News Release

Puma Biotechnology Presents Data from the Neratinib Arm of the INSIGhT Trial at the 2021 SNO Annual Meeting

LOS ANGELES, Calif., Nov. 20, 2021 – Puma Biotechnology, Inc. (Nasdaq: PBYI), a biopharmaceutical company, announced that investigators presented results from the neratinib arm of the Phase II Individualized Screening Trial of Innovative Glioblastoma Therapy (INSIGhT Trial) at the 2021 Society for Neuro-Oncology Annual Meeting. The presentation, entitled "Preliminary results of the neratinib arm in the Individualized Screening Trial of Innovative Glioblastoma Therapy (INSIGhT): a phase II platform trial using Bayesian adaptive randomization," was presented as an oral presentation in the Abstract Session: Clinical Trials II Session. A copy of the presentation is available on the Puma Biotechnology website.

The INSIGhT trial is a multisite investigator-initiated Phase II screening adaptive platform trial where patients with newly diagnosed unmethylated glioblastoma who are IDH R132H mutation negative and with genomic data available for biomarker grouping are eligible. All patients receive radiation therapy and temozolomide and then patients are randomized to receive either adjuvant temozolomide or adjuvant treatment with an experimental agent (neratinib). At the initiation of INSIGhT, three experimental arms, each with a proposed genomic biomarker, are tested simultaneously. Initial randomization is equal across arms. As the trial progresses, randomization probabilities adapt on the basis of accumulating results using Bayesian estimation of the biomarker-specific probability of treatment impact on progression-free survival. Treatment arms were allowed to drop because of low probability of treatment impact on overall survival. The primary endpoint of INSIGhT is overall survival (OS). Progression-free survival (PFS) analysis is used to influence randomization. For the neratinib arm of the trial, patients received 240 mg of neratinib daily as a single agent with mandatory loperamide prophylaxis.

For the neratinib arm of the trial, there were 149 patients in the intent-to-treat population, including 81 patients treated with neratinib and 68 patients in the control arm. For the intent-to-treat population, PFS was not significantly longer (HR 0.75; p=0.12, log rank test) with neratinib (median 6.0 months) versus the control arm (median 4.7 months) and there was no significant improvement in OS (HR 1.01; p=0.75) between neratinib (median 13.8 months) vs. the control arm (median 14.7 months). For patients with activation of the EGFR pathway, defined as patients with either *EGFR* amplification or mutation, PFS was significantly longer (HR 0.58; p=0.04, log rank test) with neratinib (median 6.3 months) vs. the control arm (median 4.6 months); however, there was no significant improvement in overall survival (HR 0.97; p= 0.94) between neratinib (median 14.4 months) vs. the control arm (median 15.3 months).

Neratinib was generally well tolerated in the trial and toxicities for neratinib were similar to that previously described. For the 81 patients treated with neratinib, there were 6 cases (7.4%) of grade 3 diarrhea and no cases of grade 4 diarrhea. No new toxicity signals were identified in the trial.

Isabel Arrillaga-Romany, MD, PhD, Director of Neuro-Oncology Clinical Trials at Mass General Cancer Center, an investigator on the trial who presented the data at SNO, said, "Although preliminary results did not achieve the primary endpoint, subgroup analyses demonstrated improved PFS in patients with EGFR activation and a non-significant trend toward improved overall survival in patients with EGFRVIII mutations, which could warrant further investigation. Additionally, we are very pleased that this trial reinforced feasibility of randomized Bayesian adaptive platform trials for newly diagnosed glioblastoma."

Alan H. Auerbach, Chief Executive Officer and President of Puma, added, "We would like to thank the INSIGHT trial investigators and the patients for their participation in the trial. This is the first data demonstrating an effect of neratinib in EGFR amplified or mutated glioblastoma. While we are not looking to pursue further clinical investigations of neratinib in this indication, we are evaluating the potential to develop a backup compound HKI-357, which has preclinically demonstrated better EGFR activity, in this indication."

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 $\geq$ 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.

Forward-Looking Statements

This press release contains forward-looking statements that involve risks and uncertainties that could cause Puma's actual results to differ materially from the anticipated results and expectations expressed in these forward-looking statements. These statements are based on current expectations, forecasts and assumptions, and actual outcomes and results could differ materially from these statements due to a number of factors, which include, but are not limited to, any adverse impact on Puma's business or the global economy and financial markets, generally, from the global COVID-19 pandemic, and the risk factors disclosed in the periodic and current reports filed by Puma with the Securities and Exchange Commission

from time to time, including Puma's Annual Report on Form 10-K for the year ended December 31, 2020. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Puma assumes no obligation to update these forward-looking statements, except as required by law.

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