



Published on *Puma Biotechnology Investor Center* (<https://investor.pumabiotechnology.com>) on 4/20/16 6:15 am PDT

## Puma Biotechnology's Neratinib Featured in Poster Presentations at the AACR Annual Meeting 2016

### Release Date:

Wednesday, April 20, 2016 6:15 am PDT

### Terms:

### Dateline City:

LOS ANGELES

LOS ANGELES--(BUSINESS WIRE)--Puma Biotechnology, Inc. (NYSE: PBYI), a biopharmaceutical company, announced that its drug candidate neratinib was highlighted in three poster presentations at the American Association for Cancer Research (AACR) Annual Meeting 2016. The AACR Annual Meeting was held at the Ernest N. Morial Convention Center in New Orleans from April 16 to April 20.

### ***Abstract Number 298: Amplification of mutant ERBB2 drives resistance to the irreversible kinase inhibitor neratinib in ERBB2-mutated breast cancer patients.***

On Sunday April 17<sup>th</sup>, preclinical data was presented from studies performed to identify possible mechanisms of acquired resistance to neratinib therapy in ERBB2-mutated breast cancers. Data from three breast cancer patients in the ongoing phase II SUMMIT basket study of neratinib in ERBB2-mutant cancers who progressed following initial benefit from neratinib treatment identified a common genomic alteration in their tumors. More specifically, targeted exome sequencing of biopsies collected at time of disease progression revealed increased copy number of the ERBB2-mutant allele. In addition, enhanced receptor activity in the ERBB2-mutant cells correlated with increased formation of ERBB2/ERBB3 dimers, activation of the PI3K/AKT pathway and in vivo tumorigenic potential. Combined ERBB2 and ERBB3 inhibition efficiently inhibited phosphorylation of ERBB2/ERBB3 and cell proliferation. These studies indicate that amplification of mutated ERBB2 may promote increased ERBB2/ERBB3 dimerization, ERBB3 activation, and subsequent downstream signaling activation and that dual ERBB2/ERBB3 blockade may be a potential strategy to delay or prevent resistance to neratinib in ERBB2-mutant breast tumors.

### ***Abstract Number 3140: Differential clonal selection in tumor tissue and cell-free DNA from a neratinib-treated refractory breast cancer patient harboring an activating ERBB2 (HER2) mutation.***

On Tuesday April 19<sup>th</sup>, data was presented from a patient who was part of the ongoing Copenhagen Prospective Personalized Oncology (CoPPO) research program. This program aims to offer patients with limited treatment options targeted treatments against actionable driver mutations that have been identified in circulating cell free DNA in patients by using whole exome sequencing. The poster presented data from a patient with metastatic HER2-negative and estrogen receptor (ER)-positive breast cancer (Luminal A) who had previously been exposed to seven lines of chemotherapy as well as ER antagonists and aromatase inhibitors. After examination by whole exome sequencing, an activating mutation in ERBB2 (S310Y) was found and consequently the patient was treated with neratinib through a compassionate use program. Neratinib caused a rapid decrease in the allelic frequency of ERBB2 (S310Y) cell free DNA after 2 days, with a continuous decline during the next 7 days. Consistent with this neratinib treatment effect, MRI scans showed regression of the liver metastases. After 5 months on neratinib, the patient progressed with the appearance of brain metastases, which were surgically removed and subject to whole exome sequencing. The ERBB2 mutation observed in the liver metastasis could not be identified in the brain metastases. However, more than 300 new variants were exclusively identified in the brain metastases, among these ERBB3 as well as new PIK3CA, and ESR1 mutations, that were not present in the pre-treatment cell free DNA samples. In conclusion, neratinib was able to suppress an activating ERBB2 mutation in a heavily pre-treated ER+ breast cancer patient. However, refractory tumor clones harboring ERBB3, PIK3CA and ESR1 mutations developed in brain. The poster indicated that combining neratinib with fulvestrant or inhibitors of the HER3/PI3K/AKT/mTOR pathway might prove beneficial to overcome potential resistance mechanisms to therapy.

### ***Abstract Number 4760: Efficacy of EGFR/HER2 dual-kinase inhibitors in PDX models harboring known and novel HER2-mutations.***

On Wednesday April 20<sup>th</sup>, preclinical studies to better understand effects of HER2 mutations were presented. Patient-derived xenograft (PDX) tumor models representing colorectal, ovary, pancreas and endometrial cancers were evaluated in vivo, testing the antitumor activity of neratinib, afatinib, lapatinib, trastuzumab and T-DM1 administered on standard treatment regimens. In vivo treatment with neratinib or afatinib resulted in tumor growth inhibition in some tested models including ST022 (HER2G366R/R678Q) ovary and ST204 (HER2A386D) pancreas and tumor regressions were reported with either agent in the ST427 (HER2V777L) colorectal line. Neratinib or afatinib were also found active in one each of four tested endometrial models. Lapatinib, trastuzumab and T-DM1 were inactive in all tested HER2-mutant models.

The abstracts of the three presentations described above are available online at:

<http://www.aacr.org/Meetings/Pages/MeetingDetail.aspx?EventItemID=63&DetailItemID=363#.Vusrr-lrKUK>.

### 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. The Company in-licenses the global development and commercialization rights to three drug candidates—PB272 (neratinib (oral)), PB272 (neratinib (intravenous)) and PB357. Neratinib is a potent irreversible tyrosine kinase inhibitor that blocks signal transduction through the epidermal growth factor receptors, HER1, HER2 and HER4. Currently, the Company is primarily focused on the development of the oral version of neratinib, and its most advanced drug candidates are directed at the treatment of HER2-positive breast cancer. The Company believes that neratinib has clinical application in the treatment of several other cancers as well, including non-small cell lung cancer and other tumor types that over-express or have a mutation in HER2.

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 that 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. 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

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**Source URL:** <https://investor.pumabiotechnology.com/press-release/puma-biotechnologys-neratinib-featured-poster-presentations-aacr-annual-meeting-2016>