PORTOLA

2019 ANNUAL REPORT
PORTOLA PHARMACEUTICALS

Therapeutic ingenuity. It's in our blood.

Dear Shareholders,

2019 was a year of significant accomplishments for Portola as we made the transition to a global commercial organization. Our flagship medicine, Andexxa® [coagulation factor Xa (recombinant), inactivated-zhzo], is now available to hospitals and patients in the United States and a growing number of European countries. We achieved several landmark milestones for Andexxa and Ondexxya™ (andexanet alfa; the trade name for Andexxa in Europe) that will drive the future growth of the company and support our vision to deliver life-saving treatments for serious blood-related disorders.

U.S. COMMERCIAL LAUNCH OF ANDEXXA

2019 was the first full year of the Andexxa launch in the U.S. following the approval of our second-generation manufacturing process on December 31, 2018. Over the course of the year, we added 425 new hospital customers for a total of 640 hospitals that have now ordered Andexxa in the U.S. Together, we estimate that these hospitals utilized Andexxa to treat over 4,000 patients with Factor Xa inhibitor-related bleeding in 2019.

We believe there is a significant opportunity to improve outcomes for more of these patients – a view that is underscored by the recommendation to use Andexxa or a specific reversal agent by 19 medical society guidelines in the United States and Europe as well as guidelines from The Joint Commission, the nation's oldest and largest standards-setting and accrediting body in healthcare.

In order to achieve broader adoption, we are executing a strategic plan to develop and disseminate clinical, health economic and other data that highlight the value of Andexxa compared to other non-specific therapies that historically have been used off-label for these patients. We began presenting this data in 2019 and have a robust schedule of new data planned for 2020 and beyond. This is backed by our educational and support programs around Andexxa's new technology add-on payment (NTAP) from the Centers for Medicare & Medicaid Services (CMS) and reimbursement best practices.

EUROPEAN APPROVAL AND LAUNCH OF ONDEXXYA

Ondexxya received marketing authorization from the European Commission in April 2019. Europe represents a large and growing opportunity, with approximately double the number of Factor Xa inhibitor patients compared to the U.S. We made important progress in building an efficient European business in our Wave 1 countries of Germany, Austria, the United Kingdom, the Netherlands, Sweden, Denmark and Finland.

Importantly, shortly after approval, our team submitted dossiers to the National Institute for Health and Care Excellence (NICE) in the United Kingdom and the Arzneimittelmarkt-Neuordnungsgesetz (AMNOG) in Germany, allowing for initial sales in these important markets in the second half of 2019 and setting the stage for reimbursement coverage decisions in 2020.

We are excited to move closer to making Ondexxya available to patients in these markets and the rest of Europe, further expanding access to the first and only approved reversal agent for patients taking rivaroxaban or apixaban.

STRATEGIC FOCUS ON ANDEXXA

During the year, we continued to invest in world-class capabilities and talent across sales, development, quality, market access, medical affairs and business information to support the launch of Andexxa. This includes expanding our U.S. sales team, establishing our European leadership and country-level teams, and, in February 2020, welcoming our new chief medical officer, who will drive the clinical development and life cycle management strategy for Andexxa. Also in early 2020, we took important steps to align our focus and resources on expanding the Andexxa customer base and driving utilization with hospital customers.

We completed an internal restructuring to reduce spending on research programs and focus our resources on the Andexxa revenue drivers and life cycle management. As a result, we discontinued our efforts to commercialize or partner Bevyxxa® (betrixaban) and paused the initiation of the CELTIC-1 trial for our SYK/JAK inhibitor, cerdulatinib, until we secure a development partner.

Portola will continue to focus on the foundation of our business, which is to fuel the near-term and future growth of Andexxa and drive shareholder value by working toward our vision to be best-in-class in the treatment of serious blood-related disorders.

ANDEXXA POISED FOR GROWTH IN 2020 AND BEYOND

2020 will be an important year of execution, growth and expansion for Andexxa against the backdrop of the large and growing Factor Xa inhibitor market. At the same time, we are operating in unprecedented times with the global COVID-19 pandemic, which has changed all aspects of our daily lives and the way in which we conduct business. As we navigate through this pandemic, Portola's first priority is the health and safety of employees, patients and healthcare providers. We have taken proactive steps to mitigate the spread of the virus while also working to provide uninterrupted support to ensure that hospitals can continue to use and re-order Andexxa for patients taking rivaroxaban or apixaban that experience life-threatening bleeds.

As we look ahead, there is significant long-term growth opportunity for Andexxa. We plan to deepen use in the U.S., expand geographically in Europe, and broaden the Andexxa label with additional Factor Xa inhibitors and an indication for patients who require urgent surgery. We remain steadfast in our efforts to educate the healthcare community with clinical and economic data that clearly demonstrates Factor Xa inhibitor patients should only be given Andexxa when an uncontrolled or life-threatening bleeding event occurs.

In closing, our successful launch and progress in 2019 would not be possible without the patients and healthcare professionals that participate in our clinical trials, the academic and clinical partners who collaborate with us, the wise counsel of our Board of Directors and the ongoing support of our shareholders. On behalf of the entire Portola executive team and our Board of Directors, thank you for your continued belief in our mission.

Sincerely,

Scott Garland

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, 2019

☐ **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	**20-0216859**
(State or other jurisdiction of incorporation or organization)	(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:	Trading Symbol(s)	Name of Each Exchange on which Registered
Common Stock, par value $0.001 per share	PTLA	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 every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth 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	☐	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 $1.1 billion computed by reference to the last sales price of $27.13 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, 2019. This calculation does not reflect a determination that certain persons are affiliates of the registrant for any other purpose.

As of February 20, 2020, the number of outstanding shares of the registrant's common stock, par value $0.001 per share, was 78,080,365.

DOCUMENTS INCORPORATED BY REFERENCE

Part III incorporates information by reference to the definitive proxy statement for the registrant's 2019 Annual Meeting of Stockholders to be filed within 120 days of the registrant's fiscal year ended December 31, 2019.

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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 financial performance;
- the projected dollar amounts of market opportunities for our products and product candidates;
- our estimates and projections for the commercial and clinical development of our products and product candidates, including launch strategies, clinical research and trials and regulatory approval, both in the United States and abroad;
- potential indications for our product candidates;
- our expectations and projections regarding existing capital resources and our estimates of our expenses, ongoing losses, future revenue, capital requirements and our needs for or ability to obtain additional financing;
- our discussion of perceived and projected competitive advantages of our products and product candidates;
- the projected patient populations targeted by our products and product candidates;
- the rate and degree of market acceptance of our approved products;
- our ability to successfully build a hospital-based sales force and commercial infrastructure;
- our ability to obtain and maintain intellectual property protection for our products;
- our ability to successfully establish and successfully maintain appropriate collaborations and derive significant value from those collaborations; 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, highly regulated 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.

Note Regarding Use of Brand Names

We generally refer to our two approved drugs in this report as Andexxa® and Bevyxxa®. If approved outside of the United States, each drug may be marketed under different brand names. In addition, an international nonproprietary name (“INN”) has been designated for each drug. Our previous INN for Andexxa in the United States was andexanet alfa; however, in the United States this INN has been replaced with “coagulation factor Xa (recombinant), inactivated-zhzo.” For other parts of the world, andexanet alfa could remain the INN for Andexxa. In April 2019, andexanet alfa received conditional approval by the European Commission ("EC") under the brand name Ondexxya™. Our use of the trade names, Andexxa or Bevyxxa, in this document in the context of continued development activities or jurisdictions for which we have not yet received regulatory approval should not be read to imply that we have received regulatory approval for any indication or in any jurisdiction not reflected in our product labels or that we will use such brand names in such jurisdictions.

PART I

ITEM 1. BUSINESS

Overview

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 diseases and inflammation for patients who currently have limited or no approved treatment options. Our headquarters is located in South San Francisco, California.

Our lead product is Andexxa [coagulation factor Xa (recombinant), inactivated-zhzo] which we are marketing under the brand name of Ondexxya in Europe. Andexxa is the first and only antidote approved by the U.S. Food and Drug Administration ("FDA") and the European Commission ("EC") for patients treated with rivaroxaban or apixaban, when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding. We are conducting clinical trials with cerdulatinib, an investigational oral, dual spleen tyrosine kinase ("SYK") and Janus kinase ("JAK") inhibitor to treat hematologic cancers.

Pipeline

	Description	Approved or Investigational Indication	Stage	Commercial rights
Andexxa	Reversal agent for certain Factor Xa (fXa) inhibitors	Patients treated with rivaroxaban or apixaban, when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding	U.S. Approval European Union ("EU") Approval	Worldwide excluding Japan
Cerdulatinib	Oral, dual Syk and JAK inhibitor	Relapsed/refractory B- and T-cell malignancies	Phase 2a	Worldwide excluding topical formulation in non-oncology indications

Our strategy

We are building a global biopharmaceutical company, focusing our efforts and resources on marketing Andexxa in the United States and Europe while we conduct additional clinical trials to obtain full regulatory approvals and expand approved indications. Additionally, we are conducting clinical trials for cerdulatinib as we pursue partnering opportunities or other strategic transactions.

Key elements of our strategy are as follows:

- Pursue and prioritize the commercial launch of Andexxa in the United States and Ondexxya in Europe;
- Increase engagement with medical, scientific and academic professionals and associations to establish Andexxa as the standard of care for treating life-threatening Factor Xa inhibitor-related bleeds;
- Continue to build our European operations and execute a phased launch of Ondexxya in Europe, with an initial focus on Germany, Austria, Denmark, Finland, Sweden, the Netherlands and the United Kingdom (together, the "Wave 1 Countries");
- Launch Ondexxya in France, Switzerland, Italy, Spain, Ireland and other countries yet to be determined (together, the "Wave 2 Countries");
- Develop clinical data supporting full approvals for Andexxa in the United States and Ondexxya in Europe;
- Pursue additional regulatory approvals for Andexxa, including reversal of additional anticoagulants such as edoxaban and enoxaparin, and reversal of Factor Xa inhibitors for emergency surgery/urgent procedures;
- Establish and improve reimbursement and market access for Andexxa/Ondexxya;
- Support our commercial marketing partners Bristol-Meyers Squibb Company ("BMS") and Pfizer, Inc. ("Pfizer") to advance the development and commercialization of Andexxa for the Japanese market; and
- Advance development of cerdulatinib for the treatment of hematologic cancers while pursuing partnering opportunities or other strategic transactions.

Approved Products

Andexxa

Andexxa is approved by the FDA as a reversal agent for patients treated with rivaroxaban or apixaban, when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding. Andexxa was approved under the FDA's Accelerated Approval pathway based on the change from baseline in anti-Factor Xa activity in healthy volunteers. Continued approval for this indication is contingent upon post-marketing study results that verify that clinical benefit is conferred to patients.

We are conducting a randomized controlled trial of Andexxa (U.S.)/Ondexxya (EU) against a usual care cohort control arm (known as "ANNEXA-I") to provide clinical data supporting full approval. ANNEXA-I was initiated in early 2019 and we anticipate that it will include approximately 440 patients with intracranial hemorrhage and compare outcomes of patients treated with Andexxa to the usual care on a 1:1 randomized scheme. We plan to conduct this study globally with our expected completion date in 2023. We are also conducting the ANNEXA-S study: a single-arm, open-label clinical trial in approximately 200 patients enrolled from approximately 80 hospitals worldwide. ANNEXA-S will evaluate the efficacy and safety in patients requiring urgent surgery while taking apixaban, edoxaban, enoxaparin, or rivaroxaban. The primary endpoint of ANNEXA-S is hemostatic efficacy, as assessed by intraoperative assessment of hemostasis. The study is expected to be completed in 2022.

In the U.S., we initially received approval from the FDA in May 2018 to market product manufactured under our Gen 1 process using the clinical-scale process at the facility that produced material for our clinical trials. We conducted a limited launch in the second half of 2018 through an Early Supply Program ("ESP") intended to reach hospitals with a large number of patients with Factor Xa bleeds and who were able to start using Andexxa during the ESP period. On December 31, 2018, the FDA approved our Gen 2 manufacturing process, which provides commercial scale volume that we believe is sufficient to support a global launch. In early January 2019, we began shipping Gen 2 product and commenced a full-scale commercial launch in the U.S..

Andexanet alfa received conditional approval under the brand name Ondexxya by the EC on April 26, 2019. This conditional approval included several post-authorization requirements, including specific obligations to submit a final clinical study report for ANNEXA-I, a final clinical study report for the ANNEXA-4 study, and an obligation to provide some additional pharmacokinetic data.

We completed our first sales of Ondexxya in Europe in July 2019 and are executing a phased launch of Ondexxya in Europe, with an initial focus on the Wave 1 Countries. We also intend to launch Ondexxya in the Wave 2 countries and establish an early access program for Ondexxya through a distribution partner. We launched in the EU using Gen 2 product in July 2019.

In May 2019, we announced a new analysis of the ANNEXA-4 study among patients with spontaneous (non-traumatic) intracranial hemorrhage - a bleeding event in the brain not caused by trauma and associated with high rates of mortality and morbidity. The data presented demonstrate that, even among this important and difficult-to-treat subset of patients, the hemostatic efficacy and safety of Andexxa is compelling and consistent. Specifically, the data show:

- A high rate of hemostatic efficacy (79%) consistent with that of the full ANNEXA-4 trial across patients with all types of bleeds (82%);
- Of the patients that achieved excellent or good hemostatic efficacy within one hour-post Andexxa administration, 98% (n=55/56) maintained excellent or good hemostatic control 12 hours following Andexxa administration;
- The majority of thrombotic events occurred in patients who delayed or did not re-start anticoagulation therapy with a Factor Xa inhibitor during the follow-up period; and
- No thrombotic events were observed among the 18 patients who re-started oral anticoagulation therapy within 30 days.

Andexxa is administered almost exclusively in the hospital and urgent care setting and is reimbursed either under Medicare Part A through an applicable Medicare Severity Diagnosis Related Group ("MS-DRG") payment related to the patient condition for inpatient use, or separately reimbursed under a C code through Medicare with respect to outpatient usage covered by Medicare Part B based on Average Sales Price. In addition, the U.S. Centers for Medicare and Medicaid Services ("CMS") has supplemented Part A reimbursement with a New Technology Add-on Payment ("NTAP"), which was first effective in October 2018 at a maximum of 50% of wholesale acquisition cost ("WAC") for the standard dose, and increased in October 2019 to a maximum of 65% of WAC. The actual NTAP amount will vary based on the amount by which the cost of a case exceeds the MS-DRG payment. The CMS NTAP program was created by Congress to support timely access to innovative therapies used to treat Medicare beneficiaries in the hospital inpatient setting. For a new technology to qualify for an add-on payment, it must meet the NTAP definition of "new," demonstrate a substantial clinical improvement and meet specific cost thresholds.

The worldwide use of Factor Xa inhibitors is rapidly growing because of their efficacy and safety profile compared to warfarin and enoxaparin in preventing and treating thromboembolic conditions such as stroke, pulmonary embolism and venous

thromboembolism ("VTE"). This growth has come with a proportional increase in the incidence of hospital admissions and deaths related to bleeding, the major complication of anticoagulation. In 2018, in the United States, there were approximately 150,000 hospital admissions attributable to Factor Xa inhibitor-related bleeding. We believe that Andexxa has the potential to act as a universal reversal agent for all direct and indirect Factor Xa inhibitors. We plan to continue clinical development to support global approvals as a reversal agent for other Factor Xa inhibitors. In addition, we plan to continue clinical development to support global approvals for reversal of the anticoagulant effects in Factor Xa inhibitor-treated patients who require emergency surgery/urgent procedures.

We hold worldwide commercial rights to Andexxa with the exception of Japan. In 2016, we entered into collaboration agreements with BMS and Pfizer whereby BMS and Pfizer will seek to obtain Japanese regulatory approval and to commercialize Andexxa 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 of up to $90.0 million, as well as tiered single-digit to double-digit royalties based on net sales in Japan. BMS and Pfizer obtained the rights to develop and commercialize Andexxa in Japan and will be responsible for all development, regulatory and commercialization activities. Under the terms of the agreement, BMS and Pfizer will purchase drug from us at cost for both clinical studies and, upon approval, commercial sales in Japan.

Bevyxxa

Bevyxxa was the first anticoagulant approved in the United States for hospital and extended duration 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 for VTE. Bevyxxa was approved by the FDA in June 2017 and we commenced the commercial launch in the United States in January 2018.

Following the approval of Andexxa in May 2018, we made the business decision to focus our resources on the launch of Andexxa and significantly scaled back our commercial efforts on Bevyxxa. Throughout 2019, we engaged with potential business collaborators for Bevyxxa, and in the fourth quarter of 2019, we determined that it was unlikely that we will find a viable partner. Accordingly, we have begun to wind down Bevyxxa operations to eliminate future operational and financial obligations.

Product Candidates:

Cerdulatinib

Cerdulatinib is our investigational SYK and Janus kinase ("JAK") inhibitor that uniquely inhibits two key cell signaling pathways implicated in certain hematologic malignancies and autoimmune diseases. There is a rationale for inhibiting both SYK (B-cell receptor pathway) and JAK (cytokine receptors) in B-cell malignancies where both targets have been shown to promote cancer cell growth and survival. In addition, pre-clinical data suggest an important role for SYK and JAK in Peripheral T-Cell Lymphoma (“PTCL”) tumor survival.

There is a significant unmet need for the treatment of patients with relapsed/refractory PTCL. Current approved therapies for relapsed/refractory PTCL are all given via IV infusion and have limited activity with overall response rates of approximately 30%. In addition, most of these responses are partial responses. Based on the unmet need and on the activity to date with cerdulatinib, we have prioritized development in PTCL. Following our End of Phase 2 meeting with the FDA in January 2019, the FDA requested additional data supporting the proposed dose and we submitted the requested data. We have reached an agreement with the FDA on the design of a registration study ("CELTIC-1").

In December 2019, we presented new interim Phase 2a data for cerdulatinib in heavily pre-treated T-cell malignancies at the American Society of Hematology ("ASH") Annual Meeting. Patients with PTCL exhibited a 34% overall response rate and a subset of those patients with angioimmunoblastic T-cell lymphoma ("AITL") exhibited an overall response rate of 52% and a complete response of 37%. Additionally, patients with cutaneous T-cell lymphoma ("CTCL") exhibited a 43% overall response rate. Cerdulatinib demonstrated good tolerability in both PTCL and CTCL patients. Additionally, we presented interim Phase 2a data for cerdulatinib alone and in combination with rituximab in Follicular Lymphoma ("FL") patients at the ASH Annual Meeting in December 2019. Data among patients in the single-agent cerdulatinib arm demonstrated consistent clinical activity (including a 48% overall response rate) and good tolerability of cerdulatinib with no evidence of cumulative toxicity. The combination of cerdulatinib with rituximab resulted in improved response rates (including a 76% overall response rate) with a similar safety profile when compared to the data from the single-agent cerdulatinib arm. Follow-up analysis of these cohorts is ongoing.

The FDA granted cerdulatinib Orphan Drug Designation for the treatment of PTCL in September 2018. The FDA's Office of Orphan Products Development grants orphan status to support development of medicines for the treatment of rare diseases. Orphan Drug Designation may provide certain benefits, including a seven-year period of market exclusivity if the drug is approved, tax credits for qualified clinical trials and an exemption from FDA market application fees.

In December 2016, we licensed worldwide rights for the development and commercialization of cerdulatinib in topical applications beyond oncology to Dermavant Sciences GmbH ("Dermavant"), a subsidiary of Roivant Sciences. We retain full rights to all non-topical formulations, including oral formulations. Dermavant is evaluating cerdulatinib as a topical treatment option for vitiligo and other inflammatory skin conditions such as atopic dermatitis. Dermavant has presented Phase 1 results with topical cerdulatinib in atopic dermatitis patients and in December 2019 announced that the first patient was dosed in its Phase 2a vitiligo clinical trial.

Other Early Stage Programs

We continue to progress certain early discovery activities that align with our scientific expertise.

Sales and marketing

We target our U.S. sales and marketing efforts at the approximately 2,100 target accounts that would account for the large majority of the prescribing base for Andexxa. We market Andexxa in the United States using a hospital-based sales force. This sales force is supported by an experienced sales leadership team of regional sales managers and account managers, and our commercial team comprised of experienced professionals in marketing, access and reimbursement, managed markets, marketing research, commercial operations, and sales force planning and management. In the EU, during 2019 we established commercial operations to launch Ondexxya in the Wave 1 Countries and are establishing operations to market Ondexxya in Wave 2 Countries. Hospitals in Europe can purchase our products directly from Portola (Germany, Austria, the Netherlands and the United Kingdom) or indirectly from wholesale distributors (Sweden, Finland and Denmark). Outside of these countries, we also expect to establish an early access program for Ondexxya through a distribution partner. To achieve global commercialization, we anticipate using a variety of distribution agreements and commercial partnerships in those territories where we do not establish our own sales force.

Customers

Our products are purchased in the United States and Europe primarily by hospitals. U.S. hospitals purchase our products through a network of specialty and wholesale distributors and EU hospitals purchase directly from Portola and, to a lesser extent, distributors. We do not believe that the loss of one of these distributors would significantly impact our ability to distribute our product, as we expect that sales volume would be absorbed by the remaining distributors.

Other Key Licenses and Collaborations

As part of our business strategy, we establish collaborations with other companies, universities and medical research institutions to assist in the clinical development and/or commercialization of certain of our products and product candidates and to provide support for our research programs. We also evaluate opportunities for acquiring products or rights to products and technologies that are complementary to our business from other companies, universities and medical research institutions. For more information regarding certain of these relationships, including their ongoing financial and accounting impact on our business, see Note 3, "Revenue Recognition" and Note 7, "Asset Acquisition and License Agreements" in the Notes to our Consolidated Financial Statements included in Part II, Item 8 of this Annual Report on Form 10-K.

Andexxa

- BMS and Pfizer

  We have worked in collaboration with BMS and Pfizer to study Andexxa as a reversal agent for their jointly-owned, FDA-approved oral Factor Xa inhibitor, apixaban, since the inception of our Phase 2 proof-of-concept in 2012. We remain actively engaged with both parties as part of the 2016 collaboration and license agreement whereby BMS and Pfizer obtained exclusive rights to develop and commercialize Andexxa 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 Factor Xa 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% to 15% on net sales of Andexxa in Japan. Under this agreement, we have agreed to provide Andexxa to BMS and Pfizer at cost in order to supply clinical and commercial demand in Japan.

- Daiichi Sankyo, Inc. (“Daiichi Sankyo”)

  In 2013, we entered into an agreement with Daiichi Sankyo to include subjects dosed with edoxaban, its Factor Xa inhibitor product, in our Phase 2 proof-of-concept study of Andexxa. In July 2014, we entered into a second collaboration agreement with Daiichi Sankyo to perform the necessary development and regulatory activities to support 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. To date, we have received $5.0 million in milestone payments and are eligible to receive additional development and regulatory milestone payments of up to $2.5 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 $7.5 million. We have received $7.0 million in milestone payments under this amended agreement. This amended collaboration agreement will continue in force until the approval of andexanet alfa as a reversal agent for edoxaban by the FDA and the European Medicines Agency ("EMA").

  In 2016, we entered into a collaboration agreement with Daiichi Sankyo to include edoxoban in the clinical studies necessary for approval of Andexxa 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 Andexxa as an antidote for edoxaban.

- Bayer Pharma, AG ("Bayer").

  In 2016, we entered into a collaboration agreement with Bayer to include rivaroxaban in the clinical studies necessary for approval of Andexxa 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 Andexxa as an antidote for rivaroxaban.

Other Programs

- We have a number of licenses and collaborations with several partners - Takeda, Ora, Inc. and Astellas Pharma Inc.

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.

Andexxa

Apart from Andexxa, there are currently no therapies approved as antidotes for Factor Xa inhibitors. However, Andexxa competes with off-label treatments to attenuate bleeding including Fresh Frozen Plasma (“FFP”), 4-factor Prothrombin Complex Concentrates (“PCCs”), recombinant activated Factor VII (“rFVIIa”), Vitamin K, protamine and whole blood. In addition, several companies have conducted clinical research on compounds that are intended to reverse the effects of one or more direct Factor Xa inhibitors which, if developed and approved, may be competitive with Andexxa.

Cerdulatinib

In the market for the treatment of FL, PTCL and CTCL, cerdulatinib, if approved, will compete with existing therapies (used as a single agent or in combination with other therapies), such as rituximab and obinutuzumab which are marketed by Chugai Pharmaceutical Co. Ltd., F. Hoffmann-LaRoche Ltd and Genentech, Inc., idelalisib, which is marketed by Gilead Sciences Inc., brentuximab, which is marketed by Seattle Genetics, Inc. and Takeda, copanlisib, which is marketed by Bayer AG, duvelisib, which is marketed by Verastem, Inc., lenalidomide and romidepsin, which are marketed by Celgene Corporation (a subsidiary of BMS), pralatrexate and belinostat, which are marketed by Spectrum Pharmaceuticals, Inc., mogamulizumab, which is marketed by Kyowa Hakko Kirin; and potentially other therapies 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 Annual Report entitled "Risk factors—Risks Related to Intellectual Property."

Andexanet alfa

Our Factor Xa inhibitor antidote patent portfolio is wholly owned by us and includes 13 issued U.S. patents and 11 U.S. patent applications covering the composition of and methods of making and using andexanet alfa or its analogs. 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 relating to the composition of matter is not expected to expire before June 2030. Related international patent applications have issued in 45 countries, and additional related international patent applications are pending. 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, Japan and other countries, and international patent applications are still pending in Europe and a number of other countries.

Betrixaban

Our betrixaban patent portfolio includes 24 issued U.S. patents and five 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 Takeda. 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 the patent term extension we have timely petitioned with the U.S. Patent Office, 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 in 39 countries. These related international patents would not be due to expire before September 2020.

