PUMA BIOTECHNOLOGY, INC.
Form 424B5
October 18, 2016
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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-201603

The information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and we are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION

PRELIMINARY PROSPECTUS SUPPLEMENT DATED OCTOBER 18, 2016

PROSPECTUS SUPPLEMENT

(To prospectus dated January 20, 2015)

$150,000,000

Puma Biotechnology, Inc.

Common Stock

We are offering shares of our common stock.

Our common stock is listed on the New York Stock Exchange under the symbol PBYI. On October 17, 2016, the last reported sale price of our common stock on the New York Stock Exchange was $52.30 per share.

Investing in our common stock involves risks that are described in the Risk Factors section beginning on page S-9 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.

	Per Share	Total
Public offering price	$	$
Underwriting discounts and commissions(1)	$	$
Proceeds, before expenses, to us	$	$

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

The underwriters may also exercise their option to purchase up to an additional $22,500,000 of shares of our common stock from us, at the public offering price, less the underwriting discounts and commissions, for 30 days after the date of this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The shares will be ready for delivery on or about , 2016.

Citigroup **J.P. Morgan**

The date of this prospectus supplement is , 2016.

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PROSPECTUS SUPPLEMENT

ACCOMPANYING PROSPECTUS

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is the prospectus supplement, including the documents incorporated by reference, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. Before you invest, you should carefully read this prospectus supplement, the accompanying prospectus, all information incorporated by reference herein and therein, as well as the additional information described under Where You Can Find More Information; Incorporation by Reference on page S-25 of this prospectus supplement. These documents contain information you should consider when making your investment decision. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement that we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectuses we may provide to you in connection with this offering. Neither we nor any of the underwriters have authorized any other person to provide you with any information that is different. If anyone provides you with different or inconsistent information, you should not rely on it. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement outside the United States. This prospectus supplement does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Unless otherwise indicated, information contained in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference, concerning our industry and the markets in which we operate, including our general expectations and market position, market opportunity and market share, is based on information from our own management estimates and research, as well as from industry and general publications and research, surveys and studies conducted by third parties. Management estimates are derived from publicly available information, our knowledge of our industry and assumptions based on such information and knowledge, which we believe to be reasonable. In addition, assumptions and estimates of our and our industry s future performance are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in Risk Factors in this prospectus supplement, the accompanying prospectus and in our Annual Report on Form 10-K for the fiscal year ended December 31, 2015, which are incorporated by reference into this prospectus supplement. These and other important factors could cause our future performance to differ materially from our assumptions and estimates. See Special Note Regarding Forward-Looking Statements.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information about us, this offering and information appearing elsewhere in this prospectus supplement, in the accompanying prospectus and in the documents we incorporate by reference. This summary is not complete and does not contain all of the information you should consider before investing in our common stock pursuant to this prospectus supplement and the accompanying prospectus. Before making an investment decision, to fully understand this offering and its consequences to you, you should carefully read this entire prospectus supplement and the accompanying prospectus, including Risk Factors beginning on page S-9 of this prospectus supplement, the financial statements and related notes, and the other information that we incorporate by reference into this prospectus supplement, including the section Risk Factors in our Annual Report on Form 10-K for the fiscal year ended December 31, 2015. As used in this prospectus supplement, unless the context requires otherwise, the terms Company, we, our and us refer to Puma Biotechnology, Inc. together with our wholly-owned subsidiary, Puma Biotechnology Ltd.

Our Company

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.

Currently, the only treatment approved by the U.S. Food and Drug Administration, or 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. There is currently no FDA approved drug for the extended adjuvant treatment of early stage HER2-positive breast cancer that has been previously treated with trastuzumab.

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. Based on our internal estimates, we believe that the worldwide Herceptin adjuvant revenue was approximately $4.5 to $5.0 billion in 2015. 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.

We believe that approximately 2% of all newly diagnosed breast cancer patients have mutation in HER2 kinase (approximately 4,000 to 5,000 patients in the United States) and that approximately 4 5% of all metastatic breast cancer patients have mutation in HER2 kinase (approximately 8,000 to 10,000 patients in the United States). We believe this occurs mostly in patients with hormone receptor positive disease.

