News Release

Puma Biotechnology Presents Updates from the SUMMIT Trial at the 2021 SABCS Annual Meeting

- *Neratinib in combination with fulvestrant and trastuzumab offers promising results for patients with hormone receptor-positive, HER2-mutated metastatic breast cancer with prior exposure to CDK4/6 inhibitors*
- *Neratinib in combination with trastuzumab results in strong activity in patients with triple negative metastatic breast cancer with a HER2 mutation*

LOS ANGELES, Calif., Dec. 10, 2021 – Puma Biotechnology, Inc. (Nasdaq: PBYI), a biopharmaceutical company, presented an update from its Phase II SUMMIT trial at the ongoing 2021 San Antonio Breast Cancer Symposium (SABCS) Annual Meeting. The data presented was from the cohort of patients with hormone receptor-positive, HER2-mutant metastatic breast cancer, exposed to CDK4/6 inhibitors, and treated with a combination of neratinib with fulvestrant and trastuzumab and a separate cohort of patients with metastatic triple negative breast cancer with a HER2 mutation treated with the combination of neratinib plus trastuzumab. The presentation, entitled "Neratinib + fulvestrant + trastuzumab for hormone receptor-positive, HER2-mutant metastatic breast cancer and neratinib + trastuzumab for triple-negative disease: Latest updates from the SUMMIT trial," is being presented at an oral session (GS4-10) by Komal Jhaveri, MD, FACP, Medical Oncologist at Memorial Sloan Kettering Cancer Center, on December 10 at 11:00 a.m. CST. A copy of this oral presentation is available on the Puma Biotechnology website, https://www.pumabiotechnology.com.

The Phase II SUMMIT trial is an open-label, multicenter, multinational study to evaluate the safety and efficacy of neratinib administered daily to patients who have solid tumors with activating HER2 (ERBB2) mutations or lung cancers with EGFR exon 18 mutations (NCT01953926). In the HER2-mutant, hormone receptor (HR)-positive, metastatic breast cancer cohort, patients who have previously received CDK4/6 inhibitors were previously enrolled in a non-randomized cohort and received 240 mg of neratinib per day, 500 mg fulvestrant on day 1 and 15 of Cycle 1 and then 8mg/kg trastuzumab every 4 weeks initially and then 6mg/kg trastuzumab every 3 weeks thereafter. In the HER2-mutant, triple negative metastatic breast cancer (TNBC) cohort, patients received 240 mg of neratinib per day and 8mg/kg body weight trastuzumab initially and then 6mg/kg trastuzumab every 3 weeks. All patients received anti-diarrheal prophylaxis with loperamide alone for the first two treatment cycles.

The SUMMIT trial was later amended to randomize hormone receptor-positive, HER2-mutant metastatic breast cancer patients to receive either: (i) the combination of neratinib (N), trastuzumab (T) and fulvestrant (F), (ii) the combination of fulvestrant and trastuzumab, or (iii) fulvestrant alone. Once randomized, patients received either neratinib plus fulvestrant plus trastuzumab, fulvestrant plus trastuzumab, or fulvestrant in 1:1:1 ratio. All patients received anti-diarrheal prophylaxis with loperamide alone for the first two treatment cycles.

In the non-randomized cohort, for the 26 patients with HR+, HER2-mutated MBC who had previously received CDK4/6 inhibitors, the efficacy results showed that for the patients who received neratinib plus fulvestrant plus trastuzumab, 12 patients (46.2%) experienced a confirmed objective response, all of which were partial responses, and 15 patients (57.7%) experienced clinical benefit (clinical benefit is defined as

confirmed complete response or partial response, or stable disease for at least 24 weeks). The median duration of response was 14.4 months and the median progression-free survival was 8.2 months (Table 1).

For the randomized portion of the trial, for the patients with HR+, HER2-mutated MBC who had previously received CDK4/6 inhibitors, no patient in either the fulvestrant plus trastuzumab or fulvestrant alone arm experienced a confirmed objective response. In the 7 randomized patients who received the combination of neratinib, trastuzumab and fulvestrant, 2 patients (28.6%) experienced a confirmed objective response, including one complete response (14.3%) and one partial response (14.3%), and 2 patients (28.6%) experienced clinical benefit (clinical benefit is defined as confirmed complete response or partial response or stable disease for at least 24 weeks). The median duration of response was not reached and the median progression-free survival was 6.2 months (Table 1).

For all 33 patients with HR+, HER2-mutated MBC, who had previously received CDK4/6 inhibitors, who received the combination of neratinib plus trastuzumab plus fulvestrant, the efficacy results showed that 14 patients (42.4%) experienced a confirmed objective response, including one complete response (3.0%) and 13 partial responses (39.4%), and 17 patients (51.5%) experienced clinical benefit (clinical benefit is defined as confirmed complete response or partial response or stable disease for at least 24 weeks). The median duration of response was 14.4 months and the median progression-free survival was 7.0 months (Table 1).

