

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

or

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

For the transition period from \_\_\_\_\_ to \_\_\_\_\_

Commission File Number: 001-35703

PUMA BIOTECHNOLOGY, INC.

(Exact name of registrant as specified in its charter)

Delaware  
(State or other jurisdiction of  
incorporation or organization)

77-0683487  
(I.R.S. Employer  
Identification No.)

10880 Wilshire Boulevard, Suite 2150

Los Angeles, CA 90024

(424) 248-6500

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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

<u>Title of each class</u>	<u>Trading symbol</u>	<u>Name of each exchange on which registered</u>
Common Stock, par value \$0.0001 per share	PBYI	The NASDAQ Stock Market LLC (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 emerging growth company. See the 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	<input type="checkbox"/>	Accelerated filer	<input checked="" type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

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 to 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 voting stock held by non-affiliates of the registrant was approximately \$427.6 million as of June 28, 2019, based upon the closing price of \$12.71 per share of the registrant's common stock on the NASDAQ Global Select Market on Friday, June 28, 2019, the last business day of the registrant's most recently completed second fiscal quarter. Shares of common stock held by each executive officer, director and holder of 10% or more of the outstanding common stock have been excluded in that such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes. As of February 20, 2020, there were 39,301,587 shares of the registrant's common stock outstanding.

Documents Incorporated by Reference:

Portions of the Proxy Statement for the registrant's 2020 Annual Meeting of Stockholders, or the 2020 Proxy Statement, are incorporated by reference into Part III of the Form 10-K to the extent stated herein.

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## CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions, future events or performance are not historical facts and may be forward looking. These forward-looking statements include, but are not limited to, statements about:

- the commercialization of NERLYNX® (neratinib);
- the development of our drug candidates, including when we expect to undertake, initiate and complete clinical trials of our product candidates;
- the anticipated timing of regulatory filings;
- the regulatory approval of our drug candidates;
- our use of clinical research organizations and other contractors;
- our ability to find collaborative partners for research, development and commercialization of potential products;
- efforts of our sub-licensees to obtain regulatory approval and commercialize NERLYNX in areas outside the United States;
- our ability to market any of our products;
- our expectations regarding our costs and expenses;
- our anticipated capital requirements and estimates regarding our needs for additional financing;
- our ability to compete against other companies and research institutions;
- our ability to secure adequate protection for our intellectual property;
- our intention and ability to vigorously defend against any litigation to which we are or may become party;
- our estimates for damages that we may be required to pay in connection with the class action lawsuit to which we are a party;
- our ability to attract and retain key personnel; and
- our ability to obtain adequate financing.

These statements are often, but not always, made through the use of words or phrases such as “anticipate,” “estimate,” “plan,” “project,” “continuing,” “ongoing,” “expect,” “believe,” “intend” and similar words or phrases. Accordingly, these statements involve estimates, assumptions and uncertainties that could cause actual results to differ materially from those expressed in them. Discussions containing these forward-looking statements may be found throughout this Annual Report, including the sections entitled “Item 1. Business” in Part I and “Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations” in Part II of this Annual Report. These forward-looking statements involve risks and uncertainties, including the risks discussed in the section entitled “Item 1A. Risk Factors” in Part I of this Annual Report that could cause our actual results to differ materially from those in the forward-looking statements. We undertake no obligation to update the forward-looking statements or to reflect events or circumstances after the date of this document, except as required by law. The risks discussed in this Annual Report should be considered in evaluating our prospects and future financial performance.

## PART I

### ITEM 1. BUSINESS

#### Company Overview

*Unless otherwise provided in this Annual Report, references to the “Company,” “we,” “us,” and “our” refer to Puma Biotechnology, Inc., a Delaware corporation formed on April 27, 2007 and formerly known as Innovative Acquisitions Corp., together with its wholly-owned subsidiaries, Puma Biotechnology Ltd and Puma Biotechnology B.V., and all references to “Former Puma” refer to Puma Biotechnology, Inc., a privately-held Delaware corporation formed on September 15, 2010, that merged with and into us in October 2011. We refer to this transaction as the “Merger.”*

We are a biopharmaceutical company with a focus on the development and commercialization of innovative products to enhance cancer care. We in-license from Pfizer, Inc. or Pfizer, the global development and commercialization rights to PB272 (neratinib, oral), PB272 (neratinib, intravenous) and PB357. Neratinib is a potent irreversible tyrosine kinase inhibitor, or TKI, that blocks signal transduction through the human epidermal growth factor receptors, HER1, HER2 and HER4. Currently, we are primarily focused on the development and commercialization of the oral version of neratinib, and our most advanced drug candidates are directed at the treatment of HER2-positive breast cancer and HER2 mutated cancers. We believe neratinib has clinical application in the treatment of several other cancers as well, including other tumor types that over-express or have a mutation in HER2, such as breast cancer, cervical cancer, lung cancer or other solid tumors.

Prior to 2017, our efforts and resources had been focused primarily on acquiring and developing our pharmaceutical technologies, raising capital and recruiting personnel. In 2017, the United States Food and Drug Administration, or FDA, approved NERLYNX, formally known as PB272 (neratinib (oral)), for the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer following adjuvant trastuzumab-based therapy. We currently market NERLYNX in the United States using our direct specialty sales force consisting of approximately 80 sales specialists. Our sales specialists are supported by an experienced sales leadership team consisting of regional managers, and our commercial team of experienced professionals in marketing, access and reimbursement, managed markets, marketing research, commercial operations and sales force planning and management. In 2018, the European Commission, or EC, granted marketing authorization for NERLYNX in the European Union for the extended adjuvant treatment of adult patients with early stage hormone receptor positive HER2-overexpressed/amplified breast cancer and who are less than one year from the completion of prior adjuvant trastuzumab-based therapy.

We license the commercial rights to our current drug candidates from Pfizer, which had previously been responsible for the clinical trials regarding neratinib. Going forward, we expect to augment our product pipeline by acquiring, through license or otherwise, additional drug candidates for research and development, and potential commercialization. Our decision to acquire a drug candidate will also depend on our evaluation of the scientific merits of the underlying technology, the costs of the transaction and other economic terms of any proposed license, the amount of capital that we anticipate will be required to develop the drug candidate and the economic potential of the drug candidate if approved for commercialization. We believe this strategy minimizes our clinical development risk and allows us to accelerate the development and potential commercialization of current and future drug candidates.

We have entered into exclusive sub-license agreements with various parties to pursue regulatory approval, if necessary, and commercialize NERLYNX, if approved, in numerous regions outside the United States, including Europe (excluding Russia and Ukraine), Canada, China, Southeast Asia, and various countries and territories in Central and South America. We plan to continue to pursue commercialization of NERLYNX in other countries outside the United States, if approved.

Breast cancer is the leading cause of cancer death among women worldwide. Studies show that approximately 20% to 25% of breast cancer tumors have an over-expression of the HER2 protein. Women with breast cancer that over-expresses HER2, referred to as HER2-positive breast cancer, are at greater risk for disease progression and death than women whose tumors do not over-express HER2. Therapeutic strategies, such as the use of trastuzumab (marketed as Herceptin), pertuzumab (marketed as Perjeta) and T-DM1 (marketed as Kadcyla), each produced by Genentech, and lapatinib (marketed as Tykerb) produced by Novartis, given either alone or in combination with chemotherapy, have been developed to improve the treatment of this type of breast cancer by binding to the HER2 protein. There are a number of trials ongoing that involve various combinations of these drugs. Based on pre-clinical studies and clinical trials to date, we believe that neratinib may offer an advantage over existing treatments by more potently inhibiting HER2 at a different site and using a different mechanism than these other drugs.

In December 2016, we initiated a managed access program for neratinib. Managed access programs provide physicians and patients access to medicines when there are limited or no other therapeutic options available. Our managed access program for neratinib enables participation from countries outside the United States, including European Union member states, where permitted by applicable rules, procedures and regulatory authorities. The program provides access to neratinib for the treatment of early stage HER2-positive breast cancer (extended adjuvant setting), HER2-positive metastatic breast cancer and HER2-mutated solid tumors. In order for patients to qualify for our managed access program they must be unable to participate in any ongoing neratinib clinical trial. Patients in the managed access program are given neratinib and are instructed to take a prophylaxis during treatment to manage neratinib-related diarrhea, which consists of high dose loperamide and budesonide. We have partnered with Caligor Opco LLC, which specializes in early access to medicines, to oversee the managed access program for neratinib.

On February 25, 2020, the FDA approved our supplemental New Drug Application, or sNDA, for neratinib in combination with capecitabine for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting. The sNDA approval was based on results of our Phase III clinical trial of PB272 that we refer to as the NALA trial. In addition to continuing to follow the patients from the ExteNET trial, which was our Phase III clinical trial of neratinib for the extended adjuvant treatment of early stage HER2-positive breast cancer, as well as patients from the NALA trial, we are actively conducting the following trials to evaluate the safety and efficacy of neratinib in various indications:

- a Phase II clinical trial of neratinib for the extended adjuvant treatment of patients with early stage HER2-overexpressed/amplified breast cancer who have received prior adjuvant trastuzumab (Herceptin)-based therapy in which patients are given either: 1) antidiarrheal prophylaxis including loperamide alone or in combination with budesonide or other agents or 2) escalating doses of neratinib during the first month (dose escalation) in order to prevent and reduce the neratinib-related diarrhea;
- a Phase II clinical trial of neratinib in combination with the drug ado-trastuzumab emtansine (T-DM1, Kadcyła) in patients with HER2-positive metastatic breast cancer that has metastasized to the brain;
- a Phase II clinical trial of neratinib monotherapy or in combination with the drug trastuzumab and or other anticancer drugs in the treatment of patients with HER2-negative cancers that have a HER2 mutation; and
- a Phase II clinical trial of neratinib monotherapy in the treatment of solid tumors that have an activating EGFR exon 18, or HER4 mutation.

## Strategy

Our primary objectives are to build neratinib into a significant oncology franchise as a single agent, and potentially in combination with other therapies, and potentially to in-license or acquire additional drug candidates. The following elements comprise our strategy to achieve these objectives:

- *Successfully execute our NERLYNX commercial plan.* An important near-term objective is to continue to execute our NERLYNX commercial plan by driving market penetration and duration of therapy consistent with the current NERLYNX label. We continue to focus our efforts on commercializing NERLYNX in the United States. In addition, we have entered into exclusive sub-license agreements with various parties to pursue regulatory approval, if necessary, and commercialize NERLYNX, if approved, in additional countries worldwide.
- *Continue to advance the development of neratinib for the treatment of other HER2-positive or HER2 mutated breast cancer indications.* We are primarily focused on developing neratinib for the treatment of patients with HER2-positive breast cancer or HER2-negative cancers with a HER2 mutation.
- *Expand our product pipeline by pursuing additional applications of neratinib.* We believe there are additional applications for neratinib in the treatment of patients with HER2-negative cancers who have a HER2 mutation; and in tumor types where HER2 is over-expressed or mutated. We intend to further evaluate the safety and efficacy of neratinib for treating these cancers.
- *In-license or acquire additional drug candidates and technologies in order to build a sustainable product pipeline by employing multiple therapeutic approaches and disciplined decision criteria based on clearly defined proof of principal goals.* We seek to build a sustainable product pipeline by employing multiple therapeutic approaches and by acquiring drug candidates belonging to known drug classes. In addition, we employ disciplined decision criteria to assess drug candidates. A decision by us to license a drug candidate will depend on a variety of factors, including the scientific merits of the technology; the costs of the transaction and other economic terms of the proposed license; the amount of capital required to develop the technology; and the economic potential of the drug candidate, should it be commercialized. We believe this strategy minimizes our clinical development risk and allows us to accelerate the development and potential commercialization of current and future drug candidates.

- *Evaluate the commercialization strategies on a product-by-product basis in order to maximize the value of each.* We are currently commercializing NERLYNX using a direct sales force in the United States and using out-licenses in certain countries outside of the United States. As we move additional drug candidates through development toward regulatory approval, we plan to evaluate several options for each drug candidate's commercialization strategy. These options include building our own internal sales force; entering into a joint marketing partnership with another pharmaceutical or biotechnology company, whereby we jointly sell and market the product; and out-licensing our product, whereby another pharmaceutical or biotechnology company sells and markets our product and pays us a royalty on sales. Our decision may be different for each product that reaches commercialization and will be based on a number of factors including capital necessary to execute on each option, size of the market to be addressed and terms of potential offers from other pharmaceutical and biotechnology companies.

## **Breast Cancer Overview**

Breast cancer is the leading cause of cancer death among women worldwide, with approximately 1 million new cases reported each year and more than 400,000 deaths per year. Approximately 20% to 25% of breast cancer tumors show over-expression of the HER2 protein. Women with breast cancer that over-expresses HER2 are at greater risk for disease progression and death than women whose tumors do not over-express HER2. Therapeutic strategies have been developed to block HER2 in order to improve the treatment of this type of breast cancer.

Trastuzumab, pertuzumab, lapatinib and T-DM1 are all drugs that bind to the HER2 protein and thereby cause the cells to cease reproducing. Today, these drugs are used as single agents, in combination with other drugs and in combination with chemotherapy to treat patients with HER2-positive breast cancer at various stages.

Currently, the only treatment approved by the FDA for the treatment of neoadjuvant (newly diagnosed) HER2-positive breast cancer is the combination of pertuzumab plus trastuzumab and taxane chemotherapy. The FDA-approved treatments for the adjuvant treatment of HER2-positive early stage breast cancer is either the combination of pertuzumab plus trastuzumab and chemotherapy, or Kadcyla, which is approved specifically in patients with HER2-positive early stage breast cancer with residual disease after neoadjuvant treatment. We are also aware of a Phase III clinical trial that is comparing trastuzumab plus pertuzumab plus taxane following anthracyclines versus T-DM1 plus pertuzumab following anthracyclines as an adjuvant therapy.

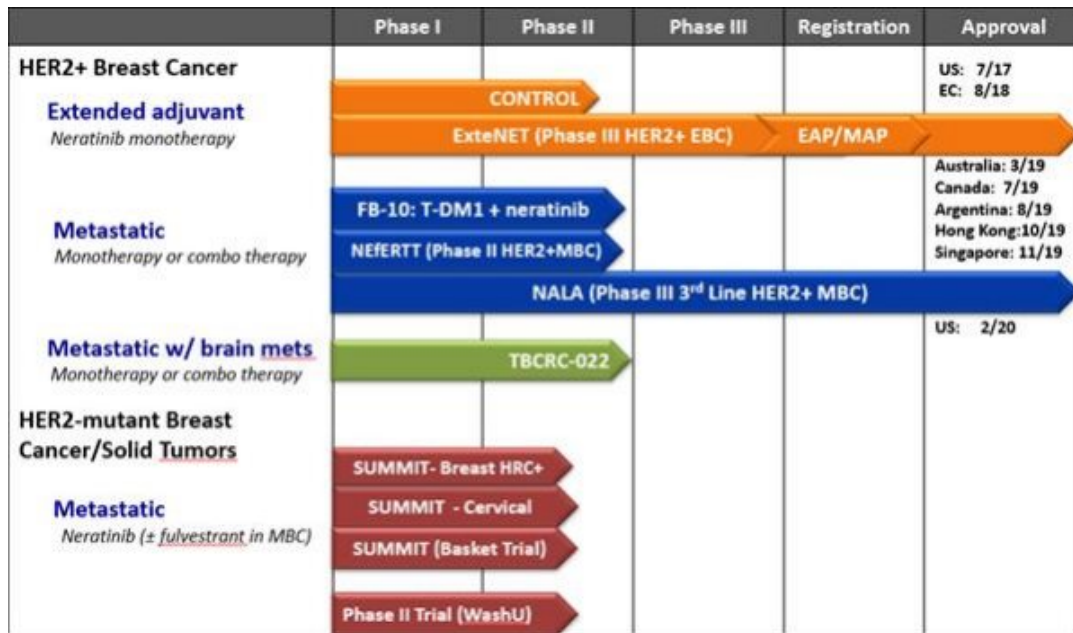
Trastuzumab and pertuzumab given in combination with taxane chemotherapy is the current first-line standard of care for HER2-positive metastatic breast cancer. Lapatinib (Tykerb), given in combination with the chemotherapy drug capecitabine, is also FDA-approved for the treatment of patients who have failed prior treatments. In a Phase II clinical trial, lapatinib demonstrated a median PFS of eight to nine weeks and a response rate of 5 – 7%. In a Phase III clinical trial, patients with HER2-positive metastatic breast cancer who received the combination of lapatinib plus capecitabine demonstrated a median progression free survival of 27.1 weeks and a response rate of 23.7%. In the Phase III EMILIA trial, the combination of lapatinib plus capecitabine demonstrated a median PFS of 25.6 weeks and a response rate of 30.8%. T-DM1 is approved by the FDA for the treatment of patients with HER2-positive metastatic breast cancer who previously received first line trastuzumab-based therapy. Unfortunately, the disease eventually progresses for most patients with HER2-positive breast cancer while on these treatments. For these reasons, there is a need for alternatives to block HER2 signaling in patients who fail treatment with prior HER2 directed treatments. Neratinib is an orally active small molecule that inhibits HER2 at a different site and uses a different mechanism than trastuzumab. As a result, we believe that neratinib may have utility in patients with HER2-positive metastatic breast cancer who have failed treatment with other HER2 inhibitors.

We believe that there are approximately 28,300 patients in the United States and 37,000 patients in the EU with early stage HER2-positive breast cancer that get treated with adjuvant treatment. We also believe that there are approximately 6,400 patients in the United States with third-line and 4,700 patients in the United States with fourth line HER2-positive metastatic breast cancer. The number of patients with third-line or later HER2 positive metastatic breast cancer may decrease in future years as the introduction of new neoadjuvant, adjuvant and extended adjuvant treatments may reduce the number of patients with recurrence of HER2 positive breast cancer and therefore reduce the number of patients with HER2 positive metastatic breast cancer.

We believe that approximately 1-12% of all cancer patients have mutation in HER2 kinase in the United States and that approximately 7 – 9% of all estrogen receptor positive metastatic breast cancer patients who have received prior endocrine treatment have a mutation in HER2 kinase (approximately 8,000 to 10,000 patients in the United States).

## **Product Development Pipeline**

The following chart shows each of our current drug candidates and their clinical development stage.



## Neratinib

Neratinib is a potent irreversible TKI that blocks signal transduction through the epidermal growth factor receptors, HER1, HER2 and HER4. Based on pre-clinical studies and clinical trials to date, we believe that neratinib may offer an advantage over existing treatments that are used in the treatment of patients with HER2-positive metastatic breast cancer who have failed prior treatments, including treatment with trastuzumab, pertuzumab, and T-DM1. Currently, the treatment of metastatic breast cancer patients involves treatment with these agents either alone or in combination with chemotherapy. We believe that by more potently inhibiting HER2 at a different site and acting via a mechanism different from other agents, neratinib may have therapeutic benefits in patients who have failed these existing treatments, most notably due to its increased selectivity and irreversible inhibition of the HER2 target enzyme.

In addition, we believe neratinib has clinical application in the treatment of other cancers, including non-small cell lung cancer and other tumor types that over-express or have a mutation in HER2.

Our initial focus is on the commercialization and development of the oral formulation of neratinib. We are also evaluating for potential development an intravenous formulation of neratinib and PB357, a back-up compound to neratinib.

### ***PB272 (neratinib oral)—Early Stage Breast Cancer***

#### *Extended Adjuvant Breast Cancer*

**Two-Year ExteNET Data.** In July 2014, we announced top line results from our ExteNET trial, a Phase III clinical trial of neratinib for the extended adjuvant treatment of early stage HER2-positive breast cancer. The data from this trial were presented in an oral presentation at the American Society of Clinical Oncology, or ASCO, Annual Meeting in June 2015 and were published online in *The Lancet Oncology* in February 2016. The ExteNET trial was a double-blind, placebo-controlled, Phase III trial of neratinib versus placebo after adjuvant treatment with Herceptin in women with early stage HER2-positive breast cancer. More specifically, the ExteNET trial enrolled 2,840 patients in 41 countries with early stage HER2-positive breast cancer who had undergone surgery and adjuvant treatment with trastuzumab. After completion of adjuvant treatment with trastuzumab, patients were randomized to receive extended adjuvant treatment with either neratinib or placebo for a period of one year. Patients were then followed for recurrent disease, ductal carcinoma in situ (DCIS), or death for a period of two years after randomization in the trial.

The safety results of the study showed that the most frequently observed adverse event for the neratinib-treated patients was diarrhea, with approximately 39.9% of the neratinib-treated patients experiencing grade 3 or higher diarrhea (one patient, 0.1%, had grade 4 diarrhea). Patients who received neratinib in this trial did not receive any prophylaxis with antidiarrheal agents to prevent the neratinib-related diarrhea. We have reported clinical data from several trials that have demonstrated that the use of high-dose prophylactic loperamide may greatly reduce the rate of grade 3 diarrhea with neratinib, with grade 3 diarrhea rates ranging from 0-17% in studies in which high-dose loperamide prophylaxis was used. We are also currently conducting an international, open-label, Phase II study (CONTROL) investigating the use of antidiarrheal prophylaxis using antidiarrheal drugs or dose escalation in the prevention and reduction of neratinib-associated diarrhea and, more specifically, grade 3 diarrhea. The interim results of this trial presented in December 2019 showed that as of the cutoff date, the incidence of grade 3 diarrhea for the 137 patients who received the loperamide prophylaxis was 31%, the incidence of grade 3 diarrhea for the 64 patients who received the combination of loperamide plus budesonide was 28%, the incidence of grade 3 diarrhea for the 136 patients who received the combination of loperamide plus colestipol was 21%, the incidence of grade 3 diarrhea for the 104 patients who received colestipol alone with loperamide as needed was 34%, and the incidence of grade 3 diarrhea for the 60 patients who used the dose escalation was 15%. See “—PB272 (neratinib, oral)—Metastatic Breast Cancer—*Safety Database*” for additional information.

The primary endpoint of the ExteNET trial was invasive disease-free survival, or DFS. The results of the trial demonstrated that treatment with neratinib resulted in a 33% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.67,  $p = 0.009$ ). The two-year DFS rate for the neratinib arm was 93.9% and the two-year DFS rate for the placebo arm was 91.6%. The secondary endpoint of the trial was disease-free survival including ductal carcinoma in situ, or DFS-DCIS. The results of the trial demonstrated that treatment with neratinib resulted in a 37% reduction of risk of disease recurrence including DCIS or death versus placebo (hazard ratio = 0.63,  $p = 0.002$ ). The two-year DFS-DCIS rate for the neratinib arm was 93.9% and the two-year DFS-DCIS rate for the placebo arm was 91.0%.

As an inclusion criteria for the ExteNET trial, patients needed to have tumors that were HER2-positive using local assessment. In addition, as a pre-defined subgroup in the trial, patients had centralized HER2 testing performed on their tumor as well. At the time the two-year data was compiled, centralized HER2 testing had been performed on 1,704 (60%) of the patients in the ExteNET trial and further central testing on available samples was currently ongoing. For the 1,463 patients whose tumors were HER2-positive by central confirmation, the results of the trial demonstrated that treatment with neratinib resulted in a 49% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.51,  $p = 0.002$ ). The two-year DFS rate for the centrally confirmed patients in the neratinib arm was 94.7% and the 2-year DFS rate for the centrally confirmed patients in the placebo arm was 90.6%. For the patients in the trial whose tumors were HER2-positive by central confirmation, the results of the trial demonstrated that treatment with neratinib resulted in a 51% reduction of risk of disease recurrence including DCIS or death versus placebo (hazard ratio = 0.49,  $p < 0.001$ ). The two-year DFS-DCIS rate for the centrally confirmed patients in the neratinib arm was 94.7% and the two-year DFS rate for centrally confirmed patients in the placebo arm was 90.2%.

For the pre-defined subgroup of patients with hormone receptor positive disease, the results of the trial demonstrated that treatment with neratinib resulted in a 49% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.51,  $p = 0.001$ ). The two-year DFS rate for the neratinib arm was 95.4% and the two-year DFS rate for the placebo arm was 91.2%. For the patients in the trial whose tumors were HER2-positive by central confirmation, the results of the trial demonstrated that treatment with neratinib resulted in a 75% reduction of risk of invasive disease recurrence or death (hazard ratio = 0.25,  $p < 0.001$ ). The two-year DFS rate for the centrally confirmed patients in the neratinib arm was 97.0% and the two-year DFS rate for centrally confirmed patients in the placebo arm was 88.4%.

Based on the results from the ExteNET trial, in June and July 2016, we submitted an MAA with the EMA and filed an NDA with the FDA, respectively, for regulatory approval of neratinib in the extended adjuvant setting, for which we have since obtained approval.

*Five-Year ExteNET Data.* In September 2017, we presented updated data from the ExteNET trial at the European Society of Medical Oncology, or ESMO, 2017 Congress in Madrid, Spain. The data represented a predefined five-year invasive disease-free survival, or iDFS, analysis as a follow-up to the primary two-year iDFS analysis of the Phase III ExteNet trial. The results of the trial demonstrated that after a median follow up of 5.2 years, treatment with neratinib resulted in a 27% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.73,  $p = 0.008$ ). The five-year iDFS rate for the neratinib arm was 90.2% and the 5-year iDFS rate for the placebo arm was 87.7%. The secondary endpoint of the trial was invasive disease-free survival including ductal carcinoma in situ, or iDFS-DCIS. The results of the trial demonstrated that treatment with neratinib resulted in a 29% reduction of risk of disease recurrence, including DCIS or death versus placebo (hazard ratio = 0.71,  $p = 0.004$ ). The five-year iDFS-DCIS rate for the neratinib arm was 89.7% and the five-year iDFS-DCIS rate for the placebo arm was 86.8%.



For the pre-defined subgroup of patients with hormone receptor positive disease, the results of the trial demonstrated that treatment with neratinib resulted in a 40% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.60,  $p = 0.002$ ). The five-year iDFS rate for the neratinib arm was 91.2% and the five-year iDFS rate for the placebo arm was 86.8%. For the pre-defined subgroup of patients with hormone receptor negative disease, the results of the trial demonstrated that treatment with neratinib resulted in a hazard ratio of 0.95 ( $p = 0.762$ ).

The results of the ExteNET trial showed that after two years of follow-up, for patients with hormone receptor positive, HER2-positive early stage breast cancer patients who were treated within one year after the completion of trastuzumab based adjuvant therapy, iDFS was 95.3% in the patients treated with neratinib compared with 90.8% in those receiving placebo (hazard ratio = 0.49; 95% CI: (0.30, 0.78);  $p=0.002$ ).

The safety results were unchanged from the primary two-year iDFS analysis of the study that showed the most frequently observed adverse event for the neratinib-treated patients was diarrhea, with approximately 39.9% of the neratinib-treated patients experiencing grade 3 or higher diarrhea (one patient, or 0.1%, had grade 4 diarrhea). Patients who received neratinib in this trial did not receive any prophylaxis with antidiarrheal agents to prevent the neratinib-related diarrhea.

### ***PB272 (neratinib, oral)—Metastatic Breast Cancer***

*Trials of Neratinib as a Single Agent.* In 2009, Pfizer presented data at the CTRC-AACR San Antonio Breast Cancer Symposium from a Phase II trial of neratinib administered as a single agent to patients with HER2-positive metastatic breast cancer. Final results from this trial were published in the Journal of Clinical Oncology in March 2010.

The trial involved a total of 136 patients, 66 of whom had received prior treatment with trastuzumab and 70 of whom had not received prior treatment with trastuzumab. The results of the study showed that neratinib was reasonably well-tolerated among both the pretreated patients and the patients who had not received prior treatment with trastuzumab. Diarrhea was the most common side effect but was manageable with antidiarrheal agents and dose modification. Efficacy results from the trial showed that the objective response rate was 24% for patients who had received prior trastuzumab treatment and 56% for patients with no prior trastuzumab treatment. Furthermore, the median PFS was 22.3 weeks for the patients who had received prior trastuzumab and 39.6 weeks for the patients who had not received prior trastuzumab.

Data from a second Phase II study, in which patients with confirmed HER2-positive metastatic breast cancer who had failed treatment with trastuzumab and taxane chemotherapy were given neratinib in combination with capecitabine, was presented at the 2011 CTRC-AACR San Antonio Breast Cancer Symposium. The results of the study showed that the combination of PB272 and capecitabine had acceptable tolerability. The efficacy results from the trial showed that for the 61 patients in the trial who had not been previously treated with the HER2 targeted anti-cancer drug lapatinib, there was an overall response rate of 64% and a clinical benefit rate of 72%. In addition, for the seven patients in the trial who had previously been treated with lapatinib, there was an overall response rate of 57% and a clinical benefit rate of 71%. The median PFS for patients who had not received prior treatment with lapatinib was 40.3 weeks and the median PFS for the patients who had received prior lapatinib treatment was 35.9 weeks.

In February 2013, we reached agreement with the FDA under an SPA for our Phase III clinical trial (PUMA-NER-1301 or the NALA trial) of neratinib in patients with HER2-positive metastatic breast cancer who have failed two or more prior treatments (third-line disease). An SPA is a written agreement between the trial's sponsor and the FDA regarding the design, endpoints, and planned statistical analysis of the Phase III trial with respect to the effectiveness of PB272 for the indication to be studied to support an NDA. The EMA also provided follow-on SA, consistent with that of the FDA regarding our Phase III trial design and endpoints used for such design to support the submission of an MAA in the EU.

Pursuant to the SPA and SA, the Phase III NALA trial was designed as a randomized controlled trial of neratinib plus capecitabine versus Tykerb® (lapatinib) plus capecitabine in patients with third-line HER2-positive metastatic breast cancer. The trial enrolled 621 patients who were randomized (1:1) to receive either neratinib plus capecitabine or lapatinib plus capecitabine. The trial was conducted globally at sites in North America, Europe, Asia-Pacific and South America. The co-primary endpoints of the trial were centrally confirmed progression free survival, or PFS, and overall survival, or OS. An alpha level of 1% was allocated to the PFS and 4% allocated to OS.

In June 2019, we announced that results from the Phase III NALA trial were presented at the American Society of Clinical Oncology (ASCO) 2019 Annual Meeting in Chicago. For the primary analysis of centrally confirmed PFS, treatment with neratinib plus capecitabine resulted in a statistically significant improvement in centrally confirmed PFS (hazard ratio=0.76,  $p=0.0059$ ) compared to treatment with lapatinib plus capecitabine. Because the hazard ratio was found to not be constant over time (i.e., the proportional hazard assumption did not hold), the statistical analysis plan for the NALA trial prespecified that a restricted means survival analysis at 24 months would be performed. In this prespecified analysis the mean PFS for the patients treated with neratinib plus capecitabine was 8.8 months and the mean PFS for the patients treated with lapatinib plus capecitabine was 6.6 months.

For the primary analyses of OS, neratinib plus capecitabine resulted in an improvement in OS that, although not statistically significant, trended numerically in favor of the neratinib plus capecitabine arm of the study (hazard ratio = 0.88, p=0.21). The median OS for the patients treated with neratinib plus capecitabine was 21.0 months and the median OS for the patients treated with lapatinib plus capecitabine was 18.7 months. In the prespecified restricted means analysis the mean OS at 48 months for the patients treated with neratinib plus capecitabine was 24.0 months and the mean OS for the patients treated with lapatinib plus capecitabine was 22.2 months.

For the secondary endpoint of time to intervention for symptomatic central nervous system disease (also referred to as brain metastases), the results of the trial showed that treatment with neratinib plus capecitabine led to an improvement over the combination of lapatinib plus capecitabine. The overall cumulative incidence of CNS metastases was 22.8% for the neratinib plus capecitabine arm and 29.2% for the lapatinib plus capecitabine arm (p=0.043). For the secondary endpoint of duration of response, neratinib plus capecitabine treatment resulted in a longer duration of response compared to lapatinib and capecitabine treatment, with a median response of 8.54 months compared to a median response of 5.55 months (HR = 0.495, p = 0.0004).

Treatment-emergent adverse events (TEAEs) were similar between arms: TEAEs leading to neratinib/lapatinib discontinuation were lower with neratinib (10.9%) than with lapatinib (14.5%). There was a higher rate of grade 3 diarrhea with neratinib plus capecitabine compared to lapatinib plus capecitabine (24.4% vs 12.5%); however, the discontinuations due to diarrhea (neratinib plus capecitabine: 2.6%, lapatinib plus capecitabine: 2.3%) were similar in both arms.

On February 25, 2020, the FDA approved our sNDA based on the results of the NALA trial for neratinib in combination with capecitabine for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting

#### *Metastatic Breast Cancer with Brain Metastases*

Approximately one-third of the patients with HER2-positive metastatic breast cancer develop metastases that spread to their brain. The current antibody-based treatments, including trastuzumab, pertuzumab and T-DM1, do not enter the brain and therefore are not believed to be effective in treating these patients. In a Phase II trial with lapatinib given as a single agent, lapatinib demonstrated a 6% objective response rate in the patients with HER2-positive metastatic breast cancer whose disease spread to their brain. In January 2012, a Phase II trial of neratinib as a single agent and in combination with the anticancer drug capecitabine in patients with HER2-positive metastatic breast cancer that has spread to their brain was initiated in conjunction with the Dana Farber Translational Breast Cancer Research Consortium. In June 2014, at the ASCO 2014 Annual Meeting, results from the first cohort (n=40) who were administered neratinib monotherapy were presented. The efficacy results from the first cohort of the trial showed that for the 40 evaluable patients, three (7.5%) patients experienced a partial response, four (10%) patients experienced prolonged stable disease for greater than or equal to six months and 12 (30%) patients experienced stable disease for less than six months. The median PFS of the 40 evaluable patients was seen to be 1.9 months and the median overall survival was seen to be 8.7 months.

In June 2017, we presented additional interim data from this trial at the ASCO 2017 Annual Meeting. The multicenter Phase II clinical trial enrolled patients with HER2-positive metastatic breast cancer who have brain metastases. The trial enrolled three cohorts of patients. Patients in the second cohort (n=5) represent patients who had brain metastases which were amenable to surgery and who were administered neratinib monotherapy prior to and after surgical resection. The third cohort (target enrollment=60) enrolled two sub-groups of patients (prior lapatinib-treated and no prior lapatinib) with progressive brain metastases who were administered neratinib in combination with the chemotherapy drug capecitabine. The oral presentation reflected only the patients in the third cohort of patients without prior lapatinib exposure (cohort 3A, n=37), who all had progressive brain metastases at the time of enrollment and who received the combination of capecitabine plus neratinib.

In cohort 3A, 30% of the patients had received prior craniotomy, 65% of the patients had received prior whole brain radiotherapy, and 35% had received prior stereotactic radiosurgery to the brain. No patients had received prior treatment with lapatinib.

The primary endpoint of the trial was CNS Objective Response Rate according to a composite criteria that included volumetric brain MRI measurements, steroid use, neurological signs and symptoms, and RECIST evaluation for non-CNS sites. The secondary endpoint of the trial was CNS response by Response Assessment in Neuro-Oncology-Brain Metastases, or RANO-BM, criteria. The efficacy results from the trial showed that 49% of patients experienced a CNS Objective Response by the composite criteria. The results also showed that the CNS response rate using the RANO-BM criteria was 24%. The median time to CNS progression was 5.5 months and the median overall survival was 13.5 months, though 49% of patients remain alive and survival data are immature.

The results for cohort 3A showed that the most frequently observed severe adverse event for the 37 patients evaluable for safety was diarrhea. Patients received antidiarrheal prophylaxis consisting of high dose loperamide, given together with the combination of capecitabine plus neratinib for the first cycle of treatment in order to try to reduce the neratinib-related diarrhea. Among the 37 patients evaluable for safety, 32% of the patients had grade 3 diarrhea and 41% had grade 2 diarrhea.

In April 2018, we announced that NERLYNX (neratinib) has been included as a recommended treatment option in the latest National Comprehensive Cancer Network, or NCCN, Clinical Practice Guidelines in Oncology Central Nervous System Cancers for Breast Cancer patients with brain metastases. The NCCN designated NERLYNX in combination with capecitabine as a category 2B treatment option and NERLYNX in combination with paclitaxel as a category 2B treatment option. Use, as designated for breast cancer patients with brain metastases, is outside the FDA-approved indication for NERLYNX and considered investigational, and we do not market or promote NERLYNX for these uses.

*Safety Database.* Our safety database includes over 3,000 patients who have been treated with neratinib. To date, the most significant grade 3 or higher adverse event associated with neratinib has been diarrhea, which occurs in approximately 30% of patients receiving the drug. Historically, once diarrhea occurred, patients were treated with loperamide and/or a reduction in the dose of neratinib.

In February 2015, we initiated a Phase II open-label trial of neratinib monotherapy for one year in 120 patients with early HER2-positive breast cancer who have completed one year of adjuvant trastuzumab, or the CONTROL trial. The CONTROL trial is an international, open-label, Phase II study investigating the use of loperamide prophylaxis with or without other agents in the reduction of neratinib-associated diarrhea that has a primary endpoint of the incidence of grade 3 diarrhea. In the CONTROL trial, patients with HER2-positive early stage breast cancer who had completed trastuzumab-based adjuvant therapy received neratinib daily for a period of one year.

In December 2019, interim results from the CONTROL trial were presented at the 2019 CTRC-AACR San Antonio Breast Cancer Symposium.

The interim analysis of the trial presented in the poster included a total of 137 patients who received neratinib plus loperamide prophylaxis, 64 patients who received neratinib plus loperamide prophylaxis for two cycles and budesonide for one cycle, 136 patients who received neratinib plus loperamide prophylaxis for one cycle and colestipol for one cycle, 104 patients who received colestipol prophylaxis for one cycle and loperamide as needed and 60 patients who were treated with a dose escalation approach which involved treating with neratinib at 120 mg per day for the first week, 160 mg per day for the second week and 240 mg per day starting at the start of the third week and until the end of treatment. The interim results showed that the incidence of grade 3 diarrhea for the 137 patients who received the loperamide prophylaxis was 31%. For the 64 patients who received the combination of loperamide plus budesonide, the interim results showed that the incidence of grade 3 diarrhea was 28%.

For the 136 patients who received the combination of loperamide plus colestipol, the interim results showed that the incidence of grade 3 diarrhea was 21%. For the 104 patients who received prophylactic colestipol and loperamide as needed the interim results showed that the incidence of grade 3 diarrhea was 34%, and for the 60 patients who were treated with the dose escalation, the incidence of grade 3 diarrhea was 15%. Further information is provided in Table 1 below:

Table 1: Incidence of Treatment-Emergent Diarrhea

	Loperamide (n=137)	Budesonide + loperamide (n=64)	Colestipol + loperamide (n=136)	Colestipol + loperamide prn (n=104)	Neratinib dose escalation + loperamide prn (n=60)
Treatment-emergent diarrhea incidence, n (%)					
No diarrhea	28 (20)	9 (14)	23 (17)	5 (5)	2 (3)
Grade 1	33 (24)	16 (25)	38 (28)	33 (32)	24 (40)
Grade 2	34 (25)	21 (33)	47 (35)	31 (30)	25 (42)
Grade 3	42 (31)	18 (28)	28 (21)	35 (34)	9 (15)
Grade 4	0	0	0	0	0
Diarrhea leading to discontinuation	28 (20.4)	7 (10.9)	5 (3.7)	8 (7.7)	2 (3.3)
Hospitalization (due to diarrhea)	2 (1.5)	0	0	0	0
Discontinuation of study (any cause)	61 (44.5)	13 (20.3)	39 (28.7)	29 (27.9)	12 (20.0)

Note: Each patient was counted only once in the highest grade category.

No Grade 4 events reported in the CONTROL study.

### **PB272 (neratinib, oral)—Other Potential Applications**

#### *HER2 Mutation-Positive Solid Tumors*

Based on the results from the Cancer Genome Atlas Study, we estimate that between 2% and 12% of each solid tumor has a mutation in HER2. In the United States, this includes new diagnoses of an estimated 7,000 – 7,500 patients with bladder cancer; 4,000 – 4,500 patients with colorectal cancer; 1,500 – 2,000 patients with glioblastoma; 1,000 patients with melanoma; 4,000 – 5,000 patients with prostate cancer; 1,000 patients with stomach cancer; and 1,000 – 2,000 patients with uterine cancer.

*Basket Trial for HER2 Mutation-Positive Solid Tumors.* In October 2013, we announced that we had initiated a Phase II clinical trial of neratinib as a single agent in patients with solid tumors that have an activating HER2 mutation, which we refer to as the SUMMIT basket trial. The Phase II SUMMIT basket trial is an open-label, multicenter, multinational study to evaluate the safety and efficacy of PB272 administered daily to patients who have solid tumors with activating HER2 or HER3 mutations. The study initially included six cohorts of patients, one for each of the following cancers: (i) bladder/urinary tract cancer; (ii) colorectal cancer; (iii) endometrial cancer; (iv) gastric/esophageal cancer; (v) ovarian cancer; and (vi) all other solid tumors (including prostate, melanoma and pancreatic cancer). Each cohort initially consists of seven patients. If a certain predetermined objective response rate is seen in the initial cohort of seven patients, the cohort will be expanded to include a larger number of patients.

#### *HER2-Mutated, Non-Amplified Breast Cancer*

A HER2 mutation in patients with HER2-negative breast cancer was identified as part of a study performed by the Cancer Genome Atlas Network and published in Cancer Discovery in December 2012. We believe this mutation may occur in an estimated 2% of patients with breast cancer. Pre-clinical data from this publication demonstrated that neratinib was active in pre-clinical models of HER2-negative breast cancer that have this HER2 mutation and that neratinib has more anti-cancer activity than either trastuzumab or lapatinib in cells with this mutation. A Phase II trial of neratinib in HER2-negative breast cancer patients who have a HER2 mutation opened for enrollment in December 2012.

As stated above, in May 2014 we expanded the first cohort from the SUMMIT basket trial. Interim results from this ongoing Phase II trial were presented at the 2017 American Association for Cancer Research Annual Meeting. All patients received loperamide (16 mg per day initially) prophylactically for the first cycle of treatment in order to reduce the neratinib-related diarrhea. Included in the presentation were data on 141 patients enrolled in the neratinib monotherapy arm of the trial, including 124 patients with HER2 mutations and 17 patients with HER3 mutations. This included patients with 21 unique tumor types, with the most common being breast, lung, bladder and colorectal cancer. There were also 30 distinct HER2 and 12 distinct HER3 mutations observed among these patients, with the most frequent HER2 variants involving S310, L755, A755\_G776insYVMA and V777.

In the HER2-mutant cohort, clinical responses were observed in tumors with S310, L755, V777, P780\_Y781insGSP and A775\_G776insYVMA mutations. When stratified by tumor type, responses were observed in patients with breast, cervical, biliary, salivary and non-small-cell lung cancers, which led to cohort expansions in these tumor types. No activity was observed in the HER3-mutant cohort. A more detailed presentation of the data is presented in the table below.

The interim safety results observed in the SUMMIT study were consistent with that observed previously in metastatic patients with HER2 amplified tumors. With anti-diarrheal prophylaxis and management, diarrhea has not been a treatment-limiting side effect in SUMMIT. The interim safety results of the study showed that the most frequently observed adverse event was diarrhea. For the 141 patients enrolled in the neratinib monotherapy arm with safety data available as of March 10, 2017, 31 patients (22%) reported grade 3 diarrhea. The median duration of grade 3 diarrhea for those patients was two days. Four patients (2.8%) permanently discontinued neratinib due to diarrhea and 21 patients (14.9%) temporarily discontinued neratinib due to diarrhea and then restarted after the diarrhea subsided.

**Table 1: SUMMIT Trial Interim Efficacy Results as of March 10, 2017**

	HER2 <sup>mut</sup> Breast (n=25)	HER2 <sup>mut</sup> Bladder (n=16)	HER2 <sup>mut</sup> Lung (n=26)	HER2 <sup>mut</sup> Colorectal (n=12)	HER2 <sup>mut</sup> Biliary tract (n=9)	HER2 <sup>mut</sup> Cervical (n=5)	HER3 <sup>mut</sup> NOS (n=17)
<b>ORR at week 8, n (%)</b> (95% CI)	8 (32.0) (14.9–53.5)	0 (0.0) (0.0–20.6)	1 (3.8) (0.1–19.6)	0 (0.0) (0.0–26.5)	2 (22.2) (2.8–60.0)	1 (20.0) (0.5–71.6)	0 (0.0) (0.0–20.6)
<b>Clinical benefit rate, n (%)</b> (95% CI)	10 (40.0) (21.1–61.3)	3 (18.8) (4.0–45.6)	11 (42.3) (23.4–63.1)	1 (8.3) (0.2–38.5)	3 (33.3) (7.5–70.1)	3 (60.0) (14.7–94.7)	2 (11.8) (1.6–38.3)
<b>Median PFS, months</b> (95% CI)	3.5 (1.9–4.3)	1.8 (1.7–3.5)	5.5 (2.7–10.9)	1.8 (1.4–1.9)	2.8 (0.5–3.7)	20.1 (0.5–NA)	1.7 (1.4–2.0)

In December 2018, we announced that updated interim results from the SUMMIT basket trial in the HER2-mutant, hormone receptor positive breast cancer cohort were presented at the San Antonio Breast Cancer Symposium. The interim results included data from 47 patients who received 240 mg of neratinib daily in combination with fulvestrant at the labeled dose. In this cohort, 43 patients (92%) had HER2-non-amplified disease, and patients had received a median of three prior lines of therapy in the metastatic setting (range 0-11 prior regimens) before entering the trial. All patients had been previously treated with an endocrine agent prior to entering the study, including 25 patients (53%) who had received prior fulvestrant. Further, 20 patients (43%) received prior cyclin-dependent kinase 4/6 (CDK4/6) -inhibitor therapy.

