PORTOLA®
PHARMACEUTICALS

2017

ANNUAL REPORT

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

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

For the Fiscal Year Ended December 31, 2017

or

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

Commission File Number: 001-35935

PORTOLA PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**2834**	**20-0216859**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification No.)

270 E. Grand Avenue
South San Francisco, California 94080
(Address of Principal Executive Offices) (Zip Code)

(650) 246-7000
(Registrant's Telephone Number, Including Area Code)

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

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

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

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

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

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

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant Section 13(a) of the Exchange Act. ☐

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates was approximately 1,956.8 million computed by reference to the last sales price of $56.17 as reported by the NASDAQ Global Select Market, as of the last business day of the registrant's most recently completed second fiscal quarter, June 30, 2017. This calculation does not reflect a determination that certain persons are affiliates of the registrant for any other purpose.

As of February 21, 2018, the number of outstanding shares of the registrant's common stock, par value $0.001 per share, was 65,392,310.

DOCUMENTS INCORPORATED BY REFERENCE

Part III incorporates information by reference to the definitive proxy statement for the registrant's 2018 Annual Meeting of Stockholders to be filed within 120 days of the registrant's fiscal year ended December 31, 2017.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This report, including the sections titled "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. In some cases you can identify these statements by forward-looking words, such as "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "could," "would," "project," "plan," "potential," "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 estimates and projections for the clinical development of our product candidates, including clinical research and trials, regulatory approvals and commercial launches, both in the United States and abroad;
- our ability to scale up manufacturing of our product candidates to commercial scale;
- potential indications for our product candidates;
- our expectation that our existing capital resources will be sufficient to enable us to complete our ongoing Phase 4 Biologics License Application, or BLA, enabling studies and related manufacturing of andexanet alfa and our Phase 2a proof-of-concept studies of cerdulatinib in hematologic cancers;
- our discussion of perceived and projected competitive advantages of our product candidates;
- the projected patient populations targeted by our product candidates;
- the projected dollar amounts of market opportunities for our product candidates;
- our ability to successfully commercialize our product candidates;
- the rate and degree of market acceptance of our product candidates;
- 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 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 ability to identify, develop, acquire and in-license new products and product candidates;
- our ability to successfully establish and successfully maintain appropriate collaborations and derive significant revenue from those collaborations;
- our financial performance; and
- developments and projections relating to our competitors or our industry.

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

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

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

PART I

ITEM 1. BUSINESS

Overview

We are a biopharmaceutical company focused on the development and commercialization of novel therapeutics in the areas of thrombosis, other hematologic disorders and inflammation for patients who currently have limited or no approved treatment options. We are advancing three programs, including our first medicine Bevyxxa® (betrixaban), an oral, once-daily Factor Xa, or fXa, inhibitor (anticoagulant), andexanet alfa (proposed tradename AndexXa®), a recombinant protein designed to reverse the anticoagulant effect in patients treated with an oral or injectable fXa inhibitor, and cerdulatinib, a spleen tyrosine kinase, or Syk, and Janus kinases, or JAK, inhibitor in development to treat hematologic cancers. We also have a partnered program, which is focused on developing selective Syk inhibitors for inflammatory conditions. These compounds come from our own internal research efforts and represent important advances that address significant unmet needs.

We are focusing our efforts on the commercialization of Bevyxxa in the United States and preparing for the potential launch of andexanet alfa pending a completion of review by the U.S. Food and Drug Administration, or FDA, anticipated in May 2018. Additionally, we are evaluating our strategy to commercialize in Europe following a positive trend vote for andexanet alfa and a negative trend vote for betrixaban received in February 2018 from the Committee for Medicinal Products for Human Use, or CHMP, regarding each product candidate's respective Marketing Authorisation Applications, or MAA. We are also continuing to advance cerdulatinib through a phase 2a clinical trial.

Our strategy

Key elements of our strategy are as follows:

- commercialize Bevyxxa and andexanet alfa, if approved, in the United States using our hospital-focused sales force;
- strategically scale up our field force and increase engagement with medical, scientific and academic professionals and associations to ensure awareness of unmet need;
- advance betrixaban and andexanet alfa through the European approval process;
- advance development of cerdulatinib for the treatment of hematologic cancers; and
- continue to advance our current development pipeline and expand it with multiple preclinical or clinical stage product candidates that align with our scientific expertise and experience; and
- continue to seek and evaluate partnerships that provide support for the further development or launch of our product candidates while retaining significant economic and commercial rights.

Marketed Product - Bevyxxa

Bevyxxa, approved by the FDA in June 2017, is the first and only anticoagulant for hospital and extended duration prophylaxis (35 to 42 days) of venous thromboembolism, or VTE, in adult patients hospitalized for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE. Bevyxxa represents an important advance in the field of thrombosis, as it significantly reduces the risk of VTE and VTE-related events without an increase in major bleeding. Portola has worldwide rights for the development and commercialization of betrixaban.

We launched Bevyxxa in the United States in January 2018 when drug supply became commercially available and we are continuing physician education activities, as well as hospital and payor negotiations regarding formulary placement. We believe we are able to address the multi-billion dollar market for VTE prophylaxis in acute medically ill patients with a targeted sales and marketing to the hospitals.

We believe the compelling health economic profile of Bevyxxa will enable us to effect a change in the treatment and care paradigm from in-hospital only VTE prophylaxis to a single-drug regimen from admission to the hospital to home. Our pivotal Phase 3 APEX study demonstrated that patients treated with betrixaban experienced a reduction in VTE with no increase in major bleeding and fewer all cause stroke events. Based on the APEX data and current cost estimates of VTE events, major bleeds and strokes, we believe that betrixaban (35 to 42 days) will be cost effective when compared to enoxaparin and unfractionated heparin. Further, each year more than 150,000 acute medically ill patients worldwide die of VTE and not from their underlying medical condition. Pulmonary embolism is the most common preventable cause of hospital death and a leading cause of increased length of hospital stay. The average annual direct medical cost of treating VTE in a hospital setting in the United States is between $7,500 and $16,500 per patient and is even greater for elderly, higher risk patients.

Product Candidates

Our development pipeline is summarized in the table below.

Development pipeline				
Product	**Description**	**Stage**	**Indication**	**Worldwide commercial rig hts**
Andexanet alfa	Antidote for Factor Xa inhibitors	Phase 3b-4	Reversal of Factor Xa inhibitor anticoagulation	Portola (excluding Japan)
Cerdulatinib	Oral, dual Syk and JAK inhibitor	Phase 2a	Relapsed/refractory B- and T-cell malignancies	Portola (excluding topical indications)
PRT2761	Tropical, selective Syk inhibitor	Phase 2	Allergic conjunctivitis	Portola / Ora
PCSK9 inhibitor	Oral, PCSK9 inhibitor	Pre-clinical	hypercholesterolemia	Portola (excluding CNS indications)

Andexanet alfa

Andexanet alfa, an FDA-designated breakthrough therapy and orphan drug, is a universal reversal agent in development for patients anticoagulated with an oral or injectable fXa inhibitor who experience a serious uncontrolled or life-threatening bleeding event, or who require urgent or emergency surgery. Currently, there is no antidote or reversal agent approved for use in reversing the anticoagulating effects of fXa inhibitors. Leading clinicians and the FDA have recognized that the lack of an effective reversal agent represents a significant unmet clinical need.

The use of fXA inhibitors is continuing to grow at a significant steady pace. Based on our research and relevant market data, we estimate that by 2020, fXa inhibitors will have a majority share of the market in each major anti-coagulation indication. As sales of fXa inhibitors increase, the need for an effective antidote or reversal agent will increase correspondingly. We estimate that by 2020, over 440,000 patients annually in the G7 countries will require an fXa reversal agent due to a major bleeding episode (approximately 300,000), emergency surgery (approximately 100,000) and traumatic injury (approximately 100,000).

Major 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 major bleeding associated with the administration of fXa inhibitors ranges from 1% to 4% per year, depending on the underlying medical condition and the specific fXa inhibitor. The clinical costs of a major bleeding event in fXa inhibitor treated patients are estimated to be $28,000 per patient on average and greater than $100,000 per patient for the top 20% or most severe bleeds. Based on the frequency of bleeding rates suggested by clinical trials and our projection of 23 million to 36 million patients treated annually with fXa inhibitors in the G7 countries, we believe that the annual costs to the healthcare system to treat major bleeding episodes in patients treated with an fXa inhibitor may exceed $10 billion by 2020. We believe that an effective fXa antidote represents a potentially cost-effective way to manage these healthcare system costs.

The current standard treatment for patients who experience major bleeding while taking a non-oral fXa inhibitor 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; and is dependent upon the particular fXa. The treatment is dependent upon which fXa-inhibitor the patient is taking. 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. These treatments can have potentially serious side effects, including increased risk of prothrombotic effects such as ischemic stroke and myocardial infarction in some cases.

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

We resubmitted our BLA, to the FDA in August 2017, and in December 2017, the FDA instituted an extension to allow more time for a thorough review of the information provided and to work with us on labeling and post-marketing commitments. The new action date is May 4, 2018. In February 2018, we received a positive trend vote for andexanet alfa from the Committee for Medicinal Products for Human Use, or CHMP, regarding our Marketing Authorisation Application, or MAA, for Europe. The CHMP also communicated requests for additional data which could delay the CHMP opinion until the fourth quarter of 2018.

While the BLA is under review, we are building a limited supply of andexanet alfa product from our first generation manufacturing process. Simultaneously, we are building generation 2 supply product, which will be subject to a supplemental approval process for approval by the FDA, and will enable a broader commercial launch. During the third quarter of 2017, we executed a new long-term manufacturing services agreement that will significantly increase our commercial manufacturing capacity for a period of ten years following initial approval of the generation 2 manufacturing process.

We are continuing to enroll patients in ANNEXA-4, our Phase 3 / 4 confirmatory patient study which underwent two Data Safety and Monitoring Board reviews during 2017, and six total to date. This multi-center open-label, single-arm study is being conducted in patients receiving apixaban, rivaroxaban, edoxaban or enoxaparin (a low molecular weight heparin) who present with certain acute major bleeds. All participants receive andexanet alfa given as a bolus dose over 30 minutes followed by a two-hour infusion. Patients receive a low or high dose depending on which fXa inhibitor they have received and the time they received it. Patients are evaluated for 30 days following andexanet alfa administration. The co-primary efficacy endpoints are the percent change in anti-Factor Xa activity at two hours and assessment of hemostasis over 12 hours following the infusion. Hemostatic efficacy is assessed by an independent endpoint adjudication committee as either excellent, good or poor/none. To date, ANNEXA-4 has enrolled more than 250 patients of the approximately 350 patients targeted for inclusion.

Cerdulatinib

Our third product candidate, cerdulatinib, is an orally available dual kinase inhibitor that inhibits Syk and JAK enzymes that regulate important signaling pathways. Cerdulatinib is being developed for hematologic, or blood, cancers and inflammatory disorders. We are currently conducting a Phase 2a proof-of-concept study for cerdulatinib in patients with B- and T-cell Non-Hodgkin's Lymphoma, or NHL, including patients with Follicular Lymphoma, or FL, Peripheral T-cell Lymphoma, or PTCL, and Chronic Lymphocytic Leukemia, or CLL, who have failed or relapsed on existing marketed therapies or products in development, including patients with identified mutations. Cerdulatinib has the potential for broad activity in hematologic cancers because it blocks the B-cell receptor pathway via Syk and key cytokine receptors via JAK. In addition, pre-clinical evidence suggests that Syk is also expressed in PTCL and activating mutations in JAK pathway are frequently observed in PTCL.

Our strategy for cerdulatinib is to focus on patients that have shown limited response to other therapies or have relapsed or do not respond due to mutations. The heterogeneity and severity of B- and T-cell malignancies may warrant simultaneous targeting of multiple disease-relevant pathways. With its dual inhibition pathway, cerdulatinib 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.

Other early stage product candidates

In addition to our lead product candidates, we have other early research and development programs including an exclusive in-license agreement with SRX Cardio LLC to explore a novel approach to develop a drug in the field of hypercholesterolemia.

Additionally, PRT2761 is currently in a phase 2 study for the treatment of allergic conjunctivitis. Allergic conjunctivitis is a disease of allergen-mediated BCR and stimulation and IgE crosslinking of FcεR1 leading to basophil and mast cell degranulation. SYK is critical for BCR and FcεR1 signaling and functional responses, and therefore represents a potentially important target for therapeutic intervention. A single-center, randomized, blinded, dose-ranging phase 2 study evaluating the efficacy and safety of PRT2761 for the treatment of allergic conjunctivitis is ongoing.

Sales and marketing

We intend to commercialize both Bevyxxa and andexanet alfa, pending regulatory approvals, using a hospital-based sales force in the United States, and in major markets in Europe. 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 2,000 hospitals and out-patient acute care settings that would account for the large majority of the prescribing base for our product and product candidate. We believe Bevyxxa and andexanet alfa, if approved, can be successfully commercialized in the United States with a hospital-based field force that includes approximately 150 sales representatives. Additionally, we intend to develop and publish health economic models demonstrating the value of Bevyxxa and andexanet alfa to hospital administrators and third party payors.

Research and development

We invest significant effort defining and refining our research and development process and internally teaching our approach to drug development. We favor programs with early decision points, well-validated targets, predictive preclinical models and clear paths to regulatory approval, all in the context of a target product profile that can address significant unmet or underserved clinical needs. Members of our discovery, research and development team have played central roles in discovering and developing a number of promising candidates over more than 20 years. 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 increase that 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. 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.

License and collaboration agreements

Betrixaban

Millennium agreements

In 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. We are obligated to pay royalties to Millennium at tiered single-digit percentages of net sales of certain ADP Program products if product sales are ever achieved. These royalty payments will continue until the expiration of the relevant patents or ten years after launch, whichever is later.

In 2004, we entered into an agreement to license from Millennium certain exclusive rights to research, develop and commercialize certain compounds that inhibit fXa from Millennium, including betrixaban. We refer to this arrangement as the fXa 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 fXa Program. 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 fXa Program. In addition, we are obligated to pay Millennium royalties at tiered single-digit percentages of net sales of any fXa 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 2005, we amended both the asset purchase agreement for the ADP Program and the license agreement for the fXa Program. In connection with these amendments, we have made aggregate cash payments to Millennium of $6.0 million and issued to Millennium equity securities with an aggregate value of $1.8 million through December 31, 2016.

Andexanet alfa

BMS and Pfizer agreements

In 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. In 2014, we entered into a second collaboration agreement with BMS and Pfizer to further study the safety and efficacy of andexanet alfa as a reversal agent to apixaban through our ongoing Phase 3 studies. Under the terms of the Phase 3 agreement, we received an upfront payment of $13.0 million and are eligible to receive additional development and regulatory milestone payments of up to $12.0 million. This Phase 3 collaboration agreement will continue in force until the approval of andexanet alfa as a reversal agent for apixaban by the FDA and EMA.

In 2016, we entered into collaboration agreements with BMS and Pfizer to obtain Japanese regulatory approval and to commercialize andexanet alfa in Japan. Under the terms of the agreement we received an upfront payment of $15.0 million and are eligible to receive potential regulatory and sales-based milestone payments totaling $90.0 million, as well as double-digit royalties based on andexanet alfa net sales in Japan. BMS and Pfizer obtained the rights to develop and commercialize andexanet alfa in Japan and will be responsible for all development, regulatory and commercialization activities.

Bayer and Janssen agreements

In 2013, we entered into a clinical collaboration agreement with Bayer and Janssen to include subjects dosed with rivaroxaban, their jointly owned fXa inhibitor product, in one of our Phase 2 proof-of-concept studies of andexanet alfa. In February 2014, we entered into a second collaboration agreement with Bayer and Janssen to further study the safety and efficacy of andexanet alfa as a reversal agent to rivaroxaban through our ongoing Phase 3 studies. Under this Phase 3 collaboration agreement, we received an upfront payment of $10.0 million and the right to receive additional development and regulatory milestone payments of up to $15.0 million. This Phase 3 collaboration agreement will continue in force until the approval of andexanet alfa as a reversal agent for rivaroxaban by the FDA and EMA.

In 2016, we entered into collaboration agreements with Bayer to include rivaroxaban in the clinical studies for approval of andexanet alfa in Japan. Under the terms of the agreement, we received an upfront payment of $5.0 million and are eligible to receive up to $10.0 million in additional milestone payments based on Japanese regulatory approval of andexanet alfa as an antidote for rivaroxaban. Bayer will provide technical support as well as fund clinical studies of andexanet alfa with rivaroxaban in Japan. Bayer received no commercial rights under this agreement.

Daiichi Sankyo agreement

In 2013, we entered into an agreement with Daiichi Sankyo to include subjects dosed with edoxaban, its fXa inhibitor product, in one of our Phase 2 proof-of-concept studies of andexanet alfa. In July 2014, we entered into a second collaboration agreement with Daiichi Sankyo to perform the necessary development and regulatory activities to support a potential U.S. and EU regulatory approval of andexanet alfa as a reversal agent for edoxaban. Under this Phase 3 collaboration agreement we received an upfront payment of $15.0 million and are eligible to receive additional development and regulatory milestone payments of up to $25.0 million. In 2016, we amended the 2014 agreement to expedite development activities in exchange for $15.0 million and a net increase in total eligible milestones of $8.0 million. This amended collaboration agreement will continue in force until the approval of andexanet alfa as a reversal agent for edoxaban by the FDA and EMA.

In 2016, we entered into collaboration agreements with Daiichi Sankyo to include edoxoban in the clinical studies necessary for approval of andexanet alfa in Japan. Under the terms of the agreement, we will receive an upfront payment of $5.0 million and are eligible to receive up to $10.0 million in additional milestone payments based on Japanese regulatory approval of andexanet alfa as an antidote for edoxaban.

Syk Selective Inhibitors

Astellas agreement

In 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 2010. The agreement with Astellas, as amended, requires us to make certain milestone, royalty and sublicense revenue sharing payments to Astellas as we develop, commercialize or sublicense Syk inhibitors. Pursuant to our agreement with Astellas, we made cash milestone payments to Astellas of $0.5 million in 2005, $0.5 million in 2006, and $1.0 million in 2008, as we elected to continue our development of Syk inhibitors. In addition, for each Syk inhibitor product, we may be required to make up to $71.5 million in additional milestone payments to Astellas if the product is approved for multiple distinct indications in the United States, Europe and Japan and the product attains certain sales levels. If we grant a sublicense to develop and commercialize Syk inhibitors, we are required to pay Astellas 20% of any payments (excluding royalties) received under the sublicense agreement. In 2011, in connection with our receipt of the upfront payment under our agreement with Biogen Idec, we made a cash payment to Astellas of $7.2 million. In addition, we are required to pay Astellas royalties at low single-digit percentages for worldwide sales for any Syk inhibitor product made by us or our sublicensees. This agreement will continue in force, on a product-by-product and country-by-country basis, until the expiration of relevant patents or ten years after the launch, whichever is later, or termination by either party pursuant to the agreement. The agreement may be terminated by us for convenience upon 60 days' written notice to Astellas or immediately upon written notice if all major claims of all of the patents covered by the agreement are invalidated by competent judicial or administrative authorities in the U.S. and no measure has

been taken to appeal the invalidation. Either party may terminate the agreement upon written notice if the other party is in material breach of its obligations under the agreement for reasons within its control and responsibility and has not remedied the breach within 30 days of receiving written notice or in the event of bankruptcy, liquidation or receivership of the other party.

Cerdulatinib

Aciex agreement (Nicox)

In 2013, we entered into a license and collaboration agreement with Aciex Therapeutics, Inc., or Aciex, pursuant to which we granted Aciex an exclusive license to co-develop and co-commercialize cerdulatinib and certain related compounds for nonsystemic indications, such as the treatment and prevention of ophthalmological diseases by topical administration and allergic rhinitis by intranasal administration. In 2014, this agreement was amended to release all rights for cerdulatinib to us. The collaboration is now focused on development of other related compounds for topical ophthalmic indications. 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.

Ora agreement

In 2015, we entered into a license and collaboration agreement with Ora pursuant to which we granted Ora an exclusive license to co-develop and co-commercialize one of our specific Syk inhibitors, PRT2761. Ora has the primary responsibility for conducting the research and development and regulatory 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.

Under the terms of this risk and cost sharing agreement, each party will incur its own share of development costs. Third-party related development costs will be shared by Ora and us at approximately 60% and 40%, respectively, until an End of Phase 2 meeting with the FDA, and then equally thereafter. We are entitled to receive either 50% of the profits, if any, generated by future sales of the products developed under the agreement or royalty payments on such sales, should we opt out of the agreement.

We may opt out of the agreement any time prior to 90 days after an End of Phase 2 meeting with the FDA. The timing of the exercise of our opt-out rights would impact future royalties we would be entitled to receive from Ora. Each party may also buy out the rights and interests in the licensed compound by paying the greater of $6.0 million or two times the actual aggregate development cost incurred by both parties on or before the date that is 90 days after an End of Phase 2 meeting with the FDA.

Dermavant agreement

In 2016, we granted an exclusive, worldwide license to Dermavant Sciences GmbH, or, Dermavant, to develop and commercialize cerdulatinib in topical formulation for all indications, excluding oncology, in exchange for a non-refundable upfront payment of $8.8 million and contingent development and regulatory milestones and commercial milestone payments based on worldwide annual net sales. Additionally, Dermavant is required to pay us royalties on worldwide net sales of all products commercialized under the agreement throughout the license term, which continues on a country-by-country basis until the later of the 10th anniversary of the first commercial sale or the expiration of the last valid patent.

See Note 6 and Note 8 in the Notes to Consolidated Financial Statements contained in the section of this report entitled “Financial Statements and Supplementary Data” for a more detailed description of the agreements and accounting assessments associated with certain of these agreements.

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 will compete with enoxaparin, which is marketed as Lovenox by Sanofi-Aventis U.S. LLC 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 fXa 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 GbmH, although none of these molecules is currently approved for use in that population. We believe, that in light of the significant opportunity in this acute medically ill population, other agents will likely be tested in a Phase 3 study. For example, in 2014, Janssen initiated a Phase 3 study designed to evaluate the efficacy and safety of rivaroxaban compared with placebo in the prevention of symptomatic VTE events and VTE-related death post-hospital discharge in high-risk, medically ill patients. Janssen also announced in 2014 that it had initiated a Phase 3 study designed to evaluate the efficacy and safety of rivaroxaban to reduce the risk of deep vein thrombosis, or DVT, and pulmonary embolism due to a concurrent medical illness for up to 45 days after hospital discharge. In the future, owners of approved direct fXa 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 fXa inhibitors. However, andexanet alfa, if approved, may compete with currently approved treatments designed to enhance coagulation including FFP, PCCs, rFVIIa, Vitamin K, protamine or whole blood. In addition, several companies have conducted clinical research on compounds that are intended to reverse the effects of one or more direct fXa inhibitors and which, if developed, may be competitive with andexanet alfa.

Cerdulatinib

In the market for the treatment of FL, PTCL, and CLL, cerdulatinib, if approved, will compete with existing therapies, such as rituximab and obinutuzumab which are marketed by Chugai Pharmaceutical Co., F. Hoffmann-LaRoche Ltd. and Genentech, Inc., idelalisib, which is marketed by Gilead, copanlisib, which is marketed by Bayer, romidepsin, which is marketed by Celgene, pralatrexate, which is marketed by Spectrum Pharmaceuticals, Inc., ibrutinib, which is marketed by Janssen and Pharmacyclics, Inc., venetoclax, which is marketed by Abbvie and Genentech, Inc.; and potentially other therapies currently in development by a number of different companies.

Syk Selective Inhibitors

In the market for treatment of allergic conjunctivitis, PRT02761, if approved, will compete with existing products, such as topical antihistamines, corticosteroids, and mast cell stabilizers 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 the section of this Report entitled "Risk factors—Risks related to intellectual property."

As of December 31, 2017, we owned 50 issued U.S. patents, 16 U.S. patent applications and 321 issued patents and 130 patent applications in other jurisdictions. We also co-owned 17 additional patents and patent applications. In addition, as of December 31, 2017, we have licensed 200 issued patents and 32 patent applications from third parties, mostly on an exclusive basis. The patent portfolios for our leading product candidates as of December 31, 2017 are summarized below**.**

Betrixaban

Our betrixaban patent portfolio includes 24 issued U.S. patents and three 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 from Millennium. The U.S. issued patents relating to the composition of matter of betrixaban are not due to expire before September 2020 and may be extended up to September 2025, if betrixaban receives regulatory approval and if the necessary eligibility requirements are met, pursuant to the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act. Related international patent applications have issued or been allowed in 37 countries and are pending in 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 Hatch-Waxman Act permits a patent term extension of up to five years for one patent related to an approved therapy. The length of the extension is based upon the period of time the therapy has been under regulatory review. We believe that we are eligible for a full five year patent term extension for one patent relating to betrixaban.

In addition, we have planned a pediatric study of betrixaban in the United States as 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.

Andexanet alfa

Our fXa inhibitor antidote patent portfolio is wholly owned by us and includes 12 issued U.S. patents and nine U.S. patent applications covering the composition of and methods of making and using andexanet alfa or its analogs. We retain full commercialization rights to andexanet alfa on a worldwide basis except for Japan where commercial rights have been licensed to BMS and Pfizer.

The last to expire of the U.S. patents is not expected to expire before June 2030.A related international patent application has issued in Australia, New Zealand, China, Japan, Mexico, Singapore, Canada, South Africa, Hong Kong, South Korea, and Europe, another related international patent application has issued in China, Japan, New Zealand, Mexico, Singapore, Australia, and South Korea. These international patents and patent applications, if issued, would not be due to expire before September 2028. Several other international patent applications have issued in Europe and other countries, and international patent applications are still pending in Europe and a number of other countries.

Cerdulatinib

Our dual Syk-JAK inhibitor patent portfolio is owned in part by us and licensed in part from Astellas and includes five issued U.S. patents covering the composition of and methods of making and using cerdulatinib or its analogs. The last to expire of the U.S. patents is not expected to expire before July 2029. Related international patent applications have issued or been allowed in 49 countries and are pending in a number of other countries. These international patents and patent applications, if issued, would not be due to expire before April 2029.

Syk Selective Inhibitors

Our Syk-specific inhibitor patent portfolio is owned by us and includes five issued U.S. patents covering the composition of and methods of making and using PRT2607 or its analogs. The last to expire of the U.S. patents is currently expected to expire in July 2029. Related international patent applications have issued or been allowed in 24 countries and, have been granted in Europe and are pending in a couple of other countries. These international patents and patent applications, if issued, would not be due to expire before April 2029.

PCSK9

Our PCSK9 patent portfolio includes three U.S. patent applications covering the composition of and methods of making and using PCSK9 inhibitors, including those owned by us and those licensed from Serometrix. The U.S. patents relating to the composition of matter of PCSK9 inhibitors, if issued, are not due to expire before February 2034. Related international patent applications are pending in seven countries. These international patent applications, if issued, would not be due to expire before February 2034. Several international patent applications are still pending and if issued would not be due to expire before 2035.

