PORTOLA PHARMACEUTICALS INC
Form 424B4
October 17, 2013
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Filed Pursuant to Rule 424(b)(4)
Registration No. 333-191609

Prospectus

6,366,513 Shares

Portola Pharmaceuticals, Inc.

Common Stock

We are offering 4,457,710 shares of our common stock and the selling stockholders are offering 1,908,803 shares of our common stock. We will not receive any proceeds from the sale of shares by the selling stockholders. Our common stock is listed on The NASDAQ Global Market under the trading symbol PTLA. On October 16, 2013, the last reported sale price of our common stock on The NASDAQ Global Market was $25.55 per share.

We are an emerging growth company under the federal securities laws and are subject to reduced public company reporting requirements.

Investing in our common stock involves a high degree of risk. See Risk factors beginning on page 12.

	Per Share	Total
Public offering price	$ 23.75	$ 151,204,684
Underwriting discounts and commissions[(1)]	$ 1.425	$ 9,072,281
Proceeds, before expenses, to us	$ 22.325	$ 99,518,376
Proceeds, before expenses, to selling stockholders	$ 22.325	$ 42,614,027

(1) See Underwriting for additional disclosure regarding underwriting discounts, commissions and expenses.

To the extent that the underwriters sell more than 6,366,513 shares of common stock, the underwriters have an option to purchase 954,976 additional shares from us at the public offering price, after deducting underwriting discounts and commissions.

The underwriters expect to deliver the shares against payment in New York, New York on October 22, 2013.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

Morgan Stanley **Credit Suisse**

Cowen and Company **William Blair** **Sanford C. Bernstein**

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Neither we, the selling stockholders nor the underwriters have authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We and the selling stockholders take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus is accurate only as of its date regardless of the time of delivery of this prospectus or of any sale of common stock.

Neither we, the selling stockholders nor the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons who come into possession of this prospectus and any free writing prospectus related to this offering in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus and any such free writing prospectus applicable to that jurisdiction.

This document has been prepared on the basis that any offer of shares in any relevant European Economic Area member state will be made pursuant to an exemption under European prospectus law from the requirement to publish a prospectus for offers of shares and does not constitute an offer to or solicitation of anyone to purchase shares in any jurisdiction in which such offer or solicitation is not authorized, nor to any person to whom it is unlawful to make such an offer or solicitation.

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We obtained the industry, market and similar data set forth in this prospectus from our own internal estimates and research, and from industry publications and research, surveys and studies conducted by third parties. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. See the section titled Market, industry and other data for further information.

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Prospectus summary

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before deciding to invest in our common stock, you should read this entire prospectus carefully, including the sections of this prospectus entitled Risk factors and Management s discussion and analysis of financial condition and results of operations and our financial statements and related notes. Unless the context otherwise requires, references in this prospectus to the company, Portola, we, us and our refer to Portola Pharmaceuticals, Inc.

Portola Pharmaceuticals, Inc.

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 (pINN) Andexanet alfa, formerly PRT4445, which has completed the first of a series of Phase 2 proof-of-concept studies, 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, 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 PRT2070 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.

Members of our management team, working together or individually, have played central roles at prior companies in discovering, developing and commercializing a number of successful therapeutics in the area of thrombosis, including Integrilin® and Xarelto®. Our approach has been to identify key enzymes and cellular signaling pathways and to apply our translational expertise to discover compounds with unique properties that have potential for clear clinical and pharmacoeconomic value. To increase the likelihood that our programs will succeed, we enhance our internal discovery and development expertise by collaborating with academic leaders at major universities, including Cornell University, Duke University, Harvard University, King s College, McMaster University, Stanford University and The University of Texas MD Anderson Cancer Center, and by proactively engaging regulatory authorities early in the development process.

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We have full worldwide commercial rights to Betrixaban and Andexanet alfa, and to PRT2070 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 on building a successful commercial enterprise to commercialize Betrixaban and Andexanet alfa globally, 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:

Development Pipeline				
Product	**Description**	**Stage**	**Indication**	**Worldwide commercial rights**
Betrixaban	Oral Factor Xa inhibitor	Phase 3	Extended duration VTE prophylaxis in acute medically ill patients for up to 35 days	Portola
Andexanet alfa	Antidote for Factor Xa inhibitors	Phase 2	Reversal of Factor Xa inhibitor anticoagulation	Portola
PRT2070	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 Aciex
PRT2607	Syk inhibitor	Pre-clinical	Allergic asthma and other inflammatory disorders	Biogen Idec

Betrixaban. Betrixaban is a novel oral once-daily inhibitor of Factor Xa in development for extended duration VTE prophylaxis in acute medically ill patients 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. 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, 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, worldwide sales of enoxaparin for the 12 months through June 2012 were in excess of $4.8 billion. We believe that the 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. 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 these patients.

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In 2012, we initiated our pivotal Phase 3 APEX study, a randomized, double-blind, active-controlled, multicenter, multinational study comparing a once-daily dose of Betrixaban for a total of 35 days with in-hospital administration of enoxaparin once daily for 6 to 14 days followed by placebo. 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.

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. Leveraging the data from our extensive clinical and preclinical studies of Betrixaban and learnings from previous trials of other Factor Xa inhibitors, we believe that we have designed APEX with a dosing regimen and for a study population that significantly increase the probability that it will demonstrate both safety and efficacy in extended duration VTE prophylaxis in acute medically ill patients both in the hospital and after discharge. We can provide no assurance that APEX will be successful and, if APEX is unsuccessful, our ability to commercialize Betrixaban would be materially adversely affected.

In July 2009, we entered into an exclusive worldwide license and collaboration agreement with Merck & Co., Inc., or Merck, to develop and commercialize Betrixaban for a different indication than the one we are currently pursuing. In March 2011, Merck exercised its right to terminate the agreement for convenience, and we and Merck agreed to a plan for Merck to return all rights to Betrixaban to us and to terminate the agreement, effective September 30, 2011.

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.

As of September 30, 2013, our Betrixaban patent portfolio included 14 issued U.S. patents and nine 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 Pharmaceuticals, Inc. The issued U.S. patents relating to the composition of matter of Betrixaban are not due to expire before September 2020 and may be extended until up to September 2025 pursuant to the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as 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.

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. 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.

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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, but do not prove, 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 recently completed the first 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 this first study demonstrates that Andexanet alfa produces a rapid, sustained and dose-related reversal of anticoagulant activity of the Factor Xa inhibitor apixaban. We are currently conducting two additional Phase 2 proof-of-concept studies evaluating Andexanet alfa for reversal of the anticoagulant activity of the Factor Xa inhibitors rivaroxaban and enoxaparin. We expect results from the study involving rivaroxaban in the second half of 2013 and results from the study involving enoxaparin in the first half of 2014. We plan to initiate similar Phase 2 proof-of-concept studies evaluating the reversal of edoxaban and Betrixaban in the first half of 2014.

We have entered into a collaboration agreement with Bristol-Myers Squibb Company, or BMS, and Pfizer Inc., or Pfizer, a collaboration agreement 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 the Phase 2 Andexanet alfa studies, but we retain full commercial rights with respect to 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. Based on our discussions with the FDA, we believe that the FDA supports our pursuit of an expedited approval process. Subject to further discussions with and approval by the FDA on the protocol, we plan to initiate a Phase 3 registration study for Andexanet alfa in the first half of 2014 followed by a Phase 4 confirmatory study. Additionally, we plan to request a formal scientific advice meeting with the European Medicines Authority in 2014 to discuss the process for approval in Europe.

As of September 30, 2013, our Factor Xa inhibitor antidote patent portfolio was wholly owned by us and included four issued U.S. patents and 12 U.S. patent applications covering the composition of and methods of making and using Andexanet alfa or its analogs. The issued U.S. patents are due to expire between September 2028 and June 2030. A related international patent application has issued in New Zealand, another related international patent application has issued in New Zealand and Mexico 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.

PRT2070. PRT2070 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 PRT2070 for treatment of certain B-cell hematologic cancers, with a particular focus on patients who have NFkB activating mutations or acquired mutations to other novel B-cell targeted therapies that cause treatment failure or disease relapse. PRT2070 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. We initiated a Phase 1/2 proof-of-concept study for PRT2070 in non-Hodgkin s lymphoma and chronic lymphocytic leukemia patients in October 2013. In February 2013, we entered into a license and collaboration agreement with Aciex Therapeutics, Inc., or Aciex, pursuant to which we

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granted Aciex an exclusive license to co-develop and co-commercialize PRT2070 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.

PRT2607. PRT2607 is an orally available, potent and selective inhibitor of Syk. We partnered PRT2607 and other highly selective Syk inhibitors on a worldwide basis with Biogen Idec in October 2011. Pursuant to our agreement, Biogen Idec made an upfront cash payment to us of $36.0 million and we are entitled to additional payments of up to approximately $370 million based on the occurrence of certain development and regulatory events. We are also entitled to receive royalties from any eventual sales of these product candidates by Biogen Idec. 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.

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. Key elements of our strategy are as follows:

- Successfully complete the clinical development of Betrixaban;
- Seek regulatory approval for Andexanet alfa through an expedited development and approval process;
- Commercialize Betrixaban and Andexanet alfa, if approved, using a hospital-focused sales force;
- Independently advance PRT2070 for treatment of hematologic cancers; and
- Deploy capital strategically to develop our portfolio of product candidates and create value.

Financial overview

Our revenue to date has been generated primarily from collaboration and license revenue pursuant to our collaboration agreements with Biogen Idec, Merck and Novartis Pharma A.G., and our agreements with BMS and Pfizer and Daiichi Sankyo. We have not generated any commercial product revenue. As of June 30, 2013, we had $235.2 million of cash, cash equivalents and investments and an accumulated deficit of $242.1 million.

Risks associated with our business

Our business is subject to numerous risks and uncertainties related to our financial condition and need for additional capital, the development and commercialization of our product candidates, our reliance on third parties, the operation of our business, our intellectual property, government regulation and this offering and ownership of our common stock. These risks include those highlighted in the section entitled Risk factors immediately following this prospectus summary, including the following:

- We do not have any products approved for sale and expect to incur substantial and increasing losses for the foreseeable future;

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Our operating results may fluctuate significantly, are difficult to predict and could fall below expectations;

We will need additional funds to support our operations, and such funding may not be available on acceptable terms or at all;

Our success depends heavily on the approval and successful commercialization of our lead product candidates, Betrixaban and Andexanet alfa;

Clinical studies of our product candidates will be costly and time consuming, and if they fail to demonstrate safety and efficacy to the satisfaction of the FDA or similar regulatory authorities, we may be unable to commercialize our product candidates;

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

Our APEX study of Betrixaban may fail due to a potential risk of increased bleeding or lack of efficacy, as experienced in two of our competitors clinical trials evaluating Factor Xa inhibitors for VTE prophylaxis in acute medically ill patients;

If Betrixaban or any of our other product candidates is approved for sale, we will be allowed to market it only for the specific indication for which it receives approval, which may be more limited than we currently anticipate;

If the FDA does not determine that an expedited approval process is available for Andexanet alfa, then the development or commercialization of Andexanet alfa could be delayed or abandoned;

We face substantial competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies;

Our product candidates have never been manufactured on a commercial scale, and there are risks associated with scaling up manufacturing to commercial scale;

Our business may be adversely affected if we are unable to obtain and maintain effective intellectual property rights or fail to comply with our obligations in our intellectual property licenses with third parties; and

Our stock price may be volatile, and purchasers of our common stock could incur substantial losses.

Corporate information

We were incorporated in Delaware in September 2003. Our principal executive offices are located at 270 E. Grand Avenue, South San Francisco, California 94080, and our telephone number is (650) 246-7300. Our website address is *www.portola.com*. The information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information contained on, or that can be accessed through, our website as part of this prospectus or in deciding whether to purchase our common stock.

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

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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.

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

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The offering

Common stock offered	
By us	4,457,710 shares
By the selling stockholders	1,908,803 shares
Total	6,366,513 shares
Common stock to be outstanding immediately after this offering	39,629,479 shares
Underwriters option	The underwriters have an option to purchase up to 954,976 additional shares of common stock from us as described in Underwriting.
Use of proceeds	The net proceeds from the issuance of our common stock in this offering will be approximately $98.8 million or approximately $120.1 million if the underwriters exercise their option in full, based on the public offering price of $23.75 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use all of the net proceeds from this offering, along with our other capital resources, to fund our ongoing Phase 3 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 PRT2070 in hematologic cancers, and for working capital, capital expenditures and other general corporate purposes, which may include the acquisition or licensing of other products, businesses or technologies. We will not receive any of the proceeds from the sale of shares of common stock by the selling stockholders. See Use of proceeds for additional information.
Risk factors	See Risk factors beginning on page 12 and the other information included in this prospectus for a discussion of factors you should carefully consider before deciding to invest in our common stock.
NASDAQ Global Market symbol	PTLA

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The number of shares of our common stock to be outstanding after this offering is 39,629,479, based on 35,171,769 shares of our common stock outstanding as of June 30, 2013, and excludes the following:

- 3,787,915 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2013 at a weighted-average exercise price of $7.50 per share;
- 334,070 shares of common stock reserved for future issuance under our 2013 Equity Incentive Plan, or 2013 Plan;
- 1,000,000 shares of our common stock reserved for future issuance under our 2013 Employee Stock Purchase Plan; and
- 82,575 shares of our common stock issuable upon the exercise of common stock warrants outstanding at a weighted-average exercise price of $12.92 per share.

Unless otherwise indicated, all information in this prospectus reflects and assumes no exercise of the underwriters option to purchase additional shares of our common stock.

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Summary financial data

The following tables summarize our financial data and should be read together with the sections in this prospectus entitled Selected financial data and Management s discussion and analysis of financial condition and results of operations and our financial statements and related notes included elsewhere in this prospectus.

We have derived the statement of operations data for the years ended December 31, 2010, 2011 and 2012 from our audited financial statements included elsewhere in this prospectus. We have derived the statement of operations data for the six months ended June 30, 2012 and 2013 and the balance sheet data as of June 30, 2013 from our unaudited interim condensed financial statements included elsewhere in this prospectus. We have prepared the unaudited financial statements on the same basis as the audited financial statements and 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 that should be expected in the future, and our unaudited interim results are not necessarily indicative of the results that should be expected for the full year or any other period.

	Year ended December 31,			Six months ended June 30,	
	2010	2011	2012	2012	2013
	(in thousands, except share and per share data)			(unaudited)	
Statement of operations data:					
Collaboration and license revenue[1]	$ 35,268	$ 78,029	$ 72,042	$ 69,346	$ 5,709
Operating expenses:					
Research and development	43,260	46,089	49,717	26,049	38,556
General and administrative	10,762	12,071	11,469	5,865	6,747
Total operating expenses	54,022	58,160	61,186	31,914	45,303
Income (loss) from operations	(18,754)	19,869	10,856	37,432	(39,594)
Interest and other income (expense), net	1,659	136	510	(796)	(147)
Interest expense	(380)	(21)			
Income (loss) before income taxes	(17,475)	19,984	11,366	36,636	(39,741)
Provision for income taxes	2,794				
Net income (loss)	$ (20,269)	$ 19,984	$ 11,366	$ 36,636	$ (39,741)
Net income (loss) attributable to common stockholders:					
Basic	$ (20,269)	$ 79	$	$ 1,257	$ (39,741)
Diluted	$ (20,269)	$ 127	$	$ 1,816	$ (39,741)
Net income (loss) per share attributable to common stockholders[2]:					
Basic	$ (16.79)	$ 0.06	$ 0.00	$ 0.95	$ (4.92)
Diluted	$ (16.79)	$ 0.06	$ 0.00	$ 0.92	$ (4.92)
Shares used to compute net income (loss) per share attributable to common stockholders:					
Basic	1,207,106	1,249,778	1,350,939	1,329,133	8,078,308
Diluted	1,207,106	2,089,206	2,048,867	1,968,821	8,078,308

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(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 our exclusive worldwide license and collaboration agreement with Merck, 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 our exclusive worldwide license agreement with Novartis Pharma A.G., effective July 1, 2012. See the section of this prospectus 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.

(2) See Note 2 to our audited financial statements included in this prospectus for an explanation of the calculations of our basic and diluted net income (loss) per share attributable to common stockholders for the years ended December 31, 2010, December 31, 2011 and December 31, 2012. See Note 1 to our unaudited interim condensed financial statements included in this prospectus for an explanation of the calculations of our basic and diluted net income (loss) per share attributable to common stockholders for the six months ended June 30, 2012 and June 30, 2013.

Stock-based compensation included in the statement of operations data above was as follows:

	Year ended December 31,			Six months ended June 30,	
	2010	2011	2012	2012	2013
			(in thousands)		
				(unaudited)	
Research and development	$ 1,170	$ 1,164	$ 1,452	$ 749	$ 945
General and administrative	764	1,189	1,357	662	978
Total stock-based compensation	$ 1,934	$ 2,353	$ 2,809	$ 1,411	$ 1,923

	As of June 30, 2013	
	Actual	As Adjusted[1]
	(in thousands) (unaudited)	
Balance sheet data:		
Cash, cash equivalents and investments[2]	$ 235.2	$ 333.9
Working capital	185.7	284.5
Total assets	245.4	344.1
Total stockholders equity	214.6	313.4

(1) The as adjusted column reflects the sale by us of 4,457,710 shares of our common stock at the public offering price of $23.75 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

(2) Includes $27.6 million classified as long-term investments.

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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 prospectus, 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 six months ended June 30, 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 six months ended June 30, 2013 and expect to incur substantial and increasing losses for the foreseeable future. As of June 30, 2013, we had an accumulated deficit of $242.1 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, 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

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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;
- 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;

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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 June 30, 2013, we had approximately $235.2 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,

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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 PRT2070 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, PRT2070 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;

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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 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 first Phase 2 proof-of concept study of Andexanet alfa, evaluating the effect of Andexanet alfa in healthy volunteers taking apixaban, 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

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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;
- 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;

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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

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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 the study to be completed by mid-2015. 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 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 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 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.

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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 expedited approval process, and if the FDA does not determine that such a process is available for Andexanet alfa, then the development or commercialization of Andexanet alfa could be delayed or abandoned.

We currently plan to seek FDA approval of Andexanet alfa through an expedited approval process, such as Accelerated Approval, which is a process allowing drugs that treat serious diseases for which there is an unmet medical need to be approved on a shortened timetable based on use of a surrogate endpoint in clinical studies or with restrictions to promote safe use. However, we have not reached agreement with the FDA on a development plan for Andexanet alfa under Accelerated Approval or any other expedited process. If the FDA does not allow us to pursue an expedited approval process for Andexanet alfa or determines that a study based on a surrogate endpoint will not be acceptable, the time and expense associated with developing Andexanet alfa would be significantly greater than we currently anticipate, and we might be required to enter into a partnership in order to develop Andexanet alfa or delay or abandon development of Andexanet alfa. Even if we are able to pursue an expedited approval process, 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;

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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,

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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.

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We are developing our lead product candidate Betrixaban for extended duration VTE prophylaxis in acute medically ill patients 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 PRT2070 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.

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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.

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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

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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

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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 recently engaged Lonza Group Ltd., or Lonza, to be the sole manufacturer of Andexanet alfa. 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 a new manufacturer, Lonza, and are also engaging a new sole-source vendor to perform lyophilization and packaging. In connection with the transfer of 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 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 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

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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 a collaboration agreement with each of Lee s, BMS and Pfizer, Bayer and Janssen, Daiichi Sankyo, Biogen Idec and Aciex 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 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 PRT2070 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;

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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;

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

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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 August 31, 2013, we had 58 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.

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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.

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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.

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.

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In connection with our Betrixaban 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, PRT2070 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.

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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

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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

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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.

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Risks related to government regulation

The regulatory approval process is expensive, time consuming and uncertain and may prevent us or our collaboration partners 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. Neither we nor our collaboration partners are permitted to market our product candidates in the United States until we receive approval of an NDA or a BLA from the FDA. Neither we nor our collaboration partners have 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;

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

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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.

In addition, on October 1, 2013, the U.S. federal government entered a shutdown suspending services deemed non-essential as a result of the failure by Congress to enact regular appropriations for the 2014 fiscal year. If the shutdown continues for a prolonged period of time, it could result in significant delays in the FDA s ability to timely review and process any submissions we have filed or may file or cause other regulatory delays, which could have a material adverse effect on our business.

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

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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;
- 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

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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;

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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 this offering and 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 experiences 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;

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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.

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A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future. This could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of June 30, 2013, we had outstanding 35,171,769 shares of common stock. 26,985,598 of these shares are currently restricted as a result of securities laws or lock-up agreements (except to the extent of any shares being sold by the selling stockholders in this offering). Moreover, as of June 30, 2013, and without giving effect to the shares being sold by the selling stockholders in this offering, holders of an aggregate of up to 24,107,872 shares of our common stock, including shares of our common stock issuable upon exercise of outstanding warrants, have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also intend to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements.

After this offering, our executive officers, directors and principal stockholders will continue to maintain the ability to control or significantly influence all matters submitted to stockholders for approval.

Upon the closing of this offering, our executive officers, directors and stockholders who owned more than 5% of our outstanding common stock before this offering will, in the aggregate, beneficially own shares representing approximately 39% of our common stock, based on 35,229,352 shares of common stock outstanding as of August 31, 2013 and after giving effect to the sale of shares in this offering. 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 is 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

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December 31, 2013. 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 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 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 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.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the balance of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds

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effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

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.

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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 $2.8 million for severance and other benefits and acceleration of vesting of stock options with a value of approximately $16.4 million (as of June 30, 2013, based on the closing price of our common stock of $24.57 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.

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Cautionary statement concerning forward-looking statements

This prospectus, including the sections titled Prospectus summary, Risk factors, Use of proceeds, Management s discussion and analysis of financial condition and results of operations, Market, industry and other data, Business and Shares eligible for future sale, 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, seek, expect, 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:

our expected uses of the net proceeds to us from this offering;

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 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 PRT2070;

our expectation that our existing capital resources and the net proceeds from this offering 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 PRT2070 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;

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;

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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;

our ability to retain and recruit key personnel;

our ability to obtain and maintain intellectual property protection for our products;

the actual receipt and timing of any milestone payments or royalties from our collaborators;

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 prospectus 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 prospectus to conform these statements to actual results or to changes in our expectations.

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

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Market, industry and other data

We obtained the industry, market and similar data set forth in this prospectus from our own internal estimates and research, and from industry publications and research, surveys and studies conducted by third parties. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates.

Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

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Use of proceeds

The net proceeds from our issuance and sale of shares of our common stock in this offering will be approximately $98.8 million, or approximately $120.1 million if the underwriters exercise their option in full, based on the public offering price of $23.75 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We will not receive any proceeds from the sale of common stock by the selling stockholders.

As of June 30, 2013, we had cash, cash equivalents and investments of approximately $235.2 million. We currently estimate that we will use the net proceeds from this offering, together with our cash, cash equivalents and investments, as follows:

- approximately $125.0 million to fund our ongoing Phase 3 study of Betrixaban;
- approximately $110.0 million to fund our Phase 3/4 Biologics License Application, or BLA, enabling studies and related manufacturing of Andexanet alfa;
- approximately $20.0 million to fund our Phase 1/2 proof-of-concept studies of PRT2070 in hematologic cancers; and
- the balance to fund working capital, capital expenditures and other general corporate purposes, which may include the acquisition or licensing of other products, businesses or technologies.

This expected use of the net proceeds from this offering and our existing cash, cash equivalents and investments represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development and commercialization efforts and the status of and results from clinical studies, as well as any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering. We have no current understandings, agreements or commitments for any material acquisitions or licenses of any products, businesses or technologies.

Based on our planned use of the net proceeds from this offering and our existing cash, cash equivalents and investments described above, we expect that such funds will be sufficient to enable us to complete our ongoing Phase 3 clinical study of Betrixaban, our Phase 2 proof-of-concept studies and Phase 3 registration study (assuming an expedited approval process) of Andexanet alfa and a Phase 1/2 proof-of-concept study in non-Hodgkin s lymphoma and chronic lymphocytic leukemia for PRT2070, and to initiate our Phase 4 confirmatory study for Andexanet alfa and related BLA-enabling commercial scale manufacturing. However, it is possible that we will not achieve the progress that we expect because the actual costs and timing of drug development, particularly clinical studies, are difficult to predict, subject to substantial risks and delays and often vary depending on the particular indication and development strategy. We do not expect that the net proceeds from this offering and our existing cash, cash equivalents and investments will be sufficient to enable us to fund substantial development of our other product candidates.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment grade, interest bearing instruments and U.S. government securities.

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Market price 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 (through October 16, 2013)	$ 20.72	$ 30.95

On October 16, 2013, the last reported sale price of our common stock as reported on The NASDAQ Global Market was $25.55 per share.

As of June 30, 2013, we had 227 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.

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.

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Dilution

Dilution is the amount by which the offering price paid by the purchasers of the shares of common stock sold in the offering exceeds the as adjusted net tangible book value per share of our common stock after this offering. The net tangible book value of our common stock as of June 30, 2013 was $214.6 million, or $6.10 per share. Net tangible book value per share represents our total tangible assets less our total liabilities, divided by the number of outstanding shares of common stock.

After giving effect to the receipt by us of the net proceeds from the sale by us of 4,457,710 shares of our common stock at the public offering price of $23.75 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2013 would have been approximately $313.4 million, or $7.91 per share. This represents an immediate increase in as adjusted net tangible book value of $1.81 per share to our existing stockholders and an immediate dilution of $15.84 per share to investors purchasing common stock in this offering. We will not receive any proceeds from the sale of these shares of common stock by the selling stockholders, or the transfer agent on their behalf.

The following table illustrates this dilution on a per share basis to new investors:

Assumed public offering price per share		$ 23.75
Net tangible book value per share as of June 30, 2013	$ 6.10	
Increase in net tangible book value per share attributable to new investors purchasing shares in this offering	1.81	
As adjusted net tangible book value per share after giving effect to this offering		7.91
Dilution in net tangible book value per share to new investors in this offering		$ 15.84

If the underwriters option to purchase additional shares in this offering is exercised in full, sales by us in this offering will reduce the percentage of shares of our common stock held by existing stockholders prior to this offering to 86.7% of the total number of shares of our common stock outstanding after this offering, and the number of shares purchased from us by investors participating in this offering will increase to 5,412,686 shares, or 13.3% of the total number of shares of our common stock outstanding after this offering.

The number of shares of our common stock reflected in the discussion and table above is based on 35,171,769 shares of our common stock outstanding as of June 30, 2013, assumes the issuance and sale of 4,457,710 shares of our common stock and excludes the following:

- 3,787,915 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2013 at a weighted-average exercise price of $7.50 per share;
- 334,070 shares of common stock reserved for future issuance under our 2013 Equity Incentive Plan, or 2013 Plan;
- 1,000,000 shares of our common stock reserved for future issuance under our 2013 Employee Stock Purchase Plan; and

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82,575 shares of our common stock issuable upon the exercise of common stock warrants outstanding at a weighted-average exercise price of $12.92 per share.

To the extent that any outstanding options or warrants are exercised, new options are issued under our stock-based compensation plans or we issue additional shares of common stock in the future, there will be further dilution to investors participating in this offering.

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Capitalization

The following table sets forth our cash, cash equivalents and investments and capitalization as of June 30, 2013:

- on an actual basis;
- on an as adjusted basis to give effect to the issuance and sale by us of 4,457,710 shares of our common stock in this offering at the public offering price of $23.75 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table together with the sections in this prospectus entitled Selected financial data, and Management s discussion and analysis of financial condition and results of operations and our financial statements and related notes included elsewhere in this prospectus.

	As of June 30, 2013	
	Actual	As adjusted
	(in thousands, except share and per share data) (unaudited)	
Cash, cash equivalents and investments[1]	$ 235,190	$ 333,948
Stockholders equity:		
Preferred stock, $0.001 par value; 5,000,000 shares authorized, no shares issued and outstanding, actual and as adjusted		
Common stock, $0.001 par value; 100,000,000 shares authorized, 35,171,769 shares issued and outstanding, actual; 39,629,479 shares issued and outstanding, as adjusted	35	40
Additional paid-in capital	456,657	555,409
Accumulated deficit	(242,060)	(242,060)
Accumulated other comprehensive (loss)	(36)	(36)
Total stockholders equity	214,596	313,353
Total capitalization	$ 214,596	$ 313,353

(1) Includes $27.6 million classified as long-term investments.

The outstanding share information in the table above is based on 35,171,769 shares of our common stock outstanding as of June 30, 2013, and excludes the following:

- 3,787,915 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2013 at a weighted-average exercise price of $7.50 per share;
- 334,070 shares of common stock reserved for future issuance under our 2013 Equity Incentive Plan, or 2013 Plan;

1,000,000 shares of our common stock reserved for future issuance under our 2013 Employee Stock Purchase Plan; and

82,575 shares of our common stock issuable upon the exercise of common stock warrants outstanding at a weighted-average exercise price of $12.92 per share.

