

PORTOLA PHARMACEUTICALS INC
Form 10-K
March 03, 2014

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the Fiscal Year Ended December 31, 2013

or

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT
OF 1934
Commission File Number: 001-35935

PORTOLA PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	2834	20-0216859
(State or other jurisdiction of	(Primary Standard Industrial	(I.R.S. Employer

incorporation or organization) Classification Code Number) Identification No.)

270 E. Grand Avenue

South San Francisco, California 94080

(Address of Principal Executive Offices) (Zip Code)

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(650) 246-7000

(Registrant's Telephone Number, Including Area Code)

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

Title of Each Class:	Name of Each Exchange on which Registered
Common Stock, par value \$0.001 per share	The NASDAQ Global Market

Securities registered pursuant to Section 12(g) of the 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 ☐ No ☒

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

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 ☒ No ☐

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 during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

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 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. ☒

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.

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates was \$322.4 million computed by reference to the last sales price of \$24.57 as reported by the NASDAQ Global Market, as of the last business day of the registrant's most recently completed second fiscal quarter, June 28, 2013. This calculation does not reflect a determination that certain persons are affiliates of the registrant for any other purpose.

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As of February 28, 2014, the number of outstanding shares of the registrant's common stock, par value \$0.001 per share, was 41,029,043.

DOCUMENTS INCORPORATED BY REFERENCE

Part III incorporates information by reference to the definitive proxy statement for the registrant's Annual Meeting of Stockholders to be held on or about May 16, 2014, to be filed within 120 days of the registrant's fiscal year ended December 31, 2013.

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“Portola Pharmaceuticals,” our logo and other trade names, trademarks and service marks of Portola appearing in this report are the property of Portola. Other trade names, trademarks and service marks appearing in this report are the property of their respective holders.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This report, including the sections titled “Business,” “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. In some cases you can identify these statements by forward-looking words, such as “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “could,” “would,” “project,” “plan,” “potential,” “goal” or the negative or plural of these words or similar expressions. These forward-looking statements include, but are not limited to, statements concerning the following:¹

- our ability to enroll patients in our clinical studies at the pace that we project;
- the timing and the success of the design of our Phase 3 clinical study of Betrixaban, or APEX;
- the timing of our anticipated additional Phase 2 proof-of-concept studies of Andexanet alfa;
- the timing of our anticipated Phase 3 registration study and Phase 4 confirmatory study of Andexanet alfa;
- our ability to design and implement a registration program of Andexanet alfa in the time frame we project;
- whether the results of our APEX study will be sufficient to support global regulatory approvals for Betrixaban;
- our ability to obtain and maintain regulatory approval of our product candidates;
- the success of our biomarker or genetic approach to clinical development;
- the possibility that we will come to an agreement with the FDA for an expedited regulatory approval process for Andexanet alfa;
- our ability to conduct a proof-of-concept study in hematologic cancers for Cerdulatinib;
- our expectation that our existing capital resources will be sufficient to enable us to complete our ongoing Phase 3 clinical study of Betrixaban, our Phase 3/4 Biologics License Application enabling studies and related manufacturing of Andexanet alfa and our Phase 1/2 proof-of-concept studies of Cerdulatinib in hematologic cancers;
- the projected number of acute medically ill patients who would benefit from the use of Betrixaban;
- the projected dollar amounts of future sales of established and novel anticoagulants and reversal agents;
- our ability to successfully commercialize our products;
- the rate and degree of market acceptance of our products;
- our ability to scale up manufacturing of our product candidates to commercial scale;
- our ability to successfully build a hospital-based sales force and commercial infrastructure;
- our ability to compete with branded and generic Factor Xa inhibitors;
- our reliance on third parties to conduct our clinical studies;
- our reliance on third-party contract manufacturers to manufacture and supply our product candidates for us;
- our reliance on our collaboration partners’ performance over which we do not have control;
- the actual receipt and timing of any milestone payments or royalties from our collaborators;
- our ability to retain and recruit key personnel;
- our ability to obtain and maintain intellectual property protection for our products;

our estimates of our expenses, ongoing losses, future revenue, capital requirements and our needs for or ability to obtain additional financing;
our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act;
our ability to identify, develop, acquire and in-license new products and product candidates;
our ability to successfully establish and successfully maintain appropriate collaborations and derive significant revenue from those collaborations;
our financial performance; and
developments and projections relating to our competitors or our industry.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in “Risk factors.” Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this report may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. Moreover, except as required by law, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this report to conform these statements to actual results or to changes in our expectations.

You should read this report and the documents that we reference in this report and have filed with the Securities and Exchange Commission as exhibits to this report with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.

PART I

ITEM 1. BUSINESS

Overview

We are a biopharmaceutical company focused on the development and commercialization of novel therapeutics in the areas of thrombosis, other hematologic disorders and inflammation for patients who currently have limited or no approved treatment options. Our current development-stage portfolio consists of three compounds discovered through our internal research efforts and one discovered by Portola scientists during their time at a prior company.

Our two lead programs address significant unmet medical needs in the area of thrombosis, or blood clots. Our lead compound Betrixaban is a novel oral once-daily inhibitor of Factor Xa in Phase 3 development for extended duration prophylaxis, or preventive treatment, of a form of thrombosis known as venous thromboembolism, or VTE, in acute medically ill patients. Currently, there is no anticoagulant approved for extended duration VTE prophylaxis in this population. Our second lead development candidate Andexanet alfa, formerly PRT4445, expected to enter into Phase 3 registration studies in the first half of 2014, is a recombinant protein designed to reverse the anticoagulant activity in patients treated with a Factor Xa inhibitor who suffer an uncontrolled bleeding episode or undergo emergency surgery. Our third product candidate, Cerdulatinib, formerly PRT2070, is an orally available kinase inhibitor that inhibits spleen tyrosine kinase, or Syk, and janus kinases, or JAK, enzymes that regulate important signaling pathways and is being developed for hematologic, or blood, cancers and inflammatory disorders. In October 2013, we initiated a Phase 1/2 proof-of-concept study for Cerdulatinib in patients with non-Hodgkin's lymphoma, or NHL, or chronic lymphocytic leukemia, or CLL, who have failed or relapsed on existing marketed therapies or products in development, including patients with identified mutations. Our fourth program, PRT2607 and other highly selective Syk inhibitors, is partnered with Biogen Idec Inc., or Biogen Idec.

We have full worldwide commercial rights to Betrixaban and Andexanet alfa, and to Cerdulatinib for systemic indications. We believe we can maximize the value of our company by retaining substantial global commercialization rights to these three product candidates and, where appropriate, entering into partnerships to develop and commercialize our other product candidates. We plan to build a successful commercial enterprise using a hospital-based sales team in the United States and possibly other major markets and with partners in other territories.

We currently have the following product candidates in development:

Betrixaban is a novel oral once-daily inhibitor of Factor Xa in development for extended duration VTE prophylaxis in acute medically ill patients both in-hospital and post-discharge for up to 35 days. Acute medically ill patients are those who are hospitalized for serious non-surgical conditions, such as heart failure, stroke, infection, rheumatic disorders and pulmonary disorders. Based on our research, we estimate that in the G7 countries in 2012 there were 22.3 million acute medically ill patients for whom VTE prophylaxis was recommended by medical treatment guidelines. The current standard of care for VTE prophylaxis in this population is enoxaparin, marketed as Lovenox by Sanofi S. A., or Sanofi, and as a generic drug by several manufacturers. Enoxaparin is an injectable drug that is approved for a usual administration period of 6 to 11 days and up to 14 days and is generally not prescribed for use outside of the hospital. According to IMS Health Incorporated, a healthcare industry information provider, or IMS, worldwide sales of enoxaparin for the 12 months through June 2013 were in excess of \$4.1 billion. We believe that use of enoxaparin in acute medically ill patients accounted for at least \$2 billion of these sales. Multiple large, global trials have demonstrated that there is substantial risk of VTE in acute medically ill patients with restricted mobility and other risk factors beyond the standard course of enoxaparin. For example, the MAGELLAN trial demonstrated

that the incidence of VTE-related death rose four-fold over several weeks after hospital discharge and the discontinuation of treatment. However, there are no therapies approved for use beyond a typical hospitalization period of 6 to 14 days despite the ongoing risk of VTE faced by these patients for 35 days or more following hospital admission.

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In 2012, we initiated our pivotal Phase 3 APEX study to evaluate extended duration VTE prophylaxis with oral once-daily Betrixaban for superiority as compared to the current standard of care in acute medically ill patients. If successful, we believe APEX will be the first thrombosis study based on a biomarker approach. We believe that Betrixaban has several clinically important pharmacological properties that differentiate it from injectable enoxaparin and other oral Factor Xa inhibitors, including a long half-life, low renal clearance and a metabolic profile that limits drug-drug interaction. Renal clearance is a measurement of the degree to which a drug is excreted from the body through the kidneys. We are over 30% enrolled in APEX with over 400 clinical sites worldwide. Our goal is to complete enrollment by the end of 2015 and file for a New Drug Application, or NDA, by mid-2016. In January 2013, we entered into a clinical collaboration agreement with Lee's Pharmaceutical (HK) Ltd, or Lee's, to jointly expand our Phase 3 APEX study of Betrixaban into China with an exclusive option for Lee's to negotiate for the exclusive commercial rights to Betrixaban in China. Under the agreement, Lee's provided us with an upfront payment and will reimburse our costs in connection with the study to support the expansion of the APEX study into China. Lee's will also lead regulatory interactions with China's State Food and Drug Administration for the study.

Andexanet alfa is a recombinant protein designed to reverse the anticoagulant activity in patients treated with a Factor Xa inhibitor who suffer an uncontrolled bleeding episode or undergo emergency surgery. Currently, there is no antidote or reversal agent approved for use against Factor Xa inhibitors. Based on industry data, we estimate that in 2020 between 23 million and 36 million patients will be treated with Factor Xa inhibitors, including low molecular weight heparins, for short-term use or chronic conditions. Clinical trial results suggest that, depending on their underlying medical condition, annually between 1% and 4% of these patients will experience uncontrolled bleeding and an additional 1% will require emergency surgery. We believe that Andexanet alfa, if approved, has the long-term potential to address a total worldwide market in excess of \$2 billion. Leading clinicians have identified, and the United States Food and Drug Administration, or FDA, has recognized, the lack of an effective reversal agent for Factor Xa inhibitors as a significant unmet clinical need. Preclinical and Phase 1 studies suggest that Andexanet alfa has the potential to be a universal reversal agent for all Factor Xa inhibitors, including enoxaparin, a low molecular weight heparin. We reported clinical data from the first two of a series of Phase 2 proof-of-concept studies evaluating the safety and activity of Andexanet alfa in healthy volunteers who are administered one of several Factor Xa inhibitors. Analysis of anticoagulation markers in blood samples taken from the subjects in these studies demonstrated that Andexanet alfa produces a rapid, sustained and dose-related reversal of anticoagulant activity of the Factor Xa inhibitors apixaban and rivaroxaban. We are currently conducting a Phase 2 proof-of-concept study evaluating Andexanet alfa for reversal of the anticoagulant activity of the low molecular weight heparin, enoxaparin. We plan to initiate similar Phase 2 proof of concept studies evaluating the reversal of edoxaban in 2014 and Betrixaban thereafter. In August 2013, we held an End of Phase 2 meeting with the FDA to discuss the remaining clinical studies needed for approval of Andexanet alfa and in November 2013, the FDA granted breakthrough therapy designation for Andexanet alfa. We plan to initiate Phase 3 registration studies for Andexanet alfa in the first half of 2014 pursuant to an Accelerated Approval pathway for Andexanet alfa followed by the initiation of a Phase 4 confirmatory study. Our plan is to file a Biologics License Application, or BLA, for conditional approval at the end of 2015. Additionally, we are in the process of obtaining formal scientific advice from the European Medicines Authority, or EMA, regarding the process for regulatory approval in Europe.

We have entered into collaboration agreements with Bristol-Myers Squibb Company, or BMS, and Pfizer Inc., or Pfizer, collaboration agreements with Bayer Pharma AG, or Bayer, and Janssen Pharmaceuticals, Inc., or Janssen, and an agreement with Daiichi Sankyo, Inc., or Daiichi Sankyo, pursuant to which agreements, BMS and Pfizer, Bayer and Janssen and Daiichi Sankyo, respectively, made payments to us to collaborate with us on a portion of our Phase 2 and Phase 3 Andexanet alfa studies, but we retain full commercial rights with respect to Andexanet alfa.

Cerdulatinib is an orally available, potent inhibitor of Syk and JAK. Scientists have demonstrated that both Syk and JAK play key roles in various hematologic cancers and inflammatory diseases. We are developing Cerdulatinib for treatment of certain B-cell hematologic cancers, with a particular focus on patients who have driving mutations such as NFkB activating mutations or acquired mutations to other novel B-cell targeted therapies that cause treatment failure or disease relapse. Cerdulatinib has completed preclinical testing and has demonstrated in-vitro activity in cancer cell lines with NFkB activating mutations and in patient tumor samples with acquired mutations to novel

B-cell targeted drug candidates. In October 2013, we initiated a Phase 1/2 proof-of-concept study in NHL and CLL. In February 2013, we entered into a license and collaboration agreement with Aciex Therapeutics, Inc., or Aciex, pursuant to which we granted Aciex an exclusive license to co-develop and co-commercialize Cerdulatinib and certain related compounds for nonsystemic indications, such as the treatment and prevention of ophthalmological diseases by topical administration and allergic rhinitis by intranasal administration. Under the agreement, we will share development costs with Aciex and be entitled to receive either a share of the profits generated by any future commercial products or royalty payments. We retain rights to other non-systemic indications, including dermatologic disorders.

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PRT2607 is an orally available, potent and selective inhibitor of Syk. PRT2607 has been evaluated in 131 subjects in several Phase 1 clinical studies. Biogen Idec is leading the pre-clinical study of PRT2607 and other highly selective Syk inhibitors for allergic asthma and other inflammatory disorders and is responsible for all development-related expenses. Syk plays a critical role in mast-cell signaling and activation, which are central to immune system over-activation and resultant airway constrictions in asthma. It is estimated that allergic asthma affects 15 million people in the United States alone. Despite numerous approved treatments, approximately 25% of all emergency room visits each year are attributed to acute and severe episodes of this disease.

Our strategy

Our goal is to build an enduring biopharmaceutical company with a foundation of products and product candidates that significantly advance patient care in the areas of thrombosis, other hematologic disorders and inflammation. We have a clear strategy focused on biomarker or genetic approaches to clinical development that we believe will increase the probability of clinical, regulatory and commercial success of our first-in-class therapies. Key elements of our strategy are as follows:

Successfully complete the clinical development of Betrixaban. We have initiated APEX, our global pivotal Phase 3 clinical study, to evaluate the efficacy and safety of our lead product candidate Betrixaban for extended duration VTE prophylaxis during a hospital stay as well as post-discharge for up to 35 days in acute medically ill patients with restricted mobility and other risk factors. If APEX is successful and we receive regulatory approval, Betrixaban will be the first anticoagulant approved based on a biomarker approach for the multi-billion dollar market for extended VTE prophylaxis in acute medically ill patients, both in the hospital and after discharge.

Advance Andexanet alfa through an expedited development and approval process. We held an End of Phase 2 meeting with the FDA in August 2013. Based on our Phase 2 clinical study results and discussions with the FDA following, our breakthrough therapy designation by the FDA in November 2013, we believe that the FDA supports our pursuit of an Accelerated Approval pathway for Andexanet alfa. We plan to initiate Phase 3 registration studies for Andexanet alfa in the first half of 2014 followed by a Phase 4 confirmatory study. Our goal is to file a BLA for conditional approval at the end of 2015. Additionally, we are in the process of obtaining formal scientific advice meeting from the EMA regarding the process for approval in Europe.

Commercialize Betrixaban and Andexanet alfa, if approved, in the United States using a hospital-focused sales force. We plan to commercialize both of our thrombosis product candidates with a U.S. hospital-based sales force of approximately 100 to 140 sales representatives all focused on demonstrating the clinical and pharmacoeconomic value of our product candidates. We believe we will be able to address the multi-billion dollar markets for our thrombosis products with a targeted sales and marketing effort because hospitals represent a concentrated customer base as compared to primary care or specialty physicians.

Independently advance Cerdulatinib for treatment of hematologic cancers. Our research into cellular signaling pathways has resulted in development of Cerdulatinib, a clinical stage kinase inhibitor with what we believe to be unique pharmacological properties that strongly differentiate it from approved kinase inhibitors and those in development. We initiated a Phase 1/2 proof-of-concept study in NHL and CLL in October 2013.

Deploy capital strategically to develop our portfolio of product candidates and create value. We intend to deploy most of our capital resources to develop our two lead product candidates. It is our strategy to leverage established clinical trial design principles as well as proactive engagement with relevant regulatory authorities to advance these candidates towards key value inflection points in a capital-efficient manner. In parallel with these efforts, we have entered into and anticipate that we will continue to enter into partnerships that provide support for the further development of our clinical-stage kinase inhibitors while retaining significant economic and commercial rights. We believe that this combination of independent development and partnering activity will allow us to realize the substantial potential value

of our product candidates while reducing our capital requirements.

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Product candidates

Our development pipeline, summarized in the table below, includes three wholly owned compounds and one partnered program.

Product	Description	Stage	Indication	Worldwide commercial rights
Betrixaban	Oral Factor Xa inhibitor	Phase 3	Extended duration VTE prophylaxis in acute medically ill patients in-hospital and post discharge for up to 35 days	Portola
Andexanet alfa	Antidote for Factor Xa inhibitors	Phase 2	Reversal of Factor Xa inhibitor anticoagulation	Portola
Cerdulatinib	Oral Dual Syk and JAK inhibitor	Phase 1/2	B-cell hematologic cancers	Hematologic cancer and other systemic indications: Portola Certain nonsystemic indications: 50/50 rights with Acix
PRT2607	Syk inhibitor	Pre-clinical	Allergic asthma and other inflammatory disorders	Biogen Idec
Betrixaban				

We are developing our lead product candidate Betrixaban to be the first anticoagulant approved for extended duration VTE prophylaxis in acute medically ill patients both in-hospital and after discharge for up to 35 days. Acute medically ill patients are patients hospitalized for non-surgical conditions, such as heart failure, stroke, infection, rheumatic disorders and pulmonary disorders. Acute medically ill patients with restricted mobility and other risk factors are known to be at increased risk for VTE, both in the hospital and after discharge. Each year, more than 150,000 acute medically ill patients worldwide die of VTE and not from their underlying medical condition. Pulmonary embolism is the most common preventable cause of hospital death and a leading cause of increased length of hospital stay. The average annual direct medical cost of treating VTE in a hospital setting in the United States is between \$7,500 and \$16,500 per patient and is even greater for elderly, higher risk patients. Both the National Quality Forum and the Joint Commission on Accreditation of Healthcare Organizations include the utilization of VTE prevention measures as a leading indicator of quality of patient care.

While there are a number of anticoagulants approved for short-duration VTE prophylaxis in acute medically ill patients during the typical hospitalization period, there is no anticoagulant approved for extended duration VTE prophylaxis in this population. Acute medically ill patients at risk for VTE are typically treated with intravenous or injectable heparin or an injectable low molecular weight heparin, such as enoxaparin, marketed as Lovenox and also available in generic form, while in the hospital but not after discharge. Multiple large regional and global studies have demonstrated that there is a substantial risk of VTE after hospital discharge in acute medically ill patients with restricted mobility and other risk factors. For example, the MAGELLAN trial of 8,101 patients showed that the rate of

VTE-related death for the 10-day period while the patients were in the hospital receiving anticoagulation therapy was 0.2%, while the rate of VTE-related death for the 25-day post-discharge period when the patient did not receive anticoagulation treatment, was 0.8%, a four-fold increase. One academic study examined the medical records of approximately 11,000 acute medically ill patients for a period of 180 days after hospital admission and determined that 56.6% of VTE events in this population occurred after discharge. These studies highlight the need for more effective extended duration prophylaxis therapies.

We are developing Betrixaban to be the first oral Factor Xa inhibitor approved for use in acute medically ill patients and the first anticoagulant approved for extended duration VTE prophylaxis in those patients. We are evaluating Betrixaban in APEX, a global Phase 3 clinical study using a biomarker approach by focusing on patients that are mostly likely to benefit, specifically those with elevated D-dimer blood levels and those over the age of 75. In the field of thrombosis, it is well established that the outcomes of Phase 3 trials are significantly influenced by three factors: drug properties, dose selection and selection of the patients who will benefit most from treatment.

Historically, multiple anticoagulant drugs have effectively addressed these factors in their clinical trials and have had success where competing agents within the same class have not. Applying our knowledge of Betrixaban's properties, our clinical experience with Betrixaban and learnings from Factor Xa inhibitor clinical trials conducted by other companies, we believe we have designed the APEX study to enhance the likelihood of its success, despite the lack of success of other Factor Xa inhibitors in this indication, based on the following factors:

Drug properties. Betrixaban's unique pharmacodynamic and pharmacokinetic properties compared to other oral Factor Xa inhibitors include a long half-life suitable for once-daily dosing, low renal clearance, which reduces the risk of drug accumulation, and low drug-drug interaction potential due to lack of metabolism by the CYP3A4 pathway, a key metabolic route for many other drugs.

Dosing. The dosing regimen in our APEX study is designed to provide immediate anticoagulation for patients in the hospital and to maintain a therapeutic level of anticoagulation over 24 hours with each oral once-daily dose for 35 days to reduce variability and potential for increased bleeding risk from supratherapeutic drug levels or increased VTE risk from subtherapeutic drug levels. We chose the dosing regimen of Betrixaban administered in APEX based on extensive modeling from our preclinical and clinical experience with Betrixaban and analysis of efficacy, safety and pharmacokinetic data from clinical trials of other Factor Xa inhibitors.

Patient population. The APEX patient population, which is based on extensive review of epidemiologic studies and data from multiple large trials in acute medically ill patients, targets the specific patients with certain risk factors who are at an increased risk for VTE and can potentially benefit from extended duration VTE prophylaxis both during a hospital stay and post-discharge for up to 35 days, while excluding those at increased risk of bleeding, the main side effect of all anticoagulants.

Overview of thrombosis

Thrombosis is the leading cause of mortality and morbidity in the western world. Thrombosis arises from an abnormal or excessive activation of the body's natural clotting process, resulting in the formation of a clot inside a blood vessel that disrupts normal blood flow. If the clot detaches from the blood vessel wall and travels through the body, known as thromboembolism, it can damage vital organs, such as the brain, heart and lungs. Clots that block arteries can lead to myocardial infarctions, more commonly referred to as heart attacks, or a form of stroke known as ischemic strokes. Our Betrixaban development efforts are currently focused on VTE, with the two most common conditions being deep vein thrombosis, or DVT, which typically leads to pain and swelling in the leg, and pulmonary embolism, which occurs when a clot disrupts blood flow to the lungs, leading to lung damage or even death. In the United States, on an annual basis, 1.2 million people have a new or recurrent heart attack, 700,000 people suffer an ischemic stroke and 350,000 to 600,000 people have a VTE.

Thrombosis is generally prevented or treated using either anticoagulants, commonly known as blood thinners, or another class of drugs known as antiplatelet agents. The specific drug, dose and dosing frequency and duration of treatment depends on a patient's underlying disease and treatment setting, such as during surgery, in the hospital or at home. In some cases, these agents may be used in sequence or combination.

Prophylaxis against all forms of thrombosis is a major medical need throughout the developed world. For example, in the G7 countries, the United States, Japan, France, Germany, Italy, Spain and the United Kingdom, existing medical guidelines recommend that a population of approximately 46.4 million patients receive some form of anticoagulation drug therapy to reduce their risk of thrombosis. The largest category of patients at risk for thrombosis is the acute medically ill, whose risk is increased for those patients immobilized for more than a few days or with other risk factors. In addition to acute medically ill patients, populations at risk for thrombosis include patients with atrial fibrillation, acute coronary syndrome, recent VTE and certain genetic mutations, as well as surgical patients undergoing orthopedic or abdominal procedures.

The table below shows our estimate of the number of patients in the G7 countries, categorized by medical condition or procedure, for whom a Class I medical guideline recommendation of anticoagulation drug therapy would apply. A Class I medical guideline recommendation represents the highest level of recommendation that patients receive specified medical treatment based on the evidence of the relative risks and benefits of such treatment.

Patients with Class I medical guideline recommendation to receive anticoagulation drug therapy



Acute medically ill patients	22.3
Moderate to high risk surgery (including orthopedic surgery)	12.3
Atrial fibrillation	6.6
Acute coronary syndrome	3.5
VTE treatment and secondary prophylaxis	1.7
Total	46.4

The population of acute medically ill patients represents the largest patient segment in the anticoagulant market, accounting for nearly half of patients in the G7 countries. Despite the short duration of current VTE prophylaxis for the acute medically ill, typically 6 to 14 days, we believe that annual worldwide sales of enoxaparin for use in acute medically ill patients are at least \$2 billion.

VTE in acute medically ill patients

The standard of care for VTE prophylaxis in acute medically ill patients is to treat those patients who have certain risk factors with an anticoagulant, such as heparin or enoxaparin, for 6 to 14 days, primarily while the patient is in the hospital. Despite the fact that the approved treatment duration for enoxaparin is limited to 6 to 14 days, we believe that annual worldwide sales of enoxaparin for use in acute medically ill patients are at least \$2 billion. Factors that have been identified as increasing the risk of VTE include several days of restricted mobility, age, an elevated blood marker known as D-dimer, previous VTE event, family history of VTE, smoking, hormonal therapy and others. Almost all hospitalized non-surgical patients have at least one of these risk factors, and approximately two-thirds have two or more risk factors. In-hospital use of anticoagulation has been shown to reduce the incidence of VTEs by approximately 63% and have a net clinical benefit; however, recent registry studies and clinical trials have shown that acute medically ill patients remain at a high risk of VTE during the period after discharge.

For example, one academic study examined the medical records of approximately 11,000 acute medically ill patients for a period of 180 days after hospital admission and determined that 56.6% of VTE events in this population occurred after discharge. In the MAGELLAN trial sponsored by Bayer and Janssen, 5.7% of enoxaparin-treated patients experienced a significant thrombotic event during the trial period, and, in higher risk sub-populations, such event rate was 7% to 9%. In the ADOPT trial sponsored by BMS, the combined incidence of symptomatic VTE and VTE-related death was twice as high during the period after cessation of enoxaparin treatment as it was during the treatment period.

Currently, there are no anticoagulants approved for extended duration VTE prophylaxis in acute medically ill patients for more than a 6- to 14-day period, and most patients receive anticoagulation therapy only while in the hospital. Heparin and enoxaparin are generally not prescribed for use outside of the hospital due to the difficulty of administering the therapies and lack of data showing a benefit beyond the currently approved duration of therapy. Warfarin has not been studied in a large randomized trial and is not indicated for VTE prophylaxis in acute medically ill patients. Both rivaroxaban and apixaban have been evaluated in large Phase 3 trials of VTE prophylaxis in acute medically ill patients, both in the hospital and after discharge. The MAGELLAN trial, which evaluated rivaroxaban, demonstrated efficacy but failed to demonstrate an acceptable benefit to risk profile due to increased bleeding, and the ADOPT trial, which evaluated apixaban, showed a reduction in VTE events, but failed to demonstrate statistically significant efficacy. Importantly, the results of these trials showed that acute medically ill patients with restricted mobility and other risk factors treated with standard duration enoxaparin therapy for 6 to 14 days continue to be at increased risk of VTE post-hospital discharge for several weeks up to 35 days.

Leading clinicians have identified, and the FDA has recognized, the lack of an appropriate therapy to prevent VTE in acute medically ill patients after discharge as a significant unmet clinical need. Such a therapy should be easy to administer both within and outside of the hospital setting and would need to show a robust reduction in the incidence of VTE and an acceptable bleeding profile compared to the current standard of care. The therapy would also need to have other properties appropriate for use in acute medically ill patients. These patients are typically frail and elderly and often cannot tolerate drugs that are significantly cleared through the kidneys. Moreover, they are often taking multiple medications for concomitant conditions and need a therapy that has a low potential to interact with other medications and a simple dosing regimen.

Betrixaban for extended duration VTE prophylaxis in acute medically ill patients

We believe that Betrixaban is well suited for use in extended duration VTE prophylaxis in acute medically ill patients, both in the hospital and after discharge. Our preclinical and clinical studies suggest that it has antithrombotic activity similar to that of enoxaparin and certain novel oral Factor Xa inhibitors (dabigatran, rivaroxaban, apixaban and edoxaban). In addition, it has a number of characteristics that differentiate it from these compounds that we believe are

particularly relevant to acute medically ill patients, including:

Orally active with 23 hour half-life. Betrixaban's half-life of approximately 23 hours is ideal for once-daily dosing, unlike that of any approved oral Factor Xa inhibitor and enoxaparin. As a result, we believe it is possible to dose Betrixaban to a lower peak concentration and still maintain effective anticoagulation through a 24-hour period while avoiding increased bleeding risk from supratherapeutic drug levels or increased VTE risk from subtherapeutic drug levels. Furthermore, oral once-daily dosing is generally considered important to patients and doctors, as it reduces the risk of administration errors compared to twice-daily dose regimens or injectable administration.

Relatively low renal clearance. Unlike all currently approved Factor Xa inhibitors, Betrixaban is primarily excreted unchanged in the bile, with renal clearance of 5% to 7% of total oral administered dose. This renal clearance is lower than that of enoxaparin and the novel oral Factor Xa inhibitors. Low renal clearance is desirable because the acute medically ill patient population includes many elderly patients with reduced kidney function, which can result in higher levels of drugs remaining in the bloodstream, thereby complicating the process of dose selection and increasing the potential risk of bleeding associated with anticoagulants. We believe that Betrixaban's relatively low renal clearance will result in more predictable blood levels of the drug across the acute medically ill patient population and, therefore, an overall lower risk of severe bleeding and higher probability of net clinical benefit.

Low potential for drug-drug interaction. Unlike all currently approved direct Factor Xa inhibitors, Betrixaban is not metabolized through the CYP3A4 pathway, a key metabolic route for many approved drugs for a wide range of conditions. Many acute medically ill patients suffer from a significant underlying illness or one or more chronic conditions and are taking multiple therapies. The concurrent use of multiple CYP3A4 metabolized drugs can result in unpredictable drug levels and other undesirable drug-drug interactions. As a result of not being metabolized through the CYP3A4 pathway, we believe Betrixaban will have a lower risk of dangerous drug-drug interactions than other direct Factor Xa inhibitors.

Betrixaban clinical experience

Betrixaban has been evaluated in 22 Phase 1 and Phase 2 clinical studies involving 1,411 human subjects, 1,200 of whom received Betrixaban, including more than 100 subjects for six months or more. A series of 19 Phase 1 and clinical pharmacology studies provided substantial information regarding its safety, dosage and use in specific sub-populations. In three Phase 2 studies, Betrixaban was evaluated in specific patient populations relative to commonly used anticoagulants. Consistent with the development of other antithrombotic agents, these studies were not designed to demonstrate a statistically significant difference between groups for the studied outcomes. The Betrixaban Phase 2 studies were instead designed to demonstrate evidence of an anticoagulant effect and relative safety compared to an established comparator. In these clinical studies:

Betrixaban was well tolerated in diverse patient populations with comparable or better tolerability as compared to warfarin and enoxaparin;

Betrixaban achieved clinically relevant anticoagulant activity with comparable or less bleeding risk than existing agents; and

Betrixaban demonstrated predictable pharmacokinetic and pharmacodynamic activity.

As is typical in the development of anticoagulants, our initial Phase 2 study was conducted in patients undergoing elective total knee replacement surgery. This patient population has a very high incidence of VTE, making it an excellent population in which to evaluate the relative effectiveness and safety of different doses as compared to the standard of care. In our 215-patient EXPERT study, two different doses of Betrixaban, 15 mg and 40 mg each given twice daily, were evaluated against a U.S. standard twice-daily dose of 30 mg of enoxaparin in patients undergoing this surgery. The incidence of VTE in the Betrixaban groups was comparable to that in the enoxaparin group and lower than the rates historically observed in placebo groups, although these results were not statistically significant. In addition, the only incidence of major bleeding seen in the study was in the enoxaparin group.

In our 508-patient Phase 2 EXPLORE-Xa study, we evaluated the use of Betrixaban for ischemic stroke prevention in elderly patients with nonvalvular atrial fibrillation. Three different once-daily doses of Betrixaban, 40 mg, 60 mg and 80 mg, were evaluated against dose-adjusted warfarin. Patients with a median age of 74 years received treatment for at least 90 days and as long as 12 months. The incidence of ischemic stroke, as well as major bleeds and clinically relevant non-major bleeds, was comparable across the warfarin and Betrixaban treatment groups, suggesting similar anticoagulant activity and bleeding risk across all groups. In addition, we measured D-dimer levels. D-dimer is a byproduct of coagulation, and elevated levels have been shown to be indicative of an increased risk of

thromboembolism. In those patients receiving Betrixaban who had not previously been taking warfarin, we observed a dose-related decrease in D-dimer levels. We believe the results of the EXPLORE-Xa study, although not statistically significant, provide evidence of the anticoagulant activity of Betrixaban and indicate that the long-term use of Betrixaban is safe in an elderly population, including those with moderate to severe kidney disease.

Our Phase 2 DEC study evaluated the utility of adjusting the dose of Betrixaban based on a patient's weight. The study indicated that making such adjustments is not necessary and it provided additional evidence of the safety and activity of Betrixaban.

All of our clinical studies to date have indicated that Betrixaban is well tolerated. Subjects taking Betrixaban had an increased rate of gastrointestinal issues, such as diarrhea, nausea and vomiting, as compared to subjects taking placebo, but these increased rates appear to be similar to those of patients taking other Factor Xa inhibitors. Patients taking Betrixaban also had an increased incidence of other side effects such as back pain, dizziness, headaches, rashes and insomnia as compared with patients taking a placebo or an active comparator. These side effects do not appear to have a substantial impact on patients' tolerance of Betrixaban. There is no evidence that Betrixaban has negative effects on heart rhythm or liver function. As discussed earlier, the most significant side effect of all anticoagulants is uncontrolled bleeding. While definitive conclusions cannot be drawn from our Phase 2 studies, it does not appear from the study results that patients taking Betrixaban face a greater risk of uncontrolled bleeding than patients taking warfarin or enoxaparin.

Phase of study	Number of studies	Subjects receiving Betrixaban	Objective	Selected results
Phase 1	19	459	Safety, tolerability, pharmacokinetic, pharmacodynamic	Single doses up to 550 mg well tolerated with predictable drug properties
Phase 2 (EXPLORE-Xa 2 and DEC)		570	Safety/efficacy in atrial fibrillation patients; safety compared to warfarin	Prophylaxis and bleeding risk comparable to warfarin
Phase 2 (EXPERT) Clinical experience of Factor Xa inhibitors in acute medically ill patients	1	171	Safety/efficacy in knee replacement compared to enoxaparin	Prophylaxis and bleeding risk comparable to enoxaparin

Direct Factor Xa inhibitors rivaroxaban and apixaban have been studied in large Phase 3 trials for VTE prophylaxis in acute medically ill patients. Neither trial was successful in showing a balanced result of VTE reduction relative to major bleeding events, referred to as net clinical benefit. The MAGELLAN trial, which evaluated rivaroxaban, met its primary efficacy endpoint of decreased VTE in acute medically ill patients but achieved this result with an unfavorable bleeding risk. By comparison, the ADOPT trial, which evaluated apixaban, did not demonstrate significant clinical efficacy, although the rates of VTE in its study population were significantly lower than those observed in MAGELLAN, which we believe reflects the lower risk patient inclusion in ADOPT. Despite the lack of efficacy observed in ADOPT, the incidence of major bleeding was lower than that observed in MAGELLAN. Although neither MAGELLAN nor ADOPT was successful, both highlighted the continuing risk of VTE after hospital discharge and illustrated two major lessons that have informed the clinical development plan for Betrixaban for acute medically ill patients.

Dose selection: In the MAGELLAN trial, rivaroxaban was dosed once daily despite having a half-life of only between 5 to 9 hours. To achieve adequate therapeutic coverage in a once-daily regimen, MAGELLAN may have studied a rivaroxaban dose that produced supratherapeutic drug levels for a period after dosing, possibly explaining the unfavorable bleeding risk observed in that trial. In the ADOPT trial, apixaban with a half-life of 12 hours, was dosed twice daily in order to maintain more consistent drug levels, which may have been responsible for its relatively lower rate of bleeding than was seen in MAGELLAN.

Patient selection: Multiple studies of the acute medically ill have demonstrated that VTE incidence increases as the number of risk factors that a patient has increases. In the ADOPT trial, where enrollment was open to a broad set of acute medically ill patients, including a large number of subjects who were not at high risk of VTE, there were too few VTE events to create a statistically significant separation between the control and treatment arms. In contrast to ADOPT, MAGELLAN enrolled patients with higher levels of VTE risk and treatment with rivaroxaban produced a significant reduction in the 35-day incidence of VTE compared to standard of care treatment with enoxaparin. Neither MAGELLAN nor ADOPT excluded patients whose medical history or concurrent use of anti-platelet therapy placed them at a substantially higher risk of severe bleeding. In MAGELLAN, this failure to exclude certain high risk patients combined with the dosing regimen used may have contributed to the relatively high level of bleeding events observed in the trial and the lack of net clinical benefit.

Phase 3 APEX study

We believe that for an anticoagulant to demonstrate efficacy and safety for extended duration VTE prophylaxis in acute medically ill patients, it must have the right drug properties, be dosed at appropriate levels and target the right patient population. As discussed above, we believe that Betrixaban has a number of key pharmacokinetic and pharmacodynamic properties that make it well suited for use with the frail and elderly patients that comprise a significant portion of the acute medically ill patient population. In addition, using the data from our extensive clinical and preclinical studies of Betrixaban and learnings from ADOPT and MAGELLAN, we believe that we have designed APEX with a dosing regimen for a study population focused on patients with certain biomarkers, that we believe will increase the probability that Apex will demonstrate both safety and efficacy in VTE prophylaxis in acute medically ill patients both in the hospital and after discharge.

Dose selection. Based on standard pharmacometric modeling that integrated preclinical and clinical studies of Factor Xa inhibitors, we believe that we have identified a dosing regimen (80 mg oral once-daily dose for 34 days following a 160 mg oral loading dose on day 1) that will produce clinically meaningful anticoagulant effects in the APEX trial. In our clinical studies, we measured the concentration of Betrixaban achieved at different dose levels and showed in Phase 2 studies that at total daily doses of 30 mg and 80 mg Betrixaban had anticoagulant activity, measured by standard imaging tests to detect VTE, comparable to standard of care enoxaparin. We also observed that bleeding and anticoagulant activity, as measured by a common blood marker D-dimer, of once-daily 40 mg, 60 mg and 80 mg doses of Betrixaban were comparable to standard doses of warfarin in patients with non-valvular atrial fibrillation. We correlated those doses with levels of thrombin generation inhibition, a common pharmacodynamic measurement used to compare anticoagulant activity of different drugs, and compared those levels with those produced by other Factor Xa inhibitors, including enoxaparin, rivaroxaban and apixaban. For patients with severe renal impairment and those taking agents that are strong inhibitors of PGP enzymes, the dose of Betrixaban will be reduced to 40 mg daily, which targets a level of anticoagulant activity consistent with the overall patient population.

