Exelixis' Cabozantinib Shows Encouraging Clinical Activity in Patients With Metastatic Breast Cancer

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Tumor responses, bone scan resolution, and improvement of bone pain reported in phase 2 randomized discontinuation trial

SOUTH SAN FRANCISCO, Calif., Dec 07, 2011 (BUSINESS WIRE) --

Exelixis, Inc. (NASDAQ:EXEL) today reported positive preliminary data from a cohort of 45 patients with metastatic breast cancer (MBC) participating in the ongoing cabozantinib phase 2 randomized discontinuation trial (RDT). Sara Tolaney, M.D., M.P.H., Instructor in the Department of Medicine at Harvard Medical School and an Attending Physician, Medical Oncology, at Dana-Farber Cancer Institute, presented the data today in a poster session at the San Antonio Breast Cancer Symposium (Abstract #850463; Poster P1-17-10).

As of the October 15, 2011 data cut-off, 45 patients with previously treated estrogen receptor-positive, triple negative, or inflammatory MBC were enrolled in this cohort of the RDT and received cabozantinib at 100 mg per day. Bone metastases and visceral metastases were reported in 73% and 82% of patients, respectively. The patient population was heavily pretreated, with 87% having received at least 3 lines of prior therapy. This includes 20 patients (44%) previously treated with anti-VEGF pathway therapy.

Tumor response was evaluated by modified RECIST in 44 evaluable patients with measurable disease and at least 12 weeks of follow up, of which 6 (14%) had a confirmed partial response (PR), 26 (59%) had stable disease (SD), and 9 (20%) had progressive disease (PD). The Week 12 disease control rate (week 12 SD or PR) was 48%. Ten patients had available bone scans at baseline and at least one post-baseline bone scan and of these, 4 patients (40%) achieved partial resolution of their metastatic bone lesions on bone scan by week 12. Additionally, among 12 patients who entered the study with bone metastases and bone pain, 5 patients experienced improvement in pain at Week 6 or Week 12 per investigator report. Additionally, 2 of 11 patients who were taking narcotic medication for bone pain at baseline were able to decrease or discontinue these medications.

Cabozantinib inhibited osteoclast activity as assessed by serum NTx, a marker of bone resorption. In a subset of 16 patients with bone metastases, a detectable baseline serum NTx level, and at least one post-baseline assessment of serum NTx, 15 had decreases in serum NTx compared with baseline. These decreases were observed in bisphosphonate-treated and bisphosphonate-naïve patients.

"We are very encouraged by these data, which provide additional evidence for the potential utility of cabozantinib in treating solid tumors metastasizing to soft tissue and bone," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "Last month we announced the initiation of an investigator-sponsored trial of cabozantinib in MBC, and a Cooperative Research and Development Agreement with the National Cancer Institute's Cancer Therapy Evaluation Program to evaluate cabozantinib in a variety of indications. We expect that both of these initiatives will provide additional insight into the potential of cabozantinib to benefit the large and underserved metastatic breast cancer population."

Safety data are available for all 45 patients in the MBC cohort. The most frequently reported greater-than or equal to Grade 3 adverse events, regardless of causality, were: palmar-plantar erythrodyesthesia 13%, fatigue 11%, diarrhea 4%, constipation 4%, abdominal pain 4%, nausea 2%, decreased appetite 2%, and vomiting 2%. In general, the tolerability profile of cabozantinib observed in this cohort of MBC patients is consistent with that of other tyrosine kinase inhibitors.

The Significance of Bone Metastases in Metastatic Breast Cancer

Overall, bone is the most common site to which breast cancer metastasizes, and the site of first metastasis in approximately 50% of patients with breast cancer. Up to 75% of patients with metastatic breast cancer will develop bone metastases during the course of their disease and this number is even higher among those with hormone receptor-positive disease. For 20-25% of patients with metastatic breast cancer, especially those with hormone receptor-positive disease, bone will be their only site of metastatic involvement. Bone metastases in women with breast cancer are associated with considerable morbidity including hypercalcemia, increased fracture risk, need for surgery or radiotherapy, spinal cord compression and significant pain.

About Cabozantinib

Cabozantinib is a potent, dual inhibitor of MET and VEGFR2. Cabozantinib is an investigational agent that provides coordinated inhibition of metastasis and angiogenesis to kill tumor cells while blocking their escape pathways. The therapeutic role of cabozantinib is currently being investigated across several tumor types. MET is upregulated in many tumor types, thus facilitating tumor cell escape by promoting the formation of more aggressive phenotypes, resulting in metastasis. MET-driven metastasis may be further stimulated by hypoxic conditions in the tumor environment, which are often exacerbated by selective VEGF-pathway inhibitors. In preclinical studies, cabozantinib has shown powerful tumoricidal, antimetastatic and antiangiogenic effects, including:

- Extensive apoptosis of malignant cells
- Decreased tumor invasiveness and metastasis

- Decreased tumor and endothelial cell proliferation
- Blockade of metastatic bone lesion progression
- Disruption of tumor vasculature

About Exelixis

Exelixis, Inc. is a biotechnology company committed to developing small molecule therapeutics for the treatment of cancer. Exelixis is focusing its proprietary resources and development efforts exclusively on cabozantinib, its most advanced solely-owned product candidate, in order to maximize the therapeutic and commercial potential of this compound. Exelixis believes cabozantinib has the potential to be a high-quality, differentiated pharmaceutical product that can make a meaningful difference in the lives of patients. Exelixis has also established a portfolio of other novel compounds that it believes have the potential to address serious unmet medical needs. For more information, please visit the company's web site at www.exelixis.com.

Forward-Looking Statements

This press release contains forward-looking statements, including, without limitation, statements related to: the continued development and clinical, therapeutic and commercial potential of, and opportunities for, cabozantinib; the potential utility of cabozantinib in treating solid tumors metastasizing to soft tissue and bone; the goals and expected benefits and outcomes of the referenced investigator-sponsored trial of cabozantinib in MBC and Cooperative Research and Development Agreement; and the significance of bone metastases in MBC. Words such as "encouraging," "positive," "evidence," "potential," "expect," "will," "may," "believes," and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Exelixis' current plans, assumptions, beliefs and expectations. Forward-looking statements involve risks and uncertainties. Exelixis' actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation: risks related to the potential failure of cabozantinib to demonstrate safety and efficacy in clinical testing; Exelixis' ability to conduct clinical trials of cabozantinib sufficient to achieve a positive completion; the sufficiency of Exelixis' capital and other resources; the uncertain timing and level of expenses associated with the development of cabozantinib; the uncertainty of the FDA approval process; market competition; and changes in economic and business conditions. These and other risk factors are discussed under "Risk Factors" and elsewhere in Exelixis' quarterly report on Form 10-Q for the quarter ended September 30, 2011 and Exelixis' other filings with the Securities and Exchange Commission. Exelixis expressly disclaims any duty, obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in Exelixis' expectations with regard thereto or any change in events, conditions or circumstances on which any such statements are based.

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