The interim efficacy results summary from the breast cohort that received neratinib + fulvestrant is shown in the table below. The interim efficacy results from the trial showed that for the 47 efficacy evaluable patients, 14 patients (30%) experienced an objective response, which included four patients with a complete response and 10 patients with partial responses, and 22 patients (47%) experienced clinical benefit (clinical benefit is defined as confirmed complete response or partial response or stable disease for at least 24 weeks). The median duration of response was 9.2 months and the median progression free survival was 5.4 months. Subgroup analysis showed that patients who had received prior fulvestrant or CDK4/6 inhibitor targeted therapy prior to entering the trial also benefited from treatment of neratinib and fulvestrant. Of note, six patients (30%) with prior CDK4/6-inhibitor exposure showed confirmed responses, with the duration of responses ranging from 4.5–14.8 months. Four patients were still on treatment at the time of data reporting.

**Table 1: HER2-Mutant, HR-Positive Metastatic Breast Cancer Phase II SUMMIT Trial Interim Efficacy Summary as of October 19, 2018**

Efficacy Endpoint <sup>a</sup> :	Neratinib + Fulvestrant		
	All Patients (n=47)	Subgroups	
		Prior Fulvestrant (n=25)	Prior CDK4/6 Inhibitor -Based Therapy (n=20)
Objective response (confirmed) <sup>b</sup> – n	14	4	6
CR	4	0	1
PR	10	4	5
Objective response rate (95% CI)	<b>30</b> (17–45)	<b>16</b> (5–36)	<b>30</b> (12–54)
Median <sup>c</sup> DOR, months (95% CI)	9.2 (5.5–16.6)		
DOR for each responder		9.2; 9.3*; 14.8*; 16.6	4.5; 7.3; 9.2*; 9.3*; 11.2*; 14.8*
Clinical benefit <sup>d</sup> – n	22	9	8
CR or PR	14	4	6
SD	8	5	2
Clinical benefit rate (95% CI)	<b>47</b> (32–62)	<b>36</b> (18–58)	<b>40</b> (19–64)
Median <sup>c</sup> PFS (95% CI) time to event, months	<b>5.4</b> (3.7–9.2)	<b>3.7</b> (3.5–6.9)	<b>4.1</b> (1.9–10.9)

Efficacy Endpoint <sup>a</sup> :	Patients with RECIST v1.1 Measurable Disease		
	All Patients (n=39)	Subgroups	
		Prior Fulvestrant (n=21)	Prior CDK4/6 Inhibitor -Based Therapy (n=15)
Objective response (confirmed) <sup>b</sup> – n	12	4	5
CR	2	0	0
PR	10	4	5
Objective response rate (95% CI)	<b>31</b> (17–48)	<b>19</b> (5–42)	<b>33</b> (12–62)
Median <sup>c</sup> DOR, months (95% CI)	<b>9.0</b> (4.5–16.6)		
DOR for each responder		9.2; 9.3*; 14.8*; 16.6	4.5; 7.3; 9.2*; 9.3*; 14.8*
Clinical benefit <sup>d</sup> – n	18	8	6
CR or PR	12	4	5
SD	6	4	1
Clinical benefit rate (95% CI)	<b>46</b> (30–63)	<b>38</b> (18–62)	<b>40</b> (16–68)
Median <sup>c</sup> PFS (95% CI) time to event, months	<b>5.4</b> (3.5–10.3)	NA	NA

a Response is based on investigator tumor assessments per RECIST v1.1 or modified PERCIST for patients with only PET-evaluable lesions.

b Overall objective response (ORR) is defined as either a complete or partial response that is confirmed no less than 4-weeks after the criteria for response are initially met.

c Kaplan-Meier analysis

d Clinical benefit rate (CBR) is defined as confirmed CR or PR or stable disease (SD) for at least 24 weeks (within +/- 7 day visit window).

\* Patient still on treatment at time of data cut; DOR, duration of response; PFS, progression free survival; NA, not available

The interim safety results observed in neratinib and fulvestrant-treated breast cancer patients in the SUMMIT basket trial were consistent with that observed previously in metastatic patients with HER2 amplified tumors. With anti-diarrheal prophylaxis and management, diarrhea was not a treatment-limiting side effect in the SUMMIT basket trial. The interim safety results of the study showed that the most frequently observed adverse event was diarrhea. For the 47 patients enrolled in the trial, 11 patients (23%) reported grade 3 diarrhea. The median duration of grade 3 diarrhea for those patients was 1.5 days. No patients permanently discontinued neratinib due to diarrhea.

In December 2019, we announced that additional interim results from the SUMMIT basket trial in the HER2-mutant, hormone receptor positive breast cancer cohort were presented at the San Antonio Breast Cancer Symposium. In the HER2-mutant, HR-positive breast cancer cohort, 28 patients received 240 mg of neratinib daily in combination with trastuzumab and fulvestrant. In this cohort, patients had received a median of four prior lines of therapy in the metastatic setting (range 0-10 prior regimens) before entering the trial. All patients had been previously treated with an endocrine agent prior to entering the study, including 17 patients (61%) who had received prior fulvestrant. Further, 15 patients (54%) received prior cyclin-dependent kinase 4/6 (CDK4/6) -inhibitor therapy. 21 patients (75%) had received prior chemotherapy.

The interim efficacy results from the breast cohort that received neratinib in combination with trastuzumab and fulvestrant showed that for the 17 efficacy evaluable patients, nine patients (53%) experienced a confirmed objective response, all of which were classified as partial responses, and 10 patients (59%) experienced clinical benefit (clinical benefit is defined as confirmed complete response or partial response or stable disease for at least 24 weeks). The median duration of response was not reached, and the median progression-free survival was 9.8 months. At the time of data cut-off, five patients continued to receive treatment.

The interim safety results observed in patients treated with the combination of neratinib plus trastuzumab plus fulvestrant in the SUMMIT study was consistent with that observed previously in metastatic patients with HER2 amplified tumors. All patients received anti-diarrheal prophylaxis with loperamide alone. The interim safety results of the study showed that the most frequently observed adverse event was diarrhea. For the 28 safety evaluable patients enrolled in this cohort, 10 patients (36%) reported grade 3 diarrhea. The median duration of grade 3 diarrhea for those patients was 5.5 days. No patient permanently discontinued neratinib due to diarrhea.

#### ***PB272 (neratinib, intravenous)***

We also plan to develop neratinib as an intravenously administered agent. The intravenous version of neratinib resulted in higher exposure levels of neratinib in pre-clinical models. We believe this may result in higher blood levels of neratinib in patients and may translate into enhanced efficacy. We are evaluating the intravenous formulation of neratinib and considering options relative to its development.

#### ***PB357***

PB357 is an investigational, orally administered agent that is an irreversible TKI that is designed to block signal transduction through the epidermal growth factor receptors, HER1, HER2 and HER4. PB357 is structurally similar to PB272. Pfizer completed single-dose Phase I trials of PB357. We are evaluating PB357 and considering options relative to its development.

### **Clinical Testing of Our Products in Development**

Each of our products in development, and likely all future drug candidates we in-license, will require extensive pre-clinical and clinical testing to determine the safety and efficacy of the product applications prior to seeking and obtaining regulatory approval. This process is expensive and time consuming. In completing these trials, we are dependent upon third-party consultants, consisting mainly of investigators and collaborators, who will conduct such trials.

We and our third-party consultants conduct pre-clinical testing in accordance with Good Laboratory Practices, or GLP, and clinical testing in accordance with Good Clinical Practice standards, or GCP, which are international ethical and scientific quality standards utilized for pre-clinical and clinical testing, respectively. GCP is the standard for the design, conduct, performance, monitoring, auditing, recording, analysis and reporting of clinical trials and the FDA requires compliance with GCP regulations in the conduct of clinical trials. Additionally, our pre-clinical and clinical testing completed in the EU is conducted in accordance with applicable EU standards, such as the EU Clinical Trials Directive (Directive 2001/20/EC of April 4, 2001), or the EU Clinical Trials Directive, and the national laws of the 28 member states of the EU, or Member States, implementing its provisions.

We have entered into, and may enter into in the future, master service agreements with clinical research organizations, or CROs, with respect to initiating, managing and conducting the clinical trials of our products. These contracts contain standard terms for the type of services provided that contain cancellation clauses requiring between 30 and 45 days written notice and that obligate us to pay for any services previously rendered with prepaid, unused funds being returned to us.

## **Competition**

The development and commercialization of new products to treat cancer is highly competitive, and we face considerable competition from major pharmaceutical, biotechnology and specialty cancer companies. As a result, there are and will likely continue to be extensive research and substantial financial resources invested in the discovery and development of new cancer products. Our competitors include, but are not limited to, Genentech, Novartis, Roche, Boehringer Ingelheim, Takeda, Daiichi Sankyo and Seattle Genetics. None of these companies are developing their drugs for the extended adjuvant treatment of early stage HER2-positive breast cancer that has been previously treated with a trastuzumab-containing regimen. All of these competitors are developing their drugs for the treatment of early stage and/or metastatic HER2-positive breast cancer. We are an early commercial stage company with a limited history of operations, sales, marketing and commercial manufacturing. Many of our competitors have substantially more financial and technical resources than we do. In addition, many of our competitors have more experience than we have in pre-clinical and clinical development, manufacturing, regulatory and global commercialization. We are also competing with academic institutions, governmental agencies and private organizations that are conducting research in the field of cancer.

We anticipate that we will face intense competition if we are able to commercialize additional product candidates. We expect that our products under development and in clinical trials will address major markets within the cancer sector. Our competition will be determined in part by the potential indications for which drugs are developed and ultimately approved by regulatory authorities. Additionally, the timing of market introduction of some of our potential products or of competitors' products may be an important competitive factor. Accordingly, the speed with which we can develop products, complete pre-clinical testing, clinical trials and approval processes, and supply commercial quantities to market are expected to be important competitive factors. We expect that competition among products approved for sale will be based on various factors, including product efficacy, safety, reliability, availability, price, reimbursement and patent position.

## **Sales and Marketing**

We currently have a U.S. specialty sales force of approximately 80 sales specialists who are focused on promoting NERLYNX to oncologists. This sales force is supported by an experienced sales leadership team comprised of regional sales managers, and our experienced commercial team comprised of experienced professionals in marketing, access and reimbursement, managed markets, marketing research, commercial operations, and sales force planning and management. In addition, our commercial infrastructure includes capabilities in manufacturing, medical affairs, quality control, and compliance.

We launched NERLYNX in the United States in July 2017, and our focus is to establish NERLYNX as the first choice for extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer following adjuvant trastuzumab-based therapy.

In other markets outside of the United States in which NERLYNX may be approved, if any, we may choose to commercialize NERLYNX independently or by establishing one or more strategic alliances such as the ones we have established for commercializing NERLYNX in the territories for each of our respective licensees.

In November 2018, our board of directors formed a commercialization committee, consisting of Michael Miller, Jay Moyes and Frank Zavrl (and on which Alan H. Auerbach, our Chief Executive Officer and President, participates), to assist management in further accelerating our commercialization efforts in the United States. In particular, the committee is assessing our current commercial infrastructure and sales organization, assisting management in designing and implementing additional strategies focused on optimizing our commercial results and working with management to provide additional oversight into the commercial department. Hugh O'Dowd and Ann Miller joined the commercialization committee upon joining our Board of Directors in October 2019 and November 2019, respectively.

## **Intellectual Property and License Agreements**

We hold a worldwide exclusive license under our license agreement with Pfizer to eighteen granted U.S. patents and five pending U.S. patent applications, as well as foreign counterparts thereof, and other patent applications and patents claiming priority therefrom.

In the United States, we have a license to an issued patent, which currently will expire in 2025, for the composition of matter of neratinib, our lead compound. We also have a license to an issued U.S. patent for the use of neratinib in the treatment of breast cancer, which currently expires in 2025, an issued patent for the use of neratinib in the extended adjuvant treatment of early stage HER2 positive breast cancer that has previously been treated with a trastuzumab containing regimen that expires in 2030, and two issued patents for the formulation of NERLYNX that expire in 2030, one issued patent for the preparation of the polymorphic forms of neratinib, and three issued patents for the use of the polymorphic forms of neratinib in the treatment of breast cancer. In jurisdictions which permit such, we will seek patent term extensions where possible for certain of our patents. We plan to pursue additional patents in and outside the United States covering additional therapeutic uses of neratinib from these existing applications. In addition, we will pursue patent protection for any new discoveries or inventions made in the course of our development of neratinib.



In the United States, marketing approval for neratinib was obtained on July 17, 2017, which provided five years of non-patent data exclusivity. Requests for patent term extension under the Hatch-Waxman Act have been filed in the United States. If we obtain marketing approval in the United States for new uses or combinations therapies for neratinib, we may be eligible for additional periods of regulatory exclusivity, such as three-year market exclusivity covering the new use. If we obtain marketing approval for neratinib or other drug candidates or in certain jurisdictions outside the United States, we may be eligible for regulatory protection, such as, eight to eleven years of data and marketing exclusivity potentially are available for new drugs in the European Union; up to five years of patent extension are potentially available in Europe (Supplemental Protection Certificate), and eight years of data exclusivity are potentially available in Japan. There can be no assurance that we will qualify for any such regulatory exclusivity, or that any such exclusivity will prevent competitors from seeking approval solely on the basis of their own studies. See “Government Regulation” below.

The intellectual property portfolio that was licensed from Pfizer in 2011 when we licensed neratinib included issued patents in a number of countries, including in Europe (EP1848414), as well as pending patent applications in several countries, including the United States, relating to methods of treating gefitinib-and/or erlotinib-resistant cancer by administering an irreversible epidermal growth factor receptor inhibitor. More specifically, with respect to the United States, a Notice of Allowance was issued in January 2020 for pending application US 11/883,474, regarding its claims for methods of treating gefitinib-and/or erlotinib-resistant non-small cell lung cancer (NSCLC) cancer. A Notice of Allowance was also issued in January 2020 for the related continuation application US 15/207,349 regarding its claims for methods of treating gefitinib-and/or erlotinib-resistant NSCLC having a T790M mutation in EGFR. The issue fees for both these US applications were paid in February 2020. Regarding Europe, the EP1848414 patent that was issued in Europe in April 2011 included specific claims that included a pharmaceutical composition for use in treating cancer in a subject with a cancer having a mutation in epidermal growth factor receptor with a T790M mutation. On November 28, 2011, Boehringer Ingelheim International GmbH filed an opposition to this patent asking for this patent to be revoked. Oral proceedings were held before the Opposition Division of the European Patent Office in Munich, Germany on February 4, 2014. The decision of the Opposition Division was to uphold the granted claims of the European patent that relate to the T790M mutation without any modification. This included specific claims that include claims for the pharmaceutical composition comprising an irreversible epidermal growth factor receptor inhibitor for use in treating cancer in a subject having a T790M mutation, and claims for the pharmaceutical composition for use in the treatment of numerous cancers, including lung cancer and non-small cell lung cancer. Both parties have appealed this decision. The appeal is pending, with a hearing set to take place in December 2020.

An Opposition was filed by Hexal AG, or Hexel, on August 3, 2016 against European Patent No. EP2416774 which was licensed from Pfizer in 2011, and which claims neratinib for use in a method for treating HER-2/neu overexpressed/amplified cancer and improving IDFS, wherein the method comprises delivering neratinib therapy to HER-2/neu overexpressed/amplified cancer patients following the completion of at least one year of trastuzumab adjuvant therapy, and wherein the neratinib therapy comprises treating the cancer patients with neratinib for at least twelve months. An oral hearing was held December 8, 2017, wherein the patent was maintained as granted. Hexal then appealed, which appeal is pending.

On October 4, 2017, Hexal AG also filed an Opposition to European Patent No. EP2326329 which was licensed from Pfizer in 2011, and which claims a combination of neratinib and pharmaceutically acceptable salts thereof with capecitabine for use in a method of treating an Erb-2 positive metastatic breast cancer. An oral hearing was held on February 13, 2019, wherein the patent was maintained as granted. Hexal then appealed, which appeal is pending.

An Opposition was filed by Generics (UK) Ltd., or Generics, on September 3, 2015 against European Patent No. EP2656844, which was licensed from Pfizer in 2011, and which claims, inter alia, a pharmaceutical pack containing 50 to 300 mg of neratinib and pharmaceutically acceptable salts thereof and vinorelbine for use in a method of treating a neoplasm. An oral hearing was held July 3, 2017, wherein the patent was maintained as granted. Generics then appealed, which appeal is pending.

Unipharm filed a pre-grant opposition to Israeli Patent Application No. IL210616 on January 31, 2016. This application was licensed from Pfizer in 2011. An oral hearing was held in Jerusalem before the Israeli Patent Office on January 22, 2018. The matter is pending before the Israeli Patent Office. The application is directed to use of a combination of neratinib and capecitabine in the manufacture of a medicament for treating a neoplasm.

Our goal is to obtain, maintain and enforce patent protection for our products, formulations, processes, methods and other proprietary technologies, preserve our trade secrets, and operate without infringing on the proprietary rights of other parties, both in the United States and in other countries. Our policy is to actively seek to obtain, where appropriate, the broadest intellectual property protection possible for our current product candidates and any future product candidates, proprietary information and proprietary technology through a combination of contractual arrangements and patents, both in the United States and abroad. However, even patent protection may not always provide us with complete protection against competitors who seek to circumvent our patents. See “Risk Factors—Risks Related to Our Intellectual Property—Our proprietary rights may not adequately protect our intellectual property and potential products, and if we cannot obtain adequate protection of our intellectual property and potential products, we may not be able to successfully market our potential products.”

We depend upon the skills, knowledge and experience of our scientific and technical personnel, as well as that of our advisors, consultants and other contractors, none of which is patentable. To help protect our proprietary know-how, which is not patentable, and inventions for which patents may be difficult to obtain or enforce, we rely on trade secret protection and confidentiality agreements to protect our interests. To this end, we require all of our employees, consultants, advisors and other contractors to enter into confidentiality agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

### **In-License Agreement**

In August 2011, Former Puma entered into an agreement pursuant to which Pfizer agreed to grant to Former Puma a worldwide license for the development, manufacture and commercialization of neratinib (oral), neratinib (intravenous), PB357, and certain related compounds. Pursuant to the terms of the agreement, the license would not become effective until Former Puma closed a capital raising transaction in which it raised at least \$25 million in aggregate net proceeds and had a net worth of at least \$22.5 million. Upon the closing of the financing that preceded the Merger, this condition was satisfied.

We assumed the license agreement, in accordance with its terms, in the Merger. The license is exclusive with respect to certain patent rights owned or licensed by Pfizer. Under the license agreement, Pfizer is obligated to transfer to us certain information, records, regulatory filings, materials and inventory controlled by Pfizer and relating to or useful for developing these compounds and to continue to conduct certain ongoing clinical studies until a certain time. After that time, we are obligated to continue such studies pursuant to an approved development plan, including after the license agreement terminates for reasons unrelated to Pfizer's breach of the license agreement, subject to certain specified exceptions. We are also obligated to commence a new clinical trial for a product containing one of these compounds within a specified period of time and use commercially reasonable efforts to complete such trial and achieve certain milestones as provided in a development plan. If certain of our out-of-pocket costs in completing such studies exceed a mutually agreed amount, Pfizer will pay for certain additional out-of-pocket costs to complete such studies. We must use commercially reasonable efforts to develop and commercialize products containing these compounds in specified major-market countries and other countries in which we believe it is commercially reasonable to develop and commercialize such products.

As consideration for the license, we are required to make payments totaling \$187.5 million upon the achievements of certain milestones if all such milestones are achieved. In connection with the FDA approval of NERLYNX in July 2017, we triggered a one-time milestone payment.

The license agreement originally stipulated that should we commercialize any of the compounds licensed from Pfizer or any products containing any of these compounds, we will be obligated to pay to Pfizer incremental annual royalties between approximately 10% and 20% of net sales of all such products, subject, in some circumstances, to certain reductions.

In July 2014, we signed an amendment to the license agreement with Pfizer that, among other things reduced the annual royalties to be paid on net sales of licensed products from a tiered royalty rate structure ranging between 10% to 20% to a fixed rate in the low to mid-teens.

Our royalty obligation continues, on a product-by-product and country-by-country basis, until the later of (i) the last to expire valid claim of a licensed patent covering the applicable licensed product in such country, or (ii) the earlier of generic competition for such licensed product reaching a certain level of sales in such country or expiration of a certain time period after first commercial sale of such licensed product in such country. We can terminate the license agreement at will at any time or for safety concerns, in each case upon specified advance notice. Each party may terminate the license agreement if the other party fails to cure any breach of a material obligation by such other party within a specified time period. Pfizer may terminate the license agreement in the event of our bankruptcy, receivership, insolvency or similar proceeding. The license agreement contains other customary clauses and terms as are common in similar agreements in the industry.

### **Sub-License Agreements**

#### *Specialised Therapeutics Agreement*

On November 20, 2017, we entered into a sub-license agreement, or the Specialised Therapeutics Agreement, with Specialised Therapeutics Asia Pte Ltd., or STA. Pursuant to the Specialised Therapeutics Agreement, we granted to STA, under certain of our intellectual property rights relating to neratinib, an exclusive, sublicensable (under certain circumstances) license to commercialize any pharmaceutical product containing neratinib in finished form for the extended adjuvant treatment of women with early stage HER2-positive breast cancer and HER2-positive metastatic breast cancer in Australia, Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, New Zealand, Papua New Guinea, Philippines, Singapore, Thailand, Timor-Leste and Vietnam, or the STA Territory.

The Specialised Therapeutics Agreement sets forth the parties' respective obligations with respect to the development, commercialization, and supply of the licensed product. Within the STA Territory, STA will be generally responsible for regulatory and commercialization activities, and we will be solely responsible for the manufacturing and supply of the licensed product under a supply agreement entered into between the parties.

Pursuant to the Specialised Therapeutics Agreement, we received an upfront payment of \$1.5 million during the fourth quarter of 2017, a regulatory milestone payment of \$1.0 million during the second quarter of 2019 and will potentially receive regulatory milestone payments totaling up to \$2.0 million. In addition, we will receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products throughout the STA Territory. At this time, we cannot estimate if or when the remaining milestone-related performance obligations might be achieved.

The term of the Specialised Therapeutics Agreement continues, on a country-by-country basis, until the later of (i) the expiration or abandonment of the last patent covering the licensed product or (ii) the earlier of (a) the date upon which sales of generic versions of licensed product reach a specified level in such country, or (b) the tenth anniversary of the first commercial sale of the licensed product in such country. The Specialised Therapeutics Agreement may be terminated by either party if the other party commits a material breach, subject to a customary cure period, or if the other party is insolvent. The Specialised Therapeutics Agreement will also terminate upon the termination of the supply agreement for licensed products between the parties.

#### *CANbridge Agreement*

On January 30, 2018, we entered into a sub-license agreement, or the CANbridge Agreement, with CANbridge Limited, or CANbridge. Pursuant to the CANbridge Agreement, we granted to CANbridge, under certain of our intellectual property rights relating to neratinib, an exclusive, sublicensable (under certain circumstances) license to develop and commercialize any pharmaceutical product containing neratinib for the treatment of human disease, or for purposes of this description, the Field, in the People's Republic of China, or the CANbridge Territory, including mainland China, Hong Kong, Macao, and Taiwan, or, each, a CANbridge Region.

The CANbridge Agreement sets forth the parties' respective obligations with respect to the development, commercialization, and supply of the licensed product. CANbridge will, at its expense, develop the licensed product for the purpose of obtaining regulatory approval in the Field and in the CANbridge Territory, subject to our approval of certain aspects of clinical studies conducted by CANbridge. Within the CANbridge Territory, CANbridge will be solely responsible, at its expense, for regulatory and commercialization activities. We will be solely responsible, subject to certain exceptions, for the manufacturing and supply of the licensed product under a supply agreement that will be entered into between the parties.

Pursuant to the CANbridge Agreement, we received an upfront payment of \$30.0 million during the first quarter of 2018 and a regulatory milestone payment of \$10.0 million during the fourth quarter of 2018, and will potentially receive additional regulatory milestone payments totaling up to \$30.0 million and sales-based milestone payments totaling up to \$185.0 million. In addition, we are entitled to receive double-digit royalties on sales of the licensed products, calculated as a percentage of net sales of the licensed products in the CANbridge Territory. At this time, we cannot estimate if or when the remaining milestone-related performance obligations might be achieved.

The term of the CANbridge Agreement continues, on a CANbridge Region-by-CANbridge Region basis, until (i) the later of the expiration or abandonment of the last licensed patent covering the licensed product in such CANbridge Region or (ii) the earlier of (x) the date upon which sales of generic versions of the licensed product reach a specified level in such CANbridge Region, or (y) the tenth anniversary of the first commercial sale of the licensed product in such CANbridge Region. The CANbridge Agreement may be terminated by either party if the other party commits a material breach, subject to a customary cure period, or if the other party is insolvent; provided that if CANbridge materially breaches its development or commercialization obligations in a particular CANbridge Region, we may terminate the CANbridge Agreement solely with respect to such CANbridge Region. CANbridge may terminate the agreement at its convenience.

#### *Pint Agreement*

On March 30, 2018, we entered into a sub-license agreement, or the Pint Agreement, with Pint Pharma International SA, or Pint. Pursuant to the Pint Agreement, we granted to Pint, under certain of our intellectual property rights relating to neratinib, an exclusive, sublicensable (under certain circumstances) license to develop and commercialize any product containing neratinib and certain related compounds in Belize, Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, and Panama, Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, Guyana, Paraguay, Peru, Suriname, Uruguay, and Venezuela, French Guiana, the Falkland Islands, and Mexico, or the Pint Territory.

The Pint Agreement sets forth the parties' respective obligations with respect to the development, commercialization, and supply of the licensed product. Pint will, at its expense, develop the licensed product for the purpose of obtaining regulatory approval in the Pint Territory, subject to our consent to conduct such development activities and approval of certain aspects of clinical studies conducted by Pint. Within the Pint Territory, Pint will also be responsible for regulatory and commercialization activities. We will be solely responsible for the manufacturing and supply of the licensed product under a supply agreement that will be entered into between the parties, subject to certain exceptions therein.

Pursuant to the Pint Agreement, we received an upfront payment of \$10.0 million during the third quarter of 2018 and will potentially receive additional regulatory and sales-based milestone payments totaling up to approximately \$24.5 million. In addition, we are entitled to receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products throughout the Pint Territory. During the third quarter of 2019, we achieved a development-based milestone, which satisfied a performance obligation necessary to recognize the associated license revenue. We expect to receive the payment from Pint associated with this milestone during the third quarter of 2020. At this time, we cannot estimate if or when the remaining milestone-related performance obligations might be achieved.

The term of the Pint Agreement continues, on a country-by-country basis, until the later of (i) the expiration or abandonment of the last licensed patent covering the licensed product in such country, or (ii) the earlier of (x) the date upon which sales of generic versions of licensed product reach a specified level in such country, or (y) the tenth anniversary of the first commercial sale of the licensed product in such country. The Pint Agreement may be terminated by either party if the other party commits a material breach, subject to a customary cure period, or if the other party is insolvent. Pint may also terminate the Pint Agreement at will, for certain safety concerns.

#### *Knight Agreement*

On January 9, 2019, we entered into a sub-license agreement, or the Knight Agreement, with Knight Therapeutics, Inc., or Knight. Pursuant to the Knight Agreement, we granted to Knight, under certain of our intellectual property rights relating to neratinib, an exclusive, sublicensable (under certain circumstances) license (i) to commercialize any product containing neratinib and certain related compounds in Canada, or the Knight Territory, (ii) to seek and maintain regulatory approvals for the licensed products in the Knight Territory and (iii) to manufacture the licensed products anywhere in the world solely for the development and commercialization of the licensed products in the Knight Territory for human use, subject to the terms of the Knight Agreement and a supply agreement to be negotiated and executed by the parties.

Under the terms of the Knight Agreement, we will be solely responsible for the manufacturing and supply of the licensed products to Knight, but under limited circumstances Knight may obtain the right to manufacture the licensed products under the supply agreement.

The Knight Agreement sets forth the parties' respective obligations with respect to the commercialization of the licensed products. Within the Knight Territory, we will be solely responsible for obtaining the regulatory approval for the indication of extended adjuvant treatment of HER2-positive early stage breast cancer, or the Initial Indication, and Knight will use commercially reasonable efforts to prepare, file and manage regulatory filings for any other indications in the field of human use. Promptly after obtaining the regulatory approval for the Initial Indication in the Knight Territory, we will transfer such regulatory approval to Knight, and Knight will own and hold any regulatory approvals for the licensed products in the Knight Territory in its name.

Pursuant to the Knight Agreement, we received an upfront payment of \$1.5 million during the first quarter of 2019, a regulatory milestone payment of approximately \$0.3 million during the third quarter of 2019 and will potentially receive regulatory and commercial milestone payments totaling up to approximately \$5.6 million. In addition, we are entitled to receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products in the Knight Territory. At this time, we cannot estimate if or when the remaining milestone-related performance obligations might be achieved.

The term of the Knight Agreement continues, on a licensed product-by-licensed product basis, until the later of (i) the expiration or abandonment of the last valid claim of the licensed patents that covers such licensed product in the Territory, or (ii) the earlier of (x) the time when generic competitors to such licensed product have achieved a specified level in such country, or (y) ten (10) years following the date of first commercial sale of such licensed product in the Territory. The Knight Agreement may be terminated by either party if the other party commits a material breach, subject to a customary cure period, or if the other party is insolvent.

## *Pierre Fabre Agreement*

On March 29, 2019, we entered into a sub-license agreement, or the Pierre Fabre Agreement, with Pierre Fabre Medicament SAS, or Pierre Fabre. The Pierre Fabre Agreement granted intellectual property rights and set forth the parties' respective obligations with respect to development, commercialization and supply of any pharmaceutical product containing neratinib in European countries excluding Russia and Ukraine, along with countries in North Africa and francophone countries of West Africa, or the Pierre Fabre Territory. On November 25, 2019, we entered into a license amendment, or the Pierre Fabre Amendment, with Pierre Fabre to extend the terms of the Pierre Fabre Agreement to the Middle East, South Africa, Sudan and Turkey, or the Pierre Fabre Amendment Territory.

Under the terms of the Pierre Fabre Agreement, we are obligated to supply Pierre Fabre with the licensed product in accordance with the related supply agreement. Pierre Fabre will be responsible for conducting additional clinical studies and leading regulatory activities in connection with the EMA.

Pursuant to the Pierre Fabre Agreement, we received an upfront payment of \$60.0 million during the second quarter of 2019 and will potentially receive additional regulatory and sales-based milestone payments totaling up to \$345.0 million. In addition, we will receive double-digit royalties on sales of licensed products throughout the Pierre Fabre Territory. Pursuant to the Pierre Fabre Amendment, we received an upfront payment of \$4.0 million and will potentially receive additional regulatory and sales-based milestone payments totaling up to \$3.0 million. In addition, we will receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products throughout the Pierre Fabre Amendment Territory. At this time, we cannot estimate if or when the remaining milestone-related performance obligations might be achieved.

The term of the Pierre Fabre Agreement, as amended, continues until, on a country-by-country basis, the later of (i) the expiration or abandonment of the last licensed patent covering the licensed product in such country and (ii) the earlier of (x) the date upon which sales of generic versions of the licensed product reach a specified level in such country, or (y) the tenth anniversary of the first commercial sale of the licensed product in such country. The Pierre Fabre Agreement, as amended, may be terminated by either party if the other party commits a material breach, subject to a cure period, or if the other party is insolvent. Pierre Fabre may terminate the agreement at its convenience or if there is evidence of safety issues with the licensed product.

## **Manufacturing**

We do not currently have our own manufacturing facilities. We intend to continue to use our financial resources to accelerate commercialization of NERLYNX and development of our drug candidates rather than diverting resources to establish our own manufacturing facilities. We intend to meet our pre-clinical and clinical trial manufacturing requirements by establishing relationships with third-party manufacturers and other service providers to perform these services for us. While our drug candidates were being developed by Pfizer, both the drug substance and drug product were manufactured by third-party contractors. We are currently using the same third-party contractors to manufacture, supply, store and distribute our products in clinical trials and commercial quantities. We believe that we have manufactured sufficient quantities of the drug to support at least the launch in the extended adjuvant breast cancer indication and plan to continue to manufacture the drug in 2020 to further support the commercial launch of the drug.

Should any of our other drug candidates obtain marketing approval, we anticipate establishing relationships with third-party manufacturers and other service providers in connection with commercial production of our products. We have some flexibility in securing other manufacturers to produce our drug candidates; however, our alternatives may be limited due to proprietary technologies or methods used in the manufacture of some of our drug candidates.

## **Government Regulation**

### *United States—FDA Process*

The research, development, testing, manufacture, labeling, promotion, advertising, distribution and marketing, among other things, of drug products are extensively regulated by governmental authorities in the United States and other countries. In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or the FDCA, and its implementing regulations. Failure to comply with the applicable U.S. requirements may subject us to administrative or judicial sanctions, such as FDA refusal to approve pending NDAs, warning letters, fines, civil penalties, product recalls, product seizures, total or partial suspension of production or distribution, injunctions and/or criminal prosecution.

*Drug Approval Process.* None of our drug product candidates may be marketed in the United States until the drug has received FDA approval. The steps required before a drug may be marketed in the United States generally include the following:

- completion of extensive pre-clinical laboratory tests, animal studies, and formulation studies in accordance with the FDA's GLP requirements and other applicable regulations;
- submission to the FDA of an Investigational New Drug application, or IND, for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, or ethics committee at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with GCP requirements to establish the safety and efficacy of the drug for each proposed indication;
- submission to the FDA of an NDA after completion of all pivotal clinical trials;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the active pharmaceutical ingredient, or API, and finished drug product are produced and tested to assess compliance with current Good Manufacturing Practices, or cGMPs; and
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

Pre-clinical tests include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies. The conduct of the pre-clinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the pre-clinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND, which must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about the conduct of the trial, such as whether human research subjects will be exposed to an unreasonable health risk. In such a case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. We cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin.

Clinical trials involve administration of the investigational drug to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol must be provided to the FDA as part of a separate submission to the IND. Further, an IRB for each medical center proposing to conduct the clinical trial must review and approve the study protocol and informed consent information for study subjects for any clinical trial before it commences at that center, and the IRB must monitor the study until it is completed. There are also requirements governing reporting of ongoing clinical trials and clinical trial results to public registries. Study subjects must sign an informed consent form before participating in a clinical trial.

Clinical trials necessary for product approval typically are conducted in three sequential phases, but the phases may overlap. Phase I usually involves the initial introduction of the investigational drug into a limited population, typically healthy humans, to evaluate its short-term safety, dosage tolerance, metabolism, pharmacokinetics and pharmacologic actions, and, if possible, to gain an early indication of its effectiveness. Phase II usually involves trials in a limited patient population to (i) evaluate dosage tolerance and appropriate dosage; (ii) identify possible adverse effects and safety risks; and (iii) evaluate preliminarily the efficacy of the drug for specific targeted indications. Multiple Phase II clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase III clinical trials. Phase III trials, commonly referred to as pivotal studies, are undertaken in an expanded patient population at multiple, geographically dispersed clinical trial centers to further evaluate clinical efficacy and test further for safety by using the drug in its final form. Post-approval trials, sometimes referred to as Phase IV studies, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase IV clinical trials as a condition of approval of an NDA.

Furthermore, the sponsor, the FDA or an IRB may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, such as in the circumstances where the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. In addition, some clinical trials are overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial.

During the development of a new drug, sponsors are given an opportunity to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase II clinical testing, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach consensus on the next phase of development. Sponsors typically use the end of Phase II meeting to discuss their Phase II clinical results and present their plans for the pivotal Phase III clinical trial that they believe will support submission of an NDA.

A sponsor may request a special protocol assessment, or SPA to reach an agreement with the FDA that the protocol design, clinical endpoints, and statistical analyses are acceptable to support regulatory approval of the product candidate with respect to effectiveness in the indication studied. If such an agreement is reached, it will be documented and made part of the administrative record, and it will be binding on the FDA except in limited circumstances, such as if the FDA identifies a substantial scientific issue essential to determining the safety or effectiveness of the product after clinical studies begin, if the relevant data, assumptions, or information provided by the sponsor in a request for SPA change are found to be false statements or misstatements or omit relevant facts, or if the sponsor fails to follow the protocol that was agreed upon with the FDA. A documented SPA may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if FDA and the sponsor agree in writing to modify the protocol and such modification is intended to improve the study. There is no guarantee that a study will ultimately be adequate to support an approval, even if the study is subject to an SPA.

Concurrent with clinical trials, companies usually complete additional animal safety studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and the manufacturer must develop methods for testing the quality, purity and potency of the final drugs. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Assuming successful completion of the required clinical testing, the results of pre-clinical studies and of clinical trials, together with other detailed information, including information on the manufacture and composition of the drug, are submitted to the FDA in the form of an NDA requesting approval to market the product for one or more indications. An NDA must be accompanied by a significant user fee, which is waived for the first NDA submitted by a qualifying small business.

The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision after it the application is submitted. The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to a filing review before the FDA accepts it for filing and substantive review.

The FDA also may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA inspects the facility or the facilities at which the drug and/or its active pharmaceutical ingredient is manufactured and will not approve the product unless the manufacturing is in compliance with cGMPs and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCPs. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates an NDA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes the specific deficiencies in the NDA identified by the FDA and may require additional clinical data and/or additional pivotal Phase III clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, pre-clinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA could approve the NDA with a Risk Evaluation and Mitigation Strategy to mitigate risks of the drug, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools. Once the FDA approves a drug, the FDA may withdraw product approval if ongoing regulatory requirements are not met or if safety problems occur after the product reaches the market. In addition, the FDA may require testing, including Phase IV clinical trials, and surveillance programs to monitor the safety effects of approved products that have been commercialized. The FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs or other information. In addition, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could impact the timeline for regulatory approval or otherwise impact ongoing development programs.

*Expedited Review and Approval.* The FDA has various programs, including fast track designation, priority review, accelerated approval, and breakthrough therapy designation, which are intended to expedite or simplify the process for reviewing certain drugs and in the case of accelerated approval, provide for approval on the basis of surrogate or intermediate endpoints. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will not be shortened. Generally, drugs that may be eligible for these programs are those for serious or life-threatening diseases or conditions, those with the potential to address unmet medical needs, and those that offer meaningful benefits over existing treatments. Fast track designation, breakthrough therapy designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

For example, fast track designation is designed to facilitate the development and expedite the review of drugs to treat serious or life-threatening diseases or conditions and which demonstrate the potential to address an unmet medical need for such diseases or conditions. With regard to a fast track-designated product, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. Any product submitted to the FDA for approval, including a product with a fast track designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. A product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date as compared to ten months for review of new molecular entity NDAs under its current PDUFA review goals.

Drug products intended for serious or life threatening conditions may be eligible for accelerated approval upon a determination that the product has an effect on a surrogate endpoint, which is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome, or an effect on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform post-marketing clinical trials. In addition, the FDA currently requires pre-approval of promotional materials as a condition for accelerated approval.

The Food and Drug Administration Safety and Innovation Act established a category of drugs referred to as "breakthrough therapies" that may be eligible to receive breakthrough therapy designation. A sponsor may seek FDA designation of a product candidate as a "breakthrough therapy" if the product is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies receive all the benefits of a fast track designation, as well as intensive guidance on efficient drug development and organizational commitment involving senior managers in the FDA.

*Post-Approval Requirements.* After a drug has been approved by the FDA for sale, the FDA may require that certain post-approval requirements be satisfied, including the conduct of additional clinical studies. In addition, certain changes to an approved product, such as adding new indications, making certain manufacturing changes, or making certain additional labeling claims, are subject to further FDA review and approval. Before a company can market products for additional indications, it must obtain additional approvals from the FDA. Obtaining approval for a new indication generally requires that additional clinical studies be conducted. A company cannot be sure that any additional approval for new indications for any product candidate will be approved on a timely basis, or at all.



If post-approval conditions are not satisfied, the FDA may withdraw its approval of the drug. In addition, holders of an approved NDA are required to (i) report certain adverse reactions to the FDA and maintain pharmacovigilance programs to proactively look for these adverse events; (ii) comply with certain requirements concerning advertising and promotional labeling for their products; and (iii) continue to have quality control and manufacturing procedures conform to cGMPs after approval. The FDA periodically inspects the sponsor's records related to safety reporting and/or manufacturing facilities; this latter effort includes assessment of ongoing compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. We use third-party manufacturers to produce our products in clinical and commercial quantities, and future FDA inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA, including, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of existing product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

*Patent Term Restoration and Marketing Exclusivity.* Depending upon the timing, duration and specifics of FDA approval of the use of our drugs, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the extension must be requested prior to expiration of the patent. The U.S. Patent and Trademark Office, or USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. We have filed for patent term extension for two U.S. patents, each of which is being considered by the USPTO. Only one U.S. patent is permitted to be extended for the currently approved drug product and its uses. If both are approved, we will be asked by the USPTO to choose one of the two patents to extend.

Data and market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or an NDA submitted under section 505(b)(2) of the FDCA by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the original active agent or from accepting and reviewing an application referencing the approved drug's application. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct, or obtain a right of reference to all of the pre-clinical studies and clinical trials necessary to demonstrate safety and effectiveness.

#### *Foreign Regulation*

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries before we can commence clinical trials and approval of foreign countries or economic areas, such as the EU, before we may market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

In the European Economic Area, or EEA, which is comprised of the Member States of the EU plus Norway, Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of MAs:

- Community MAs – These are issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA, and are valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA; for products that constitute a significant therapeutic, scientific or technical innovation; or for products that are in the interest of public health in the EU.
- National MAs – These are issued by the competent authorities of the Member States of the EEA and only cover their respective territory and are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member State through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure, an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State. The competent authority of the Reference Member State prepares a draft assessment report, a draft summary of the product characteristics, or SmPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SmPC, labeling or packaging proposed by the Reference Member State, the product is subsequently granted a National MA in all the Member States, i.e., in the Reference Member State and the Member States Concerned.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA assess the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

As in the United States, it may be possible in foreign countries to obtain a period of market and/or data exclusivity that would have the effect of postponing the entry into the marketplace of a competitor's generic product. For example, if any of our products receive marketing approval in the EEA, we expect they will benefit from eight years of data exclusivity and 10 years of marketing exclusivity. An additional non-cumulative one-year period of marketing exclusivity is possible if during the data exclusivity period (the first eight years of the 10-year marketing exclusivity period), we obtain an authorization for one or more new therapeutic indications that are deemed to bring a significant clinical benefit compared to existing therapies. The data exclusivity period begins on the date of the product's first marketing authorization in the EEA and prevents generics from relying on the marketing authorization holder's pharmacological, toxicological and clinical data for a period of eight years. After eight years, a generic product application may be submitted, and generic companies may rely on the marketing authorization holder's data. However, a generic cannot launch until two years later (or a total of 10 years after the first marketing authorization in the EU of the innovator product), or three years later (or a total of 11 years after the first marketing authorization in the EU of the innovator product) if the marketing authorization holder obtains marketing authorization for a new indication with significant clinical benefit within the eight-year data exclusivity period. In Japan, our products may be eligible for eight years of data exclusivity. There can be no assurance that we will qualify for such regulatory exclusivity, or that such exclusivity will prevent competitors from seeking approval solely on the basis of their own studies.

When conducting clinical trials in the EU, we must adhere to the provisions of the European Union Clinical Trials Directive (Directive 2001/20/EC) and the laws and regulations of the EU Member States implementing them. These provisions require, among other things, that the prior authorization of an Ethics Committee and the competent Member State authority is obtained before commencing the clinical trial. In April 2014, the EU passed the Clinical Trials Regulation (Regulation 536/2014), which will replace the current Clinical Trials Directive. To ensure that the rules for clinical trials are identical throughout the European Union, the EU Clinical Trials Regulation was passed as a regulation that is directly applicable in all EU member states. All clinical trials performed in the European Union are required to be conducted in accordance with the Clinical Trials Directive until the Clinical Trials Regulation becomes applicable. According to the current plans of the EMA, the Clinical Trials Regulation is expected to become applicable in 2020.

## *Coverage and Reimbursement*

In the United States and internationally, sales of NERLYNX and any other products that we market in the future, and our ability to generate revenues on such sales, are dependent, in significant part, on the availability of adequate coverage and reimbursement from third-party payors, such as state and federal governments, managed care providers and private insurance plans. Private insurers, such as health maintenance organizations and managed care providers, have implemented cost-cutting and reimbursement initiatives and likely will continue to do so in the future. These include establishing formularies that govern the drugs and biologics that will be offered and the out-of-pocket obligations of member patients for such products. We may need to conduct pharmacoeconomic studies to demonstrate the cost-effectiveness of our products for formulary coverage and reimbursement. Even with such studies, our products may be considered less safe, less effective or less cost-effective than existing products, and third-party payors may not provide coverage and reimbursement for our product candidates, in whole or in part.

In addition, particularly in the United States and increasingly in other countries, we are required to provide discounts and pay rebates to state and federal governments and agencies in connection with purchases of our products that are reimbursed by such entities. It is possible that future legislation in the United States and other jurisdictions could be enacted to potentially impact reimbursement rates for the products we are developing and may develop in the future and could further impact the levels of discounts and rebates paid to federal and state government entities. Any legislation that impacts these areas could impact, in a significant way, our ability to generate revenues from sales of products that, if successfully developed, we bring to market.

