VERTEX PHARMACEUTICALS INC / MA
Form 10-K
February 19, 2010

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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, 2009**

**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 whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes o 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. o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or a smaller reporting company. See 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, 2009 (the last trading day of the registrant's second fiscal quarter of 2009) was $6.4 billion. As of February 16, 2010, the registrant had 200,576,408 shares of common stock outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the definitive Proxy Statement for the 2010 Annual Meeting of Stockholders to be held on May 13, 2010 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.

"Vertex" is a registered trademark of Vertex. "Lexiva" and "Telzir" are registered trademarks of GlaxoSmithKline plc. Other brands, names and trademarks contained in this Annual Report on Form 10-K are the property of their respective owners.

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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 target hepatitis C virus, or HCV, infection. Telaprevir is being evaluated in a registration program focused on treatment-naïve and treatment-failure patients with genotype 1 HCV infection. We currently intend to submit a new drug application, or NDA, for telaprevir in the United States in the second half of 2010 and to initiate sales of telaprevir in the United States in 2011, assuming the successful completion of the registration program.

We are engaged in a number of other clinical development programs and intend to continue to invest in our research programs with the goal of adding promising new compounds to our drug development pipeline. VX-770, the lead drug candidate in our cystic fibrosis, or CF, program is being evaluated in a registration program that focuses on patients with CF who have the G551D mutation in the gene responsible for CF. We are conducting or are planning to begin in 2010 a number of Phase 2a clinical trials of our earlier-stage drug candidates. These clinical trials consist of a planned clinical trial that will evaluate telaprevir in combination with the HCV polymerase inhibitor VX-222, a planned clinical trial of VX-809 in combination with VX-770 in patients with the most common mutation in the gene responsible for CF, a clinical trial of VX-509 in patients with moderate-to-severe rheumatoid arthritis and a clinical trial of VX-765 in patients with treatment-resistant epilepsy.

### OUR PIPELINE

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

| Drug or Drug Candidate | Clinical Indication(s) | Mechanism/Target | Development Stage | Collaborator(s) |
|---|---|---|---|---|
| ***HCV Infection*** | | | | |
| telaprevir (VX-950) | HCV Infection | HCV Protease Inhibitor | Phase 3 | Janssen Pharmaceutica, N.V.<br>Mitsubishi Tanabe Pharma Corporation |
| VX-222 | HCV Infection | HCV Polymerase Inhibitor | Phase 2a | |
| VX-985 | HCV Infection | HCV Protease Inhibitor | Phase 1 | |
| VX-759 | HCV Infection | HCV Polymerase Inhibitor | Phase 1 | |
| ***Cystic Fibrosis*** | | | | |
| VX-770 | Cystic Fibrosis | CFTR Potentiator | Phase 3 | Cystic Fibrosis Foundation Therapeutics Incorporated |
| VX-809 | Cystic Fibrosis | CFTR Corrector | Phase 2a | Cystic Fibrosis Foundation Therapeutics Incorporated |
| ***Immune-mediated Inflammatory Diseases*** | | | | |
| VX-509 | Rheumatoid Arthritis | JAK3 Inhibitor | Phase 2a | |
| ***Epilepsy*** | | | | |
| VX-765 | Epilepsy | Caspase-1 Inhibitor | Phase 2a | |
| ***HIV Infection*** | | | | |
| Lexiva/Telzir | HIV Infection | HIV Protease Inhibitor | Marketed | GlaxoSmithKline plc* |

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

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**OUR STRATEGY**

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

*Obtain FDA approval for and effectively commercialize telaprevir in the United States.* We are focused on obtaining approval for and effectively commercializing telaprevir as a treatment for patients infected with genotype 1 HCV who have not received previous treatment for their infections, referred to as treatment-naïve patients, and patients infected with genotype 1 HCV who have failed to achieve a sustained viral response, or SVR, after prior treatment with pegylated-interferon, or peg-IFN, and ribavirin, or RBV, referred to as treatment-failure patients. Our registration program is designed to support 24-week response-guided telaprevir-based treatment regimens for treatment-naïve patients, and to support treatment of all categories of treatment-failure patients, including null responders to peg-IFN and RBV, who are the most difficult category of patients with HCV infection to treat successfully. We expect to receive final SVR data from the ongoing registration clinical trials for telaprevir during the second and third quarters of 2010 and expect to submit the NDA for telaprevir in the second half of 2010. If we obtain positive results from the ongoing registration program and are able to obtain approval of telaprevir on our current timeline, we plan to initiate sales of telaprevir in the United States in 2011.

*Become a fully-capable biopharmaceutical company.* In order to become a fully-capable biopharmaceutical company, we believe we need to build and establish an effective sales and marketing organization to augment our existing research capabilities along with the late-stage development organization and third-party manufacturing relationships that we have built over the last several years. Although we have been expanding our commercial infrastructure, we will need to further expand these capabilities in order to effectively launch telaprevir and to position our company for the future.

*Invest in research and early and mid-stage development programs.* We intend to continue to invest significant resources in research programs and early-stage and mid-stage clinical development programs as part of our strategy to develop drug candidates in therapeutic areas with significant unmet need. In 2010, we expect to conduct Phase 2a clinical trials involving drug candidates, which we have developed internally or acquired through business development activities, that are intended to address significant unmet needs in HCV, CF, rheumatoid arthritis and epilepsy. We expect to continue focusing our research activities toward therapies addressing serious diseases, because we believe 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 have provided us with financial support and other valuable resources for our development and research programs, and business development opportunities have provided us with drug candidates and important research resources that have contributed to a number of the drug candidates in our current development pipeline. 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 opportunistically seek to license and acquire drugs, drug candidates and other technologies that have the potential to strengthen our pipeline, drug discovery platform or commercial opportunities.

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**DRUG CANDIDATES**

***HCV Infection***

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

Telaprevir, our lead drug candidate, is an orally-administered hepatitis C protease inhibitor that is being evaluated in treatment-naïve and treatment-failure patients with genotype 1 HCV infection in combination with peg-IFN and RBV. 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. We have completed dosing of all study drugs in the registration program for telaprevir. Assuming the successful completion this year of our registration program for telaprevir, we intend to submit an NDA for telaprevir in the United States in the second half of 2010 and to initiate commercial sales of telaprevir in the United States in 2011. In addition to the current registration program, we also are planning to initiate a Phase 2a clinical trial to evaluate telaprevir in combination with VX-222, a polymerase inhibitor, with and without peg-IFN and RBV.

We have collaboration agreements relating to telaprevir with Janssen Pharmaceutica, N.V., or Janssen, a Johnson & Johnson company, and Mitsubishi Tanabe Pharma Corporation, or Mitsubishi Tanabe. Pursuant to these agreements, 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. Mitsubishi Tanabe will be responsible for the commercialization of telaprevir, including the manufacture of its own commercial supply of telaprevir, in Japan and specified other countries in 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 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 other complications of cirrhosis, including liver cancer. The World Health Organization has reported that HCV infection 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.

