Cabozantinib Shows Encouraging Activity in Heavily Pretreated Patients With Advanced Renal Cell Carcinoma

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14.7 months median progression free survival

28% confirmed partial response rate & 72% disease control rate at week 16

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Feb. 3, 2012-- Exelixis, Inc. (NASDAQ:EXEL) today reported preliminary 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, will present the data (Abstract #364) in a poster session at the 2012 Genitourinary Cancers Symposium at 6:45 a.m. PST tomorrow in San Francisco.

As of the January 18, 2012 data cut-off, 25 RCC patients were enrolled with 88% having received prior anti-VEGF therapy, 60% having received prior mTOR inhibitor therapy, and 52% having received ≥1 anti-VEGF and 1 mTOR therapy. Sixty-four percent of patients received ≥ 2 prior anti-cancer agents. 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%. Kaplan Meier estimate of median progression-free survival is 14.7 months (95% CI, lower limit 7.3 months – upper limit not reached). Ten patients remain on study and progression free with treatment durations ranging up to 16.4 months.

One patient with symptomatic bone metastases was followed by bone scan. A partial bone scan resolution was observed at week 7 in this patient who 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 73.

The data presented are from a cohort of 25 RCC patients enrolled in an ongoing phase 1b drug interaction study of cabozantinib in patients with advanced solid tumors. Patients in this trial receive 140 mg of oral cabozantinib administered daily, and the study endpoints are safety, tolerability, and anti-tumor activity. The RCC 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. Bone metastases were present at baseline in 4 patients (16%), one of whom was followed by bone scan.

“The high rate of durable tumor response, very low rate of primary refractoriness to drug therapy, and the long median progression-free survival observed in these heavily pretreated RCC patients are very encouraging,” said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. “Additionally, the bone scan response and reduction in narcotic usage in two of the four patients with bone metastases are consistent with the positive effects that we have observed for cabozantinib with respect to bone lesions in patients with castration-resistant prostate cancer and metastatic breast cancer. The data presented today support continued study of cabozantinib in patients with advanced RCC, and we hope to pursue such studies as part of our recently announced Cooperative Research and Development Agreement with the National Cancer Institute’s Cancer Therapy and Evaluation Program.”

No new safety signals were observed. The most frequently reported grade ≥ 3 adverse events (AEs), regardless of causality were: hypophosphatemia (36%), hyponatremia (20%), both manageable with substitution with or without cabozantinib dose reduction or interruption, fatigue (16%), diarrhea (12%), proteinuria (8%), palmar-plantar erythrodyesthesia (4%), and vomiting (4%).

“These data indicate that cabozantinib can provide clinical benefit to patients with advanced RCC, including those who have received anti-VEGF therapy, anti-mTOR therapy, or a sequence of these targeted therapies,” said Dr. Choueiri. “While anti-VEGF and anti-mTOR therapies have advanced the treatment of RCC, many patients are refractory to these agents and experience disease progression. Dual inhibition of both VEGFR2 and MET by cabozantinib may provide an alternative or additional mechanism for controlling disease in these patients, and further study of cabozantinib in this indication is warranted.”

The clinical data poster mentioned in this press release will be available at www.exelixis.com commencing at 6:00 a.m. EST today.

About Cabozantinib

Cabozantinib is a potent, dual inhibitor of 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. The vast majority of RCC cases have an inactivation of the von Hippel-Lindau tumor suppressor gene, which mimics a hypoxic state and triggers upregulation of both VEGF and MET expression. 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 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; the belief that the referenced data is encouraging and warrant further study of cabozantinib in patients with RCC; the hope to study cabozantinib further in RCC; the potential clinical utility of cabozantinib in RCC; the belief that cabozantinib can provide clinical belief to patients with advanced RCC; and the belief that dual inhibition of both VEGFR2 and MET by cabozantinib may provide an alternative or additional mechanism for controlling disease in RCC patients.

Words such as “encouraging,” “support,” “hope,” “indicate,” “can,” “may,” “warranted,” “believes,” “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