News Release

Puma Biotechnology Presents Interim Results of Phase II CONTROL Trial of Neratinib in Extended Adjuvant Treatment of HER2-Positive Early Stage Breast Cancer at the ASCO 2019 Annual Meeting

LOS ANGELES, Calif., June 2, 2019 – Puma Biotechnology, Inc. (Nasdaq: PBYI), a biopharmaceutical company, will present updated interim results from a Phase II clinical trial of Puma's drug neratinib at the American Society of Clinical Oncology (ASCO) 2019 Annual Meeting in Chicago. The presentation entitled, "Effect of prophylaxis on neratinib-associated diarrhea and tolerability in patients with HER2+ early-stage breast cancer: Phase II CONTROL trial," will be presented at a poster session on June 2 at 8:00 a.m. CT. A full copy of the poster is available on the Puma Biotechnology website.

Neratinib was approved by the U.S. Food and Drug Administration (FDA) in July 2017 for the extended adjuvant treatment of adult patients with early stage HER2-positive breast cancer following adjuvant trastuzumab-based therapy, and is marketed in the United States as NERLYNX® (neratinib) tablets.

The main adverse event 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, prophylactic use of anti-diarrheal medications was not mandatory. In the trial, 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 median cumulative duration of grade 3 diarrhea in the ExteNET trial was 5 days and 16.8% of patients who received neratinib in the ExteNET trial discontinued the drug due to diarrhea.

The CONTROL trial is an international, open-label, Phase II study investigating the use of antidiarrheal prophylaxis or dose escalation in the reduction of neratinib-associated diarrhea that has a primary endpoint of the incidence of grade 3 diarrhea.

In the CONTROL trial, patients with HER2-positive early stage breast cancer who had completed trastuzumab-based adjuvant therapy received neratinib daily for a period of one year. The trial initially tested high dose loperamide prophylaxis given for the first 2 cycles (56 days) of treatment (12 mg on days 1-14, 8 mg on days 15-56 and as needed thereafter). The CONTROL trial was then expanded to include four additional cohorts. One cohort received the combination of loperamide and budesonide, the second cohort received the combination of loperamide plus colestipol, the third cohort received colestipol plus loperamide as needed and the fourth cohort did not use any antidiarrheal drugs as mandatory prophylaxis but instead used a dose escalation during the first month of neratinib treatment. Budesonide is a locally acting corticosteroid that Puma believes targets the inflammation identified in a preclinical model of neratinib-induced diarrhea and colestipol is a bile acid sequestrant that Puma believes targets potential bile acid malabsorption that

could result from such inflammation. The dose escalation involved treating with neratinib at 120 mg per day for the first week, 160 mg per week for the second week and 240 mg per week starting at week 3 and until the end of treatment.

The interim analysis of the CONTROL trial presented in the poster included a total of 137 patients who received neratinib plus loperamide prophylaxis, 64 patients who received neratinib plus loperamide prophylaxis for 2 cycles and budesonide for 1 cycle, 136 patients who received neratinib plus loperamide prophylaxis for 1 cycle and colestipol for 1 cycle, 104 patients who received colestipol for 1 cycle and loperamide as needed and 60 patients who received the dose escalation regimen of neratinib.

The results of the trial showed that the incidence of grade 3 diarrhea for the 137 patients who received the loperamide prophylaxis was 30.7% and that for the 137 patients in this cohort, 20.4% discontinued neratinib due to diarrhea. The median cumulative duration of grade 3 diarrhea was 3 days.

For the 64 patients who received the combination of loperamide plus budesonide, the results of the trial showed that the incidence of grade 3 diarrhea was 28.1% and that for the 64 patients in this cohort, 10.9% discontinued neratinib due to diarrhea. The median cumulative duration of grade 3 diarrhea was 2.5 days.

For the 136 patients who received the combination of loperamide plus colestipol, the results of the trial showed that the incidence of grade 3 diarrhea was 20.6% and that for the 136 patients in this cohort, 4.4% discontinued neratinib due to diarrhea. The median cumulative duration of grade 3 diarrhea was 3.5 days.

For the 104 patients who received colestipol and loperamide as needed, the results of the trial showed that the incidence of grade 3 diarrhea was 31.7% and that for the 104 patients in this cohort, 6.7% discontinued neratinib due to diarrhea. The median cumulative duration of grade 3 diarrhea was 3 days.

For the 60 patients who received no antidiarrheal drugs as mandatory prophylaxis and dose escalation of neratinib in the first month, the results of the trial showed that the incidence of grade 3 diarrhea was 11.7% and that for the 60 patients in this cohort, 3.3% discontinued neratinib due to diarrhea. The median cumulative duration of grade 3 diarrhea was 2 days.

Further information is provided in Table 1 below:

Table 1: Characteristics of Treatment-Emergent Diarrhea

	Loperamide (n=137)	Loperamide + budesonide (n=64)	Loperamide + colestipol (n=136)	Loperamide prn + colestipol (n=104)	Neratinib dose escalation + loperamide prn (n=60)
Diarrhea, %					
Any grade	79.6	85.9	83.1	95.2	95.0
Grade 1	24.1	25.0	27.9	30.8	43.3
Grade 2	24.8	32.8	34.6	32.7	40.0
Grade 3	30.7	28.1	20.6	31.7	11.7
Diarrhea leading to discontinuation, %	20.4	10.9	4.4	6.7	3.3
Hospitalization (due to diarrhea), %	1.5	0	0	0	0
Discontinuation of study (any cause), %	44.6	20.3	28.7	26.0	13.6

Note: Each patient was counted only once in the highest grade category.
No Grade 4 events reported in the CONTROL study.