Manufacturing

We rely on contract manufacturing organizations produce our drugs and drug candidates in accordance with the FDA's and EMA's current Good Manufacturing Practices, or cGMP. 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. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. Our relationships with contract manufacturing organizations are managed by internal personnel with extensive experience in pharmaceutical development and manufacturing.

Betrixaban

Betrixaban is manufactured using common chemical engineering and synthetic processes from readily available raw materials. We have relied on Hovione, Limited, or Hovione, to produce active pharmaceutical ingredient, or API, for betrixaban for our APEX study, and in April 2016 we entered into an agreement with Hovione to manufacture API for betrixaban at commercial scale. Since the date of our approval we have initiated and received approval from the FDA for multiple prior approval supplements that enabled the commercial release of Bevyxxa manufactured before and after our approval date. The prior approval supplements have also enabled us to access multiple locations within Hovione's manufacturing network, thus mitigating the single source supply risk.

Andexanet alfa

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.

Our current Phase 4 ANNEXA study is using clinical material with bulk drug substance manufactured by AGC Biologics, formerly CMC ICOS Biologics, Inc., and Lonza. Our BLA contemplates the manufacturing process in place at AGC Biologics. The Lonza, or generation 2, process will be subject to a supplemental approval by the regulatory authority before commercialization. During the third quarter of 2017, we executed a new long-term manufacturing services agreement with Lonza that will significantly increase our commercial manufacturing capacity for a period of ten years following initial approval of the generation 2 manufacturing process.

See Note 7 in the Notes to Consolidated Financial Statements contained in the section of this report entitled "Financial Statements and Supplementary Data" and refer to the "Off-balance sheet arrangements and contractual obligations" portion of this report in the section entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" for a more detailed description of the agreements, obligations and accounting assessments.

Government regulation

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

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

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

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

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

- Phase 1 – Studies are initially conducted to test the product candidate for safety, dosage tolerance, absorption, metabolism, distribution and excretion in healthy volunteers or patients.
- Phase 2 – Studies are conducted with groups of patients with a specified disease or condition to provide enough data to evaluate the preliminary efficacy, optimal dosages and dosing schedule and expanded evidence of safety. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3 – Phase 3 clinical trials are undertaken in large patient populations to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety in an expanded patient population at multiple clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product compared to placebo or current standard of care and provide an adequate basis for product labeling. These trials may be done globally to support global registrations.
- The FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called Phase 4 studies may be made a condition to be satisfied after approval. The results of Phase 4 studies can confirm the effectiveness of a product candidate and can provide important safety information gathered in routine medical practice.

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

NDA or BLA submission and review by the FDA

The results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of an NDA or BLA. The submission of an NDA or BLA requires payment of a substantial User Fee to FDA. The FDA may convene an advisory committee to provide independent expert clinical opinion on application review questions. The FDA reviews applications to determine, among other things, whether a product is safe and effective for its intended use and whether the manufacturing controls are adequate to assure consistent batch to batch purity, identity, potency, and strength of the product candidate. Before approving an NDA or BLA, the FDA will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes, equipment and facilities are in compliance with cGMP requirements. Once the NDA submission has been accepted for filing (60 days post receipt of the application by the FDA, if at all), the FDA typically takes ten months to review the application and respond to the applicant, which can take the form of either a Complete Response Letter or Approval. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA may delay or refuse approval of an NDA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product. FDA approval of any NDA or BLA submitted by us will be at a time the FDA chooses. Also, if regulatory approval of a product is granted, such approval may entail limitations on the indicated uses for which such product may be marketed and require post-marketing requirements such as a Risk Evaluation and Mitigation Procedure or a Phase 4 study. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing regulatory standards is not maintained or if problems occur after the product reaches the marketplace. In addition, the FDA may require Phase 4 post-marketing studies to monitor the effect of approved products, and may limit further marketing of the product based on the results of these post-marketing studies.

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

Post-approval requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including record-keeping requirements and reporting of adverse experiences. Drug and biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, 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 cGMP regulations and other FDA regulatory requirements. If our present or future suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, require us to recall a product from distribution, or withdraw approval of the NDA or BLA.

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

Healthcare and reimbursement regulation

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

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

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

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

Foreign regulation

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

European Union, or 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. The sponsor responds to any inquiries and the final report is issued on the 120th day from submission of application. The final report is forwarded to the EMA for review and approval. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points may eventually be referred to the European Commission, whose decision is binding on all member states.

Employees

As of December 31, 2017, we had 252 full-time employees, 28 of whom hold Ph.D. degrees and six of whom hold M.D. degrees. Of the full-time employees, 122 employees are engaged in research and development and 130 are engaged in general administration, business development, sales 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 74,000 square feet of research and office space in South San Francisco, California under a lease that expires in March 2020. Thereafter, at our option, we may extend the term for an additional three years through March 2023. We believe that our existing facilities are sufficient for our current needs for the foreseeable future.

Legal proceedings

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

Corporate and Available Information

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

Item 1A. RISK FACTORS.

Investing in our common stock involves a high degree of risk. You should consider carefully the following risks, together with all the other information in this report, 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.

In assessing these risks, you should also refer to other information contained in this annual report on Form 10-K, including our Condensed Consolidated Financial Statements and related Notes.

RISKS RELATED TO OUR FINANCIAL CONDITION AND NEED FOR ADDITIONAL CAPITAL

We have incurred significant losses, and expect to incur substantial and increasing losses as we continue to develop and commercialize our product candidates.

We are an early stage commercial biopharmaceutical company and have recently launched our first commercial product. Bevyxxa is our only approved product, and we continue to incur significant expenses related to the planned commercialization of Bevyxxa, the funding of our ongoing and planned future clinical studies and other research and development activities for our other product candidates, including andexanet alfa, and selling, general and administrative activities. Our operating expenses increased during 2017 and we do not anticipate a decrease in the near term. As of December 31, 2017, we had an accumulated deficit of approximately $1.2 billion.

To date, we have financed our operations primarily through sales of our equity securities, collaborations, including a loan from one of our collaboration partners, a sale of a royalty stream from future product sales, sales of commercial and development rights to some of our product candidates, 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. We anticipate that we will continue to incur substantial expenses as we:

- establish and scale-up manufacturing capabilities and a sales, marketing and distribution infrastructure to commercialize Bevyxxa and other products for which we may obtain regulatory approval, including process improvements in order to manufacture andexanet alfa at commercial scale;
- 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; and
- enhance operational, compliance, financial, quality and information management systems and hire more personnel, including personnel to support development of our product candidates and support our commercialization efforts.

To be profitable in the future, we must succeed in commercializing Bevyxxa and developing and commercializing other products with significant market potential. This will require us to be successful in a range of activities, including advancing our product candidates, completing clinical studies of our product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling Bevyxxa and 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 operating results are difficult to predict and will likely fluctuate from quarter to quarter and year to year. Due to the recent approval by the FDA of Bevyxxa and the absence of historical sales data, Bevyxxa sales will be difficult to predict from period to period and as a result, you should not rely on Bevyxxa sales results in any period as being indicative of future performance and sales of Bevyxxa may be below the expectation of securities analysts or investors in the future. We believe that our quarterly and annual results of operations may be affected by a variety of factors relating to Bevyxxa, and andexanet alfa and cerdulatinib if approved, including:

- the level of demand;
- the extent to which coverage and reimbursement is available from government and health administration authorities, private health insurers, managed care programs and other third-party payors;
- rebates, discount, other pricing concessions and fees that we may provide to integrated delivery networks, group purchasing organizations, other purchasers and pharmacy benefits managers and other third-party payors;
- the timing, cost and level of investment in our marketing efforts to support sales;
- the timing, cost and level of investment in our research and development activities involving approved products and product candidates;
- the cost of manufacturing, distribution and the amount of legally mandated discounts to government entities, other discounts and rebates, product returns and other gross-to-net deductions;
- the risk/benefit profile, cost and reimbursement of existing and potential future drugs which compete with approved products; and
- expenditures that we will or may incur to acquire or develop additional product candidates and technologies;

In addition, from time to time, we enter into collaboration agreements with other companies that include development funding and upfront and milestone payments, and we expect that amounts earned from our collaboration agreements will continue to be an important source of revenue. These upfront and milestone payments may vary significantly from quarter to quarter and any such variance could cause a significant fluctuation in our operating results from one quarter to the next.

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 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 have recently launched commercial operations for our first product and are advancing multiple product candidates through the research and clinical development process. The development and commercialization of Bevyxxa and our product candidates will continue to require substantial funds. Our future financing requirements will depend on many factors, some of which are beyond our control, including the following:

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

Until we can generate a sufficient amount of product revenue to finance our cash requirements, which we may never do, we expect to finance future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other financing, 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 financing, marketing and distribution arrangements or other collaborations, strategic alliances, licensing or other financial 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, research and development programs or commercialization efforts.

RISKS RELATED TO THE COMMERCIALIZATION OF BEVYXXA AND THE DEVELOPMENT AND COMMERCIALIZATION OF OUR PRODUCT CANDIDATES

Our success depends heavily on the launch and commercialization of Bevyxxa and the approval and successful commercialization of our product candidate, andexanet alfa. Our commercialization and development of andexanet alfa and our other 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 and commercialization of Bevyxxa, the development of andexanet alfa and, to a lesser extent, cerdulatinib and our selective Syk inhibitor program. Our ability to generate product revenue from Bevyxxa or from other product candidates, which will not occur until after regulatory approval, if ever, will depend on the successful development, regulatory approval and eventual commercialization of our product candidates. The success of our product candidates will depend on several factors, including the following:

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

Bevyxxa and potential future product candidates may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

The commercial success of Bevyxxa and any potential future product candidates for which we may obtain marketing approval from the FDA or other regulatory authorities will depend upon their acceptance by the medical community and third-party payors as clinically useful, cost-effective and safe. The degree of market acceptance of any drug depends on a number of factors, such as:

- the prevalence and severity of any side effects;
- efficacy and potential advantages compared to alternative treatments;
- the price we charge for our product candidates;
- interpretations of the results of our clinical trials;
- the willingness of physicians and healthcare organizations to change their current treatment practices;

- the willingness of hospitals and hospital systems to include our product candidates as treatment options;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the willingness of the target patient population to pay for our products, including co-pays under their health coverage plans;
- the strength of marketing and distribution support; and
- the availability of third-party coverage and adequate reimbursement.

Failure to attain market acceptance among the medical community and third-party payors may have an adverse impact on our operations and profitability. Although certain of our employees have commercialization experience, as a company we currently have only limited commercial capabilities. We may not be able to attract and retain qualified personnel to serve in our sales and marketing organization to effectively support our commercialization activities. If we are not successful in commercializing Bevyxxa or current or potential future product candidates in the event they receive regulatory approval, our future product revenue will suffer and we may incur significant additional losses.

We currently have limited sales and distribution personnel and are in the initial stages of developing marketing capabilities for Bevyxxa. If we are unable to develop effective sales, marketing and distribution capabilities on our own or through collaborations or other marketing partners, we will not be successful in commercializing Bevyxxa, or andexanet alfa and our other future products.

We are in the early stages of developing our sales and marketing infrastructure and have limited history of selling, marketing or distributing therapeutic products. To achieve commercial success for Bevyxxa or any current or potential product candidate, we must continue to 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 Bevyxxa globally, and andexanet alfa if it is 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, which 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 competing products more successfully than we do.

The development and commercialization of new therapeutic products is highly competitive. We face competition with respect to commercializing Bevyxxa and developing 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 anticoagulants for use in various disease states, including injectable anticoagulants for the prevention of VTE in acutely ill medical 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. Some of these competitors are or may be 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 or maintain market share and undermine the value proposition that we might otherwise be able to offer to payors. Bevyxxa is indicated for the prophylaxis of VTE in adult patients hospitalized for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors. The current standard of care for VTE prophylaxis in acute medically ill patients in the United States is a 6- to 14-day administration of enoxaparin, marketed as Lovenox ® and also available in generic form. Enoxaparin is a low cost therapy that is widely accepted by physicians, patients and third-party payors. As a result, we may face difficulties in marketing Bevyxxa in this patient population. Additionally 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 acutely ill medical patients. For example, we believe that Bayer and Janssen are near completion of their Phase 3 MARINER clinical trial to evaluate the safety and efficacy of rivaroxaban for up to 45 days post hospital discharge (after enoxaparin in hospital) to reduce the risk of symptomatic VTE in medical ill patients. If the MARINER trial is successful, Bevyxxa is expected to face increased competition in the marketplace from a drug which would be used as a different treatment strategy (post discharge only) in an overlapping patient population. Such treatment strategy would not require physicians, patients and third-party payors to replace enoxaparin with a higher priced therapy in the hospital.

While there are no therapies approved specifically as antidotes for fXa inhibitors, we are aware of at least one drug candidate that has been studied in early stage clinical trials as a potential antidote to fXa inhibitors. In addition, in December 2014, Bristol-Myers Squibb Company and Pfizer Inc. announced that a clinical trial of 15 healthy human subjects demonstrated that two 4-factor PCCs reversed the steady-state pharmacodynamic effects of Eliquis (apixaban) in several coagulation assessments. Andexanet alfa, if approved, may compete with other currently approved treatments designed to enhance coagulation, such as FFP, PCCs, rFVIIa or whole blood. Although there is no clinical evidence supporting the use of such treatments in patients taking fXa 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 fXa inhibitors.

Also, in October 2015, Boehringer Ingelheim Corporation obtained FDA and EMA approvals of idarucizumab for the reversal of the anticoagulant effect of Pradaxa (dabigatran) for emergency/urgent procedures or in life-threatening or uncontrolled bleeding. Although idarucizumab is a specific reversal agent for Pradaxa, a direct thrombin inhibitor, rather than a fXa inhibitor, to the extent the availability of a specific reversal agent leads to increased adoption of Pradaxa rather than fXa inhibitors or low molecular weight heparins, the demand for andexanet alfa as a specific reversal agent for fXa inhibitors and low molecular weight heparins could also be reduced.

There are also a number of products in clinical development for hematologic cancer, ophthalmological diseases, allergic rhinitis, allergic asthma and other inflammatory diseases that are potential indications for cerdulatinib or selective Syk inhibitors. 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 noncompetitive. Many competing products are in later stages of development than our products and, therefore, may 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.

We received a Complete Response Letter to our initial BLA for andexanet alfa from the FDA indicating that our resubmission will not be approved unless those deficiencies have been successfully addressed.

In August 2016, we received a CRL from the FDA regarding our BLA for andexanet alfa. This CRL has delayed the commercial launch of andexanet alfa and required us to re-submit our BLA with additional information requested by the FDA, and it may present additional risk that andexanet alfa will not be approved by the FDA or other regulatory authorities, including the EMA. In the CRL, the items raised by the FDA primarily related to the manufacturing process and analytical testing of andexanet alfa. The FDA also asked us for additional data to support the inclusion of edoxaban and enoxaparin in the label and indicated that it needs to finalize its review of the clinical studies required as post-marketing commitments.

In August 2017 we resubmitted our BLA to the FDA in an effort to resolve the items identified by the FDA in the CRL and obtain approval of our BLA. On August 15, 2017, the FDA notified us that our resubmitted BLA was acceptable for review and assigned it an action due date of February 3, 2018. On December 22, 2017, the FDA notified us that this action date was extended by 90 days to May 4, 2018 to allow more time for a thorough review of the information provided and to work with the company on labeling and post-marketing commitments. We can offer no assurances that the resubmission will resolve all items raised in the CRL to the satisfaction of the FDA or that the FDA will not raise previously unidentified issues or further extend the action date for the BLA. As a result, our ability to market, sell, distribute, obtain acceptable reimbursement for, set pricing for, and continue to operate, commercialize or continue the development of andexanet alfa may be further delayed, adversely affected or prevented altogether.

Even if the outstanding items identified in the CRL are resolved to the satisfaction of the FDA by our resubmission, the agency retains the right not to approve the BLA or to require additional information, or to raise additional issues to support regulatory approval of andexanet alfa, which could further delay or prevent its approval or limit the approved indications for andexanet alfa. In addition, either the substance of the items identified by the FDA in the CRL, or the CRL itself, could have an adverse impact on our efforts to obtain marketing authorization for andexanet alfa from the EMA and other regulatory authorities. Also, in response to the CRL, we have suspended our efforts to expand post-approval supply based on an expanded generation 1 manufacturing process on the 6x2,000 liter Line C manufacturing line at CMC Biologics and are focusing our efforts on expanding post approval through our generation 2 manufacturing process at the 10,000 liter scale at Lonza. As a result, even if we obtain commercial marketing approval for andexanet alfa, our ability to market andexanet may be adversely impacted by limited supply of drug until we can commercially launch our generation 2 manufacturing process.

We are seeking regulatory approval of andexanet alfa in the United States through an Accelerated Approval process. If we are not successful with this process, the development or commercialization of andexanet alfa could be delayed, abandoned or significantly more costly.

The Accelerated Approval regulations allow drugs that are being developed to treat an unmet medical need to be approved substantially based on evidence of an effect on a surrogate biomarker endpoint that is considered reasonably likely to predict clinical benefit rather than a clinical endpoint such as survival or irreversible morbidity. Our use of an Accelerated Approval pathway requires that our ANNEXA-4 clinical study with clinical endpoints that will correlate to a surrogate endpoint(s) must be ongoing at the time our BLA is submitted, and some early patient data will be required by the FDA to support the BLA. In addition, we have commenced a usual care cohort arm of the ANNEXA-4 study to evaluate the efficacy of andexanet compared to usual care. However, both the usual care cohort and the other ANNEXA-4 studies have inherent limitations as compared with a randomized controlled trial. We expect that the FDA may require a randomized controlled trial of andexanet either as a post-marketing commitment, or even as a condition to approval. The design, practical implementation and ethical considerations of a randomized controlled trial for andexanet present many complications, and we cannot be sure that we could successfully design and conduct such a trial in a manner satisfactory to the FDA. Further, the FDA may determine that the studies conducted by us, including any additional studies conducted as a result of the CRL or other FDA responses, were insufficient to support approval for all or some of the marketed direct or indirect fXa inhibitors or proposed indications, require us to conduct extensive post-approval studies, or require us to make modifications to our ongoing ANNEXA-4 study.

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. 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:

- 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;
- 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 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 unanticipated serious side effects, other unexpected characteristics or 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;
- 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 may also increase if we experience delays in testing or approvals. We do not know whether any anticipated clinical studies will begin as planned, or whether anticipated or ongoing clinical studies will need to be restructured or will be completed on schedule, or at all. 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.

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 proof-of concept studies of andexanet alfa, evaluating the effect of andexanet alfa in healthy volunteers taking apixaban, rivaroxaban, edoxaban or enoxaparin may not be predictive of success in our Phase 4 study or other later studies, if any. In addition, although part 1 of each of our Phase 3 ANNEXA-A (apixaban) and ANNEXA-R (rivaroxaban) studies demonstrated that, for the primary efficacy endpoint, an intravenous bolus of andexanet alfa immediately and significantly reversed the anticoagulation activity of apixaban and rivaroxaban, and part 2 of each of our ANNEXA-A and ANNEXA-R studies demonstrated that, for all the primary and secondary endpoints, an intravenous bolus of andexanet alfa followed by a continuous two-hour infusion sustained the reversal of anticoagulation activity of apixaban and rivaroxaban, these positive results may not be predictive of success in our ANNEXA-4 confirmatory study in certain patients receiving apixaban, rivaroxaban, edoxaban or enoxaparin who present with acute major bleeding. Reversal of fXa inhibitor anticoagulation by andexanet does not ensure hemostasis, for example, if damage to the blood vessel integrity is severe, bleeding may not stop following the administration of andexanet. Further, the ANNEXA-4 clinical trial summary data published in August 2016 may not be predictive of the results of the complete ANNEXA-4 trial. We also do not know how the results from our ANNEXA trials will translate into clinical use in patients or the effect of repeat doses. Even if we receive accelerated approval for andexanet alfa based on biomarker findings and patient data from the ANNEXA-4 trial, we cannot be certain that the FDA will accept the final results of the ANNEXA-4 trials, including the comparative results in the Usual Care Cohort study, as sufficient evidence for full approval. Finally, the favorable interim results from our Phase 2a proof-of-concept study for cerdulatinib in patients with NHL, or CLL, who have failed or relapsed on existing marketed therapies or products in development, including patients with identified mutations, may not be confirmed in future clinical studies or predictive of final results.

Failure to obtain regulatory approvals in foreign jurisdictions will prevent us from marketing our products internationally. Following the negative trend vote by the CHMP for betrixaban, it is unlikely that we will obtain marketing approval to commercialize betrixaban in the EU at this time. While the CHMP has communicated a positive trend vote for andexanet alfa, the CHMP has requested additional data with respect to andexanet and extended the timetable for the review. This will delay the CHMP opinion and could even reduce the likelihood of a favorable opinion.

In order to market Bevyxxa or 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 EMA 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 submit for regulatory approvals and even if we submit we may not receive necessary approvals to commercialize our products in any market.

In February 2018, the CHMP communicated a negative trend vote for the MAA for betrixaban for the prevention of VTE in adult patients hospitalized for an acute medical illness with risk factors for VTE. A negative trend vote means it is unlikely that the CHMP will adopt a positive opinion on the Company's MAA at the formal CHMP decision vote, and that additional steps would be needed to gain marketing approval for betrixaban in the EU.

The CHMP noted that uncertainties remained regarding a positive benefit risk analysis for betrixaban, which was not supported by a second confirmatory study, biological plausibility for betrixaban in another approved indication or external support within the class from other Factor Xa inhibitors with respect to the acute medically ill population. Failure to obtain marketing approval of betrixaban in the EU will reduce the commercial potential of betrixaban and could also have a negative impact on our efforts to commercialize and obtain market acceptance for betrixaban in the US market.

In February 2018, the CHMP also communicated a positive trend vote on the MAA for andexanet alfa. While a positive trend vote is considered a positive (although not determinative) indicator for the potential outcome for the formal CHMP opinion, the CHMP also requested additional data with respect to andexanet which will delay the date of the formal opinion until the fourth quarter of 2018. In addition, at this time we cannot be certain that we will be able to provide the additional data to the CHMP in a form satisfactory to the CHMP, or that the additional data will support a positive opinion. Failure to obtain marketing approval of andexanet in the EU would reduce the commercial potential of andexanet.

If serious adverse side effects are identified with respect to any of our product candidates or our approved product, we may need to abandon our development of that product candidate or discontinue sale of that product.

It is impossible to guarantee when or if any of our product candidates will prove safe enough to receive regulatory approval. In addition, there can be no assurance that our clinical studies will identify all relevant safety issues. Known or previously unidentified adverse side effects can adversely affect regulatory approvals or marketing of approved products. In such an event, we might need to abandon marketing efforts or development of that product or product candidate or enter into a partnership to continue development.

For example, Bevyxxa, like all currently marketed inhibitors of fXa, carries some risk of life-threatening bleeding. In addition, patients taking betrixaban in our Phase 2 studies 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.

While no serious adverse side effects have been observed in our completed healthy patient studies with andexanet alfa, there is a risk that adverse side effects could be observed through our ANNEXA-4 patient study results, additional clinical experience or repeat doses that are determined to have been caused by andexanet alfa. Some protein-based biologics have encountered problems with immunogenicity, that is, their tendency to trigger an unwanted immune response against themselves. To date, no neutralizing antibodies against andexanet alfa or antibodies to fXa have been detected; however there is still a risk that such antibodies could be identified through our ANNEXA-4 patient study results, additional clinical experience or from repeat doses. In addition, reversing the anticoagulant activity of fXa inhibitors in patients with underlying medical conditions requiring anticoagulation is associated with an increased risk of thrombotic events, as reported in the interim analysis of our ANNEXA-4 patient trial.

Even for Bevyxxa or any of our product candidates receive marketing approval, if a regulatory agency discovers adverse events of unanticipated severity or frequency it may impose restrictions on that product or us, including requiring withdrawal of the product from the market. Among other legal and administrative actions, a regulatory agency may:

- mandate modifications to product labelling or promotional materials or require us to provide corrective information to healthcare practitioners;
- suspend any regulatory approvals;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications filed by us, our partners or our potential future partners;
- impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products or require a product recall.

In addition, the occurrence of any of the foregoing, even if promptly remedied, could negatively impact the perception of us or the relevant product among the medical community, patients or third party payors.

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

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

Even if andexanet alfa is approved by the FDA, this approval may be limited to certain indications, require post-marketing commitments, and additional clinical studies and regulatory applications may be required to expand andexanet alfa indications and we can provide no assurances that such post-marketing commitments, additional clinical studies or regulatory applications will be successful.

We are developing andexanet alfa as a universal antidote for patients receiving a fXa inhibitor anticoagulant when reversal of anticoagulation is needed, such as in life-threatening or uncontrolled bleeding or for emergency surgery/urgent procedures. Our ANNEXA-4 Phase 4 study is being conducted in patients receiving either a direct or an indirect fXa inhibitor who present with an acute major bleeding, and our ANNEXA Phase 3 studies have been conducted on healthy volunteers. It is not certain at this time which indications, if any, the FDA will approve based on this data. For example, in the CRL, the FDA stated that we have not provided sufficient information to permit labeling of andexanet alfa for safe and effective use for the proposed indication as a universal antidote. The FDA has also asked us for additional data to support the inclusion of edoxaban and enoxaparin in the label, and indicated it needed to finalize its review of the clinical studies required as post-marketing commitments. These observations in the CRL creates greater risk concerning our efforts to obtain U.S. approval for andexanet alfa as a universal antidote for fXa inhibitors as the issues raised and information requested by the FDA may be costly and time-consuming to address and generate. As a result of these observations, we could decide or be required to seek our initial approval on a more narrow indication relating to serious bleedings among patients on the two most broadly used fXa inhibitors, apixaban and rivaroxaban. Our studies have also not yet included patients requiring emergency surgery or urgent procedures and we do not anticipate obtaining this indication without clinical data. Additional clinical studies will be required to support our targeted indications, which will require additional time and expense and may not prove successful. Limitations in our label for andexanet alfa will reduce the number of patients for whom andexanet alfa is indicated and could reduce the size of the anticipated market and our financial prospects. Further, there is no guarantee that any efforts that we decide to undertake will meet the FDA's requirements, and we may not receive approval at all for andexanet alfa, even in a more narrow indication despite such efforts.

There are risks associated with scaling up manufacturing to commercial scale. Our commercial manufacturing strategy for andexanet alfa is particularly complex and challenging and is currently subject to increased uncertainty due to the CRL. We have also experienced manufacturing challenges in the past in connection with validating the commercial manufacturing process for Bevyxxa, and are still in the process of qualifying an additional manufacturing facility for Bevyxxa. If our manufacturers are unable to manufacture our products on a commercial scale or scale to increased production, this will likely delay regulatory approval and commercialization or materially adversely affect our results of operations and growth prospects.

We are still in the process of qualifying an additional commercial manufacturing facility at our primary supplier of Bevyxxa. As a part of our commercial scale-up plan, we validated our commercial process at an initial Hovione manufacturing facility and plan to move commercial production to a different Hovione production facility that has greater manufacturing capacity. Before we can use material manufactured at this facility, we are required to demonstrate a successful process transfer and obtain post-marketing regulatory approval for the second facility. We can give no assurance that these efforts will be successful in a timely manner.