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

In addition to being the most prevalent form of HCV infection, infection with genotype 1 HCV is the most difficult to treat of the primary HCV genotypes. The current standard treatment for infection with 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 achieve a long-term sustained response to therapy. For example, on an intent-to-treat basis, 41% and 46%, respectively, of treatment-naïve patients in the standard therapy arms of our Phase 2b clinical trials known as PROVE 1 and PROVE 2 achieved an SVR. In another clinical trial conducted by another

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company, involving approximately 3,070 treatment-naïve patients in the United States infected with genotype 1 HCV, between 38% and 41% of patients receiving peg-IFN and RBV achieved an SVR. We believe that there are over 250,000 patients infected with genotype 1 HCV in the United States who have failed to achieve an SVR after therapy with peg-IFN and RBV.

*Telaprevir Clinical Development*

The three clinical trials in our registration program are ADVANCE and ILLUMINATE, Phase 3 clinical trials of telaprevir-based treatment regimens in treatment-naïve patients with genotype 1 HCV infection, and REALIZE, a Phase 3 clinical trial of telaprevir-based treatment regimens in treatment-failure patients with genotype 1 HCV infection. Dosing of all study groups in these three clinical trials has been completed. SVR data are expected from ADVANCE in the second quarter of 2010 and from ILLUMINATE and REALIZE in the third quarter of 2010.

The ADVANCE trial is a 3-arm double-blinded placebo-controlled clinical trial that enrolled approximately 1,050 patients with genotype 1 HCV infection. ADVANCE 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 period of time after completing telaprevir dosing. Patients in both of the telaprevir-based treatment arms who meet extended rapid viral response criteria, or eRVR, complete all treatment after 24 weeks, while patients who are responding to treatment but do not meet the eRVR criteria 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 the end of week 4 and week 12 after the start of treatment.

**ADVANCE Clinical Trial Design**

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ILLUMINATE is a Phase 3 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 an 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 benefits and risks, for patients who achieve an eRVR, of extending total treatment duration from 24 to 48 weeks.

**ILLUMINATE Clinical Trial Design**

The REALIZE trial is a 3-arm clinical trial of telaprevir-based treatment regimens in approximately 650 patients with genotype 1 HCV infection who failed to achieve an SVR after treatment with peg-IFN and RBV alone. One treatment arm is evaluating a lead-in strategy in which patients receive four weeks of pre-treatment with peg-IFN and RBV prior to starting telaprevir. REALIZE is being managed by our collaborator Tibotec Pharmaceuticals Ltd., which is a Johnson & Johnson company and an affiliate of Janssen. REALIZE includes the following patient groups:

null responders  those patients who experienced less than a 2 $\log_{10}$ reduction in HCV RNA levels at week 12 of prior therapy;

partial responders  those patients who experienced at least a 2 $\log_{10}$ reduction in HCV RNA levels at week 12 of prior therapy, but who failed to achieve undetectable HCV RNA levels by week 24; and

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

**REALIZE Clinical Trial Design**

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*Telaprevir Clinical Data*

PROVE Phase 2b Clinical Trials

We have completed three Phase 2b clinical trials of telaprevir-based combination therapy in patients infected with genotype 1 HCV, referred to as the PROVE trials. The PROVE trials enrolled an aggregate of approximately 580 treatment-naïve patients and 440 treatment-failure patients. The SVR rates on an intent-to-treat basis for patients in the 24-week telaprevir-based treatment arms and the control arms of PROVE 1 and PROVE 2, the two Phase 2b clinical trials that evaluated treatment-naïve patients, are set forth in the table below:

| | PROVE 1 | PROVE 2 |
|---|---|---|
| **24-week telaprevir-based treatment arm:** | | |
| telaprevir in combination with peg-IFN and RBV for 12 weeks, followed by peg-IFN and RBV alone for 12 weeks | 61% | 69% |
| **48-week control arm:** | | |
| 48 weeks of therapy with peg-IFN and RBV | 41% | 46% |

PROVE 3 was a Phase 2b clinical trial that evaluated telaprevir-based treatment of patients who had failed at least one course of treatment with peg-IFN and RBV, the current standard of care. The SVR rates on an intent-to-treat basis for patients in the 24-week telaprevir-based treatment arm, the 48-week telaprevir-based treatment arm and the control arm of PROVE 3 are set forth in the table below. Non-responders are patients who were not responsive to prior treatment and consist of a mixture of null and partial responders. Relapsers are patients who had viral rebound during the period following prior treatment. Breakthroughs are patients who experienced a viral rebound during prior treatment.

| | Non-responders | Relapsers | Breakthroughs | Total |
|---|---|---|---|---|
| **24-week telaprevir-based triple-therapy treatment arm:** | | | | |
| telaprevir in combination with peg-IFN and RBV for 12 weeks, followed by peg-IFN and RBV alone for 12 weeks | 39% (n=66) | 69% (n=42) | 57% (n=7) | 51% (n=115) |
| **48-week telaprevir-based treatment arm:** | | | | |
| telaprevir in combination with peg-IFN and RBV for 24 weeks, followed by peg-IFN and RBV alone for 24 weeks | 38% (n=64) | 76% (n=41) | 50% (n=8) | 52% (n=113) |
| **48-week control arm:** | | | | |
| 48 weeks of therapy with peg-IFN and RBV | 9% (n=68) | 20% (n=41) | 40% (n=5) | 14% (n=114) |

The adverse event profile of telaprevir generally was consistent across our Phase 2 clinical trials, which have principally involved clinical trial sites in North America and Europe. 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 than in the control arms were gastrointestinal events, skin events rash and pruritus and anemia. There have been reports of severe rashes in clinical trials involving telaprevir-based treatments, including several reports from the clinical trials being conducted by Mitsubishi Tanabe in Japan, where telaprevir is being evaluated in Phase 3 clinical trials in combination with peg-IFN and RBV. Rash resulted in treatment discontinuations in the telaprevir-based treatment arms in approximately 7% of patients in PROVE 1 and PROVE 2 and 5% of patients in PROVE 3. Other adverse events reported in our Phase 2 clinical trials generally were similar in type and frequency to those seen with peg-IFN and RBV treatment. Our ongoing registration program includes a rash management program that was developed based on the information from the PROVE 1 and PROVE 2 clinical trials and first implemented in our PROVE 3 clinical trial.

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Additional Phase 2 Clinical Trials of Telaprevir

In October 2009, we announced data from the C208 trial, which was an exploratory open-label clinical trial that enrolled 161 treatment-naïve patients infected with genotype 1 HCV in Europe. The purpose of the C208 trial was 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. A three-times daily dosing regimen is being used in the ongoing registration program for telaprevir and has also been used in the other clinical trials for telaprevir.

