fisher Scientific

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International. He is currently a director of Biodel Inc., Cephalon, Inc., Genentech, Inc. and Icagen, Inc. Dr. Sanders had his undergraduate education at the University of Texas, and earned an M.D. from the University of Texas Southwestern Medical School.

Mr. Brandt has been a member of our Board of Directors since 2003. Mr. Brandt is Senior Vice President and Chief Financial Officer of Broadcom Corporation, which he joined in March 2007. From September 2005 through March 2007, he was the President, Chief Executive Officer and a member of the Board of Directors of Avanir Pharmaceuticals. Prior to joining Avanir, Mr. Brandt held various positions at Allergan Inc. from 1999 to 2005, including Executive Vice President, Finance and Technical Operations and Chief Financial Officer from February 2005 to September 2005, Executive Vice President, Finance, Strategy and Business Development, and Chief Financial Officer from 2003 until February 2005, and Corporate Vice President and Chief Financial Officer from May 1999 to 2003. From January 2001 to January 2002, he also assumed the duties of President, Global Consumer Eye Care Business, at Allergan. Prior to that, he held various positions with the Boston Consulting Group, most recently serving as Vice President and Partner, and a senior member of the BCG Health Care practice. Mr. Brandt also serves as a director of Dentsply International Inc. Mr. Brandt holds a B.S. in chemical engineering from the Massachusetts Institute of Technology and an M.B.A. from Harvard University.

Dr. Brimblecombe has been a member of our Board of Directors since 1993 and a member of the Board of Vertex Pharmaceuticals (Europe) Ltd. since 2005. He served as Chairman of Vanguard Medica plc from 1991 to 2000, of Core Group plc from 1997 to 1999, of Oxford Asymmetry International plc from 1997 to 2000 and pSivida Ltd. from 2002 to 2007. From 1979 to 1990, he held various Vice Presidential posts in SmithKline & French Laboratories' research and development organization, including Vice President R&D for Europe and Japan. He is currently a Partner in MVM Life Science Partners LLP. He holds Ph.D. and D.Sc. degrees in pharmacology from the University of Bristol, England.

Dr. Collinson has been a member of our Board of Directors since July 2001. He currently serves as a Partner at Forward Ventures. Prior to our merger with Aurora Biosciences Corporation in 2001, Dr. Collinson served as the President, Chief Executive Officer and Chairman of the Board of Aurora. Dr. Collinson held senior management positions with Glaxo Wellcome from December 1994 to June 1998, most recently serving as Co-Chairman, Hospital and Critical Care Therapy Management Team and Director of Hospital and Critical Care. Dr. Collinson received his Ph.D. in physical chemistry from the University of Oxford, England and his M.B.A. from Harvard University.

Dr. Cordes has been a member of our Board of Directors since 2005, and a scientific advisor to us since 1996. Dr. Cordes was the Chairman of Vitae Pharmaceuticals, Inc., a position he held from January 2002 to March 2006. Prior to joining Vitae Pharmaceuticals, Dr. Cordes was a professor of pharmacy at the University of Michigan. Dr. Cordes received a B.S. degree in chemistry from the California Institute of Technology and a Ph.D. in biochemistry from Brandeis University.

Mr. Sachs has been a member of our Board of Directors since 1998. He is a General Partner at Charles River Ventures. From 1998 to 1999, he served as Executive Vice President and General Manager of Ascend Communications, Inc. From 1997 until 1998, Mr. Sachs served as President and Chief Executive Officer of Stratus Computer, Inc. From 1995 to 1997, he served as Executive Vice President and General Manager of the Internet Telecom Business Group at Bay Networks, Inc. From 1993 to 1995, he served as President and Chief Executive Officer at Xylogics, Inc. Mr. Sachs also currently serves as a director of BigBand Networks, Inc. Mr. Sachs holds a B.S.E.E. in electrical engineering from Bucknell University, an M.E.E. in electrical engineering from Cornell University, and an M.B.A. from Northeastern University.

Ms. Ullian has been a member of our Board of Directors since 1997. Since 1996, she has served as President and Chief Executive Officer of Boston Medical Center. From 1994 to 1996, she served as President and Chief Executive Officer of Boston University Medical Center Hospital. From 1987 to 1994, Ms. Ullian served as President and Chief Executive Officer of Faulkner Hospital. She also serves as a director of Thermo Fisher Scientific Inc. and Hologic, Inc. Ms. Ullian holds a B.A. in political science from Tufts University and a M.P.H. from the University of Michigan.