There are other risks associated with scaling up manufacturing to commercial volumes including, among others, cost overruns, technical problems with process scale-up, process reproducibility, stability issues, lot consistency and timely availability of raw materials. There is no assurance that our manufacturer will be able to manufacture our products 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 we and our manufacturers are unable to produce sufficient quantities of our products for commercialization, either on a timely basis or at all, our commercialization efforts would be impaired, which would have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We have encountered uncertainties and risks associated with scaling up the manufacturing for andexanet alfa. The manufacture of biologics involves complex processes, typically including developing cell lines or cell systems to produce the biologic, growing large quantities of such cells and harvesting and purifying the biologic produced by them. The cost to manufacture biologics is generally far higher than traditional small molecule chemical compounds, and the manufacturing process is more complex and can be difficult to reproduce. Even though we have completed our process validation campaign for generation 2 commercial scale manufacturing, there is no guarantee we will be successful in obtaining regulatory approval for this process. Due to the high cost to manufacture andexanet alfa and the inherent uncertainty related to manufacturing costs, there is a relatively greater risk that andexanet alfa may not be commercially viable.

Our commercial manufacturing strategy for andexanet alfa is also subject to substantial uncertainty due to items raised by the FDA in the CRL. Changes to our manufacturing strategy, and addressing the manufacturing items in the CRL, will require additional time and capital and may not be successful. For example, we have suspended our efforts to expand post-approval supply based on an expanded generation 1 manufacturing and are focusing our efforts on expanding supply post approval through our generation 2 manufacturing process. We still intend to seek commercial approval based on generation 1 supply from CMC Biologics. However, our generation 1 manufacturing process was designed to produce andexanet alfa for our clinical studies on a small scale and is capable of manufacturing only limited supply to support a commercial launch in relation to projected demand. We are currently discussing options with the FDA and our commercial manufacturing organizations for expanding commercial supply post-approval. Without material from an expanded capacity manufacturing facility, even if approved, commercial supply of andexanet alfa at launch will likely be limited to our generation 1 supply until such time as we can obtain approval for generation 2 material.

In order to obtain FDA approval of generation 2 material produced by Lonza, the vendor's manufacturing facility will need to pass a pre-approval regulatory inspection and we will need to demonstrate that such material is comparable to the clinical material we previously used and material produced in our generation 1 process. Demonstrating comparability can require significant pre-clinical and clinical studies. The material may also be considered a new biological entity and a new clinical program, possibly commencing with Phase 1, and a full BLA submission may be required for approval, resulting in additional time and expense. If we are not able to establish a commercial-scale manufacturing process for andexanet alfa, our business, financial condition, results of operations and growth prospects would be materially adversely affected.

RISKS RELATED TO OUR RELIANCE ON THIRD PARTIES

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

We do not independently conduct clinical studies of our product candidates. We rely on third parties, such as contract research organizations, or CROs, clinical data management organizations, medical institutions and clinical investigators, to perform this function. Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. 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 Bevyxxa or 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 Bevyxxa and 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 to find new suppliers or manufacturers. We may also face significant delays in the development and commercialization of our product candidates.

We do not own facilities for clinical-scale or commercial manufacturing of our product candidates and we rely on third-party suppliers to manufacture Bevyxxa and our product candidates. For example, we have entered into a manufacturing agreement with Hovione for the manufacture of Bevyxxa and expect to rely on this manufacturing organization to supply Bevyxxa for U.S. commercial launch and, if approved by the EMA, the EU launch. If Hovione fails for any reason to deliver adequate quantities of Bevyxxa, the commercial launch of Bevyxxa will be delayed or disrupted. We have contracted with CMC Biologics to manufacture andexanet alfa bulk drug substance to support our potential U.S. commercial launch, and we have engaged Lonza to develop a new, higher-capacity and lower cost process for andexanet alfa bulk drug substance in order to support our broader, worldwide commercialization strategy. We also rely or expect to rely on other third party providers for raw materials, drug substance and drug product manufacturing, packaging, labeling and supply chain distribution. If we and our suppliers cannot agree to the terms and conditions for them to provide the drug supply necessary for our clinical and commercial needs, or if any single source supplier breaches an agreement with us, or terminates the agreement in response to an alleged breach by us or otherwise becomes unable to fulfill its supply obligations, we would not be able to manufacture and distribute the product candidate until a qualified alternative supplier is identified, which could also significantly delay the development of, and impair our ability to commercialize, our product candidates.

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 assurance, including stability of the product candidate and quality control 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 and agreements, our ability to provide the drug supply necessary for our clinical studies and commercial needs would be jeopardized. Any delay or interruption in the supply of clinical study materials could delay the completion of our clinical studies, increase the costs associated with maintaining our clinical study programs and, depending upon the period of delay, require us to commence new studies at significant additional expense or terminate the studies completely.

All manufacturers of our product candidates must comply with cGMP requirements enforced by the FDA through its facilities inspection program. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. Manufacturers of our product candidates may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. The FDA or similar foreign regulatory agencies may also implement new standards at any time, or change their interpretation and enforcement of existing standards for manufacturing, packaging or testing of products. We have limited 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 or interruption of clinical studies, regulatory submissions, approvals or commercialization of our product candidates, entail higher costs or adversely affect our reputation.

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

We may enter into collaborations that place the development of our product candidates outside our control, require us to relinquish important rights or may otherwise be on terms unfavorable to us, and if our collaborations are not successful, our product candidates may not reach their full market potential.

We may enter into additional collaboration agreements with third parties with respect to our product candidates for the commercialization of the candidates outside the U.S., or for other purposes. For example, we have out-licensed development and commercial rights to andexanet alfa in Japan. 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 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 are subject to numerous risks, which may include the following:

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

- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to their marketing and distribution;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- 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.

Any termination or disruption of our collaboration with potential collaborators could result in delays in the development and commercialization of our product candidates, increases in our costs to develop and commercialize the product candidate, or the termination of development of a product candidate.

RISKS RELATED TO THE OPERATION OF OUR BUSINESS

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

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

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

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

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, quality, commercial compliance, medical 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.

We incur significant costs as a result of operating as a public company, and our management is required to devote substantial time to existing and new public company compliance and reporting regulations.

As a public company, we incur significant legal, accounting and other expenses. For example, 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 have and will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations are continuously being revised, 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. In addition, we are required to have our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting. Our compliance with Section 404 of the Sarbanes-Oxley Act, as applicable, requires us to incur substantial accounting expense and expend significant management efforts. We currently do not have an internal audit group, and we will need to continue to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. If we or our independent registered public accounting firm identify deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by the NASDAQ, the SEC or other regulatory authorities, which would require additional financial and management resources.

Our ability to successfully implement our business plan and comply with Section 404, as applicable, requires us to be able to prepare timely and accurate financial statements. We expect that we will need to continue to improve existing, and implement new operational and financial systems, procedures and controls to manage our business effectively. Any delay in the implementation of, or disruption in the transition to, new or enhanced systems, procedures or controls, may cause our operations to suffer and we may be unable to conclude that our internal control over financial reporting is effective and to obtain an unqualified report on internal controls from our auditors as required under Section 404 of the Sarbanes-Oxley Act. If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results, and current and potential stockholders may lose confidence in our financial reporting. 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.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit sales of Bevyxxa and 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 the manufacturing, distribution and sale of Bevyxxa, and will face an even greater risk if we commercially sell any products that we may develop. For example, the manufacturers of currently marketed fXa inhibitors and other manufacturers of anticoagulants have faced substantial litigation due to certain alleged bleeding risks. If we cannot successfully defend ourselves against claims that Bevyxxa or 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 Bevyxxa or 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.

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 biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. 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 or hazardous materials. In addition, we may be required to incur substantial costs to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

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

In connection with our Bevyxxa and andexanet alfa development, we are currently utilizing certain suppliers outside of the United States, which subjects us to certain of the above risks.

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 was 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 Bevyxxa, cerdulatinib, one of our selective Syk inhibitors, and our PCSK9 program, and we expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that our future license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, our licensors may have the right to terminate these agreements, in which event we may not be able to develop and market any product that is covered by these agreements. Termination of these licenses or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms or our not having sufficient intellectual property rights to operate our business. The occurrence of such events could materially harm our business.

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

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

We have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and products that are important to our business. This process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technologies or from developing competing products and technologies.

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, has only recently implemented various regulations, the courts have only just begun to issue decisions addressing 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 other proceedings challenging our patent rights or the patent rights of others, and the outcome of any proceedings are highly uncertain. For example, in November 2013, Zentiva k.s. and Günter SÖLCH separately filed papers with the European Patent Office opposing European Patent 2101760, assigned to Millennium Pharmaceuticals, Inc., to which we have an exclusive license. The European Patent Office decided in favor of revoking the European patent. Portola will appeal this revocation. This patent is related to a formulation of Bevyxxa. Should the appeal or other proceedings be unsuccessful, this could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

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

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

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

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

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the proprietary rights or intellectual property of third parties. We may become party to, or be threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference proceedings before the USPTO. An interference proceeding is a proceeding before the USPTO to determine the priority among multiple patents or patent applications. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third-party's intellectual property rights, we could be required to obtain a license from such third-party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all.

Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties can have a similar negative impact on our business.

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 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 proceedings could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

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

RISKS RELATED TO GOVERNMENT REGULATION

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

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, which regulations differ from country to country. We will not be permitted to market our product candidates in the United States until we receive approval of an NDA or a BLA, from the FDA. Obtaining approval of an NDA or BLA can be a lengthy, expensive and uncertain process that may not be successful. 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 submitted 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 must demonstrate with substantial evidence from well-controlled clinical studies, and to the satisfaction of the FDA and other regulatory authorities abroad, that such product candidates are safe and effective for their intended uses. Results from preclinical studies and clinical studies can be interpreted in different ways. Even if we and our collaboration partners believe the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. Administering any of our product candidates to humans may produce undesirable side effects, which could interrupt, delay or cause suspension of clinical studies of our product candidates and result in the FDA or other regulatory authorities denying approval of our product candidates for any or all targeted indications.

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

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

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

Unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives could harm our business.

There is increasing pressure on biotechnology companies to reduce healthcare costs. In the U.S., these pressures come from a variety of sources, such as managed care groups, institutional, and government purchasers. Increased purchasing power of entities that negotiate on behalf of federal healthcare programs and private sector beneficiaries could increase pricing pressures in the future. Such pressures may also increase the risk of litigation or investigation by the government regarding pricing calculations. The biotechnology industry will likely face greater regulation and political and legal action in the future.

The regulations that govern marketing approvals, pricing and reimbursement for new therapeutic products vary widely from country to country. Some countries, including EU member countries, require approval of the sale price of a product before it can be marketed. In many countries, including EU member 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. In some foreign markets, including the EU member countries, current standard of care and/or competitive products may be used as a benchmark or reference to determine pricing and reimbursement level for novel products such as andexanet alfa and betrixaban. To the extent that comparators are available at lower prices than our anticipated pricing for andexanet alfa or betrixaban, the pricing and reimbursement level of our products in the EU could be negatively impacted. 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, or even reduce the commercial viability of the product to an extent that prevents the launch altogether.

Adverse pricing limitations may hinder our ability to recoup our investment in Bevyxxa or one or more product candidates, even if our product candidates obtain regulatory approval. Adverse pricing limitations prior to approval will also adversely affect us by reducing our commercial potential. 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. Following the launch of Bevyxxa in January 2018, we continue our negotiations with hospitals and third-party payors regarding coverage reimbursement and formulary placement. We cannot be sure that coverage and 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 Bevyxxa or 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.

Healthcare reform measures could hinder or prevent the commercial success of Bevyxxa or our product candidates.

In the United States, there have been and we expect there will continue to be a number of legislative and regulatory changes to the healthcare system in ways that could affect our future revenue and profitability and the future revenue and profitability of our potential customers. Federal and state lawmakers regularly propose and, at times, enact legislation that would result in significant changes to the healthcare system, some of which are intended to contain or reduce the costs of medical products and services. For example, one of the most significant healthcare reform measures in decades, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Affordable Care Act, was enacted in 2010. The Affordable Care Act 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 Affordable Care Act, 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;
- expanded Medicaid drug rebates to cover drugs paid by Medicaid managed care organizations;
- changes the Medicaid rebate rates for line extensions or new formulations of oral solid dosage form;
- expands the types of entities eligible for the "Section 340B discounts" for outpatient drugs;
- requires manufacturers to participate in a coverage gap discount program, under which they must agree to offer 50% (and 70% commencing January 1, 2019) 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.

Legislative changes to or regulatory changes under the Affordable Care Act remain possible and appear likely in the 115th U.S. Congress and under the Trump Administration. In addition, since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the Affordable Care Act or otherwise circumvent some of the requirements for health insurance mandated by the Affordable Care Act. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the Affordable Care Act have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain Affordable Care Act-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". We cannot assure that the Affordable Care Act, 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 Affordable Care Act was enacted. For example, the Budget Control Act of 2011, or Budget Control Act, 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 April 2013, and due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, or the ATRA, which, among other things, 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.

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

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

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

Pharmaceutical companies are heavily regulated by federal, state and local regulations in the countries in which business activities occur. 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 laws and regulations governing healthcare fraud and abuse, advertising and other promotional activities, data privacy and patient rights 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 Anti-Kickback Statute, which prohibits, among other things, any person or entity 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;
- the federal Physician Payments Sunshine Act or Open Payments Program provisions and the implementing regulations which will require, among other things, extensive tracking of physician and teaching hospital payments, maintenance of a payments database, and public reporting of the payment data;
- 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;
- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- the Foreign Corrupt Practices Act and similar statutes and regulations in foreign jurisdictions, which makes it unlawful for certain classes of persons and entities to make payments to foreign government officials to assist in obtaining or retaining business;
- 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;
- the Drug Quality and Security Act which requires manufacturers and other distribution parties to create systems to trace certain prescription drugs as they are distributed in the United States; 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 Affordable Care Act, 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 Affordable Care Act 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 federal 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 substantial penalties, including civil and criminal penalties, damages, fines, possible exclusion from participation in Medicare, Medicaid, and other federal healthcare programs, integrity oversight and reporting obligations to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our ability to operate our business and our financial results. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

RISKS RELATED TO OWNERSHIP OF OUR COMMON STOCK

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

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

- our ability to meet the expectations of investors related to the commercialization of Bevyxxa;
- regulatory actions or decisions affecting Bevyxxa, including the timing and outcome of any potential future FDA or EMA decision relating to Bevyxxa, or other product candidates, including those of our competitors;
- inaccurate sales or cash forecasting of Bevyxxa;
- the timing and amount of revenues generated from sale of Bevyxxa;
- changes in laws or regulations applicable to Bevyxxa;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- results of clinical trials or regulatory actions with respect to our product candidates;
- 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. In addition, following our update call on September 5, 2017, at least three plaintiffs' securities litigation firms publicly announced that they are investigating potential securities fraud claims that they may wish to make against us. 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.

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 forecasts of analysts, our stock price will likely decline.

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

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

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

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

Our 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 or discourage third parties from seeking business combinations.

Our executive officers are parties to agreements that contain change in control and severance provisions providing for aggregate cash payments of up to approximately $4.8 million for severance and other benefits and acceleration of vesting of equity awards with a value of approximately $30.3 million as of December 31, 2017, based on the closing price of our common stock of $48.7 on such date in the event of a termination of employment in connection with a change in control of us. The accelerated vesting of equity awards could result in dilution to our existing stockholders and harm the market price of our common stock. The payment of these severance benefits could harm our financial condition and results. In addition, these potential severance payments may discourage or prevent third parties from seeking a business combination with us.

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

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

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

We lease approximately 74,000 square feet of research and office space in South San Francisco, California under a lease that expires in March 2020. Thereafter, at our option, we may extend the term for an additional three years to March 2023. We believe that our existing facilities are sufficient for our current needs for the foreseeable future.

ITEM 3. LEGAL PROCEEDINGS

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

ITEM 4. MINE SAFETY DISCLOSURES

None.

PART II

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

PRICE RANGE OF COMMON STOCK

Our common stock is listed on The NASDAQ Global Select Market under the symbol "PTLA". 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 select Market:

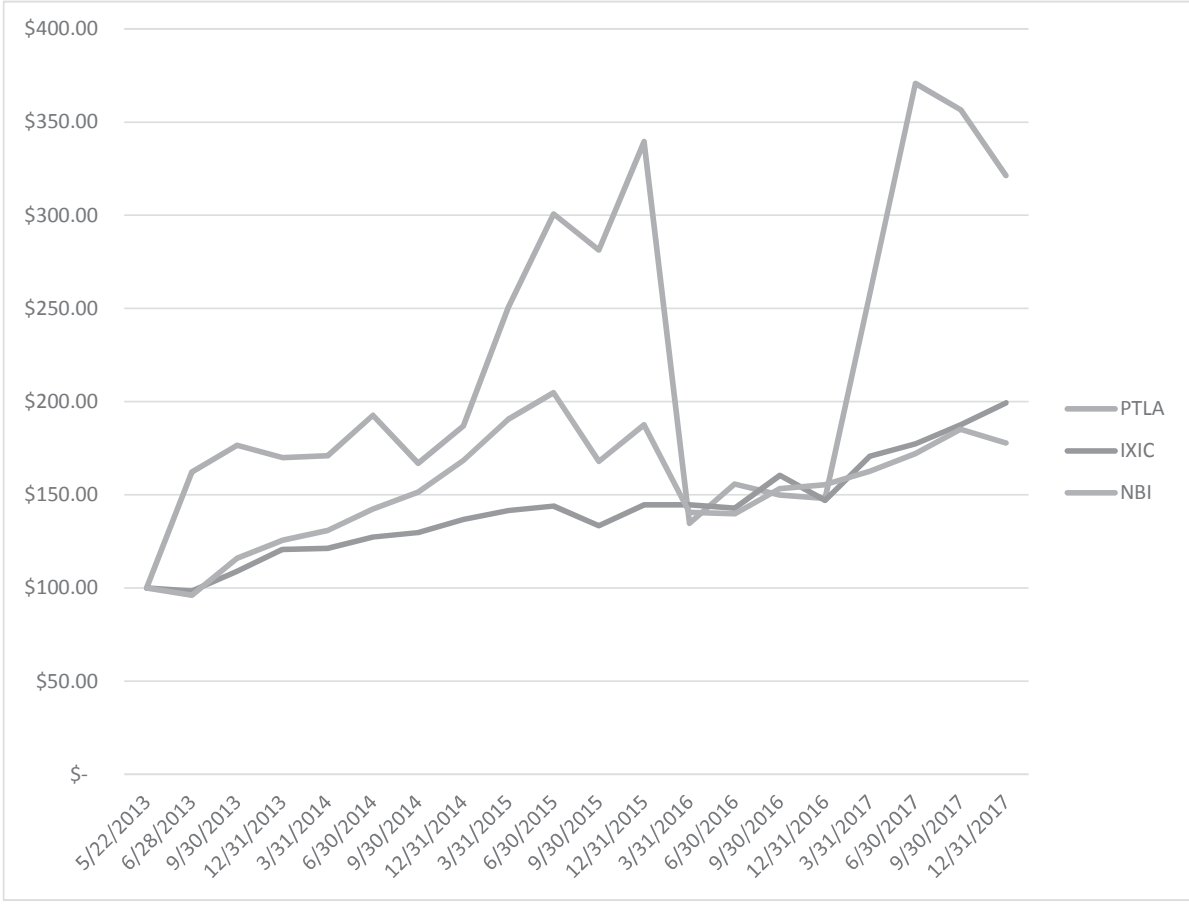
	Low	High
Fiscal Year ending December 31, 2017		
First Quarter	$ 22.53	$ 41.27
Second Quarter	$ 32.57	$ 60.00
Third Quarter	$ 49.45	$ 67.10
Fourth Quarter	$ 46.33	$ 56.70
Fiscal Year ending December 31, 2016		
First Quarter	$ 18.20	$ 51.19
Second Quarter	$ 20.17	$ 28.74
Third Quarter	$ 18.30	$ 28.60
Fourth Quarter	$ 15.68	$ 26.36

On February 21, 2018, the last reported sale price of our common stock as reported on The NASDAQ Global Select Market was $44.91 per share.

As of February 21, 2018, there were 65,392,310 shares of our common stock issued and outstanding with 15 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

STOCK PRICE PERFORMANCE GRAPH

The following stock performance graph compares our total stock return with the total return for (i) the NASDAQ Composite Index and the (ii) the NASDAQ Biotechnology Index for the period from May 22, 2013 (the date our common stock commenced trading on the NASDAQ Global Select Market) through December 31, 2017. The figures represented below assume an investment of $100 in our common stock at the closing price of $15.15 on May 22, 2013 and in the NASDAQ Composite Index and the NASDAQ Biotechnology Index on May 22, 2013 and the reinvestment of dividends into shares of common stock. The comparisons in the table are required by the Securities and Exchange Commission, or SEC, and are not intended to forecast or be indicative of possible future performance of our common stock. This graph shall not be deemed "soliciting material" or be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act of 1933, as amended, or the Securities Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.



$100 investment in stock or index	Ticker	May 22, 2013	June 30, 2013	September 30, 2013	December 31, 2013
Portola Pharmaceuticals, Inc.	PTLA	$ 100.00	$ 162.08	$ 176.57	$ 169.97
NASDAQ Composite Index	IXIC	$ 100.00	$ 96.08	$ 115.99	$ 125.56
NASDAQ Biotechnology Index	NBI	$ 100.00	$ 98.27	$ 108.90	$ 120.60

$100 investment in stock or index	Ticker	March 31, 2014	June 30, 2014	September 30, 2014	December 31, 2014
Portola Pharmaceuticals, Inc.	PTLA	$ 170.96	$ 192.61	$ 166.86	$ 186.93
NASDAQ Composite Index	IXIC	$ 121.24	$ 127.28	$ 129.74	$ 136.75
NASDAQ Biotechnology Index	NBI	$ 130.83	$ 142.35	$ 151.50	$ 168.38

$100 investment in stock or index	Ticker	March 31, 2015	June 30, 2015	September 30, 2015	December 31, 2015
Portola Pharmaceuticals, Inc.	PTLA	$ 250.56	$ 300.66	$ 281.32	$ 339.60
NASDAQ Composite Index	IXIC	$ 141.51	$ 143.99	$ 133.40	$ 144.58
NASDAQ Biotechnology Index	NBI	$ 190.61	$ 204.79	$ 167.93	$ 187.61

$100 investment in stock or index	Ticker	March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016
Portola Pharmaceuticals, Inc.	PTLA	$ 134.65	$ 155.78	$ 149.90	$ 148.12
NASDAQ Composite Index	IXIC	$ 144.50	$ 142.73	$ 160.41	$ 146.93
NASDAQ Biotechnology Index	NBI	$ 140.61	$ 139.83	$ 153.38	$ 155.43

$100 investment in stock or index	Ticker	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
Portola Pharmaceuticals, Inc.	PTLA	$ 258.68	$ 370.76	$ 356.63	$ 321.32
NASDAQ Composite Index	IXIC	$ 170.70	$ 177.30	$ 187.57	$ 199.33
NASDAQ Biotechnology Index	NBI	$ 162.64	$ 171.99	$ 185.09	$ 177.87

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.

ISSUER PURCHASES OF EQUITY SECURITIES

None.

ITEM 6. SELECTED FINANCIAL DATA

You should read the following consolidated selected financial data together with the section of this report entitled "Management's discussion and analysis of financial condition and results of operations" and our consolidated financial statements and the related notes included in this report. The consolidated statement of operations data for the years ended December 31, 2017, 2016 and 2015 and the consolidated balance sheet data as of December 31, 2017 and 2016 are derived from our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K. The consolidated statements of operations data for the years ended December 31, 2014 and 2013, and the consolidated balance sheet data as of December 31, 2015, 2014 and 2013 were derived from our audited consolidated financial statements that are not included in this Annual Report on Form 10-K.

	Year Ended December 31,				
	2017	2016	2015	2014	2013
Consolidated statements of operations data:					
Collaboration and license revenue	$ 22,546	$ 35,504	$ 12,070	$ 9,625	$ 10,531
Operating expenses:					
Cost of sales	415	–	–	–	–
Research and development	203,701	246,854	200,376	123,639	79,286
Selling general and administrative	91,109	58,235	38,869	23,552	15,423
Total operating expenses	295,225	305,089	239,245	147,191	94,709
Loss from operations	(272,679)	(269,585)	(227,175)	(137,566)	(84,178)
Interest and other income (expense), net	(1,338)	1,533	305	441	826
Interest expense	(11,603)	(61)	–	–	–
Loss before income taxes	(285,620)	(268,113)	(226,870)	(137,125)	(83,352)
Income tax benefit	–	–	(365)	–	–
Net loss	(285,620)	(268,113)	(226,505)	(137,125)	(83,352)
Net income attributable to Noncontrolling interest (SRX Cardio)	(470)	(930)	–	–	–
Net loss attributable to Portola	$ (286,090)	$ (269,043)	$ (226,505)	$ (137,125)	$ (83,352)
Net loss per share attributable to Portola stockholders:					
Basic and Diluted	$ (4.81)	$ (4.76)	$ (4.36)	$ (3.19)	$ (3.65)
Shares used to compute net loss per share attributable to Portola common stockholders:					
Basic and Diluted	59,508,156	56,480,647	51,981,463	42,977,463	22,842,443

(1) To date, substantially all of our revenue has been generated from our collaboration agreements, and we have not generated any commercial product revenue.

	As of December 31,				
	2017	2016	2015	2014	2013
Consolidated balance sheet data:					
Cash, cash equivalents and investments	$ 534,233	$ 318,771	$ 460,161	$ 392,303	$ 319,036
Working capital	397,399	263,264	414,431	273,946	247,153
Total assets	571,676	343,436	502,924	416,495	325,731
Convertible preferred stock	–	–	–	–	–
Notes Payable	50,565	49,815	–	–	–
Long term debt	54,251	–	–	–	–
Noncontrolling interest (SRX Cardio)	2,627	2,157	2,927	–	–
Total stockholders' equity	349,493	192,689	430,323	347,802	296,335

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

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

Overview

We are a biopharmaceutical company focused on the development and commercialization of novel therapeutics in the areas of thrombosis, other hematologic disorders and inflammation for patients who currently have limited or no approved treatment options. We are advancing three programs, including our first medicine Bevyxxa (betrixaban), an oral, once-daily Factor Xa, or fXa, inhibitor (anticoagulant), andexanet alfa (proposed tradename AndexXa), a recombinant protein designed to reverse the anticoagulant effect in patients treated with an oral or injectable fXa inhibitor, and cerdulatinib, a spleen tyrosine kinase, or Syk, and Janus kinases, or JAK, inhibitor in development to treat hematologic cancers.