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Selected financial data

You should read the following selected financial data together with the section of this prospectus entitled Management s discussion and analysis of financial condition and results of operations and our financial statements and the related notes included in this prospectus. The statement of operations data for the years ended December 31, 2010, 2011 and 2012 and the balance sheet data as of December 31, 2011 and 2012 are derived from our audited financial statements included elsewhere in this prospectus. The statement of operations data for the six months ended June 30, 2012 and 2013 and the balance sheet data as of June 30, 2013 are derived from our unaudited interim condensed financial statements included elsewhere in this prospectus. 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,			Six months ended June 30,	
	2010	2011	2012	2012	2013
	(in thousands, except share and per share data)			(unaudited)	
Statement of operations data:					
Collaboration and license revenue[1]	$ 35,268	$ 78,029	$ 72,042	$ 69,346	$ 5,709
Operating expenses:					
Research and development	43,260	46,089	49,717	26,049	38,556
General and administrative	10,762	12,071	11,469	5,865	6,747
Total operating expenses	54,022	58,160	61,186	31,914	45,303
Income (loss) from operations	(18,754)	19,869	10,856	37,432	(39,594)
Interest and other income (expense), net	1,659	136	510	(796)	(147)
Interest expense	(380)	(21)			
Income (loss) before income taxes	(17,475)	19,984	11,366	36,636	(39,741)
Provision for income taxes	2,794				
Net income (loss)	$ (20,269)	$ 19,984	$ 11,366	$ 36,636	$ (39,741)
Net income (loss) attributable to common stockholders:					
Basic	$ (20,269)	$ 79	$	$ 1,257	$ (39,741)
Diluted	$ (20,269)	$ 127	$	$ 1,816	$ (39,741)
Net income (loss) per share attributable to common stockholders:					
Basic	$ (16.79)	$ 0.06	$ 0.00	$ 0.95	$ (4.92)
Diluted	$ (16.79)	$ 0.06	$ 0.00	$ 0.92	$ (4.92)
Shares used to compute net income (loss) per share attributable to common stockholders:					
Basic	1,207,106	1,249,778	1,350,939	1,329,133	8,078,308
Diluted	1,207,106	2,089,206	2,048,867	1,968,821	8,078,308

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(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 our 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 our exclusive worldwide license agreement with Novartis Pharma A.G., effective July 1, 2012. See the section of this prospectus 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.

	2010	As of December 31, 2011	2012	As of June 30, 2013
		(in thousands)		(unaudited)
Balance sheet data:				
Cash, cash equivalents and investments	$ 101,417	$ 188,089	$ 137,384	$ 235,190
Restricted cash	6,000			
Working capital	55,659	169,128	116,089	185,698
Total assets	113,658	193,403	146,001	245,390
Convertible preferred stock	220,374	317,280	317,280	
Total stockholders equity (deficit)	(228,407)	(206,105)	(191,569)	214,596

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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 prospectus entitled Selected financial data and our financial statements and related notes included elsewhere in this prospectus. This discussion and other parts of this prospectus 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 prospectus 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 the first of a series of Phase 2 proof-of-concept studies. We initiated a Phase 1/2 proof-of-concept study of PRT2070 in October 2013. We also have completed multiple Phase 1 studies for PRT2607.

On May 28, 2013, we completed our initial public offering, or 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. After deducting offering expenses payable by us of approximately $5.1 million, our net proceeds were approximately $125.8 million. 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.

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 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 be completed in mid-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 prospectus entitled Business Collaboration and license agreements Millennium agreements for a more detailed description of these agreements.

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In July 2009, we entered into an exclusive worldwide license and collaboration agreement with Merck & Co., Inc., or Merck, to develop and commercialize Betrixaban, which was terminated effective September 2011. See the section of this prospectus entitled Business Collaboration and license agreements Merck agreement for a more detailed description of 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 prospectus 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. In May 2013, we completed the first of a series of Phase 2 proof-of-concept studies of Andexanet alfa in healthy volunteers who were administered a Factor Xa inhibitor, in this case Eliquis® (apixaban), which is manufactured by Bristol-Myers Squibb and Pfizer. 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 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. Based on our discussions with the FDA, we believe that the FDA supports our pursuit of an expedited approval process.

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. 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 prospectus entitled Business Collaboration and license agreements BMS and Pfizer agreement for a more detailed description of this agreement. We originally estimated the period of performance of our obligations to extend through June 2013. In March 2013, we revised our estimated period of performance to be through July 2013 and in June 2013 we revised our estimated period of performance to be through September 2013. The total consideration under this agreement of $6.0 million is being recognized as revenue on a straight-line basis over the estimated performance period through September 2013.

In February 2013, we entered into a three-way agreement with Bayer Pharma AG, or Bayer, and Janssen Pharmaceuticals, Inc., or 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 prospectus entitled Business Collaboration and license agreements Bayer and Janssen agreement 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 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 November 2013. In June 2013, we revised our estimated period of performance to be

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through January 2014. The total consideration under this agreement of $5.5 million is being recognized as revenue ratably over the estimated performance period through January 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. Should Daiichi Sankyo terminate the agreement prior to the first patient dosing in the clinical trial, it is entitled to a refund of $3.0 million. The total consideration under this agreement of $6.0 million was received in July 2013, although only the non-contingent consideration of $3.0 million was recorded as receivables from collaborations at June 30, 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. The total non-contingent consideration under this agreement of $3.0 million is being recognized as revenue ratably over the estimated non-contingent performance period through May 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 May 2014 and conclude in October 2014.

In anticipation of a potential Biologics License Application, or 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 manufacturing of Andexanet alfa to Lonza and are making process improvements in order to increase scale and efficiency. We plan to implement proposed changes with Lonza to initiate BLA-enabling studies with a manufacturing process that will allow us to launch Andexanet alfa pursuant to an expedited approval. After recent discussions with the FDA, we determined that the additional process changes needed to further reduce cost of goods will be incorporated into the commercial production later in the development of Andexanet alfa or as a supplemental BLA, if supporting studies are required.

PRT2070

In addition to our thrombosis products, we have discovered two novel orally available kinase inhibitors to treat hematologic disorders and inflammation. The first, PRT2070, 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 PRT2070 for the treatment of certain B-cell hematologic cancers. We have completed preclinical testing for PRT2070 and initiated a Phase 1/2 proof-of-concept study in non-Hodgkin s lymphoma and chronic lymphocytic leukemia patients 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 PRT2070 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, we and Aciex will each incur and report our 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 and to participate on various committees. We can opt out of our obligation to share in the

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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 three and six months ended June 30, 2013. See the section of this prospectus 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 prospectus 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 PRT2070 and PRT2607. This agreement was amended in December 2010. See the section of this prospectus 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. 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. See the section of this prospectus entitled Business Collaboration and license agreements Novartis agreement for a more detailed description of this agreement. Although we may resume development of Elinogrel in the future, we currently do not plan do to 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, Aciex, 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

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refundable contingent payment and a milestone payment in the aggregate amount of $178.7 million, of which $6.0 million was received in July 2013 pursuant to our agreement with Daiichi Sankyo.

We may also be entitled to additional milestone payments and other contingent payments upon the occurrence of specific events. We have achieved one milestone and received a milestone payment for its achievement and we have received one contingent refundable payment under our collaboration agreements as of June 30, 2013. Due to the nature of these collaboration agreements and the nonlinearity of the related revenue recognition, 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, 2010, 2011 and 2012 and the six months ended June 30, 2012 and 2013:

	Year Ended December 31,			Six Months Ended June 30,	
	2010	2011	2012	2012	2013
			(in thousands)		
				(unaudited)	
Novartis:					
Recognition of upfront license fee	$ 7,692	$ 7,692	$ 53,846	$ 53,282	$
Reimbursement of research and development expenses	898	1,879	16,238	16,064	
Novartis total	8,590	9,571	70,084	69,346	
Merck:					
Recognition of upfront license fee	21,429	21,429			
Reimbursement of research and development expenses	5,249	9,973			
Merck total	26,678	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			1,958		3,094
BMS and Pfizer total			1,958		3,094
Bayer and Janssen:					
Recognition of research and development services					2,438
Bayer and Janssen total					2,438
Lee s:					
Recognition of research and development services					52
Lee s total					52
Daiichi Sankyo:					
Recognition of research and development services					125
Daiichi Sankyo total					125

Total collaboration and license revenue	$ 35,268	$ 78,029	$ 72,042	$ 69,346	$ 5,709

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

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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 incurred during the years ended December 31, 2010, 2011 and 2012 and the six months ended June 30, 2012 and 2013:

		Year Ended December 31,			Six Months Ended June 30,	
Product candidate	**Phase of development**	**2010**	**2011**	**2012**	**2012**	**2013**
				(in thousands) (unaudited)		
Betrixaban	Phase 3	$ 6,099	$ 5,828	$ 27,297	$ 14,092	$ 22,697
Andexanet alfa	Phase 2	4,435	11,128	15,049	7,857	13,777
PRT2070	Phase 1/2	1,961	1,970	726	208	2,145
PRT2607	Pre-clinical	7,454	19,045	3,344	2,287	(206)
Elinogrel[1]	Phase 3 ready	9,371	3,221	172	100	46
Other research and development expenses[2]		13,940	4,897	3,129	1,505	97
Total research and development expenses[3]		$ 43,260	$ 46,089	$ 49,717	$ 26,049	$ 38,556

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

(2) Amount in 2010 consists primarily of costs for another compound which we are no longer developing. 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.

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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 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

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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. There have been no significant or material changes in our critical accounting policies during the three and six months ended June 30, 2013, as compared to those disclosed in Management s discussion and analysis of financial condition and results of operations Critical accounting policies and significant judgments and estimates in our prospectus dated May 21, 2013, filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act of 1933, as amended, or Securities Act.

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 ratably over the estimated period of performance, which was the same manner in which the revenue was recognized for the final deliverable.

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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;

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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 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 an expense over the employee s requisite service period on a straight-line basis. We recorded non-cash stock-based compensation expense of $1.9 million, $2.4 million, $2.8 million, $1.4 million and $1.9 million for the years ended

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December 31, 2010, 2011 and 2012 and the six months ended June 30, 2012 and 2013, respectively. At June 30, 2013, we had $8.8 million of total unrecognized stock-based compensation expense, net of estimated forfeitures, related to stock option grants that will be recognized over a weighted-average period of 2.5 years. 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 estimated 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 June 30, 2013, our total deferred tax assets were $89.1 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 each of 2009 and 2012, we performed an analysis on annual limitation as a result of ownership changes that may have occurred before January 2007 and through December 31, 2012, respectively. As a result of the analysis, we do not believe that we are currently subject to any such limitation. However, due to 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.

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Results of operations

Comparison of the six months ended June 30, 2012 and 2013

Revenue

	Six Months Ended June 30,			
	2012	2013	Increase / (Decrease)	% Increase / (Decrease)
	(dollars in thousands) (unaudited)			
Collaboration and license revenue	$ 69,346	$ 5,709	$ (63,637)	(92)%

The decrease in collaboration and license revenue during the six months ended June 30, 2013 was due to the decrease in collaboration and license 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 the six months ended June 30, 2013, compared to revenue of $69.3 million recognized from our agreement with Novartis during the six months ended June 30, 2012. This decrease in collaboration and license revenue was partially offset by revenue recognized with respect to our agreements with BMS and Pfizer, Bayer and Janssen, Lee s and Daiichi Sankyo.

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 June 2013. In March 2013, we revised our estimated period of performance to be through July 2013 and in June 2013 we revised our estimated period of performance to be through September 2013. The total consideration under this agreement of $6.0 million is being recognized as revenue on a straight-line basis over the estimated performance period through September 2013.

Pursuant to our agreement with Bayer and Janssen, we are obligated to participate on a 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 November 2013. In June 2013 we revised our estimated period of performance to be through January 2014. The total consideration under this agreement of $5.5 million is being recognized as revenue ratably over the estimated performance period through January 2014.

Pursuant to our agreement with Daiichi Sankyo, we are obligated to participate on a JCC with Daiichi Sankyo to oversee the collaboration activities under the agreement. The total consideration under this agreement is $6.0 million, of which the total non-contingent consideration of $3.0 million is being recognized as revenue ratably over the estimated non-contingent performance period through May 2014.

We expect revenue recognized in future periods, until we achieve product commercialization, 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.

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Research and development expenses

	Six Months Ended June 30,		Increase / (Decrease)	% Increase / (Decrease)
	2012	2013		
	(dollars in thousands) (unaudited)			
Research and development expenses	$ 26,049	$ 38,556	$ 12,507	48%

The increase in research and development expenses during the six months ended June 30, 2013 was primarily due to the following:

- increased program costs of $8.6 million to advance Betrixaban;
- increased program costs of $5.9 million to advance Andexanet alfa; and
- increased program costs of $1.9 million to advance PRT2070.

These increases were partially offset by:

- decreased net program costs of $2.5 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 $1.4 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 PRT2070.

We expect our research and development expenses to increase in the future as we advance our product candidates through clinical development. In particular, we expect research and development expenses to continue to increase for the remainder of 2013 and in 2014 due to the cost of additional manufacturing process changes for Andexanet alfa, our advancement of the APEX studies for Betrixaban and our expected advancement of PRT2070. 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

	Six Months Ended June 30,		Increase / (Decrease)	% Increase / (Decrease)
	2012	2013		
	(dollars in thousands) (unaudited)			
General and administrative expenses	$ 5,865	$ 6,747	$ 882	15%

The increase in general and administrative expenses during the six months ended June 30, 2013 was primarily related to increased headcount 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 $0.6 million, professional and legal fees to support business development and collaboration arrangements of $0.1 million and increased costs associated with being a public company including directors and officer s insurance and director fees of $0.1 million.

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

Interest and other income (expense), net

	Six Months Ended June 30,		Increase / (Decrease)	% Increase/ (Decrease)
	2012	2013		
	(dollars in thousands) (unaudited)			
Interest and other income (expense), net	$ (796)	$ (147)	$ 649	(82)%

The increase in interest and other income (expense), net during the six months ended June 30, 2013 of $0.6 million is primarily due to foreign currency exchange losses of $0.1 million in the six months ended June 30, 2013, compared to foreign currency exchange losses of $0.8 million in the six months ended June 30, 2012, related to fluctuations in the Euro compared to the U.S. dollar and unrealized gains and losses related to our foreign currency forward contracts.

Comparison of the years ended December 31, 2011 and 2012

Revenue

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

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Research and development expenses

	Year ended December 31,		Increase / (Decrease)	% Increase / (Decrease)
	2011	2012		
	(dollars in thousands)			
Research and development expenses	$ 46,090	$ 49,717	$ 3,627	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 December 31,		Increase / (Decrease)	% Increase / (Decrease)
	2011	2012		
	(dollars in thousands)			
General and administrative expenses	$ 12,071	$ 11,469	$ (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 December 31,		Increase / (Decrease)	% Increase / (Decrease)
	2011	2012		
	(dollars in thousands)			
Interest and other income, net	$ 116	$ 510	$ 394	341%

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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,		Increase / (Decrease)	% Increase / (Decrease)
	2011	2012		
	(dollars in thousands)			
Interest expense	$ 21	$	$ (21)	(100%)

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

Comparison of the years ended December 31, 2010 and 2011

Revenue

	Year ended December 31,		Increase / (Decrease)	% Increase / (Decrease)
	2010	2011		
	(dollars in thousands)			
Collaboration and license revenue	$ 35,268	$ 78,029	$ 42,761	121%

The increase in collaboration and license revenue was primarily due to $37.1 million of recognition of collaboration revenue pursuant to our agreement with Biogen Idec, which we entered into in October 2011, an increase of $4.7 million for recognition of collaboration revenue pursuant to our agreement with Merck and an increase of $1.0 million for recognition of collaboration revenue pursuant to our agreement with Novartis.

In October 2011, we entered into an exclusive, worldwide license and collaboration agreement with Biogen Idec to develop and commercialize PRT2607 and other highly selective Syk inhibitors. Pursuant to the agreement, Biogen Idec provided us with an upfront cash license fee of $36.0 million and paid us $9.0 million for the purchase of 636,042 shares of our Series 1 convertible preferred stock, a premium of $1.1 million above the stock s estimated fair value. For the year ended December 31, 2011, we recognized collaboration 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.

In March 2011, we agreed to a plan for Merck to return to us all rights to Betrixaban and terminate our agreement with Merck effective September 30, 2011. In connection with the termination of our agreement with Merck, we recognized revenue of $8.3 million, consisting of $5.3 million of upfront license fees and $3.0 million for reimbursement of research and development expenses. Our total Merck revenue for 2011 of $31.4 million included the foregoing amounts, as well as an additional $16.1 million of upfront license fees and $7.0 million for reimbursement of research and development expenses. We have no further performance obligations under our agreement with Merck. For 2010, we recognized total revenue from Merck of $26.7 million.

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Research and development expenses

	Year ended December 31, 2010	2011	Increase / (Decrease)	% Increase / (Decrease)
	(dollars in thousands)			
Research and development	$ 43,260	$ 46,089	$ 2,829	7%

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

- increased costs of $6.7 million for Andexanet alfa, primarily due to increased costs to advance its clinical development;
- increased net costs of $12.3 million for PRT2607 primarily due to the payment of $7.2 million to Astellas pursuant to our agreement with Astellas in connection with our agreement with Biogen Idec for the Syk program development;
- a reduction of research and development expenses for PRT2607 by $0.7 million due to reimbursement received from Biogen Idec under the cost-sharing provisions of our agreement with Biogen Idec;
- decreased clinical development costs for Elinogrel of $6.2 million; and
- decreased preclinical development costs of $9.0 million as we narrowed our focus to support clinical development of Betrixaban, Andexanet alfa and PRT2607 and preclinical development of PRT2070.

General and administrative expenses

	Year ended December 31, 2010	2011	Increase / (Decrease)	% Increase / (Decrease)
	(dollars in thousands)			
General and administrative expenses	$ 10,762	$ 12,071	$ 1,309	12%

The increase in general and administrative expenses was primarily due to increased legal and other professional costs of $1.6 million to negotiate and support our collaboration agreements and clinical studies, partially offset by decreased personnel costs of $0.2 million resulting from lower headcount and decreased facility and overhead costs of $0.1 million primarily due to favorable lease negotiations resulting in lower rent expense for our South San Francisco, California headquarters.

Interest and other income, net

	Year ended December 31, 2010	2011	Increase / (Decrease)	% Increase / (Decrease)
	(dollars in thousands)			
Interest and other income, net	$ 1,659	$ 136	$ (1,523)	(92%)

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The decrease in interest and other income, net resulted primarily from the receipt of $1.5 million of income in connection with tax credit awards received during the year ended December 31, 2010 from the U.S. Department of Treasury for six projects under the Qualifying Therapeutic Discovery Project Program to support research with the potential to produce new therapies. There were no such amounts received in 2011.

Interest expense

	Year ended December 31,		Increase / (Decrease)	% Increase / (Decrease)
	2010	2011		
	(dollars in thousands)			
Interest expense	$ 380	$ 21	$ (359)	(94%)

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

Provision for income taxes

	Year ended December 31,		Increase / (Decrease)	% Increase / (Decrease)
	2010	2011		
	(dollars in thousands)			
Provision for income taxes	$ 2,794	$	$ (2,794)	(100%)

For the year ended December 31, 2011, we did not record an income tax provision on pre-tax income because we incurred taxable losses for both state and 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 state law suspended their use in 2011. We recorded an income tax provision for the year ended December 31, 2010 on a pre-tax loss due primarily to the recognition of collaboration revenue deferred in previous years for California state income tax purposes that could not be offset by state net operating losses due to the suspension of the use of these losses under state law in 2010.

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, convertible preferred stock and payments from our collaboration partners. Our expenditures are primarily related to research and development activities. We have received additional funding from long-term debt and interest earned on investments. At June 30, 2013, we had available cash, cash equivalents and investments of $235.2 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.

In February 2009, July 2009, November 2011, December 2012, February 2013, March 2013 and April 2013, in connection with our agreements with Novartis, Merck and Biogen Idec, BMS and Pfizer, Bayer and Janssen, and Lee s we received payments of $75.0 million, $50.0 million, $36.0 million, $6.0 million, $5.0 million, and $0.7 million, respectively, as initial upfront payments and a milestone

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payment of $2.0 million. These payments are initially reflected as deferred revenue and included within cash used in operating activities. In July 2013, we received $6.0 million pursuant to our agreement with Daiichi Sankyo, of which the non-contingent consideration of $3.0 million was recorded as receivables from collaborations and deferred revenue at June 30, 2013. In addition, in 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,			Six months ended June 30,	
	2010	2011	2012	2012	2013
			(in thousands)		
				(unaudited)	
Cash used in operating activities	$ (29,646)	$ (11,321)	$ (49,225)	$ (27,560)	$ (29,327)
Cash provided by (used in) investing activities	(4,865)	32,710	(67,802)	(82,963)	(40,393)
Cash provided by (used in) financing activities	(6,492)	94,218	317	292	128,353
Net increase (decrease) in cash	$ (41,003)	$ 115,607	$ (116,710)	$ (110,231)	$ 58,633

Cash used in operating activities

Cash used in operating activities was $29.3 million for the six months ended June 30, 2013 reflecting net loss of $39.7 million, which was decreased by non-cash charges of $1.9 million for stock-based compensation, $0.4 million for unrealized losses related to foreign currency forward contracts, $0.8 million for amortization of premium on investments and $0.7 million for depreciation and amortization. Cash used in operating activities also reflected an increase in net operating assets of $6.7 million primarily due to increases in accounts payable and accrued and other liabilities of $8.0 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 $3.0 million due to an increase in deferred revenue of $5.0 million related to the upfront payments received from Bayer and Janssen, $3.0 million related to the non-contingent receivable from Daiichi Sankyo and $0.7 million related to the upfront payments received from Lee s in the six months ended June 30, 2013, partially offset by the recognition of collaboration revenue earned of $5.7 million from our collaboration agreements. Cash used in operating activities also reflected a decrease in prepaid expenses and other current assets of $0.9 million primarily reflecting payment and classification of deferred offering costs of $1.6 million, partially offset by higher prepaid corporate directors and officers insurance of $0.5 million following the renewal of our corporate insurance program and placement of our public company policies and prepaid rent of $0.2 million in the six months ended June 30, 2013. Also reflected in cash used in operating activities is a decrease in accrued compensation and employee benefits of $0.2 million due to 2012 bonuses that were paid in the six months ended June 30, 2013 and a decrease in receivables from collaborations of $2.8 million due to upfront payments received from Bayer of $6.0 million partially offset by receivables due from Daiichi Sankyo as of June 30, 2013 of $3.0 million pursuant to our agreement with Daiichi Sankyo and research and development expenses reimbursable from Biogen Idec pursuant to our agreement with Biogen Idec.

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Cash used in operating activities was $27.6 million for the six months ended June 30, 2012 reflecting net income of $36.6 million, which was increased by non-cash charges of $1.4 million for stock-based compensation, $0.7 million for depreciation and amortization and $0.6 million for amortization of premium on investments and decreased by $0.1 million for revaluation of preferred stock warrant liabilities. Cash used in operating activities also reflected a decrease in net operating assets of $66.7 million primarily due to a decrease in deferred revenue of $68.0 million following the termination of our agreement with Novartis effective July 1, 2012, the decrease in receivables from collaborations of $1.6 million due to payments related to research and development expenses reimbursable from Biogen Idec pursuant to our agreements with Biogen Idec, a decrease in accrued compensation and employee benefits of $1.1 million due to 2011 bonuses that were paid in the six months ended June 30, 2012, and a decrease in prepaid expenses and other current assets of $2.2 million primarily for clinical study costs expensed which were paid in advance to our CRO and prepaid clinical study insurance. Also reflected in cash used in operating activities is an increase in accounts payable and accrued and other liabilities of $6.5 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 $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 initial public offering. 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 operating activities was $29.6 million for the year ended December 31, 2010 reflecting a net loss of $20.3 million decreased by non-cash charges of $0.7 million for amortization of premium

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on investments, $0.8 million for depreciation and amortization and $1.9 million for stock-based compensation. Cash used in operating activities also reflected a decrease in net operating assets of $13.0 million due to the amortization of deferred revenue of $14.1 million related to initial upfront payments from our collaboration partners, decreases in accounts payable of $1.8 million primarily related to the $1.0 million purchase of laboratory equipment which was paid in 2010, accrued compensation and employee benefits of $0.4 million due to a higher bonus payout in 2010 related to 2009 performance, and accrued and other liabilities of $1.4 million primarily due to lower accrued clinical study costs. These decreases were partially offset by an increase in accrued income taxes of $2.5 million related to an income tax provision for the year ended December 31, 2010 due to the recognition of collaboration revenue deferred in previous years for state income tax purposes and an increase in other long-term liabilities by $2.2 million primarily due to increased deferred rent related to our increased leased space as we expanded our operations.

Cash used in investing activities

Cash used in investing activities of $40.4 million for the six months ended June 30, 2013 was primarily related to purchases of investments of $98.6 million and capital equipment purchases of $0.3 million, partially offset by proceeds from sales of investments of $4.6 million and proceeds from maturities of investments of $53.9 million.

Cash used in investing activities of $83.0 million for the six months ended June 30, 2012 was primarily related to capital equipment purchases of $0.4 million and purchases of investments of $117.1 million, partially offset by proceeds from sales of investments of $20.2 million and proceeds from maturities of investments of $14.3 million.

Cash used in investing activities of $67.8 million for 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 used in investing activities of $4.9 million for the year ended December 31, 2010 was primarily related to purchases of investments of $94.9 million and capital equipment purchases of $2.4 million was partially offset by proceeds from sales of investments of $1.0 million and proceeds from maturities of investments of $91.4 million.

Cash provided by financing activities

Cash provided by financing activities of $128.4 million for the six months ended June 30, 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 $2.9 million.

Cash provided by financing activities of $0.3 million for the six months ended June 30, 2012 and for the year ended December 31, 2012, was related to proceeds from the exercise of stock options.

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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.

Cash used in financing activities of $6.5 million for the year ended December 31, 2010 was primarily due to repayment of long-term debt of $6.7 million, partially offset by proceeds from the exercise of stock options of $0.2 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

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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 June 30, 2013 were as follows:

	Payments due by period				
	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years	Total
	(in thousands)				
Contractual obligations:					
Purchase commitments	$ 496	$	$	$	$ 496
Operating lease obligations	1,636	1,255			2,891
Total contractual obligations	$ 2,132	$ 1,255	$	$	$ 3,387

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 prospectus 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.

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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.

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 June 30, 2013, we had cash, cash equivalents and investments of $235.2 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 6.8 million to our European vendors during the six months ended June 30, 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 six months ended June 30, 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 $1.0 million or decreased unrealized gain by $1.4 million, respectively, at June 30, 2013. We hedge our foreign currency exposures but we have not used derivative financial instruments for speculation or trading purposes.

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Business

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, which has successfully completed the first of a series of Phase 2 proof-of-concept studies, 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, 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 PRT2070 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.

Members of our management team, working together or individually, have played central roles at prior companies, including COR Therapeutics, Inc., Millennium Pharmaceuticals, Inc. and Johnson & Johnson, in discovering, developing and commercializing a number of successful therapeutics in the area of thrombosis, including Integrilin and Xarelto. Our approach has been to identify key enzymes and cellular signaling pathways and to apply our translational expertise to discover compounds with unique properties that have potential for clear clinical and pharmacoeconomic value. To increase the likelihood that our programs will succeed, we enhance our internal discovery and development expertise by collaborating with academic leaders at major universities, including Cornell University, Duke University, Harvard University, King s College, McMaster University, Stanford University and The University of Texas MD Anderson Cancer Center, and by proactively engaging regulatory authorities early in the development process.

We have full worldwide commercial rights to Betrixaban and Andexanet alfa, and to PRT2070 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 for up to 35 days. Acute medically ill patients are those who are hospitalized for serious non-surgical conditions, such as heart

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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 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 2012 were in excess of $4.8 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.

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. 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. 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 will provide us with an upfront payment and 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 recently completed the first 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

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blood samples taken from the subjects in this first study demonstrates that Andexanet alfa produces a rapid, sustained and dose-related reversal of anticoagulant activity of the Factor Xa inhibitor apixaban. 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. Based on our discussions with the FDA, we believe that the FDA supports our pursuit of an expedited approval process. Subject to further discussions with and approval by the FDA on the protocol, we plan to initiate a Phase 3 registration study for Andexanet alfa in the first half of 2014 followed by a Phase 4 confirmatory study. We are currently conducting two additional Phase 2 proof-of-concept studies evaluating Andexanet alfa for reversal of the anticoagulant activity of the Factor Xa inhibitors rivaroxaban and enoxaparin. We expect results from the study involving rivaroxaban in the second half of 2013 and results from the study involving enoxaparin in the first half of 2014. We plan to initiate similar Phase 2 proof-of-concept studies evaluating the reversal of edoxaban and Betrixaban in the first half of 2014. Additionally, we plan to request a formal scientific advice meeting with the European Medicines Authority in 2014 to discuss the process for approval in Europe.

We have entered into a collaboration agreement with Bristol-Myers Squibb Company, or BMS, and Pfizer Inc., or Pfizer, a collaboration agreement 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 these Phase 2 studies, but we retain full commercial rights with respect to Andexanet alfa.

PRT2070 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 PRT2070 for treatment of certain B-cell hematologic cancers, with a particular focus on patients who have NFkB activating mutations or acquired mutations to other novel B-cell targeted therapies that cause treatment failure or disease relapse. PRT2070 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 PRT2070 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 non-systemic indications, including dermatologic disorders.

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.

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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. 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 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 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 recently completed the first of a series of Phase 2 proof-of-concept studies of Andexanet alfa in healthy volunteers receiving anticoagulation therapy with apixaban. 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. Based on our discussions with the FDA, we believe that the FDA supports our pursuit of an expedited approval process. Subject to further discussions with and approval by the FDA on the protocol, we plan to initiate a Phase 3 registration study for Andexanet alfa in the first half of 2014 followed by a Phase 4 confirmatory study. Additionally, we plan to request a formal scientific advice meeting with the European Medicines Authority in 2014 to discuss 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 PRT2070 for treatment of hematologic cancers. Our research into cellular signaling pathways has resulted in development of PRT2070, 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, including the proceeds from this offering, 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.

Development pipeline				
Product	**Description**	**Stage**	**Indication**	**Worldwide commercial rights**
Betrixaban	Oral Factor Xa inhibitor	Phase 3	Extended duration VTE prophylaxis in acute medically ill patients for up to 35 days	Portola
Andexanet alfa	Antidote for Factor Xa inhibitors	Phase 2	Reversal of Factor Xa inhibitor anticoagulation	Portola
PRT2070	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 Aciex
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 for up to 35 days, both in the hospital and after discharge. 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 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. 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 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.

