News Release

Puma Biotechnology Submits a Supplemental New Drug Application to U.S. FDA for Neratinib to Treat HER2-Positive Metastatic Breast Cancer

LOS ANGELES, Calif., July 1, 2019 – Puma Biotechnology, Inc. (NYSE: PBYI), a biopharmaceutical company, has submitted a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) for neratinib in combination with capecitabine for the treatment of patients with HER2-positive metastatic breast cancer who have failed two or more prior lines of HER2-directed treatments (third-line disease).

Neratinib was originally 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® tablets. In September 2018 NERLYNX was granted marketing authorization by the European Commission for the extended adjuvant treatment of adult patients with early stage hormone receptor-positive HER2-overexpressed/amplified breast cancer and are less than one year from completion of prior adjuvant trastuzumab-based therapy.

The sNDA is supported by the results of the Phase III NALA trial, a randomized controlled trial of neratinib plus capecitabine versus Tykerb® (lapatinib) plus capecitabine in patients with third-line HER2-positive metastatic breast cancer.

For the primary analysis of centrally confirmed PFS, treatment with neratinib plus capecitabine resulted in a statistically significant improvement in centrally confirmed PFS (hazard ratio=0.76, p=0.0059) compared to treatment with lapatinib plus capecitabine. Because the proportional hazard assumption did not hold, the statistical analysis plan for the NALA trial prespecified that a restricted means survival analysis at 24 months would be performed. In this prespecified analysis the mean PFS for the patients treated with neratinib plus capecitabine was 8.8 months and the mean PFS for the patients treated with lapatinib plus capecitabine was 6.6 months.

For the primary analyses of OS, neratinib plus capecitabine resulted in an improvement in OS that trended positively in favor of the neratinib plus capecitabine arm of the study (hazard ratio = 0.88, p=0.21). The median OS for the patients treated with neratinib plus capecitabine was 21.0 months and the median OS for the patients treated with lapatinib plus capecitabine was 18.7 months. In the prespecified restricted means analysis the mean OS at 48 months for the patients treated with neratinib plus capecitabine was 24.0 months and the mean OS for the patients treated with lapatinib plus capecitabine was 22.2 months.

For the secondary endpoint of time to intervention for symptomatic central nervous system disease (also referred to as brain metastases), the results of the trial showed that treatment with neratinib plus capecitabine led to an improvement over the combination of lapatinib plus capecitabine. The overall cumulative incidence for intervention for CNS metastases at 54 months was 22.8% of patients for the neratinib plus capecitabine arm and 29.2% of patients for the lapatinib plus capecitabine arm (p=0.043, descriptive). For the secondary endpoint of duration of response, neratinib plus capecitabine treatment resulted in a longer duration of response compared to lapatinib and capecitabine treatment, with a median response of 8.54 months compared to a median response of 5.55 months (HR = 0.495, p = 0.0004, descriptive).

Treatment-emergent adverse events (TEAEs) were similar between arms: TEAEs leading to neratinib/lapatinib discontinuation were lower with neratinib (10.9%) than with lapatinib (14.5%). There

was a higher rate of grade 3 diarrhea with neratinib plus capecitabine compared to lapatinib plus capecitabine (24.4% vs 12.5%); however, the discontinuations due to diarrhea (neratinib plus capecitabine: 2.6%, lapatinib plus capecitabine: 2.3%) were similar in both arms.

"We are very pleased to announce this important regulatory milestone," said Alan H. Auerbach, Chief Executive Officer and President of Puma. "Although the use of HER2 directed agents in the metastatic setting has positively impacted the treatment of the disease in the first and second line settings, patients with HER2 positive metastatic breast cancer who have progressed on two or more prior treatments continue to need additional treatment options. We look forward to working with the FDA during its review of this submission."

About NALA

The NALA trial is a randomized controlled Phase III trial of neratinib plus capecitabine versus Tykerb® (lapatinib) plus capecitabine in patients with third-line HER2-positive metastatic breast cancer. The trial enrolled 621 patients who were randomized (1:1) to receive either neratinib plus capecitabine or lapatinib plus capecitabine. The trial was conducted globally at sites in North America, Europe, Asia-Pacific and South America. The co-primary endpoints of the trial are centrally confirmed progression free survival (PFS) and overall survival (OS). An alpha level of 1% was allocated to the PFS and 4% allocated to OS. The study was to be considered positive if either of the co-primary endpoints was positive. Puma reached agreement with the FDA under a Special Protocol Assessment (SPA) for the design of the Phase III clinical trial and the European Medicines Agency (EMA) also provided follow-on scientific advice (SA) consistent with that of the FDA regarding the Company's Phase III trial design and endpoints used in the trial.

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, oral was approved by the FDA 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.

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 $\geq$ 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.

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

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