In the U.S., the Hatch-Waxman Act permits a patent term extension of up to five years for one patent related to an approved therapy. We believe that we are eligible for a full five-year patent term extension for one patent relating to betrixaban.

In addition, the Best Pharmaceuticals for Children Act provides that the period of patent exclusivity for a drug may be extended for six months if the owner of the drug conducts studies of the drug in children pursuant to a request from the FDA. We have commenced a pediatric study of bextrixaban in the United States.

Cerdulatinib

Our dual SYK-JAK inhibitor patent portfolio is owned in part by us and licensed in part from Astellas and includes six 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 in 51 countries and a related patent application is pending in Brazil.

Trademarks

We plan to market all of our products under a trademark or trademarks we select and we will own all rights, title and interest, including goodwill, associated with such trademarks. In the United States, Andexxa, Annexa, Bevyxxa and Portola Pharmaceuticals, Inc. and our logo are our registered trademarks. The Ondexxya trademark has been registered in the United States and in the EU. Andexxa and Ondexxya are our registered trademarks in Japan.

Manufacturing

We rely exclusively on contract manufacturing organizations to manufacture our drugs and drug candidates. The manufacture of pharmaceuticals is subject to extensive U.S. and foreign 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. We believe that our current agreements and purchase orders with third-party manufacturers provide for sufficient operating capacity to support anticipated commercial and clinical supply needs for the next several years.

Andexxa

Andexxa 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.

Primary commercial manufacturing of Andexxa bulk drug substance is conducted at Lonza AG ("Lonza"). Drug product manufacturing is conducted at Baxter Pharmaceutical Solutions LLC ("Baxter"). We expect that future clinical studies of Andexxa will also be conducted primarily using product manufactured by these third party-manufacturing organizations. We also rely on other third-party manufacturers for packaging, testing and shipping.

Government regulation

Healthcare and reimbursement regulation

Our research, sales, marketing, promotion, medical education and other activities are subject to regulation by numerous regulatory and law enforcement authorities in the United States, including the FDA, the Federal Trade Commission, the Department of Justice, the CMS, other divisions of the U.S. Department of Health and Human Services ("HHS") including the Office of Inspector General ("OIG") and state and local governments. Our marketing, promotional, and scientific/educational programs and interactions with health care professionals, patients, third-party payers, pharmacies, distributors and others must comply with, among other laws, the Food, Drug and Cosmetic Act the anti-kickback provisions of the Social Security Act and analogous state laws, federal and state false claims laws including the federal civil False Claims Act, the Veterans Health Care Act, federal and state price reporting laws, the Foreign Corrupt Practices Act, and federal and state transparency laws.

Our interactions with health care professionals, third-party payers, patients, distributors, pharmacies and others are subject to scrutiny and enforcement under one or more federal or state health care fraud and abuse laws and regulations, which could affect our ability to operate our business, including:

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, in whole or in part, under federal healthcare programs, such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical companies on one hand and prescribers, purchasers, payers, and formulary managers on the other. Liability under the Anti-Kickback Statute may be established without proving actual knowledge of the statute or specific intent to violate it. In addition, 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 civil False Claims Act. Although there are a number of statutory exceptions and regulatory safe harbors to the federal Anti-Kickback Statute protecting certain common business arrangements and activities from prosecution or regulatory sanctions, the exceptions and safe harbors are drawn narrowly. Failure to meet all the requirements of a particular statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute, but the legality of the arrangement will be evaluated on a case-by-case basis based on the totality of the facts and circumstances. Practices that involve remuneration to those who prescribe, purchase, or recommend pharmaceutical and biological products, including certain discounts, or engaging such individuals as consultants, advisors and speakers, may be subject to scrutiny if they do not fit squarely within an exception or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. Moreover, there are no safe harbors for many common practices, such as educational and research grants, charitable donations, product and reimbursement support and patient assistance programs.

The federal civil False Claims Act, which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, false or fraudulent claims for payment of government funds, or knowingly making, using, or causing to be made or used a false record or statement material to an obligation to pay money to the government, or knowingly concealing or knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by private individuals in the name of the government, who may then share in any monetary recovery. Many pharmaceutical manufacturers have been investigated and have reached substantial financial settlements with the federal government under the civil False Claims Act for

a variety of alleged improper activities including causing false claims to be submitted as a result of the marketing of their products for unapproved and thus non-reimbursable uses, inflating prices reported to private price publication services which are used to set drug payment rates under government healthcare programs, and other interactions with prescribers and other customers including those that may have affected their billing or coding practices and submission to the federal government. Because of the potential for treble monetary damages and significant mandatory penalties per false or fraudulent claim or statement, healthcare and pharmaceutical companies often resolve allegations without admissions of liability for significant and material amounts to avoid the uncertainty of significant potential damages and penalties that may be awarded in litigation proceedings. Settlements may require companies to enter into corporate integrity agreements with the government, which may impose substantial costs on companies to ensure compliance. Pharmaceutical and other healthcare companies also are subject to other federal false claims laws, including, among others, federal criminal healthcare fraud and false statement statutes that extend to non-government health benefit programs.

The federal Physician Payments Sunshine Act, implemented as the Open Payments Program, requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS, information related to payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, applicable manufacturers also will be required to report information regarding payments and transfers of value provided during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry, in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal healthcare Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation.

State law equivalents 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; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state and local laws that restrict certain marketing-related activities and require pharmaceutical companies to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; state laws that require the reporting of information related to drug pricing or laws that restrict the ability of manufacturers to offer co-pay support to patients for certain prescription drugs; and state and local laws requiring the registration of pharmaceutical sales representatives.

Violations of any of the laws described above or any other governmental regulations are punishable by significant civil, criminal and administrative penalties, imprisonment of individuals, damages, fines, government-imposed remediation programs and exclusion from government-funded healthcare programs, such as Medicare and Medicaid. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

Coverage and Reimbursement

Sales of pharmaceutical products depend significantly on the availability of third-party coverage and reimbursement. Third-party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. 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 studies to demonstrate the cost-effectiveness of our products and the product candidates that we develop may not ultimately 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.

In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost effectiveness of a particular drug candidate to currently available therapies. For example, the EU provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU member states may approve a

specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross border imports from low priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that 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 on a timely basis, or at all, or is available only to limited levels, we may not be able to successfully commercialize any product candidate that we successfully develop.

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.

For example, the Patient Protection and Affordable Care Act has substantially changed the way healthcare is financed by both governmental and private insurers. The Affordable Care Act and uncertainty regarding various constitutional and other legal challenges to the Act, will likely continue to significantly impact the U.S. pharmaceutical industry. Additionally, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several 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, review the differences between domestic and international pricing for drug products and reform government program reimbursement methodologies for drug products.

Reporting and Other Obligations Under the Medicaid Drug Rebate Program and Other Federal Programs

We participate in and have certain price reporting obligations to the Medicaid Drug Rebate Program. Under the Medicaid Drug Rebate Program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being available for our drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data we are required to report on a monthly and quarterly basis to CMS, the federal agency that administers the Medicaid Drug Rebate Program. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the United States in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions. Our failure to comply with these price reporting and rebate payment obligations could negatively impact our financial results, as described in the risk factor entitled "*If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs that we participate in, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, and results of operations*" in the Risk Factors section of this Annual Report.

We participate in the Medicaid Drug Rebate program and, as a result, federal law requires us to also participate in the 340B drug pricing program. The 340B program, which is administered by the Health Resources and Services Administration (HRSA), requires us to agree to charge statutorily-defined covered entities no more than the 340B "ceiling price" for our covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The Affordable Care Act expanded the list of covered entities to include certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, but exempts "orphan drugs" from the ceiling price requirements for these covered entities. The 340B ceiling price is calculated using a statutory formula based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate program, and in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. Any additional future changes to the definition of average manufacturer price and the

Medicaid rebate amount under the Affordable Care Act or other legislation or regulation could lower our 340B ceiling price calculations and negatively impact our results of operations.

HRSA issued a final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities, which became effective on January 1, 2019. It is currently unclear how HRSA will apply its enforcement authority under the new regulation. HRSA also has implemented a reporting requirement pursuant to which we are required to report the 340B ceiling prices for our drugs to HRSA every quarter. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting.

Federal law also requires that companies participating in the Medicaid Drug Rebate program report average sales price information each quarter to CMS for certain categories of drugs that are paid under the Medicare Part B program. Manufacturers calculate the average sales price based on a statutorily defined formula as well as regulations and interpretations of the statute by CMS. CMS uses these submissions to determine payment rates for drugs under Medicare Part B.

In order to be eligible to have our products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies and grantees, we also are required to participate in the U.S. Department of Veterans Affairs (VA), Federal Supply Schedule (FSS), pricing program. As part of this program, we are obligated to make our products available for procurement on an FSS contract under which we must comply with standard government terms and conditions and charge a price that is no higher than the statutory Federal Ceiling Price (FCP), to four federal agencies (VA, U.S. Department of Defense (DOD), Public Health Service, and U.S. Coast Guard).

The FCP is based on the Non-Federal Average Manufacturer Price (Non-FAMP), which we are required to calculate and report to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to significant civil monetary penalties for each item of false information. The FSS pricing and contracting obligations also contain extensive disclosure and certification requirements. For additional information regarding obligations under federal health care programs, refer to the risk factor entitled "*If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs that we participate in, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, and results of operations*" in the Risk Factors section of this Annual Report.

Foreign healthcare regulation

The regulations that govern marketing approvals, pricing and reimbursement for new therapeutic products vary widely from country to country. Some countries, including many 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 some 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 Andexxa. To the extent that comparators are available at lower prices than our anticipated pricing for Andexxa, the pricing and reimbursement level of our products in the EU and other foreign markets 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.

Clinical Development, Marketing Approvals and Commercialization of Prescription Drug Products

The FDA and comparable regulatory agencies impose substantial requirements upon the clinical development, manufacture and marketing of pharmaceutical products. Numerous agencies 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 regulatory authorities before product candidates may be marketed generally involves:

- nonclinical laboratory and animal testing of the product;
- submission of an investigational new drug application ("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 investigational drug for its intended use;

- pre-approval inspection of manufacturing facilities and selected clinical investigators for their compliance with manufacturing and clinical practice standards; and
- Approval of a marketing application prior to commercial marketing for specific indications.

These steps require substantial time, effort and financial resources. 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 patients with a specified disease or condition to provide data regarding preliminary efficacy, optimal dosages and dosing schedule and expanded evidence of safety. Multiple Phase 2 clinical trials may be conducted.
- Phase 3 - Clinical trials are undertaken in larger patient populations to further evaluate dose, 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 regulatory authorities may require, or companies may pursue, additional clinical trials after a product is approved. The results of post-marketing studies can confirm the effectiveness of a product candidate and can provide important safety information gathered in routine medical practice. Their failure to do so can result in adverse consequences for the product and the company.

In addition, 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 in accordance with regulatory manufacturing requirements. The manufacturing process must be capable of consistently producing quality batches and, among other things, the sponsor must also develop methods for testing the identity, strength, quality and purity of the final product. Appropriate packaging must be selected and tested and stability studies must be conducted to establish an appropriate shelf life for the drug.

Under EU regulatory systems, marketing authorization applications may be submitted under a centralized or decentralized procedure. The centralized procedure, which is compulsory for medicines produced by certain biotechnological processes, orphan medicinal products and certain other innovative medical products and is optional for certain other medicinal products, provides for the grant of a single marketing authorization that is valid for all EU member states. For drugs without approval in a EU member state, the decentralized procedure provides for assessment of a marketing application by one-member state, known as the reference member state, and review and possible approval of that assessment by one or more other, or concerned, member states. Under this procedure, an applicant submits an application and related materials to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of related materials. Each concerned member state must decide whether to approve the assessment report and related materials. The decentralized procedure must be completed within 210 days, excluding potential clock-stops, during which the applicant can respond to questions. If a member state cannot approve the assessment report and related materials on grounds of potential serious risk to public health, the disputed points may be referred to the EC, whose decision is binding on all member states. It is also possible to apply for a marketing authorization in one EU member state only, which could thereafter serve as a reference medicinal product for obtaining marketing authorization in one or more other EU Member States through a mutual recognition procedure.

Post-approval requirements and enforcement

Any products manufactured or distributed by us are subject to continuing regulation, including record-keeping requirements and reporting of adverse experiences. Our contracted third-party drug and biologic manufacturers and their subcontractors are required to register their establishments with the regulatory authorities and certain state agencies, and are subject to periodic unannounced inspections by them, which impose certain procedural and documentation requirements upon us and our third-party contract manufacturers. We cannot be certain that we or our present or future suppliers will be able to comply with regulatory manufacturing regulations and other regulatory requirements. If our suppliers are not able to comply with these requirements, the regulatory authorities may halt our manufacturing or clinical trials, require us to recall a product from distribution, or withdraw approval of the marketing application.

Andexxa was granted an Accelerated Approval by the FDA with a requirement for a post-marketing study to verify and describe Andexxa's clinical benefit via an open-label, randomized, controlled trial of Andexxa in acute intracranial hemorrhage in patients receiving oral Factor Xa inhibitors. In the EU, marketing authorization was granted for Ondexxya in 2019, subject to several post-approval commitments, including an obligation to submit a final clinical study report from the randomized controlled trial of Ondexxya and an obligation to provide some additional pharmacokinetic data.

Discovery of previously unknown problems with a product or clinical practices associated with the product through adverse event monitoring and reporting or otherwise, or the failure to comply with applicable FDA or foreign regulatory requirements, can have negative consequences, including adverse publicity, administrative enforcement, warning or untitled letters from the FDA or foreign regulators, mandated corrective advertising or communications with doctors, and civil penalties or criminal prosecution, among others. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

The FDA closely regulates the marketing and promotion of drugs, and a company's failure to comply with FDA requirements may 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.

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, False Claims Act actions, including "qui tam" actions brought by individual whistleblowers in the name of the government, refusal to allow us to enter into supply contracts, including government contracts, administrative actions, or integrity oversight and reporting obligations. Separately, FDA has authority to regulate the manufacturing of drug products, and failure to comply with good manufacturing practices can result in total or partial suspension of production, enforcement actions including import alerts, and suspension of regulatory review of a pending application.

Research and Development

We invested $124.6 million, $216.2 million and $203.7 million in research and development during the years ended December 31, 2019, 2018 and 2017, respectively.

Employees

As of December 31, 2019, we had 408 full-time employees. Our employees are not represented by labor unions or covered by collective bargaining agreements. We consider our employee relations to be good.

Legal proceedings

On January 16, 2020, a stockholder filed a putative class action against the Company and certain officers (the "Defendants") in the U.S. District Court for the Northern District of California, captioned *Hayden v. Portola Pharmaceuticals, Inc., et al.,* No. 3:20-cv-00367-VC (N.D. Cal.). On February 7, 2020, another stockholder filed a related putative class action against Defendants, captioned *McCutcheon v. Portola Pharmaceuticals, Inc., et al.*, No. 3:20-cv-00949 (N.D. Cal.).

The stockholder plaintiffs allege that the Defendants violated the antifraud provisions of the Securities Exchange Act by making misrepresentations and omissions in public disclosures concerning the Company's sales of andexanet alfa, marketed as Andexxa in the United States and Ondexxya in Europe, between May 8, 2019 and January 9, 2020. Specifically, plaintiffs allege that the Defendants made materially false and/or misleading statements about the demand for Andexxa, and usage of Andexxa by hospitals and healthcare organizations. Plaintiffs also allege that the Defendants made materially false and/or misleading statements about the Company's accounting for its reserve for returns, and that the Defendants failed to disclose that the Company was shifting from a short-dated version of Andexxa to a longer-dated version, impacting the reserve for returns and impacting revenue for the Company. The Plaintiffs contend that the alleged fraud was revealed on January 9, 2020, when the Company announced its preliminary unaudited financial results for the fourth quarter of 2019. A lead plaintiff has not yet been appointed, and the Company has not yet responded to the complaints.

The plaintiffs seek to recover unspecified monetary relief, interest, and attorneys' fees and costs. Given the early stage of these proceedings, we cannot presently predict the likelihood of obtaining dismissal of the case, nor can we estimate the possible loss or range of loss at this time.

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. 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 or connected to it 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 Consolidated Financial Statements and related Notes.

1) RISKS RELATED TO OUR FINANCIAL CONDITION AND NEED FOR ADDITIONAL CAPITAL

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 and the EC of our products and the short period of historical sales data, our product sales will be difficult to predict from period to period and as a result, you should not rely on sales results in any period as being indicative of future performance and sales 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, including:

- the level of demand and market acceptance;
- the results of our clinical trials;
- our ability to obtain and maintain desired regulatory approvals in the United States, EU and other foreign jurisdictions;
- 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;
- trends and developments in the pricing of prescription drugs in the United States and abroad, especially in the EU;
- 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;
- actual and estimated product returns;
- the timing, cost and level of investment in our marketing efforts to support sales;
- the timing, cost and level of investment in our medical affairs field teams to initiate relevant disease state education;
- 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;

- the timing and amount of non-cash items such as stock compensation expenses, reserves, cost of goods sold and non-recurring charges such as inventory write-offs;
- our ability to control expenses;
- costs, expenses and damages or fines arising from litigation or government investigations;
- the filing, maintenance, prosecution, defense and enforcement of patent claims and other intellectual property rights; and
- expenditures that we will or may incur to acquire or develop additional product candidates and technologies.

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 securities 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 have incurred significant operating losses, and expect to incur substantial losses in the near term as we continue to develop and commercialize our products and product candidates.

We are a commercial biopharmaceutical company. We launched our two commercial products in 2018 and continue to incur significant expenses related to commercialization, our ongoing and planned future clinical studies, research and development activities, and selling, general and administrative activities. As of December 31, 2019, we had an accumulated deficit of approximately $1.8 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, a term loan, 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 product commercialization, research and development, including manufacturing and clinical studies. We anticipate that we will continue to incur substantial expenses as we:

- establish, maintain and scale-up manufacturing capabilities and a sales, marketing and distribution infrastructure to commercialize our products in the United States and abroad;
- initiate or continue clinical studies, including a post-marketing randomized controlled trial of Andexxa;
- continue the research and development of our product candidates;
- seek to discover or in-license additional product candidates; and
- enhance operational, compliance, financial, quality and information management systems.

To be profitable in the future, we must succeed in commercializing our products and developing and commercializing other products with significant market potential. This will require us to be successful in a range of activities, including manufacturing, marketing and selling our products and any other products for which we may obtain regulatory approval, obtaining additional regulatory approvals and successfully completing additional clinical studies. 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.

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, reduce future profitability or require us to relinquish rights to our product candidates and technologies.

We will continue to require substantial funds to support commercial operations and pursue further research and development efforts. Our financing requirements will depend on many factors, some of which are beyond our control, including the following:

- product sales of Andexxa and Ondexxya, and if approved for commercial marketing, our product candidates;
- the costs of commercialization activities, including product sales, marketing, manufacturing and distribution and general corporate and commercial infrastructure;
- the scope and timing of our entry into additional foreign markets and establishment of commercial infrastructure;
- the costs and timing of international expansion;
- the timing of, and costs involved in, seeking and obtaining and maintaining approvals from the FDA, EC 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 and our repayment obligations may reduce future financial performance. 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.

Our obligations under our credit facility are secured by substantially all of our assets, so if we default on those obligations, the lenders could foreclose on our assets. As a result of these security interests, such assets would only be available to satisfy claims of our general creditors or to holders of our equity securities if we were to become insolvent at a time when the value of such assets exceeded the amount of our indebtedness and other obligations. Additionally, our credit facility contains restrictions and limitations that could significantly affect our ability to operate our business.

Pursuant to the Credit Agreement by and among us, the guarantor and lenders ("Lenders") party thereto, and HCR Collateral Management, LLC, as Administrative Agent (as defined therein), dated February 28, 2019 (the "Credit Facility"), the Administrative Agent, in its capacity as Collateral Agent for the Lenders, has been granted a security interest in substantially all of our assets. As a result, if we default under our obligations to the Lenders, the Collateral Agent could foreclose on its security interest and liquidate some or all of these assets, which would harm our business, financial condition and results of operations.

In the event of a default in connection with our bankruptcy, insolvency, liquidation, or reorganization, the Collateral Agent would have a prior right to substantially all of our assets to the exclusion of our general unsecured creditors. In that event, our assets would first be used to repay in full all indebtedness and other obligations under the Credit Facility, resulting in all or a portion of our assets being unavailable to satisfy the claims of any unsecured indebtedness. Only after satisfying the claims of the Lenders and any unsecured creditors would any amount be available for distribution to our equity holders. Events of default under the Credit Facility include, among other things, our failure to pay any amounts due under the Credit Facility or any of the

other loan documents, a breach of covenants under the Credit Facility, our insolvency, a material adverse effect occurring, the occurrence of certain defaults under certain other indebtedness for which we are obligated or certain final judgments against us.

The pledge of these assets and other restrictions imposed in the Credit Facility may limit our flexibility in raising capital for other purposes. Because substantially all of our assets are pledged to secure the Credit Facility obligations, our ability to incur additional secured indebtedness or to sell or dispose of assets to raise capital may be impaired, which could have an adverse effect on our financial flexibility.

If we are unable to comply with certain financial and operating restrictions in the Credit Facility, we may be limited in our business activities and access to credit or may default under the Credit Facility.

Provisions in the Credit Facility impose restrictions or require prior approval on our ability, and the ability of certain of our subsidiaries to, among other things:

- Incur additional debt;
- Make certain investments and acquisitions;
- Guarantee the indebtedness of others or our subsidiaries;
- Create liens or encumbrances;
- Engage in new lines of business;
- Enter into transactions with affiliates;
- Pay cash dividends and make distributions;
- Redeem or repurchase capital shares;
- Sell, lease or transfer certain parts of our business or property;
- Prepay other indebtedness; and
- Acquire new companies and merge or consolidate.

The Credit Facility also contains other customary covenants, including covenants that require us to maintain a minimum cash balance of up to $50 million, dependent on borrowings and levels of sales of Andexxa. We may not be able to comply with these covenants in the future. Our failure to comply with these covenants may result in the declaration of an event of default, which, if not cured or waived, may result in the acceleration of the maturity of indebtedness outstanding under the Credit Facility and would require us to pay all amounts outstanding. If the maturity of our indebtedness is accelerated, we may not have sufficient funds then available for repayment or we may not have the ability to borrow or obtain sufficient funds to replace the accelerated indebtedness on terms acceptable to us or at all. Our failure to repay our indebtedness would result in the Collateral Agent foreclosing on all or a portion of our assets and possibly force us to curtail or cease our operations.

2) RISKS RELATED TO COMMERCIAL AND MARKETING OPERATIONS AND THE DEVELOPMENT AND COMMERCIALIZATION OF OUR PRODUCTS AND PRODUCT CANDIDATES

Our ability to grow our company is critically dependent upon the commercial success of Andexxa

We anticipate that for the foreseeable future, our ability to generate revenue from operations to fund our business will depend substantially upon the commercial success of Andexxa in the United States and Ondexxya in the EU. If sales of Andexxa or Ondexxya fail to grow, decrease or remain flat, we may need to reduce our operating expenses, access other sources of cash or otherwise modify our business plans, which would likely have a material adverse impact on our business, financial condition and results of operations.

Our products may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

Our success depends heavily on the launch and commercialization of our products. The commercial success of our products 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 products;
- interpretations of the results of our clinical trials and availability of sufficient data demonstrating safety and efficacy of our products;
- the willingness of physicians and healthcare organizations to change their current treatment practices;
- the willingness of hospitals and hospital systems to include our products 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. If we are not successful in commercializing Andexxa, our future product revenue will suffer, we may incur significant additional losses and our business will be materially harmed.

We obtained regulatory approval of Andexxa in the United States through an Accelerated Approval process and in the EU under a conditional approval. The data supporting these approvals may limit our ability to market Andexxa. Continued approval may also be contingent upon the results of ongoing patient studies to demonstrate an improvement in hemostasis.

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 biomarker endpoint that is considered reasonably likely to predict clinical benefit rather than a clinical endpoint such as survival or irreversible morbidity. Our approval of Andexxa was supported by data from two Phase 3 ANNEXA studies (ANNEXA-R and ANNEXA-A), which evaluated the safety and efficacy of Andexxa in reversing the anticoagulant activity of the Factor Xa inhibitors rivaroxaban and apixaban in healthy volunteers, and interim patient data from our ongoing ANNEXA-4 single-arm, open-label study in patients on a Factor Xa inhibitor experiencing a life threatening or uncontrolled bleeding episode. However, these studies have inherent limitations as compared with a randomized controlled trial. For example, we do not have comparator arm data, including clinical head to head data against the treatment options which were used by hospitals prior to the availability of Andexxa, which we believe continue to be widely used, including off-label use of 4F-PCCs and other coagulation factors. In addition, the efficacy statements in our product label are limited as the result of our single-arm, open-label study. These limitations have a significant impact on our ability to market Andexxa and establish it as the standard of care, as pharmaceutical companies are generally prohibited from making product claims not set forth in their product labels. These limitations can also increase resistance to utilization by hospital formulary committees and may also negatively impact government pricing discussions in the EU and abroad.