Bevyxxa, approved by the U.S. Food and Drug Administration, or FDA, in June 2017, is the first and only anticoagulant for hospital and extended duration prophylaxis (35 to 42 days) of venous thromboembolism, or VTE, in adult patients hospitalized for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE. Bevyxxa represents an important advance in the field of thrombosis as it significantly reduces the risk of VTE and VTE-related events without an increase in major bleeding. We launched Bevyxxa in the United States in January 2018 when drug supply became commercially available and we are continuing physician education activities, as well as hospital and payor negotiations regarding formulary placement. Additionally, we are working through supplemental approvals associated with our manufacturing processes and certain changes that will enable us to satisfy commercial demand. In February 2018, we received a negative trend vote for betrixaban from the Committee for Medicinal Products for Human Use, or CHMP, regarding our Marketing Authorisation Application, or MAA, in Europe and are continuing the dialogue with the Committee to better understand the basis for the vote and to determine an appropriate strategy to address the unmet need within the European patient population.

Andexanet alfa, an FDA-designated breakthrough therapy and orphan drug, is a universal reversal agent in development for patients anticoagulated with an oral or injectable fXa inhibitor who experience a serious uncontrolled or life-threatening bleeding event, or who require urgent or emergency surgery. Currently, there is no antidote or reversal agent approved for use in reversing the anticoagulating effects of fXa inhibitors. Leading clinicians and the FDA have recognized that the lack of an effective reversal agent represents a significant unmet clinical need.

We resubmitted our Biologics License Application, or BLA, to the FDA in August 2017 and in December the FDA communicated to us that the action date will be updated to May 4, 2018 to allow more time for a thorough review of the information provided and to work with us on labeling and post-marketing commitments. While the BLA is under review, we are building limited supply of bulk drug substance from our first generation manufacturing process and are continuing to build generation 2 supply of bulk drug substance, which will be subject to a supplemental approval process, and enable a broader commercial launch. During the third quarter of 2017, we executed a new long-term manufacturing services agreement that will significantly increase our commercial manufacturing capacity for a period of ten years following initial approval of the generation 2 manufacturing process. In February 2018, we received a positive trend vote for andexanet alfa from the CHMP regarding our MAA. The CHMP also communicated requests for additional data which could delay the CHMP opinion until the fourth quarter of 2018.

Our third product candidate, cerdulatinib, is an orally available dual kinase inhibitor that inhibits Syk and JAK, enzymes that regulate important signaling pathways. Cerdulatinib is being developed for hematologic, or blood, cancers and inflammatory disorders. We are currently conducting a Phase 2a proof-of-concept study for cerdulatinib in patients with B- and T-cell NHL, including patients with FL, PTCL, and CLL, who have failed or relapsed on existing marketed therapies or products in development, including patients with identified mutations. Cerdulatinib has the potential for broad activity in hematologic cancers because it blocks the B-cell receptor pathway via Syk and key cytokine receptors via JAK. In addition, pre-clinical evidence suggests that Syk is also expressed in PTCL and activating mutations in JAK pathway are frequently observed in PTCL. On June 15, 2017, we announced the presentation of the interim results of this Phase 2a study demonstrating evidence of activity of cerdulatinib in patients with relapsed/refractory CLL follicular lymphoma, and peripheral T-cell lymphoma. We are currently enrolling patients in the Phase 2a study evaluating the safety and efficacy of cerdulatinib in patients with relapsed/refractory B-cell malignancies who have failed multiple therapies.

In addition to our three lead product candidates, we have other early research and development programs including a collaboration with Ora Inc. for the development of ocular Syk-selective inhibitors for allergic conjunctivitis and an exclusive in-license agreement with SRX Cardio LLC to explore a novel approach to develop a drug in the field of hypercholesterolemia.

Collaboration and License agreements

We obtained exclusive rights to research, develop and commercialize certain compounds that inhibit fXa, including betrixaban, from Millennium Pharmaceuticals, Inc., or Millennium, in August 2004. 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 the fXa Program.

We have entered into multiple collaboration and license agreements with BMS and Pfizer, Bayer and Janssen, and Daiichi since 2013 aimed at advancing andexanet alfa through late stage development and regulatory approval by the FDA, EMA and Japan. We retained all commercial rights under these agreements, except for the 2016 collaboration and license agreement with BMS and Pfizer that provided them exclusive rights to develop and commercialize andexanet alfa in Japan.

We obtained certain exclusive rights to research, develop and commercialize Syk inhibitors, including cerdulatinib, from Astellas Pharma, Inc., or Astellas, in 2005. In December 2016, we entered into an agreement with Dermavant Sciences GmbH, or Dermavant, whereby they obtained an exclusive worldwide license to develop and commercialize cerdulatinib in topical formulation for all indications, excluding oncology.

See “Collaboration and License Agreements” contained in the section of this report entitled “Business” for a detailed description of historical terms with our collaborators, licensees and licensors. Also see Note 6 and Note 8 in the Notes to Consolidated Financial Statements contained in the section of this report entitled “Financial Statements and Supplementary Data” for a more detailed description of the agreements and accounting assessments associated with these agreements.

Financial operations overview

Revenue

Our revenue to date has been generated from collaboration and license revenue pursuant to our collaboration agreements. We may be entitled to additional milestone payments and other contingent payments upon the occurrence of specific events primarily related to clinical, manufacturing and regulatory events specified in our collaboration agreements. Due to the nature of these collaboration agreements and the nonlinearity of the earnings process associated with certain payments and milestones, we expect that our revenue will continue to fluctuate in future periods.

In the future, we may receive revenue from the sale of Bevyxxa in the United States or our other product candidates, if approved. Betrixaban and andexanet alfa are currently under review by the EMA and our BLA with the FDA for andexanet alfa is under review with an action date of May 4, 2018.

The following table summarizes the sources of our collaboration and license revenue for the years ended December 31, 2017, 2016, and 2015:

	Year Ended December 31,		
	2017	2016	2015
		(in thousands)	
Bristol-Myers Squibb Company and Pfizer Inc.	$ 4,862	$ 6,583	$ 1,540
Daiichi Sankyo, Inc.	7,486	10,421	4,578
Bayer Pharma, AG and Janssen Pharmaceuticals, Inc.	5,424	8,248	5,740
Bayer	1,024	1,450	–
Dermavant Sciences GmbH	3,750	8,750	–
Other	–	52	212
Total collaboration and license revenue	$ 22,546	$ 35,504	$ 12,070

Research and development expenses

Research and development expenses represent costs incurred to conduct research, such as the discovery and development of our un-partnered 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.

Payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods are received or services are rendered.

We expect our research and development expenses to be consistent in the near term and to begin to decrease if and when we receive regulatory approval of our product candidates as the costs associated with our manufacturing processes may qualify for capitalization as inventory and will be subsequently expensed as costs of goods sold when the inventory is sold. The timing and amount of expenses incurred will depend upon regulatory approval of our product candidates and associated manufacturing processes and the outcomes of current or future clinical studies for our product candidates as well as the related regulatory requirements, start-up manufacturing and supply chain costs and any costs associated with the advancement of our preclinical programs.

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

	Phase of Development	Year Ended December 31,		
		2017	2016	2015
			(in thousands)	
Product candidate				
Betrixaban	Phase 3	$ 45,105	$ 58,438	$ 80,425
Andexanet alfa	Phase 2/3/4	138,800	171,460	106,754
Cerdulatinib	Phase 1/2a	13,858	12,900	10,723
Syk selective inhibitor	Pre-clinical	155	172	117
Other research and development expenses[(1)]		5,783	3,884	2,357
Total research and development expenses		$ 203,701	$ 246,854	$ 200,376

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

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 and manufacturing of our product candidates.

Selling, general and administrative expenses

Selling, 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 and sales and marketing expenses related to commercial launch preparation. Personnel costs consist of salaries, benefits and stock-based compensation.

We expect selling, general and administrative expenses to increase significantly in the future as we incur significant additional expenses associated with the establishment of a hospital-based sales force in the United States and possibly other major markets, as well as commercial infrastructure initiatives including information technology systems quality and compliance systems, and personnel support for the commercial organization.

Interest and other income, net

Interest and other income, net consists primarily of interest received on our cash, cash equivalents and investments, unrealized gains and losses from the remeasurement of our embedded derivatives associated with BMS and Pfizer promissory notes and a royalty-based financing arrangement with HealthCare Royalty Partners and its affiliates (HCR), and foreign currency deposits.

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

While our significant accounting policies are described in more detail in the Notes to Consolidated Financial Statements contained in the section of this report entitled "Financial Statements and Supplementary Data", we believe the following accounting policies to be critical to the judgments and estimates used in the preparation of our financial statements.

Variable Interest Entities

We review agreements we enter into with third party entities, pursuant to which we may have a variable interest in the entity, in order to determine if the entity is a variable interest entity, or VIE. If the entity is a VIE, we assess whether or not we are the primary beneficiary of that entity. In determining whether we are the primary beneficiary of an entity, we apply a qualitative approach that determines whether we have both (1) the power to direct the economically significant activities of the entity and (2) the obligation to absorb losses of, or the right to receive benefits from, the entity that could potentially be significant to that entity. If we determine we are the primary beneficiary of a VIE, we consolidate the statements of operations and financial condition of the VIE into our consolidated financial statements.

Our determination about whether we should consolidate such VIEs is made continuously as changes to existing relationships or future transactions may result in a consolidation or deconsolidation event.

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 or partially 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 clinical drug supply, obligation to provide regulatory approval services and obligations to participate on certain development and/or commercialization committees with the collaborators. If we determine that multiple deliverables exist, the consideration is allocated to one or more units of accounting based upon the best estimate of the selling price of each deliverable. The selling price used for each deliverable will be based on vendor-specific objective evidence, if available, third-party evidence if vendor-specific objective evidence is not available, or estimated selling price if neither vendor-specific or third-party evidence is available. In order to account for multiple element arrangements, we identify the deliverables at the inception of the arrangement and each deliverable within a multiple deliverable revenue arrangement is accounted for as a separate unit of accounting if both of the following criteria are met: (1) the delivered item or items have value to the customer on a standalone basis and (2) for an arrangement that includes a general right of return relative to the delivered items, delivery or performance of the undelivered items is considered probable and substantially in our control. A delivered item or items that do not qualify as a separate unit of accounting within the arrangement shall be combined with the other applicable undelivered items within the arrangement. For a combined unit of accounting, non-refundable upfront payments are recorded as deferred revenue in our consolidated balance sheet and are recognized as collaboration revenue over our estimated period of performance that is consistent with the terms of the research and development obligations contained in each collaboration agreement. We regularly review the estimated periods of performance related to our collaborations based on the progress made under each arrangement. Our estimates of our performance period may change over the course of the collaboration term. Such a change could have a material impact on the amount of revenue we record in future periods.

Payments that are contingent upon achievement of a substantive milestone are recognized in their entirety in the period in which the milestone is achieved. A milestone is 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. Payments contingent upon achievement of events that are not considered substantive milestones are allocated to the respective arrangements' unit of accounting when received and recognized as revenue based on the revenue recognition policy for that unit of accounting.

Amounts from sales of licenses are recognized as revenue. Amounts received as funding of research and development or regulatory approval activities are recognized as revenue if the collaboration arrangement involves the sale of our research or development and regulatory approval 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 and regulatory approval 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 expenses and related accruals

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

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

Manufacturing start-up costs are a component of research and development expenses. Additionally, manufacturing costs incurred after regulatory approval but in connection with significant changes and/or enhancements to the approved manufacturing process are recorded as research and development expenses. We accrue and expense manufacturing activities performed by third parties based upon actual work completed in accordance with agreements established with contract manufacturers.

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

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

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

- fees paid to CROs in connection with preclinical and toxicology studies and clinical studies;
- fees paid to investigative sites in connection with clinical studies;
- fees paid to contract manufacturing organizations in connection with the production of our product candidates prior to qualifying for capitalization as inventory; 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 may be required to 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.

Inventory

We capitalize inventory costs associated with our product candidates after regulatory approval and when future commercialization is considered probable and the future economic benefit is expected to be realized. Manufacturing costs for product candidates incurred prior to regulatory approval are expensed as research and development costs.

Inventory, currently consisting of work in-process products, and finished goods, is stated at the lower of cost or estimated net realizable value. We primarily use actual costs to determine our cost basis for inventories. Inventory is valued on a first-in, first-out basis and includes third-party manufacturing costs and indirect overhead costs. Quarterly, we evaluate whether reserves are necessary for potentially excess, dated or obsolete inventory based on an analysis of forecasted demand compared to quantities on hand and any firm purchase orders as well as product shelf life.

Stock-based compensation

We recognize compensation costs related to stock options granted to employees based on the estimated fair value of the options on the date of grant. We estimate the grant date fair value, and the resulting stock-based compensation expense, using the Black-Scholes option-pricing model. The grant date fair value of the stock-based option is generally recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective options.

The Black-Scholes option-pricing model requires the use of highly subjective and complex assumptions which determine the fair value of stock-based awards, including the expected term and the price volatility of the underlying stock. The expected term of employee options granted is determined using the simplified method (based on the midpoint between the vesting date and the end of the contractual term). As sufficient trading history does not yet exist for our common stock, our estimate of expected volatility is based on the weighted average volatility of other companies with similar products under development, market, size and other factors and our volatility.

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 term, which is assumed to be the remaining contractual term of the option. The compensation costs of these arrangements are subject to remeasurement over the vesting terms as earned.

We estimate the fair value of restricted stock units, or RSUs, and performance stock units, or PSUs, based on the fair market values of the underlying stock on the dates of grant. The estimated fair value of RSUs is expensed over the vesting period and the estimated fair value of PSUs is expensed using an accelerated method over the requisite service period based on management's best estimate as to whether it is probable that the shares awarded are expected to vest. We assess the probability of the performance indicators being met on a continuous basis.

We estimate fair value of market-based PSUs, or M-PSUs, based on Monte Carlo simulation models with assistance from an independent third-party valuation specialist. The Monte Carlo simulation models require the use of highly subjective and complex assumptions which determine the fair value of M-PSUs including price volatility of the underlying stock and derived service periods. The assumptions used in calculating the fair value of M-PSUs and expected attainment of performance-based PSUs represent our best estimates, but these estimates involve inherent uncertainties and the application of management judgment.

We expect to continue to grant stock options and awards in the future, and to the extent that we do, our actual stock-based compensation expense recognized in future periods will likely increase.

Interest expense

In the fourth quarter of 2016 and first quarter of 2017, we entered into two financing arrangements that, under relevant accounting literature, are required to be recorded as debt (see Note 9, Long-Term Debt). Both arrangements are eligible to be repaid based on royalties from our yet to be marketed product candidate, andexanet alfa. The recognition of interest expense requires us to estimate the total amount of future royalty payments to be generated from product sales by jurisdiction over the life of the agreements. The sum of the amounts paid to our financing partners less the net proceeds we received will be recorded as interest expense over the life of the agreements. Consequently, we impute interest on the carrying value of the notes payable and long-term debt and record interest expense using an imputed effective interest rate. We reassess the expected royalty payments each reporting period and account for any changes through an adjustment to the effective interest rate on a prospective basis, with a corresponding impact to the classification of our debt and note payable liabilities.

Income taxes

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

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.

As of December 31, 2017, our total deferred tax assets were $362.9 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. We have previously determined that a change occurred during 2013 and, as a result of this change, our net operating loss and tax credit carryforwards will not be subject to limitation in total, but we may be subject to a limitation as it relates to the timing of utilization. However, due to a lack of historical earnings and uncertainties surrounding our ability to generate future taxable income to realize these tax assets, a full valuation allowance has been established to offset our deferred tax assets.

Comparison of the years ended December 31, 2017 and 2016

Collaboration and license revenue

	Year Ended December 31,			
	2017	2016	Decrease	% Decrease
	(in thousands, except percentages)			
Collaboration and license revenue	$ 22,546	$ 35,504	$ (12,958)	-36%

The decrease in collaboration and license revenue during 2017 compared to 2016 was primarily due to:

- a decrease of $7.0 million in milestone achievement from our phase 3 agreements as the amounts ascribed to acceptance of our BLA and MAA filing in 2016 were greater than the manufacturing-related milestone achieved in 2017; and
- a decrease of $5.0 million driven by our license agreement with Dermavant owing to the difference between the upfront payment earned in 2016 and the milestone achieved in 2017 upon Dermavant's filing an IND.

Research and development expenses

	Year Ended December 31,			
	2017	2016	Decrease	% Decrease
	(in thousands, except percentages)			
Research and development expenses	$ 203,701	$ 246,854	$ (43,153)	-17%

The decrease in research and development expenses during 2017 compared to 2016 was primarily due to:

- decreased program costs of $32.7 million related to andexanet alfa driven by our decision in 2016 to cease activity on CMC's "Line C" manufacturing line. This decision resulted in a $27.3 million write-off of prepaid manufacturing costs related to the discontinued manufacturing process ;
- decreased program costs of $13.3 million related to betrixaban, largely due to a decrease in regulatory filing costs after FDA approval; and
- increased program costs of $1.8 million related to early-stage research programs that are not related to our primary development programs.

Selling, general and administrative expenses

	Year Ended December 31,			
	2017	2016	Increase	% Increase
	(in thousands, except percentages)			
Selling, general and administrative expenses	$ 91,109	$ 58,235	$ 32,874	56%

The increase in selling, general and administrative expenses during 2017 compared to 2016 was primarily due to:

- increased headcount- related costs of $20.0 million which includes an increase in stock-based compensation expense of $6.0 million;
- increased commercial launch preparation activities and business development related costs of $8.4 million; and
- increased costs associated with legal, professional and accounting fees of $3.1 million.

Interest and other income (expense), net

	Year Ended December 31,			
	2017	2016	Decrease	% Decrease
	(in thousands, except percentages)			
Interest and other income (expense), net	$ (1,338)	$ 1,533	$ (2,871)	-187%

The decrease in interest and other income (expense), net, during 2017 compared to 2016 was primarily due to:

- $4.6 million of expense recognized upon remeasurement of the embedded derivative liabilities; and
- an increase in interest income of $1.7 million earned from higher investment balances in the current period.

Interest expense

	Year Ended December 31,			
	2017	2016	Increase	% Decrease
	(in thousands, except percentages)			
Interest expense	$ (11,603)	$ (61)	$ (11,542)	18921%

The increase in interest expense during 2017 compared to 2016 was due to:

- notes payable to BMS and Pfizer were outstanding for a full twelve-month period during 2017 as compared to only a one-month period in 2016; and
- additional interest bearing financing was obtained from HealthCare Royalty Partners and its affiliates in February 2017.

Comparison of the years ended December 31, 2016 and 2015

Revenue

	Year Ended December 31,			
	2016	2015	Increase	% Increase
	(in thousands, except percentages)			
Collaboration and license revenue	$ 35,504	$ 12,070	$ 23,434	194%

The increase in collaboration and license revenue during 2016 compared to 2015 was primarily due to:

- an increase in revenue related to our license agreement with Dermavant of $8.8 million;
- incremental revenue of $7.0 million from three collaboration and license agreements executed in the first quarter of 2016 to develop and commercialize andexanet alfa in Japan; and
- an achievement of $10.0 million in milestones related to our collaboration agreements compared to $2.0 million in 2015.

Research and development expenses

	Year Ended December 31,			
	2016	2015	Increase	% Increase
	(in thousands, except percentages)			
Research and development expenses	$ 246,854	$ 200,376	$ 46,478	23%

The increase in 2016 research and development expenses compared to 2015 was primarily due to:

- increased program costs of $64.7 million to advance andexanet alfa, inclusive of a $27.3 million one-time charge of CMC Biologics prepaid balance in the third quarter of 2016 which was intended to be credited against future batch manufacturing costs;
- decreased program cost of $22.0 million in development costs related to betrixaban following the completion of our APEX clinical trial enrollment in the fourth quarter of 2015;
- increased program costs of $2.2 million to support cerdulatinib; and
- increased program costs of $1.6 million to support early research programs that are not related to our primary programs of development.

Selling, general and administrative expenses

	Year Ended December 31,			
	2016	2015	Increase	% Increase
	(in thousands, except percentages)			
Selling, general and administrative expenses	$ 58,235	$ 38,869	$ 19,366	50%

The increase in selling, general and administrative expenses during 2016 compared to 2015 was primarily due to:

- increased headcount- related costs of $12.7 million which includes an increase in stock-based compensation expense of $7.0 million;
- increased commercial launch preparation activities and business development related costs of $5.2 million; and
- increased costs associated with professional and accounting fees of $2.0 million.

Interest and other income (expense), net

	Year Ended December 31,			
	2016	2015	Increase	% Increase
	(in thousands, except percentages)			
Interest and other income (expense), net	$ 1,533	$ 305	$ 1,228	403%

Interest and other income (expense), net increased during 2016 compared to 2015 primarily due to:

- increase in interest income of $0.7 million due to higher investment balances in 2016; and
- a decrease in foreign exchange losses of $0.6 million resulting from fluctuations in the Euro and British pound sterling compared to the U.S. dollar and its impact on services we purchase from vendors denominated in foreign currencies.

Liquidity and capital resources

Due to our significant research and development expenditures, we have generated significant operating losses since our inception. We have financed our operations primarily through sales of our equity securities, collaborations, including loans from our collaboration partners, a royalty-based financing arrangement, and sales of commercial and development rights to some of our product candidates. Our expenditures are primarily related to research and development activities, including clinical trial and manufacturing related costs, and commercial preparation costs. At December 31, 2017 we had available cash, cash equivalents and investments of $534.2 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.

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 from the date of this filing. 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 the $100.0 million payment from HCR contingent upon the FDA's approval of andexanet alfa and potential milestones receivable under our current collaboration and license agreements. Our future funding requirements will depend on many factors, including the following:

- the cost, timing and outcomes of regulatory approvals;
- the cost of manufacturing our product candidates, including process improvements in order to manufacture product candidates at commercial scale, and establishing commercial supplies of our product candidates;

- the cost and timing of establishing sales, marketing and distribution capabilities;
- the timing, receipt and amount of sales, profit sharing or royalties, if any, from our potential products;
- the terms and timing of any other collaborative, licensing and other arrangements that we may establish;
- the receipt of any collaboration payments;
- the number and characteristics of product candidates that we pursue;
- the scope, rate of progress, results and cost of our clinical studies, preclinical testing and other related activities;
- 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.

Since inception, in connection with our agreements with Novartis, Merck, Biogen Idec, BMS and Pfizer, Bayer and Janssen, Lee's, Daiichi Sankyo and Dermavant, we have received payments in the aggregate amount of $288.5 million, as initial upfront payments, contingent consideration and milestone payments. Of this amount, $8.3 million is subject to a refund provision included in our Phase 3 clinical collaboration agreement with BMS and Pfizer and $8.0 million is contingently reimbursable to Daiichi Sankyo upon approval of andexanet alfa based on 1% of world-wide net sales. Further, in December 2016, we entered into a supplemental funding support loan agreement with BMS and Pfizer and received $50.0 million, to be used exclusively for the development of andexanet alfa, in exchange for promissory notes that require us to repay an amount in the range of $60.0 million to $65.0 million based on 5% of net sales of andexanet alfa in the U.S. and EU. The maximum repayment of $65.0 million is payable in December 2024 irrespective of our commercial status. See Note 6 and Note 9 in the Notes to Consolidated Financial Statements contained in the section of this report entitled "Financial Statements and Supplementary Data" for a more detailed description of these arrangements.

Additionally, in February 2017, we entered into a $150.0 million royalty agreement with HealthCare Royalty Partners, or HCR. Under the terms of the agreement, we received $50.0 million at closing and may receive an additional $100.0 million upon FDA approval of andexanet alfa in exchange for a tiered, mid-single-digit royalty based on worldwide net sales of andexanet alfa. The maximum total royalty payments under the agreement is 195% of the amount funded by HCR. If andexanet alfa is not approved we will not receive the additional $100 million and we will have no obligation to repay the $50 million received previously at closing.

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

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

	Year Ended December 31,		
	2017	2016	2015
	(in thousands)		
Cash used in operating activities	$ (225,125)	$ (196,455)	$ (207,252)
Cash provided by/(used in) investing activities	$ (228,767)	$ 140,706	$ 52,945
Cash provided by financing activities	$ 446,980	$ 57,741	$ 283,282
Net increase (decrease) in cash	$ (6,912)	$ 1,992	$ 128,974

Cash used in operating activities

Cash used in operating activities was $225.1 million for the year ended December 31, 2017, compared to cash used of $196.5 million and $207.3 million for the years ended December 31, 2016 and 2015. Operating cash flows can differ from our consolidated net loss as a result of differences in the timing of cash receipts and non-cash charges.

Cash used in operating activities for the year ended December 31, 2017, included payments made to our contract manufacturing organizations for the manufacture of andexanet alfa and betrixaban totaling $55.3 million and $15.5 million, respectively, $109.6 million of disbursements to third party vendors to support ongoing research and development and selling, general and administrative operations, and $43.2 million in payroll and related employee costs. These cash outflows were partially offset by cash receipts of $4.5 million, which was primarily from $3.2 million receipt following achievement of milestones from existing collaboration arrangements

Cash used in operating activities for the year ended December 31, 2016 included payments made to our contract manufacturing organizations for the manufacture of andexanet alfa and betrixaban totaling $83.0 million and $22.1 million, respectively, $116.0 million of disbursements to third party vendors to support ongoing research and development and selling, general and administrative operations, and $32.1 million in payroll and related employee costs. These cash outflows were partially offset by cash receipts of $56.3 million. Our cash receipts related primarily to upfront payments due upon entering into new or amended arrangements with collaborators and licensees in 2016 totaling $40.8 million, and the receipt of $13.8 million in cash following achievement of milestones from existing collaboration arrangements.

Cash used in operating activities for the year ended December 31, 2015, was $207.3 million, reflecting a net loss of $226.5 million, which was decreased by non-cash charges of $22.9 million for stock-based compensation, $3.2 million for amortization of premium on investments and $1.3 million for depreciation and amortization. Cash used in operating activities also reflected an increase in net operating assets of $7.7 million, primarily due to an increase in prepaid research and development expense of $15.3 million partially offset by a decrease in prepaid and other long-term assets of $3.6 million related to batch initiation payments for andexanet alfa manufacturing, and amortization of upfront payments for andexanet alfa manufacturing. Prepaid and other current assets decreased by $1.0 million, mainly due to a decrease in interest receivable on our investment portfolio of $0.5 million due to the timing and duration of investments. Our receivables from collaborators increased by $1.0 million relating to achievement of a milestone under our Phase 3 collaboration agreement with Bayer and Janssen. Cash used in operating activities also reflected an increase in accrued research and development costs of $11.7 million related to higher clinical study and related costs as we continued to increase our research and development activities, an increase in accrued compensation and employee benefits of $2.1 million related to our increased headcount, an increase in short term deferred rent balance of $0.6 million and long term deferred rent balance of $2.3 million related to our corporate office lease. Accounts payable decreased by $4.1 million, due to timely resolution and processing of invoices. Our deferred revenue decreased by $9.6 million due to amortization and recognition of revenue from various Phase 3 collaboration agreements entered into in 2014.

Cash provided by (used in) investing activities

Cash used in investing activities of $228.8 million for the year ended December 31, 2017 was primarily related to purchases of investments of $575.6 million, intangible assets purchase of $5.0 million and fixed assets purchases of $1.2 million, partially offset by proceeds from maturities of investments of $353.1 million.

Cash provided by investing activities of $140.7 million for the year ended December 31, 2016 was primarily related to proceeds from maturities of investments of $394.7 million, offset by purchases of investments of $252.3 million and capital equipment of $1.9 million.

