Exelixis Initiates Phase 3 Clinical Trial of Cabozantinib in Patients With Advanced Hepatocellular Carcinoma

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-- Five pivotal trials of cabozantinib now ongoing --

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Sep. 10, 2013-- Exelixis, Inc. (NASDAQ:EXEL) today announced that it has initiated CELESTIAL, a phase 3 pivotal trial comparing cabozantinib with placebo in patients with advanced hepatocellular carcinoma (HCC) who have previously been treated with sorafenib. The primary endpoint for the trial is overall survival (OS).

“Patients with advanced HCC who have progressed on sorafenib have few therapeutic options, and new approaches to managing their disease are much needed,” said Ghassan K. Abou-Alfa, M.D., Associate Attending at Memorial Sloan-Kettering Cancer Center, New York and the lead investigator on CELESTIAL. “Phase 2 data investigating cabozantinib in this patient population are worthy of more study, and cabozantinib’s target profile, which includes inhibition of both MET and VEGFR, is highly relevant in HCC.”

CELESTIAL is a randomized, double blind, placebo controlled study of cabozantinib in patients with advanced HCC that is being conducted at up to 200 sites globally in up to 30 countries. The trial is expected to enroll 760 patients with advanced HCC who have received prior sorafenib. Patients will be randomized 2:1 to receive 60 mg of cabozantinib daily or placebo.

The primary endpoint for the trial is OS, and the secondary endpoints include objective response rate (ORR) and progression-free survival (PFS). Exploratory endpoints include patient-reported outcomes, biomarkers, and safety.

Based on available clinical trial data, the primary endpoint assumes a median OS of 8.2 months for the placebo arm. A total of 621 events provide the study with 90% power to detect a 32% increase in OS (HR = 0.76). Interim analyses are planned once 50% and 75% of events have been observed, respectively.

“The initiation of the CELESTIAL trial is an important milestone as we work to expand the cabozantinib franchise into additional indications with substantial unmet medical needs,” said Gisela Schwab, M.D., executive vice president and chief medical officer of Exelixis. “CELESTIAL is the fifth pivotal trial for cabozantinib overall, and the second phase 3 trial to initiate this year. It was designed with the input of leading oncologists and HCC experts, and we believe that the data will provide important insight into the role that cabozantinib may play in improving the care of patients with this disease.”

About Cabozantinib

Cabozantinib inhibits the activity of tyrosine kinases including RET, MET and VEGFR2. These receptor tyrosine kinases are involved in both normal cellular function and in pathologic processes such as oncogenesis, metastasis, tumor angiogenesis, and maintenance of the tumor microenvironment. COMETRIQ® (cabozantinib) is currently approved by the U.S. Food and Drug Administration for the treatment of progressive, metastatic medullary thyroid cancer.

COMETRIQ® Important Safety Information, including Boxed Warning

WARNING: PERFORATIONS AND FISTULAS, and HEMORRHAGE

- **Serious and sometimes fatal gastrointestinal perforations and fistulas occur in COMETRIQ-treated patients.**
- **Severe and sometimes fatal hemorrhage occurs in COMETRIQ-treated patients.**
- COMETRIQ treatment results in an increase in thrombotic events, such as heart attacks.
- Wound complications have been reported with COMETRIQ.
- COMETRIQ treatment results in an increase in hypertension.
- Osteonecrosis of the jaw has been observed in COMETRIQ-treated patients.
- Palmar-Plantar Erythrodysesthesia (PPE) Syndrome occurs in patients treated with COMETRIQ.
- The kidneys can be adversely affected by COMETRIQ. Proteinuria and nephrotic syndrome have been reported in patients receiving COMETRIQ.
- Reversible Posterior Leukoencephalopathy Syndrome has been observed with COMETRIQ.
- COMETRIQ is not recommended for use in patients with moderate or severe hepatic impairment.
- COMETRIQ can cause fetal harm when administered to a pregnant woman.

Adverse Reactions – The most commonly reported adverse drug reactions (≥25%) are diarrhea, stomatitis, palmar-plantar erythrodysesthesia syndrome (PPES), decreased weight, decreased appetite, nausea, fatigue, oral pain, hair color changes, dysgeusia, hypertension, abdominal pain, and constipation. The most common laboratory abnormalities (≥25%) are increased AST, increased ALT, lymphopenia, increased alkaline

phosphatase, hypocalcemia, neutropenia, thrombocytopenia, hypophosphatemia, and hyperbilirubinemia.

Drug Interactions – COMETRIQ is a CYP3A4 substrate. Co-administration of strong CYP3A4 inhibitors can increase cabozantinib exposure. Chronic co-administration of strong CYP3A4 inducers can reduce cabozantinib exposure.

For full prescribing information, including Boxed Warning, please visit www.COMETRIQ.com.

About Exelixis

Exelixis 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 COMETRIQ® (cabozantinib). 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 phase 2 data investigating cabozantinib in patients with advanced HCC are worthy of more study; the belief that cabozantinib's target profile, which includes inhibition of both MET and VEGFR, is highly relevant in HCC; Exelixis' plans to expand the cabozantinib franchise and the importance of the CELESTIAL trial to such plans; the belief that the data from the CELESTIAL trial will provide important insight into the role that cabozantinib may play in improving the care of patients with HCC; and the design, plans and goals for the CELESTIAL trial, and the potential success thereof. Words such as "options," "new," "investigating," "target," "may," "conducted," "expected," "will," "endpoint," "assumes," "provide," "important," "milestone," "expand," "unmet," "designed," "believe," "insight," "role," "improving," "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: the availability of data at the expected times; risks related to the potential failure of cabozantinib to demonstrate safety and efficacy in clinical testing; the uncertain timing and level of expenses associated with the development of cabozantinib; Exelixis' ability to conduct clinical trials of cabozantinib sufficient to achieve a positive completion; the sufficiency of Exelixis' capital and other resources; 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 three months ended June 28, 2013, filed with the Securities and Exchange Commission (SEC) on August 6, 2013, and Exelixis' other filings with the SEC. 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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