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ITEM 1A. RISK FACTORS

RISK FACTORS

Investing in our common stock involves a high degree of risk, and you should carefully consider the risks and uncertainties described below in addition to the other information included or incorporated by reference in this Annual Report on Form 10-K. If any of the following risks or uncertainties actually occurs, our business, financial condition or results of operations would likely suffer, possibly materially. In that case, the trading price of our common stock could decline.

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 continue 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 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;
- 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;

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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 in 2009 and thereafter through public offerings or private placements of our debt or equity securities. Any such capital transactions may or may not be similar to 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 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.

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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 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.

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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.

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 4.75% convertible senior subordinated notes due 2013, or 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

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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.

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, 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 December 31, 2008, we had approximately 151.2 million shares of common stock issued and outstanding. We also had outstanding options to purchase approximately 16.5 million shares of common stock with a weighted-average exercise price of $29.16 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.

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 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 IRBs 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;

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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;

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 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.

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

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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 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

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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 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

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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.

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.

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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 and Avalon.

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.

- 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 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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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, 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.

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 and drugs, 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

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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 and the European Union, 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 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,

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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 progess 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;

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

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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.

THE LOSS OF THE SERVICES OF KEY EMPLOYEES OR THE FAILURE TO EFFECTIVELY INTEGRATE KEY EMPLOYEES COULD NEGATIVELY IMPACT OUR BUSINESS AND FUTURE GROWTH.

Our future success will depend in large part on our ability to retain the services of our key scientific and management personnel and to integrate new scientific and management personnel into our business. As we expand our capabilities in anticipation of the possible launch of commercial products, a loss of key personnel or a failure to properly integrate new personnel could be disruptive. We have entered into employment agreements with some individuals and provide compensation-related benefits to all of our key employees that vest over time and therefore induce them to remain with us. However, the employment agreements can be terminated by the employee on relatively short notice. The value to employees of stock-related benefits that vest over time such as options and restricted stock will be significantly affected by movements in our stock price that we cannot control, and may at any point in time be insufficient to counteract more lucrative offers from other companies. A failure to retain, as well as hire, train and effectively integrate into our organization a sufficient number of qualified scientists, professionals, sales personnel and senior management would negatively affect our business and our ability to grow our business.

IF OUR PATENTS DO NOT PROTECT OUR DRUGS, OR OUR DRUGS 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

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and maintain United States and foreign patent protection for our drugs, 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 pharmaceutical 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 similar drugs 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, regardless of whether or not 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 drugs, any of which outcomes could have a material adverse effect on our business.

OUR BUSINESS HAS A SUBSTANTIAL RISK OF PRODUCT LIABILITY CLAIMS. IF WE ARE UNABLE TO OBTAIN APPROPRIATE LEVELS OF INSURANCE, A PRODUCT LIABILITY CLAIM COULD ADVERSELY AFFECT OUR BUSINESS.

Our business exposes us to significant potential product liability risks that are inherent in the development, manufacturing and sales and marketing of human therapeutic products. We currently have clinical trial insurance and will seek to obtain product liability insurance prior to the sales and marketing of any of our drug candidates. However, our insurance may not provide adequate coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to maintain current amounts of insurance coverage or obtain additional or sufficient insurance at a reasonable cost to protect against losses that could have a material adverse effect on us. If a claim is brought against us, we might be required to pay legal and other expenses to defend the claim, as well as uncovered damages awards resulting from a claim brought successfully against us. Furthermore, whether or not we are ultimately successful in defending any such claims, we might be required to direct significant financial and managerial resources to such defense, and adverse publicity is likely to result.

IF WE DO NOT COMPLY WITH LAWS REGULATING THE PROTECTION OF THE ENVIRONMENT AND HEALTH AND HUMAN SAFETY, OUR BUSINESS COULD BE ADVERSELY AFFECTED.

