Exelixis Initiates COMET-1 Pivotal Trial Focused on Overall Survival in Men With Advanced Prostate Cancer

May 30, 2012

-- Cabozantinib now being investigated in two phase 3 pivotal trials in prostate cancer --

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--May. 30, 2012-- Exelixis, Inc. (NASDAQ:EXEL) today announced the initiation of COMET-1, a phase 3 pivotal trial of cabozantinib in men with metastatic castration-resistant prostate cancer (mCRPC). The primary endpoint for COMET-1 is overall survival (OS) in mCRPC patients who have had disease progression after treatment with docetaxel and abiraterone acetate and/or MDV3100. Exelixis expects data from COMET-1 to be available in the first half of 2014.

“COMET-1 is a well-designed global study of a compound with the potential to address many of the unmet medical needs for men with mCRPC,” said Matthew R. Smith, M.D., Ph.D., director of the Genitourinary Malignancies Program at Massachusetts General Hospital Cancer Center and lead investigator for COMET-1. “The phase 2 studies of cabozantinib provide early evidence of impressive effects on measurable tumor, progression-free survival, bone scan response, pain alleviation, and circulating tumor cell (CTC) counts. Several of these measures, including reduction in pain and CTC counts, are associated with improved overall survival in mCRPC. If COMET-1 confirms these early findings and demonstrates a survival benefit, I believe cabozantinib could become an important new treatment option for men with mCRPC.”

COMET-1 is a double-blind, placebo-controlled phase 3 study that will include up to 240 international sites. The trial is designed to enroll 960 patients with mCRPC who have previously been treated with docetaxel, and abiraterone acetate and/or MDV3100. All patients will have bone metastases and there is no limit to the number or type of prior treatments. Patients will be randomized 2:1 to receive cabozantinib (60 mg daily, N=640) or prednisone (5 mg twice daily, N=320). Each arm will also receive placebo in order to account for the once-daily versus twice-daily dosing regimens of cabozantinib and prednisone. The trial has 90% power to detect a 25% reduction in the risk of death (HR = 0.75). The final analysis will be event driven, with 578 events required. A single interim analysis is planned after 387 events. The secondary endpoint is bone scan response as assessed by an independent radiology facility (IRF).

“The initiation of the COMET-1 trial, which is focused on demonstrating the potential for cabozantinib to improve overall survival in mCRPC patients, is an important milestone in the cabozantinib development program in prostate cancer,” said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. “A successful outcome for COMET-1 and for the ongoing COMET-2 pivotal trial would document the ability of cabozantinib to extend survival and to provide significant pain palliation in mCRPC, a distinct and differentiated profile that we believe provides the best opportunity to maximize cabozantinib’s clinical and commercial potential.”

Cabozantinib Clinical Trial Program

Cabozantinib is also currently being evaluated for its ability to reduce pain associated with bone metastases in the COMET-2 phase 3 trial in men with mCRPC. The compound also is the subject of a phase 3 pivotal trial in medullary thyroid cancer, the EXAM trial, for which positive top-line data was announced in October, 2011. In phase 1 and phase 2 trials, cabozantinib has also demonstrated clinical activity in multiple indications including ovarian cancer, breast cancer, differentiated thyroid cancer, metastatic melanoma, hepatocellular carcinoma, glioblastoma, renal cell carcinoma, and non-small cell lung cancer.

On May 3, 2012, Exelixis announced a broad expansion of the cabozantinib clinical development program under a Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute’s Cancer Therapy Evaluation Program, with the approval of the initial program of 13 proposed clinical trials under the agreement. The CRADA provides for funding for as many as 20 active clinical trials each year for a five-year period, which Exelixis believes will allow for broad expansion of the cabozantinib development program in a cost-efficient manner. When initiated, these trials will substantially increase the number of indications and disease settings in which cabozantinib is being investigated, and will aid in prioritizing the next set of pivotal trials. Exelixis also has an Investigator-Sponsored Trial program that is generating additional data on cabozantinib in a variety of treatment settings.

About Cabozantinib

Cabozantinib is a potent targeted therapy that inhibits 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 therapies for the treatment of cancer. Exelixis is focusing its proprietary resources and development efforts exclusively on cabozantinib (XL184), its most advanced 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, broadly-active, 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, many of which are being advanced by partners as part of collaborations. 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 design of, and expected availability of data from, the COMET-1 pivotal phase 3 trial in mCRPC; the belief that cabozantinib could become an important new treatment option for men with mCRPC; the potential success of the COMET-1 and COMET-2 pivotal phase 3 trials in mCRPC and the expected benefits thereof; the belief that cabozantinib has a distinct and differentiated profile in mCRPC that provides the best opportunity to maximize cabozantinib's clinical and commercial potential; the expansion of the cabozantinib development program; the plans and conduct of the parties to, and scope, goals and expected benefits of, CRADA; the design, conduct, goals and other expected benefits arising from the first program of approved trials under the CRADA; the planned initiation of the first program of approved trials under the CRADA; and the design, scope, conduct, goals and expected benefits and outcome of Exelixis' Investigator-Sponsored Trial program. Words such as "expects," "potential," "if," "demonstrates," "believe," "could," "will," "outcome," "opportunity," "expansion," 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 availability of data at the referenced times; 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; timely receipt of potential reimbursements, milestones, royalties and profits under Exelixis' collaborative agreements; Exelixis' ability to enter into new collaborations; 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 March 30, 2012 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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