



Interim Data for Cabozantinib 40 mg Dose Cohort in Metastatic Castration-Resistant Prostate Cancer Presented at ESMO 2012 Congress

September 30, 2012

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Sep. 30, 2012-- Exelixis, Inc. (NASDAQ:EXEL) today announced interim data from 51 patients with metastatic castration-resistant prostate cancer (CRPC) and bone metastases receiving a 40 mg daily dose of cabozantinib in an ongoing non-randomized expansion (NRE) cohort of a phase 2 randomized discontinuation trial. The data suggest that the 40 mg daily dose has similar clinical activity to the 100 mg daily dose previously reported from this trial for key parameters, including reduction of metastatic bone and soft tissue disease, and reduction of bone-related pain and narcotic use, with apparent improvement in adverse event rates and tolerability. Johann de Bono, M.D., Ph.D., leader of the prostate cancer targeted therapy team at The Institute of Cancer Research, London, and honorary consultant at The Royal Marsden NHS Foundation Trust, and an investigator on the trial, presented the data today in an oral presentation session on prostate cancer at the European Society for Medical Oncology (ESMO) 2012 Annual Meeting (Abstract #897O) in Vienna, Austria.

"The results presented today at ESMO are consistent with interim data previously reported for the 40 mg cohort of an ongoing investigator-sponsored trial evaluating low-dose cabozantinib in men with CRPC and bone metastases," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "The data suggest that the 40 mg daily dose has activity with respect to a number of key metrics, including bone and soft tissue responses, as well as changes in pain scores and narcotic use. Additionally, the 40 mg daily dose appears to be well-tolerated in patients with metastatic CRPC."

The interim results reported today include data from 51 men enrolled in the 40 mg NRE cohort of an ongoing phase 2 randomized discontinuation trial. All patients had bone metastases on bone scan and 41% had measurable soft tissue disease. All patients had received prior docetaxel, 67% had received prior abiraterone or enzalutamide (MDV3100), and 25% had received prior cabazitaxel. Bone-directed therapies such as zoledronic acid, denosumab, and radionuclides were used in 45%, 41% and 6% of patients, respectively. Seventy-one percent of patients had received at least 2 prior lines of therapy for CRPC. Clinically significant pain, defined as baseline pain score by Brief Pain Inventory (BPI) ≥ 4 , was present in 53% of patients, with 45% of these patients receiving chronic narcotic administration.

Bone Scan Response (BSR). Computer-assisted evaluation of bone scan lesion area (BSLA) was performed and response evaluated by an Independent Radiology Committee (IRC). An overall BSR rate (complete response + partial response) of 49% was observed, with another 29% of patients having stable disease, and 14% having a best response of progressive disease.

Initial results from ongoing efforts focused on documenting the direct impact of cabozantinib on tumor lesions in the bone of prostate cancer patients were presented, and suggest that cabozantinib's effects on bone scan may be linked to induction of tumor necrosis in bone metastases. In a patient with complete resolution of pelvic metastatic lesions on bone scan, diffusion-weighted magnetic resonance imaging (MRI) findings were consistent with tumor necrosis occurring within the bone metastases. Additional evidence for the tumor selective effect of cabozantinib on bone scans was also presented, based on an analysis of a patient with concurrent osteoarthritis. In this patient, near complete resolution of bone scan tracer uptake at sites of metastatic tumor lesions was observed, while bone scan tracer uptake was maintained at sites of osteoarthritis. To gain further insights into the effects of cabozantinib on bone lesions, there are other ongoing clinical trials using MRI, other imaging techniques, and bone-metastatic tumor biopsies.

Soft Tissue Response. Twenty-one patients had measurable soft tissue or visceral lesions at baseline and 19 patients had at least one post-baseline assessment. Evidence of tumor regression was seen in 79% of the 19 patients with at least one post-baseline assessment. Overall response by RECIST among 21 patients with at least baseline data was partial response in 10%, stable disease in 71%, and progressive disease in 10%. Soft tissue responses were independent of prior therapy.