In addition, as a condition to approval, the FDA and EMA have required us to conduct a post-marketing randomized controlled trial of Andexxa. This trial will randomize patients to receive either Andexxa or the type of care the enrolling institution would provide in the absence of Andexxa. This study has been opened to enrollment and we expect it to be reported in 2023. We expect the practical implementation and ethical considerations of a randomized controlled trial for Andexxa to present challenges, and we cannot be sure that we will be able to successfully conduct and enroll such a trial in a manner satisfactory, or within the time period required by the FDA and EMA. Also, the data may be inconclusive or difficult to interpret since the control arm will consist of the standard of care among many hospitals and may vary from site to site. In addition to the post-marketing study, the EMA has also requested the final study reports for the ANNEXA-4 study and additional pharmacokinetic data. If the randomized controlled trial is not successful, the FDA and/or EMA could modify or withdraw our marketing approval for Andexxa. Further, even if the randomized controlled trial results support full approvals by the FDA and EMA, the data may still be subject to varying interpretations by the medical community and payors, including government payors in the EU and abroad.

Approval of Andexxa is limited to patients treated with rivaroxaban and apixaban, when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding, and additional clinical studies and regulatory applications will be required to expand Andexxa indications. We can provide no assurances that such clinical studies or regulatory applications will be successful.

We are developing Andexxa as a universal antidote for patients receiving a Factor Xa inhibitor when reversal of anticoagulation is needed, such as in life-threatening or uncontrolled bleeding or for emergency surgery/urgent procedures. Our approval of

Andexxa is currently limited to patients treated with rivaroxaban and apixaban, when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding. Our studies have not yet produced clinical data regarding patients requiring emergency surgery or urgent procedures and we do not anticipate obtaining this indication without clinical data. We expect that we will also be required to provide additional clinical data to support addition to our label of other Factor Xa inhibitors, including edoxaban and enoxaparin. Additional clinical studies will require additional time and expense and may not prove successful. Limitations in our label for Andexxa will reduce the number of patients for whom Andexxa is indicated and could reduce the size of the anticipated market and our financial prospects. In addition, our label for Andexxa includes a boxed warning that treatment with Andexxa has been associated with serious and life-threatening adverse events, thromboembolic events, ischemic events, cardiac arrest and sudden deaths. This boxed warning may adversely impact market acceptance and the commercial potential of Andexxa. There can be no assurance that further clinical experience will provide a basis to remove this boxed warning.

If serious adverse side effects are identified with respect to any of our product candidates or either of our approved products, 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.

While no serious adverse side effects have been observed in our completed healthy subject studies with Andexxa, adverse effects have been observed in our ANNEXA-4 study in bleeding patients. Additionally, there is a risk that adverse events may be reported in our post-marketing randomized controlled trial of Andexxa, additional clinical experience or repeat doses that are determined to have been caused by Andexxa. 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 Andexxa or antibodies to Factor X or Xa 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, in our ANNEXA-4 patient trial, reversing the anticoagulant activity of Factor Xa inhibitors in patients with life threatening or uncontrolled bleeding who have underlying medical conditions requiring anticoagulation has been associated with thromboembolic events, ischemic events, cardiac arrest and sudden deaths, and the FDA has included a boxed warning in the Andexxa label to this effect.

Bevyxxa, like all currently marketed inhibitors of Factor Xa, carries some risk of life-threatening bleeding. In addition, patients taking Bevyxxa in our clinical 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.

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.

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 our products or our other future products.

We are still in the early stages of developing our global sales and marketing infrastructure. To achieve commercial success for our products 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 expand our hospital-based sales force in additional markets and work with partners in other parts of the world to commercialize our products globally. There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services.

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 our products and developing our current product candidates, and we 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.

While there are no therapies other than Andexxa approved specifically as antidotes for Factor Xa inhibitors, we are aware of at least one drug candidate that has been studied in early stage clinical trials as a potential antidote to Factor Xa inhibitors. In addition, Andexxa may compete with the off-label use of other treatments designed to enhance coagulation, such as Fresh Frozen Plasma, 4-factor Prothrombin Complex Concentrates, recombinant activated Factor VII or whole blood. Although there is no approved indication for these products in patients taking Factor Xa inhibitors, physicians may choose to use them because of familiarity, cost or other reasons. In addition, we are aware that several companies have conducted preclinical research on compounds intended to be antidotes for Factor Xa inhibitors.

For Bevyxxa, Bayer and Janssen recently received FDA approval for use of Xarelto® for the prevention of VTE in hospitalized acutely ill medical patients at risk for thromboembolic complications who are not at high risk of bleeding during hospitalization and continued after discharge for a total recommended duration of 31 to 39 days. This approval generally will allow Xarelto to compete with Bevyxxa in a similar indication. Bayer and Janssen have significantly greater resources to market Xarelto in this indication and prescribers and payors will likely have significantly more experience with Xarelto than Bevyxxa. In addition, 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. 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 of this and other factors, we have faced 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.

There are also a number of products in clinical development for hematologic cancer, ophthalmological diseases, allergic rhinitis, allergic asthma and other inflammatory or autoimmune 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.

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 future 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.

Failure to obtain regulatory approvals in foreign jurisdictions will prevent us from marketing our products internationally. Following the negative decision by the European Commission, we will not obtain marketing approval to commercialize Bevyxxa in the EU at this time, or potentially ever.

In order to market Bevyxxa or our future products in the European Economic Area ("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 ("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.

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. In addition, 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 March 2018, the CHMP issued a negative opinion, recommending that the EMA reject the marketing application for Bevyxxa in the EU. We requested a re-examination of the initial opinion and in July 2018, we received a negative re-examination opinion from the CHMP. The European Commission adopted the CHMP decision in September 2018. Failure to obtain marketing approval of Bevyxxa in the EU will reduce the commercial potential of Bevyxxa and could also have a negative impact on our efforts to commercialize and obtain market acceptance for Bevyxxa in the U.S. market.

3) RISKS RELATED TO OUR RELIANCE ON THIRD PARTIES

We rely on single source third-party contract manufacturing organizations to manufacture and supply Andexxa, 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 Andexxa, Bevyxxa and our product candidates. For example, we have contracted with Lonza to manufacture Andexxa bulk drug substance and Baxter International, Inc. to manufacture drug product. We also rely on third parties to manufacture drug product to supply Bevyxxa. In addition, we rely or expect to rely on other third party providers for raw materials, packaging, labeling and supply chain warehousing and 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 disrupt, delay the development of, and impair our ability to commercialize, our product candidates.

Lead times for our manufacturing and contractual requirements of our third-party manufacturers require us to estimate product demand in advance. If our forecasts are not accurate, we may experience shortfalls or surplus of product. If we do not manufacture enough product, we may experience stock-outs and interruption of supply of our products. If we manufacture a surplus of product, we may experience spoilage from product expiration and incur manufacturing expenses which were not required and from which we may receive no benefit. We have fixed manufacturing commitments with our third-party manufacturers which are on a “take-or-pay” basis which requires us to pay for manufacturing costs even if we do not need the capacity forecasted at the time we entered into such commitments. The financial impact of either stock-outs or a product surplus could be significant with respect to financial commitments and the effect on our financial performance.

The manufacture of pharmaceutical products in compliance with U.S. and foreign regulatory manufacturing requirements, 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 regulatory 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. Interruptions in commercial supply could adversely affect our ability to supply the market and could have a materially adverse effect on our product revenue and growth prospects.

All manufacturers of our product candidates must comply with regulatory manufacturing requirements enforced by the U.S. and foreign regulatory authorities through their facilities inspection programs. 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 manufacturing 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, the ability to import product into countries, 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 regulatory 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 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 ("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 regulatory authorities require 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 develop our products and 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 may enter into collaborations that place the development and commercialization of our products and 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 both inside and outside the United States, or for other purposes. For example, we have out-licensed development and commercial rights to Andexxa 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 pursue pricing which is not consistent with our global strategies;
- 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 may 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.

4) RISKS RELATED TO THE OPERATION OF OUR BUSINESS

Our future success depends on our ability to retain our key executives, and if we are not able to retain these members of our management, or retain or recruit additional management and other key personnel, our business will suffer.

Recruiting and retaining leadership and other key personnel is critical to our success. We are highly dependent on our President and Chief Executive Officer and the other principal members of our executive and leadership teams. We may not be able to attract and retain management and other key personnel in the future, due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the San Francisco Bay Area. We also 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 personnel from universities, research institutions and technology companies. In addition, we rely on consultants and advisors to assist us in formulating our business strategies. Our consultants and advisors may also perform services for companies other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

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 continue to expand our development, regulatory and sales and marketing capabilities in the United States and Europe, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience continued growth in the number of our employees and the scope of our operations, in the United States and Europe, 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, 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 Securities and Exchange Commission ("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 of the Sarbanes-Oxley Act, 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 and claims against us could cause us to incur substantial liabilities and could limit product sales.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical studies, and the commercial manufacturing, distribution and sale of Andexxa and Bevyxxa. For example, the manufacturers of currently marketed Factor Xa inhibitors and other manufacturers of anticoagulants have faced substantial litigation due to certain alleged bleeding risks.

In addition, in our ANNEXA-4 patient trial, reversing the anticoagulant activity of Factor Xa inhibitors in patients with underlying medical conditions requiring anticoagulation has been associated with thromboembolic events, ischemic events, cardiac arrest and sudden deaths, and the FDA has included a boxed warning in the Andexxa label to this effect. If we receive claims that Andexxa, Bevyxxa or our product candidates or products caused injuries, we could incur substantial liabilities if we are not able to successfully defend ourselves against these claims. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for our products;
- 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 additional products that we may develop.

We may not have sufficient insurance coverage for future product liability claims. We may not be able to obtain insurance in amounts or scope sufficient to provide us with adequate coverage against all potential liabilities. Any product liability claims brought against us, with or without merit, could increase our product liability insurance rates or prevent us from securing continuing coverage, harm our reputation in the industry, significantly increase our expenses, and reduce product sales. Product liability claims in excess of our insurance coverage would be paid out of cash reserves, harming our financial condition and operating results.

We may expend our limited resources to pursue a particular product, product candidate or indication and fail to capitalize on products, 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 sales, marketing and research programs and products and product candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other products or 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 or product candidate, we may relinquish valuable rights 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.

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 Andexxa and Bevyxxa development and commercialization, we are currently utilizing certain suppliers outside of the United States, which subjects us to certain of the above risks.

We may be subject to information technology system failures, network disruptions and breaches in data security.

We are increasingly dependent upon information technology systems and infrastructure to conduct critical operations and generally operate our business, which includes using information technology systems to process, transmit and store electronic information in our day-to-day operations, including customer, employee and company data. The size and complexity of our computer systems make them potentially vulnerable to breakdown, malicious intrusion and random attack. We also store certain information with third parties. Our information systems and those of our third-party vendors are subjected to computer viruses or other malicious codes, unauthorized access attempts, and cyber- or phishing-attacks and also are vulnerable to an increasing threat of continually evolving cybersecurity risks and external hazards. Disruption, degradation, or manipulation of these systems and infrastructure through intentional or accidental means could impact key business processes. Cyber-attacks against the Company's systems and infrastructure could result in exposure of confidential information, the modification of critical data, and/or the failure of critical operations. Likewise, improper or inadvertent employee behavior, including data privacy breaches by employees and others with permitted access to our systems, may pose a risk that sensitive data may be exposed to unauthorized persons or to the public. Any such breach could compromise our networks, and the information stored therein could be accessed, publicly disclosed, lost or stolen. Such attacks could result in our intellectual property and other confidential information being lost or stolen, disruption of our operations, and other negative consequences, such as increased costs for security measures or remediation costs, and diversion of management attention. 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. In addition, with planned operations in EU, we will need to comply with the General Data Protection Regulation ("GDPR") provisions relating to personal data, use of third party processors, data breach notifications and transfer of personal data out of the EU to the United States. The GDPR imposes large penalties for noncompliance and has the potential to increase our responsibility and liability in relation of personal data that we process, including in clinical trials, and we are required to put in place and maintain additional mechanisms to ensure compliance with the GDPR, including increased company and vendor technology and data management measures and cybersecurity investments.

5) RISKS RELATED TO INTELLECTUAL PROPERTY

If we fail to comply with our obligations in our intellectual property licenses from 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, and other early stage programs, 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 supply, support, 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 or pursue other remedies, in which event we may not be able to develop and market any product that is covered by these agreements or be liable for damages. Termination of 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 our current or future licensors, licensees, or collaboration partners fail to establish or maintain such patents and other intellectual property rights, or lose rights to those patents and other intellectual property rights, such rights 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 that protect our technology or products or that 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, or vice versa. Further, we may not be aware of all third-party intellectual property rights potentially relating to our product candidates. 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.

The Leahy-Smith America Invents Act, or the America Invents Act ("AIA") implemented significant changes to United States patent law. The AIA could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We have been and may again become involved in opposition, derivation, reexamination, *inter partes review*, post-grant review, or other proceedings challenging our patent rights or the patent rights of our licensors, 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 to which we have an exclusive license. The European Patent Office decided in favor of revoking the European patent. Portola has appealed this revocation. Should any of these proceedings or appeals 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, or by successfully seeking to narrow or invalidate our patents or render them unenforceable. The issuance of a patent is not conclusive as to its inventorship 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 substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us, and may result in loss of exclusivity or freedom to operate or 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.

If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our owned or licensed U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act. Similar extensions as compensation for patent term lost during regulatory review processes are also available in certain foreign countries and territories, such as in Europe under a Supplementary Patent Certificate. However, we may not be granted an extension in the United States and/or foreign countries and territories because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. For example, we have applied for patent term extensions at the U.S. Patent and Trademark Office (USPTO) within the applicable deadline after receiving approval for Andexxa and Bevyxxa, but have not yet received a final determination. If we are unable to obtain patent term extension or the term of any such extension is shorter than what we request or we fail to choose the most optimal patents to extend, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations and prospects could be materially harmed.

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

Competitors or other parties 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. 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.

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 products and 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 third party intellectual property rights with respect to our products, product candidates, 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. Any litigation involving defense against claims of infringement, misappropriation or other violation of proprietary or intellectual property rights, regardless of the merit of such claims, would involve substantial litigation expense and would be a substantial diversion of management time. If we are found to infringe a third-party's intellectual property rights, we could be required to pay substantial damages, including treble damages and attorneys' fees if we are found to be willfully infringing a third party's patents. We may also be required to indemnify parties with whom we have contractual relationships against such claims. If a patent infringement suit were brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. We also 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. A finding of infringement could prevent us from commercializing our products or 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.

6) 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 are not permitted to market our product candidates in the United States until we receive approval from the FDA for the indications for which we seek approval. Obtaining approval is 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.

In order to receive regulatory approvals, we must demonstrate with substantial evidence from well-controlled clinical studies, and to the satisfaction of the FDA and other regulatory authorities abroad, that our 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, even indications for which we have previously received approval.

The regulatory approval process is expensive and usually takes several years. The regulatory authorities also have 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 desired regulatory approvals, our business and results of operations will be materially and adversely harmed.

Unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives in the United States, Europe and other foreign jurisdictions could harm our business.

Sales of pharmaceutical products depend significantly on the availability of third-party coverage and reimbursement. Third-party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. 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 studies to demonstrate the cost-effectiveness of our products and the product candidates that we develop may not ultimately 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.

There is increasing pressure on biotechnology companies to reduce healthcare costs. In the United States, 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.

In some foreign markets, including some 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 Andexxa. To the extent that comparators are available at lower prices than our anticipated pricing for Andexxa, 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. If we do not obtain pricing approval or if we obtain unfavorable pricing decisions in one or more countries, we may not be able to commercially launch our product in that market. This could, for example, affect our ability to successfully commercialize our product in important European markets such as Germany and the United Kingdom.

Adverse pricing limitations may hinder our ability to recoup our investment in Andexxa, Bevyxxa or one or more product candidates. Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and 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 cover and establish reimbursement levels. For example, in October 2018, CMS granted reimbursement for the NTAP to Andexxa, and in August 2019, CMS announced it would increase the reimbursement amount for the NTAP to Andexxa from 50% to 65% of the wholesale acquisition cost of the standard dose, effective October 1, 2019. While NTAP is expected to remain in effect for a period of two to three years, is no assurance, however, that this reimbursement will continue in the future at the same rate, if at all.

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 our existing 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 our products 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, legislative proposals have been introduced by members of Congress to overhaul provisions of the Patient Protection and Affordable Care Act, to allow commercial-level re-importation of prescription medications from Canada

or other countries and to enable Medicare to negotiate drug prices with biopharmaceutical manufacturers. Congressional focus on drug pricing has increased in recent years.

Certain provisions of the Affordable Care Act have been subject to judicial challenges as well as efforts to repeal or replace them or to alter their interpretation or implementation. 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, bills affecting the implementation of the Affordable Care Act have been signed into law. For example, the Tax Cuts and Jobs Act of 2017 ("Tax Act") included a provision which repealed, 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". The Bipartisan Budget Act of 2018 ("BBA"), among other things, amended 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". In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the Affordable Care Act's mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. On December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. It is unclear how this decision, future decisions, subsequent appeals, and other efforts to repeal and replace the Affordable Care Act will impact the Affordable Care Act and 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, on average, 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 2029 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, 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 administration's budget proposal for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. Further, the Presidential administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. The Department of Health and Human Services, or HHS, has solicited feedback on some of these measures and has implemented others under its existing authority. While some of these and other proposed measures may require additional authorization to become effective, Congress and the Presidential 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.

Our relationships with customers and third-party payors are subject to applicable anti-kickback, fraud and abuse, transparency and other healthcare laws and regulations. If we fail to comply with federal and state health care laws and

regulations, we could face substantial penalties, including criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings, 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. Our arrangements and interactions with health care professionals, third-party payors, pharmacies and distributors, among others, are subject to laws and regulations addressing health care 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, as well as by healthcare regulators in the EU and other foreign jurisdictions where we may market our products. 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, in whole or in part, under federal healthcare programs, such as the Medicare and Medicaid programs;
- the federal civil False Claims Act, which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, false or fraudulent claims for payment of government funds, or knowingly making, using, or causing to be made or used a false record or statement material to an obligation to pay money to the government, or knowingly concealing or knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government;
- the federal Physician Payments Sunshine Act, implemented as the Open Payments Program, requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the Centers for Medicare & Medicaid Services (CMS), information related to payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors) and teaching hospitals (and beginning in 2022 report payments and other transfers of value provided during the previous year to certain other practitioners), as well as ownership and investment interests held by physicians and their immediate family members;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry, in connection with the delivery of or payment for healthcare benefits, items or services. ;
- 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;
- state law equivalents 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; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state and local laws that restrict certain marketing-related activities and require pharmaceutical companies to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; state laws that require the reporting of information related to drug pricing or laws that restrict the ability of manufacturers to offer co-pay support to patients for certain prescription drugs; and state and local laws requiring the registration of pharmaceutical sales representatives; and
- EU member states' laws and the industry self-regulation codes of conduct governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices.

The number and complexity of both U.S. federal and state laws continue to increase, and are subject to evolving interpretation which can make compliance efforts more challenging. For example, the Bipartisan Budget Act of 2018 increased the criminal and civil penalties that can be imposed for violating certain federal health care laws, including the federal health care Anti-Kickback Statute. Enforcement agencies also continue to pursue novel theories of liability under these laws. In particular,

government agencies recently have increased regulatory scrutiny and enforcement activity with respect to manufacturer reimbursement support activities and patient support programs, including bringing criminal charges.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. 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 imprisonment, significant administrative, civil and criminal monetary penalties, damages, fines, 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, 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, and cause reputational harm. Moreover, achieving and sustaining compliance with applicable federal and state anti-fraud and abuse laws may prove costly. For a fuller discussion of the requirements of the anti-kickback, fraud and abuse, transparency and other healthcare laws and regulations applicable to our business, see Item 1, "Description of Business - Government Regulation" of this Annual Report.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other federal programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, and results of operations

We participate in, and have certain price reporting obligations to the Medicaid Drug Rebate Program. Under the Medicaid Drug Rebate Program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being available for our drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data we are required to report on a monthly and quarterly basis to the CMS, the federal agency that administers the Medicaid Drug Rebate Program. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the United States in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions. Our failure to comply with these price reporting and rebate payment obligations could negatively impact our financial results.

Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the 340B drug pricing program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B program, which is administered by the Health Resources and Services Administration (HRSA), requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The Affordable Care Act expanded the list of covered entities to include certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, but exempts "orphan drugs" from the ceiling price requirements for these covered entities. The 340B ceiling price is calculated using a statutory formula based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate program, and in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. Any additional future changes to the definition of average manufacturer price and the Medicaid rebate amount under the Affordable Care Act or other legislation or regulation could affect our 340B ceiling price calculations and negatively impact our results of operations.

HRSA issued a final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities, which became effective on January 1, 2019. It is currently unclear how HRSA will apply its enforcement authority under the new regulation. HRSA also has implemented a reporting requirement pursuant to which we are required to report the 340B ceiling prices for our drugs to HRSA every quarter. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting. We believe that Andexxa is used to a large extent in the inpatient setting and if we were required to provide 340B pricing in this setting it would likely have a significant negative impact on our operating results.

Because we participate in the Medicaid Drug Rebate program, federal law requires us to report average sales price information each quarter to CMS for certain categories of our drugs that are paid under the Medicare Part B program. Manufacturers calculate the average sales price based on a statutorily defined formula as well as regulations and interpretations of the statute by CMS. CMS uses these submissions to determine payment rates for drugs under Medicare Part B.

Pricing and rebate calculations vary among products and programs. The calculations are complex and are often subject to interpretation by us, governmental or regulatory agencies, and the courts. We could be held liable for errors associated with our submission of pricing data. In addition to retroactive Medicaid rebates and the potential for issuing 340B program refunds, if we are found to have knowingly submitted false average manufacturer price or best price information to the government, we may be liable for significant civil monetary penalties per item of false information. If we are found to have made a misrepresentation in the reporting of our average sales price, the Medicare statute provides for significant civil monetary penalties for each misrepresentation for each day in which the misrepresentation was applied. Civil monetary penalties can also be applied if we are found to have charged 340B covered entities more than the statutorily mandated ceiling price. Our failure to submit monthly/quarterly average manufacturer price and best price data on a timely basis could result in a significant civil monetary penalty per day for each day the information is late beyond the due date. Such failure also could be grounds for CMS to terminate our Medicaid drug rebate agreement, pursuant to which participate in the Medicaid Drug Rebate Program. In the event that CMS terminates our rebate agreement, no federal payments would be available under Medicaid or Medicare Part B for our covered outpatient drugs.

CMS and the Department of Health & Human Services Office of Inspector General have pursued manufacturers that were alleged to have failed to report these data to the government in a timely manner. Governmental agencies may also make changes in program interpretations, requirements or conditions of participation, some of which may have implications for amounts previously estimated or paid. We cannot assure you that our submissions will not be found to be incomplete or incorrect.

In order to be eligible to have our products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies and grantees, we also are required to participate in the U.S. Department of Veterans Affairs (VA), Federal Supply Schedule (FSS), pricing program. As part of this program, we are obligated to make our products available for procurement on an FSS contract under which we must comply with standard government terms and conditions and charge a price that is no higher than the statutory Federal Ceiling Price (FCP), to four federal agencies (VA, U.S. Department of Defense (DOD), Public Health Service, and U.S. Coast Guard). The FCP is based on the Non-Federal Average Manufacturer Price (Non-FAMP), which we would be required to calculate and report to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to significant civil monetary penalties for each item of false information. The FSS pricing and contracting obligations also contain extensive disclosure and certification requirements, with which we must comply.

We also participate in the Tricare Retail Pharmacy program, under which we are required to pay quarterly rebates on utilization of innovator products that are dispensed through the Tricare Retail Pharmacy network to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP. We are required to list our innovator products on a Tricare Agreement in order for them to be eligible for DOD formulary inclusion. If we overcharge the government in connection with our FSS contract or Tricare Agreement, whether due to a misstated FCP or otherwise, we would be required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges could result in allegations against us under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We are subject to privacy, security, and breach notification laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, fines, and diminished profits and future earnings.

We are subject to federal and state, and foreign laws and regulations governing data privacy and security of health information, and the collection, use, disclosure, and protection of health-related and other personal information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues that may affect our business, including recently enacted laws in jurisdictions where we operate. Numerous U.S. federal and state laws, including state security breach notification laws, state health information privacy laws, state genetic privacy laws, and federal and state consumer protection and privacy laws, (including, for example, Section 5 of the FTC Act, and the California Consumer Privacy Act ("CCPA")) govern the collection, use and disclosure of personal information. Compliance with these laws is difficult, constantly evolving, and time consuming. These laws may differ from each other in significant ways, thus complicating compliance efforts. Federal regulators, state attorneys general, and plaintiffs' attorneys have been and will likely continue to be active in this space. These laws include, but are not limited to:

- the EU general data privacy regulation ("GDPR"). The GDPR imposes strict obligations on the processing of personal data, including relating to the transfer of personal data from the European Economic Area to third countries such as the US. If we act in violation of the GDPR we may face significant penalties of up to 10,000,000 Euros or up to 2% of our total worldwide annual turnover for certain violations, or up to 20,000,000 Euros or up to 4% of our total worldwide annual turnover for more serious violations;

- Health Insurance Portability and Accountability Act of 1996 (“HIPAA”) and its implementing regulations also impose obligations on certain covered entity health care providers, health plans and health care clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. We may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA. Although we are not directly subject to HIPAA - other than with respect to providing certain employee benefits - we could potentially be subject to criminal penalties if we, our affiliates, or our agents knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA;
- numerous federal and state laws and regulations that address privacy and data security, including the CCPA, state data breach notification laws, state health information and/or genetic privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act, or FTC Act), govern the collection, use, disclosure and protection of health-related and other personal information, many of which differ from each other in significant ways, thus complicating compliance efforts. Compliance with these laws is difficult, constantly evolving, and time consuming, and companies that do not comply with these laws may face civil penalties.