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The following diagram illustrates various forms of thrombosis:

Both normal blood clotting and thrombosis are driven by a similar activation of the body s coagulation system. That system integrates biochemical signals from two distinct cascades known as the extrinsic and intrinsic pathways. Through a series of protein interactions, both of these pathways lead to the activation of Factor Xa. Factor Xa forms an active complex with other clotting factors, leading to generation of thrombin. Thrombin then converts fibrinogen into fibrin, the basic building block of a clot. Other elements, such as platelets and various blood factors, may also be recruited to stabilize or amplify the clotting response depending on the type and severity of the underlying cause. Current research indicates that venous thrombosis does not significantly involve platelets whereas arterial thrombosis has a large platelet component.

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The following diagram depicts elements of the coagulation cascade:

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.

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

Population	Number of G7 patients (in millions)
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.

All anticoagulant therapies used in the prophylaxis or treatment of thrombosis carry a risk of uncontrolled bleeding resulting from excessive inhibition of the coagulation cascade. Uncontrolled bleeding can occur in anticoagulated patients spontaneously in multiple forms, including intracranial bleeding, intestinal bleeding and bleeding as a result of trauma or during emergency surgery. As a result of this risk, the use of any particular antithrombotic medicine is typically limited to those patient populations where the clinical benefit achieved by the therapy has been clearly shown to outweigh the risk of uncontrolled bleeding.

Established and novel anticoagulants

A number of well-established anticoagulants are used for the prophylaxis and treatment of thrombosis, including heparin, low molecular weight heparins, fondaparinux and warfarin. While all of these therapies generally work through inhibiting the coagulation process, each drug has specific properties that have led to approval and use in specific indications or target populations. For example, prior to the recent approval of novel oral anticoagulants, warfarin was the only oral anticoagulant for long-term use in the outpatient setting for patients at high chronic risk of VTE, with over 33.9 million prescriptions for various forms of warfarin written in the United States in 2011. Warfarin has significant limitations, including the need to gradually adjust, or titrate, the dose a specific patient receives over multiple weeks, a slow therapeutic onset and offset (two to five days), the need to monitor patients with a blood test (typically monthly) and a high propensity for interactions with diet or other drugs leading to increased bleeding risk from supratherapeutic drug levels or increased VTE risk from subtherapeutic drug levels. Importantly, warfarin is neither approved nor routinely used to prevent blood clots in the population of acute medically ill patients.

In the hospital, where acute medically ill patients are typically treated for VTE prophylaxis, intravenous and subcutaneous heparin and injectable low molecular weight heparins, such as enoxaparin, are the most widely used anticoagulants. Heparin is typically prescribed to patients with an active clot or undergoing surgery, but due to its short half-life (less than one hour) and intravenous administration it is generally used for only a few hours at a time. In addition, measurement of a patient s activated partial thromboplastin time is needed to determine appropriate dosing. Patients receiving heparin must also be monitored for signs of thrombocytopenia, a serious debilitating decrease of platelet levels in the blood that can result in increased risk of thrombosis.

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Low molecular weight heparins are chemically modified heparins with extended half-lives (four to five hours) that can be administered subcutaneously, typically once or twice daily by a physician or nurse. In hospitals, low molecular weight heparins are used to prevent blood clots in a number of different patient populations, including acute medically ill patients, patients with acute coronary syndrome, patients with a DVT or pulmonary embolism and patients who have just undergone major surgery. Low molecular weight heparins are rarely prescribed for use outside of the hospital setting either because they are not approved for extended use or due to the difficulty of training patients to self-inject. Enoxaparin is cleared extensively through the kidneys, increasing the risk of bleeding in patients with moderate and severe kidney disease. In addition, low molecular weight heparins carry a risk of inducing thrombocytopenia. Despite these limitations, heparins and low molecular weight heparins have been demonstrated to be generally safe and effective across a broad range of patient populations. Therefore, the market for low molecular weight heparins is substantial.

According to IMS, worldwide sales of enoxaparin for the 12 months through June 2012 were in excess of $4.8 billion. We believe that use of enoxaparin in acute medically ill patients accounted for at least $2 billion of these sales in the G7 markets. Enoxaparin was the second highest drug expenditure in non-federal U.S. hospitals in 2010, according to a paper published in the American Journal of Health System Pharmacy in 2011. Overall, we estimate that approximately 55% of acute medically ill patients in the G7 countries currently receive some form of VTE prophylaxis.

Recently, a number of new oral anticoagulants have been developed and commercialized to replace enoxaparin or warfarin in specific indications and settings. These agents are designed to give consistent and targeted levels of anticoagulation without the need for ongoing monitoring and are based on a detailed understanding of the biochemical mechanism of action of heparin and enoxaparin. Heparin and enoxaparin both work by indirectly inhibiting Factor Xa and thrombin, with enoxaparin having greater anti-Factor Xa activity. Based on these observations, novel orally available anticoagulants have been developed that directly target either thrombin, in the case of dabigatran, or Factor Xa, in the case of rivaroxaban, apixaban and edoxaban.

These novel agents have been extensively studied in multiple Phase 3 clinical trials, which have enrolled more than 130,000 patients worldwide. These trials, which were sponsored by the owners of the novel agents (Bayer, Janssen, BMS, Pfizer, Daiichi Sankyo and Boehringer Ingelheim) have demonstrated superior or equivalent efficacy compared to enoxaparin and/or warfarin with equal or better bleeding profiles in multiple populations, including atrial fibrillation, acute coronary syndrome, treatment of VTE and VTE prophylaxis in major orthopedic surgery. Some of these agents have received regulatory approval in the United States and Europe for prevention of stroke in atrial fibrillation patients, treatment and secondary prophylaxis in patients with a DVT or pulmonary embolism and VTE prophylaxis in orthopedic surgery patients. Additional regulatory decisions relating to their use in patients with acute coronary syndrome are pending. We estimate that the global market for all anticoagulants will reach $15.5 billion by 2018 and that the global market for all Factor Xa and direct thrombin inhibitors will grow to $10 billion to $14 billion by 2020.

While both thrombin and Factor Xa are logical targets for an anticoagulant, an analysis of the coagulation cascade suggests a number of reasons that Factor Xa may be a better target. First, Factor Xa is the first step in the final common cascade for the intrinsic and extrinsic pathways and is effectively a point of convergence in the coagulation process. Furthermore, activation of a single Factor Xa molecule generates 1,000 thrombin molecules and, unlike thrombin, Factor Xa has limited biological activity outside of the coagulation cascade, potentially limiting off-target side effects as

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compared to direct thrombin inhibitors. This hypothesis has been borne out in clinical trials that have indicated that direct Factor Xa inhibitors may be safer and more effective than direct thrombin inhibitors, such as dabigatran. For example, the recent approval of apixaban in Europe for stroke prevention in atrial fibrillation includes differentiated label claims, such as mortality benefit as compared to warfarin, not included in dabigatran s product label. In addition, administration of direct Factor Xa inhibitors in large clinical trials has not resulted in increased myocardial infarction risk, which was observed with dabigatran in similar patient populations.

Although the novel oral anticoagulants have been successfully developed for a number of thrombotic indications, none has been approved or, to our knowledge, is currently in clinical development for prophylactic use in the acute medically ill patient population, creating an opportunity for Betrixaban to be first to market for this important patient population.

Established and novel anticoagulants

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 the novel oral Factor Xa inhibitors. 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

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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

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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.

Betrixaban clinical development

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 and DEC)	2	570	Safety/efficacy in atrial fibrillation patients; safety compared to warfarin	Prophylaxis and bleeding risk comparable to warfarin
Phase 2 (EXPERT)	1	171	Safety/efficacy in knee replacement compared to enoxaparin	Prophylaxis and bleeding risk comparable to enoxaparin

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Clinical experience of Factor Xa inhibitors in acute medically ill patients

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 and for a study population that significantly increase the probability that it will demonstrate both safety and efficacy in VTE prophylaxis in acute medically ill patients both in the hospital and after discharge.

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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, we are more likely to demonstrate net clinical benefit from extended duration VTE prophylaxis.

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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 for up to 35 days in acute medically ill patients with restricted mobility and certain 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 the study to be completed by mid-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 2014 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.

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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 $33.06 compared to rivaroxaban at $8.84 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 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.

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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 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.

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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

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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.

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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. Based on our discussions with the FDA, we believe that the FDA supports our pursuit of an expedited approval process. Subject to further discussions with and approval by the FDA on the protocol, we plan to initiate a Phase 3 registration study for Andexanet alfa in the first half of 2014 followed by a Phase 4 confirmatory study. Additionally, we plan to request a formal scientific advice meeting with the European Medicines Authority in 2014 to discuss the process for 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 a Phase 2 study evaluating subjects taking rivaroxaban is ongoing.

Subjects in the first study 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.

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The following diagram depicts the data from our first Phase 2 study of Andexanet alfa:

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.

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. Furthermore, because these subjects were receiving apixaban, the degree of elevation was substantially lower than in the Phase 1 subjects. 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. In addition, none of the subjects receiving Andexanet alfa generated detectable levels of antibodies against Andexanet alfa. 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.

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

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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. Interim 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.

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 initial portion of the Phase 2 study, there were no serious adverse events. The safety follow-up for the extension of the Phase 2 study is ongoing, but there have been no serious adverse events reported to date. 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 the pursuit of an expedited approval process because of the significant unmet clinical need for a reversal

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agent for Factor Xa inhibitors. For example, under the FDA s Accelerated Approval process, therapies targeting a significant unmet clinical need may be approved based upon their showing adequate safety as well as efficacy against a surrogate endpoint in a clinical trial. Utilizing an expedited approval process would significantly decrease the time and expense associated with the development program for Andexanet alfa. If permitted by the FDA, we believe that under an expedited approval process, our development program for Andexanet alfa might consist of a 100 to 200 subject Phase 3 registration study with a design similar to our proof-of-concept studies together with an open label study evaluating the safety and activity of Andexanet alfa in patients treated with Factor Xa inhibitors who are experiencing severe bleeding or undergoing emergency surgery. At the conclusion of the registration study, we would plan to submit that data along with available interim data from the open label study as part of a Biologics License Application, or BLA, for Accelerated Approval. If the registration study is successful, we believe this 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 registration study 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 expedited approval process 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 two additional Phase 2 proof-of-concept studies evaluating Andexanet alfa for reversal of the anticoagulant activity of the Factor Xa inhibitors rivaroxaban and enoxaparin. We expect results from the study involving rivaroxaban in the second half of 2013 and results from the study involving enoxaparin in the first half of 2014. We plan to initiate similar Phase 2 proof-of-concept studies evaluating the reversal of edoxaban and Betrixaban in the first half of 2014. Additionally, we plan to request a formal scientific advice meeting with the European Medicines Authority in 2014 to discuss the process for 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. This agreement does not grant BMS or Pfizer any other rights with respect to the development or commercialization of Andexanet alfa.

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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 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. This agreement does not grant Bayer or Janssen any other rights with respect to the development or commercialization of Andexanet alfa.

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. Should Daiichi Sankyo terminate the agreement prior to the first patient dosing in the clinical trial, it is entitled to a refund of $3.0 million. The total consideration under this agreement of $6.0 million was received in July 2013, although only the non-contingent consideration of $3.0 million was recorded as receivables from collaborations at June 30, 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. The total non-contingent consideration under this agreement of $3.0 million is being recognized as revenue ratably over the estimated non-contingent performance period through May 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 May 2014 and conclude in October 2014.

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 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.

PRT2070 dual Syk/JAK inhibitor

The lead compound in our kinase development effort, PRT2070, is a potent inhibitor of both Syk and JAK. We believe that PRT2070 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 PRT2070 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 Aciex to co-develop and co-commercialize formulations of PRT2070 and certain related compounds for nonsystemic indications, such as the treatment and

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prevention of ophthalmological diseases by topical administration and allergic rhinitis by intranasal administration. We retain rights to 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.

PRT2070 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 PRT2070, was active in a broad panel of B-cell lymphoma cell lines. PRT2070 was more effective than Syk-specific inhibition in these cell lines, suggesting that PRT2070 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, PRT2070 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 PRT2070 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 PRT2070 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 PRT2070 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 PRT2070 is well-

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tolerated and activity is seen in the escalation phase, we would expect to expand the study and evaluate the activity of PRT2070 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 PRT2070 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

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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 pharmacoeconmic 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 making. 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.

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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.

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., or Merck, each as described below, 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. Pursuant to the amendment, we also terminated a 2004 System Development Agreement between us and Millennium.

Merck agreement

In July 2009, we entered into an exclusive worldwide license and collaboration agreement with Merck to develop and commercialize Betrixaban for a different indication than the one we are currently pursuing. Pursuant to our agreement with Merck, Merck made an upfront cash payment to us of $50.0 million. Our agreement with Merck also provided for additional payments to us of up to $420.0 million based on the achievement of certain development, regulatory and commercialization milestones. In March 2011, Merck exercised its right to terminate the agreement for convenience, and we and Merck

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agreed to a plan for Merck to return all rights to Betrixaban to us and to terminate the agreement, effective September 30, 2011. As of the time of termination, no milestones had been achieved and no royalties had been triggered under our agreement with Merck.

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 will provide us with an upfront and non-refundable payment of $700,000 and 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 agreement

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. This agreement does not grant BMS or Pfizer any other rights with respect to the development or commercialization of Andexanet alfa.

Bayer and Janssen agreement

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. This agreement does not grant Bayer or Janssen any other rights with respect to the development or commercialization of Andexanet alfa.

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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,

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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.

PRT2070

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 PRT2070 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.

Elinogrel

Novartis agreement

In February 2009, we entered into an exclusive worldwide license agreement with Novartis to develop and commercialize Elinogrel, which was amended in December 2010. Pursuant to our agreement with Novartis, Novartis made an upfront cash payment to us of $75.0 million. The agreement with Novartis also provided for additional payments to us of up to $505.0 million based on the achievement of certain development, regulatory and commercialization milestones. In April 2012, Novartis exercised its right to terminate the agreement, and we and Novartis agreed to a plan for Novartis to return all rights to Elinogrel to us and to terminate the 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.

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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 a New Drug Application, or 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 manufacturing of Andexanet alfa to Lonza and are making process improvements in order to increase scale and efficiency. We plan to implement proposed changes with Lonza to initiate BLA-enabling studies with a manufacturing process that will allow us to launch Andexanet alfa pursuant to an expedited approval. After recent discussions with the FDA, we determined that the additional process changes needed to further improve cost of goods will be incorporated into the commercial production later in the development of Andexanet alfa or as a supplemental BLA, if supporting studies are required.

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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. 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.

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PRT2070

In the market for the treatment of CLL and NHL, PRT2070, 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 September 30, 2013, we owned 29 issued U.S. patents, 35 U.S. patent applications and 91 issued patents and 182 patent applications in other jurisdictions. We also co-owned 12 additional patents and patent applications. In addition, as of September 30, 2013, we have licensed 160 issued patents and 72 patent applications from third parties, mostly on an exclusive basis. The patent portfolios for our four leading product candidates as of September 30, 2013 are summarized below:

Betrixaban

Our Betrixaban patent portfolio includes 14 issued U.S. patents and nine 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 issued U.S. 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

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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 12 U.S. patent applications covering the composition of and methods of making and using Andexanet alfa or its analogs.

The issued U.S. patents are due to expire between September 2028 and June 2030. A related international patent application has issued in New Zealand, another related international patent application has issued in New Zealand and Mexico 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.

PRT2070

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 PRT2070 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 three 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, PRT2070 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 using our proprietary process and to our specified

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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 tests including some that must be conducted in accordance with Good Laboratory Practices;
- submission of an investigational new drug application, or IND, which must become effective before 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; and
- FDA approval of an NDA for a drug or a BLA for a biologic to permit commercial marketing for particular indications for use.

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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 safety concerns or questions about the conduct of the clinical trial by imposing 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 a data safety monitoring board, 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.

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 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.

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, must 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 demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

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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 clinical insight 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 and preserve the product s identity, strength, quality and purity. 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 and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Once the NDA submission has been accepted for filing, the FDA typically takes one year 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 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. 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 for review on a rolling basis sections of the NDA before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. A fast track designated drug candidate may also qualify for priority review, under which the FDA reviews the NDA in a total of eight months rather than 12 months time.

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.

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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

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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 August 31, 2013, we had 58 full-time employees, 15 of whom hold Ph.D. degrees and three of whom hold M.D. degrees. Of the full-time employees, 38 employees are engaged in research and development and 20 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. 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.

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Management

Executive officers and directors

The following table sets forth information regarding our executive officers and directors as of August 31, 2013:

Name	Age	Position
William Lis	49	Chief Executive Officer and Director
John T. Curnutte, M.D., Ph.D.	61	Executive Vice President, Research and Development
Mardi C. Dier	49	Senior Vice President and Chief Financial Officer
Hollings C. Renton[1][3]	66	Co-chairman of our board of directors
Charles J. Homcy, M.D.[3]	65	Co-chairman of our board of directors
Jean-Jacques Bienaimé[1]	60	Director
Jeffrey W. Bird, M.D., Ph.D.[2]	53	Director
Robert M. Califf, M.D.[3]	61	Director
Nicholas G. Galakatos, Ph.D.[1][2]	55	Director
James N. Topper, M.D., Ph.D.	51	Director
H. Ward Wolff[2]	65	Director

(1) Member of the compensation committee
(2) Member of the audit committee
(3) Member of the nominating and corporate governance committee

William Lis. William Lis has served as our Chief Executive Officer and a member of our board of directors since April 2010. Mr. Lis served as our Chief Operating Officer from November 2009 to April 2010, as our Vice President of Business and Commercial Operations from May 2008 to October 2009 and as our Senior Director of Business Development from May 2005 to August 2005. Prior to Portola, Mr. Lis held various management positions at Scios Inc., a biotechnology company and a subsidiary of Johnson & Johnson, including as Vice President Business and Commercial Operations from November 2007 to April 2008, as Vice President of Business and New Product Development from August 2005 to November 2007 and as Director of Cardiovascular Marketing and New Products from January 2004 to May 2005. From November 2003 to December 2003, Mr. Lis served as a consultant to Biosite Incorporated, a medical diagnostics company, and Millennium Pharmaceuticals, Inc., a biopharmaceutical company, or Millennium. From October 1999 to February 2002, Mr. Lis held various positions, including Product Director, at COR Therapeutics, Inc., a biopharmaceutical company, or COR. Following the acquisition of COR by Millennium in 2002, he held various positions, including Director, Marketing and New Product Development from February 2002 to November 2003. Mr. Lis holds a B.S. in Business Management and Finance from the University of Maryland, College Park. Because of Mr. Lis extensive knowledge of our company, the pharmaceutical industry and our competitors, we believe he is able to make valuable contributions to our board of directors.

John T. Curnutte, M.D., Ph.D. John Curnutte has served as our Executive Vice President of Research and Development since February 2011. From April 2010 to January 2011, Dr. Curnutte served as an independent consultant. From May 2008 to March 2010, Dr. Curnutte served as the Chief Executive Officer of 3-V Biosciences, Inc., a biotechnology company. From September 2000 to May 2008, he served as President of Schering-Plough Biopharma, a biopharmaceutical subsidiary of Schering-Plough Corporation, and Vice President of Discovery Research at Schering Plough Research Institute, a

pharmaceutical and healthcare company. From August 1993 to September 2000, he held various senior management positions at Genentech, Inc., a biotechnology company. Dr. Curnutte is currently an adjunct clinical professor of pediatrics at the Stanford University School of Medicine and a member of the medical staff. Dr. Curnutte holds a B.S. in Biochemistry and Molecular Biology from Harvard University and an M.D. and a Ph.D. in Biological Chemistry from Harvard Medical School.

Mardi C. Dier. Mardi Dier has served as our Senior Vice President and Chief Financial Officer since August 2006. From June 2003 to July 2006, Ms. Dier served as Vice President of Investor Relations at Chiron Corporation, a biopharmaceutical company. From 1994 to 2001, Ms. Dier served as a Director, Investment Banking at Prudential Securities, Inc., a securities firm. Ms. Dier previously was a supervising senior accountant at the audit department of KPMG LLP, an accounting firm, from 1986 to 1990. Ms. Dier holds a B.S. in Biology from Stanford University and an M.B.A. from the Anderson Graduate School of Management at the University of California, Los Angeles.

Hollings C. Renton. Hollings Renton has served as a member and the co-chairman of our board of directors since March 2010. Mr. Renton retired as Chairman of the board of directors at Onyx Pharmaceuticals, Inc., a biopharmaceutical and biotherapeutics company, in March 2008, where he also served as the President and Chief Executive Officer from 1993 and as a director from 1992. Mr. Renton currently serves as a member of the boards of directors of Affymax, Inc., Rigel Pharmaceuticals and Cepheid Corporation. Mr. Renton holds an M.B.A. from the University of Michigan and a B.S. in Mathematics from Colorado State University. Because of Mr. Renton s extensive experience building successful biotechnology companies and commercializing drug products, we believe he is able to bring valuable insights to our board of directors.

Charles J. Homcy, M.D. Charles Homcy has served as a member of our board of directors since September 2003, as co-chairman of our board of directors since March 2010 and as chairman of our board of directors from September 2003 to March 2010. Since May 2010, Dr. Homcy has served as a Venture Partner of Third Rock Ventures, a venture capital firm. Dr. Homcy has served as the acting chief executive officer of MyoKardia, Inc. since June 2012. Dr. Homcy is a co-founder of Portola and served as President and Chief Executive Officer of Portola from September 2003 to April 2010 and was employed as an adviser to us from May 2010 to February 2012. He served as President, Research and Development at Millennium from February 2002 to January 2003 and the senior advisor of Research and Development at Millennium from January 2003 to November 2003. From May 1995 to March 2002, he served as Executive Vice President of Research and Development of COR. Since 1997, Dr. Homcy has served as Clinical Professor of Medicine, University of California at San Francisco Medical School and as an attending physician at the San Francisco Veteran s Administration Hospital. Dr. Homcy holds an A.B. in Biology and an M.D. from Johns Hopkins University. Because of Dr. Homcy s executive experience in the life sciences industry, we believe he is able to make valuable contributions to our board of directors.

Jean-Jacques Bienaimé. Jean-Jacques Bienaimé has served as a member of our board of directors since September 2010. Since May 2005, Mr. Bienaimé has served as the Chief Executive Officer and a member of the board of directors of BioMarin Pharmaceutical Inc., a biopharmaceutical company. From August 2005 to August 2010, Mr. Bienaimé served on the board of directors of Ensemble Discovery Corporation. From November 2002 to April 2005, Mr. Bienaimé served as the Chairman, Chief Executive Officer and President of Genencor International, a biotechnology company acquired by Danisco A/S. From June 1998 to October 2002, Mr. Bienaimé served as the Chief Executive Officer and President of SangStat Medical, a biotechnology company. Mr. Bienaimé also currently serves as a

member of the board of directors of InterMune, Inc. Mr. Bienaimé holds a B.S. in Economics from the Ecole Supérieure de Commerce de Paris and an M.B.A. from the Wharton School at the University of Pennsylvania. Because of Mr. Bienaimé s expertise in business management in the biotechnology industry, we believe he is able to contribute valuable input on our strategic and business affairs to our board of directors.

Jeffrey W. Bird, M.D., Ph.D. Jeffrey Bird has served as a member of our board of directors since November 2003. Since July 2003, Dr. Bird has been a managing director of Sutter Hill Ventures, a venture capital firm. Dr. Bird also currently serves as a member of the board of directors of Threshold Pharmaceuticals, Inc. and Horizon Pharma, Inc. Dr. Bird holds a B.S. in Biological Sciences from Stanford University and a Ph.D. in Cancer Biology and an M.D. from Stanford Medical School. Because of Dr. Bird s experience investing in life science companies and serving as an executive at biopharmaceutical companies, we believe he is able to bring important insights to our board of directors.

Robert M. Califf, M.D. Robert Califf has served as a member of our board of directors since July 2012. He has held various academic positions at Duke University Medical Center, including Vice Chancellor for Clinical and Translational Research since July 2012, Professor of Medicine since 1995 and Vice Chancellor for Clinical Research from July 2006 to June 2011. Dr. Califf was the founding director of the Duke Clinical Research Institute. He also currently serves as co-chair of the Clinical Trials Transformation Initiative, a partnership focused on improving the clinical trials system. Dr. Califf holds a B.S. in Psychology and an M.D. from Duke University. Because of Dr. Califf s expertise in cardiology, clinical research, translational medicine and regulatory affairs, we believe he is able to make valuable contributions to our board of directors.

Nicholas G. Galakatos, Ph.D. Nicholas Galakatos has served as a member of our board of directors and as a member of our nominating and corporate governance committee since November 2003. Dr. Galakatos has been a co-founder and Managing Director of Clarus Ventures, a venture capital firm, since 2005. Dr. Galakatos has also been a General Partner of MPM BioVentures II GP, LP and BioVentures III GP, LP, both venture funds, since April 2000 and December 2002, respectively. From 1997 to 2000, he served as Vice President, New Business, and a member of the management team at Millennium. He was a founder of Millennium Predictive Medicine and TransForm Pharmaceuticals, where he also was the Chairman and founding Chief Executive Officer. Dr. Galakatos has served as the lead director at Affymax Inc. and a director of Cornerstone Therapeutics, Inc. (formerly Critical Therapeutics Inc.) and Aveo Pharmaceuticals, Inc. Dr. Galakatos holds a B.A. in Chemistry from Reed College and a Ph.D. in Organic Chemistry from the Massachusetts Institute of Technology and performed postdoctoral studies in molecular biology at Harvard Medical School. Because of Dr. Galakatos extensive experience in venture capital investments, we believe he is able to bring important insights to our board of directors.

James N. Topper, M.D., Ph.D. James Topper has served as a member of our board of directors since March 2011. Since August 2003, he has been a partner with Frazier Healthcare, a venture capital firm, holding the position of General Partner since August 2005. Prior to joining Frazier Healthcare, Dr. Topper served as head of the Cardiovascular Research and Development Division of Millennium from February 2002 to August 2003. Prior to the merger of COR and Millennium in 2002, Dr. Topper served as the Vice President of Biology at COR from August 1999 to February 2002. He holds an appointment as a Clinical Assistant Professor of Medicine at Stanford University and as a Cardiology Consultant to the Palo Alto Veterans Administration Hospital. Dr. Topper also currently serves as a

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member of the board of directors of Amicus Therapeutics, Inc. Dr. Topper holds a B.S. in Biology from the University of Michigan and an M.D. and a Ph.D. in Biophysics from Stanford University School of Medicine. Because of Dr. Topper s management experience in our industry and knowledge of medical and scientific matters, we believe he is able to provide important industry insights to our board of directors.

H. Ward Wolff. Ward Wolff has served as a member of our board of directors since November 2007. Since December 2007, Mr. Wolff has served as Executive Vice President and Chief Financial Officer of Sangamo BioSciences, Inc., a biopharmaceutical company. Mr. Wolff served as the Senior Vice President, Finance and Chief Financial Officer of Nuvelo, Inc., a biopharmaceutical company, from July 2006 until its restructuring in August 2007. He was Senior Vice President, Finance and Chief Financial Officer of Abgenix, Inc., a biopharmaceutical company, from September 2004 until it merged with Amgen Inc. in April 2006. Prior to joining Abgenix, Inc., Mr. Wolff held financial management positions in both public and private emerging growth companies, including serving as Senior Vice President and Chief Financial Officer of DoubleTwist, Inc., a life sciences company. Mr. Wolff holds a B.A. in Economics from the University of California at Berkeley and an M.B.A. from Harvard Business School. Because of Mr. Wolff s management experience in several public companies, we believe he is able to bring financial expertise to our board of directors.

Each of our executive officers serves at the discretion of our board of directors and holds office until his or her successor is duly elected and qualified or until his or her earlier resignation or removal. There are no family relationships among any of our directors or executive officers.

Board composition

Our business and affairs are managed under the direction of our board of directors, which currently consists of nine members. The members of our board of directors were elected in compliance with the provisions of our amended and restated certificate of incorporation.

In accordance with our amended and restated certificate of incorporation, our board of directors is divided into three classes with staggered three-year terms. At each annual general meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. Our directors are divided among the three classes as follows:

- The Class I directors are Dr. Bird, Dr. Topper and Mr. Wolff, and their terms will expire at our annual meeting of stockholders to be held in 2014;
- The Class II directors are Mr. Bienaimé, Dr. Galakatos and Dr. Homcy, and their terms will expire at our annual meeting of stockholders to be held in 2015; and
- The Class III directors are Mr. Renton, Dr. Califf and Mr. Lis, and their terms will expire at our annual meeting of stockholders to be held in 2016.

We expect that additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change in control.

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Director independence

Under the listing requirements and rules of The NASDAQ Global Market, independent directors must comprise a majority of a listed company s board of directors within twelve months of our initial public offering.

Our board of directors has undertaken a review of its composition, the composition of its committees, and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment, and affiliations, including family relationships, our board of directors has determined that all of our board of directors except Dr. Homcy and Mr. Lis do not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is independent as that term is defined under the applicable rules and regulations of the Securities and Exchange Commission, or the SEC, and the listing requirements and rules of The NASDAQ Global Market. In making this determination, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director.

Board committees

Our board of directors has the authority to appoint committees to perform certain management and administration functions. Our board of directors has an audit committee, a compensation committee and a nominating and corporate governance committee. The composition and responsibilities of each committee are described below. Members will serve on these committees until their resignation or until otherwise determined by the board of directors. The charters for each of these committees are available on our website at *www.portola.com*.