The following diagram depicts pharmacometric modeling of thrombin generation inhibition over time for rivaroxaban, apixaban and Betrixaban, reflecting the dosing regimen used in MAGELLAN, ADOPT and APEX, respectively:

Patient selection: efficacy. We used the findings of MAGELLAN, ADOPT and other trials to help define the population of patients to be included in APEX. APEX is enrolling patients that have a combination of specific medical conditions and risk factors that put them at an elevated risk of VTE for up to 35 days after enrollment. The APEX inclusion criteria specify that patients must be admitted to the hospital with one of five categories of acute medical illness: heart failure, respiratory failure, infection, rheumatic disease or stroke. The inclusion criteria also require that patients have a high degree of immobilization. Further, a patient must meet one of the following three additional criteria: have a D-dimer level of at least twice the upper limit of normal, be older than 75 years or have at least two additional risk factors for VTE, such as obesity, ongoing hormonal treatment, or previous episode of VTE. We believe that by enrolling these high risk patients and focusing on prognostic indicators such as elevated D-dimer blood levels and those over the age of 75, we are more likely to demonstrate net clinical benefit from extended duration VTE prophylaxis.

Patient selection: safety. Consistent with our approach to enroll patients into the APEX study that are at an elevated risk for VTE for 35 days or more, we likewise designed the trial to exclude patients at high risk for bleeding. We believe this further increases the probability that APEX will demonstrate a net clinical benefit for Betrixaban. For example, we exclude patients with a previous history of major surgery, gastrointestinal bleeding, hemorrhagic stroke or bleeding pulmonary lesions. In addition, patients taking daily doses of aspirin are limited to low doses and must also take a proton-pump inhibitor to reduce the risk of gastrointestinal bleeding.

Other study design features and operations measures. We have implemented various measures to improve data quality, ensure we maintain a high degree of statistical power and reduce confounding clinical and statistical issues compared to MAGELLAN and ADOPT. For example, we are transmitting ultrasound images electronically rather than by mail so that quality can be assessed in real time. We do not require an ultrasound at day 10, which was required in an earlier study and that we believe led to patients failing to return for a second ultrasound at day 35. We also instituted patient outreach measures intended to increase patient compliance with follow-up appointments after hospital discharge. We expect our approach to result in a lower incidence of missing data in the primary endpoint analysis and therefore increase study power for a given number of patients.

We designed our Phase 3 APEX study to demonstrate the safety and efficacy of Betrixaban for extended duration VTE prophylaxis during a hospital stay and post-discharge for up to 35 days in acute medically ill patients with restricted mobility and certain biomarkers and additional risk factors. If APEX is successful, we expect it to be sufficient to support global regulatory approvals. We can provide no assurance that APEX will be successful and, if APEX is not successful, our ability to commercialize Betrixaban would be materially adversely affected. APEX is a randomized, double-blind, active-controlled, multicenter, multinational study comparing a once-daily dose of 80 mg of Betrixaban for a total of 35 days (including both in the hospital and after discharge) with in-hospital administration of 40 mg of enoxaparin once daily for 6 to 14 days followed by placebo. It is expected to enroll approximately 6,850 patients at approximately 400 study sites throughout the world. The primary study objective is to demonstrate superiority as compared to the current standard of care in the reduction of VTE-related events at 35 days while maintaining a favorable benefit to risk profile. The APEX study is adequately powered to show a clinically relevant benefit with a p-value of less than 0.01 on the primary endpoint of total asymptomatic proximal DVT (as detected by ultrasound), symptomatic DVT (proximal or distal), non-fatal pulmonary embolism and VTE-related death. The first patient was enrolled in March 2012, and, based on current enrollment, we expect patient enrollment to be completed by the end of 2015. In March 2013 and again in August 2013, an independent monitoring committee reviewed preliminary safety data from the study and recommended that the study continue as planned. We anticipate that in early 2015 the committee will conduct a futility analysis of the interim data from APEX to determine whether the results up to that point indicate that the APEX study should be halted because it is unlikely to be successful.

The following schematic depicts the APEX study design:

We believe that Betrixaban's unique pharmacological profile combined with APEX's study design positions Betrixaban to be the first novel anticoagulant approved for use in acute medically ill patients and the first anticoagulant approved for extended duration VTE prophylaxis in the acute medically ill patient population. We anticipate that such an approval, if obtained, would be for the use of Betrixaban in those acute medically ill patients with medical profiles consistent with those of patients enrolled in APEX. Based upon a review of epidemiological data, we believe that such patients constitute approximately two thirds of the acute medically ill patient population subject to a medical guideline recommendation to receive pharmacological VTE prophylaxis, or approximately 14 million patients in the G7 countries.

Betrixaban pharmacoeconomics

Oral drugs are typically less expensive than injectable agents. Currently in thrombosis, based on our research, we estimate that the average daily wholesale acquisition cost of a 40 mg Lovenox pre-filled syringe in the United States is \$33.08 compared to rivaroxaban at \$8.85 per day for both the 10 mg and 20 mg strengths. In addition, the cost to treat a VTE in a hospital setting in the United States can reach \$16,500 per patient in direct medical expenses. Therefore, we believe that, if our APEX Phase 3 study is successful, Betrixaban could represent a cost-effective preventive therapy against VTE in acute medically ill patients as compared to the current standard of care. We estimate that by 2016, the total potential market for VTE prophylaxis in the acute medically ill population, including extended duration VTE prophylaxis, will be \$3 billion to \$4 billion.

Andexanet alfa

Uncontrolled bleeding is the most clinically meaningful side effect of direct and indirect Factor Xa inhibitors, including apixaban, rivaroxaban, Betrixaban and enoxaparin. Andexanet alfa is a recombinant protein designed to reverse anticoagulant activity in patients treated with a Factor Xa inhibitor who suffer an uncontrolled bleeding episode or undergo emergency surgery.

Overview of anticoagulant-related bleeding

In patients using anticoagulation therapy, there is an increased risk of uncontrolled bleeding, which is common across all anticoagulants regardless of the reason for anticoagulation therapy, the patient setting or the duration of therapy. For patients at an elevated risk of thrombosis, the benefits provided by anticoagulation products generally outweigh the related risk of bleeding, however, major bleeding remains a significant cause of morbidity and mortality in these patients. For example, atrial fibrillation patients taking Factor Xa inhibitors on a chronic basis had a 1% to 4% annual rate of a major bleed in the Phase 3 ARISTOTLE trial of apixaban, sponsored by BMS and Pfizer, and the Phase 3 ROCKET trial of rivaroxaban, sponsored by Bayer and Janssen. Based on other clinical trials, we believe that annually an additional 1% of patients taking Factor Xa inhibitors will require emergency surgery. Patients on anticoagulation who suffer trauma have a higher risk of death than similar patients not on anticoagulation. The cost of treating an uncontrolled bleed can be between \$15,000 and \$52,000 per patient in direct medical expenses.

The current standard treatment for patients taking established anticoagulants who experience uncontrolled bleeding is to administer products that directly or indirectly support clotting, such as Vitamin K; fresh frozen plasma, or FFP; prothrombin complex concentrates, or PCCs; protamine; and recombinant Factor VIIa, or rFVIIa. Which of these approaches is used for a given patient depends on the particular anticoagulant being taken. For example, common treatments for warfarin reversal are Vitamin K, FFP and, more recently, PCCs, while low molecular weight heparin patients needing reversal are often managed with FFP or protamine. We estimate that Vitamin K alone is administered approximately 400,000 times each year in the United States to reverse the effects of anticoagulants. While the existing reversal agents are effective to varying degrees to reverse the effects of established anticoagulants, they can have potentially serious side effects, including in some cases increased risk of prothrombotic effects such as ischemic stroke and myocardial infarction.

There are, however, no approved antidotes or reversal agents for the new oral Factor Xa inhibitors. Moreover, the reversal agents used for established anticoagulants have not been extensively studied in clinical trials of oral Factor Xa inhibitor treated patients, and preliminary data suggest that they may not be effective to treat uncontrolled bleeding in these patients. The existing reversal agents work mostly in the early steps of the coagulation cascade prior to the involvement of Factor Xa and simply supplement the factor deficiency caused by established anticoagulants. For the reversal agents to affect bleeding in patients taking oral Factor Xa inhibitors, sufficiently large quantities would need to be given to overwhelm the inhibitor, an approach that we believe could lead to dangerous prothrombotic effects. As

there are no currently approved therapies designed to reverse or overcome Factor Xa inhibitors, patients taking those therapies face a risk of uncontrolled bleeding. Leading clinicians have identified, and the FDA has recognized, the lack of a reversal agent for Factor Xa inhibitors as a significant unmet clinical need.

The following diagram depicts where the existing reversal agents and novel oral anticoagulants interact with the coagulation cascade:

Despite the risk of uncontrolled bleeding, sales of Factor Xa inhibitors are expected to increase dramatically in the coming years as they have significant clinical benefits over standard products for preventing thrombosis, such as warfarin or enoxaparin. Based on our research and relevant market data, we estimate that by 2020, Factor Xa inhibitors will have a majority share of the market in each major anti-coagulation indication. As sales of Factor Xa inhibitors increase, the need for an effective antidote or reversal agent will correspondingly increase. We estimate that by 2020, over 500,000 patients annually will need a Factor Xa reversal agent, with approximately 300,000 of these cases arising from an uncontrolled bleeding episode, approximately 100,000 of these cases arising from emergency surgery and approximately 100,000 of those cases arising from traumatic injury.

Andexanet alfa — a universal antidote for Factor Xa inhibitors

Building on the insights gained during the development of Betrixaban, we designed Andexanet alfa as a universal reversal agent for direct Factor Xa inhibitors, such as rivaroxaban, apixaban, edoxaban and Betrixaban, as well as indirect Factor Xa inhibitors, such as enoxaparin. Andexanet alfa is structurally very similar to native Factor Xa, but it has a number of limited modifications intended to restrict its biological activity to reversing the effects of Factor Xa inhibitors. Andexanet alfa acts as a Factor Xa decoy that binds to Factor Xa inhibitors in the blood. Once bound to Andexanet alfa, the inhibitors are unable to bind to and inhibit native Factor Xa. The native Factor Xa then becomes available to participate in the coagulation process and restore hemostasis, or normal clotting.

In designing Andexanet alfa, we started with native Factor Xa protein and used our knowledge of its functional domains to make three changes by protein engineering. First, we made a small modification to the active site, or catalytic pocket, of native Factor Xa so that Andexanet alfa cannot drive the coagulation process but still binds to Factor Xa inhibitors with high affinity. Second, we removed most of the section of the native Factor Xa that facilitates binding to the thrombin activating complex to reduce the risk that Andexanet alfa would interfere with the activity of native Factor Xa. Importantly, while removing this section we retained a small portion at the end so that Andexanet alfa looks more like native Factor Xa to the immune system, thereby decreasing the likelihood of an immune system response against Andexanet alfa. Third, we made a minor modification in the peptide section that links the two parts of Factor Xa to facilitate Andexanet alfa's manufacture using standard processes. The end result is a recombinant protein that we believe can bind with and inactivate any Factor Xa inhibitor, thereby allowing native Factor Xa to drive coagulation and restore hemostasis.

Andexanet alfa preclinical results

We have evaluated Andexanet alfa in numerous in-vitro and animal studies and have developed substantial evidence supporting the safety, efficacy and rapid activity of Andexanet alfa. Key findings from this preclinical program include:

In isolated human plasma, we have measured multiple pharmacodynamic measures of coagulation, such as anti-Factor Xa units, prothrombin time and activated partial thromboplastin time as well as key pharmacokinetic measures and have shown that Andexanet alfa reverses the effects of all Factor Xa inhibitors we have studied, including rivaroxaban, Betrixaban, apixaban, enoxaparin and fondaparinux.

In tail transection blood loss models in rats and mice, we have shown that Andexanet alfa significantly reduces the amount of blood loss compared to placebo in animals treated with enoxaparin, fondaparinux, or rivaroxaban plus aspirin. In studies where Andexanet alfa was given five or ten minutes after the transection, blood loss was significantly reduced compared to animals not given Andexanet alfa.

In a rabbit liver laceration model, we have shown that Andexanet alfa reduces the level of bleeding in rivaroxaban-treated rabbits to levels comparable to those of rabbits not anticoagulated with rivaroxaban whether given before or after the liver incisions. We have also shown that administration of pro-thrombotic agents, rFVIIa and prothrombin complex concentrates, fails to decrease the amount of blood loss in rabbits treated with rivaroxaban. In addition, we have shown that in rabbits treated with Andexanet alfa, but without rivaroxaban, bleeding levels were comparable to those of untreated rabbits, suggesting that Andexanet alfa alone does not have significant pro-coagulative effects.

In a cynomolgus monkey safety study, animals were dosed multiple times with Andexanet alfa, both alone and in the presence of several Factor Xa inhibitors, without any evidence of significant toxicity.

In a cynomolgus monkey study, administration of Andexanet alfa alone was associated with a transient increase in certain coagulation markers consistent with a known interaction between Andexanet alfa and tissue factor pathway inhibitor, or TFPI, another element in the coagulation process. These blood markers, which are indicative of increased thrombin generation, were not associated, however, with any evidence of clot formation or fibrin deposition in detailed histopathological examination of the monkeys at necropsy.

Taken together, these and other studies suggest, but do not prove, that Andexanet alfa will be a safe and effective Factor Xa reversal agent.

Andexanet alfa clinical results and development strategy

We have initiated a clinical development program for Andexanet alfa. Based on the results of our initial Phase 2 study, we held an End of Phase 2 meeting with the FDA in August 2013 to discuss the remaining clinical studies needed for approval of Andexanet alfa. In November 2013, the FDA granted breakthrough therapy designation for Andexanet alfa and we are pursuing an Accelerated Approval pathway for Andexanet alfa. We plan to initiate Phase 3 registration studies for Andexanet alfa in the first half of 2014 followed by a Phase 4 confirmatory study. Our goal is to file a BLA for conditional approval by the end of 2015. Additionally, we are in the process of obtaining formal scientific advice from the EMA regarding the process for regulatory approval in Europe.

In September 2012, we completed our initial Phase 1 study of Andexanet alfa in healthy volunteers. In this study, a total of 24 subjects each received a single dose of Andexanet alfa (30 mg, 90 mg, 300 mg or 600 mg) while eight subjects received a placebo. Andexanet alfa was generally well tolerated with no apparent safety signals. Numerous markers of coagulation, inflammation and platelet activity were assessed in this study. While the majority of markers were unaffected by Andexanet alfa administration, there was a transient, dose-dependent elevation in the same markers indicative of thrombin generation observed in our preclinical cynomolgus monkey study discussed above. Consistent with that study, there was no clinical evidence of thrombosis in any of the Phase 1 subjects.

In December 2012, we initiated the first of a series of Phase 2 proof-of-concept studies evaluating the effect of Andexanet alfa in healthy volunteers who are administered one of several Factor Xa inhibitors, including Betrixaban. The purpose of these studies is to evaluate further the safety of Andexanet alfa and to determine the dose of Andexanet alfa required to reverse the effect of each anticoagulant as measured by pharmacodynamic endpoints and an in-vitro clotting assay. We have completed the first Phase 2 study, which evaluated Andexanet alfa in subjects taking apixaban, and reported initial results from a Phase 2 study evaluating subjects taking rivaroxaban.

In our first Phase 2 study, subjects received the highest approved dose of apixaban twice daily for 5 days and were then on day 6 administered a single dose of apixaban followed by either Andexanet alfa or a placebo. A total of 18 subjects each received a single dose of Andexanet alfa (90 mg, 210 mg or 420 mg) while nine subjects received a placebo. Analysis of anticoagulation markers in blood samples taken from the subjects indicated that Andexanet alfa had a rapid, sustained and dose-related effect on reversing the anticoagulant activity of apixaban. For example, in blood samples taken 2 minutes and 30 minutes after administration of Andexanet alfa, the anti-Factor Xa activity of apixaban was reversed 77% and 40%, respectively, with the 210 mg dose, and 95% and 80%, respectively, with the 420 mg dose, compared to placebo. These results for all three doses were statistically significant with p-values of less than or equal to 0.0005 compared to placebo. In the rabbit liver laceration model discussed above, reversal of anti-Factor Xa activity by 91% at 15 minutes is correlated with significantly reduced blood loss.

Other assays were also indicative of the activity of Andexanet alfa. In an in-vitro assay of blood coagulation, the clotting time of blood taken at 2, 10 and 30 minutes after Andexanet alfa administration from subjects who had received a 420 mg dose Andexanet alfa was well within the range expected for a person not on an anticoagulant. For blood taken from these subjects 90 minutes after administration of Andexanet alfa, clotting time was at the upper end of the normal range. In contrast, blood taken from subjects receiving placebo had a clotting time longer than the normal range at the same time points. The difference between clotting time for the Andexanet alfa-treated subjects and the subjects receiving placebo was statistically significant for all three doses at 30 minutes with p-values of less than 0.0005 and for the 210 mg and 420 mg doses at 90 minutes with p-values of less than 0.005.

In June 2013, we initiated an extension of our initial Phase 2 proof-of-concept study in order to evaluate additional dosing regimens for Andexanet alfa. In this extension, healthy volunteers received the highest approved dose of apixaban twice daily for 6 days as in the original portion of the study, and then received either (i) a 420 mg bolus dose of Andexanet alfa followed by a repeat bolus dose of 180 mg of Andexanet alfa 45 minutes later, (ii) a 420 mg bolus dose of Andexanet alfa followed by a continuous infusion of a 180 mg dose of Andexanet alfa over the next 45 minutes, (iii) a 420 mg bolus dose of Andexanet alfa followed by a continuous infusion of a 480 mg dose of Andexanet alfa over the next 2 hours, or (iv) a placebo. In the extension, there were 6 subjects in each group that received Andexanet alfa and 3 subjects in the placebo group. Analysis of the results of the extension demonstrates that each of the three dosing regimens resulted in the near complete reversal of the anticoagulation activity of apixaban for an extended period. For example, in blood samples taken from subjects receiving the bolus dose and the 2 hour infusion, the anti-Factor Xa activity of apixaban was reversed by 92% at 2 minutes as compared to placebo and remained reversed by approximately 91% at 2 hours. The p-value at both time points was less than 0.0001.

The chart below compares the effect of the 420 mg bolus dose and 2 hour infusion evaluated in the extension of the Phase 2 study with the 420 mg bolus dose only and with the placebo evaluated in the initial portion of the study.

In our second proof-of-concept Phase 2 double-blind, placebo-controlled study, we treated healthy volunteers with an oral dose of rivaroxaban at 20 mg once daily for six days and then randomized volunteers in a 6:3 ratio to Andexanet alfa in four different dosing cohorts. Andexanet alfa was administered intravenously on Day 6, three hours after the last rivaroxaban dose – the approximate time of maximum rivaroxaban concentration (mean \pm SD: 0.64 \pm 0.22 mM, n=18). Pharmacodynamic and safety data were collected through Day 48 with pharmacokinetic data through Day 10.

The first three cohorts received a single IV bolus of Andexanet alfa at 210 mg, 420 mg or 600 mg, respectively. A fourth cohort received a single IV bolus of Andexanet alfa at 720 mg followed by a 4 mg/minute infusion for one hour. We examined the reversal by Andexanet alfa of the anticoagulant activity of rivaroxaban, as well as the pharmacokinetics and safety in healthy subjects.

Immediately following completion of the 210 mg, 420 mg, 600 mg and 720 mg bolus doses of Andexanet alfa, anti-Factor Xa activity decreased dose-dependency by 20%, 53%, 70% and 81%, respectively, from the pre-Andexanet alfa level and returned to placebo levels approximately two hours after treatment. Four out of six subjects in the 720 mg bolus cohort achieved greater than 90% reversal of their anti-Factor Xa activity. In parallel, the plasma concentrations of unbound rivaroxaban were decreased by 32%, 51%, 75% and 70% respectively, relative to pre-Andexanet alfa levels. Rivaroxaban-induced inhibition of thrombin generation and prolongation of both prothrombin time and activated clotting time approached normal levels with Andexanet alfa in a dose-dependent manner.

Andexanet alfa infusion was not associated with increases in prothrombin fragments 1+2 (F1+2), thrombin-antithrombin complex (TAT), or D-dimer (all levels were within normal ranges). As expected, tissue factor pathway inhibitor activity decreased due to its binding to Andexanet alfa. Andexanet alfa was well tolerated and there were no thrombotic events, serious, or severe adverse events.

A fifth cohort in this rivaroxaban Phase 2 proof-of-concept study will be evaluating a bolus of Andexanet alfa at 800 mg followed by a 8 mg/minute infusion for one hour. This cohort is ongoing and these results are expected in the first half of 2014.

The following diagram depicts the data from our second Phase 2 study of Andexanet alfa in subjects taking rivaroxaban:

As in the Phase 1 study, subjects receiving Andexanet alfa showed a transient dose-dependent elevation in markers indicative of thrombin generation, but there was no clinical evidence of thrombosis. Importantly, none of the subjects receiving Andexanet alfa generated detectable levels of antibodies against either Factor X or Factor Xa. Generation of such antibodies could lead to serious side effects. Only one subject receiving Andexanet alfa generated an antibody against Andexanet alfa, but it was deemed to be non-neutralizing. Generation of significant levels of neutralizing antibodies against Andexanet alfa could result in the activity of Andexanet alfa being blocked if it were re-administered within approximately 10 to 60 days after the initial administration.

Based on our limited human data, Andexanet alfa appears to be safe and well tolerated. In our Phase 1 study, there was one serious adverse event, a case of pneumonia, and one subject had an unplanned pregnancy approximately 10 days after administration of Andexanet alfa which ended in a miscarriage. In the Phase 2 study results reported, there were no serious adverse events. Based on unblinded data from the Phase 1 and ongoing Phase 2 studies, a total of seven out of 42 subjects administered Andexanet alfa had mild or moderate infusion-related reactions as compared to one out of 17 subjects administered placebo. These findings are not unexpected for a biological agent such as Andexanet alfa.

Based on the results of our initial Phase 2 study, we held an End of Phase 2 meeting with the FDA in August 2013 to discuss the remaining clinical studies needed for approval of Andexanet alfa. Typically the FDA requires at least one large-scale, randomized, placebo controlled study for approval of a new therapeutic. However, based on our discussions with the FDA, we believe that the FDA supports our pursuit of an Accelerated Approval pathway because of the significant unmet clinical need for a reversal agent for Factor Xa inhibitors. For example, under the FDA's "Accelerated Approval" pathway, therapies targeting a significant unmet clinical need may be approved based upon their showing adequate safety as well as efficacy against a surrogate biomarker endpoint in a clinical trial. Utilizing an expedited approval process would significantly decrease the time and expense associated with our development program. In November 2013, the FDA granted breakthrough therapy designation for Andexanet alfa and therefore we are pursuing an Accelerated Approval pathway for Andexanet alfa. We believe that under an Accelerated Approval pathway, our development program for Andexanet alfa might consist of a 100 to 200 subject Phase 3 program with a study design similar to our proof-of-concept studies together with a Phase 4 study (either controlled or open label) evaluating the safety and activity of Andexanet alfa in patients treated with Factor Xa inhibitors who are experiencing severe bleeding or undergoing emergency surgery. These Phase 3 studies will be similar in design to our Phase 2 studies and will be conducted under an Accelerated Approval pathway using biomarker endpoints for conditional approval. These biomarkers will include anti-Factor Xa levels, plasma free fraction of the anticoagulant, and thrombin generation. At the conclusion of the registration study, we would plan to submit that data along with available interim data from the Phase 4 study as part of a BLA, for Accelerated Approval. If the registration study is successful, we believe these data could be sufficient to obtain approval for Andexanet alfa from the FDA. We anticipate that both studies could be initiated in the first half of 2014 with the Phase 3 studies possibly being completed in 2015. However, the FDA has not confirmed that such a development program, even if successful, would be sufficient to support the approval of a BLA nor can we provide assurance that we would be able to complete such a program. If an Accelerated Approval pathway is not available, it is likely that we would need to enter into a partnership arrangement to continue the development of Andexanet alfa, and the approval, if received, would be substantially delayed.

We are currently conducting a Phase 2 proof-of-concept study evaluating Andexanet alfa for reversal of the anticoagulant activity of the Factor Xa inhibitor enoxaparin. We expect results from this study in 2014. We plan to initiate similar Phase 2 proof-of-concept studies evaluating the reversal of edoxaban in 2014 and Betrixaban thereafter. Additionally, we are in the process of obtaining formal scientific advice from the EMA regarding the process for regulatory approval in Europe.

Collaboration with BMS and Pfizer

In October 2012, we entered into a three-way agreement with BMS and Pfizer to include subjects dosed with apixaban, their jointly owned product candidate, in one of our Phase 2 proof-of-concept studies of Andexanet alfa. We are responsible for the cost of conducting these clinical studies. BMS and Pfizer will work closely with us on both development and regulatory aspects of Andexanet alfa in connection with our Phase 2 proof-of-concept studies to the extent such matters relate to apixaban. Under the terms of the agreement, we received an upfront non-refundable payment of \$2.0 million. We also received an additional non-refundable payment of \$4.0 million upon the first dosing of a patient in a clinical trial. These payments represent the full amount of consideration under this agreement. This agreement will continue in force until our anticipated meeting with the FDA or termination by either party pursuant to the agreement. BMS and Pfizer may terminate this agreement if the parties cannot agree on certain changes to the development plan, for convenience after the first year with 60 days' advance written notice or for our bankruptcy or change of control. In addition, either party may terminate this agreement for the other party's uncured material breach or for material safety issues.

In January 2014, we entered into a second collaboration agreement with BMS and Pfizer to further study Andexanet alfa as an antidote for their jointly owned product candidate apixaban through Phase 3 studies. The Phase 3 studies are

expected to start in the first half of 2014. Under the terms of the agreement, we will receive an upfront payment of \$13.0 million and are eligible to receive additional development and regulatory milestone payments of up to \$12.0 million. These payments represent the total consideration under this agreement. BMS and Pfizer will continue to provide development and regulatory guidance for the program.

Under both agreements, we retain full, worldwide development and commercial rights to Andexanet alfa.

This second collaboration agreement will continue in force until the approval of Andexanet alfa as a reversal agent for apixaban by the FDA and EMA. BMS and Pfizer may terminate this agreement for convenience with 60 days' advance written notice or for our bankruptcy or change of control. In addition, either party may terminate this agreement for the other party's uncured material breach, material safety issues, or failure of the Phase 3 studies.

Collaboration with Bayer and Janssen

In February 2013, we entered into a three-way agreement with Bayer and Janssen to include subjects dosed with rivaroxaban, their Factor Xa inhibitor product, in one of our Phase 2 proof-of-concept studies of Andexanet alfa. We are responsible for the cost of conducting such clinical studies. Pursuant to the agreement, Bayer and Janssen will work closely with us on both development and regulatory aspects of Andexanet alfa in connection with our Phase 2 proof-of-concept studies. Under the agreement, Bayer and Janssen have each provided us with an upfront and non-refundable fee of \$2.5 million, for an aggregate fee of \$5.0 million, and will each provide us with an additional payment of \$250,000, for an aggregate fee of \$500,000, following the delivery of the final written study report of our Phase 2 proof-of-concept studies of Andexanet alfa, as further specified in the agreement. This agreement will continue in force until the later of the completion of the studies and the fulfillment of certain other conditions set forth in the agreement, unless earlier terminated by either party pursuant to the agreement. This agreement may be terminated by either party for material safety issues or the other party's uncured material breach. In addition, Bayer and Janssen may terminate this agreement with 60 days' advance written notice for convenience at any time, or immediately for our bankruptcy or change of control.

In February 2014, we entered into a second collaboration agreement with Bayer and Janssen to evaluate Andexanet alfa as a reversal agent for the FDA-approved oral Factor Xa inhibitor rivaroxaban through Phase 3 studies. Our original collaboration agreement with Bayer and Janssen covers the conduct of a Phase 2 proof-of-concept study. The new collaboration agreement will cover the conduct of Phase 3 studies of Andexanet alfa with rivaroxaban and any potential U.S. and EU regulatory approval of Andexanet alfa as reversal agent of rivaroxaban. The Phase 3 studies are expected to start in the first half of 2014. Under this new collaboration agreement, we will receive an upfront payment of \$10 million and are eligible to receive additional development and regulatory milestone payments of up to \$15.0 million. These payments represent the total consideration under this agreement. Bayer and Janssen will continue to provide development and regulatory guidance for the program.

Under both agreements, we retain full, worldwide development and commercial rights to Andexanet alfa.

This second collaboration agreement will continue in force until the approval of Andexanet alfa as a reversal agent for rivaroxaban by the FDA and EMA. Bayer and Janssen may terminate this agreement for convenience with 60 days' advance written notice or for our bankruptcy or change of control. In addition, either party may terminate this agreement for the other party's uncured material breach or material safety issues, and we can also terminate this agreement for failure of the Phase 3 studies.

Collaboration with Daiichi Sankyo

In June 2013, we entered into an agreement with Daiichi Sankyo, Inc., or Daiichi Sankyo, to include subjects dosed with edoxaban, Daiichi Sankyo's Factor Xa inhibitor product, in one of our proof-of-concept studies of Andexanet alfa. We are responsible for the cost of conducting this clinical study. Under the terms of the agreement, Daiichi Sankyo provided us with an upfront fee of \$6.0 million. Daiichi Sankyo may terminate the agreement at any time. The total consideration under this agreement of \$6.0 million was received in July 2013. We are obligated to perform preclinical proof-of-concept studies and participate on a JCC with Daiichi Sankyo to oversee the collaboration activities under the agreement. We originally estimated the non-contingent period of performance to be through the second quarter of 2014. In December 2013, we revised our estimated period of performance to be through the first quarter of 2014. The total non-contingent consideration under this agreement of \$3.0 million is being recognized as collaboration and license revenue on a straight-line basis over our estimated non-contingent performance period. In February 2014, we resolved the contingent portion of the arrangement which was tied to pre-clinical studies. The contingent consideration under this agreement of \$3.0 million will be recognized over the remaining performance period, which is currently estimated to begin in the first quarter of 2014 and conclude in the first quarter of 2015.

Antidote pharmacoeconomics

Uncontrolled bleeding is the most clinically relevant side effect of anticoagulant treatment across all anticoagulants and clinical settings. Clinical trial results suggest that the frequency of uncontrolled bleeding associated with the administration of Factor Xa inhibitors ranges from 1% to 4% per year, depending on the underlying medical condition. The clinical costs of a major bleeding event in anticoagulant treated patients are estimated to be \$15,000 to \$52,000 per patient during the year following the event. Based on the frequency of bleeding rates suggested by clinical trials and our projection of 23 million to 36 million patients treated annually with Factor Xa inhibitors in the G7 countries, we believe that by 2020, the annual costs to the healthcare system to treat major bleeding episodes in patients treated with a Factor Xa inhibitor may exceed \$10 billion. We believe that an effective Factor Xa antidote represents a potentially cost-effective way to manage these healthcare system costs.

Our hematologic cancer and inflammation product candidates

Our early stage development programs are focused on developing small molecule kinase inhibitors for the treatment of hematologic cancers and inflammatory diseases. Kinases are enzymes that act on and modify the activity of different proteins. Syk and JAK are clinically validated kinase targets involved in key signaling pathways that are important in certain hematologic cancers and inflammatory disorders. We have focused on the discovery and development of specific inhibitors of Syk and dual inhibitors of both Syk and JAK based on the unique roles of these kinases in NHL, CLL, allergic asthma, rheumatoid arthritis, or RA, and other inflammatory diseases.

Syk overview

Syk is a cell signaling enzyme that is found in certain white blood cells, including B-cells, basophils, neutrophils, monocytes, and tissue macrophages and mast cells, and is important for controlling the activity and recruitment of these cells. Scientists have focused on the role of Syk in B-cell cancers, such as NHL and CLL, as well as certain inflammatory diseases, such as allergic asthma and RA. B-cell activation is driven by the B-cell receptor, or BCR, whose signaling promotes cell proliferation, adhesion and survival in NHL and CLL. Syk acts downstream of the BCR, and blocking Syk activity in preclinical models results in an inhibition of proliferation, a disruption of tumor cell adhesion and cell death in malignant B-cells. Inhibitors of the BCR pathway, including the Syk inhibitor fostamatinib being developed by Rigel Pharmaceuticals, have been shown to have activity in NHL and CLL.

JAK overview

The JAK kinases are a family of related tyrosine kinases that play key roles in cytokine signaling involved in immune processes. JAK activation and signaling is directly downstream from receptors for several cytokines that are integral to normal lymphocyte activation, proliferation and function. JAK also plays a role in malignant lymphocytes, including the survival and proliferation of CLL cells as well as cytokine signaling in certain NHL and other cancers. Leading clinicians have hypothesized that these JAK-related cytokines play a key role in promoting tumor survival and growth and that JAK inhibition may be effective in interrupting signaling processes involved in tumor cells that have mutated and are no longer entirely dependent on B-cell signaling via BCR.

Cerdulatinib—dual Syk/JAK inhibitor

The lead compound in our kinase development effort, Cerdulatinib, is a potent inhibitor of both Syk and JAK. We believe that Cerdulatinib may be able to treat certain diseases that involve Syk-BCR signaling and cytokine-JAK signaling. Based on the inhibition of these key pathways, we are currently focused on developing Cerdulatinib for NHL, CLL and other hematologic cancers, with a focus on patients with certain treatment-resistant mutations, including those targeting the BTK and PI3K kinases, and certain inflammatory diseases. In October 2013, we initiated a Phase 1/2 proof-of-concept study in NHL and CLL and anticipate initial proof of activity from this trial in 2014. In addition, we have entered into a license and collaboration agreement with Acix to co-develop and co-commercialize formulations of Cerdulatinib and certain related compounds for nonsystemic indications, such as the treatment and prevention of ophthalmological diseases by topical administration and allergic rhinitis by intranasal administration. We retain rights to all systemic indications and other non-systemic indications, including dermatologic disorders.

NHL and CLL

Lymphoma is a large class of hematologic cancer that affects the B-cell and T-cell lymphocytes in lymph nodes. In 2011, lymphoma affected an estimated 660,000 people in the United States, with 500,000 of them suffering from the NHL varieties of the disease. NHL is often aggressive, marked by rapidly growing tumors in the lymph nodes, spleen, liver, bone marrow and other organs.

CLL is also a hematologic cancer that affects B-cell lymphocytes in the blood and bone marrow and is the most common type of leukemia. In 2011, approximately 100,000 patients had CLL in the United States. As it advances, usually slowly, CLL results in swollen lymph nodes, spleen and liver and eventually in anemia and infections.

Despite the introduction of novel therapies for B-cell NHL and CLL, some patients fail to go into remission and of those who do attain remission, many relapse and develop refractory disease and therefore need alternative therapies. The heterogeneity and severity of B-cell malignancies may warrant simultaneous targeting of multiple disease-relevant pathways. Dual inhibition of Syk and JAK represents such a strategy and may have several benefits relative to selective kinase inhibition, such as gaining control over a broader array of disease etiologies, reducing the probability of selection of alternate disease growth mechanisms, and the potential that an overall lower level suppression of multiple targets may be sufficient to modulate disease activity.

Cerdulatinib is a highly potent inhibitor of Syk and JAK activity in blood cells from human volunteers. In preclinical studies, inhibition of Syk and JAK, via Cerdulatinib, was active in a broad panel of B-cell lymphoma cell lines. Cerdulatinib was more effective than Syk-specific inhibition in these cell lines, suggesting that Cerdulatinib may be useful in the treatment of a broad range of B-cell lymphomas, including patients with diffuse large B-cell lymphoma, or DLBCL, an aggressive form of NHL that affects over 80,000 patients in the G7 countries, and patients with hard to treat mutations. For example, Cerdulatinib was shown to be effective in cell lines dependent on NFkB mutations for their survival. Current therapies and those in development, including those targeting the BTK and PI3K kinases, have limited activity in DLBCL patients with these mutations. In addition, preclinical data suggest that dual Syk/JAK inhibition with Cerdulatinib may also have activity in patients with an inadequate response to novel specific kinase inhibitors in development for NHL and CLL. Our strategy includes targeting Cerdulatinib for certain CLL and NHL patient populations, such as those with specific genetic mutations or those who have not responded adequately to other treatments. For example, it is estimated that approximately one third of patients become refractory to standard CLL therapy. We believe these indications could potentially represent a significant commercial opportunity if we are able to develop an effective therapy.

Based on the preclinical data and our understanding of the role of Syk and JAK signaling in B-cell cancers, we initiated an open label Phase 1/2 proof-of-concept study in NHL and CLL patients who have failed or relapsed on existing marketed therapies or products in development, including patients with identified mutations, in October 2013. In the initial phase of this study, we will evaluate the safety and activity of Cerdulatinib using escalating doses. We anticipate that initial results of the escalation phase of the study will be available in the first half of 2014. In addition, we anticipate that we may see clinical responses in some patients in this phase of the study by the end of 2014. If Cerdulatinib is well-tolerated and activity is seen in the escalation phase, we would expect to expand the study and evaluate the activity of Cerdulatinib in a larger cohort of patients at a dose that was active and well-tolerated in the escalation phase. We anticipate that the results from the expansion phase of the study would be available in the second half of 2015. Depending on the overall results of the study, we would expect to further study Cerdulatinib in CLL and/or NHL either alone or in combination with other approved products.

PRT2607 — potent and selective Syk inhibitor

PRT2607 is an oral, small molecule targeting Syk. It has been shown to be a highly potent and selective inhibitor of Syk in a broad range of in vitro assays. When tested against a broad panel of 270 purified kinases, Syk was the most potently inhibited kinase with an 80-fold margin over the next most potently inhibited kinase.

PRT2607 has been studied in 131 subjects in Phase 1 studies. It has been found to be well tolerated in completed studies of both single doses up to 400 mg and multiple doses up to 110 mg given once daily for ten days. The pharmacokinetic properties of PRT2607, including long half-life and low peak-to-trough ratio, are appropriate for once-daily administration. The exposures of PRT2607 in these studies also demonstrated dose dependent, high level inhibition of Syk-dependent cellular signaling pathways, B-cell activation and immunoglobulin E, or IgE, mediated basophil degranulation, which reversed in relation to the decline in PRT2607 drug levels.

We have entered into a collaboration agreement with Biogen Idec, pursuant to which Biogen Idec is leading the development and commercialization of PRT2607 and certain other selective Syk inhibitors for inflammatory disorders. Biogen Idec is currently evaluating inhaled versions of PRT2607 and certain highly selective Syk inhibitors for allergic asthma.

Allergic asthma

Allergic asthma is a chronic inflammatory disorder of the lungs and respiratory passages that arises from a response to an allergen or pathogen. Asthma affects the lower respiratory tract and is marked by episodic flare-ups, or attacks, that

can be life threatening. In patients with this disorder, allergens, such as pollen, bind to and trigger cross-linking of the IgE/Fc receptor complexes on the surface of mast cells. This results in the initiation of a cascade of intracellular signals to mount an immune response resulting in swelling and inflammation of the airways. When this process occurs repeatedly over time, it creates persistent inflammation of the upper and lower airway passages, resulting in the chronic congestion and airway obstruction associated with allergic rhinitis and asthma, respectively.

PRT2607 is designed to bind to Syk in mast cells to interrupt the signal from the IgE/Fc receptor complex, potentially inhibiting the immune response to the allergen in a way that may be effective in both the short and long-term control of allergic asthma. Based on the unique role Syk plays in allergic diseases, the selectivity profile of PRT2607, and the high solubility and other good physicochemical properties of PRT2607, we believe that PRT2607 is differentiated from other kinase inhibitors in development for allergic asthma.

Elinogrel — P2Y₁₂ receptor inhibitor

Our product candidate Elinogrel is an oral and intravenous, competitive and reversible inhibitor of the P2Y₁₂ platelet receptor. Products that block P2Y₁₂, such as clopidogrel, prasugrel and ticagrelor, are indicated to reduce myocardial infarction, stroke and death in patients at high risk of a myocardial infarction. The current agents have a number of limitations that reduce efficacy or decrease safety, such as slow onset, lack of reversibility, lack of intravenous delivery and non-competitive mechanism of action. Elinogrel has been studied in two Phase 2 studies and was previously partnered with Novartis Pharma A.G., or Novartis. We re-acquired full development and commercial rights to the program from Novartis in 2012. We are not currently pursuing development of Elinogrel due to the expense of the large Phase 3 studies needed for approval in current indications, however, we may pursue development of Elinogrel in smaller indications or with a partner in the future.

