News Release

Puma Biotechnology Presents Outcomes from the Metastatic Breast Cancer Cohort of the SUMMIT Trial at the ASCO 2022 Annual Meeting

LOS ANGELES, Calif., June 6, 2022 -- Puma Biotechnology, Inc. (NASDAQ: PBYI), a biopharmaceutical company, presented results from the Phase II SUMMIT trial, assessing the efficacy of combined neratinib, fulvestrant, and trastuzumab in patients with hormone receptor positive, HER2-negative, *HER2*-mutant metastatic breast cancer, at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting held in person from June 3-7 in Chicago, IL, and online. The poster, entitled "Neratinib + fulvestrant + trastuzumab (N+F+T) for hormone receptor-positive (HR+), HER2-negative, *HER2*-mutant metastatic breast cancer (MBC): outcomes and biomarker analysis from the SUMMIT trial," was presented at the Breast Cancer -- Metastatic Poster Session (poster #1028) by Komal L. Jhaveri, MD, FACP, Medical Oncologist at Memorial Sloan Kettering Cancer Center on June 6 at 9:00 a.m. ET.

Earlier genomic analyses from a cohort treated with a combination of neratinib and fulvestrant suggest that resistance to neratinib may occur via mutant allele amplification or secondary *HER2* mutations. The addition of trastuzumab to the combination of neratinib and fulvestrant in this trial demonstrated positive durable responses in patients with HR-positive, *HER2*-mutant MBC who had received prior CDK4/6 inhibitors (CDK4/6i).

The Phase II SUMMIT basket trial is an open-label, multicenter, multinational study that included a cohort evaluating the efficacy of the triplet combination of neratinib (N), plus fulvestrant (F), plus trastuzumab (T), in patients with HR-positive, HER2-negative, *HER2*-mutant metastatic breast cancer, as identified by local genomic sequencing, who had previously received CDK4/6 inhibitors. In order to confirm the contribution of neratinib to the combination, a small, randomized cohort comparing neratinib plus fulvestrant plus trastuzumab versus fulvestrant plus trastuzumab versus fulvestrant was also included. A range of *HER2* allelic variants was represented in the cohort. Patients who received the triplet regimen were enrolled in the non-randomized cohort and received 240 mg of neratinib per day intramuscularly, 500 mg intravenous fulvestrant on days 1 and 15 of Cycle 1 and then every 4 weeks, 8mg/kg body weight trastuzumab initially and then 6mg/kg every 3 weeks. Patients in the randomized cohort received either a combination of neratinib, fulvestrant, and trastuzumab, or fulvestrant and trastuzumab, or fulvestrant alone in a 1:1:1 ratio. To counter the side effects of diarrhea, loperamide prophylaxis was mandatory for the first two treatment cycles. Patients who were randomized to the combination of fulvestrant and trastuzumab, or fulvestrant alone, could cross over to receive neratinib, fulvestrant, and trastuzumab at progression. Efficacy was assessed using objective response rate (ORR) and clinical benefit rate (CBR). Tumor tissue was retrospectively assessed by central next-generation sequencing (NGS).

The table below summarizes the efficacy of SUMMIT MBC patients who received neratinib plus fulvestrant plus trastuzumab, those who received fulvestrant plus trastuzumab, and those who received fulvestrant alone; and also those who received fulvestrant plus trastuzumab or fulvestrant and then crossed over to neratinib plus fulvestrant plus trastuzumab upon progression. Patients who received neratinib plus fulvestrant plus trastuzumab (non-randomized + randomized) had a 35.3% investigator-assessed objective response rate, 14.3-month duration of response, 41.7% clinical benefit rate, and 8.2-month median progression-free survival. Neratinib appears to be a critical component of the combination therapy, as

demonstrated by lack of response in the small cohort of patients treated with fulvestrant or fulvestrant plus trastuzumab, and by response in a subset of those patients upon crossover to neratinib plus fulvestrant plus trastuzumab.

Table: Efficacy Findings from HR+ Metastatic Breast Cancer Patients

	Non-randomized + Randomized HR+ Prior CDK4/6i (N+F+T, n=51)	Randomized HR+ Prior CDK4/6i (F+T, n=7)	After crossover from F+T to N+F+T (n=4)	Randomized HR+ Prior CDK4/6i (F, n=7)	After crossover from F to N+F+T (n=6)
Objective response (confirmed CR/PR)[a], n (%)	18 (35.3)	0	1 (25.0)	0	2 (33.3)
CR	1 (2.0)	0	0	0	0
PR	17 (33.3)	0	1 (25.0)	0	2 (33.3)
Best overall response* (confirmed or unconfirmed PR or CR), n (%)	25 (49.0)	0	1 (25.0)	0	2 (33.3)
Median DOR[b], months (95% CI)	14.3 (6.4–NE)	No response	6.2 (NE–NE)	No response	6.3 (6.2–6.4)
Clinical benefit[c], n (%)	24 (47.1)	0	1 (25.0)	0	5 (83.3)
Median PFS, months (95% CI)	8.2 (4.7–12.7)	3.9 (1.9–4.1)	8.25 (NE–NE)	4.1 (1.6–4.1)	NE

Data cut-off: 15 April 2022. Tumor response based on: investigator tumor assessments (RECIST v1.1)

CR, confirmed response; PR, partial response; CI, confidence interval; DOR, duration of response; NA, not applicable; NE, not estimable; PFS, progression-free survival

[a] Objective response defined as either a complete or partial response that is confirmed no less than 4-weeks after the criteria for response are initially met;

[b] Kaplan-Meier analysis. For crossover patients, calculated from time of crossover to N+F+T.

[c] Clinical benefit is defined as confirmed CR or PR or stable disease (SD) for ≥24 weeks (within +/– 7-day visit window)

These results suggest that the combination of neratinib, fulvestrant, and trastuzumab together is promising for treating HR+ and HER2-mutated MBC with prior exposure to CDK4/6i across a range of HER2 mutations.

Dr. Jhaveri, an investigator of the trial, said, “Patients with hormone receptor-positive, HER2-negative, *HER2*-mutant metastatic breast cancer who had received prior treatment with CDK4/6 inhibitors demonstrated encouraging clinical activity with durable responses when treated with the triplet combination of neratinib with fulvestrant and trastuzumab. These responses were observed in patients whose tumors harbored a wide spectrum of *HER2* mutations, including those with co-occurring *HER3* mutations, regardless of ductal or lobular histology, and with a range of HER2 protein expression.”

Alan H. Auerbach, Chief Executive Officer, and President of Puma Biotechnology added, “*HER2* mutations can be readily and accurately identified and are clinically actionable for targeted therapy in metastatic breast cancers. We are very pleased with the updated activity seen with the combination of neratinib plus trastuzumab plus fulvestrant therapy in this heavily pretreated metastatic breast cancer patient population with *HER2*-mutated disease.”

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 https://www.pumabiotechnology.com.

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

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: 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 https://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 H_2-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.

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 1-855-816-5421.

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