Audit committee

Our audit committee consists of Dr. Bird, Dr. Galakatos and Mr. Wolff, each of whom satisfies the independence requirements under The NASDAQ Global Market listing standards and Rule 10A-3(b)(1) of the Exchange Act. The chairperson of our audit committee is Mr. Wolff, whom our board of directors has determined to be an audit committee financial expert within the meaning of SEC regulations. Each member of our audit committee can read and understand fundamental financial statements in accordance with audit committee requirements. In arriving at this determination, the board has examined each audit committee member s scope of experience and the nature of their employment in the corporate finance sector.

Our audit committee oversees our corporate accounting and financial reporting process. The audit committee has the following responsibilities, among others things, as set forth in the audit committee charter:

- reviewing disclosures by prospective registered public accounting firm of relationships between such firm or its members and the Company or our personnel in financial oversight roles to determine independence of prospective registered public accounting firm;

- reviewing and pre-approving the engagement of our independent registered public accounting firm to perform audit services and any permissible non-audit services;

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evaluating the performance and assessing qualifications of our independent registered public accounting firm and deciding whether to retain their services;

monitoring the rotation of partners of our independent registered public accounting firm on our engagement team as required by law;

reviewing disclosures by our independent registered public accounting firm of relationships between such firm or its members and the Company or our personnel in financial oversight roles to affirm independence of our independent registered public accounting firm;

considering and adopting clear policies regarding pre-approval by our audit committee of our employment of individuals employed or formerly employed by our independent registered accounting firm and engaged on our account;

reviewing our annual and quarterly financial statements and reports and discussing the statements and reports with our independent registered public accounting firm and management, including a review of disclosures under the section of this prospectus entitled Management s discussion and analysis of financial condition and results of operations;

preparing the audit committee report required by the SEC to be included in our annual proxy statement;

reviewing, with our independent registered public accounting firm and management, significant issues that may arise regarding accounting principles and financial statement presentation, as well as matters concerning the scope, adequacy and effectiveness of our financial controls;

reviewing and discussing with management and our independent registered accounting firm, our guidelines and policies with respect to risk assessment and risk management, any management or internal control letters, and any conflicts or disagreements regarding financial reporting, accounting practices of policies or other matters significant to our financial statements or the report of our independent registered accounting firm;

reviewing and establishing appropriate additional insurance coverage for our directors and executive officers;

considering and reviewing with our management, our independent registered accounting firm, and outside counsel or advisors, correspondence with regulatory or governmental agencies and any published reports that may raise material issues regarding our financial statements or accounting policies;

conducting an annual assessment of the performance of the audit committee and its members, and the adequacy of its charter;

establishing procedures for the receipt, retention and treatment of complaints received by us regarding financial controls, accounting or auditing matters; and

reporting to our board of directors material issues in connection with our auditor committee s responsibilities.

Compensation committee

Our compensation committee consists of Mr. Bienaimé, Dr. Galakatos and Mr. Renton, each of whom our board of directors has determined to be independent under The NASDAQ Global Market listing

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standards, a non-employee director as defined in Rule 16b-3 promulgated under the Exchange Act, and an outside director as that term is defined in Section 162(m) of the Internal Revenue Code. The chairperson of our compensation committee is Mr. Bienaimé.

Our compensation committee reviews and recommends policies relating to compensation and benefits of our officers and employees. The compensation committee has the following responsibilities, among other things, as set forth in the compensation committee s charter:

- determining the appropriate relationship of compensation to the market to achieve corporate objectives;
- recommending to our board of directors for determination and approval the compensation and other terms of employment of our chief executive officer and his performance in light of relevant corporate performance goals and objectives;
- reviewing and approving the compensation and other terms of employment of our executive officers (other than our chief executive officer) and other employees, and corporate performance goals and objectives relevant to such compensation, and assessing the attainment of the prior year s corporate goals and objectives;
- appointing, compensating, and overseeing the work of compensation consultants, independent legal counsel or any other advisors engaged for the purpose of advising the committee after assessing the independence of such person in accordance with applicable NASDAQ rules;
- after consulting with compensation consultants, independent legal counsel or other advisor to our compensation committee, reviewing and recommending to our board of directors the compensation of our directors;
- reviewing and recommending to our board of directors and administering the equity incentive plans, compensation plans, and similar programs advisable for us, as well as evaluating and approving modification or termination of existing plans and programs;
- establishing policies with respect to equity compensation arrangements;
- reviewing and discussing annually with management the executive compensation disclosure and analysis required to be disclosed by SEC rules;
- recommending to our board of directors compensation-related proposals to be considered at our annual meeting of stockholders, including the frequency of advisory votes on executive compensation;
- preparing the compensation committee report required by the SEC to be included in our annual proxy statement;
- reviewing and discussing with management any conflicts of interest raised by the work of a compensation consultant or advisor retained by our compensation committee or management and how such conflict is being addressed, and preparing any necessary disclosure in our annual proxy statement in accordance with applicable SEC rules; and

reviewing and evaluating, at least annually, the performance of the compensation committee and the adequacy of its charter.

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Nominating and corporate governance committee

Our nominating and corporate governance committee consists of Dr. Califf, Dr. Homcy and Mr. Renton, each of whom our board of directors has determined to be independent under The NASDAQ Global Market listing standards. The chairperson of our nominating and corporate governance committee is Mr. Renton.

Our nominating and corporate governance committee makes recommendations regarding corporate governance, the composition of our board of directors, identification, evaluation and nomination of director candidates and the structure and composition of committees of our board of directors. The nominating and corporate governance committee has the following responsibilities, among other things, as set forth in the nominating and corporate governance committee s charter:

- reviewing periodically and evaluating director performance on our board of directors and its applicable committees, and recommending to our board of directors and management areas for improvement;
- interviewing, evaluating, nominating and recommending individuals for membership on our board of directors;
- overseeing and reviewing our processes and procedures to provide information to our board of directors and its committees;
- reviewing and recommending to our board of directors any amendments to our corporate governance policies; and
- reviewing and assessing, at least annually, the performance of the nominating and corporate governance committee and the adequacy of its charter.

Code of business conduct and ethics

Our board of directors has adopted a code of business conduct and ethics that applies to all of our employees, officers and directors, including those officers responsible for financial reporting. The code of business conduct and ethics is available on our website at *www.portola.com*. We intend to disclose any amendments to the code, or any waivers of its requirements, on our website to the extent required by the applicable rules and exchange requirements. The inclusion of our website address in this prospectus does not incorporate by reference the information on or accessible through our website into this prospectus.

Compensation committee interlocks and insider participation

None of the members of our Compensation Committee has ever been an officer or employee of the Company. None of our executive officers serve, or have served during the last fiscal year, as a member of the board of directors, compensation committee or other board committee performing equivalent functions of any entity that has one or more executive officers serving as one of our directors or on our Compensation Committee.

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Director compensation

We currently provide cash compensation to certain of our non-employee directors. From time to time, we have granted stock options to certain of our non-employee directors as compensation for their services. Mr. Lis, who is also an employee, is compensated for his service as an employee and does not receive any additional compensation for his service on our board of directors.

The following table sets forth information regarding compensation earned by our non-employee directors during the fiscal year ended December 31, 2012.

Name	Cash compensation	Option awards[1]	Other compensation	Total
Jean-Jacques Bienaimé	$ 50,000	$ 21,780[2]		$ 71,780
Jeffrey W. Bird, M.D., Ph.D.				
Robert M. Califf, M.D.[3]	$ 22,778	$ 52,272[4]		$ 75,050
Farah H. Champsi[5]				
Nicholas G. Galakatos, Ph.D.				
Jean M. George[5]				
Russell C. Hirsch, M.D., Ph.D.[5]				
Charles J. Homcy, M.D.	$ 71,875	$ 21,780[2]	$ 3,125[6]	$ 96,780
Peggy V. Phillips[5]	$ 37,500	$ 21,780[2]		$ 59,280
Hollings C. Renton	$ 75,000	$ 21,780[2]		$ 96,780
James N. Topper, M.D., Ph.D.				
H. Ward Wolff	$ 37,500	$ 21,780[2]		$ 59,280

(1) The amounts in this column reflect the aggregate grant date fair value of each option award granted during the fiscal year, computed in accordance with FASB ASC Topic 718. The valuation assumptions used in determining such amounts are described in Note 12 to our financial statements included in this prospectus. The table below lists the aggregate number of shares and additional information with respect to the outstanding option awards held by each of our non-employee directors.

Name	Number of shares subject to outstanding options as of December 31, 2012
Jean-Jacques Bienaimé	22,520
Jeffrey W. Bird, M.D., Ph.D.	
Robert M. Califf, M.D.	12,000
Farah H. Champsi	
Nicholas G. Galakatos, Ph.D.	
Jean M. George	
Russell C. Hirsch, M.D., Ph.D.	
Charles J. Homcy, M.D.	715,491
Peggy V. Phillips	32,520
Hollings C. Renton	30,520
James N. Topper, M.D., Ph.D.	
H. Ward Wolff	27,520

(2) Represents an option to purchase 5,000 shares of our common stock that was issued to such director on September 25, 2012 under our 2003 Equity Incentive Plan, or 2003 Plan. The grant date fair value of such option award is $21,780, as computed in accordance with FASB ASC Topic 718. The valuation assumptions used in determining such amounts are described in Note 12 to our financial statements included in this prospectus.

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(3) Dr. Califf joined our board of directors in July 2012.
(4) Represents an option to purchase 12,000 shares of our common stock that was issued to such director on July 18, 2012 under our 2003 Plan. The grant date fair value of such option award is $52,272, as computed in accordance with FASB ASC Topic 718. The valuation assumptions used in determining such amount are described in Note 12 to our financial statements included in this prospectus.
(5) Such individual resigned as a director immediately prior to the closing of our initial public offering.
(6) Dr. Homcy was also an employee in January of 2012, and this amount reflects compensation for his service as an employee. He did not receive any additional compensation for his service on our board of directors during the time he was an employee.

In April 2013, our board of directors adopted a non-employee director compensation policy, which became effective for all of our non-employee directors upon the closing of our initial public offering, pursuant to which we compensate our non-employee directors with a combination of cash and equity. Each such director who is not affiliated with one of our principal stockholders will receive an annual base cash retainer of $50,000 for such service, to be paid quarterly. Each chairperson, vice-chairperson and lead independent director of our board of directors will receive an additional annual base cash retainer of $25,000 for such service, to be paid quarterly.

The policy also provides that we compensate the members of our board of directors for service on our committees as follows:

The chairperson of our audit committee will receive an annual cash retainer of $20,000 for such service, paid quarterly, and each of the other members of the audit committee will receive an annual cash retainer of $6,500, paid quarterly.

The chairperson of our compensation committee will receive an annual cash retainer of $20,000 for such service, paid quarterly, and each of the other members of the compensation committee will receive an annual cash retainer of $6,500, paid quarterly.

The chairperson of our nominating and corporate governance committee will receive an annual cash retainer of $15,000 for such service, paid quarterly, and each of the other members of the nominating and corporate governance committee will receive an annual cash retainer of $5,000, paid quarterly.

The chairperson of our research and development committee will receive an annual cash retainer of $15,000 for such service, paid quarterly, and each of the other members of the research and development committee will receive an annual cash retainer of $5,000, paid quarterly.

The policy further provides for the grant of equity awards as follows:

For each new director that joins our board of directors after the closing of this offering, an initial stock option grant to purchase that number of shares equal to approximately 0.08% of our then-outstanding shares, including the conversion and exercise of all convertible and exercisable securities and the shares reserved for issuance under the equity plans described in the section of this prospectus entitled Executive compensation Employee benefit and stock plans, vesting monthly over 36 months; and

Annually, for each director continuing to serve on our board of directors, a stock option grant to purchase that number of shares of our common stock equal to approximately 0.04% of our

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then-outstanding shares, including the conversion and exercise of all convertible and exercisable securities and the shares reserved for issuance under our equity plans, vesting monthly over 12 months.

Each of these options will be granted with an exercise price equal to the fair market value of our common stock on the date of such grant. The exact number of shares to be granted in each such grant shall be subject to adjustment based on the review by our board of directors or compensation committee of the market value of the grant implied by the foregoing percentages at the time of grant.

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Executive compensation

2012 and 2011 summary compensation table

The following table provides information regarding the compensation of our principal executive officer and each of our three other most highly compensated executive officers during the fiscal years ended December 31, 2012 and December 31, 2011. We refer to these executive officers in this prospectus as our named executive officers.

Name and principal position	Year	Salary	Option awards[1]	Non-equity incentive plan compensation	All other compensation	Total
William Lis	2012	$ 405,000	$ 1,392,329	$ 121,500	$ 500[2]	$ 1,919,329
Chief Executive Officer	2011	$ 391,800	$ 701,720	$ 175,500	$ 500[2]	$ 1,269,520
John T. Curnutte, M.D., Ph.D.	2012	$ 376,980	$ 332,716	$ 90,475	$ 23,986[3]	$ 824,157
Executive Vice President, Research and Development	2011	$ 320,769[4]	$ 1,261,797	$ 131,760	$ 21,736[3]	$ 1,736,062
Mardi C. Dier	2012	$ 326,795	$ 357,904	$ 68,625	$ 500[2]	$ 753,824
Senior Vice President and Chief Financial Officer	2011	$ 317,269	$ 25,392	$ 174,939	$ 500[2]	$ 518,100
Michael M. Kitt, M.D.	2012	$ 370,484	$ 127,564	$ 80,099	$ 500[2]	$ 578,647
Senior Vice President and Chief Medical Officer	2011	$ 182,500[5]	$ 1,288,294	$ 62,488	$ 45,500[6]	$ 1,578,782

(1) The amounts in this column reflect the aggregate grant date fair value of each option award granted during the fiscal year, computed in accordance with FASB ASC Topic 718. The valuation assumptions used in determining such amounts are described in Note 12 to our financial statements included in this prospectus.

(2) Represents amounts contributed to such executive officers 401(k) plans as described in the section of this prospectus entitled Executive compensation Employee benefit and stock plans 401(k) plan.

(3) Represents amounts paid to Dr. Curnutte in lieu of his participation in the Company s medical benefits program.

(4) Dr. Curnutte s employment with us began in February 2011.

(5) Dr. Kitt s employment with us began in July 2011 and terminated in August 2013.

(6) Represents a signing bonus that was paid to Dr. Kitt in connection with the commencement of his employment and $500 contributed to Dr. Kitt s 401(k) plan as described in the section of this prospectus entitled Executive compensation Employee benefit and stock plans 401(k) plan.

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Outstanding equity awards as of December 31, 2012

The following table provides information regarding outstanding equity awards held by our named executive officers as of December 31, 2012.

	Number of securities underlying unexercised options[1]		Option exercise price	Option expiration date
Name	**Exercisable**	**Unexercisable**		
William Lis	18,867[2]		$5.30	6/18/2018
	82,228[2]		$5.30	6/18/2018
	25,429[2]		$4.10	12/23/2018
	15,462[3]		$5.10	2/25/2019
	19,607[3]		$5.10	2/25/2019
	1,956[4]		$5.10	6/9/2019
	11,111[5]		$9.00	2/24/2020
	28,888[5]		$9.00	2/24/2020
	211,820[6]		$9.00	7/14/2020
	11,764[7]		$8.50	3/23/2021
	107,070[7]		$8.50	3/23/2021
	190,014[8]		$7.00	3/8/2022
	14,285[8]		$7.00	3/8/2022
John T. Curnutte	11,764[9]		$8.50	3/23/2021
	201,918[9]		$8.50	3/23/2021
	15,714[8]		$7.00	3/8/2022
	14,285[8]		$7.00	3/8/2022
	24,148[10]		$9.50	12/13/2022
Mardi C. Dier	30,303[2]		$3.30	9/6/2016
	20,000[2]		$5.00	9/20/2017
	4,476[2]		$5.00	9/20/2017
	6,908[2]		$4.10	12/23/2018
	24,390[2]		$4.10	12/23/2018
	5,868[3]		$5.10	2/25/2019
	1,956[4]		$5.10	6/9/2019
	10,000[5]		$9.00	2/24/2020
	4,300[7]		$8.50	3/23/2021
	14,285[8]		$7.00	3/8/2022
	5,714[8]		$7.00	3/8/2022
	38,470[10]		$9.50	12/13/2022
Michael M. Kitt[11]	11,764[12]		$8.50	7/13/2021
	201,918[12]		$8.50	7/13/2021
	10,000[8]		$7.00	3/8/2022
	3,157[10]		$9.50	12/13/2022
	9,482[10]		$9.50	12/13/2022

(1) The options listed are fully vested or are subject to an early exercise right and may be exercised in full prior to vesting of the shares underlying such options. Vesting of all options is subject to continued service on the applicable vesting date.
(2) The shares subject to these options were fully vested as of December 31, 2013.
(3) 95.8% of the shares subject to these options were vested as of December 31, 2012 and the remainder vested in approximately equal increments on a monthly basis thereafter through February 25, 2013.
(4) 85.4% of the shares subject to these options were vested as of December 31, 2012 and the remainder vested in approximately equal increments on a monthly basis thereafter through July 2, 2013.

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(5) 75% of the shares subject to these options were vested as of December 31, 2012 and the remainder vest in approximately equal increments on a monthly basis thereafter through December 9, 2013.
(6) 64.6% of the shares subject to these options were vested as of December 31, 2012 and the remainder vest in approximately equal increments on a monthly basis thereafter through May 1, 2014.
(7) 43.7% of the shares subject to these options were vested as of December 31, 2012 and the remainder vest in approximately equal increments on a monthly basis thereafter through March 23, 2015.
(8) 25% of the shares subject to these options vest as of March 8, 2013 and the remainder vest in approximately equal increments on a monthly basis thereafter through March 8, 2016.
(9) 45.8% of the shares subject to these options were vested as of December 31, 2012 and the remainder vest in approximately equal increments on a monthly basis thereafter through February 14, 2015.
(10) 25% of the shares subject to these options vest as of December 12, 2013 and the remainder vest in approximately equal increments on a monthly basis thereafter through December 12, 2016.
(11) Dr. Kitt s employment with us terminated in August 2013.
(12) 35.4% of the shares subject to these options were vested as of December 31, 2012 and the remainder vest in approximately equal increments on a monthly basis thereafter through July 1, 2015.

Change in control severance benefits agreements

We have entered into change in control severance benefits agreements with each of William Lis, John Curnutte and Mardi Dier that contain severance provisions providing for continued payment of salary and provision of certain benefits for a specified period of time in connection with termination of employment under various circumstances, including involuntary termination by us or termination by the employee for good reason.

The actual amounts that would be paid or distributed to an eligible executive officer as a result of a termination of employment occurring in the future may be different than those described below as many factors will affect the amount of any payments and benefits upon a termination of employment. For example, some of the factors that could affect the amounts payable include the executive officer s base salary and the market price of our common stock. Although we have entered into a written agreement to provide severance payments and benefits in connection with a termination of employment under particular circumstances, we may mutually agree with the executive officers to provide payments and benefits on terms that vary from those currently contemplated. In addition to the amounts presented below, each executive officer is eligible to receive any benefits accrued under our broad-based benefit plans, such as accrued vacation pay, in accordance with those plans and policies.

To receive any of the severance benefits under these agreements, the executive officer would be required to execute a release of claims against us and comply with further cooperation, confidentiality and noncompetition provisions.

Severance payments

In the event of a termination without cause by us or an executive officer s resignation for good reason at any time during the period that is within three months prior to or 12 months following a change in control of Portola, which termination we refer to as a Covered Termination, such executive officer is eligible to receive the following payments and benefits:

a cash amount equal to one twelfth of the aggregate amount of such executive officer s annual base salary and pro-rata bonus multiplied by 15, which shall be paid over 15 months immediately following the termination date; and

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health insurance premiums under our group health insurance plans as provided under the Consolidated Omnibus Budget Reconciliation Act, or COBRA, until the earlier of (i) 15 months after termination of employment, (ii) such time as the executive officer is eligible for health insurance coverage with a subsequent employer and (iii) such time as the executive officer is no longer eligible for COBRA coverage.

Equity awards

In addition, in the event of a Covered Termination, the vesting and exercisability of all outstanding options to purchase our common stock held by an eligible executive officer will be accelerated in full, and any repurchase rights held by us with respect to our common stock issued or issuable pursuant to any other stock award granted to such executive officer will lapse.

For purposes of these agreements, the term change in control means the occurrence of any of the following: (i) any natural person, entity or group within the meaning of Section 13(d) or 14(d) of the Securities Exchange Act of 1934, as amended, becoming the owner of more than 50% of the combined outstanding voting power of Portola; (ii) the consummation of a merger, consolidation or similar transaction involving us that results in our stockholders immediately prior to such transaction not owning more than 50% of the combined outstanding voting power of the surviving entity or the parent of such surviving entity; (iii) approval by our stockholders or our board of directors of a plan of complete dissolution or liquidation of Portola, or a complete dissolution or liquidation of Portola; or (iv) the consummation of a sale, lease, license or other disposition of all or substantially all of our assets, with certain exceptions.

For purposes of these agreements, the term cause means any of the following: (i) the executive officer s willful and material failure to perform duties or follow lawful and reasonable directions following written notice of such failure from our board of directors; (ii) conviction of a felony or a crime involving moral turpitude or dishonesty; (iii) willful engagement in gross misconduct that is materially and demonstrably injurious to us or (iv) material breach of such executive officer s confidentiality agreement by the executive officer.

For purposes of these agreements, the term good reason means any of the following: subject to certain exceptions, (i) a decrease in the executive officer s total target compensation of more than 10% which both we and the executive officer acknowledge as a diminution in such person s base compensation and a material breach by us of such executive officer s employment agreement with us; (ii) a material diminution of position, duties and responsibilities; (iii) an increase in the executive officer s round-trip driving distance of more than 50 miles from such person s principal personal residence to the principal business location or (iv) our failure to obtain a satisfactory agreement from any successor to assume and agree to perform under the material terms of the change in control severance benefits agreement.

Before an executive officer may terminate employment for good reason, the executive officer must notify us in writing, we must fail to remedy or cure the alleged good reason and the executive officer must then terminate employment, all within prescribed time periods.

Employment agreements

We have entered into agreements with each of the executive officers in connection with his or her employment with us. With the oversight and approval of our board of directors, each of these

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employment agreements was negotiated on our behalf by our Chief Executive Officer, William Lis, with the exception of his own employment agreement. These agreements provided for at will employment and set forth the terms and conditions of employment of each named executive officer, including base salary, target annual bonus opportunity, standard employee benefit plan participation, initial stock option grant and vesting provisions with respect to the initial stock option grant. These employment agreements were each subject to execution of our standard confidential information and invention assignment agreement.

Employee benefit and stock plans

2003 equity incentive plan

Our board of directors adopted our 2003 Equity Incentive Plan, or the 2003 Plan, in November 2003, and our stockholders subsequently approved the 2003 Plan in November 2003. The 2003 Plan was amended by our board of directors on March 8, 2012 and February 27, 2013. Our 2003 Plan provides for the grant of incentive stock options, or ISOs, within the meaning of Section 422 of the Internal Revenue Code of 1986, as amended, or the Code, to our employees, and for the grant of nonstatutory stock options, or NSOs, stock bonuses, and rights to acquire restricted stock to our employees, directors and consultants. We expect no further grants will be made under our 2003 Stock Plan.

Authorized shares. As of June 30, 2013, the maximum number of shares of our common stock that may be issued under our 2003 Plan is 3,787,915, which consists solely of shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2013.

Shares issued under our 2003 Plan include any authorized but unissued or reacquired shares of our common stock. Shares subject to stock awards granted under our 2003 Plan that expire or terminate without being exercised in full, shares that are tendered to pay the exercise price or tax withholding obligation on an award, and shares subject to awards that are paid out in cash rather than in shares, will not be returned to the 2003 Plan but rather will be added to the number of shares available for issuance under our 2013 Equity Incentive Plan, or the 2013 Plan.

Plan administration. Our board of directors, or a duly authorized committee of our board of directors, may administer our 2003 Plan. Subject to the terms of our 2003 Plan, the board of directors has the authority to determine and amend the terms of awards, including recipients, the exercise, purchase or strike price of stock awards, if any, the number of shares subject to each stock award, the fair market value of a share of our common stock, the vesting schedule applicable to the awards, together with any vesting acceleration and the form of consideration, if any, payable upon exercise or settlement of the award and the terms of the award agreements for use under our 2003 Plan.

Corporate transactions. Our 2003 Plan provides that in the event of a specified corporate transaction, as defined under our 2003 Plan, each outstanding stock award may be assumed or an equivalent stock award may be substituted by a successor corporation. If the successor corporation does not agree to assume the stock award or to substitute an equivalent stock award, such stock awards will become fully vested and exercisable prior to the closing, and if not exercised by the closing, the stock awards will terminate at the closing of the transaction.

Plan amendment or termination. Our board of directors has the authority to amend, suspend or terminate our 2003 Plan, provided that such action does not materially impair the existing rights of any participant without such participant s written consent.

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2013 equity incentive plan

Our board of directors adopted our 2013 Plan on January 30, 2013. Our board of directors amended the 2013 Plan on February 27, 2013. Our stockholders approved the 2013 Plan, as amended, on March 8, 2013. The 2013 Plan became effective immediately upon the signing of the underwriting agreement for our initial public offering. The 2013 Plan will terminate on January 29, 2023, unless sooner terminated by our board of directors. Our 2013 Plan provides for the grant of ISOs to our employees and for the grant of NSOs, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance-based stock awards, performance-based cash awards and other forms of equity compensation to our employees, directors and consultants. Additionally, our 2013 Plan provides for the grant of performance cash awards to our employees, directors and consultants.

Authorized shares. As of June 30, 2013, the maximum number of shares of our common stock that may be issued under our 2013 Plan consists of (i) 334,070 shares available for issuance under the 2013 Plan as of June 30, 2013 and (ii) the shares of our common stock subject to awards granted under the 2003 Plan that expire or terminate for any reason prior to exercise or settlement, are forfeited because of the failure to vest in those shares, or are otherwise reacquired or withheld to satisfy a tax withholding obligation in connection with such awards if, as, and when such shares are subject to such events, which aggregate number of shares will not exceed 4,121,985 shares, with such shares subject to adjustment to reflect any split of our common stock. Additionally, the number of shares of our common stock reserved for issuance under our 2013 Plan will automatically increase on January 1 of each year, beginning on January 1, 2014 and ending on and including January 1, 2023, by 5% of the total number of shares of our capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by our board of directors. The maximum number of shares that may be issued upon the exercise of ISOs under our 2013 Plan is 8,100,000 (subject to adjustment to reflect any split of our common stock).

Shares issued under our 2013 Plan include authorized but unissued or reacquired shares of our common stock. Shares subject to stock awards granted under our 2013 Plan that expire or terminate without being exercised in full, or that are paid out in cash rather than in shares, do not reduce the number of shares available for issuance under our 2013 Plan. Additionally, shares issued pursuant to stock awards under our 2013 Plan that we repurchase or that are forfeited, as well as shares used to pay the exercise price of a stock award or to satisfy the tax withholding obligations related to a stock award, become available for future grant under our 2013 Plan.

Plan administration. Our board of directors, or a duly authorized committee of our board of directors, will administer our 2013 Plan. Our board of directors may also delegate to one or more of our officers the authority to (i) designate employees (other than officers) to receive specified stock awards, and (ii) determine the number of shares of our common stock to be subject to such stock awards. Subject to the terms of our 2013 Plan, the board of directors has the authority to determine the terms of awards, including recipients, the exercise, purchase or strike price of stock awards, if any, the number of shares subject to each stock award, the fair market value of a share of our common stock, the vesting schedule applicable to the awards, together with any vesting acceleration, and the form of consideration, if any, payable upon exercise or settlement of the award and the terms of the award agreements.

The board of directors has the power to modify outstanding awards under our 2013 Plan. The board of directors has the authority to reprice any outstanding option or stock appreciation right, cancel any

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outstanding stock award in exchange for new stock awards, cash or other consideration, or take any other action that is treated as a repricing under generally accepted accounting principles, with the consent of any adversely affected participant.

Section 162(m) limits. At such time as necessary for compliance with Section 162(m) of the Code, no participant may be granted stock awards covering more than 1,000,000 shares of our common stock (subject to adjustment to reflect any split of our common stock) under our 2013 Plan during any calendar year pursuant to stock options, stock appreciation rights and other stock awards whose value is determined by reference to an increase over an exercise price or strike price of at least 100% of the fair market value of our common stock on the date of grant. Additionally, no participant may be granted in a calendar year a performance stock award covering more than 1,000,000 shares of our common stock (subject to adjustment to reflect any split of our common stock) or a performance cash award having a maximum value in excess of $2,000,000 under our 2013 Plan. These limitations are intended to give us the flexibility to grant compensation that will not be subject to the $1,000,000 annual limitation on the income tax deductibility imposed by Section 162(m) of the Code.

Performance awards. We believe our 2013 Plan permits the grant of performance-based stock and cash awards that may qualify as performance-based compensation that is not subject to the $1,000,000 limitation on the income tax deductibility imposed by Section 162(m) of the Code. Our compensation committee may structure awards so that the stock or cash will be issued or paid only following the achievement of certain pre-established performance goals during a designated performance period. However, we retain the discretion to grant awards under the 2013 Plan that may not qualify for full deductibility.

Our compensation committee may establish performance goals by selecting from one or more performance criteria, including:

earnings before interest, taxes, depreciation and amortization;

total stockholder return;

return on equity or average stockholders equity;

return on assets, investment, or capital employed;

stock price;

income (before or after taxes);

operating income;

pre-tax profit;

operating cash flow;

sales or revenue targets;

increases in revenue or product revenue;

expenses and cost reduction goals;

improvement in or attainment of working capital levels;

implementation or completion of projects or processes;

employee retention;

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stockholders equity;

capital expenditures;

operating profit or net operating profit;

growth of net income or operating income;

initiation of phases of clinical trials and/or studies by specified dates;

patient enrollment rates;

budget management;

regulatory body approval with respect to products, studies and/or trials; and

to the extent that an award is not intended to comply with Section 162(m) of the Code, other measures of performance selected by our board of directors.

