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# Puma Biotechnology Presents Results from Phase III NALA Trial of Neratinib in Patients with HER2-Positive Metastatic Breast Cancer at the ASCO 2019 Annual Meeting

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LOS ANGELES--(**BUSINESS WIRE**)--Puma Biotechnology, Inc. (Nasdaq: PBYI), a biopharmaceutical company, announced that results from the Phase III NALA trial of PB272 (neratinib) in patients with HER2-positive metastatic breast cancer who have failed two or more prior lines of HER2-directed treatments (third-line disease) in the setting of metastatic disease, were presented at the American Society of Clinical Oncology (ASCO) 2019 Annual Meeting in Chicago. "Neratinib + capecitabine versus lapatinib + capecitabine in patients with HER2+ metastatic breast cancer previously treated with  $\geq 2$  HER2-directed regimens: Findings from the multinational, randomized, phase III NALA trial," was presented as an oral presentation by Adam M. Brufsky, MD, PhD, Professor of Medicine, Co-Director, Comprehensive Breast Cancer Center, Magee Women's Hospital of the University of Pittsburgh Medical Center. Slides from the presentation are available on the Puma Biotechnology website.

The Phase III NALA trial is a randomized controlled trial of neratinib plus capecitabine versus Tykerb® (lapatinib) plus capecitabine in patients with third-line HER2-positive metastatic breast cancer. The trial enrolled 621 patients who were randomized (1:1) to receive either neratinib plus capecitabine or lapatinib plus capecitabine. The trial was conducted globally at sites in North America, Europe, Asia-Pacific and South America. The co-primary endpoints of the trial are centrally confirmed progression free survival (PFS) and overall survival (OS). An alpha level of 1% was allocated to the PFS and 4% allocated to OS. The study was to be considered positive if either of the co-primary endpoints was positive. Puma reached agreement with the U.S. Food and Drug Administration (FDA) under a Special Protocol Assessment (SPA) for the design of the Phase III clinical trial and the European Medicines Agency (EMA) also provided follow-on scientific advice (SA) consistent with that of the FDA regarding the Company's Phase III trial design and endpoints used in the trial.

For the primary analysis of centrally confirmed PFS, treatment with neratinib plus capecitabine resulted in a statistically significant improvement in centrally confirmed PFS (hazard ratio=0.76,  $p=0.0059$ ) compared to treatment with lapatinib plus capecitabine. Because the proportional hazard assumption did not hold, the statistical analysis plan for the NALA trial prespecified that a restricted means survival analysis at 24 months would be performed. In this prespecified analysis the mean PFS for the patients treated with neratinib plus capecitabine was 8.8 months and the mean PFS for the patients treated with lapatinib plus capecitabine was 6.6 months.

For the primary analyses of OS, neratinib plus capecitabine resulted in an improvement in OS that trended positively in favor of the neratinib plus capecitabine arm of the study (hazard ratio = 0.88,  $p=0.21$ ). The median OS for the patients treated with neratinib plus capecitabine was 21.0 months and the median OS for the patients treated with lapatinib plus capecitabine was 18.7 months. In the prespecified restricted means analysis the mean OS at 48 months for the patients treated with neratinib plus capecitabine was 24.0 months and the mean OS for the patients treated with lapatinib plus capecitabine was 22.2 months.

For the secondary endpoint of time to intervention for symptomatic central nervous system disease (also referred to as brain metastases), the results of the trial showed that treatment with neratinib plus capecitabine led to an improvement over the combination of lapatinib plus capecitabine. The overall cumulative incidence of CNS metastases was 22.8% for the neratinib plus capecitabine arm and 29.2% for the lapatinib plus capecitabine arm ( $p=0.043$ , descriptive). For the secondary endpoint of duration of response, neratinib plus capecitabine treatment resulted in a longer duration of response compared to lapatinib and capecitabine treatment, with a median response of 8.54 months compared to a median response of 5.55 months (HR = 0.495,  $p = 0.0004$ , descriptive).

Treatment-emergent adverse events (TEAEs) were similar between arms: TEAEs leading to neratinib/lapatinib discontinuation were lower with neratinib (10.9%) than with lapatinib (14.5%). There was a higher rate of grade 3 diarrhea with neratinib plus capecitabine compared to lapatinib plus capecitabine (24.4% vs 12.5%); however, the discontinuations due to diarrhea (neratinib plus capecitabine: 2.6%, lapatinib plus capecitabine: 2.3%) were similar in both arms.

Puma plans to submit its New Drug Application to the U.S. Food and Drug Administration based on the Phase III NALA trial results in the second quarter/third quarter of 2019.

"Patients with HER2 positive metastatic breast cancer who have progressed on two or more prior treatments continue to need additional treatment options," said Adam M. Brufsky, MD, PhD, Professor of Medicine, Co-Director, Comprehensive Breast Cancer Center, Magee Women's Hospital of the University of Pittsburgh Medical Center. "The results of the Phase III NALA trial are promising not only for a significant PFS improvement and a trend toward an OS improvement, but also for the

potential to prevent progression of CNS metastases, which is a growing concern in HER2 positive metastatic breast cancer.”

Alan H. Auerbach, Chief Executive Officer and President of Puma Biotechnology, said, “We are highly encouraged by these results from the NALA trial with the combination of neratinib plus capecitabine in patients with HER2-positive metastatic breast cancer who have failed two or more prior lines of HER2-directed treatments. We look forward to working with the regulatory authorities in the hope of bringing another potential treatment option to patients with HER2-positive metastatic breast cancer as soon as possible.”

### **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 three drug candidates — PB272 (neratinib, oral), PB272 (neratinib, intravenous) and PB357. Neratinib, oral was approved by the U.S. Food and Drug Administration in July 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. NERLYNX was granted marketing authorization by the European Commission in September 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](http://www.pumabiotechnology.com).

### **Forward-Looking Statements**

This press release contains forward-looking statements, including statements regarding anticipated timing for submissions with regulatory authorities. All forward-looking statements 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, 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, 2018. 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.

### **Language:**

English

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