Sales and marketing

Assuming Betrixaban and Andexanet alfa are approved by the FDA and other regulatory authorities, we intend to commercialize both molecules using a hospital-based sales force in the United States, and possibly other major markets. To achieve global commercialization, we anticipate using a variety of distribution agreements and commercial partnerships in those territories where we do not establish a sales force. We expect to target our U.S. sales and marketing efforts at the approximately 1,500 hospitals and out-patient acute care settings that would account for the large majority of the prescribing base for our product candidates, if approved. We plan to commercialize both of our thrombosis product candidates with a U.S. hospital-based sales force of approximately 100 to 140 sales representatives all focused on demonstrating the clinical and pharmacoeconomic value of our product candidates. We expect that our commercial infrastructure would be comprised of several proven, experienced marketing and sales management professionals along with a reimbursement support and hospital formulary specialist team. In addition, we intend to develop and publish health economic models demonstrating the value of Betrixaban and Andexanet alfa to hospital administrators and third party payors.

Research and development

We invest significant effort defining and refining our research and development process and internally teaching our approach to drug development. We favor programs with early decision points, well-validated targets, predictive preclinical models and clear paths to regulatory approval, all in the context of a target product profile that can address significant unmet or underserved clinical needs. Members of our discovery, research and development team have played central roles in discovering and developing a number of promising candidates over the past 20 plus years while at Portola, and while at Millennium Pharmaceuticals, Inc., or Millennium, and COR Therapeutics, Inc., two early developers of thrombosis therapies. They have used unique biological insights to develop in vitro and in vivo models that speed development. We also selectively leverage outside collaborators to expand into potential additional indications. As our product candidates progress through clinical development, we have focused and will increasingly focus our scientific efforts on supporting that development.

We emphasize data-driven decision making, strive to advance or terminate projects early based on clearly defined go/no go criteria, prioritize programs at all stages and allocate our capital to the most promising programs. Our current development-stage portfolio consists of three compounds discovered through our internal research efforts and one discovered by Portola scientists during their time at a prior company. In addition we are actively seeking to identify attractive external opportunities. We utilize the same critical filters for investment when evaluating external programs as we do with our own, internally-derived candidates.

Collaboration and license agreements

Betrixaban

Millennium agreements

In November 2003, we entered into an asset purchase agreement to acquire patent rights and intellectual property to an ADP Receptor Antagonist Program, or the ADP Program, and a Platelet Research Program from Millennium. Pursuant to the asset purchase agreement, we issued Millennium 100,000 shares of our Series A convertible preferred stock valued at \$10.00 per share and made a cash payment to Millennium of \$249,000. We are obligated to pay to Millennium royalties at tiered single-digit percentages of net sales of certain ADP Program products if product sales are ever achieved, which royalty payments will continue until the expiration of the relevant patents or ten years after launch, whichever is later.

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In August 2004, we entered into an agreement to license from Millennium certain exclusive rights to research, develop and commercialize certain compounds that inhibit Factor Xa, including Betrixaban, or the Factor Xa Program. The license agreement requires us to make certain license fee, milestone, royalty and sublicense sharing payments to Millennium as we develop, commercialize or sublicense Betrixaban and other products from the Factor Xa Program. In November 2007, we made a cash payment to Millennium of \$5.0 million pursuant to the license agreement. The Millennium license agreement further provides for additional payments to Millennium of up to \$35.0 million based on the achievement of regulatory filing and approval milestones related to the Factor Xa Program. In addition, we are obligated to pay Millennium royalties at tiered single-digit percentages of net sales of any Factor Xa Program products if product sales are ever achieved. This license agreement will continue in force, on a product-by-product and country-by-country basis, until the expiration of the relevant patents or ten years after the launch, whichever is later, or termination by either party pursuant to the agreement. This license agreement may be terminated by either party for the other party's uncured material breach. In addition, we may terminate this agreement for convenience with 30 days' advance written notice.

In December 2005, we amended both the asset purchase agreement for the ADP Program and the license agreement for the Factor Xa Program. In connection with this amendment, we made a cash payment to Millennium of \$500,000 and issued to Millennium 38,167 shares of our Series B convertible preferred stock valued at \$13.10 per share. In addition, pursuant to the amendment, in connection with our entry into both the agreement with Novartis and agreement with Merck & Co., Inc., we made a cash payment to Millennium of \$250,000 and issued Millennium 17,667 shares of our Series C convertible preferred stock valued at \$14.15 per share.

Lee's agreement

In January 2013, we entered into a clinical collaboration agreement with Lee's to jointly expand our Phase 3 APEX study of Betrixaban into China. Under the agreement, Lee's provided us with an upfront and non-refundable payment of \$700,000 and will reimburse our costs in connection with the study to support the expansion of the APEX study into China. Lee's will also lead regulatory interactions with China's State Food and Drug Administration for the study. We granted Lee's an exclusive option to negotiate for the exclusive commercial rights to Betrixaban in China, which may be exercised by Lee's for 60 days after it receives the primary data analysis report from the study. We may, at any time prior to the unblinding of the APEX study data, terminate the option and the agreement by providing Lee's with written notification and making a termination payment. We reserved the right to terminate Lee's option under certain specified circumstances. If the parties fail to reach agreement on the terms of the commercial rights and we commercialize Betrixaban in China ourselves or grant a third party the right to do so, or if we terminate Lee's option under the agreement, we are required to make certain payments to Lee's.

Unless earlier terminated, this agreement will continue until superseded by the execution of the agreement that grants to Lee's the commercial rights to Betrixaban in China. This agreement may be terminated by Lee's for convenience with 90 days' advance written notice, or by either party for the other party's uncured material breach or any material safety issue of Betrixaban. In addition, this agreement will automatically terminate if we fail to reach agreement to grant Lee's the commercial rights to Betrixaban in China, or if we terminate Lee's option.

Andexanet alfa

BMS and Pfizer agreements

In October 2012, we entered into a collaboration agreement with BMS and Pfizer, to include subjects dosed with apixaban, their jointly owned product candidate, in one of our Phase 2 proof-of-concept studies of Andexanet alfa. We are responsible for the cost of conducting such clinical studies. This agreement will continue in force until the completion of the studies or termination by either party pursuant to the agreement.

In January 2014, we entered into a second collaboration agreement with BMS and Pfizer to further study Andexanet alfa as a reversal agent for their jointly owned product candidate apixaban through Phase 3 studies. The Phase 3 studies are expected to start in the first half of 2014. Under the terms of the agreement, we will receive an upfront payment of \$13.0 million and are eligible to receive additional development and regulatory milestone payments of up to \$12.0 million. These payments represent the total consideration under this agreement. BMS and Pfizer will continue to provide development and regulatory guidance for the program.

Under both agreements, we retain full, worldwide development and commercial rights to Andexanet alfa.

This second collaboration agreement will continue in force until the approval of Andexanet alfa as a reversal agent for apixaban by the FDA and EMA. BMS and Pfizer may terminate this agreement for convenience with 60 days' advance written notice or for our bankruptcy or change of control. In addition, either party may terminate this agreement for the other party's uncured material breach, material safety issues, or failure of the Phase 3 studies.

Bayer and Janssen agreements

In February 2013, we entered into a clinical collaboration agreement with Bayer and Janssen to include subjects dosed with rivaroxaban, their Factor Xa inhibitor product, in one of our Phase 2 proof-of-concept studies of Andexanet alfa. We are responsible for the cost of conducting such clinical studies. This agreement will continue in force until the later of the completion of the studies and the fulfillment of certain other conditions set forth in the agreement, unless earlier terminated by either party pursuant to the agreement.

In February 2014, we entered into a second collaboration agreement with Bayer and Janssen to evaluate Andexanet alfa as a reversal agent for the FDA-approved oral Factor Xa inhibitor rivaroxaban through Phase 3 studies. Our original collaboration agreement with Bayer and Janssen covers the conduct of a Phase 2 proof-of-concept study. The new collaboration agreement covers the conduct of Phase 3 studies of Andexanet alfa with rivaroxaban and any potential U.S. and EU regulatory approval of Andexanet alfa as reversal agent of rivaroxaban. The Phase 3 studies are expected to start in the first half of 2014. Under this new collaboration agreement, we will receive an upfront payment of \$10 million and are eligible to receive additional development and regulatory milestone payments of up to \$15.0 million. These payments represent the total consideration under this agreement. Bayer and Janssen will continue to provide development and regulatory guidance for the program.

Under both agreements, we retain full, worldwide development and commercial rights to Andexanet alfa.

This second collaboration agreement will continue in force until the approval of Andexanet alfa as a reversal agent for rivaroxaban by the FDA and EMA. Bayer and Janssen may terminate this agreement for convenience with 60 days' advance written notice or for our bankruptcy or change of control. In addition, either party may terminate this agreement for the other party's uncured material breach or material safety issues, and we can also terminate this agreement for failure of the Phase 3 studies..

Daiichi Sankyo agreement

In June 2013, we entered into an agreement with Daiichi Sankyo to include subjects dosed with edoxaban, their Factor Xa inhibitor product, in one of our proof-of-concept studies of Andexanet alfa. We are responsible for the costs of conducting this clinical study. This agreement will continue in force until the later of the completion of the studies and the fulfillment of certain other conditions set forth in the agreement, unless earlier terminated by either party pursuant to the agreement. This agreement does not grant Daiichi Sankyo any other rights with respect to the development or commercialization of Andexanet alfa.

PRT2607

Biogen Idec agreement

In October 2011, we entered into an exclusive worldwide license and collaboration agreement with Biogen Idec to develop and commercialize PRT2607 and certain highly selective Syk inhibitors. Biogen Idec made an upfront cash payment to us of \$36.0 million and purchased 636,042 shares of our Series 1 convertible preferred stock for an aggregate purchase price of \$9.0 million. Pursuant to the agreement, we had an option to lead development and commercialization efforts in the United States for select smaller indications, as well as discovery efforts for follow-on Syk inhibitors and an option to co-promote the drug alongside Biogen Idec with major indications in the United States. In November 2012, we elected to exercise our option to convert the agreement to a fully out-licensed agreement. After such election, we relinquished our right to share profits from sales of products related to Syk inhibitors, but are entitled to receive tiered royalties at low-double-digit percentages (not greater than 20%) from sales of these products by Biogen Idec if product sales are ever achieved. We no longer have an obligation to fund the

program under the agreement. The agreement also provides for additional payments to us of up to approximately \$370 million based on the occurrence of certain development and regulatory events. Biogen Idec has elected to assume all future development work for Syk inhibitors, including the major indications, such as rheumatoid arthritis and allergic asthma. To date, no development or regulatory events provided by the agreement have occurred and no royalties have been triggered under our agreement with Biogen Idec. This agreement will continue in force until either party terminates the agreement pursuant to the agreement or until the expiration of Biogen Idec's royalty obligations pursuant to the agreement, which is the later of the expiration of all relevant patents and regulatory exclusivities or 10 years after first commercial sale. Biogen Idec may terminate the agreement without cause upon 120 days' written notice or for cause if Portola commits a material breach of its obligations under the agreement and fails to cure the breach. We may terminate the agreement with proper written notice for cause if Biogen Idec commits a material breach of its obligations under the agreement and fails to cure the breach for 90 days (or 60 days for nonpayment of an amount due) after written notice is given, if Biogen Idec commences a legal action challenging the validity, enforceability or scope of any of the patents subject to the agreement or in the event of bankruptcy, reorganization, liquidation or receivership of Biogen Idec. In such event, we would regain all development rights and Biogen Idec would have no further payment obligations pursuant to the agreement.

Astellas agreement

In June 2005, we entered into an agreement to license certain exclusive rights to research, develop and commercialize Syk inhibitors from Astellas Pharma, Inc., or Astellas, which agreement was subsequently amended and restated in December 2010. The agreement with Astellas, as amended, requires us to make certain milestone, royalty and sublicense revenue sharing payments to Astellas as we develop, commercialize or sublicense Syk inhibitors. Pursuant to our agreement with Astellas, we made cash milestone payments to Astellas of \$500,000 in May 2005, \$500,000 in May 2006 and \$1.0 million in December 2008, as we elected to continue our development of Syk inhibitors. In addition, for each Syk inhibitor product, we may be required to make up to \$71.5 million in additional milestone payments to Astellas if the product is approved for multiple distinct indications in the United States, Europe and Japan and the product attains certain sales levels. If we grant a sublicense to develop and commercialize Syk inhibitors, we are required to pay Astellas 20% of any payments (excluding royalties) received under the sublicense agreement. In 2011, in connection with our receipt of the upfront payment under our agreement with Biogen Idec, we made a cash payment to Astellas of \$7.2 million. In addition, we are required to pay Astellas royalties at low single-digit percentages for worldwide sales for any Syk inhibitor product made by us or our sublicensees. This agreement will continue in force, on a product-by-product and country-by-country basis, until the expiration of relevant patents or ten years after the launch, whichever is later, or termination by either party pursuant to the agreement. The agreement may be terminated by us for convenience upon 60 days' written notice to Astellas or immediately upon written notice if all major claims of all of the patents covered by the agreement are invalidated by competent judicial or administrative authorities in the U.S. and no measure has been taken to appeal the invalidation. Either party may terminate the agreement upon written notice if the other party is in material breach of its obligations under the agreement for reasons within its control and responsibility and has not remedied the breach within 30 days of receiving written notice or in the event of bankruptcy, liquidation or receivership of the other party.

Cerdulatinib

Aciex agreement

In February 2013, we entered into a license and collaboration agreement with Aciex pursuant to which we granted Aciex an exclusive license to co-develop and co-commercialize Cerdulatinib and certain related compounds for nonsystemic indications, such as the treatment and prevention of ophthalmological diseases by topical administration and allergic rhinitis by intranasal administration. Under the agreement, we will share development costs with Aciex and be entitled to receive either a share of the profits generated by any eventual products or royalty payments. We retain rights to other indications, including dermatologic disorders.

Manufacturing and clinical research agreements

PPD development agreement

In January 2012, we entered into a master contract services agreement with PPD Development, LP, or PPD, under which PPD provides administrative, data management and statistical analysis services relating to our APEX study. Pursuant to this agreement as amended, PPD is responsible for overseeing and managing the conduct of the APEX study in Asia and parts of Europe and Latin America. We will remain ultimately responsible for the study and have separate agreements with the sites performing the study, other clinical research organizations and other third party vendors. This agreement will remain in effect until the later of three years after its effective date or the completion of services by PPD. Portola may terminate the agreement with 30 days' notice or immediately upon a material breach of the agreement by PPD that cannot be cured. PPD may terminate the agreement immediately upon a material breach of the agreement by us that cannot be cured or, 30 days after giving notice of a curable material breach of the agreement by us, if we have not cured such breach.

Hovione manufacturing agreement

In January 2007, we entered into a development and manufacturing service agreement with Hovione Inter Limited, or Hovione, as amended on February 1, 2013, pursuant to which Hovione is producing the active pharmaceutical ingredient, or API, for Betrixaban for use in our APEX study. Under the agreement, Hovione produces the API using our proprietary process and to our specified quality standards and in compliance with applicable regulations. Hovione produces the API pursuant to work orders submitted by us and agreed to by Hovione, though Hovione is not under any obligation to enter into any work order. We expect that we will need to enter into additional work orders with Hovione in order to produce the remaining API necessary to file an NDA. The agreement remains in effect until the later of seven years after its effective date or the completion of any outstanding work orders. The agreement may be extended continuously for additional two-year periods upon agreement of the parties. We may terminate the agreement for convenience with 60 days' written notice and either party may terminate the agreement with 60 days' written notice upon the bankruptcy of the other party, the failure of the other party to cure a material breach of the agreement within 30 days of receiving notice of such breach, the occurrence of events that prevents the other party from performing its obligations or if either party determines that the agreement is detrimental to its interests and can demonstrate that it would be in the best interests of both parties to terminate the agreement.

Lonza manufacturing agreement

In anticipation of a potential BLA filing and subsequent commercialization, we signed an agreement in June 2013 with Lonza Group Ltd, or Lonza, to develop a commercial-scale manufacturing process for Andexanet alfa. We have transferred the manufacturing process previously run at CMC-ICOS for Andexanet alfa to Lonza and have started commercial scale manufacturing at Lonza. Our Phase 3 studies will start with clinical material from CMC ICOS. Non-clinical studies are planned to establish comparability between CMC-ICOS and Lonza material such that Lonza material can be used in in the BLA-enabling clinical program. The process at Lonza requires further demonstration and validation prior to BLA filing for conditional approval. In parallel, we are making process improvements in order to increase scale and efficiency to further improve cost of goods which will be incorporated into the commercial production of Andexanet alfa through a supplemental BLA filing.

Competition

Our industry is highly competitive and subject to rapid and significant technological change. While we believe that our development experience and scientific knowledge provide us with competitive advantages, we may face competition from large pharmaceutical and biotechnology companies, smaller pharmaceutical and biotechnology companies, specialty pharmaceutical companies, generic drug companies, academic institutions, government agencies and research institutions and others.

Many of our competitors may have significantly greater financial, technical and human resources than we have. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Our commercial opportunity could be reduced or eliminated if our competitors develop or market products or other novel technologies that are more effective, safer or less costly than any that will be commercialized by us, or obtain regulatory approval for their products more rapidly than we may obtain approval for ours. Our success will be based in part on our ability to identify, develop and manage a portfolio of drugs that are safer, more efficacious and/or more cost-effective than alternative therapies.

Betrixaban

In the market for VTE prophylaxis in acute medically ill patients, Betrixaban, if approved, will compete with enoxaparin, which is marketed as Lovenox by Sanofi and as a generic pharmaceutical by several manufacturers, and

to a lesser extent with other low molecular weight heparins. In addition, Betrixaban may face competition in the market for acute medically ill patients from other Factor Xa inhibitors including apixaban, which is marketed by BMS and Pfizer, edoxaban, which is marketed by Daiichi Sankyo, rivaroxaban, which is marketed by Bayer and Janssen, and the direct thrombin inhibitor dabigatran, which is marketed by Boehringer Ingelheim, although none of these molecules is currently approved for use in that population. We believe, however, that in light of the significant opportunity in this acute medically ill population, one of these agents will likely be tested in a Phase 3 study. As the dosing regimen for an anticoagulant typically varies based on the indication in which it is used and anticoagulants often work in one indication but not another, we and our clinical advisors think it is unlikely that a significant number of physicians will choose to prescribe a Factor Xa inhibitor in the acute medically ill patient population absent a relevant regulatory approval or clinical evidence supporting its use. In the future, owners of approved direct Factor Xa or thrombin inhibitors may decide to develop them for VTE prophylaxis in the acute medically ill patient population although nothing is in development for that indication to our knowledge. In addition, they or other competitors may decide to develop new therapies for VTE prophylaxis in acute medically ill patients.

Andexanet alfa

Currently there are no therapies approved as antidotes for Factor Xa inhibitors. However, Andexanet alfa, if approved, may compete with currently approved treatments designed to enhance coagulation including fresh frozen plasma, prothrombin complex concentrates, rFVIIa, Vitamin K, protamine or whole blood. In addition, several companies have conducted preclinical research on compounds that are intended to reverse the effects of one or more direct Factor Xa inhibitors and which, if developed, may be competitive with Andexanet alfa. One of the companies, Perosphere Inc., has initiated a Phase 1 trial of its reversal agent in 2013.

Cerdulatinib

In the market for the treatment of CLL and NHL, Cerdulatinib, if approved, will compete with existing therapies, such as rituximab, which is marketed by Chugai Pharmaceutical Co., F. Hoffmann-LaRoche Ltd. and Genentech, Inc., and potentially other therapies currently in development by a number of different companies.

PRT2607

In the market for treatment of allergic asthma, PRT2607, if approved, will compete with existing products, such as inhaled corticosteroids, leukotriene modifiers and long-acting beta agonists and potentially with other products currently in development by a number of different companies.

Intellectual property

Our success will significantly depend upon our ability to obtain and maintain patent and other intellectual property and proprietary protection for our drug candidates, including composition-of-matter, dosage and formulation patents, as well as patent and other intellectual property and proprietary protection for our novel biological discoveries and other important technology inventions and know-how. In addition to patents, we rely upon unpatented trade secrets, know-how, and continuing technological innovation to develop and maintain our competitive position. We protect our proprietary information, in part, using confidentiality agreements with our commercial partners, collaborators, employees and consultants and invention assignment agreements with our employees. We also have confidentiality agreements or invention assignment agreements with our commercial partners and selected consultants. Despite these measures, any of our intellectual property and proprietary rights could be challenged, invalidated, circumvented, infringed or misappropriated, or such intellectual property and proprietary rights may not be sufficient to permit us to take advantage of current market trends or otherwise to provide competitive advantages. For more information, please see “Risk factors—Risks related to intellectual property.”

As of December 31, 2013, we owned 29 issued U.S. patents, 33 U.S. patent applications and 96 issued patents and 177 patent applications in other jurisdictions. We also co-owned 11 additional patents and patent applications. In addition, as of December 31, 2013, we have licensed 164 issued patents and 67 patent applications from third parties, mostly on an exclusive basis. The patent portfolios for our leading product candidates as of December 31, 2013 are summarized below:

Betrixaban

Our Betrixaban patent portfolio includes 15 issued U.S. patents and 8 U.S. patent applications covering the composition of and methods of making and using Betrixaban or its analogs, including those owned by us and those licensed in from Millennium. The U.S. issued patents relating to the composition of matter of Betrixaban are not due to expire before September 2020 and may be extended to up to September 2025 pursuant to the Hatch-Waxman Act, and Betrixaban may also be eligible for an additional 6 months of pediatric exclusivity under the Best Pharmaceuticals

for Children Act as described below. Related international patent applications have issued or been allowed in 35 countries and are pending in Europe and a number of other countries. These international patents and patent applications, if issued, would not be due to expire before September 2020.

In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act, permits a patent term extension of up to five years for one patent related to an approved therapy. The length of the extension is based upon the period of time the therapy has been under regulatory review. We believe that, if Betrixaban is approved, we will be eligible for a full five year patent term extension for one patent relating to Betrixaban.

In addition, in the United States, the Best Pharmaceuticals for Children Act provides that the period of patent exclusivity for a drug may be extended for six months if the owner of the drug conducts studies of the drug in children pursuant to a request from the FDA. We believe that there may be pediatric applications for Betrixaban and, therefore, that it may be possible for us to obtain an additional 6 months of pediatric exclusivity of Betrixaban by conducting FDA-requested studies in children.

Andexanet alfa

Our Factor Xa inhibitor antidote patent portfolio is wholly owned by us and includes four issued U.S. patents and 11 U.S. patent applications covering the composition of and methods of making and using Andexanet alfa or its analogs.

The U.S. issued patents are not due to expire before June 2030. A related international patent application has issued in New Zealand and China, another related international patent application has issued in New Zealand and allowed in Singapore and international patent applications are pending in Europe and a number of other countries. These international patents and patent applications, if issued, would not be due to expire before September 2028.

Cerdulatinib

Our dual Syk-JAK inhibitor patent portfolio is owned in part by us and licensed in part from Astellas and includes four issued U.S. patents covering the composition of and methods of making and using Cerdulatinib or its analogs. The last to expire of the U.S. patents is currently expected to expire in July 2029. Related international patent applications have issued or been allowed in 12 countries and are pending in Europe and a number of other countries. These international patents and patent applications, if issued, would not be due to expire before April 2029.

PRT2607

Our Syk-specific inhibitor patent portfolio is owned by us and includes five issued U.S. patents covering the composition of and methods of making and using PRT2607 or its analogs. The last to expire of the U.S. patents is currently expected to expire in July 2029. Related international patent applications have issued or been allowed in five countries and are pending in Europe and a number of other countries. These international patents and patent applications, if issued, would not be due to expire before April 2029.

Manufacturing

We rely on contract manufacturing organizations, or CMOs, to produce our drug candidates in accordance with the FDA's current Good Manufacturing Practices, or cGMP, regulations for use in our clinical studies. The manufacture of pharmaceuticals is subject to extensive cGMP regulations, which impose various procedural and documentation requirements and govern all areas of record keeping, production processes and controls, personnel and quality control. Our small molecule drug candidates, Betrixaban, Cerdulatinib and PRT2607, are manufactured using common chemical engineering and synthetic processes from readily available raw materials. We rely on Hovione to produce API for Betrixaban for our APEX study. Pursuant to a development and manufacturing service agreement between us and Hovione, Hovione produces the API for Betrixaban using our proprietary process and to our specified quality standards and in compliance with applicable regulations. Hovione produces the API pursuant to work orders submitted by us and agreed to by Hovione, though Hovione is not under any obligation to enter into any work order and may terminate the agreement under certain conditions. We expect that we will need to enter into additional work orders with Hovione in order to produce the remaining API necessary to file an NDA. Andexanet alfa is a recombinant biologic molecule produced in living cells, a process that is inherently complex and requires specialized knowledge and extensive process optimization and product characterization to transform laboratory scale processes into reproducible commercial manufacturing processes. We have signed a development and manufacturing service agreement with Lonza and are currently working on multiple strategies to develop an economical, commercial scale production process for Andexanet alfa. Pursuant to that agreement, Lonza will fully develop a commercial scale manufacturing process for Andexanet alfa and produce approval enabling validation lots.

We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. To meet our projected needs for clinical supplies to support our activities through regulatory approval and commercial

manufacturing, the CMOs with whom we currently work will need to increase scale of production or we will need to secure alternate suppliers. We believe that there are multiple potential sources for our contract manufacturing, but we have not engaged alternate suppliers in the event that our current CMOs are unable to scale production. Our relationships with CMOs are managed by internal personnel with extensive experience in pharmaceutical development and manufacturing.

If we are unable to obtain sufficient quantities of drug candidates or receive raw materials in a timely manner, we could be required to delay our ongoing clinical studies and seek alternative manufacturers, which would be costly and time-consuming.

Government regulation

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the clinical development, manufacture and marketing of pharmaceutical products. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion of our products.

The process required by the FDA before product candidates may be marketed in the United States generally involves the following:

- nonclinical laboratory and animal testing of the product including some that must be conducted in accordance with Good Laboratory Practices or GLPs;
- submission of an investigational new drug application, or IND, which must become effective before human clinical trials may begin;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug candidate for its intended use;
- pre-approval inspection of manufacturing facilities and selected clinical investigators for their compliance with Good Manufacturing Practices, or GMP, and Good Clinical Practices or GCPs; and
- Approval of an NDA, for a drug or a BLA, for a biologic prior to commercial marketing for specific indications for use.

The testing and approval process requires substantial time, effort and financial resources. Prior to commencing the first clinical trial with a product candidate, we must submit an IND to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns about the supporting safety data or questions about the design of the clinical trial and imposes a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development. Further, an independent institutional review board for each medical center proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial commences at that center. Regulatory authorities or an institutional review board or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. Some studies also include an Independent Data Monitoring Committee, or IDMC, which receives special access to unblinded data during the clinical trial and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. The IDMC may halt a trial if it feels that the data demonstrate efficacy of the drug and it is no longer ethical to withhold the drug from patients in the control arm of the study.

For purposes of NDA or BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap.

Phase 1 – Studies are initially conducted to test the product candidate for safety, dosage tolerance, absorption, metabolism, distribution and excretion in healthy volunteers or patients.

Phase 2 – Studies are conducted with groups of patients with a specified disease or condition to provide enough data to evaluate the preliminary efficacy, optimal dosages and dosing schedule and expanded evidence of safety. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

Phase 3 – Phase 3 clinical trials are undertaken in large patient populations to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety in an expanded patient population at multiple clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product

compared to placebo or current standard of care and provide an adequate basis for product labeling. These trials may be done globally to support global registrations.

The FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called Phase 4 studies may be made a condition to be satisfied after approval. The results of Phase 4 studies can confirm the effectiveness of a product candidate and can provide important safety information gathered in routine medical practice.

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Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must also develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to establish an appropriate shelf life for the product candidate including data demonstrating that the product candidate does not undergo unacceptable deterioration over its shelf life.

NDA or BLA submission and review by the FDA

The results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of an NDA or BLA. The submission of an NDA or BLA requires payment of a substantial User Fee to FDA. The FDA may convene an advisory committee to provide independent expert clinical opinion on application review questions. The FDA reviews applications to determine, among other things, whether a product is safe and effective for its intended use and whether the manufacturing controls are adequate to assure consistent batch to batch purity, identity, potency, and strength of the product candidate. Before approving an NDA or BLA, the FDA will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes, equipment and facilities are in compliance with cGMP requirements. Once the NDA submission has been accepted for filing (sixty days post receipt of the application by the FDA), the FDA typically takes ten months to review the application and respond to the applicant, which can take the form of either a Complete Response Letter or Approval. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA may delay or refuse approval of an NDA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product. FDA approval of any NDA or BLA submitted by us will be at a time the FDA chooses. Also, if regulatory approval of a product is granted, such approval may entail limitations on the indicated uses for which such product may be marketed and require post-marketing requirements such as a Risk Evaluation and Mitigation Procedure or a Phase 4 study. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing regulatory standards is not maintained or if problems occur after the product reaches the marketplace. In addition, the FDA may require Phase 4 post-marketing studies to monitor the effect of approved products, and may limit further marketing of the product based on the results of these post-marketing studies.

The FDA has a fast track program that is intended to expedite or facilitate the process for reviewing new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for fast track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. For a fast track product, the FDA may consider review of completed sections of an NDA or BLA on a rolling basis provided the sponsor provides, and the FDA accepts, a schedule for the submission of the completed sections of the NDA or BLA. Under these circumstances, the sponsor pays any required user fees upon submission of the first section of the NDA or BLA. A fast track designated drug candidate may also qualify for priority review, under which the FDA reviews the NDA or BLA in a total of six months rather than ten months after it is accepted for filing.

Post-approval requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including record-keeping requirements and reporting of adverse experiences. Drug and biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with GMP, which

impose certain procedural and documentation requirements upon us and our third-party manufacturers. We cannot be certain that we or our present or future suppliers will be able to comply with the GMP regulations and other FDA regulatory requirements. If our present or future suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, require us to recall a product from distribution, or withdraw approval of the NDA or BLA.

The FDA closely regulates the marketing and promotion of drugs. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use.

Healthcare and reimbursement regulation

Our sales, promotion, medical education and other activities following product approval will be subject to regulation by numerous regulatory and law enforcement authorities in the United States in addition to FDA, including potentially the Federal Trade Commission, the Department of Justice, the Centers for Medicare and Medicaid Services, other divisions of the Department of Health and Human Services and state and local governments. Our promotional and scientific/educational programs must comply with the anti-kickback provisions of the Social Security Act, the Foreign Corrupt Practices Act, the False Claims Act, the Veterans Health Care Act and similar state laws.

Depending on the circumstances, failure to meet these applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of pre-marketing product approvals, private “qui tam” actions brought by individual whistleblowers in the name of the government or refusal to allow us to enter into supply contracts, including government contracts.

Sales of pharmaceutical products depend significantly 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 products. However, these third-party payors are increasingly challenging the price and examining the cost-effectiveness of medical products and services. In addition, significant uncertainty exists as to the reimbursement status of newly approved healthcare products. We may need to conduct expensive pharmacological studies to demonstrate the cost-effectiveness of our products. The product candidates that we develop may not be considered cost-effective. It is time consuming and expensive for us to seek reimbursement from third-party payors. Reimbursement may not be available or sufficient to allow us to sell our products on a competitive and profitable basis.

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

Foreign regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products to the extent we choose to develop or sell any products outside of the United States. The approval process varies from country to country and the time may be longer or shorter than that required to obtain FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

EU member states require both regulatory clearances by the national competent authority and a favorable ethics committee opinion prior to the commencement of a clinical trial. Under the EU regulatory systems, we may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all EU member states. The centralized procedure is compulsory for medicines produced by certain biotechnological processes, products with a new active substance indicated for the treatment of certain diseases, such as neurodegenerative disorder or diabetes and products designated as orphan medicinal products and optional for those products which are highly innovative or for which a centralized process is in the interest of patients. The decentralized procedure of approval provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state, known

as the reference member state. Under the decentralized approval 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.

Employees

As of December 31, 2013, we had 70 full-time employees, 14 of whom hold Ph.D. degrees and four of whom hold M.D. degrees. Of the full-time employees, 45 employees are engaged in research and development and 25 are engaged in general administration, business development and marketing. Our employees are not represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Facilities

We lease approximately 50,000 square feet of research and office space in South San Francisco, California under a lease that expires in March 2015. Thereafter, at our option, we may extend the term for an additional three years to March 2018. In January 2014, we signed a letter of intent to extend our lease for five years through 2019. We believe that our existing facilities are sufficient for our current needs for the foreseeable future.

Legal proceedings

We are not currently a party to any material legal proceedings.

Corporate and Available Information

Our principal corporate offices are located at 270 E. Grand Avenue, South San Francisco, California 94080 and our telephone number is (650) 246-7000. We were incorporated in Delaware in September 2003. Our internet address is www.portola.com. We make available on our website, free of charge, our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission, or the SEC. Our SEC reports can be accessed through the Investors section of our internet website. Further, a copy of this Annual Report on Form 10-K is located at the SEC's Public Reference Rooms at 100 F Street, N.E., Washington, D. C. 20549. Information on the operation of the Public Reference Room can be obtained by calling the SEC at 1-800-SEC-0330. The SEC maintains a website that contains reports, proxy and information statements and other information regarding our filings at <http://www.sec.gov>. The information found on our internet website is not incorporated by reference into this Annual Report on Form 10-K or any other report we file with or furnish to the SEC.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012. As such, we are eligible for exemptions from various reporting requirements applicable to other public companies that are not emerging growth companies, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002 and reduced disclosure obligations regarding executive compensation. We will remain an emerging growth company until the earlier of (1) December 31, 2018, (2) the last day of the fiscal year (a) in which we have total annual gross revenue of at least \$1.0 billion or (b) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th, and (3) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period.

Item 1A. RISK FACTORS.

Investing in our common stock involves a high degree of risk. You should consider carefully the following risks, together with all the other information in this Annual Report on Form 10-K, including our financial statements and notes thereto, before you invest in our common stock. If any of the following risks actually materializes, our operating results, financial condition and liquidity could be materially adversely affected. As a result, the trading price of our common stock could decline and you could lose part or all of your investment.

RISKS RELATED TO OUR FINANCIAL CONDITION AND NEED FOR ADDITIONAL CAPITAL

Although we reported net income for the years ended December 31, 2012 and December 31, 2011, we have incurred significant losses prior to 2011 and for the year ended December 31, 2013 and expect to incur substantial and increasing losses for the foreseeable future.

We are a clinical-stage biopharmaceutical company. We do not currently have any products approved for sale, and we continue to incur significant research and development and general and administrative expenses related to our operations. Although we reported net income for the years ended December 31, 2012 and December 31, 2011, this was primarily due to the recognition of all remaining deferred revenue following the termination of two of our collaboration agreements. We have incurred significant operating losses prior to 2011 and for the year ended December 31, 2013 and expect to incur substantial and increasing losses for the foreseeable future. As of December 31, 2013, we had an accumulated deficit of \$285.7 million.

To date, we have financed our operations primarily through private placements of our convertible preferred stock, sale of our common stock in our initial public offering and follow-on offering, collaborations and, to a lesser extent, government grants, equipment leases, venture debt and with the benefit of tax credits made available under a federal stimulus program supporting drug development. We have devoted substantially all of our efforts to research and development, including clinical studies, but have not completed development of any product candidates. We anticipate that our expenses will increase substantially as we:

- initiate or continue clinical studies of our three most advanced product candidates;
- continue the research and development of our product candidates;
- seek to discover or in-license additional product candidates;
- seek regulatory approvals for our product candidates that successfully complete clinical studies;
- establish a sales, marketing and distribution infrastructure and scale-up manufacturing capabilities to commercialize products for which we may obtain regulatory approval, including process improvements in order to manufacture Andexanet alfa, formerly PRT4445, at commercial scale; and
- enhance operational, financial and information management systems and hire more personnel, including personnel to support development of our product candidates and, if a product candidate is approved, our commercialization efforts.

To be profitable in the future, we must succeed in developing and eventually commercializing products with significant market potential. This will require us to be successful in a range of activities, including advancing our product candidates, completing clinical studies of our product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling those products for which we may obtain regulatory approval. We are only in the preliminary stages of some of these activities. We may not succeed in these activities and may never generate revenue that is sufficient to be profitable in the future. Even if we are profitable, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to achieve sustained profitability would depress the value of our company and could impair our ability to raise capital, expand our business, diversify our product candidates, market our product candidates, if approved, or continue our operations.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.

Our quarterly and annual operating results may fluctuate significantly in the future, which makes it difficult for us to predict our future operating results. From time to time, we enter into collaboration agreements with other companies that include development funding and significant upfront and milestone payments, and we expect that amounts earned from our collaboration agreements will continue to be an important source of our revenue. Accordingly, our revenue will depend on development funding and the achievement of development and clinical milestones under our existing collaboration arrangements, as well as any potential future collaboration and license agreements and sales of our products, if approved. These upfront and milestone payments may vary significantly from period to period and any such variance could cause a significant fluctuation in our operating results from one period to the next. For example, in the year ended December 31, 2011, we recognized all remaining deferred revenue of approximately \$8.3 million following the termination of our exclusive worldwide license and collaboration agreement with Merck & Co., Inc., or Merck, and in the year ended December 31, 2012, we recognized all remaining deferred revenue of approximately \$65.1 million following the termination of our worldwide license agreement with Novartis Pharma A.G., or Novartis. In addition, we measure compensation cost for stock-based awards made to employees at the grant date of the award, based on the fair value of the award as determined by our board of directors, and recognize the cost as an expense over the employee's requisite service period. As the variables that we use as a basis for valuing these awards change over time, including our underlying stock price and stock price volatility, the magnitude of the expense that we must recognize may vary significantly. Furthermore, our operating results may fluctuate due to a variety of other factors, many of which are outside of our control and may be difficult to predict, including the following:

the timing and cost of, and level of investment in, research and development activities relating to our product candidates, which may change from time to time;

the cost of manufacturing our product candidates, which may vary depending on United States Food and Drug Administration, or FDA, guidelines and requirements, the quantity of production and the terms of our agreements with manufacturers;

expenditures that we will or may incur to acquire or develop additional product candidates and technologies;

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the level of demand for our product candidates, should they receive approval, which may vary significantly; future accounting pronouncements or changes in our accounting policies; the timing and success or failure of clinical studies for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners; the risk/benefit profile, cost and reimbursement policies with respect to our products candidates, if approved, and existing and potential future drugs that compete with our product candidates; and the changing and volatile global economic environment.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue and/or earnings guidance we may provide.

We will need additional funds to support our operations, and such funding may not be available to us on acceptable terms, or at all, which would force us to delay, reduce or suspend our research and development programs and other operations or commercialization efforts. Raising additional capital may subject us to unfavorable terms, cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our product candidates and technologies.

We are advancing multiple product candidates through the research and clinical development process. The completion of the development and the potential commercialization of our product candidates, should they receive approval, will require substantial funds. As of December 31, 2013, we had \$319.0 million in cash, cash equivalents and investments. We believe that our available cash, cash equivalents and investments will be sufficient to fund our anticipated level of operations for at least the next 12 months. Our future financing requirements will depend on many factors, some of which are beyond our control, including the following:

the rate of progress and cost of our clinical studies;
the timing of, and costs involved in, seeking and obtaining approvals from the FDA and other regulatory authorities;
the costs of commercialization activities if any of our product candidates is approved, including product sales, marketing, manufacturing and distribution;
the degree and rate of market acceptance of any products launched by us or future partners;
our ability to enter into additional collaboration, licensing, commercialization or other arrangements and the terms and timing of such arrangements; and
the emergence of competing technologies or other adverse market developments.