Corporate transactions. Our 2013 Plan provides that in the event of certain specified significant corporate transactions, as defined under our 2013 Plan, each outstanding award will be treated as the administrator determines. The administrator may (i) arrange for the assumption, continuation or substitution of a stock award by a successor corporation, (ii) arrange for the assignment of any reacquisition or repurchase rights held by us to a successor corporation, (iii) accelerate the vesting, in whole or in part, of the stock award and provide for its termination prior to the transaction and arrange for the lapse, in whole or in part, of any reacquisition or repurchase rights held by us or (iv) cancel the stock award prior to the transaction in exchange for a cash payment, if any, determined by our board of directors. The plan administrator is not obligated to treat all stock awards or portions of stock awards, even those that are of the same type, in the same manner.

Plan amendment or termination. Our board of directors has the authority to amend, suspend, or terminate our 2013 Plan, provided that such action does not materially impair the existing rights of any participant without such participant s written consent. No ISOs may be granted after the tenth anniversary of the date our board of directors adopted our 2013 Plan.

2013 employee stock purchase plan

Our board of directors adopted our 2013 Employee Stock Purchase Plan, or the ESPP, on January 30, 2013. Our stockholders approved the ESPP on March 8, 2013. The maximum aggregate number of shares of our common stock that may be issued under our ESPP is 1,000,000 shares (subject to adjustment to reflect any split of our common stock). Additionally, the number of shares of our common stock reserved for issuance under our ESPP will increase automatically each year, beginning on January 1, 2014 and continuing through and including January 1, 2023, by the lesser of (i) 2% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year; (ii) 2,500,000 shares of common stock (subject to adjustment to reflect any split of our common stock); or (iii) such lesser number as determined by our board of directors. Shares subject to purchase rights granted under our ESPP that terminate without having been exercised in full will not reduce the number of shares available for issuance under our ESPP. To date, we have not issued any shares under our ESPP.

Our board of directors will administer our ESPP. Our board of directors may delegate authority to administer our ESPP to our compensation committee.

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Our employees, including executive officers, may have to satisfy one or more of the following service requirements before participating in our ESPP, as determined by the administrator: (i) customary employment for more than 20 hours per week and more than five months per calendar year, or (ii) continuous employment for a minimum period of time, not to exceed two years. An employee may not be granted rights to purchase stock under our ESPP if such employee (i) immediately after the grant would own stock possessing 5% or more of the total combined voting power or value of our common stock, or (ii) holds rights to purchase stock under our ESPP that would accrue at a rate that exceeds $25,000 worth of our stock for each calendar year that the rights remain outstanding. Under our ESPP, we may grant purchase rights that do not meet the requirements of an employee stock purchase plan because of deviations necessary to permit participation by employees who are foreign nationals or employed outside of the United States, as required by applicable foreign laws.

The administrator may approve offerings with a duration of not more than 27 months, and may specify one or more shorter purchase periods within each offering. Each offering will have one or more purchase dates on which shares of our common stock will be purchased for the employees who are participating in the offering. The administrator, in its discretion, will determine the terms of offerings under our ESPP including determining which of our designated affiliates will be eligible to participate in the 423 component of our ESPP and which of our designated affiliates will be eligible to participate in the non-423 component of our ESPP. No offerings have been approved at this time.

Our ESPP permits participants to purchase shares of our common stock through payroll deductions or other methods with up to 15% of their earnings. The purchase price of the shares will be not less than 85% of the lower of the fair market value of our common stock on the first day of an offering or on the date of purchase.

A participant may not transfer purchase rights under our ESPP other than by will, the laws of descent and distribution or as otherwise provided under our ESPP.

In the event of a specified corporate transaction, such as a merger or change in control, a successor corporation may assume, continue or substitute each outstanding purchase right. If the successor corporation does not assume, continue or substitute for the outstanding purchase rights, the offering in progress may be shortened and a new exercise date will be set, so that the participants purchase rights can be exercised and terminate immediately thereafter.

Our ESPP will remain in effect until terminated by the administrator in accordance with the terms of the ESPP. Our board of directors has the authority to amend, suspend or terminate our ESPP, at any time and for any reason.

401(k) plan

We maintain a tax-qualified retirement plan that provides eligible U.S. employees with an opportunity to save for retirement on a tax advantaged basis. Eligible employees are able to defer eligible compensation subject to applicable annual Code limits. We have the ability to make discretionary contributions to the 401(k) plan and currently match employee contributions up to $500 per person on an annual basis. Employees pre-tax contributions are allocated to each participant s individual account and are then invested in selected investment alternatives according to the participants directions. Employees are immediately and fully vested in their contributions. The 401(k) plan is intended to be qualified under Section 401(a) of the Code with the 401(k) plan s related trust intended to be tax

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exempt under Section 501(a) of the Code. As a tax-qualified retirement plan, contributions to the 401(k) plan and earnings on those contributions are not taxable to the employees until distributed from the 401(k) plan.

Limitation on liability and indemnification matters

Our amended and restated certificate of incorporation contains provisions that limit the liability of our current and former directors for monetary damages to the fullest extent permitted by Delaware law. Delaware law provides that directors of a corporation will not be personally liable for monetary damages for any breach of fiduciary duties as directors, except liability for:

- any breach of the director s duty of loyalty to the corporation or its stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions; or
- any transaction from which the director derived an improper personal benefit.

Such limitation of liability does not apply to liabilities arising under federal securities laws and does not affect the availability of equitable remedies, such as injunctive relief or rescission.

Our amended and restated certificate of incorporation and our amended and restated bylaws provide that we are required to indemnify our directors to the fullest extent permitted by Delaware law. Our amended and restated bylaws also provide that, upon satisfaction of certain conditions, we shall advance expenses incurred by a director in advance of the final disposition of any action or proceeding, and permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in that capacity regardless of whether we would otherwise be permitted to indemnify him or her under the provisions of Delaware law. Our amended and restated certificate of incorporation and amended and restated bylaws also provide our board of directors with discretion to indemnify our officers and employees when determined appropriate by the board. We have entered and expect to continue to enter into agreements to indemnify our directors and executive officers. With certain exceptions, these agreements provide for indemnification for related expenses including, among other things, attorneys fees, judgments, fines and settlement amounts incurred by any of these individuals in any action or proceeding. We believe that these bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers. We also maintain customary directors and officers liability insurance.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against our directors for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and other stockholders. Further, a stockholder s investment may be adversely affected to the extent that we pay the costs of settlement and damage awards against directors and officers as required by these indemnification provisions. At present, there is no pending litigation or proceeding involving any of our directors, officers or employees for which indemnification is sought and we are not aware of any threatened litigation that may result in claims for indemnification.

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Certain relationships and related party transactions

Other than compensation arrangements, we describe below transactions and series of similar transactions, since January 1, 2010, to which we were a party or will be a party, in which:

- the amounts involved exceeded or will exceed $120,000; and
- any of our directors, executive officers, or holders of more than 5% of our capital stock, or any member of the immediate family of the foregoing persons, had or will have a direct or indirect material interest.

Compensation arrangements for our directors and named executive officers are described elsewhere in this prospectus.

Participation in our initial public offering

Maxwell (Mauritius) Pte Ltd, Eastern Capital Limited and Brookside Capital Partners Fund LP, or Brookside, each of whom were holders of more than 5% of our capital stock at the time of our initial public offering, or IPO, purchased a total of 1,200,000 shares of our common stock in our IPO. The underwriters received the same underwriting discount from the sale of the shares of our common stock to these securityholders as they did from other shares of our common stock sold to the public in that offering. The shares purchased by these existing securityholders are subject to lock-up restrictions described in the section titled Shares eligible for future sale, except that the shares purchased by Brookside in our IPO are not subject to any lock-up restrictions.

Sales of preferred stock

In November 2011, we sold an aggregate of 6,287,026 shares of our Series D convertible preferred stock at a purchase price of $14.15 per share for an aggregate purchase price of approximately $89.0 million. In December 2011, we sold an aggregate of 636,042 shares of our Series 1 convertible preferred stock at a purchase price of $14.15 per share for an aggregate purchase price of approximately $9.0 million. The following table summarizes purchases of shares of our convertible preferred stock by our executive officers, directors and holders of more than 5% of our capital stock since January 1, 2010.

Stockholder	Number of shares of Series D convertible preferred stock
Maxwell (Mauritius) Pte Ltd	3,533,568
Eastern Capital Limited	1,766,784
Entities affiliated with MPM BioVentures[1]	144,836
Entities affiliated with Prospect Venture Partners[2]	107,730
Brookside Capital Partners Fund LP	105,899
Entities affiliated with Advanced Technology Ventures[3]	91,556
Entities affiliated with Sutter Hill Ventures[4]	109,102
Entities affiliated with Frazier Healthcare[5]	85,205
Hollings C. Renton[6]	2,826
Jean-Jacques Bienaimé	706
Peggy V. Phillips[7]	7,067
H. Ward Wolff	1,766

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(1) Represents 120,566 shares purchased by MPM BioVentures III-QP, L.P., 10,189 shares purchased by MPM BioVentures III GmbH & Co. Beteiligungs KG, 8,106 shares purchased by MPM BioVentures III, L.P., 3,641 shares purchased by MPM BioVentures III Parallel Fund, L.P., and 2,334 shares purchased by MPM Asset Management Investors 2003 BVIII LLC. MPM BioVentures III-QP, L.P.; MPM BioVentures III GmbH & Co. Beteiligungs KG; MPM BioVentures III, L.P., MPM BioVentures III Parallel Fund, L.P.; and MPM Asset Management Investors 2003 BVIII LLC are collectively referred to as the Entities affiliated with MPM BioVentures. Nicholas G. Galakatos, Ph.D., a member of our board of directors, is a Series A Member of MPM BioVentures III LLC and a Manager of MPM Asset Management Investors 2003 BVIII LLC.

(2) Represents 106,114 shares purchased by Prospect Venture Partners II, L.P. and 1,616 shares purchased by Prospect Associates II, L.P. Prospect Venture Partners II, L.P. and Prospect Associates II, L.P. are collectively referred to as the Entities affiliated with Prospect Venture Partners. Russell C. Hirsch, M.D., Ph.D. is a managing director of Prospect Management Co. II, L.L.C.

(3) Represents 85,939 shares purchased by Advanced Technology Ventures VII, L.P., 3,448 shares purchased by Advanced Technology Ventures VII (B), L.P., 1,657 shares purchased by Advanced Technology Ventures VII (C), L.P and 512 shares purchased by ATV Entrepreneurs VII, L.P. ATV Associates VII, L.L.C. is the general partner of each of Advanced Technology Ventures VII, L.P., Advanced Technology Ventures VII (B), L.P., Advanced Technology Ventures VII (C), L.P. and ATV Entrepreneurs VII, L.P, which are collectively referred to as the Entities affiliated with Advanced Technology Ventures. Jean M. George is a Managing Director of ATV Associates VII, LLC.

(4) Represents 65,818 shares purchased by Sutter Hill Ventures, a California limited partnership, 4,368 shares purchased by Jeffrey W. Bird and Christina R. Bird as Trustees of Jeffrey W. and Christina R. Bird Trust over which Jeffrey W. Bird, a member of our board of directors, may be deemed to have share voting and investment power, and 38,916 shares purchased by individuals other than Dr. Bird who are affiliated with Sutter Hill Ventures or entities affiliated with such individuals. Dr. Bird may also be deemed to have shared voting and investment power with respect to the shares purchased by Sutter Hill Ventures.

(5) Includes 84,775 shares purchased by Frazier Healthcare IV, LP and 430 shares purchased by Frazier Affiliates IV, LP. Frazier Healthcare IV, LP and Frazier Affiliates IV, LP. are collectively referred to as the Entities affiliated with Frazier Healthcare. James Topper, M.D., Ph.D., a member of our board of directors, is a venture capitalist with Frazier Healthcare, but does not hold voting or dispositive power over the shares purchased by the entities affiliated with Frazier Healthcare and disclaims beneficial ownership thereof except to the extent of his proportionate pecuniary interest in such shares.

(6) Purchased by The Renton Family Community Property Trust, for which Mr. Renton holds voting or dispositive power.

(7) Purchased by Thomas W. Phillips and Peggy V. Phillips.

Investor rights agreement

We are party to an investor rights agreement that provides holders of our convertible preferred stock, including certain holders of 5% of our capital stock and entities affiliated with certain of our directors, with certain registration rights, including the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing. The investor rights agreement also provided for a right of first refusal in favor of certain holders of our stock with regard to certain issuances of our capital stock. The rights of first refusal did not apply to, and terminated upon, the closing of our initial public offering. For a more detailed description of these registration rights, see the section of this prospectus entitled Description of capital stock Registration rights.

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Voting agreement

Prior to our initial public offering, we were party to a voting agreement under which certain holders of our capital stock, including certain holders of 5% of our capital stock and entities affiliated with certain of our directors, have agreed to vote in a certain way on certain matters, including with respect to the election of directors. The voting agreement terminated upon our initial public offering and none of our stockholders have any special rights regarding the election or designation of members of our board of directors.

Right of first refusal and co-sale agreement

Prior to our initial public offering, we were party to a right of first refusal and co-sale agreement with holders of our convertible preferred stock and our founders, including certain holders of 5% of our capital stock and entities affiliated with certain of our directors, pursuant to which the holders of convertible preferred stock have a right of first refusal and co-sale in respect of certain sales of securities by our founders. The right of first refusal and co-sale agreement terminated upon our initial public offering.

Indemnification agreements

Our amended and restated certificate of incorporation contains provisions limiting the liability of directors and our amended and restated bylaws provide that we will indemnify each of our directors to the fullest extent permitted under Delaware law. Our amended and restated certificate of incorporation and amended and restated bylaws also provide our board of directors with discretion to indemnify our officers and employees when determined appropriate by the board. In addition, we have entered and expect to continue to enter into agreements to indemnify our directors and executive officers. For more information regarding these agreements, see the section of this prospectus entitled Executive compensation Limitations on liability and indemnification matters.

Change in control arrangements

We have entered into change in control severance benefits agreements with each of our executive officers, as described in greater detail in the section of this prospectus titled Executive Compensation Change in control severance benefits agreements.

Agreements with Global Blood Therapeutics, Inc. and MyoKardia, Inc.

Charles Homcy, a member and co-chairman of our board of directors and our former President and Chief Executive Officer, is also a co-founder and member of the board of directors of Global Blood Therapeutics, Inc., or Global Blood, and the interim Chief Executive Officer and a member of the board of directors of MyoKardia, Inc., or MyoKardia. We entered into Master Services Agreements with Global Blood on November 2, 2012, and with MyoKardia on November 13, 2012, respectively, which provide that we provide certain consulting, preclinical, laboratory and clinical research related services to Global Blood and MyoKardia, respectively. As each of these agreements were deemed not material to our business or operations, they were not formally approved or ratified by our board of directors or audit committee.

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Policies and procedures for related party transactions

Our board of directors adopted a policy, effective upon the closing of our initial public offering, that our executive officers, directors, nominees for election as a director, beneficial owners of more than 5% of any class of our common stock and any members of the immediate family of any of the foregoing persons are not permitted to enter into a related person transaction with us without the prior consent of our audit committee. Any request for us to enter into a transaction with an executive officer, director, nominee for election as a director, beneficial owner of more than 5% of any class of our common stock or any member of the immediate family of any of the foregoing persons in which the amount involved exceeds $120,000 and such person would have a direct or indirect interest must first be presented to our audit committee for review, consideration and approval. In approving or rejecting any such proposal, our audit committee is to consider the material facts of the transaction, including, but not limited to, whether the transaction is on terms no less favorable than terms generally available to an unaffiliated third party under the same or similar circumstances and the extent of the related person s interest in the transaction. We did not have a formal review and approval policy for related party transactions at the time of any of the transactions described above. However, all of the transactions described above were entered into after presentation, consideration and approval by our board of directors, except as noted above.

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Principal and selling stockholders

The following table sets forth information regarding the beneficial ownership of our common stock as of August 31, 2013 by the following:

- each of our directors and named executive officers;
- all of our directors and executive officers as a group;
- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock; and
- each of the selling stockholders.

Beneficial ownership is determined according to the rules of the Securities and Exchange Commission and generally means that a person has beneficial ownership of a security if he, she or it possesses sole or shared voting or investment power of that security, including options and warrants that are currently exercisable or exercisable within 60 days of August 31, 2013. Shares of our common stock issuable pursuant to stock options and warrants are deemed outstanding for computing the percentage of the person holding such options or warrants and the percentage of any group of which the person is a member but are not deemed outstanding for computing the percentage of any other person. Except as indicated by the footnotes below, we believe, based on the information furnished to us, that the persons named in the table below have sole voting and investment power with respect to all shares of common stock shown that they beneficially own, subject to community property laws where applicable. The information does not necessarily indicate beneficial ownership for any other purpose, including for purposes of Section 13(d) and 13(g) of the Securities Act of 1933, as amended.

Our calculation of the percentage of beneficial ownership prior to this offering is based on 35,229,352 shares of common stock outstanding as of August 31, 2013. Our calculation of the percentage of beneficial ownership after this offering is based on 39,687,062 shares of common stock outstanding immediately after the closing of this offering, assuming no exercise of outstanding options or warrants and no exercise of the underwriters option to purchase additional shares of our common stock.

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Unless otherwise indicated, the address of each beneficial owner listed in the table below is c/o Portola Pharmaceuticals, Inc., 270 E. Grand Avenue, South San Francisco, California 94080.

	Shares beneficially owned prior to the offering		Shares being offered	Shares beneficially owned after the offering	
Name of beneficial owner	**Number**	**Percent**		**Number**	**Percent**
5% Stockholders:					
Maxwell (Mauritius) Pte Ltd[1]	4,233,568	12.0%		4,233,568	10.7%
Entities affiliated with MPM BioVentures III, L.P.[2]	2,441,344	6.9%		2,441,344	6.2%
Entities affiliated with Prospect Venture Partners II, L.P.[3]	1,815,884	5.2%		1,815,884	4.6%
Brookside Capital Partners Fund LP[4]	2,185,013	6.2%	1,785,013	400,000	1.0%
Entities affiliated with Sutter Hill Ventures[5]	1,782,081	5.1%		1,782,081	4.5%
Eastern Capital Limited[6]	1,866,784	5.3%		1,866,784	4.7%
Named executive officers and directors:					
William Lis[7]	838,501	2.3%		838,501	2.1%
John T. Curnutte, M.D., Ph.D.[8]	267,829	*		267,829	*
Mardi C. Dier[9]	236,319	*		236,319	*
Michael M. Kitt, M.D.[10]	114,833	*		114,833	*
Hollings C. Renton[11]	38,046	*		38,046	*
Charles J. Homcy, M.D.[12]	959,624	2.7%	95,962	863,662	2.1%
Jean-Jacques Bienaimé[13]	27,926	*		27,926	*
Jeffrey W. Bird, M.D., Ph.D.[14]	1,180,725	3.4%		1,180,725	3.0%
Robert M. Califf, M.D.[15]	16,700	*		16,700	*
Nicholas G. Galakatos, Ph.D.[16]	2,446,044	6.9%		2,446,044	6.2%
James N. Topper, M.D., Ph.D.[17]	1,440,906	4.1%		1,440,906	3.6%
H. Ward Wolff[18]	33,986	*		33,986	*
All executive officers and directors as a group (11 persons)[19]	7,486,606	20.0%	95,962	7,390,644	17.7%
Other Selling Stockholders:					
David R. Phillips, Ph.D.[20]	278,288	*	27,828	250,460	*

* Less than 1% of the outstanding shares of common stock

(1) Maxwell (Mauritius) Pte Ltd is a wholly owned subsidiary of Cairnhill Investments (Mauritius) Pte Ltd, which is a wholly owned subsidiary of Fullerton Management Pte Ltd, which is a wholly owned subsidiary of Temasek Holdings (Private) Limited. Each of these entities, through the ownership described above, may be deemed to beneficially own and share voting and dispositive power over the shares held by Maxwell (Mauritius) Pte Ltd. The address for Maxwell (Mauritius) Pte Ltd is Les Cascades, Edith Cavell Street, Port Louis, Mauritius.

(2) Represents 2,032,239 shares held by MPM BioVentures III-QP, L.P., 171,747 shares held by MPM BioVentures III GmbH & Co. Beteiligungs KG, 136,641 shares held by MPM BioVentures III, L.P., 61,373 shares held by MPM BioVentures III Parallel Fund, L.P., and 39,344 shares held by MPM Asset Management Investors 2003 BVIII LLC. MPM BioVentures III-QP, L.P.; MPM BioVentures III GmbH & Co. Beteiligungs KG; MPM BioVentures III, L.P., MPM BioVentures III Parallel Fund, L.P.; and MPM Asset Management Investors 2003 BVIII LLC are collectively referred to as the Entities affiliated with MPM BioVentures. MPM BioVentures III GP, L.P. is the general partner of each of MPM BioVentures III-QP, L.P., MPM BioVentures III, L.P. and MPM BioVentures III Parallel Fund, L.P. and the managing limited partner of MPM BioVentures III GmbH & Co. Beteiligungs KG. MPM BioVentures III LLC is the General Partner of MPM BioVentures III GP, L.P. Ansbert Gadicke, Luke Evnin, Nicholas Galakatos, Dennis Henner, Nicholas Simon, Michael Steinmetz and Kurt Wheeler are the Series A Members of MPM BioVentures III LLC and Managers of MPM Asset Management Investors 2003 BVIII LLC and share

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voting and dispositive power over the shares held by MPM BioVentures III-QP, L.P., MPM BioVentures III GmbH & Co. Beteiligungs KG, MPM BioVentures III, L.P., MPM BioVentures III Parallel Fund, L.P. and MPM Asset Management Investors 2003 BVIII LLC, and each disclaims beneficial ownership of the shares identified in this footnote except to the extent of his or her respective proportionate pecuniary interest in such shares. The address for the Entities affiliated with MPM BioVentures is 200 Clarendon Street, 54th Floor, Boston, Massachusetts 02116.

(3) Represents 1,788,647 shares held by Prospect Venture Partners II, L.P. and 27,237 shares held by Prospect Associates II, L.P. Prospect Venture Partners II, L.P. and Prospect Associates II, L.P. are collectively referred to as the Entities affiliated with Prospect Venture Partners. Prospect Management Co. II, L.L.C. is the general partner of the Entities affiliated with Prospect Venture Partners. Russell Hirsch and David Schnell are the managing directors of Prospect Management Co. II, L.L.C. and share voting and dispositive power over the shares held by the Entities affiliated with Prospect Venture Partners, and each disclaims beneficial ownership of the shares identified in this footnote except to the extent of his or her respective proportionate pecuniary interest in such shares. The address for the Entities affiliated with Prospect Venture Partners is 435 Tasso Street, Suite 200, Palo Alto, California 94301.

(4) Brookside Capital Management, LLC is the general partner of Brookside Capital Investors, L.P., which is the general partner of Brookside Capital Partners Fund LP. Brookside Capital Management, LLC is controlled by an executive committee whose members include Dewey J. Awad, Domenic J. Ferrante, Matthew V. McPherron, William E. Pappendick IV and John M. Toussaint, who may be deemed to share voting and dispositive power over the shares held by Brookside Capital Partners Fund LP, and each disclaims beneficial ownership of the shares identified in this footnote except to the extent of his respective proportionate pecuniary interest in such shares. The address for Brookside Capital Partners Fund LP is 111 Huntington Ave, Boston, Massachusetts 02199.

(5) Represents 1,102,824 shares held by Sutter Hill Ventures, a California limited partnership, or Sutter Hill Ventures, 36,599 shares held by Jeffrey W. Bird and Christina R. Bird as Trustees of Jeffrey W. and Christina R. Bird Trust, 36,602 shares held by NestEgg Holdings, LP, 4,700 shares issuable pursuant to stock options held directly by Dr. Bird exercisable within 60 days of August 31, 2013 and 601,356 shares held by individuals other than Dr. Bird who are affiliated with Sutter Hill Ventures or entities affiliated with such individuals. Dr. Bird is a trustee of Jeffrey W. and Christina R. Bird Trust, which is a general partner of NestEgg Holdings, LP, and shares voting and investment power with respect to the shares held by both entities. Dr. Bird and Sutter Hill Ventures do not have any voting or investment power with respect to the shares held by the individuals and entities described in this footnote other than shares held by Dr. Bird, his affiliated entities and Sutter Hill Ventures. Dr. Bird, David L. Anderson, William H. Younger, Jr., Tench Coxe, James C. Gaither, James N. White, G. Leonard Baker Jr., David E. Sweet, Andrew T. Sheehan, Michael L. Speiser, Stefan A. Dyckerhoff and Samuel J. Pullara III are managing directors of Sutter Hill Ventures and share voting and investment power with respect to the shares held by Sutter Hill Ventures. Each of these individuals disclaims beneficial ownership of the shares held by Sutter Hill Ventures except to the extent of his individual pecuniary interest therein. The address for Sutter Hill Ventures and affiliates is 755 Page Mill Road, Suite A-200, Palo Alto, California 94304.

(6) Eastern Capital Limited is a direct wholly owned subsidiary of Portfolio Services Ltd. Kenneth B. Dart is the beneficial owner of all of the outstanding shares of Portfolio Services Ltd., which in turn owns all the outstanding shares of Eastern Capital Limited. The address for Eastern Capital Limited is 10 Market Street #773, Camana Bay, KY1-9006, Grand Cayman, Cayman Islands.

(7) Represents shares issuable pursuant to stock options exercisable within 60 days of August 31, 2013.

(8) Represents shares issuable pursuant to stock options exercisable within 60 days of August 31, 2013.

(9) Represents 69,649 shares held directly by Ms. Dier and 166,670 shares issuable pursuant to stock options exercisable within 60 days of August 31, 2013.

(10) Represents 114,833 shares issuable pursuant to stock options exercisable within 60 days of August 31, 2013. Dr. Kitt s employment with us terminated in August 2013.

(11) Represents 2,826 shares held by The Renton Family Community Property Trust, over which Mr. Renton shares voting and dispositive power and 35,220 shares issuable pursuant to stock options held directly by Mr. Renton exercisable within 60 days of August 31, 2013.

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(12) Represents 219,433 shares held directly by Dr. Homcy, 720,191 shares issuable pursuant to stock options held directly by Dr. Homcy exercisable within 60 days of August 31, 2013 and 20,000 shares held by The Charles J. Homcy 2009 Grantor Retained Annuity Trust, for which Dr. Homcy holds voting or dispositive power.

(13) Represents 706 shares held directly by Mr. Bienaimé and 27,220 shares issuable pursuant to stock options held directly by Mr. Bienaimé exercisable within 60 days of August 31, 2013.

(14) Represents 1,102,824 shares held by Sutter Hill Ventures, 36,599 shares held by Jeffrey W. Bird and Christina R. Bird as Trustees of Jeffrey W. and Christina R. Bird Trust, 36,602 shares held by NestEgg Holdings, LP and 4,700 shares issuable pursuant to stock options held directly by Dr. Bird exercisable within 60 days of August 31, 2013. Dr. Bird is a trustee of the Jeffrey W. and Christina R. Bird Trust, which is a general partner of NestEgg Holdings, LP, and a managing director of Sutter Hill Ventures. Dr. Bird may be deemed to share voting and investment powers for the shares identified in this footnote, and disclaims beneficial ownership of all such shares except to the extent of his pecuniary interest in such shares.

(15) Represents shares issuable pursuant to stock options exercisable within 60 days of August 31, 2013.

(16) Represents 2,032,239 shares held by MPM BioVentures III-QP, L.P., 171,747 shares held by MPM BioVentures III GmbH & Co. Beteiligungs KG, 136,641 shares held by MPM BioVentures III, L.P., 61,373 shares held by MPM BioVentures III Parallel Fund, L.P., 39,344 shares held by MPM Asset Management Investors 2003 BVIII LLC and 4,700 shares issuable pursuant to stock options held directly by Dr. Galakatos exercisable within 60 days of August 31, 2013. Dr. Galakatos is a Series A Member of MPM BioVentures III LLC, which is the general partner of MPM BioVentures III GP, L.P., which is the general partner of each of MPM BioVentures III-QP, L.P., MPM BioVentures III, L.P. and MPM BioVentures III Parallel Fund, L.P., and a manager of MPM Asset Management Investors 2003 BVIII LLC and shares voting and dispositive power over the shares held by MPM BioVentures III-QP, L.P., MPM BioVentures III GmbH & Co. Beteiligungs KG, MPM BioVentures III, L.P., MPM BioVentures III Parallel Fund, L.P. and MPM Asset Management Investors 2003 BVIII LLC. Dr. Galakatos disclaims beneficial ownership of the shares identified in this footnote except to the extent of his respective proportionate pecuniary interest in such shares.

(17) Represents 1,428,954 shares held by Frazier Healthcare IV, LP, 7,252 shares held by Frazier Affiliates IV, LP and 4,700 shares issuable pursuant to stock options held directly by Dr. Topper exercisable within 60 days of August 31, 2013. Dr. Topper is a venture capitalist with Frazier Healthcare. Dr. Topper does not hold voting or dispositive power over the shares held by the Entities affiliated with Frazier Healthcare and disclaims beneficial ownership thereof except to the extent of his pecuniary interests therein.

(18) Represents 1,766 shares held directly by Mr. Wolff and 32,220 shares issuable pursuant to stock options held directly by Mr. Wolff exercisable within 60 days of August 31, 2013.