Our research and development efforts involve the controlled use of hazardous materials, chemicals and various radioactive compounds. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards prescribed by state and federal regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens and the handling of biohazardous materials. Although we maintain workers' compensation insurance to cover us for costs we may incur due to injuries to our employees resulting from the use of these materials, this insurance may not provide adequate coverage against potential liabilities. Due to the small amount of hazardous materials that we generate, we have determined that the cost to secure insurance coverage for environmental liability and toxic tort claims far exceeds the benefits. Accordingly, we do not maintain any insurance to cover pollution conditions or other extraordinary or unanticipated events relating to our use and disposal of hazardous materials. Additional federal, state and local laws and regulations affecting our operations may be adopted in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate, any of these laws or regulations.

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WE HAVE ADOPTED ANTI-TAKEOVER PROVISIONS AND ARE SUBJECT TO MASSACHUSETTS CORPORATE LAWS THAT MAY FRUSTRATE ANY ATTEMPT TO REMOVE OR REPLACE OUR CURRENT MANAGEMENT.

Our corporate charter and by-law provisions, Massachusetts state laws, and our stockholder rights plan may discourage certain types of transactions involving an actual or potential change of control of Vertex that might be beneficial to us or our security holders. 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 our 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. Massachusetts state law prohibits us from engaging in specified business combinations, unless the combination is approved or consummated in a prescribed manner, and prohibits voting by any stockholder who acquires 20% or more of our voting stock without stockholder approval. As a result, stockholders 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. From January 1, 2007 to December 31, 2008, our common stock traded between $13.84 and $41.42 per share. 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 trials or nonclinical studies relating to our drug candidates or those of our competitors;
- announcements of financial results and other operating performance measures, or capital structuring or financing activities;
- technological innovations or the introduction of new drugs by our competitors;
- government regulatory action;
- public concern as to the safety of drugs 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;
- developments relating specifically to other companies and market conditions for pharmaceutical and biotechnology stocks or stocks in general; and
- general worldwide or national economic, political and capital market conditions.

OUR ESTIMATES OF OUR LIABILITY UNDER OUR KENDALL SQUARE LEASE MAY BE INACCURATE.

We leased a 290,000 square foot facility in Kendall Square, Cambridge, Massachusetts in January 2003 for a 15-year term. We currently are not occupying the entire facility. We have sublease arrangements in place for the remaining rentable square footage of the facility. In determining our

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obligations under the lease for the part of the facility that we are not occupying, we have made certain assumptions relating to the time necessary to sublease the space after the expiration of the initial subleases, projected future sublease rental rates and the anticipated durations of future subleases. Our estimates have changed in the past, and may change in the future, resulting in additional adjustments to the estimate of liability, and the effect of any such adjustments could be material.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K and, in particular, the description of our Business set forth in Item 1, the Risk Factors set forth in this Item 1A and our Management's Discussion and Analysis of Financial Condition and Results of Operations set forth in Item 7 contain or incorporate a number of forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, including statements regarding:

our expectations regarding clinical trials, development timelines and regulatory authority filings for telaprevir, VX-770 and other drug candidates under development by us and our collaborators;

our expectations regarding the number of patients that will be evaluated, the trial design that will be utilized, the anticipated date by which enrollment will be completed and the expected date by which SVR data, interim data and/or final data will be available and/or publicly announced for our ADVANCE, REALIZE and ILLUMINATE trials, the other ongoing or planned clinical trials of telaprevir, the registration program for VX-770, the Phase 1 clinical trials and Phase 2a clinical trials of VX-809, the Phase 1 clinical trial of VX-813, and the clinical trials being conducted by our collaborators of drug candidates for the treatment of cancer;

expectations regarding trends with respect to our costs and expenses;

the data that will be generated by ongoing and planned clinical trials, and the ability to use that data for the design and initiation of further clinical trials and to support regulatory filings, including potentially applications for marketing approval for telaprevir and VX-770;

our ability to potentially register telaprevir for marketing across a range of genotypes and patient populations;

our intention to work with regulatory authorities in North America and Europe to design a registration program for VX-770, which, if approved, could begin the first half of 2009;

our expectations regarding the future market demand and medical need for telaprevir and our other drug candidates;

our beliefs regarding the support provided by clinical trials and preclinical and nonclinical studies of our drug candidates for further investigation, clinical trials or potential use as a treatment of those drug candidates;

our ability to successfully market telaprevir and VX-770 if we are able to obtain regulatory approval;

the focus of our drug development efforts and our financial and management resources and our plan to invest significant resources in telaprevir and our other drug candidates;

the establishment, development and maintenance of collaborative relationships;

potential business development activities, including with respect to our JAK3 program and drug candidates that could be complimentary to our HCV protease inhibitors;

our ability to use our research programs to identify and develop new drug candidates to address serious diseases and significant unmet medical needs;

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our estimates regarding obligations associated with a lease of a facility in Kendall Square, Cambridge, Massachusetts; and

our liquidity and our expectations regarding our needs for and ability to raise additional capital.