Failure to comply with such laws and regulations could result in government enforcement actions and create liability for us (including the imposition of significant penalties), private litigation and/or adverse publicity that could negatively affect our business. In addition, if we successfully commercialize our product candidates, we may obtain patient health information from healthcare providers who prescribe our products and research institutions we collaborate with, and they are subject to privacy and security requirements under HIPAA. Although we are not directly subject to HIPAA other than potentially with respect to providing certain employee benefits, we could potentially be subject to criminal penalties if we, our affiliates or our agents knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. In California, the CCPA took effect on January 1, 2020. The CCPA establishes certain requirements for data use and sharing transparency and creates new data privacy rights for consumers. Failure to comply could result in penalties, and individuals have a private right of action.

These laws and regulations are evolving and subject to interpretation, and may impose limitations on our activities or otherwise adversely affect our business. Any associated claims, inquiries, or investigations or any other government actions may lead to unfavorable outcomes including increased compliance costs, delays or impediments in the development of new products, negative publicity, increased operating costs, diversion of management time and attention, and remedies that harm our business, including fines or demands or orders that we modify or cease existing business practices.

The United Kingdom’s withdrawal from the EU may have a negative effect on our business, global economic conditions, and financial markets.

As of January 31, 2020, the United Kingdom is no longer an EU Member State. As a result of the United Kingdom’s vote to leave the EU, the EMA has relocated its headquarters from London to Amsterdam. Since a significant proportion of the regulatory framework in the United Kingdom is derived from EU directives and regulations, Brexit could materially impact the regulatory regime with respect to the approval of product candidates, disrupt the manufacture of our products and product candidates in the United Kingdom or the EU, disrupt the importation and export of active substances and other components of drug formulations, and disrupt the supply chain for clinical trial product and final authorized formulations. While negotiations continue regarding the future relation between the United Kingdom and the EU, the specific impact to the supervision, regulation and supply of medicines in the United Kingdom and Europe remain unclear. The cumulative effect of disruptions to the regulatory framework or supply chains may add considerably to the development lead time to, and expense of, marketing authorization and commercialization of products in the EU and/or the United Kingdom. In view of the uncertainty surrounding the Brexit implementation, we are unable to predict the effects of such disruption to the regulatory framework and supply chain in Europe.

Our products and marketing efforts are subject to extensive post-approval government regulation.

Once a drug receives marketing approval, numerous post-approval requirements apply. Among other things, the holder of an approved new drug application ("NDA") or biologics license application ("BLA") is subject to periodic and other monitoring and reporting obligations enforced by the FDA and other regulatory bodies, including obligations to monitor and report adverse events and instances of the failure of a product to meet the specifications in the approved application. Application holders must

also submit advertising and other promotional material to regulatory authorities and report on ongoing postmarketing clinical trials.

With respect to sales and marketing activities, advertising and promotional materials must comply with regulatory requirements in the United States and in other countries. Governments may scrutinize our promotional efforts or otherwise monitor our business closely. Industry-sponsored scientific and educational activities also must comply with FDA and other requirements. In the United States, the distribution of product samples to physicians must comply with the requirements of the U.S. Prescription Drug Marketing Act, and the Drug Supply Chain Security Act requires that we track distribution of Andexxa in commerce. Manufacturing facilities remain subject to FDA inspection and must continue to adhere to the FDA's pharmaceutical current good manufacturing practice requirements ("cGMPs"). Application holders must obtain FDA approval for product and manufacturing changes, depending on the nature of the change.

Depending on the circumstances, failure to meet post-approval 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, or refusal to allow us to enter into supply contracts, including government contracts. Even if we comply with FDA and other requirements, new information regarding the safety or effectiveness of a product could lead the FDA to modify or withdraw a product approval. Newly discovered or developed safety or effectiveness data may require changes to a drug's approved labeling and marketing, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures.

7) RISKS RELATED TO OWNERSHIP OF OUR COMMON STOCK

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

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

- the timing and amount of revenues generated from sale of our products or product candidates;
- our ability to meet the expectations of investors related to the commercialization of our products and product candidates;
- regulatory actions or decisions, including the timing and outcome of any potential future FDA or EMA decision, or other products or product candidates, including those of our competitors;
- inaccurate sales or cash forecasting of our products or product candidates;
- changes in laws or regulations;
- 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 products or product candidates;
- market conditions in the pharmaceutical and biotechnology sectors;
- changes in the structure of healthcare payment systems;
- 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. For example, 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. In addition, following our preliminary announcement of 2019 Andexxa revenues on January 9, 2020, a number of plaintiffs' firms have initiated legal action alleging certain violations of the U.S. federal securities laws; see Item 3 "Legal proceedings" in this

Annual Report on Form 10-K for additional information. Such litigation 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 and acceleration of vesting of equity awards. 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 our existing debt agreement preclude us from paying dividends and future debt agreements or other restrictive covenants could also preclude us from paying dividends in the future. 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 87,000 square feet of research and office space in South San Francisco, California under a lease that expires in March 2023. Thereafter, at our option, we may extend the term for an additional eight years to March 2031. We believe that our existing facilities are sufficient for our current needs for the foreseeable future.

ITEM 3. LEGAL PROCEEDINGS

On January 16, 2020, a stockholder filed a putative class action against the Company and certain officers (the "Defendants") in the U.S. District Court for the Northern District of California, captioned *Hayden v. Portola Pharmaceuticals, Inc., et al.,* No. 3:20-cv-00367-VC (N.D. Cal.). On February 7, 2020, another stockholder filed a related putative class action against Defendants, captioned *McCutcheon v. Portola Pharmaceuticals, Inc., et al.*, No. 3:20-cv-00949 (N.D. Cal.).

The stockholder plaintiffs allege that the Defendants violated the antifraud provisions of the Securities Exchange Act by making misrepresentations and omissions in public disclosures concerning the Company's sales of andexanet alfa, marketed as Andexxa in the United States and Ondexxya in Europe, between May 8, 2019 and January 9, 2020. Specifically, plaintiffs allege that the Defendants made materially false and/or misleading statements about the demand for Andexxa, and usage of Andexxa by hospitals and healthcare organizations. Plaintiffs also allege that the Defendants made materially false and/or misleading statements about the Company's accounting for its reserve for returns, and that the Defendants failed to disclose that the Company was shifting from a short-dated version of Andexxa to a longer-dated version, impacting the reserve for returns and impacting revenue for the Company. The Plaintiffs contend that the alleged fraud was revealed on January 9, 2020, when the Company announced its preliminary unaudited financial results for the fourth quarter of 2019. A lead plaintiff has not yet been appointed, and the Company has not yet responded to the complaints.

The plaintiffs seek to recover unspecified monetary relief, interest, and attorneys' fees and costs. Given the early stage of these proceedings, we cannot presently predict the likelihood of obtaining dismissal of the case, nor can we estimate the possible loss or range of loss at this time.

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

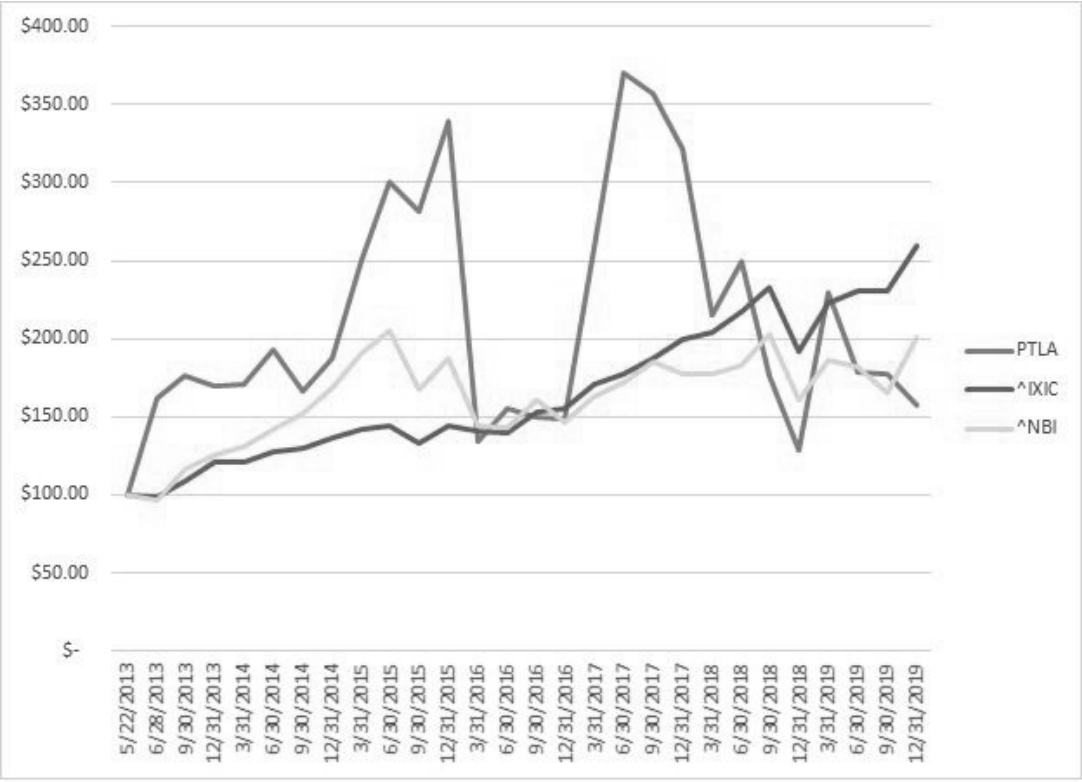
PRICE RANGE OF COMMON STOCK

Our common stock is listed on The Nasdaq Global Select Market under the symbol “PTLA”.

On February 20, 2020, the last reported sale price of our common stock as reported on The Nasdaq Global Select Market was $13.22 per share. As of February 20, 2020, there were 78,080,365 shares of our common stock issued and outstanding with 16 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, 2019. 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	$ 140.61	$ 139.83	$ 153.38	$ 155.43
Nasdaq Biotechnology Index	^NBI	$ 144.50	$ 142.73	$ 160.41	$ 146.93

$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

$100 investment in stock or index	Ticker	March 31, 2018	June 30, 2018	September 30, 2018	December 31, 2018
Portola Pharmaceuticals, Inc.	PTLA	$ 215.58	$ 249.31	$ 175.78	$ 128.84
Nasdaq Composite Index	^IXIC	$ 203.95	$ 216.85	$ 232.33	$ 191.59
Nasdaq Biotechnology Index	^NBI	$ 177.75	$ 183.00	$ 203.24	$ 161.28

$100 investment in stock or index	Ticker	March 31, 2019	June 30, 2019	September 30, 2019	December 31, 2019
Portola Pharmaceuticals, Inc.	PTLA	$ 229.04	$ 179.08	$ 177.03	$ 157.62
Nasdaq Composite Index	^IXIC	$ 223.18	$ 231.17	$ 230.97	$ 259.08
Nasdaq Biotechnology Index	^NBI	$ 186.12	$ 181.65	$ 165.74	$ 200.65

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. The terms of our existing debt agreement entered with HCR and Athyrium Opportunities III Acquisition LP in 2019 precludes us from paying dividends. 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, 2019, 2018 and 2017 and the consolidated balance sheet data as of December 31, 2019 and 2018 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, 2016 and 2015, and the consolidated balance sheet data as of December 31, 2017, 2016 and 2015 were derived from our audited Consolidated Financial Statements that are not included in this Annual Report on Form 10-K.

	Year Ended December 31,				
	2019	2018	2017	2016	2015
Consolidated statements of operations data:					
Revenues:					
Product revenue, net	$ 111,644	$ 24,117	$ —	$ —	$ —
Collaboration and license revenue	4,996	16,013	22,546	35,504	12,070
Total revenues	116,640	40,130	22,546	35,504	12,070
Operating expenses:					
Cost of sales	44,378	18,081	415	—	—
Research and development	124,627	216,205	203,701	246,854	200,376
Selling general and administrative	218,919	151,164	91,109	58,235	38,869
Total operating expenses	387,924	385,450	295,225	305,089	239,245
Loss from operations	(271,284)	(345,320)	(272,679)	(269,585)	(227,175)
Interest and other income (expense), net	9,698	13,516	(1,338)	1,533	305
Interest expense	(31,290)	(18,740)	(11,603)	(61)	—
Loss before income taxes	(292,876)	(350,544)	(285,620)	(268,113)	(226,870)
Income tax benefit	—	—	—	—	(365)
Net loss	(292,876)	(350,544)	(285,620)	(268,113)	(226,505)
Net loss (income) attributable to noncontrolling interest	2,213	321	(470)	(930)	—
Net loss attributable to Portola	$ (290,663)	$ (350,223)	$ (286,090)	$ (269,043)	$ (226,505)
Net loss per share attributable to Portola common stockholders:					
Basic and Diluted	$ (4.06)	$ (5.31)	$ (4.81)	$ (4.76)	$ (4.36)
Shares used to compute net loss per share attributable to Portola common stockholders:					
Basic and Diluted	71,555,220	66,017,330	59,508,156	56,480,647	51,981,463

	As of December 31,				
	2019	2018	2017	2016	2015
Consolidated balance sheet data:					
Cash, cash equivalents and investments	$ 466,244	$ 316,964	$ 534,233	$ 318,771	$ 460,161
Working capital	359,715	284,322	397,399	263,264	414,431
Total assets	578,483	386,419	571,676	343,436	502,924
Notes payable, less current portion	43,100	48,298	50,565	49,815	—
Long term royalty-based debt, less current portion	162,897	155,256	54,251	—	—
Long-term debt	118,096	—	—	—	—
Noncontrolling interest	—	2,166	2,627	2,157	2,927
Total stockholders' equity	129,825	90,567	349,493	192,689	430,323

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

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 diseases and inflammation for patients who currently have limited or no approved treatment options. Our headquarters are located in South San Francisco, California. Our lead product is Andexxa® [coagulation factor Xa (recombinant), inactivated-zhzo], the first and only antidote approved by the U.S. FDA for patients treated with rivaroxaban or apixaban, when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding. We are conducting clinical trials with cerdulatinib, an investigational oral, SYK-JAK inhibitor to treat hematologic cancers while we pursue partnering opportunities or other strategic transactions for this drug candidate.

Business Highlights:

Andexxa

- Commenced full scale commercial launch of Andexxa in the U.S. in January 2019, recording $105.0 million net revenues in 2019.
- Over 425 new U.S. hospitals purchased Andexxa during 2019.
- Added to the Veterans Affairs National Formulary in the third quarter of 2019.
- The CMS increased Andexxa's eligible reimbursement amount for the New Technology Add-on Payment ("NTAP") from 50% to 65% of the wholesale acquisition cost of the standard dose, effective October 1, 2019.
- The Joint Commission on Accreditation of Healthcare Organizations ("JCAHO") updated the U.S. accreditation measure, requiring hospitals to use approved protocols and evidence-based practice guidelines to reverse anticoagulation and management of bleeding events related to each Factor Xa inhibitor.
- Received conditional approval under the brand name Ondexxya by the European Commission in April 2019.
- Commenced a phased launch of Ondexxya in Europe in July 2019, recording $7.0 million net revenues in 2019.
- Initiated both ANNEXA-I, a randomized controlled trial, and ANNEXA-S, a single-arm urgent surgery study.

Cerdulatinib

- Continued enrollment and treatment of patients in ongoing Phase 2 B- and T-cell Non-Hodgkin Lymphoma ("NHL") study.
- Released interim Phase 2a data demonstrating good tolerability and clinical response in patients with relapsed/refractory peripheral T-Cell lymphoma ("PTCL") and cutaneous T-Cell lymphoma ("CTCL") including a 52% overall response rate for patients with angioimmunoblastic T-Cell lymphoma ("AITL") and rapid and significant reduction in itch among patients with CTCL.
- Released interim Phase 2a data demonstrating improved overall response rate (76%) for patients in the cerdulatinib and rituximab combination cohort.

Bevyxxa

- Curtailed discretionary spend in order to focus resources on the commercialization and continuing development of Andexxa.
- Concluded our process to evaluate potential partners and other strategic transactions.

- Began preparations in the fourth quarter of 2019 to wind down operations and eliminate future operational and financial obligations.

Results of Operations

Revenue

Product revenue is primarily derived from sales of Andexxa and Ondexxya in the United States and the EU, respectively. Collaboration and license revenue relates primarily to agreements with multiple parties centered around the advancement of our Andexxa program and regulatory approval in the United States, EU and Japan. For further discussion of our revenue recognition policy, see "Critical Accounting Policies and Significant Judgments and Estimates" below. Our ability to generate revenue and become profitable depends upon our ability to successfully commercialize Andexxa globally and any product candidates that we may develop, in-license or acquire in the future.

We adopted new revenue accounting guidance effective January 1, 2018 (Accounting Standards Codification Topic 606, Revenues from Contracts with Customers, or Topic 606). For further discussion, see Note 3, "Revenue Recognition" in the Notes to our Consolidated Financial Statements included in Part II, Item 8 of this Annual Report on Form 10-K.

Cost of Sales

Cost of sales represents primarily the costs associated with manufacturing of our commercial products, Bevyxxa net sales-based royalties payable to Takeda, amortization of an intangible asset associated with a capitalized milestone payment made to Takeda upon FDA approval of Bevyxxa, write-offs of product and prepayments for product to be manufactured that may not be recoverable based on future sales, fixed costs to our contract manufacturers, if any, for anticipated shortfall in product demand relative to committed volumes, and a write off of Bevyxxa asset group as an impairment charge following our decision in 2019 to wind down the Bevyxxa project as soon as administratively possible.

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, discovery and development of clinical candidates pursuant to our collaboration agreements, as well as costs to further develop Andexxa, including manufacturing process improvements and further clinical trials to support full approvals and label expansion. We recognize all research and development costs as they are incurred.

We expect our research and development expenses to decrease slightly in the near term as our current Andexxa manufacturing processes qualify for capitalization as inventory and will be expensed as costs of sales when the inventory is sold. The timing and amount of expenses incurred will depend largely on the progress of our randomized controlled trial for Andexxa and potentially label-expanding clinical study of Andexxa in patients requiring urgent surgery. Additionally, our research and development expenses will depend on related regulatory requirements and further initiatives that may be undertaken to enhance or expand our current manufacturing processes and decisions we may make regarding future clinical and preclinical studies of our products and product candidates.

For further discussion of the changes in our research and development expenses with respect to the year ended December 31, 2019 and the corresponding period of 2018, see "Comparison of the years ended December 31, 2019 and 2018 — Research and development expenses" below.

The program-specific expenses summarized in the table below 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, compliance, human resources, audit and accounting services and advertising and marketing expenses. Personnel costs consist of salaries, benefits and stock-based compensation.

We expect selling, general and administrative expenses to increase in the future as we incur additional expenses associated with the establishment and growth of a hospital-based sales force in the United States and Europe 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 (expense), net

Interest and other income (expense), net consists primarily of interest received on our cash, cash equivalents and investments, unrealized gains and losses from the remeasurement of our embedded derivatives associated with BMS and Pfizer promissory notes, a royalty-based financing arrangement with HealthCare Royalty Partners and its affiliates ("HCR") and secured term loans from HCR and Athyrium Opportunities III Acquisition LP ("Athyrium"), and remeasurement of foreign currency denominated monetary assets and liabilities.

Interest expense

Interest expense represents interest from our BMS and Pfizer promissory notes, a royalty-based financing arrangement with HCR and secured term loans from HCR and Athyrium.

Comparison of the years ended December 31, 2019 and 2018

Revenue

	Year Ended December 31,			
	2019	2018	Change	% Change
	(in thousands, except percentages)			
Andexxa	$ 104,529	$ 23,995	$ 80,534	336 %
Ondexxya	6,936	—	6,936	*
Bevyxxa	179	122	57	47 %
Total product revenue, net	111,644	24,117	87,527	363 %
Total collaboration and license revenue	4,996	16,013	(11,017)	(69)%
Total revenues	$ 116,640	$ 40,130	76,510	191 %

* Percentage not meaningful

The increase in total revenues during 2019 compared to 2018 was primarily attributable to:

- Commercial product revenue earned from U.S. net sales of Andexxa, which we began shipping to customers in May 2018 and more broadly in January 2019 following the FDA approval of our Gen 2 manufacturing process. During 2019, U.S. net product revenues exhibited consistent growth until the fourth quarter when flat quarter-over-quarter hospital demand led to lower ex-factory sales to specialty distributors as they began rationalizing their on-hand inventory requirements. Further, we recorded an increase to our product return reserves of $4.2 million to address potential return exposures for current year product sales with expiry in 2020;
- Commercial product revenue earned from the EU commencing in the third quarter of 2019; offset by
- A decrease in Phase 3 collaboration revenue from certain collaboration partners as related performance obligations were mostly fulfilled by the first quarter of 2019.

Cost of Sales

	Year Ended December 31,			
	2019	2018	Change	% Change
	(in thousands, except percentage)			
Cost of sales	$ 44,378	$ 18,081	$ 26,297	145%

The increase in cost of sales during 2019 compared to 2018 was primarily attributable to:

- A full year of Andexxa product sales in 2019;
- A $27.5 million charge recorded in 2019 as a result of the management's decision to wind down the Bevyxxa operation. This charge is comprised of 1) an excess and obsolescence inventory charge of $13.7 million, 2) a write-off of a long-term prepaid manufacturing assets of $7.8 million, 3) an impairment charge for an intangible asset related to a payment made to Takeda of $3.7 million, and 4) an accrual for firm purchase commitments of $2.3 million; offset by
- A $6.5 million decrease of excess and obsolescence charges recorded in 2018 which did not recur in 2019 and were associated with our Gen 1 manufacturing process.

Cost of product sales also consists of certain finishing costs incurred after FDA approvals related to approved products sold, in addition to certain distribution and overhead costs. We expect costs of sales to increase in relation to product revenues as we deplete inventories that we had expensed prior to receiving FDA approvals.

Research and development expenses

		Year Ended December 31,			
		2019	2018	Change	% Change
Product candidate	**Phase of Development**	(in thousands, except percentages)			
Andexanet alfa	Phase 2/3/4	$ 74,633	$ 159,773	$ (85,140)	(53)%
Betrixaban	Phase 1/3	4,078	23,641	(19,563)	(83)%
Cerdulatinib	Phase 1/2a	33,036	25,233	7,803	31 %
Other research and development expenses(1)		12,880	7,558	5,322	70 %
Total research and development expenses		$ 124,627	$ 216,205	$ (91,578)	(42)%

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

The decrease in total research and development expenses during 2019 compared to 2018 was primarily attributable to:

- Decreased program costs related to Andexxa, which were largely the result of capitalizing Gen2 manufacturing costs that were recorded as research and development expenses in 2018; and
- Decreased program costs related to Bevyxxa, which were the result of overall decreased spending; offset by
- Increased program costs related to 1) cerdulatinib, primarily due to increased manufacturing expenses and 2) an impairment charge of $3.2 million due to the abandonment of a program with a subsidiary during the second quarter of 2019.

Selling, general and administrative expenses

	Year Ended December 31,			
	2019	2018	Change	% Change
	(in thousands, except percentage)			
Selling, general and administrative expenses	$ 218,919	$ 151,164	$ 67,755	45%

The increase in selling, general and administrative expenses during 2019 compared to 2018 was primarily attributable to:

- Increased headcount-related costs of $46.6 million resulting from the hiring of our sales force and headcount supporting commercial functions; and
- Increased external costs of $17.2 million associated with commercial and marketing initiatives to support the launch of Andexxa.

Interest and other income (expense), net

	Year Ended December 31,			
	2019	2018	Change	% Change
	(in thousands, except percentage)			
Interest and other income (expense), net	$ 9,698	$ 13,516	$ (3,818)	(28)%

The decrease in interest and other income (expense), net, during 2019 compared to 2018 was primarily attributable to

- Decrease in gain on remeasurement from embedded derivatives by $3.4 million; and
- Decrease in interest income earned from investments.

Interest expense

	Year Ended December 31,			
	2019	2018	Change	% Change
	(in thousands, except percentage)			
Interest expense	$ 31,290	$ 18,740	$ 12,550	67%

The increase in interest expense during 2019 compared to 2018 was primarily attributable to:

- An additional $95.0 million of funding received in May 2018 under the Andexxa Royalty Sales Agreement with HCR; and
- First and the second tranche fundings of $125.0 million received in 2019 under the Credit Agreement with HCR and Athyrium.

Comparison of the years ended December 31, 2018 and 2017

For the comparison of the years ended December 31, 2018 and 2017, refer to Part II, Item 7 of our Annual Report on Form 10-K for our fiscal year ended December 31, 2018, filed with the SEC on March 1, 2019.

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 and third parties, a royalty-based financing arrangement and sales of commercial and development rights to some of our product candidates. Our expenditures are related to research and development activities, including clinical trial and manufacturing-related costs, and selling, general and administrative costs, including commercial preparation, launch, and operating costs. At December 31, 2019, we had available cash, cash equivalents and investments of $466.2 million, which includes the $50.0 million minimum cash holdings required by our secured term loan agreement (See Note 8, “Long Term Obligations”, in the Notes to our Consolidated Financial Statements included in Part II, Item 8 of this Annual Report on Form 10-K). 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 potential milestones receivable under our current collaboration and license agreements. Our future funding requirements will depend on many factors, including the following:

- the timing, receipt and amount of sales, profit sharing or royalties, if any, from our current and potential products;

- the cost of manufacturing our current products and 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 in the United States and abroad;
- 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 cost, timing and outcomes of regulatory approvals;
- 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;
- 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; and
- partnerships and other strategic options for our products and product candidates.

