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

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LOS ANGELES--(BUSINESS WIRE)-- Puma Biotechnology, Inc. (NASDAQ: PBYI), a biopharmaceutical company, announced that the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Cervical Cancer were updated to include an addition involving neratinib (NERLYNX®).

The updated NCCN Practice Guidelines for Cervical Cancer include neratinib monotherapy for use as second-line or subsequent therapy for recurrent or metastatic disease as an option for patients with *HER2* -mutated tumors with a designation of Category 2A. The NCCN Guidelines Category of Preference is designated as "useful in certain circumstances" as a treatment option for patients with *HER2* -mutated tumors.

This addition was based on results from the Phase II SUMMIT trial (NCT01953926), which enrolled a cohort of patients who were required to have histologically confirmed recurrent/metastatic cervical cancer for which no curative treatment existed, along with documented evidence of a somatic, activating *HER2* mutation (Friedman CF, D'Souza A, Bello Roufai D, et al. Targeting HER2-mutant metastatic cervical cancer with neratinib: Final results from the Phase II SUMMIT basket trial. *Gynecol Oncol.* 2024;181:162-169. doi: 10.1016/j.ygyno.2023.12.004).

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 Cervical 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 cervical cancer."

About HER2-Mutated Cervical Cancer

Despite recent advancements in the therapeutic landscape for recurrent and metastatic cervical cancer, there is a need to identify robust biomarkers to direct therapy choices to target mutational drivers. Somatic *HER2 (ERBB2)* mutations have been reported in up to 9%[1,2,3] of cervical cancers and are associated with poor prognosis [1,2] . In a recent real-world study, prospective genomic profiling of cervical cancer patients identified *HER2* mutations as one of the more prevalent genomic alterations in the studied cervical cancer population[3] .

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-licensed the global development and commercialization rights to PB272 (neratinib, oral), in 2011. 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. In February 2024, Puma initiated ALISCA™-Lung1, a Phase II clinical trial of alisertib monotherapy for the treatment of patients with extensive-stage small cell lung cancer. In November 2024, Puma initiated ALISCA™-Breast1, a Phase II clinical trial of alisertib in combination with endocrine therapy for the treatment of patients with HER2-negative, HR-positive metastatic 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.

[1] Xiang L, Jiang W, Ye S, He T, Pei X, Li J, et al. ERBB2 mutation: A promising target in non-squamous cervical cancer. *Gynecol Oncol* . 2018;148(2):311-316.

[2] Zammataro L, Lopez S, Bellone S, Pettinella F, Bonazzoli E, Perrone E, et al. Whole-exome sequencing of cervical carcinomas identifies activating ERBB2 and PIK3CA mutations as targets for combination therapy. *Proc Natl Acad Sci U S A* .

2019;116(45):22730-22736.

[3] Friedman CF, Ravichandran V, Miller K, et al. Assessing the genomic landscape of cervical cancers: clinical opportunities and therapeutic targets. *Clin Cancer Res* . 2023;29(22):4660-4668. doi: 10.1158/1078-0432.CCR-23-1078. PMID: 37643132; PMCID: PMC10644000.

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