In the C208 trial, patients received telaprevir, peg-IFN and RBV for 12 weeks followed by an additional period of therapy of peg-IFN and RBV alone in a response-guided trial design. The design is response-guided because the time period during which a patient remains on therapy with peg-IFN and RBV alone after completion of therapy with a combination of telaprevir, peg-IFN and RBV is adjusted depending on the nature of the patient's early response to treatment. Patients who achieved at week 4 HCV RNA levels of less than 25 IU/mL, which is undetectable in the test used and is referred to as a rapid viral response or RVR, and also demonstrated undetectable HCV RNA through week 20, were able to stop all treatment after 24 weeks. Patients who did not meet the response-guided criteria were treated for a total of 48 weeks. 18% of patients across the treatment arms were required to continue treatment for 48 weeks.

The following table summarizes the RVR and SVR data on an intent-to-treat basis from the C208 trial.

| Telaprevir Dosing | Combination Therapy | Total Number of Patients | RVR (undetectable at week 4 on treatment) | SVR (undetectable 24 weeks after end-of-treatment) |
|---|---|---|---|---|
| 1,125 mg every 12 hours | alfa-2a (PEGASYS)/RBV | 40 | 83% (n=33) | 83% (n=33) |
| 1,125 mg every 12 hours | alfa-2b (PEGINTRON)/RBV | 39 | 67% (n=26) | 82% (n=32) |
| 750 mg every 8 hours | alfa-2a (PEGASYS)/RBV | 40 | 80% (n=32) | 85% (n=34) |
| 750 mg every 8 hours | alfa-2b (PEGINTRON)/RBV | 42 | 69% (n=29) | 81% (n=34) |

The frequency and severity of adverse events and the rate of treatment discontinuations were similar to those reported in prior telaprevir trials. The most common adverse events reported in patients in this clinical trial were pruritis, nausea, rash, anemia, flu-like illness, fatigue and headache, and the adverse events were similar overall across the patient groups receiving three-times daily dosing and those receiving twice-daily dosing. Serious adverse events leading to permanent treatment discontinuation of all drugs occurred in 5% of patients and were mainly related to rash, which resulted in discontinuation of 4 out of 161, or 3%, of patients, and anemia, which resulted in discontinuation of 3 out of 161, or 2%, of patients.

We also provided interim data in 2009 from an exploratory clinical trial, referred to as the 107 Trial, in patients from the control arms of the PROVE 1, PROVE 2 or PROVE 3 clinical trials who did not achieve an SVR. We expect to present final data from the 107 Trial during 2010.

*Mitsubishi Tanabe Clinical Program*

Mitsubishi Tanabe has three ongoing Phase 3 trials of telaprevir-based combination therapy in approximately 300 treatment-naïve and treatment-failure patients with HCV infection in Japan. Mitsubishi Tanabe has completed the telaprevir dosing portion of these Phase 3 clinical trials.

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**VX-222 (investigational oral HCV polymerase inhibitor for the treatment of HCV infection)**

HCV polymerase inhibitors, including our HCV polymerase inhibitor VX-222, are direct-acting antiviral agents that inhibit the replication of HCV, but through a mechanism distinct from HCV protease inhibitors such as telaprevir. VX-222 was evaluated by ViroChem Pharma Inc., or ViroChem, in Phase 1 clinical trials prior to our acquisition of ViroChem in March 2009. In this Phase 1 viral kinetics clinical trial, which involved five treatment-naïve patients with genotype 1 HCV infection, VX-222 dosed at 750 mg twice daily resulted in a median 3.7 $\log_{10}$ decrease in HCV RNA equivalent to a 5,000-fold reduction in virus in the blood at the end of three days of dosing. The results were consistent from patient to patient, and across HCV genotype 1 subtypes. We recently reported interim data from a multiple-dose Phase 1b viral kinetic clinical trial of VX-222 that we are conducting to evaluate the antiviral activity, safety, tolerability and pharmacokinetics of VX-222 in patients with genotype 1 HCV infection. Interim results were consistent with the findings of the previously-conducted three-day viral kinetics clinical trial. No serious adverse events were reported in this trial.

We are engaged in late-stage discussions with the FDA and other international regulatory authorities, regarding the initiation of a Phase 2a combination trial of telaprevir and VX-222. This clinical trial is expected to begin in the first quarter of 2010 and to evaluate SVR rates using multiple regimens of telaprevir/VX-222-based therapy in patients with HCV infection.

**Additional HCV Research Activities and Development Programs**

In addition to our development activities focused on telaprevir and VX-222, we are conducting a number of earlier-stage research and development activities aimed at identifying compounds that have advantageous characteristics for potential use against HCV infection. As we obtain new data and scientific, business and commercial insights into our own drug candidates and the drug candidates being developed by other companies, we may periodically change our focus and priority with respect to the drug candidates we are developing and the research programs we are pursuing. We currently consider VX-759, a second polymerase inhibitor that we acquired in our ViroChem acquisition, to be a back-up drug candidate to VX-222. VX-759 has been evaluated in Phase 1 clinical trials, and there are no ongoing clinical trials for VX-759. VX-985, an investigational HCV protease inhibitor that we discovered, is currently in Phase 1 clinical development. VX-813, another investigational HCV protease inhibitor, is no longer in development. We have an ongoing research program directed at identifying NS5A inhibitors, a third class of specifically targeted anti-viral compounds that we believe may be useful in the treatment of HCV infection.

***Cystic Fibrosis***

Cystic fibrosis is a genetic disorder that affects about 30,000 people in the United States and 70,000 worldwide. The drug candidates that we are developing for CF were selected because of their potential to address the underlying cause of CF by increasing the function of a defective protein in CF patients, known as the cystic fibrosis transmembrane conductance regulator, or CFTR. 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 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 2008, the predicted median 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.

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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 results in a defect known as a gating defect, in which the CFTR protein reaches the cell surface but does not efficiently transport chloride ions across the cell membrane. The F508del mutation results in a defect known as a trafficking defect, in which the CFTR protein does not reach the cell surface in sufficient quantities.

According to the 2007 Cystic Fibrosis Foundation Patient Registry Annual Data Report in the United States, approximately 4% of patients with CF have the G551D mutation on at least one allele, 49% of patients with CF have the F508del mutation on both alleles and an additional approximately 38% of patients with CF have the F508del mutation on one allele.

There 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. The $FEV_1$ test has been used as an efficacy end-point during testing of 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 percent 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 selected because of their potential to improve the function of defective CFTR proteins in patients with CF. We discovered VX-770 and VX-809 in our research collaboration with The 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 will pay royalties to CFFT on any future sales of VX-770 or VX-809.