Political, economic and regulatory influences are subjecting the healthcare industry in the United States to fundamental changes. There have been, and we expect there will continue to be, legislative and regulatory proposals to change the healthcare system in ways that could significantly affect our future business. For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, enacted in March 2010, substantially changes the way healthcare is financed by both governmental and private insurers. Among other cost containment measures, ACA establishes:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents;
- a new Medicare Part D coverage gap discount program, in which pharmaceutical manufacturers who wish to have their drugs covered under Part D must offer discounts to eligible beneficiaries during their coverage gap period, or the donut hole; and
- a new formula that increases the rebates a manufacturer must pay under the Medicaid Drug Rebate Program.

We expect that the current presidential administration and U.S. Congress will likely continue to seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA. Most recently, the Tax Cuts and Jobs Act was enacted, which, among other things, removes penalties for not complying with the Affordable Care Act's individual mandate to carry health insurance. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, ruled that the individual mandate is a critical and inseparable feature of the ACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the U.S. Court of Appeals for the Fifth Circuit ruled that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. It is unclear how these decisions, subsequent appeals, if any, and other efforts to challenge repeal or replace the ACA will impact the ACA.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, the Budget Control Act of 2011, among other things, included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, 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 types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical 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. Recently, there has also been heightened governmental scrutiny over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills 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 drug products. For example, the 21st Century Cures Act changes the reimbursement methodology for infusion drugs and biologics furnished through durable medical equipment in an attempt to remedy over- and underpayment of certain drugs.

Similar political, economic and regulatory developments are occurring in the EU and may affect the ability of pharmaceutical companies to profitably commercialize their products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could restrict or regulate post-approval activities and affect the ability of pharmaceutical companies to commercialize their products. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

In the future, there may continue to be additional proposals relating to the reform of the U.S. healthcare system and international healthcare systems. Future legislation, or regulatory actions implementing recent or future legislation may have a significant effect on our business. Our ability to successfully commercialize products depends in part on the extent to which reimbursement for the costs of our products and related treatments will be available in the United States and worldwide from government health administration authorities, private health insurers and other organizations. The adoption of certain proposals could limit the prices we are able to charge for our products, the amounts of reimbursement available for our products, and limit the acceptance and availability of our products. Therefore, substantial uncertainty exists as to the reimbursement status of newly approved health care products by third-party payors.

### ***Sales and Marketing***

The FDA regulates all advertising and promotion activities for products under its jurisdiction prior to and after approval, including standards and regulations for direct-to-consumer advertising, dissemination of off-label information, industry-sponsored scientific and educational activities and promotional activities involving the Internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved label. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, we may be required to submit and obtain FDA approval of a new or supplemental NDA, which may require us to collect additional data or conduct additional pre-clinical studies and clinical trials. Failure to comply with applicable FDA requirements may subject a company to adverse publicity, enforcement action by the FDA, corrective advertising, consent decrees and the full range of civil and criminal penalties available to the FDA.

Physicians may prescribe legally available drugs for uses that are not described in the drug's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties, and often reflect a physician's belief that the off-label use is the best treatment for the patient. The FDA does not regulate the behavior of physicians in their choice of treatments, but FDA regulations do impose stringent restrictions on manufacturers' communications regarding off-label uses. Failure to comply with applicable FDA requirements may subject a company to adverse publicity, enforcement action by the FDA, corrective advertising, consent decrees and the full range of civil and criminal penalties available to the FDA.

Outside the United States, our ability to market a product is contingent upon obtaining marketing authorization from the appropriate regulatory authorities. The requirements governing marketing authorization, pricing and reimbursement vary widely from country to country.

### ***Other Healthcare Laws***

We may also be subject to various federal and state laws pertaining to health care "fraud and abuse," including anti-kickback laws and false claims laws, data privacy and security laws and transparency laws.

The federal Anti-Kickback Statute, or AKS, prohibits, among other things, any person or entity from knowingly and willfully soliciting, receiving, offering or paying any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of an item or service reimbursable, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. The term "remuneration" has been broadly interpreted to include anything of value. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution; however, these are drawn narrowly and require strict compliance in order to offer protection. Additionally, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Moreover, a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the federal False Claims Act, or the FCA.

Federal civil and criminal false claims laws, such as the FCA, prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented false, fictitious or fraudulent claims for payment or approval by the federal government, including federal health care programs, such as Medicare and Medicaid, and knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim, or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government. Private individuals can bring “qui tam” actions under the FCA, on behalf of the government and such individuals, commonly known as “whistleblowers,” may share in amounts paid by the entity to the government in fines or settlement.

The federal Civil Monetary Penalties law prohibits, among other things, offering or transferring remuneration to a federal healthcare beneficiary that a person knows or should know is likely to influence the beneficiary’s decision to order or receive items or services reimbursable by the government from a particular provider or supplier.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the AKS, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

The federal transparency requirements under the Physician Payments Sunshine Act, created under the ACA, requires, among other things, certain manufacturers of drugs, devices, biologics and medical supplies reimbursed under Medicare, Medicaid, or the Children’s Health Insurance Program to annually report to CMS information related to payments and other transfers of value provided to physicians, certain other healthcare professionals beginning in 2022, and teaching hospitals and physician ownership and investment interests, including such ownership and investment interests held by a physician’s immediate family members.

There are also state and foreign law equivalents of each of the above federal laws, such as state anti-kickback and false claims laws, that may impose similar or more prohibitive restrictions, and may apply to items or services reimbursed by any non-governmental third-party payors, including private insurers. Similar restrictions are also imposed on the promotion and marketing of medicinal products in the EU and other countries. Laws (including those governing promotion, marketing and anti-kickback provisions), industry regulations and professional codes of conduct often are strictly enforced.

Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including fines and civil monetary penalties, the possibility of exclusion from federal health care programs (including Medicare and Medicaid) and corporate integrity agreements, which impose, among other things, rigorous operational and monitoring requirements on companies. Similar sanctions and penalties also may be imposed upon executive officers and employees, including criminal sanctions against executive officers under the so-called “responsible corporate officer” doctrine, even in situations where the executive officer did not intend to violate the law and was unaware of any wrongdoing. Given the penalties that may be imposed on companies and individuals if convicted, allegations of such violations often result in settlements even if the company or individual being investigated admits no wrongdoing. Settlements often include significant civil sanctions, including fines and civil monetary penalties, and corporate integrity agreements. In addition, private individuals have the ability to bring similar actions.

### ***Data Privacy and Security***

Pharmaceutical companies may be subject to U.S. federal and state and foreign health information privacy, security and data breach notification laws, which may govern the collection, use, disclosure and protection of health-related and other personal information. In the U.S., HIPAA imposes privacy, security and breach reporting obligations with respect to individually identifiable health information upon “covered entities” (health plans, health care clearinghouses and certain health care providers), and their respective business associates, individuals or entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HIPAA mandates the reporting of certain breaches of health information to HHS, affected individuals and if the breach is large enough, the media. Entities that are found to be in violation of HIPAA as the result of a breach of unsecured protected health information, a complaint about privacy practices or an audit by HHS, may be subject to significant civil, criminal and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance. Even when HIPAA does not apply, according to the Federal Trade Commission or the FTC, failing to take appropriate steps to keep consumers’ personal information secure constitutes unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act, or the FTCA, 15 U.S.C § 45(a). The FTC expects a company’s data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards. The FTC’s guidance for appropriately securing consumers’ personal information is similar to what is required by the HIPAA Security Rule.

In addition, certain state and non-U.S. laws, such as the European Union General Data Protection Regulation 2016/679, or GDPR, govern the privacy and security of health information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. For example, California recently enacted legislation, the California Consumer Privacy Act, or CCPA, which went into effect January 1, 2020. The CCPA, among other things, creates new data privacy obligations for covered companies and provides new privacy rights to California residents, including the right to opt out of certain disclosures of their information. The CCPA also creates a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. Although the law includes limited exceptions, including for “protected health information” maintained by a covered entity or business associate, it may regulate or impact our processing of personal information depending on the context. In Europe, the GDPR went into effect in May 2018 and introduces strict requirements for processing the personal data of European Union data subjects. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater.

#### ***Other Laws and Regulatory Processes***

We are subject to a variety of financial disclosure and securities trading regulations as a public company in the United States with securities traded on the NASDAQ Global Select Market, including laws relating to the oversight activities of the Securities and Exchange Commission, or the SEC, and the rules and regulations of The NASDAQ Stock Market LLC. In addition, the Financial Accounting Standards Board, or FASB, the SEC, and other bodies that have jurisdiction over the form and content of our accounts, our financial statements and other public disclosure are constantly discussing and interpreting proposals and existing pronouncements designed to ensure that companies best display relevant and transparent information relating to their respective businesses.

Our present and future business has been and will continue to be subject to various other laws and regulations. Various laws, regulations and recommendations relating to safe working conditions, laboratory practices, experimental use of animals, and the purchase, storage, movement, import and export, and use and disposal of hazardous or potentially hazardous substances used in connection with our research work are or may be applicable to our activities. Certain agreements entered into by us involving exclusive license rights or acquisitions may be subject to national or supranational antitrust regulatory control, the effect of which cannot be predicted. The extent of government regulation that might result from future legislation or administrative action cannot accurately be predicted.

#### **Research and Development Expenses**

Research and development activities, which include personnel costs, research supplies, clinical and pre-clinical study costs, are the primary source of our overall expenses. Such expenses related to the research and development of our product candidates totaled \$132.9 million for the year ended December 31, 2019, \$164.9 million for the year ended December 31, 2018 and \$207.8 million for the year ended December 31, 2017.

## Employees

As of December 31, 2019, we had 269 employees, all of whom are full-time employees. We believe our relations with our employees are good. Over the course of the next year, we anticipate hiring approximately 30 additional full-time employees.

In addition, we intend to continue to use CROs and third parties to perform our clinical studies and manufacturing.

## Corporate Information and History

Our principal executive offices are located at 10880 Wilshire Boulevard, Suite 2150, Los Angeles, California 90024 and our telephone number is (424) 248-6500. Our internet address is [www.pumabiotechnology.com](http://www.pumabiotechnology.com). Our annual, quarterly and current reports, and any amendments to those reports, filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 may be accessed free of charge through our website after we have electronically filed or furnished such material with the SEC. We also make available free of charge on or through our website our Code of Business Conduct and Ethics, Corporate Governance Guidelines, Audit Committee Charter, Compensation Committee Charter, Nominating and Corporate Governance Committee Charter and Research and Development Committee Charter. We will disclose on a current report on Form 8-K or on our website information any amendment or waiver of the Code of Business Conduct and Ethics for our executive officers and directors. Any amendment or waiver disclosed on our website will remain available on our website for at least 12 months after the initial disclosure.

The reference to [www.pumabiotechnology.com](http://www.pumabiotechnology.com) (including any other reference to such address in this Annual Report) is an inactive textual reference only, meaning that the information contained on or accessible from the website is not part of this Annual Report on Form 10-K and is not incorporated in this report by reference.

We were originally incorporated in the State of Delaware in April 2007 under the name Innovative Acquisitions Corp. We were a “shell” company registered under the Exchange Act with no specific business plan or purpose until we acquired Former Puma in the Merger. As a result of this transaction, Former Puma become our wholly-owned subsidiary and subsequently merged with and into us, at which time we adopted Former Puma’s business plan and changed our name to “Puma Biotechnology, Inc.”

## ITEM 1A. RISK FACTORS

*In addition to the other information contained in this Annual Report, the following risk factors should be considered carefully in evaluating our company. Our business, financial condition, liquidity or results of operations could be materially adversely affected by any of these risks. Our business, financial condition, liquidity or results of operations could be materially adversely affected by any of these risks. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties that we are unaware of, or that we currently believe are not material, may also become important factors that affect us.*

### Risks Related to our Business

***We have a limited operating history and are not profitable and may never become profitable.***

We have a limited operating history and have a history of operating losses, with net losses of \$75.6 million, \$113.6 million and \$292.0 million for the years ended December 31, 2019, 2018 and 2017, respectively. As of December 31, 2019, we had an accumulated deficit of approximately \$1,277.6 million.

Although we received FDA approval and commenced commercialization of NERLYNX in the United States in July 2017 and the EC granted marketing authorization for NERLYNX in the European Union in 2018, we may continue to incur losses and may never become profitable. Moreover, even if we succeed in developing and commercializing one or more of other drug candidates, we may never become profitable. The successful development and commercialization of any drug candidate will require us to perform a variety of functions, including:

- undertaking pre-clinical development and clinical trials;
- hiring additional personnel;
- participating in regulatory approval processes;
- formulating and manufacturing products;
- initiating and conducting sales and marketing activities; and
- implementing additional internal systems and infrastructure.

We will need to generate significant revenue in order to achieve and maintain profitability. We may not be able to generate this revenue or achieve profitability in the future. As a result, we expect our losses to continue for the foreseeable future. Accordingly, we cannot assure you that we will achieve profitability in the future or that, if we do become profitable, we will sustain profitability. Our failure to achieve or maintain profitability could negatively impact the value of our common stock.

***Our success depends on our ability to commercialize NERLYNX successfully. We are currently a single product company with limited commercial sales experience, which makes it difficult to evaluate our current business, predict our future prospects and forecast our financial performance and growth.***

We have invested a significant portion of our efforts and financial resources in the development and commercialization of our lead product, NERLYNX, and we expect NERLYNX to constitute the vast majority of our product revenue for the foreseeable future. Our success depends on our ability to commercialize NERLYNX successfully. Successful commercialization of NERLYNX is subject to many risks. We have never, as an organization, launched or commercialized a product, and there is no guarantee that we will be able to do so successfully with NERLYNX. There are numerous examples of unsuccessful product launches and failures to meet high expectations of market potential, including by pharmaceutical companies with more experience and resources than we have. The commercial success of NERLYNX depends on the extent to which patients and physicians accept and adopt NERLYNX. For example, if the expected patient population is smaller than we estimate or if physicians are unwilling to prescribe or patients are unwilling to take or continue to take NERLYNX, due to the related side effects, including diarrhea, or otherwise, the commercial success of NERLYNX will be limited. Thus, significant uncertainty remains regarding the commercial potential of NERLYNX. Moreover, our ability to effectively generate product revenue from NERLYNX will depend on our ability to, among other things:

- achieve and maintain compliance with regulatory requirements;
- create and sustain market demand for and achieve market acceptance of NERLYNX through our marketing and sales activities and other arrangements established for the promotion of NERLYNX;
- compete with other breast cancer drugs (either in the present or in the future);
- educate physicians and patients about the benefits, administration and use of NERLYNX;



- train, deploy and support a qualified sales force;
- secure formulary approvals for NERLYNX at a substantial number of targeted hospitals;
- ensure that our third-party manufacturers manufacture NERLYNX in sufficient quantities, in compliance with requirements of the FDA and similar foreign regulatory agencies where NERLYNX is approved, and at acceptable quality and pricing levels in order to meet commercial demand;
- ensure that our third-party manufacturers develop, validate and maintain commercially viable manufacturing processes that are compliant with current Good Manufacturing Practice, or cGMP, regulations;
- implement and maintain agreements with wholesalers, distributors and group purchasing organizations on commercially reasonable terms;
- ensure that our entire supply chain efficiently and consistently delivers NERLYNX to our customers;
- receive adequate levels of coverage and reimbursement for NERLYNX from commercial health plans and governmental health programs;
- provide co-pay assistance to help qualified patients with out-of-pocket costs associated with their NERLYNX prescription and/or other programs to ensure patient access to our products;
- obtain acceptance of NERLYNX as safe and effective by patients and the medical community;
- influence the nature of publicity related to our product relative to the publicity related to our competitors' products;
- obtain regulatory approvals for additional indications for the use of NERLYNX; and
- maintain and defend our patent protection and regulatory exclusivity for NERLYNX and to comply with our obligations under, and otherwise maintain, our intellectual property license with Pfizer and our license agreements with third parties.

In addition, we are dependent on international third-party sub-licensees for the development and commercialization of NERLYNX in several countries outside the United States. The failure of these sub-licensees to meet their contractual, regulatory or other obligations could adversely affect international sales of NERLYNX and hinder our ability to generate revenue.

***We have limited experience as a company in marketing or distributing pharmaceutical products. If we are unable to expand our marketing capabilities and successfully commercialize NERLYNX, our business, results of operations and financial condition may be materially adversely affected.***

A key part of our strategy is to build our sales, marketing and distribution capabilities to commercialize NERLYNX successfully in the United States. While we are continuing to establish our commercial team and hire our U.S. sales force, we have limited experience commercializing pharmaceutical products as an organization. In order to market NERLYNX successfully, we must continue to build our sales, marketing, managerial, compliance, and related capabilities or make arrangements with third parties to perform these services. If we are unable to establish adequate sales, marketing, and distribution capabilities, whether independently or with third parties, we may not be able to commercialize NERLYNX appropriately and may not become profitable.

Part of our strategy to commercialize NERLYNX in the United States is to develop a direct sales force. These efforts will continue to be expensive and time-consuming, and we cannot be certain that we will be able to successfully develop this capability. NERLYNX is a newly-marketed drug and, therefore, none of the members of our sales force had ever promoted NERLYNX prior to its commercial launch. In addition, we must train our sales force to ensure that a consistent and appropriate message about NERLYNX is being delivered to our potential customers. If we are unable to effectively train our sales force and equip them with effective materials, including medical and sales literature to help them inform and educate potential customers about the benefits of NERLYNX and its proper administration, our efforts to commercialize NERLYNX successfully could be harmed, which would negatively impact our ability to generate product revenue.

Additionally, we will need to maintain and further develop our sales force to achieve commercial success, and we will be competing with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel. In the event we are unable to continue to develop and effectively maintain our commercial team, including our U.S. sales force, our ability to successfully commercialize NERLYNX would be limited, and we would not be able to generate product revenue successfully.

There are risks involved both with establishing our own sales and marketing capabilities, and with entering into arrangements with third parties to perform these services. For example, any efforts to develop a direct sales and marketing organization are subject to numerous risks, including:

- the expense and time required to recruit and train a sales force;
- our inability to recruit, retain or motivate adequate numbers of effective and qualified sales and marketing personnel;
- the inability to provide adequate training to sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or convince adequate numbers of physicians to prescribe any product;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization; and
- the premature or unnecessary incurrence of significant commercialization expenses if the commercial launch of a product is delayed or does not occur for any reason.

Similarly, if we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or the profitability associated with any product revenue may be lower than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our products or may be unable to do so on terms that are favorable to us. We may 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. Moreover, we may be negatively impacted by other factors outside of our control relating to such third parties, including, but not limited to, their inability to comply with regulatory requirements. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our products.

***We depend on a limited number of customers for a significant amount of our total revenue, and if we lose any of our significant customers, our business could be harmed.***

The majority of our revenue comes from a limited number of customers. In 2019, two customers, CVS/Caremark and Accredo/Acaria, individually comprised approximately 34% and 22%, respectively, of our total product revenue. We expect that revenue from a limited number of customers will continue to account for a large portion of our revenue in the future. The loss by us of any of these customers, or a material reduction in their purchases or their market pricing, could harm our business, results of operations, financial condition and prospects. In addition, if any of these customers were to fail to pay us in a timely manner, it could harm our cash flow.

***We are dependent on international third-party sub-licensees for the development and commercialization of NERLYNX in several countries outside the United States. The failure of these sub-licensees to meet their contractual, regulatory or other obligations could adversely affect our business.***

We have entered into exclusive sub-license agreements with several third parties that provide these sub-licensees exclusive rights to the development and commercialization of NERLYNX in various specified regions outside of the United States. As a result, we are entirely dependent on these parties to achieve regulatory approval of NERLYNX for marketing in these countries and for the commercialization of NERLYNX, if approved. The timing and amount of any milestone and royalty payments we may receive under these agreements, as well as the commercial success of NERLYNX in those regions outside of the United States, will depend on, among other things, the efforts, allocation of resources and successful commercialization of NERLYNX by the licensees. We also depend on these third parties to comply with all applicable laws relative the development and commercialization of our products in those countries. We do not control the individual efforts of these licensees and have limited ability to terminate these agreements if the licensees do not perform as anticipated. The failure of these licensees to devote sufficient time and effort to the development and commercialization of NERLYNX, or the failure of these licensees to meet their obligations to us, including for future royalty and milestone payments; to adequately deploy business continuity plans in the event of a crisis; and/or satisfactorily resolve significant disagreements with us or address other factors, could have an adverse impact on our financial results and operations. In addition, if these third parties violate, or are alleged to have violated, any laws or regulations during the performance of their obligations for us, it is possible that we could suffer financial and reputational harm or other negative outcomes, including possible legal consequences.

Any termination, breach or expiration of any of these sub-license agreements could have a material adverse effect on our financial position by reducing or eliminating the potential for us to receive license fees, milestones and royalties. In such an event, we may be required to devote additional efforts and to incur additional costs associated with pursuing regulatory approval and commercialization of the applicable products and product candidates. Alternatively, we may attempt to identify and transact with a new sub-licensee, but there can be no assurance that we would be able to identify a suitable sub-licensee or transact on terms that are favorable to us.

***We may not be able to secure additional financing on favorable terms, or at all, to meet our future capital needs and our failure to obtain additional financing when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development or commercialization efforts or other operations.***

Our operations have consumed substantial amounts of cash since inception. Our costs and expenses may increase in the future as we continue to commercialize NERLYNX, on account of, among other things, the cost of a direct sales force and the cost of manufacturing. We will also continue to expend substantial amounts on research and development of our other product candidates, including conducting clinical trials. Our future capital requirements will depend on many factors, including:

- the costs and expenses of our U.S. sales and marketing infrastructure, and of manufacturing;
- the degree of success we experience in commercializing NERLYNX;
- the revenue generated by the sale of NERLYNX and any other products that may be approved;
- the costs, timing and outcomes of clinical trials and regulatory reviews associated with our other product candidates;
- the emergence of competing products;
- the extent to which NERLYNX is adopted by the physician community and patients;
- the number and types of future products we develop and commercialize;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;
- the costs of operating as a public company and compliance with existing and future regulations; and
- the extent and scope of our general and administrative expenses.

While our consolidated financial statements have been prepared on a going concern basis, we expect to continue incurring significant losses for the foreseeable future and will continue to remain dependent on our ability to obtain sufficient funding to sustain operations and successfully commercialize NERLYNX. We are party to a credit facility with Oxford Finance LLC, or Oxford, providing for term loans equaling a total of \$100 million, which mature on June 1, 2024. As of December 31, 2019, we had \$100 million in principal amounts outstanding. While we have been successful in raising financing in the past, there can be no assurance that we will be able to do so in the future. Additional financing may not be available on a timely basis on terms acceptable to us, or at all. We may raise funds in equity or debt financings to access funds for our capital needs. If we raise additional funds through further issuances of equity or convertible debt securities, our existing stockholders could suffer significant dilution in their percentage ownership of our company, and any new equity securities we issue could have rights, preferences and privileges senior to those of holders of our common stock. Any debt financing obtained by us in the future would cause us to incur debt service expenses and could include restrictive covenants relating to our capital raising activities and other financial and operational matters, which may make it more difficult for us to obtain additional capital and pursue business opportunities. If we are unable to obtain adequate financing or financing on terms satisfactory to us when we require it, we may terminate or delay the development of one or more of our product candidates, delay clinical trials necessary to market our products, or delay establishment of sales and marketing capabilities or other activities necessary to commercialize our products. If this were to occur, our ability to continue to grow and support our business and to respond to business challenges could be significantly limited. Furthermore, our ability to obtain funding may be adversely impacted by uncertain market conditions, our success in commercializing neratinib, unfavorable decisions of regulatory authorities or adverse clinical trial results. The outcome of these matters cannot be predicted at this time.

***The terms of our credit facility place restrictions on our ability to operate our business and on our financial flexibility, and we may be unable to achieve the revenue necessary for us to incur additional borrowings under the credit facility or to satisfy the minimum revenue covenants.***

The terms of our credit facility place restrictions on our ability to operate our business and our financial flexibility. As of December 31, 2019, we had \$100 million in principal amounts outstanding under the credit facility. The credit facility is secured by substantially all of our personal property, other than our intellectual property.

The credit facility includes affirmative and negative covenants applicable to us, our current subsidiaries and any subsidiaries we create in the future. The affirmative covenants include, among others, covenants requiring us to maintain our legal existence and governmental approvals, deliver certain financial reports, maintain insurance coverage and satisfy certain requirements regarding deposit accounts. We must also achieve product revenue, measured as of the last day of each fiscal quarter on a trailing year to date basis. New minimum revenue levels will be established for each subsequent fiscal year by mutual agreement of us, Oxford, as collateral agent, and the lender. The negative covenants include, among others, restrictions on us transferring collateral, incurring additional indebtedness, engaging in mergers or acquisitions, paying dividends or making other distributions, making investments, creating liens, selling assets and suffering a change in control, in each case subject to certain exceptions. These covenants may make it difficult for us to operate our business. In addition, we are in the early stages of commercializing NERLYNX and we cannot assure you that we will be able to achieve the minimum revenue requirements provided for in the credit facility. Our failure to satisfy the revenue, or any other, covenant could result in an event of default under the loan.

The credit facility also includes events of default, the occurrence and continuation of which could cause interest to be charged at the rate that is otherwise applicable plus 5% and would provide Oxford, as collateral agent, with the right to exercise remedies against us and the collateral securing the credit facility, including foreclosure against the property securing the credit facility, including our cash. These events of default include, among other things, our failure to pay principal or interest due under the credit facility, a breach of certain covenants under the credit facility, our insolvency, a material adverse change, the occurrence of any default under certain other indebtedness in an amount greater than \$500,000 and one or more judgments against us in an amount greater than \$500,000 individually or in the aggregate that remains unsatisfied, unvacated, or unstayed for a period of 10 days after its entry.

***Interim, “topline” and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.***

From time to time, we may publicly disclose preliminary or topline data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Preliminary and topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. Consequently, preliminary and topline data should be viewed with caution until the final data are available.

Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock after this offering.

In addition, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

***NERLYNX or our other drug candidates may cause undesirable side effects or have other properties when used alone or in combination with other approved products or investigational new drugs that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any, as applicable.***

Undesirable side effects caused by NERLYNX or our other drug candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. To date, subjects treated with NERLYNX have experienced drug-related side effects including diarrhea. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete clinical trials or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Additionally, if we or others later identify undesirable side effects caused by any approved product, including in combination with other approved products or investigational new drugs, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of NERLYNX or the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

***Even though the FDA and EC have granted approval of NERLYNX for the extended adjuvant treatment of early stage, HER2-positive breast cancer, the terms of the approvals may limit its commercial potential.***

Even though the FDA and EC have granted approval of NERLYNX, the scope and terms of the approvals may limit our ability to commercialize NERLYNX and, therefore, our ability to generate substantial sales revenue. The FDA and EC have approved NERLYNX only for the extended adjuvant treatment of early stage, HER2-positive breast cancer in patients who are less than one year from the completion of prior adjuvant trastuzumab-based therapy. In connection with the FDA and EC approvals, we have committed to conduct certain post-marketing studies. We have completed the post-marketing commitments related to the FDA approval, and the post-marketing studies related to the EC approval are ongoing. If we fail to comply with all of our post-marketing commitments, or if the results of the post-marketing studies, or any other ongoing clinical studies of NERLYNX, are negative, the FDA or the EC could decide to withdraw its respective approval, add warnings or narrow the approved indication in the product label.

***NERLYNX is still under clinical development for various additional indications, and we cannot be certain that NERLYNX will receive regulatory approval for any other indication for which we may seek approval.***

The FDA and the EC have approved NERLYNX only for the extended adjuvant treatment of adult patients with early stage hormone receptor positive HER2-overexpressed/amplified breast cancer and who are less than one year from the completion of prior adjuvant trastuzumab-based therapy. We expect that a substantial portion of our efforts and expenditures over the next few years will be devoted to the development of NERLYNX in various additional indications. Accordingly, our business currently depends heavily on the successful development and regulatory approval of NERLYNX for additional indications. The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of drug products are and will remain subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries that each have differing regulations. We are not permitted to market NERLYNX for other indications or any of our other drug candidates in the United States until we receive approval of an NDA from the FDA or in the EU until we receive approval from the EC, as applicable, for such indications, or, in any foreign countries, until requisite approval from such countries.

Approval of NERLYNX by the FDA or the EC for the extended adjuvant treatment of adult patients with early stage hormone receptor positive HER2-overexpressed/amplified breast cancer and who are less than one year from the completion of prior adjuvant trastuzumab-based therapy does not ensure that a foreign jurisdiction will also approve NERLYNX for that indication, nor does it ensure that NERLYNX will be approved by the FDA for any other indications. Obtaining approval of an NDA or foreign marketing application is an extensive, lengthy, expensive and inherently uncertain process, and the FDA or a foreign regulator may delay, limit or deny approval of a drug candidate for many reasons, including:

- we may not be able to demonstrate that NERLYNX or any other drug candidate is safe and effective as a treatment for our targeted indications to the satisfaction of the FDA or other regulator;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or other regulator for marketing approval;
- the FDA or other regulator may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the clinical research organization, or CRO, that we retain to conduct clinical trials or any other third parties involved in the conduct of trials may take actions outside of our control that materially adversely impact our clinical trials;
- the FDA or other regulator may not find the data from pre-clinical studies and clinical trials sufficient to demonstrate that the clinical and other benefits of NERLYNX or any other drug candidate outweigh the safety risks;
- the FDA or other regulator may disagree with our interpretation of data from our pre-clinical studies and clinical trials or may require that we conduct additional studies or trials;
- the FDA or other regulator may not accept data generated at our clinical trial sites;
- if our NDA is reviewed by an advisory committee, the FDA may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the FDA require, as a condition of approval, additional pre-clinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;
- the advisory committee may recommend that the FDA require, as a condition of approval, additional pre-clinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;
- the FDA may require development of a Risk Evaluation and Mitigation Strategy as a condition of approval;
- the FDA or other regulator may identify deficiencies in the manufacturing processes or facilities of our third-party manufacturers; or
- the FDA or other regulator may change its approval policies or adopt new regulations.

If we do not obtain regulatory approval of NERLYNX for other indications, whether in the United States or in other jurisdictions, we will not be able to market NERLYNX for such indications in those jurisdictions, which will limit our commercial revenue.

***We have no experience in drug formulation or manufacturing and rely exclusively on third parties to formulate and manufacture NERLYNX and our drug candidates, and any disruption or loss of these relationships could delay our development and commercialization efforts.***

We have no experience in drug formulation or manufacturing and do not intend to establish our own manufacturing facilities. We lack the resources and expertise to formulate or manufacture NERLYNX and our drug candidates. While our drug candidates were being developed by Pfizer, both the drug substance and drug product were manufactured by third-party contractors. We are using the same third-party contractors to manufacture, supply, store and distribute drug supplies for our clinical trials and the commercialization of NERLYNX. If we are unable to continue our relationships with one or more of these third-party contractors, we could experience delays in our development or commercialization efforts as we locate and qualify new manufacturers. We intend to rely on one or more third-party contractors to manufacture the commercial supply of our drugs. Our anticipated future reliance on a limited number of third-party manufacturers exposes us to the following risks:

- We may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited, and the FDA must approve any replacement manufacturer. This approval would require new testing and compliance inspections. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of our products after receipt of FDA approval.
- Our third-party manufacturers might be unable to formulate and manufacture our drugs in the volume and of the quality required to meet our clinical and/or commercial needs.

- Our future contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store and distribute our products for commercialization, as applicable.
- The facilities used by our contract manufacturers to manufacture NERLYNX and our other drug candidates must be approved by the FDA pursuant to inspections that are conducted following submission of an NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMP regulations for manufacture of both active drug substances and finished drug products. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the Drug Enforcement Administration for controlled substances, similar non-U.S. regulatory agencies and corresponding state agencies to ensure strict compliance with cGMP regulations and other government regulations and corresponding foreign standards. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our drug candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for our other drug candidates, if approved, or market NERLYNX.
- If any third-party manufacturer makes improvements in the manufacturing process for our products, we may not own, or may have to share, the intellectual property rights to the innovation.

Each of these risks could delay our clinical trials, the approval, if any, of our drug candidates by the FDA or the commercialization of NERLYNX or our other drug candidates, or result in higher costs or deprive us of potential product revenue.

***If our third-party manufacturers fail to manufacture NERLYNX in sufficient quantities and at acceptable quality and pricing levels, or fail to fully comply with cGMP regulations, we may face delays in commercialization or be unable to meet market demand, and may lose potential revenues.***

The manufacture of NERLYNX requires significant expertise and capital investment, including the development of advanced manufacturing techniques, process controls and the use of specialized processing equipment. Our third-party manufacturers must comply with federal, state and foreign regulations, including the FDA's regulations governing cGMP, enforced by the FDA through its facilities inspection program and by similar regulatory authorities in other jurisdictions where we do business. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. The FDA or similar foreign regulatory authorities at any time may implement new standards or change their interpretation and enforcement of existing standards for manufacture, packaging or testing of our products. Any failure by us or our third-party manufacturers to comply with applicable regulations may result in fines and civil penalties, suspension of production, product seizure or recall, operating restrictions, imposition of a consent decree, modification or withdrawal of product approval or criminal prosecution and would limit the availability of our product. Any manufacturing defect or error discovered after products have been produced and distributed also could result in significant consequences, including costly recall procedures, re-stocking costs, damage to our reputation and potential for product liability claims.

If our third-party manufacturers are unable to produce the required commercial quantities of NERLYNX to meet market demand for NERLYNX on a timely basis or at all, or if they fail to comply with applicable laws for the manufacturing of NERLYNX, we will suffer damage to our reputation and commercial prospects and we will lose potential revenue.

***Clinical trials are very expensive, time-consuming and difficult to design and implement.***

Although NERLYNX has been approved by the FDA for the extended adjuvant treatment of early stage, HER2-positive breast cancer, NERLYNX is still under development for various indications in the United States, and our other drug candidates are in development, as well, all of which will require extensive clinical testing before we can submit any NDA for regulatory approval. We cannot predict with any certainty that any NDA or supplemental NDA seeking to expand the indication for NERLYNX will be approved by the FDA. Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. The clinical trial process is also time consuming. We estimate that clinical trials of our other drug candidates will take at least several years to complete. Furthermore, failure can occur at any stage of the trials, and we could encounter problems that cause us to abandon or repeat clinical trials. The results of pre-clinical studies and early clinical trials of our drug candidates may not be predictive of the results of later-stage clinical trials. Drug candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through pre-clinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Our future clinical trial results may not be successful.

We do not know whether our future clinical trials will begin on time or enroll patients on time, or whether our ongoing and/or future clinical trials will be completed on schedule or at all. Clinical trials can be delayed for a variety of reasons, including delays related to:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical studies;
- obtaining regulatory authorizations to commence a trial or reaching a consensus with regulatory authorities on trial design;
- any failure or delay in reaching an agreement with CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining approval from one or more institutional review boards, or IRBs;
- IRBs refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing their approval of the trial;
- changes to clinical trial protocol;
- clinical sites deviating from trial protocol or dropping out of a trial;
- manufacturing sufficient quantities of product candidate or obtaining sufficient quantities of combination therapies for use in clinical trials;
- subjects failing to enroll or remain in our trial at the rate we expect, or failing to return for post-treatment follow-up;
- subjects choosing an alternative treatment for the indication for which we are developing our product candidates, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trial;
- subjects experiencing severe or unexpected drug-related adverse effects;
- occurrence of serious adverse events in trials of the same class of agents conducted by other companies;
- selection of clinical end points that require prolonged periods of clinical observation or analysis of the resulting data;
- a facility manufacturing our product candidates or any of their components being ordered by the FDA or comparable foreign regulatory authorities to temporarily or permanently shut down due to violations of current good manufacturing practice, or cGMP, regulations or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process;
- any changes to our manufacturing process that may be necessary or desired;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, good clinical practices, or GCP, or other regulatory requirements;
- third-party contractors not performing data collection or analysis in a timely or accurate manner; or
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications.

Further, we, the FDA, foreign regulatory authorities, or an Institutional Review Board, or IRB, may suspend our clinical trials at any time if it appears that we or our collaborators are failing to conduct a trial in accordance with regulatory requirements, that we are exposing participants to unacceptable health risks, or if the FDA or such other regulator finds deficiencies in our IND or comparable submissions or the conduct of these trials. Therefore, we cannot predict with any certainty the schedule for commencement and completion of future clinical trials. If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of our drug candidates could be harmed, and our ability to generate revenue from the drug candidates may be delayed. In addition, any delays in our clinical trials could increase our costs, slow down the approval process and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may harm our business, financial condition and results of operations. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our drug candidates.



***Enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control.***

We may encounter delays in enrolling, or be unable to enroll, a sufficient number of patients to complete any of our clinical trials, and even once enrolled we may be unable to retain a sufficient number of patients to complete any of our trials. Patient enrollment and retention in clinical trials depends on many factors, including the size of the patient population, the nature of the trial protocol, the existing body of safety and efficacy data with respect to the study drug, the number and nature of competing treatments and ongoing clinical trials of competing drugs for the same indication, the proximity of patients to clinical sites and the eligibility criteria for the study. Furthermore, any negative results we may report in clinical trials of any of our drug candidates may make it difficult or impossible to recruit and retain patients in other clinical studies of that same drug candidate. Delays or failures in planned patient enrollment and/or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop our drug candidates or could render further development impossible. In addition, we expect to rely on CROs and clinical trial sites to ensure proper and timely conduct of our future clinical trials and, while we intend to enter into agreements governing their services, we will be limited in our ability to compel their actual performance.

***The results of our clinical trials may not support our drug candidate claims.***

Even if our clinical trials are completed as planned, we cannot be certain that their results will support the safety and effectiveness of our drug candidates for our targeted indications. Success in pre-clinical testing and early clinical trials does not ensure that later clinical trials will be successful, and we cannot be sure that the results of later clinical trials will replicate the results of prior clinical trials and pre-clinical testing. A failure of a clinical trial to meet its predetermined endpoints would likely cause us to abandon a drug candidate and may delay development of other drug candidates.

Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA, EMA or comparable foreign regulatory authority approval. We cannot guarantee that the FDA or foreign regulatory authorities will interpret trial results as we do, and more trials could be required before we are able to submit applications seeking approval of our product candidates. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates. Even if regulatory approval is secured for any of our product candidates, the terms of such approval may limit the scope and use of our product candidate, which may also limit its commercial potential. Furthermore, the approval policies or regulations of the FDA, EMA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval, which may lead to the FDA, EMA or comparable foreign regulatory authorities delaying, limiting or denying approval of our product candidates.

***Engaging in international business subjects us to additional business and regulatory risks, and there can be no assurance that our products will be accepted in those markets.***

We have entered into exclusive sub-license agreements providing for third parties to pursue regulatory approval and commercialize NERLYNX, if approved, in various specified regions outside of the United States. We plan to continue to pursue commercialization of NERLYNX in additional countries outside the United States where it has been approved. Engaging in international business inherently involves a number of difficulties and risks, including:

- competition from established companies, many of which are well-positioned within their local markets with longer operating histories, more recognizable names and better established distribution networks;
- the availability and level of coverage and reimbursement within prevailing foreign healthcare payment systems and the ability of patients to elect to privately pay for NERLYNX and our other products, if approved;
- difficulties in enforcing intellectual property rights;
- pricing pressure;
- required compliance with existing and changing foreign regulatory requirements and laws;
- laws and business practices favoring local companies;
- longer sales and payment cycles;
- difficulties in enforcing agreements and collecting receivables through certain foreign legal systems;
- political and economic instability;
- foreign currency risks that could adversely affect our financial results;
- potentially adverse tax consequences, tariffs and other trade barriers;
- exposure to liabilities under anti-corruption and anti-money laundering laws, including the U.S. Foreign Corrupt Practices Act, or FCPA, and similar laws and regulations in other jurisdictions;

- international terrorism and anti-American sentiment;
- difficulties and costs associated with staffing and managing foreign operations; and
- export restrictions and controls relating to technology.

If we or our sub-licensees or third-party manufacturers are unable to address these international risks, we may fail to establish and maintain an international presence, and our business, financial condition and results of operations would suffer.

***The failure to comply with anti-bribery, anti-corruption, and anti-money laundering laws, including the FCPA and similar laws associated with our activities outside of the United States, could subject us to penalties and other adverse consequences.***

We are subject to the FCPA, regulations of the U.S. Office of Foreign Assets Control, the United Kingdom Bribery Act of 2010 and other anti-corruption, anti-bribery and anti-money laundering laws around the world where we conduct activities, including, if approved in such countries, the sale of NERLYNX. We face significant risks and liability if we fail to comply with the FCPA and other anti-corruption and anti-bribery laws that prohibit companies and their employees and third-party business partners, such as distributors or resellers, from authorizing, offering or providing, directly or indirectly, improper payments or benefits to foreign government officials, political parties or candidates, employees of public international organizations including healthcare professionals, or private-sector recipients for the corrupt purpose of obtaining or retaining business, directing business to any person, or securing any advantage. We currently rely on various third parties for certain services outside the United States, including continued development of NERLYNX and, if approved, its subsequent commercialization. We may be held liable for the corrupt or other illegal activities of these third parties and intermediaries, our employees, representatives, contractors, partners, and agents, even if we do not explicitly authorize such activities.

Any violation of the FCPA, other applicable anti-bribery, anti-corruption laws, and anti-money laundering laws could result in whistleblower, adverse media coverage, investigations, loss of export privileges, severe criminal or civil sanctions and, in the case of the FCPA, suspension or debarment from U.S. government contracts, which could have a material and adverse effect on our reputation, business, operating results and prospects. In addition, responding to any enforcement action or related investigation may result in a materially significant diversion of management's attention and resources and significant defense costs and other professional fees.

***If we fail to comply with United States export control and economic sanctions or fail to expand and maintain an effective sales force or successfully develop our international distribution network, our business, financial condition and operating results may be adversely affected.***

When selling any products outside of the United States, including NERLYNX, we are subject to United States export control and economic sanctions laws, the violation of which could result in substantial penalties being imposed against us. More broadly, if we fail to comply with export control laws, any sales could fail to grow or could decline, and our ability to grow our business could be adversely affected.

***Regulatory approval for any approved product is limited by the FDA to those specific indications and conditions for which clinical safety and efficacy have been demonstrated as set forth on the product label. If we market NERLYNX for uses beyond such approved indications, we could be subject to enforcement action, which could have a material adverse effect on our business.***

The FDA strictly regulates marketing, labeling, advertising and promotion of prescription drugs. These regulations include standards and restrictions for direct-to-consumer advertising, industry-sponsored scientific and educational activities, promotional activities involving the internet and off-label promotion. Any regulatory approval that the FDA grants is limited to those specific diseases and indications for which a product is deemed to be safe and effective by the FDA. For example, the FDA-approved label for NERLYNX is limited to the extended adjuvant treatment of adult patients with early stage, HER2-positive breast cancer following adjuvant trastuzumab-based therapy. In addition to the FDA approval required for new formulations, any new indication for an approved product also requires FDA approval. If we are not able to obtain FDA approval for any desired future indications for our drugs and drug candidates, our ability to effectively market and sell our products may be reduced and our business may be adversely affected.

While physicians in the United States may choose, and are generally permitted, to prescribe drugs for uses that are not described in the product's labeling and for uses that differ from those tested in clinical trials and approved by the regulatory authorities, our ability to promote the products is narrowly limited to those indications that are specifically approved by the FDA. These "off-label" uses are common across medical specialties and may constitute an appropriate treatment for some patients in varied circumstances. For example, in April 2018 we announced that NERLYNX (neratinib) has been included as a recommended treatment option in the latest NCCN Clinical Practice Guidelines in Oncology Central Nervous System Cancers for Breast Cancer patients with brain metastases. The NCCN designated NERLYNX in combination with capecitabine as a category 2A treatment option and NERLYNX in combination with paclitaxel as a category 2B treatment option. Use, as designated for breast cancer patients with brain metastases, is outside the FDA approved indication for NERLYNX and considered investigational, and we do not market or promote NERLYNX

for these uses. Regulatory authorities in the United States generally do not regulate the behavior of physicians in their choice of treatments. Regulatory authorities do, however, restrict communications by pharmaceutical companies on the subject of off-label use. Although recent court decisions suggest that certain off-label promotional activities may be protected under the First Amendment, the scope of any such protection is unclear. If our promotional activities fail to comply with the FDA's regulations or guidelines, we may be subject to warnings from, or enforcement action by, these authorities. In addition, our failure to follow FDA rules and guidelines relating to promotion and advertising may cause the FDA to issue warning letters or untitled letters, bring an enforcement action against us, suspend or withdraw an approved product from the market, require a recall or institute fines or civil fines, or could result in disgorgement of money, operating restrictions, injunctions or criminal prosecution, any of which could harm our reputation and our business.

***Even though the FDA has approved NERLYNX for the extended adjuvant treatment of early stage, HER2-positive breast cancer in adult patients following adjuvant trastuzumab-based therapy, we will be subject to ongoing obligations and continued regulatory review with regard to NERLYNX and any other drug candidates that receive FDA approval, which may result in significant additional expense. Additionally, NERLYNX and our drug candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.***

The FDA's approval of the NDA for NERLYNX and any regulatory approvals that we receive for our other drug candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase IV clinical trials, and surveillance to monitor the safety and efficacy of the drug candidate. In addition, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these Executive Orders will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

***We rely on third parties to conduct our pre-clinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for our drug candidates.***

We depend upon independent investigators and collaborators, such as CROs, universities and medical institutions, to conduct our pre-clinical studies and clinical trials under agreements with us. These collaborators are not our employees and we cannot control the amount or timing of resources that they devote to our programs. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with regulatory requirements, including GCP requirements, and the applicable protocol. If we, or any of our CROs or third party contractors, fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be

conducted with product produced under current cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, third party contractors and investigators may not assign as great a priority to our programs or pursue them as diligently as we would if we were undertaking such programs ourselves. If outside collaborators fail to devote sufficient time and resources to our drug-development programs, or if their performance is substandard or otherwise fails to satisfy applicable regulatory requirements, the approval of our FDA applications, if any, and our introduction of new drugs, if any, will be delayed. These collaborators may also have relationships with other commercial entities, some of whom may compete with us. If our collaborators assist our competitors to our detriment, our competitive position would be harmed. If any of our relationships with these third-party collaborators terminate, we may not be able to enter into arrangements with alternative third parties on commercially reasonable terms, or at all. Switching or adding additional third parties to our clinical trial programs can involve substantial costs and require extensive management time and focus.

