# News Release

## Puma Biotechnology's NERLYNX® Included in NCCN Clinical Practice Guidelines for the Treatment of Breast Cancer with a HER2 Mutation

**LOS ANGELES, Calif., Feb. 1, 2023** –Puma Biotechnology, Inc. (NASDAQ: PBYI), a biopharmaceutical company, announced that the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer were updated to include an addition involving neratinib (NERLYNX®).

The updated NCCN Practice Guidelines for Breast Cancer include neratinib combinations as category 2B potential targeted therapies for patients with ER+/HER2- or ER-/HER2- metastatic (stage IV) breast cancer and activating mutations in the *HER2* gene as detected by next generation sequencing of tumor tissue or ctDNA. Neratinib is included 1) with or without fulvestrant, and 2) with or without trastuzumab/fulvestrant. The NCCN Guidelines' Category of Preference is designated as "useful in certain circumstances" and for ER+/HER2- disease, "useful in certain circumstances in patients who have already received CDK 4/6 inhibitor therapy." This update is described in a table entitled, "Emerging Biomarkers to Identify Novel Therapies for Patients with Stage IV (M1) Disease."

This addition was based on results from the Phase 2 SUMMIT trial (NCT01953926), which enrolled a cohort of patients with locally assessed HR+/ HER2- metastatic breast cancer with activating *HER2* mutations who had received prior CDK4/6 inhibitor therapy (Jhaveri KL, J Clin Oncol 2022; 40:1028-1028*), as well as results from the Phase 2 MutHER trial (NCT01670877), a single-arm, multi-cohort trial that evaluated neratinib in combination with fulvestrant in patients with *HER2*-mutated, non-amplified metastatic breast cancer (Ma CX, Clin Cancer Res 2022; 28:1258-1267**).

Additionally, in its recent update, NCCN included dose escalation in the neratinib dosing schedule for recurrent unresectable or metastatic breast cancer. The neratinib dose escalation schedule was previously included in the 2022 NCCN Guidelines for Breast Cancer under preoperative/adjuvant therapy regimens as an approach to improve the tolerability of neratinib in the treatment of adjuvant HER2-positive breast cancer. This latest update aligns with the labeling supplement to the U.S. Prescribing Information approved by the U.S. Food and Drug Administration in June 2021, which incorporated the use of NERLYNX dose escalation as evaluated in the Phase II CONTROL study.

Alan H. Auerbach, Chief Executive Officer and President of Puma, said, "We are pleased with the additional inclusion of neratinib in the NCCN Guidelines for Breast Cancer for patients with *HER2* activating mutations. Physicians use the NCCN Guidelines as the standard resource for determining the best course of treatment for patients. We believe the updated NCCN guidelines will increase awareness, which will help assist patients, their caregivers and their healthcare providers in making informed decisions while treating this significant unmet need in advanced breast cancer."

**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 the National Comprehensive Cancer Network**

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of leading cancer centers devoted to patient care, research, and education. NCCN is dedicated to improving and facilitating quality, effective, efficient, and accessible cancer care so patients can live better lives. The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) provide transparent, evidence-based, expert consensus recommendations for cancer treatment, prevention, and supportive services; they are the recognized standard for clinical direction and policy in cancer management and the most thorough and frequently updated clinical practice guidelines available in any area of medicine. The NCCN Guidelines for Patients® provide expert cancer treatment information to inform and empower patients and caregivers, through support from the NCCN Foundation®. NCCN also advances continuing education, global initiatives, policy, and research collaboration and publication in oncology. Visit NCCN.org for more information.

**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.

In September 2022, Puma entered into an exclusive license agreement for the development and commercialization of the anti-cancer drug alisertib, a selective, small molecule, orally administered inhibitor of aurora kinase A. Initially, Puma intends to focus the development of alisertib on the treatment of small cell lung cancer and breast cancer.

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 https://www.NERLYNX.com or by dialing 1-855-816-5421.

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

**INDICATIONS**

- NERLYNX® (neratinib) tablets, for oral use, 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.

**Important Safety Information Regarding NERLYNX® (neratinib) U.S. Indication**

**CONTRAINDICATIONS: None**

**WARNINGS AND PRECAUTIONS:**

- Diarrhea: Manage diarrhea through either NERLYNX dose escalation or loperamide prophylaxis. 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. Separate NERLYNX by at least 2 hours before or 10 hours after H2-receptor antagonists. Or separate NERLYNX by at least 3 hours with antacids.
- Strong CYP3A4 inhibitors: Avoid concomitant use.
- P-gp and moderate CYP3A4 dual inhibitors: Avoid concomitant use.
- Strong or moderate CYP3A4 inducers: Avoid concomitant use.
- Certain P-gp substrates: Monitor for adverse reactions of P-gp substrates for which minimal concentration change may lead to serious adverse reactions when used concomitantly with NERLYNX.

**USE IN SPECIFIC POPULATIONS**:

- Lactation: Advise women not to breastfeed.

Please see Full Prescribing Information for additional safety information.

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* Jhaveri KL, Goldman JW, Hurvitz SA, et al. Neratinib plus fulvestrant plus trastzuzumab (N+F+T) for hormone receptor-positive (HR+), HER2-negative, HER2-mutant metastatic breast cancer (MBC): Outcomes and biomarker analysis from the SUMMIT trial. J Clin Oncol 2022; 40:1028-1028.

** Ma CX, Luo J, Freedman RA, et al. The phase II MutHER study of neratinib alone and in combination with fulvestrant in HER2-mutated, non-amplified metastatic breast cancer. Clin Cancer Res 2022; 28:1258-1267.