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

VX-770 is an investigational oral drug candidate that was selected because of its potential to increase chloride ion transport across cell membranes by partially restoring the activity of defective CFTR protein. In May 2009, we initiated a registration program, referred to as ENDEAVOR, for VX-770. The VX-770 registration program focuses on patients with the G551D mutation. The registration program consists of three clinical trials.

The primary clinical trial, which is referred to as STRIVE, is a Phase 3 clinical trial of VX-770 that enrolled approximately 170 patients 12 years and older with the G551D mutation on at least one of the patient's two *CFTR* genes, or alleles. In this randomized, placebo-controlled, double-blind, parallel-group clinical trial, patients will receive either VX-770 or placebo for 48 weeks. The second clinical trial, which is referred to as ENVISION, is a Phase 3 clinical trial of VX-770 in patients between 6 to 11 years of age with the G551D mutation on at least one allele. ENVISION is a two-part, randomized, placebo-controlled, double-blind, parallel-group clinical trial of VX-770. We have completed part 1 of ENVISION, which evaluated single-dose pharmacokinetics to determine the dose selection for children ages 6 to 11. We expect that Part 2 of the ENVISION trial will enroll approximately 30 patients who will receive either VX-770 or placebo for 48 weeks. The primary endpoint for the STRIVE and ENVISION clinical trials is absolute change from baseline in $FEV_1$

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through week 24. Additional $FEV_1$ measurements will be taken through 48 weeks as a secondary endpoint. Secondary endpoints, including sweat chloride levels, will be measured to evaluate the effectiveness of VX-770 in improving the function of the defective CFTR protein.

The third clinical trial, which is referred to as DISCOVER, is a Phase 2 exploratory clinical trial of VX-770 that enrolled approximately 120 patients with CF who are 12 years and older and with the F508del mutation on both alleles. In this randomized, placebo-controlled, double-blind, parallel-group trial, patients will receive either VX-770 or placebo for 16 weeks. The primary endpoints of the DISCOVER clinical trial are safety and change from baseline in $FEV_1$ through week 16. Additional secondary endpoints, including sweat chloride levels, will be measured to evaluate the effectiveness of VX-770 in improving the function of the defective CFTR protein. We currently anticipate that further clinical trials in patients homozygous for the F508del mutation will involve a combination of VX-770 and VX-809.

STRIVE and DISCOVER are fully-enrolled and we expect to complete enrollment in ENVISION in the first half of 2010. If our registration program for VX-770 is successful and completed on the timeline that we currently anticipate, we could submit an NDA for VX-770 in the second half of 2011.

*Completed Phase 2a Clinical Trial of VX-770*

We have completed a Phase 2a clinical trial of VX-770 that 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 this 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 period. Also in Part 2, all reported adverse advents were mild or moderate in severity.

Lung Function and CFTR Protein Function (secondary endpoints)

In this 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 evaluated through measurements of sweat chloride levels 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 ducts. 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

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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 oral corrector compound that was selected because of its potential to increase the concentration of CFTR proteins on cell surfaces, in patients with the F508del mutation, a mutation that results in a trafficking defect. *In vitro*, studies of correctors have suggested that these compounds can 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.

We recently completed a Phase 2a, 28-day clinical trial of VX-809 as a single agent in 89 patients 18 years or older with the F508del mutation on both alleles. This Phase 2a clinical trial was a randomized, double-blind, placebo-controlled, multiple dose clinical trial. Patients received one of four doses of VX-809, or placebo, in addition to standard therapies for 28 days. The trial was designed primarily to evaluate the safety and tolerability of VX-809. Multiple secondary endpoints were utilized to determine any effect of VX-809 on CFTR protein function and lung function.

Based on a preliminary analysis of the data from the trial, VX-809 was well-tolerated through 28 days of 25 mg, 50 mg, 100 mg and 200 mg once-daily dosing. In the trial, one patient discontinued treatment in each of the VX-809 treatment arms due to adverse events. Respiratory-related adverse events were the most commonly reported adverse event in the trial. Safety and tolerability were the primary endpoints of the trial, and a detailed safety analysis is ongoing.

We also evaluated several secondary endpoints in the Phase 2a clinical trial. In the trial, there was a statistically significant decline in sweat chloride at both the 100 mg and 200 mg once-daily doses, suggesting that the activity of the CFTR protein was increased in patients during dosing. Additionally, we observed a dose response in change in sweat chloride across the four dose groups. A summary of the preliminary data regarding sweat chloride levels from this Phase 2a clinical trial is set forth in the table below. The patients' mean baseline sweat chloride levels were approximately 100 mmol/L, which is consistent with sweat chloride measurements of patients with severe CF.

| Treatment Arm | Mean Change in Sweat Chloride Levels from Baseline at Day 28 | p-value |
|---|---|---|
| 25 mg (once-daily) | 0.10 mmol/L | .9753 |
| 50 mg (once-daily) | -4.61 mmol/L | .1323 |
| 100 mg (once-daily) | -6.13 mmol/L | .0498 |
| 200 mg (once-daily) | -8.21 mmol/L | .0092 |

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The trial also included additional secondary endpoints to evaluate CFTR protein function, including CFTR protein trafficking, and lung function. Additional sub-analyses are ongoing to determine any potential trends in other measures of CFTR-dependent chloride ion transport, such as nasal potential difference; or CFTR maturation, as measured by an exploratory Western blot assay, however no statistically significant changes in these measures were observed in the preliminary analysis of data from this trial. The results from this Phase 2a clinical trial did not show any change in lung function, as measured by $FEV_1$. Based on the results of this clinical trial, we expect to initiate a combination trial of VX-770 and VX-809 in the second half of 2010 in patients with the F508del mutation on both alleles.

Prior to the above mentioned Phase 2a clinical trial, we completed two Phase 1 clinical trials of VX-809 in healthy volunteers and a Phase 1 clinical trial of VX-809 in CF patients who carry the F508del mutation on at least one of the two alleles. The first clinical trial in healthy volunteers 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. The Phase 1 clinical trial in patients with CF was an escalating dose pharmacokinetics and safety clinical trial.

***Immune-mediated Inflammatory Diseases***

**VX-509 (investigational oral JAK3 inhibitor for the treatment of immune-mediated inflammatory diseases)**

VX-509 is designed to inhibit Janus kinase 3, or JAK3, which is involved in signaling pathways that control the survival and proliferation of a type of white blood cells referred to as lymphocytes. Because of JAK3's role in lymphocyte biology, we believe it is a promising target for the design of immunosuppressant drugs for treatment of a variety of immune-based diseases. Based on *in vitro* data, VX-509 appears to be a potent and selective inhibitor of JAK3. We have completed Phase 1 clinical trials of VX-509, including a Phase 1 single dose and a multiple dose-ranging 14-day clinical trial of VX-509 in healthy volunteers.

