Exelixis to Initiate Cabozantinib '306 Trial with Pain Endpoint in mCRPC

October 31, 2011

-Company plans to initiate '306 trial without an SPA-
-Company plans to initiate '307 overall survival trial in first half of 2012-
-Management to hold conference call at 6:00 p.m. EDT/3:00 p.m. PDT today-

SOUTH SAN FRANCISCO, Calif., Oct 31, 2011 (BUSINESS WIRE) --

Exelixis, Inc. (NASDAQ:EXEL) announced today that it has decided to initiate the '306 trial, the company's first phase 3 pivotal trial of cabozantinib in patients with metastatic castration-resistant prostate cancer (CRPC). Based on the regulatory feedback obtained from both the United States Food and Drug Administration (FDA) and European Medicines Agency (EMA) to date, the company has determined that pain will be the primary efficacy endpoint for the '306 trial. The company did not reach a timely agreement under a special protocol assessment (SPA) with the FDA on the proposed design and analysis of the '306 trial. The company expects to initiate the '306 trial by the end of 2011 and is no longer pursuing a SPA.

"We have had a valuable dialogue with the FDA on the '306 trial protocol and gained important insight throughout this process, including on the definition of pain response and that pain may be an appropriate efficacy endpoint in the phase 3 '306 trial if the treatment effect is pronounced. The FDA also stated that the trial can be conducted without a SPA under the normal regulatory framework," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. Moderate-to-severe bone pain is a major unmet medical need in patients with symptomatic metastatic CRPC. Based on advice from leading investigators and regulatory consultants, we believe it is in the best interests of both patients and Exelixis to initiate the trial as soon as possible. In addition, we also plan to initiate our '307 trial in metastatic CRPC patients with an overall survival endpoint in the first half of 2012. Both trials provide a compelling opportunity to differentiate cabozantinib from other agents if improvements in both the quality and quantity of life are achieved."

The double-blind '306 trial is designed to enroll 246 patients with CRPC metastatic to bone, who are suffering from moderate to severe bone pain despite optimized narcotic medication, and who have failed prior treatment with docetaxel and abiraterone in no particular order. The '306 trial will be conducted in English speaking regions including the United States, Canada and the United Kingdom.

Patients will be randomized 1:1 to receive either cabozantinib or mitoxantrone/prednisone.Alleviation of bone pain will be the primary endpoint, and will be measured by comparing the percentage of patients in the two treatment arms who achieve a pain response at week 9 that is confirmed at week 15. Prior to randomization on the study, patients will undergo a period during which their pain medication is optimized using one long-acting narcotic and one immediate-release narcotic medication. This optimization follows a standard approach defined in the National Comprehensive Cancer Network guidelines.

"This phase 3 trial builds on the extended phase 2 experience with cabozantinib in patients with metastatic CRPC that showed favorable effects on bone and soft tissue lesions, and in particular relief of bone metastasis-related pain, which can cause significant suffering for patients with the disease," said Howard I. Scher MD, Chief of the Genitourinary Oncology Service at Memorial Sloan-Kettering Cancer Center and contributor to the design of this study. "Effectively managing pain is a particular challenge for symptomatic patients in the metastatic setting. Cabozantinib has the potential to become an important agent in the treatment of CRPC that can impact multiple aspects of the disease."

Overall survival (OS) will be a secondary endpoint to demonstrate that there is no negative impact on survival for the cabozantinib arm. Bone scan response will be a secondary endpoint and will be evaluated by an independent radiology facility (IRF).

The company has previously communicated a comprehensive development plan and regulatory strategy in metastatic CRPC that includes a pivotal trial focused on overall survival, consistent with the FDA's feedback in connection with the SPA process related to the '306 trial. In that context, the company plans to initiate its phase 3 '307 trial in the first half of 2012. The '307 trial is expected to be a global trial powered to evaluate overall survival time comparing cabozantinib versus prednisone in patients who have failed prior docetaxel and abiraterone.

