PUMA BIOTECHNOLOGY, INC.
Form 8-K
December 11, 2015

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d)

of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): December 10, 2015

PUMA BIOTECHNOLOGY, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**001-35703**	**77-0683487**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

10880 Wilshire Boulevard, Suite 2150

Los Angeles, California 90024

(Address of principal executive offices) (Zip Code)

(424) 248-6500

(Registrant s telephone number, including area code)

N/A

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

¨ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

¨ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

¨ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

¨ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 8.01 Other Events.

Results of Phase II Trial of PB272 in Neoadjuvant Treatment of HER2-Positive Locally Advanced Breast Cancer

On December 10, 2015, Puma Biotechnology, Inc. (the Company or Puma) announced that results from a randomized Phase II clinical trial of Puma s investigational drug PB272 (neratinib) in the neoadjuvant treatment of locally advanced HER2-positive breast cancer were presented at the 2015 CTRC-AACR San Antonio Breast Cancer Symposium (SABCS). The presentation entitled NSABP FB-7: A Phase II Randomized Trial Evaluating Neoadjuvant Therapy Regimens with Weekly Paclitaxel plus Trastuzumab or Neratinib or Trastuzumab and Neratinib Followed by Doxorubicin and Cyclophosphamide with Postoperative Trastuzumab in Women with Locally Advanced HER2-Positive Breast Cancer was presented at the poster discussion session. This trial was sponsored by the NSABP Foundation, Inc.

The FB-7 trial is a randomized Phase II clinical trial for women with HER2-positive locally advanced stage IIB-IIIC invasive breast cancer. Patients were randomly assigned to trastuzumab (T) or neratinib (N) or the combination (T+N) with weekly paclitaxel (P) followed by standard doxorubicin and cyclophosphamide chemotherapy (AC) administered prior to surgery. 126 U.S., Canadian, and European patients were randomly assigned to Arm 1 (T+P followed by AC), Arm 2 (N+P followed by AC) or Arm 3 (T+N+P followed by AC). The primary endpoint of the trial is pathological complete response rate (pCR) in the breast and lymph nodes.

Tumor tissue was collected on patients at the time of diagnosis. This tissue will be analyzed for several biomarkers including AKT, cMET, EGFR, ESR-alpha, HER2, HER3, HER4, p95 HER2 and PI3K and intrinsic subtypes. A key secondary endpoint of this trial is the molecular and genetic correlates of response for each of these biomarkers. The analysis of these biomarkers is ongoing and will be presented at a medical meeting in 2016.

For the intent-to-treat patient population (hormone receptor positive (HR+) and hormone receptor negative (HR-)), the pCR rate for Arm 1 was 38.1%, for Arm 2 was 33.3% and for Arm 3 was 50.0%. For the HR+ patients, the pCR rate for Arm 1 was 29.6%, for Arm 2 was 27.6% and for Arm 3 was 30.4%. For the HR- patients, the pCR rate for Arm 1 was 57.1%, for Arm 2 was 46.2% and for Arm 3 was 73.7%.

Pathological Complete Response Rate (pCR, breast and lymph nodes)

Arm	**Arm 1 (T)**	**Arm 2 (N)**	**Arm 3 (N+T)**
Intent-to-Treat Population	38.1%	33.3%	50.0%
HR+ Patients	29.6%	27.6%	30.4%
HR- Patients	57.1%	46.2%	73.7%

The most frequently observed severe adverse event in the two neratinib treated arms of the trial (Arm 2 and Arm 3) was diarrhea. In the first 19 patients treated in Arm 2 of the trial, high dose loperamide (16 mg per day initially) as primary prophylaxis was not given to prevent the neratinib-related diarrhea. In this subset of patients the grade 3 diarrhea rate was 42% (8/19). In the next 10 patients treated in Arm 2 and the first 20 patients treated in Arm 3, high dose primary prophylaxis (16 mg per day initially) with loperamide was given during the initial two weeks of the first cycle of treatment. Using two weeks of intensive loperamide prophylactically, the grade 3 diarrhea rate in Arm 2 was 30% (3/10) and the grade 3 diarrhea rate in Arm 3 was 35% (7/20). In the next 13 patients in Arm 2 and 22 patients in Arm 3, high dose prophylaxis (16 mg per day initially) was given for the entire first cycle of treatment (4 weeks). The grade 3 diarrhea rate was 15% (2/13) in Arm 2 and 23% (5/22) in Arm 3.