In January 2010, we initiated a Phase 2a clinical trial of VX-509 in patients with moderate-to-severe rheumatoid arthritis, or RA, expected to enroll approximately 200 patients. This double-blind, randomized, placebo-controlled trial will evaluate the safety, tolerability and clinical activity of four doses of VX-509. Patients will receive 12 weeks of treatment with VX-509 dosed twice daily compared to placebo. The primary endpoints of the clinical trial are to evaluate safety and to measure clinical signs and symptoms of RA in patients after 12 weeks of treatment. Efficacy assessments will include the American College of Rheumatology criteria ACR20, ACR50 and ACR70 for defining clinical improvement in patients with RA. ACR20, ACR50 and ACR70 are standardized measures of the number of patients who achieve at least a 20, 50 or 70 percent improvement, respectively, in ACR-specified measures of RA activity. The trial will also utilize disease activity score, or DAS, and European League Against Rheumatism, or EULAR, response criteria as additional efficacy assessments. We expect to obtain interim clinical data from this clinical trial, including measurements of safety, tolerability and clinical activity, as early as the second half of 2010.

We plan to pursue collaborative opportunities for VX-509 with major pharmaceutical companies, but expect that we would not enter into a collaboration until after the receipt of clinical data from the Phase 2a trial.

***Epilepsy***

**VX-765 (investigational oral Caspase-1 inhibition for the treatment of epilepsy)**

VX-765 is designed to inhibit the interleukin-1 converting enzyme, which is an enzyme that controls the generation of cytokines, IL-1β and IL-18, that are believed to mediate a wide range of immune and inflammatory responses in many cell types. Epilepsy is a chronic neurological disorder that

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is defined by recurrent seizures that are the result of overactive neurons in the brain. Recent studies suggest that inflammation and overproduction of IL-1β may be associated with the initiation and maintenance of epileptic seizures. While there are a number of currently approved anticonvulsant medications used to treat patients with epilepsy, a substantial portion of patients are considered to be treatment-resistant because they continue to have seizures while taking approved anti-epileptic drugs.

VX-765 has been shown to inhibit acute seizures in preclinical models. In addition, VX-765 has shown activity in preclinical models of chronic epilepsy that do not respond to approved anti-epileptic drugs. VX-765 previously has been dosed in over 100 patients in Phase 1 and Phase 2a clinical trials relating to other indications, including a 28-day Phase 2a clinical trial in patients with psoriasis. We terminated development for psoriasis in 2006 because patients did not show an adequate response to therapy with VX-765. We believe that the data we have from the nonclinical studies together with safety information from previous clinical trials in humans for VX-765 provide a rationale to explore the clinical potential of this drug candidate as a treatment for epilepsy. We expect that VX-765 will be the first clinical drug candidate to target epilepsy through the inflammation pathway.

The Phase 2a trial for VX-765 we initiated in the first quarter of 2010 is expected to enroll approximately 75 patients with treatment-resistant epilepsy. The double-blind, randomized, placebo-controlled clinical trial is expected to evaluate the safety, tolerability and clinical activity of VX-765. Patients will be monitored for seizure frequency during an initial six week baseline period and then for six weeks while they are receiving treatment with VX-765. The primary endpoints of the trial are safety and tolerability. The secondary endpoints will evaluate clinical efficacy relative to baseline measured by reduction in seizure frequency and number of patients with a 50 percent or greater reduction in seizure frequency versus baseline.

**COMMERCIAL ORGANIZATION**

We plan to market telaprevir in North America, and we hold worldwide commercial rights to the other drug candidates in our pipeline. Over the past several years, we have expanded our commercial organization with a focus on building our understanding of the HCV market, developing our commercial strategy for the potential launch of telaprevir, and planning the infrastructure necessary to support future commercial activities. In addition, our commercial organization has continued to provide market insight to our research and development organization regarding VX-770 and our earlier-stage drug candidates.

We believe that we have developed a deep understanding of the HCV market in the United States. Our understanding incorporates information regarding the current standard of care as well as both patient and health care providers' attitudes toward current and potential, future therapies. Based on this information and the data obtained from our Phase 2 clinical trials of telaprevir, we have begun developing our marketing strategy for telaprevir, which we intend to update and refine as we obtain additional information regarding the potential commercial profile for telaprevir. In particular, we plan to incorporate the information we obtain regarding the efficacy and safety of telaprevir from our registration program into our marketing strategy.

In the period prior to the anticipated launch of telaprevir, we will expand our commercial organization to an even more significant extent. This expansion will include implementation of internal systems and infrastructure in order to support commercial sales, incorporation of appropriate compliance policies and procedures, establishment of patient-focused programs and hiring a sales force to promote telaprevir, if approved, to health care providers. We are assembling a group of executives with broad experience in marketing, sales, distribution, and reimbursement of drugs. We will continue to expand our commercial infrastructure by hiring a sales management team followed by a commercial sales force in the United States.

In addition, our government affairs and public policy group has begun the process of advocating with state and federal legislatures, government agencies, public health officials and other policy-makers.

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We are advocating policies that promote life sciences innovation and greater awareness regarding HCV infection.

Under our collaboration agreement with Janssen we will be reliant on Janssen to effectively market telaprevir in the European Union and the rest of its territory. Mitsubishi Tanabe will market telaprevir in Japan and specified other countries in the Far East. If we obtain approval, we may further develop our own capabilities to market and sell one or more of our other drug candidates in markets outside North America. We are assessing various scenarios to support VX-770, both within and beyond the United States. CF markets tend to be highly concentrated and are therefore accessible through a variety of promotional approaches.

**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 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 attempting to identify multiple targets within each indication that, either as a stand-alone therapy or combination therapy, 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 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 2010.

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, we have 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.

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***Janssen Pharmaceutica, N.V.***

In June 2006, we entered into a license, development, manufacturing and commercialization agreement with Janssen. Under the collaboration agreement, we 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 lead the development plan for telaprevir in North America and the Janssen territories. Janssen has 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. As of December 31, 2009, we had received $100.0 million of contingent milestone payments related to the development of telaprevir under the collaboration agreement. In addition, the agreement provides for additional contingent milestone payments to us of up to $250.0 million related to the regulatory filing with and approval of telaprevir by the European Medicines Evaluation Agency, and the launch of telaprevir in the European Union. In the third quarter of 2009, we entered into two financial transactions related to these $250.0 million in potential future milestone payments, which are discussed in detail in the consolidated financial statements and management's discussion and analysis contained in this Annual Report on Form 10-K. In the first transaction, we issued a note in the amount of $155.0 million secured by the first $155.0 million of these milestone payments, and in the second transaction we sold our rights to the remaining $95.0 million in future milestone payments. Our collaboration agreement with Janssen was unchanged by these transactions.