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,		
	2019	2018	2017
	(in thousands)		
Cash used in operating activities	$ (237,923)	$ (326,058)	$ (225,125)
Cash (used in) provided by investing activities	(73,002)	174,081	(228,772)
Cash provided by financing activities	389,564	110,249	446,980
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(2)	—	—
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 78,637	$ (41,728)	$ (6,917)

Cash used in operating activities

Cash used in operating activities for the year ended December 31, 2019 includes payments made to our contract manufacturing organizations for the manufacture of Andexxa and Bevyxxa, totaling $73.3 million and $1.2 million, respectively, $174.0 million of disbursements to third-party vendors to support research and development and selling and general and administrative operations, and $95.3 million in payroll and related employee costs. These cash outflows were partially offset by cash receipts of $109.9 million associated with Andexxa commercial sales and $10.8 million from our Andexxa collaboration agreements.

Cash used in operating activities for the year ended December 31, 2018, includes payments made to our contract manufacturing organizations for the manufacture of Andexxa and Bevyxxa, totaling $125.1 million and $8.7 million, respectively, $156.7 million of disbursements to third-party vendors to support planned research and development and selling and general and administrative operations, and $66.5 million in payroll and related employee costs. These cash outflows were partially offset by

cash receipts of $39.1 million, primarily $15.1 million from our Andexxa collaboration agreements, $3.8 million associated with a milestone earned pursuant to our out-license of cerdulatinib to Dermavant, and $20.1 million associated with Andexxa and Bevyxxa commercial sales.

Cash (used in) provided by investing activities

Cash used in investing activities for the year ended December 31, 2019 was primarily related to purchases of investments of $368.7 million partially offset by proceeds from maturities of investments of $297.3 million.

Cash provided by investing activities of $174.1 million for the year ended December 31, 2018 was primarily related to proceeds from maturities of investments of $435.7 million, partially offset by investment purchases of $259.1 million and fixed asset purchases of $2.6 million.

Cash provided by financing activities

Cash provided by financing activities for the year ended December 31, 2019 was primarily related to net proceeds from our public offering of common stock in August 2019 of $243.9 million, net proceeds from debt issuance of $121.7 million, and net proceeds from the issuance of common stock pursuant to equity awards of $24.9 million.

Cash provided by financing activities of $110.2 million for the year ended December 31, 2018 was primarily related to net proceeds of $95.0 million of royalty-based financing from our agreement with HCR and net proceeds from the issuance of common stock pursuant to equity awards of $15.4 million.

For the cash flow information for the year ended December 31, 2017, please refer to Part II, Item 7 of our Annual Report on Form 10-K for our fiscal year ended December 31, 2018, filed with the SEC on March 1, 2019.

Off-balance sheet arrangements and contractual obligations

The following table summarizes our future contractual obligations as of December 31, 2019:

	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:					
Manufacturing and service contracts (1)	$ 94,526	$ 143,597	$ 83,537	$ 76,150	$ 397,810
Notes payable, debt and obligation to collaborator (2)	43,060	147,875	155,557	175,353	521,845
Operating lease obligations	4,908	9,650	1,188	—	15,746
Total contractual obligations	$ 142,494	$ 301,122	$ 240,282	$ 251,503	$ 935,401

(1) We are contractually obligated to pay for raw materials procured by our contract manufacturers or for raw materials they have entered into firm orders with their vendors in support of manufacturing process. Our contract manufactures generally plan for and procure such raw materials one year in advance of the commencement of the associated manufacturing campaign.

(2) For more detailed description of the obligations, see Note 8, "Long Term Obligation" and Note 3, "Revenue Recognition" in the Notes to our Consolidated Financial Statements included in Part II, Item 8 of this Annual Report. This line includes estimated future royalty payments, our long-term obligation to collaborator, Daiichi Sankyo and payments for principal and interest related to the secured term loans arrangement made with HCR and Athyrium.

We lease our corporate headquarters, laboratory and other U.S. facilities under an operating lease expiring in March 2023. 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 $99.5 million have not been recorded on our consolidated balance sheet as of December 31, 2019.

Our commercial manufacturing agreements include cancellable purchase commitments aggregating approximately $77.9 million that are incremental to the amounts shown in the commitment table above. These commitments are 100% cancellable as of December 31, 2019 without any cancellation fee and are not included in the contractual obligations table above as a purchase commitment.

In addition to the above, in August 2017, we executed a Manufacturing Services Agreement with Lonza AG ("Lonza") to develop our Gen 2 manufacturing process for Andexxa bulk drug substance. The manufacturing commitments included therein are contingent upon marketing approval by either the FDA or the EMA of Andexxa manufactured at the current Porrino facility under the Gen 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 $1.00 per share, contingent upon certain events.

The first purchase right was earned by Lonza upon the approval of the Gen 2 process and after the commencement of process transfer activities to an additional new facility in the first quarter of 2019. Lonza exercised their right to purchase 500,000 shares of our common stock at $1.00 per share. For the first purchase right, we marked to market the liability-classified award up to the settlement date using the valuation assumptions described in Note 4, "Fair Value Measurements" in the Notes to our Consolidated Financial Statements included in Part II, Item 8 of this Annual Report on Form 10-K.

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 second purchase right is capped at the lesser of either: (1) the number of shares with an aggregate market value of $15.0 million based on a 20 days trailing market value average from the date such purchase right is earned by Lonza, or (2) 500,000 shares. As of December 31, 2019, we have not recognized any expense for the second purchase right because the related performance conditions include a regulatory approval condition and regulatory approvals are not considered probable until actually achieved.

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, ("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 our Consolidated Financial Statements included in Part II, Item 8 of this Annual Report on Form 10-K, we believe the following accounting policies to be critical to the judgments and estimates used in the preparation of our financial statements.

Revenue recognition

Product Revenue, Net and Reserves for Variable Consideration

We recognize revenue when our customers obtain control of promised goods or services, in an amount that reflects the consideration to which we are entitled in exchange for those goods or services. We calculate gross product revenues based on the price that we charge to the specialty distributors and wholesalers in the U.S and the customers in the EU. We estimate our net product revenues by deducting from our gross product revenues various forms of variable considerations, which include (a) product returns, (b) estimated government rebates and chargebacks, (c) fees paid to specialty distributors and wholesalers, and (d) cash discounts. Variable consideration requires significant judgment by management. Estimates are assessed each period and updated to reflect current information.

We initially record estimates for these deductions at the time we recognize the related gross product revenue. Our estimates for the expected utilization are based on customer and payor data received from specialty distributors and wholesalers, and historical utilization rates. For a further description of our variable considerations, see Note 2, "Summary of Significant Accounting Policies" in the Notes to our Consolidated Financial Statements included in Part II, Item 8 of this Annual Report on Form 10-K.

Collaboration and License Revenue

We enter into collaboration and license agreements for the development and commercialization of our products. The terms of collaboration and license agreements typically include payments to us of one or more of the following: non-refundable or partially refundable upfront or license fees, development, regulatory and commercial milestone payments, manufacturing supply services, partial or complete reimbursement of research and development costs, and royalties on net sales of licensed products. Each of these payments results in collaboration and license revenue, except for royalties on net sales of licensed products, which are classified as royalty revenues. To date, we have not received any royalty revenues.

As part of the accounting for these arrangements, we must apply judgment to determine whether the performance obligations are distinct, and develop assumptions in determining the stand-alone selling price for each distinct performance obligation identified in the contract. To determine the stand-alone selling price, we rely on assumptions which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success.

At the inception of each arrangement that includes development milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or that of the licensee, such as regulatory approvals, are constrained until those milestones are achieved. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such development milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration and license revenue in the period of adjustment.

Amounts related to research and development and regulatory activities 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. We use internal development projected cost estimates to determine the amount of revenue to record as we satisfy this performance obligation, known as the inputs method.

Inventory

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. We analyze our inventory levels quarterly and write down inventory that is subject to expiry in excess of expected requirements, that has a cost basis in excess of its expected net realizable value or that is in excess of expected sales requirements. These write downs are recognized as cost of sales. On a quarterly basis, we analyze our estimated production levels for the following twelve-month period, which is our normal operating cycle, and reclassify inventory we expect to use or sell in periods beyond the next twelve months into Inventories, noncurrent portion in our Consolidated Balance Sheets. The bulk drug substance in Andexxa has undergone significant manufacturing specific to their intended purposes at the point they are purchased by us, therefore, we classify BDS as work-in-process inventory.

Clinical trial accruals

All of our clinical trials have been executed with support from contract research organizations and other vendors. We accrue costs for clinical trial activities performed by contract research organizations based upon the estimated amount of work completed on each trial. For clinical trial expenses, the significant factors used in estimating accruals include the number of patients enrolled, the activities to be performed for each patient, the number of active clinical sites and the duration for which the patients will be enrolled in the trial. We monitor patient enrollment levels and related activities to the extent possible through internal reviews, correspondence with contract research organizations and review of contractual terms. We base our estimates on the best information available at the time. However, additional information may become available to us, which may allow us to make a more accurate estimate in future periods. 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.

Stock-based compensation

We recognize compensation costs related to stock options 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). Our estimate of expected volatility is based on our volatility and the weighted average volatility of other companies with similar products under development, market, size and other factors. The expected term of nonemployee options assumes the remaining contractual term of the respective option.

Income taxes

We provide for income taxes under the asset and liability method. Significant estimates are required in determining our income taxes. Some of these estimates are based on interpretations of existing tax laws or regulations. We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Under this method, deferred tax assets and liabilities are determined on the basis of the difference between the tax basis of assets and liabilities and their respective financial reporting amounts (temporary differences) at enacted tax rates in effect for the years in which the differences are expected to reverse. A valuation allowance is established for deferred tax assets for which it is more likely than not that some portion or all of the deferred tax assets, including net operating losses and tax credits, will not be realized. We periodically re-assess the need for a valuation allowance against our deferred tax assets based on various factors including our historical loss experience by taxing jurisdiction, and forecasts of future operating results and utilization of net operating losses and tax credits prior to their expiration. 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.

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, 2019, we had cash, cash equivalents and investments of $466.2 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 €62.4 million and €89.7 million to our European vendors during the year ended December 31, 2019 and 2018, respectively. 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, 2019, the effect of the exposure to these fluctuations in foreign exchange rates was not material.

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, 2019 and 2018, 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, 2019, and the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2019 and 2018, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2019, 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, 2019, 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 February 28, 2020 expressed an unqualified opinion thereon.

Adoption of New Accounting Standard

As discussed in Note 2 to the consolidated financial statements, the Company changed its method for recognizing revenue as a result of the adoption of Accounting Standards Update (ASU) No. 2014-09, Revenue from Contracts with Customers (Topic 606), effective January 1, 2018.

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.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Reserves for returns on product revenue

Description of the Matter

As described in Note 3 to the consolidated financial statements, the Company had product revenue of $111.6 million for the year ended December 31, 2019, which was net of $20.6 million recorded as a reduction in revenue, which includes estimates of variable consideration for which reserves are established, including reserves for product returns.

Auditing the Company's measurement of reserves for product returns under its contracts with customers was especially challenging because (1) the calculation involves subjective management assumptions about inventory remaining in the distribution channel as of the balance sheet date (i.e., units held by hospitals) that could be subject to return in future periods under the Company's returns policy, and (2) the Company has limited commercial sales history on which to base its assumptions.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of internal controls that address the identified risks related to the Company's process used to determine reserves for returns on product revenue. For example, we tested controls over management's review of the completeness and accuracy of the data used in the process, the assumptions about customer reorder patterns and units in the channel as of the balance sheet date.

To test the Company's reserves for returns on product revenue, our audit procedures included, among other procedures, testing the accuracy and completeness of the underlying data used in the calculations and evaluating the significant assumptions used by management to estimate its reserves. To test management's significant assumptions, we inspected agreements with significant customers to evaluate whether such contracts allow for extended rights of return beyond the Company's standard policy, obtained written representations from members of executive management to assess whether all contract provisions were subject to accounting analyses, including oral or side agreements (if any), examined credit memos issued during and after year end for unusual items or trends not consistent with the Company's analysis of product returns, performed revenue cutoff testing at period end to assess whether there were unusual trends that should have been considered in the Company's analysis of product returns, compared the Company's product shipment reports to distributor sell through information to assess the extent of inventory in the distribution channel and examined hospital reorder information. We also performed sensitivity analyses to assess the effect of changes in assumptions.

/s/ Ernst & Young LLP

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

Redwood City, California
February 28, 2020

PORTOLA PHARMACEUTICALS, INC.

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

	December 31, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 215,229	$ 138,951
Short-term investments	214,054	178,013
Restricted cash	3,421	1,062
Trade and other receivables, net	13,547	5,849
Unbilled - collaboration and license revenue	3,783	9,880
Inventories	4,101	7,873
Prepaid and other current assets	7,998	11,699
Total current assets	462,133	353,327
Property and equipment, net	4,264	5,236
Intangible assets	—	7,279
Operating lease right-of-use assets	12,064	—
Inventories, noncurrent portion	56,096	9,645
Long-term investments	36,961	—
Prepaid and other long-term assets	6,965	10,932
Total assets	$ 578,483	$ 386,419
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 12,739	$ 13,215
Accrued research and development	19,249	19,831
Accrued and other liabilities	49,773	22,310
Deferred revenue, current portion	1,623	1,847
Current portion of notes payable and long-term royalty-based debt	19,034	11,802
Total current liabilities	102,418	69,005
Notes payable, less current portion	43,100	48,298
Long term royalty-based debt, less current portion	162,897	155,256
Long term debt	118,096	—
Long term obligation to collaborator, less current portion	5,060	6,881
Deferred revenue, long-term	4,352	4,488
Long-term portion of lease liabilities	8,850	—
Other long-term liabilities	3,885	11,924
Total liabilities	448,658	295,852
Commitments and contingencies (Note 9)		
Stockholders' equity:		
Preferred stock, $0.001 par value, 5,000 shares authorized; no shares issued and outstanding	—	—
Common stock, $0.001 par value, 150,000 shares authorized at December 31, 2019 and 2018; 77,925 and 66,618 shares issued and outstanding at December 31, 2019 and 2018, respectively	80	68
Additional paid-in capital	1,946,077	1,614,320
Accumulated deficit	(1,816,367)	(1,525,704)
Accumulated other comprehensive income (loss)	35	(283)
Total Portola stockholders' equity	129,825	88,401
Noncontrolling interest	—	2,166
Total stockholders' equity	129,825	90,567
Total liabilities and stockholders' equity	$ 578,483	$ 386,419

See accompanying notes

PORTOLA PHARMACEUTICALS, INC.

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

	Year Ended December 31,		
	2019	**2018**	**2017**
Revenues:			
Product revenue, net	$ 111,644	$ 24,117	$ —
Collaboration and license revenue	4,996	16,013	22,546
Total revenues	116,640	40,130	22,546
Operating expenses:			
Cost of sales	44,378	18,081	415
Research and development	124,627	216,205	203,701
Selling, general and administrative	218,919	151,164	91,109
Total operating expenses	387,924	385,450	295,225
Loss from operations	(271,284)	(345,320)	(272,679)
Interest and other income (expense), net	9,698	13,516	(1,338)
Interest expense	(31,290)	(18,740)	(11,603)
Net loss	(292,876)	(350,544)	(285,620)
Net loss (income) attributable to noncontrolling interest	2,213	321	(470)
Net loss attributable to Portola	$ (290,663)	$ (350,223)	$ (286,090)
Net loss per share attributable to Portola common stockholders:			
Basic and diluted	$ (4.06)	$ (5.31)	$ (4.81)
Shares used to compute net loss per share attributable to Portola common stockholders:			
Basic and diluted	71,555,220	66,017,330	59,508,156

See accompanying notes

PORTOLA PHARMACEUTICALS, INC.

Consolidated Statements of Comprehensive Loss
(In thousands)

	Year Ended December 31,		
	2019	**2018**	**2017**
Net loss	$ (292,876)	$ (350,544)	$ (285,620)
Other comprehensive income (loss):			
Unrealized gain (loss) on available-for-sale securities	318	126	(397)
Comprehensive loss	(292,558)	(350,418)	(286,017)
Comprehensive loss (income) attributable to noncontrolling interest	2,213	321	(470)
Total comprehensive loss attributable to Portola	$ (290,345)	$ (350,097)	$ (286,487)

See accompanying notes

PORTOLA PHARMACEUTICALS, INC.

Consolidated Statements of Stockholders' Equity
(In thousands)

	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Non-controlling Interest (SRX Cardio)	Total Stockholders' Equity
	Shares	Amount					
Balance at December 31, 2016	56,544	$ 57	$ 1,108,832	$ (918,345)	$ (12)	$ 2,157	$ 192,689
Cumulative effect of a change in accounting principal	—	—	84	(84)	—	—	—
Issuance of common stock pursuant to equity award plans	1,450	2	19,641	—	—	—	19,643
Issuance of common stock in connection with public offering, net	7,303	7	379,887	—	—	—	379,894
Stock-based compensation expense	—	—	43,284	—	—	—	43,284
Other comprehensive loss	—	—	—	—	(397)	—	(397)
Net (loss) gain	—	—	—	(286,090)	—	470	(285,620)
Balance at December 31, 2017	65,297	$ 66	$ 1,551,728	$ (1,204,519)	$ (409)	$ 2,627	$ 349,493
Adjustment to accumulated deficit due to adoption of ASC 606	—	—	—	29,038	—	—	29,038
Issuance of common stock pursuant to equity award plans	1,321	2	15,387	—	—	—	15,389
Stock-based compensation expense	—	—	47,205	—	—	—	47,205
Other comprehensive income	—	—	—	—	126	—	126
Net loss	—	—	—	(350,223)	—	(321)	(350,544)
Change in noncontrolling interest	—	—	—	—	—	(140)	(140)
Balance at December 31, 2018	66,618	$ 68	$ 1,614,320	$ (1,525,704)	$ (283)	$ 2,166	$ 90,567
Issuance of common stock pursuant to equity award plans	2,066	3	39,918	—	—	—	39,921
Issuance of common stock pursuant to public offering, net	9,241	9	243,931	—	—	—	243,940
Stock-based compensation expense	—	—	47,908	—	—	—	47,908
Other comprehensive income	—	—	—	—	318	—	318
Net loss	—	—	—	(290,663)	—	(2,213)	(292,876)
Change in noncontrolling interest	—	—	—	—	—	47	47
Balance at December 31, 2019	77,925	$ 80	$ 1,946,077	$ (1,816,367)	$ 35	$ —	$ 129,825

See accompanying notes

PORTOLA PHARMACEUTICALS, INC.

Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,		
	2019	**2018**	**2017**
Operating activities			
Net loss	$ (292,876)	$ (350,544)	$ (285,620)
Adjustments to reconcile net loss to cash used in operating activities:			
Depreciation and amortization	3,000	3,102	2,410
Amortization of operating lease right-of-use assets	3,224	—	—
Accretion of discount on investment securities	(1,225)	(1,864)	(235)
Non-cash interest expense	25,371	18,740	11,603
Stock-based compensation expense, net of capitalized labor	52,075	55,360	43,284
Charge associated with our Gen 1 manufacturing process transition	—	10,311	—
Remeasurement (gain) loss on embedded derivatives liabilities	(2,931)	(6,357)	4,562
Provision for excess and obsolete inventories	4,152	2,246	—
Loss on impairment and provision for excess and obsolete inventories of Bevyxxa asset group	27,451	—	—
Loss on impairment of SRX intangible asset	3,151	—	—
Others	195	15	52
Changes in operating assets and liabilities:			
Inventories	(58,830)	(12,612)	(1,099)
Trade and other receivables, net	(7,698)	607	(3,750)
Unbilled - collaboration and license revenue	6,097	(3,186)	—
Prepaid and other current assets	3,812	(7,496)	235
Prepaid and other long-term assets	(3,813)	(10,968)	(4,395)
Accounts payable	(2,652)	1,881	(5,242)
Accrued research and development	(582)	(25,142)	21,155
Accrued and other liabilities	17,668	3,514	8,576
Deferred revenue	(360)	(1,288)	(15,796)
Notes payable and long term royalty-based debt	(13,152)	(1,412)	—
Other long-term liabilities	—	(965)	(865)
Net cash used in operating activities	(237,923)	(326,058)	(225,125)
Investing activities			
Capital expenditures, net	(1,544)	(2,559)	(1,236)
Purchase of intangible assets	—	—	(5,000)
Purchases of investments	(368,747)	(259,083)	(575,624)
Proceeds from maturities of investments	297,289	435,723	353,088
Net cash (used in) provided by investing activities	(73,002)	174,081	(228,772)
Financing activities			
Proceeds from debt issuance, net	121,703	95,000	47,444
Proceeds from issuance of common stock from public offering, net	243,941	—	379,894
Proceeds from issuance of common stock pursuant to equity award plans	24,896	15,389	19,642
Payments of long-term obligation to collaborator	(976)	—	—
Other	—	(140)	—
Net cash provided by financing activities	389,564	110,249	446,980
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(2)	—	—
Net increase (decrease) in cash, cash equivalents and restricted cash	78,637	(41,728)	(6,917)
Cash, cash equivalents and restricted cash at beginning of period	140,013	181,741	188,658
Cash, cash equivalents and restricted cash at end of period	$ 218,650	$ 140,013	$ 181,741

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 is located in South San Francisco, California. We have operations in the United States and in Europe, and we operate in one segment.

Our lead product, Andexxa [coagulation factor Xa (recombinant), inactivated-zhzo], which we are marketing under the brand name of Ondexxya in Europe, is the first and only antidote approved by the U.S. Food and Drug Administration ("FDA") and the European Commission ("EC"), respectively, for patients treated with rivaroxaban or apixaban, when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding. Bevyxxa (betrixaban) is an oral, once-daily Factor Xa inhibitor approved by the FDA for the prevention of venous thromboembolism ("VTE") in adult patients hospitalized for an acute medical illness. We are conducting clinical trials on cerdulatinib, an investigational oral, dual spleen tyrosine kinase ("SYK") and Janus kinase ("JAK") inhibitor in development to treat hematologic cancers.

Public Offerings

In August 2019, we completed an underwritten public offering of 9,241,072 shares of our common stock, which included 1,205,357 shares of common stock issued pursuant to the over-allotment option granted to our underwriters, at a public offering price of $28.00 per share. The total proceeds from the offering and over-allotment, net of underwriting discounts and commissions of approximately $14.2 million, were approximately $244.5 million. After deducting offering expenses of approximately $0.6 million, net proceeds to us were approximately $243.9 million.

2. Summary of Significant Accounting Policies

Consolidation and Basis of Presentation

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, our wholly owned subsidiaries and SRX Cardio,LLC ("SRX Cardio") that is a variable interest entity (a "VIE") for which Portola was deemed, under applicable accounting guidance, to be the primary beneficiary. During the third quarter of 2019, we deconsolidated SRX Cardio, a VIE we had consolidated since 2015, and as such, we do not have any consolidated VIE as of December 31, 2019. All intercompany transactions and balances have been eliminated upon consolidation.

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. Management bases its estimates on historical experience and on various other market-specific and relevant assumptions that management believes to be reasonable under the circumstances. Actual results may differ from those estimates.

Cash and Cash Equivalents

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

Cash as Reported in Consolidated Statements of Cash Flows

Cash as reported in the consolidated statements of cash flows includes the aggregate amounts of cash and cash equivalents and restricted cash. As of December 31, 2019, restricted cash represents cash restricted for royalty payments to HealthCare Royalty Partners and its Affiliates ("HCR") and cash held as a security deposit for our office lease in Europe.

Cash as reported in these consolidated statements of cash flows consists of the following (in thousands):

	December 31, 2019	December 31, 2018	December 31, 2017
Cash and cash equivalents	$ 215,229	$ 138,951	$ 181,568
Restricted cash (SRX Cardio)	—	30	173
Restricted cash for royalty payments to HealthCare Royalty Partners and its affiliates ("HCR")	3,375	1,032	—
Restricted cash (Lease)	46	—	—
Total cash balance in consolidated statements of cash flows	$ 218,650	$ 140,013	$ 181,741

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, trade and other receivables, 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.

Trade receivables and 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.

We are dependent on third-party manufacturers to manufacture our drugs and drug candidates. In particular, we rely and expect to continue to rely on a small number of manufacturers to supply us with the requirements for the bulk drug substance and active pharmaceutical ingredients related to our drugs and drug candidates. We could be adversely affected by a significant interruption in the supply of bulk drug substance and active pharmaceutical ingredients.

Trade Receivables

Trade receivables are recorded net of estimates of variable consideration for which reserves are established and which result from chargebacks for government and other programs, discounts that are offered within contracts between us and a limited number of specialty distributors and wholesalers in the United States and hospitals and clinics in the EU (“Customers”) and fees for distribution services. Estimates for chargebacks for government and other programs are based on contractual terms, historical trends and our expectations regarding the utilization rates for these programs. Estimates for discounts and fees are based on contractual terms and our expectation regarding customers earning the discounts and fees. Estimates of our allowance for doubtful accounts are determined based on existing contractual payment terms, historical payment patterns of our customers and individual customer circumstances. Historically, estimates for uncollectible accounts receivable has been insignificant and we have not recorded any reserves.

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. To the extent inventories are not scheduled to be sold within twelve months of the balance sheet date, it is reported as inventories, noncurrent portion in our Consolidated Balance Sheets.

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 Bevyxxa when it was determined that the inventory had a probable future economic benefit after Bevyxxa received the FDA approval in June 2017. This inventory capitalization process began to be applied to Andexxa Gen 1 and Gen2 supply upon their approval dates of May 3, 2018 and December 31, 2018, respectively.

We assess our inventory levels each reporting period and write-down inventory that is expected to be at risk for expiration, that has a cost basis in excess of its expected net realizable value and inventory quantities in excess of expected requirements. In evaluating the sufficiency of our inventory reserves or liabilities for firm purchase commitments, we also take into consideration our firm purchase commitments for future inventory production. If we were to decide to cancel our manufacturing commitment, such cancellation would trigger the payment of a cancellation fee. If we project to have excess inventories and that it would be more cost-efficient to pay the cancellation fee, we may accrue the cancellation fee as a liability. Our assessment of excess inventories, including future firm purchase commitments, requires management to utilize judgment in formulating estimates and assumptions that we believe to be reasonable under the circumstances. Actual results may differ from those estimates and assumptions. When we recognize a loss on such inventory or firm purchase commitments, it establishes a new, lower cost basis for that inventory, and subsequent changes in facts and circumstances will not result in the restoration or increase in that newly established cost basis. If inventory with a lower cost basis is subsequently sold, it will result in higher gross margin for those sales. The portion of our inventory that is most at risk for product dating issues is the finished goods inventory.