***We rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cybersecurity incidents, could harm us.***

Our internal computer systems and those of third parties with which we contract may be vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures despite the implementation of security measures. System failures, accidents or security breaches could cause interruptions in our operations and could result in a material disruption of our clinical activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. The loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and our research and development programs and the development of our drug candidates could be delayed.

***Compliance with governmental regulation and other legal obligations related to privacy, data protection and information security could result in additional costs and liabilities to us or inhibit our ability to collect and process data, and the failure to comply with such requirements could have a material adverse effect on our business, financial condition or results of operations.***

Privacy and data security have become significant issues in the United States, Europe and in many other jurisdictions where we may in the future conduct our operations. As we receive, collect, process, use and store personal and confidential data, we are subject to diverse laws and regulations relating to data privacy and security, including, in the United States, HIPAA, and, in the EU, GDPR. In addition, in the United States, certain states have also enacted data privacy and security laws. For example, in June 2018, California enacted the California Consumer Privacy Act, or CCPA, which went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA may increase our compliance costs and potential liability, and similar laws have been proposed at the federal level and in other states. Compliance with these privacy and data security requirements is rigorous and time-intensive and may increase our cost of doing business, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation and reputational harm, which could materially and adversely affect our business, financial condition and results of operations.

In addition, the regulatory framework for the receipt, collection, processing, use, safeguarding, sharing and transfer of personal and confidential data is rapidly evolving and is likely to remain uncertain for the foreseeable future as new global privacy rules are being enacted and existing ones are being updated and strengthened. For example, on May 25, 2018, GDPR took effect in Europe. GDPR is directly applicable in each European Union member state and applies to companies established in the European Union as well as companies that collect and use personal data to offer goods or services to, or monitor the behavior of, individuals in the European Union. GDPR introduces more stringent data protection obligations for processors and controllers of personal data, and penalties and fines for failure to comply with GDPR are significant, including fines of up to €20 million or 4% of total worldwide annual turnover, whichever is higher.

***Health care reform measures may hinder or prevent our products' and product candidates' commercial success.***

The United States and some foreign jurisdictions have enacted or are considering enacting a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to profitably sell our product and product candidates, if and when they are approved. 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.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, became law in the United States. The ACA substantially changed and will continue to change the way healthcare is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. Among the provisions of the ACA, of greatest importance to the pharmaceutical industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals, which began in April 2010, and by adding new eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level beginning in 2014, thereby potentially increasing manufacturers' Medicaid rebate liability;
- increase in the number of entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians;
- a licensure framework for follow-on biologic products; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA. As a result, there have been delays in the implementation of, and action taken to repeal or replace, certain aspects of the ACA. Most recently, the Tax Cuts and Job Act was enacted, which, among other things, removes the penalties for not complying with the ACA's individual mandate to carry health insurance. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, ruled that the individual mandate is a critical and inseparable feature of the ACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the U.S. Court of Appeals for the Fifth Circuit ruled that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. It is unclear how these decisions, subsequent appeals, if any, and other efforts to challenge, repeal or replace the ACA will impact the ACA and our business. We cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, the Budget Control Act of 2011 resulted in aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments, will remain in effect through 2029 unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012, among other things, also reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Recently, there has been heightened governmental scrutiny over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills 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 drug products. For example, the 21st Century Cures Act changes the reimbursement methodology for infusion drugs and biologics furnished through durable medical equipment in an attempt to remedy over- and underpayment of certain drugs. We cannot predict all of the ways in which future federal or state legislative or administrative changes relating to healthcare reform will affect our business.

Individual states in the United States have also become increasingly active in 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. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs.

We anticipate that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product, and could seriously harm our business. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product and product candidates, if approved.

In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize NERLYNX and our other product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could restrict or regulate post-approval activities and affect our ability to commercialize NERLYNX and our other product candidates, if approved. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our collaborators are not able to maintain regulatory compliance, NERLYNX may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

***Failure to obtain or maintain adequate coverage and reimbursement for our products or product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.***

Successful commercial sales of any approved products will depend on the availability of adequate coverage and reimbursement from government health administration authorities, private health insurers and other third-party payors. Each third-party payor separately decides which products it will cover and establishes the reimbursement level, and there is no guarantee that any of our approved products or product candidates that may be approved for marketing by regulatory authorities will receive adequate coverage or reimbursement levels. Obtaining and maintaining coverage approval for a product is time-consuming, costly and may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of coverage and reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or limited, we may not be able to successfully commercialize any product or product candidate for which we obtain marketing approval. Government authorities and 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 drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs and biologics. Even if we obtain coverage for a given product, the resulting reimbursement rates may be inadequate and may affect the demand for, or the price of, any product candidate for which we obtain marketing approval.

We expect to experience pricing pressures in connection with the sale of our current or future commercial products, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals. There may be additional pressure by payors and healthcare providers to use generic drugs that contain the active ingredients found in neratinib (oral), neratinib (intravenous), PB357 or any other drug candidates that we may develop. If we fail to successfully secure and maintain adequate coverage and reimbursement for our products or are significantly delayed in doing so, we will have difficulty achieving market acceptance of our products and expected revenue and profitability which would have a material adverse effect on our business, results of operations and financial condition.

***We are subject, directly and indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, physician payment transparency laws and health information privacy and security laws. Failure to comply with these laws may subject us to substantial penalties.***

We do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors. However, federal and state healthcare laws and regulations pertaining to fraud and abuse, physician payment transparency, privacy and security laws and regulations may apply to us depending on programs we operate and have been asserted by the government and others to apply to companies like us, and our arrangements with healthcare providers, customers and other entities, including our marketing practices, educational programs and pricing policies. These laws include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- federal false claims laws, including, without limitation, the False Claims Act, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid or other federal third-party payors that are false or fraudulent, such as engaging in improper promotion of products or submitting inaccurate price reports to the Medicaid Drug Rebate program;
- the federal Civil Monetary Penalties law, which prohibits, among other things, offering or transferring remuneration to a federal healthcare beneficiary that a person knows or should know is likely to influence the beneficiary's decision to order or receive items or services reimbursable by the government from a particular provider or supplier;
- federal criminal laws that prohibit executing a scheme to defraud any federal healthcare benefit program or making false statements relating to healthcare matters; similar to the federal 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;
- HIPAA, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information held by certain covered entities and their business associates, and imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal Physician Payment Sunshine Act, which requires 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 Centers for Medicare & Medicaid Services, or CMS, information related to payments or other “transfers of value” made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other healthcare professionals starting in 2022, and teaching hospitals, and requires applicable manufacturers and group purchasing organizations to report annually to CMS ownership and investment interests held by the physicians described above and their immediate family members and payments or other “transfers of value” to such physician owners (manufacturers are required to submit reports to CMS by the 90th day of each calendar year);
- analogous state equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the industry’s voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts; and
- European and other foreign law equivalents of each of these laws, including reporting requirements detailing interactions with and payments to healthcare providers and laws governing the privacy and security of certain protected information, such as GDPR, which imposes obligations and restrictions on the collection and use of personal data relating to individuals located in the EU (including health data).

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available under such laws, it is possible that some of our business activities, including our relationships with physicians and other healthcare providers, some of whom recommend, purchase and/or prescribe our products, and the manner in which we promote our products, could be subject to challenge under one or more of such laws.

We are also exposed to the risk that our employees, independent contractors, principal investigators, consultants, vendors, distributors and agents may engage in fraudulent or other illegal activity. While we have policies and procedures in place prohibiting such activity, misconduct by these parties could include, among other infractions or violations, intentional, reckless and/or negligent conduct or unauthorized activity that violates FDA requirements, including those laws that require the reporting of true, complete and accurate information to the FDA, manufacturing standards, federal and state healthcare fraud and abuse laws and regulations, laws that require the true, complete and accurate reporting of financial information or data or other commercial or regulatory laws or requirements. It is not always possible to identify and deter misconduct by our employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations.

If our operations are found to violate any of the laws described above or any other laws and regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment of officers involved, any of which could adversely affect our ability to market our current and any future products, once approved, and materially adversely affect our business, results of operations and financial condition. 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.

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

We participate in the Medicaid Drug Rebate Program, as administered by CMS, and other federal and state government pricing programs in the United States, and we may participate in additional government pricing programs in the future. These programs generally require us to pay rebates or otherwise provide discounts to government payors in connection with drugs, including NERLYNX, that are dispensed to beneficiaries of these programs. In some cases, such as with the Medicaid Drug Rebate Program, the rebates are based on pricing and rebate calculations that we report on a monthly and quarterly basis to the government agencies that administer the programs. Pricing and rebate calculations are complex, vary among products and programs, and are often subject to interpretation by governmental or regulatory agencies and the courts. The terms, scope and complexity of these government pricing programs change frequently. Responding to current and future changes may increase our costs and the complexity of compliance will be time consuming.



In addition, there is increased focus by the Office of Inspector General on the methodologies used by manufacturers to calculate average manufacturer price, or AMP, and best price, or BP, to assess manufacturer compliance with reporting requirements under the Medicaid Drug Rebate Program. We are liable for errors associated with our submission of pricing data and for any overcharging of government payors. For example, failure to submit monthly/quarterly AMP and BP data on a timely basis could result in a civil monetary penalty per day for each day the submission is late beyond the due date. Failure to make necessary disclosures and/or to identify overpayments could result in allegations against us under the Federal False Claims Act and other laws and regulations.

Any required refunds to the U.S. government or responding to a government investigation or enforcement action would be expensive and time consuming and could have a material adverse effect on our business, results of operations and financial condition. In the event that CMS were to terminate our rebate agreement, no federal payments would be available under Medicaid or Medicare for our covered outpatient drugs.

***If we cannot compete successfully for market share against other drug companies, we may not achieve sufficient product revenue and our business will suffer.***

The market for our drugs and drug candidates is characterized by intense competition and rapid technological advances. NERLYNX competes, and any of our other drug candidates that receives FDA approval will compete, with a number of existing and future drugs and therapies developed, manufactured and marketed by others. Existing or future competing products may provide greater therapeutic convenience or clinical or other benefits for a specific indication than our products or may offer comparable performance at a lower cost. In addition, a large number of companies are pursuing the development of pharmaceuticals that target the same diseases and conditions that we are targeting. If our products fail to capture and maintain market share, we may not achieve sufficient product revenue and our business will suffer.

We compete against fully integrated pharmaceutical companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors have oncology compounds that have already been approved or are in development. In addition, many of these competitors, either alone or together with their collaborative partners, operate larger research and development programs or have substantially greater financial resources than we do, as well as significantly greater experience in the following:

- developing drugs;
- undertaking pre-clinical testing and clinical trials;
- obtaining FDA and other regulatory approvals of drugs;
- formulating and manufacturing drugs; and
- launching, marketing and selling drugs.

***We may be exposed to liability claims associated with the use of hazardous materials and chemicals.***

Our research and development activities may involve the controlled use of hazardous materials and chemicals. Although we believe that our safety procedures for using, storing, handling and disposing of these materials comply with federal, state and local laws and regulations, we cannot completely eliminate the risk of accidental injury or contamination from these materials. In the event of such an accident, we could be held liable for any resulting damages and any liability could materially adversely affect our business, financial condition and results of operations. In addition, the federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous or radioactive materials and waste products may require us to incur substantial compliance costs that could materially adversely affect our business, financial condition and results of operations.

***The loss of one or more key members of our management team could adversely affect our business.***

Our success and future growth depend, to a significant degree, on the skills and continued services of our management team, in particular Alan H. Auerbach, our Chief Executive Officer and President. If Mr. Auerbach resigns or becomes unable to continue in his present role and is not adequately replaced, our business operations could be materially adversely affected. We do not maintain “key man” life insurance for Mr. Auerbach.

***If we are unable to hire additional qualified personnel, our ability to grow our business may be harmed.***

As of December 31, 2019, we had 269 employees. Our future success depends on our ability to identify, attract, hire, train, retain and motivate other highly skilled scientific, technical, marketing, managerial and financial personnel. Although we will seek to hire and retain qualified personnel with experience and abilities commensurate with our needs, there is no assurance that we will succeed despite their collective efforts. Competition for personnel is intense, and any failure to attract and retain the necessary

technical, marketing, managerial and financial personnel would have a material adverse effect on our business, prospects, financial condition and results of operations.

***We may not successfully manage our growth.***

Our success will depend upon the expansion of our operations and our ability to successfully manage our growth. Our future growth, if any, may place a significant strain on our management and on our administrative, operational and financial resources. Our ability to manage our growth effectively will require us to implement and improve our operational, financial and management systems and to expand, train, manage and motivate our employees. These demands may require the hiring of additional management personnel and the development of additional expertise by management. Any increase in resources devoted to research and product development without a corresponding increase in our operational, financial and management systems could have a material adverse effect on our business, financial condition and results of operations.

***We may be adversely affected by the current economic environment.***

Our ability to attract and retain collaborators or customers, invest in and grow our business and meet our financial obligations depends on our operating and financial performance, which, in turn, is subject to numerous factors, including the prevailing economic conditions and financial, business and other factors beyond our control, such as the rate of unemployment, the number of uninsured persons in the United States and inflationary pressures. We cannot anticipate all the ways in which the current economic climate and financial market conditions could adversely impact our business.

We are exposed to risks associated with reduced profitability and the potential financial instability of our collaborators or customers, many of which may be adversely affected by volatile conditions in the financial markets. For example, unemployment and underemployment, and the resultant loss of insurance, may decrease the demand for healthcare services and pharmaceuticals. If fewer patients are seeking medical care because they do not have insurance coverage, our collaboration partners or customers may experience reductions in revenues, profitability and/or cash flow that could lead them to modify, delay or cancel orders for our products once commercialized. If collaboration partners or customers are not successful in generating sufficient revenue or are precluded from securing financing, they may not be able to pay, or may delay payment of, accounts receivable that are owed to us. This, in turn, could adversely affect our financial condition and liquidity. In addition, if economic challenges in the United States result in widespread and prolonged unemployment, either regionally or on a national basis, a substantial number of people may become uninsured or underinsured. To the extent economic challenges result in fewer individuals pursuing or being able to afford our products once commercialized, our business, results of operations, financial condition and cash flows could be adversely affected.

***We may incur substantial liabilities and may be required to limit commercialization of our products in response to product liability lawsuits and product recalls.***

The testing and marketing of medical products entail an inherent risk of product liability. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our products. If we are unable to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims, the commercialization of pharmaceutical products we develop, alone or with collaborators, could be prevented or inhibited.

Product recalls may be issued at our discretion, or at the discretion of government agencies and other entities that have regulatory authority for pharmaceutical sales. Any recall of NERLYNX could materially adversely affect our business by rendering us unable to sell NERLYNX for some time and by adversely affecting our reputation.

***We may in the future engage in strategic transactions that increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.***

We actively evaluate various strategic transactions on an ongoing basis, including licensing or otherwise acquiring complementary products, technologies or businesses. Any potential future acquisitions or in-licensing transactions entail numerous risks, including but not limited to:

- risks associated with satisfying the closing conditions relating to such transactions and realizing their anticipated benefits;
- increased operating expenses and cash requirements;
- difficulty integrating acquired technologies, products, operations, and personnel with our existing business;
- the potential disruption of our historical core business;
- diversion of management's attention in connection with both negotiating the acquisition or license and integrating the business, technology or product;

- retention of key employees;
- difficulties in assimilating employees and corporate cultures of any acquired companies;
- uncertainties in our ability to maintain key business relationships of any acquired companies;
- strain on managerial and operational resources;
- difficulty implementing and maintaining effective internal control over financial reporting at businesses that we acquire, particularly if they are not located near our existing operations;
- exposure to unanticipated liabilities of acquired companies or companies in which we invest;
- the potential need to write down assets or recognize impairment charges; and
- potential costly and time-consuming litigation, including stockholder lawsuits.

As a result of these or other problems and risks, businesses, technologies or products we acquire or invest in or obtain licenses to may not produce the revenues, earnings or business synergies that we anticipated, acquired or licensed product candidates or technologies may not result in regulatory approvals, and acquired or licensed products may not perform as expected. As a result, we may incur higher costs and realize lower revenues than we had anticipated. We cannot assure you that any acquisitions or investments we have made or may make in the future will be completed or that, if completed, the acquired business, licenses, investments, products, or technologies will generate sufficient revenue to offset the negative costs or other negative effects on our business. Failure to effectively manage our growth through acquisition or in-licensing transactions could adversely affect our growth prospects, business, results of operations, financial condition, and cash flow.

In addition, we may spend significant amounts, issue dilutive securities, assume or incur significant debt obligations, incur large one-time expenses and acquire intangible assets or goodwill in connection with acquisitions and in-licensing transactions that could result in significant future amortization expense and write-offs. Moreover, we may not be able to locate suitable acquisition opportunities and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business. Other pharmaceutical companies, many of which may have substantially greater financial, marketing and sales resources, compete with us for these opportunities. Even if appropriate opportunities are available, we may not be able to successfully identify them or we may not have the financial resources necessary to pursue them, and if pursued, we may be unable to structure and execute transactions in the anticipated timeframe, or at all.

#### **Risks Related to Our Intellectual Property**

***We depend significantly on intellectual property licensed from Pfizer and the termination of this license would significantly harm our business and future prospects.***

We depend significantly on our license agreement with Pfizer. Our license agreement with Pfizer may be terminated by Pfizer if we materially breach the agreement and fail to cure our breach during an applicable cure period. Our failure to use commercially reasonable efforts to develop and commercialize licensed products in certain specified major market countries would constitute a material breach of the license agreement. Pfizer may also terminate the license agreement if we become involved in bankruptcy, receivership, insolvency or similar proceedings. In the event our license agreement with Pfizer is terminated, we will lose all of our rights to develop and commercialize the drug candidates covered by such license, which would significantly harm our business and future prospects.

***Our proprietary rights may not adequately protect our intellectual property and potential products, and if we cannot obtain adequate protection of our intellectual property and potential products, we may not be able to successfully market our potential products.***

Our commercial success will depend in part on obtaining and maintaining intellectual property protection for our products, formulations, processes, methods and other technologies. We will only be able to protect these technologies and products from unauthorized use by third parties to the extent that valid and enforceable intellectual property rights, including patents, cover them, or other market exclusionary rights apply. The patent positions of pharmaceutical companies, like ours, can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in such companies' patents has emerged to date in the United States. The general environment for pharmaceutical patents outside the United States also involves significant uncertainty. Accordingly, we cannot predict the breadth of claims that may be allowed (if any are allowed at all) or enforced, or that the scope of these patent rights could provide a sufficient degree of future protection that could permit us to gain or keep our competitive advantage with respect to these products and technology. For example, we cannot predict:

- the degree and range of protection any patents will afford us against competitors, including whether third parties will find ways to make, use, sell, offer to sell or import competitive products without infringing our patents;

- if and when patents will issue;
- whether or not others will obtain patents claiming inventions similar to those covered by our patents and patent applications; or
- whether we will need to initiate litigation or administrative proceedings in connection with patent rights, which may be costly whether we win or lose, and the outcome of which is unpredictable.

The patents we have licensed may be challenged and could be invalidated or rendered unenforceable by third parties. Changes in either the patent laws or in the interpretations of patent laws in the United States or other countries may diminish the value of our intellectual property.

The patents we have licensed may be affected by certain provisions of the America Invents Act, or AIA, enacted in 2011. For example, under the AIA, members of the public may seek to challenge an issued patent by petitioning the USPTO to institute a post grant proceeding, such as a Post Grant Review, or PGR, or Inter Partes Review, or IPR. Once a post grant proceeding is instituted, the USPTO may find grounds to revoke the challenged patent or specific claims therein. A similar procedure (known as a patent opposition) has existed in Europe for many years and we have defended, and continue to defend, our European patents in certain of those proceedings. We cannot predict whether any other licensed patents will become the subject of a post grant proceeding or patent opposition. If a significant product patent is successfully challenged in a post grant proceeding or patent opposition, it may be revoked, which would have a serious negative impact on our ability to maintain exclusivity in the market-place for our commercial products affected by such revocation and could adversely affect our future revenues and profitability.

In addition, others may independently develop similar or alternative products and technologies that may be outside the scope of our intellectual property. Furthermore, others may have invented technology claimed by our patents before we or our licensors did so, and they may have filed patents claiming such technology before we did so, weakening our ability to obtain and maintain patent protection for such technology. Should third parties obtain patent rights to similar products or technology, this may have an adverse effect on our business.

We may also rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. Trade secrets, however, are difficult to protect. While we believe that we will use reasonable efforts to protect our trade secrets, our own or our strategic partners' employees, consultants, contractors or advisors may unintentionally or willfully disclose our information to competitors. Such disclosure could adversely affect our ability to prevent further disclosures of our trade secrets. We seek to protect this information, in part, through the use of non-disclosure and confidentiality agreements with employees, consultants, advisors and others. These agreements may be breached, and we may not have adequate remedies for a breach. In addition, we cannot ensure that those agreements will be enforceable, provide adequate protection for our trade secrets, know-how or other proprietary information, or prevent their unauthorized use or disclosure.

To the extent that consultants or key employees apply technological information independently developed by them or by others to our potential products, disputes may arise as to the proprietary rights in such information, which may not be resolved in our favor. Consultants and key employees who work with our confidential and proprietary technologies are required to assign all intellectual property rights in their discoveries to us. However, these consultants or key employees may terminate their relationship with us, and we cannot preclude them indefinitely from dealing with our competitors. If our trade secrets become known to competitors with greater experience and financial resources, the competitors may copy or use our trade secrets and other proprietary information in the advancement of their products, methods or technologies. If we were to prosecute a claim that a third party had illegally obtained and was using our trade secrets, it could be expensive and time consuming and the outcome could be unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets than courts in the United States. Moreover, if our competitors independently develop equivalent knowledge, we would lack any legal or contractual claim to prevent them from using such information, and our business could be harmed.

*We may not be able to protect our intellectual property rights throughout the world.*

Filing, prosecuting, and defending our intellectual property rights in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Further, licensing partners may not prosecute patents in certain jurisdictions in which we may obtain commercial rights, thereby precluding the possibility of later obtaining patent protection in these countries. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products, and our intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our intellectual property rights or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our proprietary rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our proprietary rights at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

***Our ability to commercialize our potential products will depend on our ability to sell such products without infringing the patent or proprietary rights of third parties. If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.***

Our ability to commercialize our potential products will depend on our ability to sell such products without infringing the patents or other proprietary rights of third parties. Third-party intellectual property rights in our field are complicated and continuously evolving. The coverage of patents is subject to interpretation by the courts, and this interpretation is not always consistent.

Other companies may have or may acquire intellectual property rights that could be enforced against us. If they do so, we may be required to alter our products, formulations, processes, methods or other technologies, obtain a license, assuming one can be obtained, or cease our product-related activities. Holders of such intellectual property rights are not required to give us a license if one were required. If our products or technologies infringe the intellectual property rights of others, such parties could bring legal action against us or our licensors or collaborators claiming damages and seeking to enjoin any activities that they believe infringe their intellectual property rights. If we are sued for patent infringement, we would need to demonstrate that our products or methods of use either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving the invalidity of a patent is particularly difficult in the United States, since it requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. If we are found to infringe a third-party patent, we may need to cease the commercial sale of our products.

Because patent applications can take many years to issue, there may be currently pending applications unknown to us or reissue applications that may later result in issued patents upon which our products or technologies may infringe. There could also be existing patents of which we are unaware that our products or technologies may infringe. In addition, if third parties file patent applications or obtain patents claiming products or technologies also claimed by us in pending applications or issued patents, we may have to participate in interference proceedings in the U.S. Patent and Trademark Office, or USPTO, to determine priority of invention. If third parties file inter partes review or post-grant review petitions in the USPTO to invalidate our issued U.S. patents, we may have to participate in such proceedings to defend such patents. If third parties file oppositions in foreign countries, we may also have to participate in opposition proceedings in foreign tribunals to defend the patentability of our filed foreign patent applications. The outcome of such proceedings in the United States and foreign countries is predictable. Some of our competitors may be able to sustain the costs of such proceedings and of complex patent litigation more effectively than we can because they have substantially greater resources. Additionally, any uncertainties resulting from the initiation and continuation of any such proceedings or litigation may have a material adverse effect on our ability to raise the funds necessary to continue our operations.

If a third-party claims that we infringe its intellectual property rights, it could cause our business to suffer in a number of ways, including:

- we may become involved in time-consuming and expensive litigation, even if the claim is without merit, the third party's patent is ultimately invalid or unenforceable, or we are ultimately found to have not infringed;
- we may become liable for substantial damages for past infringement if a court decides that our technologies infringe upon a third party's patent;
- we may be ordered by a court to stop making, using, selling, offering for sale, importing or licensing our products or technologies without a license from a patent holder, and such license may not be available on commercially acceptable terms, if at all, or may require us to pay substantial royalties or grant cross-licenses to our patents; and
- we may have to redesign our products so that they do not infringe upon others' patent rights, which may not be possible or could require substantial investment and/or time.

If any of these events occur, our business could suffer, and the market price of our common stock may decline.

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at other companies in these industries, including our competitors or potential competitors. We may become subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers, although no such claims are pending. Litigation may be necessary to defend against these claims. Even if we successfully defend any such claims, we may incur substantial costs in such defense, and our management may be distracted by these claims.

### **Risks Related to Owning our Common Stock**

#### ***The price of our common stock could be subject to volatility related or unrelated to our operations.***

The trading price of our common stock has been highly volatile and could continue to be subject to wide fluctuations in response to various factors, some of which are beyond our control. These factors include:

- the level of sales of NERLYNX;
- the overall demand for NERLYNX, including the customer ordering and discontinuation patterns;
- actual or anticipated quarterly variation in our results of operations or the results of our competitors;
- announcements regarding results of any clinical trials relating to our drug candidates;
- announcements of medical innovations or new products by our competitors;
- developments involving our sublicensees;
- issuance of new or changed securities analyst reports or recommendations for our stock;
- developments or disputes concerning our intellectual property or other proprietary rights;
- commencement of, or developments in, litigation involving us;
- market conditions in the biopharmaceutical industry;
- timing and announcement of regulatory approvals;
- changes in government regulation that affect us or the biopharmaceutical industry more generally;
- any future sales of our common stock or other securities in connection with raising additional capital or otherwise;
- any major change to the composition of our board of directors or management; and
- general economic conditions and slow or negative growth of our markets.

The stock market in general, and market prices for the securities of biotechnology companies like ours in particular, have from time to time experienced volatility that often has been unrelated to the operating performance of the underlying companies. These broad market and industry fluctuations may adversely affect the market price of our common stock, regardless of our operating performance.

***We have been subject to securities litigation in the past, and volatility in the price of our common stock may subject us to securities litigation in the future.***

In the past, securities class action litigation has often been brought against a company following periods of volatility in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. These types of lawsuits are subject to inherent uncertainties, and are expensive and time-consuming to investigate, defend and resolve. For instance, in *Hsu v. Puma Biotechnology, Inc., et al.*, the plaintiff alleged that we and certain of our executive officers made false or misleading statements and failed to disclose material adverse facts about our business, operations, prospects and performance in violation of the Exchange Act. In February 2019, a jury found that we had liability on one of four alleged misstatements, and awarded a maximum of \$4.50 per share in damages, representing approximately 5% of total claimed damages. Trading models suggest that approximately ten million shares traded during the class period may be eligible to claim damages. Based on prior lawsuits, we believe that the number of stockholders who submit proof of claims sufficient to recover damages is typically in the range of 20% to 40% of the total eligible shares, and based on these assumptions, total damages after claims could range from \$9 million to \$18 million. However, the total amount of aggregate class-wide damages remains uncertain and will be ascertained only after an extensive claims process and the exhaustion of any appeals, and it is possible that the total damages will be higher than this estimate. It is also possible, as a result of the verdict, that our insurance carriers may assert a right to be paid back litigation cost reimbursements previously received by us, due to certain provisions in our insurance coverage policy.

Any other litigation to which we are a party may similarly divert our management's attention and financial and other resources, or result in an onerous or unfavorable judgment that may not be reversed upon appeal or in payments of substantial monetary damages or fines. Additionally, we may decide to settle such lawsuits on similarly unfavorable terms, which could adversely affect our business, financial condition, results of operations or stock price.

***Issuance of stock to fund our operations may dilute your investment and reduce your equity interest.***

We may need to raise capital in the future to fund the development of our drug candidates or for other purposes. Any equity financing may have a significant dilutive effect to stockholders and a material decrease in our existing stockholders' equity interest in us. Equity financing, if obtained, could result in substantial dilution to our existing stockholders. At its sole discretion, our board of directors may issue additional securities without seeking stockholder approval, and we do not know when we will need additional capital or, if we do, whether it will be available to us.

***Upon the exercise of our outstanding warrant, holders of our common stock may experience immediate dilution and the market price of our common stock may be adversely affected.***

Our founder, Chief Executive Officer and President, Alan H. Auerbach, holds a warrant for 2,116,250 shares with an exercise price of \$16.00 per share. If any portion of the outstanding warrant is exercised for shares of our common stock prior to its expiration in October 2021, our stockholders may experience immediate dilution and the market price of our common stock may be adversely affected.

***We incur increased costs and demands upon management as a result of complying with the laws and regulations affecting public companies.***

As a public company, we incur significant legal, accounting and other expenses, including costs associated with public company reporting requirements. We also incur costs associated with current corporate governance requirements, including requirements under Section 404 and other provisions of the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, as well as rules implemented by the SEC, or NASDAQ or any stock exchange or inter-dealer quotations system on which our common stock may be listed in the future. The expenses incurred by public companies for reporting and corporate governance purposes have increased dramatically in recent years. These rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly.

These rules and regulations may also make it difficult and expensive for us to maintain the appropriate level of director and officer insurance for a company with our market capitalization. If we are unable to maintain an appropriate level of such insurance, we may be required to accept reduced policy limits and coverage or larger deductible limits. As a result, it may be more difficult for us to attract and retain qualified individuals to serve on our board of directors or as our executive officers.

***If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, our ability to operate our business and investors' views of us.***

We are subject to the rules and regulations of the SEC, including those rules and regulations mandated by the Sarbanes-Oxley Act. Section 404 of the Sarbanes-Oxley Act requires public companies to include in their annual report a statement of management's responsibilities for establishing and maintaining adequate internal control over financial reporting, together with an assessment of the effectiveness of those internal controls. Section 404 also requires the independent auditors of certain public companies to attest to, and report on, this management assessment. Ensuring that we have adequate internal financial and accounting controls and procedures

in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that will need to be evaluated frequently. Our failure to maintain the effectiveness of our internal controls in accordance with the requirements of the Sarbanes-Oxley Act could have a material adverse effect on our business. We could lose investor confidence in the accuracy and completeness of our financial reports, which could have an adverse effect on the price of our common stock. In addition, if our efforts to comply with new or changed laws, regulations, and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to practice, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

***If securities or industry analysts do not publish, or cease publishing, research reports about us, our business or our market, or if they change their recommendations regarding our stock adversely, our stock price and trading volume could decline.***

The trading market for our common stock is and will be influenced by whether industry or securities analysts publish research and reports about us, our business, our market or our competitors and, if any analysts do publish such reports, what they publish in those reports. We may not obtain analyst coverage in the future. Any analysts who do cover us may make adverse recommendations regarding our stock, adversely change their recommendations from time to time, and/or provide more favorable relative recommendations about our competitors. If any analyst who may cover us in the future were to cease coverage of our company or fail to regularly publish reports on us, or if analysts fail to cover us or publish reports about us at all, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

***We do not foresee paying cash dividends in the foreseeable future.***

We currently intend to retain any future earnings for funding growth. We do not anticipate paying any dividends in the foreseeable future, and the payment of dividends is also restricted under our credit facility. As a result, you should not rely on an investment in our securities if you require dividend income. Capital appreciation, if any, of our shares may be your sole source of gain for the foreseeable future. Moreover, you may not be able to re-sell your shares in us at or above the price you paid for them.

***Our ability to use our net operating losses and research and development credit carryforwards to offset future taxable income may be subject to certain limitations.***

In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an “ownership change,” generally defined as a greater than 50% change (by value) in its equity ownership over a three year period, is subject to limitations on its ability to utilize its pre-change net operating losses, or NOLs, and its research and development credit carryforwards to offset future taxable income. Our existing NOLs and research and development credit carryforwards may be subject to limitations arising from previous ownership changes, and if we undergo an ownership change, our ability to utilize NOLs and research and development credit carryforwards could be further limited by Sections 382 and 383 of the Code. Future changes in our stock ownership, some of which might be beyond our control, could result in an ownership change under Sections 382 and 383 of the Code. Furthermore, our ability to utilize NOLs and research and development credit carryforwards of any companies we may acquire in the future may be subject to limitations, in accordance with Sections 382 and 383 of the Code. For these reasons, in the event we experience a change of control, we may not be able to utilize a material portion of the NOLs and research and development credit carryforwards, even if we attain profitability.



**ITEM 1B. UNRESOLVED STAFF COMMENTS**

Not applicable.

**ITEM 2. PROPERTIES**

We lease approximately 65,656 square feet of office space in the building located at 10880 Wilshire Boulevard, Los Angeles, California for use as our corporate headquarters. This lease commenced in December 2011 and over time has been amended to add rentable square footage. The lease terminates in March 2026. We also lease approximately 29,470 square feet of office space in the building located at 701 Gateway Blvd, South San Francisco, California. The lease for the South San Francisco facility commenced in October 2012. The lease will terminate around March 2026, with an option to extend for an additional five-year term. We believe that our existing office space, along with the additional office space in South San Francisco, is adequate to meet current and anticipated future requirements and that additional or substitute space will be available as needed to accommodate any expansions that our operations require.

**ITEM 3. LEGAL PROCEEDINGS*****Hsu vs. Puma Biotechnology, Inc., et. al.***

On June 3, 2015, Hsingching Hsu, individually and on behalf of all others similarly situated, filed a class action lawsuit against us and certain of our executive officers in the United States District Court for the Central District of California (Case No. 8:15-cv-00865-AG-JCG). On October 16, 2015, lead plaintiff Norfolk Pension Fund filed a consolidated complaint on behalf of all persons who purchased our securities between July 22, 2014 and May 29, 2015. A trial on the claims relating to four statements alleged to have been false or misleading was held from January 15 to January 29, 2019. At trial, the jury found that three of the four challenged statements were not false or misleading, and thus found in the defendants' favor on those claims. The jury found liability as to one statement and awarded a maximum of \$4.50 per share in damages, which represents approximately 5% of the total claimed damages of \$87.20 per share. Trading models suggest that approximately ten million shares traded during the class period may be eligible to claim damages. Based on prior lawsuits, we believe that the number of stockholders who submit proof of claims sufficient to recover damages is typically in the range of 20% to 40% of the total eligible shares. Based on these assumptions, total damages after claims could range from \$9 million to \$18 million. The total amount of aggregate class-wide damages remains uncertain and will be ascertained only after an extensive claims process and the exhaustion of any appeals, and it is reasonably possible that the total damages will be higher than this estimate. However, the amount is not estimable at this time.

On September 9, 2019, the Court entered an order specifying the rate of prejudgment interest to be awarded on any valid claims at the 52-week Treasury Bill rate. The Court's order also established a claims process, which is expected to take about twelve months. A final judgment has not been entered.

***Eshelman vs. Puma Biotechnology, Inc., et. al.***

In February 2016, Fredric N. Eshelman filed a lawsuit against our Chief Executive Officer and President, Alan H. Auerbach, and us in the United States District Court for the Eastern District of North Carolina (Case No. 7:16-cv-00018-D). The complaint generally alleged that we and Mr. Auerbach made defamatory statements regarding Dr. Eshelman in connection with a proxy contest. In May 2016, Dr. Eshelman filed a notice of voluntary dismissal of the claims against Mr. Auerbach. A trial on the remaining defamation claims against us took place from March 11 to March 15, 2019. At trial, the jury found us liable and awarded Dr. Eshelman \$15.9 million in compensatory damages and \$6.5 million in punitive damages. The plaintiff has since filed motions seeking attorneys' fees and pre-judgment interest, which if granted could increase the judgment amount. We strongly disagree with the verdict and, on April 22, 2019, filed a motion for a new trial or, in the alternative, a reduced damages award. If the verdict is upheld, pending the outcome of that motion, we intend to appeal the verdict. We estimate the high end of potential damages in the matter could be approximately \$26.3 million; however, the actual amount of damages payable by us is still uncertain and will be ascertained only after completion of post-trial proceedings and the exhaustion of any appeals, and such amount could be greater than the amount of expense already recognized or the high end of the estimate.

**ITEM 4. MINE SAFETY DISCLOSURE**

Not applicable.

## **PART II**

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

#### **Market for Common Stock**

Our common stock has been quoted on the NASDAQ Global Select Market, or NASDAQ, under the symbol "PBYI" since January 3, 2017. Prior to January 3, 2017, shares of our common stock had been listed on the New York Stock Exchange since October 19, 2012.

#### **Record Holders**

On February 20, 2020, we had eight 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. We believe approximately 14,586 additional owners held our common stock in "Street Name" as of February 20, 2020.

#### **Dividends**

We have never declared or paid any cash dividends on our capital stock. Currently, we anticipate that we will retain all available funds for use in the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination relating to dividend policy will be made at the discretion of our board of directors and will depend on our future earnings, capital requirements, financial condition, prospects, applicable Delaware law, which provides that dividends are only payable out of surplus or current net profits, and other factors that our board of directors deems relevant. Additionally, we are restricted from paying cash dividends under our credit facility with Oxford.

#### **Securities Authorized for Issuance Under Equity Compensation Plans**

The information included under Item 12 of Part III of this Annual Report, "Securities Authorized for Issuance Under Equity Compensation Plans," is hereby incorporated by reference into this Item 5 of Part II of this Annual Report.

#### **Recent Sales of Unregistered Securities**

We did not make any sales of unregistered securities during fiscal year 2019.

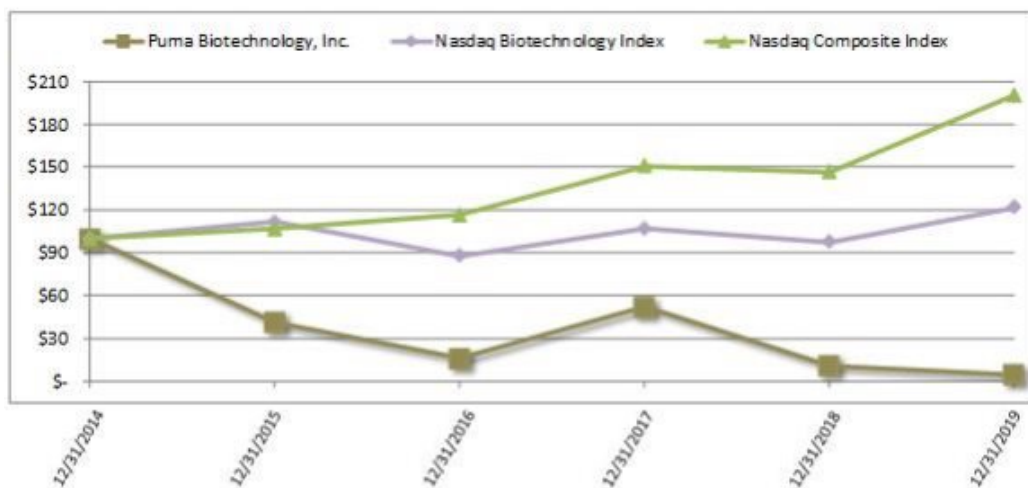
#### **Purchases of Equity Securities by the Issuer and Affiliated Purchasers**

Neither we nor any "affiliated purchasers" within the definition of Rule 10b-18(a)(3) made any purchases of our equity securities during the fourth quarter of 2019.

#### **Performance Graph**

The graph and table below compare the cumulative total return of our common stock from December 31, 2014, through December 31, 2019, with the cumulative total returns on (i) the Nasdaq Biotechnology Index and (ii) the Nasdaq Composite Index. The comparison assumes investment of \$100 on December 31, 2014, in our common stock and in each index and, for each index, assumes reinvestment of all dividends.

The historical price performance included below is not necessarily indicative of future stock price performance.



**Cumulative Total Return**  
**Puma Biotechnology, Inc. Compared to the Nasdaq Biotechnology Index and Nasdaq Composite Index**

	12/31/2014	12/31/2015	12/31/2016	12/31/2017	12/31/2018	12/31/2019
Puma Biotechnology, Inc.	100.00	41.42	16.22	52.23	10.75	4.62
Nasdaq Biotechnology Index	100.00	111.77	87.91	106.92	97.45	121.92
Nasdaq Composite Index	100.00	106.96	116.45	150.96	146.67	200.49

\* On October 19, 2012, shares of Puma common stock were listed and began trading on the New York Stock Exchange.

On January 3, 2017, the listing of shares of Puma common stock was moved to the Nasdaq Stock Market.

The material in this performance graph is not soliciting material, is not deemed filed with the SEC and is not incorporated by reference in any of our filings under the Securities Act of 1933, as amended, or the Exchange Act, whether made on, before or after the date of this filing and irrespective of any general incorporation language in such filing.

**ITEM 6. SELECTED FINANCIAL DATA**

The following financial data should be read in conjunction with our consolidated financial statements and the related notes thereto appearing elsewhere in this Annual Report and with the section entitled “Management’s Discussion and Analysis of Financial Condition and Results of Operations.”

The Consolidated Statement of Operations Data and Other Financial Data for the years ended December 31, 2019, 2018 and 2017 and the Consolidated Balance Sheet Data as of December 31, 2019 and 2018 have been derived from our audited consolidated financial statements included elsewhere in this Annual Report. The Consolidated Statement of Operations Data and Other Financial Data for the years ended December 31, 2016 and 2015 and the Consolidated Balance Sheet Data as of December 31, 2017, 2016 and 2015 have been derived from our audited consolidated financial statements not included herein. Historical results are not necessarily indicative of the results to be expected in the future, and the results for the years presented should not be considered indicative of our future results of operations.

	Years Ended December 31,				
	2019	2018	2017	2016	2015
	(in millions, except share and per share data)				
<i>Statement of Operations Data:</i>					
Product revenue, net	\$ 211.6	\$ 200.5	\$ 26.2	\$ —	\$ —
License revenue	60.3	50.5	1.5	—	—
Royalty revenue	0.4	—	—	—	—
<i>Expenses:</i>					
Cost of sales	36.8	34.6	5.6	—	—
Selling, general and administrative	141.7	146.2	106.7	53.8	31.8
Research and development	132.9	164.9	207.8	222.8	208.5
Operating loss	(39.1)	(94.7)	(292.4)	(276.6)	(240.3)
Interest income	2.8	1.8	1.2	1.0	1.0
Interest expense	(15.0)	(11.0)	(0.7)	—	—
Legal verdict expense	(16.4)	(9.0)	—	—	—
Loss on debt extinguishment	(8.1)	—	—	—	—
Other income (expense)	0.2	(0.7)	(0.1)	(0.4)	—
Total other income (expense)	(36.5)	(18.9)	0.4	0.6	1.0
Net loss	(75.6)	(113.6)	(292.0)	(276.0)	(239.3)
Net loss attributable to common stock	(75.6)	(113.6)	(292.0)	(276.0)	(239.3)
Net loss per common share—basic and diluted	\$ (1.95)	\$ (2.99)	\$ (7.85)	\$ (8.29)	\$ (7.45)
Weighted-average common shares outstanding—basic and diluted	38,768,653	37,942,411	37,169,678	33,295,114	32,126,094

	As of December 31,				
	2019	2018	2017	2016	2015
	(in millions)				
<i>Balance Sheet Data:</i>					
Total assets	\$ 234.9	\$ 259.1	\$ 165.5	\$ 252.8	\$ 239.8
Total liabilities	217.4	224.8	112.2	43.0	33.8
Total stockholders' equity	17.5	34.3	53.3	209.8	206.0

	Years Ended December 31,				
	2019	2018	2017	2016	2015
	(in millions)				
<i>Other Financial Data:</i>					
Net cash provided by (used in) operating activities	\$ 22.4	\$ (24.1)	\$ (172.5)	\$ (141.7)	\$ (154.5)
Net cash provided by (used in) investing activities	5.2	(57.6)	(15.4)	142.2	(85.9)
Net cash provided by (used in) financing activities	(67.1)	108.5	75.1	162.4	233.4

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

*This Annual Report on Form 10-K contains forward-looking statements within the meanings of the federal securities laws. These statements are subject to risks and uncertainties that could cause actual results and events to differ materially from those expressed or implied by such forward-looking statements. For a detailed discussion of these risks and uncertainties, see the "Risk Factors" section in Item 1A of Part I of this Form 10-K. We caution the reader not to place undue reliance on these forward-looking statements, which reflect management's analysis only as of the date of this Form 10-K. We undertake no obligation to update forward-looking statements to reflect events or circumstances occurring after the date of this Form 10-K.*

**Overview**

We are a biopharmaceutical company with a focus on the development and commercialization of innovative products to enhance cancer care. We in-license from Pfizer the global development and commercialization rights to PB272 (neratinib (oral)), PB272 (neratinib (intravenous)) and PB357. Neratinib is a potent irreversible TKI that blocks signal transduction through the epidermal growth factor receptors, HER1, HER2 and HER4. Currently, we are primarily focused on the development and commercialization of the oral version of neratinib, and our most advanced drug candidates are directed at the treatment of HER2-positive breast cancer and HER2 mutated cancers. We believe neratinib has clinical application in the treatment of several other cancers as well, including other tumor types that over-express or have a mutation in HER2, such as breast cancer, cervical cancer, lung cancer or other solid tumors.