(19) Represents 314,380 shares held by our current directors and executive officers, 2,118,651 shares issuable pursuant to stock options exercisable within 60 days of August 31, 2013 and 5,053,575 shares held by entities affiliated with certain of our directors.

(20) Represents 178,557 shares held directly by Dr. Phillips and 99,731 shares issuable pursuant to stock options held directly by Dr. Phillips exercisable within 60 days of August 31, 2013. Dr. Phillips is one of our co-founders and was an employee until January 2012. Dr. Phillips has served as a consultant since such time.

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Description of capital stock

General

Our amended and restated certificate of incorporation authorizes common stock and authorizes shares of undesignated preferred stock, the rights, preferences and privileges of which may be designated from time to time by our board of directors.

Our authorized capital stock consists of 105,000,000 shares, all with a par value of $0.001 per share, of which:

- 100,000,000 shares are designated as common stock; and
- 5,000,000 shares are designated as preferred stock.

As of June 30, 2013, we had outstanding no shares of preferred stock and 35,171,769 shares of our common stock. Our outstanding capital stock was held by 227 stockholders of record as of June 30, 2013. As of June 30, 2013, we also had outstanding options to acquire 3,787,915 shares of common stock held by employees, directors and consultants pursuant to our 2003 Equity Incentive Plan and 2013 Equity Incentive Plan, having a weighted-average exercise price of $7.50 per share.

Common stock

Voting rights

Each holder of our common stock is entitled to one vote for each share of common stock held on all matters submitted to a vote of stockholders, except as otherwise expressly provided in our amended and restated certificate of incorporation or required by applicable law. Cumulative voting for the election of directors is not provided for in our amended and restated certificate of incorporation, which means that the holders of a majority of our shares of common stock can elect all of the directors then standing for election.

Economic rights

Dividends and distributions. Subject to preferences that may apply to any shares of convertible preferred stock outstanding at the time, the holders of outstanding shares of our common stock are entitled to receive dividends out of funds legally available at the times and in the amounts that our board of directors may determine.

Liquidation rights. Upon our liquidation, dissolution or winding-up, the assets legally available for distribution to our stockholders would be distributable ratably among the holders of our common stock and any participating convertible preferred stock outstanding at that time after payment of liquidation preferences, on any outstanding shares of convertible preferred stock and payment of other claims of creditors.

The rights, preferences, and privileges of holders of our common stock are subject to, and may be adversely affected by, the rights of holders of shares of any series of convertible preferred stock that we may designate and issue in the future.

Preemptive or similar rights. Our common stock is not entitled to preemptive rights and is not subject to conversion or redemption.

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Preferred stock

As of June 30, 2013, there were no shares of our convertible preferred stock outstanding.

Our board of directors may, without further action by our stockholders, fix the rights, preferences, privileges and restrictions of up to an aggregate of 5,000,000 shares of preferred stock in one or more series and authorize their issuance. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of our common stock. The issuance of our preferred stock could adversely affect the voting power of holders of our common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change of control or other corporate action. No shares of preferred stock are outstanding, and we have no present plan to issue any shares of preferred stock.

Warrants

As of June 30, 2013, we had three warrants to purchase an aggregate of 1,500 shares of our common stock with an exercise price of $13.10 per share outstanding. Each of these warrants has a net exercise provision under which the holder, in lieu of payment of the exercise price in cash, can surrender the warrant and receive a net number of shares of our common stock based on the fair market value of such stock at the time of exercise of the warrant after deduction of the aggregate exercise price. Unless earlier exercised, these warrants will expire on May 22, 2020.

As of June 30, 2013, we had a warrant to purchase the number of shares of our common stock equal to 1.9% of our utilization of the credit line provided by General Electric Capital Corporation, rounded down to the nearest whole share, with an exercise price of $10.00 per share outstanding. As of June 30, 2013, there were 4,740 shares of our common stock issuable pursuant to the exercise of this warrant. This warrant has a net exercise provision under which the holder, in lieu of payment of the exercise price in cash, can surrender the warrant and receive a net number of shares of common stock based on the fair market value of such stock at the time of exercise of the warrant after deduction of the aggregate exercise price. Unless earlier exercised, this warrant will expire on January 21, 2015.

As of June 30, 2013, we had two warrants to purchase an aggregate of 76,335 shares of our common stock with an exercise price of $13.10 per share outstanding. Each of these warrants has a net exercise provision under which the holder, in lieu of payment of the exercise price in cash, can surrender the warrant and receive a net number of shares of our common stock based on the fair market value of such stock at the time of exercise of the warrant after deduction of the aggregate exercise price. Unless earlier exercised, these warrants will expire on September 29, 2016.

Registration rights

Stockholder registration rights

We are party to an investor rights agreement which provides that holders of shares of our common stock issued pursuant to the conversion of our convertible preferred stock have certain registration rights, as set forth below. This investor rights agreement was entered into in November 2003 and has been amended and/or restated from time to time in connection with our preferred stock financings. The

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registration of shares of our common stock pursuant to the exercise of registration rights described below would enable the holders to sell these shares without restriction under the Securities Act of 1933, as amended, when the applicable registration statement is declared effective. We will pay the registration expenses, other than underwriting discounts and commissions, of the shares registered pursuant to the demand, piggyback and Form S-3 registrations described below.

Generally, in an underwritten offering, the managing underwriter, if any, has the right, subject to specified conditions, to limit the number of shares such holders may include. The demand, piggyback and Form S-3 registration rights described below will expire the later of (i) May 22, 2014 or (ii) with respect to each stockholder, at such time as (A) our capital stock is publicly traded and (B) such stockholder is entitled to sell all of its shares pursuant to Rule 144 of the Securities Act during any 90-day period.

Demand registration rights

The holders of an aggregate of 24,103,132 shares of our common stock issued upon the conversion of our convertible preferred stock and shares of common stock currently subject to certain outstanding warrants, without giving effect to the sale of shares in this offering by the selling stockholders, will be entitled to certain demand registration rights. At any time beginning 180 days after the closing of our initial public offering, the holders of a majority of these shares may, on not more than two occasions, request that we file a registration statement having an aggregate offering price to the public of not less than $10,000,000 to register all or a portion of their shares.

Piggyback registration rights

In connection with this offering, the holders of an aggregate of 24,107,872 shares of our common stock issued upon the conversion of our convertible preferred stock and shares of common stock currently subject to certain outstanding warrants, without giving effect to the sale of shares in this offering by the selling stockholders, were entitled to, and the necessary percentage of holders waived, their rights to include their shares of registrable securities in this offering. In the event that we propose to register any of our securities under the Securities Act of 1933, as amended, either for our own account or for the account of other security holders, the holders of these shares will be entitled to certain piggyback registration rights allowing them to include their shares in such registration, subject to certain marketing and other limitations. As a result, whenever we propose to file a registration statement under the Securities Act of 1933, as amended, including a registration statement on Form S-3 as discussed below, other than with respect to a demand registration or a registration statement on Forms S-4 or S-8, the holders of these shares are entitled to notice of the registration and have the right, subject to limitations that the underwriters may impose on the number of shares included in the registration, to include their shares in the registration.

Form S-3 registration rights

The holders of an aggregate of 24,103,132 shares of our common stock issued upon the conversion of our convertible preferred stock and shares of common stock currently subject to certain outstanding warrants, without giving effect to the sale of shares in this offering by the selling stockholders, will be entitled to certain Form S-3 registration rights. Such holders may make a request that we register their shares on Form S-3 if we are qualified to file a registration statement on Form S-3. Such request for registration on Form S-3 must cover securities the aggregate offering price of which, before payment of underwriting discounts and commissions, is at least $5,000,000.

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Anti-takeover provisions

Certificate of incorporation and bylaws

Our amended and restated certificate of incorporation provides for our board of directors to be divided into three classes with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. Because our stockholders do not have cumulative voting rights, our stockholders holding a majority of the voting power of our shares of common stock outstanding will be able to elect all of our directors. The directors may be removed by the stockholders only for cause upon the vote of holders of a majority of the shares then entitled to vote at an election of directors. Furthermore, the authorized number of directors may be changed only by resolution of our board of directors, and vacancies and newly created directorships on our board of directors may, except as otherwise required by law or determined by our board, only be filled by a majority vote of the directors then serving on the board, even though less than a quorum. Our amended and restated certificate of incorporation and amended and restated bylaws provide that all stockholder actions must be effected at a duly called meeting of stockholders and not by a consent in writing. A special meeting of stockholders may be called only by a majority of our whole board of directors, the chair of our board of directors, our chief executive officer or our president. Our amended and restated bylaws also provide that stockholders seeking to present proposals before a meeting of stockholders to nominate candidates for election as directors at a meeting of stockholders must provide timely advance notice in writing, and will specify requirements as to the form and content of a stockholder s notice.

Our amended and restated certificate of incorporation further provides that the affirmative vote of holders of at least 66 2/3% of the voting power of all of the then outstanding shares of voting stock, voting as a single class, is required to amend certain provisions of our certificate of incorporation, including provisions relating to the structure of our board of directors, the size of the board, removal of directors, special meetings of stockholders, actions by written consent and cumulative voting. The affirmative vote of holders of at least 66 2/3% of the voting power of all of the then outstanding shares of voting stock, voting as a single class, is required to amend or repeal our bylaws, although our bylaws may be amended by a simple majority vote of our board of directors.

The foregoing provisions will make it more difficult for our existing stockholders to replace our board of directors as well as for another party to obtain control of the Company by replacing our board of directors. Since our board of directors has the power to retain and discharge our officers, these provisions could also make it more difficult for existing stockholders or another party to effect a change in management. In addition, the authorization of 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 change the control of the Company.

These provisions are intended to enhance the likelihood of continued stability in the composition of our board of directors and its policies and to discourage certain types of transactions that may involve an actual or threatened acquisition of the Company. These provisions are also designed to reduce our vulnerability to an unsolicited acquisition proposal and to discourage certain tactics that may be used in proxy rights. However, such provisions could have the effect of discouraging others from making tender offers for our shares and may have the effect of deterring hostile takeovers or delaying changes in control of the Company or our management. As a consequence, these provisions also may inhibit fluctuations in the market price of our stock that could result from actual or rumored takeover attempts.

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Section 203 of the Delaware general corporation law

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years after the date that such stockholder became an interested stockholder, with the following exceptions:

- before such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon closing of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction began, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned by (i) persons who are directors and also officers and (ii) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or after such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of the stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

In general, Section 203 defines business combination to include the following:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;
- subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loss, advances, guarantees, pledges or other financial benefits by or through the corporation.

In general, Section 203 defines an interested stockholder as an entity or person who, together with the person s affiliates and associates, beneficially owns, or within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

Limitations of liability and indemnification

See the section of this prospectus entitled Executive compensation Limitation on liability and indemnification matters.

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Listing

Our common stock is listed on The NASDAQ Global Market under the trading symbol PTLA.

Transfer agent and registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

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Shares eligible for future sale

Future sales of our common stock in the public market, or the availability of such shares for sale in the public market, could adversely affect market prices prevailing from time to time. As described below, only a limited number of shares are currently available for sale due to contractual and legal restrictions on resale. Nevertheless, sales of our common stock in the public market after such restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price at such time and our ability to raise equity capital in the future.

Based on the number of shares outstanding as of June 30, 2013, upon the closing of this offering, 39,629,479 shares of our common stock will be outstanding, assuming no exercise of the underwriters option to purchase additional shares of common stock and no exercise of outstanding options or warrants. Of the outstanding shares, all of the shares sold in this offering and in our initial public offering, in each case not subject to any lock-up agreements as described below, will be freely tradable, except that any shares held by our affiliates, as that term is defined in Rule 144 under the Securities Act of 1933, as amended, or the Securities Act, may only be sold in compliance with the limitations described below.

The remaining shares of our common stock outstanding after this offering are restricted securities, as such term is defined in Rule 144 under the Securities Act, or are subject to lock-up agreements with us as described below. Following the expiration of the lock-up period, restricted securities may be sold in the public market only if registered or if they qualify for an exemption from registration under Rule 144 or 701 promulgated under the Securities Act, described in greater detail below.

Rule 144

In general, a person who has beneficially owned restricted shares of our common stock for at least six months would be entitled to sell their securities provided that (i) such person is not deemed to have been one of our affiliates at the time of, or at any time during the 90 days preceding a sale and (ii) we are subject to the periodic reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, for at least 90 days before the sale. Persons who have beneficially owned restricted shares of our common stock for at least six months but who are our affiliates at the time of, or any time during the 90 days preceding, a sale, would be subject to additional restrictions, by which such person would be entitled to sell within any three-month period only a number of securities that does not exceed the greater of either of the following:

- 1% of the number of shares of our common stock outstanding after this offering, which will equal approximately 396,295 shares immediately after the closing of this offering, based on the number of common shares outstanding as of June 30, 2013 and assuming no exercise of the underwriters option to purchase additional shares of our common stock; or

- the average weekly trading volume of our common stock on The NASDAQ Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale;

provided, in each case, that we are subject to the periodic reporting requirements of the Exchange Act for at least 90 days before the sale. Such sales both by affiliates and by non-affiliates must also comply with the manner of sale, current public information and notice provisions of Rule 144.

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Rule 701

In general, under Rule 701 of the Securities Act, any of an issuer s employees, consultants or advisors who purchased shares from the issuer in connection with a qualified compensatory stock plan or other written agreement before the effective date of a registration statement under the Securities Act is eligible to resell those shares in reliance on Rule 144. An affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding period requirements of Rule 144, and a non-affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding period requirements of Rule 144 and without regard to the volume of such sales or the availability of public information about the issuer.

The Securities and Exchange Commission has indicated that Rule 701 will apply to typical stock options granted by an issuer before it becomes subject to the reporting requirements of the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after an issuer becomes subject to the reporting requirements of the Exchange Act. In 2013 we filed a registration statement on Form S-1 under the Securities Act to register shares in connection with our initial public offering and a registration statement on Form S-8 under the Securities Act to register all of the shares of our common stock subject to outstanding options and other awards issuable pursuant to our 2003 Equity Incentive Plan and 2013 Equity Incentive Plan.

Lock-up agreements

In connection with our initial public offering, we, our directors and officers, and substantially all of our stockholders and optionholders agreed with the underwriters that through November 17, 2013, we will not offer, sell, assign, transfer, pledge, contract to sell or otherwise dispose of or hedge any shares of our common stock or any securities convertible into or exchangeable for shares of our common stock, subject to specified exceptions. Morgan Stanley & Co. LLC and Credit Suisse Securities (USA) LLC may, in their sole discretion, at any time, release all or any portion of the shares from the restrictions in this agreement and have released us and the selling stockholders from such restrictions solely with respect to the shares being sold in this offering.

In addition, in connection with this offering, we, all of our directors and executive officers, each of the selling stockholders and certain of our other stockholders have agreed to abide by the restrictions described above for their shares of common stock for an additional period ending 90 days after the date of this prospectus as described in further detail under the section of this prospectus titled Underwriting.

Registration rights

The holders of shares of our common stock issued upon the conversion of our convertible preferred stock and certain warrants to purchase shares of our common stock, or their transferees, are entitled to certain rights with respect to the registration of those shares under the Securities Act of 1933, as amended. For a description of these registration rights, see the section of this prospectus entitled Description of capital stock Registration rights. If these shares are registered, they will be freely tradable without restriction under the Securities Act of 1933, as amended.

Equity incentive plans

We have filed a Form S-8 registration statement under the Securities Act of 1933, as amended, to register shares of our common stock issued or reserved for issuance under our equity compensation

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plans and agreements. Accordingly, the shares covered by this registration statement are eligible for sale in the public markets, subject to vesting restrictions, the lock-up agreements described above and Rule 144 limitations applicable to affiliates. For a more complete discussion of our equity compensation plans, see the section of this prospectus entitled Executive compensation Employee benefit and stock plans.

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Material United States federal income tax consequences to non-U.S. holders

The following is a summary of the material United States federal income and estate tax consequences to non-U.S. holders (as defined below) of the acquisition, ownership and disposition of our common stock issued pursuant to this offering. This discussion is not a complete analysis of all potential United States federal income tax consequences relating thereto, does not address the potential application of the Medicare contribution tax and does not address any gift tax consequences or any tax consequences arising under any state, local or foreign tax laws, or any other United States federal tax laws. This discussion is based on the Internal Revenue Code of 1986, as amended, or the Code, Treasury Regulations promulgated thereunder, judicial decisions and published rulings and administrative pronouncements of the Internal Revenue Service, or IRS, all as in effect as of the date of this prospectus. These authorities may change, possibly retroactively, resulting in United States federal income tax consequences different from those discussed below.

This discussion is limited to non-U.S. holders who purchase our common stock issued pursuant to this offering and who hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all of the United States federal income tax consequences that may be relevant to a particular holder in light of such holder s particular circumstances. This discussion also does not consider any specific facts or circumstances that may be relevant to holders subject to special rules under the United States federal income tax laws, including, without limitation, certain former citizens or long-term residents of the United States, partnerships or other pass-through entities, controlled foreign corporations, passive foreign investment companies, corporations that accumulate earnings to avoid United States federal income tax, banks, financial institutions, investment funds, insurance companies, brokers, dealers or traders in securities, commodities or currencies, tax-exempt organizations, tax-qualified retirement plans, persons subject to the alternative minimum tax, persons that own, or have owned, actually or constructively, more than 5% of our common stock and persons holding our common stock as part of a hedging or conversion transaction or straddle, or a constructive sale, or other risk reduction strategy.

PROSPECTIVE INVESTORS SHOULD CONSULT THEIR TAX ADVISORS REGARDING THE PARTICULAR UNITED STATES FEDERAL INCOME TAX CONSEQUENCES TO THEM OF ACQUIRING, OWNING AND DISPOSING OF OUR COMMON STOCK, AS WELL AS ANY TAX CONSEQUENCES ARISING UNDER ANY STATE, LOCAL OR FOREIGN TAX LAWS AND ANY OTHER UNITED STATES FEDERAL TAX LAWS.

Definition of non-U.S. holder

For purposes of this discussion, a non-U.S. holder is any beneficial owner of our common stock that is not a United States person or a partnership (including any entity or arrangement treated as a partnership) for United States federal income tax purposes. A United States person is any of the following:

- an individual citizen or resident of the United States;
- a corporation (or other entity treated as a corporation for United States federal income tax purposes) created or organized under the laws of the United States, any state thereof or the District of Columbia;
- an estate, the income of which is subject to United States federal income tax regardless of its source; or

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a trust (1) whose administration is subject to the primary supervision of a United States court and which has one or more United States persons who have the authority to control all substantial decisions of the trust, or (2) that has a valid election in effect under applicable Treasury Regulations to be treated as a United States person.

Distributions on our common stock

If we make cash or other property distributions on our common stock, such distributions will constitute dividends for United States federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under United States federal income tax principles. Amounts not treated as dividends for United States federal income tax purposes will constitute a return of capital and will first be applied against and reduce a holder s tax basis in our common stock, but not below zero. Any excess will be treated as gain realized on the sale or other disposition of our common stock and will be treated as described under the section of this prospectus entitled Gain on disposition of our common stock below.

Dividends (out of earnings and profits) paid to a non-U.S. holder of our common stock generally will be subject to United States federal withholding tax at a rate of 30% of the gross amount of the dividends, or such lower rate specified by an applicable income tax treaty. To receive the benefit of a reduced treaty rate, a non-U.S. holder must furnish to us or our paying agent a valid IRS Form W-8BEN (or applicable successor form) including a United States taxpayer identification number and certifying such holder s qualification for the reduced rate. This certification must be provided to us or our paying agent prior to the payment of dividends and must be updated periodically. If the non-U.S. holder holds the stock through a financial institution or other agent acting on the non-U.S. holder s behalf, the non-U.S. holder will be required to provide appropriate documentation to the agent, which then will be required to provide certification to us or our paying agent, either directly or through other intermediaries.

Non-U.S. holders that do not timely provide us or our paying agent with the required certification, but that qualify for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS.

If a non-U.S. holder holds our common stock in connection with the conduct of a trade or business in the United States, and dividends paid on our common stock are effectively connected with such holder s United States trade or business (and are attributable to such holder s permanent establishment in the United States if required by an applicable tax treaty), the non-U.S. holder will be exempt from United States federal withholding tax. To claim the exemption, the non-U.S. holder must generally furnish to us or our paying agent a properly executed IRS Form W-8ECI (or applicable successor form).

Any dividends paid on our common stock that are effectively connected with a non-U.S. holder s United States trade or business (and if an income tax treaty applies, are attributable to a permanent establishment maintained by the non-U.S. holder in the United States) generally will be subject to United States federal income tax on a net income basis at the regular graduated United States federal income tax rates in much the same manner as if such holder were a resident of the United States. A non-U.S. holder that is a foreign corporation also may be subject to an additional branch profits tax equal to 30% (or such lower rate specified by an applicable income tax treaty) of its effectively connected earnings and profits for the taxable year, as adjusted for certain items. Non-U.S. holders should consult any applicable income tax treaties that may provide for different rules.

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Gain on disposition of our common stock

Subject to the discussion below regarding backup withholding and certain recently enacted legislation, a non-U.S. holder generally will not be subject to United States federal income tax on any gain realized upon the sale or other disposition of our common stock, unless:

- the gain is effectively connected with the non-U.S. holder s conduct of a trade or business in the United States, and if an income tax treaty applies, is attributable to a permanent establishment maintained by the non-U.S. holder in the United States;

- the non-U.S. holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition, and certain other requirements are met; or

- our common stock constitutes a United States real property interest by reason of our status as a United States real property holding corporation, or USRPHC, for United States federal income tax purposes at any time within the shorter of the five-year period preceding the disposition or the non-U.S. holder s holding period for our common stock, and our common stock has ceased to be regularly traded on an established securities market prior to the beginning of the calendar year in which the sale or other disposition occurs. The determination of whether we are a USRPHC depends on the fair market value of our United States real property interests relative to the fair market value of our other trade or business assets and our foreign real property interests. We believe we are not currently and do not anticipate becoming a USRPHC for United States federal income tax purposes.

Gain described in the first bullet point above generally will be subject to United States federal income tax on a net income basis at the regular graduated United States federal income tax rates in the same manner as if such holder were a resident of the United States. A non-U.S. holder that is a foreign corporation also may be subject to an additional branch profits tax equal to 30% (or such lower rate specified by an applicable income tax treaty) of its effectively connected earnings and profits for the taxable year, as adjusted for certain items.

Non-U.S. holders should consult any applicable income tax treaties that may provide for different rules.

Gain described in the second bullet point above will be subject to United States federal income tax at a flat 30% rate (or such lower rate specified by an applicable income tax treaty), but may be offset by United States-source capital losses (even though the individual is not considered a resident of the United States), provided that the non-U.S. holder has timely filed United States federal income tax returns with respect to such losses.

Information reporting and backup withholding

We must report annually to the IRS and to each non-U.S. holder the amount of dividends on our common stock paid to such holder and the amount of any tax withheld with respect to those dividends. These information reporting requirements apply even if no withholding was required because the dividends were effectively connected with the holder s conduct of a United States trade or business, or withholding was reduced or eliminated by an applicable income tax treaty. This information also may be made available under a specific treaty or agreement with the tax authorities in the country in which the non-U.S. holder resides or is established. Backup withholding, currently at a 28% rate, generally will not apply to payments to a non-U.S. holder of dividends on or the gross proceeds of a disposition

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of our common stock provided the non-U.S. holder furnishes to us or our paying agent the required certification as to its non-U.S. status, such as by providing a valid IRS Form W-8BEN or IRS Form W-8ECI, or certain other requirements are met. Notwithstanding the foregoing, backup withholding may apply if either we or our paying agent has actual knowledge, or reason to know, that the holder is a United States person who is not an exempt recipient.

Backup withholding is not an additional tax. If any amount is withheld under the backup withholding rules, the non-U.S. holder should consult with a United States tax advisor regarding the possibility of and procedure for obtaining a refund or a credit against the non-U.S. holder s United States federal income tax liability, if any.

Recently enacted legislation affecting taxation of our common stock held by or through foreign entities

Sections 1471 through 1474 of the Code (commonly referred to as FATCA) will impose a United States federal withholding tax of 30% on certain payments made to a foreign financial institution (as specially defined under these rules) unless such institution enters into an agreement with the United States government to withhold on certain payments and to collect and provide to the United States tax authorities substantial information regarding United States account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with United States owners) or an exemption applies. FATCA also generally will impose a United States federal withholding tax of 30% on certain payments made to a non-financial foreign entity unless such entity provides the withholding agent a certification identifying the direct and indirect United States owners of the entity or an exemption applies. Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of such taxes. Under certain transition rules, these withholding taxes would be imposed on dividends paid on our common stock after June 30, 2014, and on gross proceeds from sales or other dispositions of our common stock after December 31, 2016.

Prospective investors are encouraged to consult with their own tax advisors regarding the possible implications of this legislation on their investment in our common stock.

Estate tax

Individual non-U.S. holders and entities whose property is potentially includible in such an individual s gross estate for United States federal estate tax purposes (for example, a trust funded by such an individual and with respect to which the individual has retained certain interests or powers), should note that, absent an applicable treaty benefit, our common stock will be treated as United States situs property subject to United States federal estate tax.

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Underwriting

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus, the underwriters named below, for whom Morgan Stanley & Co. LLC and Credit Suisse Securities (USA) LLC are acting as representatives, have severally agreed to purchase from us and the selling stockholders, and we and the selling stockholders have agreed to sell to them, the number of shares indicated below:

Name	Number of shares
Morgan Stanley & Co. LLC	2,705,768
Credit Suisse Securities (USA) LLC	2,069,117
Cowen and Company, LLC	954,977
William Blair & Company, L.L.C.	381,991
Sanford C. Bernstein & Co., LLC	254,660
Total:	6,366,513

The underwriters and the representatives are collectively referred to as the underwriters and the representatives, respectively. The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters option to purchase additional shares described below.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the public offering price listed on the cover page of this prospectus and part to certain dealers at a price that represents a concession not in excess of $0.855 a share under the public offering price. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to 954,976 additional shares of common stock at the public offering price listed on the cover page of this prospectus, less underwriting discounts and commissions. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase about the same percentage of the additional shares of common stock as the number listed next to the underwriter s name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table.

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The following table shows the per share and total public offering price, underwriting discounts and commissions, and proceeds before expenses to us and the selling stockholders. These amounts are shown assuming both no exercise and full exercise of the underwriters option to purchase up to an additional 954,976 shares of our common stock.

		Total	
	Per share	**No exercise**	**Full exercise**
Public offering price	$ 23.75	$ 151,204,684	$ 173,885,364
Underwriting discounts and commissions paid by us and the selling stockholders	$ 1.425	$ 9,072,281	$ 10,433,122
Proceeds, before expenses, to us and the selling stockholders	$ 22.325	$ 142,132,403	$ 163,452,242

The estimated offering expenses payable by us, exclusive of underwriting discounts and commissions, are approximately $760,000. We have agreed to reimburse the underwriters for expenses of approximately $10,000 relating to the clearance of this offering with the Financial Industry Regulatory Authority, Inc. The underwriters have agreed to reimburse us for a portion of our expenses relating to this offering.

Our common stock is listed on The NASDAQ Global Market under the trading symbol PTLA.

In connection with our initial public offering, we and all directors and officers and the holders of substantially all of our outstanding stock and stock options agreed that, without the prior written consent of Morgan Stanley & Co. LLC and Credit Suisse Securities (USA) LLC on behalf of the underwriters, we and they will not, during the period ending November 17, 2013, or the restricted period:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for shares of common stock;

- file any registration statement with the Securities and Exchange Commission relating to the offering of any shares of common stock or any securities convertible into or exercisable or exchangeable for common stock; or

- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of our common stock;

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. In addition, we and each such person agreed that, without the prior written consent of Morgan Stanley & Co. LLC and Credit Suisse Securities (USA) LLC on behalf of the underwriters, we or such other person will not, during the restricted period, make any demand for, or exercise any right with respect to, the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock.

The restrictions described in the immediately preceding paragraph do not apply to:

- the sale of shares to the underwriters;

- our issuance of common stock upon the exercise of an option or a warrant or the conversion of a security outstanding on the date of this prospectus and disclosed in this prospectus;

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our issuance of shares or options to purchase shares of our common stock to our employees, officers, directors, advisors or consultants pursuant to employee benefit plans described in this prospectus, provided that, prior to the issuance of any such shares or the grant of any such options, we shall cause each recipient of such grant or issuance to execute and deliver a lock-up agreement;

our filing of registration statements on Form S-8 with respect to the employee benefit plans described in this prospectus;

the sale or issuance of or entry into an agreement to sell or issue shares of our common stock in connection with our acquisition of one or more businesses, products or technologies (whether by means of merger, stock purchase, asset purchase or otherwise) or in connection with joint ventures, commercial relationships or other strategic transactions; provided, that, the aggregate number of shares of our common stock that we may sell or issue or agree to sell or issue pursuant to this clause shall not exceed 5% of the total number of shares of our common stock issued and outstanding immediately following the closing of our initial public offering and provided further that we shall cause each recipient of such shares to execute and deliver, on or prior to such issuance, a lock-up agreement;

transfers of shares as a bona fide gift, distributions to limited partners, members or stockholders, transfers by will or intestate succession or to any trust or partnership for the benefit of the lock-up signatory or members of the lock-up signatory s immediate family, or the net exercise of stock options issued under our equity incentive plans, provided in each case that (1) each donee, distributee and transferee shall sign and deliver a lock-up agreement to the underwriters and (2) no filing under Section 16(a) of the Exchange Act shall be required or voluntarily made during the restricted period;

the establishment of a trading plan pursuant to Rule 10b5-1 under the Securities Exchange Act of 1934, as amended, or the Exchange Act, for the transfer of shares of common stock, provided that (i) such plan does not provide for the transfer of common stock during the restricted period and (ii) no public announcement or filing under the Exchange Act is required of or voluntarily made by or on behalf of the lock-up signatory or us regarding the establishment of such plan; or

for entities affiliated with our existing stockholders that are not our affiliates, the sale or transfer of any shares purchased in this offering.