Cash provided by investing activities of $52.9 million for the year ended December 31, 2015 was primarily related to purchases of investments of $266.1 million, capital equipment purchases of $4.7 million, and increase in restricted cash (SRX Cardio) of $0.3 million, offset by proceeds from maturities of investments of $324.1 million.

Cash provided by financing activities

Cash provided by financing activities of $447.0 million for the year ended December 31, 2017 was primarily related to proceeds from our public offering in September 2017, net of underwriting discounts and commissions, of $380.6 million, debt issuance of $48.0 million, and proceeds from the issuance of common stock of $19.6 million pursuant to equity plan awards. These cash receipts were partially offset by payments of public offering costs of $0.7 million and debt issuance costs of $0.6 million.

Cash provided by financing activities of $57.7 million for the year ended December 31, 2016, was primarily related to $50.0 million in proceeds from a supplemental funding support loan agreement that we entered into with BMS and Pfizer and a further $8.0 million in funding from Daiichi Sankyo.

Cash provided by financing activities of $283.3 million for the year ended December 31, 2015 was primarily related to proceeds from our 2015 public offering, net of underwriting discounts and commissions, of $272.2 million, partially offset by payments of offering costs of $0.9 million, proceeds from the exercise of stock options of $11.1 million and proceeds from purchases under our Employee Stock Purchase Plan of $0.8 million.

Off-balance sheet arrangements and contractual obligations

In August 2017, we executed a Manufacturing Services Agreement with Lonza AG, or Lonza, to increase the amount of commercial manufacturing capacity available by adding an additional Lonza manufacturing facility. The manufacturing commitments included in the agreement are contingent upon marketing approval by either the FDA or the EMA of andexanet alfa manufactured at the current Porrino facility under the generation 2 process, and after effectiveness may also be canceled or terminated with three years advance notice to be communicated no earlier than the fifth anniversary of the related marketing approval. Additionally, the agreement provides Lonza two separate rights to purchase shares of our common stock at a purchase price of one dollar per share. The first purchase right will be earned by Lonza upon the approval of the generation 2 process and the commencement of process transfer activities to the new facility. The number of shares subject to the first purchase right will be the lesser of either the number of shares with an aggregate market value of $15.0 million based on a 20 day trailing market value average from the date the first purchase right is earned by Lonza, or 500,000 shares. The second purchase right will be earned by Lonza upon the approval of the drug substance manufactured at the new facility and the number of shares will be determined based on the achievement of specified performance metrics at the new facility. The maximum number of shares will be capped at the lesser of either the number of shares with an aggregate market value of $15.0 million based on a 20 day trailing market value average from the date the second purchase right is earned by Lonza, or 500,000 shares.

The following table summarizes our future contractual obligations, exclusive of the contingent commitments included in the Manufacturing Services agreement with Lonza discussed above, as of December 31, 2017:

	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:					
Batch purchase commitments	$ 64,762	$ 2,850	$ –	$ –	$ 67,612
Purchase commitments	7,172	1,389	77	39	8,677
Notes Payable[(1)]	–	–	–	65,000	65,000
Operating lease obligations	3,026	3,460	–	–	6,486
Total contractual obligations	$ 74,960	$ 7,699	$ 77	$ 65,039	$ 147,775

(1) See Note 9 in the Notes to Consolidated Financial Statements contained in the section of this report entitled "Financial Statements and Supplementary Data" for a more detailed description of the obligation. Also, see Note 9 for detailed description of the $50 million royalty-based contingent obligation from the arrangement made with HealthCare Royalty Partners and its affiliates (HCR) and which is not repayable to HCR if we do not achieve regulatory approval of andexanet alfa.

We lease our corporate, laboratory and other facilities under an operating lease expiring in March 2020. These leases require us to pay taxes, insurance, maintenance and minimum lease payments.

In addition to the above, we have committed to make potential future milestone payments to third parties as part of licensing and development programs. Payments under these agreements become due and payable only upon the achievement by us or our sub-licensees of certain developmental, regulatory and/or commercial milestones. Because it is uncertain if and when these milestones will be achieved, such contingencies, aggregating up to $260.0 million have not been recorded on our consolidated balance sheet as of December 31, 2017.

We are also obligated to pay royalties, ranging generally from 1% to 6% of the selling price of the licensed component. We are unable to determine precisely when and if our payment obligations under the agreements will become due as these obligations are based on future events, the achievement of which is subject to a significant number of risks and uncertainties.

We have also entered into agreements with contract manufacturers to develop approval-enabling validation batches and commercial scale manufacturing batches for andexanet alfa and betrixaban. These agreements include cancellable purchase commitments aggregating approximately $135.8 million over several years. These commitments are 100% cancellable as of December 31, 2017 without any cancellation fee and are not included in the contractual obligations table above as a purchase commitment.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The primary objective of our investment activities is to preserve our capital to fund our operations. We also seek to maximize income from our investments without assuming significant risk. To achieve our objectives, we maintain a portfolio of cash equivalents and investments in a variety of securities of high credit quality. As of December 31, 2017, we had cash, cash equivalents and investments of $534.2 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. We made payments in the aggregate amount of €37.0 million and £3.0 million to our European vendors during the year ended December 31, 2017. 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 and British Pounds, to a lesser extent. For the year ended December 31, 2017, the effect of the exposure to these fluctuations in foreign exchange rates was not material.

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ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The Consolidated Financial Statements and related disclosures included in Part IV, Item 15 of this annual report are incorporated by reference into this Item 8.

PORTOLA PHARMACEUTICALS, INC.

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Portola Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Portola Pharmaceuticals, Inc. (the Company) as of December 31, 2017 and 2016, the related consolidated statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2017, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2017, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated March 1, 2018 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2004.

Redwood City, California
March 1, 2018

PORTOLA PHARMACEUTICALS, INC.

Consolidated Balance Sheets
(In thousands, except share and per share data)

	December 31, 2017	December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	$ 181,568	$ 188,480
Short-term investments	281,589	130,291
Restricted cash (SRX Cardio)	173	178
Receivables from collaborators	3,750	–
Inventory	1,099	–
Prepaid research and development	734	7,299
Prepaid expenses and other current assets	9,010	2,680
Total current assets	477,923	328,928
Property and equipment, net	5,217	6,143
Intangible assets	7,851	3,151
Long-term investments	71,076	–
Prepaid and other long-term assets	9,609	5,214
Total assets	$ 571,676	$ 343,436
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 9,304	$ 14,546
Accrued compensation and employee benefits	11,526	4,806
Accrued research and development	44,973	23,818
Accrued and other liabilities	3,552	1,696
Deferred revenue, current portion	11,169	20,798
Total current liabilities	80,524	65,664
Notes payable, long-term	50,565	49,815
Long term debt	54,251	–
Long term obligation to Collaborator	8,000	8,000
Deferred revenue, long-term	18,798	24,965
Other long-term liabilities	10,045	2,303
Total liabilities	222,183	150,747
Stockholders' equity:		
Preferred stock, $0.001 par value, 5,000,000 shares authorized; no shares issued and outstanding	–	–
Common stock, $0.001 par value, 100,000,000 shares authorized at December 31, 2017 and 2016; 65,296,643 shares and 56,544,218 shares issued and outstanding at December 31, 2017 and 2016, respectively	66	57
Additional paid-in capital	1,551,728	1,108,832
Accumulated deficit	(1,204,519)	(918,345)
Accumulated other comprehensive loss	(409)	(12)
Total Portola stockholders' equity	346,866	190,532
Noncontrolling interest (SRX Cardio)	2,627	2,157
Total stockholders' equity	349,493	192,689
Total liabilities and stockholders' equity	$ 571,676	$ 343,436

Amounts include the assets and liabilities of SRX Cardio, LLC, a consolidated variable interest entity ("VIE"). Portola's interests and obligations with respect to the VIE's assets and liabilities are limited to those accorded to Portola in its agreement with the VIE. See Note 8, "Asset Acquisition and License Agreements," to these consolidated financial statements.

See accompanying notes

PORTOLA PHARMACEUTICALS, INC.

Consolidated Statements of Operations
(In thousands, except share and per share data)

	Year Ended December 31,		
	2017	2016	2015
Collaboration and license revenue	$ 22,546	$ 35,504	$ 12,070
Operating expenses:			
Cost of sales	415	–	–
Research and development	203,701	246,854	200,376
Selling, general and administrative	91,109	58,235	38,869
Total operating expenses	295,225	305,089	239,245
Loss from operations	(272,679)	(269,585)	(227,175)
Interest and other income (expense), net	(1,338)	1,533	305
Interest expense	(11,603)	(61)	–
Loss before taxes	(285,620)	(268,113)	(226,870)
Income tax benefit	–	–	365
Net loss	(285,620)	(268,113)	(226,505)
Net income attributable to noncontrolling interest (SRX Cardio)	(470)	(930)	–
Net loss attributable to Portola	$ (286,090)	$ (269,043)	$ (226,505)
Net loss per share attributable to Portola common stockholders:			
Basic and diluted	$ (4.81)	$ (4.76)	$ (4.36)
Shares used to compute net loss per share attributable to Portola common stockholders:			
Basic and diluted	59,508,156	56,480,647	51,981,463

See accompanying notes

PORTOLA PHARMACEUTICALS, INC.

Consolidated Statements of Comprehensive Loss
(In thousands)

	Year Ended December 31,		
	2017	2016	2015
Net loss	$ (285,620)	$ (268,113)	$ (226,505)
Other comprehensive income:			
Unrealized gain (loss) on available-for-sale securities, net of tax	(397)	138	89
Comprehensive loss	(286,017)	(267,975)	(226,416)
Comprehensive income attributable to noncontrolling interest (SRX Cardio)	(470)	(930)	–
Total comprehensive loss attributable to Portola	$ (286,487)	$ (268,905)	$ (226,416)

See accompanying notes

PORTOLA PHARMACEUTICALS, INC.
Consolidated Statements of Stockholders' Equity
(In thousands, except share and per share data)

	Common Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Non-controlling Interest	Total Stockholders'
	Shares	Amount	Capital	Deficit	Loss	(SRX Cardio)	Equity
Balance at December 31, 2014	48,766,806	$ 49	$ 770,789	$ (422,797)	$ (239)	$ -	$ 347,802
Exercise of employee stock options for cash	1,095,486	1	11,110	–	–	–	11,111
Lapse of repurchase rights related to common shares issued pursuant to early exercises	125	–	–	–	–	–	–
Issuance of common stock upon cashless exercise of common stock warrants	3,041	–	–	–	–	–	–
Issuance of common stock pursuant to ESPP purchase	30,307	1	836	–	–	–	837
Issuance of common stock in connection with public offering, net of underwriting discounts, commissions and issuance costs	6,463,750	6	271,090	–	–	–	271,096
Employee stock-based compensation expense	–	–	20,172	–	–	–	20,172
Compensation expense relating to stock options granted to consultants	–	–	2,794	–	–	–	2,794
Unrealized gain on available-for-sale securities, net of tax	–	–	–	–	89	–	89
Development Partner's non-controlling interest upon consolidation	–	–	–	–	–	2,927	2,927
Net loss	–	–	–	(226,505)	–	–	(226,505)
Balance at December 31, 2015	56,359,515	$ 57	$ 1,076,791	$ (649,302)	$ (150)	$ 2,927	$ 430,323
Exercise of employee stock options for cash	54,045	–	401	–	–	–	401
Issuance of common stock pursuant to ESPP purchase	62,293	–	1,278	–	–	–	1,278
Issuance of common stock pursuant to RSU and PSU release	68,365	–	–	–	–	–	–
Employee stock-based compensation expense	–	–	30,285	–	–	–	30,285
Compensation expense relating to stock options granted to consultants	–	–	77	–	–	–	77
Unrealized gain on available-for-sale securities, net of tax	–	–	–	–	138	–	138
Net income attributable to non-controlling interest (SRX Cardio)	–	–	–	–	–	930	930
Dividends to non-controlling interest (SRX Cardio)'s shareholders	–	–	–	–	–	(1,700)	(1,700)
Net loss	–	–	–	(269,043)	–	–	(269,043)
Balance at December 31, 2016	56,544,218	$ 57	$ 1,108,832	$ (918,345)	$ (12)	$ 2,157	$ 192,689
Cumulative effect of a change in accounting principal	–	–	84	(84)	–	–	–
Exercise of employee stock options for cash	1,092,539	1	17,696	–	–	–	17,697
Issuance of common stock pursuant to ESPP purchase	85,170	–	1,945	–	–	–	1,945
Issuance of common stock pursuant to RSU and PSU release	272,256	1	–	–	–	–	1
Employee stock-based compensation expense	–	–	38,638	–	–	–	38,638
Compensation expense relating to stock options granted to consultants	–	–	4,646	–	–	–	4,646
Unrealized loss on available-for-sale securities, net of tax	–	–	–	–	(397)	–	(397)
Net income attributable to non-controlling interest (SRX Cardio)	–	–	–	–	–	470	470
Issuance of common stock in connection with public offering, net of underwriting discounts, commissions and issuance costs	7,302,500	7	379,887	–	–	–	379,894
Net loss	–	–	–	(286,090)	–	–	(286,090)
Balance at December 31, 2017	65,296,683	$ 66	$ 1,551,728	$ (1,204,519)	$ (409)	$ 2,627	$ 349,493

See accompanying notes

PORTOLA PHARMACEUTICALS, INC.
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,		
	2017	**2016**	**2015**
Operating activities			
Net loss	$ (285,620)	$ (268,113)	$ (226,505)
Adjustments to reconcile net loss to cash used in operating activities:			
Depreciation and amortization	2,410	1,924	1,311
Net amortization/accretion on investment securities	(235)	1,113	3,174
Non-cash interest expense	11,603	61	–
Stock-based compensation expense	43,284	30,362	22,858
Remeasurement loss on embedded derivatives liabilities	4,562	–	–
Loss on assets disposal	52	–	–
Change in reserve for uncertain tax position	–	–	(365)
Changes in operating assets and liabilities:			
Inventories	(1,099)	–	–
Receivables from collaborations	(3,750)	1,000	(943)
Prepaid research and development	6,565	9,677	(15,290)
Prepaid expenses and other current assets	(6,330)	378	1,001
Prepaid and other long-term assets	(4,395)	6,779	3,619
Accounts payable	(5,242)	4,308	(4,061)
Accrued compensation and employee benefits	6,720	(653)	2,054
Accrued research and development	21,155	(377)	11,650
Accrued and other liabilities	1,856	(892)	1,531
Deferred revenue	(15,796)	18,747	(9,569)
Other long-term liabilities	(865)	(769)	2,281
Net cash used in operating activities	(225,125)	(196,455)	(207,252)
Investing activities			
Purchases of property and equipment	(1,236)	(1,864)	(4,746)
Decrease (increase) in restricted cash (SRX Cardio)	5	163	(341)
Purchase of intangible assets	(5,000)	–	–
Purchases of investments	(575,624)	(252,323)	(266,068)
Proceeds from maturities of investments	353,088	394,730	324,100
Net cash (used in) provided by investing activities	(228,767)	140,706	52,945
Financing activities			
Proceeds from debt issuance, net	48,000	–	–
Proceeds from issuance of common stock, net	380,552	–	272,216
Debt issuance costs paid	(556)	–	–
Payment of public offering costs	(658)	(242)	(882)
Proceeds from issuance of common stock pursuant to equity award plans	19,642	1,683	11,948
Dividends to Noncontrolling interest (SRX Cardio)'s shareholders	–	(1,700)	–
Proceeds from long-term notes payable	–	50,000	–
Proceeds from long-term obligation to Collaborator	–	8,000	–
Net cash provided by financing activities	446,980	57,741	283,282
Net increase/(decrease) in cash and cash equivalents	(6,912)	1,992	128,974
Cash and cash equivalents at beginning of year	188,480	186,488	57,514
Cash and cash equivalents at end of year	$ 181,568	$ 188,480	$ 186,488
Noncash investing and financing activities:			
Net change in accrued offering cost	$ –	$ (238)	$ 238
Net change in accounts payable related to purchase of property and equipment	$ –	$ –	$ 5

See accompanying notes

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.

On June 23, 2017, we received marketing approval from the U.S. Food and Drug Administration ("FDA") for Bevyxxa® (betrixaban), an oral once-daily inhibitor of fXa, for the prophylaxis of venous thromboembolism ("VTE") in adult patients hospitalized for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE. Our second compound, andexanet alfa, an FDA-designated breakthrough therapy and orphan drug, is a recombinant protein designed to reverse anticoagulant activity in patients treated with an fXa inhibitor. Our third compound, cerdulatinib, is being developed for hematologic cancers and inflammatory disorders. Cerdulatinib is an orally available dual kinase inhibitor that inhibits Syk and JAK, enzymes that regulate important signaling pathways. We also have an early stage program of highly selective Syk inhibitors, one of which is partnered with Ora, Inc. ("Ora") and another early stage program to develop a drug in the field of hypercholesterolemia.

Public Offerings

In March 2015, we completed an underwritten public offering of 2,870,000 shares of our Common Stock, which included 374,348 shares of Common Stock issued pursuant to the over-allotment option granted to the underwriters, at a public offering price of $40.00 per share. The net proceeds from the offering to us including the over-allotment option, net of underwriting discounts, commissions and offering expenses of approximately $358,000, were approximately $108.4 million.

In December 2015, we completed an underwritten public offering of 3,593,750 shares of our Common Stock, which included 468,750 shares of Common Stock issued pursuant to the over-allotment option granted to the underwriters, at a public offering price of $48.00 per share. The net proceeds from the offering to us including the over-allotment option, net of underwriting discounts, commissions and offering expenses of approximately $765,000 were approximately $162.7 million.

In September 2017, we completed an underwritten public offering of 7,302,500 shares of our common stock, which included 952,500 shares of common stock issued pursuant to the over-allotment option granted to the underwriters, at a public offering price of $55.00 per share. The total proceeds from the offering and over-allotment, net of underwriting discounts and commissions of approximately $21.1 million, were approximately $380.6 million. After deducting offering expenses of approximately $0.7 million, net proceeds to us were approximately $379.9 million.

2. Summary of Significant Accounting Policies

Basis of Consolidation

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP"). The accompanying consolidated financial statements include the accounts of Portola and its wholly owned subsidiaries and SRX Cardio,LLC ("SRX Cardio') that is a variable interest entity (a "VIE") for which Portola is deemed, under applicable accounting guidance to be the primary beneficiary as of December 31, 2017. For the consolidated VIE, we record net income attributable to noncontrolling interests in our Consolidated Statements of Operations equal to the percentage of the economic or ownership interest retained in such VIE by the respective noncontrolling parties. Unless otherwise specified, references to the Company are references to Portola and its consolidated subsidiaries and VIE. All intercompany transactions and balances have been eliminated upon consolidation.

Reclassification

Certain immaterial reclassifications have been made to prior period amounts to conform to current period presentation. This reclassification did not have an impact on our results of operations or financial condition as of December 31, 2017.

Use of Estimates

The preparation of consolidated 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 liabilities and the reported amounts of revenues and expenses in the consolidated 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, in-process research and development, carrying value of notes payable and long term debt, the consolidation of VIEs and deconsolidation of VIEs 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. Our estimated periods of performance associated with our collaboration and license agreements are based in part on our estimated regulatory approval dates and thus require us to make estimates about future requirements that may be imposed upon us by regulatory agencies. Actual results may differ from those estimates.

Variable Interest Entities

We review agreements we enter into with third-party entities, pursuant to which we may have a variable interest in the entity, in order to determine if the entity is a VIE. If the entity is a VIE, we assess whether or not we are the primary beneficiary of that entity. In determining whether we are the primary beneficiary of an entity, we apply a qualitative approach that determines whether we have both (1) the power to direct the economically significant activities of the entity and (2) the obligation to absorb losses of, or the right to receive benefits from, the entity that could potentially be significant to that entity. If we determine we are the primary beneficiary of a VIE, we consolidate the statements of operations and financial condition of the VIE into our consolidated financial statements.

Our determination about whether we should consolidate such VIEs is made continuously as changes to existing relationships or future transactions may result in a consolidation or deconsolidation event.

Intangible Assets

Intangible assets include an in-process research and development asset related to our consolidated VIE and a milestone payment made to Millennium Pharmaceuticals, Inc. (“Millennium) upon FDA approval of betrixaban.

The in-process research and development asset is considered to be indefinite-lived until the completion or abandonment of the associated research and development efforts. If the project is completed, which generally occurs if and when regulatory approval to market a product is obtained, the carrying value of the related intangible asset is amortized as a part of cost of sales over the remaining estimated life of the asset beginning in the period in which the project is completed. If the asset becomes impaired or is abandoned, the carrying value of the related intangible asset is written down to its fair value and an impairment charge is taken in the period in which the impairment occurs. The in-process research and development asset is tested for impairment on an annual basis, and more frequently if indicators are present or changes in circumstances suggest that impairment may exist. Please refer to Note 8, “Asset Acquisition and License Agreements,” for further information.

A milestone payment made pursuant to the regulatory approval of betrixaban in the United States is considered to be finite-lived and will be amortized on a straight-line basis over the remaining estimated patent life. The intangible asset with finite useful life is reviewed for impairment when facts or circumstances suggest that the carrying value of the asset may not be recoverable.

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.

Inventories

Inventories are stated at the lower of cost or estimated net realizable value, on a first-in, first-out, or FIFO, basis. We primarily use actual costs to determine our cost basis for inventories.

Prior to the regulatory approval of our product candidates, we incur expenses for the manufacture of drug product that could potentially be available to support the commercial launch of our products. Until the first reporting period when regulatory approval has been received, we record all such costs as research and development expense. Beginning in the fourth quarter of 2017, we began to capitalize inventory costs associated with betrixaban when it was determined that the inventory had a probable future economic benefit. We periodically analyze our inventory levels, and write down inventory that has become obsolete, inventory that has a cost basis in excess of its estimated realizable value and inventory in excess of expected sales requirements as cost of sales. The determination of whether inventory costs will be realizable requires estimates by management and if actual market conditions are less favorable than projected by management, write-downs of inventory may be required which would be recorded as cost of sales in the consolidated statements of operations.

The active pharmaceutical ingredient (API) in betrixaban is currently produced by a single supplier. As the API has undergone significant manufacturing specific to its intended purpose at the point it is purchased by us, we classify the API as work-in-process inventory.

Investments in Marketable Securities

All investments in marketable securities 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.

Concentration of Risk

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

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

Collaboration Customer Concentration

Collaboration customers who accounted for 10% or more of total collaboration and license revenues were as follows:

	Year Ended December 31,		
	2017	2016	2015
Daiichi Sankyo, Inc.	33%	29%	38%
Bayer Pharma, AG and Janssen Pharmaceuticals, Inc.	29%	27%	48%
Dermavant Sciences GmbH	16%	25%	–
Bristol-Myers Squibb Company and Pfizer Inc.	22%	19%	13%

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 for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Specific potential indicators of impairment include a significant decrease in the fair value of an asset, a significant change in the extent or manner in which an asset is used or a significant physical change in an asset, a significant adverse change in legal factors or in the business climate that affects the value of an asset, an adverse action or assessment by the FDA or another regulator or a projection or forecast that demonstrates continuing losses associated with an income producing asset. 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, 2017, there have been no such losses.

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 or partially 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 may include the transfer of intellectual property rights (licenses), obligations to provide research and development services and related clinical drug supply, obligations to provide regulatory approval services and obligations to participate on certain development and/or commercialization committees with the collaborators. If we determine that multiple deliverables exist, the consideration is allocated to one or more units of accounting based upon the best estimate of the selling price of each deliverable. The selling price used for each deliverable will be based on vendor-specific objective evidence, if available, third-party evidence if vendor-specific objective evidence is not available, or estimated selling price if neither vendor-specific or third-party evidence is available. In order to account for multiple element arrangements, we identify the deliverables at the inception of the arrangement and each deliverable within a multiple deliverable revenue arrangement is accounted for as a separate unit of accounting if both of the following criteria are met: (1) the delivered item or items have value to the customer on a standalone basis and (2) for an arrangement that includes a general right of return relative to the delivered items, delivery or performance of the undelivered items is considered probable and substantially in our control. A delivered item or items that do not qualify as a separate unit of accounting within the arrangement shall be combined with the other applicable undelivered items within the arrangement. For a combined unit of accounting, non-refundable upfront payments are recognized in a manner consistent with the final deliverable, which has generally been ratably over the period we provide research and development services. Amounts received in advance of performance are recorded as deferred revenue in our consolidated balance sheet and are recognized as collaboration revenue. We regularly review the estimated periods of performance related to our collaborations based on the progress made under each arrangement. Our estimates of our performance period may change over the course of the collaboration term. Such a change could have a material impact on the amount of revenue we record in future periods.

Payments that are contingent upon achievement of a substantive milestone are recognized in their entirety in the period in which the milestone is achieved. A milestone is 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. Payments contingent upon achievement of events that are not considered substantive milestones are allocated to the respective arrangements unit of accounting when received and recognized as revenue based on the revenue recognition policy for that unit of accounting.

Amounts received from our collaboration and license agreements are recognized as revenue if the collaboration arrangement involves the sale of services associated with the development and commercialization of our products at amounts that exceed our cost. Under certain collaboration arrangements we receive reimbursement for a portion of our research and development costs. 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 and regulatory approval 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.

Cost of Sales – Intangible Asset Amortization

Cost of sales for intangible asset amortization consists of the amortization of a capitalized milestone payment made to Millennium Pharmaceuticals, Inc. (Millennium) upon FDA approval of betrixaban. The milestone payment is amortized on a straight-line basis over the estimated remaining patent life of betrixaban.

Research and Development

Research and development costs are expensed as incurred and consist of salaries and benefits, lab supplies, materials and facility costs, as well as fees paid to 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 are received or services are rendered.

Clinical Trial Accruals

Clinical trial costs are a component of research and development expenses. We accrue and expense clinical trial activities performed by third parties based upon actual work completed in accordance with agreements established with clinical research organizations and clinical sites. We determine the actual costs through monitoring patient enrollment and discussions with internal personnel and external service providers as to the progress or stage of completion of trials or services and the agreed-upon fee to be paid for such services. We have not experienced any material deviations between the accrued clinical trial expenses and actual clinical trial expenses. However, actual services performed, number of patients enrolled and the rate of patient enrollment may vary from our estimates, resulting in adjustments to clinical trial expense in futures periods.

Stock-Based Compensation

Employee stock-based compensation cost is measured at the grant date, based on the fair value of the award. The compensation cost is recognized as expense on a straight-line basis over the vesting period for options and restricted stock units ("RSUs") and on an accelerated basis for performance stock options ("PSOs"), market-based performance stock units ("M-PSUs") and performance-based stock units ("PSUs"). For stock option grants including PSOs, we use the Black-Scholes option pricing model to determine the fair value of stock options. This model requires us to make assumptions such as expected term and volatility that determine the stock options fair value. We are also required to make estimates as to the probability of achieving the specific performance criteria underlying the PSOs and PSUs. For M-PSU awards, we use the Monte-Carlo option pricing model to determine the fair value of awards at the date of issue. The Monte-Carlo option-pricing model uses similar input assumptions as the Black-Scholes model; however, it further incorporates into the fair-value determination the possibility that the performance-based market condition may not be satisfied. Compensation costs related to awards with a market-based condition are recognized regardless of whether the market condition is ultimately satisfied. Compensation cost is not reversed if the achievement of the market condition does not occur. For RSUs and PSU awards, we base the fair value of awards on the closing market value of our common stock at the date of grant.

