# News Release

## Puma Biotechnology Presents Data Comparing Findings from the Phase II CONTROL Trial with the Neratinib Arm of the Phase III ExteNET Trial at the ASCO 2021 Annual Meeting

*Dose escalation of neratinib lowers the frequency of severe diarrhea and improves overall tolerability in patients with HER2-positive early stage breast cancer*

**LOS ANGELES, Calif., June 4, 2021** – Puma Biotechnology, Inc. (NASDAQ: PBYI), a biopharmaceutical company, presented results at the virtual 2021 ASCO Annual Meeting comparing the diarrhea mitigation strategies investigated in the Phase II CONTROL trial with the neratinib treatment arm of the ExteNET trial where diarrhea prophylaxis was not required. The presentation, entitled "Dose escalation for mitigating diarrhea: Ranked tolerability assessment of antidiarrheal regimens in patients receiving neratinib for early-stage breast cancer," is included in the **Breast Cancer—Local/Regional/Adjuvant** Poster Session (#536).

The CONTROL trial is an international, open-label, Phase II study investigating the use of antidiarrheal prophylaxis or dose escalation to improve the tolerability of neratinib-associated diarrhea. The primary endpoint of the trial is the incidence of grade 3 diarrhea. Patients ≥18 years of age with stage I–IIIc HER2-positive breast cancer received neratinib (240 mg/day orally for 1 year) together with one of the regimens investigated: loperamide alone, in combination with budesonide or colestipol, or neratinib dose escalation (DE): 120 mg/day on days 1–7, 160 mg/day on days 8–14, then 240 mg/day thereafter + loperamide PRN.

In the analysis presented at ASCO 2021, five CONTROL cohorts that had completed follow up were evaluated for 13 endpoints related to tolerability. The DE cohort ranked the best among the CONTROL cohorts and was then compared with the neratinib arm of the ExteNET trial, which included patients ≥18 years of age with stage I–III HER2-positive breast cancer receiving neratinib 240 mg/day or matching placebo for one year, without mandated anti-diarrheal treatment. ExteNET was a multicenter, randomized, double-blind, Phase III trial (NCT00878709) of 2,840 HER2-positive early stage breast cancer patients who received neratinib after neoadjuvant and/or adjuvant therapy with chemotherapy and a trastuzumab-based regimen.

Comparison of the CONTROL DE cohort with the ExteNET neratinib arm demonstrated that grade 3 diarrhea was substantially lower in CONTROL DE compared to ExteNET (13.3% vs. 39.9%). Neratinib DE also resulted in fewer total days of grade 3 diarrhea compared to ExteNET (2.5 days vs 5 days). Dose escalation also led to fewer discontinuations due to diarrhea in the first three months of treatment compared to ExteNET (3.3% vs 14.5%). Additionally, the average duration of treatment with neratinib was much longer in the DE cohort versus ExteNET. Overall, the findings of this analysis suggest that escalating the dose of neratinib in the first 2 weeks of treatment may help patients stay on neratinib longer, allowing them the opportunity to complete the recommended 1-year of treatment.

"Dose escalation of neratinib with loperamide PRN is an effective way of minimizing the extent of grade 3 diarrhea. This strategy showed improvements in overall tolerability as compared to ExteNET and resulted in more patients being able to remain on therapy," said Gavin M. Marx, MBBS, Sydney Adventist Hospital.

“These results confirm that dose escalation of neratinib lowered the incidence and duration of grade 3 diarrhea as well as discontinuations due to diarrhea, said Adam M. Brufsky, MD, PhD University of Pittsburgh School of Medicine. “Using dose escalation, the average duration of neratinib was longer (compared to ExteNET)."

Alan H. Auerbach, Chief Executive Officer and President of Puma, added, “We are committed to research that seeks to understand how to improve the tolerability of neratinib. The CONTROL trial evaluated multiple diarrhea mitigation strategies and dose escalation of neratinib resulted in the best tolerability, allowing more patients to stay on treatment for the recommended duration.”

**About HER2-Positive Breast Cancer**

Up to 20% of patients with breast cancer tumors over-express the HER2 protein (HER2-positive disease) and in the ExteNET study, 57% of patients were found to have tumors that were hormone-receptor positive. 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 recurring, up to 25% of patients treated with trastuzumab experience recurrence within 10 years, the majority of which are metastatic recurrences.

**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 PB272 (neratinib, oral), PB272 (neratinib, intravenous) and PB357. Neratinib, oral was approved by the U.S. Food and Drug Administration in 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. In February 2020, NERLYNX was also approved by the FDA in combination with capecitabine for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting. NERLYNX was granted marketing authorization by the European Commission in 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 may be found at www.pumabiotechnology.com.

**IMPORTANT SAFETY INFORMATION**

**NERLYNX® (neratinib) tablets, for oral use**

**INDICATIONS AND USAGE:** NERLYNX is a kinase inhibitor indicated:

- As a single agent, for the extended adjuvant treatment of adult patients with early-stage HER2-positive breast cancer, to follow adjuvant trastuzumab-based therapy.
- In combination with capecitabine, for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer, who have received two or more prior anti-HER2 based regimens in the metastatic setting.

**CONTRAINDICATIONS:** None

**WARNINGS AND PRECAUTIONS:**

- **Diarrhea:** Aggressively manage diarrhea. If diarrhea occurs despite recommended prophylaxis, treat 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 (reported in ≥ 5% of patients) were as follows:

- NERLYNX as a single agent: Diarrhea, nausea, abdominal pain, fatigue, vomiting, rash, stomatitis, decreased appetite, muscle spasms, dyspepsia, AST or ALT increased, nail disorder, dry skin, abdominal distention, epistaxis, weight decreased, and urinary tract infection.
- NERLYNX in combination with capecitabine: Diarrhea, nausea, vomiting, decreased appetite, constipation, fatigue/asthenia, weight decreased, dizziness, back pain, arthralgia, urinary tract infection, upper respiratory tract infection, abdominal distention, renal impairment, and muscle spasms.

**To report SUSPECTED ADVERSE REACTIONS, contact Puma Biotechnology, Inc. at 1-844-NERLYNX (1-844-637-5969) 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 CYP3A4 inhibitors: Avoid concomitant use.
- Moderate CYP3A4 and P-glycoprotein (P-gp) dual 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.**

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.

**Forward-Looking Statements**

This press release contains forward-looking statements, that involve risks and uncertainties that could cause Puma'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, any adverse impact on Puma's business or the global economy and financial markets, generally, from the global COVID-19 pandemic, and the risk factors disclosed in the periodic and current reports filed by Puma with the Securities and Exchange Commission from time to time, including Puma's Annual Report on Form 10-K for the year ended December 31, 2020. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Puma assumes no obligation to update these forward-looking statements, except as required by law.

**Contacts**

Alan H. Auerbach or Mariann Ohanesian, Puma Biotechnology, Inc., +1 424 248 6500

info@pumabiotechnology.com

ir@pumabiotechnology.com

David Schull or Maggie Beller, Russo Partners, +1 212 845 4200

david.schull@russopartnersllc.com

maggie.beller@russopartnersllc.com

**# # # # #**