Any or all of our forward-looking statements in this Annual Report on Form 10-K 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 this Annual Report on Form 10-K will be important in determining future results. Consequently, no forward-looking statement can be guaranteed. Actual future results may vary materially from expected results. We also provide a cautionary discussion of risks and uncertainties under "Risk Factors" above in this Item 1A. These are factors and uncertainties that we think could cause our actual results to differ materially from expected results. Other factors and uncertainties besides those listed there could also adversely affect us.

Without limiting the foregoing, the words "believes," "anticipates," "plans," "intends," "expects" and similar expressions are intended to identify forward-looking statements. There are a number of factors and uncertainties that could cause actual events or results to differ materially from those indicated by such forward-looking statements, many of which are beyond our control, including the factors and uncertainties set forth under "Risk Factors" above in this Item 1A. In addition, the forward-looking statements contained herein represent our estimate only as of the date of this filing and should not be relied upon as representing our estimate as of any subsequent date. While we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so to reflect actual results, changes in assumptions or changes in other factors affecting such forward-looking statements.

ITEM 1B. UNRESOLVED STAFF COMMENTS

We did not receive any written comments from the Securities and Exchange Commission prior to the date 180 days before the end of the fiscal year ending December 31, 2008 regarding our filings under the Securities Exchange Act of 1934, as amended, that have not been resolved.

ITEM 2. PROPERTIES

We lease an aggregate of approximately 829,000 square feet of laboratory and office space in facilities located in Cambridge, Massachusetts, San Diego, California, Washington, DC, Coralville, Iowa, and the United Kingdom. We believe our facilities are adequate for our current needs.

Cambridge, Massachusetts

We lease an aggregate of 684,000 square feet of space in nine facilities situated in close proximity to our corporate headquarters facility located at 130 Waverly Street in Cambridge, Massachusetts. We lease approximately 100,000 square feet of laboratory and office space in our 130 Waverly Street corporate headquarters and approximately 192,000 square feet of laboratory and office space at 200 Sidney Street, located adjacent to our corporate headquarters. The 130 Waverly Street and 200 Sidney Street leases expire on December 31, 2015, with two options to extend for five year terms. The lease for 21,000 square feet of office space at 21 Erie Street, also located adjacent to our corporate headquarters, expires in May 2012, with an option to extend for two additional consecutive five-year terms.

The lease for our Kendall Square, Cambridge, Massachusetts facility will expire in 2018. We have the option to extend that lease for two consecutive ten-year terms. We have subleased approximately 145,000 square feet of Kendall Square facility, and are using the remaining square feet of space leased in the facility for our research operations. The subleases are for terms ending in 2011 and 2012 with extension options to 2015 and 2018. One of the subleases has certain termination provisions beginning in 2010.

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San Diego, California

We lease approximately 81,000 square feet of laboratory and office space in San Diego, California. The lease for this space will expire on September 30, 2013. We have the option to extend this lease for one additional term of five years.

United Kingdom

We lease approximately 22,000 square feet of laboratory and office space in Milton Park, Abingdon, England, for our United Kingdom business and research and development activities, under a lease expiring in 2013. We also have an agreement to lease an additional 41,000 square feet of laboratory and office space in Milton Park beginning later in 2009 with a term that expires in 2024. This lease has certain termination provisions in 2014 and 2019.

ITEM 3. LEGAL PROCEEDINGS

We are not a party to any material legal proceedings. We are not a party to any litigation in any court with any governmental authority, and management is not aware of any contemplated proceeding by any governmental authority against us.

In the fourth quarter of 2008, the purported shareholder class action brought against us on March 13, 2008 and referred to as *Waterford Township Police Fire Retirement System v. Vertex Pharmaceuticals Incorporated, et al.*, was dismissed with prejudice, and without any payments by the defendant to the plaintiffs.

ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

There were no matters submitted to a vote of security holders during the quarter ended December 31, 2008.