Diarrhea	No Prophylaxis	2-week Prophylaxis		4-week Prophylaxis	
Arm	Arm 2 (N) (n=19)	Arm 2 (N) (n=10)	Arm 3 (N+T) (n=20)	Arm 2 (N) (n=13)	Arm 3 (N+T) (n=22)
Grade 3 Diarrhea (All Cycles)	8 (42%)	3 (30%)	7 (35%)	2 (15%)	5 (23%)

Interim Results of Phase II Trial of PB272 for ERBB2 Mutant, HER2 Non-Amplified, Metastatic Breast Cancer

On December 10, 2015, the Company announced that interim results from an ongoing Phase II clinical trial of PB272 (neratinib) were presented at the 2015 CTRC-AACR San Antonio Breast Cancer Symposium (SABCS). The presentation entitled Neratinib for ERBB2 mutant, HER2 non-amplified, metastatic breast cancer: preliminary analysis from SUMMIT a multicenter, open-label, multi-histology phase II basket trial was presented as a poster discussion by Dr. David Hyman, Acting Director, Developmental Therapeutics at Memorial Sloan Kettering Cancer Center.

In May 2014 Puma announced that it expanded the first cohort from the Phase II clinical trial of PB272 (neratinib) in patients with solid tumors who have an activating *ERBB2* (HER2) mutation (SUMMIT basket trial). These interim results are the first presentation of data from this expanded cohort of patients with metastatic breast cancer and whose tumors have a HER2 mutation but are neither HER2 amplified or overexpressed (HER2 negative).

In the cohort, patients with HER2 mutant metastatic breast cancer were enrolled and 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 20 patients in the cohort presented, 20 patients (100%) had HER2-negative disease, 17 patients (85%) were hormone receptor positive (estrogen receptor or progesterone receptor positive), and patients had received a median of 4 prior regimens in the metastatic setting (range 0-11 prior regimens) before entering the trial.

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 confirmed objective response (complete response or partial response), clinical benefit rate and progression free survival (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 progression free survival 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.

The interim safety results of the study showed that the most frequently observed adverse event was diarrhea. For the 130 patients enrolled across all solid tumor cohorts in the SUMMIT study, 25 patients (19%) 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.

The Company anticipates advancing the combination of PB272 and fulvestrant into a pivotal trial in 2016.

3-Year Disease Free Survival Data from Phase III Trial of PB272 in Extended Adjuvant Breast Cancer (ExteNET Trial)

On December 11, 2015, the Company announced the presentation of updated results from the Phase III clinical trial of PB272 (neratinib) for the extended adjuvant treatment of breast cancer (ExteNET trial). The ExteNET trial is a double-blind, placebo-controlled, Phase III trial of neratinib versus placebo after adjuvant treatment with trastuzumab (Herceptin) in women with early stage HER2-positive breast cancer. The data was presented in an oral presentation at the 2015 CTRC-AACR San Antonio Breast Cancer Symposium (SABCS). Previous safety and efficacy data from this trial were reported in June at the American Society of Clinical Oncology (ASCO) 2015 Annual Meeting in Chicago, Illinois.

The ExteNET 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 (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%. These results were previously reported at the 2015 American Society of Clinical Oncology meeting in June.

The presentation at SABCS involved an exploratory sensitivity analysis of the 3-year disease free survival data to examine the durability of treatment effect beyond the 2-year data included in the primary analysis. This analysis was not a pre-planned analysis in the statistical analysis plan for the trial. For the primary endpoint of the trial, invasive disease free survival (DFS), the 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, two sided p = 0.023). The 3-year DFS rate for the neratinib arm was 92.0% and the 3-year DFS rate for the placebo arm was 89.9%.