Janssen is 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 payable to us 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 such an event, all manufacturing, commercialization and intellectual property rights to telaprevir in the Janssen territories 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 territories, 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 collaboration agreement with Mitsubishi Tanabe pursuant to which Mitsubishi Tanabe agreed to provide financial and other support for the development and commercialization of telaprevir. Under the terms of the agreement, Mitsubishi Tanabe has the right to develop and commercialize telaprevir in Japan and specified other Far East countries. The original agreement provided for payments by Mitsubishi Tanabe to us through Phase 2 clinical development, including an up-front license fee, development stage milestone payments and reimbursement of certain drug development costs for telaprevir.

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In July 2009, we amended the collaboration agreement with Mitsubishi Tanabe. Under the amended agreement, we received $105.0 million in the third quarter of 2009, and will be eligible to receive a further contingent milestone payment, which if realized would range between $15.0 million and $65.0 million. The amended agreement provides Mitsubishi Tanabe with a fully-paid license to commercialize telaprevir to treat HCV infection in Japan and specified other countries in the Far East, as well as the right to manufacture telaprevir for sale in its territory. Mitsubishi Tanabe is responsible for its own development and manufacturing costs in its territory. Mitsubishi Tanabe may terminate the agreement at any time without cause upon 60 days' prior written notice to us.

***Cystic Fibrosis Foundation Therapeutics Incorporated***

In May 2004, we entered into a collaboration agreement with CFFT, the non-profit drug discovery and development affiliate of the Cystic Fibrosis Foundation, pursuant to which CFFT provided us with funding for our CF research and development programs, which funding was completed in 2008. Two drug candidates currently in clinical development for CF, 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 collaboration with Merck to discover, develop and commercialize Aurora kinase inhibitors. Under the agreement, Merck was responsible for developing and commercializing the drug candidates that resulted from the collaboration worldwide and would have paid 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. Merck is conducting a Phase 1 clinical trial of MK-5108 (VX-689) involving patients with advanced and/or refractory tumors, but has indicated to us, based on its analysis of its broader portfolio of drug development programs, that it does not anticipate continuing further development activities with respect to MK-5108 after the completion of dosing of patients currently enrolled in this Phase 1 clinical trial. Merck is not conducting any other clinical trials of drug candidates that resulted from the collaboration.

***GlaxoSmithKline plc***

In 1993, we entered into a collaboration with GlaxoSmithKline plc covering the research, development and commercialization of HIV protease inhibitors. The agreement provides that GlaxoSmithKline will pay us a royalty on all net sales of the HIV protease inhibitors covered by the agreement. 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 to us 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

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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.

While we have numerous issued patents and pending patent applications in our patent portfolio, we believe that the patents and patent applications in the United States and the European Union that are the most important to our business are those that claim the composition-of-matter of drug candidates that have progressed at least into Phase 2 clinical trials. The following table sets forth the status of the primary patents and patent applications in the United States and the European Union covering the composition-of-matter of these drug candidates:

| Drug Candidate | Status of United States Patent (Anticipated Expiration, Subject to Potential Extensions) | Status of European Union Patent (Anticipated Expiration, Subject to Potential Extensions) |
|---|---|---|
| telaprevir (VX-950) | Application Pending (2021) | Granted (2021) |
| VX-770 | Granted (2025) | Application Pending (2025) |
| VX-222 | Application Pending (2027) | Application Pending (2027) |
| VX-809 | Application Pending (2026) | Application Pending (2026) |
| VX-509 | Application Pending (2025) | Application Pending (2025) |
| VX-765 | Granted (2021) | Application Pending (2021) |

We hold issued patents and pending patent applications in the United States, and in foreign countries we deem appropriate, claiming intellectual property developed as part of each of our significant research and development programs. In addition to the composition-of-matter patents and patent applications listed above, our intellectual property holdings include but are not limited to:

United States and foreign patents and patent applications covering telaprevir, VX-222, VX-759, VX-985 and other HCV protease and polymerase inhibitors and the use of these compounds to treat HCV infection.

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 patents and patent applications covering caspase-1 inhibitors, including VX-765.

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.

We cannot be certain, however, that issued patents will be enforceable or provide adequate protection or that pending patent applications will result in issued patents

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**

*Manufacturing Approach and Philosophy*

As we advance our proprietary drug candidates through clinical development toward commercialization, we will continue to build and maintain our supply chain and quality assurance resources. We rely on an international network of third parties to manufacture and distribute our drug candidates for clinical trials, and we expect that we will continue to rely on third parties for the foreseeable future to meet our commercial supply needs for any of our drug candidates that are approved for sale.

Our supply chain for sourcing raw materials and manufacturing drug product ready for distribution is a multi-step international endeavor. Third-party contract manufacturers, including some in Asia, supply us with raw materials, and contract manufacturers in the European Union and the United States convert these raw materials into drug substance, and convert the drug substance into final dosage form. Establishing and managing this global supply chain requires a significant financial commitment and the creation and maintenance of numerous third-party contractual relationships.

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.

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.

*Manufacture of Telaprevir Clinical and Commercial Supplies*

We require a supply of telaprevir for our clinical trials and have agreed to exercise our contractual rights from our third-party manufacturers to provide a supply of telaprevir to Janssen and Mitsubishi Tanabe for their clinical trials. We will require a supply of telaprevir for sale in North America if we obtain marketing approval and have agreed to exercise our contractual rights from our third-party manufacturers to provide, until April 2012, a supply of telaprevir drug substance to Mitsubishi Tanabe for their use in manufacturing final dosage telaprevir for sale, if approved, in its territory.

We have completed the technical development work for our commercial formulation of telaprevir, established relationships with multiple third-party manufacturers for the manufacture of clinical and commercial supply of telaprevir, and completed contracts for our primary supply of drug substance, drug product and key raw materials. We are manufacturing telaprevir, through our third-party manufacturer network, to meet our, Janssen's and Mitsubishi Tanabe's clinical supply needs. 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 have completed 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

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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.

*Manufacture of VX-770 Clinical and Commercial Supplies*

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 required to produce VX-770 at a commercial scale. We are in the process of expanding our existing relationships with our third-party manufacturers and establishing new relationships with third-party manufacturers, in order to establish a supply chain for VX-770 to support the potential commercial launch of VX-770.

**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 competitors' 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, stockpiling 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***

*Current HCV Market*

A 48 week course of both peg-IFN, which requires weekly injections, and RBV, which is an oral drug, 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 infected with HCV, we believe that there are a significant number of patients with HCV who have been diagnosed but not yet achieved an SVR that may consider treatment with new therapies that are more effective.