Prior to 2017, our efforts and resources were focused primarily on acquiring and developing our pharmaceutical technologies, raising capital and recruiting personnel. In 2017, the FDA approved NERLYNX, formally known as PB272 (neratinib(oral)), for the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer following trastuzumab-based therapy. In 2018, the EC granted marketing authorization for NERLYNX in the European Union for the extended adjuvant treatment of adult patients with early state hormone receptor positive HER-2-overexpressed/amplified breast cancer and who are less than one year from the completion of prior adjuvant trastuzumab-based therapy.

We have entered into exclusive sub-license agreements with various parties to pursue regulatory approval, if necessary, and commercialize NERLYNX, if approved, in various specified regions outside of the United States, including Europe (excluding Russia and Ukraine), Canada, China, Southeast Asia, and various countries and territories in Central and South America. We plan to continue to pursue commercialization of NERLYNX in other countries outside the United States, if approved.

Our expenses to date have been related to hiring staff, commencing company-sponsored clinical trials and the build out of our corporate infrastructure and, since 2017, the commercial launch of NERLYNX. Accordingly, our success depends not only on the safety and efficacy of our product candidates, but also on our ability to finance product development. To date, our major sources of working capital have been proceeds from product and license revenue, public offerings of our common stock, proceeds from our credit facility and sales of our common stock in private placements.

**Summary of Income and Expenses**

*Product revenue, net*

Product revenue, net consists of revenue from sales of NERLYNX. We sell NERLYNX to a limited number of specialty pharmacies and specialty distributors in the United States. We record revenue at the net sales price, which includes an estimate for variable consideration for which reserves are established. Variable consideration consists of trade discounts and allowances, product returns, provider chargebacks and discounts, government rebates and other incentives.

*License revenue*

License revenue consists of consideration earned for performance obligations satisfied pursuant to our sub-license agreements.

*Royalty revenue*

Royalty revenue consists of consideration earned related to product sales made by our sub-licensees in their respective territories pursuant to our license agreements.

### *Cost of sales*

Cost of sales consists of third-party manufacturing costs, freight, and indirect overhead costs associated with sales of NERLYNX. Cost of product sales may also include period costs related to royalty charges payable to Pfizer, the amortization of a milestone payment made to Pfizer after obtaining FDA approval of NERLYNX, certain inventory manufacturing services, inventory adjustment charges, unabsorbed manufacturing and overhead costs, and manufacturing variances.

### *Selling, general and administrative expenses*

Selling, general and administrative, or SG&A, expenses consist primarily of salaries and related personnel costs, including stock-based compensation expense, professional fees, business insurance, rent, general legal activities, and other corporate expenses. Internal expenses primarily consist of payroll-related costs, but also include facilities and equipment costs, travel expenses and supplies. External expenses primarily consist of legal fees, insurance expenses and consulting for activities such as sales, marketing and software implementations to support corporate growth.

### *Research and development expenses*

Research and development, or R&D, expenses include costs associated with services provided by consultants who conduct clinical services on our behalf, contract organizations for manufacturing of clinical materials and clinical trials. During the years ended December 31, 2019, 2018 and 2017, our R&D expenses consisted primarily of clinical research organization, or CRO, fees; fees paid to consultants; salaries and related personnel costs; and stock-based compensation. We expense our clinical R&D costs as they are incurred. Internal R&D expenses primarily consist of payroll-related costs, but also include equipment costs, travel expenses and supplies.

## **Results of Operations**

The following summarizes our results of operations for the years ended December 31, 2019 and 2018. For discussion related to the results of operations and changes in financial condition for the year ended December 31, 2018 compared to the year ended December 31, 2017, please refer to Item 7 of Part II, “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in our Annual Report for the Year Ended December 31, 2018, which was filed with the United States Securities and Exchange Commission on March 1, 2019.

### *Total revenue*

Total revenue was approximately \$272.3 million for the year ended December 31, 2019, compared to \$251.0 million for the year ended December 31, 2018.

### *Product revenue, net*

Product revenue, net was approximately \$211.6 million for the year ended December 31, 2019, compared to \$200.5 million for the year ended December 31, 2018. The increase in product revenue, net was primarily attributable to a 10% increase in gross selling price that occurred in the first quarter of 2019 and again in the third quarter of 2019, partially offset by an increase in variable consideration of approximately 14% for the year ended December 31, 2019 as compared to approximately 7% for the year ended December 31, 2018. The increase in variable consideration is primarily due to a increase in government rebates.

### *License revenue*

License revenue was approximately \$60.3 million for the year ended December 31, 2019, compared to \$50.5 million for the year ended December 31, 2018. The increase in license revenue was primarily due to upfront payments for the satisfaction of our performance obligations and the satisfaction of performance-based milestones related to sub-license agreements, which resulted in greater payments than the upfront payments received in 2018.

### *Royalty revenue*

Royalty revenue was approximately \$0.4 million for the year ended December 31, 2019, compared to no royalty revenue for the year ended December 31, 2018. The increase was due to royalty revenue recognized related to the start of product sales by our sub-licensees.

### Cost of sales

Cost of sales was approximately \$36.8 million for the year ended December 31, 2019, compared to \$34.6 million for the year ended December 31, 2018. The increase in cost of sales was primarily attributable to increased royalty expense due to Pfizer, directly related to the increase in product revenue, net.

### Selling, general and administrative expenses:

Selling, general, and administrative expenses in thousands	For the Year Ended December 31,		Change	
	2019	2018	\$	%
Payroll and related costs	\$ 41,415	\$ 42,730	\$ (1,315)	-3.1%
Professional fees and expenses	49,060	46,366	2,694	5.8%
Travel and meetings	10,987	11,771	(784)	-6.7%
Facilities and equipment costs	5,803	5,902	(99)	-1.7%
Loss on impairment of asset	1,183	-	1,183	100.0%
Stock-based compensation	27,892	34,913	(7,021)	-20.1%
Other	5,352	4,506	846	18.8%
	<u>\$ 141,692</u>	<u>\$ 146,188</u>	<u>\$ (4,496)</u>	<u>-3.1%</u>

Total SG&A expenses decreased approximately 3.1% to \$141.7 million for the year ended December 31, 2019 from \$146.2 million for the year ended December 31, 2018. The decrease is primarily attributable to the following:

- a decrease in stock-based compensation expense of approximately \$7.0 million, primarily due to a decrease of approximately \$8.6 million for stock options and restricted stock units that have fully vested, and a decrease of approximately \$5.6 million from employee turnover, partially offset by an increase of approximately \$5.4 million from new grants, an increase of approximately \$1.1 million from stock award modifications, and other immaterial fluctuations; and
- a decrease in payroll and related costs of approximately \$1.3 million, primarily due to employee turnover and a decrease in sales commission;

which were partially offset by:

- an increase in professional fees and expenses of approximately \$2.7 million, consisting of an increase of approximately \$5.5 million in legal fees for various lawsuits and an increase of approximately \$1.1 million in insurance premiums, partially offset by a decrease of approximately \$2.8 million for consultancy efforts related to marketing and commercialization support, and other immaterial fluctuations; and
- a loss of approximately \$1.2 million in connection with our decision to sublease the right to use a portion of our leased office space recorded as an operating asset in accordance with ASC 842.

### Research and development expenses:

Research and development expenses in thousands	For the Year Ended December 31,		Change	
	2019	2018	\$	%
Clinical trial expense	\$ 51,545	\$ 55,736	\$ (4,191)	-7.5%
Internal R&D	39,603	44,279	(4,676)	-10.6%
Consultant and contractors	12,268	12,813	(545)	-4.3%
Stock-based compensation	29,435	52,026	(22,591)	-43.4%
	<u>\$ 132,851</u>	<u>\$ 164,854</u>	<u>\$ (32,003)</u>	<u>-19.4%</u>

Total R&D expenses decreased approximately 19.4% to \$132.9 million for the year ended December 31, 2019 from \$164.9 million for the year ended December 31, 2018. The decrease is primarily attributable to the following:

- a decrease in stock-based compensation expense of approximately \$22.6 million, primarily due to a decrease of approximately \$18.5 million for stock options and restricted stock units that have fully vested, a decrease of approximately \$8.7 million due to employee turnover, and other immaterial fluctuations, partially offset by an increase of approximately \$5.1 million from new grants;
- a decrease in internal R&D expense of approximately \$4.7 million, primarily due to a decrease in payroll and payroll related expenses of approximately \$5.3 million due to a reduction in headcount, and other immaterial fluctuations, partially offset by an increase in recruitment costs of approximately \$0.6 million and other immaterial fluctuations; and
- a decrease in clinical trial expenses of approximately \$4.2 million, primarily due to the close out of certain clinical trials.

*Other income and expenses:*

Other income (expenses) in thousands	For the Year Ended		Change	
	December 31,		\$	%
	2019	2018		
Interest income	\$ 2,847	\$ 1,796	\$ 1,051	58.5%
Interest expense	(15,019)	(10,985)	(4,034)	36.7%
Legal verdict expense	(16,350)	(9,000)	(7,350)	81.7%
Loss on debt extinguishment	(8,103)	—	(8,103)	-100.0%
Other income (expenses)	128	(714)	842	-117.9%
	<u>\$ (36,497)</u>	<u>\$ (18,903)</u>	<u>\$ (17,594)</u>	<u>93.1%</u>

*Interest income*

For the year ended December 31, 2019, we recognized approximately \$2.8 million in interest income compared to approximately \$1.8 million of interest income for the year ended December 31, 2018. The increase in interest income reflects more cash invested in money market accounts and “high yield” savings accounts in 2019 compared to 2018.

*Interest expense*

For the year ended December 31, 2019, we recognized approximately \$15.0 million in interest expense compared to \$11.0 million of interest expense for the year ended December 31, 2018. The increase in interest expense is primarily attributable to us having greater outstanding borrowings over the course of 2019 as well as a higher interest rate year over year.

*Legal verdict expense*

For the year ended December 31, 2019, we recognized approximately \$16.4 million in legal verdict expense related to the *Eshelman v. Puma Biotechnology, Inc., et al.* verdict. The legal verdict of \$16.4 million is the result of our estimate of total damages payable in the matter of \$22.4 million, net of \$6.0 million in insurance reimbursements. For the year ended December 31, 2018, we recognized \$9.0 million in legal verdict expense that represents an estimate of potential amounts that may be owed to class action participants as a result of the recent jury verdict in *Hsu v. Puma Biotechnology, Inc., et al.* However, the total amount of aggregate class-wide damages is uncertain and will be ascertained only after an extensive claims process and the exhaustion of any appeals. It is also possible that the total damages will be higher than this estimate.

*Loss on debt extinguishment*

For the year ended December 31, 2019, we recognized approximately \$8.1 million in loss on debt extinguishment related to the fees paid in connection with our debt refinancing during the second quarter of 2019 that resulted in the reduction of our long-term debt by approximately \$55.0 million.



## Non-GAAP Financial Measures:

In addition to our operating results, as calculated in accordance with U.S. generally accepted accounting principles, or GAAP, we use certain non-GAAP financial measures when planning, monitoring, and evaluating our operational performance. The following table presents our net loss and net loss per share, as calculated in accordance with GAAP, as adjusted to remove the impact of stock-based compensation. For the years ended December 31, 2019 and 2018, stock-based compensation represented approximately 75.8% and 76.5% of our net loss, respectively. Our management believes that these non-GAAP financial measures are useful to enhance understanding of our financial performance, are more indicative of our operational performance and facilitate a better comparison among fiscal periods. These non-GAAP financial measures are not, and should not be viewed as, substitutes for GAAP reporting measures.

### Reconciliation of GAAP Net Loss to Non-GAAP Adjusted Net Loss and GAAP Net Loss Per Share to Non-GAAP Adjusted Net Loss Per Share (in thousands except share and per share data)

	For the Year Ended December 31,	
	2019	2018
GAAP net loss	\$ (75,595)	\$ (113,575)
Adjustments:		
Stock-based compensation -		
Selling, general and administrative	27,892	34,914 (1)
Research and development	29,435	52,025 (2)
Non-GAAP adjusted net loss	\$ (18,268)	\$ (26,636)
GAAP net loss per share—basic	\$ (1.95)	\$ (2.99)
Adjustment to net loss (as detailed above)	1.48	2.29
Non-GAAP adjusted basic loss per share	\$ (0.47)	\$ (0.70) (3)

(1) To reflect a non-cash charge to operating expense for selling, general, and administrative stock-based compensation.

(2) To reflect a non-cash charge to operating expense for research and development stock-based compensation.

(3) Non-GAAP adjusted basic net loss per share was calculated based on 38,768,653 and 37,942,411 weighted-average shares of common stock outstanding for the years ended 2019 and 2018, respectively.

## Liquidity and Capital Resources

### Operating Activities

We recorded net losses of approximately \$75.6 million and \$113.6 million for the years ended December 31, 2019 and 2018, respectively. We reported positive cash flows from operating activities of approximately \$22.4 million for the year ended December 31, 2019 and reported negative cash flows from operating activities of \$24.1 million for the year ended December 31, 2018.

Net cash provided by operating activities for the year ended December 31, 2019 included a net loss of \$75.6 million, adjusted for non-cash items of approximately \$57.3 million for stock-based compensation expense, approximately \$8.1 million for depreciation and amortization, approximately \$8.0 million for debt extinguishment fees, and a loss of approximately \$1.2 million for the impairment of an operating lease asset. Further changes in cash flows from operations included an increase in accrued expenses of approximately \$22.6 million, an increase in post-marketing commitment liability of approximately \$9.0 million, a decrease in other current assets of approximately \$1.5 million, and a decrease in prepaid expenses and other of approximately \$0.6 million. These changes were offset by an increase in accounts receivable, net of approximately \$8.1 million, a decrease in accounts payable of approximately \$1.5 million, an increase in inventory, net of approximately \$0.5 million, and an increase in deferred rent of approximately \$0.2 million.

Net cash used in operating activities for the year ended December 31, 2018, included a net loss of \$113.6 million adjusted for non-cash items of approximately \$86.9 million for stock-based compensation expense and approximately \$7.4 million for depreciation and amortization. Further changes in cash flows from operations included an increase in accounts receivable, net of approximately \$11.1 million, a decrease in accounts payable of approximately \$7.0 million, and increases in other current assets of approximately \$1.8 million, prepaid expenses and other of approximately \$0.8 million, and inventory, net of approximately \$0.6 million. These changes were offset by an increase in accrued expenses of approximately \$15.8 million and deferred rent of approximately \$0.4 million.

### *Investing Activities*

During the year ended December 31, 2019, cash provided by investing activities was approximately \$5.2 million. This included the purchase of available-for-sale securities of approximately \$127.2 million and the purchase of property and equipment of approximately \$0.3 million, offset by the maturity of available-for-sale securities of approximately \$104.6 million and the sale of available-for-sale securities of approximately \$28.1 million.

During the year ended December 31, 2018, cash used in investing activities was approximately \$57.6 million. This included the purchase of available-for-sale securities of approximately \$107.5 million and cash used for the purchase of property and equipment of approximately \$0.6 million in connection with the expansion of our salesforce and the commercial launch of NERLYNX, offset by the maturity of available-for-sale securities of approximately \$50.5 million.

### *Financing Activities*

During the year ended December 31, 2019, cash used in financing activities was approximately \$67.1 million, which consisted of \$80.0 million in debt repayments, approximately \$7.8 million in debt extinguishment costs, and approximately \$5.6 million in debt issuance costs, offset by \$25.0 million in proceeds from long-term debt and approximately \$1.3 million in net proceeds from the exercise of stock options.

During the year ended December 31, 2018, cash provided by financing activities was approximately \$108.5 million, which consisted of \$105.0 million of incremental proceeds from the Amended Credit Facility and approximately \$7.7 million of net proceeds from the exercise of stock options, partially offset by approximately \$4.2 million in debt issuance costs.

### *Loan and Security Agreement*

In October 2017, we entered into a loan and security agreement with Silicon Valley Bank, or SVB, as administrative agent, and the lenders party thereto from time to time, or the Original Lenders, including Oxford and SVB. Pursuant to the terms of the credit facility provided for by the loan and security agreement, or the Original Credit Facility, we borrowed \$50 million. In May 2018, we entered into an amendment to the loan and security agreement, which provided for an amended credit facility, or the Amended Credit Facility. Under the Amended Credit Facility, the Original Lenders agreed to make term loans available to us in an aggregate amount of \$155 million, consisting of (i) a term loan in an aggregate amount of \$125 million, the proceeds of which, in part, were used to repay the \$50 million we borrowed under the Original Credit Facility, and (ii) a term loan in an aggregate amount of \$30 million that we drew in December 2018, which was available to us under the Amended Credit Facility as a result of achieving a specified minimum revenue milestone. We were in compliance with all applicable financial covenants during the entire term of the Amended Credit Facility.

On June 28, 2019, or the Effective Date, we entered into a new credit facility, or the New Credit Facility, with Oxford, as collateral agent, and the lenders party thereto from time to time, including Oxford, pursuant to which we repaid the \$155.0 million outstanding under the Amended Credit Facility, as well as all applicable exit and prepayment fees owed to the Original Lenders under the Amended Credit Facility, using cash on hand and \$100.0 million in new borrowings from the New Credit Facility. Under the New Credit Facility, we issued to Oxford new and/or replacement secured promissory notes in an aggregate principal amount for all such promissory notes of \$100.0 million evidencing the New Credit Facility. No additional capacity remains available to us under the New Credit Facility.

The New Credit Facility is secured by substantially all of our personal property other than our intellectual property. We also pledged 65% of the issued and outstanding capital stock of our subsidiaries, Puma Biotechnology Ltd. and Puma Biotechnology B.V. The New Credit Facility limits our ability to grant any interest in our intellectual property to certain permitted licenses and permitted encumbrances set forth in the agreement.

The term loans under the New Credit Facility bear interest at an annual rate equal to the greater of (i) 9.0% and (ii) the sum of (a) the “prime rate,” as reported in The Wall Street Journal on the last business day of the month that immediately precedes the month in which the interest will accrue, plus (b) 3.5%. We are required to make monthly interest-only payments on each term loan under the New Credit Facility commencing on the first calendar day of the calendar month following the funding date of such term loan, and continuing on the first calendar day of each calendar month thereafter through August 1, 2021, or the Amortization Date. Commencing on the Amortization Date, and continuing on the first calendar day of each calendar month thereafter, we will make consecutive equal monthly payments of principal, together with applicable interest, in arrears to each lender under the New Credit Facility, calculated pursuant to the New Credit Facility. All unpaid principal and accrued and unpaid interest with respect to each term loan under the New Credit Facility is due and payable in full on June 1, 2024, or the Maturity Date. Upon repayment of such term loans, we are also required to make a final payment to the new lenders equal to 7.5% of the aggregate principal amount of such term loans outstanding as of the Effective Date.

At our option, we may prepay the outstanding principal balance of any term loan in whole but not in part, subject to a prepayment fee of 3.0% of the amount prepaid if the prepayment occurs through and including the first anniversary of the funding date of such term loan, 2.0% of the amount prepaid if the prepayment occurs after the first anniversary of the funding date of such term loan through and including the second anniversary of the funding date of such term loan, and 1.0% of the amount prepaid if the prepayment occurs after the second anniversary of the funding date of such term loan and prior to the Maturity Date.

The New Credit Facility includes affirmative and negative covenants applicable to us, our current subsidiaries and any subsidiaries we create in the future. The affirmative covenants include, among others, covenants requiring us to maintain our legal existence and governmental approvals, deliver certain financial reports, maintain insurance coverage and satisfy certain requirements regarding deposit accounts. We must also achieve certain product revenue targets, measured as of the last day of each fiscal quarter on a trailing year to date basis. New minimum revenue levels will be established for each fiscal year by mutual agreement of us, Oxford, as collateral agent, and the lenders under the New Credit Facility. The negative covenants include, among others, restrictions on our transferring collateral, incurring additional indebtedness, engaging in mergers or acquisitions, paying dividends or making other distributions, making investments, creating liens, selling assets and suffering a change in control, in each case subject to certain exceptions.

The New Credit Facility also includes events of default, the occurrence and continuation of which could cause interest to be charged at the rate that is otherwise applicable plus 5.0% and would provide Oxford, as collateral agent, with the right to exercise remedies against us and the collateral securing the New Credit Facility, including foreclosure against the property securing the New Credit Facility, including our cash. These events of default include, among other things, our failure to pay principal or interest due under the New Credit Facility, a breach of certain covenants under the New Credit Facility, our insolvency, a material adverse change, the occurrence of any default under certain other indebtedness in an amount greater than \$500,000 and one or more judgments against us in an amount greater than \$500,000 individually or in the aggregate that remains unsatisfied, unvacated, or unstayed for a period of 10 days after its entry.

As of December 31, 2019, there was \$100.0 million in principal amounts outstanding under the New Credit Facility, representing all of our long-term debt outstanding as of that date, and we were in compliance with all applicable covenants under the New Credit Facility.

#### *Current and Future Financing Needs*

We did not receive or record any product revenues until the third quarter of 2017. We have spent, and expect to continue to spend, substantial amounts in connection with implementing our business strategy, including our planned product development efforts, our clinical trials, our R&D efforts and our commercialization efforts.

We may choose to begin new R&D efforts or we may choose to launch additional marketing efforts. These efforts may require funding in addition to the cash and cash equivalents totaling approximately \$60.0 million and \$51.6 million in marketable securities available at December 31, 2019. While our consolidated financial statements have been prepared on a going concern basis, we expect to continue incurring significant losses for the foreseeable future and will need to generate significant revenue to sustain operations and successfully commercialize neratinib. While we have been successful in raising financing in the past, there can be no assurance that we will be able to do so in the future. Our ability to obtain funding may be adversely impacted by uncertain market conditions, our success in commercializing neratinib, unfavorable decisions of regulatory authorities or adverse clinical trial results. The outcome of these matters cannot be predicted at this time. We believe that our existing cash and cash equivalents and marketable securities as of December 31, 2019 and proceeds that will become available to us through product sales and license payments are sufficient to satisfy our operating cash and capital needs for at least one year after the filing of this Annual Report.

In addition, we have based our estimate of capital needs on assumptions that may prove to be wrong. Changes may occur that would consume our available capital faster than anticipated, including changes in and progress of our development activities, the impact of commercialization efforts, acquisitions of additional drug candidates and changes in regulation. Potential sources of financing include strategic relationships, public or private sales of equity or debt and other sources of funds. We may seek to access the public or private equity markets when conditions are favorable due to our long-term capital requirements. If we raise funds by selling additional shares of common stock or other securities convertible into common stock, the ownership interests of our existing stockholders will be diluted. If we are not able to obtain financing when needed, we may be unable to carry out our business plan. As a result, we may have to significantly limit our operations, and our business, financial condition and results of operations would be materially harmed. In such an event, we will be required to undertake a thorough review of our programs, and the opportunities presented by such programs, and allocate our resources in the manner most prudent.

## Off-Balance Sheet Arrangements

We do not have any “off-balance sheet arrangements,” as defined by the SEC regulations.

## Contractual Obligations

Contractual obligations represent future cash commitments and liabilities under agreements with third parties and exclude contingent liabilities for which we cannot reasonably predict future payment. Our contractual obligations result from leases for office space and office equipment and the principal and interest owed under our credit facility. We also have unrecognized tax benefits that, if recognized, would affect the effective tax rate at December 31, 2019. We do not have tax positions for which it is reasonably possible that the total amounts of unrecognized tax benefit will significantly increase or decrease within 12 months of the reporting date. Additionally, the expected timing of payment of the obligations presented below is estimated based on current information.

The following table represents our contractual obligations as of December 31, 2019, aggregated by type (in thousands):

Contractual Obligations	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
Operating lease obligations	\$ 34,982	\$ 5,207	\$ 10,848	\$ 11,436	\$ 7,491
Long term debt obligations (principal and interest)	135,659	9,150	63,865	62,644	—
<b>Total</b>	<b>\$ 170,641</b>	<b>\$ 14,357</b>	<b>\$ 74,713</b>	<b>\$ 74,080</b>	<b>\$ 7,491</b>

Although we do have obligations for CRO services, the table above excludes potential payments we may be required to make under our agreements with CROs because timing of payments and actual amounts paid under those agreements may be different depending on the timing of receipt of goods or services or changes to agreed-upon terms or amounts for some obligations, and those agreements are cancelable upon written notice by us and therefore, not long-term liabilities. The contracts also contain variable costs and milestones that are hard to predict as they are based on such things as patients enrolled and clinical trial sites, which can vary and therefore, are also not included in the table above. The contracts held by us as of December 31, 2019, are summarized as follows (in thousands):

Indication	Estimated Contractual Obligation as of December 31, 2019	Months Remaining on Contract
HER2 Overexpressed/Amplified Breast Cancer (Extension)	\$ 16,402	12
HER2 Overexpressed/Amplified Breast Cancer (Licensor Legacy Clinical Trials)	695	3
HER2 Mutated Breast Cancer and HER2 Mutated Breast Cancer with Brain Metastases	697	36
Metastatic & Adjuvant Breast Cancer	24,839	6
Pre-Clinical Research	2,288	10
Post-Clinical Research	2,335	6
HER2 Mutated Solid Tumors	22,117	14
Other	28,425	19
<b>Total</b>	<b>\$ 97,798</b>	

In regards to our contractual obligations in relation to the Pfizer in-license agreement, as consideration for the license, we are required to make substantial payments upon the achievement of certain milestones totaling approximately \$187.5 million if all such milestones are achieved. These milestone amounts were not included in the table above as the timing of when or if these payments will be made is uncertain. In connection with the FDA approval of NERLYNX in July of 2017, we triggered a one-time milestone payment pursuant to the agreement. Should we commercialize any more of the compounds licensed from Pfizer or any products containing any of these compounds, we will be obligated to pay to Pfizer annual royalties at a fixed rate in the low-to-mid teens of net sales of all such products, subject to certain reductions and offsets in some circumstances. Our royalty obligation continues, on a product-by-product and country-by-country basis, until the later of (1) the last to expire licensed patent covering the applicable licensed product in such country, or (2) the earlier of generic competition for such licensed product reaching a certain level in such country or expiration of a certain time period after first commercial sale of such licensed product in such country. In the event that we sublicense the rights granted to us under the license agreement with Pfizer to a third party, the same milestone and royalty payments are required. We can terminate the license agreement at will, or for safety concerns, in each case upon specified advance notice.

See Note 13—Income Taxes and Note 14—Commitments and Contingencies in the accompanying notes to the financial statements for a summary of our uncertain tax positions and contracts held by us as of December 31, 2019. As of December 31, 2019, the amount of unrecognized tax benefit was \$2.0 million, and is also not included in the table above as the timing of when or if these payments will be made is uncertain.

### **Critical Accounting Policies**

The discussion and analysis of our consolidated financial condition and results of operations are based upon our consolidated financial statements, which have been prepared in conformity with GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, and expenses, and related disclosure of contingent assets and liabilities reported in our consolidated financial statements. The estimation process requires assumptions to be made about future events and conditions and, as a result, is inherently subjective and uncertain. Actual results could differ materially from our estimates.

The SEC defines critical accounting policies as those that are, in management's view, most important to the portrayal of our financial condition and results of operations and most demanding of our judgment. We consider the following policies to be critical to an understanding of our consolidated financial statements and the uncertainties associated with the complex judgments made by us that could impact our results of operations, financial position, and cash flows.

#### ***Revenue Recognition:***

We adopted Accounting Standards Codification, or ASC, Topic 606 - *Revenue from Contracts with Customers*, or ASC 606, on January 1, 2017. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements, and financial instruments. Under ASC 606, an entity recognizes revenue when its customer obtains control of the promised goods or services, in an amount that reflects the consideration which the entity expects to be entitled in exchange for those goods or services. We had no contracts with customers until the FDA approved NERLYNX on July 17, 2017. Subsequent to receiving FDA approval, we entered into a limited number of arrangements with specialty pharmacies and specialty distributors in the United States to distribute NERLYNX. These arrangements are our initial contracts with customers. We have determined that these sales channels with customers are similar.

#### ***Product Revenue, Net:***

We sell NERLYNX to a limited number of specialty pharmacies and specialty distributors in the United States. These customers subsequently resell our products to patients and certain medical centers or hospitals. In addition to distribution agreements with these customers, we enter into arrangements with health care providers and payors that provide for government mandated and/or privately negotiated rebates, chargebacks and discounts with respect to the purchase of our products.

We recognize revenue on product sales when the specialty pharmacy or specialty distributor, as applicable, obtains control of our product, which occurs at a point in time (upon delivery). Product revenue is recorded net of applicable reserves for variable consideration.

Shipping and handling costs for product shipments occur prior to the customer obtaining control of the goods and are recorded in cost of sales.

#### ***Reserves for Variable Consideration:***

Revenue from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established. Components of variable consideration include trade discounts and allowances, product returns, provider chargebacks and discounts, government rebates, payor rebates, and other incentives, such as voluntary patient assistance, and other allowances that are offered within contracts between us and our customers, payors, and other indirect customers relating to the sale of our products. These reserves, as detailed below, are based on the amounts earned, or to be claimed on the related sales, and are classified as reductions of accounts receivable or a current liability. These estimates take into consideration a range of possible outcomes which are probability-weighted in accordance with the expected value method in ASC 606 for relevant factors such as current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which it is entitled based on the terms of the respective underlying contracts.

The amount of variable consideration which 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 under the contract will not occur in a future period. Our analyses also contemplated application of the constraint in accordance with the guidance, under which it determined a material reversal of revenue would not occur in a future period for the estimates detailed below as of December 31, 2019 and, therefore, the transaction price was not reduced further during the year ended December 31, 2019. 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.

***Trade Discounts and Allowances:***

We generally provide customers with discounts which include incentive fees that are explicitly stated in our contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, we compensate (through trade discounts and allowances) our customers for sales order management, data, and distribution services. However, we have determined such services received to date are not distinct from our sale of products to the customer and, therefore, these payments have been recorded as a reduction of revenue within the statement of operations.

***Product Returns:***

Consistent with industry practice, we offer the specialty pharmacies and specialty distributors limited product return rights for damaged and expiring products, provided it is within a specified period around the product expiration date as set forth in the applicable individual distribution agreement. 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, as well a reduction to accounts receivables, net on the consolidated balance sheets. We currently estimate product returns using our sales information, including our visibility into the inventory remaining in the distribution channel. We have an insignificant amount of returns to date and believe that returns of our products will continue to be minimal.

***Provider Chargebacks and Discounts:***

Chargebacks for fees and discounts to providers represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to customers who directly purchase the product from us. Customers charge us for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and a reduction to accounts receivable, net on the consolidated balance sheets. Chargeback amounts are generally determined at the time of resale to the qualified healthcare provider by customers, and we generally issue credits for such amounts within a few weeks of the customer's notification to us of the resale. Chargebacks consist of credits that we expect to issue for units that remain in the distribution channel at each reporting period-end that we expect will be sold to qualified healthcare providers, and chargebacks that customers have claimed, but for which we have not yet issued a payment.

***Government Rebates:***

We are subject to discount obligations under state Medicaid programs and Medicare. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses on the consolidated balance sheets. Our liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel at the end of each reporting period.

***Payor Rebates:***

We contract with certain private payor organizations, primarily insurance companies and pharmacy benefit managers, for the payment of rebates with respect to utilization of its products. We estimate these rebates and records such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability.

### ***Other Incentives:***

Other incentives which we offer include voluntary patient assistance programs, such as the co-pay assistance program, which are intended to provide financial assistance to qualified commercially-insured patients with prescription drug co-payments required by payors. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that we expect to receive associated with product that has been recognized as revenue, but remains in the distribution channel at the end of each reporting period. The adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included as a component of accrued expenses on the consolidated balance sheets.

### ***License Revenue:***

We recognize license revenue under certain of our sub-license agreements that are within the scope of ASC 606. The terms of these agreements may contain multiple performance obligations, which may include licenses and research and development activities. We evaluate these agreements under ASC 606 to determine the distinct performance obligations. Non-refundable, up-front fees that are not contingent on any future performance and require no consequential continuing involvement by us, are recognized as revenue when the license term commences and the licensed data, technology or product is delivered. We defer recognition of non-refundable upfront license fees if the performance obligations are not satisfied.

Prior to recognizing revenue, we make estimates of the transaction price, including variable consideration that is subject to a constraint. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur and when the uncertainty associated with the variable consideration is subsequently resolved.

If there are multiple distinct performance obligations, we allocate the transaction price to each distinct performance obligation based on its relative standalone selling price. The standalone selling price is generally determined based on the prices charged to customers or using expected cost-plus margin. Revenue is recognized by measuring the progress toward complete satisfaction of the performance obligations using an input measure.

### ***CANbridge Agreement***

During the first quarter of 2018, we entered into the CANbridge Agreement with CANbridge, to pursue regulatory approval and commercialize NERLYNX, if approved, in the CANbridge Territory. The license agreement granted intellectual property rights and set forth the parties' respective obligations with respect to development, commercialization and supply of the licensed product. Pursuant to the license agreement, a non-refundable, upfront license fee was received and recognized by us as license revenue in accordance with ASC 606. The license agreement met the contract existence criteria and contained distinct, identifiable performance obligations for which the stand-alone selling prices were readily determinable and allocable. We are obligated to supply CANbridge with the licensed product in accordance with the supply agreement entered into in connection with the license agreement. This supply arrangement has been identified as a separate performance obligation. We also identified the Joint Steering Committee as a separate, distinct performance obligation. To determine the stand-alone selling price, we estimated the transaction prices, including any variable consideration, at contract inception and determined the fair value of such obligations based on similar arrangements. When determining the transaction prices, we assumed that the goods or services will be transferred to the customer based on the terms of the existing contract, and did not take into consideration the possibility of a contract being canceled, renewed, or modified. We noted there was no additional variable consideration, significant financing components, noncash consideration, or consideration payable to the customer in this agreement. This license agreement also includes potential future milestone and royalty payments due to us upon successful completion of certain separate, distinct performance obligations. Pursuant to the CANbridge Agreement, we received an upfront payment of \$30.0 million during the first quarter of 2018 and a regulatory milestone payment of \$10.0 million during the fourth quarter of 2018 and will potentially receive regulatory milestone payments totaling up to \$30.0 million and sales-based milestone payments totaling up to \$185.0 million. In addition, we are entitled to receive double-digit royalties calculated as a percentage of net sales of the licensed products in the CANbridge Territory. At this time, we cannot estimate if or when these milestone-related performance obligations might be achieved.

### *Pint Agreement*

During the first quarter of 2018, we entered into the Pint Agreement with Pint. The Pint Agreement granted intellectual property rights and set forth the respective obligations with respect to development, commercialization and supply of NERLYNX in the Pint Territory. The Pint Agreement met the contract existence criteria and contained distinct, identifiable performance obligations for which the stand-alone selling prices were readily determinable and allocable. We are obligated to supply Pint with the licensed product during development pursuant to a supply agreement. This supply arrangement has been identified as a separate performance obligation. To determine the respective stand-alone selling prices, we estimated the transaction prices, including any variable consideration, at contract inception and determined the fair value of such obligations based on similar arrangements. When determining the transaction prices, we assumed that the goods or services will be transferred to the customer based on the terms of the existing contract, and did not take into consideration the possibility of a contract being canceled, renewed, or modified. We noted there was no additional variable consideration, significant financing components, noncash consideration, or consideration payable to the customer in these agreements. Pursuant to the Pint Agreement, we received a non-deductible, non-creditable upfront payment of \$10.0 million upon providing certain required documents on or before September 30, 2018 to the satisfaction of Pint. During the quarter ended September 30, 2018 we satisfied this performance obligation and revenue has been recognized under the terms of the arrangement. The Pint Agreement also includes potential future milestone and royalty payments due to us upon successful completion of certain separate, distinct events, such as achieving regulatory approvals. The non-deductible, non-creditable milestones consist of certain development and commercial performance obligations, and we could earn up to approximately \$24.5 million if all remaining, respective performance obligations are achieved. In addition, we are entitled to receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products throughout the Pint Territory. During the third quarter of 2019, we achieved a certain development-based milestone, which satisfied a performance obligation necessary to recognize the associated license revenue. The payment associated with this license revenue is expected to be received from Pint during the third quarter of 2020. At this time, we cannot estimate if or when the remaining milestone-related performance obligations are expected to be achieved.

### *Knight Agreement*

During the first quarter of 2019, we entered into the Knight Agreement with Knight. Pursuant to the Knight Agreement, we granted to Knight, under certain of our intellectual property rights relating to neratinib, an exclusive, sublicensable (under certain circumstances) license (i) to commercialize any product containing neratinib and certain related compounds in the Knight Territory, (ii) to seek and maintain regulatory approvals for the licensed products in the Knight Territory and (iii) to manufacture the licensed products anywhere in the world solely for the development and commercialization of the licensed products in the Knight Territory for human use, subject to the terms of the Knight Agreement and the related supply agreement. During the first quarter of 2019, a non-refundable, upfront license fee was received and recognized as license revenue in accordance with ASC 606. We satisfied the necessary performance obligations to recognize this license revenue under the terms of the arrangement. This license agreement met the contract existence criteria and contained distinct, identifiable performance obligations for which the stand-alone selling prices were readily determinable and allocable. As a separate promise under the terms of the license agreement, we are obligated to supply Knight with the licensed product in accordance with the supply agreement entered in connection with the license agreement. We are also obligated to participate in a Joint Steering Committee, which was identified as a separate performance obligation. To determine the stand-alone selling price, we estimated the transaction prices, including any variable consideration, at contract inception and determined the fair value of such obligations based on similar arrangements. When determining the transaction prices, we assumed that the goods or services will be transferred to the customer based on the terms of the existing contract, and did not take into consideration the possibility of a contract being canceled, renewed, or modified. We noted there was no additional variable consideration, significant financing components, non-cash consideration, or consideration payable to the customer in this agreement. This license agreement also includes potential future milestone and royalty payments due to us upon successful completion of certain separate, distinct performance obligations. Pursuant to the Knight Agreement, we received an upfront payment of \$1.5 million during the first quarter of 2019 and a milestone payment of approximately \$0.3 million during the third quarter of 2019, and will potentially receive regulatory and commercial milestone payments totaling up to approximately \$5.6 million. In addition, we are entitled to receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products in the Knight Territory. At this time, we cannot estimate if or when these milestone-related performance obligations might be achieved.



### *Pierre Fabre Agreement and Amendment*

During the first quarter of 2019, we entered into the Pierre Fabre Agreement with Pierre Fabre. The Pierre Fabre Agreement granted intellectual property rights and set forth the parties' respective obligations with respect to development, commercialization and supply of any pharmaceutical product containing neratinib in the Pierre Fabre Territory. During the first quarter of 2019, we received a non-refundable, upfront license fee of \$60.0 million, of which \$51.0 million was recognized as license revenue in accordance with ASC 606. We satisfied the necessary performance obligations to recognize this license revenue under the terms of the arrangement. The Pierre Fabre Agreement met the contract existence criteria and contained distinct, identifiable performance obligations for which the stand-alone selling prices were readily determinable and allocable. As a separate promise under the terms of the Pierre Fabre Agreement, we are obligated to supply Pierre Fabre with the licensed product in accordance with the related supply agreement. We are also obligated to participate in a Joint Steering Committee and Transition Plan, which were identified as separate performance obligations. To determine the respective stand-alone selling prices, we estimated the transaction prices, including any variable consideration, at contract inception and determined the fair value of such obligations based on similar arrangements. When determining the transaction prices, we assumed that the goods or services will be transferred to the customer based on the terms of the existing contract and did not take into consideration the possibility of a contract being canceled, renewed, or modified. We noted there was approximately \$9.0 million of additional variable consideration in this agreement related to a post-marketing commitment liability, while there were no significant financing components, non-cash consideration, or consideration payable to the customer. The Pierre Fabre Agreement also includes potential future milestone and royalty payments due to us upon successful completion of certain separate, distinct performance obligations. Pursuant to the Pierre Fabre Agreement, we will potentially receive additional regulatory and commercial milestone payments totaling up to \$345.0 million. In addition, we will receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products throughout the Pierre Fabre Territory. At this time, we cannot estimate if or when these milestone-related performance obligations might be achieved.

During the fourth quarter of 2019, we entered into the Pierre Fabre Amendment with Pierre Fabre to extend the terms of the Pierre Fabre Agreement to the Pierre Fabre Amendment Territory. Pursuant to the Pierre Fabre Amendment, we received an upfront payment of \$4.0 million and will potentially receive additional regulatory and sales-based milestone payments totaling up to \$3.0 million. In addition, we will receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products throughout the Pierre Fabre Amendment Territory. At this time, we cannot estimate if or when these milestone-related performance obligations might be achieved.

### **Recently Issued Accounting Standards**

In February 2016, the FASB issued ASU No. 2016-02, Leases (Topic 842). The amendments in ASU 2016-02 require organizations that lease assets, with lease terms of more than 12 months, to recognize on their balance sheet the assets and liabilities for the rights and obligations created by those leases. Consistent with GAAP, the recognition, measurement, and presentation of expenses and cash flows arising from a lease by a lessee primarily depends on its classification as a finance or operating lease. However, unlike previous GAAP that requires only capital leases to be recognized on the balance sheet, ASU 2016-02 requires both types of leases to be recognized on the balance sheet. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. For lessees, the income statement presentation and expense recognition pattern for financing and operating leases is similar to the current model for capital and operating leases, respectively. Companies may elect to exclude short-term leases. The update also requires additional disclosures that will better enable users of financial statements to assess the amount, timing, and uncertainty of cash flows arising from leases. We adopted ASU 2016-02 in the first quarter of 2019 using the effective date transition method. As permitted under the effective date transition method, financial information and disclosures for periods prior to the date of initial application will not be updated. The adoption of ASU 2016-02 resulted in an increase in assets and liabilities on our consolidated balance sheets related to recording right-of-use assets and corresponding lease liabilities of approximately \$21.6 million and \$27.4 million, respectively. The difference between the additional lease assets and lease liabilities represent deferred rent for leases that existed as of the date of adoption. As a result of the adoption there was no material impact to the consolidated statement of operations or statement of cash flows.

In June 2018, the FASB issued ASU No. 2018-07, Compensation-Stock Compensation (Topic 718) - Improvements to Nonemployee Share-Based Payment Accounting, as part of its Simplification Initiative to reduce the cost and complexity in accounting for nonemployee share-based payment transactions. The amendments in ASU 2018-07, specify that Topic 718 applies to all share-based payment transactions in which a grantor acquires goods or services to be used or consumed in a grantor's own operations by issuing share-based payment awards, including nonemployees. ASU 2018-07 is effective for public entities for fiscal years beginning after December 15, 2018. The adoption of ASU 2018-07 did not have a material effect on our current financial position, results of operations or financial statement disclosures.

In July 2018, the FASB issued ASU No. 2018-09, Codification Improvements. The amendments in ASU 2018-09 do not prescribe any new accounting guidance, but instead makes minor improvements and clarifications of several different FASB ASC areas based on comments and suggestions made by various stakeholders. Certain updates are applicable immediately while others provide for a transition period to adopt in fiscal years beginning after December 15, 2018. The adoption of ASU 2018-09 did not have a material effect on our current financial position, results of operations or financial statement disclosures.

In August 2018, the FASB issued ASU No. 2018-13, Fair Value Measurement (Topic 820): Disclosure Framework-Changes to the Disclosure Requirements for Fair Value Measurement. The amendments in ASU 2018-13 modifies the disclosure requirements on fair value measurements. ASU 2018-13 is effective for fiscal years beginning after December 15, 2019, with early adoption permitted for any removed or modified disclosures. The removed and modified disclosures will be adopted on a retrospective basis and the new disclosures will be adopted on a prospective basis. We do not expect ASU 2018-13 to have a material effect on our current financial position, results of operations or financial statement disclosures.

In December 2019, the FASB issued ASU No. 2019-12, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes, as part of its Simplification Initiative to reduce the cost and complexity in accounting for income taxes. The amendments in ASU 2019-12 removes certain exceptions related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. ASU 2019-12 also amends other aspects of the guidance to help simplify and promote consistent application of GAAP. The guidance is effective for interim and annual periods beginning after December 15, 2020, with early adoption permitted. We do not expect ASU 2019-12 to have a material effect on our current financial position, results of operations or financial statement disclosures.

#### **ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK**

Some of the securities in which we invest have market risk in that a change in prevailing interest rates may cause the principal amount of the cash equivalents to fluctuate. Financial instruments that potentially subject us to significant concentrations of credit risk consist primarily of cash and cash equivalents. We invest our excess cash primarily in cash equivalents such as money market investments as of December 31, 2019. The primary objectives of our investment activities are to ensure liquidity and to preserve principal while at the same time maximizing the income we receive from our cash and cash equivalents without significantly increasing risk. Additionally, we established guidelines regarding approved investments and maturities of investments, which are designed to maintain safety and liquidity.

Because of the short-term maturities of our cash equivalents, we do not believe that a 10% increase in interest rates would have a material effect on the realized value of our cash equivalents.