Marketing Authorization Application and New Drug Application

In June and July 2016, we submitted a Marketing Authorization Application, or MAA, to the European Medicines Agency, or the EMA, and filed a New Drug Application, or NDA, with the FDA, respectively, for neratinib for the extended adjuvant treatment of patients with early-stage HER2-overexpressed/amplified breast cancer who have received prior adjuvant trastuzumab-based therapy. We recently announced that the EMA validated the MAA and the FDA accepted for review the NDA. The MAA and NDA submissions are based upon the results of the ExteNET Phase III study, or the ExteNET trial, which reached its primary endpoint whereby neratinib demonstrated a statistically significant reduction of risk of invasive disease recurrence or death versus placebo. The ExteNET trial is a double-blind, placebo-controlled, Phase III trial of neratinib versus placebo after adjuvant treatment with trastuzumab in women with early-stage HER2-positive breast cancer. The trial randomized 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, or death for a period of two years after randomization in the trial. The primary endpoint of the trial was invasive disease free survival, or DFS.

In the ExteNET trial, 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 invasive DFS rate for the neratinib arm was 93.9% and the 2-year DFS rate for the placebo arm was 91.6%. 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). For the patients with hormone receptor positive disease, 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%. Results of the study were published online in *The Lancet Oncology* in February 2016.

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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 patient (0.1%) had grade 4 diarrhea). Patients who received neratinib in the ExteNET trial did not receive any prophylaxis with antidiarrheal agents to prevent the neratinib-related diarrhea. Interim results of a Phase II study of neratinib monotherapy in patients with HER2-positive early stage breast cancer who have previously been treated with adjuvant trastuzumab, where patients received anti-diarrheal prophylaxis with loperamide, demonstrated that treatment with prophylactic loperamide reduced the rate of grade 3 or higher diarrhea to between 13.0% and 18.5%.

In July 2016, we announced updated results from the ExteNET trial. As part of the data analysis for the NDA filing in the United States and the MAA submission in Europe, an updated analysis that included an interim 5-year invasive DFS analysis was performed. This data analysis was performed in order to examine the durability of treatment effect beyond the 2-year data included in the primary analysis. This interim analysis was not a pre-planned analysis in the statistical analysis plan for the trial. For the primary endpoint of the trial, invasive DFS, the 5-year interim results of the trial demonstrated that treatment with neratinib resulted in a 26% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.74, p = 0.017). The 5-year interim invasive DFS rate for the neratinib arm was 90.4% and the 5-year interim invasive DFS rate for the placebo arm was 87.9%. Additional updated results for the 3-year invasive DFS rate and 4-year invasive DFS rate are shown in the table below:

DFS for Intent to Treat (ITT) Population

	3-Year DFS	4-Year DFS	5-Year Interim DFS
Neratinib	92.5%	91.4%	90.4%
Placebo	90.3%	89.2%	87.9%
Absolute invasive DFS Difference	2.2%	2.2%	2.5%

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. To date, centralized HER2 testing has been performed on 2,140 (75%) of the patients in the ExteNET trial, and further central testing on available samples is currently ongoing. For the 1,777 patients whose tumors were HER2 positive by central confirmation, the interim results of the trial demonstrated that treatment with neratinib resulted in a 30% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.70, p = 0.026). The 5-year interim invasive DFS rate for the centrally confirmed patients in the neratinib arm was 90.8% and the 5-year interim invasive DFS rate for the centrally confirmed patients in the placebo arm was 88.1%.

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For the pre-defined subgroup of 1,631 patients with hormone receptor positive disease, the interim results of the trial demonstrated that treatment with neratinib resulted in a 41% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.59, p = 0.002). The 5-year interim invasive DFS rate for the neratinib arm was 91.7% and the 5-year interim invasive DFS rate for the placebo arm was 86.9%. Additional updated results for the 3-year invasive DFS rate and 4-year invasive DFS rate are shown in the table below:

DFS for Hormone Receptor Positive (HR-positive) Population

	3-Year DFS	4-Year DFS	5-Year Interim DFS
Neratinib	93.8%	92.9%	91.7%
Placebo	89.9%	88.6%	86.9%
Absolute invasive DFS Difference	3.9%	4.3%	4.8%

We anticipate that the full 5-year DFS data will be available in 2017.

Phase II Trial of Neratinib with HER2-Mutated, Non-Amplified Breast Cancer

In December 2015, we announced interim results from an ongoing Phase II clinical trial of neratinib that were presented at the 2015 CTRC-AACR San Antonio Breast Cancer Symposium (SABCS). These interim results were the first presentation of data from the expanded cohort of patients from our ongoing Phase II clinical trial of neratinib in patients with solid tumors who have an activating ERBB2 (HER2) mutation (SUMMIT basket trial). This expanded cohort included patients with metastatic breast cancer and whose tumors have a HER2 mutation but are neither HER2 amplified or overexpressed (HER2 negative).