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*Initial Anticipated Competitive Landscape*

While we are aware of numerous companies that are developing potentially competitive drug candidates, Merck's (previously Schering-Plough's) protease inhibitor, boceprevir, is the only protease inhibitor that is being developed on a timeline comparable to telaprevir. Merck is conducting Phase 3 clinical trials of boceprevir and has indicated that it expects to submit an NDA for boceprevir in 2010, which would put it on a timeline to potentially launch boceprevir in 2011. Merck's Phase 3 clinical trials include a clinical trial that enrolled approximately 404 treatment-failure patients but excluded null responders to prior treatment and a Phase 3 clinical trial involving approximately 1,100 treatment-naïve patients with genotype 1 HCV infection. In November 2009, Merck initiated another Phase 3 clinical trial for boceprevir that it estimates will enroll approximately 660 patients infected with genotype 1 HCV to compare the effect on efficacy of erythropoietin use versus reducing the dose of RBV for the management of anemia.

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, dosing regimen, cost, cost of co-therapies and side-effect profiles.

*Long-term Competitive Landscape*

We are aware of numerous other compounds in clinical trials that target HCV infection through a number of different mechanisms of action, and we believe that there are many additional potential HCV treatments in research or early development. There are a number of earlier-stage protease inhibitors, HCV polymerase inhibitors and HCV NS5A inhibitors, each of which is a specifically targeted anti-viral compound. We believe that these earlier-stage drug candidates, if approved, would be launched several years after telaprevir. If any of these drug candidates is approved as a treatment for HCV infection, we expect that such drug candidates would compete with telaprevir on the basis of the factors described above.

Future competition in the HCV treatment market may result from the administration of combinations of new oral therapies, and we are aware of a number of companies focusing on developing combinations of specifically-targeted antiviral compounds. We are planning a Phase 2a clinical trial to evaluate a combination of VX-222, our lead polymerase inhibitor, and telaprevir with and without peg-IFN and RBV. We also are aware that Bristol-Myers Squibb Company is conducting Phase 2 clinical trials of an NS5A inhibitor it is developing in combination with a protease inhibitor it is developing, and Intermune, Inc. and Pharmasset, Inc., in collaboration with Roche, are evaluating a combination of a protease inhibitor being developed by Intermune and a polymerase inhibitor being developed by Pharmasset.

***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-inflammatory drug candidates. PTC Therapeutics, Inc. is evaluating ataluren, which was formerly known as PTC124, in a Phase 3 clinical trial in patients with CF. Ataluren is 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.

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**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 might 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 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.

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Data from nonclinical testing and all clinical trials, along with descriptions of the manufacturing process, analytical tests, proposed labeling and the proposed risk evaluation and mitigation strategies 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. In addition, the company developing a drug candidate typically must submit a plan setting forth its risk evaluation and mitigation strategies.

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 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 regimen 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.

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**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 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,

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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 are and 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, 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

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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 statutes and regulations, now or hereafter in effect.

**EMPLOYEES**

As of December 31, 2009, we had 1,432 employees (1,422 full-time, 10 part-time). The number of our full-time employees increased by 6% during 2009, from 1,339 on December 31, 2008. We are likely to further increase our headcount in 2010 as we invest in expanding our commercialization capabilities. Of our employees, 1,119 were based in Massachusetts, 177 were based in California, 103 were based in Europe and 33 were based in Canada. 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.

**OTHER MATTERS**

**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; Montreal, Canada and Milton Park, U.K. We also have an office in Washington, D.C.

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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 |
|---|---|---|
| Matthew W. Emmens | 58 | Chief Executive Officer, Chairman of the Board and President |
| Peter Mueller, Ph.D. | 53 | Executive Vice President, Global Research and Development, and Chief Scientific Officer |
| Ian F. Smith, C.P.A., A.C.A. | 44 | Executive Vice President and Chief Financial Officer |
| Nancy J. Wysenski | 52 | Executive Vice President and Chief Commercial Officer |
| Kenneth S. Boger, M.B.A., J.D. | 63 | Senior Vice President and General Counsel |
| Lisa Kelly-Croswell | 43 | Senior Vice President, Human Resources |
| Amit K. Sachdev, J.D. | 42 | Senior Vice President, Corporate Affairs and Public Policy |
| Paul M. Silva | 44 | Vice President and Corporate Controller |
| Charles A. Sanders, M.D. | 78 | Lead Independent Director |
| Joshua S. Boger, Ph.D. | 58 | Director |
| Roger W. Brimblecombe, Ph.D., D.Sc. | 80 | Director |
| Stuart J.M. Collinson, Ph.D. | 50 | Director |
| Eugene H. Cordes, Ph.D. | 73 | Director |
| Jeffrey M. Leiden, M.D., Ph.D. | 54 | Director |
| Bruce I. Sachs | 50 | Director |
| Elaine S. Ullian | 62 | Director |
| Dennis L. Winger | 62 | Director |

Mr. Emmens has been our Chairman, Chief Executive Officer and President since May 2009. He has been a member of our Board of Directors since 2004 and became our President in February 2009. Mr. Emmens is the Chairman of the Board of Directors of Shire plc, a specialty biopharmaceutical company, 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 plc, which had more than 2,500 employees and revenues of $1.8 billion in 2006. 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, Inc., its United States prescription pharmaceutical business. Mr. Emmens 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 was a member of the Board of Directors of Incyte Corporation from 2006 through February 2009. Mr. Emmens received a B.S. degree in business management from Farleigh Dickinson University.

Dr. Mueller is our Executive Vice President, Global Research and Development, a position he has held since May 2009, and has been our Chief Scientific Officer since July 2003. Dr. Mueller was our Executive Vice President, Drug Innovation and Realization, from February 2006 to May 2009, and our Senior Vice President, Drug Discovery and Innovation, from July 2003 to February 2006. Prior to joining us, 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

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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 us, 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., 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.

Ms. Wysenski is our Executive Vice President and Chief Commercial Officer, a position she has held since December 2009. Prior to joining us, Ms. Wysenski held the position of Chief Operating Officer of Endo Pharmaceuticals, a 1,200-person specialty pharmaceutical company, where she led sales, marketing, commercial operations, supply chain management, human resources and various business development initiatives. Prior to her role at Endo, Ms. Wysenski participated in the establishment of EMD Pharmaceuticals, Inc., where she held various leadership positions, including the role of President and Chief Executive Officer from 2001 to 2006 and Vice President of Commercial from 1999 to 2001. From 1984 to 1998, Ms. Wysenski held several sales-focused roles at major pharmaceutical companies, including Vice President of Field Sales for Astra Merck, Inc. Ms. Wysenski serves on the North Carolina Central University Board of Trustees and is a founder of the Research Triangle Park chapter of the Healthcare Business Women's Association. Ms. Wysenski holds a B.S. from Kent State University and an Executive Masters in Business Administration from Baldwin Wallace College.

Mr. Kenneth Boger is our Senior Vice President and General Counsel, a position he has held since joining us in 2001. He came to us 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, one of our directors.