We do not have any material committed external source of funds or other support for our development efforts other than our exclusive worldwide license and collaboration agreement with Biogen Idec Inc., or Biogen Idec, for the development and commercialization of PRT2607 and other highly selective Syk inhibitors, which is terminable by Biogen Idec without cause upon 120 days' notice. Until we can generate a sufficient amount of product revenue to finance our cash requirements, which we may never do, we expect to finance future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing and distribution arrangements. Additional financing may not be available to us when we need it or it may not be available on favorable terms. If we raise additional capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish certain valuable rights to our product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us. If we raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we are unable to obtain adequate financing when needed, we may have to delay, reduce the scope of, or suspend one or more of our clinical studies or research and development programs or our commercialization efforts.

Risks related to the development and commercialization of our product candidates

Our success depends heavily on the approval and successful commercialization of our lead product candidates, Betrixaban and Andexanet alfa along with Cerdulatinib and our selective Syk inhibitor program. Clinical studies of these product candidates may not be successful. If we are unable to commercialize one or more of our product candidates, or experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources into the development of Betrixaban, a novel oral once-daily inhibitor of Factor Xa, an enzyme involved in the body's coagulation system, that seeks to inhibit the blood coagulation process, and Andexanet alfa, a recombinant protein designed to reverse the anticoagulant activity in patients treated with a Factor Xa inhibitor who suffer an uncontrolled bleeding episode or undergo emergency surgery, and, to a lesser extent, Cerdulatinib and our selective Syk inhibitor program. Our ability to generate product revenue, which we do not expect to occur for at least the next several years, if ever, will depend heavily on the successful development, regulatory approval and eventual commercialization of one of our product candidates. The success of our product candidates will depend on several factors, including the following:

- successful enrollment in, and completion of, clinical studies;
- our ability to reach agreement with the FDA and other regulatory authorities on the appropriate regulatory path for approval of our product candidates, particularly Andexanet alfa;
- receipt of marketing approvals from the FDA and similar regulatory authorities outside the United States for our product candidates;
- establishing commercial manufacturing arrangements with third parties;
- ability to manufacture product at commercially acceptable costs;
- launching commercial sales of any product candidate that may be approved, whether alone or in collaboration with others;
- acceptance of any approved product by the medical community, third-party payors and patients;
- effectively competing with other therapies;
- a continued acceptable safety profile of the product following approval; and
- obtaining, maintaining, enforcing and defending intellectual property rights and claims.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business.

If clinical studies of our product candidates fail to demonstrate safety and efficacy to the satisfaction of the FDA or similar regulatory authorities outside the United States or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

Before obtaining regulatory approval for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of our product candidates in humans. Clinical studies are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. A failure of one or more of our clinical studies could occur at any stage of testing. The outcome of preclinical testing and early clinical studies may not be predictive of the success of later clinical studies, and interim results of a clinical study do not necessarily predict final results.

For example, the favorable results from our Phase 2 clinical studies of Betrixaban, which involved the prophylaxis, or preventive treatment, against venous thromboembolism, or VTE, in patients receiving total knee replacements and the prevention of stroke in patients with atrial fibrillation, may not be predictive of success in our current Phase 3 clinical study of Betrixaban, which we refer to as APEX, for extended duration VTE prophylaxis both in-hospital and post-discharge for up to 35 days in acute medically ill patients with restricted mobility and other risk factors, as the Phase 2 studies were not designed to demonstrate statistically significant effectiveness, were in different medical conditions, involved different patient populations or dosing regimens, were of different duration or had different comparators. Any of these factors and other factors could result in Betrixaban showing decreased activity or increased safety risks in our APEX study as compared to the Phase 2 studies. Moreover, the probability of our APEX study succeeding is highly dependent on the adequacy of its design. Two other Factor Xa inhibitors have failed in Phase 3 trials for the indication that we are pursuing for Betrixaban. We have reviewed publicly available data from those studies and incorporated the results of our analysis into the design of our APEX study, but we could have misinterpreted the data or performed a flawed analysis. Furthermore, relevant information from the studies may not be publicly available or, if available, may not have been obtained by us. As a result, there could be flaws in the design of our APEX study that could cause it to fail. For example, our patient inclusion criteria for the APEX study selects for patients with a higher risk of VTE, and these patients may be more likely to experience a severe bleeding event, even though we attempt to exclude certain patients at higher risk of bleeding. If patients in the APEX study experience a higher than expected rate of severe bleeding events, the APEX study may fail to demonstrate a sufficient safety profile for Betrixaban. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain regulatory approval for the marketing of their products.

Similarly, the favorable results from our initial Phase 2 proof-of concept studies of Andexanet alfa, evaluating the effect of Andexanet alfa in healthy volunteers taking apixaban or rivaroxaban, may not be predictive of success in our other Phase 2 proof-of-concept studies or other later studies. We do not yet know how the results from our Phase 1 studies of Andexanet alfa or our Phase 2 study in healthy volunteers taking Andexanet alfa will translate into clinical outcomes in our intended target population of patients treated with a Factor Xa inhibitor who suffer an uncontrolled bleeding episode or undergo emergency surgery. Moreover, the results from our study to date of Andexanet alfa may not address the effect of repeat doses or allow a determination of the optimal therapeutic dose of Andexanet alfa for our intended target patient population.

We may experience numerous unforeseen events during, or as a result of, clinical studies that could delay or prevent our ability to receive regulatory approval or commercialize our product candidates, including the following:

clinical studies of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical studies or abandon product development programs;

the number of patients required for clinical studies of our product candidates may be larger than we anticipate, enrollment in these clinical studies may be insufficient or slower than we anticipate or patients may drop out of these clinical studies at a higher rate than we anticipate;

the cost of clinical studies or the manufacturing of our product candidates may be greater than we anticipate;

our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

we might have to suspend or terminate clinical studies of our product candidates for various reasons, including a finding that our product candidates have unanticipated serious side effects or other unexpected characteristics or that the patients are being exposed to unacceptable health risks;

regulators may not approve our proposed clinical development plans;

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regulators or institutional review boards may not authorize us or our investigators to commence a clinical study or conduct a clinical study at a prospective study site;
regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements; and
the supply or quality of our product candidates or other materials necessary to conduct clinical studies of our product candidates may be insufficient or inadequate.

If we are required to conduct additional clinical studies or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical studies of our product candidates or other testing, if the results of these studies or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications that are not as broad as intended;
- have the product removed from the market after obtaining marketing approval;
- be subject to additional post-marketing testing requirements; or
- be subject to restrictions on how the product is distributed or used.

Our product development costs will also increase if we experience delays in testing or approvals. We do not know whether any clinical studies will begin as planned, will need to be restructured or will be completed on schedule, or at all. For example, in 2010, we suspended our Phase 1 clinical study of PRT2607 in order to investigate potentially adverse toxicology findings in an animal study that was being conducted concurrently. A follow-up study determined that there was not a significant safety risk, but the completion of the study was delayed by approximately nine months.

Significant clinical study delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which would impair our ability to commercialize our product candidates and harm our business and results of operations.

If serious adverse side effects are identified during the development of any of our product candidates, we may need to abandon our development of that product candidate.

None of our leading product candidates has completed clinical development. The risk of failure of clinical development is high. It is impossible to predict when or if any of our product candidates will prove safe enough to receive regulatory approval. For example, our lead product candidate Betrixaban, like all currently marketed inhibitors of Factor Xa, carries some risk of life-threatening bleeding. In addition, subjects taking Betrixaban had an increased rate of gastrointestinal issues, such as diarrhea, nausea and vomiting, and other side effects such as back pain, dizziness, headaches, rashes and insomnia as compared to subjects taking a placebo or an active comparator. There can be no assurance that our APEX study will not fail due to safety issues. In such an event, we might need to abandon development of Betrixaban or enter into a partnership to continue development.

The failure of two of our competitors' clinical trials evaluating Factor Xa inhibitors for VTE prophylaxis in acute medically ill patients may suggest an increased risk that our APEX trial for Betrixaban will also fail.

Two of our competitors' clinical trials evaluating Factor Xa inhibitors for VTE prophylaxis in acute medically ill patients have failed. The MAGELLAN trial sponsored by Bayer Pharma AG, or Bayer, and Janssen Pharmaceuticals, Inc., or Janssen, which evaluated rivaroxaban, demonstrated efficacy but failed to demonstrate an acceptable benefit to risk profile due to increased bleeding. The ADOPT trial sponsored by Bristol-Myers Squibb Company, which evaluated apixaban, showed a reduction in VTE events, but failed to demonstrate statistically significant efficacy and also showed an increase in bleeding. Betrixaban, like rivaroxaban and apixaban, may fail its clinical trials if it does not show a statistically significant level of efficacy or if the resulting bleeding risk is too high compared to its benefits.

Delays in the enrollment of patients in any of our clinical studies could increase our development costs and delay completion of the study.

We may not be able to initiate or continue clinical studies for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these studies as required by the FDA or other regulatory authorities. Even if we are able to enroll a sufficient number of patients in our clinical studies, if the pace of enrollment is slower than we expect, the development costs for our product candidates may increase and the completion of our studies may be delayed or our studies could become too expensive to complete.

For example, our APEX study is expected to enroll approximately 6,850 patients at approximately 400 study sites throughout the world. We have never previously conducted a study of this magnitude and can provide no assurance that we will be able to enroll patients at a sufficient pace to complete the study within our projected time frame. The first patient was enrolled in APEX in March 2012, and, based on current enrollment, we expect patient enrollment to be completed by the end of 2015, later than we initially estimated. Completing the study by that date will require us to continue to activate new clinical study sites and to enroll patients at forecasted rates at both new and existing clinical study sites. Our forecasts regarding the rates of clinical site activation and patient enrollment at those sites are based on a number of assumptions including assumptions based on past experience with our APEX study. However, there can be no assurance that those forecasts will be accurate or that we will complete our APEX study by the currently anticipated date. During the initial months of the APEX study, the number of clinical sites activated and the number of patients enrolled at each clinical site per month was lower than we had anticipated and, as a result, we made a number of adjustments to the clinical study plan, including increasing the number of clinical study sites. We can provide no assurance that those adjustments will be sufficient to enable us to complete the APEX study within our anticipated time frame. If we experience delays in enrollment, our ability to complete our APEX study could be materially adversely affected.

If we are unable to enroll the patients at the projected rate, the completion of the study could be delayed and the costs of conducting the study could increase, either of which could have a material adverse effect on our business. For example, in October 2012, we decided to increase the number of study sites for our APEX study and make certain changes to the management of the study in order to increase the enrollment rate, which had been slower than originally anticipated. These adjustments increased the cost of the study.

Even if our APEX study demonstrates statistically significant safety and efficacy of Betrixaban for extended duration VTE prophylaxis in acute medically ill patients both in-hospital and post-discharge for up to 35 days, the FDA or similar regulatory authorities outside the United States may not approve Betrixaban for marketing or may approve it with restrictions on the label, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Assuming the success of our APEX study, we anticipate seeking regulatory approval for Betrixaban in the United States for extended duration VTE prophylaxis in acute medically ill patients both in-hospital and post-discharge for up to 35 days. It is possible that the FDA may not consider the results of our APEX study to be sufficient for approval of Betrixaban for this indication. In general, the FDA suggests that sponsors complete two adequate and well-controlled clinical studies to demonstrate effectiveness because a conclusion based on two persuasive studies will be more compelling than a conclusion based on a single study. Although the FDA has informed us that our APEX study, plus supportive Phase 2 data obtained to date, could potentially provide sufficient safety and efficacy data for extended duration VTE prophylaxis in acute medically ill patients both in-hospital and post-discharge for up to 35 days, the FDA has further advised us that whether one or two adequate and well-controlled clinical studies are required will be a review issue in connection with a new drug application, or NDA, submission. Even if we achieve favorable results in our APEX study, the FDA may nonetheless require that we conduct additional clinical studies, possibly using a different clinical study design.

Even if the FDA or other regulatory authorities approve Betrixaban for VTE prophylaxis in acute medically ill patients, the approval may include additional restrictions on the label that could make Betrixaban less attractive to physicians and patients than other products that may be approved for broader indications, which could limit potential sales of Betrixaban.

If we fail to obtain FDA or other regulatory approval of Betrixaban or if the approval is for an indication that is narrower than what we seek, it could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We anticipate seeking regulatory approval of Andexanet alfa in the United States through an accelerated approval process, and since we have limited experience with this process, the development or commercialization of Andexanet alfa could be delayed or abandoned.

In November 2013, the FDA granted breakthrough therapy designation for Andexanet alfa which allows for an Accelerated Approval process. We currently plan to seek FDA approval of Andexanet alfa under the Accelerated Approval regulations. These regulations allow drugs that are being developed to treat an unmet medical need to be approved based on evidence of an effect on a surrogate biomarker endpoint rather than a clinical endpoint such as survival or irreversible morbidity. A surrogate or biomarker endpoint is defined as a laboratory or physical sign that is expected to predict the effect of the therapy. Use of an Accelerated Approval process provides a shortened timetable to approval, but a Phase 4 clinical study with clinical endpoints that will confirm the validity of the surrogate endpoint(s) must be ongoing at the time the License Application (BLA or NDA) is filed. We expect that this study will continue into commercialization. Because we have limited experience with the Accelerated Approval process, we may require more time and incur greater costs than anticipated and may not succeed in obtaining regulatory approval of Andexanet alfa. In addition, the FDA may subsequently determine that the studies conducted by us were insufficient to support approval or require us to conduct extensive post-approval studies. If the FDA determines that a randomized, placebo-controlled study demonstrating superior efficacy of Andexanet alfa in Factor Xa inhibitor treated patients experiencing a severe bleeding event is required for approval of Andexanet alfa, it may not be feasible to conduct such a trial or may take many years to complete at substantially greater cost.

Even if our product candidates receive regulatory approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

If any of our product candidates receive regulatory approval, they may nonetheless fail to gain sufficient market acceptance by physicians, hospital administrators, patients, healthcare payors and others in the medical community. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including the following:

- the prevalence and severity of any side effects;
- efficacy and potential advantages compared to alternative treatments;
- the price we charge for our product candidates;
- the willingness of physicians to change their current treatment practices;
- the willingness of hospitals and hospital systems to include our product candidates as treatment options;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support; and
- the availability of third-party coverage or reimbursement.

For example, while there are no approved therapies for VTE prophylaxis in acute medically ill patients approved for use beyond the typical hospitalization period, there are therapies available for in-hospital use and physicians may not be willing to change their current in-hospital treatment practices in favor of Betrixaban. If our product candidates, if approved, do not achieve an adequate level of acceptance, we may not generate significant product revenue and we may not become profitable on a sustained basis.

Our product candidates have never been manufactured on a commercial scale, and there are risks associated with scaling up manufacturing to commercial scale. In particular, we will need to develop a larger scale manufacturing process that is more efficient and cost-effective to commercialize Andexanet alfa, which may not be successful, and which will require us to transfer our production to another manufacturer, potentially delaying regulatory approval and commercialization.

Our product candidates have never been manufactured on a commercial scale, and there are risks associated with scaling up manufacturing to commercial scale including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, lot consistency and timely availability of raw materials. Even if we could otherwise obtain regulatory approval for any product candidate, there is no assurance that our manufacturer will be able to manufacture the approved product to specifications acceptable to the FDA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product or to meet potential future demand. If our manufacturer is unable to produce sufficient quantities of the approved product for commercialization, our commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

In particular, we face uncertainties and risks associated with scaling up the manufacturing for Andexanet alfa. Andexanet alfa is a biological molecule, or biologic, rather than a small molecule chemical compound like our other product candidates. The manufacture of biologics involves complex processes, including developing cells or cell systems to produce the biologic, growing large quantities of such cells and harvesting and purifying the biologic produced by them. As a result, the cost to manufacture biologics is generally far higher than traditional small molecule chemical compounds, and the manufacturing process is less reliable and is difficult to reproduce. Andexanet alfa is currently produced for us by a third-party contract manufacturer using a small-scale process that is too expensive and inefficient to support the commercialization of Andexanet alfa in the dosages and at the sales volumes and price that would be necessary for a commercially viable drug. We have entered into an agreement with a third party manufacturer to develop a more efficient, larger-scale commercial manufacturing process. However, scaling up and improving a biologic manufacturing process is a difficult and uncertain task, and we can give no assurance that we will be successful in developing and implementing this new process. In particular, we will need to demonstrate that the new process produces material that is comparable to the material we previously used. Demonstrating comparability can require significant pre-clinical and clinical studies. If we are not able to demonstrate comparability, then the material would be considered a new biological entity and a full Biologics License Application, or BLA, submission would be required for approval. Additionally, if the therapeutically effective dosage of Andexanet alfa is higher than we anticipate or the obtainable sales price is lower than we anticipate, we may not be able to successfully commercialize Andexanet alfa.

We currently have no sales or distribution personnel and only limited marketing capabilities. If we are unable to develop a sales and marketing and distribution capability on our own or through collaborations or other marketing partners, we will not be successful in commercializing Betrixaban, Andexanet alfa or other future products.

We do not have a significant sales or marketing infrastructure and have no experience in the sale, marketing or distribution of therapeutic products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. We plan to establish a hospital-based sales force in the United States and possibly other major markets and work with partners in other parts of the world to commercialize both Betrixaban and Andexanet alfa globally, if they are approved.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we

would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

We also may not be successful entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively and could damage our reputation. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new therapeutic products is highly competitive. We face competition with respect to our current product candidates, and will face competition with respect to any products that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. For example, several large pharmaceutical and biotechnology companies currently market and sell direct or indirect Factor Xa inhibitors for use in various disease states, including the treatment of acute medically ill patients. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Many of these competitors are attempting to develop therapeutics for our target indications. In addition, many of our competitors are large pharmaceutical companies that will have a greater ability to reduce prices for their competing drugs in an effort to gain market share and undermine the value proposition that we might otherwise be able to offer to payors.

We are developing our lead product candidate Betrixaban for extended duration VTE prophylaxis in acute medically ill patients both in-hospital and post-discharge for up to 35 days. The current standard of care for VTE prophylaxis in acute medically ill patients in the United States is a 6- to 14-day hospital administration of enoxaparin, marketed as Lovenox® and also available in generic form, an indirect Factor Xa inhibitor. Enoxaparin is widely accepted by physicians, patients and third-party payors. As a result, we may face difficulties in marketing Betrixaban as a substitute therapy for the current standard of care, enoxaparin. Furthermore, the FDA has already approved a number of therapies that, like Betrixaban, are direct Factor Xa inhibitors and that have already achieved substantial market acceptance. Although these products have not been approved for VTE prophylaxis in acute medically ill patients, the owners of the products may decide to seek such approval or physicians may decide to prescribe these products for the treatment of VTE in acute medically ill patients absent such approval, known as prescribing “off-label.” Further, our competitors may have the financial and other resources to conduct additional clinical studies in an effort to obtain regulatory approval for use of their drugs for VTE prophylaxis in acute medically ill patients, even in cases where they have previously run clinical trials that have failed.

While there are no therapies approved specifically as antidotes for Factor Xa inhibitors, Andexanet alfa, if approved, may compete with other currently approved treatments designed to enhance coagulation, such as fresh frozen plasma, prothrombin complex concentrates, recombinant Factor VIIa or whole blood. Although there is no clinical evidence supporting the use of such treatments in patients taking Factor Xa inhibitors, physicians may choose to use them because of familiarity, cost or other reasons. In addition, we are aware that several companies have conducted preclinical research on compounds intended to be antidotes for Factor Xa inhibitors and that at least one company has initiated a Phase 1 clinical trial of an antidote.

There are also a number of products in clinical development for hematologic cancer, ophthalmological diseases, allergic rhinitis, allergic asthma and other inflammatory diseases that are potential indications for Cerdulatinib or PRT2607. Our competitors may develop products that are more effective, safer, more convenient or less costly than any that we are developing or that would render our product candidates obsolete or non-competitive. Many competing products are in later stages of development than our products and are, therefore, likely to obtain FDA or other regulatory approval for their products before we obtain approval for ours.

Many of our competitors, including a number of large pharmaceutical companies that compete directly with us, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be

significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical study sites and patient registration for clinical studies, as well as in acquiring technologies complementary to, or necessary for, our programs.

If we are able to commercialize any product candidates, the products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, thereby harming our business.

The regulations that govern marketing approvals, pricing and reimbursement for new therapeutic products vary widely from country to country. Some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product and negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain regulatory approval.

Our ability to commercialize any products successfully also will depend in part on the extent to which reimbursement for these products and related treatments becomes available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Reimbursement may impact the demand for, or the price of, any product for which we obtain marketing approval. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with products administered under the supervision of a physician. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate that we successfully develop.

There may be significant delays in obtaining reimbursement for approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA or regulatory authorities in other countries. Moreover, eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Payment rates may vary according to the use of the product and the clinical setting in which it is used, may be based on payments allowed for lower cost products that are already reimbursed and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of products from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government funded and private payors for new products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical studies and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of patients from clinical studies or cancellation of studies;
- significant costs to defend the related litigation;
- substantial monetary awards to patients;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

We currently hold \$10.0 million in product liability insurance coverage, which may not be adequate to cover all liabilities that we may incur. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products.

If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights.

Risks related to our reliance on third parties

We rely on third parties to conduct our clinical studies, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such studies.

We do not independently conduct clinical studies of our product candidates. We rely on third parties, such as contract research organizations, or CROs, clinical data management organizations, medical institutions and clinical investigators, to perform this function. For example, we rely on PPD Development, LP and other CROs to oversee and manage our APEX study. Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. Furthermore, most of the clinical study sites for our APEX study are outside the United States, including several developing countries. The performance of these sites may be adversely affected by various issues, including less advanced medical infrastructure, lack of familiarity with conducting clinical studies using U.S. standards, insufficient training of personnel and communication difficulties. We remain responsible for ensuring that each of our clinical studies is conducted in accordance with the general investigational plan and protocols for the study. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices, for conducting, recording and reporting the results of clinical studies to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of patients in clinical studies are protected. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical studies in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, regulatory approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

We also rely on other third parties to store and distribute supplies for our clinical studies. Any performance failure on the part of our existing or future distributors could delay clinical development or regulatory approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We rely on third-party contract manufacturing organizations to manufacture and supply our product candidates for us. If one of our suppliers or manufacturers fails to perform adequately or fulfill our needs, we may be required to incur significant costs and devote significant efforts, particularly with respect to Andexanet alfa, to find new suppliers or manufacturers. We may also face delays in the development and commercialization of our product candidates.

We currently have limited experience in, and we do not own facilities for, clinical-scale manufacturing of our product candidates and we rely upon third-party contract manufacturing organizations to manufacture and supply drug product

for our clinical studies. The manufacture of pharmaceutical products in compliance with the FDA's current good manufacturing practices, or cGMPs, requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, including difficulties with production costs and yields, quality control, including stability of the product candidate and quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced cGMP requirements, other federal and state regulatory requirements and foreign regulations. If our manufacturers were to encounter any of these difficulties or otherwise fail to comply with their obligations to us or under applicable regulations, our ability to provide study drugs in our clinical studies would be jeopardized. Any delay or interruption in the supply of clinical study materials could delay the completion of our clinical studies, increase the costs associated with maintaining our clinical study programs and, depending upon the period of delay, require us to commence new studies at significant additional expense or terminate the studies completely.

All manufacturers of our product candidates must comply with cGMP requirements enforced by the FDA through its facilities inspection program. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. Manufacturers of our product candidates may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. The FDA or similar foreign regulatory agencies may also implement new standards at any time, or change their interpretation and enforcement of existing standards for manufacture, packaging or testing of products. We have little control over our manufacturers' compliance with these regulations and standards. A failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall or withdrawal of product approval. If the safety of any product supplied is compromised due to our manufacturers' failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize our products and we may be held liable for any injuries sustained as a result. Any of these factors could cause a delay of clinical studies, regulatory submissions, approvals or commercialization of our product candidates, entail higher costs or impair our reputation.

We currently rely on a single source supplier for each of our product candidates. For example, we rely on Hovione Inter Limited to produce the active pharmaceutical ingredient for Betrixaban for our APEX study, and we have engaged Lonza Group Ltd., or Lonza, to be the sole commercial manufacturer of Andexanet alfa bulk drug substance. Our current agreements with our suppliers do not provide for the entire supply of the drug product necessary for all anticipated clinical studies or for full scale commercialization. If we and our suppliers cannot agree to the terms and conditions for them to provide the drug product necessary for our clinical and commercial supply needs, or if any single source supplier terminates the agreement in response to a breach by us or otherwise becomes unable to fulfill its supply obligations, we would not be able to manufacture the product candidate until a qualified alternative supplier is identified, which could also delay the development of, and impair our ability to commercialize, our product candidates. One of our leading product candidates, Andexanet alfa, is a biologic and therefore requires a complex production process. We have transferred production of Andexanet alfa to Lonza, for commercial production and engaged a new sole-source vendor to perform lyophilization and packaging. In connection with the transfer of commercial production, we intend to make certain changes to the manufacturing process in order to increase its scale and efficiency. There can be no assurance that we will be able to successfully implement these transitions or implement the proposed improvements to the manufacturing process. In particular, in order to obtain FDA approval of material produced by a new vendor or using a new process, we will need to demonstrate that such material is comparable to the clinical material we previously used. Demonstrating comparability can require significant pre-clinical and clinical studies. If we are not able to demonstrate comparability, then the material would be considered a new biological entity and a full BLA submission would be required for approval, resulting in additional time and expense. If we are not able to implement the proposed transitions in a timely manner, or establish comparability of the new material, or obtain the anticipated improvements in efficiency, our business, results of operations and growth prospects would be materially adversely affected.

Although alternative sources of supply exist, the number of third-party suppliers with the necessary manufacturing and regulatory expertise and facilities is limited, and it could be expensive and take a significant amount of time to arrange for alternative suppliers, which could have a material adverse effect on our business. New suppliers of any product candidate would be required to qualify under applicable regulatory requirements and would need to have sufficient rights under applicable intellectual property laws to the method of manufacturing the product candidate. Obtaining the necessary FDA approvals or other qualifications under applicable regulatory requirements and ensuring non-infringement of third-party intellectual property rights could result in a significant interruption of supply and could require the new manufacturer to bear significant additional costs which may be passed on to us.

We have entered into collaboration agreements with each of Lee's, BMS and Pfizer, Bayer and Janssen, Daiichi Sankyo, Biogen Idec and Acix with respect to our product candidates. These collaborations may place the development of these product candidates outside our control, may require us to relinquish important rights or may otherwise be on terms unfavorable to us, and if our collaborations are not successful, these product candidates may not reach their full market potential.

In January 2013, we entered into a clinical collaboration agreement with Lee's Pharmaceutical (HK) Ltd, or Lee's, to jointly expand our Phase 3 APEX study of Betrixaban into China with an exclusive option for Lee's to negotiate for the exclusive commercial rights to Betrixaban in China. In October 2012, we entered into a three-way agreement with Bristol-Myers Squibb Company, or BMS, and Pfizer Inc., or Pfizer, to include subjects dosed with apixaban, their jointly owned Factor Xa inhibitor product, in one of our proof-of-concept studies of Andexanet alfa. In February 2013, we entered into a three-way agreement with Bayer and Janssen to include subjects dosed with rivaroxaban, their Factor Xa inhibitor product, in one of our proof-of-concept studies of Andexanet alfa. In June 2013, we entered into an agreement with Daiichi Sankyo, Inc., or Daiichi Sankyo, to include subjects dosed with edoxaban, their Factor Xa inhibitor product, in one of our proof-of-concept studies of Andexanet alfa. In January 2014, we entered into a second clinical collaboration agreement with BMS and Pfizer to further study Andexanet alfa as an antidote for their jointly owned product candidate apixaban through Phase 3 studies. In February 2014, we entered into a second clinical collaboration agreement with Bayer and Janssen to evaluate Andexanet alfa as a reversal agent for the FDA-approved oral Factor Xa inhibitor rivaroxaban through Phase 3 studies. In February 2013, we entered into a license and collaboration agreement with Acix Therapeutics, Inc., or Acix, pursuant to which we granted Acix an exclusive license to co-develop and co-commercialize Cerdulatinib and certain related compounds for nonsystemic indications, such as the treatment and prevention of ophthalmological diseases by topical administration and allergic rhinitis by intranasal administration.

We retain rights to other non-systemic indications including dermatologic disorders. In October 2011, we entered into a collaboration agreement with Biogen Idec pursuant to which Biogen Idec has ultimate decision-making authority with respect to the research, development and commercialization of PRT2607 and other highly selective Syk inhibitors. We may enter into additional collaboration agreements with third parties with respect to our other product candidates for the commercialization of the candidates outside the United States. In addition, depending on our capital requirements, development and commercialization costs, need for additional therapeutic expertise and other factors, it is possible that we will enter into broader development and commercialization arrangements with respect to our other product candidates. Our likely collaborators for any distribution, marketing, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We will have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenue from these arrangements will depend in part on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates, such as our collaboration with Biogen Idec, are subject to numerous risks, which may include the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to any such collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical study results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical studies, provide insufficient funding for a clinical study program, stop a clinical study, abandon a product candidate, repeat or conduct new clinical studies or require a new formulation of a product

candidate for clinical testing;

collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates;

a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to their marketing and distribution;

collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;

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disputes may arise between us and a collaborator that causes the delay or termination of the research, development or commercialization of our product candidates or that results in costly litigation or arbitration that diverts management attention and resources;

collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates; and

collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property.

For example, we previously had an exclusive worldwide license and collaboration agreement with Merck for the development and commercialization of Betrixaban and an exclusive worldwide license agreement with Novartis for the development and commercialization of Elinogrel, a novel anti-platelet agent. In each case, the collaborator chose to terminate the collaboration for internal business reasons. As a result of these terminations, we were required to revise the development plan for Betrixaban and raise additional financing to support that plan, and we also decided to halt our development efforts with respect to Elinogrel. Any termination or disruption of our collaboration with Biogen Idec or other potential collaborators could result in delays in the development of product candidates, increases in our costs to develop the product candidate or the termination of development of a product candidate.

Risks related to the operation of our business

Our future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on William Lis, our Chief Executive Officer, and the other principal members of our executive and scientific teams. Under the terms of their employment, our executives may terminate their employment with us at any time. The loss of the services of any of these people could impede the achievement of our research, development and commercialization objectives. We maintain “key person” insurance for Mr. Lis but not for any other executives or employees. Any insurance proceeds we may receive under our “key person” insurance on Mr. Lis would not adequately compensate us for the loss of his services.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

We expect to expand our development, regulatory and sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of December 31, 2013, we had 70 employees. Over the next several years, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and radioactive and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We also store certain low level radioactive waste at our facilities until the materials can be properly disposed of. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may be required to incur substantial costs to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Requirements associated with being a public company will increase our costs significantly, as well as divert significant company resources and management attention.

Prior to the completion of our initial public offering in May 2013, we were not subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or Securities Exchange Act, or the other rules and regulations of the Securities and Exchange Commission, or SEC, or any securities exchange relating to public companies. With the assistance of our legal, independent accounting and financial advisors we have identified those areas in which changes should be made to our financial and management control systems to manage our growth and our obligations as a public company. These areas include corporate governance, corporate control, internal audit, disclosure controls and procedures and financial reporting and accounting systems. Making those changes has resulted, and will continue to result in our incurring significant expenses. In addition, compliance with the various reporting and other requirements applicable to public companies requires considerable time and attention of management. There can be no assurance that the changes we have made and will make will be sufficient to allow us to satisfy our obligations as a public company on a timely basis.

In addition, as a public company, it may be more difficult or more costly for us to obtain certain types of insurance, including directors' and officers' liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified personnel to serve on our board of directors, our board committees or as executive officers.

We are an "emerging growth company," and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act, or the JOBS Act, which was enacted in April 2012. For as long as we continue to be an emerging growth company, we may take advantage of

exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years, although circumstances could cause us to lose that status earlier. We will remain an emerging growth company until the earlier of (1) December 31, 2018, (2) the last day of the fiscal year (a) in which we have total annual gross revenue of at least \$1.0 billion, or (b) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th, and (3) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may suffer or be more volatile.

Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards, and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or manmade disasters or business interruptions. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. Our corporate headquarters is located in California and certain clinical sites for our product candidates, operations of our existing and future partners and suppliers are or will be located in California near major earthquake faults and fire zones. The ultimate impact on us, our significant partners, suppliers and our general infrastructure of being located near major earthquake faults and fire zones and being consolidated in certain geographical areas is unknown, but our operations and financial condition could suffer in the event of a major earthquake, fire or other natural or manmade disaster.

If we obtain approval to commercialize any approved products outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If any product candidates that we may develop are approved for commercialization outside the United States, we will be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

In connection with our Betrixaban and Andexanet alfa studies, we are currently utilizing certain suppliers outside of the United States, which subjects us to certain of the above risks, but our risks will be significantly increased if we establish operations internationally.

Our internal computer systems, or those of our CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our drug development programs.

Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could

result in a material disruption of our drug development programs. For example, the loss of clinical study data from completed or ongoing clinical studies for any of our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

Risks related to intellectual property

If we fail to comply with our obligations in our intellectual property licenses with third parties, we could lose license rights that are important to our business.

We are a party to intellectual property license agreements with third parties, including with respect to Betrixaban, Cerdulatinib and PRT2607, and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that our future license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, our licensors may have the right to terminate these agreements, in which event we may not be able to develop and market any product that is covered by these agreements. Termination of these licenses or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms or our not having sufficient intellectual property rights to operate our business. The occurrence of such events could materially harm our business.

Our ability to successfully commercialize our technology and products may be materially adversely affected if we are unable to obtain and maintain effective intellectual property rights for our technologies and product candidates.

Our success depends in large part on our and our licensors' ability to obtain and maintain patent and other intellectual property protection in the United States and in other countries with respect to our proprietary technology and products. In some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology or products that we license from third parties. Therefore, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. In addition, if third parties who license patents to us fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated.

We have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and products that are important to our business. This process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technologies or from developing competing products and technologies. Under our collaboration agreement with Biogen Idec, we are obligated to use commercially reasonable efforts to file and prosecute patent applications, and maintain patents, covering PRT2607 and other highly selective Syk inhibitors in specified jurisdictions, and these patent rights are licensed to Biogen Idec.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain and involves complex legal and factual questions for which legal principles remain unresolved. In recent years patent rights have been the subject of significant litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our and our licensors' patent rights are highly uncertain. Our and our licensors' pending and future patent applications may not result in patents being issued which protect our technology or products or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned and licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions. Assuming the other requirements for patentability are met, prior to March 16, 2013, in the United States, the first to make the claimed invention is entitled

to the patent, while outside the United States, the first to file a patent application is entitled to the patent. On March 16, 2013, under the recently enacted America Invents Act, the United States moved to a first to file system. The effects of these changes are currently unclear as the United States Patent and Trademark Office, or USPTO, must still implement various regulations, the courts have yet to address any of these provisions and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. We may become involved in opposition or interference proceedings challenging our patent rights or the patent rights of others, and the outcome of any proceedings are highly uncertain. An adverse determination in any such proceeding could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. The issuance of a patent is not conclusive as to its scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop or prevent us from stopping others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours or otherwise provide us with a competitive advantage.

We may become involved in lawsuits to protect or enforce our patents, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the proprietary rights or intellectual property of third parties. We may become party to, or be threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference proceedings before the USPTO. An interference proceeding is a proceeding before the USPTO to determine the priority among multiple patents or patent applications. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third-party's intellectual property rights, we could be required to obtain a license from such third-party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties can have a similar negative impact on our business.

For example, in August 2011, the USPTO declared an interference proceeding involving U.S. Patent No. 7,727,982 assigned to Millennium Pharmaceuticals, Inc., to which we have an exclusive license, and U.S. Application No. 12/203,640 assigned to Yamanouchi Pharmaceuticals Co., Ltd. Both of these patent applications potentially

covered a Factor Xa inhibitor being developed by a competitor, but not Betrixaban or its lead backup compounds. As the competitor had ceased clinical development of its compound, we decided against contesting the interference proceeding and priority was given to U.S. Application No. 12/203,640. We do not believe this result will have a material impact on our business.

We may be unable to protect the confidentiality of our trade secrets, thus harming our business and competitive position.

In addition to our patented technology and products, we rely upon trade secrets, including unpatented know-how, technology and other proprietary information to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our collaborators and consultants. We also have agreements with our employees and selected consultants that obligate them to assign their inventions to us. However, it is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees, consultants or collaborators that are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could be disclosed, misappropriated or otherwise become known or be independently discovered by our competitors. In addition, intellectual property laws in foreign countries may not protect our intellectual property to the same extent as the laws of the United States. If our trade secrets are disclosed or misappropriated, it would harm our ability to protect our rights and have a material adverse effect on our business.

We may be subject to claims that our employees have wrongfully used or disclosed intellectual property of their former employers. Intellectual property litigation or proceeding could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could have a material adverse effect on our ability to compete in the marketplace.

Risks related to government regulation

The regulatory approval process is expensive, time consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates.

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, which regulations differ from country to country. We will not be permitted to market our product candidates in the United States until we receive approval of an NDA or a BLA, from the FDA. We have not submitted an application or received marketing approval for any of our product candidates. Obtaining approval of an NDA or BLA can be a lengthy, expensive and uncertain process. In addition, failure to comply with FDA and other applicable U.S.

and foreign regulatory requirements may subject us to administrative or judicially imposed sanctions, including the following:

- warning letters;
- civil or criminal penalties and fines;
- injunctions;
- suspension or withdrawal of regulatory approval;
- suspension of any ongoing clinical studies;
- voluntary or mandatory product recalls and publicity requirements;

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refusal to accept or approve applications for marketing approval of new drugs or biologics or supplements to approved applications filed by us;
restrictions on operations, including costly new manufacturing requirements; or
seizure or detention of our products or import bans.

Prior to receiving approval to commercialize any of our product candidates in the United States or abroad, we and our collaboration partners must demonstrate with substantial evidence from well-controlled clinical studies, and to the satisfaction of the FDA and other regulatory authorities abroad, that such product candidates are safe and effective for their intended uses. Results from preclinical studies and clinical studies can be interpreted in different ways. Even if we and our collaboration partners believe the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. Administering any of our product candidates to humans may produce undesirable side effects, which could interrupt, delay or cause suspension of clinical studies of our product candidates and result in the FDA or other regulatory authorities denying approval of our product candidates for any or all targeted indications.

Regulatory approval of an NDA or BLA is not guaranteed, and the approval process is expensive and may take several years. The FDA also has substantial discretion in the approval process. Despite the time and expense exerted, failure can occur at any stage, and we could encounter problems that cause us to abandon or repeat clinical studies, or perform additional preclinical studies and clinical studies. The number of preclinical studies and clinical studies that will be required for FDA approval varies depending on the product candidate, the disease or condition that the product candidate is designed to address and the regulations applicable to any particular product candidate. The FDA can delay, limit or deny approval of a product candidate for many reasons, including, but not limited to, the following:

- a product candidate may not be deemed safe or effective;
- FDA officials may not find the data from preclinical studies and clinical studies sufficient;
- the FDA might not approve our or our third-party manufacturer's processes or facilities; or
- the FDA may change its approval policies or adopt new regulations.

If any of our product candidates fails to demonstrate safety and efficacy in clinical studies or does not gain regulatory approval, our business and results of operations will be materially and adversely harmed.

Even if we receive regulatory approval for a product candidate, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and subject us to penalties if we fail to comply with applicable regulatory requirements.

