Published on *Puma Biotechnology Investor Center* (https://investor.pumabiotechnology.com) on 9/4/18 5:03 am PDT

European Commission Grants Marketing Authorisation for Puma Biotechnology's NERLYNX® (neratinib) for Extended Adjuvant Treatment of Hormone Receptor Positive HER2-Positive Early Stage Breast Cancer

Release Date:
Tuesday, September 4, 2018 5:03 am PDT

Terms:

Dateline City:
LOS ANGELES

- *Neratinib becomes the first anti-HER2 treatment to be EC-approved as extended adjuvant therapy for early stage hormone receptor positive HER2-positive breast cancer following adjuvant trastuzumab-based therapy*
- *Treatment with neratinib in the approved European indication resulted in a 51% reduction in the risk of invasive disease recurrence or death versus placebo after patients completed one year of therapy following a trastuzumab-based regimen*
- *Neratinib addresses an unmet medical need, as up to 25% of HER2-positive early stage breast cancer patients treated with trastuzumab-based adjuvant treatment experience a recurrence*

LOS ANGELES--(BUSINESS WIRE)--Puma Biotechnology, Inc. (Nasdaq:PBYI) announced that the European Commission (EC), has granted marketing authorisation for *NERLYNX® (neratinib) 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 the completion of prior adjuvant trastuzumab based therapy.*

EC approval was based on the Phase III ExteNET trial, a multicenter, randomized, double-blind, placebo-controlled trial of neratinib following adjuvant trastuzumab treatment. Patients (n=2,840) with early stage HER2-positive breast cancer and within two years of completing adjuvant trastuzumab were randomized to receive either neratinib (n=1420) or placebo (n=1420) for one year.

The results of the ExteNET trial demonstrated that after two years of follow-up, for patients with hormone receptor positive, HER2-positive early stage breast cancer patients who were treated within one year after the completion of trastuzumab based adjuvant therapy, invasive disease-free survival (iDFS) was 95.3% in the patients treated with neratinib compared with 90.8% in those receiving placebo (hazard ratio = 0.49; 95% CI: (0.30, 0.78); p=0.002)

The most common adverse reactions (>5%) were diarrhea, nausea, abdominal pain, fatigue, vomiting, rash, stomatitis, decreased appetite, muscle spasms, dyspepsia, AST or ALT increase, nail disorder, dry skin, abdominal distention, weight loss, and urinary tract infection. The most common adverse reaction leading to discontinuation was diarrhea, which was observed in 16.8% of neratinib-treated patients. Hepatotoxicity or increases in liver transaminases led to drug discontinuation in 1.7% of neratinib-treated patients.

"Reducing the risk of disease recurrence remains a need for patients, despite advances in the treatment of early stage HER2-positive breast cancer," said Puma Biotechnology CEO and President Alan H. Auerbach. "We are pleased to bring this new medicine to patients in Europe and would like to express our appreciation to the patients, caregivers and physicians who contributed to the neratinib clinical development program and, more specifically, the ExteNET trial. We are committed to continuing to expand NERLYNX accessibility to patients worldwide. We expect NERLYNX to be commercially available in Europe in 2019, beginning with our launch in Germany during the first half of 2019 and followed by additional countries throughout Europe in the second half of 2019."

The approval of NERLYNX by the European Commission follows the positive opinion issued by the Committee for Medicinal Products for Human Use of the European Medicines Agency in June 2018.

Neratinib was approved by the U.S. Food and Drug Administration (FDA) in July 2017 for the extended adjuvant treatment of adult patients with early stage HER2-positive breast cancer following adjuvant trastuzumab-based therapy, and is marketed in the United States as NERLYNX® (neratinib) tablets.

About HER2-Positive Breast Cancer

Approximately 20 to 25 percent of breast cancer tumors over-express the HER2 protein. 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 returning after surgery, up to 25% of patients treated with trastuzumab experience recurrence.

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 is a registered trademark of Puma Biotechnology, Inc.

Important EU NERLYNX ® (neratinib) Safety Information

All suspected adverse reactions should be reported in accordance with the national reporting system.

The adverse reactions described in this section were identified in the randomized Phase 3 clinical trial (n=2840). The most common adverse reactions of any grade were diarrhoea (93.6%), nausea (42.5%), fatigue (27.3%), vomiting (26.8%), abdominal pain (22.7%), rash (15.4%), decreased appetite (13.7%), abdominal pain upper (13.2%), stomatitis (11.2%), and muscle spasms (10.0%).

The most common Grade 3-4 adverse reactions were diarrhoea (Grade 3, 36.9% and Grade 4, 0.2%) and vomiting (Grade 3, 3.4% and Grade 4, 0.1%).

Adverse reactions reported as serious included diarrhoea (1.9%), vomiting (1.3%), dehydration (1.1%), nausea (0.5%), alanine aminotransferase increased (0.4%), aspartate aminotransferase increased (0.4%), abdominal pain (0.3%), fatigue (0.3%) and decreased appetite (0.2%).

For full European prescribing information, please refer to the NERLYNX (neratinib) Summary of Product Characteristics on the European Medicines Agency website (http://www.ema.europa.eu/ema/).

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

NERLYNX® (neratinib) tablets, for oral use

INDICATIONS AND USAGE: NERLYNX is a kinase inhibitor indicated for the extended adjuvant treatment of adult patients with HER2 overexpressed/amplified breast cancer, to follow adjuvant trastuzumab-based therapy.

CONTRAINDICATIONS: None

WARNINGS AND PRECAUTIONS:

• **Diarrhea:** Aggressively manage diarrhea occurring despite recommended prophylaxis 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 inpatients 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 (≥ 5%) were diarrhea, nausea, abdominal pain, fatigue, vomiting, rash, stomatitis, decreased appetite, muscle spasms, dyspepsia, AST or ALT increase, nail disorder, dry skin, abdominal distention, epistaxis, weight decreased and urinary tract infection.

To report SUSPECTED ADVERSE REACTIONS, contact Puma Biotechnology, Inc. at 1-844-NERLYNX (1-844-637-5969) and www.NERLYNX.com 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 (PPI) and H2-receptor antagonists. Separate NERLYNX by 3 hours after antacid dosing.
- Strong or moderate CYP3A4 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 health care 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.

The recommended dose of NERLYNX is 240 mg (six 40 mg tablets) given orally once daily with food, continuously for one year. Antidiarrheal prophylaxis should be initiated with the first dose of NERLYNX and continued during the first 2 months (56 days) of treatment and as needed thereafter.

Further information about Puma Biotechnology can be found at www.pumabiotechnology.com.

Forward-Looking Statements

This press release contains forward-looking statements, including statements regarding the worldwide expansion of NERLYNX. All forward-looking statements involve risks and uncertainties that could cause the Company'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 the Company with the Securities and Exchange Commission from time to time, including the Company's Annual Report on Form 10-K for the year ended December 31, 2017 and its Quarterly Report on Form 10-Q for the quarter ended June 30, 2018. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. The Company assumes no obligation to update these forward-looking statements, except as required by law.

Language:
English

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