



## Cabozantinib Demonstrates Evidence of Anti-Tumor Effects in Heavily Pretreated Patients with Hepatocellular Carcinoma

June 2, 2012

*Data Show High Rates of Objective Tumor Regression, AFP Response and Encouraging Progression-Free and Overall Survival*

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jun. 2, 2012-- Exelixis, Inc. (NASDAQ:EXEL) today reported positive updated interim data from the cohort of hepatocellular carcinoma (HCC) patients participating in the ongoing phase 2 randomized discontinuation trial (RDT) of cabozantinib. Chris Verslype, M.D., Ph.D., professor of medicine at the Departments of Digestive Oncology/Hepatology at the University Hospitals Gasthuisberg, Leuven, Belgium, and an investigator on the trial, presented the data today in an oral session at the American Society of Clinical Oncology 2012 Annual Meeting (Abstract #4007). The meeting is taking place in Chicago, Illinois. Slides from the presentation are available at <http://www.exelixis.com/resources/events/asco-2012>.

The results comprise data from 41 patients with advanced hepatocellular carcinoma with measurable disease at baseline and documented progressive disease per RECIST criteria. Patients in the open label 12-week Lead-In Stage of the trial received a daily dose of 100 mg cabozantinib. Eligible patients had Child-Pugh Score A. Eighty percent had received 1-2 prior lines of systemic therapy: 56% had prior tyrosine kinase inhibitor (TKI) therapy, including 51% previously treated with sorafenib. At baseline, extrahepatic spread of disease (which is associated with a poorer prognosis) was present in 73% of subjects, 39% had hemoglobin (Hb) < 11 g/dL, 34% had thrombocytopenia, and median alpha-fetoprotein (AFP) level was 368 ng/ml. Tumor assessments per original RECIST 1.0 were conducted using conventional CT/MRI at baseline and every 6 weeks thereafter.

**Progression-Free survival (PFS) and Overall Survival (OS).** Median PFS was 4.4 months, and was similar for sorafenib-pretreated and sorafenib-naïve patients. Median OS in the 41 patients was 15.1 months.

**Response Rate.** The week 12 disease control rate (partial response [PR] and stable disease [SD] at week 12) was 66%. 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 PR in 2 patients (5%) and SD in 32 patients (78%).

"The progression-free survival and overall survival results observed to date are encouraging," said Eric Van Cutsem, M.D., Ph.D., professor of internal medicine and digestive oncology at the University Hospitals Gasthuisberg, Leuven, Belgium, and senior investigator on the presentation. "It is also interesting that the activity of cabozantinib in this population was irrespective of sorafenib pre-treatment status. The data suggest that dual inhibition of MET and VEGF with cabozantinib may provide clinical benefit beyond what can be achieved through inhibition of either pathway alone."

**AFP Biomarker and hemoglobin.** A decrease of >50% in serum AFP was observed in 9 of 26 patients (35%) with baseline values  $\geq$  20 ng/mL. The median maximum rise in Hb for the 13 patients with baseline Hb < 11 g/dL was 3.1 g/dL (range 1.3 to 7.8 g/dL).

"These interim data are encouraging and support the potential utility of cabozantinib in the treatment of HCC," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "As previously announced, a trial evaluating cabozantinib in a second-line randomized phase 2 trial in HCC is planned under our Cooperative Research and Development Agreement with the National Cancer Institute's Cancer Therapy Evaluation Program. We believe this planned trial will help to prioritize the development of cabozantinib in HCC in the context of the multiple indications in which the compound appears to provide clinical benefit."

### Safety Results

The tolerability of cabozantinib in patients with HCC was similar to that of other TKIs. The most frequently reported adverse events (AEs) of grade  $\geq$  3, regardless of causality in the 41 patients in the HCC cohort were: diarrhea (20%), hand-foot syndrome (15%), thrombocytopenia (15%), aspartate aminotransferase increased (10%), asthenia (7%), hypertension (7%), fatigue (10%), nausea (2%), vomiting (2%), and weight decreased (2%). There were no grade 5 events related to cabozantinib and no clinically significant bleeding was reported.

### Randomized Discontinuation Trial Design

The presented 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 Stage, 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 randomization and blinded allocation to placebo vs. cabozantinib. Patients progressing on placebo have the option of receiving salvage therapy with cabozantinib.

### 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](http://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 are encouraging and suggest that dual inhibition of MET and VEGF with cabozantinib may provide clinical benefit beyond what can be achieved through inhibition of either pathway alone; the potential utility of cabozantinib in the treatment of HCC; and the referenced planned randomized phase 2 trial of cabozantinib in HCC and the expected benefits of such planned trial. Words such as "demonstrates," "positive," "encouraging," "suggest," "may," "can," "support," "planned," "believe," "will" "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 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.

Exelixis, Inc.  
Charles Butler, 650-837-7277  
Vice President  
Investor Relations and Corporate Communications  
[cbutler@exelixis.com](mailto:cbutler@exelixis.com)