



Published on *Puma Biotechnology Investor Center* (<https://investor.pumabiotechnology.com>) on 6/1/15 8:25 am PDT

Puma Biotechnology Announces Phase III Trial of PB272 in Extended Adjuvant Breast Cancer (ExteNET Trial) Demonstrates Statistically Significant Improvement in Disease Free Survival

Release Date:

Monday, June 1, 2015 8:25 am PDT

Terms:

Dateline City:

LOS ANGELES

LOS ANGELES--([BUSINESS WIRE](#))--Puma Biotechnology, Inc. (NYSE: PBYI), a development stage biopharmaceutical company, announced the presentation of positive results from the Phase III clinical trial of Puma's investigational drug PB272 (neratinib) for the extended adjuvant treatment of breast cancer (ExteNET trial). The ExteNET trial is a double-blind, placebo-controlled, Phase III trial of neratinib versus placebo after adjuvant treatment with trastuzumab (Herceptin) in women with early stage HER2-positive breast cancer. The data was presented today in an oral presentation at the American Society of Clinical Oncology (ASCO) 2015 Annual Meeting in Chicago, Illinois.

The ExteNET trial randomized 2,840 patients in 41 countries with early-stage HER2-positive breast cancer who had undergone surgery and adjuvant treatment with trastuzumab. After completion of adjuvant treatment with trastuzumab, patients were randomized to receive extended adjuvant treatment with either neratinib or placebo for a period of one year. Patients were then followed for recurrent disease, ductal carcinoma in situ (DCIS), or death for a period of two years after randomization in the trial.

The patient characteristics in the trial were well balanced between the neratinib and placebo arms of the trial. For the 1,420 patients in the neratinib arm of the trial, 1,085 (76.4%) were node positive while for the 1,420 patients in the placebo arm of the trial, 1,084 (76.3%) were node positive. Additionally, in the neratinib arm of the trial, 816 (57.5%) patients were hormone receptor positive, and in the placebo arm of the trial, 815 (57.4%) patients were hormone receptor positive. The median time from the last trastuzumab dose to entry into the trial was 4.4 months for the neratinib-treated patients and 4.6 months for the placebo-treated patients.

The safety results of the study showed that the most frequently observed adverse event for the neratinib-treated patients was diarrhea, with approximately 39.9% of the neratinib-treated patients experiencing grade 3 or higher diarrhea (1 (0.1%) patient had grade 4 diarrhea). Patients who received neratinib in this trial did not receive any prophylaxis with antidiarrheal agents to prevent the neratinib-related diarrhea. Puma's recently reported clinical data from several trials have demonstrated that the use of high dose prophylactic loperamide greatly reduces the rate of grade 3 diarrhea with neratinib, with grade 3 diarrhea rates ranging from 0-17% in studies in which high dose loperamide prophylaxis was used. In all of its current ongoing studies Puma is instituting the use of high dose loperamide for the first cycle of treatment in order to continue to reduce the neratinib-related diarrhea.

The primary endpoint of the trial was invasive disease free survival (DFS). The results of the trial demonstrated that treatment with neratinib resulted in a 33% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.67, $p = 0.009$). The 2-year DFS rate for the neratinib arm was 93.9% and the 2-year DFS rate for the placebo arm was 91.6%.

The secondary endpoint of the trial was disease free survival including ductal carcinoma in situ (DFS-DCIS). The results of the trial demonstrated that treatment with neratinib resulted in a 37% reduction of risk of disease recurrence including DCIS or death versus placebo (hazard ratio = 0.63, $p = 0.002$). The 2-year DFS-DCIS rate for the neratinib arm was 93.9% and the 2-year DFS-DCIS rate for the placebo arm was 91.0%.

As an inclusion criteria for the ExteNET trial, patients needed to have tumors that were HER2 positive using local assessment. In addition, as a pre-defined subgroup in the trial, patients had centralized HER2 testing performed on their tumor as well. To date, centralized HER2 testing has been performed on 1,704 (60%) of the patients in the ExteNET trial, and further central testing on available samples is currently ongoing. For the 1,463 patients whose tumor was HER2 positive by central confirmation, the results of the trial demonstrated that treatment with neratinib resulted in a 49% reduction of risk of invasive disease recurrence or death versus placebo (hazard ratio = 0.51, $p = 0.002$). The 2-year DFS rate for the centrally confirmed patients in the neratinib arm was 94.7% and the 2-year DFS rate for the centrally confirmed patients in the placebo arm was 90.6%. For the patients in the trial whose tumor was HER2 positive by central confirmation, the results of the trial demonstrated that treatment with neratinib resulted in a 51% reduction of risk of disease recurrence including DCIS or death versus placebo (hazard ratio = 0.49, $p < 0.001$). The 2-year DFS-DCIS rate for the centrally confirmed patients in the neratinib arm was 94.7% and the 2-year DFS rate for centrally confirmed patients in the placebo arm was 90.2%.