For the purposes of this offering, the representatives intend to waive, solely with respect to the shares being offered in this offering, the restrictions under these lock-up agreements applicable to us and the selling stockholders.

In addition, in connection with this offering, we, our directors and executive officers, each of the selling stockholders and certain other stockholders, with respect to an aggregate of 10,989,682 shares of our outstanding common stock, have agreed to abide by the restrictions described above for their shares of common stock for an additional period ending 90 days after the date of this prospectus.

Morgan Stanley & Co. LLC and Credit Suisse Securities (USA) LLC, in their sole discretion, may release our common stock and other securities subject to the lock-up agreements described above in whole or in part at any time with or without notice.

In order to facilitate the offering of our common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of our common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting

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agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the option. The underwriters can close out a covered short sale by exercising the option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the option. The underwriters may also sell shares in excess of the option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of common stock on The NASDAQ Global Market to stabilize the price of our common stock. These activities may raise or maintain the market price of our common stock above independent market levels or prevent or retard a decline in the market price of our common stock. The underwriters are not required to engage in these activities and may end any of these activities at any time. Neither we, the selling stockholders, nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of the common stock. In addition, neither we, the selling stockholders, nor any of the underwriters make any representation that the representatives will engage in these stabilizing transactions or that any transaction, once commenced, will not be discontinued without notice.

We and the selling stockholders have agreed to indemnify the underwriters, and the underwriters have agreed to indemnify us and the selling stockholders, in each case against certain liabilities, including liabilities under the Securities Act.

A prospectus in electronic format may be made available on websites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The representatives may agree to allocate a number of shares of common stock to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters that may make Internet distributions on the same basis as other allocations.

Selling restrictions

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State) an offer to the public of any shares of our common stock may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any shares of our common stock may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;
(b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or
(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

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For the purposes of this provision, the expression an offer to the public in relation to any shares of our common stock in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of our common stock to be offered so as to enable an investor to decide to purchase any shares of our common stock, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State, and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

United Kingdom

Each underwriter has represented and agreed that:

(a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000, as amended (the FSMA)) received by it in connection with the issue or sale of the shares of our common stock in circumstances in which Section 21(1) of the FSMA does not apply to us; and

(b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares of our common stock in, from or otherwise involving the United Kingdom.

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Legal matters

Cooley LLP, San Francisco and Palo Alto, California, will pass upon the validity of the shares of common stock offered hereby. The underwriters are being represented by Davis Polk & Wardwell LLP, Menlo Park, California, in connection with the offering.

Experts

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements at December 31, 2011 and 2012, and for each of the three years in the period ended December 31, 2012, as set forth in their report. We have included our financial statements in this prospectus and elsewhere in the registration statement in reliance on Ernst & Young LLP s report, given on their authority as experts in accounting and auditing.

Where you can find more information

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to this offering of our common stock. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement, some items of which are contained in exhibits to the registration statement as permitted by the rules and regulations of the SEC. For further information with respect to us and our common stock, we refer you to the registration statement, including the exhibits and the financial statements and notes filed as a part of the registration statement. Statements contained in this prospectus concerning the contents of any contract or any other document are not necessarily complete. If a contract or document has been filed as an exhibit to the registration statement, please see the copy of the contract or document that has been filed. Each statement in this prospectus relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit. The exhibits to the registration statement should be referenced for the complete contents of these contracts and documents. A copy of the registration statement and the exhibits filed therewith may be inspected without charge at the public reference room of the SEC, located at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You may obtain information on the operation of the public reference rooms by calling the SEC at 1-800-SEC-0330. The SEC also maintains an Internet website that contains reports, proxy statements, and other information about issuers, like us, that file electronically with the SEC. The address of that website is *www.sec.gov*.

We are subject to the information and reporting requirements of the Exchange Act and, in accordance with this law, we file periodic reports, proxy statements, and other information with the SEC. These periodic reports, proxy statements, and other information are available for inspection and copying at the SEC s public reference facilities and the website of the SEC referred to above. We also maintain a website at *www.portola.com*. You may access our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not incorporated by reference into this prospectus.

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PORTOLA PHARMACEUTICALS, INC.

INDEX TO FINANCIAL STATEMENTS

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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, 2011 and 2012, and the related statements of operations, comprehensive income (loss), convertible preferred stock and stockholders deficit, and cash flows for each of the three years in the period ended December 31, 2012. 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, 2011 and 2012, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2012, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Redwood City, California

March 12, 2013, except for the last paragraph of Note 2, as to which the date is May 17, 2013.

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PORTOLA PHARMACEUTICALS, INC.

Balance Sheets

(In thousands, except share and per share data)

	December 31, 2011	December 31, 2012
Assets		
Current assets:		
Cash and cash equivalents	$ 170,323	$ 53,613
Short-term investments	17,766	77,656
Receivables from collaborations	955	662
Prepaid expenses and other current assets	471	2,982
Total current assets	189,515	134,913
Property and equipment, net	3,888	2,861
Long-term investments		6,115
Other assets		2,112
Total assets	$ 193,403	$ 146,001
Liabilities, convertible preferred stock and stockholders (deficit)		
Current liabilities:		
Accounts payable	$ 2,823	$ 4,840
Accrued compensation and employee benefits	2,840	1,860
Accrued and other liabilities	4,034	7,399
Deferred revenue, current portion	9,924	4,042
Convertible preferred stock warrant liability	766	683
Total current liabilities	20,387	18,824
Deferred revenue, long-term	59,544	
Other long-term liabilities	2,297	1,466
Total liabilities	82,228	20,290
Commitments and contingencies (Note 12)		
Convertible preferred stock, $0.001 par value, 243,258,300 shares authorized at December 31, 2011 and 2012, and 24,026,797 shares issued and outstanding at December 31, 2011 and 2012; redemption value of $317,280 at December 31, 2011 and 2012	317,280	317,280
Stockholders (deficit):		
Common stock, $0.001 par value, 300,000,000 shares authorized at December 31, 2011 and 2012, 1,279,732 and 1,385,508 shares issued and outstanding at December 31, 2011 and 2012	1	1
Additional paid-in capital	7,581	10,717
Accumulated deficit	(213,686)	(202,320)
Accumulated other comprehensive income (loss)	(1)	33
Total stockholders (deficit)	(206,105)	(191,569)
Total liabilities, convertible preferred stock and stockholders (deficit)	$ 193,403	$ 146,001

See accompanying notes

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PORTOLA PHARMACEUTICALS, INC.

Statements of Operations

(In thousands, except share and per share data)

	Year Ended December 31,		
	2010	**2011**	**2012**
Collaboration and license revenue	$ 35,268	$ 78,029	$ 72,042
Operating expenses:			
Research and development	43,260	46,089	49,717
General and administrative	10,762	12,071	11,469
Total operating expenses	54,022	58,160	61,186
Income (loss) from operations	(18,754)	19,869	10,856
Interest and other income, net	1,659	136	510
Interest expense	(380)	(21)	
Income (loss) before income taxes	(17,475)	19,984	11,366
Provision for income taxes	2,794		
Net income (loss)	$ (20,269)	$ 19,984	$ 11,366
Net income (loss) attributable to common stockholders:			
Basic	$ (20,269)	$ 79	$
Diluted	$ (20,269)	$ 127	$
Net income (loss) per share attributable to common stockholders:			
Basic	$ (16.79)	$ 0.06	$ 0.00
Diluted	$ (16.79)	$ 0.06	$ 0.00
Shares used to compute net income (loss) per share attributable to common stockholders:			
Basic	1,207,106	1,249,778	1,350,939
Diluted	1,207,106	2,089,206	2,048,867

See accompanying notes

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PORTOLA PHARMACEUTICALS, INC.

Statements of Comprehensive Income (Loss)

(In thousands)

	Year Ended December 31,		
	2010	**2011**	**2012**
Net income (loss)	$ (20,269)	$ 19,984	$ 11,366
Other comprehensive income (loss):			
Unrealized gain on available-for-sale securities, net of tax	3	3	34
Total comprehensive income (loss)	$ (20,266)	$ 19,987	$ 11,400

See accompanying notes

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PORTOLA PHARMACEUTICALS, INC.

Statements of Convertible Preferred Stock and Stockholders Deficit

(In thousands, except share and per share data)

	Convertible Preferred Stock		Common Stock					
	Shares	Amount	Shares	Amount	Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders Deficit
Balance at December 31, 2009	17,103,729	$ 220,374	1,165,850	$ 1	$ 3,154	$ (213,401)	$ (7)	$ (210,253)
Exercise of employee stock options for cash			37,545		101			101
Lapse of repurchase rights related to common shares issued pursuant to early exercises			21,387		77			77
Employee stock-based compensation expense					1,763			1,763
Compensation expense relating to stock options granted to consultants					171			171
Unrealized gain on available-for-sale securities, net of tax							3	3
Net loss						(20,269)		(20,269)
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 at $14.15 per share, net of issuance costs of $115	6,287,026	88,962			(115)			(115)
Issuance of Series 1 convertible preferred stock at $14.15 per share, net of issuance costs of $91	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)

See accompanying notes

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PORTOLA PHARMACEUTICALS, INC.

Statements of Cash Flows

(In thousands)

	Year Ended December 31,		
	2010	**2011**	**2012**
Operating activities			
Net income (loss)	$ (20,269)	$ 19,984	$ 11,366
Adjustments to reconcile net income (loss) to cash used in operating activities:			
Depreciation and amortization	829	1,382	1,389
Noncash interest expense	113	7	
Amortization of premium on investment securities	724	751	1,469
Stock-based compensation expense	1,934	2,353	2,809
Loss on disposal of leasehold improvements	32		
Revaluation of convertible preferred stock warrant liability	(11)	(23)	(83)
Unrealized gain on foreign currency forward contracts			(51)
Changes in operating assets and liabilities:			
Receivables from collaborations	798	(955)	293
Prepaid expenses and other current assets	(717)	1,615	(2,481)
Other assets			(2,091)
Accounts payable	(1,824)	1,437	2,017
Accrued compensation and employee benefits	(417)	117	(980)
Accrued and other liabilities	(1,395)	(171)	3,375
Deferred revenue	(14,095)	(35,387)	(65,426)
Other long-term liabilities	2,176	45	(831)
Accrued income taxes	2,476	(2,476)	
Net cash used in operating activities	(29,646)	(11,321)	(49,225)
Investing activities			
Decrease in restricted cash		6,000	
Purchases of property and equipment	(2,390)	(1,477)	(362)
Purchases of investments	(94,911)	(33,805)	(144,644)
Proceeds from sales of investments	1,000	2,163	36,517
Proceeds from maturities of investments	91,436	59,829	40,687
Net cash provided by (used in) investing activities	(4,865)	32,710	(67,802)
Financing activities			
Repayment of debt	(6,667)	(2,598)	
Proceeds from issuance of common stock, including early exercise of stock options	176	167	317
Repurchase of unvested common stock	(1)	(51)	
Proceeds from issuance of convertible preferred stock, net of issuance costs		96,700	
Net cash provided by (used in) financing activities	(6,492)	94,218	317
Net increase (decrease) in cash and cash equivalents	(41,003)	115,607	(116,710)
Cash and cash equivalents at beginning of year	95,719	54,716	170,323

Cash and cash equivalents at end of year	$ 54,716	$ 170,323	$ 53,613
Supplemental disclosure of cash flow information			
Interest paid	$ 267	$ 14	$
Income taxes paid	$	$ 2,476	$ 57
Noncash investing activities			
Net change in accounts payable related to purchase of property and equipment	$ 362	$ (362)	$

See accompanying notes

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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, 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. Our fourth program, PRT2607 and other highly selective Syk inhibitors, is partnered with Biogen Idec Inc.

Additional Capital Requirements

The accompanying financial statements have been prepared assuming that we will continue as a going concern. We have incurred significant losses and negative cash flows from operations. At December 31, 2012, we had an accumulated deficit of $202.3 million and cash, cash equivalents and investments of $137.4 million. Our management believes that currently available resources will provide sufficient funds to enable us to meet our obligations through at least December 31, 2013. However, if our anticipated operating results are not achieved in future periods, our management believes that planned expenditures may need to be reduced in order to extend the time period over which the then-available resources would be able to fund our operations. We will need to raise additional capital to fully implement our business plan.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States (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 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, convertible preferred stock and related warrants, common stock, 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 could differ from those estimates.

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PORTOLA PHARMACEUTICALS, INC.

Notes to Financial Statements

(continued)

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, accounts receivable 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.

Accounts receivable 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 our receivables.

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PORTOLA PHARMACEUTICALS, INC.

Notes to Financial Statements

(continued)

Customer Concentration

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

	Year Ended December 31,		
	2010	2011	2012
Merck	76%	40%	
Novartis	24%	12%	97%
Biogen Idec		48%	

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, 2012, there have been no such losses.

Deferred Offering Costs

Deferred offering costs, which primarily consist of direct incremental legal and accounting fees relating to the initial public offering (IPO), are capitalized. The deferred offering costs will be offset against IPO proceeds upon the consummation of the offering. In the event the offering is terminated, deferred offering costs will be expensed. As of December 31, 2012, $1.6 million of deferred offering costs were capitalized in other assets on the balance sheet.

Convertible Preferred Stock

We record all shares of convertible preferred stock at their respective fair values on the dates of issuance. In the event of a change of control of the Company, proceeds will be distributed in accordance with the liquidation preferences set forth in our Amended and Restated Certificate of Incorporation unless the holders of convertible preferred stock have converted their convertible preferred shares into common shares. Therefore, convertible preferred stock is classified outside of stockholders deficit on the accompanying balance sheets as events triggering the liquidation preferences are not solely within the Company s control.

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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 will continue to adjust the carrying value of the warrants until the earlier of the exercise of the warrants or the completion of a liquidation event, including the completion of an IPO, at which time the liabilities will be reclassified to stockholders 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 ratably over the estimated period of performance.

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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 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 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, including stock options, 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

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basis over the employee s requisite service period (generally the vesting period). 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 gains and losses 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.

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, net income attributable to common

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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.

Newly Adopted Accounting Pronouncements

In May 2011, Accounting Standards Codification Topic 820, *Fair Value Measurement*, was amended to develop common requirements for measuring fair value and for disclosing information about fair value measurements in accordance with U.S. generally accepted accounting principles and international financial reporting standards. We adopted this guidance as of January 1, 2012 on a retrospective basis and this adoption did not have a material effect on our financial statements.

In June 2011, Accounting Standards Codification Topic 220, *Comprehensive Income*, was amended to increase the prominence of items reported in other comprehensive income. Accordingly, a company can present all nonowner changes in stockholders (deficit) equity either in a single continuous statement of comprehensive income or in two separate but consecutive statements. We adopted this guidance as of January 1, 2012 on a retrospective basis and this adoption did not have a material effect on our financial statements.

Reverse Stock Split

In April 2013, our board of directors and our stockholders approved an amendment to our amended and restated certificate of incorporation to effect a reverse split of shares of our common stock on a 1-for-9, 1-for-10 or 1-for-11 basis (the Reverse Stock Split), with the determination of the exact ratio to be determined by a committee of our board of directors. On May 10, 2013, this committee determined that the ratio for the Reverse Stock Split would be 1-for-10. The par value and the authorized shares of the common and convertible preferred stock were not adjusted as a result of the Reverse Stock Split. All issued and outstanding common stock, convertible preferred stock, options and warrants for common stock, warrants for preferred stock, and per share amounts contained in the financial statements have been retroactively adjusted to reflect this Reverse Stock Split for all periods presented. The Reverse Stock Split was effected on May 17, 2013.

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

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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 derivatives, 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.

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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 is classified as Level 3. The fair values of the outstanding convertible preferred stock warrants are measured using the Black-Scholes option-pricing model. Inputs used to determine estimated fair value include 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, 2011			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 166,696	$	$	$ 166,696
Corporate notes and commercial paper		9,893		9,893
U.S. government agency securities		7,873		7,873
Total financial assets	$ 166,696	$ 17,766	$	$ 184,462
Financial Liabilities:				
Convertible preferred stock warrant liability	$		$ 766	$ 766

	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

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Level 3 liabilities include the convertible preferred stock warrant liability (see Note 11). 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, 2009	$ 800
Recognized gain	(11)
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

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, 2011			December 31, 2012		
	Cost	Unrealized Gain (Loss)	Estimated Fair Value	Cost	Unrealized Gain	Estimated Fair Value
Money market funds	$ 166,696	$	$ 166,696	$ 43,303	$	$ 43,303
Corporate notes and commercial paper	9,895	(2)	9,893	64,403	22	64,425
U.S. government agency securities	7,872	1	7,873	19,335	11	19,346
	$ 184,463	$ (1)	$ 184,462	$ 127,041	$ 33	$ 127,074

At December 31, 2012, 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, 2012, we had foreign currency forward contracts with notional amounts of 16.8 million

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($22.2 million based on the exchange rate as of December 31, 2012) that were not designated as hedges. As of December 31, 2012, we recorded a derivative asset within prepaid expenses and other current assets and other long-term assets of $30,000 and $21,000, respectively, related to these foreign currency forward contracts. We had no foreign currency forward contracts outstanding in 2011.

For the year ended December 31, 2012, we recorded an unrealized gain of $51,000 in interest and other income, net on our statement of operations related to these foreign currency forward 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,	
	2011	**2012**
Computer equipment	$ 442	$ 515
Capitalized software	424	423
Equipment	2,934	3,224
Leasehold improvements	3,499	3,499
	7,299	7,661
Less accumulated depreciation and amortization	(3,411)	(4,800)
Property and equipment, net	$ 3,888	$ 2,861

Accrued and Other Liabilities

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

	December 31,	
	2011	**2012**
Research and development related	$ 2,451	$ 4,217
Legal and accounting fees	399	1,523
Deferred rent	786	831
Other	398	828
Total accrued liabilities	$ 4,034	$ 7,399

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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,		
	2010	**2011**	**2012**
Novartis:			
Recognition of upfront license fee	$ 7,692	$ 7,692	$ 53,846
Reimbursement of research and development expense	898	1,879	16,238
Novartis total	8,590	9,571	70,084
Merck:			
Recognition of upfront license fee	21,429	21,429	
Reimbursement of research and development expense	5,249	9,973	
Merck total	26,678	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			1,958
BMS and Pfizer total			1,958
Total collaboration and license revenue	$ 35,268	$ 78,029	$ 72,042

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

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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

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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

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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

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

As of December 31, 2012, the one milestone in the agreement had not been achieved and no royalties had been triggered under this agreement.

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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. 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. Any costs associated with preclinical studies required by regulatory authorities that are not part of the development plan within the agreement will be funded solely by us. Also, we are obligated to participate on a Joint Collaboration Committee (JCC) with BMS and Pfizer 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, 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 through June 2013.

The total consideration under this agreement of $6.0 million is being recognized as revenue on a straight-line basis over the estimated performance period through June 2013.

In connection with this agreement, we recognized $2.0 million in collaboration revenue for the year ended December 31, 2012. The deferred revenue balance was $4.0 million as of December 31, 2012.

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.

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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 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 24 employees, 16 of whom were immediately terminated, five of whom were terminated on January 31, 2013, two of whom will be terminated on April 30, 2013 and one of whom will be terminated on June 30, 2013. The total restructuring charge of $727,000 includes severance and related costs associated with the termination of the employees. For the year ended December 31, 2012, we recorded a restructuring charge of $618,000 which is included within research and development on our statement of operations. The remaining restructuring charge will be recorded in the first half of 2013 as the eight employees must be employed through various dates in 2013 in order to receive their severance payments. As of December 31, 2012, the accrued restructuring liability, which is included within accrued and other liabilities on the balance sheet, was $143,000.

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10. Long-Term Debt

In September 2006, we entered into a Loan and Security Agreement (the Loan Agreement) with Hercules Technology Growth Capital (Hercules) and Comerica Bank (Comerica). Under the terms of the Loan Agreement, we were initially entitled to draw up to $15.0 million. In March 2007, we met a scientific development milestone that qualified as a credit enhancement event under the Loan Agreement with Hercules and Comerica (the Credit Enhancement Event). As a result, our available credit under the Loan Agreement was increased by $5.0 million to $20.0 million, the interest-only period was extended to April 2008 and the loan term was extended to March 2011. In 2007, we had drawn down all of the available funds under the Loan Agreement.

In connection with the Loan Agreement, we were required to pay $215,000 in facility and other fees. These fees were capitalized and were amortized to interest expense over the term of the loan. Additionally, we were required to pay an exit fee equal to 2% of the aggregate principal amount of each advance. This obligation was amortized to interest expense over the term of the loan. Total amortization expense was $38,000, $3,000 and $0 for the years ended December 31, 2010, 2011 and 2012, respectively.

Also in connection with the Loan Agreement and the Credit Enhancement Event, we issued Hercules and Comerica warrants to purchase an aggregate of 76,335 shares of Series B convertible preferred stock at an exercise price of $13.10 per share. These warrants were valued using the Black-Scholes option-pricing model with the following assumptions: exercise price and fair value of $13.10 per share, expected volatility of 71%, risk-free interest rate of 4.5% to 4.64%, dividend yield of zero and contractual life of 10 years. This resulted in an estimated fair value of $794,000, which was recorded as a debt discount to the credit facility. The discount was amortized to interest expense over the repayment period. Interest expense related to the warrant was $76,000, $4,000 and $0 for the years ended December 31, 2010, 2011 and 2012, respectively.

Under the terms of the Loan Agreement, we were required to maintain a money market or investment account with Comerica, or one of its affiliates, with a minimum balance of $6.0 million. In April 2011, we repaid all of our obligations under the Loan Agreement in full, along with the exit fee obligation. This repayment terminated the $6.0 million minimum balance requirement with Comerica and released the security interest in our personal property.

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11. Convertible Preferred Stock Warrant Liability

Convertible preferred stock warrants were valued using the Black-Scholes option-pricing model upon their issuance and remeasured to estimated fair value at the end of each reporting period. The following table sets forth the estimated fair value for each of the convertible preferred stock warrants as of December 31, 2011 and 2012 (in thousands, except share and per share data):

Preferred Stock	Expiration Date	Exercise Price Per Share	Shares as of December 31, 2011	Shares as of December 31, 2012	Estimated Fair Value December 31, 2011	Estimated Fair Value 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	$ 42	$ 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	724	647
Total			81,075	81,075	$ 766	$ 683

Concurrent with the closing of an IPO, all convertible preferred stock warrants will convert into warrants to purchase shares of common stock at the applicable conversion rate for the related preferred stock (currently, 1-for-1 for all series of preferred stock). All warrants are exercisable upon issuance.

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

	Year Ended December 31, 2010	2011	2012
Risk-free interest rate	1.5-2.4%	0.4-0.9%	0.3-0.6%
Estimated term equal to the remaining contractual term	4.1-6.2 years	3.1-5.2 years	2.1-4.2 years
Volatility	78%	85%	82%
Dividend yield			

As a private company, we cannot rely on the volatility of our own stock price because there is no public market for the stock. Therefore, the estimated volatility is based on the volatility of other

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companies with similar products under development, market, size and other factors. We developed a broad peer group to provide a representative sample of comparable companies. 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.

12. 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.

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.

In conjunction with entering into the original lease agreement in December 2006, we issued to the landlord a warrant to purchase up to 1,500 shares of our common stock at an exercise price of $13.10 per share. The shares subject to the warrant were valued using Black-Scholes option-pricing model, resulting in an estimated fair value of $3,000, which was amortized to rent expense over the original term of the lease. The fair value of the warrants to purchase common stock was fully amortized as of December 31, 2009.

At December 31, 2012, our future minimum commitments under our non-cancelable operating leases were as follows (in thousands):

Year ending December 31:	
2013	$ 1,613
2014	1,660
2015	418
Total	$ 3,691

Rent expense was $1.4 million, $1.0 million and $800,000 for the years ended December 31, 2010, 2011 and 2012, 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

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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.

13. Convertible Preferred Stock and Stockholders Deficit

Common Stock

As of December 31, 2011 and 2012, we had reserved shares of common stock, on an as-if-converted basis, for issuance as follows:

	December 31,	
	2011	2012
Conversion of Series A convertible preferred stock	4,309,972	4,309,972
Conversion of Series B convertible preferred stock	3,579,597	3,579,597
Conversion of Series C convertible preferred stock	9,214,160	9,214,160
Conversion of Series D convertible preferred stock	6,287,026	6,287,026
Conversion of Series 1 convertible preferred stock	636,042	636,042
Options issued and outstanding	3,104,399	3,451,178
Options available for grant under stock option plan	45,259	593,011
Common and convertible preferred stock warrants	82,575	82,575
Total	27,259,030	28,153,561

Convertible Preferred Stock

As of December 31, 2011 and 2012, we had outstanding convertible preferred stock as follows (in thousands, except share data):

	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

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Dividends and Distributions

The holders of the outstanding shares of convertible preferred stock are 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 shall 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 will be distributed among all holders of convertible preferred stock and common stock in proportion to the number of shares of common stock that would then be held by each such holder if all shares of convertible preferred stock were converted into common stock. No dividends have been declared to date.

Conversion and Voting Rights

The preferred stock is 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 is entitled upon conversion shall be 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 converts into common stock in the event of an initial public offering of our common stock with gross proceeds of at least $50.0 million and the price per share is equal to or exceeds the Series D convertible preferred stock conversion price, which is $14.15, as adjusted for any stock dividends, combinations, splits, recapitalizations and the like. In addition, each share of convertible preferred stock shall automatically be converted into common stock at any time upon the affirmative election of the holders of at least two-thirds of the outstanding shares of voting convertible preferred stock.

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

Holders of Series D convertible preferred stock are granted a separate vote. For so long as any shares of Series D convertible preferred stock remain outstanding, 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 shall be necessary for effecting or validating certain actions as outlined in our Amended and Restated Certificate of Incorporation.

Liquidation Rights

Upon liquidation, dissolution, or winding up of the Company (whether voluntary or involuntary) (a Liquidation Event), before any distribution or payment shall 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 shall be entitled to be paid out of our assets legally available for

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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 shall be 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 available for distribution to stockholders will be distributed ratably to the holders of our common stock.

Asset Transfer or Acquisition Rights

In the event that the Company is a party to an Acquisition or Asset Transfer (each as defined below), then each holder of convertible preferred stock shall be entitled to receive, for each share of convertible preferred stock then held, out of the proceeds of such Acquisition or Asset Transfer, the amount of cash, securities or other property to which such holder would be entitled to receive in a Liquidation Event.

Acquisition shall mean (A) any consolidation or merger of the Company with or into any other corporation or other entity or person, or any other corporate reorganization, in which the stockholders of the Company immediately prior to such consolidation, merger or reorganization, own less than 50% of the voting power of the surviving entity (or, if the surviving entity is a wholly owned subsidiary, its parent) immediately after such consolidation, merger or reorganization; or (B) any transaction or series of related transactions to which the Company is a party in which in excess of fifty percent (50%) of the Company s voting power is transferred; provided that an Acquisition shall not include (x) any consolidation or merger effected exclusively to change the domicile of the Company, or (y) any transaction or series of transactions principally for bona fide equity financing purposes in which cash is received by the Company or any successor or indebtedness of the Company is cancelled or converted or a combination thereof in consideration solely for the issuance of equity securities; and (C) Asset Transfer shall mean a sale, lease or other disposition of all or substantially all of the assets of the Company (including the exclusive license of all or substantially all of the Company s intellectual property, following which the Company retains no operational obligations).

14. Stock-Based Compensation

In November 2003, we adopted the 2003 Equity Incentive Plan (the 2003 Plan). The 2003 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. The Board of Directors determines the estimated fair value of common stock. Stock options are generally granted with terms of up to ten years and vest over a period of four years.

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As of December 31, 2012, 4,753,323 shares of common stock were reserved under the 2003 Plan for the issuance of options and restricted stock.

The following summarizes option activity under the 2003 Plan and related information during the years ended December 31, 2010, 2011 and 2012:

	Shares Available for Grant	Shares Subject to Outstanding Options	Weighted-Average Exercise Price Per Share
Balance at December 31, 2009	108,911	1,986,475	$ 4.16
Options authorized	900,000		
Options granted	(471,915)	471,915	9.00
Options exercised		(52,127)	3.36
Options canceled	12,670	(12,670)	5.30
Options repurchased	167		
Balance at December 31, 2010	549,833	2,393,593	5.13
Options authorized	250,000		
Options granted	(850,977)	850,977	8.35
Options exercised		(53,336)	3.10
Options canceled	86,835	(86,835)	5.86
Options repurchased	9,568		
Balance at December 31, 2011	45,259	3,104,399	6.03
Options authorized	998,948		
Options granted	(658,789)	658,789	7.38
Options exercised		(104,417)	3.04
Options canceled	207,593	(207,593)	6.36
Balance at December 31, 2012	593,011	3,451,178	$ 6.35

Additional information related to the status of options at December 31, 2012, is as follows (aggregate intrinsic value in thousands):

	Shares	Weighted-Average Exercise Price Per Share	Remaining Contractual Life	Aggregate Intrinsic Value
Outstanding and exercisable	3,451,178	$ 6.35	6.2	$ 11,891
Vested and expected to vest	3,387,447	$ 6.33	6.2	$ 11,762
Vested	2,229,151	$ 5.51	4.9	$ 9,568

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 estimated fair value of our common stock as determined by the Board of Directors as of December 31, 2012.

The aggregate intrinsic value of options exercised was $284,000, $290,000 and $451,000 for the years ended December 31, 2010, 2011 and 2012, respectively.