The bulk drug substance in Andexxa has undergone significant manufacturing specific to its intended purposes at the point it is are purchased by us, therefore, we classify BDS as work-in-process inventory.

Customer Concentration

During the year ended December 31, 2019, we had four Andexxa specialty distributor customers who each accounted for 10% or more of total net revenues, and no collaboration revenue customers who each accounted for more than 10% of total net revenues. As of December 31, 2019, we had four Andexxa specialty distributor customers who each accounted for 10% or more of total trade and other receivables, and two collaboration revenue customers who each accounted for more than 10% of total unbilled - collaboration and license revenue.

During the year ended December 31, 2018, we had three Andexxa specialty distributor customers who each accounted for 10% or more of total net revenues, and two collaboration revenue customers who each accounted for 10% or more of total net revenues. As of December 31, 2018, we had three Andexxa specialty distributor customers who each accounted for 10% or more of total trade and other receivables, and two collaboration revenue customers who each accounted for more than 10% of total unbilled - collaboration and license revenue.

During the year ended December 31, 2017, we had four collaboration revenue customers who each accounted for 10% or more of total net revenues.

Intangible Assets

Intangible assets as of December 31, 2018 include an in-process research and development asset related to our consolidated VIE and a milestone payment made to Takeda Pharmaceutical Company Ltd. ("Takeda") upon FDA approval of Bevyxxa. We review our intangible assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. We have a zero balance for intangible assets as of December 31, 2019. During 2019, SRX Cardio was deconsolidated and the related in-process research and development asset was derecognized. Also during 2019, the intangible asset related to the milestone payment to Takeda was fully impaired. Throughout 2019, we engaged with potential business collaborators for Bevyxxa. In the fourth quarter of 2019, we determined that it was unlikely that we will find a viable partner. Accordingly, we have begun to wind down Bevyxxa operations to eliminate future operational and financial obligations. We no longer expect to commercialize Bevyxxa or support any further development efforts.

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. See Note 14, "Costs from Wind Down of Bevyxxa Activities" for additional details of charges recorded in 2019 related to the wind down of the Bevyxxa-related activities.

Revenue Recognition

On January 1, 2018, we adopted Accounting Standards Codification (“ASC”), Topic 606 (ASC 606), *Revenue from Contracts with Customers*, (created by Accounting Standards Update ("ASU") 2014-09) using the modified retrospective method to all contracts that were not completed as of January 1, 2018. Pursuant to ASC 606, we recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration that we expect to receive in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract, determine those that are performance obligations, and assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Product Revenue, Net

Our product revenue consists of the U.S. sales of Andexxa and Bevyxxa, which we began shipping to customers in May 2018 and January 2018, respectively, and the EU sales of Ondexxya, which we began shipping to customers in July 2019. Prior to January 2018 we had no product revenues. We sell Andexxa and Bevyxxa to a limited number of specialty distributors and wholesalers in the United States, and Ondexxya primarily to hospitals and clinics, many of which are government-owned or supported in the EU (“Customers”). Our Customers in the United States subsequently resell our products to hospitals, pharmacies and long-term care centers. In addition to distribution agreements with Customers, we enter into arrangements with payors that provide for government-mandated and/or privately negotiated chargebacks, rebates, distribution costs and discounts with respect to the purchase of our products. Our payment terms are approximately 30 days for Andexxa in the United States and consistent with prevailing practice in the EU markets.

We recognize revenue from product sales when control of the product transfers, generally upon shipment or delivery, to the Customer. Upon recognition of revenue from product sales, reserves are made for various forms of variable consideration, which include expected product returns, government rebates such as Medicaid reimbursements, government and other chargebacks, distributor fees and customer incentives such as cash discounts for prompt payment and other distributor costs. Liabilities for expected product returns and government rebates are classified as “Accrued and other liabilities”in our Consolidated Balance Sheets. Government and other chargebacks, distributor fees and customer discounts are recorded as a reduction to “Trade and other receivables, net” in our Consolidated Balance Sheets.

Where appropriate, these estimates take into consideration a range of possible outcomes that are probability-weighted in accordance with the expected value method under ASC 606 for relevant factors. These factors include current contractual and statutory requirements, specific known historical data, specific known market events and trends, and/or forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the respective underlying contracts.

The amount of variable consideration that is included in the transaction price may be constrained, and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, we will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known. For product revenue reserves established for the sales made in the prior period, please see Note 3, "Revenue Recognition".

We expense incremental costs of obtaining a contract when incurred, if the expected amortization period of the asset that we would have recognized is one year or less. To date, we have not incurred any such costs.

Reserves for Variable Consideration

Product Returns: We generally offer Customers a right of return based on the product's expiration date and certain spoilage instances for product that has been purchased from us. We estimate the amount of our product sales that may be returned by our Customers and record this estimate as a reduction of revenue in the period the related product revenue is recognized. Our estimates for expected returns are based primarily on an ongoing analysis of our historical return patterns, our own sales information and our visibility into the inventory remaining in the distribution channel.

Chargebacks: Chargebacks are discounts that occur when contracted customers, which currently consist primarily of Public Health Service institutions, Federal government entities purchasing via the Federal Supply Schedule, and group purchasing organizations, purchase directly from our specialty distributors and wholesalers at a discounted price. The specialty distributors and wholesalers, in turn, charge us back the difference between the price initially paid by them and the discounted price paid by the healthcare providers. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and receivables. We generally issue credits for such amounts within a few weeks of the Customer's notification to us of the resale. Reserves for chargebacks consist of (i) credits that we expect to issue for units that remain in the distribution channel inventories at each reporting period end that we expect will be sold to qualified healthcare providers, and (ii) chargebacks that Customers have claimed but for which we have not yet issued a credit.

Distributor Fees: Under our inventory management agreements with our Customers, we pay the specialty distributors and wholesalers a fee primarily for compliance with certain contractually determined covenants such as the maintenance of agreed upon inventory levels. These distributor fees are based on a contractually determined fixed percentage of sales.

Discounts: We estimate cash discounts based on contractual terms, historical customer payment patterns and our expectations regarding future Customer payment patterns.

Collaboration and License Revenue

We enter into collaboration and license agreements for the development and commercialization of our products that are within the scope of ASC 606. The terms of collaboration and license agreements typically include payments to us of one or more of the following: non-refundable or partially refundable upfront or license fees; development, regulatory and commercial milestone payments; manufacturing supply services; partial or complete reimbursement of research and development costs; and royalties on net sales of licensed products. Each of these payments results in collaboration and license revenue, except for royalties on net sales of licensed products, which are classified as royalty revenues. To date, we have not received any royalty revenues.

As part of the accounting for these arrangements, we must apply judgment to determine whether the performance obligations are distinct, and develop assumptions in determining the stand-alone selling price for each distinct performance obligation identified in the contract. To determine the stand-alone selling price, we rely on assumptions which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success.

Licenses of Intellectual Property: If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenues from non-refundable, up-front fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Milestone Payments: At the inception of each arrangement that includes development milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or that of the licensee, such as regulatory approvals, are constrained until those approvals are received. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such development milestones and any related constraint and, if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration and license revenue in the period of adjustment.

Manufacturing Supply Services: Arrangements that include a promise for future supply of drug substance or drug product for either clinical development or commercial supply at the licensee's discretion are generally considered as options. We assess whether these options provide a material right to the licensee, and if so, they are accounted for as separate performance obligations. If we are entitled to additional payments when the licensee exercises these options, any additional payments are recorded in collaboration and license revenue when the licensee obtains control of the goods, which is upon delivery.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any royalty revenue resulting from any of our out-licensing arrangements.

Research and Development Activities: Amounts related to research and development and regulatory activities 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.

We receive payments from our collaborators based on billing schedules established in each contract. Upfront payments and fees may be recorded as deferred revenue upon receipt or when due, and may require deferral of revenue recognition to a future period until we perform our obligations under these arrangements. Amounts are recorded as accounts receivable when our right to consideration is unconditional. We do not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the collaborators and the transfer of the promised goods or services to the collaborators will be one year or less.

Cost of Sales

Cost of sales represents primarily the costs associated with manufacturing of Andexxa and Bevyxxa, amortization of an intangible asset associated with a capitalized milestone payment made to Takeda upon FDA approval of Bevyxxa, and fixed costs to our contract manufacturers, if any, for anticipated shortfall in product demand relative to committed volumes. We periodically analyze our inventory levels, and write-down inventory for estimated excess, obsolete and non-sellable inventories based on assumptions about future demand, past usage, changes to manufacturing processes and overall market conditions. See Note 14, "Costs from Wind Down of Bevyxxa Activities" for additional details of charges recorded in 2019 related to the wind down of the Bevyxxa related activities.

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 RSU and PSU awards, we base the fair value of awards on the closing market value of our common stock at the date of grant. Upon our adoption of Accounting Standards Update ("ASU") No. 2016-9, *Improvements to Employee Share-Based Payment Accounting*, on January 1, 2017, we made an accounting policy election to account for the forfeitures as they occur. After our adoption of ASU No. 2018-7, *Stock-based Compensation: Improvements to Nonemployee Share-based Payment Accounting,* as of January 1, 2019, compensation costs for nonemployee awards are fixed at the grant date.

BMS and Pfizer Promissory Notes, HCR Royalty-based Financing, and Interest Expense

Notes payable and long-term royalty-based debt are eligible to be repaid based on royalties from our Andexxa net sales. Interest expense is accrued using the effective interest rate method over the estimated period the related debts will be paid. This 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. Consequently, we impute interest on the carrying value of the Notes payable and long-term royalty-based 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 Notes payable and royalty-based debt. 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 the debt carrying values, as well as the period over which debt issuance costs will be amortized.

Embedded Derivatives Related to Debt Instruments

Embedded derivatives that are required to be bifurcated from their host contract are evaluated and valued separately from the debt instrument. Under our Notes payable agreement with BMS and Pfizer and the credit agreement with HCR and Athyrium, upon the occurrence of a change in control, we are required to make accelerated payments of the borrowings to BMS and Pfizer, and we are required to make accelerated payments of the borrowings and a prepayment penalty to HCR and Athyrium. These prepayments and prepayment penalty are considered embedded derivatives, as the holder of the loans may exercise the option to require prepayment by us. The embedded derivatives are classified as "Other long-term liabilities" in our Consolidated Balance Sheets. We remeasure the embedded derivatives each reporting period and report changes in the estimated fair value as gains or losses in "Interest and other income (expense), net" in our Consolidated Statements of Operations.

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 our 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 and Translations

We have certain transactions denominated in currencies other than our functional currencies, and, as a result, are exposed to changes in foreign currency exchange rates. Foreign currency exchange gains (losses) generated from the settlement and remeasurement of these transactions are recognized in earnings and presented within interest and other income (expense), net in our consolidated statements of operations.

Non-U.S. entity operations are recorded in the functional currency of each entity. Results of operations for non-U.S. dollar functional currency entities are translated into U.S. dollars using average currency rates. Assets and liabilities are translated using currency rates at period end. Foreign currency translation adjustments are recorded as a component of accumulated other comprehensive income (loss) within stockholders' equity.

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 the same as basic net loss per share attributable to Portola Common Stockholders, since the effects of potentially dilutive securities are antidilutive.

Net Loss (Income) Attributable to SRX

Net loss (income) attributable to SRX represents the results of operations of SRX during the periods in which we were deemed to be the primary beneficiary of SRX and consolidated the statements of operations and financial condition of SRX into our Consolidated Financial Statements.

Recent Accounting Pronouncements Not Yet Adopted

In September 2016, the Financial Accounting Standards Board ("FASB") issued ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326)*. This ASU implements an impairment model, known as the current expected credit loss model that is based on expected losses rather than incurred losses, and applies to most financial assets measured at amortized cost, such as trade and other receivable, and certain other instruments, such as available-for-sale debt securities. Entities are required to estimate expected credit losses over the life of financial assets and record an allowance against the assets' amortized cost basis to present them at the amount expected to be collected. Additionally, the guidance amends the impairment model for available-for-sale debt securities and requires entities to determine whether all or a portion of the unrealized loss on such debt security is a credit loss. This ASU is effective for all interim and annual reporting periods beginning after December 15, 2019. We do not expect the adoption of this standard to have a material effect on our Consolidated Financial Statements.

In August 2018, the FASB issued ASU No. 2018-15, *Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract*. This ASU aligns the requirements for capitalizing implementation costs incurred in a hosting arrangement that is a service contract with the requirements for capitalizing implementation costs incurred to develop or obtain internal-use software. Accordingly, this ASU requires a customer in a hosting arrangement that is a service contract to follow the guidance in Subtopic 350-40 to determine which implementation costs to capitalize as an asset related to the service contract and which costs to expense. This ASU is effective for us for all interim and annual reporting periods beginning after December 15, 2019. We do not expect the adoption of this standard to have a material effect on our Consolidated Financial Statements.

In November 2018, the FASB issued ASU 2018-18, *Collaborative arrangements (Topic 808): Clarifying the interaction between Topic 808 and Topic 606*. ASU 2018-18 clarifies that certain transactions between participants in a collaborative arrangement should be accounted for under ASC 606 when the counterparty is a customer and precludes an entity from presenting consideration from a transaction in a collaborative arrangement as revenue from contracts with customers if the counterparty is not a customer for that transaction. For public business entities, these amendments are effective for fiscal years beginning after December 2019, and interim periods therein. We do not expect the adoption of this standard to have an effect on our Consolidated Financial Statements.

Recent Accounting Pronouncements Adopted

In February 2016, the FASB issued ASU No. 2016-2, *Leases (Topic 842)*, which amends the existing accounting standards for leases. The new standard requires lessees to record a right-of-use ("ROU") asset and a corresponding lease liability on the balance sheet (with the exception of short-term leases). We adopted this new standard effective January 1, 2019, using the optional transition method, which allows us to recognize a cumulative-effect adjustment to the opening balance of accumulated deficit at the date of adoption and apply the new disclosure requirements beginning in the period of adoption. Our adoption of

the standard added approximately $2.1 million in ROU assets and $3.3 million in lease liabilities to our Consolidated Balance Sheet upon adoption and did not significantly impact financial results.

The new standard provides a number of optional practical expedients and we elected the following:

Transition Elections. We elected the package of practical expedients that permits us to not reassess under the new standard our prior conclusions about lease identification, lease classification, and initial direct costs. We also elected the practical expedient to not separate lease and non-lease components to new or modified leases beginning on or after the adoption date. That is, we will account for each separate lease component of a contract and its associated non-lease components as a single lease component.

Ongoing Accounting Policy Elections. We elected the short-term lease recognition exemption whereby ROU assets and lease liabilities will not be recognized for leasing arrangements with terms less than one year.

In June 2018, the FASB issued ASU No. 2018-7, *Stock-based Compensation: Improvements to Nonemployee Share-based Payment Accounting*, which amends the existing accounting standards for share-based payments to nonemployees. This ASU aligns much of the guidance on measuring and classifying nonemployee awards with that of awards to employees. Under the new guidance, the measurement of nonemployee equity awards is fixed on the grant date. We adopted this new standard effective January 1, 2019. Adoption of this standard did not result in an adjustment to our opening balance of accumulated deficit at the date of adoption, and did not significantly impact our Consolidated Financial Statements.

3. Revenue Recognition

Revenues are recognized when control of the promised goods or services is transferred to our customers, in an amount that reflects the consideration we expect to be entitled to in exchange for those goods or services.

The following tables present our revenues disaggregated by timing of transfer of goods or services (in thousands):

	Year Ended December 31, 2019			Year Ended December 31, 2018		
	Product Revenue, net	Collaboration and License Revenue	Total	Product Revenue, net	Collaboration and License Revenue	Total
Timing of revenue recognition:						
Transferred at a point in time	$ 111,644	$ —	$ 111,644	$ 24,117	$ —	$ 24,117
Transferred over time	—	4,996	4,996	—	16,013	16,013
Total	$ 111,644	$ 4,996	$ 116,640	$ 24,117	$ 16,013	$ 40,130

The following table presents our net product revenues disaggregated by geographic region (in thousands):

	Year Ended December 31,		
	2019	2018	2017
United States	$ 104,708	$ 24,117	$ —
Europe	6,936	—	—
Total revenues	$ 111,644	$ 24,117	$ —

Net product revenues are attributed to geographic region based on the bill-to location. Collaboration and license revenues are all attributed to the United States based on the location of our collaboration partners' headquarters.

Product Revenue, Net

To date, our sources of product revenue have been from the U.S. sales of Andexxa and Bevyxxa, which we began shipping to customers in May 2018 and January 2018, respectively, and from the EU sales of Ondexxya, which we began shipping to customers in July 2019. No costs to obtain or fulfill the contracts have been capitalized. For the year ended December 31, 2019 and 2018, we recorded a total of $20.6 million and $3.6 million, respectively, as a reduction to revenue consisting primarily of reserves for product returns, chargebacks and estimated distribution fees.

Product Revenue Reserves

The activities and ending reserve balances for each significant category of product revenue reserves (which constitute variable considerations) were as follows (in thousands):

	Returns	Chargebacks	Others	Total
Balance at December 31, 2017	$ —	$ —	$ —	$ —
Provision related to sales made in:				
Current period	2,611	289	633	3,533
Prior period	—	—	—	—
Payments and customer credits issued	(2,312)	(113)	(409)	(2,834)
Balance at December 31, 2018	$ 299	$ 176	$ 224	$ 699
Provision related to sales made in:				
Current period	10,254	4,026	3,988	18,268
Prior period	2,373	—	—	2,373
Payments and customer credits issued	(5,366)	(3,303)	(1,550)	(10,219)
Balance at December 31, 2019	$ 7,561	$ 899	$ 2,661	$ 11,121

Collaboration and License Revenue

The following table presents changes in our contract assets and liabilities for the year ended December 31, 2019 (in thousands):

	Balance at Beginning of Period	Addition	Deduction	Balance at End of Period
Contract assets:				
Unbilled - collaboration and license revenue	$ 9,880	$ 5,628	$ (11,725)	$ 3,783
Total contract assets	$ 9,880	$ 5,628	$ (11,725)	$ 3,783
Contract liabilities:				
Deferred revenue	$ 6,335	$ 2,628	$ (3,445)	$ 5,518
Total contract liabilities	$ 6,335	$ 2,628	$ (3,445)	$ 5,518

Significant changes in the contract liabilities balances during the period are as follows (in thousands):

	Year Ended December 31, 2019
Revenue recognized according to the current period performance that was included in the contract liability at the beginning of the period	$ 884

The following table includes estimated revenue expected to be recognized in the future related to performance obligations that are unsatisfied or partially unsatisfied as of December 31, 2019 (in thousands):

Collaborator	Transaction Price Allocated to the Remaining Performance Obligation as of December 31, 2019	Expected Year By Which Revenue Recognition Will Be Completed	Percentage of Revenue Recognized
BMS and Pfizer - 2016 agreement	$ 451	2021	96%
Daiichi Sankyo - 2014 agreement	673	2021	98%
Daiichi Sankyo - 2016 agreement	2,355	2025	86%
Bayer - 2016 agreement	1,697	2025	90%
Total	$ 5,176		

Milestone payments or refundable advance payments that are not considered probable of being achieved are excluded from the transaction price until they are probable.

Sales-based royalties, including milestone payments based on the level of sales, related to license arrangements are excluded from variable consideration and will be recognized at the later of (a) when the related sales occur, or (b) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any royalty revenue resulting from any of our licensing arrangements.

BMS and Pfizer

Agreement Terms

In January 2014, we entered into an agreement with BMS and Pfizer to further study Andexxa as a reversal agent for their jointly-owned, U.S. FDA-approved oral Factor Xa inhibitor, apixaban, through Phase 3 studies (the "2014 BMS and Pfizer Agreement"). We are responsible for the cost of conducting this clinical study.

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 Andexxa in Japan (the "2016 BMS and Pfizer Agreement"). 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 Factor Xa 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% to 15% on net sales of Andexxa in Japan.

Revenue Recognition

We assessed the 2014 BMS and Pfizer Agreement and the 2016 BMS and Pfizer Agreement in accordance with ASC 606 and concluded that BMS and Pfizer are customers.

For the 2014 BMS and Pfizer Agreement, we determined that the duration of the contract began on the effective date in January 2014 and ends upon Andexxa approval in the United States and Europe, which was achieved in 2019. All the performance obligations under this agreement were delivered and we recognized all related revenues by the first quarter of 2019. For the years ended December 31, 2019, 2018, and 2017, we recognized less than $0.1 million, $1.5 million, and $1.8 million, respectively, as license and collaboration revenue under the 2014 BMS and Pfizer Agreement.

For the 2016 BMS and Pfizer Agreement, we determined that the duration of the contract begins on the effective date in February 2016 and ends upon estimated completion of the Andexxa Phase 4 expansion clinical trial in Japan.

We determined that the transaction price of the 2016 BMS and Pfizer Agreement was $10.6 million as of December 31, 2019 which includes routine updates for estimated costs that BMS and Pfizer will incur in developing Andexxa in Japan. In determining the transaction price, we evaluated all the payments to be received during the duration of the contract. As of December 31, 2019, the transaction price included a $15.0 million upfront payment, $5.0 million for acceptance of the Japan New Drug Application ("JNDA") in Japan, as management expects it to be probable of achievement, $4.3 million of estimated variable consideration for cost-sharing payments from BMS and Pfizer for agreed upon research and development services for clinical trials outside of Japan, and $0.7 million for the cost of Andexxa clinical supply provided to BMS and Pfizer for Andexxa Phase 4 expansion clinical trial in Japan. Our transaction price is reduced by $14.4 million for estimated payments to be made to BMS and Pfizer for costs they will incur in developing Andexxa in Japan. Regulatory approval milestones were fully constrained and therefore are not included in the transaction price, as the receipts of such milestones are outside of our control. In determining whether to constrain other milestones, we considered numerous factors, including whether receipt of the milestones is within our control, contingent upon success in future clinical trials and/or the licensee's efforts. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to BMS and Pfizer and therefore have also been excluded from the transaction price. We will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

For the year ended ended December 31, 2019, we recognized a $1.1 million reversal of license and collaboration revenue under the 2016 BMS and Pfizer Agreement and recorded $4.8 million as deferred revenue under contract liabilities as of December 31, 2019 on our Consolidated Balance Sheets.

For the year ended December 31, 2018, we recognized $0.8 million as license and collaboration revenue under the 2016 BMS and Pfizer Agreement and recorded $6.3 million as deferred revenue under contract liabilities as of December 31, 2018 on our Consolidated Balance Sheets.

For the year ended December 31, 2017, we recognized $3.1 million as license and collaboration revenue under the 2016 BMS and Pfizer Agreement.

Daiichi Sankyo, Inc. ("Daiichi Sankyo")

Agreement Terms

In July 2014, we entered into an agreement with Daiichi Sankyo to study the safety and efficacy of Andexxa as a reversal agent to edoxaban, in our Phase 3 and Phase 4 studies (the "2014 Daiichi Sankyo Agreement"). 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 manufacture and supply Andexxa 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 Andexxa as a reversal agent to edoxaban by the FDA and the 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 Andexxa. 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.

In March 2016, we entered into an agreement with Daiichi Sankyo 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 Andexxa in Japan with BMS and Pfizer (the "2016 Daiichi Sankyo Agreement"). 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.

Revenue Recognition

We assessed the 2014 Daiichi Sankyo Agreement as amended in October 2016 and the 2016 Daiichi Sankyo Agreement in accordance with ASC 606 and concluded that Daiichi Sankyo is a customer.

For the 2014 Daiichi Sankyo Agreement, we determined that the duration of the contract begins on the effective date in July 2014 and ends upon Andexxa approval as a reversal agent to edoxaban in the United States and Europe, which we expect to be achieved in 2021. The contract duration is defined as the period in which parties to the contract have present enforceable rights and obligations. We analyzed the impact of Daiichi Sankyo's terminating the agreement prior to Andexxa approval and determined that there were substantive non-monetary penalties to Daiichi Sankyo for doing so. We considered quantitative and qualitative factors to reach this conclusion.

We determined that the transaction price of the 2014 Daiichi Sankyo Agreement and October 2016 amendment of this agreement was $34.0 million as of December 31, 2019. In order to determine the transaction price, we evaluated all the payments to be received during the duration of the contract. As of December 31, 2019, the transaction price included $22.0 million of upfront payments and $12.0 million in milestones already received upon achievement of specified events. As of December 31, 2019, we had $5.5 million of further milestone payments eligible to be included in the transaction price but have determined that achievement of these milestones is not probable and therefore constrained. As part of our evaluation of the constraint, we considered numerous factors, including whether receipt of the milestones is outside of our control and/or contingent upon success in a future clinical trial. We will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

For the year ended December 31, 2019, we recognized $0.9 million as license and collaboration revenue under the combined 2014 Daiichi Sankyo Agreement and October 2016 amendment and recorded $0.7 million as deferred revenue under contract liabilities as of December 31, 2019 on our Consolidated Balance Sheets. There were no costs incurred to obtain or fulfill the contract.

For the year ended December 31, 2018, we recognized $2.9 million, as license and collaboration revenue under the combined 2014 Daiichi Sankyo Agreement and October 2016 amendment and recorded $1.4 million as Unbilled - collaboration and license revenue as of December 31, 2018 on our Consolidated Balance Sheets. There were no costs incurred to obtain or fulfill the contract.