For the pre-defined subgroup of patients with hormone receptor positive disease, the results of the trial demonstrated that treatment with neratinib resulted in a 49% reduction of risk of invasive disease recurrence or death versus placebo (hazard

ratio = 0.51, p = 0.001). The 2-year DFS rate for the neratinib arm was 95.4% and the 2-year DFS rate for the placebo arm was 91.2%. For the patients in the trial whose tumor was HER2 positive by central confirmation, the results of the trial demonstrated that treatment with neratinib resulted in a 75% reduction of risk of invasive disease recurrence or death (hazard ratio = 0.25, p < 0.001). The 2-year DFS rate for the centrally confirmed patients in the neratinib arm was 97.0% and the 2-year DFS rate for centrally confirmed patients in the placebo arm was 88.4%.

"While the use of trastuzumab in the adjuvant setting has led to a reduction in disease recurrence in patients with early stage HER2-positive breast cancer, there remains an unmet clinical need for further improvement in outcome in order to attempt to further reduce this risk of recurrence," said Professor Arlene Chan, medical oncologist at Mount Hospital and the Vice Chair of the Breast Cancer Research Centre WA. "The results of the ExteNET study demonstrate that we may be able to provide this type of improvement with neratinib to further help the patients with this disease."

"We are very pleased with the results of the ExteNET trial with neratinib. This represents the first trial with a HER2 targeted agent that has shown a statistically significant benefit in the extended adjuvant setting, which we believe provides a meaningful point of differentiation for neratinib in the treatment of HER2 positive breast cancer," said Alan H. Auerbach, Chief Executive Officer and President of Puma. "We are also intrigued by the activity in the hormone receptor positive subgroup of patients, which we believe may be the result of neratinib inhibiting the cross talk between the estrogen receptor and the HER2 receptor and which may help the tumor increase its sensitivity to endocrine therapy. We look forward to proceeding with the regulatory filing for neratinib for the extended adjuvant treatment of breast cancer currently anticipated in the first quarter of 2016."

Webcast

The Company will host a meeting and webcast to discuss the results of the Phase III ExteNET trial beginning at approximately 7:00 p.m. CDT (8:00 p.m. EDT) on Monday, June 1, 2015. The webcast will be accessible through the Investor Relations section of Puma's website at http://www.pumabiotechnology.com/ir_events.html and will be archived there for 30 days.

About Puma Biotechnology

Puma Biotechnology, Inc. is a development stage biopharmaceutical company that acquires and develops innovative products for the treatment of various forms of cancer. The Company focuses on in-licensing drug candidates that are undergoing or have already completed initial clinical testing for the treatment of cancer and then seeks to further develop those drug candidates for commercial use. The Company is initially focused on the development of PB272 (oral neratinib), a potent irreversible tyrosine kinase inhibitor, for the treatment of patients with HER2-positive breast cancer and patients with non-small cell lung cancer, breast cancer and other solid tumors that have a HER2 mutation.

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

Forward-Looking Statements:

This press release contains forward-looking statements, including, but not limited to, statements regarding the development of our drug candidates and the anticipated timing of regulatory filings. All forward-looking statements included in this press release 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 fact that the Company has no product revenue and no products approved for marketing; the Company's dependence on PB272, which is still under development and may never receive regulatory approval; the challenges associated with conducting and enrolling clinical trials; the risk that the results of clinical trials may not support the Company's drug candidate claims; even if approved, the risk that physicians and patients may not accept or use the Company's products; the Company's reliance on third parties to conduct its clinical trials and to formulate and manufacture its drug candidates; the Company's dependence on licensed intellectual property; and the other risk factors disclosed in the periodic 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, 2014. 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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Ticker Slug:

Ticker: PBYI

Exchange: NYSE

ISIN:

US74587V1070

Source URL: <https://investor.pumabiotechnology.com/press-release/puma-biotechnology-announces-phase-iii-trial-pb272-extended-adjuvant-breast-cancer-ext>