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The total estimated grant date fair value of options vested during the years ended December 31, 2010, 2011 and 2012 was $1.6 million, $1.8 million and $3.0 million, respectively.

Additional information regarding our stock options outstanding and vested and exercisable as of December 31, 2012 is summarized below:

	Options Outstanding and Exercisable			Options Vested	
Exercise Prices	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	56,914	1.8	$ 1.27	56,914	$ 1.27
$3.30	426,894	3.2	3.30	426,895	3.30
$3.60	10,000	4.2	3.60	10,000	3.60
$4.10	383,446	4.6	4.10	383,446	4.10
$4.50	2,500	4.5	4.50	2,500	4.50
$5.00	349,925	4.1	5.00	349,925	5.00
$5.10 - $5.30	364,471	4.8	5.22	355,155	5.22
$7.00	615,389	9.0	7.00	37,709	7.00
$8.50	708,349	8.0	8.50	300,740	8.50
$9.00 - $9.50	533,290	7.3	9.09	305,867	9.00
	3,451,178	6.2	$ 6.35	2,229,151	$ 5.51

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,		
	2010	2011	2012
Research and development	$ 1,170	$ 1,164	$ 1,452
General and administrative	764	1,189	1,357
Total stock-based compensation	$ 1,934	$ 2,353	$ 2,809

As of December 31, 2012, total unamortized employee and nonemployee stock-based compensation was $5.4 million, which is expected to be recognized over the remaining vesting period of 2.7 years. The weighted-average fair value of employee options granted during the years ended December 31, 2010, 2011 and 2012 was $5.90, $5.90 and $4.70 per share, respectively, as of the grant date.

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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,		
	2010	**2011**	**2012**
Risk-free interest rate	2.3%	1.1%	1.1%
Expected life	5.7 years	6.0 years	6.0 years
Volatility	78%	85%	72%
Dividend yield			

The risk-free rate is based on U.S. Treasury zero-coupon issues with remaining terms similar to the expected terms of the options. 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 a private company, we cannot rely on the volatility of our own stock price because there is no public market for the stock. Therefore, the estimated 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.

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 33,750 and 6,380 shares with average exercise prices of $9.00 and $7.00 per share, respectively, during the years ended December 31, 2010 and 2012, respectively. There were no such grants during the year ended December 31, 2011. These options vest upon grant or various terms up to four years. We recognized consultant stock compensation expense of $172,000, $65,000 and $144,000 during the years ended December 31, 2010, 2011 and 2012, respectively. The fair value of consultants 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.

Liability for Early Exercise of Stock Options

As of December 31, 2011 and 2012, there were 2,484 and 1,125, respectively, of unvested common shares outstanding that were exercised early and subject to repurchase by us at the original issuance price upon termination of the stockholders services. We may repurchase these shares at average prices of $7.85 and $8.45 per share as of December 31, 2011 and 2012, respectively. Our right to repurchase these shares generally lapses 25% after one year and 1/48 of the original grant per month for 36 months thereafter.

The shares purchased by the employees pursuant to the early exercise of stock options are not deemed, for accounting purposes, to be issued until those shares vest. The cash received in exchange for exercised and unvested shares related to stock options granted is recorded as a liability for the early exercise of stock options on the accompanying balance sheets and will be transferred into common

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stock and additional paid-in capital as the shares vest. As of December 31, 2011 and 2012, we recorded $20,000 and $10,000, respectively, as accrued and other liabilities associated with shares issued with repurchase rights.

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

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,		
	2010	2011	2012
Net income (loss)	$ (20,269)	$ 19,984	$ 11,366
Noncumulative dividends on convertible preferred stock		(18,757)	(11,366)
Undistributed earnings allocated to participating securities		(1,148)	
Net income (loss) attributable to common stockholders, basic	(20,269)	79	
Adjustment to undistributed earnings allocated to participating securities		48	
Net income (loss) attributable to common stockholders, diluted	$ (20,269)	$ 127	$
Shares used in computing net income (loss) per share attributable to common stockholders, basic	1,207,106	1,249,778	1,350,939
Dilutive effect of common stock options		839,428	697,928
Shares used in computing net income (loss) per share attributable to common stockholders, diluted	1,207,106	2,089,206	2,048,867
Net income (loss) per share attributable to common stockholders:			
Basic	$ (16.79)	$ 0.06	$ 0.00
Diluted	$ (16.79)	$ 0.06	$ 0.00

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,		
	2010	2011	2012
Convertible preferred stock	17,103,729	24,026,797	24,026,797
Common stock subject to repurchase	13,662		
Stock options to purchase common stock	290,166	962,225	1,653,298
Convertible preferred stock warrants	81,075	81,075	81,075
Common stock warrants	1,500	1,500	1,500

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PORTOLA PHARMACEUTICALS, INC.

Notes to Financial Statements

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16. 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. We recognized total expense of $38,000, $35,000 and $31,000 for the years ended December 31, 2010, 2011 and 2012, respectively.

17. Income Taxes

The income tax provision is summarized as follows (in thousands):

	Year Ended December 31,		
	2010	**2011**	**2012**
Current:			
Federal	$ (47)	$	$
State	2,841		
Provision for income tax	$ 2,794	$	$

The effective tax rate of our provision for income taxes differs from the federal statutory rate as follows:

	Year Ended December 31,		
	2010	**2011**	**2012**
Federal statutory income tax rate	34.0%	34.0%	34.0%
State income taxes, net of federal benefit	4.6	(3.8)	22.8
Federal and state research credits	5.3	(5.7)	0.8
Stock based compensation	(1.5)	1.3	0.4
Other	(0.1)	0.6	(0.1)
Change in valuation allowance	(58.3)	(26.4)	(57.9)
	(16.0)%	0.0%	0.0%

We recorded an income tax provision in 2010 on a pre-tax loss due primarily to the recognition of collaboration revenue deferred in previous years for California state income tax purposes that could not be offset by state net operating losses due to the suspension of the use of these losses under state law in 2010. In 2011 and 2012, 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 2011 and 2012 state law suspended their use. Our valuation allowance at December 31, 2011 and 2012 appropriately considers the balances of both net operating losses and deferred revenue.

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Notes to Financial Statements

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

	December 31, 2011	December 31, 2012
Deferred tax assets:		
Federal and state net operating loss carryforwards	$ 54,551	$ 74,390
Federal and state research tax credit carryforwards	7,240	7,551
Deferred revenue	26,160	1,434
Stock options	1,749	2,362
Capitalized research and development	1,627	
Capitalized acquisition costs	1,930	1,503
Other	2,627	1,859
Total deferred tax assets	95,884	89,099
Valuation allowance	(95,884)	(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 decreased by $5.4 million for the year ended December 31, 2011. The valuation allowance decreased by $6.8 million for the year ended December 31, 2012.

As of December 31, 2012, we had net operating loss carryforwards for federal income tax purposes of approximately $177.4 million and federal research tax credits of approximately $7.6 million, which expire at various dates in the period from 2024 to 2032. We used approximately $68.0 million of federal net operating loss carryforwards during 2009 primarily in connection with the receipt of taxable upfront license payments totaling $125.0 million. We elected to defer such taxable amounts into 2010 for state income tax purposes. We also have state net operating loss carry forwards of approximately $224.4 million which expire at various dates in the period from 2013 to 2032 and state research tax credits of $1.6 million. Utilization of the net operating loss carryforwards and credits may be subject to a substantial 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 2012, remain open to U.S. federal and California state tax examinations.

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PORTOLA PHARMACEUTICALS, INC.

Notes to Financial Statements

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

	Year Ended December 31,		
	2010	**2011**	**2012**
Unrecognized tax benefits, beginning of period	$	$ 973	$ 1,344
Gross increases tax position in prior period	856		
Gross increases current period tax positions	117	371	91
Unrecognized tax benefits, end of period	$ 973	$ 1,344	$ 1,435

The amount of unrecognized income tax benefits that, if recognized, would affect our effective tax rate was $365,000 as of December 31, 2011 and 2012. If the $1.3 million and $1.4 million of unrecognized income tax benefits as of December 31, 2011 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.

18. 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 the interim Chief Executive Officer 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, 2012, we recorded a reduction in research and development expense of $57,000 owed to us by Global Blood and Myokardia under the Master Services Agreements.

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

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PORTOLA PHARMACEUTICALS, INC.

Condensed Balance Sheets

(In thousands, except share and per share data)

	December 31, 2012	June 30, 2013
ASSETS	**(Note 2)**	**(Unaudited)**
CURRENT ASSETS:		
Cash and cash equivalents	$ 53,613	$ 112,246
Short-term investments	77,656	95,358
Receivables from collaborations	662	3,494
Prepaid expenses and other current assets	2,982	3,970
Total current assets	134,913	215,068
Property and equipment, net	2,861	2,516
Long-term investments	6,115	27,586
Other assets	2,112	220
TOTAL ASSETS	$ 146,001	$ 245,390
LIABILITIES, CONVERTIBLE PREFERRED STOCK, AND STOCKHOLDERS EQUITY (DEFICIT)		
CURRENT LIABILITIES:		
Accounts payable	$ 4,840	$ 4,676
Accrued compensation and employee benefits	1,860	1,673
Accrued and other liabilities	7,399	16,325
Deferred revenue current portion	4,042	6,696
Convertible preferred stock warrant liability	683	
Total current liabilities	18,824	29,370
Deferred revenue noncurrent portion		337
Other long-term liabilities	1,466	1,087
TOTAL LIABILITIES	$ 20,290	$ 30,794
Commitments and contingencies		
Convertible preferred stock, $0.001 par value. 0 and 243,258,300 shares authorized at June 30, 2013 and December 31, 2012; 0 shares and 24,026,797 shares issued and outstanding at June 30, 2013 and December 31, 2012	317,280	
STOCKHOLDERS EQUITY (DEFICIT):		
Preferred stock, $0.001 par value. 5,000,000 shares authorized at June 30, 2013; 0 issued and outstanding		
Common stock, $0.001 par value. 100,000,000 and 300,000,000 shares authorized; 35,171,769 and 1,385,508 shares issued and outstanding at June 30, 2013 and December 31, 2012	1	35
Additional paid-in capital	10,717	456,657
Accumulated deficit	(202,320)	(242,060)
Accumulated other comprehensive income (loss)	33	(36)
Total stockholders equity (deficit)	(191,569)	214,596
	$ 146,001	$ 245,390

TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK, AND STOCKHOLDERS EQUITY (DEFICIT)

See accompanying notes

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PORTOLA PHARMACEUTICALS, INC.

Condensed Statements of Operations

(Unaudited)

(In thousands, except share and per share data)

	Six Months Ended June 30,	
	2012	**2013**
Collaboration and license revenue	$ 69,346	$ 5,709
Operating expenses:		
Research and development	26,049	38,556
General and administrative	5,865	6,747
Total operating expenses	31,914	45,303
Income (loss) from operations	37,432	(39,594)
Interest and other (expense), net	(796)	(147)
Net income (loss)	$ 36,636	$ (39,741)
Net income (loss) attributable to common stockholders:		
Basic	$ 1,257	$ (39,741)
Diluted	$ 1,816	$ (39,741)
Shares used to compute net income (loss) per share attributable to common stockholders:		
Basic	1,329,133	8,078,308
Diluted	1,968,821	8,078,308
Net income (loss) per share attributable to common stockholders:		
Basic	$ 0.95	$ (4.92)
Diluted	$ 0.92	$ (4.92)

See accompanying notes

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PORTOLA PHARMACEUTICALS, INC.

Condensed Statements of Comprehensive Income (Loss)

(Unaudited)

(In thousands)

	Six Months Ended June 30,	
	2012	**2013**
Net income (loss)	$ 36,636	$ (39,741)
Other comprehensive income (loss):		
Unrealized (loss) on available-for-sale securities, net of tax	(33)	(69)
Total comprehensive income (loss)	$ 36,603	$ (39,810)

See accompanying notes

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PORTOLA PHARMACEUTICALS, INC.

Condensed Statements of Cash Flows

(Unaudited)

(In thousands)

	Six Months Ended June 30	
	2012	**2013**
Operating activities		
Net income (loss)	$ 36,636	$ (39,741)
Adjustments to reconcile net income (loss) to cash used in operating activities:		
Depreciation and amortization	699	679
Amortization of premium on investment securities	578	818
Stock-based compensation expense	1,411	1,923
Revaluation of convertible preferred stock warrant liability	(127)	(24)
Unrealized loss on foreign currency forward contracts	694	352
Changes in operating assets and liabilities:		
Receivables from collaborations	(1,585)	(2,832)
Prepaid expenses and other current assets	(2,244)	(1,091)
Other assets	(271)	229
Accounts payable	6,434	(164)
Accrued compensation and employee benefits	(1,099)	(187)
Accrued and other liabilities	454	8,153
Deferred revenue	(68,730)	2,991
Other long-term liabilities	(410)	(433)
Net cash used in operating activities	(27,560)	(29,327)
Investing activities		
Purchases of property and equipment	(354)	(333)
Purchases of investments	(117,147)	(98,640)
Proceeds from sales of investments	20,209	4,644
Proceeds from maturities of investments	14,329	53,936
Net cash used in investing activities	(82,963)	(40,393)
Financing activities		
Proceeds from initial public offering, net of underwriters discount		131,027
Payment of initial public offering costs		(2,927)
Proceeds from issuance of common stock, including early exercise of stock options	292	253
Net cash provided by financing activities	292	128,353
Net increase (decrease) in cash and cash equivalents	(110,231)	58,633
Cash and cash equivalents at beginning of period	170,323	53,613
Cash and cash equivalents at end of period	$ 60,092	$ 112,246

See accompanying notes

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PORTOLA PHARMACEUTICALS, INC.

Notes to Condensed 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 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, 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. Our fourth program, PRT2607 and other highly selective Syk inhibitors, is partnered with Biogen Idec Inc.

Initial Public Offering

In May 2013, the Company completed its initial public offering (IPO) of 9,686,171 shares of its 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 total proceeds from the offering to the Company, net of underwriting discounts and commissions of approximately $9.4 million, were approximately $131.0 million. After deducting offering expenses payable by the Company of approximately $5.2 million, net proceeds to the Company were $125.8 million. As of June 30, 2013, $2.1 million of accrued offering costs remained unpaid and these costs are expected to be paid by the end of the Company s fiscal year. 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 the Company s convertible preferred stock warrants were converted into warrants to purchase common stock.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying unaudited condensed financial statements have been prepared in accordance with U.S. generally accepted accounting principles (U.S. GAAP), and following the requirements of the Securities and Exchange Commission (SEC) for interim reporting. As permitted under those rules, certain footnotes or other financial information that are normally required by U.S. GAAP can be condensed or omitted. These financial statements have been prepared on the same basis as the Company s annual financial statements and, in the opinion of management, reflect all adjustments, consisting only of normal recurring adjustments, that are necessary for a fair statement of the Company s financial information. The results of operations for the six months ended June 30, 2013 are

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PORTOLA PHARMACEUTICALS, INC.

Notes to Condensed Financial Statements

(continued)

not necessarily indicative of the results to be expected for the year ending December 31, 2013. The condensed balance sheet as of December 31, 2012 has been derived from audited financial statements at that date but does not include all of the information required by U.S. GAAP for complete financial statements.

The accompanying condensed financial statements and related financial information should be read in conjunction with the audited financial statements and the related notes thereto for the year ended December 31, 2012 included in the Company s Prospectus filed pursuant to Rule 424(b)(4) on May 22, 2013 with the SEC.

Reverse Stock Split

On May 17, 2013, the Company effected a 1-for-10 reverse split of its 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 condensed financial statements, on a retroactive basis, to reflect the 1-for-10 reverse stock split.

Additional Capital Requirements

We have incurred significant losses and negative cash flows from operations. As of June 30, 2013, we had an accumulated deficit of $242.4 million and cash, cash equivalents and investments of $235.2 million. Our management believes that currently available resources will provide sufficient funds to enable us to meet our obligations for at least the next twelve months based on our current business plans. However, if our anticipated operating results are not achieved in future periods, our management believes that planned expenditures may need to be reduced in order to extend the time period over which the then-available resources would be able to fund our operations. We will need to raise additional capital to fully implement our business plan.

Use of Estimates

The preparation of condensed 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.

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PORTOLA PHARMACEUTICALS, INC.

Notes to Condensed Financial Statements

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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 its 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. 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 (expense), net. The cost of securities sold is based on the specific-identification method. Interest on marketable securities is included in interest and other income (expense), net.

Customer Concentration

Customers whose collaborative research and development revenue accounted for 10% or more of total revenues were as follows:

	Six Months Ended June 30,	
	2012	2013
Novartis AG	100%	
Bristol-Myers Squibb Company and Pfizer Inc.		54%
Bayer Pharma, AG and Janssen Pharmaceuticals, Inc.		43%

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 June 30, 2013.

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.

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PORTOLA PHARMACEUTICALS, INC.

Notes to Condensed Financial Statements

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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.

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 gains and losses in the condensed 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.

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

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PORTOLA PHARMACEUTICALS, INC.

Notes to Condensed Financial Statements

(continued)

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, 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.

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PORTOLA PHARMACEUTICALS, INC.

Notes to Condensed Financial Statements

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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, 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

	June 30, 2013			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 103,302	$	$	$ 103,302
Corporate notes and commercial paper		77,004		77,004
U.S. government agency securities		45,940		45,940
Total financial assets	$ 103,302	$ 122,944	$	$ 226,246
Financial Liabilities:				
Foreign currency forward contracts	$	$ 228	$	$ 228

We have elected to use the income approach to value the derivatives (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.

Our convertible preferred stock warrant liability was classified as a Level 3 liability. The fair values of the outstanding 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 convertible preferred stock at the valuation measurement date, the remaining contractual

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PORTOLA PHARMACEUTICALS, INC.

Notes to Condensed Financial Statements

(continued)

term of the warrants, risk-free interest rates, expected dividends and estimated volatility. The significant unobservable input used in the fair value measurement of the convertible preferred stock warrant liability was the fair value of the underlying convertible preferred stock at the valuation remeasurement date. Generally, increases (decreases) in the fair value of the underlying convertible preferred stock would result in a directionally similar impact to the fair value measurement. The preferred stock warrants were converted to common stock warrants upon the completion of the IPO and are no longer subject to remeasurement.

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 until their conversion to common stock warrants and related reclassification to additional paid-in capital (in thousands):

Balance as of December 31, 2012	$ 683
Recognized gain upon final remeasurement	(24)
Reclassification of warrant liability to additional paid-in capital	(659)
Balance as of June 30, 2013	$

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

The estimated fair value of the convertible preferred stock warrants was determined as of May 22, 2013, the date remeasurement was no longer applicable, and June 30, 2012 using the Black-Scholes option-pricing model using the following assumptions:

	June 30, 2012	May 22, 2013
Risk free interest rate	0.33 0.72%	0.11 0.91 %
Estimated term equal to the remaining contractual term	2.6 4.7 years	1.7 3.8 years
Volatility	70%	79 %
Dividend yield		

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PORTOLA PHARMACEUTICALS, INC.

Notes to Condensed Financial Statements

(continued)

4. Financial Instruments

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

	December 31, 2012			June 30, 2013		
	Cost	Unrealized Gain (Loss)	Estimated Fair Value	Cost	Unrealized Gain (Loss)	Estimated Fair Value
Money market funds	$ 43,303	$	$ 43,303	$ 103,302	$	$ 103,302
Corporate notes and commercial paper	64,403	22	64,425	77,020	(16)	77,004
U.S. government agency securities	19,335	11	19,346	45,960	(20)	45,940
	$ 127,041	$ 33	$ 127,074	$ 226,282	$ (36)	$ 226,246
Classified as:						
Cash equivalents			$ 43,303			$ 103,302
Short-term investments			77,656			95,358
Long-term investments			6,115			27,586
Total cash equivalents and investments			$ 127,074			$ 226,246

At June 30, 2013 and December 31, 2012, 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, 2012 and June 30, 2013, we had foreign currency forward contracts with notional amounts of 16.8 million ($22.2 million based on the exchange rate as of December 31, 2012) and 12.0 million ($15.6 million based on the exchange rate as of June 30, 2013), respectively, that were not designated as hedges. As of December 31, 2012, we recorded a derivative asset within prepaid expenses and other current assets and other long-term assets of $30,000 and $21,000, respectively, related to these foreign currency forward contracts. As of June 30, 2013, we recorded a derivative liability within accrued liabilities and other noncurrent liabilities of $175,000 and $53,000, respectively, related to these foreign currency forward contracts.

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We recorded an unrealized loss of $352,000 in interest and other income (expense), net on our condensed statements of operations related to these foreign currency forward contracts for the six months ended June 30, 2013. During the six months ended June 30, 2013, we settled foreign currency forward contracts and recognized a realized gain of $73,000, respectively, in interest and other income (expense), net. During the three and six months ended June 30, 2012 we recognized no realized gains or losses.

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

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

	December 31, 2012	June 30, 2013
Research and development related	$ 4,217	$ 12,461
Legal and accounting fees	507	523
Deferred rent	831	854
Foreign currency forward contracts		175
Deferred offering costs	1,506	2,107
Other	338	205
Total accrued and other liabilities	$ 7,399	$ 16,325

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7. Collaboration and License Agreements

Summary of Collaboration Related Revenue

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

	Six Months Ended June 30,	
	2012	2013
Novartis:		
Recognition of upfront license fee	$ 53,282	$
Reimbursement of research and development expense	16,064	
Novartis total	69,346	
BMS and Pfizer:		
Recognition of research and development services		3,094
BMS and Pfizer total		3,094
Bayer and Janssen:		
Recognition of research and development services		2,438
Bayer and Janssen total		2,438
Lee s:		
Recognition of research and development services		52
Lee s total		52
Daiichi Sankyo:		
Recognition of research and development services		125
Daiichi Sankyo total		125
Total collaboration and license revenue	$ 69,346	$ 5,709

Novartis AG (Novartis)

In February 2009, we entered into a license agreement with Novartis to develop and commercialize Elinogrel. We estimated the term of our obligation to participate in the Joint Steering Committee and Joint Development Committee (collectively, 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. All remaining deferred revenue was recognized as revenue through July 2012, 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.

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Biogen Idec, Inc. (Biogen Idec)

In October 2011, we entered into an exclusive, worldwide license and collaboration agreement with Biogen Idec, under which Portola and Biogen Idec were to jointly develop and commercialize selective, novel oral Syk inhibitors for the treatment of autoimmune and inflammatory diseases.

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. As all contingent consideration payments are based solely on the performance of Biogen Idec, the milestone method of accounting will not be applied to such amounts. 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 three and six months ended June 30, 2013 and 2012, we recorded a reduction in research and development expense of $164,000 and $494,000, and $2.1 million and $4.8 million, respectively, owed by Biogen Idec to us under the cost-sharing terms of the 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 June 2013. In March 2013, we revised our estimated period of performance to be through July 2013. In June 2013, we revised our estimated period of performance to be through September 2013. The effect of this change in estimate was not significant.

The total consideration under this agreement of $6.0 million is being recognized as revenue on a straight-line basis over the estimated performance period through September 2013.

During the three and six months ended June 30, 2013, we recognized $1.1 million and $3.1 million in collaboration revenue, respectively. During the three and six months ended June 30, 2012 we did not recognize any revenue from the BMS and Pfizer agreement. The deferred revenue balance as of June 30 2013 was $900,000.

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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 paid us 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 ratably over the estimated period of performance. Any reimbursements we may receive from Lee s for the costs we incur in connection with this agreement are expected to be immaterial.

During the three and six months ended June 30, 2013, we recognized $52,000 of collaboration revenue. The deferred revenue balance as of June 30, 2013 was $648,000.

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 PRT2070 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. We have not incurred any such costs during the three and six months ended June 30, 2013 related to this agreement.

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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 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 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 November 2013. In June 2013, we revised our estimated period of performance to be through January 2014. The total consideration under this agreement is being recognized as revenue ratably over the estimated performance period through January 2014. The effect of this change was not significant.

During the three and six months ended June 30, 2013, we recognized $1.3 million and $2.4 million in collaboration revenue, respectively. During the three and six months ended June 30, 2012, we did not recognize any revenue from our Bayer and Janssen agreement. The deferred revenue balance as of June 30, 2013 was $2.6 million.

Daiichi Sankyo, Inc. (Daiichi Sankyo)

In June 2013, we entered into an agreement with 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. Should Daiichi Sankyo terminate the agreement prior to the first patient dosing in the clinical trial, it is entitled to a refund of $3.0 million. The total consideration under this agreement of $6.0 million was received in July 2013, although only the non-contingent consideration of $3.0 million was recorded as receivables from collaborations at June 30, 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 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

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Notes to Condensed Financial Statements

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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 through May 2014. The total non-contingent consideration under this agreement of $3.0 million is being recognized as revenue ratably over the estimated non-contingent performance period through May 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 May 2014 and conclude in October 2014.

During the six months ended June 30, 2013, we recognized $125,000 in collaboration revenue associated with the non-contingent element of the arrangement. The payment due from Daiichi Sankyo of $3.0 million at June 30, 2013 relating to the non-contingent portion of the arrangement was recorded in receivables from collaborations and the unearned portion of the non-contingent upfront fee of $2.9 million was recorded as deferred revenue as of June 30, 2013.

8. 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, 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 six months ended June 30, 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 condensed statements of operations. During the six months ended June 30, 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 June 30, 2013.

9. Stock-Based Compensation

In January 2013, our Board of Directors adopted our 2013 Equity Incentive Plan, or the 2013 Plan, which became effective upon of the closing of our IPO in May 2013. As of June 30, 2013, there are 334,070 shares reserved under the 2013 Plan for the issuance of options and restricted stock.

The estimated grant date fair values of the employee stock options were calculated using the Black-Scholes valuation model, based on the following assumptions:

	Six Months Ended June 30,	
	2012	2013
Risk-free interest rate	1.2%	1.1%
Expected life	6.0 years	6.0 years
Volatility	70%	79%
Dividend yield		

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The following table summarizes option activity under the 2003 Plan and the 2013 Plan and related information during the six months ended June 30, 2013:

	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	(560,854)	560,854	13.98
Options exercised		(72,204)	3.52
Options cancelled	151,913	(151,913)	7.33
Balance at June 30, 2013	334,070	3,787,915	$ 7.50

The table below sets forth the functional classification of stock-based compensation expense, net of estimated forfeitures, for the periods presented (in thousands):

	Six Months Ended June 30,	
	2012	2013
Research and development	$ 749	$ 945
General and administrative	662	978
Total stock-based compensation	$ 1,411	$ 1,923

10. 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:

	Six Months Ended June 30,	
	2012	2013
Convertible preferred stock	24,026,797	
Common stock subject to repurchase		875
Stock options to purchase common stock	1,540,613	3,787,915
Preferred stock warrants	81,075	
Common stock warrants	1,500	82,575

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Notes to Condensed Financial Statements

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

	Six Months Ended June 30,	
	2013	**2012**
Net income (loss)	$ (39,741)	$ 36,636
Noncumulative dividends on convertible preferred stock		(12,664)
Undistributed earnings allocated to participating securities		(22,715)
Net income (loss) attributable to common stockholders, basic	(39,741)	1,257
Adjustment to undistributed earnings allocated to participating securities		559
Net income (loss) attributable to common stockholders, diluted	$ (39,741)	$ 1,816
Basic shares:		
Weighted average common shares outstanding	8,078,308	1,329,133
Diluted shares:		
Weighted average common shares outstanding	8,078,308	1,329,133
Weighted average effect of dilutive stock options		639,688
	8,078,308	1,968,821
Net income (loss) per share attributable to common stockholders:		
Basic	$ (4.92)	$ 0.95
Diluted	$ (4.92)	$ 0.92

11. Income Taxes

For the three and six months ended June 30, 2012, 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, California state law suspended their use. We maintain deferred tax assets that reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. These deferred tax assets include net operating loss carryforwards, research credits and capitalized research and development. Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain based on our history of losses. Accordingly, our deferred tax assets have been fully offset by a valuation allowance. Utilization of operating losses and credits may be subject to substantial annual limitation due to ownership change provisions of 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.

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12. Supplementary Financial Data

The following table presents certain unaudited quarterly financial information for the ten quarters in the period ended June 30, 2013. 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.

	For the Three Months Ended[1]			
	March 31	June 30	September 30	December 31
	(in thousands except per share data)			
	(unaudited)			
2013:				
Collaboration and license revenue	$ 3,108	$ 2,601		
Operating expenses	(20,761)	(24,541)		
Loss from operations	(17,653)	(21,940)		
Net loss	(18,142)	(21,598)		
Basic and diluted net loss per share	$ (12.94)	$ (1.47)		
2012:				
Collaboration and license revenue	$ 2,481	$ 66,865	$ 738	$ 1,958
Operating expenses	(15,768)	(16,147)	(12,833)	(16,438)
Income (loss) from operations	(13,287)	50,718	(12,095)	(14,480)
Net income (loss)	(13,127)	49,762	(11,488)	(13,781)
Basic net income (loss) per share	$ (10.08)	$ 1.71	$ (8.38)	$ (10.02)
Diluted net income (loss) per share	$ (10.08)	$ 1.67	$ (8.38)	$ (10.02)
2011:				
Collaboration and license revenue	$ 9,875	$ 10,080	$ 18,563	$ 39,511
Operating expenses	(12,855)	(13,771)	(11,990)	(19,545)
Income (loss) from operations	(2,980)	(3,691)	6,573	19,966
Net income (loss)	(2,971)	(3,643)	6,595	20,004
Basic net income (loss) per share	$ (2.42)	$ (2.95)	$ 0.12	$ 0.65
Diluted net income (loss) per share	$ (2.42)	$ (2.95)	$ 0.11	$ 0.62

(1) The amounts were computed independently for each quarter, and the sum of the quarters may not total the annual amounts.

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