Exelixis Reports Positive Preliminary Phase 2 Cabozantinib Data in Patients with Hepatocellular Carcinoma

January 20, 2012

Data Highlight Progression Free Survival of 4.2 months in both sorafenib-pretreated and -naïve patients

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jan. 20, 2012-- Exelixis, Inc. (NASDAQ:EXEL) today reported positive preliminary data from the cohort of hepatocellular carcinoma (HCC) patients participating in the ongoing phase 2 randomized discontinuation trial (RDT) of cabozantinib. Allan Lee Cohn, M.D., Medical Director of Research at the Rocky Mountain Cancer Centers, will present the data today at 11:45 a.m. PST as part of the 2012 Gastrointestinal Cancers Symposium (Abstract #261). The meeting is taking place in San Francisco, California.

The week 12 disease control rate (PR and SD at week 12) was 68%. Evidence of objective tumor regression was observed in 78% of patients, including those with or without prior sorafenib therapy. The best radiologic response per RECIST in the lead-in stage of the study for 36 patients with at least one post-baseline measurement was confirmed partial response (cPR) in 2 patients and stable disease (SD) in 32 patients. One additional patient had a partial response that was confirmed after the patient completed the lead-in stage and proceeded to the randomized component of the trial. Median progression-free survival (PFS) was 4.2 months, and was similar for sorafenib-pretreated and sorafenib-naïve patients.

The results include data from 41 patients with advanced hepatocellular carcinoma (HCC) with measurable disease at baseline and documented progressive disease per RECIST criteria. Eligible patients had Child-Pugh Score A. Seventy-one percent of patients had one prior line of systemic therapy: 24% had received prior chemotherapy and 56% prior tyrosine kinase inhibitor (TKI) therapy, including 51% previously treated with sorafenib. Extrahepatic spread of disease was present in 70% of subjects, median AFP level was 368 and thrombocytopenia was present in 34%. Patients in the open label 12 week lead-in stage of the trial received a starting dose of 100 mg of oral cabozantinib daily.

A >50% reduction in the tumor marker alpha-fetoprotein (AFP) serum level was observed in 10 (38%) of 26 patients with AFP levels of ≥ 20 ng/mL at baseline and at least one post baseline measurement.

“We are very encouraged by the disease control rates observed in this population of patients with hepatocellular carcinoma,” said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. “Importantly, the similar PFS data in patients with and without prior sorafenib therapy is noteworthy, given the widespread use of this treatment as first-line therapy for HCC. These data warrant further study and we hope to investigate cabozantinib further in HCC as part of our recently announced Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute’s Cancer Therapy and Evaluation Program.”

The tolerability of cabozantinib in patients with HCC was similar to that of other TKIs. The most frequently reported ≥ grade 3 adverse events (AEs), regardless of causality in the 41 patients in the HCC cohort were: diarrhea (17%), palmar-plantar erythrodyesthesia (15%), thrombocytopenia (10%), asthenia (7%), aspartate aminotransferase elevation (5%), and fatigue, nausea, vomiting, hypertension, and weight decrease (2% each).There were no grade 5 events related to cabozantinib.

“These compelling results highlight cabozantinib’s potential clinical utility in HCC,” said Dr. Cohn. “In particular, the anti-tumor activity in patients with and without prior sorafenib therapy suggests that we may see additional benefit for pretreated and treatment-naïve patients through simultaneous inhibition of MET and VEGF signaling, rather than VEGF alone. Further study of cabozantinib in patients with HCC is clearly warranted.”

The clinical data poster mentioned in this press release will be available at www.exelixis.com commencing at 11:45 a.m. PST today.

Randomized Discontinuation Trial Design

The data above are from the HCC cohort from the randomized discontinuation trial evaluating the activity of cabozantinib in multiple tumor types. In the RDT design, patients initially receive open label cabozantinib at 100 mg daily (free base equivalents, corresponding to 125 mg salt form) during a 12-week Lead-In phase, which evaluates the effects of uninterrupted cabozantinib administration. Patients achieving a PR per RECIST criteria at week 12 are eligible for continued open label treatment with cabozantinib, and patients with progressive disease discontinue treatment. Patients with SD enter the randomized discontinuation phase, which assesses the progression free survival of these patients after random allocation to blinded placebo vs. cabozantinib. Patients progressing on placebo have the option of receiving salvage therapy with cabozantinib.

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. 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 noteworthy and warrant further study of cabozantinib in patients with HCC; the hope to study cabozantinib further in HCC; the potential clinical utility of cabozantinib in HCC; and the suggestion that there may be additional benefit for pretreated and treatment-naïve patients through simultaneous inhibition of MET and VEGF signaling, rather than VEGF alone. Words such as “positive,” “encouraged,” “noteworthy,” “warrant,” “hope,” “compelling,” “potential,” “suggests,” “may,” “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 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.

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