'306 Trial Details

Inclusion Criteria. In order to be considered for inclusion in the '306 trial, patients must have: CRPC that has metastasized to the bone; moderate to severe bone pain despite optimized narcotic medication; and investigator-assessed prostate cancer progression during or after docetaxel and abiraterone in no particular order. Patients may have received prior cabazitaxel therapy, but this is not required.

Cabozantinib Dosing. Patients in the cabozantinib arm will be dosed at 60 mg daily until the patient no longer receives clinical benefit. This dosing schedule is based on data from the phase 2 randomized discontinuation trial (RDT) of cabozantinib. In that trial, approximately 50% of patients receiving the 100 mg daily dose experienced dose reductions to 60 mg. The median time to dose reduction for CRPC patients in the RDT was approximately 30 days. Further dose reductions were much less frequent, and patients who had a dose reduction to 60 mg appeared to maintain their pain and tumor responses.

Definition of Pain Response. The definition of a response with respect to the bone pain endpoint is a greater-than or equal to 30% decrease from baseline in the average of the daily worst pain intensity collected over 7 days in week 9 and confirmed in week 15, with neither a concomitant increase in average daily dose of any narcotic pain medication, nor addition of any new narcotic pain medication.The worst pain intensity item, taken from the Brief Pain Inventory (BPI), is widely used in contemporary pain studies. It is considered to be a robust, reliable and sensitive measure of pain, as described by Atkinson et al in 2010.

Potential to Validate Bone Scan Response. Bone scan response will be assessed as a secondary endpoint. To be a bone-scan responder, patients

must have both a response on bone scan using computer aided detection methodology by independent radiology facility (IRF) and absence of soft tissue progression. A response per bone scan is defined as a greater-than or equal to 30% decrease in the lesion area of all bone lesions as compared with the baseline bone scan per IRF analysis.

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 with metastatic disease. 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 alkaline phosphatase (ALP) and crosslinked C-terminal telopeptides of type 1 collagen, markers for osteoblast and osteoclast activity, respectively, are often observed in CRPC patients with bone metastases, and elevated ALP in particular is associated with shorter overall survival.

Conference Call and Webcast Information

Exelixis' management will discuss the company's plans to initiate the '306 and '307 trials and feedback from the FDA through the company's SPA process during a conference call beginning at 6:00 p.m. EDT / 3:00 p.m. PDT today, Monday, October 31, 2011. To listen to a live webcast of the discussion, visit the Event Calendar page under Investors at www.exelixis.com.

An archived replay of the webcast will be available on the Event Calendar page under Investors at www.exelixis.com and via phone until 11:59 p.m. EST on November 30, 2011. Access numbers for the phone replay are: 1-888-286-8010 (domestic) and 1-617-801-6888 (international); the passcode is 87143958.

About Cabozantinib

Cabozantinib is a potent inhibitor of MET and VEGFR2 that inhibits tumor growth, metastasis and angiogenesis in preclinical models. MET is up-regulated in many tumor types, and promotes tumor cell survival, invasion and metastasis. Further up-regulation of MET occurs under hypoxic conditions, which are often exacerbated by VEGF-pathway inhibitors, promoting increased tumor cell invasion and metastases. The therapeutic role of cabozantinib is currently being investigated across several tumor types.

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; plans to initiate the '306 trial and the timing thereof; plans to initiate the '307 trial and the timing thereof; the belief that completion of the '306 and '307 trials may provide a compelling opportunity to differentiate cabozantinib from other agents by demonstrating improvements in both the quality and quantity of life; the design and conduct of the '306 and '307 trials; the potential success of the '306 and '307 trials; a potential regulatory submission for product approval and the FDA's response thereto; and the potential for cabozantinib to become an important agent in the treatment of CRPC that impacts multiple aspects of the disease. Words such as "plans," "design," "expected," "believe," "could," "may," "appropriate," "will," "compelling," "opportunity," "potential," 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.

Exelixis, Inc.
Charles Butler, 650-837-7277
Vice President, Investor Relations and Corporate Communications
cbutler@exelixis.com