The primary endpoint of the trial was objective response at week 8 assessed by anatomic or metabolic imaging. The interim efficacy results from the trial showed that for the 19 efficacy evaluable patients in the breast cancer cohort, 6 patients (32%) experienced a response at week 8. This included one patient with a complete response and five patients with partial responses. The secondary endpoints of the trial included duration of response, clinical benefit rate and progression free survival, or PFS. The results of the trial showed that 3 patients (16%) had a confirmed objective response, 8 patients (42%) demonstrated clinical benefit and the median PFS was 4.0 months.

The presentation also discussed that a bidirectional cross-talk between hormone receptor and HER2 signaling pathways can lead to endocrine resistance due to activated HER2 signaling and ER-mediated tumor proliferation as a potential resistance mechanism to sustained HER2 inhibition. Preclinical data has demonstrated that the combination of an anti-estrogen with a HER2 inhibitor results in enhanced anti-tumor activity in preclinical models of estrogen receptor positive/HER2-positive breast tumors. Based on this, the SUMMIT study was amended to allow for the combination of neratinib plus fulvestrant in eligible postmenopausal hormone receptor positive breast cancer patients. For the 3 response-evaluable patients who have been enrolled and received the combination of neratinib plus fulvestrant, 3 (100%) of 3 patients have shown a response, including one patient with a complete response and two patients with partial responses. There have also been two patients enrolled on the combination of neratinib plus fulvestrant after progressing on neratinib monotherapy. One (50%) of these two patients has demonstrated a partial response.

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The interim safety results of the study showed that the most frequently observed adverse event was diarrhea. Patients received loperamide (16 mg per day initially) prophylactically for the first cycle of treatment in order to reduce the neratinib-related diarrhea. For the 130 patients enrolled across all solid tumor cohorts in the SUMMIT study, 26 patients (20%) reported grade 3 diarrhea. The median duration of grade 3 diarrhea for the patients in the entire SUMMIT study was 2 days. 2 patients (2%) in the SUMMIT study have permanently discontinued neratinib due to diarrhea and 20 patients (15%) have temporarily discontinued neratinib due to diarrhea and then restarted after the diarrhea subsided. For the breast cancer mutation cohort, 7 of 20 patients (35%) experienced grade 3 diarrhea. The median duration of grade 3 diarrhea was 1 day. No patient (0%) in the breast cancer cohort permanently discontinued neratinib due to diarrhea and 4 patients (20%) temporarily discontinued neratinib due to diarrhea and then restarted after the diarrhea subsided.

In June 2016, we announced that positive results from an investigator sponsored Phase II trial of neratinib with HER2-mutated, non-amplified breast cancer were presented in a poster discussion session at the American Society of Clinical Oncology, or ASCO, 2016 Annual Meeting.

In the trial, patients with HER2 mutated breast cancer (either in their primary or metastatic tumor) received 240 mg of neratinib daily. Patients received loperamide (16 mg per day initially) prophylactically for the first cycle of treatment in order to reduce the neratinib-related diarrhea. For the 16 patients enrolled in the trial, 16 patients (100%) had HER2-negative disease, 15 patients (94%) were hormone receptor positive (estrogen receptor or progesterone receptor positive), and for the patients with metastatic disease, patients had received a median of 3 prior regimens (range 2-10 prior regimens) before entering the trial. Among these 16 patients, 14 had activating HER2 mutations and 2 patients had HER2 mutations of unknown significance.

The primary endpoint of the Phase II trial was clinical benefit rate, or CBR, defined as complete response, or CR, partial response, or PR, or stable disease, or SD, greater than or equal to six months. The trial was designed to detect a CBR of 20%. In the 14 patients with activating HER2 mutations, 5 (36%) achieved clinical benefit, including 1 patient (7%) with a CR, 1 patient (7%) with a PR, and 3 patients (21%) with SD for greater than or equal to six months. The median duration of response in these 5 patients was 6 (range 6-14+) months. The median progression-free survival for all 14 patients with activating HER2 mutations in the trial was 5.0 months. In the 2 patients with HER2 mutations of unknown significance, there was no clinical benefit seen with neratinib.