Equity instruments issued to nonemployees, consisting of stock options granted to consultants and restricted stock units and performance stock units granted to employees that have converted to nonemployees, are valued using the Black-Scholes option-pricing model for stock options and period-end market price for restricted stock units and performance stock units. 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.

Interest Expense

Notes payable and long-term debt are eligible to be repaid based on royalties from our yet to be marketed product, andexanet alfa. The recognition of interest expense requires us to estimate the total amount of future royalty payments to be generated from product sales by jurisdiction over the life of the agreement. Consequently, we impute interest on the carrying value of the notes payable and long-term debt and record interest expense using an imputed effective interest rate. We reassess the expected royalty payments each reporting period and account for any changes through an adjustment to the effective interest rate on a prospective basis, with a corresponding impact to the reclassification of our debt and note payable liabilities. The assumptions used in determining the expected repayment term of the debt and amortization period of the issuance costs requires that we make estimates that could impact the short and long-term classification of these costs, as well as the period over which these costs will be amortized.

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 consolidated financial statement reporting and tax basis 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

We have financial transactions denominated in foreign currencies, primarily the Euro and British Pound, and, as a result, are exposed to changes in foreign currency exchange rates.

Net Loss per Share Attributable to Portola Common Stockholders

Basic net loss per share attributable to Portola Common Stockholders is calculated by dividing the net loss attributable to Portola Common Stockholders by the weighted-average number of shares of Common Stock outstanding for the period. Diluted net loss per share attributable to Portola Common Stockholders is computed by giving effect to all potential dilutive Common Stock equivalents outstanding for the period. Diluted net loss per share attributable to Portola Common Stockholders is the same as basic net loss per share attributable to Portola Common Stockholders, since the effects of potentially dilutive securities are antidilutive.

Recent Accounting Pronouncements

In March 2016, the Financial Accounting Standards Board, or the FASB, issued Accounting Standards Update, or ASU, No. 2016-09, *Improvements to Employee Share-Based Payment Accounting*. This ASU simplifies certain aspects of the accounting for share-based payment transactions, including income tax requirements, forfeitures, and presentation on the balance sheet and the statement of cash flows. The amendments in this ASU are effective for annual periods beginning after December 15, 2016 and for the interim periods therein. We adopted the standards as of January 1, 2017, with a cumulative-effect adjustment to increase our deferred tax assets by $14.0 million with a corresponding increase to our valuation allowance. In addition, we made an accounting policy election to account for the forfeitures as they occur, which resulted in a cumulative-effect adjustment to increase additional paid-in capital by $84 thousand with a corresponding increase to our accumulated deficit as of January 1, 2017. Lastly, as required by the standard, excess tax benefits recognized on stock-based compensation expense were reflected in our provision for income taxes rather than additional paid-in capital on a prospective basis. Accordingly, we recorded excess tax benefits within our provision for income taxes, rather than additional paid-in-capital, for the year ended December 31, 2017.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting.* This ASU includes guidance on determining which changes to the terms and conditions of share-based payment awards require an entity to apply modification accounting under Topic 718. This guidance is effective for annual and interim periods of public entities beginning after December 15, 2017, with early adoption permitted. We have evaluated the effect that this guidance will have on our consolidated financial statements and related disclosures and have determined that it will not have a material impact.

In January 2017, the FASB issued ASU No. 2017-01, *Business Combinations (Topic 805): Clarifying the Definition of a Business.* This ASU clarifies the definition of a business when evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. Our effective date for adoption of this guidance is our fiscal year beginning January 1, 2018. We have evaluated the effect that this guidance will have on our consolidated financial statements and related disclosures and determined it will not have a material impact.

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 842), which amends the existing accounting standards for leases.* The new standard requires lessees to record a right-of-use lease asset and a corresponding lease liability on the balance sheet (with the exception of short-term leases). For lessees, leases will continue to be classified as either operating or financing in the income statement. This ASU becomes effective for us in the first quarter of fiscal year 2019 and early adoption is permitted. We are currently evaluating the impact that ASU 2016-02 will have on our consolidated financial statements.

In May 2014, the FASB issued ASU 2014-09, Revenue from Contracts with Customers (Topic 606), which amends the existing accounting standards for revenue recognition. Subsequently, the FASB has issued the following standards related to ASU 2014-09: ASU No. 2016-08, Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations; ASU No. 2016-10, Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing; and ASU No. 2016-12, Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients. ASU 2016-08, ASU 2016-10 and ASU 2016-12 with ASU 2014-09 (collectively, the "new revenue standard") is effective for annual and interim periods beginning after December 15, 2017 and early adoption is permitted.

The new revenue standard permits two methods of adoption: retrospectively to each prior reporting period presented (full retrospective method), or retrospectively with the cumulative effect of initially applying the guidance recognized at the date of initial application (the modified retrospective method). We plan to adopt the standard in the first quarter of 2018 using the modified retrospective method. Expected impacts from the adoption of this standard could differ upon the final adoption and implementation of the standard. In connection with the adoption of the standard, we have evaluated the primary terms of our collaborative arrangements, including the performance obligations under collaboration arrangements, the allocation of consideration under these agreements, the estimated variable considerations, and the pattern of recognition for each performance obligation under the new standard.

The estimated effect of adopting ASU No. 2014-09 is principally the result of applying the new standard's guidance in accounting for variable consideration, including milestone payments or contingent payments. Under our current accounting policy, we recognize contingent or milestone payments as revenue in the period that the payment-triggering event occurred or is achieved. However, under the new revenue standard, it is possible to start to recognize contingent or milestone payments before the payment-triggering event is completely achieved, subject to management's assessment of whether it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved.

While we are still in the process of completing our adoption efforts, at a minimum, we preliminarily expect revenues we had historically deferred as a result of the payments being refundable to our collaboration partner upon the occurrence of certain events and milestones we deem to be probable of achievement, totaling approximately $15 million, to be recognized as an adjustment to accumulated deficit upon the recording of our transition adjustment in the first quarter of 2018.

In addition, we are in the process of implementing several new internal controls, including controls to monitor the probability of achievement of contingent milestone payments and the pattern of performance of certain performance obligations.

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, restricted cash, short-term investments, receivables from collaborations, prepaid research and development, prepaid expenses and other current assets and accounts payable, accrued research and development, accrued compensation and employee benefits, accrued and other liabilities and deferred revenue, 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. Treasury bills and government agency securities and foreign currency forward contracts as Level 2. 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. 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.

In certain cases where there is limited activity or less transparency around inputs to valuation, the related assets or liabilities are classified as Level 3. Our embedded derivative liabilities are measured at fair value using a Monte Carlo simulation model and are included as a component of other long-term liabilities on the consolidated balance sheets. The embedded derivative liabilities are subject to remeasurement at the end of each reporting period, with changes in fair value recognized as a component of interest and other income (expense), net, in our consolidated statements of operations. The assumptions used in the Monte Carlo simulation model include: 1) our estimates of both the probability and timing of regulatory approval of andexanet alfa by geographical region and other related events; 2) the probability weighted net sales of andexanet alfa; 3) our risk adjusted discount rate that includes a company specific risk premium; 4) our cost of debt; 5) volatility; 6) the probability of a change in control occurring during the term of the note; and 7) the probability of an event of default. The valuation of our embedded derivative liabilities is most sensitive to the probability of andexanet alfa achieving regulatory approval given the binary nature of such an approval event and the correlation to other assumptions included in the model.

There were no transfers between Level 1, Level 2 and Level 3 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 noncontrolling interest (SRX Cardio) includes the fair value of the contingent milestone and royalty payments, which is valued based on Level 3 inputs. Please refer to Note 8, "Asset Acquisition and License Agreements," for further information.

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

	December 31, 2017			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 31,836	$ –	$ –	$ 31,836
Corporate notes and commercial paper	–	313,164	–	313,164
U.S. Treasury bills and government agency securities	–	170,458	–	170,458
Total financial assets	$ 31,836	$ 483,622	$ –	$ 515,458
Financial Liabilities:				
Embedded derivative liabilities	$ –	$ –	$ 8,854	$ 8,854

	December 31, 2016			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 6,254	$ –	$ –	$ 6,254
Corporate notes and commercial paper	–	133,099	–	133,099
U.S. Treasury bills and government agency securities	–	55,936	–	55,936
Total financial assets	$ 6,254	$ 189,035	$ –	$ 195,289
Financial Liabilities:				
Embedded derivative liabilities	$ –	$ –	$ 246	$ 246

Level 3 liabilities are comprised of embedded derivative liabilities as described in Note 9.

We estimate the fair value of our corporate notes, commercial paper and U.S. Treasury bills and government agency securities by taking into consideration valuations obtained from third-party pricing services. The pricing services utilize industry standard valuation models, including both income- and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker/dealer quotes on the same or similar securities, issuer credit spreads, benchmark securities, prepayment/default projections based on historical data, and other observable inputs.

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, 2017				December 31, 2016			
	Cost	Unrealized Gains	Unrealized (Losses)	Estimated Fair Value	Cost	Unrealized Gains	Unrealized (Losses)	Estimated Fair Value
Money market funds	$ 31,836	$ –	$ –	$ 31,836	$ 6,254	$ –	$ –	$ 6,254
Corporate notes and commercial paper	313,307	2	(145)	313,164	133,112	1	(14)	133,099
U.S. Treasury bills and government agency securities	170,724	–	(266)	170,458	55,934	5	(3)	55,936
	$515,867	$ 2	$ (411)	$515,458	$195,300	$ 6	$ (17)	$195,289
Classified as:								
Cash equivalents				$162,793				$ 64,998
Short-term investments				281,589				130,291
Long-term investments				71,076				–
Total cash equivalents and Investments				$515,458				$195,289

At December 31, 2017, 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. Available-for-sale debt securities that were in a continuous loss position but were not deemed to be other than temporarily impaired were immaterial at both December 31, 2017 and 2016.

5. Balance Sheet Components

Inventories

Inventories as of December 31, 2017 consisted of the following (in thousands):

	December 31, 2017	December 31, 2016
Work in process	$ 1,032	$ –
Finished goods	67	–
Total inventories	$ 1,099	$ –

We began capitalizing inventory during the year ended December 31, 2017 as a result of the FDA's approval of betrixaban, as the related costs are expected to be recoverable through the commercialization of the product. As of December 31, 2017, prepaid expenses and other current assets on the Consolidated Balance Sheet include a prepayment of $2.3 million made to a manufacturer for the purchase of inventories which we expect to be converted to finished goods within the next twelve months. A prepayment of $9.6 million is classified as prepaid and other long-term assets as the production is expected after the next twelve months and the amount is deemed recoverable.

No losses were incurred on valuation of inventories at lower of cost or market value or write-off of obsolete inventories during the year ended December 31, 2017.

Property and Equipment

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

	December 31,	
	2017	2016
Computer equipment	$ 1,329	$ 1,207
Capitalized software	1,518	1,569
Equipment	6,973	6,747
Leasehold improvements	8,000	7,529
	17,820	17,052
Less accumulated depreciation and amortization	(12,603)	(10,909)
Property and equipment, net	$ 5,217	$ 6,143

6. Collaboration and License Agreements

Summary of Collaboration and License Revenue

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

	Year Ended December 31,		
	2017	2016	2015
BMS and Pfizer	$ 4,862	$ 6,583	$ 1,540
Daiichi Sankyo	7,486	10,421	4,578
Bayer and Janssen	5,424	8,248	5,740
Bayer	1,024	1,450	–
Dermavant	3,750	8,750	–
Other	–	52	212
Total collaboration and license revenue	$ 22,546	$ 35,504	$ 12,070

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

In January 2014, we entered into an agreement with BMS and Pfizer to further study andexanet alfa as a reversal agent for their jointly-owned, FDA-approved oral Factor Xa inhibitor, apixaban, through Phase 3 studies. 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, development and regulatory approval services and participate in the Joint Collaboration Committee ("JCC") in exchange for a partially refundable upfront fee of $13.0 million and up to $12.0 million of contingent milestone payments due upon achievement of certain development and regulatory events. All consideration received and to be earned under this agreement is subject to a 50% refund contingent upon certain regulatory and/or clinical events.

We identified the following non-cancellable performance deliverables under the January 2014 agreement: 1) the obligation to provide research and development services, which include manufacturing and supplying andexanet alfa and providing various reports, 2) the obligation to provide regulatory approval services, and 3) the obligation to participate in the JCC. We considered the provisions of the multiple-elements arrangement guidance and determined that none of the deliverables have standalone value; all of these obligations will be delivered throughout the estimated period of performance and will be accounted for as a single unit of accounting. The non-contingent upfront consideration under this agreement of $6.5 million is being recognized as collaboration revenue on a straight-line basis over the estimated period of performance. The contingent upfront consideration of $6.5 million will be recognized if and when the refundable nature of these amounts lapses based upon the achievement of specified regulatory and/or clinical events.

As of December 31, 2017, we have no further milestone payments eligible for achievement under this agreement and continue to recognize the non-contingent payments received on a straight-line basis over the period of

performance, which is estimated to be through the third quarter of 2018. In the second quarter of 2017, we updated our estimated period of performance from the first quarter of 2018 to the third quarter of 2018 to reflect a modification to our clinical development and regulatory plans. The effect of this change in estimate was not significant. The contingent milestone payments under the January 2014 agreement are not considered substantive because 50% may be refunded upon certain events.

During the years ended December 31, 2017, 2016 and 2015, we recognized $1.8 million, $2.2 million and $1.5 million, respectively, in collaboration revenue under this agreement. The deferred revenue balance under this agreement as of December 31, 2017 and 2016 was $9.4 million and $11.2 million, respectively.

In February 2016, we entered into a collaboration and license agreement with BMS and Pfizer whereby BMS and Pfizer obtained exclusive rights to develop and commercialize andexanet alfa in Japan. BMS and Pfizer are responsible for all development, regulatory and commercial activities in Japan and we will reimburse BMS and Pfizer for expenses they incur for research and development activities specific to fXa inhibitors other than apixaban. Pursuant to this agreement, we are obligated to provide certain research and development activities outside of Japan, provide clinical drug supply and related manufacturing services and to participate on various committees in exchange for a non-refundable upfront fee of $15.0 million. We are also eligible to receive, contingent payments totaling up to $20.0 million which may be earned upon achievement of certain regulatory events and up to $70.0 million which may be earned upon achievement of specified annual net sales volumes in Japan. We are also entitled to receive royalties ranging from 5% to15% on net sales of andexanet alfa in Japan.

We concluded that the January 2014 and February 2016 agreements should each be accounted for as standalone agreements. We identified the following non-cancellable performance deliverables under the February 2016 agreement: 1) grant of intellectual property license, 2) the obligation to provide research and development services, 3) the obligation to manufacture and provide clinical supply of andexanet alfa, and 4) the obligation to participate in various committees. The February 2016 agreement also contains an obligation to manufacture and provide commercial supply of andexanet alfa which we concluded was a contingent deliverable because andexanet alfa is not yet a commercially approved product and is currently subject to additional clinical studies prior to commercial approval in Japan. We considered the provisions of the multiple-elements arrangement guidance and determined that none of the deliverables have standalone value because of our required expertise associated with the manufacturing process of andexanet alfa and the interdependency of the remaining deliverables on the clinical supply of andexanet alfa.

We evaluated the timing of delivery for each of the deliverables and concluded that our obligation to participate on the various committees would be the last delivered element under the arrangement and therefore would be the basis for revenue recognition for the combined unit of accounting. The total upfront consideration under this agreement is being recognized as collaboration revenue on a straight-line basis over the estimated performance period. In the second quarter of 2017, we updated our estimated period of performance from the first quarter of 2019 to the fourth quarter of 2020 to reflect a modification to our clinical development and regulatory plans. The effect of this change in estimate was not significant.

We have determined that the future contingent payments meet the definition of a milestone and that such milestones are substantive in that the consideration is reasonable relative to all of the deliverables and payment terms within the agreement are commensurate with our performance to achieve the milestone after commencement of the agreement. As of December 31, 2017, no amounts had been recognized as collaboration revenue for any of these milestones and all the contingent payments remained eligible for achievement.

During the years ended December 31, 2017 and 2016, we recognized $3.1 million and $4.4 million, respectively, in collaboration revenue under this agreement. The deferred revenue balance under this agreement as of December 31, 2017 and 2016 was $7.6 million and $10.6 million, respectively.

Daiichi Sankyo, Inc. ("Daiichi Sankyo")

In July 2014, we entered into an agreement with Daiichi Sankyo to study the safety and efficacy of andexanet alfa as a reversal agent to edoxaban, in our Phase 3 and Phase 4 studies. We are responsible for the cost of conducting these clinical studies. Pursuant to our agreement with Daiichi Sankyo we are obligated to provide research, development and regulatory services and to participate in a JCC in exchange for an upfront nonrefundable fee of $15.0 million, up to two contingent payments totaling $5.0 million which are payable upon the initiation of our Phase 3 study and achievement of certain events associated with scaling up our manufacturing process to support a commercial launch, and up to four payments totaling $20.0 million which are payable upon acceptance of filing and regulatory approval of andexanet alfa as a reversal agent to edoxaban by the FDA and EMA.

In October 2016, we amended this agreement to expedite the expansion of our Phase 4 trial in exchange for an upfront fee of $15.0 million, $8.0 million of which is payable back to Daiichi Sanko based solely on quarterly royalty payments of 1% of world-wide net sales of andexanet alfa. We are also eligible to receive up to three contingent payments totaling $10.0 million payable upon achieving specified clinical site activation and patient enrollment targets. Additionally, the $2.5 million contingent payment associated with scaling up our manufacturing process from the original agreement has been removed by this amendment.

We concluded that the July 2014 agreement and the October 2016 amendment are linked and should be accounted as a combined agreement. We identified the following non-cancellable performance deliverables under the combined agreement: 1) the obligation to provide research and development services, which include manufacturing and supplying andexanet alfa and providing various reports, 2) the obligation to provide regulatory approval services, and 3) the obligation to participate on the JCC. We considered the provisions of the multiple-element arrangement guidance in determining how to recognize the total consideration of the combined agreement. We determined that none of the deliverables have standalone value; all of these obligations will be delivered throughout the estimated period of performance and therefore are accounted for as a single unit of accounting. The $7.0 million nonrefundable portion of the upfront payment received pursuant to the amendment is being recognized as revenue on a straight-line basis over the estimated period of performance through the second quarter of 2019. In the fourth quarter of 2017, we updated our estimated period of performance from the third quarter of 2018 to the second quarter of 2019 to reflect a modification to our clinical development and regulatory plans. The effect of this change in estimate was not significant. The $8.0 million refundable portion of the upfront consideration represents an obligation to collaborator and will be relieved as we make royalty payments or written off should we fail to commercialize andexanet alfa.

We have determined all but one of the future contingent payments meets the definition of a milestone and that such milestones are substantive in that the consideration is reasonable relative to all of the deliverables and payment terms within the agreement are commensurate with our performance to achieve the milestone after commencement of the agreement. We recognized zero and $5.0 million, respectively, as collaboration revenue associated with the achievement of milestones during the years ended December 31, 2017 and 2016.

As of December 31, 2017, we have milestone payments totaling up to $12.5 million that remain eligible for achievement upon the occurrence of certain clinical events and patient enrollment targets.

During the years ended December 31, 2017, 2016 and 2015, we recognized $6.4 million, $9.2 million and $3.5 million, respectively, in collaboration revenue under this agreement. The deferred revenue balance under this agreement as of December 31, 2017 and 2016 was $6.1 million and $12.6 million, respectively.

In March 2016, we entered into an agreement with Daiichi Sankyo to perform an ethnic sensitivity study ("ESS-Study") of Japanese ethnicity, perform any further studies requested by the Japanese regulatory authorities and to deliver services in connection with our collaboration agreement to commercialize andexanet alfa in Japan with BMS and Pfizer. Daiichi Sankyo will reimburse us for 33% of our costs and expenses incurred to conduct the ESS-Study and between 33% and 100% of costs and expenses we incur for other studies that involve edoxaban under the terms of the arrangement.

Pursuant to our agreement with Daiichi Sankyo, we are obligated to provide research and development services, clinical drug supply and related manufacturing services, regulatory approval services and to participate in a JCC in exchange for an upfront nonrefundable fee of $5.0 million. We are eligible to receive, up to two contingent payments totaling $10.0 million payable upon the initial and final regulatory approval for andexanet alfa as a reversal agent to edoxaban in Japan. The $10.0 million contingent payments will be reduced to $7.0 million if the Japanese regulatory approval is attained based only upon the ESS-study results.

We concluded that the March 2016 agreement should be accounted for as a standalone agreement. We identified the following non-cancellable performance deliverables under the March 2016 agreement: 1) the obligation to provide research and development services 2) the obligation to provide regulatory approval services, 3) the obligation to manufacture and provide clinical supply of andexanet alfa, and 4) the obligation to participate in the JCC. We considered the provisions of the multiple-element arrangement guidance and determined that none of the deliverables have standalone value and accordingly will be accounted for as a single unit of accounting. The total upfront consideration received under this agreement is being recognized as collaboration revenue on a straight-line basis over the estimated performance period associated with our participation in the JCC. In the second quarter of 2017, we updated our estimated period of performance from the first quarter of 2019 to the fourth quarter of 2020 to reflect a modification to our clinical development and regulatory plans. The effect of this change in estimate was not significant.

We have determined that the future contingent payments meet the definition of a milestone and that such milestones are substantive in that the consideration is reasonable relative to all of the deliverables and payment term within the agreement are commensurate with our performance to achieve the milestones after commencement of the agreement. As of December 31, 2017, no amounts had been recognized as collaboration revenue for any of these milestones and all the contingent payments remained eligible for achievement.

During the years ended December 31, 2017 and 2016, we recognized $1.1 million and $1.3 million, respectively, in collaboration revenue under this agreement. The deferred revenue balance under this agreement as of December 31, 2017 and 2016 was $2.7 million and $3.7 million, respectively.

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 FXa inhibitor product, in one of our Phase 2 proof-of-concept studies of andexanet alfa. Bayer and Janssen paid us an upfront fee of $5.0 million and $0.5 million upon delivery of the final written study report. During the year ended December 31, 2015, we recognized $0.5 million in collaboration revenue under this agreement. There was no remaining deferred revenue balance under this agreement as of December 31, 2015.

In January 2014, we entered into an agreement with Bayer and Janssen to study andexanet alfa as a reversal agent to rivaroxaban in our Phase 3 studies. As of December 31, 2017, we have a milestone payment of $2.0 million that remains eligible for achievement upon the occurrence of certain events associated with our manufacturing process. We continue to recognize non-contingent consideration received under the agreement on a straight-line basis over the period of performance, which is estimated to be through the third quarter of 2018. In the second quarter of 2017 we updated our estimated period of performance from the first quarter of 2018 to the third quarter of 2018 to reflect a modification to our clinical development and regulatory plans. The effect of this change in estimate was not significant.

For the years ended December 31, 2017 and 2016, we recognized $3.0 million and $5.0 million, respectively, in collaboration revenue associated with achievement of milestones.

During the years ended December 31, 2017, 2016 and 2015, we recognized $5.4 million, $8.2 million and $5.2 million, respectively, in collaboration revenue under this agreement. The deferred revenue balance under this agreement as of December 31, 2017 and 2016 was $1.6 million and $4.0 million, respectively.

Bayer

In February 2016, we entered into an agreement with Bayer to perform an ESS-Study of Japanese ethnicity, perform any further studies requested by the Japanese regulatory authorities and to deliver services, in connection with our collaboration agreement to commercialize andexanet alfa in Japan with BMS and Pfizer. Bayer will reimburse us 33% of our costs and expenses incurred to conduct the ESS-Study and between 33% and 100% of costs and expenses we incur for other studies that involve rivaroxaban under the terms of the arrangement.

Pursuant to our agreement with Bayer we are obligated to provide research and development services, provide clinical drug supply and related manufacturing services, provide regulatory approval services and to participate in a JCC in exchange for an upfront nonrefundable fee of $5.0 million. We are also eligible to receive, one contingent payment of $10.0 million which is payable upon the initial regulatory approval for andexanet alfa for rivaroxaban in Japan. The $10.0 million contingent payment will be reduced to $7.0 million if Japanese regulatory approval is attained based only upon the ESS study results.

We concluded that the January 2014 agreement with Bayer and Janssen and February 2016 agreement with Bayer should each be accounted for as standalone agreements. We identified the following non-cancellable performance deliverables under the February 2016 agreement: 1) the obligation to provide research and development services 2) the obligation to provide regulatory approval services, 3) the obligation to manufacture and provide clinical supply of andexanet alfa, and 4) the obligation to participate in the JCC. We considered the provisions of the multiple-element arrangement guidance and determined that none of the deliverables had standalone value and all of these obligations will be delivered throughout the estimated period of performance and accounted for as a single unit of accounting. The total upfront consideration under this agreement is being recognized as collaboration revenue on a straight-line basis over the estimated performance period through the fourth quarter of 2020. In the second quarter of 2017 we updated our estimated period of performance from the first quarter of 2019 to the fourth quarter of 2020 to reflect a modification to our clinical development and regulatory plans. The effect of this change in estimate was not significant.

We have determined that the future contingent payment meets the definition of a milestone and that such milestone is substantive in that the consideration is reasonable relative to all of the deliverables and payment terms within the agreement are commensurate with our performance to achieve the milestone after commencement of the agreement. As of December 31, 2017, no amounts had been recognized as collaboration revenue for this milestone and the contingent payment remained eligible for achievement.

During the years ended December 31, 2017 and 2016, we recognized $1.0 million and $1.5 million, respectively, in collaboration revenue under this agreement. The deferred revenue balance under this agreement as of December 31, 2017 and 2016 was $2.5 million and $3.5 million, respectively.

Dermavant Sciences GmbH ("Dermavant")

In December 2016, we granted an exclusive, worldwide license to Dermavant to develop and commercialize cerdulatinib in topical formulation for all indications, excluding oncology, in exchange for a non-refundable upfront payment of $8.8 million and contingent development and regulatory milestones of $36.3 million and up to $100.0 million in commercial milestone payments based on worldwide annual net sales. Additionally, Dermavant is required to pay us a 9% royalty on worldwide net sales of all products commercialized under the agreement throughout the license term, which continues on a country-by-country basis until the later of the 10th anniversary of the first commercial sale or the expiration of the last valid patent.

We identified the following non-contingent deliverables under the agreement, all of which had been satisfied as of December 31, 2016: 1) grant of an exclusive license to develop and commercialize cerdulatinib in topical formulation, excluding oncology; 2) obligation to transfer scientific knowledge and know-how; and 3) obligation to transfer manufacturing knowledge and know-how. Other deliverables referenced in the agreement were either contingent or deemed to be inconsequential and perfunctory. Dermavant has sole responsibility to develop, manufacture and commercialize the product. In the fourth quarter of 2017 we received notice that Dermavant achieved a specified regulatory milestone that requires a payment of $3.8 million to us.

