Exelixis Initiates Phase 3 Pivotal Trial of Cabozantinib in Patients With Metastatic Renal Cell Carcinoma

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SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--May. 31, 2013-- Exelixis, Inc. (NASDAQ:EXEL) today announced it has initiated METEOR, a phase 3 pivotal trial comparing cabozantinib to everolimus in patients with metastatic renal cell carcinoma (mRCC) who have experienced disease progression following treatment with at least one prior VEGFR tyrosine kinase inhibitor (TKI). The primary endpoint for the trial is progression-free survival.

“RCC patients who progressed after or who are refractory to initial treatment with VEGFR-TKI therapy have limited treatment options,” said METEOR Principal Investigator Toni K. Choueiri, M.D., Director of the Kidney Cancer Center at the Dana-Farber Cancer Institute and an Associate Professor of Medicine at Harvard Medical School. “The cabozantinib data to date in RCC patients previously treated with VEGFR-TKIs showed encouraging anti-tumor activity, and provide a sound rationale for the design of the METEOR phase 3 study comparing cabozantinib to everolimus in this indication.”

METEOR is an open-label trial of cabozantinib in patients with mRCC that is being conducted at up to 200 sites in up to 26 countries. The trial is expected to enroll 650 patients with clear cell RCC who have received and progressed on at least one VEGFR-TKI. Patient enrollment will be weighted toward Western Europe, North America, and Australia, and patients will be stratified based on the number of prior VEGFR-TKI therapies received and commonly applied RCC risk criteria developed by Motzer et al. Patients will be randomized 1:1 to receive 60 mg of cabozantinib daily or 10 mg of everolimus daily. No cross-over is allowed between the study arms.

The primary endpoint is progression-free survival (PFS) and the secondary endpoint is overall survival (OS). Exploratory endpoints include patient-reported outcomes, biomarkers, safety, and pharmacokinetics. PFS is an established acceptable endpoint for RCC clinical trials and has been used to support approval of sorafenib, sunitinib, everolimus, axitinib, and pazopanib in this indication.

Based on available clinical trial data, the primary endpoint assumes a median PFS of 5 months for the everolimus arm and 7.5 months for cabozantinib arm. This provides for a hazard ratio (HR) of 0.67 and 90% power and requires 259 PFS events among the first 375 patients randomized. The secondary endpoint assumes a median OS of 15 months for the everolimus arm and 20 months for the cabozantinib arm. This provides for a HR of 0.75 and 80% power and requires 413 events.

“Initiation of this phase 3 pivotal trial in mRCC is an important component of our development strategy to expand the cabozantinib franchise by exploring additional indications with the goal of providing patients with new treatment options,” said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. “Our pre-phase 3 meetings with regulatory authorities in the U.S. and Europe, as well as feedback gathered from expert oncologists around the globe, have helped us design a trial that is intended to provide for a robust examination of cabozantinib’s clinical potential as a treatment for mRCC. We also remain on track to begin a phase 3 pivotal trial of cabozantinib in patients with metastatic hepatocellular carcinoma in the third quarter of this year.”

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 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 cabozantinib data to date in RCC patients previously treated with VEGFR-TKIs provide a sound rationale for the design of the METEOR trial; the design, plans and goals for the METEOR trial, and the potential success thereof; Exelixis' development strategy to expand the cabozantinib franchise; Exelixis' plans to explore cabozantinib in additional indications; Exelixis' goal of providing patients with new treatment options; and Exelixis' plan to begin a phase 3 pivotal trial of cabozantinib in metastatic hepatocellular carcinoma and the expected timing thereof. Words such as "endpoint," "encouraging," "provide," "rationale," "design," "conducted," "expected," "will," "assumes," "strategy," "expand," "exploring," "goal," "new," "options," "intended," "potential," "on track," 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 March 29, 2013, filed with the Securities and Exchange Commission (SEC) on May 7, 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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