Table 1: Efficacy findings from HR+ MBC patients

	Non-randomized (N+F+T, n=26)	Randomized (N+F+T, n=7)	Randomized (F+T, n=7)	Randomized (F, n=7)	All N+F+T (N+F+T, n=33)
Objective response (confirmed CR/PR)[a], n (%)	12 (46.2)	2 (28.6)	0	0	14 (42.4)
CR	0	1 (14.3)	0	0	1 (3.0)
PR	12 (46.2)	1 (14.3)	0	0	13 (39.4)
Best overall response (confirmed or unconfirmed PR or CR), n (%)	15 (57.7)	3 (42.9)	0	0	18 (54.5)
Median DOR[b], months (95% CI)	14.4 (6.4–NE)	NE	NE	NE	14.4 (6.4–NE)
Clinical benefit[c], n (%)	15 (57.7)	2 (28.6)	0	0	17 (51.5)
Median PFS, months (95% CI)	8.2 (4.0–15.1)	6.2 (2.1–NE)	3.9 (1.9–4.1)	4.1 (1.6–4.1)	7.0 (4.2–12.7)
Median duration of treatment, months (range)	8.7 (1.0–22.1)	5.0 (0.7–13.2)	3.5 (0.8–4.1)	2.1 (0.7–4.1)	6.5 (0.7–22.1)

Note: Data cut-off: 10 September 2021. Tumor response based on: investigator tumor assessments (RECIST v1.1) for HR+ cohorts
CR, confirmed response; PR, partial response; CI, confidence interval; DOR, duration of response; 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
[c] Clinical benefit is defined as confirmed CR or PR or stable disease (SD) for ≥24 weeks (within +/– 7-day visit window)

Based on the results from the randomized portion of the trial, for patients with hormone receptor-positive, HER2-mutant metastatic breast cancer, the Independent Data Monitoring Committee (IDMC) recommended closing enrollment to the fulvestrant plus trastuzumab and fulvestrant alone arms of the trial and recommended continuing enrollment in the neratinib plus trastuzumab plus fulvestrant arm of the trial. To date, the Company has enrolled 19 additional patients in this triplet arm of the trial.

For the 18 patients with HER2-mutant triple negative breast cancer (TNBC) who received fulvestrant plus trastuzumab, 6 patients (33.3%) experienced a confirmed objective response, including one complete response (5.6%) and 5 partial responses (27.8%), and 7 patients (38.9%) experienced clinical benefit (clinical benefit is defined as confirmed complete response or partial response or stable disease for at least 24 weeks). The median duration of response has not been reached and the median progression-free survival was 6.2 months (Table 2).

Table 2: Efficacy findings from TNBC patients

	TNBC (N+T, n=18)
Objective response (confirmed CR/PR)[a], n (%)	6 (33.3)
CR	1 (5.6)
PR	5 (27.8)
Best overall response (confirmed or unconfirmed PR or CR), n (%)	7 (38.9)
Median DOR[b], months (95% CI)	NE
Clinical benefit[c], n (%)	7 (38.9)
Median PFS, months (95% CI)	6.2 (2.1–8.2)
Median duration of treatment, months (range)	4.4 (0.3–15.4)

Note: Data cut-off: 10 September 2021. Tumor response based on: investigator tumor assessments (RECIST v1.1 or modified PERCIST) for TNBC cohorts; TNBC cohort analysis ongoing

CR, confirmed response; PR, partial response; CI, confidence interval; DOR, duration of response; 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

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

The safety profile observed in patients treated with neratinib in the SUMMIT study was consistent with that observed previously in metastatic patients with HER2 amplified tumors. The interim safety results of the study showed that the most frequently observed adverse event was diarrhea. For the 33 safety-evaluable HR-positive breast cancer patients who received the combination of neratinib plus trastuzumab plus fulvestrant, 15 patients (45.5%) reported grade 3 diarrhea. One patient (3.0%) permanently discontinued neratinib due to diarrhea. For the 18 safety-evaluable triple negative breast cancer patients who received the combination of neratinib plus trastuzumab, 3 patients (16.7%) reported grade 3 diarrhea. No patient permanently discontinued neratinib due to diarrhea.

“For patients treated with CDK4/6 inhibitors without seeing tumor reversal, combination therapy with neratinib, fulvestrant and trastuzumab presents a promising new treatment option,” said Dr. Jhaveri. “Neratinib is not only effective in treating early stage HER2-positive breast cancer but has been seen as being efficacious in helping combat secondary HER2 mutations as well.”

Alan H. Auerbach, Chief Executive Officer and President of Puma, added, “We are pleased to see the activity of neratinib in both the hormone receptor-positive and triple negative breast cancer cohorts of the SUMMIT trial. We look forward to obtaining data from the 19 additional patients who have been enrolled post expansion of the neratinib plus trastuzumab plus fulvestrant arm of the randomized trial, as per the IDMC, which we anticipate we will be able to present in the first half of 2022.”

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 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 dose escalation or loperamide, treat with loperamide, 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 3 hours with antacids. 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 www.NERLYNX.com or 1-855-816-5421.

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