During the years ended December 31, 2017 and 2016, we recognized $3.8 million and $8.8 million, respectively, in revenue under this agreement as we completed our obligations under these deliverables.

Refer to Note 8 "Asset Acquisition and License Agreements" for discussion regarding sublicensing fees due to Astellas Pharma, Inc. ("Astellas") resulting from this agreement.

Ora, Inc. ("Ora")

In May 2015, we entered into a license and collaboration agreement with Ora pursuant to which we granted Ora an exclusive license to co-develop and co-commercialize one of our specific Syk inhibitors, PRT2761. Ora has the primary responsibility for conducting the research and development and regulatory 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.

Under the terms of this risk and cost sharing agreement, each party will incur its own share of development costs. Third-party related development costs will be shared by Ora and us at approximately 60% and 40%, respectively, until an End of Phase 2 meeting with the FDA, and equally thereafter. We are entitled to receive either 50% of the profits, if any, generated by future sales of the products developed under the agreement or royalty payments on such sales, should we opt out of the agreement.

We may opt out of the agreement any time prior to 90 days after an End of Phase 2 meeting with the FDA. The timing of the exercise of our opt-out rights would impact future royalties we would be entitled to receive from Ora. Each party may also buy out the rights and interests in the licensed compound by paying the greater of $6.0 million or two times the actual aggregate development cost incurred by both parties, before or 90 days after an End of Phase 2 meeting with the FDA.

All costs we incur in connection with this agreement will be recognized as research and development expenses. During the years ended December 31, 2017 and 2016, costs of $1,495,000 and $629,000, respectively, have been incurred related to this agreement.

7. Purchase Commitments

Commercial Supply Agreement ("CSA")

In July 2014, we entered into a CSA with AGC Biologics, formerly CMC ICOS Biologics, Inc. ("CMC"), a subsidiary of CMC Biologics S.à.r.l., a privately-held contract manufacturing organization, pursuant to which CMC will manufacture clinical and commercial supply of andexanet alfa. The terms of the CSA required us to purchase an aggregate fixed number of batches of andexanet alfa from CMC beginning in 2015 through 2021. The fixed commitment to purchase batches was divided between two manufacturing lines at CMC: (i) the 2,500 liter manufacturing line which has been used since inception of the program to supply clinical drug product, referred to as "Line A/B"; and (ii) the 6x2,000 liter manufacturing line referred to as "Line C" which was intended to satisfy the drug product requirements of our initial commercial launch.

In February 2016, we filed a BLA based on the Line A/B manufacturing process and on August 17 2016, we received a Complete Response Letter ("CRL") from the FDA that focused primarily on Line A/B manufacturing. Given the time and effort required to address the deficiencies raised in the CRL and re-submit the BLA, we made the decision to suspend manufacturing activities on Line C in order to focus on getting andexanet alfa approved using Line A/B. We recorded a charge of $27.3 million in research and development expense in the third quarter of 2016 due to this decision and related uncertainty about whether we would receive future benefits related to advance payments made for Line C manufacturing since inception of the CSA.

In December 2016, we entered into an Amended Restated Commercial Supply Agreement ("aCSA") with CMC that amends and restates the terms of the original CSA. Under the aCSA, CMC will continue to manufacture bulk drug substance for andexanet alfa under our first generation manufacturing process and will support other regulatory and manufacturing activities. The aCSA increases the number of batches to be manufactured on Line A/B, releases both parties from any obligations related to Line C, and details other services to be provided by CMC to support our regulatory applications in the United States and EU. Under the aCSA, the batch price is fixed at $1.0 million.

Pursuant to the terms of the aCSA, we received a $33.7 million credit for amounts previously paid to CMC pursuant to the original 2014 agreement, which may be applied to either satisfy or partially offset specified amounts owed to CMC for services rendered under the aCSA, existing obligations/payables to CMC as of the execution date and future services to be rendered. For the year ended December 31, 2017, we utilized $8.0 million of these credits as a reduction of R&D expenses associated with the manufacture of 2017 batches and $5.7 million of the credits were used to settle accounts payable and accrued liabilities related to specified services rendered by CMC.

The term of the aCSA is two years and may be earlier terminated by either party for the other party's uncured material breach or insolvency. We may terminate the aCSA unilaterally if our applications for regulatory approval for andexanet alfa in the United States and EU are rejected, for any other safety, efficacy or commercial reasons that lead to the discontinuation, reduction in market demand or commercial infeasibility of andexanet alfa.

Under the consolidation guidance, we determined that CMC is a VIE and we are not the primary beneficiary and therefore consolidation of CMC is not required. As of December 31, 2017, we have not provided financial or other support to CMC that was not previously contractually required. We have recorded $47,000 of accounts payable and $1.2 million of accrued research and development in the consolidated balance sheet as of December 31, 2017. The original CSA and aCSA does not require us to fund operations at CMC and therefore, historically we have quantified our maximum exposure to loss as the aggregate value of prepaid manufacturing services as of each reporting date. No such amounts were recorded as of the reporting date and thus we have no further financial exposure to losses at December 31, 2017. Further, we believe that our total exposure to losses associated with the fixed pricing terms of this agreement is de minimis given the cost per batch, number of batches and time frame over which the batches will be manufactured, pursuant to the amended agreement.

Betrixaban Manufacturing Agreement

In April 2016, we entered into a Manufacturing Agreement ("the Hovione Agreement") with Hovione, Limited ("Hovione"), pursuant to which Hovione will manufacture active pharmaceutical ingredient ("API") for betrixaban at commercial scale and perform process validation during the term of the agreement.

As of December 31, 2017, we have recorded $2.3 million in prepaid expenses and other current assets and $9.6 million in prepaid and other long-term under the agreement, and will make up to $10.8 million of additional payments throughout the term of the Hovione Agreement ending June 2019.

Lonza Manufacturing Services Agreement

In August 2017, we executed a Manufacturing Services Agreement with Lonza AG ("Lonza") to develop a higher-capacity and lower cost process ("generation 2 process") for andexanet alfa bulk drug substance. The manufacturing commitments included therein are contingent upon marketing approval by either the FDA or the EMA of andexanet alfa manufactured at the current Porrino facility under the generation 2 process and will remain in effect for a period of ten years. Additionally, the agreement provides Lonza with two separate rights to purchase shares of our common stock at a purchase price of one dollar per share, contingent upon certain events. The first purchase right will be earned by Lonza upon the approval of the generation 2 process and the commencement of process transfer activities to an additional, new facility in Switzerland. The second purchase right will be earned by Lonza upon the approval of the drug substance manufactured at the new facility and the number of shares will be determined based on the achievement of specified performance metrics at the new facility. The number of shares subject to the first and the second purchase right, each, will be the lesser of either the number of shares with an aggregate market value of $15 million based on a 20 day trailing market value average from the date the first or the second purchase right is earned by Lonza, or 500,000 shares.

We measure the fair value of the equity instrument contingently issuable to Lonza by using the stock price and other measurement assumptions as of the earlier of the date at which either: (1) a commitment for performance by the counterparty has been reached; or (2) the counterparty's performance is complete. We determined that Lonza does not have a performance commitment in this arrangement because there is no substantive disincentive for nonperformance. As such, our measurement date for the contingently issuable equity awards will be when the specified performance criteria have been achieved. Until such achievement, the contingently issuable equity awards will be measured at their then-current lowest aggregate fair value at each financial reporting date. As of December 31, 2017, the awards' lowest aggregate fair value was zero.

8. Asset Acquisition and License Agreements

SRX Cardio, LLC ("SRX Cardio")

In December 2015, we entered into an option agreement with SRX Cardio to explore a novel approach to develop a drug in the field of hypercholesterolemia. This agreement provided us an option to enter into an exclusive license agreement as well as responsibility to lead and fund the development effort during the option period. We made an upfront payment of $0.5 million.

In September 2016, we exercised our right to enter into an exclusive license agreement. Pursuant to the terms of the agreement, we made an upfront payment of $2.2 million to acquire the license and are obligated to pay up to $152.5 million in research and development milestones related to the advancement of the program and royalties in the range of 2% to 6% of worldwide net sales. We may terminate the license agreement upon 90 days' notice for convenience and the agreement may also be terminated by either party for a material breach by the other party.

We determined that SRX Cardio is and continues to be a variable interest entity and that we hold a variable interest in SRX Cardio's intellectual property assets and the related potential future product candidates these assets may produce. Due to the absence of other significant development programs at SRX Cardio, we concluded that the variable interest was in the entity as a whole. Given the stage of development, we concluded that SRX Cardio is not considered a business as they lack the processes required to generate outputs. Further, because we control those activities most significant to SRX Cardio, we are considered to be the primary beneficiary of SRX Cardio. Accordingly, SRX Cardio is subject to consolidation and we have consolidated the financial statements of SRX Cardio by (a) eliminating all intercompany balances and transactions; and (b) allocating income or loss attributable to the noncontrolling interest in SRX Cardio to net income or loss attributable to noncontrolling interest in our consolidated statement of operations and reflecting noncontrolling interest on our consolidated balance sheet. Our interest in SRX Cardio is limited to the development of the intellectual property asset. The upfront payments of $0.5 million and $2.2 million and the obligation to fund the development plan represent our maximum exposure to loss under the agreement. We did not acquire any equity interest in SRX Cardio, any interest in SRX Cardio's cash and cash equivalents or any control over their activities that do not relate to the exclusive license agreement. SRX Cardio does not have any right to our assets except as provided in the exclusive license agreement.

At the inception of the agreement, the identifiable assets, assumed liabilities and non-controlling interest of SRX Cardio were recorded at their estimated fair value upon the initial consolidation of SRX Cardio, including the in-process research and development intangible asset. We estimated the fair value of these indefinite lived intangible assets to be $3.2 million and the noncontrolling interest to be $2.9 million. The fair value was estimated using present-value models on potential contingent milestones and royalty payments ("contingent future payments"), based on assumptions regarding the probability of achieving the development milestones, estimate of time to develop the drug candidate, estimates of future cash flows from potential product sales and assumptions regarding the appropriate discount rate.

As of December 31, 2017, we have not provided financial or other support to SRX Cardio that was not previously contracted or required. We recorded SRX Cardio's $173,000 and $178,000 of cash as restricted cash as of December 31, 2017 and 2016, respectively, because (a) we do not have any interest in or control over SRX Cardio's cash and (b) the agreement does not provide for these assets to be used for the development of the intellectual property assets developed pursuant to this agreement. We recorded $470,000 as net income attributable to noncontrolling interest (SRX Cardio) on our consolidated statements of operations, reflecting a $476,000 change in fair value of our contingent future payments liability to SRX Cardio as of December 31, 2017.

Should the development program make substantive advancement, we expect to record increases in the fair value of the contingent milestone and royalty payments with a corresponding increase to net loss or decrease to net income attributable to Portola Shareholders.

Millennium Pharmaceuticals, Inc. ("Millennium")

In 2004, we entered into an agreement to license from Millennium certain exclusive rights to research, develop and commercialize certain compounds that inhibit fXa, including betrixaban. The license agreement requires us to make license fee, milestone, royalty and sublicense sharing payments to Millennium as we develop, commercialize or sublicense betrixaban. The license agreement will continue in force, on a 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.

Under the agreement, milestone payments are determined based on the indication included in our filing and become payable upon acceptance of our NDA and regulatory approval in the United States and Europe. In December 2016, the FDA accepted our NDA for betrixaban for extended-duration prophylaxis of VTE, triggering a $2.0 million milestone payment to Millennium which is recorded as a research and development expense in the consolidated statement of operations. In June 2017, betrixaban received regulatory approval in the United States, triggering a $5.0 million milestone payment to Millennium which is recorded as finite-lived intangible assets in our consolidated balance sheet and is being amortized to cost of sales on a straight-line basis over the remaining estimated patent life. Amortization expense was $300,000 for the year ended December 31, 2017. Should betrixaban receive approval in Europe, another $5.0 million will become payable by us. Future net product sales generated by us will be subject to a tier royalty ranging between 2% and 8%.

A further $23.0 million in milestone payments would become due if betrixaban was approved for other indications specified in the agreement in the United States and Europe.

Astellas Pharma, Inc. ("Astellas")

In 2010, we amended and restated the original license agreement with Astellas executed in August 2005. The amended and restated license agreement provides us certain exclusive rights to research, develop and commercialize Syk inhibitors. Pursuant to the agreement, we may be required to pay Astellas up to $71.5 million in milestone payments upon the achievement of certain regulatory, approval and sales events for each Syk inhibitor we develop. Additionally, 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.

In December 2016, we out-licensed exclusive rights to cerdulatinib in topical formulation, excluding oncology, to Dermavant Sciences GmbH ("Dermavant"). Twenty percent of the milestone payments received from Dermavant are payable to Astellas. We recognized research and development expense in our consolidated statement of operations of $0.8 million and $1.8 million for the periods ended December 31, 2017 and 2016, respectively, associated with our payment obligation to Astellas.

9. Notes Payable

BMS and Pfizer Promissory Notes

In December 2016, we entered into a supplemental funding support agreement with BMS and Pfizer whereby we received $50.0 million in exchange for two promissory notes totaling $65.0 million that become due in December 2024 ("Notes"). The use of funds is for the development activities needed for regulatory approval of andexanet alfa by the FDA and EMA as provided for in the agreement.

Pursuant to the terms of the agreement, we are required to pay down the Notes each quarter in an amount equal to 5% of net sales of andexanet alfa in the United States and the EU. Should the initial regulatory approval of andexanet alfa in the United States and EU not be achieved by January 1, 2019, one hundred percent of payments due to us under the Japan License agreement and fifty percent of all other andexanet alfa license fees and milestone payments received from third party collaborators will be applied to the notes payable. In addition, if the approval of andexanet alfa in the United States and EU is not achieved by January 1, 2019, we are able to reduce the repayment amount to $60.0 million if such amount is paid by December 31, 2021 and regardless of the timing of regulatory approval, we may reduce the repayment amount to $62.5 million if such amount is paid by December 31, 2023. Any unpaid amounts shall become immediately due upon: 1) a change of control of Portola; 2) an event of default; and 3) termination of the agreement for breach. We have the right to prepay the repayment amount at any time without any penalty.

The accounting for such funding agreement requires us to make certain estimates and assumptions, including timing of andexanet alfa approval, timing of royalty payments due to BMS and Pfizer, the expected rate of return to BMS and Pfizer, the split between current and long-term portions of the obligation and accretion of related interest expense.

The upfront cash receipt of $50.0 million is recorded as notes payable, long term at issuance. We are accruing for interest over the term of the related note at issuance. The carrying value of the Notes at December 31, 2017, including accrued interest of $4.2 million, is $50.6 million. The total carrying value of the Notes, including accrued interest, will be classified as long-term on the consolidated balance sheet until we receive regulatory approval of andexanet alfa or until amounts are contractually payable to BMS and Pfizer.

We evaluated the features of the Notes and determined that certain features require acceleration of payments such as pursuant to a change of control or an event of default, as well as the terms that adjust the total amount of interest required to be paid based upon the timing of initial regulatory approval in the United States and EU. We determined that these features (embedded derivatives) require bifurcation and fair value recognition. We determined the fair value of each derivative using a Monte Carlo simulation model taking into account the probability of these events occurring and potential repayment amounts and timing of such payments that would result under various scenarios (see Note 3). We will remeasure the embedded derivatives to fair value each reporting period until the repayment, termination or maturity of the long-term note payable. The fair value of the embedded derivatives was not material at December 31, 2017.

The estimated fair value of the Notes payable at December 31, 2017 was $55.5 million and the fair value was measured using Level 3 inputs. The estimated fair market value was calculated using a Monte Carlo simulation model with inputs consistent with those used in determining the embedded derivative values as described in Note 3.

Royalty-based Financing

In February 2017, we entered into a purchase and sale agreement, or ("Royalty Sales Agreement") with HealthCare Royalty Partners and its affiliates. ("HCR") whereby HCR acquired a royalty interest in future worldwide net sales of andexanet alfa. We received $50.0 million upon closing and are due to receive an additional $100.0 million if U.S. regulatory approval of andexanet alfa is received prior to October 2018.

We are required to pay HCR a royalty of 2.0% based on tiered net worldwide sales of andexanet alfa. If the additional $100.0 million is received from HCR, the tiered royalty rate will increase to a range of 7.85% to 3.58%, as the applicable rate decreases starting at worldwide net sales levels above $150 million. Total royalty payments are capped at 195% of the funded amount, however, the royalty rates are subject to increase if the timing of marketing and manufacturing approvals from the FDA is not received before the dates within 2018 specified in the Royalty Sales Agreement. If andexanet alfa is not approved for commercial sale, we have no repayment obligations under this agreement. We have evaluated the terms of the Royalty Sales Agreement and concluded that the features of the funded amount are similar to those of a debt instrument. Accordingly, we have accounted for the transaction as long-term debt.

As the repayment of the funded amount is contingent upon the sales volumes of andexanet alfa, the repayment term may be shortened or extended depending on the actual sales of andexanet alfa. The repayment period is commencing from the first commercial sale of andexanet alfa in any country and expiring on the date when HCR has received cash payments totaling an aggregate of 195% of the funded amounts.

We evaluated the terms of the debt and determined that certain features, such as the increase in the repayment amount up to $125.0 million upon a change of control and the variability in the royalty rates based upon the timing of regulatory approvals in the United States and EU, are embedded derivatives that require bifurcation from the debt instrument and fair value recognition. We determined the fair value of each derivative using a Monte Carlo simulation model taking into account the probability of these events occurring and potential repayment amounts and timing of such payments that would result under various scenarios, as further described in Note 3 to these consolidated financial statements. We will remeasure the embedded derivatives to fair value each reporting period until the time the features lapse and/or termination of the Royalty Sales Agreement. For the year ended December 31, 2017, we recognized a loss of $6.2 million upon remeasurement of the embedded derivatives.

The effective interest rate as of December 31, 2017 was 17.5%. For the year ended December 31, 2017, accrued interest in the amount of $7.4 million was added to the principal balance of the debt.

In connection with the Royalty Sales Agreement, we paid HCR a fee of $2.0 million and incurred additional debt issuance costs totaling $0.6 million, which includes expenses that we paid on behalf of HCR and expenses incurred directly by us. Debt issuance costs have been netted against the debt as of December 31, 2017 and are being amortized over the estimated term of the debt using the effective interest method. For the year ended December 31, 2017, we recognized interest expense, including amortization of the debt discount, related to the debt of $7.4 million. The assumptions used in determining the expected repayment term of the debt and amortization period of the issuance costs requires that we make estimates that could impact the short and long-term classification of these costs, as well as the period over which these costs will be amortized. The carrying value of the debt as of December 31, 2017 was $54.3 million, inclusive of accrued interest expense of $7.4 million and net of unamortized debt discount of $2.3 million. The total carrying value of the debt, including accrued interest, will be classified as long-term on the consolidated balance sheet until we achieve regulatory approval of andexanet alfa.

The estimated fair value of long-term debt at December 31, 2017 was $58.8 million and the fair value was measured using Level 3 inputs. The estimated fair market value was calculated using a Monte Carlo simulation model with inputs consistent with those used in determining the embedded derivative values as described in Note 3.

10. Commitments and Contingencies

We conduct product research and development programs through a combination of internal and collaborative programs that include, among others, arrangements with universities, contract research organizations and clinical research sites. We have contractual arrangements with these organizations; however, these contracts are cancelable on 30 days' notice and our obligations under these contracts are largely based on services performed with the exception of our contract manufacturers. Non-cancelable purchase commitments with contract manufacturing organizations amount to $71.9 million, $4.0 million and $0.2 million for services to be performed in 2018, 2019 and 2020, respectively.

Facility Leases

We lease our corporate, laboratory and other facilities under an operating lease, which has been subject to several amendments necessary to secure additional space and extend the lease term through March 2020. These amendments provided for aggregate tenant improvement allowances of $6.3 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, provides for an early termination right effective March 2018 with nine months advance notice and a termination fee of $1.0 million. The facility lease agreement, as amended, contains scheduled rent increases over the lease term. The related rent expense for this lease is calculated on a straight-line basis, with the difference recorded as deferred rent.

At December 31, 2017, our future minimum commitments under our non-cancelable operating leases were as follows (in thousands):

Year ending December 31:	
2018	3,026
2019	2,764
2020	696
Total	$ 6,486

Rent expense was $1.8 million, $1.8 million and $1.7 million for the years ended December 31, 2017, 2016 and 2015, respectively.

Guarantees and Indemnifications

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

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

11. Stock-Based Compensation

Equity Incentive Plan

In January 2013, our Board of Directors adopted our 2013 Equity Incentive Plan, or the 2013 Plan, which became effective upon the closing of our IPO in May 2013. As of December 31, 2017, we are authorized to issue 15,032,633 shares of common stock under the 2013 Plan. The 2013 Plan had 3,735,201 shares of common stock available for future issuance as of December 31, 2017, subject to automatic annual increases each January 1st and will continue through January 1, 2023. The automatic annual share increase is equal to 5 % of the total number of outstanding shares of our common stock on December 31st of the preceding fiscal year, unless our Board of Directors elects to forego or reduce such increase. Further, all remaining shares available under the 2003 Equity Incentive Plan, or the 2003 Plan, were transferred to the 2013 Plan upon adoption. The 2013 Plan provides for the granting of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance stock awards, performance cash awards and other stock awards 2017 to employees, officers, directors and consultants.

In September 2017, our Board of Directors adopted an Inducement Plan ("2017 Plan") with 1,500,000 shares authorized for issuance to new employees entering into employment with Portola in accordance with NASDAQ Listing Rule 5635(c)(5). The 2017 Plan had 864,600 shares of common stock available for future issuance as of December 31, 2017.

Stock Options

Incentive stock options may be granted with exercise prices of not less than 100% of the estimated fair value of our common stock and nonstatutory stock options may be granted with an exercise price of not less than 85% of the estimated fair value of the common stock on the date of grant. Stock options granted to a stockholder owning more than 10% of our voting stock must have an exercise price of not less than 110% of the estimated fair value of the common stock on the date of grant. Stock options are generally granted with terms of up to ten years and vest over a period of four years.

The following table summarizes stock option activities under our 2013 Plan and 2017 Plan and related information:

	Shares Subject to Outstanding Stock Options	Weighted-Average Exercise Price Per Share
Balance at December 31, 2016	5,817,116	$ 25.26
Options granted	2,139,750	40.43
Options exercised	(1,080,570)	16.11
Options canceled	(361,758)	32.33
Balance at December 31, 2017	6,514,538	$ 31.36

Additional information related to the status of stock options at December 31, 2017, is as follows (aggregate intrinsic value in thousands):

	Shares	Weighted-Average Exercise Price Per Share	Remaining Contractual Life	Aggregate Intrinsic Value
Outstanding	6,514,538	$ 31.36	7.0	$ 120,071
Vested	3,629,244	$ 25.35	5.5	$ 84,886

The aggregate intrinsic values of stock options outstanding and vested were calculated as the difference between the exercise price of the stock options and the fair value of our common stock as of December 31, 2017. The aggregate intrinsic value of stock options exercised was $39.3 million, $1.0 million and $35.9 million for the years ended December 31, 2017, 2016 and 2015, respectively.

The weighted-average grant date fair value of employee stock options granted during the years ended December 31, 2017, 2016 and 2015 was $24.08, $17.15 and $22.84 per share, respectively. The total estimated grant date fair value of stock options vested during the years ended December 31, 2017, 2016 and 2015 was $23.0 million, $20.8 million and $12.0 million, respectively.

We recognized stock-based compensation expenses of $25.5 million, $21.2 million and $15.8 million in 2017, 2016 and 2015 respectively relating to the employee stock options. As of December 31, 2017, total unamortized employee and nonemployee stock-based compensation was $62.2 million, which is expected to be recognized over the remaining estimated vesting period of 2.8 years.

Performance Stock Options ("PSOs")

In May 2016, the Compensation Committee of our Board of Directors approved the commencement of granting performance stock option awards to our executive and senior officers. PSOs represent a contingent right to purchase our Common Stock upon achievement of specified conditions. The PSOs granted in May 2016 will vest upon the achievement of certain regulatory and manufacturing goals related to our lead programs.

We recognized stock-based compensation expense of $2.3 million and $0.5 million in 2017 and 2016, respectively, relating to these PSOs. As of December 31, 2017, the stock-based compensation expense for these PSOs had been fully recognized.

The following table summarizes PSO activities under our 2013 Plan and related information:

	Shares Subject to Outstanding Stock Options	Weighted-Average Exercise Price Per Share
Balance at December 31, 2016	180,752	$ 23.76
Options granted	–	–
Options exercised	(11,969)	23.76
Options canceled	(4,000)	23.76
Balance at December 31, 2017	164,783	$ 23.76

Additional information related to the status of PSOs at December 31, 2017, is as follows (aggregate intrinsic value in thousands):

	Shares	Weighted-Average Exercise Price Per Share	Remaining Contractual Life	Aggregate Intrinsic Value
Outstanding	164,783	$ 23.76	7.9	$ 4,106
Vested	164,783	$ 23.76	7.9	$ 4,106

The aggregate intrinsic value of PSOs exercised was $0.4 million for the year ended December 31, 2017. The weighted-average grant date fair value of PSOs granted during the year ended December 31, 2017 was $23.76 per share. The total estimated grant date fair value of PSOs vested during the years ended December 31, 2017 and 2016 was $2.4 million and zero, respectively.

Restricted stock units ("RSUs")

In January 2015, the Compensation Committee of our Board of Directors approved the commencement of granting restricted stock units to our employees. RSUs are share awards that entitle the holder to receive freely tradable shares of our Common Stock upon vesting. The RSUs cannot be transferred, and until they vest, the awards are subject to forfeiture if employment terminates prior to the release of the vesting restrictions. The RSUs, generally vest in equal amounts on each of the first three year anniversaries of the grant date, provided the employee remains continuously employed with us. The fair value of the RSUs is equal to the closing price of our Common Stock on the grant date.

The following table summarizes RSU activities under our 2013 Plan and 2017 Plan and related information:

	Shares Subject to Outstanding RSU's	Weighted-Average grant date fair value per share
Balance at December 31, 2016	546,507	$ 28.38
RSUs granted	343,800	27.15
RSUs released	(211,882)	28.26
RSUs canceled	(78,091)	27.19
Balance at December 31, 2017	600,334	$ 27.87

Additional information related to the status of RSUs at December 31, 2017, is as follows (aggregate intrinsic value in thousands):

	Shares	Remaining Contractual Life	Aggregate Intrinsic Value
Outstanding	600,334	0.9	$ 29,224

The total grant date fair value and the total vest date fair value of RSUs vested during the years ended December 31, 2017 and 2016 was $6.0 million and $1.7 million, respectively. The weighted-average grant date fair value of RSUs granted during the years ended December 31, 2017, 2016 and 2015 was $27.15, $28.01 and $30.74 per share respectively.

We recognized stock-based compensation expenses of $8.1 million, $5.3 million and $1.5 million in the years ended December 31, 2017, 2016 and 2015, respectively, relating to these RSUs. As of December 31, 2017, there was $9.8 million of unrecognized compensation costs related to these RSUs, which is expected to be recognized over an estimated weighted-average period of 1.5 years.

