Exelixis' Cabozantinib Phase 2 Data Demonstrate Reduction in Bone Pain and Narcotic Analgesic Use in Patients with Previously Treated mCRPC

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48% of Patients with Moderate to Severe Pain at Baseline Achieve Durable Pain Response

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Nov. 12, 2011-- Exelixis, Inc. (NASDAQ:EXEL) today reported interim data on pain relief and related reduction in narcotic analgesic use with cabozantinib in castration-resistant prostate cancer (CRPC) patients with bone metastases. Howard Scher, M.D., chief of the Genitourinary Oncology Service at Memorial Sloan-Kettering Cancer Center, will present the data on November 14, 2011 in a poster session at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in San Francisco (Abstract B57). The poster will be available at http://www.exelixis.com/resources/presentations.

Study Results

Effects on pain intensity were measured prospectively in CRPC patients enrolled in the ongoing non-randomized expansion (NRE) cohort of the company's phase 2 randomized discontinuation trial. Sixty-seven patients were enrolled in the NRE cohort at least 6 weeks prior to data cutoff. All patients had bone metastases and 29 (43%) had measurable soft tissue disease. All patients had received prior docetaxel, 16 (24%) had received prior cabazitaxel, 15 (22%) had prior abiraterone or MDV3100, 4 (6%) had prior radionuclides, and 53 (79%) had previously been treated with bisphosphonates and/or denosumab. The median of the average worst pain at baseline determined by the Brief Pain Inventory (BPI) was 3.3 (range 0-7.9). Twenty-nine patients (43%) had moderate to severe pain as evidenced by average worst pain ≥4 at baseline, of which 27 (40%) were taking narcotics for pain. This latter population is the focus of the poster presentation.

Patient compliance with scheduled pain assessment was high; 67 patients completed a total of 268 of 295 (91%) pain assessment intervals. Twenty-nine patients with average worst pain ≥4 at baseline completed 115 of 126 (91%) pain assessment intervals.

Average worst pain improved in 28 of the 29 patients with average worst pain ≥4 at baseline, including 17 patients previously treated with docetaxel alone and 11 previously treated with docetaxel plus abiraterone and/or cabazitaxel. Three of these patients also previously received a systemic radionuclide therapy. Median best pain reduction from baseline was 46%, and 17 (59%) patients had at least a 30% decrease in average worst pain, including patients with 1-3 prior therapies. Of 25 patients with average worst pain ≥4 at baseline and a minimum of 12 weeks of follow-up, 12 (48%) had a durable ≥30% decrease in average worst pain relative to baseline at 2 completed time points which were at least 6 weeks apart. Onset of pain improvement was documented at the first pain assessment at 3 weeks in the majority of patients.

Of the 27 patients with average worst pain ≥4 and taking narcotics at baseline, 15 (56%) decreased their dose by at least 30%, including 7 (26%) who discontinued narcotic drugs completely, 4 (15%) had a stable dose (no change or change ≤30%), and 8 (30%) increased narcotic drug usage.

Pain relief (≥30% pain alleviation relative to baseline) was also accompanied by improved sleep and reduced interference with activities of daily living. Twelve patients with a ≥ 30% pain alleviation at week 12 had a 32% median improvement in sleep and 17% median improvement in interference with activities of daily living. Six patients not experiencing pain relief (<30% improvement in pain relative to baseline) had worsening median interference with sleep (16%) and activities of daily living (20%).

"The improvements in pain observed in this study are significant and suggest that cabozantinib could have an important role in the control of pain related to bone metastases in men with progressive CRPC," said Howard Scher, M.D., an investigator on the trial and chief of the Genitourinary Oncology Service at Memorial Sloan-Kettering Cancer Center. "Cancer-related pain is one of the most feared complications of prostate cancer and a predictor for increased mortality from the disease. New treatment options to relieve and control these debilitating symptoms are urgently needed."

"These prospectively collected data indicate that cabozantinib has a meaningful impact on pain and narcotic use in CRPC patients with bone metastases," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "These results importantly corroborate our initial investigator-reported data presented at this year's ASCO meeting, and suggest that cabozantinib can provide meaningful clinical benefit to patients suffering from pain and who have limited treatment options."

Patients in this single-arm study received a starting dose of 100 mg of cabozantinib daily. All patients in the NRE cohort had bone metastases, had received prior docetaxel chemotherapy, and could have received additional systemic therapy including cabazitaxel. Upon study entry, patients were required to have demonstrated objective evidence of disease progression during or within 6 months of docetaxel or cabazitaxel therapy.

Pain and Analgesic Medication Assessment

Pain was assessed using an Interactive Voice Response System comprising a 4-item questionnaire. The questionnaire assessed pain at its worst, disturbed sleep at its worst, and interference with activities of daily living, all within the previous 24 hours. These three items were measured using an 11-point rating scale (0-10), in which 0 indicates absence of the symptom. The worst pain intensity rating is derived from the BPI, which is widely used and accepted in contemporary pain studies (Atkinson et al., 2010). Changes in a patient's pain were assessed relative to their baseline pain score. Narcotic analgesic medication use was assessed by Patient Diary. All pain and analgesic medication use assessments were reported as the average daily score over a 7-day interval. The baseline assessment was taken within 14 days prior to the first dose of cabozantinib, while the post-baseline assessments were taken at Week 3, Week 6, and every 6 weeks thereafter. For the assessment interval to be considered valid, the patient had to complete a minimum of 4 of the 7 questionnaires administered during the 7-day assessment interval.

Changes in pain assessment were evaluated in patients with moderate-to-severe baseline pain, defined as an average daily worst pain score ≥4. Patients were evaluated for achieving a ≥30% decrease in average daily worst pain relative to baseline. Patients were also evaluated for changes in

narcotic analgesic use relative to baseline.

Safety and anti-tumor activity in the NRE cohort of CRPC patients will be summarized in a future presentation.

The Significance of Bone Metastases in CRPC

The primary cause of morbidity and mortality in patients with CRPC is metastasis to the bone, which occurs in about 90% of cases. Bone metastases cause local disruption of normal bone remodeling, with lesions generally showing a propensity for an osteoblastic (bone-forming) phenotype on imaging. These lesions often lead to increased skeletal fractures, spinal cord compression, and severe bone pain. Osteoblastic lesions are typically visualized in CRPC patients by bone scan, which detects rapid incorporation of 99mTc-labeled methylene-diphosphonate radiotracer into newly forming bone. In addition, increased blood levels of ALP and CTx, markers for osteoblast and osteoclast activity, respectively, are often observed in CRPC patients with bone metastases, and are associated with shorter overall survival.

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 http://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 reducing pain and narcotic analgesic use in CRPC patients with bone metastases; the need for new treatment options to relieve and control symptoms in CRPC patients with bone metastases; the potential for cabozantinib to provide a meaningful clinical benefit to patients suffering from pain; and the future presentation of safety and anti-tumor activity in the NRE cohort of CRPC patients. Words such as "demonstrate," "suggest," "could," "predictor," "can," “will,” "potential," “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.

Source: Exelixis, Inc.

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