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 through 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, for the Health Care Division and Service Operations, of CIGNA, an employee benefits company. 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.

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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 and 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 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 and has been our lead outside director since May 2009. Dr. Sanders served as our Chairman from May 2006 through May 2009 and was our lead outside director from 2003 through May 2006. 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. He is currently a director of Biodel Inc., Biocryst Pharmaceuticals Inc., Cephalon, Inc., and Icagen, Inc. Dr. Sanders was a member of the Board of Directors of Genentech, Inc. from 1999 through its acquisition by Roche in March 2009, Fisher Scientific International from 2004 through its merger in November 2006, BioPure Corporation from 1997 through 2007 and Trimeris, Inc. from 1996 through 2006. Dr. Sanders also has served in the past on the boards of Merrill Lynch, Reynolds Metals Co. and Morton International 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.

Dr. Joshua Boger is the founder of Vertex and has been a director since our inception in 1989. He was our Chief Executive Officer from 1992 through May 2009. He was our Chairman of the Board from 1997 until May 2006 and our President from our inception until December 2000, and from 2005 through February 2009. He was our Chief Scientific Officer from 1989 until May 1992. 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 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.

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 an advisor to MVM Life Science Partners LLP, a venture capital firm. He holds Ph.D. and D.Sc. degrees in pharmacology from the University of Bristol, England.

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Dr. Collinson has been a member of our Board of Directors since July 2001. He currently serves as a Partner at Forward Ventures, a venture capital firm. Prior to our acquisition of 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.

Dr. Leiden has been a member of our Board of Directors since July 2009. He has more than 20 years of experience in the biomedical and pharmaceutical sectors. Dr. Leiden was President and Chief Operating Officer of Abbott Laboratories, Pharmaceuticals Products Group, and a member of the Board of Directors of Abbott Laboratories from 2001 to 2006. From 1987 to 2000, Dr. Leiden held several academic appointments, including the Rawson Professor of Medicine and Pathology and Chief of Cardiology and Director of the Cardiovascular Research Institute at the University of Chicago, the Elkan R. Blout Professor of Biological Sciences at the Harvard School of Public Health, and Professor of Medicine at Harvard Medical School. He is an elected member of both the American Academy of Arts and Sciences, and the Institute of Medicine of the National Academy of Sciences. Dr. Leiden is currently a Managing Director at Clarus Ventures, a life sciences venture capital firm he joined in 2006. Dr. Leiden is also currently a director and the non-executive Vice Chairman of the board of Shire plc, and a director of several private biotechnology companies. Dr. Leiden was a member of the Board of Directors of Millennium Pharmaceuticals, Inc. from October 2007 until it was acquired in June 2008. Dr. Leiden received both his M.D. and Ph.D. degrees from the University of Chicago.

Mr. Sachs has been a member of our Board of Directors since 1998. He is a General Partner at Charles River Ventures, a venture capital firm he joined in 1999. 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 was a director of BigBand Networks, Inc. from 2005 through June 2009. 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. From 1996 through January 2010, she served as President and Chief Executive Officer of Boston Medical Center, a private, not-for-profit, 626-bed, academic medical center with a community-based focus. 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. In addition, Ms. Ullian was a member of the Board of Directors of Valeant Pharmaceuticals, Inc. during 2005 through 2007. Ms. Ullian holds a B.A. in political science from Tufts University and an M.P.H. from the University of Michigan.

Mr. Winger has been a member of our Board of Directors since July 2009. Mr. Winger has over 30 years of experience as a financial executive, the majority of which has focused on the life sciences industry. He retired in 2008 from Applera Corporation, a life sciences company, where he had been

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Senior Vice President and Chief Financial Officer since 1997. He was previously Senior Vice President of Finance and Administration, and Chief Financial Officer at Chiron Corporation. Before joining Chiron, Mr. Winger held various financial executive positions, including Chief Financial Officer of The Cooper Companies, Inc. Mr. Winger is currently a director of the following public companies: Accuray Incorporated; Cephalon Inc.; and Nektar Therapeutics. In addition, Mr. Winger was a member of the Board of Directors of A.P. Pharma, Inc. during 2005 and 2006 and a member of the Board of Directors of Cell Genesys, Inc. until its merger with BioSante Pharmaceuticals in October 2009. He holds an M.B.A. from Columbia University Graduate School of Business and he earned his undergraduate degree from Siena College.

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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.*

### Risks Related to Our Business

***We expect to incur future losses, and we may never become profitable.***

We have incurred significant operating losses each year since our inception, including net losses of $642.2 million, $459.9 million and $391.3 million during the years ended December 31, 2009, 2008 and 2007, respectively, and expect to incur significant operating losses in 2010. We expect to continue to incur operating losses at least until we are able to obtain approval for and successfully commercialize telaprevir, because we are continuing to invest significant amounts in the late-stage development of telaprevir and VX-770, and in clinical development of our earlier-stage drug candidates and 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 provide assurance that we will ever become profitable.

***We depend heavily on the success of our lead drug candidate, telaprevir, which is still being evaluated in a registration program. 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 attributed to our company by investors relates to the commercial potential of telaprevir. We expect that we will be making significant additional investments in telaprevir in order to be prepared for the potential commercial launch of telaprevir in the United States in 2011, including the establishment of a sales force and marketing capabilities and additional investment in commercial inventory. The clinical development and commercial success of telaprevir will depend on many 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 comparable foreign regulatory authorities;
- receipt and timing of marketing approvals from the FDA and comparable foreign regulatory authorities for products being developed for the treatment of HCV infection by our competitors, including Merck's boceprevir;
- additional discussions with the FDA and similar foreign authorities regarding the quality of our manufacturing process for telaprevir and our clinical trial results, including the results we expect to obtain in the second and third quarters of 2010 from our Phase 3 clinical trials of telaprevir;

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- interactions with regulatory authorities regarding the contents of any NDA submission, including the data from our clinical trials and nonclinical studies, any plan setting forth risk evaluation and mitigation strategies and our manufacturing processes;

- 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 infection;

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

- the effect of new health care legislation currently being considered in the United States;

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

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

If the data from our ongoing clinical trials or nonclinical 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.

***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 the ability of our collaborators, if any, to develop and commercialize our drug candidates, including telaprevir and VX-770, 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 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 comparable foreign regulatory authorities for sale. To satisfy these standards, we and/or our collaborators must allocate 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 longer for each drug candidate. 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.

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In addition to our ongoing registration programs for telaprevir and VX-770, we have ongoing and planned Phase 2a clinical trials for a number of our earlier-stage drug candidates, including a planned clinical trial of telaprevir in combination with VX-222 in patients infected with HCV, a planned clinical trial of VX-809 in combination with VX-770 in patients with the most common CF mutation, a clinical trial of VX-509 in patients with moderate-to-severe RA and a clinical trial of VX-765 in patients with epileps