Performance stock units ("PSUs")

In January 2015, the Compensation Committee of our Board of Directors approved the commencement of granting performance stock units to our employees. PSUs are share awards that entitle the holder to receive freely tradable shares of our Common Stock upon achievement of specified market or performance conditions. In January 2016, the Compensation Committee of our Board of Directors approved a program to award up to 102,906 PSUs to the management team based on the achievement of certain commercial and regulatory goals related to andexanet alfa and betrixaban, respectively. In January 2017, the Compensation Committee of our Board of Directors approved a program to award up to 143,750 PSUs to the management team based on the achievement of certain regulatory goals related to andexanet alfa.

The following table summarizes PSU activities under our 2013 Plan and related information:

	Shares Subject to Outstanding PSU's	Weighted-Average grant date fair value per share
Balance at December 31, 2016	285,866	$ 29.24
PSUs granted	143,750	25.54
PSU's released	(60,374)	35.97
PSUs canceled	(64,488)	33.09
Balance at December 31, 2017	304,754	$ 25.34

Additional information related to the status of PSUs at December 31, 2017, is as follows (aggregate intrinsic value in thousands):

	Shares	Remaining Contractual Life	Aggregate Intrinsic Value
Outstanding	304,754	1.0	$ 14,835

The total grant date fair value and the total vest date fair value of PSUs vested in 2017 was $2.1 million and $3.1 million, respectively. The total grant date fair value and the total vest date fair value of PSUs vested in 2016 was $0.7 million and $0.4 million, respectively. None of the PSUs vested in 2015. The weighted-average grant date fair value of PSUs granted during the years ended December 31, 2017, 2016 and 2015 was $25.54, $33.49 and $29.35 per share, respectively.

We recognized stock-based compensation expenses of $2.4 million, $2.5 million and $2.3 million in the years ended December 31, 2017, 2016 and 2015, respectively, relating to these PSUs. As of December 31, 2017, there was $18,000 of unrecognized compensation costs related to these PSUs, which is expected to be recognized over an estimated weighted-average period of 1.0 year.

Employee Stock Purchase Plan ("ESPP")

The Board of Directors adopted the 2013 ESPP, effective upon the completion of the initial public offering of our common stock. As of December 31, 2017, we reserved a total of 1,818,314 shares of common stock for issuance under the 2013 ESPP. The reserve for shares available under the ESPP automatically increases on January 1st each year, beginning in 2014, by an amount equal to 2% of the total number of outstanding shares of our common stock on December 31st of the preceding fiscal year unless the Board of Directors elects to forego or reduce such increases. In 2015, the Board of Directors elected to completely forego the automatic 2016 increase of shares available under the ESPP. The ESPP had 1,611,807 shares of common stock available for future issuance as of December 31, 2017. Eligible employees may purchase common stock at 85% of the lesser of the fair market value of our Common Stock on the first or last day of the offering period.

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 50,000, 52,000 and 66,041 shares with average exercise prices of $38.14, $24.85 and $40.85 per share, respectively, during the years ended December 31, 2017, 2016, and 2015, respectively. These options vest upon grant or various terms up to four years. We recognized non-employees stock compensation expense of $3.9 million, less than $0.1 million and $2.8 million during the years ended December 31, 2017, 2016 and 2015 respectively. The fair value of non-employees' options was measured using the Black-Scholes option-pricing model reflecting the same assumptions as applied to employee options in each of the reported years, other than the expected life assumption, 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.

Stock-Based Compensation

Stock-based compensation expense is reflected in the consolidated statements of operations as follows (in thousands):

	Year Ended December 31,		
	2017	2016	2015
Research and development	$ 19,779	$ 12,905	$ 11,653
Selling, general and administrative	23,505	17,457	11,205
Total stock-based compensation	$ 43,284	$ 30,362	$ 22,858

Valuation Assumptions

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

The following table illustrates the weighted-average assumptions for the Black-Scholes option-pricing model used in determining the fair value of these awards:

	Year Ended December 31,		
	2017	2016	2015
Risk-free interest rate			
Stock options	1.70%-2.27%	1.01%-2.10%	1.54%-1.93%
Performance stock options	–	1.34%-1.50%	–
ESPP	0.47%-1.10%	0.26%-0.50%	0.14%
Expected term			
Stock options	5.0 -6.1 years	5.0 -6.1 years	6.0 years
Performance stock options	–	5.4 -6.4 years	–
ESPP	0.5 years	0.5 years	0.5 years
Expected volatility			
Stock options	60%-65%	62% - 66%	64% - 66%
Performance stock options	–	65%-66%	–
ESPP	61%-80%	54%-99%	62%
Dividend yield			
Stock options	–	–	–
Performance stock options	–	–	–
ESPP	–	–	–

12. Net Loss per Share Attributable to Portola Common Stockholders

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

	Year Ended December 31,		
	2017	2016	2015
Stock options to purchase Common Stock	6,514,538	5,817,116	4,731,483
Performance stock options	164,783	180,752	–
Restricted stock units	600,334	546,507	167,750
Performance stock units	304,754	285,866	205,261
Employee stock purchase plan	32,325	37,368	15,606
Common stock warrants	1,500	1,500	1,500

Up to one million shares may be contingently issued, if certain performance conditions are met under an agreement with one of our contract manufacturers.

13. 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 3% of employee salary for the years ended December 31, 2017, 2016 and 2015. During the years ended December 31, 2017, 2016 and 2015, we recognized total expense of $910,000, $819,000 and $525,000, respectively.

14. Income Taxes

The income tax provision consists of the following (in thousands):

	Year Ended December 31,	
	2017	2016
Current:		
Federal	$ –	$ –
State	–	–
Foreign	–	–
	–	–
Deferred:		
Federal	$ –	$ –
State	–	–
Foreign	–	–
	–	–
Total provision for income taxes	$ –	$ –

We did not record an income tax expense for the year ended December 31, 2017 and 2016. We recorded an income tax benefit of $0.4 million for the year ended December 31, 2015. The effective tax rate of our provision for income taxes differs from the federal statutory rate as follows:

	Year Ended December 31,		
	2017	2016	2015
Federal statutory income tax rate	34.0%	34.0%	34.0%
State income taxes, net of federal benefit	0.0%	0.0%	-6.6%
Federal and state credits	8.9%	9.5%	2.5%
Excess tax benefit	8.6%	0.0%	0.0%
Stock based compensation	0.1%	-0.1%	0.0%
FIN 48 release	0.0%	0.0%	0.2%
Other	-0.1%	0.1%	0.0%
Tax impact due to tax rate reduction	-47.7%	0.0%	0.0%
Change in valuation allowance	2.6%	-38.6%	-29.9%
Foreign Rate Differential	-6.4%	-4.9%	0.0%
Total tax benefit	0.0%	0.0%	0.2%

The components of U.S. deferred tax assets and (liabilities) are as follows (in thousands):

	December 31,	
	2017	2016
Deferred tax assets:		
Federal and state net operating loss carryforwards	$ 203,897	$ 235,015
Federal and state research tax credit carryforwards	21,238	17,927
Federal Orphan Drug Credit	96,750	60,822
Deferred revenue	17,538	15,566
Stock options	15,995	18,734
Capitalized acquisition costs	–	819
Other	7,529	16,298
Net deferred tax assets before valuation allowance	362,947	365,181
Valuation allowance	(362,947)	(365,181)
Net deferred tax assets	$ –	$ –

We received orphan designation and were eligible to claim a federal orphan drug credit starting in 2015 and reported the credit in 2017 and 2016.

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, we believe 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 approximately $2.2 million for the year ended December 31, 2017, which consists of $133.9 million increase offset by $136.1 million decrease due to the remeasurement of the ending deferred tax assets and liabilities at 21%. The valuation allowance increased by approximately $114.2 million for the year ended December 31, 2016.

As of December 31, 2017, we had net operating loss carryforwards for federal income tax purposes of approximately $865 million and federal research tax credits of approximately $18 million and orphan drug credit of $114 million, which expire at various dates in the period from 2024 to 2037. We also have California net operating loss carry forwards of approximately $222 million which expire at various dates in the period from 2018 to 2032 and California research tax credits of approximately $8 million, which can be carried forward indefinitely. Our federal and state net operating loss carryforwards as of December 31, 2017 include amounts resulting from exercises and sales of stock option awards to employees and non-employees. When we realize the tax benefit associated with these stock option exercises as a reduction to taxable income in our returns, we will account for the tax benefit as a reduction of our income tax provision in our consolidated financial statements.

Internal Revenue Code Section 382 limits the use of net operating loss and tax credit carryforwards in certain situations where changes occur in the stock ownership of a company. In the event that we had a change of ownership, utilization of the net operating loss and tax credit carryforwards may be limited under section 382.

Uncertain Tax Positions

We are subject to taxation in the United States. We have not been audited by the Internal Revenue Service or any state tax authority. We are no longer subject to audit by the Internal Revenue Service for income tax returns filed before 2015, and by the material state and local tax authorities for tax returns filed before 2014. However, carryforward tax attributes that were generated prior to these years may still be adjusted upon examination by tax authorities.

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

	Year Ended December 31,		
	2017	2016	2015
Unrecognized tax benefits, beginning of period	$ 13,865	$ 3,228	$ 2,906
Increases due to current period positions	7,046	6,919	1,091
Decreases due to current period positions	–	–	–
Increase due to prior period positions	–	4,266	–
Decreases due to prior period positions	(181)	(548)	(404)
Decreases due to the lapse of statutes of limitations	–	–	(365)
Unrecognized tax benefits, end of period	$ 20,730	$ 13,865	$ 3,228

The amount of unrecognized income tax benefits that, if recognized, would affect our effective tax rate was $0 as of December 31, 2017 and December 31, 2016. If the $20.7 million and $13.9 million of unrecognized income tax benefits as of December 31, 2017 and 2016, respectively, is recognized, there would be no impact to the effective tax rate as any change will fully offset the valuation allowance. We do not expect that the unrecognized tax benefit will change within the next 12 months.

We recognize interest and penalties related to unrecognized tax benefits within income tax expense. Accrued interest and penalties are included within the related tax liability line in the accompanying consolidated balance sheets. Due to our net operating losses, we have not accrued any interest or penalty for any of our uncertain tax benefits as of December 31, 2017 and 2016.

On December 22, 2017 President Donald Trump signed into U.S. law the Tax Reform Act. ASC Topic 740, Accounting for Income Taxes, requires companies to recognize the effect of tax law changes in the period of enactment even though the effective date for most provisions is for tax years beginning after December 31, 2017, or in the case of certain other provisions of the law, January 1, 2018. As a result of Tax Reform Act, the U.S. statutory tax rate was lowered from 35% to 21%, effective on January 1, 2018. We are required to remeasure our U.S. deferred tax assets and liabilities to the new tax rate. We reduced our net deferred tax assets by $136.1 million as a provisional amount due to the remeasurement which was offset by a full valuation allowance, and therefore, it had no impact to our provision for income taxes for the year ended December 31, 2017.

Given the significance of the legislation, the SEC staff issued Staff Accounting Bulletin ("SAB") No. 118 (SAB 118), which allows registrants to record provisional amounts during a one year “measurement period”. However, the measurement period is deemed to have ended earlier when the registrant has obtained, prepared, and analyzed the information necessary to finalize its accounting. During the measurement period, impacts of the law are expected to be recorded at the time a reasonable estimate for all or a portion of the effects can be made, and provisional amounts can be recognized and adjusted as information becomes available, prepared, or analyzed.

Amounts recorded, where we consider accounting to be provisional for the year ended December 31, 2017, principally relate to the impact of corporate income tax rate reduction on the deferred tax assets, on the corresponding change of deferred tax assets’ valuation allowance, and limitations on deductibility of compensation paid to certain highly paid employees.

The changes included in the Tax Reform Act are broad and complex. The final transition impacts of the Tax Reform Act may differ from the above estimate, possibly materially, due to, among other things, changes in interpretations of the Tax Reform Act, any legislative action to address questions that arise because of the Tax Reform Act, and changes in accounting standards for income taxes or related interpretations in response to the Tax Reform Act, or any updates or changes to estimates that we have utilized to calculate the transition impacts.

15. Related Party Transactions

Our former President and Chief Executive Officer, who is currently a member of our board of directors, is also a co-founder and member of the board of directors of Global Blood Therapeutics, Inc. ("Global Blood"), and a member of the board of directors of MyoKardia, Inc. ("MyoKardia"). In November 2012, we entered into Master Services Agreements with Global Blood and MyoKardia under which we provide certain consulting, preclinical, laboratory and clinical research related services to each of these companies. For the years ended December 31, 2017, 2016, and 2015, we recorded a reduction in research and development expense of $292,000, $313,000, and $352,000, respectively, related to amounts owed to us by Global Blood under the Master Services Agreement.

As of December 31, 2017 and 2016, receivables due from these related parties in the amount of $26,000 and $44,000, respectively, were included in prepaid expenses and other current assets on the consolidated balance sheet.

16. Quarterly Financial Data (unaudited)

The following table presents certain unaudited quarterly financial information. This information has been prepared on the same basis as the audited consolidated 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.

	2017				2016			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Collaboration and license revenue	$ 5,128	$ 3,787	$ 3,828	$ 9,803	$ 8,258	$ 4,231	$ 9,322	$ 13,693
Operating expenses	$(45,666)	$(69,621)	$(84,284)	$(95,654)	$(73,564)	$(61,867)	$(100,765)	$(68,893)
Net loss	$(41,764)	$(69,414)	$(82,941)	$(91,501)	$(64,974)	$(57,339)	$ (91,036)	$(54,764)
Net loss (income) attributable to noncontrolling interest (SRX Cardio)	$ 45	$ (240)	$ 5	$ (280)	$ –	$ –	$ (1,853)	$ 923
Net loss attributable to Portola	$(41,719)	$(69,654)	$(82,936)	$(91,781)	$(64,974)	$(57,339)	$ (92,889)	$(53,841)
Net loss per share attributable to Portola common stockholders:								
Basic and diluted	$ (0.74)	$ (1.22)	$ (1.41)	$ (1.41)	$ (1.15)	$ (1.02)	$ (1.64)	$ (0.95)

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

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

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

As required by Rule 13a-15(b) under the Exchange Act, our management, under the supervision and with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of December 31, 2017. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2017, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is a process designed by, or under the supervision of, our Chief Executive Officer and Chief Financial Officer to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that (1) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the consolidated financial statements.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on criteria established in "Internal Control—Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Our management concluded that our internal control over financial reporting was effective as of December 31, 2017.

Our independent registered public accounting firm, Ernst & Young LLP, has audited the effectiveness of our internal control over financial reporting as of December 31, 2017 as stated in their report which is included herein.

Limitations on Effectiveness of Controls and Procedures and Internal Control over Financial Reporting

In designing and evaluating the disclosure controls and procedures and internal control over financial reporting, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures and internal control over financial reporting must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal controls over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended December 31, 2017 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Portola Pharmaceuticals, Inc.

Opinion on Internal Control over Financial Reporting

We have audited Portola Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2017, based on criteria established in Internal Control— Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework)(the COSO criteria). In our opinion, Portola Pharmaceuticals, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2017, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the 2017 consolidated financial statements of the Company and our report dated March 1, 2018, expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Redwood City, California
March 1, 2018

PART III

Certain information required by Part III is omitted from this annual report on Form 10-K and is incorporated herein by reference to our definitive Proxy Statement for our 2018 Annual Meeting of Stockholders, or the Proxy Statement, which we intend to file pursuant to Regulation 14A of the Securities Exchange Act of 1934, as amended, within 120 days after December 31, 2017.

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

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

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

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item regarding executive compensation is incorporated by reference to the information set forth in the sections titled "Executive Compensation", and "Compensation Committee Interlocks and Insider Participation" in our Proxy Statement.

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

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

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

The information required by this item regarding certain relationships and related transactions and director independence is incorporated by reference to the information set forth in the sections titled "Certain Relationships and Related Party Transactions" and "Election of Directors", respectively, in our Proxy Statement.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

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

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

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

(1) FINANCIAL STATEMENTS

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

(2) FINANCIAL STATEMENT SCHEDULES

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

(b) Exhibits. The following exhibits are filed, or incorporated by reference into, this report.

Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
3.1	Amended and Restated Certificate of Incorporation of Portola Pharmaceuticals, Inc.	8-K	001-35935	3.1	5/28/2013
3.2	Amended and Restated Bylaws of Portola Pharmaceuticals, Inc.	8-K	001-35935	3.2	5/28/2013
4.1	Form of Common Stock Certificate of Portola Pharmaceuticals, Inc.	S-1	333-187901	4.1	5/17/2013
4.2	Warrant to Purchase Shares of Series A Preferred Stock by and between the registrant and General Electric Capital Corporation, dated January 21, 2005.	10-Q	001-35935	4.4	11/6/13
4.3	Warrant to Purchase Shares of Series B Preferred Stock by and between the registrant and Comerica Incorporated, dated September 26, 2006.	10-Q	001-35935	4.6	11/6/13
4.4	Warrant to Purchase Shares of Common Stock by and between the registrant and Laurence Shushan and Magdalena Shushan Acosta, Trustees, The Laurence and Magdalena Shushan Family Trust, Under Agreement Dated October 8, 1997, dated December 15, 2006.	10-Q	001-35935	4.7	11/6/13
4.5	Warrant to Purchase Shares of Common Stock by and between the registrant and HCP Life Science Assets TRS, LLC, dated December 15, 2006.	10-Q	001-35935	4.8	11/6/13
4.6	Warrant to Purchase Shares of Common Stock by and between the registrant and Bristow Investments, L.P., dated December 15, 2006.	10-Q	001-35935	4.9	11/06/13
4.7	Reference is made to Exhibits 3.1 and 3.2.				
10.1	Form of Indemnity Agreement between the Registrant and its directors and officers.	S-1	333-187901	10.1	4/12/2013
10.2+	Portola Pharmaceuticals, Inc. 2003 Equity Incentive Plan, as amended, and Form of Stock Option Grant Notice, Option Agreement and Form of Notice of Exercise.	S-1	333-187901	10.2	4/12/2013
10.3+	Portola Pharmaceuticals, Inc. 2013 Equity Incentive Plan and Form of Stock Option Agreement and Form of Stock Option Grant Notice thereunder.	S-1	333-187901	10.3	4/12/2013

Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
10.4+	Form of Executive Severance Benefits Agreement (amends and restates Form of 2006 Executive Change in Control Severance Benefits Agreement)	10-Q	001-35935	10.4	8/6/2014
10.5+	Amended Non-Employee Director Compensation Policy.	10-Q	001-35935	10.5	5/6/2016
10.6†	License Agreement by and between the registrant and Millennium Pharmaceuticals, Inc., dated as of August 4, 2004.	S-1	333-187901	10.8	4/12/2013
10.7†	Asset Purchase Agreement by and between the registrant and Millennium Pharmaceuticals, Inc., dated as of November 7, 2003.	S-1	333-187901	10.9	4/12/2013
10.8†	Letter by and between the registrant and Millennium Pharmaceuticals, Inc., dated as of December 6, 2005.	S-1	333-187901	10.10	4/12/2013
10.9†	Second Amended and Restated License Agreement by and between the registrant and Astellas Pharma, Inc., dated as of December 20, 2010.	S-1	333-187901	10.11	4/12/2013
10.10	Lease by and between the registrant and Britannia Pointe Grand Limited Partnership, dated as of December 15, 2006.	S-1	333-187901	10.13	4/12/2013
10.11	First Amendment to Lease by and between the registrant and Britannia Pointe Grand Limited Partnership, dated as of May 21, 2010.	S-1	333-187901	10.14	4/12/2013
10.12	Offer Letter by and between the Registrant and William Lis, dated as of April 29, 2008.	S-1	333-187901	10.15	4/12/2013
10.13	Offer Letter by and between the Registrant and Mardi C. Dier, dated as of July 28, 2006.	S-1	333-187901	10.17	4/12/2013
10.14	Portola Pharmaceuticals, Inc. 2013 Employee Stock Purchase Plan.	10-Q	001-35935	10.19	11/9/2017
10.15	Second Amendment to Lease made and entered into as of the 14th day of March 2014, by and between Portola Pharmaceuticals, Inc. and Britannia Pointe Grand Limited Partnership.	8-K	001-35935	10.22	3/19/2014
10.16+	Form of Restricted Stock Unit Award Grant Notice and Award Agreement—2013 Equity Incentive Plan.	10-K	001-35935	10.25	3/2/2015
10.17+	Form of Performance Stock Unit Award Grant Notice and Award Agreement—2013 Equity Incentive Plan.	10-K	001-35935	10.26	2/29/2016
10.18+	Offer Letter by and between Portola Pharmaceuticals, Inc. and Tao Fu, dated as of May 8, 2015.	10-Q	001-35935	10.27	8/5/2015
10.19+	Form of Stock Option Grant Notice for Non-Employees — 2013 Equity Incentive Plan.	10-Q	001-35935	10.28	8/9/2016
10.20+	Form of Performance Stock Option Grant Notice —2013 Equity Incentive Plan.	10-Q	001-35935	10.29	8/9/2016
10.21+	Form of Restricted Stock Unit Award Grant Notice and Award Agreement for Directors—2013 Equity Incentive Plan.	10-Q	001-35935	10.30	8/9/2016
10.22+	Form of Restricted Stock Unit Award Grant Notice for Officers —2013 Equity Incentive Plan.	10-Q	001-35935	10.31	8/9/2016
10.23+	Form of Performance Stock Unit Award Grant Notice — 2013 Equity Incentive Plan.	10-Q	001-35935	10.32	8/9/2016

Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
10.24+	Market Based Performance Stock Unit Award Grant Notice—2013 Equity Incentive Plan.	10-Q	001-35935	10.33	8/9/2016
10.25+	Amended and Restated Offer Letter by and between Portola and John T. Curnutte, M.D., Ph.D., dated as of January 25, 2017.	8-K	001-35935	10.1	2/3/2017
10.26	Purchase and Sale Agreement dated as of February 2, 2017 between Portola Pharmaceuticals, Inc. and certain entities managed by Healthcare Royalty Management LLC.	10-Q	001-359351	10.37	5/9/2017
10.27*	Supplemental Funding Support Loan Agreement among Portola, Bristol-Myers Squibb Company and Pfizer Inc. dated as of December 16, 2016.	10-K	001-35935	10.35	3/1/2017
10.28+	Portola Pharmaceuticals, Inc. Inducement Plan	10-Q	001-35935	10.39	11/9/2017
10.29+	Form of Stock Option Grant Notice - Inducement Plan	10-Q	001-35935	10.40	11/9/2017
10.30+	Form of Stock Option Grant Notice for Officers - Inducement Plan	10-Q	001-35935	10.41	11/9/2017
10.31+	Form of Option Agreement - Inducement Plan	10-Q	001-35935	10.42	11/9/2017
10.32+	Form of Restricted Stock Unit Award Grant Notice - Inducement Plan	10-Q	001-35935	10.43	11/9/2017
10.33+	Form of Restricted Stock Unit Award Grant Notice for Officers - Inducement Plan	10-Q	001-35935	10.44	11/9/2017
10.34	Form of Award Agreement - Inducement Plan	10-Q	001-35935	10.45	11/9/2017
23.1*	Consent of Independent Registered Public Accounting Firm				
24.1	Power of Attorney (see signature page).				
31.1*	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended.				
31.2*	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended.				
32.1*	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.(1)				
101.INS	XBRL Instance Document. (2)				
101.SCH	XBRL Taxonomy Extension Schema Document. (2)				
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document. (2)				
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document. (2)				
101.LAB	XBRL Taxonomy Extension Label Linkbase Document. (2)				
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document. (2)				

† Confidential Treatment Granted

+ Management contract or compensatory plan
* Filed herewith

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

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

ITEM 16. FORM 10–K SUMMARY

Not applicable

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of South San Francisco, State of California, on the 1st day of March 2018.

PORTOLA PHARMACEUTICALS, INC.

By: /s/ WILLIAM LIS
William Lis
Chief Executive Officer

POWER OF ATTORNEY

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

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

Signature	Title	Date
/ S / WILLIAM LIS William Lis	Chief Executive Officer and Director (Principal Executive Officer)	March 1, 2018
/ S / MARDI C. DIER Mardi C. Dier	Chief Financial Officer (Principal Financial and Accounting Officer)	March 1, 2018
/ S / HOLLINGS C. RENTON Hollings C. Renton	Chairman of the Board of Directors	March 1, 2018
/ S / JEFFREY W. BIRD Jeffrey W. Bird, M.D., Ph.D.	Director	March 1, 2018
/ S / LAURA A. BREGE Laura A. Brege	Director	March 1, 2018
/ S / DENNIS FENTON, PH.D. Dennis Fenton, Ph.D.	Director	March 1, 2018
/ S / CHARLES J. HOMCY, M.D. Charles J. Homcy, M.D	Director	March 1, 2018
/ S / JOHN H. JOHNSON John H. Johnson	Director	March 1, 2018
/ S / DAVID C. STUMP, M.D. David C. Stump, M.D.	Director	March 1, 2018
/ S / H. WARD WOLFF H. Ward Wolff	Director	March 1, 2018

CORPORATE INFORMATION

EXECUTIVE TEAM

William Lis
Chief Executive Officer

John T. Curnutte, M.D., Ph.D.
Executive Vice President,
Research and Development

Mardi C. Dier
Executive Vice President,
Chief Financial Officer

Tao Fu
Executive Vice President,
Chief Commercial and Business Officer

John H. (Jack) Lawrence, M.D.
Senior Vice President,
Chief Medical Officer

John B. Moriarty, J.D.
Executive Vice President,
General Counsel

BOARD OF DIRECTORS

Hollings C. Renton
Chairman of the Board

William Lis
Chief Executive Officer,
Portola Pharmaceuticals, Inc.

Jeffrey W. Bird, M.D., Ph.D.
Managing Director, Sutter Hill Ventures

Laura Brege
Former President and Chief Executive Officer, Nodality, Inc.

Dennis Fenton, Ph.D.
Owner and Chief Executive Officer,
Fenton and Associates

Charles Homcy, M.D.
Former President and Chief Executive Officer, Portola Pharmaceuticals, Inc.

John H. Johnson
Founder, Plum Brook Advisors

David C. Stump, M.D.
Former Executive Vice President,
Research and Development,
Human Genome Sciences, Inc.

H. Ward Wolff
Former Executive Vice President and Chief Financial Officer,
Sangamo Therapeutics, Inc.

CORPORATE INFORMATION

Independent Auditors
Ernst & Young LLP
275 Shoreline Drive, Suite 600
Redwood City, CA 94065
Phone: 650.802.4500

Investor Relations
Inquiries and requests for information, including copies of Portola's Annual Report on Form 10-K may be obtained without charge by contacting Investor Relations or visiting our website.

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Corporate Counsel
Cooley LLP
3175 Hanover Street
Palo Alto, CA 94304
Phone: 650.843.5000

Annual Meeting
June 8, 2018 at 9:00 am PT
Portola Pharmaceuticals, Inc.
270 E. Grand Avenue
South San Francisco, CA 94080

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