Puma Biotechnology's 5-Year Analysis of Phase III ExteNET Study Published Online in The Lancet Oncology

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Data Demonstrates Continued Benefit from Neratinib after 5 years in Extended Adjuvant HER2-Positive Breast Cancer

LOS ANGELES--(BUSINESS WIRE)--Puma Biotechnology, Inc. (Nasdaq: PBYI), a biopharmaceutical company, announced the publication of previously presented results from the ExteNET Phase III clinical trial of Puma's drug neratinib in patients with early stage HER2-positive breast cancer in the journal *The Lancet Oncology*.

The article, entitled "Neratinib after trastuzumab-based adjuvant therapy in early stage HER2-positive breast cancer (ExteNET): 5-year analysis of a randomized, double blind, placebo-controlled phase III trial," appears in the November 13th online issue of *The Lancet Oncology* and will be published in a future print issue of the journal.

The ExteNET trial is a double-blind, placebo-controlled, Phase III trial of neratinib versus placebo after adjuvant treatment with trastuzumab (Herceptin) in patients with early stage HER2-positive breast cancer. The predefined 5-year invasive disease free survival (iDFS) analysis as a follow-up to the primary 2-year iDFS analysis of the Phase III ExteNET trial was published online today.

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 invasive recurrent disease, ductal carcinoma in situ (DCIS), or death for a period of five years after randomization in the trial.

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 primary endpoint of the trial was invasive disease free survival (iDFS). The results of the trial demonstrated that after a median follow up of 5.2 years, treatment with neratinib resulted in a 27% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.73, p = 0.008). The 5-year iDFS rate for the neratinib arm was 90.2% and the 5-year iDFS rate for the placebo arm was 87.7%.

The secondary endpoint of the trial was invasive disease free survival including ductal carcinoma in situ (iDFS-DCIS). The results of the trial demonstrated that treatment with neratinib resulted in a 29% reduction of risk of disease recurrence including DCIS or death versus placebo (hazard ratio = 0.71, p = 0.004). The 5-year iDFS-DCIS rate for the neratinib arm was 89.7% and the 5-year iDFS-DCIS rate for the placebo arm was 86.8%.

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 40% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.60, p = 0.002). The 5-year iDFS rate for the neratinib arm was 91.2% and the 5-year iDFS rate for the placebo arm was 86.8%. For the pre-defined subgroup of patients with hormone receptor negative disease, the results of the trial demonstrated that treatment with neratinib resulted in a hazard ratio of 0.95 (p = 0.762).

"ExteNET represents the first trial with a HER2-targeted agent that has shown a benefit in the extended adjuvant setting, which we believe provides a meaningful point of differentiation for neratinib in the treatment of HER2-positive breast cancer. We are pleased that *The Lancet Oncology* has chosen to publish these results," said Alan H. Auerbach, Chief Executive Officer and President of Puma.

The safety results were unchanged from the primary 2-year iDFS analysis of the study that showed 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). No evidence of increased risk of long-term toxicity or long-term adverse consequences of neratinib-associated diarrhea were identified in the analysis. Patients who received neratinib in this trial did not receive any prophylaxis with antidiarrheal agents to prevent the neratinib-

related diarrhea. Puma is currently running the ongoing CONTROL trial to investigate the use of loperamide-based prophylaxis to reduce the incidence of grade 3 or higher diarrhea in patients with early stage HER2-positive breast cancer who have completed adjuvant trastuzumab-based treatment. The most recently reported clinical data from CONTROL in June 2017 demonstrated that the use of loperamide-based prophylaxis reduced the rate of grade 3 diarrhea with neratinib, with grade 3 diarrhea rates ranging from 8-31% when loperamide-based prophylaxis was used.

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, epistaxis, 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 (PPI) and H2-receptor antagonists. Separate NERLYNX by 3 hours after antacid dosing.
- 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. The Company in-licenses the global development and commercialization rights to three drug candidates — PB272 (neratinib (oral)), PB272 (neratinib (intravenous)) and PB357. NERLYNX® (neratinib) is approved for commercial use by prescription in the United States as extended adjuvant therapy for early stage HER2-positive breast cancer following adjuvant trastuzumab-based therapy and is marketed as NERLYNX. 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 commercialization of NERLYNX and the continued development of its other advanced drug candidates directed at the treatment of HER2-positive breast cancer. The Company believes that NERLYNX has clinical application in the potential treatment of several other cancers 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 benefits of NERLYNX® and neratinib, the Company's clinical trials and the announcement of data relative to those trials. 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 only recently commenced commercialization and shipment of its only FDA approved product; the Company's dependence upon the commercial success of NERLYNX (neratinib); the Company's history of operating losses and its expectation that it will continue to incur losses for the foreseeable future; risks and uncertainties related to the Company's ability to achieve or sustain profitability; the Company's ability to predict its future prospects and forecast its financial performance and growth; failure to obtain sufficient capital to fund the Company's operations; the effectiveness of sales and marketing efforts; the Company's ability to obtain FDA approval or other regulatory approvals in the United States or elsewhere for other indications for neratinib or other product candidates; 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; risks pertaining to securities class action, derivative and defamation lawsuits; 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2017. 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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