News Release

Puma Biotechnology Presents Interim Results of Phase II CONTROL Trial of PB272 in Extended Adjuvant Treatment of HER2-Positive Early Stage Breast Cancer at the 2016 San Antonio Breast Cancer Symposium

LOS ANGELES, Calif., Dec. 8, 2016 – Puma Biotechnology, Inc. (NYSE: PBYI), a biopharmaceutical company, announced that interim results from a Phase II clinical trial of Puma's investigational drug PB272 (neratinib) were presented at the 2016 CTRC-AACR San Antonio Breast Cancer Symposium (SABCS) that is currently taking place in San Antonio, Texas. The presentation entitled "Incidence and severity of diarrhea with neratinib plus intensive loperamide prophylaxis in patients with HER2-positive early-stage breast cancer (EBC): Interim analysis from the multicenter, open-label, phase II CONTROL trial" was presented as a poster presentation.

The main adverse event that has been seen to date in clinical trials of neratinib is diarrhea and more specifically grade 3 diarrhea. In the Phase III ExteNET trial of neratinib as extended adjuvant treatment of HER2-positive early stage breast cancer that has previously been treated with adjuvant Herceptin, 95.4% of the patients experienced all grade diarrhea and 39.8% of the patients experienced grade 3 or higher diarrhea (there was one event of grade 4 diarrhea). The CONTROL trial is an international, open-label, phase II study investigating the use of loperamide prophylaxis with or without other agents in the prevention and reduction of neratinib-associated diarrhea and more specifically grade 3 diarrhea.

In the trial, patients with HER2-positive early-stage breast cancer who had completed trastuzumab-based adjuvant therapy received neratinib daily for a period of one year. High dose loperamide prophylaxis was given for the first 2 cycles (56 days) of treatment. Initially, the loperamide dosing used was 16 mg on day 1, then 12 mg on days 2 and 3 and then 6-8 mg on days 4-56 (original dosing). The protocol was later amended to simplify the regimen such that patients took 12 mg on days 1-14 and 8 mg on days 15-56 (modified dosing). The CONTROL trial has recently been expanded to include prophylaxis with the combination of loperamide and budesonide, a locally acting corticosteroid that the Company believes targets the inflammation identified in a preclinical model of neratinib-induced diarrhea.

The interim analysis of the trial presented in the poster included a total of 135 patients who received neratinib plus loperamide prophylaxis (28 patients taking the original dosing and 107 patients taking the modified dosing) and 40 patients who received neratinib plus loperamide prophylaxis for 2 cycles and budesonide for 1 cycle.

The results of the trial showed that the incidence of grade 3 diarrhea for the total 135 patients who received the loperamide prophylaxis was 28.1%. For the 28 patients who received loperamide using the original dosing regimen the grade 3 diarrhea rate was 25.0% and for the 107 patients who received the modified loperamide dosing regimen the grade 3 diarrhea rate was

29.0%. For the patients in the original dosing group, 71% of the patients who experienced grade 3 diarrhea were known to be non-compliant with the loperamide regimen and for the patients in the modified loperamide dosing regimen, 35% of the patients were known to be non-compliant with their loperamide dosing regimen. For the 135 patients who received the loperamide prophylaxis, the median number of grade 3 diarrhea episodes per patient was 1 and the median cumulative duration of grade 3 diarrhea was 3 days. For the 135 patients who received loperamide prophylaxis, 18.5% discontinued neratinib due to diarrhea.

For the 40 patients who received the combination of loperamide plus budesonide, the results of the trial showed that the incidence of grade 3 diarrhea was 15.0%. None of the patients who experienced grade 3 diarrhea were non-compliant with the loperamide plus budesonide regimen. The median number of grade 3 diarrhea episodes per patient was 1 and the median cumulative duration of grade 3 diarrhea was 2.5 days. For the 40 patients who received loperamide plus budesonide prophylaxis, 5.0% discontinued neratinib due to diarrhea. Further information is provided in Table 1 below:

Table 1: Characteristics of Treatment-Emergent Diarrhea

Study	**CONTROL**				**ExteNET**
	Loperamide cohort			**Budesonide cohort**	**Neratinib arm**
Prophylaxis	**Original schedule (n=28)**	**Modified schedule (n=107)**	**Loperamide total (N=135)**	**Loperamide + budesonide (N=40)**	**Loperamide prn (N=1408)**
Diarrhea, %					
Any grade	82.1	73.8	75.6	65.0	95.4
Grade 1	35.7	21.5	24.4	32.5	22.9
Grade 2	21.4	23.4	23.0	17.5	32.5
Grade 3[a]	25.0	29.0	28.1	15.0	39.8
Grade 4	0	0	0	0	0.1
Median cumulative duration, days					
Grade ≥2	5.0	4.0	4.0	3.0	10.0
Grade ≥3[b]	2.0	3.0	3.0	2.5	5.0
Median diarrhea episodes/patient					
Any grade	2	2	2	2	8
Grade ≥2	2	1	2	1	3
Grade ≥3[b]	1	1	1	1	2
Action taken, %					
Dose hold	7.1	12.1	11.1	7.5	33.9
Dose reduction	10.7	7.5	8.1	5.0	26.4
Discontinuation	28.6	15.9	18.5	5.0	16.8
Hospitalization	0	1.9	1.5	0	1.4
Duration of neratinib treatment, months					
Median	9.7	7.4	7.5	1.8	11.6
Range	0.1–13.1	0.1–12.8	0.1–13.1	0.1–6.3	0.03–13.3

