Cabozantinib (XL184) Phase 2 Data Demonstrate Encouraging Clinical Activity in Patients with Castration-Resistant Prostate Cancer

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High rates of complete or partial bone scan resolution (85%), pain relief, improvements in hemoglobin, and tumor regression observed

SOUTH SAN FRANCISCO, Calif., Feb 17, 2011 (BUSINESS WIRE) -- Exelixis, Inc. (NASDAQ:EXEL) today reported updated interim data from the cohort of patients with metastatic castration-resistant prostate cancer (CRPC) treated with cabozantinib (XL184) in an ongoing phase 2 adaptive randomized discontinuation trial. The data support the findings that cabozantinib reduces or stabilizes metastatic bone lesions in nearly all patients evaluable by bone scan, reduces bone pain and narcotic analgesic medication and results in an increase in hemoglobin in patients with anemia. The data also suggest that cabozantinib shows an encouraging early signal of durable clinical benefit in both docetaxel-naïve and pretreated patients.

David C. Smith, M.D., Professor, Departments of Internal Medicine and Urology at the University of Michigan, presented the data on Thursday, February 17 in a poster session at the American Society of Clinical Oncology's 2011 Genitourinary Cancers Symposium (Abstract #127) in Orlando, Florida.

As of the January 27, 2011 cut-off date, accrual in this cohort was complete at 168 patients, randomization was halted, and randomized patients were unblinded based on an observed high rate of clinical activity.

The efficacy-evaluable population for tumor response per mRECIST includes 100 patients with at least 12 weeks of follow-up. The bone scan evaluable population includes 62 patients with a baseline bone scan, evidence of bone metastasis, and at least 1 post-baseline assessment. All patients had measurable soft tissue disease, approximately half (47%) had evidence of visceral disease (e.g., liver or lung), and approximately half (47%) were docetaxel-pretreated.

High Rates of Complete or Partial Bone Scan Resolution

Of 62 patients evaluable by bone scan, 53 (85%) achieved either complete or partial resolution of metastatic lesions on bone scan by independent radiologist review. Eight other patients (13%) had stable disease (SD) on bone scan, resulting in an overall rate of disease control in bone of 98% (61/62). Only one patient (2%) had progressive disease as their best assessment. High rates of bone scan resolution were observed in both docetaxel-pretreated and docetaxel-naïve subgroups.

Increase in Hemoglobin in Patients with Anemia

CRPC patients with bone metastases frequently experience anemia, which in prior studies has been associated with a worse prognosis. In this study, the majority of patients with anemia (hemoglobin < 11g/dL) had sustained treatment-emergent increases in hemoglobin as compared with baseline. The median maximum rise in hemoglobin in anemic patients (Hb < 11 g/dL) was 2.2 g/dL (range, 0.6-3.5).

Preliminary Progression-Free Survival Results are Encouraging

The median follow-up for all 100 patients is 3.8 months (range, 0.7 to 15.2 months). In the Randomized Discontinuation Phase, a total of 31 patients with SD at Week 12 were randomized to either placebo or cabozantinib. The median progression free survival (PFS), assessed by investigators, is 40 days (95% Confidence Interval: 37, 82 days) for the placebo group (n=17), while median PFS data for the cabozantinib group (n=14) are not yet mature with a censoring rate of 79%.

For the overall population, excluding those randomized to placebo, the median PFS data for patients continuously treated with cabozantinib are not yet mature with censoring rates of 85% and 79% for the docetaxel-naïve and -pretreated populations, respectively. However, PFS appears to be independent of prior docetaxel therapy, which historically has conveyed a worse prognosis.

Improvement in Symptomatic Bone Pain

Data on bone pain and narcotic use, as assessed by the investigator, were collected retrospectively. A total of 43 patients had bone metastases and bone pain reported at baseline, and at least one post-baseline assessment of pain status. Of these patients, 26 (60%) had pain improvement at either Week 6 or 12. Narcotic analgesic medication was required at baseline for control of bone pain in 28 patients assessable for post-baseline review of narcotic consumption. Thirteen of 28 (46%) patients were able to decrease or discontinue narcotic medication for bone pain.