Carlos H. Barcenas, MD, MS, Assistant Professor in the Department of Breast Medical Oncology of The University of Texas MD Anderson Cancer Center, said, “We are pleased to see the maturation of the data supporting observations of a reduction in incidence, severity and duration of neratinib-associated diarrhea with loperamide prophylaxis, loperamide plus budesonide prophylaxis or the loperamide plus colestipol prophylaxis. We are pleased to see the initial results of the dose escalation regimen. Along with the continued reduction in the incidence and severity of grade 3 diarrhea with neratinib, diarrhea appears to be early onset, acute, self-limiting and manageable. Not only does the addition of budesonide or colestipol to loperamide prophylaxis appear to greatly improve the tolerability of neratinib, the dose escalation regimen appears as another promising option since there is no mandatory prophylaxis. We look forward to the completion of the dose escalation cohort.”

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 antidiarrheal regimens and the dose escalation. The reduction in the discontinuations due to diarrhea are encouraging and appear to represent a marked improvement in tolerability over what was seen in the ExteNET trial.”

About HER2-Positive Breast Cancer

Approximately 20% to 25% of breast cancer tumors over-express the HER2 protein. HER2-positive breast cancer is often more aggressive than other types of breast cancer, increasing the risk of disease progression and death. Although research has shown that trastuzumab can reduce the risk of early stage HER2-positive breast cancer returning after surgery, up to 25% of patients treated with trastuzumab experience recurrence.

IMPORTANT SAFETY INFORMATION

NERLYNX® (neratinib) tablets, for oral use

INDICATIONS AND USAGE: NERLYNX is a kinase inhibitor indicated for the extended adjuvant treatment of adult patients with early-stage HER2 overexpressed/amplified breast cancer, to follow adjuvant trastuzumab-based therapy.

CONTRAINDICATIONS: None

WARNINGS AND PRECAUTIONS:

- **Diarrhea:** Aggressively manage diarrhea occurring despite recommended prophylaxis with additional antidiarrheals, fluids, and electrolytes as clinically indicated. Withhold NERLYNX in patients experiencing severe and/or persistent diarrhea. Permanently discontinue NERLYNX in patients experiencing Grade 4 diarrhea or Grade ≥ 2 diarrhea that occurs after maximal dose reduction.

- **Hepatotoxicity:** Monitor liver function tests monthly for the first 3 months of treatment, then every 3 months while on treatment and as clinically indicated. Withhold NERLYNX in patients experiencing Grade 3 liver abnormalities and permanently discontinue NERLYNX in patients experiencing Grade 4 liver abnormalities.

- **Embryo-Fetal Toxicity:** NERLYNX can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception.

ADVERSE REACTIONS: The most common adverse reactions (≥ 5%) were diarrhea, nausea, abdominal pain, fatigue, vomiting, rash, stomatitis, decreased appetite, muscle spasms, dyspepsia, AST or ALT increase, nail disorder, dry skin, abdominal distention, weight decreased and urinary tract infection.

To report SUSPECTED ADVERSE REACTIONS, contact Puma Biotechnology, Inc. at 1-844-NERLYNX (1-844-637-5969) and www.NERLYNX.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS:

- Gastric acid reducing agents: Avoid concomitant use with proton pump inhibitors. When patients require gastric acid reducing agents, use an H_2-receptor antagonist or antacid. Separate NERLYNX by at least 3 hours with antacids. Separate NERLYNX by at least 2 hours before or 10 hours after H_2-receptor antagonists.
- Strong or moderate CYP3A4 inhibitors: Avoid concomitant use.
- Strong or moderate CYP3A4 inducers: Avoid concomitant use.
- P-glycoprotein (P-gp) substrates: Monitor for adverse reactions of narrow therapeutic agents that are P-gp substrates when used concomitantly with NERLYNX.

USE IN SPECIFIC POPULATIONS:

- **Lactation:** Advise women not to breastfeed.

Please see Full Prescribing Information for additional safety information.

The recommended dose of NERLYNX is 240 mg (six 40 mg tablets) given orally once daily with food, continuously for one year. Antidiarrheal prophylaxis should be initiated with the first dose of NERLYNX and continued during the first 2 months (56 days) of treatment and as needed thereafter.

To help ensure patients have access to NERLYNX, Puma has implemented the Puma Patient Lynx support program to assist patients and healthcare providers with reimbursement support and referrals to resources that can help with financial assistance. More information on the Puma Patient Lynx program can be found at www.NERLYNX.com or 1-855-816-5421.

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. Puma in-licenses the global development and commercialization rights to three drug candidates — PB272 (neratinib, oral), PB272 (neratinib, intravenous) and PB357. Neratinib, oral was approved by the U.S. Food and Drug Administration in July 2017 for the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer, following adjuvant trastuzumab-based therapy, and is marketed in the United States as NERLYNX® (neratinib) tablets. NERLYNX was granted marketing authorization by the European Commission in September 2018 for the extended adjuvant treatment of adult patients with early stage hormone receptor-positive HER2-overexpressed/amplified breast cancer and who are less than one year from completion of prior adjuvant trastuzumab-based therapy. NERLYNX is a registered trademark of Puma Biotechnology, Inc.

Further information about Puma Biotechnology can be found at www.pumabiotechnology.com.

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