[a] Non-compliance with loperamide prophylaxis in patients with grade 3 diarrhea was 71% with the original loperamide schedule, 35% with the modified loperamide schedule, and 0% with loperamide prophylaxis plus budesonide.

[b] No grade 4 events in the CONTROL study; one grade 4 event in the ExteNET study.

In the ExteNET trial, higher grade (grade 2 and grade 3) diarrhea occurred early and persisted throughout the duration of the 12-month treatment period. In the CONTROL trial, in both the loperamide prophylaxis and loperamide plus budesonide prophylaxis arms, the results showed that higher grade diarrhea (grade 2 and 3) occurred early but did not typically recur. This is shown in more detail in Figure 1: Treatment Emergent Diarrhea, which is attached to this news release.

The grade 3 diarrhea rates seen in the loperamide cohort have increased over what was previously reported in December 2015 (n=50, grade 3 diarrhea rate 16%). During the course of the CONTROL trial there has been an increase in the proportion of patients previously treated with pertuzumab (mainly in the neoadjuvant setting). More specifically in the data reported in December 2015, 18% (9 of 50 patients) had previously received pertuzumab. In the current data set 40% (54 of 135 patients) of the patients in the combined loperamide prophylaxis arms received prior pertuzumab and 55% (22 of 40 patients) received prior pertuzumab in the budesonide arm.

For the 54 patients in the loperamide prophylaxis cohort who received prior pertuzumab, the grade 3 diarrhea rate was 35.2% (Table 2). For the 81 patients who did not receive prior pertuzumab, the grade 3 diarrhea rate was 23.5%. For the 22 patients in the budesonide cohort who received prior pertuzumab, the grade 3 diarrhea rate was 13.6%. For the 18 patients in the budesonide cohort who did not receive prior pertuzumab, the grade 3 diarrhea rate was 16.7%. This analysis suggests that prior pertuzumab exposure may have led to a higher rate of grade 3 diarrhea in CONTROL that was not effectively managed by loperamide prophylaxis alone but was more effectively managed by loperamide plus budesonide.

Table 2: Incidence of Grade 3 Diarrhea in CONTROL by Prior Pertuzumab Treatment

	Loperamide Cohort		**Budesonide Cohort**	
	Yes (n = 54)	No (n = 81)	Yes (n = 22)	No (n = 18)
Grade 3 Diarrhea	35.2%	23.5%	13.6%	16.7%

Dr. Carlos H. Barcenas, Assistant Professor, Department of Breast Oncology and Associate Medical Director, Breast Cancer Survivorship for the University of Texas MD Anderson Cancer Center, said, "We are pleased to see the reduction in incidence, severity and duration of neratinib-associated diarrhea when using the loperamide prophylaxis and the loperamide plus budesonide prophylaxis. When using either the loperamide prophylaxis or the loperamide plus budesonide prophylaxis there appears to be a reduction in the incidence and severity of grade 3 diarrhea with neratinib. Importantly, the severe grade 2 and grade 3 diarrhea, when using the prophylaxis, appears to be acute, self-limiting and manageable. We look forward to completing the loperamide plus budesonide cohort and to the testing of additional investigational agents as well."

Alan H. Auerbach, Chief Executive Officer and President of Puma Biotechnology, said, "We are pleased to see the reductions in the incidence of severe neratinib-related diarrhea in the CONTROL trial when using the loperamide and/or loperamide plus budesonide combination.

We are further pleased to see the severe diarrhea become more acute, whereby it does not typically recur after the first month."

About Puma Biotechnology

Puma Biotechnology, Inc. is a biopharmaceutical company with a focus on the development and commercialization of innovative products to enhance cancer care. The Company in-licenses 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 that blocks signal transduction through the epidermal growth factor receptors, HER1, HER2 and HER4. Currently, the Company is primarily focused on the development of the oral version of neratinib, and its most advanced drug candidates are directed at the treatment of HER2-positive breast cancer. The Company believes that neratinib has clinical application in the treatment of several other cancers as well, including non-small cell lung cancer and other tumor types that over-express or have a mutation in HER2. Further information about Puma Biotechnology can be found at www.pumabiotechnology.com.

Forward-Looking Statements:

This press release contains forward-looking statements, including statements regarding the development of the Company's drug candidates. All forward-looking statements included in this press release 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 and current 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, 2015. 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.

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