Based on the preclinical data described above that has demonstrated that the combination of an anti-estrogen with a HER2 inhibitor results in enhanced anti-tumor activity in preclinical models of estrogen receptor positive/HER2-mutated breast tumors, the study has been amended to administer the combination of neratinib plus fulvestrant in eligible hormone receptor positive breast cancer patients who have an activating HER2 mutation in the tumor. Enrollment in this cohort is currently ongoing and results from this cohort receiving the combination of fulvestrant plus neratinib is expected to be presented at a future medical meeting.

The interim safety results of the study showed that the most frequently observed adverse event was diarrhea. For the 16 patients enrolled in the study, 4 patients (25%) reported grade 3 diarrhea. The median duration of grade 3 diarrhea for the patients in the study was 1.5 days.

Special Protocol Assessment for Planned Phase III Clinical Trial of Neratinib in Patients with HER2-Positive Metastatic Breast Cancer

In February 2013, we reached agreement with the 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 EMA has also provided follow-on scientific advice 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 and we anticipate that results of this trial may be available in the first half of 2017.

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Additional Neratinib Trials

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:

- 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 prophylactic treatment with loperamide in order to prevent and reduce the neratinib-related diarrhea;

- a Phase II clinical trial of neratinib in combination with the chemotherapy drug capecitabine in patients with HER2-positive metastatic breast cancer that has metastasized to the brain;

- a Phase II clinical trial of neratinib in combination with the endocrine therapy fulvestrant in the treatment of patients with HER2-negative breast cancer that have a HER2 mutation;

- a Phase II clinical trial of neratinib monotherapy in the treatment of solid tumors that have an activating HER2 mutation;

- Phase II clinical trials in the neoadjuvant treatment of HER2-positive breast cancer; and

- a Phase II clinical trial in the treatment of HER2-mutated non-small cell lung cancer.

We anticipate reporting additional data from the Phase II trial of neratinib as an extended adjuvant treatment in HER2-positive early stage breast cancer using loperamide prophylaxis in the fourth quarter of 2016, reporting additional Phase II data from the FB-7 neoadjuvant HER2-positive breast cancer trial in the subgroup of patients who are MammaPrint High in the fourth quarter of 2016, reporting data from the Phase II trial of neratinib plus fulvestrant in patients with HER2 non-amplified breast cancer that has a HER2 mutation during the fourth quarter of 2016, reporting data from the Phase III trial of neratinib in third-line HER2-positive metastatic breast cancer patients during the first half of 2017, and reporting data from the Phase II trial of neratinib in metastatic breast cancer patients with brain metastases during the first half of 2017.

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, a Phase II clinical trial for the neoadjuvant treatment of patients with triple negative breast cancer who have phosphorylated HER1 (EGFR) and HER2 and a Phase II randomized trial of neratinib plus endocrine in patients with hormone receptor positive HER2-positive metastatic 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. Additionally, we are planning to commence an expanded access program/clinical trial for neratinib for the extended adjuvant treatment of patients with early stage HER2-overexpressed/amplified breast cancer who have received prior adjuvant trastuzumab-based therapy. Patients in this trial will be given prophylactic loperamide in order to prevent and reduce the neratinib-related diarrhea.

Risks Affecting Us

Our business is subject to numerous risks, as more fully described in the section titled Risk Factors of this prospectus supplement, the accompanying prospectus and our Annual Report on Form 10-K for the fiscal year ended December 31, 2015, which is incorporated by reference into this prospectus supplement, including the following:

We currently have no product revenues and no products approved for marketing, and will need to raise additional capital to operate our business.

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

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We are heavily dependent on the success of neratinib (oral), our lead drug candidate, which is still under clinical development, and we cannot be certain that neratinib (oral) will receive regulatory approval or be successfully commercialized even if we receive regulatory approval.

We currently have no sales, marketing or distribution capabilities. If we are unable to establish such capabilities on our own or through third parties, we may not be successful in commercializing neratinib in the extended adjuvant indication or in any other indication if and when it is approved.

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

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

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

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 any such litigation would have a material adverse effect on our business.

Additionally, as disclosed under Legal Proceedings in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2016, a securities class action lawsuit was filed against us and certain of our executive officers in the United States District Court for the Central District of California. On November 30, 2015, we filed a motion to dismiss, and on September 30, 2016, the motion to dismiss was denied by the Court. We intend to vigorously defend this matter.

Corporate Information

Our principal executive offices are located at 10880 Wilshire Boulevard, Suite 2150, Los Angeles, California 90024. Our telephone number is (424) 248-6500. Our website is *www.pumabiotechnology.com*. Information contained on our website is not incorporated by reference into, and should not be considered a part of, this prospectus supplement.