For the year ended December 31, 2017, we recognized $6.4 million as license and collaboration revenue under the combined 2014 Daiichi Sankyo Agreement and October 2016 amendment.

For the 2016 Daiichi Sankyo Agreement, we determined that the transaction price of the 2016 Daiichi Sankyo Agreement was $16.4 million as of December 31, 2019 which includes routine updates for estimated reimbursable costs to be incurred in future periods. In order to determine the transaction price, we evaluated all the payments to be received during the duration of the contract. As of December 31, 2019, the transaction price included $5.0 million of upfront payment and $4.5 million of estimated variable consideration for cost-sharing payments from Daiichi Sankyo for agreed upon research and development services incurred and to be incurred outside of Japan including the ESS-study, and $6.9 million of estimated variable consideration for cost-sharing payments from Daiichi Sankyo associated with the development of Andexxa in Japan. As of December 31, 2019, we had $10.0 million of further regulatory milestone payments eligible for achievement, however, regulatory milestones have been fully constrained and thus are not included in the transaction price. In determining whether to constrain these milestones, we considered numerous factors, including whether receipt of the milestones is within our control and/or contingent upon success in future clinical trials. We will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

For the year ended December 31, 2019, we recognized $2.4 million as license and collaboration revenue under the 2016 Daiichi Sankyo Agreement and recorded $1.6 million as Unbilled - collaboration and license revenue as of December 31, 2019 on our Consolidated Balance Sheets. None of the costs to obtain or fulfill the contract were capitalized.

For the year ended December 31, 2018, we recognized $3.5 million as license and collaboration revenue under the 2016 Daiichi Sankyo Agreement and recorded $3.1 million as Unbilled - collaboration and license revenue as of December 31, 2018 on our Consolidated Balance Sheets. None of the costs to obtain or fulfill the contract were capitalized.

For the year ended December 31, 2017, we recognized $1.1 million as license and collaboration revenue under the 2016 Daiichi Sankyo Agreement.

Bayer Pharma, AG (“Bayer”) and Janssen Pharmaceuticals, Inc. (“Janssen”)

Agreement Terms

In January 2014, we entered into an agreement with Bayer and Janssen to study Andexxa as a reversal agent to rivaroxaban in our Phase 3 studies and to seek regulatory approval in the United States and Europe (the “2014 Bayer and Janssen Agreement”). We are responsible for the costs associated with this agreement.

Revenue Recognition

We assessed the 2014 Bayer and Janssen Agreement in accordance with ASC 606 and concluded that Bayer and Janssen are customers.

For the 2014 Bayer and Janssen Agreement, we determined that the duration of the contract begins on the effective date of the 2014 Bayer and Janssen Agreement and ends upon Andexxa approval in the United States and Europe for rivaroxaban, which was achieved in 2019. All the performance obligations under this agreement were delivered and we recognized all related revenues by the first quarter of 2019.

For the year ended December 31, 2019, we recognized less than $0.1 million as license and collaboration revenue under the 2014 Bayer and Janssen Agreement. None of the costs to obtain or fulfill the contract were capitalized.

For the year ended December 31, 2018, we recognized $4.1 million as license and collaboration revenue under the 2014 Bayer and Janssen Agreement and recorded $2.0 million as Unbilled - collaboration and license revenue as of December 31, 2018 on our consolidated balance sheets. None of the costs to obtain or fulfill the contract were capitalized.

For the year ended December 31, 2017, we recognized $5.4 million as license and collaboration revenue under the 2014 Bayer and Janssen Agreement.

Bayer Pharma, AG ("Bayer")

Agreement Terms

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 Andexxa in Japan with BMS and Pfizer (the "2016 Bayer Agreement"). 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.

We are obligated to provide research and development services, to provide clinical drug supply and related manufacturing services and to provide regulatory approval services in exchange for an upfront nonrefundable fee of $5.0 million. We are also eligible to receive, one payment of $10.0 million which is payable upon the initial regulatory approval for Andexxa for rivaroxaban in Japan. The $10.0 million payment will be reduced to $7.0 million if Japanese regulatory approval is attained based only upon the ESS Study results.

Revenue Recognition

We assessed the 2016 Bayer Agreement in accordance with ASC 606 and concluded that Bayer is a customer.

We determined that the transaction price of the 2016 Bayer Agreement was $16.4 million as of December 31, 2019 which includes routine updates for estimated reimbursable costs to be incurred in future periods. In order to determine the transaction price, we evaluated all the payments to be received during the duration of the contract. As of December 31, 2019, the transaction price included a $5.0 million upfront payment, $4.5 million of estimated variable consideration for cost-sharing payments from Bayer for agreed upon research and development services incurred and to be incurred outside of Japan including the ESS-study and $6.9 million of estimated variable consideration for cost-sharing payments from Bayer associated with the development of Andexxa in Japan. As of December 31, 2019, we had $10.0 million of further regulatory milestone payments eligible for achievement, however, regulatory milestones have been fully constrained and thus are not included in the transaction price. In determining whether to constrain these milestones, we considered numerous factors, including whether receipt of the milestones is within our control and/or contingent upon success in future clinical trials. We will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

For the year ended December 31, 2019, we recognized $2.7 million as license and collaboration revenue under the 2016 Bayer Agreement and recorded $2.2 million as Unbilled - collaboration and license revenue as of December 31, 2019 on our Consolidated Balance Sheets. There were no costs incurred to obtain or fulfill the contract.

For the year ended December 31, 2018, we recognized $3.4 million as license and collaboration revenue under the 2016 Bayer Agreement and have recorded $3.5 million as Unbilled - collaboration and license revenue as of December 31, 2018 on our Consolidated Balance Sheets. There were no costs incurred to obtain or fulfill the contract.

For the year ended December 31, 2017, we recognized $1.0 million as license and collaboration revenue under the 2016 Bayer and Janssen Agreement.

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. During the year ended December 31, 2017, we recognized $3.8 million in revenue under this agreement as we completed our obligations under these deliverables. There was no revenue recognized in 2019 and 2018.

Refer to Note 7 “Asset Acquisition and License Agreements” for discussion regarding sublicensing fees due to Astellas Pharma, Inc. (“Astellas”) resulting from this agreement.

4. Fair Value Measurements

Financial assets and liabilities are recorded at fair value. The carrying amounts of our trade and other receivables, receivables from collaborations, prepaid and other current assets, accounts payable, accrued research and development and accrued and other liabilities 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 in the sale of 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.

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 or a discounted cash flow model and are included as a component of other long-term liabilities on our 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, and as remeasurement gain or loss on embedded derivatives liabilities in our consolidated statements of cash flows. The assumptions used in the Monte Carlo simulation model or the discounted cash flow model include: (1) our estimates of both the probability and timing of regulatory approval of Andexxa and other related events; (2) the probability-weighted net sales of Andexxa; (3) our risk-adjusted discount rate that includes a company specific risk premium; (4) our cost of debt; (5) volatility; and (6) the probability of a change in control occurring during the term of the note.

Our liability-classified Lonza AG (“Lonza”) award, consisting of their first purchase right of our common stock, was measured at fair value using a Black-Scholes model until the settlement date during the first quarter of 2019. Changes in the fair value of the liability-classified Lonza award were recognized as research and development expense in our consolidated statements of operations. The assumptions used in the Black-Scholes model include: (1) expected risk free rate; (2) expected volatility; and (3) expected dividend yield rate. See Note 6, "Contract Manufacturing Agreement" for further information.

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.

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

		December 31, 2019				December 31, 2018			
	Fair Value Hierarchy	Amortized Cost	Unrealized Gain	Unrealized (Loss)	Estimated Fair Value	Amortized Cost	Unrealized Gain	Unrealized (Loss)	Estimated Fair Value
Money market funds	Level 1	$ 23,826	$ —	$ —	$ 23,826	$ 19,500	$ —	$ —	$ 19,500
Corporate notes and commercial paper	Level 2	284,410	9	(20)	284,399	166,363	1	(205)	166,159
U.S. Treasury bills and government agency securities	Level 2	96,196	48	(1)	96,243	110,270	1	(81)	110,190
		$ 404,432	$ 57	$ (21)	$ 404,468	$ 296,133	$ 2	$ (286)	$ 295,849

	December 31, 2019				December 31, 2018			
Classified as:	Amortized Cost	Unrealized Gain	Unrealized (Loss)	Estimated Fair Value	Amortized Cost	Unrealized Gain	Unrealized (Loss)	Estimated Fair Value
Cash equivalents	$ 153,453	$ —	$ —	$ 153,453	$ 117,837	$ 1	$ (2)	$ 117,836
Short-term investments	214,029	35	(10)	214,054	178,296	1	(284)	178,013
Long-term investments	36,950	22	(11)	36,961	—	—	—	—
	$ 404,432	$ 57	$ (21)	$ 404,468	$ 296,133	$ 2	$ (286)	$ 295,849

At December 31, 2019, the remaining contractual maturities of available-for-sale securities classified as short-term investments were less than one year. At December 31, 2019, the remaining contractual maturities of available-for-sale securities classified as long-term investments were more than one year, but less than two years. There have been no significant realized losses on available-for-sale securities for the periods presented. We do not intend to sell the investments with unrealized losses at December 31, 2019, and it is not more likely than not that we will be required to sell those investments with unrealized losses before recovery of their amortized cost bases, which may be maturity. 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, 2019 and December 31, 2018.

Level 3 liabilities are comprised of embedded derivative liabilities as described in Note 8, “Long Term Obligations” and includes a liability-classified Lonza award that was settled in the first quarter of 2019. The estimated fair value of the Notes, long term royalty-based debt and long term debt are discussed in Note 8, "Long Term Obligations". The following table sets forth a summary of the changes in the estimated fair value of our embedded derivative liabilities and Lonza award during the year ended December 31, 2019 (in thousands):

	Embedded derivative liabilities	Lonza award	Total
Balance as of December 31, 2018	$ 2,497	$ 9,201	$ 11,698
Net change in the fair value	(2,931)	5,824	2,893
Addition of derivative related to 2019 Secured Term Loan	4,300	—	4,300
Settlement of Lonza award	—	(15,025)	(15,025)
Balance as of December 31, 2019	$ 3,866	$ —	$ 3,866

5. Balance Sheet Components

Inventories

Inventories consisted of the following (in thousands):

	December 31, 2019	December 31, 2018
Raw materials	$ 9,504	$ 279
Work in process	49,307	14,395
Finished goods	1,386	2,844
Total inventories	$ 60,197	$ 17,518
Balance Sheet Classification		
Inventories	$ 4,101	$ 7,873
Inventories, noncurrent portion	56,096	9,645
Total inventories	$ 60,197	$ 17,518

We began capitalizing inventory for costs associated with Andexxa Gen 1 and Gen 2 supply upon FDA approval on May 3, 2018 and December 31, 2018, respectively. We began capitalizing inventory for costs associated with Bevyxxa during the fourth quarter of 2018 when it was determined that the inventory had a probable future economic benefit. As of December 31, 2019 and 2018, long-term inventories of $56.1 million and $9.6 million, respectively are classified as prepaid and other long-term assets as these inventories are not expected to be sold within the next twelve months, and the amount is deemed recoverable.

As of December 31, 2019 and 2018, we have made prepayments to manufacturers for the purchase of inventories. We classify prepayments to manufacturers as short or long-term assets based on whether the related inventories are expected to be utilized in the manufacturing process and/or sold within the next twelve months. As of December 31, 2019 and 2018, long-term prepaid manufacturing assets of $4.7 million and $10.9 million, respectively, are classified as prepaid and other long-term assets.

We recorded an excess and obsolescence inventory charge of $17.8 million and $12.6 million to cost of sales during 2019 and 2018, respectively. In developing our inventory reserve estimate, we consider forecasted demand, current inventory levels and our firm purchase commitments. If it is determined that inventory utilization will further diminish based on estimates of demand compared to product expiration, additional inventory write-downs may be required. See Note 14, "Costs from Wind Down of Bevyxxa Activities" for additional details of charges recorded in 2019 related to the planned wind down of the Bevyxxa project.

Property and Equipment

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

	December 31, 2019	December 31, 2018
Computer equipment	$ 1,546	$ 1,335
Capitalized software	1,940	1,322
Equipment	8,600	8,737
Leasehold improvements and others	8,304	8,143
Total acquisition costs	20,390	19,537
Less accumulated depreciation and amortization	(16,126)	(14,301)
Property and equipment, net	$ 4,264	$ 5,236

Accrued and Other Liabilities

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

	December 31, 2019	December 31, 2018
Manufacturing related	$ 11,485	$ 5,465
Compensation and employee benefits	16,099	10,794
Product revenue reserves	7,680	329
Current portion of lease liabilities	4,715	—
Accruals for sponsorship	4,433	—
Others	5,361	5,722
Total accrued and other liabilities	$ 49,773	$ 22,310

6. Contract Manufacturing Agreement

Lonza Manufacturing Services Agreement

In August 2017, we executed a Manufacturing Services Agreement with Lonza AG ("Lonza") to develop a second manufacturing site and to continue to develop our Gen 2 manufacturing process for Andexxa bulk drug substance and to manufacture commercial supply. The manufacturing commitments included therein were contingent upon marketing approval by either the FDA or the EMA of Andexxa manufactured under the Gen 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 $1.00 per share, contingent upon certain events.

The first purchase right was earned by Lonza upon the FDA approval of the Gen 2 process on December 31, 2018 and after Lonza commenced process transfer activities to an additional new facility in the first quarter of 2019. During the first quarter of 2019, Lonza exercised their right to purchase 500,000 shares of our common stock at $1.00 per share. We marked to market the liability-classified award up to the settlement date using the valuation assumptions described in Note 4, "Fair Value Measurements" and recognized $5.8 million of non-employee stock based compensation expense classified as research and development expense during the first quarter of 2019.

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 second purchase rights is capped at the lesser of either: (1) 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 such purchase right is earned by Lonza, or (2) 500,000 shares. As of December 31, 2019, we have not recognized any expense for the second purchase right because the related performance conditions include a regulatory approval condition and regulatory approvals are not considered probable until actually achieved.

7. 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.

During 2019, the exclusive license agreement signed in September 2016 was formally terminated, and SRX Cardio was deconsolidated from our consolidated financial statements as of September 30, 2019. As such, during 2019, we recorded (1) a full impairment charge of $3.2 million related to the in-process research and development intangible asset, which was recorded in research and development expense, and (2) a gain of $2.3 million for the de-recognition of the contingent milestone payable to SRX Cardio associated with the licensed hypercholesterolemia program, which was recorded in net loss attributable to noncontrolling interest in our consolidated financial statements. In addition, upon deconsolidation, we recorded a loss of $76 thousand which was measured as a difference between the carrying amount of noncontrolling interest in SRX and the carrying amount of SRX's net assets. There was no fair value associated with consideration received or any retained noncontrolling

interest in SRX upon the deconsolidation. In addition, our discontinuance of the hypercholesterolemia program from SRX was not a development that represented a significant strategic shift that has a material impact on our operations and financial results. As such, the deconsolidation of SRX was not presented as a discontinued operation in our consolidated financial statements for 2019.

Astellas Pharma, Inc. ("Astellas")

In 2010, we amended and restated our original license agreement with Astellas which was 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 2017, 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, 2018 and 2017, respectively, associated with our payment obligation to Astellas. There was no research and development expense incurred during 2019 because we did not earn any associated milestone from Dermavant during 2019.

8. Long Term Obligations

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"). We may reduce the repayment amount to $62.5 million if such amount is paid by December 31, 2023. The use of funds is restricted to development activities needed for regulatory approval of Andexxa by the FDA and the EMA as provided 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 Andexxa in the United States and the EU.

The upfront cash receipt of $50.0 million is recorded as Notes payable at issuance. We are accruing for interest over the term of the Notes. The carrying values of the Notes payable includes accrued interest of $10.7 million and $7.6 million at December 31, 2019 and 2018, respectively.

Our payment obligations for BMS and Pfizer Promissory Notes are as follows (in thousands):

	December 31, 2019	December 31, 2018
Total repayment obligations	$ 62,500	$ 62,500
Less: interest to be accreted in future periods	(5,565)	(8,643)
Less: payments made	(5,374)	(497)
Carrying value of notes payable	51,561	53,360
Less: current portion of royalties	(8,461)	(5,062)
Non-current portion of notes payable	$ 43,100	$ 48,298

We evaluated the features of the Notes and determined that certain features require acceleration of payments such as pursuant to a change of control. 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 4, "Fair Value Measurements", to these Consolidated Financial Statements). We will remeasure the embedded derivatives to fair value each reporting period until the repayment, termination or maturity of the Notes. For the years ended December 31, 2019 and 2018, we recognized a gain of $1.6 million and a loss of $0.4 million, respectively, upon remeasurement of the embedded derivatives.

The estimated fair value of the Notes at December 31, 2019 and December 31, 2018 was $47.3 million and $53.2 million, respectively, 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 4, “Fair Value Measurements”, to these Consolidated Financial Statements.

Royalty-based Financing

In February 2017, we entered into a purchase and sale agreement (the “Royalty Sales Agreement”) with HCR whereby HCR acquired a term royalty interest in future worldwide net sales of Andexxa. We received $50.0 million upon closing and received an additional $100.0 million following the U.S. regulatory approval of Andexxa in May 2018. We are required to pay royalties to HCR based on tiered net worldwide sales of Andexxa in a range of 8.46% to 4.19%. The applicable rate decreases start when worldwide net annual sales levels are above $150.0 million. Total royalty payments are capped at 195% of the funding received less certain transaction expenses, or $290.6 million.

Upon the closing of the Royalty Sales Agreement in February 2017, we incurred a fee to HCR of $2.0 million and paid additional debt issuance costs totaling $0.6 million, which included expenses that we paid on behalf of HCR and expenses incurred directly by us. Upon the subsequent funding of $100.0 million in May 2018, we incurred fees to HCR of $5.0 million. Fees and debt issuance costs have been netted against the debt and are being amortized over the estimated term of the debt using the effective interest method.

The effective interest rate for the HCR royalty-based debt as of December 31, 2019 was 11.4%. We are accruing for interest over the term of the royalty-based debt. The carrying value of the royalty-based debt includes accrued interest of $44.4 million and $22.9 million, net of unamortized debt discount of $5.9 million and $6.8 million, at December 31, 2019 and December 31, 2018, respectively.

Our payment obligations for HCR royalty-based debt are as follows (in thousands):

	December 31, 2019	December 31, 2018
Total repayment obligations	$ 290,550	$ 290,550
Less: interest to be accreted in future periods	(104,268)	(125,851)
Less: payments made	(9,069)	(816)
Carrying value of long term royalty-based debt	177,213	163,883
Less: current portion of royalties	(14,316)	(8,627)
Non-current portion of long term royalty-based debt	$ 162,897	$ 155,256

We determined that certain features, such as the variability in the royalty payments based upon the timing of regulatory approval, were embedded derivatives that required bifurcation from the royalty-based debt instrument. Upon the Andexxa Gen 2 FDA approval on December 31, 2018, it was determined that there was no longer a derivative associated with the debt contract.

The estimated fair value of the royalty-based debt at December 31, 2019 and December 31, 2018 was $142.0 million and $154.2 million, respectively, 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 as described in Note 4, “Fair Value Measurements”, to these Consolidated Financial Statements.

Secured Term Loans

In February 2019, we entered into a credit agreement (the “Credit Agreement”) with HCR and Athyrium Opportunities III Acquisition LP (“Athyrium”) whereby we received the first tranche of $62.5 million in March 2019 and the second tranche of $62.5 million in November 2019 (collectively, “Secured Term Loans”).

All obligations under the Credit Agreement are due on February 28, 2025 with certain scheduled payments of the principal starting from March 31, 2022. The outstanding principal balance of the loans bear interest at 9.75% per annum. The loans are secured by substantially all of our assets. The Credit Agreement contains certain covenants that, among others, require us to deliver financial reports at designated times of the year and limit or restrict our ability to incur additional indebtedness or liens, acquire, own or make any investments, pay cash dividends or enter into certain corporate transactions, including mergers and changes of control, and require us to maintain $50.0 million of cash. Violating covenants would put us in default and the lenders would then have the option to demand repayment plus certain penalties or allow us to continue to service the Secured Term Loans, but at the default interest rate of 12.75%. As of December 31, 2019, we were not in violation of any covenants.

For the year ended December 31, 2019, we accrued interest of $6.3 million and we paid in cash interest of $5.6 million under the Secured Term Loans. Upon the closing of the Credit Agreement, we incurred fees of $2.8 million to HCR and Athyrium and other debt issuance cost of $0.5 million. Loan origination fees and debt issuance costs are netted against the loan balance and are amortized over the contractual term of the loan using the effective interest method. The weighted average effective interest rate was 11.5% as of December 31, 2019.

The future principal maturities of our Secured Term Loans for each of the next five years are as follows (in thousands):

Year ended December 31,	
2022	$ 19,231
2023	19,231
2024	19,231
Thereafter	67,307
Total	$ 125,000

We evaluated the terms of the loans and determined that one feature could require acceleration of payments and a prepayment penalty (make-whole provision) upon a change of control if it occurs prior to the 30-month anniversary period from the funding date in March 2019. We determined that this feature (embedded derivative) requires bifurcation from the debt instrument and fair value recognition. We determined the fair value of the derivative using a discounted cash flow model taking into account the probability of a change of control occurring and potential repayment amounts and timing of such payments that would result under various scenarios, as further described in Note 4, “Fair Value Measurements”, to these Consolidated Financial Statements. We will remeasure the embedded derivative to fair value each reporting period until the make-whole provision lapses 30 months after the funding date of March 2019. For the year ended December 31, 2019, we recognized a gain of $1.4 million upon remeasurement of the embedded derivatives.

The estimated fair value of long-term debt at December 31, 2019 was $123.7 million, and the fair value was measured using Level 3 inputs. The estimated fair market value was calculated using a discounted cash flow model with inputs consistent with those used in determining the embedded derivative values as described in Note 4, “Fair Value Measurements” to these Consolidated Financial Statements.

9. 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 $94.5 million, $101.7 million and $41.8 million, for services to be performed in 2020, 2021, and 2022, 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 2023. The facility lease agreement, as amended, contains scheduled rent increases over the lease term. Lease expense was $3.6 million, $2.1 million and $1.8 million for the years ended December 31, 2019, 2018 and 2017, respectively. Our future minimum commitments under our non-cancelable operating leases are disclosed in Note 13, "Leases" to these consolidated financial statements.

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.

Contingencies

While there are no material legal proceedings we are aware of, there is one matter described below, and we may become party to various additional claims and complaints arising in the ordinary course of business. Management does not believe that any ultimate liability resulting from any of these claims will have a material adverse effect on its results of operations, financial position, or liquidity. However, management cannot give any assurance regarding the ultimate outcome of these claims, and their resolution could be material to operating results for any particular period, depending upon the level of income for the period.

We recognize accruals for such actions to the extent that we conclude that a loss is both probable and reasonably estimable. We accrue for the best estimate of a loss within a range; however, if no estimate in the range is better than any other, then we accrue the minimum amount in the range. If we determine that a loss is reasonably possible and the loss or range of loss can be estimated, we disclose the possible loss. Unless otherwise noted, it is not possible to determine the outcome of these matters, and we cannot reasonably estimate the maximum potential exposure or the range of possible loss. We did not recognize any accruals for the action described below in our Consolidated Balance Sheets as of December 31, 2019 and 2018, as we did not believe losses were probable.

Legal Proceedings

On January 16, 2020, a stockholder filed a putative class action against the Company and certain officers (the "Defendants") in the U.S. District Court for the Northern District of California, captioned *Hayden v. Portola Pharmaceuticals, Inc., et al.,* No. 3:20-cv-00367-VC (N.D. Cal.). On February 7, 2020, another stockholder filed a related putative class action against Defendants, captioned *McCutcheon v. Portola Pharmaceuticals, Inc., et al.*, No. 3:20-cv-00949 (N.D. Cal.).

The stockholder plaintiffs allege that the Defendants violated the antifraud provisions of the Securities Exchange Act by making misrepresentations and omissions in public disclosures concerning the Company's sales of andexanet alfa, marketed as Andexxa in the United States and Ondexxya in Europe, between May 8, 2019 and January 9, 2020. Specifically, plaintiffs allege that the Defendants made materially false and/or misleading statements about the demand for Andexxa, and usage of Andexxa by hospitals and healthcare organizations. Plaintiffs also allege that the Defendants made materially false and/or misleading statements about the Company's accounting for its reserve for returns, and that the Defendants failed to disclose that the Company was shifting from a short-dated version of Andexxa to a longer-dated version, impacting the reserve for returns and impacting revenue for the Company. The Plaintiffs contend that the alleged fraud was revealed on January 9, 2020, when the Company announced its preliminary unaudited financial results for the fourth quarter of 2019. A lead plaintiff has not yet been appointed, and the Company has not yet responded to the complaints.

The plaintiffs seek to recover unspecified monetary relief, interest, and attorneys' fees and costs. Given the early stage of these proceedings, we cannot presently predict the likelihood of obtaining dismissal of the case, nor can we estimate the possible loss or range of loss at this time.

10. Stock-Based Compensation

Equity Incentive Plan

In January 2013, our Board of Directors adopted our 2013 Equity Incentive Plan ("2013 Plan"), which became effective upon the closing of our IPO in May 2013. As of December 31, 2019, we are authorized to issue 21,628,351 shares of common stock under the 2013 Plan. The 2013 Plan had 6,640,145 shares of common stock available for future issuance as of December 31, 2019, 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 to employees, officers, directors and consultants.

In July 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). In December 2018, our Board of Directors authorized an additional 1,000,000 shares under the 2017 Plan, bringing the total to 2,500,000 shares, for issuance to new employees entering into employment with Portola in accordance with NASDAQ Listing Rule 5635(c)(5). The 2017 Plan had 1,132,267 shares of common stock available for future issuance as of December 31, 2019.