The previously published analysis of previous adjuvant trials of Herceptin have demonstrated that patients are at the highest risk of disease progression closest to the completion of their treatment with adjuvant trastuzumab (Perez et al, Journal of Clinical Oncology, 2014). For the 2,297 patients in the ExteNET trial who were treated in ExteNET less than one year from the completion of their adjuvant treatment with trastuzumab, the results of the trial demonstrated that treatment with neratinib resulted in a 28% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.72, two sided p = 0.02). For this group of patients, the 3-year DFS rate for the neratinib arm was 91.5% and the 3-year DFS rate for the placebo arm was 88.9%.

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 2,041 (72%) of the patients in the ExteNET trial, and further central testing on available samples is currently ongoing. For the 1,709 patients whose tumors were HER2 positive by central confirmation, the 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, two

sided p = 0.037). The 3-year DFS rate for the centrally confirmed patients in the neratinib arm was 91.8% and the 3-year DFS rate for the centrally confirmed patients in the placebo arm was 89.6%. For the 1,392 patients in the ExteNET trial with centrally confirmed HER2 positive disease who were treated in ExteNET less than one year from the completion of their adjuvant treatment with trastuzumab, the results of the trial

demonstrated that treatment with neratinib resulted in a 37% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.63, two sided p = 0.009). For this group of patients, the 3-year DFS rate for the neratinib arm was 91.7% and the 3-year DFS rate for the placebo arm was 88.2%.

For the pre-defined subgroup of 1,631 patients with hormone receptor positive disease, the results of the trial demonstrated that treatment with neratinib resulted in a 43% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.57, two sided p = 0.003). The 3-year DFS rate for the neratinib arm was 93.6% and the 3-year DFS rate for the placebo arm was 89.3%. For the 1,334 hormone receptor positive patients in the ExteNET trial who were treated in ExteNET less than one year from the completion of their adjuvant treatment with trastuzumab, the results of the trial demonstrated that treatment with neratinib resulted in a 43% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.57, two sided p = 0.004). For this group of patients, the 3-year DFS rate for the neratinib arm was 93.3% and the 3-year DFS rate for the placebo arm was 88.6%. For the 903 patients in the trial whose tumors were hormone receptor positive and HER2 positive by central confirmation, the results of the trial demonstrated that treatment with neratinib resulted in a 57% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.43, two sided p < 0.001). The 3-year DFS rate for the hormone receptor positive patients who also had HER2 centrally confirmed disease in the neratinib arm was 94.4% and the 3-year DFS rate for centrally confirmed patients in the placebo arm was 88.0%.

Forward-Looking Statements:

This Current Report on Form 8-K contains forward-looking statements, including, but not limited to, statements regarding the development of our drug candidates and the anticipated timing of various clinical trials and the announcement of data relative to these trials. All forward-looking statements included in this Current Report on Form 8-K involve risks and uncertainties that could cause the Company s actual results to differ materially from the anticipated results and expectations expressed in these forward-looking statements. These statements are based on current expectations, forecasts and assumptions, and actual outcomes and results could differ materially from these statements due to a number of factors, which include, but are not limited to, the fact that the Company has no product revenue and no products approved for marketing; the Company s dependence on PB272, which is still under development and may never receive regulatory approval; the challenges associated with conducting and enrolling clinical trials; the risk that the results of clinical trials may not support the Company s drug candidate claims; even if approved, the risk that physicians and patients may not accept or use the Company s products; the Company s reliance on third parties to conduct its clinical trials and to formulate and manufacture its drug candidates; the Company s dependence on licensed intellectual property; and the other risk factors disclosed in the periodic reports filed by the Company with the Securities and Exchange Commission from time to time, including the Company s Annual Report on Form 10-K for the year ended December 31, 2014 and any subsequently filed Quarterly Reports on Form 10-Q and Current Reports on Form 8-K. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. The Company assumes no obligation to update these forward-looking statements, except as required by law.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

PUMA BIOTECHNOLOGY, INC.

Date: December 11, 2015

By: /s/ Alan H. Auerbach
Alan H. Auerbach
President and Chief Executive Officer