Once regulatory approval has been granted, the approved product and its manufacturer are subject to continual review by the FDA and/or non-U.S. regulatory authorities. Any regulatory approval that we or our collaboration partners receive for our product candidates may be subject to limitations on the indicated uses for which the product may be marketed or contain requirements for potentially costly post-marketing follow-up studies to monitor the safety and efficacy of the product. In addition, if the FDA and/or non-U.S. regulatory authorities approve any of our product candidates, we will be subject to extensive and ongoing regulatory requirements by the FDA and other regulatory authorities with regard to the labeling, packaging, adverse event reporting, storage, advertising, promotion and recordkeeping for our products. In addition, manufacturers of our drug products are required to comply with cGMP regulations, which include requirements related to quality control and quality assurance as well as the corresponding maintenance of records and documentation. Further, regulatory authorities must approve these manufacturing facilities before they can be used to manufacture our drug products, and these facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations. If we or a third party discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory authority may impose restrictions on that product, the manufacturer or us, including requiring withdrawal of the product from the market or suspension of manufacturing. If we, our product candidates or the manufacturing facilities for our product candidates

fail to comply with regulatory requirements of the FDA and/or other non-U.S. regulatory authorities, we could be subject to administrative or judicially imposed sanctions, including the following:

warning letters;

civil or criminal penalties and fines;

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injunctions;
suspension or withdrawal of regulatory approval;
suspension of any ongoing clinical studies;
voluntary or mandatory product recalls and publicity requirements;
refusal to accept or approve applications for marketing approval of new drugs or biologics or supplements to approved applications filed by us;
restrictions on operations, including costly new manufacturing requirements; or
seizure or detention of our products or import bans.

The regulatory requirements and policies may change and additional government regulations may be enacted for which we may also be required to comply. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or in other countries. If we are not able to maintain regulatory compliance, we may not be permitted to market our future products and our business may suffer.

Failure to obtain regulatory approvals in foreign jurisdictions will prevent us from marketing our products internationally.

We intend to seek a distribution and marketing partner for Betrixaban outside the United States and may market future products in international markets. In order to market our future products in the European Economic Area, or EEA, and many other foreign jurisdictions, we must obtain separate regulatory approvals. Specifically, in the EEA, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA.

Before granting the MA, the European Medicines Agency or the competent authorities of the member states of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

We have had limited interactions with foreign regulatory authorities, and the approval procedures vary among countries and can involve additional clinical testing, and the time required to obtain approval may differ from that required to obtain FDA approval. Clinical studies conducted in one country may not be accepted by regulatory authorities in other countries. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one or more foreign regulatory authorities does not ensure approval by regulatory authorities in other foreign countries or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. We may not be able to file for regulatory approvals and even if we file we may not receive necessary approvals to commercialize our products in any market.

Healthcare reform measures could hinder or prevent our product candidates' commercial success.

In the United States, there have been and we expect there will continue to be a number of legislative and regulatory changes to the healthcare system in ways that could affect our future revenue and profitability and the future revenue and profitability of our potential customers. Federal and state lawmakers regularly propose and, at times, enact legislation that would result in significant changes to the healthcare system, some of which are intended to contain or reduce the costs of medical products and services. For example, one of the most significant healthcare reform measures in decades, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, collectively, the PPACA, was enacted in 2010. The PPACA contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse measures, all of which will impact existing government healthcare programs and will result in the development of new programs. The PPACA, among other things:

imposes a non-deductible annual fee on pharmaceutical manufacturers or importers who sell “branded prescription drugs,” effective 2011;

increases the minimum level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1%, effective 2011;

could result in the imposition of injunctions;

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requires collection of rebates for drugs paid by Medicaid managed care organizations;
requires manufacturers to participate in a coverage gap discount program, under which they must agree to offer 50% point-of-sale discounts off negotiated prices of applicable branded drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and
creates a process for approval of biologic therapies that are similar or identical to approved biologics.
While the U.S. Supreme Court upheld the constitutionality of most elements of the PPACA in June 2012, other legal challenges are still pending final adjudication in several jurisdictions. In addition, Congress has also proposed a number of legislative initiatives, including possible repeal of the PPACA. At this time, it remains unclear whether there will be any changes made to the PPACA, whether to certain provisions or its entirety. We cannot assure that the PPACA, as currently enacted or as amended in the future, will not adversely affect our business and financial results and we cannot predict how future federal or state legislative or administrative changes relating to healthcare reform will affect our business.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. For example, the Budget Control Act of 2011, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee did not achieve a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, which triggered the legislation's automatic reduction to several government programs, including aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, or the ATRA, which delayed for another two months the budget cuts mandated by the sequestration provisions of the Budget Control Act of 2011. The ATRA, among other things, also reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. On March 1, 2013, the President signed an executive order implementing sequestration, and on April 1, 2013, the 2% Medicare reductions went into effect.

There likely will continue to be legislative and regulatory proposals at the federal and state levels directed at containing or lowering the cost of health care. We cannot predict the initiatives that may be adopted in the future or their full impact. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of health care may adversely affect:

our ability to set a price we believe is fair for our products;
our ability to generate revenue and achieve or maintain profitability; and
the availability of capital.

Further, changes in regulatory requirements and guidance may occur and we may need to amend clinical study protocols to reflect these changes. Amendments may require us to resubmit our clinical study protocols to Institutional Review Boards for reexamination, which may impact the costs, timing or successful completion of a clinical study. In light of widely publicized events concerning the safety risk of certain drug products, regulatory authorities, members of Congress, the Governmental Accounting Office, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the recall and withdrawal of drug products, revisions to drug labeling that further limit use of the drug products and establishment of risk management programs that may, for instance, restrict distribution of drug products or require safety surveillance and/or patient education. The increased attention to drug safety issues may result in a more cautious approach by the FDA to clinical studies and the drug approval process. Data from clinical studies may receive greater scrutiny with respect to safety, which may make the FDA or other regulatory authorities more likely to terminate or suspend clinical studies before completion, or require longer or additional clinical studies that may result in substantial additional expense and a delay or failure in obtaining approval or approval for a more limited indication than originally sought.

Given the serious public health risks of high profile adverse safety events with certain drug products, the FDA may require, as a condition of approval, costly risk evaluation and mitigation strategies, which may include safety

surveillance, restricted distribution and use, patient education, enhanced labeling, special packaging or labeling, expedited reporting of certain adverse events, preapproval of promotional materials and restrictions on direct-to-consumer advertising.

If we fail to comply with healthcare regulations, we could face substantial penalties and our business, operations and financial condition could be adversely affected.

Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. We could be subject to healthcare fraud and abuse and patient privacy regulation by both the federal government and the states in which we conduct our business. The regulations that may affect our ability to operate include, without limitation:

the federal healthcare program Anti-Kickback Statute, which prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs, such as the Medicare and Medicaid programs; federal Physician Payment Sunshine or Open Payments Program provisions which will require extensive tracking of physician and teaching hospital payments, maintenance of a payments database, and public reporting of the payment data;

indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs, such as the Medicare and Medicaid programs;

the federal False Claims Act, which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, false claims, or knowingly using false statements, to obtain payment from the federal government, and which may apply to entities like us which provide coding and billing advice to customers;

federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

the federal transparency requirements under the Health Care Reform Law requires manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests;

the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information; and

state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers.

The PPACA, among other things, amends the intent requirement of the Federal Anti-Kickback Statute and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. In addition, the PPACA provides that the government may assert that a claim including items or services resulting from a violation of the Federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our ability to operate our business and our financial results. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

Risks related to ownership of our common stock

Our stock price may be volatile, and investors in our common stock could incur substantial losses.

Our stock price has fluctuated in the past and may be volatile in the future. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may experience losses on their investment in our stock. The market price for our common stock may be influenced by many factors, including the following:

- the success of competitive products or technologies;
- results of clinical studies of our product candidates or those of our competitors;
- regulatory or legal developments in the United States and other countries, especially changes in laws or regulations applicable to our products;
- introductions and announcements of new products by us, our commercialization partners, or our competitors, and the timing of these introductions or announcements;
- actions taken by regulatory agencies with respect to our products, clinical studies, manufacturing process or sales and marketing terms;
- variations in our financial results or those of companies that are perceived to be similar to us;
- the success of our efforts to acquire or in-license additional products or product candidates;
 - developments concerning our collaborations, including but not limited to those with our sources of manufacturing supply and our commercialization partners;
- developments concerning our ability to bring our manufacturing processes to scale in a cost-effective manner;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments
- developments or disputes concerning patents or other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our products;
- our ability or inability to raise additional capital and the terms on which we raise it;
- the recruitment or departure of key personnel;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- actual or anticipated changes in earnings estimates or changes in stock market analyst recommendations regarding our common stock, other comparable companies or our industry generally;
- trading volume of our common stock;
- sales of our common stock by us or our stockholders;
- general economic, industry and market conditions; and
- the other risks described in this “Risk factors” section.

These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. In the past, following periods of volatility in the market, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

Our executive officers, directors and principal stockholders have the ability to control or significantly influence all matters submitted to stockholders for approval.

Our executive officers, directors and stockholders who own more than 5% of our outstanding common stock beneficially own shares representing approximately 32% of our common stock as of the date of this report. As a result, if these stockholders were to choose to act together, they would be able to control or significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these stockholders, if they choose to act together, will control or significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

We are incurring significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a newly public company, we are incurring significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act, and rules of the SEC and those of The NASDAQ Stock Market, or the NASDAQ, have imposed various requirements on public companies including requiring establishment and maintenance of effective disclosure and financial controls. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased and will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal control over financial reporting and disclosure controls and procedures. In particular, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act, beginning with our annual report on Form 10-K for the fiscal year ended December 31, 2014. In addition, we will be required to have our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting beginning with our annual report on Form 10-K following the date on which we are no longer an emerging growth company. Our compliance with Section 404 of the Sarbanes-Oxley Act, as applicable, will require that we incur substantial accounting expense and expend significant management efforts. We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. If we are not able to comply with the requirements of Section 404, as applicable, in a timely manner, or if we or our independent registered public accounting firm identify deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by the NASDAQ, the SEC or other regulatory authorities, which would require additional financial and management resources.

Our ability to successfully implement our business plan and comply with Section 404, as applicable, requires us to be able to prepare timely and accurate financial statements. We expect that we will need to continue to improve existing, and implement new operational and financial systems, procedures and controls to manage our business effectively. Any delay in the implementation of, or disruption in the transition to, new or enhanced systems, procedures or controls, may cause our operations to suffer and we may be unable to conclude that our internal control over financial

reporting is effective and to obtain an unqualified report on internal controls from our auditors as required under Section 404 of the Sarbanes-Oxley Act. This, in turn, could have an adverse impact on trading prices for our common stock, and could adversely affect our ability to access the capital markets.

An active trading market for our common stock may not be maintained

Our stock is currently traded on the NASDAQ, but we can provide no assurance that we will be able to maintain an active trading market for our shares on the NASDAQ or any other exchange in the future. If an active market for our common stock is not maintained, it may be difficult for our stockholders to sell shares without depressing the market price for the shares or at all.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, our stock price and trading volume could decline.

The trading market for our common stock depends, in part, on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts may cease to publish research on our company at any time in their discretion. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline. In addition, if one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. If our operating results fail to meet the forecast of analysts, our stock price will likely decline.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Because our board of directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team. Among others, these provisions include the following:

- our board of directors is divided into three classes with staggered three-year terms which may delay or prevent a change of our management or a change in control;
- our board of directors has the right to elect directors to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- our stockholders may not act by written consent or call special stockholders' meetings; as a result, a holder, or holders, controlling a majority of our capital stock would not be able to take certain actions other than at annual stockholders' meetings or special stockholders' meetings called by the board of directors, the chairman of the board, the chief executive officer or the president;
- our certificate of incorporation prohibits cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- stockholders must provide advance notice and additional disclosures in order to nominate individuals for election to the board of directors or to propose matters that can be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror's own slate of directors or otherwise attempting to obtain control of our company; and
- our board of directors may issue, without stockholder approval, shares of undesignated preferred stock; the ability to issue undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to acquire us.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Our employment agreements with our executive officers may require us to pay severance benefits to any of those persons who are terminated in connection with a change in control of us, which could harm our financial condition or results.

Certain of our executive officers are parties to employment agreements that contain change in control and severance provisions providing for aggregate cash payments of up to approximately \$2.2 million for severance and other benefits and acceleration of vesting of stock options with a value of approximately \$33.4 million as of December 31, 2013, based on the closing price of our common stock of \$25.75 on such date in the event of a termination of employment in connection with a change in control of us. The accelerated vesting of options could result in dilution to our existing stockholders and harm the market price of our common stock. The payment of these severance benefits could harm our financial condition and results. In addition, these potential severance payments may discourage or prevent third parties from seeking a business combination with us.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be our stockholders' sole source of gain.

We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of existing or any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

We lease approximately 50,000 square feet of research and office space in South San Francisco, California under a lease that expires in March 2015. Thereafter, at our option, we may extend the term for an additional three years to March 2018. In January 2014, we entered into a letter of intent to lease our existing space from our landlord for a period of five years, expiring in 2019. We believe that our existing facilities are sufficient for our current needs for the foreseeable future.

ITEM 3. LEGAL PROCEEDINGS

We are not currently a party to any material legal proceedings.

ITEM 4. MINE SAFETY DISCLOSURES

None.

PART II

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

PRICE RANGE OF COMMON STOCK

Our common stock has been listed on The NASDAQ Global Market under the symbol "PTLA" since May 22, 2013. Prior to that date, there was no public trading market for our common stock. Our initial public offering was priced at \$14.50 per share on May 22, 2013. The following table sets forth for the periods indicated the high and low sales prices per share of our common stock as reported on The NASDAQ Global Market:

	Low	High
Fiscal Year ending December 31, 2013		
Second Quarter (beginning May 22, 2013)	\$ 14.75	\$26.12
Third Quarter	\$20.15	\$28.77
Fourth Quarter	\$20.72	\$30.95

On February 28 2014, the last reported sale price of our common stock as reported on The NASDAQ Global Market was \$24.39 per share.

As of February 28 2014, there were 41,029,043 shares of our common stock issued and outstanding with 92 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

STOCK PRICE PERFORMANCE GRAPH

The following stock performance graph compares our total stock return with the total return for (i) the NASDAQ Composite Index and the (ii) the [NASDAQ Biotechnology Index] for the period from May 22, 2013 (the date our common stock commenced trading on the NASDAQ Global Market) through December 31, 2013. The figures represented below assume an investment of \$100 in our common stock at the closing price of \$15.15 on May 22, 2013 and in the NASDAQ Composite Index and the NASDAQ Biotechnology Index on May 22, 2013 and the reinvestment of dividends into shares of common stock. The comparisons in the table are required by the Securities and Exchange Commission, or SEC, and are not intended to forecast or be indicative of possible future performance of our common stock. This graph shall not be deemed “soliciting material” or be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act of 1933, as amended, or the Securities Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

\$100 investment in

stock or index	Ticker	May 22, 2013	June 30, 2013	September 30, 2013	December 31, 2013
Portola Pharmaceuticals, Inc.	PTLA	\$ 100.00	\$ 162.08	\$ 176.57	\$ 169.97
NASDAQ Composite Index	IXIC	\$ 100.00	\$ 96.08	\$ 115.99	\$ 125.56
NASDAQ Biotechnology Index	NBI	\$ 100.00	\$ 98.27	\$ 108.90	\$ 120.60

DIVIDEND POLICY

We have never declared or paid, and do not anticipate declaring, or paying in the foreseeable future, any cash dividends on our capital stock. Future determination as to the declaration and payment of dividends, if any, will be at the discretion of our board of directors and will depend on then existing conditions, including our operating results, financial conditions, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

USE OF PROCEEDS

On May 21, 2013, our registration statement on Form S-1 (File No. 333-187901) was declared effective for our initial public offering. As a result of our initial public offering and the exercise of the overallotment option, both of which closed on May 28, 2013, we received net proceeds of approximately \$131.0 million, after underwriting discounts and commissions of approximately \$9.4 million. In addition, we incurred other expenses associated with our initial public offering of approximately \$5.2 million. No payments for such expenses were made directly or indirectly to any of our officers or directors.

On October 16, 2013, our registration statement on Form S-1 (File No. 333-191609) was declared effective for our follow-on public offering. As a result of our follow-on public offering and the exercise of the overallotment which closed on October 22, 2013 and November 14, 2013, respectively, we received net proceeds of approximately \$120.8 million, after underwriting discounts and commissions of approximately \$7.7 million. We did not receive any proceeds from the sale of common stock by certain of our existing stockholders in the follow-on public offering. In addition, we incurred other expenses associated with our follow-on public offering of approximately \$0.9 million. No payments for such expenses were made directly or indirectly to any of our officers or directors.

The net proceeds from the offerings described above have been used and will be used, together with our cash, cash equivalents and investments, to fund continued advancement of our Betrixaban, Andexanet alfa and Cerdulatinib programs, anticipated to be approximately \$285.0 million, with the balance to be used to fund working capital, capital expenditures and other general corporate purposes, which may include the acquisition or licensing of other products, businesses or technologies.

There has been no material change in the planned use of proceeds from our initial public offering as described in our prospectus dated May 22, 2013, filed with the SEC pursuant to Rule 424(b) of the Securities Act or the planned use of proceeds from our public offering as described in our prospectus dated October 17, 2013, filed with the SEC pursuant to Rule 424(b) of the Securities Act.

RECENT SALE OF UNREGISTERED SECURITIES

During the year ended December 31, 2013, we granted options in unregistered transactions to purchase an aggregate of 1,022,601 shares of common stock at a weighted average exercise price of \$18.03 per share to our employees, directors and consultants. During such period, options were exercised in unregistered transactions to purchase 403,468 shares for cash consideration in the aggregate amount of \$2.6 million. The sales of the above securities were exempt from registration under Rule 701 promulgated under the Securities Act as transactions pursuant to a compensatory benefit plan or a written contract relating to compensation. Shares of common stock to be issued pursuant to awards (including options) under our equity incentive plans were registered on a Registration Statement on Form S-8, filed with the SEC on May 31, 2013.

Issuer Purchases of Equity Securities

None.

ITEM 6. SELECTED FINANCIAL DATA

You should read the following selected financial data together with the section of this report entitled “Management’s discussion and analysis of financial condition and results of operations” and our financial statements and the related notes included in this report. The statement of operations data for the years ended December 31, 2013, 2012 and 2011 and the balance sheet data as of December 31, 2013 and 2012 are derived from our audited financial statements included elsewhere in this report. We have included, in our opinion, all adjustments, consisting only of normal recurring adjustments that we consider necessary for a fair presentation of the financial information set forth in those statements. Our historical results are not necessarily indicative of the results to be expected in the future, and our unaudited interim results are not necessarily indicative of the results to be expected for the full year or any other period.

	Year Ended December 31,		
	2013	2012	2011
Collaboration and license revenue	\$10,531	\$72,042	\$78,029
Operating expenses:			
Research and development	79,286	49,717	46,089
General and administrative	15,423	11,469	12,071
Total operating expenses	94,709	61,186	58,160
Income (loss) from operations	(84,178)	10,856	19,869
Interest and other income, net	826	510	136
Interest expense	-	-	(21)
Net income (loss)	\$(83,352)	\$11,366	\$19,984
Net income (loss) attributable to common stockholders:			
Basic	\$(83,352)	\$-	\$79
Diluted	\$(83,352)	\$-	\$127
Net income (loss) per share attributable to common stockholders:			
Basic	\$(3.65)	\$-	\$0.06
Diluted	\$(3.65)	\$-	\$0.06
Shares used to compute net income (loss) per share attributable to common stockholders:			
Basic	22,842,443	1,350,939	1,249,778
Diluted	22,842,443	2,048,867	2,089,206

- (1) To date, substantially all of our revenue has been generated from our collaboration agreements, and we have not generated any commercial product revenue. Revenue in the year ended December 31, 2011 includes \$8.3 million that represents the recognition of all remaining deferred revenue following the termination of an exclusive worldwide license and collaboration agreement with Merck & Co., Inc., effective September 30, 2011. Revenue in the year ended December 31, 2012 includes \$65.1 million that represents the recognition of all remaining deferred revenue following the termination of an exclusive worldwide license agreement with Novartis Pharma A.G., effective July 1, 2012. See the section of this report entitled “Management’s discussion and analysis of financial condition and results of operations—Financial operations overview—Revenue” for a more detailed description of our revenue recognition with respect to these agreements.

	As of December 31,		
	2013	2012	2011
Balance sheet data:			
Cash, cash equivalents and investments	\$319,036	\$137,384	\$188,089
Working capital	247,153	116,089	169,128
Total assets	325,731	146,001	193,403
Convertible preferred stock	—	317,280	317,280
Total stockholders' equity (deficit)	296,335	(191,569)	(206,105)

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with the section of this report entitled "Selected financial data" and our financial statements and related notes included elsewhere in this report. This discussion and other parts of this report contain forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations and intentions. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section of this report entitled "Risk factors."

Overview

We are a biopharmaceutical company focused on the development and commercialization of novel therapeutics in the areas of thrombosis, other hematologic disorders and inflammation for patients who currently have limited or no approved treatment options. Since our inception in 2003, we have advanced several innovative compounds into clinical development. Our lead product candidate Betrixaban is in a pivotal Phase 3 clinical study, and our second lead development candidate Andexanet alfa, formerly PRT4445, has completed two Phase 2 proof-of-concept studies and we plan to initiate our Phase 3 registration studies in the first half of 2014. We initiated a Phase 1/2 proof-of-concept study of Cerdulatinib, formerly PRT2070, one of our other product candidates, in October 2013. We also have completed multiple Phase 1 studies for PRT2607.

Our product candidates and collaboration agreements

Betrixaban

Betrixaban is a novel oral once-daily inhibitor of Factor Xa in development for extended duration prophylaxis, or preventive treatment, of a form of thrombosis, or blood clots, known as venous thromboembolism, or VTE, in acute medically ill patients for in-hospital and post-discharge for up to 35 days. In March 2012, we initiated a pivotal Phase 3 study to evaluate oral once-daily Betrixaban for superiority as compared to subcutaneous injection of enoxaparin for extended VTE prophylaxis in acute medically ill patients with restricted mobility and other risk factors. This study is anticipated to enroll approximately 6,850 patients. Based on current enrollment, we expect our current Phase 3 study of Betrixaban, or APEX, to complete patient enrollment by the end of 2015.

We entered into an asset purchase agreement with Millennium Pharmaceuticals, Inc., or Millennium, in November 2003 to acquire patent rights and intellectual property to a platelet research program, and a license agreement with Millennium in August 2004, to obtain certain exclusive rights to research, develop and commercialize certain compounds that inhibit Factor Xa, including Betrixaban. Both of these agreements were amended in December 2005. See the section of this report entitled "Business—Collaboration and license agreements—Millennium agreements" for a more detailed description of these agreements.

In July 2009, we entered into an exclusive worldwide license and collaboration agreement with Merck & Co., Inc., or Merck, to develop and commercialize Betrixaban. Merck made an upfront cash payment to us of \$50.0 million, and this agreement provided for additional payments to us based on the achievement of certain development, regulatory and commercialization milestones. This agreement was terminated effective September 2011, and as of the time of termination, no milestones had been achieved and no royalties had been triggered under this agreement. In January 2013, we entered into a clinical collaboration agreement with Lee's Pharmaceutical (HK) Ltd, or Lee's, to jointly expand the Phase 3 APEX study of Betrixaban into China with an exclusive option for Lee's to negotiate for the exclusive commercial rights to Betrixaban in China. See the section of this report entitled "Business—Collaboration and license agreements—Lee's agreement" for a more detailed description of this agreement.

Andexanet alfa

Andexanet alfa is a recombinant protein designed to reverse the anticoagulant activity in patients treated with a Factor Xa inhibitor who suffer an uncontrolled bleeding episode or undergo emergency surgery. We are pursuing an Accelerated Approval pathway for Andexanet alfa and plan to initiate registration-enabling studies in 2014. We completed two Phase 2 proof-of-concept studies of Andexanet alfa in healthy volunteers who were administered a Factor Xa inhibitor Eliquis[®] (apixaban), which is manufactured by Bristol-Myers Squibb Company, or BMS and Pfizer Inc., or Pfizer, and XARELTO[®] (rivaroxaban), which is manufactured by Bayer Pharma AG, or Bayer, and Janssen Pharmaceuticals, Inc., or Janssen. Andexanet alfa is the first therapy to demonstrate reversal of a Factor Xa inhibitor in a clinical study. Based on the results of our initial Phase 2 studies, we anticipate initiating our Phase 3 registration studies in 2014. In November 2013, the FDA granted breakthrough therapy designation for Andexanet alfa for which we are pursuing an Accelerated Approval pathway.

In October 2012, we entered into a three-way agreement with BMS and Pfizer to include subjects dosed with apixaban, their jointly owned Factor Xa inhibitor product, in one of our proof-of-concept studies of Andexanet alfa. We are responsible for the cost of conducting this clinical study. Pursuant to our agreement with BMS and Pfizer, we are obligated to provide research and development services and participate on various committees. See the section of this report entitled “Business—Collaboration and license agreements—BMS and Pfizer agreements” for a more detailed description of this agreement. We originally estimated the period of performance of our obligations to extend through the second quarter of 2013. During 2013, we added cohorts that were not planned as part of the original study design at the inception of the agreement and therefore revised our estimated period of performance to now be through 2013. The total consideration under this agreement of \$6.0 million was recognized as revenue on a straight-line basis over the estimated performance period through 2013.

In February 2013, we entered into a three-way agreement with Bayer and Janssen to include subjects dosed with rivaroxaban, their jointly owned Factor Xa inhibitor product, in one of our proof-of-concept studies of Andexanet alfa. See the section of this report entitled “Business—Collaboration and license agreements—Bayer and Janssen agreements” for a more detailed description of this agreement. We are responsible for the cost of conducting this clinical study. Under the terms of the agreement, Bayer and Janssen have each provided us with an upfront and non-refundable fee of \$2.5 million, for an aggregate fee of \$5.0 million. The agreement also provides for additional non-refundable payments to us from Bayer and Janssen of \$250,000 each for an aggregate fee of \$500,000 following the delivery of the final written study report of our Phase 2 proof-of-concept studies of Andexanet alfa. We are also obligated to participate on a Joint Collaboration Committee, or JCC, with Bayer and Janssen to oversee the collaboration activities under the agreement. We originally estimated the period of performance of our obligations to extend through the fourth quarter of 2013. During 2013, we added cohorts that were not planned as part of the initial study design at the inception of the agreement and therefore revised our estimated period of performance to now be through 2014. The total consideration under this agreement of \$5.5 million is being recognized as revenue on a straight-line basis over the estimated performance period through 2014.

In June 2013, we entered into an agreement with Daiichi Sankyo, Inc., or Daiichi Sankyo, to include subjects dosed with edoxaban, Daiichi Sankyo’s Factor Xa inhibitor product, in one of our proof-of-concept studies of Andexanet alfa. We are responsible for the cost of conducting this clinical study. Under the terms of the agreement, Daiichi Sankyo provided us with an upfront fee of \$6.0 million. Daiichi Sankyo may terminate the agreement at any time. The total consideration under this agreement of \$6.0 million was received in July 2013. We are obligated to perform preclinical proof-of-concept studies and participate on a JCC with Daiichi Sankyo to oversee the collaboration activities under the agreement. We originally estimated the non-contingent period of performance to be through the second quarter of 2014. In December 2013, the JCC agreed to forego certain preclinical studies that were planned in the original study design at the inception of the agreement. As a result of this change, we revised our estimated period of performance to be through the first quarter of 2014. The total non-contingent consideration under this agreement of \$3.0 million is being recognized as revenue on a straight-line basis over our estimated non-contingent performance period through the first quarter of 2014. The contingent consideration under this agreement of \$3.0 million will be recognized when the contingency is resolved over the remaining performance period, which is currently estimated to begin in the first quarter of 2014 and conclude in the first quarter of 2015.

In anticipation of a potential BLA filing and subsequent commercialization, we signed an agreement in June 2013 with Lonza Group Ltd, or Lonza, to develop a commercial-scale manufacturing process for Andexanet alfa. We have transferred the manufacturing process previously run at CMC-ICOS for Andexanet alfa to Lonza and have started commercial scale manufacturing at Lonza. Our Phase 3 studies will be initiated with clinical material from CMC ICOS. Non-clinical studies are planned to establish comparability between CMC-ICOS and Lonza material such that Lonza material may be used in the BLA-enabling studies. The commercial manufacturing process at Lonza requires further demonstration and validation prior to filing a BLA. In parallel, we are making process improvements in order to increase scale and efficiency to further improve cost of goods which will be incorporated into the commercial

production of Andexanet alfa through a supplemental BLA.

In January 2014, we entered into a second collaboration agreement with BMS and Pfizer to further study Andexanet alfa as a reversal agent for their jointly owned product candidate apixaban through Phase 3. The Phase 3 studies are expected to start in the first half of 2014. Under the terms of the agreement, we will receive an upfront payment of \$13.0 million and are eligible to receive additional development and regulatory milestone payments of up to \$12.0 million. These payments represent the total consideration under this agreement. BMS and Pfizer will continue to provide development and regulatory guidance for the program.

Under both agreements, we retain full, worldwide development and commercial rights to Andexanet alfa.

This second collaboration agreement will continue in force until the approval of Andexanet alfa as a reversal agent for apixaban by the FDA and EMA. BMS and Pfizer may terminate this agreement for convenience with 60 days' advance written notice or for our bankruptcy or change of control. In addition, either party may terminate this agreement for the other party's uncured material breach, material safety issues, or failure of the Phase 3 studies.

In February 2014, we entered into a second collaboration agreement with Bayer and Janssen to evaluate Andexanet alfa as a reversal agent for the FDA-approved oral Factor Xa inhibitor rivaroxaban through Phase 3 studies. Our original collaboration agreement with Bayer and Janssen, covers the conduct of a Phase 2 proof-of-concept study. The new collaboration agreement covers the conduct of Phase 3 studies of Andexanet alfa with rivaroxaban and any potential U.S. and EU regulatory approval of Andexanet alfa as a reversal agent for rivaroxaban. The Phase 3 studies are expected to start in the first half of 2014. Under this new collaboration agreement, we will receive an upfront payment of \$10.0 million and are eligible to receive additional development and regulatory milestone payments of up to \$15.0 million. These payments represent the total consideration under this agreement. Bayer and Janssen will continue to provide development and regulatory guidance for the program.

Under both agreements, we retain full, worldwide development and commercial rights to Andexanet alfa.

This second collaboration agreement will continue in force until the approval of Andexanet alfa as a reversal agent for rivaroxaban by the FDA and EMA. Bayer and Janssen may terminate this agreement for convenience with 60 days' advance written notice or for our bankruptcy or change of control. In addition, either party may terminate this agreement for the other party's uncured material breach or material safety issues, and we can also terminate this agreement for failure of the Phase 3 studies.

Cerdulatinib

In addition to our thrombosis products, we have discovered two novel orally available kinase inhibitors to treat hematologic disorders and inflammation. The first, Cerdulatinib, is an orally available, potent inhibitor of enzymes that regulate two important signaling pathways, spleen tyrosine kinase, or Syk, and janus kinase. We are developing Cerdulatinib for the treatment of certain B-cell hematologic cancers. We have completed preclinical testing for Cerdulatinib and initiated a Phase 1/2 proof-of-concept study in non-Hodgkin's lymphoma and chronic lymphocytic leukemia in October 2013.

In February 2013, we entered into an agreement with Aciex Therapeutics, Inc., or Aciex, for topical and intranasal co-development and co-commercialization of Cerdulatinib and certain related compounds for nonsystemic indications, such as the treatment and prevention of ophthalmological diseases by topical administration and allergic rhinitis by intranasal administration. We retain rights to other non-systemic indications, including dermatologic disorders. Under the terms of this risk and cost sharing agreement, Portola and Aciex will each incur and report their own internal research and development costs. Third-party related development costs incurred pursuant to this agreement will be shared by Aciex and us 60% and 40%, respectively, until the end of the Phase 2 clinical study, and shared equally thereafter. Aciex has the primary responsibility for conducting the research and development activities under this agreement. We are obligated to provide assistance in accordance with the agreed-upon development plan as well as participate on various committees. We can opt out of our obligation to share in the development costs at various points in time, the timing of which impacts future royalties we may receive based on product sales made by Aciex. All net costs we incur in connection with this agreement will be recognized as research and development expenses. No costs related to this agreement were incurred during the year ended December 31, 2013. See the section of this report entitled "Business—Collaboration and license agreements—Aciex agreement" for a more detailed description of this agreement.

PRT2607

Our second kinase inhibitor, PRT2607, is an orally available, potent and selective inhibitor of Syk. Syk is an important mediator of immune response in a number of different types of immune cells. PRT2607 has been successfully evaluated in 131 subjects in several Phase 1 clinical studies. Biogen Idec Inc., or Biogen Idec, is leading the pre-clinical study of PRT2607 and other highly selective Syk inhibitors for allergic asthma and other inflammatory

disorders and is responsible for all development-related expenses.

In October 2011, we entered into an exclusive, worldwide license and collaboration agreement with Biogen Idec to develop and commercialize selective Syk kinase inhibitors for the treatment of autoimmune and inflammatory diseases. See the section of this report entitled “Business—Collaboration and license agreements—Biogen Idec agreement” for a more detailed description of this agreement.

In June 2005, we entered into a license agreement with Astellas Pharma, Inc., or Astellas, pursuant to which we licensed from Astellas certain rights to research, develop and commercialize Syk kinase inhibitors, including Cerdulatinib and PRT2607. This agreement was amended in December 2010. See the section of this report entitled “Business—Collaboration and license agreements—Astellas agreement” for a more detailed description of this agreement.

Other

Prior to 2012, we were developing Elinogrel, a novel anti-platelet agent. In February 2009, we entered into a worldwide collaboration and license agreement with Novartis Pharma A.G., or Novartis, to develop and commercialize Elinogrel. Novartis made an upfront cash payment to us of \$75.0 million, and the agreement also provided for additional payments based on the achievement of certain development, regulatory and commercialization milestones. In April 2012, we and Novartis agreed to a plan for Novartis to return all rights to Elinogrel to us and to terminate our agreement, effective July 1, 2012. As of the time of termination, no milestones had been achieved and no royalties had been triggered pursuant to our agreement with Novartis. Although we may resume development of Elinogrel in the future, we currently do not plan to do so.

For purposes of this discussion and analysis of our financial condition and results of operations, we refer to our agreements with Millennium, Merck, Lee's, BMS and Pfizer, Bayer and Janssen, Daiichi Sankyo, Acix, Biogen Idec, Astellas and Novartis collectively as our collaboration agreements.

Financial operations overview

Revenue

Our revenue to date has been generated primarily from collaboration and license revenue pursuant to our collaboration agreements. We have not generated any revenue from commercial product sales to date. Under our agreements with Biogen Idec, Merck, Novartis, BMS and Pfizer, Bayer and Janssen, Daiichi Sankyo and Lee's, we received payments including non-refundable upfront license fees, a refundable contingent payment and a milestone payment in the aggregate amount of \$178.7 million.

We may also be entitled to additional milestone payments and other contingent payments upon the occurrence of specific events.. Due to the nature of these collaboration agreements and the nonlinearity of the earnings process associated with certain payments and milestones, we expect that our revenue will continue to fluctuate in future periods.

The following table summarizes the sources of our revenue for the years ended December 31, 2013, 2012 and 2011, in thousands:

	Year Ended December 31,		
	2013	2012	2011
Novartis:			
Recognition of upfront license fee	\$-	\$53,846	\$7,692
Reimbursement of research and development expense	-	16,238	1,879
Novartis total	-	70,084	9,571
Merck:			
Recognition of upfront license fee	-	-	21,429
Reimbursement of research and development expense	-	-	9,973
Merck total	-	-	31,402
Biogen Idec:			
Recognition of upfront license fee	-	-	37,056
Biogen Idec total	-	-	37,056
BMS and Pfizer:			

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Recognition of research and development services	4,042	1,958	-
BMS and Pfizer total	4,042	1,958	-
Bayer and Janssen:			
Recognition of research and development services	3,876	-	-
Bayer and Janssen total	3,876	-	-
Lee's:			
Recognition of research and development services	194	-	-
Lee's total	194	-	-
Daiichi Sankyo:			
Recognition of research and development services	2,419		
Daiichi Sankyo total	2,419	-	-
Total collaboration and license revenue	\$10,531	\$72,042	\$78,029

In accordance with the accounting guidance we adopted on January 1, 2011, we recognized collaboration revenue of \$37.1 million pursuant to our agreement with Biogen Idec and recorded a reduction for research and development expenses of \$0.7 million for reimbursement of research and development expenses received from Biogen Idec for the year ended December 31, 2011. Under the previous accounting guidance for multiple element arrangements, we would have recognized revenue of approximately \$3.4 million pursuant to our agreement with Biogen Idec for the year ended December 31, 2011. We expect that our revenue will continue to fluctuate in future periods.

Research and development expenses

Research and development expenses represent costs incurred to conduct research, such as the discovery and development of our unpartnered product candidates, as well as discovery and development of clinical candidates pursuant to our collaboration agreements. We recognize all research and development costs as they are incurred.

Our research and development expenses may increase or decrease by amounts we may pay or receive under various cost-sharing provisions of our collaboration and license agreements.

We expect our research and development expenses to increase as we continue to advance our product candidates through clinical development. We intend to identify partnerships to further develop other product candidates that strengthen our pipeline, which may offset a portion of our research and development expenses through reimbursement from these partners. In addition, if any of our product candidates receive regulatory approval for commercial sale, we expect to incur significant expenses associated with the establishment of a hospital-based sales force in the United States and possibly other major markets. Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of expenses incurred or when, or if, we will be able to achieve and sustain profitability.

The following table summarizes our research and development expenses by product candidate:

	Phase of development (in thousands) (unaudited)	Year Ended December 31		
		2013	2012	2011
Product candidate				
Betrixaban	Phase 3	\$40,641	\$27,297	\$5,828
Andexanet alfa	Phase 2	33,420	15,049	11,128
Cerdulatinib	Phase 1/2	5,242	726	1,970
PRT2607	Pre-clinical	(113)	3,344	19,045
Elinogrel ⁽¹⁾	Phase 3 ready	59	172	3,221
Other research and development expenses ⁽²⁾		37	3,129	4,897
Total research and development expenses ⁽³⁾		\$79,286	\$49,717	\$46,089

(1) Although we may resume development of Elinogrel in the future, we currently do not plan to do so.

(2) Amounts in all periods include costs for other potential product candidates.

(3)

Our research and development expenses have been reduced by reimbursements of certain research and development expenses pursuant to the cost-sharing provisions of our agreements with Biogen Idec commencing in the fourth quarter of 2011 and MyoKardia, Inc. and Global Blood Therapeutics, Inc. commencing in the fourth quarter of 2012. Reimbursement of research and development expenses of the cost-sharing provisions of our agreements with Merck and Novartis were recognized as revenue pursuant to the revenue recognition accounting policy applicable to these agreements.

The program-specific expenses summarized in the table above include costs directly attributable to our product candidates. We allocate research and development salaries, benefits, stock-based compensation and indirect costs to our product candidates on a program-specific basis, and we include these costs in the program-specific expenses. The largest component of our total operating expenses has historically been our investment in research and development activities, including the clinical development of our product candidates. We expect our research and development expenses to increase in the future. The process of conducting the necessary clinical research to obtain FDA approval is costly and time consuming. We consider the active management and development of our clinical pipeline to be crucial to our long-term success. The actual probability of success for each product candidate and clinical program may be affected by a variety of factors including: the quality of the product candidate, early clinical data, investment in the program, competition, manufacturing capability and commercial viability. Furthermore, in the past we have entered into collaborations with third parties to participate in the development and commercialization of our product candidates, and we may enter into additional collaborations in the future. In situations in which third parties have control over the preclinical development or clinical study process for a product candidate, the estimated completion dates are largely under the control of such third parties and not under our control. We cannot forecast with any degree of certainty which of our product candidates, if any, will be subject to future collaborations or how such arrangements would affect our development plans or capital requirements. As a result of the uncertainties discussed above, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates.

