Exelixis Announces Initiation of Phase 2 Investigator-Sponsored Trial of Cabozantinib in Women with Hormone Receptor-Positive Metastatic Breast Cancer and Bone Metastases

November 21, 2011

SOUTH SAN FRANCISCO, Calif., Nov 21, 2011 (BUSINESS WIRE) --

Exelixis, Inc. (NASDAQ:EXEL) today announced the initiation of an investigator-sponsored trial (IST) of cabozantinib in women with hormone receptor-positive breast cancer with bone metastases. This study is currently being conducted at the Massachusetts General Hospital Cancer Center under the direction of Michaela J. Higgins, M.D., MRCPI, (Principal Investigator) and José Baselga, M.D., Ph.D. (Chief of Hematology/Oncology and Associate Director of the Massachusetts General Hospital Cancer Center). This multi-center trial will also be conducted at the Memorial Sloan-Kettering Cancer Center under the direction of Monica Fornier, M.D. (Assistant Professor), and at Dana-Farber/Brigham and Women's Cancer Center and at Beth Israel Deaconess Medical Center under the direction of Sara M. Tolaney, M.D., M.P.H., and Steven Come M.D., respectively.

"The previously reported positive responses observed with cabozantinib in the breast cancer cohort of the phase 2 randomized discontinuation trial are encouraging and suggest that cabozantinib may have a positive impact on bone and soft tissue lesions in these patients. This new phase 2 trial should provide important insight into the potential role that cabozantinib could play in the treatment of hormone receptor-positive metastatic breast cancer," said Dr. Baselga.

"This phase 2 trial will enroll women with hormone receptor-positive breast cancer that has metastasized to the bone and whose disease has progressed after initial treatment for metastatic disease. Important therapeutic goals for the treatment of these women are to control the disease in the bone and in other tissues, decrease the risk of bone complications and pain, and delay the need for chemotherapy," said Dr. Higgins.

The open label, single arm trial is expected to enroll 50 women. Patients will receive cabozantinib once daily until disease progression or unacceptable toxicity, and will have their disease evaluated every 12 weeks. At baseline and at the 12-week assessment, subjects may undergo an optional bone biopsy to obtain tissue samples for correlative studies.

The primary endpoint of the trial is bone scan response rate determined by local institutions and by an independent radiology facility. Secondary endpoints are objective response rate, overall survival, progression-free survival, effects of cabozantinib on tumor markers and biochemical markers of bone turnover, skeletal-related events, and positron emission tomography (PET) response rate. The identification of surrogate biomarkers associated with the clinical activity of cabozantinib is included as an exploratory endpoint.

"The results from this IST will play a critical role in evaluating the clinical and commercial potential of cabozantinib in a large indication with substantial unmet medical need," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "With its primary endpoint of bone scan response rate, this trial will complement our first pivotal trial of cabozantinib in metastatic castration-resistant prostate cancer, the '306 trial, which will use bone scan response as a secondary endpoint and is expected to start by the end of the year. We believe that these two trials together should provide important further insights into the compound's activity on bone metastases, and build a foundation for further clinical inquiry. The initiation of this IST reflects a high level of enthusiasm for cabozantinib among oncologists, and we are pleased to support the efforts of Dr. Higgins and her colleagues."

Trial Rationale

Despite the availability of multiple treatment options for women with breast cancer, including surgery, radiation, hormonal therapy, and cytotoxic agents, there is still a significant unmet medical need for new treatment options. Hormonal therapy is the main option for patients with hormone receptor-positive breast cancer, although resistance to this treatment is often associated with ligand-independent activation of the estrogen receptor. Several studies have implicated MET, VEGFR2, and RET, targets of cabozantinib, in the onset, progression, metastasis, and recurrence of breast cancer.

The phase 2 randomized discontinuation trial of cabozantinib included 20 women with measurable metastatic breast cancer (ASCO 2011). Despite the typically poor prognosis of these patients, 2 of 20 experienced a partial response and 15 of 20 patients had tumor shrinkage as their best response with cabozantinib treatment. The responders had hormone receptor-positive disease. Three patients had baseline and on-treatment bone scans. Two of these patients had partial resolution of their lesions on bone scan, which was associated with a decrease in pain. The third patient had stable disease on bone scan.

Metastatic bone lesions from cancer as imaged on bone scan, FDG-PET scan or X-ray are not considered 'measurable' by the RECIST criteria. As a result, patients with bone-only or bone-predominant metastatic breast cancer without measurable disease have typically been excluded from clinical trials that include response measurements as a primary endpoint. However, such patients are common in the breast clinic and there is an unmet need to evaluate novel agents that may effectively treat their metastatic disease burden in bone as well as soft tissue sites.

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, and spinal cord compression.

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 design, conduct, goals and expected benefits and outcome of the IST; the potential success of the IST; the belief that previously reported positive responses observed with cabozantinib in the breast cancer cohort of the phase 2 randomized discontinuation trial are encouraging and suggest that cabozantinib may have a positive impact on bone and soft tissue lesions in these patients; the belief that the IST should provide important insight into the potential role that cabozantinib could play in the treatment of hormone receptor-positive metastatic breast cancer; the belief that the results from the IST will play a critical role in evaluating the clinical and commercial potential of cabozantinib in a large indication with substantial unmet medical need; the belief that the IST will complement the '306 trial; the plans to initiate the '306 trial and the timing thereof; the design, conduct and potential success of the '306 trial; the belief that the IST and the '306 trial together should provide important further insights into cabozantinib's activity on bone metastases, and build a foundation for further clinical inquiry; and the belief that initiation of the IST reflects a high level of enthusiasm for cabozantinib among oncologists. Words such as "will," "encouraging," "suggest," "may," "should," "could," "goals," "expected," "believe," 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.

SOURCE: Exelixis, Inc.

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