Cabozantinib Demonstrates Encouraging Activity in Patients with Heavily Pretreated Metastatic Renal Cell Carcinoma

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Median Overall Survival Not Yet Reached After Median Follow-up of 14.7 Months

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jun. 2, 2012-- Exelixis, Inc. (NASDAQ:EXEL) today reported positive updated interim data from a cohort of heavily pretreated patients with metastatic refractory renal cell carcinoma (RCC) participating in an ongoing phase 1b trial of cabozantinib. Toni K. Choueiri, M.D., Director of the Kidney Cancer Center at the Dana-Farber Cancer Institute, presented the data in an oral session at the American Society of Clinical Oncology 2012 Annual Meeting (Abstract #4504), which is taking place in Chicago, Illinois. Slides from the presentation are available at http://www.exelixis.com/resources/events/asco-2012.

The data presented are from a cohort of 25 RCC patients enrolled in an ongoing phase 1b drug-drug interaction study of cabozantinib at the phase 1 maximum tolerated dose (MTD) in patients with advanced solid tumors. Patients in this trial receive 140 mg of oral cabozantinib administered daily and a single dose of rosiglitazone at day 22. The study endpoints are safety, tolerability, and anti-tumor activity. All patients had histologically confirmed RCC (with clear cell components) and metastases, were refractory to or had progressed following standard therapy, and had measurable disease per RECIST. This was a heavily pre-treated population, with 68% of patients receiving ≥2 prior systemic agents and 32% receiving ≥4 prior systemic agents. Prior therapies included anti-VEGF pathway therapy (88%) and mTOR inhibitor therapy (60%), with 52% of patients receiving both an mTOR inhibitor and at least 1 anti-VEGF pathway therapy. Bone metastases were present at baseline in 4 patients (16%), one of whom was followed by bone scan.

Tumor Regression. Objective evidence of tumor regression was observed in 19 of 21 patients (90%) with ≥1 post-baseline assessment. Best overall response was determined per RECIST criteria with 7 of 25 patients (28%) showing a confirmed partial response (PR). Importantly, PRs were observed in heavily pretreated patients, including 3 patients with 2-4 prior systemic therapies, and 2 patients with >4 prior systemic therapies. Thirteen additional patients (52%) had stable disease (SD) as their best response, and only a single patient (4%) demonstrated evidence of primary refractoriness to cabozantinib with a best overall response of progressive disease. The rate of disease control (PR + SD) at week 16 for all 25 patients is 72%.

Progression-Free Survival, Overall Survival, and Treatment Duration. Kaplan Meier estimate of median progression-free survival (PFS) is 14.7 months (95% CI, lower limit 7.3 months – upper limit not reached). Median overall survival (OS) has not yet been reached after median follow-up of 14.7 months. The estimated 1-year survival rate is 60%. Seven patients remain on study and progression free with treatment durations ranging up to 21.8+ months.

Radiographic and Bone Scan Response. One patient with sarcomatoid differentiation and bone and soft tissue involvement who had previously been treated with four systemic agents including sunitinib and everolimus had a radiographic response at week 8. Also, as previously reported, a partial bone scan resolution was observed at week 7 in a patient with bone metastases who was followed by bone scan and had previously been treated with sorafenib, sunitinib, and everolimus. The patient also substantially reduced narcotic use by week 7 and continued on reduced narcotics until week 25. A second patient with bone metastases and bone pain at baseline reported complete resolution of pain by week 4 and remains pain free at week 90.

“Up to 25% of RCC patients initially treated with anti-VEGF pathway therapy are refractory to such agents, and these patients have few treatment options,” said Dr. Choueiri. “The clinical benefit observed with cabozantinib is encouraging, particularly in highly pretreated patients who are refractory to anti-VEGF and anti-mTOR therapies or who have had disease progression while on these agents. Additionally, the improvements in bone lesions and bone pain are also encouraging, especially given that bone metastases occur in up to 30% of RCC patients. Existing RCC therapies have minimal impact on bone disease, and cabozantinib may be able to address this medical need. Cabozantinib has the potential to be a meaningful addition to the treatment of RCC.”

Safety results for the Phase 1 MTD of 140 mg are consistent with those observed in other trials of cabozantinib and with other tyrosine kinase inhibitor therapies. The most frequently reported adverse events (AEs) Grade ≥ 3 or higher, regardless of causality, were: hypophosphatemia (36%), hyponatremia (20%), fatigue (16%), diarrhea (12%), proteinuria (8%), decreased appetite (4%), vomiting (4%), hand-foot syndrome (4%). Grade ≥ 3 hypertension was seen in 8% of patients and was considered an AE of interest due to the increased incidence of hypertension observed with other VEGF inhibitors. No grade 5 AEs were reported.

“We continue to be encouraged by the high tumor response rate, PFS time, and the estimated 60% 1-year survival rate from this trial in a very heavily-pretreated patient population,” said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. “Taken together, the data demonstrate cabozantinib’s potential role to improve care and outcomes for patients with RCC. A randomized phase 2 trial in first-line RCC using a 60 mg dose is planned under our Cooperative Research and Development Agreement with the National Cancer Institute’s Cancer Therapy Evaluation Program and should provide further insight into cabozantinib’s clinical and commercial potential in this indication.”

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 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 belief that the observed clinical benefit is encouraging; belief that cabozantinib may address bone disease in RCC patients; the belief that cabozantinib has the potential to be a meaningful addition to the treatment of RCC; the belief that the referenced data are encouraging and demonstrate cabozantinib's potential role in the treatment of RCC patients; and the referenced planned randomized phase 2 trial of cabozantinib in RCC and the expected benefits of such planned trial. Words such as "demonstrates," "positive," "encouraging," "may," "potential," "addition," "planned," "should," "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 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.

Source: Exelixis, Inc.

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