PUMA BIOTECHNOLOGY, INC.
Form 10-K
February 29, 2016

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2015

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	77-0683487
(State or other jurisdiction of incorporation or organization)	(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:

Title of each class	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	New York Stock Exchange

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 x 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 x

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 x No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate website, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes x No ¨

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

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

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

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

The aggregate market value of voting stock held by non-affiliates of the registrant as of June 30, 2015, was $2,044,234,826 based upon the closing price of $116.75 per share of the registrant's common stock on the New York Stock Exchange on Tuesday, June 30, 2015, 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 19, 2016, there were 32,486,842 shares of the registrant's common stock outstanding.

Documents Incorporated by Reference:

Portions of the Proxy Statement for the registrant's 2016 Annual Meeting of Stockholders, or the 2016 Proxy Statement, are incorporated by reference in 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 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;
- the anticipated timing of product revenues and the commercial availability 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;
- our ability to market any of our products;
- our history of operating losses;
- 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 ability to vigorously defend against a purported securities class action and a defamation lawsuit;
- 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 state 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” 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 Part I of this Annual Report, in the section entitled “Item 1A. Risk Factors,” 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. 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 subsidiary, Puma Biotechnology Ltd., 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 the global development and commercialization rights to three drug candidates—PB272 (neratinib (oral)), PB272 (neratinib (intravenous)) and PB357. Neratinib is a potent irreversible tyrosine kinase inhibitor, or TKI, that blocks signal transduction through the epidermal growth factor receptors, HER1, HER2 and HER4. Currently, we are primarily focused on the development of the oral version of neratinib, and our most advanced drug candidates are directed at the treatment of HER2-positive breast cancer. We believe neratinib has clinical application in the treatment of several other cancers as well, including non-small cell lung cancer, or NSCLC, and other tumor types that over-express or have a mutation in HER2.

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 cancer by binding to the HER2 protein. There are also a number of trials ongoing that involve various combinations of these drugs (for example, Perjeta plus Kadcyla). 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.

We recently completed a Phase III clinical trial of neratinib for the extended adjuvant treatment of women with early stage HER2-positive breast cancer, which we refer to as the ExteNET trial. Based on the results from the ExteNET trial, we expect to file for regulatory approval of neratinib in the extended adjuvant setting in the United States in the first quarter of 2016 and in the European Union in the first half of 2016.

Separately, in February 2013, we reached agreement with the U.S. Food and Drug Administration, or FDA, under a Special Protocol Assessment, or SPA, for a planned Phase III clinical trial of PB272 in patients with HER2-positive metastatic breast cancer who have failed two or more prior treatments (third-line disease). The European Medicines Agency, or EMA, has also provided follow-on scientific advice, or SA, consistent with that of the FDA regarding our ability to use the trial to support regulatory approval in the European Union. We refer to this trial as PUMA-NER-1301. We initiated this trial in June 2013.

In addition to continuing to follow the patients from the ExteNET trial and continuing the PUMA-NER-1301 trial, we are actively conducting the following trials to evaluate the safety and efficacy of neratinib in various indications:

- Phase II clinical trials in the neoadjuvant treatment of HER2-positive breast cancer;
- a Phase II clinical trial in patients with HER2-positive metastatic breast cancer that has metastasized to the brain;
- a Phase II trial in the treatment of HER2-mutated non-small cell lung cancer;
- a Phase II trial in the treatment of patients with HER2-negative breast cancer that have a HER2 mutation; and

a Phase II trial in the treatment of solid tumors that have an activating HER2 mutation.

During the next 12 to 18 months, we expect to commence a Phase III trial of neratinib for the neoadjuvant treatment of HER2-positive breast cancer and a Phase II clinical trial for the neoadjuvant treatment of a subset of patients with HER2-negative breast cancer. We also plan to continue to evaluate the application of neratinib in the treatment of other forms of HER2-positive or HER2-mutated cancers where there may be unmet medical needs.

We license the commercial rights to our current drug candidates from Pfizer, Inc., 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. In evaluating potential drug candidates, we employ disciplined decision criteria that favor drug candidates that have undergone at least some clinical study. 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.

Strategy

Our strategy is to become a leading oncology-focused biopharmaceutical company. The key elements of our strategy are as follows:

Seek regulatory approval and commence commercialization of neratinib in our lead indication. We recently completed our ExteNET trial, a Phase III clinical trial of neratinib for the extended adjuvant treatment of women with early stage HER2-positive breast cancer. Based on the results from the ExteNET trial, we expect to file for regulatory approval of neratinib in the extended adjuvant setting in the United States in the first quarter of 2016 and in the European Union in the first half of 2016. We are continuing to evaluate potential commercialization options for the extended adjuvant setting, including developing a direct sales force, contracting with third parties to provide sales and marketing capabilities, some combination of these two options or other strategic options. Additionally, we believe we currently have sufficient inventory on hand to support at least the first year of commercialization in the extended adjuvant setting and will continue to monitor and evaluate our third party manufacturers' ability to provide commercial supply of the product.

