News Release

Puma Biotechnology Announces Publication of Overall Survival Results from Phase III ExteNET Trial Evaluating Neratinib in HER2-Positive, Hormone Receptor-Positive, Early Stage Breast Cancer

*Data published online in **Clinical Breast Cancer***

LOS ANGELES, Calif., Oct. 5, 2020 – Puma Biotechnology, Inc. (NASDAQ: PBYI), a biopharmaceutical company, announced that efficacy results of neratinib in HER2-positive, hormone receptor-positive (HR+), early stage breast cancer (eBC) from the Phase III ExteNET trial were published in *Clinical Breast Cancer*. The manuscript appears in the October 5, 2020 online issue accessible at https://www.clinical-breast-cancer.com/article/S1526-8209(20)30258-5/fulltext.

ExteNET was a multicenter, randomized, double-blind, Phase III trial of 2,840 HER2-positive eBC patients who received neratinib after neoadjuvant and/or adjuvant therapy with chemotherapy and trastuzumab. Patients were stratified by hormone receptor status and randomly assigned to one year of treatment with either oral neratinib 240 mg/day or placebo. The primary endpoint of the trial was invasive disease-free survival (iDFS) with overall survival as a key secondary endpoint. Within the European Union, neratinib is approved in patients with HR+ breast cancer who initiated treatment within one year of completing an adjuvant trastuzumab containing regimen.

The manuscript presents data focusing on HR+ patients who initiated treatment within a year of completing an adjuvant trastuzumab containing treatment (HR+ /< 1 yr) and subgroups of clinical interest including patients who did not achieve a pathological complete response (no pCR) after neoadjuvant treatment and therefore were at a high risk of disease recurrence. (HR+/ <1 yr, no pCR)

In the HR+ /< 1 yr patient population, the absolute 5-year invasive disease-free survival benefit versus placebo was 5.1% (HR=0.58, 95% CI 0.41–0.82) and absolute 8-year overall survival benefit was 2.1%. (HR=0.79, 95% CI 0.55–1.13). The 5 year cumulative incidence of CNS metastases was 0.7% in the neratinib arm and 2.1% in the placebo arm.

In the HR+/ <1 yr, no pCR subgroup of patients that were at a high risk of disease recurrence the absolute 5-year iDFS benefit in the neratinib arm versus placebo was 7.4% (HR=0.60; 95% CI 0.33–1.07) and the 8- year overall survival benefit was 9.1% (HR=0.47; 95% CI 0.23– 0.92).

Most common grade 3 adverse events were diarrhea (39% vs placebo, 1%; without mandatory anti-diarrheal prophylaxis), vomiting (4% vs <1%), and fatigue (2% vs <1%).

Professor Arlene Chan, Vice Chair Breast Cancer Research Centre – WA, said, “Deciding on which patients benefit most from a given therapy is an important goal for clinicians. This newly published study provides consistent and durable benefits of neratinib in a subset of HER2-positive early stage breast cancer patients who are considered to be at greater risk of relapse: namely patients with HR+ tumors that did not achieve a pCR after neoadjuvant treatment (no pCR). The benefits demonstrated are meaningful in all endpoints evaluated, including iDFS, OS and CNS recurrence, and thus should help guide future clinical decisions.”

Hope S. Rugo, MD, Professor of Medicine, University of California San Francisco Comprehensive Cancer Center, said, "HER2-positive HR+ patients who do not achieve a pCR are at increased risk of recurrence, even after receiving current standard of care treatment. In a descriptive subset analysis, extended adjuvant therapy with neratinib demonstrated a positive benefit in these patients not only in iDFS, but also in OS. In addition, the trend toward lower CNS involvement is a very important consideration, given the profound impact of CNS metastasis on future prognosis. These data coupled with the recently published data from the CONTROL study, which shows improved tolerability with dose escalation, should allow more patients to benefit from this important therapy."

Alan H. Auerbach, Chief Executive Officer and President of Puma, added, "Although there have been many new treatment options for patients with early stage HER2-positive breast cancer, the risk of disease recurrence remains significant and more must be done. These newly published data demonstrate that neratinib provides a clinically meaningful reduction in the risk of recurrence and provides a very important option for these high risk patients."

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) 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 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.

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

# # # # #