We also have interest rate exposure as a result of our outstanding term loans. As of December 31, 2019, the aggregate outstanding principal amounts of the term loans was \$100 million. The term loans bear interest at an annual rate equal to the greater of (i) 9.00% and (ii) the sum of (a) the “prime rate,” as reported in The Wall Street Journal on the last business day of the month that immediately precedes the month in which the interest will accrue, plus (b) 3.5%. If overall interest rates had increased by 100 basis points during the year ended December 31, 2019 our interest expense would not have been materially affected.

#### **ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

All financial statements and supplementary data required by this Item are listed in Part IV, Item 15 of this Annual Report and are presented beginning on Page F-1.

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

Not applicable.

## 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 Exchange Act, is recorded, processed, summarized and reported within the timelines 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 timely decisions regarding required disclosures. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can only provide reasonable assurance of achieving the desired control objectives and in reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we have evaluated the effectiveness of our disclosure controls and procedures (as defined under Exchange Act Rule 13a-15(e)), as of December 31, 2019. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that these disclosure controls and procedures were effective as of December 31, 2019.

### Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting that occurred during the year ended December 31, 2019, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

### Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. 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 accounting principles generally accepted in the United States of America.

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.

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 as of December 31, 2019. Management based its assessment on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control—Integrated Framework - 2013* (COSO 2013 framework). Based on this evaluation, our management concluded that, as of December 31, 2019, our internal control over financial reporting was effective.

Our internal control over financial reporting as of December 31, 2019 has been audited by KPMG LLP, our independent registered public accounting firm, as stated in their report, which expresses an unqualified opinion on the effectiveness of our internal control over financial reporting as of December 31, 2019.

## Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors  
Puma Biotechnology, Inc.:

### *Opinion on Internal Control Over Financial Reporting*

We have audited Puma Biotechnology, Inc. and subsidiaries' (the Company) internal control over financial reporting as of December 31, 2019, based on criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control – Integrated Framework - 2013*. In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2019, based on criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control – Integrated Framework - 2013*.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of 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 years in the three-year period ended December 31, 2019, and the related notes (collectively, the consolidated financial statements), and our report dated February 27, 2020 expressed an unqualified opinion on those consolidated financial statements.

### *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 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 of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included 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/ KPMG LLP

Los Angeles, California  
February 27, 2020

**ITEM 9B. OTHER INFORMATION**

None.

**Part III**

**ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE**

The information required by this Item will be included in our 2020 Proxy Statement, which will be filed with the SEC, and is incorporated by reference herein.

**ITEM 11. EXECUTIVE COMPENSATION**

The information required by this Item will be included in our 2020 Proxy Statement, which will be filed with the SEC, and is incorporated by reference herein.

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

The information required by this Item will be included in our 2020 Proxy Statement, which will be filed with the SEC, and is incorporated by reference herein.

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

The information required by this Item will be included in our 2020 Proxy Statement, which will be filed with the SEC, and is incorporated by reference herein.

**ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES**

The information required by this Item will be included in our 2020 Proxy Statement, which will be filed with the SEC, and is incorporated by reference herein.

**Part IV**

**ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES**

Reference is made to the Index to Consolidated Financial Statements beginning on Page F-1 hereof.

## Consolidated Financial Statement Schedules

(a) Documents Filed as Part of Report

(1) Consolidated Financial Statements

- [Report of Independent Registered Public Accounting Firm](#) F-2
- [Consolidated Balance Sheets at December 31, 2019 and 2018](#) F-3
- [Consolidated Statements of Operations for the Years Ended December 31, 2019, 2018 and 2017](#) F-4
- [Consolidated Statements of Comprehensive Loss for the Years Ended December 31, 2019, 2018 and 2017](#) F-5
- [Consolidated Statements of Stockholders' Equity for the Years Ended December 31, 2019, 2018 and 2017](#) F-6
- [Consolidated Statements of Cash Flows for the Years Ended December 31, 2019, 2018 and 2017](#) F-7
- [Notes to Consolidated Financial Statements](#) F-8

(2) Consolidated Financial Statement Schedules

Consolidated Financial Statement Schedules have been omitted because they are either not required or not applicable, or because the information required to be presented is included in the consolidated financial statements or the notes thereto included in this Annual Report.

(3) Exhibits

The exhibits listed on the accompanying Exhibit Index are filed or incorporated by reference as part of this Annual Report and such Exhibit Index is incorporated by reference herein.

## ITEM 16. Form 10-K SUMMARY

None.

## EXHIBIT INDEX

<b>Exhibit Number</b>	<b>Description</b>
2.1	<a href="#"><u>Agreement and Plan of Merger, dated September 29, 2011, by and among Innovative Acquisitions Corp., IAC Merger Corporation, a Delaware corporation and wholly-owned subsidiary of the Company, and Puma Biotechnology, Inc., a Delaware corporation (filed as Exhibit 2.1 to the Company's Current Report on Form 8-K filed with the SEC on October 4, 2011 and incorporated herein by reference)</u></a>
3.1	<a href="#"><u>Certificate of Merger relating to the merger of IAC Merger Corporation with and into Puma Biotechnology, Inc., filed with the Secretary of State of Delaware on October 4, 2011 (filed as Exhibit 3.1 to the Company's Current Report on Form 8-K filed with the SEC on October 11, 2011 and incorporated herein by reference)</u></a>
3.2	<a href="#"><u>Certificate of Ownership and Merger relating to the merger of Puma Biotechnology, Inc. with and into Innovative Acquisitions Corp., filed with the Secretary of State of the State of Delaware on October 4, 2011 (filed as Exhibit 3.2 to the Company's Current Report on Form 8-K filed with the SEC on October 11, 2011 and incorporated herein by reference)</u></a>
3.3	<a href="#"><u>Certificate of Merger relating to the merger of IAC Merger Corporation with and into Puma Biotechnology, Inc., filed with the Secretary of State of Delaware on October 4, 2011 (filed as Exhibit 3.1 to the Company's Current Report on Form 8-K filed with the SEC on October 11, 2011 and incorporated herein by reference)</u></a>
3.4	<a href="#"><u>Second Amended and Restated Certificate of Incorporation of the Company, as filed with the Secretary of State of the State of Delaware on June 14, 2016 (filed as Exhibit 3.1 to the Company's Current Report on Form 8-K filed with the SEC on June 15, 2016 and incorporated herein by reference)</u></a>
3.5	<a href="#"><u>Third Amended and Restated Bylaws of the Company (filed as Exhibit 3.1 to the Company's Current Report on Form 8-K filed with the SEC on May 28, 2019 and incorporated herein by reference)</u></a>
4.1	<a href="#"><u>Form of Common Stock Certificate (filed as Exhibit 4.1 to the Company's Registration Statement on Form S-1/A filed with the SEC on February 1, 2012 and incorporated herein by reference)</u></a>
4.2#	<a href="#"><u>Warrant to Purchase Shares of Common Stock of Puma Biotechnology, Inc., dated October 4, 2011, issued to Alan H. Auerbach (filed as Exhibit 4.2 to the Company's Current Report on Form 8-K filed with the SEC on October 11, 2011 and incorporated herein by reference)</u></a>
4.3+	<a href="#"><u>Description of the Company's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934</u></a>
10.1(a)*	<a href="#"><u>License Agreement, dated August 18, 2011, by and between the Company, as successor to Puma Biotechnology, Inc., and Pfizer Inc. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K/A filed with the SEC on December 16, 2011 and incorporated herein by reference)</u></a>
10.1(b)*	<a href="#"><u>Amendment No. 1 to License Agreement dated July 18, 2014, between the Company and Pfizer, Inc. (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on November 10, 2014 and incorporated herein by reference)</u></a>
10.2(a)#	<a href="#"><u>Puma Biotechnology, Inc. 2011 Incentive Award Plan (filed as Exhibit 10.4 to the Company's Current Report on Form 8-K filed with the SEC on October 11, 2011 and incorporated herein by reference)</u></a>
10.2(b)#	<a href="#"><u>First Amendment to Puma Biotechnology, Inc. 2011 Incentive Award Plan (filed as Appendix A to the Company's Proxy Statement on Form DEF 14A filed with the SEC on April 30, 2014 and incorporated herein by reference)</u></a>
10.2(c)#	<a href="#"><u>Second Amendment to Puma Biotechnology, Inc. 2011 Incentive Award Plan (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 10, 2015 and incorporated herein by reference)</u></a>
10.2(d)#	<a href="#"><u>Third Amendment to Puma Biotechnology, Inc. 2011 Incentive Award Plan (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on June 14, 2017 and incorporated herein by reference)</u></a>
10.2(e)#	<a href="#"><u>Fourth Amendment to Puma Biotechnology, Inc. 2011 Incentive Award Plan (filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed with the SEC on June 14, 2017 and incorporated herein by reference)</u></a>
10.2(f)#	<a href="#"><u>Puma Biotechnology, Inc. 2017 Employment Inducement Incentive Award Plan (filed as Exhibit 99.1 to the Company's Registration Statement on Form S-8 filed with the SEC on May 31, 2017 and incorporated herein by reference)</u></a>

- 10.2(g)# [Form of Stock Option Grant Notice and Stock Option Agreement, issued pursuant to the 2011 Incentive Award Plan \(filed as Exhibit 10.5 to the Company's Annual Report on Form 10-K filed with the SEC on March 29, 2012 and incorporated herein by reference\)](#)
- 10.2(h)# [Form of Chief Executive Officer Stock Option Grant Notice and Stock Option Agreement, issued pursuant to the 2011 Incentive Award Plan \(filed as Exhibit 10.6 to the Company's Annual Report on Form 10-K filed with the SEC on March 29, 2012 and incorporated herein by reference\)](#)
- 10.2(i)# [Form of Performance Share Award Agreement, issued pursuant to the 2011 Incentive Award Plan \(filed as Exhibit 10.2\(d\) to the Company's Annual Report on Form 10-K filed with the SEC on March 3, 2014 and incorporated herein by reference\)](#)
- 10.2(j)# [Form of Restricted Stock Unit Award Agreement, issued pursuant to the 2011 Incentive Award Plan \(filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on October 17, 2016 and incorporated herein by reference\)](#)
- 10.2(k)# [Form of Stock Option Grant Notice and Stock Option Agreement, issued pursuant to the 2017 Employment Inducement Incentive Award Plan \(filed as Exhibit 10.2\(k\) to the Company's Annual Report on Form 10-K filed with the SEC on March 1, 2019 and incorporated herein by reference\)](#)
- 10.3(a) [Registration Rights Agreement, dated October 4, 2011, by and among Puma, the investors listed on Exhibit A attached thereto and the Company \(filed as Exhibit 10.5 to the Company's Current Report on Form 8-K/A filed with the SEC on December 16, 2011 and incorporated herein by reference\)](#)
- 10.3(b) [Amendment No. 1 to Registration Rights Agreement \(filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed with the SEC on November 23, 2011 and incorporated herein by reference\)](#)
- 10.4(a) [Office Lease by and between the Company and CA - 10880 Wilshire Limited Partnership, executed on December 7, 2011 \(filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on December 13, 2011 and incorporated herein by reference\)](#)
- 10.4(b) [First Amendment to the Office Lease, dated as of November 28, 2012, by and between the Company and CA - 10880 Wilshire Limited Partnership \(filed as Exhibit 10.13\(b\) to the Company's Annual Report on Form 10-K filed with the SEC on April 1, 2013 and incorporated herein by reference\)](#)
- 10.4(c) [Second Amendment to the Office Lease, dated as of December 3, 2013, by and between the Company and CA - 10880 Wilshire Limited Partnership \(filed as Exhibit 10.6\(c\) to the Company's Annual Report on Form 10-K filed with the SEC on March 3, 2014 and incorporated herein by reference\)](#)
- 10.4(d) [Third Amendment to the Office Lease, dated as of March 18, 2014, by and between the Company and CA - 10880 Wilshire Limited Partnership \(filed as Exhibit 10.5\(d\) to the Company's Annual Report on Form 10-K filed with the SEC on March 2, 2015 and incorporated herein by reference\)](#)
- 10.4(e) [Fourth Amendment to the Office Lease, dated as of July 31, 2015, by and between the Company and CA - 10880 Wilshire Limited Partnership \(filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on November 9, 2015 and incorporated herein by reference\)](#)
- 10.5# [Employment Agreement, dated January 19, 2012, by and between the Company and Alan H. Auerbach \(filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on January 24, 2012 and incorporated herein by reference\)](#)
- 10.6(a) [Office Lease by and between DWF III Gateway, LLC and the Company, executed June 7, 2012 \(filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on June 13, 2012 and incorporated herein by reference\)](#)
- 10.6(b) [First Amendment to Lease, dated as of May 19, 2014, by and between DWF III Gateway, LLC and Puma Biotechnology, Inc. \(filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on May 23, 2014 and incorporated herein by reference\)](#)
- 10.6(c) [Second Amendment to Lease, dated as of June 10, 2014, by and between DWF III Gateway, LLC and Puma Biotechnology, Inc. \(filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 10, 2015 and incorporated herein by reference\)](#)



- 10.6(d) [Third Amendment to Lease, dated as of July 21, 2015, by and between PR 707 Gateway, LLC \(as successor in interest to DWF III Gateway, LLC\) and the Company \(filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed with the SEC on November 9, 2015 and incorporated herein by reference\)](#)
- 10.7# [Letter Agreement, dated May 2, 2012, between the Company and Richard P. Bryce \(filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on June 26, 2012 and incorporated herein by reference\)](#)
- 10.8# [Form of Indemnification Agreement \(filed as Exhibit 10.17 to the Company's Registration Statement on Form S-1/A filed with the SEC on October 15, 2012 and incorporated herein by reference\)](#)
- 10.9(a)# [Amended Non-Employee Director Compensation Program \(filed as Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 9, 2018 and incorporated herein by reference\)](#)
- 10.9(b)# [Amended Non-Employee Director Compensation Program \(filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on November 7, 2019 and incorporated herein by reference\)](#)
- 10.10(a)\* [License Agreement, dated November 20, 2017, by and between the Company and Specialised Therapeutics Asia Pte Ltd. \(filed as Exhibit 10.13 to the Company's Annual Report on Form 10-K filed with the SEC on March 9, 2018 and incorporated herein by reference\)](#)
- 10.10(b)\* [Amendment No. 1, dated April 20, 2018, to the License Agreement by and between the Company and Specialised Therapeutics Asia Pte Ltd. \(filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 9, 2018 and incorporated herein by reference\)](#)
- 10.11(a)\*\* [Amended and Restated Loan and Security Agreement dated June 28, 2019, by and among the Company and Oxford Finance LLC, as collateral agent and lender \(filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 9, 2019 and incorporated herein by reference\)](#)
- 10.12# [Letter Agreement, dated December 8, 2017, between the Company and Douglas Hunt \(filed as Exhibit 10.15 to the Company's Annual Report on Form 10-K filed with the SEC on March 9, 2018 and incorporated herein by reference\)](#)
- 10.13(a)\* [Collaboration and License Agreement, dated January 30, 2018, between the Company and CANbridge Biomed Limited \(as successor in interest to CANbridgepharma Limited\) \(filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on May 10, 2018 and incorporated herein by reference\)](#)
- 10.13(b)\* [Side Letter Agreement, dated November 19, 2018, between the Company and CANbridge Biomed Limited \(as successor in interest to CANbridgepharma Limited\) \(filed as Exhibit 10.15\(b\) to the Company's Annual Report on Form 10-K filed with the SEC on March 1, 2019 and incorporated herein by reference\)](#)
- 10.14\* [License Agreement, dated March 30, 2018, between the Company and Pint Pharma International SA \(filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed with the SEC on May 10, 2018 and incorporated herein by reference\)](#)
- 10.15\* [Supply Agreement, dated April 20, 2018, by and between the Company and Specialised Therapeutics Asia Pte. Ltd. \(filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 9, 2018 and incorporated herein by reference\)](#)
- 10.16# [Letter Agreement, dated September 28, 2018, between the Company and Maximo F. Nougues \(filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on November 9, 2018 and incorporated herein by reference\)](#)
- 10.17(a)\* [License Agreement, dated January 9, 2019, by and between the Company and Knight Therapeutics Inc. \(filed as Exhibit 10.19 to the Company's Annual Report on Form 10-K filed with the SEC on March 1, 2019 and incorporated herein by reference\)](#)
- 10.17(b)+\*\* [Amendment to the License Agreement, dated December 18, 2019, by and between the Company and Knight Therapeutics, Inc.](#)
- 10.18(a)\*\* [License Agreement, dated March 29, 2019, by and between the Company and Pierre Fabre Medicament SAS \(filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed with the SEC on May 10, 2019 and incorporated herein by reference\)](#)
- 10.18(b)+\*\* [First Amendment to the License Agreement, dated September 17, 2019, by and between the Company and Pierre Fabre Medicament SAS](#)

- 10.18(c)+\*\* [Second Amendment to the License Agreement, dated November 25, 2019, by and between the Company and Pierre Fabre Medicament SAS](#)
- 21.1+ [Subsidiaries](#)
- 23.1+ [Consent of KPMG LLP](#)
- 24.1+ [Power of Attorney \(included on signature page\)](#)
- 31.1+ [Certification of Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002](#)
- 31.2+ [Certification of Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002](#)
- 32.1++ [Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002](#)
- 32.2++ [Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002](#)
- 101.INS+ Inline XBRL Instance Document
- 101.SCH+ Inline XBRL Taxonomy Extension Schema Document
- 101.CAL+ Inline XBRL Taxonomy Extension Calculation Linkbase Document
- 101.DEF+ Inline XBRL Taxonomy Extension Definition Linkbase Document
- 101.LAB+ Inline XBRL Taxonomy Extension Label Linkbase Document
- 101.PRE+ Inline XBRL Taxonomy Extension Linkbase Document
- 104+ Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)
- + Filed herewith.
- ++ Furnished herewith.
- \* Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment pursuant to Rule 24b-2 under the Securities Exchange Act of 1934.
- \*\* Portions of this exhibit (indicated by asterisks) have been omitted pursuant to Regulation S-K, Item 601(b)(10). Such omitted information is not material and would likely cause competitive harm to the registrant if publicly disclosed. Additionally, certain schedules and attachments to certain of these exhibits have been omitted pursuant to Regulation S-K, Item 601(a)(5).
- # Management contract or compensatory plan or arrangement.

## Signatures

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, on February 27, 2020.

PUMA BIOTECHNOLOGY, INC.

By: /s/ Alan H. Auerbach

Alan H. Auerbach

*President & Chief Executive Officer*

(Principal Executive Officer)

KNOWN BY ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Alan H. Auerbach and Maximo Nougues, or either of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K and any documents related to this report and filed pursuant to the Securities Exchange Act of 1934, 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 and necessary to be done in connection therewith as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or their substitute or substitutes may lawfully do or cause to be done by virtue hereof. This power of attorney shall be governed by and construed with the laws of the State of Delaware and applicable federal securities laws.

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

<b>Signature</b>	<b>Title</b>	<b>Date</b>
<u>/s/ Alan H. Auerbach</u> Alan H. Auerbach	Chairman of the Board of Directors, President and Chief Executive Officer (Principal Executive Officer)	February 27, 2020
<u>/s/ Maximo Nougues</u> Maximo Nougues	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	February 27, 2020
<u>/s/ Ann C. Miller</u> Ann C. Miller	Director	February 27, 2020
<u>/s/ Michael P. Miller</u> Michael P. Miller	Director	February 27, 2020
<u>/s/ Jay M. Moyes</u> Jay M. Moyes	Director	February 27, 2020
<u>/s/ Hugh O'Dowd</u> Hugh O'Dowd	Director	February 27, 2020
<u>/s/ Adrian M. Senderowicz</u> Adrian M. Senderowicz	Director	February 27, 2020
<u>/s/ Troy E. Wilson</u> Troy E. Wilson	Director	February 27, 2020
<u>/s/ Frank E. Zavrl</u> Frank E. Zavrl	Director	February 27, 2020

**PUMA BIOTECHNOLOGY, INC. AND SUBSIDIARIES**  
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## Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors  
Puma Biotechnology, Inc.:

### *Opinion on the Consolidated Financial Statements*

We have audited the accompanying consolidated balance sheets of Puma Biotechnology, Inc. and subsidiaries (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 years in the three-year period ended December 31, 2019, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2019 and 2018, and the results of its operations and its cash flows for each of the years in the three-year 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 set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control – Integrated Framework (2013)*, and our report dated February 27, 2020, expressed an unqualified opinion on the effectiveness of the Company's internal control over financial reporting.

### *Change in Accounting Principle*

As discussed in Note 2 to the consolidated financial statements, the Company has changed its method of accounting for Leases as of January 1, 2019, due to the adoption of Financial Accounting Standards Board's Accounting Standards Codification (ASC) Topic 842, *Leases*.

### *Basis for Opinion*

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated 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 consolidated 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 consolidated 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 consolidated 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 consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG LLP

We have served as the Company's auditor since 2017.

Los Angeles, California  
February 27, 2020

**PUMA BIOTECHNOLOGY, INC. AND SUBSIDIARIES**  
**CONSOLIDATED BALANCE SHEETS**  
(in thousands, except share and per share data)

	December 31, 2019	December 31, 2018
<b>ASSETS</b>		
Current assets:		
Cash and cash equivalents	\$ 60,037	\$ 108,419
Marketable securities	51,607	57,002
Accounts receivable, net	28,896	20,773
Inventory, net	3,170	2,625
Prepaid expenses, current	13,259	12,397
Deferred rent	154	—
Restricted cash, current	8,850	—
Other current assets	323	1,787
<b>Total current assets</b>	<b>166,296</b>	<b>203,003</b>
Lease right-of-use assets, net	18,522	—
Property and equipment, net	3,304	3,963
Intangible assets, net	40,461	44,408
Restricted cash, long-term	4,323	4,319
Prepaid expenses and other, long-term	1,999	3,429
<b>Total assets</b>	<b>\$ 234,905</b>	<b>\$ 259,122</b>
<b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>		
Current liabilities:		
Accounts payable	\$ 19,183	\$ 20,684
Accrued expenses	69,030	46,431
Lease liabilities, current	2,624	—
<b>Total current liabilities</b>	<b>90,837</b>	<b>67,115</b>
Deferred rent	—	5,815
Lease liabilities, long-term	22,643	—
Post-marketing commitment liability	9,000	—
Long-term debt	94,962	151,886
<b>Total liabilities</b>	<b>217,442</b>	<b>224,816</b>
Commitments and contingencies (Note 14)		
Stockholders' equity:		
Common stock - \$.0001 par value per share; 100,000,000 shares authorized; 39,203,304 shares issued and outstanding at December 31, 2019 and 38,325,037 issued and outstanding at December 31, 2018	4	4
Additional paid-in capital	1,295,033	1,236,355
Accumulated other comprehensive income (loss)	62	(12)
Accumulated deficit	(1,277,636)	(1,202,041)
<b>Total stockholders' equity</b>	<b>17,463</b>	<b>34,306</b>
<b>Total liabilities and stockholders' equity</b>	<b>\$ 234,905</b>	<b>\$ 259,122</b>

See Accompanying Notes to the Consolidated Financial Statements

**PUMA BIOTECHNOLOGY, INC. AND SUBSIDIARIES**  
**CONSOLIDATED STATEMENTS OF OPERATIONS**  
(in thousands, except share and per share data)

	For the Year Ended December 31,		
	2019	2018	2017
<b>Revenue:</b>			
Product revenue, net	\$ 211,619	\$ 200,491	\$ 26,185
License revenue	60,250	50,500	1,500
Royalty revenue	391	—	—
<b>Total revenue</b>	<b>272,260</b>	<b>250,991</b>	<b>27,685</b>
<b>Operating costs and expenses:</b>			
Cost of sales	36,815	34,621	5,572
Selling, general and administrative	141,692	146,188	106,693
Research and development	132,851	164,854	207,810
<b>Total operating costs and expenses</b>	<b>311,358</b>	<b>345,663</b>	<b>320,075</b>
<b>Loss from operations</b>	<b>(39,098)</b>	<b>(94,672)</b>	<b>(292,390)</b>
<b>Other income (expenses):</b>			
Interest income	2,847	1,796	1,256
Interest expense	(15,019)	(10,985)	(720)
Legal verdict expense	(16,350)	(9,000)	—
Loss on debt extinguishment	(8,103)	—	—
Other income (expenses)	128	(714)	(101)
<b>Total other income (expenses):</b>	<b>(36,497)</b>	<b>(18,903)</b>	<b>435</b>
<b>Net loss</b>	<b>\$ (75,595)</b>	<b>\$ (113,575)</b>	<b>\$ (291,955)</b>
<b>Net loss applicable to common stockholders</b>	<b>\$ (75,595)</b>	<b>\$ (113,575)</b>	<b>\$ (291,955)</b>
<b>Net loss per share of common stock—basic and diluted</b>	<b>\$ (1.95)</b>	<b>\$ (2.99)</b>	<b>\$ (7.85)</b>
<b>Weighted-average shares of common stock outstanding—basic and diluted</b>	<b>38,768,653</b>	<b>37,942,411</b>	<b>37,169,678</b>

See Accompanying Notes to the Consolidated Financial Statements



**PUMA BIOTECHNOLOGY, INC. AND SUBSIDIARIES**  
**CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS**  
(in thousands)

	<u>For the Year Ended December 31,</u>		
	<u>2019</u>	<u>2018</u>	<u>2017</u>
Net loss	\$ (75,595)	\$ (113,575)	\$ (291,955)
Other comprehensive loss			
Unrealized gain (loss) on available-for-sale securities, net of tax of \$0, \$0, and \$0	72	(12)	13
Reclassifications of gain on available-for-sale securities, included in "Other income (expenses)", net of tax of \$0, \$0, and \$0	2	—	—
Comprehensive loss	<u>\$ (75,521)</u>	<u>\$ (113,587)</u>	<u>\$ (291,942)</u>

See Accompanying Notes to the Consolidated Financial Statements

**PUMA BIOTECHNOLOGY, INC. AND SUBSIDIARIES**  
**CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY**  
(in thousands, except share and per share data)

	Common Stock		Additional Paid-in Capital	Receivables from Exercises of Options	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total
	Shares	Amount					
Balance at December 31, 2016	36,826,010	\$ 4	\$ 1,006,344	\$ —	\$ (13)	\$ (796,511)	\$ 209,824
Stock-based compensation	—	—	108,735	—	—	—	108,735
Shares issued or restricted stock units vested under employee stock plans	768,841	—	27,134	(449)	—	—	26,685
Reclassification of gain on available-for-sale securities	—	—	—	—	—	—	—
Unrealized gain on available-for-sale securities	—	—	—	—	13	—	13
Net loss	—	—	—	—	—	(291,955)	(291,955)
Balance at December 31, 2017	37,594,851	4	1,142,213	(449)	—	(1,088,466)	53,302
Stock-based compensation	—	—	86,939	—	—	—	86,939
Shares issued or restricted stock units vested under employee stock plans	730,186	—	7,203	449	—	—	7,652
Reclassification of gain on available-for-sale securities	—	—	—	—	—	—	—
Unrealized loss on available-for-sale securities	—	—	—	—	(12)	—	(12)
Net loss	—	—	—	—	—	(113,575)	(113,575)
Balance at December 31, 2018	38,325,037	4	1,236,355	—	(12)	(1,202,041)	34,306
Stock-based compensation	—	—	57,327	—	—	—	57,327
Shares issued or restricted stock units vested under employee stock plans	878,267	—	1,351	—	—	—	1,351
Reclassification of gain on available-for-sale securities	—	—	—	—	2	—	2
Unrealized gain on available-for-sale securities	—	—	—	—	72	—	72
Net loss	—	—	—	—	—	(75,595)	(75,595)
Balance at December 31, 2019	39,203,304	\$ 4	\$ 1,295,033	\$ —	\$ 62	\$ (1,277,636)	\$ 17,463

See Accompanying Notes to the Consolidated Financial Statements

**PUMA BIOTECHNOLOGY, INC. AND SUBSIDIARIES**  
**CONSOLIDATED STATEMENTS OF CASH FLOWS**  
(in thousands)

	For the Year Ended December 31,		
	2019	2018	2017
<b>Operating activities:</b>			
Net loss	\$ (75,595)	\$ (113,575)	\$ (291,955)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:			
Depreciation and amortization	8,077	7,384	2,811
Stock-based compensation	57,327	86,939	108,735
Disposal of property and equipment	54	—	—
Loss on impairment of asset	1,183	—	—
Loss on debt extinguishment	8,047	—	—
Debt modification fees	—	289	—
Changes in operating assets and liabilities:			
Accounts receivable, net	(8,123)	(11,103)	(9,670)
Inventory, net	(545)	(596)	(2,029)
Prepaid expenses and other	568	(840)	(1,142)
Other current assets	1,464	(1,787)	—
Accounts payable	(1,526)	(7,008)	7,657
Accrued expenses	22,599	15,783	13,222
Deferred rent	(154)	409	(99)
Post-marketing commitment liability	9,000	—	—
<b>Net cash provided by (used in) operating activities</b>	<b>22,376</b>	<b>(24,105)</b>	<b>(172,470)</b>
<b>Investing activities:</b>			
Purchase of intangible assets	—	—	(50,000)
Purchase of property and equipment	(306)	(439)	(431)
Expenditures for leasehold improvements	—	(170)	—
Purchase of available-for-sale securities	(127,198)	(107,502)	(79,729)
Sale of available-for-sale securities	28,135	—	—
Maturity of available-for-sale securities	104,532	50,488	114,724
<b>Net cash provided by (used in) investing activities</b>	<b>5,163</b>	<b>(57,623)</b>	<b>(15,436)</b>
<b>Financing activities:</b>			
Net proceeds from shares issued under employee stock plans	1,351	7,652	26,685
Proceeds from long-term debt	25,000	105,000	50,000
Payment of debt	(80,000)	—	—
Payment of debt extinguishment costs	(7,793)	—	—
Payment of debt issuance costs	(5,625)	(4,201)	(1,575)
<b>Net cash (used in) provided by financing activities</b>	<b>(67,067)</b>	<b>108,451</b>	<b>75,110</b>
<b>Net (decrease) increase in cash, cash equivalents and restricted cash</b>	<b>(39,528)</b>	<b>26,723</b>	<b>(112,796)</b>
Cash, cash equivalents and restricted cash, beginning of period	112,738	86,015	198,811
<b>Cash, cash equivalents and restricted cash, end of period</b>	<b>\$ 73,210</b>	<b>\$ 112,738</b>	<b>\$ 86,015</b>
<b>Supplemental disclosures of non-cash investing and financing activities:</b>			
Property and equipment purchases in accounts payable	\$ 25	\$ —	\$ 27
Receivables related to stock option exercises	\$ —	\$ —	\$ 449
<b>Supplemental disclosure of cash flow information:</b>			
Interest paid	\$ 11,739	\$ 8,055	\$ 344

See Accompanying Notes to the Consolidated Financial Statements

**PUMA BIOTECHNOLOGY, INC. AND SUBSIDIARIES**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**Note 1—Business and Basis of Presentation:**

**Business:**

Puma Biotechnology, Inc., or the Company, is a biopharmaceutical company based in Los Angeles, California with a focus on the development and commercialization of innovative products to enhance cancer care. The Company in-licenses from Pfizer, Inc., or Pfizer, the global development and commercialization rights to PB272 (neratinib (oral)), PB272 (neratinib (intravenous)) and PB357. Neratinib is a potent irreversible tyrosine kinase inhibitor that blocks signal transduction through the epidermal growth factor receptors HER1, HER2 and HER4. Currently, the Company is primarily focused on the development and commercialization of the oral version of neratinib, and its most advanced drug candidates are directed at the treatment of HER2-positive breast cancer and HER2 mutated cancers. The Company believes neratinib has clinical application in the treatment of several other cancers as well, including other tumor types that over-express or have a mutation in HER2, such as breast cancer, cervical cancer, lung cancer or other solid tumors.

The Company has two subsidiaries, Puma Biotechnology Ltd., a United Kingdom company, and Puma Biotechnology, B.V., a Netherlands company. These subsidiaries were established for the purpose of legal representation in the United Kingdom and the European Union.

**Basis of Presentation:**

The Company is focused on developing and commercializing neratinib for the treatment of patients with HER2-positive breast cancer, HER2 mutated non-small cell lung cancer, HER2-negative breast cancer that has a HER2 mutation and other solid tumors that have an activating mutation in HER2. The Company has reported a net loss of approximately \$75.6 million and cash flows from operations of approximately \$22.4 million for the year ended December 31, 2019. The Company believes that it will continue to incur net losses and may incur negative net cash flows from operating activities through the drug development process and global commercialization.

The Company has incurred significant operating losses since its inception. In 2017, the Company received FDA approval for its first product, NERLYNX® (neratinib), formerly known as PB272 (neratinib (oral)), for the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer following adjuvant trastuzumab-based therapy. Following FDA approval in July 2017, NERLYNX became available by prescription in the United States, and the Company commenced commercialization.

The Company in-licenses PB272 (neratinib (oral)), PB272 (neratinib (intravenous)) and PB357, as well as certain related compounds, from Pfizer. The Company is required to make substantial payments to Pfizer upon the achievement of certain milestones and has contractual obligations for clinical trial contracts.

The Company has entered into other exclusive sub-license agreements with various parties to pursue regulatory approval, if necessary, and commercialize NERLYNX, if approved, in numerous regions outside the United States, including Europe (excluding Russia and Ukraine), Canada, China, Southeast Asia, and various countries and territories in Central and South America. The Company plans to continue to pursue commercialization of NERLYNX in other countries outside the United States, if approved.

The Company's commercialization, research and development, or R&D, or marketing efforts may require funding in addition to the cash and cash equivalents totaling approximately \$60.0 million and marketable securities totaling approximately \$51.6 million available at December 31, 2019. The Company believes that its existing cash and cash equivalents and marketable securities as of December 31, 2019 and proceeds that will become available to the Company through product sales and license payments are sufficient to satisfy its operating cash needs for at least one year after the filing of the Annual Report on Form 10-K in which these financial statements are included. The Company continues to remain dependent on its ability to obtain sufficient funding to sustain operations and continue to successfully commercialize neratinib. While the Company has been successful in raising capital in the past, there can be no assurance that it will be able to do so in the future. The Company's ability to obtain funding may be adversely impacted by uncertain market conditions, the Company's success in commercializing neratinib, unfavorable decisions of regulatory authorities or adverse clinical trial results. The outcome of these matters cannot be predicted at this time. Additionally, the terms of the Company's loan and security agreement place restrictions on the Company's ability to operate the business and on the Company's financial flexibility, and the Company may be unable to achieve the revenue necessary to incur additional borrowings under its loan and security agreement or to satisfy the minimum revenue covenants.

Since its inception through December 31, 2019, the Company's financing has primarily been proceeds from product and license revenue, public offerings of its common stock, private equity placements, and borrowings under its loan and security agreement.

**Note 2—Significant Accounting Policies:**

The significant accounting policies followed in the preparation of these consolidated financial statements are as follows:

**Principles of Consolidation:**

The consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

**Segment Reporting:**

Management has determined that the Company operates in one business segment, which is the development and commercialization of innovative products to enhance cancer care.

**Use of Estimates:**

The preparation of consolidated financial statements in conformity with U.S. generally accepted accounting principles, or GAAP, requires management to make estimates and assumptions that affect reported amounts of assets and liabilities, and disclosure of contingent assets and liabilities at the date of the balance sheet, and reported amounts of revenues and expenses for the period presented. Accordingly, actual results could differ from those estimates.

Significant estimates include estimates for variable consideration for which reserves were established. These estimates are included in the calculation of net revenues and include trade discounts and allowances, product returns, provider chargebacks and discounts, government rebates, payor rebates, and other incentives, such as voluntary patient assistance, and other allowances that are offered within contracts between the Company and its customers, payors, and other indirect customers relating to the Company's sale of its products.

**Net Loss per Share of Common Stock:**

Basic net loss per share of common stock is computed by dividing net loss applicable to common stockholders by the weighted average number of shares of common stock outstanding during the periods presented, as required by Accounting Standards Codification, or ASC, 260, *Earnings per Share*. For purposes of calculating diluted loss per share of common stock, the denominator includes both the weighted average number of shares of common stock outstanding and the number of dilutive common stock equivalents, such as stock options, restricted stock units, or RSUs and warrants. A common stock equivalent is not included in the denominator when calculating diluted earnings per common share if the effect of such common stock equivalent would be anti-dilutive. For the year ended December 31, 2019, potentially dilutive securities excluded from the calculations were 5,042,325 shares issuable upon exercise of options, 2,116,250 shares issuable upon exercise of a warrant, and 1,991,125 shares underlying RSUs that were subject to vesting and were antidilutive. For the year ended December 31, 2018, potentially dilutive securities excluded from the calculations were 5,708,544 shares issuable upon exercise of options, 2,116,250 shares issuable upon exercise of a warrant, and 1,838,670 shares underlying RSUs that were subject to vesting and were antidilutive. For the year ended December 31, 2017, potentially dilutive securities excluded from the calculations were 6,134,513 shares issuable upon exercise of options, 2,116,250 shares issuable upon exercise of a warrant, and 1,637,662 shares underlying RSUs that were subject to vesting and were antidilutive.

**Revenue Recognition:**

The Company adopted ASC Topic 606, *Revenue from Contracts with Customers*, or ASC 606, on January 1, 2017. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements, and financial instruments. Under ASC 606, an entity recognizes revenue when its customer obtains control of the promised goods or services, in an amount that reflects the consideration which the entity expects to be entitled in exchange for those goods or services. The Company had no contracts with customers until the FDA approved NERLYNX on July 17, 2017. Subsequent to receiving FDA approval, the Company entered into a limited number of arrangements with specialty pharmacies and specialty distributors in the United States to distribute NERLYNX. These arrangements are the Company's initial contracts with customers. The Company has determined that these sales channels with customers are similar.

To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identifies the contract(s) with a customer, (ii) identifies the performance obligations in the contract, (iii) determines the transaction price, (iv) allocates the transaction price to the performance obligations in the contract, and (v) recognizes revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to arrangements that meet the definition of a contract under ASC 606, including when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. For a complete discussion of accounting for product revenue, see *Product Revenue, Net* (below).

***Product Revenue, Net:***

The Company sells NERLYNX to a limited number of specialty pharmacies and specialty distributors in the United States. These customers subsequently resell the Company’s products to patients and certain medical centers or hospitals. In addition to distribution agreements with these customers, the Company enters into arrangements with health care providers and payors that provide for government mandated and/or privately negotiated rebates, chargebacks and discounts with respect to the purchase of the Company’s products.

The Company recognizes revenue on product sales when the specialty pharmacy or specialty distributor, as applicable, obtains control of the Company's product, which occurs at a point in time (upon delivery). Product revenue is recorded net of applicable reserves for variable consideration, including discounts and allowances. The Company’s payment terms range between 10 and 65 days.

Shipping and handling costs for product shipments occur prior to the customer obtaining control of the goods and are recorded in cost of sales.

If taxes should be collected from customers relating to product sales and remitted to governmental authorities, they will be excluded from revenue. The Company expenses incremental costs of obtaining a contract when incurred, if the expected amortization period of the asset that the Company would have recognized is one year or less. However, no such costs were incurred during the year ended December 31, 2019.

Product revenue from each of the Company’s customers who individually accounted for 10% or more of total revenues consisted of the following:

	For the Year Ended December 31, 2019	For the Year Ended December 31, 2018	For the Year Ended December 31, 2017
CVS/Caremark	34%	39%	38%
Accredo/Acaria	22%	25%	23%
Diplomat	10%	13%	13%

***Reserves for Variable Consideration:***

Revenue from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established. Components of variable consideration include trade discounts and allowances, product returns, provider chargebacks and discounts, government rebates, payor rebates, and other incentives, such as voluntary patient assistance, and other allowances that are offered within contracts between the Company and its customers, payors, and other indirect customers relating to the Company’s sale of its products. These reserves, as detailed below, are based on the related sales, and are classified as reductions of accounts receivable, net or as a current liability. These estimates take into consideration a range of possible outcomes that are probability-weighted in accordance with the expected value method in ASC 606 for relevant factors such as current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns. Overall, these reserves reflect the Company’s best estimates of the amount of consideration to which it is 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 under the contract will not occur in a future period. The Company's analyses also contemplated application of the constraint in accordance with the guidance, under which it determined a material reversal of revenue would not occur in a future period for the estimates detailed below as of December 31, 2019 and, therefore, the transaction price was not reduced further during the year ended December 31, 2019. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from the Company's estimates, the Company will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

***Trade Discounts and Allowances:***

The Company generally provides customers with discounts, which include incentive fees that are explicitly stated in the Company's contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. The reserve for discounts is established in the same period that the related revenue is recognized, together with reductions to accounts receivables, net on the consolidated balance sheets. In addition, the Company compensates its customers for sales order management, data, and distribution services. The Company has determined such services received to date are not distinct from the Company's sale of products to its customers and, therefore, these payments have been recorded as a reduction of revenue within the statement of operations.

***Product Returns:***

Consistent with industry practice, the Company offers the specialty pharmacies and specialty distributors that are its customers limited product return rights for damaged and expiring product, provided it is within a specified period around the product expiration date as set forth in the applicable individual distribution agreement. The Company estimates the amount of its product sales that may be returned by its customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized, as well as a reduction to accounts receivables, net on the consolidated balance sheets. The Company currently estimates product returns using its own sales information, including its visibility into the inventory remaining in the distribution channel. The Company has an insignificant amount of returns to date and believes that returns of its products will continue to be minimal.

***Provider Chargebacks and Discounts:***

Chargebacks for fees and discounts to providers represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to its customers who directly purchase the product from the Company. Customers charge the Company for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. The reserve for chargebacks are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and a reduction to accounts receivable, net on the consolidated balance sheets. Chargeback amounts are generally determined at the time of resale to the qualified healthcare provider by customers, and the Company generally issues credits for such amounts within a few weeks of the customer's notification to the Company of the resale. Chargebacks consist of credits the Company expects to issue for units that remain in the distribution channel at each reporting period-end that the Company expects will be sold to qualified healthcare providers and chargebacks that customers have claimed, but for which the Company has not yet issued a payment.

***Government Rebates:***

The Company is subject to discount obligations under state Medicaid programs and Medicare. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability, which is included in accrued expenses on the consolidated balance sheets. The Company's liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimates of future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel at the end of each reporting period.

***Payor Rebates:***

The Company contracts with certain private payor organizations, primarily insurance companies and pharmacy benefit managers, for the payment of rebates with respect to utilization of its products. The Company estimates these rebates and records such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability.

### ***Other Incentives:***

Other incentives the Company offers include voluntary patient assistance programs, such as the co-pay assistance program, which are intended to provide financial assistance to qualified commercially-insured patients with prescription drug co-payments required by payors. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that the Company expects to receive associated with product that has been recognized as revenue, but remains in the distribution channel at the end of each reporting period. The adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability, which is included as a component of accrued expenses on the consolidated balance sheets.

### ***License Revenue:***

The Company also recognizes license revenue under certain of the Company's sub-license agreements that are within the scope of ASC 606. The terms of these agreements may contain multiple performance obligations, which may include licenses and research and development activities. The Company evaluates these agreements under ASC 606 to determine the distinct performance obligations. Non-refundable, upfront fees that are not contingent on any future performance and require no consequential continuing involvement by the Company, are recognized as revenue when the license term commences and the licensed data, technology or product is delivered. The Company defers recognition of non-refundable upfront license fees if the performance obligations are not satisfied.

Prior to recognizing revenue, the Company makes estimates of the transaction price, including variable consideration that is subject to a constraint. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur and when the uncertainty associated with the variable consideration is subsequently resolved.

If there are multiple distinct performance obligations, the Company allocates the transaction price to each distinct performance obligation based on its relative standalone selling price. The standalone selling price is generally determined based on the prices charged to customers or using expected cost-plus margin. Revenue is recognized by measuring the progress toward complete satisfaction of the performance obligations using an input measure.

### ***CANbridge Agreement***

During the first quarter of 2018, the Company entered into a sub-license agreement, or the CANbridge Agreement, with CANbridge Limited, or CANbridge, to pursue regulatory approval and commercialize NERLYNX, if approved, in the People's Republic of China (including mainland China, Hong Kong, Macao, and Taiwan), or the CANbridge Territory. The CANbridge Agreement granted intellectual property rights and set forth the parties' respective obligations with respect to development, commercialization and supply of the licensed product. Pursuant to the CANbridge Agreement, a non-refundable, upfront license fee was received and recognized by the Company as license revenue in accordance with ASC 606. The CANbridge Agreement met the contract existence criteria and contained distinct, identifiable performance obligations for which the stand-alone selling prices were readily determinable and allocable. The Company is obligated to supply CANbridge with the licensed product in accordance with the supply agreement entered into in connection with the CANbridge Agreement. This supply arrangement has been identified as a separate performance obligation. The Company also identified the Joint Steering Committee as a separate, distinct performance obligation. To determine the stand-alone selling price, the Company estimated the transaction prices, including any variable consideration, at contract inception and determined the fair value of such obligations based on similar arrangements. When determining the transaction prices, the Company assumed that the goods or services will be transferred to the customer based on the terms of the existing contract, and did not take into consideration the possibility of a contract being canceled, renewed, or modified. The Company noted there was no additional variable consideration, significant financing components, noncash consideration, or consideration payable to the customer in this agreement. The CANbridge Agreement also includes potential future milestone and royalty payments due to the Company upon successful completion of certain separate, distinct performance obligations. Pursuant to the CANbridge Agreement, the Company received an upfront payment of \$30.0 million during the first quarter of 2018 and a regulatory milestone payment of \$10.0 million during the fourth quarter of 2018 and will potentially receive regulatory milestone payments totaling up to \$30.0 million and sales-based milestone payments totaling up to \$185.0 million. In addition, the Company is entitled to receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products in the CANbridge Territory. At this time, the Company cannot estimate if or when these milestone-related performance obligations might be achieved.