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THE OFFERING

Common Stock Offered by Us	shares
Common Stock Outstanding After this Offering	shares (or shares if the underwriters exercise their option to purchase additional shares in full)
Option to Purchase Additional Shares	The underwriters have a 30-day option to purchase up to an additional $22.5 million of shares of our common stock at the public offering price less the underwriting discounts and commissions.
Use of Proceeds	We intend to use the net proceeds of this offering for the overall development of our drug candidates, including, but not limited to, research and development and clinical trial expenditures, pre-commercialization activities and general corporate and working capital purposes. See Use of Proceeds.
Risk Factors	You should read the Risk Factors section beginning on page S-9 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement, for a discussion of factors to consider before deciding to invest in shares of our common stock.
New York Stock Exchange Symbol	PBYI

Unless otherwise noted, the number of shares of our common stock outstanding prior to and after this offering is based on 32,493,092 shares outstanding as of June 30, 2016, and excludes:

- 5,765,520 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2016 at a weighted average exercise price of $99.77 per share;
- a maximum of 9,469 shares of common stock issuable pursuant to performance share awards outstanding as of June 30, 2016;
- 3,222,579 shares of common stock reserved for future issuance under our incentive award plan as of June 30, 2016, 645,019 of which are issuable upon the vesting of restricted stock units granted subsequent to June 30, 2016; and
- 2,116,250 shares of our common stock issuable upon the exercise of a warrant held by Alan H. Auerbach, our President and Chief Executive Officer, at $16.00 per share.

Unless otherwise indicated, the information in this prospectus supplement assumes no exercise by the underwriters of their option to purchase additional shares of common stock from us.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should carefully consider the risks discussed below, together with the other information contained in this prospectus supplement, the accompanying prospectus or incorporated by reference herein or therein, including the risks and uncertainties discussed under Risk Factors in our Annual Report on Form 10-K for the fiscal year ended December 31, 2015, which are incorporated by reference into this prospectus supplement. If any of the risks incorporated by reference or set forth below occurs, our business, results of operations and financial condition could suffer significantly. As a result, you could lose some or all of your investment in our common stock. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business.

Risks Related to this Offering

Our stock price may fluctuate significantly and you may have difficulty selling your shares based on current trading volumes of our stock. In addition, numerous other factors could result in substantial volatility in the trading price of our stock.

Our common stock has been listed on the New York Stock Exchange, or NYSE, since October 19, 2012. Prior to October 2012, shares of our common stock had been quoted for trading on the OTC Bulletin Board and OTCQB Market in limited volumes. We cannot predict the extent to which investor interest in our company will be sufficient to maintain an active trading market on the NYSE or any other exchange in the future. We have several stockholders, including affiliated stockholders, who hold substantial blocks of our stock. As of December 31, 2015, we had 32,466,842 shares of common stock outstanding, and stockholders holding at least 5% of our stock, individually or with affiliated entities, collectively owned or controlled approximately 77.2% of such shares. Sales of large numbers of shares by any of our large stockholders could adversely affect our trading price. If stockholders holding shares of our common stock sell, indicate an intention to sell, or if it is perceived that they will sell, substantial amounts of their common stock in the public market, the trading price of our common stock could decline. Moreover, if there is a less active trading market, holders of our common stock may have difficulty selling their shares.

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 historically experienced volatility. The high and low sales prices for our common stock were $252.92 and $56.11, respectively, in fiscal 2015 and $77.99 and $19.74, respectively, in fiscal 2016 through September 30, 2016. The trading price of our common stock may continue to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. These factors include:

- 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;

issuance of new or changed securities analysts reports or recommendations for our stock;

developments or disputes concerning our intellectual property or other proprietary rights;

commencement of, or involvement in, litigation;

market conditions in the biopharmaceutical industry;

timing and announcement of regulatory approvals;

any future sales of our common stock or other securities in connection with raising additional capital or otherwise;

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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. In several recent situations where the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit against us, the defense and disposition of the lawsuit could be costly and divert the time and attention of our management and harm our operating results.

Investors in this offering will suffer immediate and substantial dilution in the book value of their investment.

If you purchase common stock in this offering, you will pay more for your shares than our net tangible book value per share. Based upon the public offering price of $ per share, you will incur immediate and substantial dilution of $ per share, representing the difference between our public offering price and our as adjusted net tangible book value per share as of June 30, 2016. You may experience additional dilution upon exercise of any warrant, upon exercise of options to purchase shares of common stock under our incentive award plan, or if we otherwise issue additional shares of our common stock. For a further description of the dilution that you will experience immediately after this offering, see Dilution.