General and administrative expenses

General and administrative expenses consist primarily of personnel costs, allocated facilities costs and other expenses for outside professional services, including legal, human resources, audit and accounting services. Personnel costs consist of salaries, benefits and stock-based compensation. We are incurring additional expenses as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the Securities and Exchange Commission, or SEC, and those of The NASDAQ Global Market, additional insurance expenses, investor relations activities and other administration and professional services.

Interest and other income (expense), net

Interest and other income (expense), net consists primarily of interest received on our cash, cash equivalents and investments, unrealized gains and losses from the remeasurement of our foreign currency bank balances and foreign currency forward contracts and gains and losses resulting from the remeasurement of our convertible preferred stock warrant liability. We recorded adjustments to the estimated fair value of the convertible preferred stock warrants until they were converted into warrants to purchase shares of our common stock upon the closing of our initial public offering, or IPO. At that time, we reclassified the convertible preferred stock warrant liability to additional paid-in capital and we will no longer record any related periodic fair value adjustments.

Critical accounting policies and significant judgments and estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with United States generally accepted accounting principles, or U.S. GAAP. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenue generated and expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 of our financial statements included in this Annual Report on Form 10-K, we believe the following accounting policies to be critical to the judgments and estimates used in the preparation of our financial statements.

Revenue recognition

We generate revenue from collaboration and license agreements for the development and commercialization of our product candidates. Collaboration and license agreements may include non-refundable upfront payments, partial or complete reimbursement of research and development costs, contingent payments based on the occurrence of specified events under our collaboration arrangements, license fees and royalties on sales of product candidates if they are successfully approved and commercialized. Our performance obligations under the collaborations may include the transfer of intellectual property rights in the form of licenses, obligations to provide research and development services and related materials and obligations to participate on certain development and/or commercialization committees with the collaboration partners. We make judgments that affect the periods over which we recognize revenue. We periodically review our estimated periods of performance based on the progress under each arrangement and account for the impact of any changes in estimated periods of performance on a prospective basis.

On January 1, 2011, we adopted an accounting standards update that amends the guidance on accounting for new or materially modified multiple-element arrangements that we enter into subsequent to January 1, 2011. This guidance removed the requirement for objective and reliable evidence of fair value of the undelivered items in order to consider a deliverable a separate unit of accounting. It also changed the allocation method such that the relative-selling-price method must be used to allocate arrangement consideration to all the units of accounting in an arrangement. This guidance established the following hierarchy that must be used in estimating selling price under the relative-selling-price method: (1) vendor-specific objective evidence of fair value of the deliverable, if it exists, (2) third-party evidence of selling price, if vendor-specific objective evidence is not available or (3) vendor's best estimate of selling price if neither vendor-specific nor third-party evidence is available. The adoption of this guidance had a material effect on the revenue recognized for the year ended December 31, 2011 as we entered into a multiple-element agreement with Biogen Idec. We determined that the deliverables under our agreement with Biogen Idec had stand-alone value and there were no rights of return, thus we accounted for each deliverable as a separate unit of accounting. For multiple element arrangements entered into prior to January 1, 2011, we determined whether the elements had stand-alone value and whether there was objective and reliable evidence of fair value. When the delivered element did not have stand-alone value or there was insufficient evidence of fair value for the undelivered element(s), we recognized the consideration for the combined unit of accounting on a straight-line basis over the estimated period of performance, which was the same manner in which the revenue was recognized for the final deliverable.

Based upon the relative estimated selling prices of the units of accounting for the year ended December 31, 2011, we recognized collaboration and license revenue of \$37.1 million pursuant to our agreement with Biogen Idec, and recorded a reduction in our research and development expenses of \$0.7 million for reimbursement of research and development expenses received from Biogen Idec pursuant to the cost-sharing provisions of our agreement with Biogen Idec. Under the previous accounting guidance for multiple element arrangements, we would have recognized revenue of approximately \$3.4 million pursuant to our agreement with Biogen Idec for the year ended December 31, 2011. We would have concluded that all deliverables are combined into a single unit of accounting in the absence of vendor-specific objective evidence of fair value of undelivered services, and we would have recognized the funds received over an estimated performance period through November 2013.

On January 1, 2011, we also adopted an accounting standards update that provides guidance on revenue recognition using the milestone method. Payments that are contingent upon achievement of a substantive milestone are recognized in their entirety in the period in which the milestone is achieved. Milestones are defined as events that can be achieved based only on our performance and as to which, at the inception of the arrangement, there is substantive uncertainty about whether the milestone will be achieved. Events that are contingent only on the passage of time or only on third-party performance are not considered milestones subject to this guidance. Further, the amounts received must relate solely to prior performance, be reasonable relative to all of the deliverables and payment terms in the agreement

and commensurate with our performance to achieve the milestone after commencement of the agreement.

Amounts received from licensing of intellectual property are recognized as revenue, as such licensing is one of our principal or major ongoing activities. Amounts received as funding of research and development activities are recognized as revenue if the collaboration arrangement involves the sale of our research or development services at amounts that exceed our cost. However, such funding is recognized as a reduction of research and development expenses when we engage in a research and development project jointly with another entity, with both entities participating in project activities and sharing costs and potential benefits of the project. Accordingly, reimbursement of research and development expenses pursuant to the cost-sharing provisions of our agreements with Merck and Novartis, which were entered into in 2009 and prior to the adoption of the accounting standards update explained above, were recognized as revenue pursuant to our revenue recognition accounting policy in effect at that time. Reimbursement of research and development expenses pursuant to the cost-sharing provisions of our agreement with Biogen Idec, which was entered into in 2011 following the adoption of the accounting standards update explained above, are recognized as a reduction of research and development expenses. In November 2012, we elected to exercise our option to fully out-license PRT2607 under our agreement with Biogen Idec and accordingly we and Biogen Idec no longer have any further obligation pursuant to the cost-sharing provisions of the agreement.

Accrued research and development expenses

As part of the process of preparing financial statements, we are required to estimate and accrue expenses, the largest of which are research and development expenses. This process involves the following:

- communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost;
- estimating and accruing expenses in our financial statements as of each balance sheet date based on facts and circumstances known to us at the time; and
- periodically confirming the accuracy of our estimates with selected service providers and making adjustments, if necessary.

Examples of estimated research and development expenses that we accrue include:

- fees paid to CROs in connection with preclinical and toxicology studies and clinical studies;
- fees paid to investigative sites in connection with clinical studies;
- fees paid to CMOs in connection with the production of clinical study materials; and
- professional service fees for consulting and related services.

We base our expense accruals related to clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and clinical research organizations that conduct and manage clinical studies on our behalf. The financial terms of these agreements vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors, such as the successful enrollment of patients and the completion of clinical study milestones. Our service providers invoice us monthly in arrears for services performed. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates.

To date, we have not experienced significant changes in our estimates of accrued research and development expenses after a reporting period. However, due to the nature of estimates, we cannot assure you that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical studies and other research activities.

Estimated fair value of convertible preferred stock warrants

Freestanding warrants for the purchase of convertible preferred stock that are either subject to a put right or redeemable are classified as liabilities on the balance sheet at their estimated fair value. At the end of each reporting period, changes in estimated fair value during the period are recorded in interest and other income, net. We continued to adjust the carrying value of these warrants until the completion of our IPO, at which time the liabilities were reclassified to stockholders' deficit.

We estimate the fair values of the convertible preferred stock warrants using the Black-Scholes option-pricing model based on inputs as of the valuation measurement dates for the estimated fair value of the underlying convertible preferred stock, the remaining contractual terms of the warrants, risk-free interest rates, expected dividend rates and the estimated volatility of the price of the convertible preferred stock.

Stock-based compensation

Stock-based compensation cost is recorded at fair value as of the grant date using the Black-Scholes option-pricing model and recognized as expense on a straight-line basis over the requisite service period. Prior to our IPO in May 2013, stock based compensation cost was measured at the date of grant, based on the estimated fair value of the award as determined by our board of directors and recognized as expense on a straight-line basis over the requisite service period. We expect to continue to grant stock options in the future, and to the extent that we do, our actual stock-based compensation expense recognized in future periods will likely increase.

We account for stock-based compensation arrangements with non-employees using a fair value approach. The fair value of these options is measured using the Black-Scholes option pricing model reflecting the same assumptions as applied to employee options in each of the reported periods, other than the expected life, which is assumed to be the remaining contractual life of the option. The compensation costs of these arrangements are subject to remeasurement over the vesting terms as earned.

Option grants are based on the fair value of our common stock on the date of grant. Prior to our IPO in May 2013, our board of directors, with the assistance of management and, in some cases, an independent third-party valuation consultant, determined the estimated fair value of our common stock. In determining the estimated fair value of our common stock, our board of directors used a combination of the market multiple approach and the IPO value approach to estimate the enterprise value of our company in accordance with the American Institute of Certified Public Accountants Accounting and Valuation Guide: Valuation of Privately-Held-Company Equity Securities Issued as Compensation. The per share common stock value was estimated by allocating the enterprise value using the probability-weighted expected return method at each valuation date prior to December 2011 and commencing in December 2012. The per share common stock value was estimated by using the option pricing method at each valuation date between December 2011 and December 2012.

Income taxes

We file U.S. federal income tax returns and California, Alaska and Massachusetts state tax returns. To date, we have not been audited by the Internal Revenue Service or any state income tax authority.

As of December 31, 2013, our total deferred tax assets were \$119.7 million. The deferred tax assets were primarily comprised of federal and state tax net operating losses and tax credit carryforwards. Utilization of the net operating loss and tax credit carryforwards may be subject to an annual limitation due to historical or future ownership percentage change rules provided by the Internal Revenue Code of 1986, and similar state provisions. The annual limitation may result in the expiration of certain net operating loss and tax credit carryforwards before their utilization. In 2013, we performed an analysis on annual limitation as a result of ownership changes that may have occurred through November 2013. Our analysis indicates that a change occurred during 2013. As a result of this change, our net operating loss and tax credit carryforwards will not be subject to limitation in total, but we may be subject to a limitation as it relates to the timing of utilization. However, due to a lack of historical earnings and uncertainties surrounding our ability to generate future taxable income to realize these tax assets, a full valuation allowance has been established to offset our deferred tax assets.

Comparison of the years ended December 31, 2013 and 2012

Revenue

	Year ended December 31, 2013	2012	Increase / (Decrease)	% Increase / (Decrease)
	(dollars in thousands)			
Collaboration and license revenue	\$10,531	\$72,042	\$ (61,511)	(85)%

The decrease in collaboration and license revenue during 2013 was due to the decrease in revenue from Novartis following the termination of our agreement with Novartis effective July 1, 2012. We recognized no revenue from our agreement with Novartis during 2013, compared to revenue of \$70.1 million recognized from our agreement with Novartis during 2012. This decrease in collaboration and license revenue was partially offset by revenue recognized

during 2013 with respect to our agreements with BMS and Pfizer of \$4.0 million, Bayer and Janssen of \$3.9 million, Lee's of \$0.2 million and Daiichi Sankyo of \$2.4 million.

We expect revenue recognized in future periods to fluctuate as we recognize revenue related to our existing collaboration agreements and enter into new collaboration agreements.

Research and development expenses

	Year ended December 31, 2013 2012		Increase / (Decrease)	% Increase / (Decrease)	
	(dollars in thousands)				
Research and development expenses	\$79,286	\$49,717	\$ 29,569	59	%

The increase in research and development expenses was primarily due to the following:

increased program costs of \$13.3 million to advance Betrixaban;
 increased program costs of \$18.4 million to advance Andexanet alfa;
 increased program costs of \$4.5 million to advance Cerdulatinib;
 These increases were partially offset by:

decreased net program costs of \$3.5 million related to PRT2607, primarily due to reimbursements received from Biogen Idec to fund clinical and manufacturing costs pursuant to the cost-sharing provisions of our agreement with Biogen Idec; and

decreased development costs of \$3.2 million as we reduced costs for programs that are not related to or in support of our primary programs of development; Betrixaban, Andexanet alfa and Cerdulatinib.

We expect our research and development expenses to increase in the future as we advance our product candidates through clinical development. The timing and amount of expenses incurred will depend largely upon the outcomes of current or future clinical studies for our product candidates as well as the related regulatory requirements, manufacturing costs and any costs associated with the advancement of our preclinical programs.

General and administrative expenses

	Year ended December 31, 2013 2012		Increase / (Decrease)	% Increase / (Decrease)	
	(dollars in thousands)				
General and administrative expenses	\$15,423	\$11,469	\$ 3,954	34	%

The increase in general and administrative expenses during 2013 was primarily related to increased headcount related costs including an increase in stock based compensation expense resulting from the increased fair value of new stock options following our IPO in May 2013 of \$3.3 million, and increased costs associated with being a public company including directors and officer's insurance and director fees of \$0.5 million, and higher professional and legal fees to support business development and collaboration arrangements of \$0.1 million.

We expect general and administrative expenses to continue to increase in order to support the costs of being a public company and our growing business.

Interest and other income, net

	Year ended December 31, 2013 2012		Increase / (Decrease)	% Increase / (Decrease)	
	(dollars in thousands)				
Interest and other income, net	\$826	\$510	\$ 316	62	%

Interest and other income, net increased as a result of interest income of \$0.1 million earned on higher cash, cash equivalents and investments balances and foreign currency exchange gains of \$0.3 million primarily related to favorable fluctuations in the Euro compared to the U.S. dollar and the unrealized gains related to our Euro forward contracts. The increase was partially offset by decreased other income of \$0.1 million due to the fair value remeasurement of our convertible preferred stock warrants.

Comparison of the years ended December 31, 2012 and 2011

Revenue

	Year ended December 31, 2012 2011		Increase / (Decrease)	% Increase / (Decrease)
	(dollars in thousands)			
Collaboration and license revenue	\$72,042	\$78,029	\$ (5,987)	(8)%

The decrease in collaboration and license revenue was due to the decrease in revenue recognized with respect to our agreements with Biogen Idec, which we entered into in the fourth quarter of 2011, and Merck, which was terminated in the third quarter of 2011. We recognized no revenue from our agreement with Biogen Idec during 2012, compared to revenue of \$37.1 million recognized from this same agreement during 2011. We recognized no revenue from our agreement with Merck during 2012, compared to revenue of \$31.4 million recognized from this same agreement during 2011.

The decrease in collaboration and license revenue recognized with respect to our agreements with Biogen Idec and Merck was partially offset by the recognition of all remaining deferred revenue following the termination of our agreement with Novartis effective July 1, 2012. In connection with the termination of our agreement with Novartis, we recognized revenue of \$65.1 million, consisting of \$50.0 million of upfront license fees and \$15.1 million of reimbursement of research and development expenses. Our total Novartis revenue for 2012 of \$70.1 million included the foregoing amounts. In addition, we recognized \$3.8 million of upfront collaboration and license revenue and \$1.1 million of reimbursement of research and development expenses prior to the termination of our agreement with Novartis. For 2011, we recognized total Novartis revenue of \$9.6 million.

We expect revenue recognized in future periods to be lower than that in 2012 primarily due to no further revenue being recognized in connection with our terminated agreement with Novartis, which may be partially offset by an increase in revenue recognized in connection with new collaboration agreements.

Research and development expenses

	Year ended December 31, 2012 2011		Increase / (Decrease)	% Increase / (Decrease)
	(dollars in thousands)			
Research and development expenses	\$49,717	\$46,089	\$ 3,628	8 %

The increase in research and development expenses was primarily due to the following:

increased program costs of \$21.5 million to advance Betrixaban;
increased program costs of \$3.9 million to advance Andexanet alfa;
decreased net program costs of \$15.7 million related to PRT2607, primarily due to reimbursements received from Biogen Idec to fund clinical and manufacturing costs pursuant to the cost-sharing provisions of our agreement with Biogen Idec; and
decreased program costs of \$3.0 million related to Elinogrel in connection with the termination of our agreement with Novartis effective July 1, 2012.

We expect our research and development expenses to increase in the future as we advance our product candidates through clinical development. The timing and amount of expenses incurred will depend largely upon the outcomes of current or future clinical studies for our product candidates as well as the related regulatory requirements, manufacturing costs and any costs associated with the advancement of our preclinical programs.

General and administrative expenses

	Year ended		Increase /	% Increase /
	December 31,		(Decrease)	(Decrease)
	2012	2011		
	(dollars in thousands)			
General and administrative expenses	\$11,469	\$12,071	\$ (602)	(5)%

The decrease in general and administrative expenses was primarily related to decreased professional and legal costs of \$1.1 million, partially offset by increased facilities and overhead-related costs of \$0.5 million.

We expect general and administrative expenses to continue to increase in order to support the costs of being a public company.

Interest and other income, net

	Year ended		Increase /	% Increase /	
	December 31,		(Decrease)	(Decrease)	
	2012	2011			
	(dollars in thousands)				
Interest and other income, net	\$510	\$136	\$ 374	322	%

The increase in interest and other income, net is from increased interest income of \$0.2 million on higher cash, cash equivalents and investments, increased other income of \$0.1 million due to the fair value remeasurement of our convertible preferred stock warrants, and foreign currency exchange gains of \$0.1 million primarily related to favorable fluctuations in the Euro compared to the U.S. dollar and the unrealized gains related to our Euro forward contracts.

Interest expense

	Year ended December 31, 20122011 (dollars in thousands)	Increase / (Decrease)	% Increase / (Decrease)
Interest expense	\$—\$ 21	\$ (21)	(100 %)

The decrease in interest expense was due to the repayment of our long-term debt in April 2011.

Liquidity and capital resources

Due to our significant research and development expenditures, we have generated significant operating losses since our inception. We have funded our operations primarily through sales of our common stock as part of our IPO and follow-on public offering, and our convertible preferred stock and payments from our collaboration partners. Our expenditures are primarily related to research and development activities. At December 31, 2013, we had available cash, cash equivalents and investments of \$319.0 million. Our cash, cash equivalents and investments are held in a

variety of interest-bearing instruments, including investments backed by U.S. government agencies, corporate debt securities and money market accounts. Cash in excess of immediate requirements is invested with a view toward liquidity and capital preservation, and we seek to minimize the potential effects of concentration and degrees of risk.

On May 28, 2013, we closed our IPO, of 9,686,171 shares of our common stock, which included 1,263,413 shares of common stock issued pursuant to the over-allotment option granted to the underwriters. The public offering price of the shares sold in the offering was \$14.50 per share. The offer and sale of all of the shares in the IPO were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-187901), which was declared effective by the SEC on May 21, 2013. The total proceeds from the offering to us, net of underwriting discounts and commissions of approximately \$9.4 million, were approximately \$131.0 million. After deducting offering expenses payable by us of approximately \$5.1 million, our net proceeds were approximately \$125.8 million. As of December 31, 2013, no accrued offering costs remained unpaid. Upon the closing of the IPO, 24,026,797 shares of convertible preferred stock then outstanding automatically converted into 24,026,797 shares of our common stock.

On October 22, 2013, we closed a follow-on public offering of 6,366,513 shares of our common stock, which included 4,457,710 shares issued and sold by us and 1,908,803 shares of common stock sold by certain existing stockholders of Portola. The public offering price of the shares sold in the offering was \$23.75 per share. In addition, on November 14, 2013, the underwriters of the offering exercised their over-allotment option to purchase an additional 954,976 shares from us at the public offering price. The offer and sale of all of the shares in the offering were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-191609), which was declared effective by the SEC on October 16, 2013. The total proceeds from the offering to us including the over-allotment option, net of underwriting discounts and commissions of approximately \$7.7 million, were approximately \$120.8 million. After deducting offering expenses payable by us of approximately \$0.9 million, our net proceeds were approximately \$119.9 million.

In February 2009, July 2009, November 2011, December 2012, February 2013, March 2013, April 2013, and July 2013, in connection with our agreements with Novartis, Merck and Biogen Idec, BMS and Pfizer, Bayer and Janssen, Lee's and Daiichi Sankyo we received payments of \$75.0 million, \$50.0 million, \$36.0 million, \$6.0 million, \$5.0 million, \$0.7 million, and \$6.0 million, respectively, as initial upfront payments and a milestone payment of \$2.0 million from BMS and Pfizer. These payments are initially reflected as deferred revenue and included within cash used in operating activities. November 2011, we received proceeds of \$98.0 million from the sale of our convertible preferred stock.

The following table summarizes our cash flows for the periods indicated:

	Year Ended December 31,		
	2013	2012	2011
Cash used in operating activities	\$(63,615)	\$(49,225)	\$(11,321)
Cash provided by (used in) investing activities	(120,736)	(67,802)	32,710
Cash provided by (used in) financing activities	248,511	317	94,218
Net increase (decrease) in cash	\$64,160	\$(116,710)	\$115,607

Cash used in operating activities

Cash used in operating activities was \$63.6 million for the year ended December 31, 2013 reflecting a net loss of \$83.4 million, which was decreased by non-cash charges of \$5.0 million for stock-based compensation, \$2.3 million for amortization of premium on investments and \$1.4 million for depreciation and amortization. Cash used in operating activities also reflected an increase in net operating assets of \$11.1 million primarily due to increases in accounts payable and accrued and other liabilities of \$10.1 million related to higher clinical study and related costs as we continue to increase our research and development activities, an increase in deferred revenue of \$1.2 million due to an increase in deferred revenue of \$5.0 million related to the upfront payments received from Bayer and Janssen, \$6.0 million related to the upfront payments received from Daiichi Sankyo and \$0.7 million related to the upfront payments received from Lee's in the year ended December 31, 2013, partially offset by the recognition of collaboration revenue earned of \$10.5 million from our collaboration agreements and an increase in accrued compensation and employee benefits of \$0.7 million to support our increased headcount. Cash used in operating activities also reflected an increase in prepaid expenses and other current assets of \$0.7 million primarily reflecting higher interest receivable on our investment portfolio of \$0.4 million, unrealized gains on our foreign currency forward contracts of \$0.4 million, other receivables of \$0.4 million related to our agreements with Myokardia and Global Blood Therapeutics, prepaid premiums for corporate director's and officer's insurance of \$0.1 million following the renewal of our corporate insurance program and placement of our public company policies, and prepaid rent of \$0.2 million in 2013 partially offset by recognition of clinical trial upfront fees upon contract execution of \$0.7 million. Also reflected in cash used in operating activities is a decrease in other assets following payment and classification of deferred offering costs of

\$1.6 million and a decrease in receivables from collaborations of \$0.4 million due to the receipt of research and development expenses reimbursable from Biogen Idec pursuant to our agreement with Biogen Idec.

Cash used in operating activities was \$49.2 million for the year ended December 31, 2012 reflecting net income of \$11.4 million, which was increased by non-cash charges of \$1.4 million for depreciation and amortization, \$1.5 million for amortization of premium on investments, \$2.8 million for stock-based compensation and \$0.1 million for unrealized gains related to foreign currency forward contracts. Cash used in operating activities also reflected a decrease in net operating assets of \$66.1 million primarily due to the recognition of all remaining deferred revenue of \$65.1 million related to the upfront payments received from Novartis in prior periods following the termination of our agreement with Novartis effective July 1, 2012 and the recognition of collaboration revenue earned of \$6.9 million; an increase in prepaid expenses and other current assets of \$2.5 million primarily for clinical study costs paid in advance to our CRO and prepaid clinical study insurance; and an increase in other assets of \$2.1 million related to deferred offering costs and legal fees related to our IPO. Also reflected in cash used in operating activities is a decrease in accrued compensation and employee benefits of \$1.0 million due to 2011 bonuses that were paid in the first quarter of 2012 and a decrease in receivables from collaboration agreements of \$0.3 million due to increased research and development expenses reimbursable from Biogen Idec pursuant to our agreements with Biogen Idec, MyoKardia, Inc. and Global Blood Therapeutics, Inc., and increases in accounts payable and accrued and other liabilities of \$5.4 million related to higher clinical study and related costs as we continue to increase our research and development activities.

Cash used in operating activities was \$11.3 million for the year ended December 31, 2011 reflecting net income of \$20.0 million, which was increased by non-cash charges of \$0.8 million for amortization of premium on investments, \$1.4 million for depreciation and amortization and \$2.4 million for stock-based compensation. Cash used in operating activities also reflected a decrease in net operating assets of \$35.8 million due to the amortization of deferred revenue of \$35.4 million related to initial upfront payments from our collaboration partners, a decrease in accrued income taxes of \$2.5 million for taxes paid in the first quarter of 2011 and decreases in prepaid expenses and other current assets of \$1.6 million primarily related to the receipt of reimbursable leasehold improvement costs from our landlord and timing of prepaid research and development expenses and the increase in accounts payable of \$1.4 million due to higher research and development related costs and timing of such payments.

Cash used in investing activities

Cash used in investing activities of \$120.7 million for the year ended December 31, 2013 was primarily related to purchases of investments of \$219.8 million and capital equipment purchases of \$0.9 million, partially offset by proceeds from sales of investments of \$8.0 million and proceeds from maturities of investments of \$92.0 million.

Cash used in investing activities of \$67.8 million for the year ended December 31, 2012 was primarily related to purchases of investments of \$144.6 million and capital equipment purchases of \$0.4 million, partially offset by proceeds from sales of investments of \$36.5 million and proceeds from maturities of investments of \$40.7 million.

Cash provided by investing activities of \$32.7 million for the year ended December 31, 2011 was primarily related to proceeds from maturities of investments of \$59.8 million, the contractual release of restricted cash of \$6.0 million and proceeds from sales of investments of \$2.2 million. These increases were partially offset by purchases of investments of \$33.8 million and capital equipment purchases of \$1.5 million.

Cash provided by financing activities

Cash provided by financing activities of \$248.5 million for the year ended December 31, 2013, was primarily related to proceeds from our IPO, net of underwriting discounts and commissions, of \$131.0 million, partially offset by payments of deferred offering costs of \$5.0 million and proceeds from our follow-on public offering, net of underwriting discounts and commissions, of \$120.8 million, partially offset by payments of deferred offering costs of \$0.9 million, and proceeds from the exercise of stock options of \$2.5 million.

Cash provided by financing activities of \$0.3 million for the year ended December 31, 2012, was related to proceeds from the exercise of stock options.

Cash provided by financing activities of \$94.2 million for the year ended December 31, 2011 was primarily related to net proceeds from issuance of convertible preferred stock of \$96.7 million and proceeds from the exercise of stock options of \$0.2 million, partially offset by repayment of long-term debt of \$2.6 million.

We believe that our existing capital resources, together with interest thereon, will be sufficient to meet our projected operating requirements for at least the next 12 months. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Further, our operating plan may change, and we may need additional funds to meet operational needs and capital requirements for product development and commercialization sooner than planned. We currently have no credit facility or committed sources of capital other than potential milestones receivable under our current collaboration. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates and the extent to which we may enter into additional collaborations with third parties to participate in their development and commercialization, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical studies. Our future funding requirements will depend on many factors, including the following:

- the scope, rate of progress, results and cost of our clinical studies, preclinical testing and other related activities;
- the cost of manufacturing clinical supplies, and establishing commercial supplies, of our product candidates and any products that we may develop, including process improvements in order to manufacture Andexanet alfa at commercial scale;
- the receipt of any collaboration payments;
- the number and characteristics of product candidates that we pursue;
- the cost, timing and outcomes of regulatory approvals;
- the cost and timing of establishing sales, marketing and distribution capabilities;
- the terms and timing of any other collaborative, licensing and other arrangements that we may establish;
- the timing, receipt and amount of sales, profit sharing or royalties, if any, from our potential products;
- the cost of preparing, filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights; and
- the extent to which we acquire or invest in businesses, products or technologies, although we currently have no commitments or agreements relating to any of these types of transactions.

If we need to raise additional capital to fund our operations, funding may not be available to us on acceptable terms, or at all. If we are unable to obtain adequate financing when needed, we may have to delay, reduce the scope of or suspend one or more of our clinical studies, research and development programs or commercialization efforts. We may seek to raise any necessary additional capital through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing and distribution arrangements. To the extent that we raise additional capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we do raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

Off-balance sheet arrangements

Since our inception, we have not engaged in any off-balance sheet arrangements, including the use of structured finance, special purpose entities or variable interest entities.

Contractual obligations

Our future contractual obligations at December 31, 2013 were as follows:

	Payments due by period				Total
	Less than 1 year (in thousands)	1 to 3 years	3 to 5 years	More than 5 years	
Contractual obligations:					
Purchase commitments	\$5,243	\$—	\$ —	\$ —	\$5,243
Operating lease obligations	1,660	418			2,078
Total contractual obligations	\$6,903	\$418	\$ —	\$ —	\$7,321

Pursuant to our asset purchase agreement with Millennium, we are obligated to pay to Millennium royalties on sales of certain products if product sales are ever achieved, which royalty payments will continue until the expiration of the relevant patents or 10 years after the launch, whichever is later. Pursuant to the license agreement between Millennium and us, we are required to make certain license fee, milestone, royalty and sublicense sharing payments to Millennium as we develop, commercialize or sublicense Betrixaban and other products from certain Factor Xa programs as described in the agreement. In November 2007, we made a cash payment to Millennium of \$5.0 million pursuant to the license agreement. The Millennium license agreement further provides for additional payments to Millennium of up to \$35.0 million based on the achievement of certain milestones related to Betrixaban and the Factor Xa programs. See the section of this report entitled “Business—Collaboration and license agreements—Millennium agreements” for a more detailed description of these agreements.

We entered into an agreement pursuant to which a manufacturer, Lonza, will fully develop a commercial scale manufacturing process for Andexanet alfa and produce approval-enabling validation lots. The agreement includes purchase commitments aggregating approximately \$4.4 million over several years of which \$2.6 million is non-cancellable and included in the contractual obligations table above as a purchase commitment.

JOBS Act accounting election

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards, and, therefore, are subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The primary objective of our investment activities is to preserve our capital to fund our operations. We also seek to maximize income from our investments without assuming significant risk. To achieve our objectives, we maintain a portfolio of cash equivalents and investments in a variety of securities of high credit quality. As of December 31, 2013, we had cash, cash equivalents and investments of \$319.0 million consisting of cash and liquid investments deposited in highly rated financial institutions in the United States. A portion of our investments may be subject to

interest rate risk and could fall in value if market interest rates increase. However, because our investments are primarily short-term in duration, we believe that our exposure to interest rate risk is not significant and a 1% movement in market interest rates would not have a significant impact on the total value of our portfolio. We actively monitor changes in interest rates.

We contract for the conduct of certain clinical development and manufacturing activities with vendors in Europe. Beginning in 2012, we have utilized foreign currency forward contracts to mitigate our exposure to foreign currency gains and losses. We made payments in the aggregate amount of €17.8 million to our European vendors during the year ended December 31, 2013. We are subject to exposure due to fluctuations in foreign exchange rates in connection with these agreements and with our cash balance denominated in Euros. For the year ended December 31, 2013, the effect of the exposure to these fluctuations in foreign exchange rates was not material. A 10% change in the exchange rates upward or downward in our portfolio of foreign currency forward contracts would have increased unrealized gain by \$0.8 million or decreased unrealized gain by \$5.3 million, respectively, at December 31, 2013. We hedge our foreign currency exposures but we have not used derivative financial instruments for speculation or trading purposes.

PORTOLA PHARMACEUTICALS, INC.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders

Portola Pharmaceuticals, Inc.

We have audited the accompanying balance sheets of Portola Pharmaceuticals, Inc. (the “Company”) as of December 31, 2013 and 2012, and the related statements of operations, comprehensive income (loss), convertible preferred stock and stockholders’ equity (deficit), and cash flows for each of the three years in the period ended December 31, 2013. These financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company’s internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company’s internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Portola Pharmaceuticals, Inc. at December 31, 2013 and 2012, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2013, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Redwood City, California

March 3, 2014

PORTOLA PHARMACEUTICALS, INC.

Balance Sheets

(In thousands, except share and per share data)

	December 31,	
	2013	2012
Assets		
Current assets:		
Cash and cash equivalents	\$ 117,773	\$ 53,613
Short-term investments	150,892	77,656
Receivables from collaborations	309	662
Prepaid expenses and other current assets	3,733	2,982
Total current assets	272,707	134,913
Property and equipment, net	2,600	2,861
Long-term investments	50,371	6,115
Other assets	53	2,112
Total assets	\$ 325,731	\$ 146,001
Liabilities, convertible preferred stock and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	\$ 3,232	\$ 4,840
Accrued compensation and employee benefits	2,569	1,860
Accrued and other liabilities	17,796	7,399
Deferred revenue, current portion	1,958	4,042
Convertible preferred stock warrant liability	—	683
Total current liabilities	25,555	18,824
Deferred revenue, long-term	3,253	—
Other long-term liabilities	588	1,466
Total liabilities	29,396	20,290
Commitments and contingencies (Note 11)		
Convertible preferred stock, \$0.001 par value, 0 and 243,258,300 shares authorized at December 31, 2013 and 2012; 0 and 24,026,797 shares issued and outstanding at December 31, 2013 and 2012; redemption value of \$317,280 at December 31, 2012	—	317,280
Stockholders' equity (deficit):		
Preferred stock, \$0.001 par value, 5,000,000 shares authorized at December 31, 2013; 0 shares issued and outstanding at December 31, 2013; 0 authorized, issued and outstanding at December 31, 2012	—	—
Common stock, \$0.001 par value, 100,000,000 and 300,000,000 shares authorized at December 31, 2013 and 2012; 40,915,130 and 1,385,508 shares issued and outstanding at December 31, 2013 and 2012	41	1
Additional paid-in capital	581,911	10,717
Accumulated deficit	(285,672)	(202,320)
Accumulated other comprehensive income	55	33
Total stockholders' equity (deficit)	296,335	(191,569)

Total liabilities, convertible preferred stock and stockholders' equity (deficit)	\$325,731	\$146,001
See accompanying notes		

PORTOLA PHARMACEUTICALS, INC.

Statements of Operations

(In thousands, except share and per share data)

	Year Ended December 31,		
	2013	2012	2011
Collaboration and license revenue	\$10,531	\$72,042	\$78,029
Operating expenses:			
Research and development	79,286	49,717	46,089
General and administrative	15,423	11,469	12,071
Total operating expenses	94,709	61,186	58,160
Income (loss) from operations	(84,178)	10,856	19,869
Interest and other income, net	826	510	136
Interest expense	-	-	(21)
Net income (loss)	\$(83,352)	\$11,366	\$19,984
Net income (loss) attributable to common stockholders:			
Basic	\$(83,352)	\$-	\$79
Diluted	\$(83,352)	\$-	\$127
Net income (loss) per share attributable to common stockholders:			
Basic	\$(3.65)	\$-	\$0.06
Diluted	\$(3.65)	\$-	\$0.06
Shares used to compute net income (loss) per share attributable to common stockholders:			
Basic	22,842,443	1,350,939	1,249,778
Diluted	22,842,443	2,048,867	2,089,206

See accompanying notes

PORTOLA PHARMACEUTICALS, INC.

Statements of Comprehensive Income (Loss)

(In thousands)

	Year Ended December 31,		
	2013	2012	2011
Net income (loss)	\$(83,352)	\$11,366	\$19,984
Other comprehensive income:			
Unrealized gain on available-for-sale securities, net of tax	22	34	3
Total comprehensive income (loss)	\$(83,330)	\$11,400	\$19,987

See accompanying notes

PORTOLA PHARMACEUTICALS, INC.

Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)

(In thousands, except share and per share data)

	Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Capital	Deficit	(Loss)	Equity (Deficit)
Balance at December 31, 2010	17,103,729	\$ 220,374	1,224,782	\$ 1	\$ 5,266	\$ (233,670)	\$ (4)	\$ (228,407)
Exercise of employee stock options for cash	—	—	51,336	—	149	—	—	149
Lapse of repurchase rights related to common shares issued pursuant to early exercises	—	—	3,614	—	19	—	—	19
Issuance of Series D convertible preferred stock, net of issuance costs	6,287,026	88,962	—	—	(115)	—	—	(115)
Issuance of Series 1 convertible preferred stock, net of issuance costs	636,042	7,944	—	—	(91)	—	—	(91)
Employee stock-based compensation expense	—	—	—	—	2,288	—	—	2,288
Compensation expense relating to stock options granted to consultants	—	—	—	—	65	—	—	65
Unrealized gain on available-for-sale securities, net of tax	—	—	—	—	—	—	3	3
Net income	—	—	—	—	—	19,984	—	19,984
Balance at December 31, 2011	24,026,797	317,280	1,279,732	1	7,581	(213,686)	(1)	(206,105)

Exercise of employee stock options for cash	—	—	104,417	—	317	—	—	317
Lapse of repurchase rights related to common shares issued pursuant to early exercises	—	—	1,359	—	10	—	—	10
Employee stock-based compensation expense	—	—	—	—	2,665	—	—	2,665
Compensation expense relating to stock options granted to consultants	—	—	—	—	144	—	—	144
Unrealized gain on available-for-sale securities, net of tax	—	—	—	—	—	—	34	34
Net income	—	—	—	—	—	11,366	—	11,366
Balance at December 31, 2012	24,026,797	317,280	1,385,508	1	10,717	(202,320)	33	(191,569)
Exercise of employee stock options for cash	—	—	403,468	—	2,529	—	—	2,529
Lapse of repurchase rights related to common shares issued pursuant to early exercises	—	—	500	—	4	—	—	4
Conversion of preferred stock warrants to common stock warrants	—	—	—	—	659	—	—	659
Conversion of preferred stock to common stock	(24,026,797)	(317,280)	24,026,797	24	317,256	—	—	317,280
Issuance of common stock in connection with initial public offering, net of underwriting discounts, commissions and issuance costs	—	—	9,686,171	11	125,861	—	—	125,872
Issuance of common stock in connection with follow-on offering, net of underwriting	—	—	5,412,686	5	119,970	—	—	119,975

discounts, commissions and issuance costs								
Employee stock-based compensation expense	—	—	—	—	4,140	—	—	4,140
Compensation expense relating to stock options granted to consultants	—	—	—	—	775	—	—	775
Unrealized gain on available-for-sale securities, net of tax	—	—	—	—	—	—	22	22
Net loss	—	—	—	—	—	(83,352)	—	(83,352)
Balance at December 31, 2013	—	\$-	40,915,130	\$ 41	\$581,911	\$(285,672)	\$ 55	\$ 296,335
See accompanying notes								

PORTOLA PHARMACEUTICALS, INC.

Statements of Cash Flows

(In thousands)

	Year Ended December 31,		
	2013	2012	2011
Operating activities			
Net income (loss)	\$(83,352)	\$ 11,366	\$ 19,984
Adjustments to reconcile net income (loss) to cash used in operating activities:			
Depreciation and amortization	1,359	1,389	1,382
Noncash interest expense	–	–	7
Amortization of premium on investment securities	2,333	1,469	751
Stock-based compensation expense	4,974	2,809	2,353
Revaluation of convertible preferred stock warrant liability	(24)	(83)	(23)
Unrealized gain on foreign currency forward contracts	(261)	(51)	–
Changes in operating assets and liabilities:			
Receivables from collaborations	353	293	(955)
Prepaid expenses and other current assets	(469)	(2,481)	1,615
Other assets	396	(2,091)	–
Accounts payable	(1,773)	2,017	1,437
Accrued compensation and employee benefits	650	(980)	117
Accrued and other liabilities	11,908	3,375	(171)
Deferred revenue	1,169	(65,426)	(35,387)
Other long-term liabilities	(878)	(831)	45
Accrued income taxes	–	–	(2,476)
Net cash used in operating activities	(63,615)	(49,225)	(11,321)
Investing activities			
Decrease in restricted cash	–	–	6,000
Purchases of property and equipment	(933)	(362)	(1,477)
Purchases of investments	(219,813)	(144,644)	(33,805)
Proceeds from sales of investments	8,009	36,517	2,163
Proceeds from maturities of investments	92,001	40,687	59,829
Net cash (used in) provided by investing activities	(120,736)	(67,802)	32,710
Financing activities			
Proceeds from public offering of common stock, net of underwriters discount	251,865	–	–
Payment of public offering costs	(5,883)	–	–
Proceeds from issuance of common stock, including early exercise of stock options	2,529	317	167
Repurchase of unvested common stock	–	–	(51)
Proceeds from issuance of convertible preferred stock, net of issuance costs	–	–	96,700
Repayment of debt	–	–	(2,598)
Net cash provided by financing activities	248,511	317	94,218
Net increase (decrease) in cash and cash equivalents	64,160	(116,710)	115,607
Cash and cash equivalents at beginning of year	53,613	170,323	54,716
Cash and cash equivalents at end of year	117,773	53,613	170,323

Supplemental disclosure of cash flow information

Interest paid	\$—	\$—	\$ 14
Income taxes paid	\$—	\$57	\$2,476
Noncash investing activities			
Net change in accounts payable related to purchase of property and equipment	\$ 165	\$—	\$(362)
See accompanying notes			

PORTOLA PHARMACEUTICALS, INC.