Continue to advance the development of neratinib for the treatment of other HER2-positive breast cancer indications. We are primarily focused on developing neratinib for the treatment of patients with HER2-positive breast cancer, HER2-negative breast cancer who have a HER2 mutation and other solid tumors with an activating mutation in HER2, and HER2-mutated non-small cell lung cancer. In addition to our recently completed ExteNET trial, we have several ongoing clinical trials focused on the treatment of patients with HER2-positive breast cancer. In June 2013, we commenced a Phase III clinical trial of neratinib in patients with HER2-positive metastatic breast cancer who have failed two or more prior treatments (third-line disease), and in the next 12 to 18 months we expect to commence another Phase III clinical trial of neratinib in combination with chemotherapy for the neoadjuvant treatment of HER2-positive breast cancer. We also have several ongoing Phase II clinical trials evaluating the use of neratinib in combination with various other drugs, including Xeloda, Paclitaxel and Torisel, to treat patients with HER2-positive metastatic breast cancer and HER2-positive metastatic breast cancer that has metastasized to the brain.

Expand our product pipeline by pursuing additional applications of neratinib. We believe there are additional applications for neratinib in the treatment of HER2-mutated non-small cell lung cancer, which we also believe may be underserved by current treatment alternatives; in the treatment of patients with HER2-negative breast cancer 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.

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, favoring drug candidates that have undergone at least some clinical study. Our decision to license a drug candidate will also depend on 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. We intend to pursue regulatory approval for a majority of our drug candidates in multiple indications.

Evaluate the commercialization strategies on a product-by-product basis in order to maximize the value of each. As we move our 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 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 therapy for the adjuvant treatment of HER2-positive early stage breast cancer is the combination of trastuzumab and paclitaxel (Taxol) following anthracyclines, trastuzumab following chemotherapy and the combination of docetaxel (Taxotere) and trastuzumab following anthracyclines. In addition, we are aware of the ongoing APHINITY trial, which is comparing pertuzumab plus trastuzumab and chemotherapy versus placebo plus trastuzumab and chemotherapy as an adjuvant therapy, and the KAITLIN trial, which 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 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%. T-DM1 is approved by the FDA for the treatment of patients with HER2-positive metastatic breast cancer who previously received trastuzumab and a taxane chemotherapy, separately or in combination. Unfortunately, most patients with HER2-positive breast cancer eventually develop resistance to these treatments, resulting in disease progression. 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 trastuzumab.

We believe that there are approximately 36,000 patients in the United States and 34,000 patients in the European Union, or EU, with newly diagnosed HER2-positive breast cancer, representing an estimated total market opportunity for neoadjuvant HER2-positive breast cancer between $1 billion and $2 billion. We believe that the worldwide Herceptin adjuvant revenue was approximately $4.3 billion in 2013. We also believe that there are between 5,000 and 6,000 patients in the United States with third-line or later HER2-positive metastatic breast cancer. In 2013, worldwide sales of Tykerb for this indication were approximately $325 million.

Product Development Pipeline

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

Neratinib

Neratinib is a potent irreversible tyrosine kinase inhibitor, or 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 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 the Phase III clinical trial of neratinib for the extended adjuvant treatment of early stage HER2-positive breast cancer (ExteNET Trial). The data from this trial was presented in an oral presentation at the American Society of Clinical Oncology (ASCO) 2015 Annual Meeting in June 2015 and was recently published online in the journal The Lancet Oncology and will be published in a future print issue of the journal. The ExteNET trial is 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 (1 (0.1%) patient 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. Puma's recently reported clinical data from several trials have demonstrated that the use of high dose prophylactic loperamide greatly reduces 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. In all of its current ongoing studies Puma is instituting the use of high dose loperamide for the first cycle of treatment in order to continue to reduce the neratinib-related diarrhea.

The primary endpoint of the trial was invasive disease free survival (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 2-year DFS rate for the neratinib arm was 93.9% and the 2-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 (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 2-year DFS-DCIS rate for the neratinib arm was 93.9% and the 2-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 2-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 2-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 2-year DFS-DCIS rate for the centrally confirmed patients in the neratinib arm was 94.7% and the 2-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 2-year DFS rate for the neratinib arm was 95.4% and the 2-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 2-year DFS rate for the centrally confirmed patients in the neratinib arm was 97.0% and the 2-year DFS rate for centrally confirmed patients in the placebo arm was 88.4%.

We intend to use the 2-year data from the ExteNET trial to file for regulatory approval of neratinib in the extended adjuvant setting in the United States during the first quarter of 2016 and in the European Union in the first half of 2016.

Three-Year ExteNET Data. In December 2015, updated results from the ExteNET trial were presented at the 2015 CTRC-AACR San Antonio Breast Cancer Symposium. This presentation involved an exploratory sensitivity analysis of the 3-year disease free survival data to examine the durability of treatmen