A substantial number of shares of common stock may be sold in the market following this offering, which may depress the market price for our common stock.

Sales of a substantial number of shares of our common stock in the public market following this offering could cause the market price of our common stock to decline. A substantial majority of the outstanding shares of our common stock are, and the shares of common stock sold in this offering upon issuance will be, freely tradable without restriction or further registration under the Securities Act of 1933, as amended.

Our management will have broad discretion over the use of the proceeds we receive in this offering and might not apply the proceeds in ways that increase the value of your investment.

Our management will have broad discretion over the use of proceeds from this offering, and we could spend the proceeds from this offering in ways our stockholders may not agree with or that do not yield a favorable return, if at all. We intend to use the net proceeds of this offering for the overall development of our drug candidates, including, but not limited to, research and development and clinical trial expenditures, pre-commercialization activities and general corporate and working capital purposes. However, our use of these proceeds may differ substantially from our current plans. If we do not invest or apply the proceeds of this offering in ways that improve our operating results, we may fail to achieve expected financial results, which could cause our stock price to decline.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, and the SEC filings that are incorporated by reference into this prospectus supplement and the accompanying prospectus contain or incorporate by reference forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, which we refer to as the Securities Act, and Section 21E of the Securities Exchange Act of 1934, which we refer to as the Exchange Act. 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. Any statements abo expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. Accordingly, these statements involve estimates, assumptions, risks and uncertainties, including the risks discussed in the section titled Risk Factors, that could cause actual results to differ materially from those expressed in them. You should not place undue reliance on these forward-looking statements. Although forward-looking statements reflect management s good faith beliefs, reliance should not be placed on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, which may cause the actual results, performance or achievements to differ materially from anticipated future results, performance or achievements expressed or implied by such forward-looking statements. 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, and when we expect to announce results of such trials;
- 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 intention to vigorously defend against a purported securities class action lawsuit, derivative lawsuits and a defamation lawsuit;

our ability to attract and retain key personnel;

our ability to obtain adequate financing; and

the intended use of proceeds from this offering.

Discussions containing these forward-looking statements may be found throughout this prospectus supplement, the accompanying prospectus, and the SEC filings that are incorporated by reference into this prospectus supplement and the accompanying prospectus. Forward-looking statements speak only as of the date the statements are made. We undertake no obligation to update the forward-looking statements or to reflect events or circumstances. The risks discussed in this prospectus supplement, the accompanying prospectus, and the SEC filings that are incorporated by reference into this prospectus supplement and the accompanying prospectus should be considered in evaluating our prospects and future financial performance.

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USE OF PROCEEDS

We estimate that the net proceeds from this offering will be approximately $ million (or $ million if the underwriters exercise their option to purchase additional shares in full), after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds to us from this offering for the overall development of our drug candidates, including, but not limited to, research and development and clinical trial expenditures, pre-commercialization activities and general corporate and working capital purposes. Pending the application of the net proceeds as described above, we intend to invest the net proceeds of the offering in short-term, investment-grade, interest-bearing securities.

We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds to us from this offering and investors will be relying on the judgment of our management regarding the application of the proceeds from this offering. We reserve the right to change the use of these proceeds as a result of certain contingencies such as competitive developments, the results of our commercialization efforts, acquisition and investment opportunities and other factors.

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DIVIDEND POLICY

We never have 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 after the offering and for 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.

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DILUTION

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the public offering price per share of our common stock and the as adjusted net tangible book value per share of our common stock upon closing of this offering. Net tangible book value per share of our common stock is determined at any date by subtracting our total liabilities from the amount of our total tangible assets (total assets less intangible assets) and dividing the difference by the number of shares of our common stock deemed to be outstanding at that date.

Our net tangible book value as of June 30, 2016 was approximately $127.1 million, or $3.91 per share, based on 32,493,092 shares of common stock outstanding as of June 30, 2016. After giving effect to our sale of shares of common stock in this offering at the public offering price of $ per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2016 would have been approximately $ million, or $ per share. This amount represents an immediate increase in net tangible book value of approximately $ per share of our common stock to existing stockholders and an immediate dilution in net tangible book value of approximately $ per share of our common stock to new investors purchasing shares of common stock in this offering.

The following tables illustrate this dilution on a per share basis:

Public offering price per share	$
Net tangible book value per share as of June 30, 2016 before giving effect to this offering	