Notes to Financial Statements

1. Organization

Portola Pharmaceuticals, Inc. (the “Company” or “we” or “our” or “us”) is a biopharmaceutical company focused on the development and commercialization of novel therapeutics in the areas of thrombosis, other hematologic disorders and inflammation for patients who currently have limited or no approved treatment options. We were incorporated in September 2003 in Delaware. Our headquarters and operations are located in South San Francisco, California and we operate in one segment.

Our two lead programs address the area of thrombosis, or blood clots. Our lead compound Betrixaban is a novel oral once-daily inhibitor of Factor Xa in Phase 3 development for extended duration prophylaxis, or preventive treatment, of a form of thrombosis known as venous thromboembolism, in acute medically ill patients. Our second lead development candidate Andexanet alfa, formerly PRT4445, is a recombinant protein designed to reverse the anticoagulant activity in patients treated with a Factor Xa inhibitor who suffer an uncontrolled bleeding episode or undergo emergency surgery. Our third product candidate, Cerdulatinib, formerly PRT2070, is an orally available kinase inhibitor being developed for hematologic, or blood, cancers and inflammatory disorders. Our fourth program, PRT2607 and other selective Syk inhibitors, is being developed in partnership with Biogen Idec Inc.

Initial Public and Follow-on Offering

In May 2013, we closed our initial public offering (“IPO”) of 9,686,171 shares of our common stock, which included 1,263,413 shares of common stock issued pursuant to the over-allotment option granted to our underwriters. The public offering price of the shares sold in the offering was \$14.50 per share. The total proceeds from the offering to us, net of underwriting discounts and commissions of approximately \$9.4 million, were approximately \$131.0 million. After deducting offering expenses payable by us of approximately \$5.2 million, net proceeds to us were \$125.8 million. Upon the closing of the IPO, all shares of convertible preferred stock then outstanding converted into 24,026,797 shares of common stock. In addition, all of our convertible preferred stock warrants were converted into warrants to purchase common stock.

In October 2013, we completed a follow-on offering of 6,366,513 shares of our common stock, which included 1,908,803 shares of common stock sold by certain existing stockholders, at a public offering price of \$23.75 per share. In November 2013, the underwriters exercised their over-allotment option to purchase an additional 954,976 shares from us at the public offering price. The total proceeds from the offering and over-allotment option, net of underwriting discounts and commissions of approximately \$7.7 million, were approximately \$120.8 million. After deducting offering expenses of approximately \$862,000, net proceeds to us were \$119.9 million.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities and

the reported amounts of revenues and expenses in the condensed financial statements and the accompanying notes. On an ongoing basis, management evaluates its estimates, including those related to revenue recognition, clinical trial accruals, fair value of assets and liabilities, income taxes and stock-based compensation. Management bases its estimates on historical experience and on various other market-specific and relevant assumptions that management believes to be reasonable under the circumstances. Actual results may differ from those estimates.

Cash and Cash Equivalents

Cash and cash equivalents consist of cash and other highly liquid investments with original maturities of three months or less from the date of purchase.

Investments

All investments have been classified as “available-for-sale” and are carried at estimated fair value as determined based upon quoted market prices or pricing models for similar securities. Management determines the appropriate classification of our investments in debt securities at the time of purchase and reevaluates such designation as of each balance sheet date. Unrealized gains and losses are excluded from earnings and were reported as a component of accumulated comprehensive income (loss). Realized gains and losses and declines in fair value judged to be other than temporary, if any, on available-for-sale securities are included in interest and other income, net. The cost of securities sold is based on the specific-identification method. Interest on marketable securities is included in interest and other income, net.

Fair Value Measurements

Fair value accounting is applied for all financial assets and liabilities and non-financial assets and liabilities that are recognized or disclosed at fair value in the financial statements on a recurring basis (at least annually).

Concentration of Credit Risk

Financial instruments that potentially subject us to concentrations of credit risk consist of cash, cash equivalents, receivables from collaborations and investments. Our investment policy limits investments to certain types of debt securities issued by the U.S. government, its agencies and institutions with investment-grade credit ratings and places restrictions on maturities and concentration by type and issuer. We are exposed to credit risk in the event of a default by the financial institutions holding our cash, cash equivalents and investments and issuers of investments to the extent recorded on the balance sheets.

Receivables from collaborations are typically unsecured and are concentrated in the pharmaceutical industry. Accordingly, we may be exposed to credit risk generally associated with pharmaceutical companies or specific to our collaboration agreements. To date, we have not experienced any losses related to these receivables.

Customer Concentration

Customers that accounted for 10% or more of total revenues were as follows:

	Year Ended December 31,		
	2013	2012	2011
Bristol-Myers Squibb Company and Pfizer Inc.	38%	—	—
Bayer Pharma, AG and Janssen Pharmaceuticals, Inc.	37%	—	—
Daiichi Sankyo, Inc	23%	—	—
Novartis, AG	—	97%	12%
Biogen Idec	—	—	48%
Merck & Co., Inc.	—	—	40%

Property and Equipment

Property and equipment are stated at cost and depreciated using the straight-line method over the estimated useful lives of the assets, ranging from two to five years. Leasehold improvements are amortized over the shorter of their estimated useful lives or the related lease term.

Impairment of Long-Lived Assets

We review long-lived assets, including property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. Impairment, if any, is assessed using discounted cash flows or other appropriate measures of fair value. Through December 31, 2013, there have been no such losses.

Deferred Offering Costs

Deferred offering costs, which primarily consist of direct incremental legal, accounting and printing fees incurred in the preparation of the IPO, were capitalized. The deferred offering costs were offset against IPO proceeds upon completion of the offering in May 2013. As of December 31, 2012, \$1.6 million of deferred offering costs were capitalized in other assets on the balance sheets. There were no remaining amounts deferred at December 31, 2013.

Convertible Preferred Stock

We recorded all shares of convertible preferred stock at their respective fair values on the dates of issuance. As of December 31, 2012, convertible preferred stock was classified outside of stockholders' equity (deficit) on the balance sheet as events triggering the liquidation preferences were not solely within the Company's control. Upon the closing of the IPO, all shares of our convertible preferred stock then outstanding converted into 24,026,797 shares of our common stock.

Convertible Preferred Stock Warrant Liability

Warrants for shares that are puttable and warrants for shares that are contingently redeemable are classified as liabilities on the accompanying balance sheets and carried at their estimated fair value. At the end of each reporting period, any changes in fair value are recorded as a component of interest and other income, net. We continued to adjust the carrying value of the warrants until the closing of the IPO, at which time the warrants became exercisable for shares of our common stock and were reclassified to stockholders' equity (deficit).

Deferred Rent

We recognize rent expense on a straight-line basis over the noncancelable term of our operating lease and, accordingly, record the difference between cash rent payments and the recognition of rent expense as a deferred rent liability. We also record lessor-funded lease incentives, such as reimbursable leasehold improvements, as a deferred rent liability, which is amortized as a reduction of rent expense over the noncancelable term of our operating lease.

Revenue Recognition

We generate revenue from collaboration and license agreements for the development and commercialization of our products. Collaboration and license agreements may include non-refundable upfront license fees, partial or complete reimbursement of research and development costs, contingent consideration payments based on the achievement of defined collaboration objectives and royalties on sales of commercialized products. Our performance obligations under our collaborations include the transfer of intellectual property rights (licenses), obligations to provide research and development services and related materials and obligations to participate on certain development and/or commercialization committees with the collaborators.

On January 1, 2011, we adopted an accounting standards update that amends the guidance on accounting for new arrangements or those materially modified, with multiple deliverables. This guidance eliminates the requirement for objective and reliable evidence of fair value of the undelivered items in order to consider a deliverable a separate unit of accounting. It also changes the allocation method such that the relative-selling-price method must be used to allocate arrangement consideration to the units of accounting in an arrangement. This guidance establishes the following estimation hierarchy that must be used in estimating selling price under the relative-selling-price method: (1) vendor-specific objective evidence of fair value of the deliverable, if it exists, (2) third-party evidence of selling price, if vendor-specific objective evidence is not available or (3) vendor's best estimate of selling price, if neither vendor-specific nor third-party evidence is available. The adoption of this guidance had a material effect on the

revenue recognized for the year ended December 31, 2011 (see Note 7). For multiple element arrangements entered into prior to January 1, 2011, we determined whether the elements had stand-alone value and whether there was objective and reliable evidence of fair value. When the delivered element did not have stand-alone value or there was insufficient evidence of fair value for the undelivered element(s), we recognized the consideration for the combined unit of accounting in the same manner as the revenue was recognized for the final deliverable, which was on a straight-line basis over the estimated period of performance.

On January 1, 2011, we adopted an accounting standards update that provides guidance on revenue recognition using the milestone method. Payments that are contingent upon achievement of a substantive milestone are recognized in their entirety in the period in which the milestone is achieved. Milestones are defined as an event that can only be achieved based on our performance and there is substantive uncertainty about whether the event will be achieved at the inception of the arrangement. Events that are contingent only on the passage of time or only on counterparty performance are not considered milestones subject to this guidance. Further, the amounts received must relate solely to prior performance, be reasonable relative to all of the deliverables and payment terms within the agreement and commensurate with our performance to achieve the milestone after commencement of the agreement.

Amounts from sales of licenses are recognized as revenue, as licensing of intellectual property is one of our principal or major ongoing activities. Amounts received as funding of research and development activities are recognized as revenue if the collaboration arrangement involves the sale of our research or development services at amounts that exceed our cost. However, such funding is recognized as a reduction in research and development expense when we engage in a research and development project jointly with another entity, with both entities participating in project activities and sharing costs and potential benefits of the arrangement.

Amounts related to research and development funding are recognized as the related services or activities are performed, in accordance with the contract terms. Payments may be made to or by us based on the number of full-time equivalent researchers assigned to the collaboration project and the related research and development expenses incurred.

Research and Development

Research and development costs are expensed as incurred and consist of salaries and benefits, lab supplies, materials and facility costs, as well as fees paid to other nonemployees and entities that conduct certain research and development activities on our behalf. Amounts incurred in connection with collaboration and license agreements are also included in research and development expense. Payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received.

Clinical Trial Accruals

Clinical trial costs are a component of research and development expenses. We accrue and expense clinical trial activities performed by third parties based upon actual work completed in accordance with agreements established with clinical research organizations and clinical sites. We determine the actual costs through monitoring patient enrollment and discussions with internal personnel and external service providers as to the progress or stage of completion of trials or services and the agreed-upon fee to be paid for such services.

Stock-Based Compensation

Stock-based awards issued to employees, are recorded at fair value as of the grant date using the Black-Scholes option-pricing model and recognized as expense on a straight-line basis over the vesting period of the award. Because noncash stock compensation expense is based on awards ultimately expected to vest, it is reduced by an estimate for future forfeitures. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from estimates.

Equity instruments issued to nonemployees, consisting of stock options granted to consultants, are valued using the Black-Scholes option-pricing model. Stock-based compensation expense for nonemployee services is subject to remeasurement as the underlying equity instruments vest and is recognized as an expense over the period during which services are received.

Income Taxes

We provide for income taxes under the asset and liability method. Current income tax expense or benefit represents the amount of income taxes expected to be payable or refundable for the current year. Deferred income tax assets and liabilities are determined based on differences between the financial statement reporting and tax bases of assets and liabilities and net operating loss and credit carryforwards, and are measured using the enacted tax rates and laws that will be in effect when such items are expected to reverse. Deferred income tax assets are reduced, as necessary, by a valuation allowance when management determines it is more likely than not that some or all of the tax benefits will not be realized. The recognition, derecognition and measurement of a tax position is based on management's best judgment given the facts, circumstances and information available at the reporting date. Our policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense or benefit. To date, there have been no interest or penalties charged in relation to the underpayment of income taxes.

Foreign Currency Transactions and Hedging

We have transactions denominated in foreign currencies, primarily the Euro, and, as a result, are exposed to changes in foreign currency exchange rates. We manage a portion of these cash flow exposures through the purchase of Euros and the use of foreign currency forward contracts. Our foreign currency forward contracts are not designated as hedges for accounting purposes. Gains or losses on foreign currency forward contracts are intended to offset gains or losses on the underlying net exposures in an effort to reduce the earnings and cash flow volatility resulting from fluctuating foreign currency exchange rates. Foreign currencies and our foreign currency forward contracts are marked to market at the end of each period and recorded as interest and other income, net in the statements of operations.

Our foreign exchange forward contracts expose us to credit risk to the extent that the counterparty, a major financial institution, is unable to meet the terms of the agreement. Our management does not expect material losses as a result of defaults by the counterparty.

Reverse Stock Split

On May 17, 2013, we effected a 1-for-10 reverse split of our preferred stock and common stock. Upon the effectiveness of the reverse stock split every 10 shares of outstanding preferred stock and common stock was decreased to one share of preferred stock or common stock, as applicable, the number of shares of common stock into which each outstanding option to purchase common stock is exercisable was proportionately decreased on a 1-for-10 basis, and the exercise price of each outstanding option to purchase common stock was proportionately increased on a 1-for-10 basis. All the shares numbers, share prices and exercise prices have been adjusted within the financial statements, on a retroactive basis, to reflect the 1-for-10 reverse stock split.

Net Income (Loss) per Share Attributable to Common Stockholders

Basic and diluted net income (loss) per share attributable to common stockholders is calculated in conformity with the two-class method required for companies with participating securities. Under the two-class method, in periods when we have net income, basic net income attributable to common stockholders is determined by allocating undistributed earnings, calculated as net income less current period convertible preferred stock noncumulative dividends, between the common stock and the convertible preferred stock. In computing diluted net income attributable to common stockholders, undistributed earnings are re-allocated to reflect the potential impact of dilutive securities. Basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding for the period. The diluted net income per share attributable to common stockholders is computed by giving effect to all potential dilutive common stock equivalents outstanding for the period. In periods when we have incurred a net loss, convertible preferred stock, options and warrants to purchase common stock and convertible preferred stock warrants are considered common stock equivalents but have been excluded from the calculation of diluted net loss per share attributable to common stockholders as their effect is antidilutive.

3. Fair Value Measurements

Financial assets and liabilities are recorded at fair value. The carrying amounts of certain of our financial instruments, including cash and cash equivalents, short-term investments, receivables and accounts payable, approximate their fair value due to their short maturities. The accounting guidance for fair value provides a framework for measuring fair value, clarifies the definition of fair value and expands disclosures regarding fair value measurements. Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (an exit price) in an orderly

transaction between market participants at the reporting date. The accounting guidance establishes a three-tiered hierarchy, which prioritizes the inputs used in the valuation methodologies in measuring fair value as follows:

Level 1 – Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date.

Level 2 – Inputs (other than quoted market prices included in Level 1) are either directly or indirectly observable for the asset or liability through correlation with market data at the measurement date and for the duration of the instrument's anticipated life.

Level 3 – Inputs reflect management's best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

A financial instrument's categorization within the valuation hierarchy is based upon the lowest level of input that is significant to the fair value measurement. Where quoted prices are available in an active market, securities are classified as Level 1. We classify money market funds as Level 1. When quoted market prices are not available for the specific security, then we estimate fair value by using quoted prices for identical or similar instruments in markets that are not active and model-based valuation techniques for which all significant inputs are observable in the market or can be corroborated by observable market data for substantially the full term of the assets. Where applicable, these models project future cash flows and discount the future amounts to a present value using market-based observable inputs obtained from various third party data providers, including but not limited to, benchmark yields, interest rate curves, reported trades, broker/dealer quotes and market reference data. We classify our corporate notes, commercial paper, U.S. government agency securities and foreign currency forward contracts as Level 2. We have elected to use the income approach to value the foreign currency forward contracts, using observable Level 2 market expectations at the measurement date and standard valuation techniques to convert future amounts to a single present amount assuming that participants are motivated, but not compelled to transact. Level 2 inputs for the valuations are limited to quoted prices for similar assets or liabilities in active markets and inputs other than quoted prices that are observable for the asset or liability (specifically foreign currency spot and forward rates, and credit risk at commonly quoted intervals). Mid-market pricing is used as a practical expedient for fair value measurements. The fair value measurement of any asset or liability must reflect the non-performance risk of the entity and the counterparty to the transaction. Therefore, the impact of the counterparty's creditworthiness, when in an asset position, and our creditworthiness, when in a liability position, has also been factored into the fair value measurement of the derivative instruments and did not have a material impact on the fair value of these derivative instruments. Both we and the counterparty are expected to continue to perform under the contractual terms of the instruments.

There were no transfers between Level 1 and Level 2 during the periods presented.

In certain cases where there is limited activity or less transparency around inputs to valuation, securities are classified as Level 3. Our convertible preferred stock warrant liability was classified as Level 3. The fair values of the convertible preferred stock warrants were measured using the Black-Scholes option-pricing model. Inputs used to determine estimated fair value included the estimated fair value of the underlying preferred stock at the valuation measurement date, the remaining contractual term of the warrants, risk-free interest rates, expected dividends and estimated volatility. Estimated volatility is based on the volatility of our peer group. We monitor the historical volatility of peer group companies on a quarterly basis and adjust our estimated volatility when significant changes in the peer group volatilities occur. The significant unobservable input used in the fair value measurement of the convertible preferred stock warrant liability is the fair value of the underlying preferred stock at the valuation remeasurement date. Generally, increases (decreases) in the fair value of the underlying preferred stock would result in a directionally similar impact to the fair value measurement.

The following table sets forth the fair value of our financial assets and liabilities, allocated into Level 1, Level 2 and Level 3, that was measured on a recurring basis (in thousands):

	December 31, 2013			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	\$57,296	\$-	\$ -	\$57,296
Corporate notes and commercial paper	-	182,472	-	182,472
U.S. government agency securities	-	75,289	-	75,289
Foreign currency forward contracts		372		372
Total financial assets	\$57,296	\$258,133	\$ -	\$315,429

	December 31, 2012			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	\$43,303	\$-	\$ -	\$43,303
Corporate notes and commercial paper	-	64,425	-	64,425
U.S. government agency securities	-	19,346	-	19,346
Foreign currency forward contracts	-	51	-	51
Total financial assets	\$43,303	\$83,822	\$ -	\$127,125
Financial Liabilities:				
Convertible preferred stock warrant liability	\$-	\$-	\$ 683	\$683

Level 3 liabilities include the convertible preferred stock warrant liability (see Note 10). The following table sets forth a summary of the changes in the estimated fair value of our convertible preferred stock warrants, which were measured at fair value on a recurring basis (in thousands):

Balance as of December 31, 2010	\$789
Recognized gain	(23)
Balance as of December 31, 2011	766
Recognized gain	(83)
Balance as of December 31, 2012	683
Recognized gain	(24)
Balance as of December 31, 2013	\$-

The recognized gain was included in interest and other income, net.

4. Financial Instruments

Cash equivalents and short-term and long-term investments, all of which are classified as available-for-sale securities, consisted of the following (in thousands):

	December 31, 2013				December 31, 2012			
	Cost	Unrealized Gain	Unrealized (Loss)	Estimated Fair Value	Cost	Unrealized Gain	Unrealized (Loss)	Estimated Fair Value
Money market funds	\$57,296	\$ -	\$ -	\$57,296	\$43,303	\$ -	\$ -	\$43,303
Corporate notes and commercial paper	182,426	62	(16)	182,472	64,403	25	(3)	64,425
U.S. government agency securities	75,278	23	(12)	75,289	19,335	11	-	19,346
	\$315,000	\$ 85	\$ (28)	\$315,057	\$127,041	\$ 36	\$ (3)	\$127,074
Classified as:								
Cash equivalents				\$113,794				\$43,303
Short-term investments				150,892				77,656
Long-term investments				50,371				6,115
Total cash equivalents and investments				\$315,057				\$127,074

At December 31, 2013, the remaining contractual maturities of available-for-sale securities were less than two years. There have been no significant realized gains or losses on available-for-sale securities for the periods presented.

5. Derivative Instruments

We are exposed to foreign currency exchange rates related to our business operations. To reduce our risks related to these exposures, we utilize certain derivative instruments, namely foreign currency forward contracts. We do not use derivatives for speculative trading purposes.

We enter into foreign currency forward contracts, none of which are designated as hedging transactions for accounting purposes, to reduce our exposure to foreign currency fluctuations of certain liabilities denominated in foreign currencies. These exposures are hedged on a quarterly basis. As of December 31, 2013 and 2012, we had foreign currency forward contracts with notional amounts of €7.7 million (\$10.6 million based on the exchange rate as of December 31, 2013) and €16.8 million (\$22.2 million based on the exchange rate as of December 31, 2012), respectively. As of December 31, 2013, we recorded a derivative asset within prepaid expenses and other current assets of \$372,000 related to these foreign currency forward contracts. As of December 31, 2012, we recorded a derivative asset with prepaid expenses and other current assets and other long-term assets of \$30,000 and \$21,000, respectively.

For the years ended December 31, 2013 and 2012, we recorded an unrealized gain of \$261,000 and \$51,000, respectively, in interest and other income, net on our statement of operations related to these foreign currency forward contracts. During the year ended December 31, 2013, we settled foreign currency forward contracts and recognized a realized gain of \$60,000 in interest and other income (expense), net. No realized gains or losses were recorded for the year ended December 31, 2012 related to these foreign currency contracts.

Our derivative financial instruments present certain market and counterparty risks. In general, the market risk related to these contracts is offset by corresponding gains and losses on the hedged transactions. The credit risk associated with these contracts is driven by changes in interest and currency exchange rates and, as a result, varies over time.

6. Balance Sheet Components

Property and Equipment

Property and equipment consists of the following (in thousands):

	December 31,	
	2013	2012
Computer equipment	\$618	\$515
Capitalized software	463	423
Equipment	3,690	3,224
Leasehold improvements	3,988	3,499
	8,759	7,661
Less accumulated depreciation and amortization	(6,159)	(4,800)
Property and equipment, net	\$2,600	\$2,861

Accrued and Other Liabilities

Accrued and other liabilities consist of the following (in thousands):

	December 31,	
	2013	2012
Research and development related	\$16,110	\$4,217
Legal and accounting fees	462	1,523
Deferred rent	879	831
Other	345	828
Total accrued liabilities	\$17,796	\$7,399

7. Collaboration and License Agreements

Summary of Collaboration Related Revenue

We have recognized revenue from our collaboration and license agreements as follows (in thousands):

	Year Ended December 31,		
	2013	2012	2011
Novartis:			
Recognition of upfront license fee	\$-	\$53,846	\$7,692
Reimbursement of research and development expense	-	16,238	1,879
Novartis total	-	70,084	9,571
Merck:			
Recognition of upfront license fee		-	21,429
Reimbursement of research and development expense	-	-	9,973
Merck total	-	-	31,402
Biogen Idec:			
Recognition of upfront license fee	-	-	37,056
Biogen Idec total	-	-	37,056
BMS and Pfizer:			
Recognition of research and development services	4,042	1,958	-
BMS and Pfizer total	4,042	1,958	-
Bayer and Janssen:			
Recognition of research and development services	3,876	-	-
Bayer and Janssen total	3,876	-	-
Lee's:			
Recognition of research and development services	194	-	-
Lee's total	194	-	-
Daiichi Sankyo:			
Recognition of research and development services	2,419		
Daiichi Sankyo total	2,419	-	-
Total collaboration and license revenue	\$10,531	\$72,042	\$78,029

Novartis Pharma A.G. ("Novartis")

In February 2009, we entered into an exclusive worldwide license agreement with Novartis to develop and commercialize Elinogrel, which was amended in December 2010 and terminated effective July 1, 2012. Under the terms of the license agreement, Novartis made an upfront cash payment to us of \$75.0 million in exchange for an exclusive worldwide license to develop and commercialize Elinogrel. We were eligible to receive additional cash payments totaling up to \$505.0 million upon achievement by Novartis of certain development, regulatory and commercialization milestones. We were obligated to participate on a Joint Steering Committee and a Joint Development Committee (collectively, the "Committees") with Novartis through December 31, 2018, to oversee development activities related to Elinogrel, unless Novartis agreed to disband the Committees at an earlier date. Pursuant to the license agreement, Novartis was obligated to fund development and commercialization expenses for Elinogrel after January 1, 2009, except for the first \$18.0 million of Phase 2 clinical trial costs and selected tasks, which we were obligated to fund.

Novartis had the exclusive right to market and sell drugs developed pursuant to the license agreement and was obligated to pay us tiered royalties at specified rates on net sales for each product. Under the license agreement, we had the right to elect to co-fund the development costs for the Phase 3 clinical trial in exchange for higher royalty payments and had the right to co-promote, in the United States, drugs developed pursuant to the license agreement in exchange for compensation for such co-promotion effort (on a fee-for-service basis).

We identified the following performance obligations under the license agreement with Novartis: 1) the transfer of intellectual property rights (license), 2) the obligation to provide certain limited research and development services early during the term of the license agreement and 3) the obligation to participate on the Committees. We accounted for these deliverables in accordance with accounting rules applicable to arrangements entered into prior to January 1, 2011 as a single unit of accounting, as there was no objective and reliable evidence of the fair value of our undelivered performance obligation with respect to participation on the Committees. Consideration under the license agreement consisted of an upfront license fee, milestone payments, research and development funding and royalties (if and when commercialization occurs). The amounts we received from Novartis for the upfront license fee and collaborative research efforts are recognized as collaboration revenue on a straight-line basis from the effective date of payment over the remainder of the expected performance period. Royalties on net sales will generally be recognized when royalty amounts can be reasonably estimated. No milestones have been reached since the inception of the Novartis agreement.

We estimated the term of our obligation to participate in the Committees to extend through December 31, 2018. In April 2012, we and Novartis agreed to a plan to return all rights to Elinogrel to Portola and to terminate the exclusive worldwide license agreement effective July 1, 2012. In connection with this plan, the expected term of our obligation to participate in the Committees changed from December 31, 2018 to July 1, 2012. The change in term of the obligation to participate in the Committees was accounted for as a change in accounting estimate on a prospective basis effective April 1, 2012. The change resulted in a \$65.1 million increase in collaboration revenue due to the recognition of all remaining revenue that would have otherwise been recorded over the obligation period through December 31, 2018. Absent this acceleration, the net income for the year ended December 31, 2012 would have been lower by \$65.1 million, resulting in a net loss of \$53.7 million and net loss per share would have been \$3.98 compared to net income per share of \$0.00 as reported. As a result of terminating the agreement, all remaining deferred revenue was recognized immediately, as no further performance obligations remained upon termination. As of the time of termination, no milestones had been achieved and no royalties had been triggered under our agreement with Novartis.

Merck & Co., Inc. (“Merck”)

In July 2009, we entered into an exclusive worldwide license agreement with Merck to develop and commercialize Betrixaban, which was terminated effective September 30, 2011. Under the terms of the agreement, Merck made an upfront cash payment to us of \$50.0 million in August 2009 in exchange for an exclusive worldwide license to develop and commercialize Betrixaban. We were eligible to receive additional cash payments totaling as much as \$420.0 million upon achievement by Merck of certain development, regulatory and commercialization milestones under the agreement.

We identified the following performance obligations under the license agreement with Merck: 1) the transfer of intellectual property rights (license), 2) the obligation to provide certain limited research and development services early during the term of the license agreement and 3) the obligation to participate on the Committees. We accounted for these deliverables in accordance with accounting rules applicable to arrangements entered into prior to January 1, 2011 as a single unit of accounting as there was not objective and reliable evidence of the fair value of our undelivered performance obligation with respect to participation on the Committees. Consideration under the license agreement consisted of an upfront license fee and research and development funding and could have also included milestone payments and royalties (if certain development and commercialization events occurred). Amounts received by us from Merck for the upfront license fee and collaborative research efforts were recognized as collaboration revenue on a straight-line basis from the date of payment over the remainder of the expected performance period.

In March 2011, we and Merck agreed to a plan to return all rights to Betrixaban to Portola and to terminate the exclusive worldwide license agreement effective September 2011. As a result of the termination of the agreement, all remaining deferred revenue was recognized immediately, as no further performance obligations remained upon

termination. As of the time of termination, no milestones had been achieved and no royalties had been triggered under our agreement with Merck.

Biogen Idec, Inc. (“Biogen Idec”)

In October 2011, we entered into an exclusive, worldwide license and collaboration agreement with Biogen Idec, which was subsequently converted by its terms into a fully out-licensed agreement, under which Portola and Biogen Idec were to jointly develop and commercialize highly selective, novel oral Syk inhibitors for the treatment of autoimmune and inflammatory diseases, including rheumatoid arthritis, allergic asthma and systemic lupus erythematosus.

We led the initial development effort for the Syk inhibitor program until commencement of the first Phase 2 clinical trial in late 2012. At that time, Biogen Idec assumed responsibility to lead the global development and commercialization efforts in major indications such as rheumatoid arthritis and allergic asthma. We had the option to elect to lead U.S. development and commercialization efforts for select smaller indications as well as discovery efforts for follow-on Syk inhibitors and retained an option to co-promote the drug alongside Biogen Idec in the United States in major indications. On a product-by-product basis, we had and exercised an option to opt out of our co-funding obligation of the development of such product. Pursuant to this option, we also relinquished our right to share profits from sales of such product(s), but are entitled to receive royalties from Biogen Idec's sales of these products.

Under the terms of the agreement, Biogen Idec provided us with a non-refundable upfront cash license fee of \$36.0 million and paid \$9.0 million for the purchase of 636,042 shares of our Series 1 convertible preferred stock at a premium of \$1.1 million above the stock's estimated fair value. In addition, we estimated that the agreement would provide \$22.9 million for the partial reimbursement of certain research and development services and related committee participation and delivery of drug materials. The original agreement also provided for additional payments of up to \$508.5 million based on the achievement of certain development and regulatory events. The \$508.5 million includes one milestone of \$23.0 million for commencement of the first Phase 2 trial which is considered substantive as its achievement is subject to the uncertain outcome of our development efforts over an extended period of time. All remaining payments would be associated with development and regulatory events that would be accomplished primarily based upon the performance of Biogen Idec, specifically, progress of development to Phase 3 clinical trials and filing and approval of drug applications by regulatory authorities in various countries. Accordingly, all other contingent consideration of \$485.5 million was to be allocated to the identified performance deliverables when received and recognized when those performance deliverables are completed. If the performance deliverables are fully completed at the time payment is received, such amounts would be recognized upon receipt.

We identified the following four non-contingent performance deliverables under the license agreement: 1) the transfer of intellectual property rights (license), 2) the obligation to provide research and development services, 3) the manufacture of drug material for development purposes, until commencement of the first Phase 2 clinical trial and 4) the obligation to participate on various committees. We have the right to opt out of any committees at any time after November 2013. The agreement states that consideration for the first two deliverables is \$36.0 million and \$22.9 million, respectively. There was no separate consideration identified in the agreement for the last two deliverables noted above. We are also required to contribute certain materials that we had previously acquired at a cost of approximately \$1.0 million to the collaboration for research and development use.

We considered the provisions of the multiple-element arrangement guidance in determining whether the deliverables outlined above have standalone value. We believe that Biogen Idec has research and development expertise with compounds similar to those licensed under the agreement and has the ability to engage other third parties to develop these compounds allowing Biogen Idec to realize the value of the license without receiving any of the remaining deliverables. Additionally, under the agreement, Biogen Idec has the right to sublicense this license to third parties, substantially with all the same rights and responsibilities. Therefore, the research and development services, participation in committee activities and provision of drug materials are deemed to have standalone value as Biogen Idec could negotiate for and/or acquire these from other third parties. Although participation in committee activities and provision of drug materials have standalone value, they will be delivered and utilized as the research and development services are performed and have a similar pattern of performance. These three deliverables are combined as one unit of accounting. There are no rights of return under the agreement.

The upfront license fee of \$36.0 million, the premium on the purchase of our Series 1 convertible preferred stock of \$1.1 million and research and development expense reimbursements of \$22.9 million were allocated to the two separate units of accounting using the relative estimated selling price method.

We developed our best estimates of selling prices for each deliverable in order to allocate the noncontingent arrangement consideration to the two units of accounting. For the license, we used the discounted cash flow method to estimate the price at which we could sell the license on a standalone basis. Embedded in the estimate were significant assumptions regarding probabilities of success during the development process, data regarding the potential customer market for the drug and costs of development and manufacturing and the discount rate. For the combined unit of accounting, we considered the estimated selling price of each deliverable within that unit. That is, for research and development services and committee participation, we estimated selling prices based on personnel and other costs incurred in the delivery of the services, plus an estimated margin on sales of such services on a standalone basis. For the contributed drug materials, we estimated the selling price based on our cost to purchase such materials from our third party supplier.

The arrangement consideration allocated to the license was recognized as collaboration and license revenue upon delivery in 2011. The amount allocated to the research and development services, materials and committee participation unit of accounting is being recognized over our estimated non-cancellable performance period of two years as a reduction to research and development expense. Under the terms of the agreement, we and Biogen Idec jointly shared development responsibilities prior to the conversion of this agreement into a fully out-licensed agreement, as if the two parties to the agreement incurred those costs directly.

Based upon the relative estimated selling prices for the two units of accounting for the year ended December 31, 2011, we recognized collaboration revenue of \$37.1 million and recorded a reduction in research and development expense for amounts owed by Biogen Idec to us under the cost-sharing terms of the agreement totaling \$734,000.

Under the previous accounting guidance for multiple element arrangements, we would have recognized revenues of approximately \$3.4 million from the Biogen Idec arrangement for the year ended December 31, 2011. We would have concluded that all deliverables should be combined into a single unit of accounting in the absence of objective and reliable evidence of fair value of undelivered services and recognized over an estimated performance period through November 2013.

In November 2012, we elected to exercise our option under our agreement with Biogen Idec to convert the agreement to a fully out-licensed agreement. After such election, we relinquished our right to share profits from sales of products related to PRT2607 and other selective Syk inhibitors, but are entitled to receive royalties from sales of these products by Biogen Idec. We no longer have the responsibility to fund the program under the agreement. The out-licensed agreement now provides for future payments to us of up to approximately \$370.0 million based on the occurrence of certain development and regulatory events. Biogen Idec has elected to assume all future development work for Syk inhibitors, including the major indications, such as allergic asthma. This agreement will continue in force until either party terminates the agreement pursuant to the agreement or until the expiration of Biogen Idec's royalty obligations pursuant to the agreement. Biogen Idec may terminate the agreement without cause upon 120 days' notice. In such event, we would regain all development rights and Biogen Idec would have no further payment obligations pursuant to the agreement.

During the years ended December 31, 2013 and 2012, we recorded a reduction in research and development expense of \$804,000 and \$6.5 million, respectively, owed by Biogen Idec to us under the cost-sharing terms of the agreement.

As of December 31, 2013, the one milestone in the agreement had not been achieved and no royalties had been triggered under this agreement.

Bristol-Myers Squibb Company ("BMS") and Pfizer Inc. ("Pfizer")

In October 2012, we entered into a three-way agreement with BMS and Pfizer to include subjects dosed with apixaban, their jointly owned product candidate, in one of our Phase 2 proof-of-concept studies of Andexanet alfa. We are responsible for the cost of conducting this clinical study. BMS and Pfizer will work closely with us on both development and regulatory aspects of Andexanet alfa in connection with our Phase 2 proof-of-concept studies to the extent such matters relate to apixaban. Pursuant to our agreement with BMS and Pfizer we are obligated to provide research and development services and participate on various committees. We originally estimated the period of performance of our obligations to extend through the second quarter 2013. During 2013, we added more cohorts than originally planned as part of the original study design at the inception of our agreement and therefore revised our estimated period of performance to be through the fourth quarter of 2013. The effects of these changes in estimates were not significant.

The total consideration under this agreement of \$6.0 million was recognized as revenue on a straight-line basis over the performance period through the fourth quarter of 2013. For the year ended December 31, 2013 and 2012, we recognized \$4.0 and \$2.0 million in collaboration revenue, respectively.

Lee's Pharmaceutical (HK) Ltd ("Lee's")

In January 2013, we entered into an agreement with Lee's to jointly expand our Phase 3 APEX Study of Betrixaban into China. Under the terms of the agreement, Lee's provided us with an upfront and non-refundable fee of \$700,000 and will reimburse our costs in connection with the expansion of the APEX study into China. Lee's will lead this study and the regulatory interactions with China's State Food and Drug Administration. We granted Lee's an exclusive option to negotiate for the exclusive commercial rights to Betrixaban in China, which may be exercised by Lee's for 60 days after it receives the primary data analysis report from the Phase 3 APEX study.

We identified the following deliverables under the agreement with Lee's: 1) the granting of an exclusive option to negotiate for the exclusive commercial rights to Betrixaban in China, 2) the obligation to manufacture and supply product in support of the APEX study in China, 3) the obligation to participate in a joint working group, and 4) the delivery of the primary data analysis report from the APEX study. We considered the provisions of the multiple-element arrangement guidance in determining how to recognize the total consideration of the agreement. We determined that none of the deliverables have standalone value and therefore are accounted for as a single unit of accounting with the upfront fee recognized as revenue on a straight-line basis over the estimated period of performance. Any reimbursements we may receive from Lee's for the costs we incur in connection with this agreement have not been material.

For the year ended December 31, 2013, we recognized \$194,000 of collaboration revenue. The deferred revenue balance as of December 31, 2013 was \$506,000.

Bayer Pharma, AG ("Bayer") and Janssen Pharmaceuticals, Inc. ("Janssen")

In February 2013, we entered into a three-way agreement with Bayer and Janssen to include subjects dosed with rivaroxaban, their Factor Xa inhibitor product, in one of our Phase 2 proof-of-concept studies of Andexanet alfa. We are responsible for the cost of conducting this clinical study. Under the terms of the agreement, Bayer and Janssen have each provided us with an upfront and non-refundable fee of \$2.5 million, for total consideration of \$5.0 million. The agreement also provides for additional non-refundable payments to us from Bayer and Janssen of \$250,000 each for an aggregate of \$500,000 following the delivery of the final written study report of our Phase 2 proof-of-concept studies of Andexanet alfa. Also, we are obligated to participate on a Joint Collaboration Committee ("JCC") with Bayer and Janssen to oversee the collaboration activities under the agreement.

We identified the following performance deliverables under the agreement: 1) the obligation to provide research and development services, which includes supplying Andexanet alfa and providing a final written report, and 2) the obligation to participate on the JCC. We considered the provisions of the multiple-element arrangement guidance in determining how to recognize the revenue associated with these two deliverables. We have accounted for the research and development services and our participation on the JCC as a single unit of accounting as neither deliverable has standalone value and both obligations will be delivered throughout the estimated period of performance. We originally estimated the period of performance to be through the fourth quarter of 2013. During 2013, we added more cohorts than originally planned as part of the original study design at the inception of our agreement and therefore adjusted our period of performance to be through the fourth quarter of 2014. The total consideration under this agreement is being recognized as revenue on a straight-line basis over the estimated performance period through the fourth quarter of 2014.

For the year ended December 31 2013, we recognized \$3.9 million in collaboration revenue. The deferred revenue balance as of December 31, 2013 was \$1.1 million.