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PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock is traded on The Nasdaq Global Select Market under the symbol "VRTX." The following table sets forth for the periods indicated the high and low sale prices per share of our common stock as reported by Nasdaq:

Year Ended December 31, 2007:	High	Low
First quarter	$38.95	$26.98
Second quarter	32.51	25.61
Third quarter	41.42	27.55
Fourth quarter	39.48	22.80

Year Ended December 31, 2008:		
First quarter	$24.67	$13.84
Second quarter	34.97	23.40
Third quarter	35.00	24.62
Fourth quarter	33.19	18.43

As of February 10, 2009, there were 1,717 holders of record of our common stock.

Performance Graph

CUMULATIVE TOTAL RETURN*

Based on Initial Investment of $100 on December 31, 2003
with dividends reinvested (fiscal years ending December 31)

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Dividends

We have never declared or paid any cash dividends on our common stock, and we currently expect that future earnings, if any, will be retained for use in our business.

Issuer Repurchases of Equity Securities

The table set forth below shows all repurchases of securities by us during the three months ended December 31, 2008:

Period	Total Number of Shares Purchased	Average Price Paid per Share	Total Number of Shares Purchased as part of publicly announced Plans or Programs	Maximum Number of Shares that may yet be purchased under publicly announced Plans or Programs
Oct. 1, 2008 to Oct. 31, 2008	47,927	$ 0.01		
Nov. 1, 2008 to Nov. 30, 2008	1,452	$ 0.01		
Dec. 1, 2008 to Dec. 31, 2008	4,158	$ 0.01		

The repurchases were made under the terms of our 1996 Stock and Option Plan and 2006 Stock and Option Plan. Under these plans, we may award shares of restricted stock to our employees and consultants. These shares of restricted stock typically are subject to a lapsing right of repurchase by us. We may exercise this right of repurchase in the event that a restricted stock recipient's service to us is terminated. If we exercise this right, we are required to repay the purchase price paid by or on behalf of the recipient for the repurchased restricted shares, which typically is the par value per share of $0.01. Repurchased shares are returned to the applicable Stock and Option Plan under which they were issued. Shares returned to the 2006 Stock and Option Plan are available for future awards under the terms of that plan.

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ITEM 6. SELECTED FINANCIAL DATA

The following unaudited selected consolidated financial data for each of the five years in the period ended December 31, 2008 are derived from our audited consolidated financial statements. These data should be read in conjunction with our audited consolidated financial statements and related notes that are included elsewhere in this Annual Report on Form 10-K and with "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in Item 7 below.

	Years Ended December 31,				
	2008	2007	2006	2005	2004
	(in thousands, except per share amounts)				
Consolidated Statements of Operations Data:					
Revenues:					
Royalty revenues	$ 37,483	$ 47,973	$ 41,208	$ 32,829	$ 17,322
Collaborative and other research and development revenues	138,021	151,039	175,148	128,061	85,395
Total revenues	175,504	199,012	216,356	160,890	102,717
Costs and expenses:					
Royalty expenses	15,686	13,904	12,170	10,098	5,649
Research and development expenses	516,292	518,677	379,228	248,540	192,162
Sales, general and administrative expenses	101,910	79,104	50,345	43,990	42,139
Restructuring expense	4,324	7,119	3,651	8,134	17,574
Total costs and expenses	638,212	618,804	445,394	310,762	257,524
Loss from operations	(462,708)	(419,792)	(229,038)	(149,872)	(154,807)
Other income/(expense), net	2,857	28,513	15,069	(5,332)	(7,994)
Realized gain on sale of investment(1)			11,183		
Loss on exchange of convertible subordinated notes(2)(3)			(5,151)	(48,213)	
Loss on retirement of convertible subordinated notes(4)					(3,446)
Loss before cumulative effect of change in accounting principle	$(459,851)	$(391,279)	$(207,937)	$(203,417)	$(166,247)
Cumulative effect of a change in accounting principle SFAS 123(R)(5)			1,046		
Net loss	$(459,851)	$(391,279)	$(206,891)	$(203,417)	$(166,247)
Basic and diluted loss per common share before cumulative effect of a change in accounting principle	$ (3.27)	$ (3.03)	$ (1.84)	$ (2.28)	$ (2.12)
Basic and diluted cumulative effect of a change in accounting principle per common share.			0.01		