### *Pint Agreement*

During the first quarter of 2018, the Company entered into a sub-license agreement, or the Pint Agreement, with Pint Pharma International SA, or Pint. The Pint Agreement granted intellectual property rights and set forth the respective obligations with respect to development, commercialization and supply of NERLYNX in Mexico and 21 countries and territories in Central and South America, or the Pint Territory. The Pint Agreement met the contract existence criteria and contained distinct, identifiable performance obligations for which the stand-alone selling prices were readily determinable and allocable. The Company is obligated to supply Pint with the licensed product during development pursuant to a supply agreement. This supply arrangement has been identified as a separate performance obligation. To determine the respective stand-alone selling prices, the Company estimated the transaction prices, including any variable consideration, at contract inception and determined the fair value of such obligations based on similar arrangements. When determining the transaction prices, the Company assumed that the goods or services will be transferred to the customer based on the terms of the existing contract and did not take into consideration the possibility of a contract being canceled, renewed, or modified. The Company noted there was no additional variable consideration, significant financing components, non-cash consideration, or consideration payable to the customer in these agreements. Pursuant to the Pint Agreement, the Company received a non-deductible, non-creditable upfront payment of \$10.0 million upon providing certain required documents on or before September 30, 2018 to the satisfaction of Pint. During the third quarter of 2018, the Company satisfied this performance obligation, and revenue has been recognized under the terms of the arrangement. The Pint Agreement also includes potential future milestone and royalty payments due to the Company upon successful completion of certain performance obligations, such as achieving regulatory approvals. The non-deductible, non-creditable milestones consists of certain development and commercial performance obligations, and the Company could earn up to approximately \$24.5 million if all remaining, respective performance obligations are achieved. In addition, the Company is entitled to receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products throughout the Pint Territory. During the third quarter of 2019, the Company achieved a certain development-based milestone, which satisfied a performance obligation necessary to recognize the associated license revenue. The payment associated with this license revenue is expected to be received from Pint during the third quarter of 2020. At this time, the Company cannot estimate if or when the remaining milestone-related performance obligations might be achieved.

### *Knight Agreement*

During the first quarter of 2019, the Company entered into a sub-license agreement, or the Knight Agreement, with Knight Therapeutics, Inc., or Knight. Pursuant to the Knight Agreement, the Company granted to Knight, under certain of the Company's intellectual property rights relating to neratinib, an exclusive, sublicensable (under certain circumstances) license (i) to commercialize any product containing neratinib and certain related compounds in Canada, or the Knight Territory, (ii) to seek and maintain regulatory approvals for the licensed products in the Knight Territory and (iii) to manufacture the licensed products anywhere in the world solely for the development and commercialization of the licensed products in the Knight Territory for human use, subject to the terms of the Knight Agreement and the related supply agreement. During the first quarter of 2019, a non-refundable, upfront license fee was received and recognized as license revenue in accordance with ASC 606. The Company satisfied the necessary performance obligations to recognize this license revenue under the terms of the arrangement. This license agreement met the contract existence criteria and contained distinct, identifiable performance obligations for which the stand-alone selling prices were readily determinable and allocable. As a separate promise under the terms of the license agreement, the Company is obligated to supply Knight with the licensed product in accordance with the supply agreement entered in connection with the license agreement. The Company is also obligated to participate in a Joint Steering Committee, which was identified as a separate performance obligation. To determine the stand-alone selling price, the Company estimated the transaction prices, including any variable consideration, at contract inception and determined the fair value of such obligations based on similar arrangements. When determining the transaction prices, the Company assumed that the goods or services will be transferred to the customer based on the terms of the existing contract, and did not take into consideration the possibility of a contract being canceled, renewed, or modified. The Company noted there was no additional variable consideration, significant financing components, non-cash consideration, or consideration payable to the customer in this agreement. This license agreement also includes potential future milestone and royalty payments due to the Company upon successful completion of certain separate, distinct performance obligations. Pursuant to the Knight Agreement, the Company received an upfront payment of \$1.5 million during the first quarter of 2019 and a milestone payment of approximately \$0.3 million during the third quarter of 2019 and will potentially receive upfront, regulatory and commercial milestone payments totaling up to approximately \$5.6 million. In addition, the Company is entitled to receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products in the Knight Territory. At this time, the Company cannot estimate when these milestone-related performance obligations might be achieved.

### *Pierre Fabre Agreement and Amendment*

During the first quarter of 2019, the Company entered into a sub-license agreement, or the Pierre Fabre Agreement, with Pierre Fabre Medicament SAS, or Pierre Fabre. The Pierre Fabre Agreement granted intellectual property rights and set forth the parties' respective obligations with respect to development, commercialization and supply of any pharmaceutical product containing neratinib in European countries excluding Russia and Ukraine, along with countries in North Africa and francophone countries of West Africa,

or the Pierre Fabre Territory. During the first quarter of 2019, the Company received a non-refundable, upfront license payment of \$60.0 million, of which, \$51.0 million was recognized as license revenue in accordance with ASC 606. The Company satisfied the necessary performance obligations to recognize this license revenue under the terms of the arrangement. The Pierre Fabre Agreement met the contract existence criteria and contained distinct, identifiable performance obligations for which the stand-alone selling prices were readily determinable and allocable. As a separate promise under the terms of the Pierre Fabre Agreement, the Company is obligated to supply Pierre Fabre with the licensed product in accordance with the related supply agreement. The Company is also obligated to participate in a Joint Steering Committee and Transition Plan, which were identified as separate performance obligations. To determine the respective stand-alone selling prices, the Company estimated the transaction prices, including any variable consideration, at contract inception and determined the fair value of such obligations based on similar arrangements. When determining the transaction prices, the Company assumed that the goods or services will be transferred to the customer based on the terms of the existing contract and did not take into consideration the possibility of a contract being canceled, renewed, or modified. The Company noted there was approximately \$9.0 million of additional variable consideration in this agreement related to a post-marketing commitment liability, while there were no significant financing components, non-cash consideration, or consideration payable to the customer. The post-marketing commitment liability will be reimbursed to Pierre Fabre as expenses are incurred or services performed. The Pierre Fabre Agreement also includes potential future milestone and royalty payments due to the Company upon successful completion of certain separate, distinct performance obligations. Pursuant to the Pierre Fabre Agreement, the Company will potentially receive additional regulatory and commercial milestone payments totaling up to \$345.0 million. In addition, the Company will receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products throughout the Pierre Fabre Territory. At this time, the Company cannot estimate if or when these milestone-related performance obligations might be achieved.

During the fourth quarter of 2019, the Company entered into a license amendment, or the Pierre Fabre Amendment, with Pierre Fabre to extend the terms of the Pierre Fabre Agreement to the Middle East, South Africa, Sudan and Turkey, or the Pierre Fabre Amendment Territory. Pursuant to the Pierre Fabre Amendment, the Company received an upfront payment of \$4.0 million and will potentially receive additional regulatory and sales-based milestone payments totaling up to \$3.0 million. In addition, the Company will receive double-digit royalties on sales of licensed products, calculated as a percentage of net sales of licensed products throughout the Pierre Fabre Amendment Territory. At this time, the Company cannot estimate if or when these milestone-related performance obligations might be achieved.

#### **Royalty Revenue:**

Royalty revenue consists of consideration earned related to international sales of NERLYNX made by the Company's sub-licensees in their respective territories. The Company recognizes royalty revenue when the performance obligations have been satisfied.

#### **Royalties:**

Royalties incurred in connection with the Company's license agreement with Pfizer, as disclosed in Note 14—Commitments and Contingencies, are expensed to cost of sales as revenue from product sales is recognized.

#### **Research and Development Expenses:**

Research and development expenses, or R&D, are charged to operations as incurred. The major components of research and development costs include clinical manufacturing costs, clinical trial expenses, consulting and other third-party costs, salaries and employee benefits, stock-based compensation expense, supplies and materials, and allocations of various overhead costs. Clinical trial expenses include, but are not limited to, investigator fees, site costs, comparator drug costs, and clinical research organization, or CRO, costs. In the normal course of business, the Company contracts with third parties to perform various clinical trial activities in the ongoing development of potential products. The financial terms of these agreements are subject to negotiation and variations from contract to contract and may result in uneven payment flows. Payments under the contracts depend on factors such as the achievement of certain events, the successful enrollment of patients and the completion of portions of the clinical trial or similar conditions. The Company's accruals for clinical trials are based on estimates of the services received and efforts expended pursuant to contracts with numerous clinical trial sites, cooperative groups and CROs. As actual costs become known, the Company adjusts its accruals in that period.

In instances where the Company enters into agreements with third parties for clinical trials and other consulting activities, upfront amounts are recorded to prepaid expenses and other in the accompanying consolidated balance sheets and expensed as services are performed or as the underlying goods are delivered. If the Company does not expect the services to be rendered or goods to be delivered, any remaining capitalized amounts for non-refundable upfront payments are charged to expense immediately.

Amounts due under such arrangements may be either fixed fee or fee for service, and may include upfront payments, monthly payments and payments upon the completion of milestones or receipt of deliverables.

Costs related to the acquisition of technology rights and patents for which development work is still in process are charged to operations as incurred and considered a component of research and development costs.

### **Stock-Based Compensation:**

#### ***Stock option awards:***

ASC Topic 718, *Compensation-Stock Compensation*, or ASC 718, requires the fair value of all share-based payments to employees and nonemployees, including grants of stock options, to be recognized in the statement of operations over the requisite service period. Under ASC 718, employee and nonemployee option grants are generally valued at the grant date and those valuations do not change once they have been established. The fair value of each option award is estimated on the grant date using the Black-Scholes Option Pricing Method. As allowed by ASC 718, the Company's estimate of expected volatility is based on its average volatilities using its past six years of publicly traded history. Prior to 2018, while the Company had a short period of publicly traded stock history, the Company calculated its estimate of average volatility based on a sampling of companies with similar attributes. Beginning in 2018, the Company estimated its expected volatility based on its average volatilities using its past six years of publicly traded stock history, including industry, stage of life cycle, size and financial leverage. The risk-free rate for periods within the contractual life of the option is based on the U.S. Treasury yield curve in effect at the time of grant valuation. Option forfeitures are estimated when the option is granted to reduce the option expense to be recognized over the life of the award. The estimated forfeiture rate considers historical employee turnover rates stratified into employee pools, actual forfeiture experience and other factors. The option expense is "trued-up" upon the actual forfeiture of a stock option grant and the Company periodically revises the estimated forfeiture rate in subsequent periods if actual forfeitures differ from those estimates. Due to its limited history of stock option exercises, the Company uses the simplified method to determine the expected life of the option grants. Compensation expense related to modified stock options is measured based on the fair value for the awards as of the modification date. Any incremental compensation expense arising from the excess of the fair value of the awards on the modification date compared to the fair value of the awards immediately before the modification date is recognized at the modification date or ratably over the requisite service period, as appropriate.

#### ***Restricted stock units:***

RSUs are valued on the grant date and the fair value of the RSUs is equal to the market price of the Company's common stock on the grant date. The RSU expense is recognized over the requisite service period. When the requisite service period begins prior to the grant date (because the service inception date occurs prior to the grant date), the Company is required to begin recognizing compensation cost before there is a measurement date (i.e., the grant date). The service inception date is the beginning of the requisite service period. If the service inception date precedes the grant date, accrual of compensation cost for periods before the grant date shall be based on the fair value of the award at the reporting date. In the period in which the grant date occurs, cumulative compensation cost shall be adjusted to reflect the cumulative effect of measuring compensation cost based on fair value at the grant date rather than the fair value previously used at the service inception date (or any subsequent reporting date). RSU forfeitures are estimated when the RSU is granted to reduce the RSU expense to be recognized over the life of the award. The estimated forfeiture rate considers historical employee turnover rates stratified into employee pools, actual forfeiture experience and other factors. The RSU expense is "trued-up" upon the actual forfeiture of a RSU grant and the Company periodically revises the estimated forfeiture rate in subsequent periods if actual forfeitures differ from those estimates. Compensation expense related to modified restricted stock units is measured based on the fair value for the awards as of the modification date. Any incremental compensation expense arising from the excess of the fair value of the awards on the modification date compared to the fair value of the awards immediately before the modification date is recognized at the modification date or ratably over the requisite service period, as appropriate.

#### ***Warrants:***

Warrants (refer to Note 11 for further details) granted to employees and nonemployees are normally valued at the fair value of the instrument on the grant date and are recognized in the statement of operations over the requisite service period. When the requisite service period precedes the grant date and a market condition exists in the warrant, the Company values the warrant using the Monte Carlo Simulation Method. When the terms of the warrant become fixed, the Company values the warrant using the Black-Scholes Option Pricing Method. As allowed by ASC 718 for companies with a short period of publicly traded stock history, the Company's estimate of expected volatility is based on the average volatilities of a sampling of eight to nine companies with similar attributes to the Company, including industry, stage of life cycle, size and financial leverage. The risk-free rate for periods within the contractual life of the warrant is based on the U.S. Treasury yield curve in effect at the time of grant valuation. In determining the value of the warrant until the terms are fixed, the Company factors in the probability of the market condition occurring and several possible scenarios. When the requisite service period precedes the grant date and is deemed to be complete, the Company records the fair

value of the warrant at the time of issuance as an equity stock-based compensation transaction. The grant date is determined when all pertinent information, such as exercise price and quantity are known.

### **Income Taxes:**

The Company follows ASC Topic 740, *Income Taxes*, or ASC 740, which requires recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the consolidated financial statements or tax returns. Under this method, deferred tax assets and liabilities are based on the differences between the consolidated financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance to the extent management concludes it is more likely than not that the asset will not be realized. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled.

The standard addresses the determination of whether tax benefits claimed or expected to be claimed on a tax return should be recorded in the consolidated financial statements. Under ASC 740, the Company may recognize the tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained on examination by the tax authorities, based on the technical merits of the position. The tax benefits recognized in the consolidated financial statements from such a position should be measured based on the largest benefit that has a greater than 50% likelihood of being realized upon ultimate settlement. ASC 740 also provides guidance on de-recognition, classification, interest and penalties on income taxes, accounting in interim periods and requires increased disclosures. As of December 31, 2019, the Company's uncertain tax position reserves include a reserve for its R&D credits.

### **Financial Instruments**

The carrying value of financial instruments, such as cash equivalents, accounts receivable and accounts payable, approximate their fair value because of their short-term nature. The carrying value of long-term debt approximates its fair value as the principal amounts outstanding are subject to variable interest rates that are based on market rates which are regularly reset.

### **Cash and Cash Equivalents:**

The Company classifies all highly liquid instruments with an original maturity of three months or less as cash equivalents.

### **Restricted Cash:**

Restricted cash represents cash held at financial institutions that are pledged as collateral for stand-by letters of credit for lease and legal verdict commitments. The lease related letters of credit will lapse at the end of the respective lease terms through 2026. At December 31, 2019 and 2018, the Company had restricted cash in the amount of \$13.2 million and \$4.3 million, respectively.

### **Investment Securities:**

The Company classifies all investment securities (short-term and long-term) as available-for-sale, as the sale of such securities may be required prior to maturity to implement management's strategies. These securities are carried at fair value, with the unrealized gains and losses, reported as a component of accumulated other comprehensive income (loss) in stockholders' equity until realized. Realized gains and losses from the sale of available-for-sale securities, if any, are determined on a specific identification basis. A decline in the market value of any available-for-sale security below cost that is determined to be other than temporary results in the revaluation of its carrying amount to fair value. The impairment is charged to earnings and a new cost basis for the security is established. Premiums and discounts are amortized or accreted over the life of the related security as an adjustment to yield using the straight-line method. Interest income is recognized when earned.

### **Assets Measured at Fair Value on a Recurring Basis:**

ASC Topic 820, *Fair Value Measurement*, or ASC 820, provides a single definition of fair value and a common framework for measuring fair value as well as disclosure requirements for fair value measurements used in financial statements. Under ASC 820, fair value is determined based upon the exit price that would be received by a company to sell an asset or paid by a company to transfer a liability in an orderly transaction between market participants, exclusive of any transaction costs. Fair value measurements are determined by either the principal market or the most advantageous market. The principal market is the market with the greatest level of activity and volume for the asset or liability. Absent a principal market to measure fair value, the Company uses the most advantageous market, which is the market from which the Company would receive the highest selling price for the asset or pay the lowest price to settle the liability, after considering transaction costs. However, when using the most advantageous market, transaction costs are only considered to determine which market is the most advantageous and these costs are then excluded when applying a fair

value measurement. ASC 820 creates a three-level hierarchy to prioritize the inputs used in the valuation techniques to derive fair values. The basis for fair value measurements for each level within the hierarchy is described below, with Level 1 having the highest priority and Level 3 having the lowest.

Level 1: Quoted prices in active markets for identical assets or liabilities.

Level 2: Quoted prices for similar assets or liabilities in active markets; quoted prices for identical or similar instruments in markets that are not active; and model-derived valuations in which all significant inputs are observable in active markets.

Level 3: Valuations derived from valuation techniques in which one or more significant inputs are unobservable.

Following are the major categories of assets measured at fair value on a recurring basis as of December 31, 2019 and 2018, using quoted prices in active markets for identical assets (Level 1), significant other observable inputs (Level 2), and significant unobservable inputs (Level 3) (in thousands):

<b>December 31, 2019</b>	<b>Level 1</b>	<b>Level 2</b>	<b>Level 3</b>	<b>Total</b>
Cash equivalents	\$ 41,295	\$ —	\$ —	\$ 41,295
Commercial paper	—	—	—	—
Corporate bonds	—	41,557	—	41,557
U.S. government securities	10,050	—	—	10,050
<b>Totals</b>	<b>\$ 51,345</b>	<b>\$ 41,557</b>	<b>\$ —</b>	<b>\$ 92,902</b>

<b>December 31, 2018</b>	<b>Level 1</b>	<b>Level 2</b>	<b>Level 3</b>	<b>Total</b>
Cash equivalents	\$ 83,329	\$ 2,987	\$ —	\$ 86,316
Commercial paper	—	35,941	—	35,941
Corporate bonds	—	18,077	—	18,077
U.S. government securities	2,984	—	—	2,984
<b>Totals</b>	<b>\$ 86,313</b>	<b>\$ 57,005</b>	<b>\$ —</b>	<b>\$ 143,318</b>

The Company's investments in commercial paper, corporate bonds and U.S. government securities are exposed to price fluctuations. The fair value measurements for commercial paper, corporate bonds and U.S. government securities are based upon the quoted prices of similar items in active markets multiplied by the number of securities owned.

The following tables summarize the Company's short-term investments (in thousands):

<b>December 31, 2019</b>	<b>Maturity (in years)</b>	<b>Amortized cost</b>	<b>Unrealized</b>		<b>Estimated fair value</b>
			<b>Gains</b>	<b>Losses</b>	
Cash equivalents		\$ 41,295	\$ —	\$ —	\$ 41,295
Commercial paper	Less than 1	—	—	—	—
Corporate bonds	Less than 1	41,507	50	—	41,557
U.S. government securities	Less than 1	10,038	12	—	10,050
<b>Totals</b>		<b>\$ 92,840</b>	<b>\$ 62</b>	<b>\$ —</b>	<b>\$ 92,902</b>

<b>December 31, 2018</b>	<b>Maturity (in years)</b>	<b>Amortized cost</b>	<b>Unrealized</b>		<b>Estimated fair value</b>
			<b>Gains</b>	<b>Losses</b>	
Cash equivalents		\$ 86,316	\$ —	\$ —	\$ 86,316
Commercial paper	Less than 1	35,941	—	—	35,941
Corporate bonds	Less than 1	18,089	—	(12)	18,077
U.S. government securities	Less than 1	2,984	—	—	2,984
<b>Totals</b>		<b>\$ 143,330</b>	<b>\$ —</b>	<b>\$ (12)</b>	<b>\$ 143,318</b>

#### Concentration of Risk:

Financial instruments, which potentially subject the Company to concentrations of credit risk, principally consist of cash and cash equivalents, marketable securities, and accounts receivable, net. The Company's cash and cash equivalents and restricted cash in excess of the Federal Deposit Insurance Corporation and the Securities Investor Protection Corporation insured limits at December 31, 2019, were approximately \$77.3 million. The Company does not believe it is exposed to any significant credit risk due to the quality

nature of the financial instruments in which the money is held. Pursuant to the Company's internal investment policy, investments must be rated A-1/P-1 or better by Standard and Poor's Rating Service and Moody's Investors Service at the time of purchase.

The Company sells its products in the United States primarily through specialty pharmacies and specialty distributors. Therefore, wholesale distributors and large pharmacy chains account for a large portion of its accounts receivables, net and product revenues, net. The creditworthiness of its customers is continuously monitored, and the Company has internal policies regarding customer credit limits. The Company estimates an allowance for doubtful accounts primarily based on the credit worthiness of its customers, historical payment patterns, aging of receivable balances and general economic conditions. The Company recorded \$0 as an allowance for doubtful accounts in the years ended December 31, 2019, 2018, and 2017.

The Company's success depends on its ability to successfully commercialize NERLYNX. The Company currently has a single product with limited commercial sales experience, which makes it difficult to evaluate its current business, predict its future prospects and forecast financial performance and growth. The Company has invested a significant portion of its efforts and financial resources in the development and commercialization of the lead product, NERLYNX, and expects NERLYNX to constitute the vast majority of product revenue for the foreseeable future.

The Company relies exclusively on third parties to formulate and manufacture NERLYNX and its drug candidates. The commercialization of NERLYNX and any other drug candidates, if approved, could be stopped, delayed or made less profitable if those third parties fail to provide sufficient quantities of product or fail to do so at acceptable quality levels or prices. The Company has no experience in drug formulation or manufacturing and does not intend to establish its own manufacturing facilities. The Company lacks the resources and expertise to formulate or manufacture NERLYNX and other drug candidates. While the drug candidates were being developed by Pfizer, both the drug substance and drug product were manufactured by third-party contractors. The Company is using the same third-party contractors to manufacture, supply, store and distribute drug supplies for clinical trials and the commercialization of NERLYNX. If the Company is unable to continue its relationships with one or more of these third-party contractors, it could experience delays in the development or commercialization efforts as it locates and qualifies new manufacturers. The Company intends to rely on one or more third-party contractors to manufacture the commercial supply of drugs.

#### **Inventory:**

The Company values its inventories at the lower of cost and estimated net realizable value. The Company determines the cost of its inventories, which includes amounts related to materials and manufacturing overhead, on a first-in, first-out basis. The Company performs an assessment of the recoverability of capitalized inventory during each reporting period, and it writes down any excess and obsolete inventories to their estimated realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded within the cost of sales in the consolidated statements of comprehensive loss. The determination of whether inventory costs will be realizable requires estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required, which would be recorded as a cost of sales in the consolidated statements of operations.

The Company capitalizes inventory costs associated with the Company's products after regulatory approval, if any, when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized. Inventory totaling \$4.5 million, acquired prior to receipt of marketing approval of a product candidate, was recorded as research and development expense in the year ended December 31, 2017. Inventory that can be used in either the production of clinical or commercial product is recorded as research and development expense when selected for use in a clinical trial. Starter kits, provided to patients prior to insurance approval, are expensed by the Company to selling, general and administrative expense as incurred.

As of December 31, 2019, the Company's inventory balance consisted primarily of raw materials purchased subsequent to FDA approval of NERLYNX.

#### **Property and Equipment, Net:**

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, which is generally three years for computer hardware and software, three years for phone equipment, and seven years for furniture and fixtures. Leasehold improvements are amortized using the straight-line method over the lesser of the useful life or the lease term. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are eliminated from the accounts and any resulting gain or loss is credited or charged to operations. Repairs and maintenance costs are expensed as incurred.

The Company reviews its long-lived assets used in operations for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable, as required by ASC Topic 360, *Property, Plant, and Equipment*, or ASC 360. The Company performs a recoverability test by comparing the sum of the estimated undiscounted cash flows over the life of the asset to its carrying value on the consolidated balance sheet. If the undiscounted cash flows used in the recoverability test are less than the carrying value, the Company would then determine the fair value of the long-lived asset and recognize an impairment loss for the amount in excess of the carrying value.

#### **Leases:**

In February 2016, the Financial Accounting Standards Board, or FASB, issued an accounting standards update, or ASU, which requires lessees to recognize most leases on the balance sheet with a corresponding right-of-use asset, or ROU asset. ROU assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. The assets and lease liabilities are recognized at the lease commencement date based on the estimated present value of fixed lease payments over the lease term. ROU assets are evaluated for impairment using the long-lived assets impairment guidance, as required by ASC 360. A significant indication of impairment of an ROU asset would include a change in the extent or manner in which the asset is being used. The Company must make assumptions which underlie the most significant and subjective estimates in determining whether any impairment exists. Those estimates, and the underlying assumptions, include estimates of future cash flow utilizing market lease rates and determination of fair value. If an ROU asset related to an operating lease is impaired, the carrying value of the ROU asset post-impairment should be amortized on a straight-line basis through the earlier of the end of the useful life of the ROU asset or the end of the lease term. Post impairment, a lessee must calculate the amortization of the ROU asset and interest expense on the lease liability separately, although the sum of the two continues to be presented as a single lease cost. If a lease is planned to be abandoned with no intention of subleasing, the ROU asset should be assessed for impairment.

Leases will be classified as financing or operating, which will drive the expense recognition pattern. For lessees, the income statement presentation and expense recognition pattern for financing and operating leases is similar to the current model for capital and operating leases, respectively. The Company has elected to exclude short-term leases if and when the Company has them. The update also requires additional disclosures that will better enable users of financial statements to assess the amount, timing, and uncertainty of cash flows arising from leases. The Company adopted this guidance as of January 1, 2019, the required effective date, using the effective date transition method. As permitted under the effective date transition method, financial information and disclosure for periods prior to the date of initial application will not be updated. An adjustment to opening retained earnings was not required in conjunction with the Company's adoption. For additional information, see Note 7—Leases. The Company has elected not to reassess whether expired or existing contracts contain leases, nor did it reassess the classification of existing leases as of the adoption date.

The Company leases office space and copy machines, all of which are operating leases. Most leases include the option to renew and the exercise of the renewals options is at the Company's sole discretion. Options to extend or terminate a lease are considered in the lease term to the extent that the option is reasonably certain of exercise. The leases do not include the options to purchase the leased property. The depreciable life of assets and leasehold improvements are limited by the expected lease term. Covenants imposed by the leases include letters of credit required to be obtained by the lessee.

The incremental borrowing rate, or IBR, represents the rate of interest that the Company would expect to pay on a collateralized basis to borrow an amount equal to the lease payments under similar terms. When determinable, the Company uses the rate implicit in the lease to determine the present value of lease payments. As the Company's leases do not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at the commencement date in determining the present value of lease payments. The Company's average IBR for existing leases on the transition date (January 1, 2019) was calculated as 10.9%.

Since adoption of the standard, the Company decided to cease the use of a portion of its leased office space. In connection with the decreased need for the right to use the ROU asset, the Company entered into a sublease for the underlying asset, in which the sublease income is less than the original lease payments, indicating impairment. In performing the recoverability test on the effective date, the undiscounted future estimated cash flows and carrying value were identified for the subleased portion of the leased building, as an individual asset group, defined under ASC 360. The undiscounted future cash flows were determined to be less than the carrying value of the asset. To determine if there was an impairment, the Company then compared the fair value of the asset, based on the present value of the sublessee payments using the original discount rate of 10.9% as the best representation of the market value, to the carrying value. A reduction to the carrying value of the ROU asset was recorded of approximately \$1.2 million representing the fair value amount in excess of the carrying value, with a corresponding impairment charge recorded as selling, general and administration expense, in the consolidated statements of operations for the year ended December 31, 2019.

#### **License Fees and Intangible Assets:**

The Company expenses amounts paid to acquire licenses associated with products under development when the ultimate recoverability of the amounts paid is uncertain and the technology has no alternative future use when acquired. Acquisitions of

technology licenses are charged to expense or capitalized based upon the asset achieving technological feasibility in accordance with management’s assessment regarding the ultimate recoverability of the amounts paid and the potential for alternative future use. The Company has determined that technological feasibility for its product candidates is reached when the requisite regulatory approvals are obtained to make the product available for sale. The Company capitalizes technology licenses upon reaching technological feasibility.



The Company maintains definite-lived intangible assets related to the license agreement with Pfizer. These assets are amortized over their remaining useful lives, which are estimated based on the shorter of the remaining patent life or the estimated useful life of the underlying product. Intangible assets are amortized using the economic consumption method if anticipated future revenues can be reasonably estimated. The straight-line method is used when future revenues cannot be reasonably estimated. Amortization costs are recorded as part of cost of sales.

The Company assesses its intangible assets for impairment if indicators are present or changes in circumstance suggest that impairment may exist. Events that could result in an impairment, or trigger an interim impairment assessment, include the receipt of additional clinical or nonclinical data regarding one of the Company's drug candidates or a potentially competitive drug candidate, changes in the clinical development program for a drug candidate, or new information regarding potential sales for the drug. If impairment indicators are present or changes in circumstance suggest that impairment may exist, the Company performs a recoverability test by comparing the sum of the estimated undiscounted cash flows of each intangible asset to its carrying value on the consolidated balance sheet. If the undiscounted cash flows used in the recoverability test are less than the carrying value, the Company would determine the fair value of the intangible asset and recognize an impairment loss if the carrying value of the intangible asset exceeds its fair value. In connection with the FDA approval of NERLYNX in July 2017, the Company triggered a one-time milestone payment pursuant to its license agreement with Pfizer. The Company capitalized the milestone payment as an intangible asset and is amortizing the asset to cost of sales on a straight-line basis over the estimated useful life of the licensed patent through 2030. The Company recorded amortization expense related to its intangible asset of \$3.9 million, \$3.9 million and \$1.6 million for the years ended December 31, 2019, 2018 and 2017, respectively. As of December 31, 2019, estimated future amortization expense related to the Company's intangible asset was approximately \$3.9 million for each year starting 2020 through 2029, and \$1.0 million for 2030.

#### **Recently Issued Accounting Standards:**

In February 2016, the FASB issued ASU No. 2016-02, Leases (Topic 842). The amendments in ASU 2016-02 require organizations that lease assets, with lease terms of more than 12 months, to recognize on their balance sheet the assets and liabilities for the rights and obligations created by those leases. Consistent with GAAP, the recognition, measurement, and presentation of expenses and cash flows arising from a lease by a lessee primarily depends on its classification as a finance or operating lease. However, unlike previous GAAP that requires only capital leases to be recognized on the balance sheet, ASU No. 2016-02 requires both types of leases to be recognized on the balance sheet. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. For lessees, the income statement presentation and expense recognition pattern for financing and operating leases is similar to the current model for capital and operating leases, respectively. Companies may elect to exclude short-term leases. The update also requires additional disclosures that will better enable users of financial statements to assess the amount, timing, and uncertainty of cash flows arising from leases. The Company adopted ASU No. 2016-02 in the first quarter of 2019 using the effective date transition method. As permitted under the effective date transition method, financial information and disclosure for periods prior to the date of initial application will not be updated. The adoption of ASU No. 2016-02 resulted in an increase in its assets and liabilities on its consolidated balance sheets related to recording right-of-use assets and corresponding lease liabilities of approximately \$21.6 million and \$27.4 million, respectively. The difference between the additional lease assets and lease liabilities represent deferred rent for leases that existed as of the date of adoption. As a result of the adoption there was no material impact to the consolidated statement of operations or statement of cash flows.

In June 2018, the FASB issued ASU No. 2018-07, Compensation-Stock Compensation (Topic 718) - Improvements to Nonemployee Share-Based Payment Accounting, as part of its Simplification Initiative to reduce the cost and complexity in accounting for nonemployee share-based payment transactions. The amendments in ASU 2018-07, specify that Topic 718 applies to all share-based payment transactions in which a grantor acquires goods or services to be used or consumed in a grantor's own operations by issuing share-based payment awards, including nonemployees. ASU 2018-07 is effective for public entities for fiscal years beginning after December 15, 2018. The adoption of ASU 2018-07 did not have a material effect on the Company's current financial position, results of operations or financial statement disclosures.

In July 2018, the FASB issued ASU No. 2018-09, Codification Improvements. The amendments in ASU 2018-09 do not prescribe any new accounting guidance, but instead makes minor improvements and clarifications of several different FASB ASC areas based on comments and suggestions made by various stakeholders. Certain updates are applicable immediately while others provide for a transition period to adopt in fiscal years beginning after December 15, 2018. The adoption of ASU 2018-09 did not have a material effect on the Company's current financial position, results of operations or financial statement disclosures.

In August 2018, the FASB issued ASU No. 2018-13, Fair Value Measurement (Topic 820): Disclosure Framework-Changes to the Disclosure Requirements for Fair Value Measurement. The amendments in ASU 2018-13 modifies the disclosure requirements on fair value measurements. ASU 2018-13 is effective for fiscal years beginning after December 15, 2019, with early adoption permitted for any removed or modified disclosures. The removed and modified disclosures will be adopted on a retrospective basis and the new disclosures will be adopted on a prospective basis. The Company does not expect ASU 2018-13 to have a material effect on the Company's current financial position, results of operations or financial statement disclosures.

In December 2019, the FASB issued ASU No 2019-12, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes, as part of its Simplification Initiative to reduce the cost and complexity in accounting for income taxes. The amendments in ASU 2019-12 removes certain exceptions related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. ASU 2019-12 also amends other aspects of the guidance to help simplify and promote consistent application of GAAP. The guidance is effective for interim and annual periods beginning after December 15, 2020, with early adoption permitted. The Company does not expect ASU 2019-12 to have a material effect on the Company's current financial position, results of operations or financial statement disclosures.

**Note 3—Accounts Receivable, Net:**

Accounts receivable, net consisted of the following (in thousands):

	December 31, 2019	December 31, 2018
Accounts receivable, net	\$ 26,396	\$ 20,773
License revenue receivable	2,500	—
Total accounts receivable, net	<u>\$ 28,896</u>	<u>\$ 20,773</u>

Accounts receivable, net, consists entirely of amounts owed from the Company's customers related to product sales. The license revenue receivable relates to amounts owed from Pint relating to license revenue recognized during the third quarter of 2019. The Company recorded \$0 as an allowance for doubtful accounts in the years ended December 31, 2019 and 2018.

**Note 4—Prepaid Expenses and Other:**

Prepaid expenses and other consisted of the following at December 31 (in thousands):

	December 31, 2019	December 31, 2018
Current:		
CRO services	\$ 4,810	\$ 5,824
Other clinical development	2,043	888
Insurance	3,452	2,446
Professional fees	544	272
Other	2,410	2,967
	<u>13,259</u>	<u>12,397</u>
Long-term:		
CRO services	400	1,073
Other clinical development	468	650
Other	1,131	1,706
	<u>1,999</u>	<u>3,429</u>
Totals	<u>\$ 15,258</u>	<u>\$ 15,826</u>

Other prepaid amounts consist primarily of deposits, licenses, subscriptions, and software.

**Note 5—Other Current Assets:**

Other current assets consisted of the following at December 31 (in thousands):

	December 31, 2019	December 31, 2018
Insurance receivable	\$ —	\$ 1,175
Other	323	612
Totals	<u>\$ 323</u>	<u>\$ 1,787</u>

Other current asset amounts consist primarily of capitalized sublease commission and a sublease tenant improvement allowances, net of amortization.

**Note 6—Property and Equipment:**

Property and equipment consisted of the following at December 31 (in thousands):

	December 31, 2019	December 31, 2018
Leasehold improvements	\$ 3,779	\$ 4,048
Computer equipment	2,698	2,402
Telephone equipment	340	343
Furniture and fixtures	2,346	2,346
	9,163	9,139
Less: accumulated depreciation	(5,859)	(5,176)
<b>Totals</b>	<b>\$ 3,304</b>	<b>\$ 3,963</b>

For the years ended December 31, 2019, 2018, and 2017, the Company incurred depreciation expense of \$0.9 million, \$1.1 million, and \$1.1 million, respectively.

**Note 7—Leases:**

In December 2011, the Company entered into a non-cancelable operating lease for office space in Los Angeles, California, which lease was subsequently amended in November 2012, December 2013, March 2014 and July 2015, and December 2017. The initial term of the lease was for seven years and commenced on December 10, 2011. As amended, the Company rents approximately 65,656 square feet. The term of the lease runs until March 2026, and rent amounts payable by the Company increase approximately 3% per year. Concurrent with the execution of the lease, the Company provided the landlord an automatically renewable stand-by letter of credit in the amount of \$2.5 million. The stand-by letter of credit is collateralized by a high-yield savings account which is classified as restricted cash on the accompanying consolidated balance sheets.

In June 2012, the Company entered into a long-term lease agreement for office space in South San Francisco, California, which was subsequently amended in May 2014 and July 2015. As amended, the Company rents approximately 29,470 square feet. The term of this lease runs until March 2026, with the option to extend for an additional five-year term, and rents payable by the Company increase approximately 3% per year. The Company provided the landlord an automatically renewable stand-by letter of credit in the amount of \$1.6 million. The stand-by letter of credit is collateralized by a high-yield savings account which is classified as restricted cash on the accompanying consolidated balance sheets.

The Company also leases copier equipment for use in the office spaces. Components of lease expense include fixed lease expense and variable lease expense of approximately \$4.7 million and \$0.4 million, respectively, for the year ended December 31, 2019. Rent expense for the years ended December 31, 2018 and 2017, was approximately \$4.7 million and \$3.9 million, respectively. For purposes of determining straight-line rent expense, the lease term is calculated from the date the Company first takes possession of the facility, including any periods of free rent and any renewal option periods that the Company is reasonably certain of exercising. The Company's office and equipment leases generally have contractually specified minimum rent and annual rent increases are included in the measurement of the ROU asset and related lease liability. Additionally, under these lease arrangements, the Company may be required to pay directly, or reimburse the lessors, for real estate taxes, insurance, utilities, maintenance and other operating costs. Such amounts are generally variable and therefore not included in the measurement of the ROU asset and related lease liability but are instead recognized as variable lease expense in selling, general and administrative costs in the consolidated statements of operations when they are incurred.

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

	Amount
2020	\$ 5,207
2021	5,365
2022	5,483
2023	5,631
2024	5,805
Thereafter	7,491
<b>Total</b>	<b>\$ 34,982</b>
Less: imputed interest	(9,715)
<b>Total lease liabilities</b>	<b>\$ 25,267</b>

In February 2019, the Company entered into a long-term sublease agreement for 12,429 square feet of the office space in Los Angeles, CA. The term of the lease runs until March 2026, and rent amounts payable to the Company increase approximately 3% per year. The Company recorded operating sublease income of \$0.2 million for the year ended December 31, 2019 in other income (expenses) in the consolidated statements of operations.

The future minimum lease payments to be received as of December 31, 2019 were as follows (in thousands):

	<b>Amount</b>
2020	\$ 416
2021	467
2022	481
2023	495
2024	510
Thereafter	659
<b>Total</b>	<b>\$ 3,028</b>

Supplemental cash flow information related to leases for the year ended December 31, 2019:

Operating cash flows from operating leases (in thousands)	\$ 5,438
Right-of-use assets obtained in exchange for new operating lease liabilities	—
Weighted average remaining lease term (in years)	6.2
Weighted average discount rate	10.9%

#### **Note 8—Intangible Assets:**

Intangible assets consisted of the following at December 31 (in thousands):

	<b>December 31, 2019</b>	<b>Estimated Useful Life</b>
Acquired and in-licensed rights	\$ 50,000	13 Years
Less: accumulated amortization	(9,539)	
Total intangible asset, net	<u>\$ 40,461</u>	

Estimated future intangible amortization expense as of December 31, 2019 is as follows (in thousands):

2020	\$ 3,947
2021	3,947
2022	3,947
2023	3,947
2024	3,947
Thereafter	20,726
Totals	<u>\$ 40,461</u>

#### **Note 9—Accrued Expenses:**

Accrued expenses consisted of the following at December 31 (in thousands):

	December 31, 2019	December 31, 2018
Accrued legal verdict expense	\$ 31,350	\$ 9,000
Accrued royalties	8,866	9,162
Accrued CRO services	8,502	10,187
Accrued variable consideration	7,978	3,818
Accrued bonus	1,618	1,705
Accrued compensation	4,138	4,435
Accrued other clinical development	2,546	2,380
Accrued professional fees	1,775	2,175
Accrued legal fees	266	1,379
Accrued manufacturing costs	869	788
Other	1,122	1,402
Totals	<u>\$ 69,030</u>	<u>\$ 46,431</u>

Accrued CRO services, accrued other clinical development expenses, and accrued legal fees represent the Company's estimates of such costs and are recognized as incurred. Accrued royalties represent royalties incurred in connection with the Company's license agreement with Pfizer. Accrued compensation includes accrued commissions and accrued vacation, which is accrued at the rate the employee earns vacation and reduced as vacation is used by the employee. Accrued variable consideration represents estimates of adjustments to product revenue, net for which reserves are established. Other accrued expenses consist primarily of business license fees, taxes, insurance, and marketing fees.

Accrued legal verdict expense represents an estimate of a range between \$9.0 million and \$18.0 million that may be owed to class action participants as a result of the recent jury verdict in *Hsu v. Puma Biotechnology, Inc.*, and an initial estimate of \$22.4 million that may be owed to the plaintiff as a result of the recent jury verdict in *Eshelman v. Puma Biotechnology, Inc., et al.* The total amount of damages in *Hsu* and *Eshelman* is uncertain and will be ascertained only after an extensive claims process in *Hsu*, and the completion of post-trial proceedings, and the exhaustion of any appeals in both cases. It is also reasonably possible that the total damages will be higher than these estimates.

All accrued expenses are adjusted in the period the actual costs become known.

#### Note 10—Debt:

Long-term debt consisted of the following at December 31, 2019 (in thousands):

	December 31, 2019	Maturity Date
Long-term debt	\$ 100,000	June 1, 2024
Accretion of final interest payment	1,929	
Less: deferred financing costs	(6,967)	
Total long-term debt, net	<u>\$ 94,962</u>	

In October 2017, the Company entered into a loan and security agreement with Silicon Valley Bank, or SVB, as administrative agent, and the lenders party thereto from time to time, or the Original Lenders, including Oxford Finance LLC, or Oxford, and SVB. Pursuant to the terms of the credit facility provided for by the loan and security agreement, or the Original Credit Facility, the Company borrowed \$50.0 million.

In May 2018, the Company entered into an amendment to the loan and security agreement, which provided for an amended credit facility, or the Amended Credit Facility. Under the Amended Credit Facility, the Original Lenders agreed to make term loans available to the Company in an aggregate amount of \$155.0 million, consisting of (i) an aggregate amount of \$125.0 million, the proceeds of which, in part, were used to repay the \$50.0 million borrowed under the Original Credit Facility, and (ii) an aggregate amount of \$30.0 million that the Company drew in December 2018, which was available under the Amended Credit Facility as a result of achieving a specified minimum revenue milestone. The Company was in compliance with all applicable financial covenants during the entire term of the Amended Credit Facility.

Prior to the amendment and restatement of the loan and security agreement in June 2019, which provided for a new credit facility, or the New Credit Facility, the term loans under the Amended Credit Facility bore interest at an annual rate equal to the greater of (i) 8.25% and (ii) the sum of (a) the “prime rate,” as reported in The Wall Street Journal on the last business day of the month that immediately preceded the month in which the interest accrued, plus (b) 3.5%. The Company was required to make monthly interest-only payments on each term loan commencing on the first calendar day of the calendar month following the funding date of such term loan, and continuing on the first calendar day of each calendar month thereafter through July 1, 2020. Commencing on July 1, 2020, and continuing on the first calendar day of each calendar month thereafter, the Company would have been required to make consecutive equal monthly payments of principal, together with applicable interest, in arrears to each original lender, calculated pursuant to the Amended Credit Facility. All unpaid principal and accrued and unpaid interest with respect to each term loan would have been due and payable in full on May 1, 2023. Upon repayment of the term loans, the Company was also required to make a final payment to the Original Lenders equal to 7.5% of the original principal amount of term loans funded.

The Company was also permitted to prepay the outstanding principal balance of any term loan under the Amended Credit Facility, in whole but not in part, subject to a prepayment fee of 3.0% of the amount prepaid if the prepayment were to occur through and including the first anniversary of the funding date of such term loan, 2.0% of any amount prepaid if the prepayment were to occur after the first anniversary of the funding date of such term loan through and including the second anniversary of the funding date of such term loan, and 1.0% of the amount prepaid if the prepayment were to occur after the second anniversary of the funding date of such term loan and prior to May 1, 2023.

On June 28, 2019, or the Effective Date, the Company entered into the New Credit Facility with Oxford, as collateral agent, and the lenders party thereto from time to time, including Oxford, pursuant to which the Company repaid the \$155.0 million outstanding under the Amended Credit Facility, as well as all applicable exit and prepayment fees owed to the Original Lenders under the Amended Credit Facility, using cash on hand and \$100.0 million in new borrowings from the New Credit Facility. Under the New Credit Facility, the Company issued to Oxford new and/or replacement secured promissory notes in an aggregate principal amount for all such promissory notes of \$100.0 million evidencing the New Credit Facility. No additional capacity remains available to the Company under the New Credit Facility.

The New Credit Facility is secured by substantially all of the Company’s personal property other than its intellectual property. The Company also pledged 65% of the issued and outstanding capital stock of its subsidiaries, Puma Biotechnology Ltd. and Puma Biotechnology B.V. The New Credit Facility limits the Company’s ability to grant any interest in its intellectual property to certain permitted licenses and permitted encumbrances set forth in the agreement.