Aciex Therapeutics, Inc. ("Aciex")

In February 2013, we entered into a license and collaboration agreement with Aciex pursuant to which we granted Aciex an exclusive license to co-develop and co-commercialize Cerdulatinib and certain related compounds for nonsystemic indications, such as the treatment and prevention of ophthalmological diseases by topical administration and allergic rhinitis by intranasal administration. Under the terms of this risk and cost sharing agreement, Portola and Aciex will each incur and report their own internal research and development costs. Further, third-party related development costs will be shared by Aciex and us 60% and 40%, respectively, until the end of the Phase 2 clinical study, and then equally afterwards. Also, we are entitled to receive either one-half of the profits, if any, generated by future sales of the products developed under the agreement, or royalty payments. Aciex has the primary responsibility

for conducting the research and development activities under this agreement. We are obligated to provide assistance in accordance with the agreed upon development plan as well as participate on various committees. We can opt out of our obligation to share in the development costs at various points in time, the timing of which impacts future royalties we may receive based on product sales made by Aciex. All net costs we incur in connection with this agreement will be recognized as research and development expenses. During 2013 no such costs have been incurred related to this agreement.

Daiichi Sankyo, Inc. (“Daiichi Sankyo”)

In June 2013, we entered into an agreement with Daiichi Sankyo to include subjects dosed with edoxaban, their Factor Xa inhibitor product, in one of our Phase 2 proof-of-concept studies of Andexanet alfa. We are responsible for the cost of conducting this clinical study. Under the terms of the agreement, Daiichi Sankyo will provide us with an upfront fee of \$6.0 million, \$3.0 million of which is subject to refund should Daiichi Sankyo decide to terminate the agreement. We are obligated to participate on a JCC with Daiichi Sankyo to oversee the collaboration activities under the agreement.

We identified the following performance deliverables under the agreement: 1) the obligation to provide research and development services, which includes supplying Andexanet alfa and providing a final written report, and 2) the obligation to participate on the JCC.

We considered the provisions of the multiple-element arrangement guidance in determining how to recognize the revenue associated with these two deliverables. We have accounted for the research and development services and our participation on the JCC as a single unit of accounting as neither deliverable has standalone value and both obligations will be delivered throughout the estimated period of performance. We originally estimated the non-contingent consideration under this agreement of \$3.0 million would be recorded as revenue on a straight-line basis over the estimated non-contingent performance period through the second quarter of 2014. In December 2013, the JCC agreed to forego certain preclinical studies that were planned in the original study design at the inception of the agreement. As a result of this change, we updated our period of performance to be through the first quarter of 2014. The contingent consideration under this agreement of \$3.0 million will be recognized after the contingency is resolved over the remaining performance period, which is currently estimated to begin in the first quarter of 2014 and conclude in the first quarter of 2015.

During the year ended December 31, 2013, we recognized \$2.4 million in collaboration revenue associated with the non-contingent element of the arrangement. The contingent element of the arrangement of \$3.0 million and the unearned portion of the non-contingent element of the arrangement of \$581,000 was recorded as deferred revenue as of December 31, 2013.

8. Asset Acquisition and License Agreements

Millennium Pharmaceuticals, Inc. (“Millennium”)

In November 2003, we acquired patent rights and intellectual property to an ADP Receptor Antagonist Program (“ADP Program”) and a Platelet Biology Program from Millennium. We are obligated to pay royalties on sales of products developed in the ADP Program if product sales are ever achieved.

In August 2004, we licensed rights to research, develop and commercialize compounds that inhibit Factor Xa from Millennium. We also obtained a patent license, a license for know-how and a technology license related to the lead Factor Xa compound, Betrixaban. In December 2005, we amended our agreements with Millennium for the ADP Program and for the Factor Xa Program. The effect of this amendment modified Millennium’s Right of First Negotiation in each agreement from an exclusive right to negotiate development and commercial rights to a nonexclusive right to negotiate.

In November 2007, we elected to continue our development of Betrixaban and the Factor Xa backup chemistry beyond December 1, 2007 and accordingly, paid \$5.0 million in cash to Millennium, which was charged to research and development expense, as the rights had no alternative future use. We could owe Millennium up to \$35.0 million upon the occurrence of specified events related to Betrixaban and royalties on sales of Factor Xa products, if such product sales are ever achieved.

As a result of entering into definitive agreements with third parties during 2009 for the development (and possibly commercialization) of both Elinogrel and Betrixaban, we paid Millennium an additional \$250,000 in cash and issued 17,667 shares of Series C convertible preferred stock with a fair value of \$14.15 per share. The value ascribed to the shares issued to Millennium was based upon the sale of our Series C convertible preferred stock at \$14.15 per share in May 2009 to an external investor. The value of the Series C convertible preferred stock of approximately \$250,000

was charged to research and development expense.

Astellas Pharma, Inc. (“Astellas”)

In June 2005, we licensed certain rights to research, develop and commercialize Syk inhibitors, including Cerdulatinib, from Astellas. In December 2008, under the terms of the license agreement, we elected to continue our development of Syk inhibitors and, accordingly, paid \$1.0 million in cash to Astellas, which was charged to research and development expense as the rights had no alternative future use.

In 2011, under the terms of the license agreement and in connection with the Biogen Idec collaboration agreement to develop Syk, we paid \$7.2 million in cash to Astellas, which was charged to research and development expense as the rights had no alternative future use.

We may be required to pay Astellas up to \$71.5 million upon the achievement of certain regulatory, approval and sales events for each Syk inhibitor we develop. In the event that we enter into an agreement with a third party to develop and commercialize Syk inhibitors, we would be required to pay Astellas 20% of any payments (excluding royalties) received under the collaboration. These payments would be creditable against the aforementioned milestone payments. In addition, we are required to pay Astellas royalties for worldwide sales for any commercial Syk inhibitor product.

9. Restructuring Charge

In November 2012, as part of our strategy to better align our capital resources with our clinical development plan, we reduced our workforce by 23 employees, 16 of whom were immediately terminated, five of whom were terminated on January 31, 2013, and two of whom were terminated on April 30, 2013. The final restructuring charge of \$698,000 includes severance and related costs associated with the termination of the employees. For the year ending December 31, 2013, we recorded a net restructuring charge of \$79,000, of which \$66,000 is included within research and development expense and \$13,000 is included within general and administrative expense on our statement of operations. During the year ended December 31, 2013, we paid \$223,000 of severance costs. At December 31, 2012, the accrued restructuring liability, which is included within accrued and other liabilities on the balance sheet was \$143,000. There were no remaining amounts accrued for the restructuring liability at December 31, 2013.

10. Convertible Preferred Stock Warrant Liability

Upon closing of the IPO, all convertible preferred stock warrants converted into warrants to purchase shares of common stock at a conversion rate of 1-for-1 and the estimated liability was reclassified to additional paid-in capital. The following table sets forth the estimated fair value for each of the convertible preferred stock warrants as of May 22, 2013, the date of the final remeasurement before reclassifying the liability to APIC, and December 31, 2012 (in thousands, except share and per share data):

Preferred Stock	Expiration Date	Exercise Price Per Share	Shares as of		Estimated Fair Value	
			May 22, 2013	December 31, 2012	May 22, 2013	December 31, 2012
Series A	Later of: (i) January 20, 2015 or (ii) 3 years after the closing of an initial public offering of our common stock	\$ 10.00	4,740	4,740	\$ 35	\$ 36
Series B	Later of: (i) September 28, 2016 or (ii) 5 years after the closing of an initial public offering of our common stock	\$ 13.10	76,335	76,335	624	647
Total			81,075	81,075	\$ 659	\$ 683

The estimated fair value of the above warrants was determined using the Black-Scholes option-pricing model using the following assumptions:

	May 22, 2013	December 31, 2012
Risk-free interest rate	0.1 - 0.9%	0.3 - 0.6%
Estimated term equal to the remaining contractual term	1.7 - 3.8	2.1 - 4.2 years

	years	
Volatility	79%	82%
Dividend yield	—	—

11. Commitments and Contingencies

We conduct product research and development programs through a combination of internal and collaborative programs that include, among others, arrangements with universities, contract research organizations and clinical research sites. We have contractual arrangements with these organizations; however, these contracts are cancelable on 30 days' notice and our obligations under these contracts are largely based on services performed with the exception of our contract manufacturers where we have committed to \$5.2 million in services to be performed in 2014.

Facility Leases

We lease our corporate, laboratory and other facilities under an operating lease, which was extended in May 2010 through March 31, 2015. The 2010 lease amendment provided for tenant improvement allowances of \$3.2 million, which are amortized as a reduction to rent expense on a straight-line basis over the lease term. The facility lease agreement, as amended, contains scheduled rent increases over the lease terms. Under the 2010 lease amendment, we have an option to extend the lease for an additional three-year term. The related rent expense for this lease is calculated on a straight-line basis, with the difference recorded as deferred rent.

At December 31, 2013, our future minimum commitments under our non-cancelable operating leases were as follows (in thousands):

Year ending December 31:	
2014	\$1,660
2015	418
Total	\$2,078

Rent expense was \$803,000, \$800,000 and \$1.0 million for the years ended December 31, 2013, 2012 and 2011, respectively.

Guarantees and Indemnifications

We indemnify each of our officers and directors for certain events or occurrences, subject to certain limits, while the officer or director is or was serving at our request in such capacity, as permitted under Delaware law and in accordance with our certificate of incorporation and bylaws. The term of the indemnification period lasts as long as an officer or director may be subject to any proceeding arising out of acts or omissions of such officer or director in such capacity.

The maximum amount of potential future indemnification is unlimited; however, we currently hold director and officer liability insurance. This insurance allows the transfer of risk associated with our exposure and may enable us to recover a portion of any future amounts paid. We believe that the fair value of these indemnification obligations is minimal. Accordingly, we have not recognized any liabilities relating to these obligations for any period presented.

12. Convertible Preferred Stock and Stockholders' Equity (Deficit)

Convertible Preferred Stock

As of December 31, 2013, no shares of convertible preferred stock were outstanding. The authorized, issued, and outstanding shares of convertible preferred stock at December 31, 2012 were as follows:

	Shares Authorized	Shares Issued and Outstanding	Carrying Value and Liquidation Preference
Series A	43,147,400	4,309,972	\$ 43,100
Series B	36,750,400	3,579,597	46,893
Series C	93,000,000	9,214,160	130,381
Series D	64,000,000	6,287,026	88,962
Series 1	6,360,500	636,042	7,944
Total	243,258,300	24,026,797	\$ 317,280

Conversion

The preferred stock was convertible at the option of the holder at any time into fully paid, nonassessable shares of common stock. The number of shares of common stock to which a holder was entitled upon conversion was the product obtained by multiplying the preferred conversion rate (the original issue price divided by the convertible preferred stock conversion price (the original issue price, subject to certain adjustments for antidilution)) by the number of shares being converted.

Each share of convertible preferred stock automatically converted into common stock upon closing of our IPO. Our Amended and Restated Certificate of Incorporation currently authorizes 5,000,000 shares of preferred stock, none of which have been issued by us or designated by our board of directors. A description of certain rights applicable to shares of convertible preferred stock prior to their conversion in our IPO is as follows:

Voting Rights

With the exception of the holders of Series 1 convertible preferred stock, which had no voting rights, the holders of each share of convertible preferred stock had one vote for each share of common stock into which such convertible preferred stock could have been converted.

Holders of Series D convertible preferred stock were granted a separate vote. In addition to any other vote or consent required, the vote or written consent of the holders of at least 50% of the outstanding Series D convertible preferred stock would have been necessary for effecting or validating certain actions as were previously outlined in our Certificate of Incorporation before it was amended and restated in connection with our IPO.

Dividends and Distributions

The holders of the convertible preferred stock were entitled to receive, when, as and if declared by the Board of Directors, a noncumulative cash dividend at the annual rate of 8% of the original issue price per annum on each outstanding share of convertible preferred stock. The original issue price is \$10.00 for Series A, \$13.10 for Series B and \$14.15 for Series C, Series D and Series 1. Such dividends were to be payable only when, as and if declared by the Board of Directors. After payment of dividends at the rate set forth above, any additional dividends declared would have been distributed among all holders of convertible preferred stock and common stock in proportion to the number of shares of common stock that would have then been held by each such holder if all shares of convertible preferred stock were converted into common stock. No dividends were declared prior to the conversion of all shares of preferred stock into shares of common stock in connection with the closing of our IPO.

Liquidation Rights

Upon liquidation, dissolution, or winding up of the Company (whether voluntary or involuntary) (a "Liquidation Event"), before any distribution or payment was to be made to the holders of any Series A, Series B, Series C or Series 1 convertible preferred stock or common stock, the holders of Series D convertible preferred stock would have been entitled to be paid out of our assets legally available for distribution, an amount equal to the original purchase price of the Series D convertible preferred stock plus all declared and unpaid dividends. The holders of Series A, Series B, Series C and Series 1 convertible preferred stock would have been entitled to receive, prior and in preference to any distribution of any of our assets legally available for distribution to the holders of common stock, an amount equal to the respective original purchase price of such series of convertible preferred stock plus all declared and unpaid dividends. After payments of the full liquidation preferences of the Series A, Series B, Series C, Series D and Series 1 convertible preferred stock described above, the remaining assets of the Company would have been available for distribution to stockholders.

Warrants

At December 31, 2013, warrants to purchase 82,575 shares of common stock were outstanding at exercise prices ranging between \$10.00 and \$13.10 per share and are exercisable through 2018. No warrants were granted, exercised or canceled during 2013.

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Equity Incentive Plan

In January 2013, our Board of Directors adopted our 2013 Equity Incentive Plan, or the 2013 Plan, which became effective upon the closing of our IPO in May 2013. The 2013 Plan has 81,948 shares of common stock available for future issuance as of December 31, 2013, subject to automatic annual increases beginning on January 1, 2014 through January 1, 2023. Further, all remaining shares available under the 2003 Equity Incentive Plan, or the 2003 Plan, were transferred to the 2013 Plan upon adoption. The 2013 Plan provides for the granting of incentive stock options, nonstatutory stock options, stock bonuses and rights to acquire restricted stock to employees, officers, directors and consultants. Incentive stock options may be granted with exercise prices of not less than 100% of the estimated fair value of our common stock and nonstatutory stock options may be granted with an exercise price of not less than 85% of the estimated fair value of the common stock on the date of grant. Stock options granted to a stockholder owning more than 10% of our voting stock must have an exercise price of not less than 110% of the estimated fair value of the common stock on the date of grant. Stock options are generally granted with terms of up to ten years and vest over a period of four years.

As of December 31, 2013, 4,903,323 shares of common stock were reserved under the 2013 Plan for the issuance of options and restricted stock.

A summary of Portola's stock option activity follows:

	Shares Available for Grant	Shares Subject to Outstanding Options	Weighted- Average Exercise Price Per Share
Balance at December 31, 2012	593,011	3,451,178	\$ 6.35
Options authorized	150,000	—	—
Options granted	(1,022,601)	1,022,601	18.31
Options exercised	—	(403,468)	6.40
Options canceled	361,538	(361,538)	8.58
Balance at December 31, 2013	81,948	3,708,773	\$ 9.43

Additional information related to the status of options at December 31, 2013, is as follows (aggregate intrinsic value in thousands):

	Shares	Weighted- Average Exercise Price Per Share	Remaining Contractual Life	Aggregate Intrinsic Value
Outstanding and exercisable	3,708,773	\$ 9.43	6.5	\$ 60,600
Vested and expected to vest	3,631,910	\$ 9.26	6.5	\$ 60,600
Vested	2,324,788	\$ 6.33	5.0	\$ 45,199

The aggregate intrinsic values of options outstanding and exercisable, vested and expected to vest were calculated as the difference between the exercise price of the options and the fair value of our common stock as of December 31, 2013.

The aggregate intrinsic value of options exercised was \$6.3 million, \$451,000 and \$290,000 for the years ended December 31, 2013, 2012 and 2011, respectively.

The total estimated grant date fair value of options vested during the years ended December 31, 2013, 2012 and 2011 was \$3.8 million, \$3.0 million and \$1.8 million, respectively.

Additional information regarding our stock options outstanding and vested and exercisable as of December 31, 2013 is summarized below:

Exercise Prices	Options Outstanding and Exercisable			Options Vested	
	Number of Options Outstanding and Exercisable	Weighted Average Remaining Contractual Life (Years)	Weighted Average Exercise Price per Share	Number of Options Vested	Weighted Average Exercise Price Per Share
\$1.00 - \$2.00	14,042	1.1	\$ 1.34	14,042	\$ 1.34
\$3.30	381,521	2.4	3.30	381,521	3.30
\$3.6 - \$4.10	378,399	3.9	4.09	378,399	4.09
\$4.5 - \$5.10	463,189	3.6	5.02	463,189	5.02
\$5.30	152,750	4.5	5.30	152,750	5.30
\$7.00	449,244	8.1	7.00	206,664	7.00
\$8.50	416,921	7.2	8.50	270,056	8.50
\$9.00	379,318	6.4	9.00	354,875	9.00
\$9.5 - \$10.90	406,068	9.2	10.05	26,693	9.75
\$19.74 - \$28.47	667,321	9.6	22.23	76,599	20.25
	3,708,773	6.5	\$ 9.43	2,324,788	\$ 6.33

13. Stock Based Compensation

Stock-based compensation expense, net of estimated forfeitures, is reflected in the statements of operations as follows (in thousands):

	Year Ended December 31,		
	2013	2012	2011
Research and development	\$2,295	\$1,452	\$1,164
General and administrative	2,679	1,357	1,189
Total stock-based compensation	\$4,974	\$2,809	\$2,353

As of December 31, 2013, total unamortized employee and nonemployee stock-based compensation was \$12.5 million, which is expected to be recognized over the remaining vesting period of 2.8 years. The weighted-average grant date fair value of employee options granted during the years ended December 31, 2013, 2012 and 2011 was \$12.46, \$5.90 and \$4.70 per share, respectively.

Valuation Assumptions

The employee stock-based compensation expense was determined using the Black-Scholes option valuation model. Option valuation models require the input of subjective assumptions and these assumptions can vary over time. The risk-free rate is based on U.S. Treasury zero-coupon issues with remaining terms similar to the expected terms of the awards. The expected term of employee options granted is determined using the simplified method (based on the midpoint between the vesting date and the end of the contractual term). As sufficient trading history does not yet exist for our common stock, our estimate of expected volatility is based on the volatility of other companies with similar products under development, market, size and other factors. To date, we have not declared or paid any cash dividends and do not have any plans to do so in the future. Therefore, we used an expected dividend yield of zero.

The following table illustrates the weighted-average assumptions for the Black-Scholes option-pricing model used in determining the fair value of options granted to employees:

	Year Ended December 31,		
	2013	2012	2011
Risk-free interest rate	1.43%	1.10%	1.10%
Expected life	6.0 years	6.0 years	6.0 years
Expected volatility	79%	72%	85%
Dividend yield	—	—	—

The following table illustrates the weighted-average assumptions for the Black-Scholes option-pricing model used in determining the fair value of ESPP purchase rights granted to employees:

	Year Ended December 31,		
	2013	2012	2011
Risk-free interest rate	0.10%	—	—
Expected life	0.42 years	—	—
Expected volatility	62%	—	—
Dividend yield	—	—	—

Options Granted to Nonemployees

We have granted options to purchase shares of common stock to consultants in exchange for services performed. We granted options to purchase 32,943 and 6,380 shares with average exercise prices of \$19.88 and \$7.00 per share, respectively, during the years ended December 31, 2013 and 2012, respectively. These options vest upon grant or various terms up to four years. We recognized non-employees stock compensation expense of \$775,000, \$144,000 and \$65,000 during the years ended December 31, 2013, 2012 and 2011, respectively. The fair value of non-employees' options was measured using the Black-Scholes option-pricing model reflecting the same assumptions as applied to employee options in each of the reported years, other than the expected life, which is assumed to be the remaining contractual life of the option.

Employee Stock Purchase Plan

The Board of Directors adopted the 2013 Employee Stock Purchase Plan, effective upon the completion of Portola's initial public offering of its common stock. Portola reserved a total of 1,000,000 shares of common stock for issuance under the plan. Eligible employees may purchase common stock at 85 percent of the lesser of the fair market value of Portola's common stock on the first or last day of the offering period. The reserve for shares available under the plan will automatically increase on January 1st each year, beginning in 2014, by an amount equal to 2 percent of the total number of outstanding shares of our common stock on December 31st of the preceding fiscal year.

14. Net Income (Loss) per Share Attributable to Common Stockholders

The following outstanding shares of common stock equivalents were excluded from the computation of diluted net income (loss) per share attributable to common stockholders for the periods presented because including them would have been antidilutive:

	Year Ended December 31,		
	2013	2012	2011
Convertible preferred stock	–	24,026,797	24,026,797
Stock options to purchase common stock	3,708,773	1,653,298	962,225
Convertible preferred stock warrants	–	81,075	81,075
Common stock warrants	82,575	1,500	1,500

The following table sets forth the computation of our basic and diluted net income (loss) per share attributable to common stockholders (in thousands, except share and per share data):

	Year Ended December 31,		
	2013	2012	2011
Net income (loss)	\$(83,352)	\$11,366	\$19,984
Noncumulative dividends on convertible preferred stock	–	(11,366)	(18,757)
Undistributed earnings allocated to participating securities	–	–	(1,148)
Net income (loss) attributable to common stockholders, basic	(83,352)	-	79
Adjustment to undistributed earnings allocated to participating securities	–	-	48
Net income (loss) attributable to common stockholders, diluted	\$(83,352)	\$-	\$127
Shares used in computing net income (loss) per share attributable to common stockholders, basic	22,842,443	1,350,939	1,249,778
Dilutive effect of common stock options	–	697,928	839,428
Shares used in computing net income (loss) per share attributable to common stockholders, diluted	22,842,443	2,048,867	2,089,206
Net income (loss) per share attributable to common stockholders:			
Basic	\$(3.65)	\$-	\$0.06
Diluted	\$(3.65)	\$-	\$0.06

15. Employee Benefit Plan

We sponsor a 401(k) Plan, which stipulates that eligible employees can elect to contribute to the 401(k) Plan, subject to certain limitations of eligible compensation. We match employee contributions up to a maximum of \$500 per employee each year. During the years ended December 31, 2013, 2012 and 2011, we recognized total expense of \$59,000, \$31,000 and \$35,000, respectively.

16. Income Taxes

We did not record a tax provision for the years ending December 31, 2013, 2012 and 2011. The effective tax rate of our provision for income taxes differs from the federal statutory rate as follows:

	Year Ended December 31,		
	2013	2012	2011
Federal statutory income tax rate	34.0 %	34.0 %	34.0 %
State income taxes, net of federal benefit	0.4	22.8	(3.8)
Federal and state research credits	3.4	0.8	(5.7)
Stock based compensation	(0.2)	0.4	1.3
Other	(0.5)	(0.1)	0.6

Change in valuation allowance	(37.1)	(57.9)	(26.4)
	0.0	%	0.0 %

In 2012 and 2011, we did not record an income tax provision on pre-tax income because we incurred a current taxable loss for federal income tax purposes and had available tax credits to offset all state income tax. Tax credits were used in lieu of net operating losses because in 2012 and 2011 state law suspended their use. Our valuation allowance at December 31, 2013 and 2012 appropriately considers the balances of both net operating losses and deferred revenue.

Significant components of our deferred tax assets are as follows (in thousands):

	December 31,	
	2013	2012
Deferred tax assets:		
Federal and state net operating loss carryforwards	\$ 102,478	\$ 74,390
Federal and state research tax credit carryforwards	10,750	7,551
Deferred revenue	1,755	1,434
Stock options	2,895	2,362
Capitalized acquisition costs	1,295	1,503
Other	654	1,859
Total deferred tax assets	119,827	89,099
Valuation allowance	(119,827)	(89,099)
Net deferred tax assets	\$-	\$-

Realization of the deferred tax assets is dependent upon the generation of future taxable income, if any, the amount and timing of which are uncertain. Based on available objective evidence, including the fact that we have incurred significant losses in almost every year since our inception, management believes it is more likely than not that our deferred tax assets are not recognizable. Accordingly, deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by \$30.7 million for the year ended December 31, 2013. The valuation allowance decreased by \$6.8 million for the year ended December 31, 2012.

As of December 31, 2013, we had net operating loss carryforwards for federal income tax purposes of approximately \$260.0 million and federal research tax credits of approximately \$10.9 million, which expire at various dates in the period from 2023 to 2033. We also have state net operating loss carry forwards of approximately \$227.6 million which expire at various dates in the period from 2014 to 2033 and state research tax credits of \$2.4 million. Utilization of the net operating loss carryforwards and credits will be subject to an annual limitation due to the ownership change limitations provided by the Internal Revenue Code of 1986, as amended and similar state provisions. The annual limitation may result in the expiration of net operating losses and credits before utilization.

Uncertain Tax Positions

We have not been audited by the Internal Revenue Service or any state tax authority. We are subject to taxation in the United States. Because of the net operating loss and research credit carryforwards, substantially all of our tax years, from 2003 through 2013, remain open to U.S. federal and California state tax examinations.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

	Year Ended December 31,		
	2013	2012	2011
Unrecognized tax benefits, beginning of period	\$ 1,435	\$ 1,344	\$ 973
Gross increases - current period tax positions	619	91	371
Gross decreases - tax position in prior period	(6)	-	-

Unrecognized tax benefits, end of period	\$2,048	\$1,435	\$1,344
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The amount of unrecognized income tax benefits that, if recognized, would affect our effective tax rate was \$365,000 as of December 31, 2013 and 2012. If the \$2.0 million and \$1.4 million of unrecognized income tax benefits as of December 31, 2013 and 2012, respectively, is recognized, there would be no impact to the effective tax rate as any change will fully offset the valuation allowance. We have classified the unrecognized tax benefits as long term, as we do not expect them to be realized over the next 12 months.

We do not anticipate significant changes to our uncertain tax positions through the next 12 months.

17. Related Party Transactions

Our former President and Chief Executive Officer, who is currently a member of our board of directors, is also a co-founder and member of the board of directors of Global Blood Therapeutics, Inc. (“Global Blood”), and a member of the board of directors of MyoKardia, Inc. (“MyoKardia”). In November 2012, we entered into Master Services Agreements with Global Blood and MyoKardia under which we provide certain consulting, preclinical, laboratory and clinical research related services to each of these companies. For the year ended December 31, 2013 and 2012, we recorded a reduction in research and development expense of \$816,000 and \$57,000, respectively, owed to us by Global Blood and Myokardia under the Master Services Agreements.

As of December 31, 2013 and 2012, receivables from these related parties in the amount of \$394,000 and \$57,000, respectively, are included in prepaid expenses and other current assets on the balance sheet.

18. Subsequent Events

In January 2014, we entered into a three-way agreement with BMS and Pfizer to include subjects dosed with apixaban, their jointly owned product candidate, in one of our Phase 3 studies of Andexanet alfa. We are responsible for the cost of conducting this clinical study. BMS and Pfizer will work closely with us on both development and regulatory aspects of Andexanet alfa in connection with our Phase 3 study to the extent such matters relate to apixaban. Pursuant to our agreement with BMS and Pfizer we are obligated to provide research and development services and participate on various committees.

The total consideration under this agreement of \$25.0 million consists of a \$13.0 million upfront payment and \$12.0 million of payments due upon the achievement of certain milestones associated with the progress of our Phase 3 study.

In January 2014, we entered into a three-way agreement with Bayer and Janssen to include subjects dosed with rivaroxaban, their Factor Xa inhibitor product, in one of our Phase 3 studies of Andexanet alfa. We are responsible for the cost of conducting this clinical study. Bayer and Janssen will work closely with us on both development and regulatory aspects of Andexanet alfa in connection with our Phase 3 study to the extent such matters relate to rivaroxaban. Pursuant to our agreement with Bayer and Janssen, we are obligated to provide research and development services and participate on various committees.

The total consideration under this agreement of \$25.0 million consists of a \$10.0 million upfront payment and \$15.0 million of payments due upon the achievement of certain milestones associated with the progress of our Phase 3 study.

19. Quarterly Financial Data

The following table presents certain unaudited quarterly financial information. This information has been prepared on the same basis as the audited financial statements and includes all adjustments (consisting only of normal recurring adjustments) necessary to present fairly the unaudited quarterly results of operations set forth herein. Net income (loss) per share for all periods presented have been retroactively adjusted to reflect the 1-for-10 reverse stock split effected on May 17, 2013. All data is in thousands except per share data.

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	2013				2012			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Collaboration and license revenue	\$3,108	\$2,601	\$2,766	\$2,056	\$2,481	\$66,865	\$738	\$1,958
Operating expenses	\$(20,761)	\$(24,541)	\$(21,995)	\$(27,412)	\$(15,768)	\$(16,147)	\$(12,833)	\$(16,438)
Net income (loss)	\$(18,142)	\$(21,598)	\$(18,550)	\$(25,062)	\$(13,127)	\$49,762	\$(11,488)	\$(13,781)
Net income (loss) per share:								
Basic	\$(12.94)	\$(1.47)	\$(0.53)	\$(0.63)	\$(10.08)	\$1.71	\$(8.38)	\$(10.02)
Diluted	\$(12.94)	\$(1.47)	\$(0.53)	\$(0.63)	\$(10.08)	\$1.67	\$(8.38)	\$(10.02)

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our reports under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and the rules and regulations thereunder, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow for timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As required by Rule 13a-15(b) under the Exchange Act, our management, under the supervision and with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of December 31, 2013. Based on such evaluation, our principal executive officer and principal financial officer have concluded that, as of December 31, 2013, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

This annual report does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal controls over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended December 31, 2013 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

Certain information required by Part III is omitted from this annual report on Form 10-K and is incorporated herein by reference to our definitive Proxy Statement for our 2014 Annual Meeting of Stockholders, or the Proxy Statement, which we intend to file pursuant to Regulation 14A of the Securities Exchange Act of 1934, as amended, within 120 days after December 31, 2013.

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item concerning our directors is incorporated by reference to the information set forth in the section titled “Directors and Corporate Governance” in our Proxy Statement. Information required by this item concerning our executive officers is incorporated by reference to the information set forth in the section entitled “Executive Officers of the Company” in our Proxy Statement. Information regarding Section 16 reporting compliance is incorporated by reference to the information set forth in the section entitled “Section 16(a) Beneficial Ownership Reporting Compliance” in our Proxy Statement.

Our written code of ethics applies to all of our directors and employees, including our executive officers, including without limitation our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions. The code of ethics is available on our website at <http://www.portola.com> in the Investors section under “Corporate Governance.” Changes to or waivers of the code of ethics will be disclosed on the same website. We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding any amendment to, or waiver of, any provision of the code of ethics in the future by disclosing such information on our website.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item regarding executive compensation is incorporated by reference to the information set forth in the sections titled “Executive Compensation” in our Proxy Statement.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this item regarding security ownership of certain beneficial owners and management is incorporated by reference to the information set forth in the section titled “Security Ownership of Certain Beneficial Owners and Management” and “Equity Compensation Plan Information” in our Proxy Statement.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item regarding certain relationships and related transactions and director independence is incorporated by reference to the information set forth in the sections titled “with Related Persons

Transactions” and “Election of Directors”, respectively, in our Proxy Statement.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this item regarding principal accountant fees and services is incorporated by reference to the information set forth in the section titled “Principal Accountant Fees and Services” in our Proxy Statement.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) The following documents are filed as part of this report:

(1) FINANCIAL STATEMENTS

Financial Statements—See Index to Financial Statements at Item 8 of this report.

(2) FINANCIAL STATEMENT SCHEDULES

Financial statement schedules have been omitted in this report because they are not applicable, not required under the instructions, or the information requested is set forth in the consolidated financial statements or related notes thereto.

(b) Exhibits. The exhibits listed in the accompanying index to exhibits are filed as part of, or incorporated by reference into, this report.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of South San Francisco, State of California, on the 28th day of February 2014.

PORTOLA
PHARMACEUTICALS,
INC.

By: /s/ WILLIAM LIS
William Lis

Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints William Lis and Mardi C. Dier, jointly and severally, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her, and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this report, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises hereby ratifying and confirming all that said attorneys-in-fact and agents, or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/ S / WILLIAM LIS	Chief Executive Officer and Director (Principal Executive Officer)	February 28, 2014
William Lis		
/ S / MARDI C. DIER	Chief Financial Officer (Principal Financial and Accounting Officer)	February 28, 2014

Mardi C. Dier

/ S / HOLLINGS C. RENTON Co-chairman of the Board of Directors February 28, 2014

Hollings C. Renton

/ S / CHARLES J. HOMCY, M.D. Co-chairman of the Board of Directors February 28, 2014

Charles J. Homcy, M.D.

/ S / JEAN-JACQUES BIENAIMÉ Director February 28, 2014

Jean-Jacques Bienaimé

/ S / JEFFREY W. BIRD, M.D., PH.D. Director February 28, 2014

Jeffrey W. Bird, M.D., Ph.D.

/ S / ROBERT CALIFF, M.D. Director February 28, 2014

Robert Califf, M.D.

/ S / NICHOLAS GALAKATOS, Ph.D. Director February 28, 2014

Nicholas Galakatos, Ph.D.

/ S / H. WARD WOLFF Director February 28, 2014

H. Ward Wolff

EXHIBIT INDEX

Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
3.1	Amended and Restated Certificate of Incorporation of Portola Pharmaceuticals, Inc.	8-K	001-35935	3.1	5/28/2013
3.2	Amended and Restated Bylaws of Portola Pharmaceuticals, Inc.	8-K	001-35935	3.2	5/28/2013
4.1	Form of Common Stock Certificate of Portola Pharmaceuticals, Inc.	S-1	333-187901	4.1	5/17/2013
4.2	Warrant to Purchase Shares of Series A Preferred Stock by and between the registrant and General Electric Capital Corporation, dated January 21, 2005.	10-Q	001-35935	4.4	11/06/13
4.3	Warrant to Purchase Shares of Series B Preferred Stock by and between the registrant and Hercules Technology Growth Capital, Inc., dated September 29, 2006.	10-Q	001-35935	4.5	11/06/13
4.4	Warrant to Purchase Shares of Series B Preferred Stock by and between the registrant and Comerica Incorporated, dated September 26, 2006.	10-Q	001-35935	4.6	11/06/13
4.5	Warrant to Purchase Shares of Common Stock by and between the registrant and Laurence Shushan and Magdalena Shushan Acosta, Trustees, The Laurence and Magdalena Shushan Family Trust, Under Agreement Dated October 8, 1997, dated December 15, 2006.	10-Q	001-35935	4.7	11/06/13
4.6	Warrant to Purchase Shares of Common Stock by and between the registrant and HCP Life Science Assets TRS, LLC, dated December 15, 2006.	10-Q	001-35935	4.8	11/06/13
4.7	Warrant to Purchase Shares of Common Stock by and between the registrant and Bristow Investments, L.P., dated December 15, 2006.	10-Q	001-35935	4.9	11/06/13
5.1	Opinion of Cooley LLP.				
10.1	Form of Indemnity Agreement between the Registrant and its directors and officers.	S-1	333-187901	10.1	4/12/2013
10.2+	Portola Pharmaceuticals, Inc. 2003 Equity Incentive Plan, as amended, and Form of Stock Option Grant Notice, Option Agreement and Form of Notice of Exercise.	S-1	333-187901	10.2	4/12/2013

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10.3+	Portola Pharmaceuticals, Inc. 2013 Equity Incentive Plan and Form of Stock Option Agreement and Form of Stock Option Grant Notice thereunder.	S-1	333-187901	10.3	4/12/2013
10.4+	Form of 2006 Executive Change in Control Severance Benefits Agreement.	S-1	333-187901	10.4	4/12/2013
10.5+	Non-Employee Director Compensation Policy.	S-1	333-187901	10.5	5/7/2013
10.6	Third Amended and Restated Investor Rights Agreement, dated as of November 11, 2011, by and among the registrant and certain of its stockholders.	S-1	333-187901	10.6	4/12/2013
10.7†	License and Collaboration Agreement by and between the registrant and Biogen Idec MA Inc., dated as of October 26, 2011.	S-1	333-187901	10.7	5/7/2013
10.8†	License Agreement by and between the registrant and Millennium Pharmaceuticals, Inc., dated as of August 4, 2004.	S-1	333-187901	10.8	4/12/2013
10.9†	Asset Purchase Agreement by and between the registrant and Millennium Pharmaceuticals, Inc., dated as of November 7, 2003.	S-1	333-187901	10.9	4/12/2013
10.10†	Letter by and between the registrant and Millennium Pharmaceuticals, Inc., dated as of December 6, 2005.	S-1	333-187901	10.10	4/12/2013
10.11†	Second Amended and Restated License Agreement by and between the registrant and Astellas Pharma, Inc., dated as of December 20, 2010.	S-1	333-187901	10.11	4/12/2013

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Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
10.12†	Clinical Collaboration Agreement by and among the registrant, Bristol-Myers Squibb Company and Pfizer Inc., dated as of October 16, 2012.	S-1	333-187901	10.12	4/12/2013
10.13	Lease by and between the registrant and Britannia Pointe Grand Limited Partnership, dated as of December 15, 2006.	S-1	333-187901	10.13	4/12/2013
10.14	First Amendment to Lease by and between the registrant and Britannia Pointe Grand Limited Partnership, dated as of May 21, 2010.	S-1	333-187901	10.14	4/12/2013
10.15	Offer Letter by and between the Registrant and William Lis, dated as of April 29, 2008.	S-1	333-187901	10.15	4/12/2013
10.16	Offer Letter by and between the Registrant and John T. Curnutte, M.D., Ph.D., dated as of January 6, 2011.	S-1	333-187901	10.16	4/12/2013
10.17	Offer Letter by and between the Registrant and Mardi C. Dier, dated as of July 28, 2006.	S-1	333-187901	10.17	4/12/2013
10.18	Offer Letter by and between the Registrant and Michael M. Kitt, M.D., dated as of June 17, 2011.	S-1	333-187901	10.18	4/12/2013
10.19	Portola Pharmaceuticals, Inc. 2013 Employee Stock Purchase Plan.	S-1	333-187901	10.19	4/12/2013
10.20	Master Contract Services Agreement for Preclinical and Clinical Services by and between the Registrant and PPD Development, LP, dated as of January 2, 2012, as amended by Amendment No.1 between the registrant and PPD Development, LLC (formerly PPD Development, LP).	S-1	333-187901	10.20	4/12/2013
10.21	Development and Manufacturing Services Agreement by and between the Registrant and Hovione Inter Limited, dated as of January 17, 2007, as amended by Amendment No. 1 by and between the registrant and Hovione Inter Limited, dated as of February 1, 2013.	S-1	333-187901	10.21	4/12/2013
23.1	Consent of Independent Registered Public Accounting Firm.				

24.1	Power of Attorney (see signature page).
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended.
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended.
32.1	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. ⁽¹⁾
101.INS	XBRL Instance Document. ⁽²⁾
101.SCH	XBRL Taxonomy Extension Schema Document. ⁽²⁾
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document. ⁽²⁾
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document. ⁽²⁾
101.LAB	XBRL Taxonomy Extension Label Linkbase Document. ⁽²⁾
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document. ⁽²⁾

Confidential Treatment Granted

+Indicates management contract or compensatory plan.

(1) This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Registrant under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.

(2) Pursuant to applicable securities laws and regulations, the Registrant is deemed to have complied with the reporting obligation relating to the submission of interactive data files in such exhibits and is not subject to liability under any anti-fraud provisions of the federal securities laws as long as the Registrant has made a good faith attempt to comply with the submission requirements and promptly amends the interactive data files after becoming aware that the interactive data files fail to comply with the submission requirements. These interactive data files are deemed not filed or part of a registration statement or report for purposes of sections 11 or 12 of the Securities Act of 1933, as amended, are deemed not filed for purposes of section 18 of the Securities Exchange Act of 1934, as amended, and otherwise are not subject to liability under these sections.

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