Pain Palliation. In 26 patients with clinically significant baseline pain, the median maximal reduction in pain from baseline was 49%. A clinically significant reduction of pain, defined as a $\geq 30\%$ decrease in BPI pain score, was observed in 18 patients (69%). Fifty-four percent of patients decreased their use of narcotics, including one patient who discontinued narcotics. The majority of patients in whom these improvements were observed had received both prior docetaxel and prior abiraterone or enzalutamide.

Biomarkers. Improvements were also seen in circulating tumor cells (CTCs), and two markers of bone metabolism: cross-linked C-terminal telopeptides of type 1 collagen (CTX) and bone-specific alkaline phosphatase (BSAP). Substantial reductions in CTCs were observed regardless of prior therapy in patients with baseline CTC counts $\geq 5/7.5$ mL of blood and a week 6 and/or week 12 assessment. Twenty-six of 39 patients (67%) had a $\geq 30\%$ decrease in their CTC count, and 22% converted to < 5 CTCs at week 6. Median CTC change was a 70% decrease. Median change in CTx at Week 12 was a 31% reduction, and 50% of evaluable patients had decreased BSAP at Week 12 or later.

Progression-Free Survival (PFS). Analyses of PFS based on radiographic progression per IRC in soft tissue and/or bone included either the total population (N=51) or only patients who had received prior docetaxel and abiraterone (N=32). Median PFS was 4.1 months for both the total population and for patients who had previously received docetaxel and abiraterone. The median treatment duration was 4.7 months (range: 0.3 – 8.8+ months).

Adverse Events. The most frequently reported adverse events (AEs) of grade 3 or higher, regardless of causality, were: hypertension (14%), venous thrombosis (14%), fatigue (12%), decreased appetite (8%), and back pain (4%). No grade 5 AEs were reported. Only 25% of patients experienced a dose reduction due to an AE.

"The adverse event and clinical activity data observed with the 40 mg daily dose of cabozantinib support the design of the ongoing phase 3 trials," said Dr. de Bono. "Additionally, the MRI data suggest that cabozantinib's effect on bone metastases may involve tumor-specific cell death, which potentially would differentiate cabozantinib from purely bone-targeted agents. Additional studies in CRPC and other malignancies with high rates of bone

metastases are warranted.”

Data from the 100 mg daily dose of cabozantinib in the CRPC NRE cohort were most recently presented in June 2012 at the American Society of Clinical Oncology (ASCO) 2012 Annual Meeting (Abstract #4513).

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 BSAP 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 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. 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. Exelixis submitted a new drug application (NDA) for cabozantinib as a treatment for patients with progressive, unresectable, locally advanced, or metastatic medullary thyroid cancer to the United States Food and Drug Administration. The Prescription Drug User Fee Act (PDUFA) action date for the NDA is November 29, 2012.

About The Institute of Cancer Research

Scientists and clinicians at The Institute of Cancer Research (ICR) are working every day to make a real impact on cancer patients' lives. Through its unique partnership with The Royal Marsden Hospital and 'bench-to-bedside' approach, the ICR is able to create and deliver results in a way that other institutions cannot. Together the two organisations are rated in the top four cancer centres globally.

The ICR has an outstanding record of achievement dating back more than 100 years. It provided the first convincing evidence that DNA damage is the basic cause of cancer, laying the foundation for the now universally accepted idea that cancer is a genetic disease. Today it leads the world at isolating cancer-related genes and discovering new targeted drugs for personalised cancer treatment.

As a college of the University of London, the ICR provides postgraduate higher education of international distinction. It has charitable status and relies on support from partner organisations, charities and the general public.

The ICR's mission is to make the discoveries that defeat cancer.

For more information visit www.icr.ac.uk

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 (formerly known as XL184), its most advanced product candidate, in order to maximize the therapeutic and commercial potential of this compound. 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 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 cabozantinib; the significance of the referenced data; and potential future regulatory approval of cabozantinib and the timing thereof. Words such as “suggest,” “appears,” “may,” “evidence,” “further,” “support,” “potentially,” “would,” “warranted,” 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 June 29, 2012, filed with the Securities and Exchange Commission (SEC) on August 2, 2012, and Exelixis' other filings with the SEC. 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