The term loans under the New Credit Facility bear interest at an annual rate equal to the greater of (i) 9.0% and (ii) the sum of (a) the “prime rate,” as reported in The Wall Street Journal on the last business day of the month that immediately precedes the month in which the interest will accrue, plus (b) 3.5%. The Company is required to make monthly interest-only payments on each term loan under the New Credit Facility commencing on the first calendar day of the calendar month following the funding date of such term loan, and continuing on the first calendar day of each calendar month thereafter through August 1, 2021 or, the Amortization Date. Commencing on the Amortization Date, and continuing on the first calendar day of each calendar month thereafter, the Company will make consecutive equal monthly payments of principal, together with applicable interest, in arrears to each lender under the New Credit Facility, calculated pursuant to the New Credit Facility. All unpaid principal and accrued and unpaid interest with respect to each term loan under the New Credit Facility is due and payable in full on June 1, 2024, or the Maturity Date. Upon repayment of such term loans, the Company is also required to make a final payment to the lenders equal to 7.5% of the aggregate principal amount of such term loans outstanding as of the Effective Date.

At the Company’s option, the Company may prepay the outstanding principal balance of any term loan in whole but not in part, subject to a prepayment fee of 3.0% of the amount prepaid if the prepayment occurs through and including the first anniversary of the funding date of such term loan, 2.0% of the amount prepaid if the prepayment occurs after the first anniversary of the funding date of such term loan through and including the second anniversary of the funding date of such term loan, and 1.0% of the amount prepaid if the prepayment occurs after the second anniversary of the funding date of such term loan and prior to the Maturity Date.

The New Credit Facility includes affirmative and negative covenants applicable to the Company, its current subsidiaries and any subsidiaries the Company creates in the future. The affirmative covenants include, among others, covenants requiring the Company to maintain its legal existence and governmental approvals, deliver certain financial reports, maintain insurance coverage and satisfy certain requirements regarding deposit accounts. The Company must also achieve certain product revenue targets, measured as of the

last day of each fiscal quarter on a trailing year to date basis. New minimum revenue levels will be established for each subsequent fiscal year by mutual agreement of the Company, Oxford, as collateral agent, and the new lenders. The negative covenants include, among others, restrictions on the Company's transferring collateral, incurring additional indebtedness, engaging in mergers or acquisitions, paying dividends or making other distributions, making investments, creating liens, selling assets and suffering a change in control, in each case subject to certain exceptions.

The New Credit Facility also includes events of default, the occurrence and continuation of which could cause interest to be charged at the rate that is otherwise applicable plus 5.0% and would provide Oxford, as collateral agent, with the right to exercise remedies against the Company and the collateral securing the New Credit Facility, including foreclosure against the property securing the New Credit Facility, including the Company's cash. These events of default include, among other things, the Company's failure to pay principal or interest due under the New Credit Facility, a breach of certain covenants under the New Credit Facility, the Company's insolvency, a material adverse change, the occurrence of any default under certain other indebtedness in an amount greater than \$500,000 and one or more judgments against the Company in an amount greater than \$500,000 individually or in the aggregate that remains unsatisfied, unvacated, or unstayed for a period of 10 days after its entry.

As of December 31, 2019, there was \$100.0 million in principal amounts outstanding under the New Credit Facility, representing all of the Company's long-term debt outstanding as of that date, and the Company was in compliance with all applicable covenants under the New Credit Facility.

The future minimum principal payments under the New Credit Facility as of December 31, 2019 were as follows (in thousands):

	<b>Amount</b>
2020	\$ —
2021	14,286
2022	34,286
2023	34,286
2024	17,142
Thereafter	—
<b>Total</b>	<b>\$ 100,000</b>

#### **Note 11—Stockholders' Equity:**

##### **Common Stock:**

The Company issued 87,625, 200,743, and 557,080 shares of common stock upon exercise of stock options during the years ended December 31, 2019, 2018 and 2017, respectively. The Company issued 790,642, 529,443, and 211,761 shares of common stock upon vesting of RSUs during the years ended December 31, 2019, 2018 and 2017, respectively.

##### **Authorized Shares:**

The Company has 100,000,000 shares of stock authorized for issuance, all of which 100,000,000 are common stock, par value \$0.0001 per share.

##### **Warrants:**

In October 2011, the Company issued an anti-dilutive warrant to Alan Auerbach, the Company's founder and chief executive officer. The warrant was issued to provide Mr. Auerbach with the right to maintain ownership of at least 20% of the Company's common stock in the event that the Company raised capital through the sale of its securities in the future.

In connection with the closing of a public offering in October 2012, the exercise price and number of shares underlying the warrant issued to Mr. Auerbach were established and, accordingly, the final value of the warrant became fixed. Pursuant to the terms of the warrant, Mr. Auerbach may exercise the warrant to acquire 2,116,250 shares of the Company's common stock at \$16 per share until October 4, 2021.

## Stock Options and Restricted Stock Units:

The Company's 2011 Incentive Award Plan, or the 2011 Plan, was adopted by the Company's Board of Directors on September 15, 2011. Pursuant to the 2011 Plan, the Company may grant incentive stock options and nonqualified stock options, as well as other forms of equity-based compensation. Incentive stock options may be granted only to employees, while consultants, employees, officers and directors are eligible for the grant of nonqualified options under the 2011 Plan. The maximum term of stock options granted under the 2011 Plan is 10 years and the awards generally vest over a three-year period. The exercise price of incentive stock options granted under the 2011 Plan must be at least equal to the fair value of such shares on the date of grant. Through December 31, 2019, a total of 12,529,412 shares of the Company's common stock have been reserved for issuance under the 2011 Plan.

The Company awarded only "plain vanilla options" as determined by the SEC Staff Accounting Bulletin 107, or *Share Based Payment*. As of December 31, 2019, 6,297,885 shares of the Company's common stock are issuable upon the exercise of outstanding awards granted under the 2011 Plan and 2,400,084 shares of the Company's common stock are available for future issuance under the 2011 Plan. The fair value of options granted to employees and nonemployees was estimated using the Black-Scholes Option Pricing Method (see Note 2) with the following weighted-average assumptions used during the years ended December 31:

	2019	2018
Dividend yield	0.0%	0.0%
Expected volatility	99.9%	96.5%
Risk-free interest rate	2.5%	2.7%
Expected life in years	5.76	5.85

The Company's 2017 Employment Inducement Incentive Award Plan, or the 2017 Plan, was adopted by the Company's Board of Directors on April 27, 2017. Pursuant to the 2017 Plan, the Company may grant stock options and restricted stock units, as well as other forms of equity-based compensation to employees, as an inducement to join the Company. The maximum term of stock options granted under the 2017 Plan is 10 years and the awards generally vest over a three-year period. The exercise price of stock options granted under the 2017 Plan must be at least equal to the fair market value of such shares on the date of grant. As of December 31, 2019, a total of 1,000,000 shares of the Company's common stock have been reserved for issuance under the 2017 Plan. As of December 31, 2019, 735,565 shares have been awarded under the 2017 Plan.

Stock-based compensation expense was as follows for the years ended December 31 (in thousands):

	For the Year Ended December 31, 2019		
	2019	2018	2017
Stock-based compensation:			
Options -			
Selling, general, and administrative	\$ 9,044	\$ 14,063	\$ 23,024
Research and development	7,452	26,456	67,299
Restricted stock units -			
Selling, general, and administrative	18,848	20,851	8,170
Research and development	21,983	25,569	10,242
Total stock-based compensation expense	<u>\$ 57,327</u>	<u>\$ 86,939</u>	<u>\$ 108,735</u>



During the year ended December 31, 2019, in accordance with the terms of a former executive's severance agreement, the Company modified share-based payment awards by accelerating the vesting and by extending the exercise period. As a result of the modification, the Company recorded stock-based compensation of \$2.6 million during the year ended December 31, 2019.

Activity with respect to options granted under the 2011 and 2017 Plan is summarized as follows:

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2016	6,578,522	\$ 87.52	8.0	\$ 18,442
Granted	519,791	\$ 38.87	8.4	
Forfeited	(285,377)	\$ 50.11		
Exercised	(557,080)	\$ 48.71		\$ 27,185
Expired	(121,343)	\$ 125.40		
Outstanding at December 31, 2017	6,134,513	\$ 87.91	7.2	\$ 220,060
Granted	315,566	\$ 59.13	9.3	
Forfeited	(183,837)	\$ 51.96		
Exercised	(200,743)	\$ 35.88		\$ 5,063
Expired	(356,955)	\$ 116.96		
Outstanding at December 31, 2018	5,708,544	\$ 87.49	6.1	\$ 7,762
Granted	340,241	\$ 15.40	8.6	
Forfeited	(128,406)	\$ 38.71		
Exercised	(87,625)	\$ 15.42		\$ 995
Expired	(790,429)	\$ 104.76		
Outstanding at December 31, 2019	5,042,325	\$ 82.42	5.2	\$ 1,951
Nonvested at December 31, 2019	439,194	\$ 25.14	9.2	
Exercisable	4,603,131	\$ 87.88	4.8	\$ 1,746

At December 31, 2019, total estimated unrecognized compensation cost related to non-vested stock options granted prior to that date was approximately \$7.4 million, which is expected to be recognized over a weighted-average period of 1.6 years. At December 31, 2019, the total estimated unrecognized compensation cost related to non-vested RSUs was approximately \$42.7 million, which is expected to be recognized over a weighted-average period of 1.6 years. The weighted-average grant date fair value of options granted during the years ended December 31, 2019, 2018 and 2017, was \$12.08, \$45.62 and \$24.30 per share, respectively. The weighted average grant date fair value of RSUs awarded during the year ended December 31, 2019, 2018 and 2017 was \$14.72, \$41.42, and \$94.93, respectively.

### Stock Option Rollforward

	Shares	Weighted Average Grant-Date Fair Value
Nonvested shares at December 31, 2017	1,788,436	\$ 33.37
Granted	315,566	45.62
Vested/Issued	(1,140,873)	36.81
Forfeited	(183,837)	31.43
Nonvested shares at December 31, 2018	779,292	33.75
Granted	340,241	12.08
Vested/Issued	(551,933)	33.56
Forfeited	(128,406)	26.27
Nonvested shares at December 31, 2019	439,194	\$ 19.38

## Restricted Stock Unit Rollforward

	Shares	Weighted Average Grant-Date Fair Value
Nonvested shares at December 31, 2017	1,637,662	\$ 85.58
Granted	1,175,231	41.42
Vested/Issued	(529,443)	79.98
Forfeited	(444,780)	80.99
Nonvested shares at December 31, 2018	1,838,670	60.08
Granted	1,472,417	14.72
Vested/Issued	(790,642)	62.98
Forfeited	(529,320)	51.63
Nonvested shares at December 31, 2019	<u>1,991,125</u>	<u>\$ 27.63</u>

### Note 12—401(k) Savings Plan:

During 2012, the Company adopted a 401(k) savings plan for the benefit of its employees. The Company is required to make matching contributions to the 401(k) plan equal to 100% of the first 3% of wages deferred by each participating employee and 50% on the next 2% of wages deferred by each participating employee. The Company incurred expenses for employer matching contributions of approximately \$1.5 million, \$1.9 million and \$ 0.9 million for the years ended December 31, 2019, 2018 and 2017, respectively.

### Note 13—Income Taxes:

Income tax expense (benefit) was as follows for the years ended December 31 (in thousands):

	2019	2018	2017
Current:			
Federal	\$ —	\$ —	\$ —
State	53	17	—
	<u>\$ 53</u>	<u>\$ 17</u>	<u>\$ —</u>
Deferred:			
Federal	—	—	—
State	—	—	—
	<u>\$ —</u>	<u>\$ —</u>	<u>\$ —</u>
Total	<u>\$ 53</u>	<u>\$ 17</u>	<u>\$ —</u>

The provision for income taxes in the accompanying consolidated statements of operations differs from the amount calculated by applying the statutory income tax rate to loss from continuing operations before income taxes. Approximately \$21.0 million of tax expense is due to stock-based compensation expense shortfall and the expiration of vested stock options. Approximately \$15.2 million of the tax benefit is due to R&D tax credits, of which approximately \$8.4 million is due to a release of uncertain tax positions as a result of the Company performing a R&D tax credit study. The primary components of such differences are as follows as of December 31 (in thousands):

	2019	2018	2017
Tax computed at the federal statutory rate	\$ (15,830)	\$ (23,771)	\$ (99,234)
State taxes	(2,453)	(2,791)	(15,890)
Permanent items	21,834	10,932	(1,404)
R&D credits	(14,946)	(5,630)	(6,217)
Deferred tax asset adjustment	—	—	6,805
Impact of federal statutory rate change related to the 2017 Tax Act	—	—	141,147
Prior year adjustments	(2,792)	15,750	—
Other	—	—	(20)
Change in valuation allowance	14,240	5,527	(25,187)
Total provision	<u>\$ 53</u>	<u>\$ 17</u>	<u>\$ —</u>

Temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes give rise to the Company's deferred income taxes. The components of the Company's net deferred tax assets are as follows as of December 31 (in thousands):

	2019	2018
Deferred tax assets:		
Net operating loss carry forwards	\$ 260,555	\$ 257,021
Business credit carryforwards	50,343	35,107
Organization costs	10,472	3,593
Compensation	60,967	72,804
Deferred rent	—	1,404
Lease liabilities	6,145	—
Other	13	—
Subtotal	<u>388,495</u>	<u>369,929</u>
Deferred tax liabilities:		
Lease right-of-use assets	(4,505)	—
Other deferred tax liabilities	(76)	(255)
Subtotal	<u>(4,581)</u>	<u>(255)</u>
Total deferred tax assets	383,914	369,674
Valuation allowance	(383,914)	(369,674)
Net deferred tax assets	<u>\$ —</u>	<u>\$ —</u>

As the ultimate realization of the potential benefits of the Company's deferred tax assets is considered unlikely by management, the Company has offset the deferred tax assets attributable to those potential benefits through valuation allowances. Accordingly, the Company did not recognize any benefit from income taxes in the accompanying consolidated statements of operations to offset its pre-tax losses. The valuation allowance increased \$14.2 million and \$5.5 million for the years ended December 31, 2019 and 2018, respectively. At December 31, 2019, the Company had federal and state net operating loss carryforwards, respectively, of approximately \$957.4 million and \$883.4 million, which will begin to expire in 2033 and 2031. At December 31, 2019, the Company also has federal research and development credit carryforwards of approximately \$32.1 million. If not utilized, the carryforwards will begin expiring in 2033. The Company has state research and development credit carryforwards of approximately \$18.3 million which do not expire. Pursuant to the Internal Revenue Code, Sections 382 and 383, use of the Company's net operating loss and credit carryforwards could be limited if a cumulative change in ownership of more than 50% occurs within a three-year period. The Company has not yet performed an assessment on the potential limitation on net operating loss and credit carryforwards.

The following is a tabular reconciliation of the total amounts of unrecognized tax benefits at December 31 (in thousands):

	2019	2018	2017
Unrecognized tax benefits - January 1	\$ 8,777	\$ 7,151	\$ 5,315
Gross decreases - tax positions in prior period	(8,422)	—	—
Gross increases - tax positions in a current period	1,613	1,626	1,836
Unrecognized tax benefits - December 31	<u>\$ 1,968</u>	<u>\$ 8,777</u>	<u>\$ 7,151</u>

During the current period, the Company completed a R&D credit study. As a result of the study, the Company assessed that the Company qualified under safe harbor rules, which when applied consistently results in a more conservative approach of calculating the amount of R&D credit. The Company concluded that a release of uncertain tax benefits was appropriate and released a portion of previously recorded uncertain tax positions reserve.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by the federal and state jurisdictions where applicable. There are currently no pending income tax examinations. The Company's tax years for 2009 and forward are subject to examination by the federal and California tax authorities due to the carryforward of unutilized net operating losses and research and development credits.

#### Note 14—Commitments and Contingencies:

##### License Agreement:

In August 2011, the Company entered into an agreement pursuant to which Pfizer agreed to grant it a worldwide license for the development, manufacture and commercialization of PB272 neratinib (oral), PB272 neratinib (intravenous) and PB357, and certain related compounds. The license is exclusive with respect to certain patent rights owned by or licensed to Pfizer. Under the agreement, the Company is obligated to commence a new clinical trial for a product containing one of these compounds within a specified period of time and to use commercially reasonable efforts to complete clinical trials and to achieve certain milestones as provided in a development plan. From the closing date of the agreement through December 31, 2011, Pfizer continued to conduct the existing clinical trials on behalf of the Company at the Licensor's sole expense. At the Company's request, Pfizer has agreed to continue to perform certain services in support of the existing clinical trials at the Company's expense. These services will continue through the completion of the transitioned clinical trials. The license agreement "capped" the out of pocket expense the Company would be responsible for completing the then existing clinical trials. All agreed upon costs incurred by the Company above the "cost cap" would be reimbursed by Pfizer. The Company exceeded the "cost cap" during the fourth quarter of 2012. In accordance with the license agreement, the Company billed Pfizer for agreed upon costs above the "cost cap" until December 31, 2013.

On July 18, 2014, the Company entered into an amendment to the license agreement with Pfizer. The amendment amends the agreement to (1) reduce the royalty rate payable by the Company to Pfizer on sales of licensed products; (2) release Pfizer from its obligation to pay for certain out-of-pocket costs incurred or accrued on or after January 1, 2014 to complete certain ongoing clinical studies; and (3) provide that Pfizer and the Company will continue to cooperate to effect the transfer to the Company of certain records, regulatory filings, materials and inventory controlled by Pfizer as promptly as reasonably practicable.

As consideration for the license, the Company is required to make substantial payments upon the achievement of certain milestones totaling approximately \$187.5 million if all such milestones are achieved. In connection with the FDA approval of NERLYNX in July of 2017, the Company triggered a one-time milestone payment pursuant to the agreement. Additionally, the Company may trigger a one-time milestone payment related to the commercialization efforts in certain European countries. Should the Company commercialize any more of the compounds licensed from Pfizer or any products containing any of these compounds, the Company will be obligated to pay to Pfizer annual royalties at a fixed rate in the low-to-mid teens of net sales of all such products, subject to certain reductions and offsets in some circumstances. The Company's royalty obligation continues, on a product-by-product and country-by-country basis, until the later of (1) the last to expire licensed patent covering the applicable licensed product in such country, or (2) the earlier of generic competition for such licensed product reaching a certain level in such country or expiration of a certain time period after first commercial sale of such licensed product in such country. In the event that the Company sublicenses the rights granted to the Company under the license agreement with Pfizer to a third party, the same milestone and royalty payments are required. The Company can terminate the license agreement at will, or for safety concerns, in each case upon specified advance notice.

### Clinical Trial Contracts:

The Company engages with clinical research organizations and contract manufacturing organizations, or CMOs, in addition to engaging in contracts for the management of its ongoing clinical trials and pre-commercialization efforts. The Company may cancel these agreements with a 30 to 45 day written notice to the outside vendor. The Company would be obligated to pay for services rendered up to that point. The contracts also contain variable costs that are hard to predict as they are based on such things as patients enrolled and clinical trial sites, which can vary and therefore, are not included in the table below. The contracts held by the Company as of December 31, 2019, are summarized as follows (in thousands):

<b>Indication</b>	<b>Estimated Contractual Obligation as of December 31, 2019</b>	<b>Months Remaining on Contract</b>
HER2 Overexpressed/Amplified Breast Cancer (Extension)	\$ 16,402	12
HER2 Overexpressed/Amplified Breast Cancer (Licensor Legacy Clinical Trials)	695	3
HER2 Mutated Breast Cancer and HER2 Mutated Breast Cancer with Brain Metastases	697	36
Metastatic & Adjuvant Breast Cancer	24,839	6
Pre-Clinical Research	2,288	10
Post-Clinical Research	2,335	6
HER2 Mutated Solid Tumors	22,117	14
Other	28,425	19
<b>Total</b>	<b>\$ 97,798</b>	

Included in the above are payments to be made when milestones are reached. As of December 31, 2019, Company obligations for potential milestone payments totaled approximately \$20.2 million. This amount will be paid by the Company if all milestones are reached and would reduce the overall contractual obligation if one or more milestone is never reached.

### Legal Proceedings

The Company and certain of its executive officers were named as defendants in the lawsuits detailed below. The Company records a liability in the consolidated financial statements for loss contingencies when a loss is known or considered probable and the amount can be reasonably estimated. If the reasonable estimate of a known or probable loss is a range, and no amount within the range is a better estimate than any other, the minimum amount of the range is accrued. If a loss is reasonably possible but not known or probable, and can be reasonably estimated, the estimated loss or range of loss is disclosed. When determining the estimated loss or range of loss, significant judgment is required to estimate the amount and timing of a loss to be recorded. Currently, the Company has accrued estimated losses of \$9.0 million related to *Hsu v. Puma Biotechnology, Inc.* and \$22.4 million related to *Eshelman v. Puma Biotechnology, Inc., et al.* as detailed below. For certain legal expenses related to the verdicts listed below, the Company has received reimbursements from its insurers.

#### *Hsu vs. Puma Biotechnology, Inc., et al.*

On June 3, 2015, Hsingching Hsu, individually and on behalf of all others similarly situated, filed a class action lawsuit against the Company and certain of its executive officers in the United States District Court for the Central District of California (Case No. 8:15-cv-00865-AG-JCG). On October 16, 2015, lead plaintiff Norfolk Pension Fund filed a consolidated complaint on behalf of all persons who purchased the Company's securities between July 22, 2014 and May 29, 2015. A trial on the claims relating to four statements alleged to have been false or misleading was held from January 15, 2019 to January 29, 2019. At trial, the jury found that three of the four challenged statements were not false or misleading, and thus found in the defendants' favor those claims. The jury found liability as to one statement and awarded a maximum of \$4.50 per share in damages, which represents approximately 5% of the total claimed damages of \$87.20 per share. Trading models suggest that approximately ten million shares traded during the class period may be eligible to claim damages. Based on prior lawsuits, the Company believes that the number of stockholders who submit proof of claims sufficient to recover damages is typically in the range of 20% to 40% of the total eligible shares. Based on these assumptions, total damages after claims could range from \$9.0 million to \$18.0 million. The total amount of aggregate class-wide damages remains uncertain and will be ascertained only after an extensive claims process and the exhaustion of any appeals and it is reasonably possible that the total damages will be higher than this estimate, however, the amount is not estimable at this time.

On September 9, 2019, the Court entered an order specifying the rate of prejudgment interest to be awarded on any valid claims at the 52-week Treasury Bill rate. The Court's order also established a claims process, which is expected to take about twelve months. A final judgment has not been entered. Based on the final total damages, the Company may owe a success-based legal fee to the Company's legal counsel in the amount of \$3.0 million. As the total damages remains uncertain, no liability has been recorded for the legal fee. The Company recognizes legal fees in connection with a loss contingency as incurred.

***Eshelman vs. Puma Biotechnology, Inc., et al.***

In February 2016, Fredric N. Eshelman filed a lawsuit against the Company's Chief Executive Officer and President, Alan H. Auerbach, and the Company in the United States District Court for the Eastern District of North Carolina (Case No. 7:16-cv-00018-D). The complaint generally alleged that Mr. Auerbach and the Company made defamatory statements regarding Dr. Eshelman in connection with a proxy contest. In May 2016, Dr. Eshelman filed a notice of voluntary dismissal of the claims against Mr. Auerbach. A trial on the remaining defamation claims against the Company took place from March 11 to March 15, 2019. At trial, the jury found the Company liable and awarded Dr. Eshelman \$15.9 million in compensatory damages and \$6.5 million in punitive damages. The plaintiff has since filed motions seeking attorneys' fees and pre-judgment interest, which if granted could increase the judgment amount. The Company strongly disagrees with the verdict and, on April 22, 2019, filed a motion for a new trial or, in the alternative, a reduced damages award. If the verdict is upheld, pending the outcome of that motion, the Company intends to appeal the verdict. The Company estimates the high end of potential damages in the matter could be approximately \$26.3 million; however, the actual amount of damages payable by the Company is still uncertain and will be ascertained only after completion of post-trial proceedings and the exhaustion of any appeals, and such amount could be greater than the amount of expense already recognized or the high end of the estimate. Due to the appeal, the Company secured a bond for the potential damages, which is collateralized by an automatically renewable stand-by letter of credit in the amount of \$8.9 million. The stand-by letter of credit is collateralized by a high-yield savings account which is classified as restricted cash on the accompanying consolidated balance sheets.

**Note 15—Quarterly Financial Data:**

Quarterly financial data (in thousands except share and per share data):  
(unaudited)

	Three Months Ended			
	March 31,	June 30,	September 30,	December 31,
<b>2019</b>				
Revenues	\$ 99,067	\$ 53,919	\$ 56,352	\$ 62,922
Net loss	(10,087)	(37,424)	(16,885)	(11,199)
Net loss attributable to common stock	(10,087)	(37,424)	(16,885)	(11,199)
Net loss per share—basic and diluted	\$ (0.26)	\$ (0.97)	\$ (0.44)	\$ (0.29)
Weighted-average shares of common stock outstanding—basic and diluted	38,481,824	38,647,775	38,893,757	39,043,706
<b>2018</b>				
Revenues	\$ 66,516	\$ 50,767	\$ 62,629	\$ 71,079
Net loss	(24,345)	(44,335)	(14,201)	(30,694)
Net loss attributable to common stock	(24,345)	(44,335)	(14,201)	(30,694)
Net loss per share—basic and diluted	\$ (0.65)	\$ (1.17)	\$ (0.37)	\$ (0.80)
Weighted-average shares of common stock outstanding—basic and diluted	37,699,024	37,819,767	38,043,174	38,201,056
<b>2017</b>				
Revenues	\$ —	\$ —	\$ 6,077	\$ 21,608
Net loss	(72,865)	(77,832)	(77,180)	(64,078)
Net loss attributable to common stock	(72,865)	(77,832)	(77,180)	(64,078)
Net loss per share—basic and diluted	\$ (1.97)	\$ (2.10)	\$ (2.07)	\$ (1.71)
Weighted-average shares of common stock outstanding—basic and diluted	36,931,167	36,992,017	37,214,002	37,534,410

**Note 16—Subsequent Events:**

On February 25, 2020, the FDA approved a supplemental New Drug Application, or sNDA, for neratinib in combination with capecitabine for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting. The sNDA approval was based on results of the Phase III NALA trial, a randomized controlled trial of neratinib plus capecitabine in patients with HER2-positive metastatic breast cancer who have received two or more prior anti-HER2-based regimens.

**Description of the Registrant's Securities Registered  
Pursuant to Section 12 of the Securities Exchange Act of 1934**

*Except as otherwise indicated herein or as the context otherwise requires, references in this exhibit to “we,” “us,” “our” and “our company” refer to Puma Biotechnology, Inc. The following description of our common stock and certain provisions of our second amended and restated certificate of incorporation and third amended and restated bylaws are summaries and are qualified in their entirety by reference to the full text of our second amended and restated certificate of incorporation and third amended and restated bylaws. We urge you to read those documents, each of which are incorporated by reference as exhibits to our filings with the Securities and Exchange Commission, for additional information.*

**General**

Our common stock is registered under Section 12 of the Securities Exchange Act of 1934, as amended. Our second amended and restated certificate of incorporation authorizes 100,000,000 shares of common stock, all with a par value of \$0.0001 per share. Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. The election of directors by holders of our common stock is determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of our common stock are entitled to receive proportionately any dividends as may be declared by our board of directors.

In the event of our liquidation or dissolution, the holders of our common stock are entitled to receive proportionately our net assets available for distribution to stockholders after the payment of all debts and other liabilities. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. Outstanding shares of our common stock are, when issued and paid for, validly issued, fully paid and nonassessable.

**Delaware Anti-Takeover Statute**

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

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

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

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

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



[\*\*\*] Certain information in this document has been excluded pursuant to Regulation S-K, Item 601(b)(10). Such excluded information is not material and would likely cause competitive harm to the registrant if publicly disclosed.

**AMENDING AGREEMENT**  
**Nerlynx License Agreement**

THIS AGREEMENT made effective as of the 18<sup>th</sup> day of December, 2019 (the “**Amending Agreement**”)

BY AND BETWEEN

**PUMA BIOTECHNOLOGY, INC.**, a corporation incorporated under the laws of Delaware (“**Licensor**”);

AND:

**KNIGHT THERAPEUTICS INC.**, a corporation incorporated under the laws of Canada (“**Knight**”).

(Licensor and Knight are hereinafter individually referred to as a “**Party**” and collectively as the “**Parties**”)

**WHEREAS** Licensor and Knight entered into a License Agreement dated January 9, 2019 (the “**Original Agreement**”);

**WHEREAS** the Parties wish to clarify certain aspects of the Original Agreement.

**NOW THEREFORE, THE PARTIES HEREBY AGREE AS FOLLOWS:**

1. The Original Agreement is amended by adding the following as Section 6.15 thereof:

“6.15. **Royalty Allocation.** The Parties confirm and agree that with respect to any and all royalties paid or payable by Knight to Licensor hereunder, [\*\*\*] of any such amount shall be for and in respect of the licenses as granted hereunder to the Licensor’s Patents and Know-How and the balance of [\*\*\*] shall be for and in respect to the licenses granted hereunder for the Licensor Marks, provided, however, such allocation shall in no event increase, reduce or otherwise change any of the royalty amounts payable by Knight to Licensor in the aggregate in accordance with the terms of this Agreement.”
  2. This Amending Agreement shall enure to the benefit of and be binding upon the Parties and their respective successors and legal personal representatives.
  3. This Amending Agreement may be executed by the Parties in separate counterparts each of which when so executed and delivered shall be an original, but all such counterparts shall together constitute one and the same instrument. The Parties agree that this Amending Agreement may be transmitted by facsimile and that the reproduction of signatures by facsimile will be treated as binding as if originals.
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4. All other terms of the Original Agreement shall remain in full force and effect unamended and are hereby ratified by the Parties hereto in all respects.
5. This Agreement all disputes arising out of or relating to this Agreement, or the performance, enforcement, breach or termination hereof or thereof, and any remedies relating thereto, shall be construed, governed by and interpreted in accordance with the laws of New York.

**IN WITNESS WHEREOF** the Parties hereto have executed this Amending Agreement as of the day and year first above written.

**PUMA BIOTECHNOLOGY, INC.**

Per: /s/ Maximo F. Nougues  
Name: Maximo F. Nougues  
Title: Chief Financial Officer

**KNIGHT THERAPEUTICS INC.**

Per: /s/ Amal Khouri  
Name: Amal Khouri  
Title: VP Business Development

[\*\*\*] Certain information in this document has been excluded pursuant to Regulation S-K, Item 601(b)(10). Such excluded information is not material and would likely cause competitive harm to the registrant if publicly disclosed.

### FIRST AMENDMENT TO LICENSE AGREEMENT

**This First Amendment** (the “**First Amendment**”), effective as of September 17, 2019 (“**Effective Date of the First Amendment**”), is made by and between Puma Biotechnology, Inc., a corporation organized and existing under the laws of Delaware with its principal place of business at 10880 Wilshire Blvd, Los Angeles, CA 90024 (“**Licensor**”) and Pierre Fabre Medicament SAS, a company duly organized and existing under the laws of France, having offices and principal place of business at 45, Place Abel Gance 92100 Boulogne Billancourt, France (“**Licensee**”) (each individually a “**Party**” and collectively the “**Parties**”), and amends that certain License Agreement between the Parties effective as of March 29, 2019 (the “**Agreement**”). Capitalized terms used herein without definition shall have the meaning set forth in the Agreement.

**WHEREAS**, the Parties desire to amend the provisions of the Agreement relating to the named patient, temporary use, or similar programs for the Product in the Licensee Territory (collectively, the “**Programs**” and each, a “**Program**”).

**NOW THEREFORE**, for good and valuable mutual consideration, the receipt and sufficiency of which is hereby acknowledged, the Parties hereto agree to amend the Agreement as follows:

1. Section 4.6(c)(ii) of the Agreement shall be deleted and replaced with the following:

(ii) Licensor shall maintain Regulatory Filings or approvals for the Product as existing on or prior to the Effective Date in each country of the Licensee Territory [\*\*\*], in consultation with Licensee. Licensor shall not initiate Programs in the Licensee Territory after the transfer of the Marketing Authorization to Licensee without Licensee prior written consent. Licensor shall supply all Product requirements for the Programs for each country of the Licensee Territory [\*\*\*] until calendar year end [\*\*\*] in accordance with the quality agreement for the Programs to be entered into by and among Puma, Pierre Fabre and Caligor Coghlan Pharma Services (hereinafter referred to as the “Subcontractor”), provided, such Product requirements shall be met solely through U.S. commercial supplies and Licensor shall have no obligation under this Section 4.6(c)(ii) to provide Products in any other supply form. Title to the Products intended for the Programs in the Licensee Territory shall pass from Licensor to Licensee upon delivery at the Subcontractor’s site.

2. Section 4.6(c)(iii) of the Agreement shall be added with the following:

(iii) With respect to any and all Programs, the Parties agree as follows:

(A) **Monthly Management Fee:** Licensor shall pay for [\*\*\*] monthly management fees of the Programs prior to [\*\*\*]. On or after [\*\*\*], Licensee shall pay for [\*\*\*] monthly management fees for the Programs in the Licensee Territory.

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- (B) **New Patient Fee:** Licensor shall pay for [\*\*\*] new patient fees of a Program if the first Product bottle for a patient enrolled in such Program was delivered to the patient on or after the Effective Date and prior to the MAH Transfer Date. For those Programs in which the first Product bottle for a patient enrolled in such Program was delivered to the patient on or after the MAH Transfer Date, Licensee shall pay a one-time fee of \$[\*\*\*] per new patient for each new patient who enrolls in a Program.
  - (C) **Shipping Management Fee:** Licensor shall pay for [\*\*\*] directly related to the shipping management, that are not Shipping Costs, of the Program Products, prior to the MAH Transfer Date. On or after the MAH Transfer Date, Licensee shall pay \$[\*\*\*] per shipment as shipping management fees, provided the Parties agree to use reasonable efforts to combine Product shipment.
  - (D) **Shipping Costs:** Licensor shall pay for [\*\*\*] shipping costs and expenses directly related to the shipment of the Products from Licensor's site to Subcontractor's site and from Subcontractor's site to each patient ("**Shipping Costs**") enrolled in a Program for all initial fills and refills thereafter prior to the MAH Transfer Date. On or after the MAH Transfer Date, Licensee shall pay [\*\*\*] Shipping Costs for the applicable Program.
3. **Entire Agreement.** All other terms and conditions of the Agreement, as amended and modified, are hereby ratified, confirmed and approved. This First Amendment is the integral part of the Agreement. Except as set forth in this First Amendment, the Agreement is unaffected and shall continue in full force and effect in accordance with its terms. If there is a conflict between the Agreement and this First Amendment, the terms of this First Amendment will prevail.
  4. **Counterparts.** This First Amendment may be executed in one or more counterparts by the Parties by signature of a person having authority to bind the Party, each of which when executed and delivered by facsimile, electronic transmission or by mail delivery, will be an original and all of which shall constitute but one and the same instrument.

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**IN WITNESS WHEREOF**, the Parties have executed this First Amendment as of the Effective Date of the First Amendment.

**PUMA BIOTECHNOLOGY, INC.**

BY: /s/ Alan Auerbach

NAME: Alan Auerbach

TITLE: Chief Executive Officer and President

**PIERRE FABRE MEDICAMENT SAS**

BY: /s/ Jean Luc Lowinski

NAME: Jean Luc Lowinski

TITLE: President, Pharmaceuticals Division

[\*\*\*] Certain information in this document has been excluded pursuant to Regulation S-K, Item 601(b)(10). Such excluded information is not material and would likely cause competitive harm to the registrant if publicly disclosed.

## SECOND AMENDMENT TO LICENSE AGREEMENT

This Second Amendment (the “**Second Amendment**”), effective as of November 25, 2019 (“**Effective Date of the Second Amendment**”), is made by and between Puma Biotechnology, Inc., a corporation organized and existing under the laws of Delaware with its principal place of business at 10880 Wilshire Blvd, Los Angeles, CA 90024 (“**Licensor**”) and Pierre Fabre Medicament SAS, a company duly organized and existing under the laws of France, having offices and principal place of business at 45, Place Abel Gance 92100 Boulogne Billancourt, France (“**Licensee**”) (each individually a “**Party**” and collectively the “**Parties**”), and amends that certain License Agreement between the Parties effective as of March 29, 2019, amended by the First Amendment effective as of September 17, 2019 (together, the “**Agreement**”). Capitalized terms used herein without definition shall have the meaning set forth in the Agreement.

**WHEREAS**, pursuant to Article 2.6 of the Agreement, Licensor provided a Licensor Notice to Licensee dated July 31, 2019; and

**WHEREAS**, Licensor received the Licensee Notice from Licensee on August 9, 2019, whereby Licensee indicated its interest and intent to negotiate with Licensor for the commercialization rights of the Products in certain of the Option Territory, as further described below.

**NOW THEREFORE**, for good and valuable mutual consideration, the receipt and sufficiency of which is hereby acknowledged, the Parties hereto agree to amend the Agreement as follows:

1. Article 1.95 shall be added with the following:  
  
1.95 “First Territory Extension” means Middle East Countries, South Africa, Sudan, and Turkey.
  2. As of the Effective Date of this Second Amendment, the First Territory Extension shall be deemed included in the Licensee Territory and shall no longer be included in the Option Territory.
  3. As of the Effective Date of this Second Amendment, subject to the terms and conditions of the Agreement, Licensor hereby grants to Licensee and its Affiliates an exclusive (even as to Licensor and its Affiliates), royalty bearing license under the Licensed Intellectual Property, with the right to sublicense (subject to Article 2.3 of the Agreement) through multiple tiers to Develop, Manufacture (subject to this Section 3), seek approval of Regulatory Filings and Commercialize the Product in the First Territory Extension in the Field. Notwithstanding anything to the contrary herein or the agreement, the exclusive rights Manufacture the Licensed Products shall not apply to the First Territory Extension, unless and until such rights and licenses are necessary to comply with applicable Law in any country in the First Territory Extension and shall solely extend to the extent to such country and to the extent necessary for Licensee to exercise its Commercialization rights under this Agreement in such country.
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4. As of the Effective Date of the Second Amendment, Licensee shall be responsible for the Programs (as defined in the First Amendment to the License Agreement, dated 18 September, 2019) for each country of the First Extension Territory, including without limitation Product supplies, and costs and fees related to the management fees of such Programs.

5. Payments relating to the First Territory Extension.

a. License Fee. In consideration for the license granted by Licensor to Licensee under Section 3 of this Second Amendment, Licensee shall pay to Licensor a license fee equal to four million USD (US \$4,000,000) within [\*\*\*] ([\*\*\*)] days following the Effective Date of the Second Amendment in accordance with the payment provisions of Article 7 of the Agreement. Payment made in accordance with this Section 5(a) shall be non-refundable, non-creditable and non-cancellable.

b. Milestone Payments.

i. Development Milestone Payments. In further consideration for the license granted by Licensor to Licensee under Section 3 of this Second Amendment, Licensee shall pay to Licensor the milestone payments set out below following the first achievement by Licensee, and/or any of its Affiliates or Sublicensees, of the corresponding milestone events set out below with respect to the Product in the First Territory Extension, in accordance with this Section 5(b)(i) and the payment provisions in Article 7 of the Agreement:

<b>Milestone Event</b>	<b>Milestone Payment</b>
[***]	[***]
[***]	[***]

Each development milestone payable under this Section 5(b)(i) shall be payable only once and the total of such development milestones shall not exceed [\*\*\*] ([\*\*\*)].

ii. Sales Milestone Payments. In further consideration for the license granted by Licensor to Licensee under Sections 3 of this Second Amendment, Licensee shall pay to Licensor the milestone payments set out below following the first time that the Annual Royalty Bearing Net Sales of the Product reach the following thresholds in South Africa, in accordance with this Section 5(b)(ii) and the payment provisions in Article 7 of the Agreement:

<b>Sales Milestone Events</b>	<b>Milestone Payment</b>
[***]	[***]

c. For the avoidance of doubt, Royalty Bearing Net Sales of the Product in the First Territory Extension shall be included in the calculation of sales milestones payments and royalties provided under Articles 6.2(b) and 6.4.

6. As of the Effective Date of the Second Amendment, Exhibit 1 of the Agreement shall be deleted and replaced with Addendum A to this Second Amendment, attached hereto.

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7. As of the Effective Date of the Second Amendment, Exhibit 5 of the Agreement shall be deleted and replaced with Addendum B to this Amendment, attached hereto.
8. **Entire Agreement.** All other terms and conditions of the Agreement, as amended and modified, are hereby ratified, confirmed and approved. This Second Amendment is the integral part of the Agreement. Except as set forth in this Second Amendment, the Agreement is unaffected and shall continue in full force and effect in accordance with its terms. If there is a conflict between the Agreement and this Second Amendment, the terms of this Second Amendment will prevail.
9. **Counterparts.** This Second Amendment may be executed in one or more counterparts by the Parties by signature of a person having authority to bind the Party, each of which when executed and delivered by facsimile, electronic transmission or by mail delivery, will be an original and all of which shall constitute but one and the same instrument.

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**IN WITNESS WHEREOF**, the Parties have executed this Amendment Two as of the Effective Date of the Amendment Two.

**PUMA BIOTECHNOLOGY, INC.**

BY: /s/ Alan Auerbach  
NAME: Alan Auerbach  
TITLE: Chief Executive Officer and President

**PIERRE FABRE MEDICAMENT SAS**

BY: /s/ Jean Luc Lowinski  
NAME: Jean Luc Lowinski  
TITLE: President, Pharmaceuticals Division

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## **Addendum A**

### **LICENSED PATENTS**

Omitted pursuant to Regulation S-K, Item 601(a)(5)

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## **Addendum B**

### **PRODUCT TRADEMARKS AND DOMAIN NAMES**

Omitted pursuant to Regulation S-K, Item 601(a)(5)

**Puma Biotechnology, Inc.  
Subsidiaries**

<b>Subsidiary</b>	<b>Jurisdiction of Incorporation or Organization</b>
Puma Biotechnology Ltd	England and Wales
Puma Biotechnology B.V.	Netherlands

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors  
Puma Biotechnology, Inc.:

We consent to the incorporation by reference in the registration statements (Nos. 333-181703, 333-196993, 333-205117 and 333-219347) on Form S-8 pertaining to the Puma Biotechnology, Inc. 2011 Incentive Award Plan, as amended, and in the registration statement (No. 333-218373) on Form S-8, pertaining to the Puma Biotechnology, Inc. 2017 Employment Inducement Award Plan, of our reports dated February 27, 2020, with respect to the consolidated balance sheets of Puma Biotechnology, Inc. as of December 31, 2019 and 2018, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2019, and the related notes (collectively, the financial statements), and the effectiveness of internal control over financial reporting as of December 31, 2019, which reports appear in the December 31, 2019 annual report on Form 10-K of Puma Biotechnology, Inc.

Our report contains an explanatory paragraph related to Puma Biotechnology, Inc.'s change in method of accounting for leases as of January 1, 2019 due to the adoption of Accounting Standards Codification Topic 842, Leases.

Los Angeles, California  
February 27, 2020

/s/ KPMG LLP

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**CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER  
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Alan H. Auerbach, certify that:

1. I have reviewed this Annual Report on Form 10-K of Puma Biotechnology, Inc. for the year ended December 31, 2019;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;
  - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 27, 2020

/s/ Alan H. Auerbach  
\_\_\_\_\_  
Alan H. Auerbach  
Principal Executive Officer

**CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER  
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Maximo F. Nougues, certify that:

1. I have reviewed this Annual Report on Form 10-K of Puma Biotechnology, Inc. for the year ended December 31, 2019;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;
  - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 27, 2020

/s/ Maximo F. Nougues

Maximo F. Nougues

Principal Financial and Accounting Officer

**CERTIFICATION****PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

The following certification is being furnished solely to accompany the Annual Report on Form 10-K of Puma Biotechnology, Inc. for the year ended December 31, 2019, pursuant to 18 U.S.C. § 1350 and in accordance with SEC Release No. 33-8238. This certification shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, nor shall it be incorporated by reference in any filing of Puma Biotechnology, Inc. under the Securities Act of 1933, as amended, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

**Certification of Principal Executive Officer**

I, Alan H. Auerbach, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Annual Report on Form 10-K of Puma Biotechnology, Inc. for the year ended December 31, 2019, fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended, and that the information contained in such report fairly presents, in all material respects, the financial condition and results of operations of Puma Biotechnology, Inc.

Date: February 27, 2020

/s/ Alan H. Auerbach

Alan H. Auerbach

Principal Executive Officer

A signed original of this written statement required by Section 906 has been provided to Puma Biotechnology, Inc. and will be retained by Puma Biotechnology, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.



**CERTIFICATION****PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

The following certification is being furnished solely to accompany the Annual Report on Form 10-K of Puma Biotechnology, Inc. for the year ended December 31, 2019, pursuant to 18 U.S.C. § 1350 and in accordance with SEC Release No. 33-8238. This certification shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, nor shall it be incorporated by reference in any filing of Puma Biotechnology, Inc. under the Securities Act of 1933, as amended, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

**Certification of Principal Financial Officer**

I, Maximo F. Nougues, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Annual Report on Form 10-K of Puma Biotechnology, Inc. for the year ended December 31, 2019, fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended, and that the information contained in such report fairly presents, in all material respects, the financial condition and results of operations of Puma Biotechnology, Inc.

Date: February 27, 2020

/s/ Maximo F. Nougues

Maximo F. Nougues

Principal Financial and Accounting Officer

A signed original of this written statement required by Section 906 has been provided to Puma Biotechnology, Inc. and will be retained by Puma Biotechnology, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.