News Release

Puma Biotechnology Presents Efficacy and Safety Outcomes from the Phase III NALA Trial at the 2020 SABCS

Results show improved CNS outcomes with neratinib-based regimens in the treatment and prevention of CNS metastases from HER2-positive breast cancer

LOS ANGELES, Calif., Dec. 11, 2020 – Puma Biotechnology, Inc. (NASDAQ: PBYI), a biopharmaceutical company, presented efficacy and safety outcomes in a subgroup of patients from the NALA trial who had central nervous system (CNS) metastases at baseline, with a particular focus on CNS-specific endpoints, at the 2020 Virtual San Antonio Breast Cancer Symposium (SABCS) that is currently taking place. The presentation entitled, "Impact of neratinib plus capecitabine on outcomes in HER2-positive metastatic breast cancer patients with central nervous system disease at baseline: Findings from the phase 3 NALA trial," is being presented at a Spotlight Poster Discussion Session by Cristina Saura, M.D., Ph.D., Head of Breast Cancer Unit, Vall d'Hebrón University Hospital, an investigator of the trial. A copy of this poster presentation is available on the Puma website.

The Phase III NALA trial was a randomized controlled trial of neratinib plus capecitabine (N+C) versus Tykerb® (lapatinib) plus capecitabine (L+C) in patients with third-line HER2-positive metastatic breast cancer (NCT01808573). The trial enrolled 621 patients who were randomized (1:1) to receive either N+C or L+C. The co-primary endpoints of the trial were independently adjudicated progression free survival (PFS) and overall survival (OS). The NALA study met its primary endpoint, with the neratinib arm having significantly improved PFS vs. the lapatinib arm (hazard ratio [HR], 0.76; 95% confidence interval [CI], 0.63-0.93; stratified log-rank P = .0059; mean PFS 8.8 mo vs. 6.6 mo). The data showed no statistical difference in OS between treatment arms (HR 0.88; 95% CI, 0.72-1.07; P = .2098). Time to intervention for symptomatic central nervous system disease (also referred to as brain metastases) was a predefined secondary endpoint of the trial. In the ITT population, significantly fewer interventions for CNS disease occurred with N+C versus L+C (cumulative incidence, 22.8% vs. 29.2%; P = .043).

The poster presented at the 2020 SABCS meeting describes results for the subset of patients who entered the trial with CNS metastases. Of the 621 patients randomized to study treatment, 101 (16.3%) had asymptomatic CNS metastases at baseline (N+C, n=51; L+C, n=50). Within the CNS at baseline subgroup, the data suggested an association between N+C and improved PFS compared with L+C (HR 0.66; 95% CI, 0.41-1.05). The mean PFS was 7.8 months in the neratinb arm vs. 5.5 months in the laptinib arm. Consistent with results in the overall population, there was no apparent difference in OS between arms in the CNS at baseline group. With respect to the CNS-specific outcomes, N+C was associated with fewer interventions for CNS disease compared with L+C; the 12 month incidence of interventions for CNS metastases was 25.5% in the N+C arm and 36.0% in the L+C arm. The data also suggested an association between neratinib and improved CNS progression free survival (CNS-PFS), an ad hoc composite endpoint assessing disease progression in the brain or death from any cause (HR 0.62; 95% CI, 0.32-1.18). The median CNS-PFS was 12.4 months in the patients treated with N+C and 8.3 months in the patients treated with L+C.

As described in the poster, a unique feature of the NALA trial was the inclusion of patients with leptomeningeal disease (LMD), two of whom were treated with N+C with good outcomes (progression after 5.6 and 9.8 months, and OS times of 17.4 and 19.8 months, respectively). One patient with LMD

received L+C and had disease progression after 4.3 months and an OS of 6.5 months.

The safety profile in patients with CNS metastases at baseline was consistent with that observed in the overall NALA safety population. Diarrhea, nausea, vomiting, and palmar-plantar erythrodysesthesia syndrome were the most common adverse events. Common CNS adverse events (grade 1-4) included headache (N+C, 18% vs L+C, 29%), dizziness (18% vs. 16%), hemiparesis (4% vs. 4%), seizure (4% vs. 4%), and gait disturbance (0% vs. 8%).

Cristina Saura, M.D., Ph.D., Head of Breast Cancer Unit, Vall d'Hebrón University Hospital, said, "The data suggest an association between neratinib and improved PFS and CNS outcomes in patients with CNS metastases from HER2-positive metastatic breast cancer. These findings are consistent with three other prospective studies."

Alan H. Auerbach, Chief Executive Officer and President of Puma, added, "CNS metastases from HER2-positive breast cancer present a clinical challenge due to the limited availability of effective treatments. These findings from the NALA trial add to the growing body of data on the efficacy of neratinib in patients with HER2 positive metastatic breast cancer that has metastasized to the brain and may suggest a role for neratinib as a systemic treatment option in the management of patients with HER2-positive brain metastases following antibody-based HER2-directed therapies."

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) 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

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