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 activity under our 2013 Plan and 2017 Plan, and related information during the year ended December 31, 2019:

	Shares Subject to Outstanding Options	Weighted-Average Exercise Price Per Share
Balance at December 31, 2018	7,507,690	$ 33.25
Options granted	2,199,307	27.74
Options exercised	(916,157)	21.32
Options canceled	(1,242,404)	38.62
Balance at December 31, 2019	7,548,436	$ 32.21

Additional information related to the status of stock options at December 31, 2019, is as follows (aggregate intrinsic value in thousands):

	Shares	Weighted-Average Exercise Price Per Share	Weighted-Average Remaining Contractual Life	Aggregate Intrinsic Value
Outstanding	7,548,436	$ 32.21	6.64	$ 5,913
Vested	4,361,497	$ 32.75	5.33	$ 4,514

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, 2019. The aggregate intrinsic value of stock options exercised was $7.5 million, $11.6 million and $39.3 million for the years ended December 31, 2019, 2018 and 2017, respectively, and was calculated as the difference between the exercise price of the stock options and the fair value of our common stock on the date of exercise.

The weighted-average grant date fair value of employee stock options granted during the years ended December 31, 2019, 2018 and 2017 was $16.01, $21.01 and $24.08 per share, respectively. The total estimated grant date fair value of stock options vested during the years ended December 31, 2019, 2018 and 2017 was $29.8 million, $30.6 million and $23.0 million, respectively.

We recognized stock-based compensation expenses of $28.7 million, $29.7 million and $25.5 million in 2019, 2018 and 2017 respectively relating to the employee stock options. As of December 31, 2019, total unamortized employee stock-based compensation was $51.8 million, which is expected to be recognized over the remaining estimated vesting period of 2.6 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 were fully vested by the fourth quarter of 2018 when regulatory approval of Andexxa was achieved and when the manufacturing goal related to our lead programs was met in 2017. A portion of the PSOs granted in May 2016 were forfeited and cancelled when regulatory approval of Andexxa was not achieved by the fourth quarter of 2017. In March 2019, the Compensation Committee of our Board of Directors approved a program to award up to 490,986 PSOs to the management team based on the achievement of a net revenue goal for 2019.

We recognized stock-based compensation expense of $1.3 million, $0 million and $2.3 million in 2019, 2018 and 2017, respectively, relating to these PSOs. The aggregate intrinsic value of PSOs exercised for the years ended December 31, 2019, 2018 and 2017 was $0.2 million, $0.2 million and $0.4 million, respectively. The weighted-average grant date fair value of the

PSOs granted during 2019 was $19.27. As of December 31, 2019, total unamortized stock-based compensation related to PSOs was $1.8 million.

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

	Shares Subject to Outstanding PSOs	Weighted-Average Exercise Price Per Share
Balance at December 31, 2018	143,335	$ 23.76
Options granted	490,986	33.29
Options exercised	(35,624)	23.76
Options canceled	(46,687)	33.29
Balance at December 31, 2019	552,010	$ 31.43

Additional information related to the status of PSOs at December 31, 2019, is as follows (aggregate intrinsic value in thousands):

	Shares	Weighted-Average Exercise Price Per Share	Weighted-Average Remaining Contractual Life	Aggregate Intrinsic Value
Outstanding	552,010	$ 31.43	7.78	$ 34
Vested	107,711	$ 23.76	3.00	$ 34

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 RSUs	Weighted-Average Grant Date Fair Value Per Share
Balance at December 31, 2018	979,278	$ 34.00
RSUs granted	882,646	27.86
RSUs released	(401,393)	33.62
RSUs canceled	(186,314)	34.02
Balance at December 31, 2019	1,274,217	$ 29.86

Additional information related to the status of RSUs at December 31, 2019, is as follows (aggregate intrinsic value in thousands):

	Shares	Weighted-Average Remaining Contractual Life	Aggregate Intrinsic Value
Outstanding	1,274,217	1.16	$ 30,428

The total grant date fair value of RSUs vested during the years ended December 31, 2019, 2018 and 2017 was $13.5 million, $8.0 million and $6.0 million, respectively. The weighted-average grant date fair value of RSUs granted during the years ended December 31, 2019, 2018 and 2017 was $27.86, $37.6 and $27.15 per share respectively.

We recognized stock-based compensation expenses of $13.8 million, $11.3 million and $8.1 million in the years ended December 31, 2019, 2018 and 2017, respectively, relating to these RSUs. As of December 31, 2019, there was $26.5 million of unrecognized compensation costs related to these RSUs, which is expected to be recognized over an estimated weighted-average period of 1.96 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 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. In March 2018, the Compensation Committee of our Board of Directors approved a program to award up to 102,600 PSUs to the management team based on the achievement of certain regulatory and net revenue goals.

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

	Shares Subject to Outstanding PSUs	Weighted-Average Grant Date Fair Value Per Share
Balance at December 31, 2018	153,503	$ 29.85
PSUs granted	—	—
PSUs released	(52,670)	28.29
PSUs canceled	(88,908)	30.4
Balance at December 31, 2019	11,925	32.66

Additional information related to the status of PSUs at December 31, 2019, is as follows (aggregate intrinsic value in thousands):

	Shares	Weighted-Average Remaining Contractual Life	Aggregate Intrinsic Value
Outstanding	11,925	0.03	$ 285

The total grant date fair value of PSUs vested in 2019, 2018 and 2017 was $1.5 million, $5.7 million and $2.1 million, respectively. The weighted-average grant date fair value of PSUs granted in 2019, 2018 and 2017 was zero, $32.66 and $25.54 per share, respectively.

We recognized stock-based compensation expenses of $0.2 million, $2.7 million and $2.4 million in the years ended December 31, 2019, 2018 and 2017, respectively, relating to these PSUs. As of December 31, 2019, there was less than $0.1 million of unrecognized compensation costs related to these PSUs, which is expected to be recognized over an estimated weighted-average period of 0.03 years.

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, 2019, 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. Since 2015, the Board of Directors has annually elected to completely forego the automatic share increases available under the ESPP. The ESPP had 1,345,549 shares of common stock available for future issuance as of December 31, 2019. 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 22,600, 37,000 and 50,000 shares with average exercise prices of $27.10, $45.16 and $38.14 per share, respectively, during the years ended December 31, 2019, 2018, and 2017, respectively. These options vest upon grant or various terms up to four years. We recognized non-employee stock compensation expense of $2.2 million, $2.9 million and 3.9 million during the years ended December 31, 2019, 2018 and 2017, respectively for these non-employee awards. 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.

Stock-Based Compensation

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

	Year Ended December 31,		
	2019	2018	2017
Research and development	$ 19,340	$ 27,694	$ 19,779
Selling, general and administrative	32,735	28,712	23,505
Stock-based compensation expense included in total expenses	$ 52,075	$ 56,406	$ 43,284
			—
Capitalized stock-based compensation costs	$ (1,657)	$ (1,046)	$ —

Stock-based compensation capitalized into inventory is recognized as cost of sales when the related product is sold.

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). 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,		
	2019	2018	2017
Risk-free interest rate			
Stock options	1.39% - 2.56%	2.55% - 3.03%	1.70% - 2.27%
Performance stock options	2.43%	—	—
ESPP	1.89% - 2.52%	1.10% - 2.28%	0.47% - 1.10%
Expected term			
Stock options	5.0 - 6.1 years	5.0 - 6.1 years	5.0 - 6.1 years
Performance stock options	6.0 years	—	—
ESPP	0.5 years	0.5 years	0.5 years
Expected volatility			
Stock options	59% - 61%	59% - 62%	60% - 65%
Performance stock options	61%	—	—
ESPP	43% - 67%	49% - 65%	61% - 80%
Dividend yield			
Stock options	—	—	—
Performance stock options	—	—	—
ESPP	—	—	—

Contingently issuable shares to Lonza are discussed in Note 6, "Contract Manufacturing Agreement" to these Consolidated Financial Statements.

11. 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,		
	2019	2018	2017
Stock options to purchase Common Stock	7,548,436	7,507,690	6,514,538
Performance stock options	552,010	143,335	164,783
Restricted stock units	1,274,217	979,278	600,334
Performance stock units	11,925	153,503	304,754
Employee stock purchase plan	76,036	96,219	32,325
Common stock warrants	1,500	1,500	1,500

12. 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 matched employee contributions up to a maximum of 3% of employee salary for the years ended December 31, 2019, 2018 and 2017. During the years ended December 31, 2019, 2018 and 2017, we recognized total expense of $1.7 million, $1.3 million and $0.9 million, respectively, relating to these contributions.

13. Leases

We have operating leases for our office facilities. We renewed one operating lease for our office facilities in June 2019. Upon adoption of ASC 842, we did not elect to apply the hindsight expedient in evaluating our renewal option, and as such, we did not include the renewal period in our lease term because at the inception we were not reasonably certain that we would exercise the renewal option. Our lease agreements do not contain any material residual value guarantees or material restrictive covenants.

Our operating lease right-of-use asset and liability were recognized at the adoption date of ASC 842 based on the present value of lease payments over the remaining lease term at the adoption date. In determining the net present value of lease payments, we used our incremental borrowing rate based on the information available, including remaining lease term, at the adoption date of ASC 842.

Upon the renewal of the operating lease in June 2019, we remeasured the lease liability to reflect the changes to the lease term and the lease payments using a discount rate at the date of remeasurement on the basis of the remaining lease term and the remaining lease payments. We recognized the remeasurement amount of the lease liability as an adjustment to the lease right-of-use asset. This resulted in an $11.1 million increase to the lease liability and the lease right-of-use asset at the remeasurement date in June 2019.

The components of lease expense are as follows (in thousands):

	Year Ended December 31, 2019
Operating lease costs	$ 3,224
Short-term lease cost	356
Total	$ 3,580

Cash flow information related to leases are as follows (in thousands):

	Year Ended December 31, 2019
Cash paid for amounts included in the measurement of lease liabilities:	
Operating cash flows from operating leases	$ 3,003
Supplemental non-cash information:	
Right-of-use asset obtained in exchange for lease obligation due to remeasurement	$ 11,103
Right-of-use assets obtained in exchange for new operating lease liabilities	$ 1,432

Supplemental balance sheet information related to leases are as follows (in thousands):

	Classification	As of December 31, 2019
Operating leases		
Lease right-of-use assets		
Non-current	Operating lease right-of-use assets	$ 12,064
Lease liabilities		
Current	Accrued and other liabilities	$ 4,715
Non-current	Long-term portion of lease liabilities	$ 8,850
Weighted Average Remaining Lease Term		
Operating leases		3.1 years
Weighted Average Discount Rate		
Operating leases		6.55%

As of December 31, 2019, the maturity of our lease liabilities were as follows (in thousands):

Year ending December 31,	Operating Leases
2020	4,908
2021	4,937
2022	4,713
2023	1,188
Total lease payments	15,746
Less imputed interests	(2,181)
Total lease liabilities	$ 13,565

14. Costs from Wind Down of Bevyxxa Activities

Following the approval of Andexxa in May 2018, we made the business decision to focus our resources on the launch of Andexxa and significantly scaled back our commercial efforts on Bevyxxa. Throughout 2019, we engaged with potential business collaborators for Bevyxxa, and in the fourth quarter of 2019, we determined that it was unlikely that we will find a viable partner. Accordingly, we have begun to wind down Bevyxxa operations to eliminate future operational and financial obligations. Accordingly, we recorded a charge of $27.5 million as cost of sales which is comprised of an excess and obsolescence inventory charge of $13.7 million, a write-off of a long-term prepaid manufacturing asset of $7.8 million, an impairment charge for an intangible asset related to a payment made to Takeda of $3.7 million, and an accrual of firm purchase commitments of $2.3 million which we expect to settle in the next twelve months.

15. Income Taxes

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

	Year Ended December 31,	
	2019	2018
Current:		
Federal	$ —	$ —
State	—	—
Foreign	—	—
	—	—
Deferred:		
Federal	$ —	$ —
State	—	—
Foreign	—	—
	—	—
Total provision for income taxes	$ —	$ —

We did not record an income tax expense for 2019, 2018 and 2017. The effective tax rate of our provision for income taxes differs from the federal statutory rate as follows:

	Year Ended December 31,		
	2019	2018	2017
Federal statutory income tax rate	21.0 %	21.0 %	34.0 %
Federal and state credits	3.2 %	7.4 %	8.9 %
Excess tax benefit	0.3 %	0.4 %	8.6 %
Stock based compensation	(2.5)%	(0.8)%	0.1 %
U.S. tax on foreign earnings	(0.2)%	— %	— %
Other	(0.5)%	(0.6)%	(0.1)%
Tax impact due to tax rate reduction	— %	— %	(47.7)%
Change in valuation allowance	(19.8)%	(24.1)%	2.6 %
Foreign rate differential	(1.5)%	(3.3)%	(6.4)%
Total tax provision	0.0 %	0.0 %	0.0 %

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

	December 31,	
	2019	2018
Deferred tax assets:		
Federal and state net operating loss carryforwards	$ 285,685	$ 241,881
Federal and state research tax credit carryforwards	24,782	23,917
Federal Orphan Drug Credit	112,802	120,273
Deferred revenue	44,588	29,530
Stock options	20,893	19,992
Inventories	10,617	4,350
Operating lease liabilities	3,146	—
Other	7,861	5,098
Total deferred tax assets	510,374	445,041
Deferred tax liabilities:		
Operating lease right-of-use assets	(2,793)	—
Total deferred tax liabilities	(2,793)	—
Net deferred tax assets before valuation allowance	507,581	445,041
Valuation allowance	(507,581)	(445,041)
Net deferred tax assets	$ —	$ —

We received orphan drug designation and were eligible to claim a federal orphan drug credit starting in 2015 and reported the credit in 2019, 2018, 2017, and 2016. On December 22, 2017, President Donald Trump signed into U.S. law the Tax Reform Act. The new law limits the orphan drug credit to 25% of qualified clinical testing expenses for the tax year effective for amounts paid or incurred in tax years beginning after 2017.

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 increased by approximately $62.5 million for the year ended December 31, 2019. The valuation allowance decreased by approximately $82.1 million for the year ended December 31, 2018.

As of December 31, 2019, we had net operating loss carryforwards for federal income tax purposes of approximately $1,225.5 million. Of the federal net operating loss carryforwards, $868.1 million will expire in the period from 2027 to 2037, and $357.4 million will carryforward indefinitely. We also have federal research tax credits of approximately $19.3 million and orphan drug credit of $132.7 million, which expire at various dates in the period from 2024 to 2039. Lastly, we have California net operating loss carry forwards of approximately $208.0 million which expire at various dates in the period from 2020 to 2039 and California research tax credits of approximately $12.0 million, which can be carried forward indefinitely. Our federal and state net operating loss carryforwards as of December 31, 2019 include amounts resulting from exercises and sales of stock option awards to employees and non-employees.

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 with the exception of State of Washington. We are no longer subject to audit by the Internal Revenue Service for income tax returns filed before 2017, and by the material state and local tax authorities for tax returns filed before 2016. 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,		
	2019	2018	2017
Unrecognized tax benefits, beginning of period	$ 25,421	$ 20,730	$ 13,865
Increases due to current period positions	1,875	4,879	7,046
Increase due to prior period positions	22	26	—
Decreases due to prior period positions	(3,017)	(214)	(181)
Unrecognized tax benefits, end of period	$ 24,301	$ 25,421	$ 20,730

The amount of unrecognized income tax benefits that, if recognized, would affect our effective tax rate was $0 as of December 31, 2019 and December 31, 2018. If the $24.3 million and $25.4 million of unrecognized income tax benefits as of December 31, 2019 and 2018, 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, 2019 and 2018.

On December 22, 2017, the Tax Cuts and Jobs Act (the "Tax ACT") was enacted into law, which significantly changes existing U.S. tax law and includes many provisions applicable to us, such as reducing the U.S. federal statutory tax rate and adopting a territorial tax system. The Tax Act reduced the U.S. federal statutory tax rate from 35% to 21% effective January 1, 2018.

The Tax Act also includes a provision referred to as Global Intangible Low-Taxed Income ("GILTI") which generally imposes a tax on foreign income in excess of a deemed return on tangible assets. The FASB guidance issued in January, 2018 allows companies to make an accounting policy election to either (i) account for GILTI as a component of tax expense in the period in which the tax is incurred (the "period cost method"), or (ii) account for GILTI in the measurement of deferred taxes (the "deferred method"). We elect to account for the tax effects of this provision using the period cost method.

Our foreign entities started to have earnings in 2019 and our accumulated undistributed foreign earnings as of December 31, 2019 have been subject to the current year income inclusion under subpart F or GILTI regime for U.S. tax purposes. If we were to make actual distributions of some or all of these earnings, we would generally incur no additional U.S. income tax but could incur U.S. state income tax and foreign withholding taxes. We are evaluating whether future undistributed foreign earnings would be permanently re-invested or not and have not accrued for these potential U.S. state income tax and foreign withholding taxes. However, any additional tax associated with the distribution of these earnings would be immaterial.

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 necessary to present fairly the unaudited quarterly results of operations set forth herein.

	2019				2018			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Product revenue, net	$ 20,362	$ 27,164	$ 35,743	$ 28,375	$ 606	$ 2,265	$ 7,176	$ 14,070
Collaboration and license revenue	1,807	1,260	1,056	873	6,038	1,746	7,001	1,228
Operating expenses	(95,768)	(92,384)	(80,381)	(119,391)	(91,944)	(107,706)	(83,321)	(102,479)
Net loss	(78,096)	(68,477)	(49,627)	(96,676)	(84,510)	(105,971)	(71,177)	(88,886)
Net loss (income) attributable to noncontrolling interest (SRX Cardio)	(60)	2,273	—	—	332	(223)	(126)	338
Net loss attributable to Portola	(78,156)	(66,204)	(49,627)	(96,676)	(84,178)	(106,194)	(71,303)	(88,548)
Net loss per share attributable to Portola common stockholders:								
Basic and diluted	$ (1.17)	$ (0.97)	$ (0.68)	$ (1.24)	$ (1.28)	$ (1.61)	$ (1.08)	$ (1.34)

17. Subsequent Event

Restructuring Plan

In February 2020, we undertook an organizational realignment to focus our resources on the maximizing the Andexxa/ Ondexxya commercial opportunity which included a reduction in headcount in order to conserve resources.

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, 2019. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2019, 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, 2019.

Our independent registered public accounting firm, Ernst & Young LLP, has audited the effectiveness of our internal control over financial reporting as of December 31, 2019 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, 2019 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

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, 2019, 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, 2019, 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 2019 consolidated financial statements of the Company and our report dated February 28, 2020, 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
February 28, 2020

ITEM 9B. OTHER INFORMATION

None.

PART III

Certain information required by Part III is omitted from this annual report on Form 10-K and is incorporated herein by reference to our definitive Proxy Statement for our 2019 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, 2019.

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 "Information about our Executive Officers" in our Proxy Statement. Information regarding Section 16 reporting compliance is incorporated by reference to the information set forth in the section entitled "Delinquent Section 16(a) Reports" 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 Part II, Item 8 of this Annual Report on Form 10-K.

(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.

		Incorporation By Reference			
Exhibit Number	**Exhibit Description**	**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	Certificate of Amendment to the Portola Pharmaceuticals, Inc. Amended and Restated Certificate of Incorporation	8-K	001-35935	3.1	6/11/2018
3.3	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*	Description of securities of Portola Pharmaceuticals, Inc. registered under Section 12 of the Exchange Act				
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	11/6/2013
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	11/6/2013
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	11/6/2013
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 Amendment dated February 27, 2019	10-Q	001-35935	10.3	5/8/2019
10.4+	Form of Executive Severance Benefits Agreement (amends and restates Form of 2006 Executive Change in Control Severance Benefits Agreement)	8-K	001-35935	10.4	10/12/2018
10.5+	Amended Non-Employee Director Compensation Policy.	10-Q	001-35935	10.5	8/7/2019
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
10.14	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
10.19+	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
10.24+	Market Based Performance Stock Unit Award Grant Notice—2013 Equity Incentive Plan.	10-Q	001-35935	10.33	8/9/2016
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. Amended and Restated Inducement Plan and Amendment dated February 27, 2019	10-Q	001-35935	10.28	5/8/2019
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+	Amended and Restated Non-Employee Director Compensation Policy	10-Q	001-35935	10.5	5/10/2018
10.41+	Offer Letter by and between Portola Pharmaceuticals, Inc. and John B. Moriarty dated January 18, 2018	10-Q	001-35935	10.41	8/9/2018
10.42+	Offer Letter by and between Portola Pharmaceuticals, Inc. and Glenn Brame dated June 8, 2018	10-Q	001-35935	10.42	8/9/2018
10.43+	Offer Letter by and between Portola Pharmaceuticals, Inc. and Scott Garland, dated September 10, 2018	8-K	001-35935	10.43	9/20/2018
10.45+	Form of Executive Severance Benefits Agreement	8-K	001-35935	10.4	10/12/2018

10.46	Credit Agreement by and between Portola Pharmaceuticals, Inc. (the Borrower), certain domestic subsidiaries of the Borrower (the Guarantors), HCR Collateral Management, LLC (the Administrative Agent), and Healthcare Royalty Partners III, L.P., Athyrium Opportunities III Acquisition LP, HCRP Overflow Fund, L.P., HCR Molag Fund, L.P., and HealthCare Royalty Partners IV, L.P. (collectively, the Lenders), dated February 28, 2019	10-K	001-35935	10.46	3/1/2019
10.47†	Manufacturing Services Agreement by and between Lonza AG and Portola Pharmaceuticals, Inc., effective as of August 15, 2017	10-Q	001-35935	10.47	5/8/2019
10.48+	Offer Letter by and between Portola Pharmaceuticals, Inc. and Ernie Meyer dated June 26, 2018	10-Q	001-35935	10.48	5/8/2019
10.49+	Offer Letter by and between Portola Pharmaceuticals, Inc. and Sheldon Koenig dated January 17, 2019	10-Q	001-35935	10.49	5/8/2019
10.51	Sixth Amendment to Lease dated June 28, 2019	10-Q	001-35935	10.51	8/7/2019
10.52	Amendment No. 1 to Credit Agreement, dated August 15, 2019, to the Credit Agreement, dated February 28, 2019	10-Q	001-35935	10.52	11/5/2019
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	Inline XBRL Instance Document. (2)				
101.SCH	Inline XBRL Taxonomy Extension Schema Document. (2)				
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document. (2)				
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document. (2)				
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document. (2)				
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document. (2)				
104	Cover Page Interactive Data File, formatted in Inline XBRL (included as Exhibit 101)				

† Certain confidential information contained in this document, marked by brackets, is omitted because it is both (i) not material and (ii) would be competitively harmful if publicly disclosed.

\+ 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 28th day of February 2020.

PORTOLA PHARMACEUTICALS, INC.

By: /s/ Scott Garland

Scott Garland
President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Scott Garland 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 / SCOTT GARLAND Scott Garland	Chief Executive Officer and Director (Principal Executive Officer)	February 28, 2020
/ S / MARDI C. DIER Mardi C. Dier	Chief Financial Officer (Principal Financial and Accounting Officer)	February 28, 2020
/ S / HOLLINGS C. RENTON Hollings C. Renton	Chairman of the Board of Directors	February 28, 2020
/ S / JEFFREY W. BIRD, M.D., Ph.D. Jeffrey W. Bird, M.D., Ph.D.	Director	February 28, 2020
/ S / LAURA A. BREGE Laura A. Brege	Director	February 28, 2020
/ S / DENNIS FENTON, Ph.D. Dennis Fenton, Ph.D.	Director	February 28, 2020
/ S / JOHN H. JOHNSON John H. Johnson	Director	February 28, 2020
/ S / TED W. LOVE, M.D. Ted W. Love, M.D.	Director	February 28, 2020
/ S / DAVID C. STUMP, M.D. David C. Stump, M.D.	Director	February 28, 2020
/ S / H. WARD WOLFF H. Ward Wolff	Director	February 28, 2020

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Corporate Information

EXECUTIVE TEAM

Scott Garland
President and Chief Executive Officer

Glenn Brame
Executive Vice President, Chief Technical Operations Officer

Mardi C. Dier
Executive Vice President, Chief Financial Officer and Chief Business Officer

Sheldon Koenig
Executive Vice President, Chief Commercial Officer

Ernie Meyer
Executive Vice President, Chief Human Resources Officer

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

Rajiv Patni, M.D.
Executive Vice President, Chief Medical Officer

BOARD OF DIRECTORS

Hollings C. Renton
Chairman of the Board

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

Scott Garland
President and Chief Executive Officer

John H. Johnson
Former Chief Executive Officer, Melinta Therapeutics

Ted Love, M.D.
President and Chief Executive Officer, Global Blood Therapeutics

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
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.

Portola Pharmaceuticals, Inc.

270 E. Grand Avenue
South San Francisco, CA 94080
650.246.7000
650.246.7376
IR@portola.com
www.portola.com

Transfer Agent

American Stock Transfer & Trust Company
6201 15th Avenue
Brooklyn, NY 11219
www.amstock.com
800.937.5449
info@amstock.com

Corporate Counsel

Cooley LLP
3175 Hanover Street
Palo Alto, CA 94304
650.843.5000

Annual Meeting

June 12, 2020, at 9:00 a.m. PT
Portola Pharmaceuticals, Inc.
270 E. Grand Avenue
South San Francisco, CA 94080

Portola Pharmaceuticals
270 E. Grand Avenue,
South San Francisco, CA 94080

MAIN +1.650.246.7000
FAX +1.650.246.7376

@Portola_Pharma
Portola Pharmaceuticals

portola.com