"These data are very exciting and reinforce the novel and differentiated profile of cabozantinib relative to other prostate cancer agents. Cabozantinib was effective at reducing or stabilizing metastatic bone lesions in nearly all patients evaluable by bone scan. Further, bone scan resolution observed in patients from this cohort is accompanied by important reductions of bone pain and narcotic analgesic medication as well as a sustained increase in hemoglobin in patients with anemia. Finally, cabozantinib shows an encouraging early signal of durable clinical benefit in both docetaxel naïve and pretreated patients," said Michael Morrissey, PhD, president and CEO of Exelixis, Inc. "These interim data give us further confidence in our comprehensive development plan for cabozantinib in CRPC that includes three potential pivotal trials, the first focused on a composite endpoint that incorporates bone scan resolution and improvement in bone pain, and future trials evaluating overall survival and bone metastasis prevention in CRPC

patients."

Reduction and Stabilization of Soft Tissue Lesions Observed in the Majority of Patients

One hundred patients were evaluable for response by mRECIST. The overall Week-12 disease control rate (SD + partial response (PR)) was 74%. Tumor shrinkage was observed in 61 of 91 patients (67%) with measurable soft-tissue metastatic lesions and at least one post-baseline scan. To date, 6 of 100 patients (6%) evaluable by mRECIST achieved a confirmed PR. SD was reported in 82 patients (82%), and 2 other patients have had unconfirmed PRs awaiting confirmation. Prostate-specific antigen (PSA) changes were observed to be independent of reduction or stability of tumor target lesions, resolution of bone lesions on bone scan, and changes in bone pain.

Cabozantinib Affects Markers of Bone Formation and Resorption in CRPC Patients, Regardless of Prior Bisphosphonate Therapy

Alkaline phosphatase (ALP) and type I collagen C-telopeptides (CTx), which are markers of osteoblast (bone formation) and osteoclast (bone resorption) activity, respectively, are often elevated in patients with bone metastases. Reductions in levels of CTx and ALP have been correlated in the past with a reduced risk of skeletal-related events and mortality, respectively. Of 16 patients treated with cabozantinib who had ALP levels at least twice the upper limit of normal, known bone metastases, and at least 12 weeks of follow-up, 15 had decreases in ALP. Similarly, 42 of 48 patients with known metastases experienced a decrease in CTx, regardless of prior bisphosphonate status. ALP and CTx levels decreased from baseline by approximately 60% at Weeks 12 and 24, respectively.

"Cabozantinib has to date shown impressive activity in patients with metastatic CRPC. The interim data presented today clearly indicate that cabozantinib positively impacts both soft tissue and bone disease and appears to alleviate associated symptoms," said David C. Smith, M.D., Professor, Departments of Internal Medicine and Urology at the University of Michigan. "Cabozantinib may offer a unique approach to the treatment of prostate cancer, particularly due to its effect on metastatic bone lesions, which are a key factor of morbidity and mortality in this disease and represent a major unmet medical need."

Safety and Tolerability

Safety data are available for the lead in phase of the study for 100 patients with at least 12 weeks of follow-up. The most common greater-than or equal to grade 3 adverse events (AEs), regardless of causality were fatigue (15%), hypertension (8%), PPE syndrome (5%), back pain (3%), decreased appetite, nausea, vomiting, rash, hemorrhage, abdominal pain (each 2%), diarrhea, dyspnea, and cough (each 1%). No cabozantinib-related grade 5 AEs were reported. At least one dose reduction was reported in 51% of patients.

To access the clinical data poster mentioned in this press release, please visit www.exelixis.com/sites/default/files/pdf/ASCOGU_2011_Cabozantinib-127.pdf

Cabozantinib Targets Key Pathways That Contribute to Prostate Cancer

Cabozantinib, an inhibitor of tumor growth, metastasis and angiogenesis, simultaneously targets MET and VEGFR2, key kinases involved in the development and progression of many cancers. Prominent expression of MET has been observed in primary and metastatic prostate carcinomas, with evidence for higher levels of expression in bone metastases. Overexpression of hepatocyte growth factor (HGF), the ligand for MET, has also been observed in prostate carcinoma, and increased plasma levels of HGF are associated with decreased overall survival in CRPC. Data from preclinical studies also suggest that both HGF and MET are regulated by the androgen signaling pathway in prostate cancer, where upregulation of MET signaling is associated with the transition to androgen-independent tumor growth. Additionally, both the MET and VEGFR signaling pathways also appear to play important roles in the function of osteoblasts and osteoclasts -- cells in the bone microenvironment that are often dysregulated during the establishment and progression of bone metastases.

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.

Conference Call and Webcast

An investor briefing webcast will be held in conjunction with the 2011 ASCO Genitourinary Cancers Symposium. The webcast will be held on Thursday, February 17, 2011, from 6:30-8:00 p.m. EST, and may be accessed by visiting the Event Calendar page under Investors at www.exelixis.com. An archived replay will be available on the Event Calendar page under Investors at www.exelixis.com and via phone until 11:59 p.m. EST on March 17, 2011. Access numbers for the replay are: 1-888-286-8010 (domestic) and 1-617-801-6888 (international). The replay passcode is 59328118.

About Cabozantinib

Cabozantinib, an inhibitor of tumor growth, metastasis and angiogenesis, simultaneously targets MET and VEGFR2, key kinases involved in the development and progression of many cancers. It has recently been shown in preclinical models that treatment with selective inhibitors of VEGF signaling can result in tumors that are more invasive and aggressive compared to control treatment. In preclinical studies, upregulation of MET has been shown to occur in concert with development of invasiveness after selective anti-VEGF therapy, and may constitute a mechanism of acquired or evasive resistance to agents that target VEGF signaling without inhibiting MET. Accordingly, treatment with cabozantinib in similar preclinical studies resulted in tumors that were less invasive and aggressive compared to control or selective anti-VEGF treatment. Therefore, cabozantinib has the potential for improving outcomes in a range of indications, including those where selective anti-VEGF therapy has shown minimal or no activity.

About Exelixis

Exelixis, Inc. is a development-stage biotechnology company dedicated to the discovery and development of novel small molecule therapeutics for the

treatment of cancer. The company is leveraging its biological expertise and integrated research and development capabilities to generate a pipeline of development compounds with significant therapeutic and commercial potential for the treatment of cancer. Currently, Exelixis' broad product pipeline includes investigational compounds in phase 3, phase 2, and phase 1 clinical development. Exelixis has established strategic corporate alliances with major pharmaceutical and biotechnology companies, including Bristol-Myers Squibb Company, sanofi-aventis, GlaxoSmithKline, Genentech (a wholly owned member of the Roche Group), Boehringer Ingelheim, and Daiichi-Sankyo. 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 clinical and therapeutic potential of cabozantinib, including the ability for cabozantinib to offer a unique approach to the treatment of prostate cancer, the potential for cabozantinib to provide a durable clinical benefit in both docetaxel naïve and pretreated patients, Exelixis' belief that cabozantinib has a novel and differentiated profile relative to other prostate cancer agents, the comprehensive development plan for cabozantinib, the impact of cabozantinib on soft tissue, bone disease and associated symptoms in patients with CRPC, the ability for cabozantinib to target key pathways involved in the development and progression of many cancers and Exelixis' belief that cabozantinib has the potential for improving outcomes in a range of indications. Words such as "encouraging," "support," "appears," "plan," "future," "indicate," "may," "suggest," "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 October 1, 2010 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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