Exelixis Announces Start of Phase 1 Trial of Cabozantinib in Combination with Nivolumab or Nivolumab Plus Ipilimumab in Patients with Advanced/Metastatic Urothelial Carcinoma and Other Genitourinary Tumors

July 13, 2015

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jul. 13, 2015-- Exelixis, Inc. (NASDAQ:EXEL) today announced the initiation of a phase 1 trial of cabozantinib in combination with nivolumab alone or in combination with nivolumab plus ipilimumab in patients with advanced/metastatic urothelial (bladder) and other genitourinary tumors. The primary endpoint of the trial is the determination of dose-limiting toxicities (DLT) and a recommended phase 2 dose (RP2D) for the combination of cabozantinib and nivolumab, and separately, for the combination of cabozantinib, nivolumab and ipilimumab, in patients with genitourinary solid tumors. Secondary endpoints include evaluating the activity of the two combinations by objective response rate, as well as progression-free survival (PFS) and overall survival (OS), in cohorts of patients with urothelial carcinoma of the bladder, urethra, ureter or renal pelvis.

The trial is sponsored by the U.S. National Cancer Institute (NCI) through Cooperative Research and Development Agreements between the NCI's Cancer Therapy Evaluation Program (CTEP), Division of Cancer Treatment and Diagnosis, and both Bristol-Myers Squibb and Exelixis. Andrea Apolo, M.D., of the NCI's Genitourinary Malignancies Branch, is the principal investigator. The trial will be conducted by the NCI and includes centers from its Experimental Therapeutics Clinical Trials Network.

"In the United States, bladder cancer is one of the ten most common malignancies for men and women alike, and there are no drugs approved for use in the second-line setting," said Dr. Apolo. "In a previous study, single-agent cabozantinib demonstrated intriguing clinical activity in bladder cancer. Now, with this trial, we'll explore the safety and tolerability, and the antitumor activity of the combination of cabozantinib with the immune checkpoint inhibitor nivolumab, alone or together with ipilimumab, in this and other important genitourinary cancer settings."

This open label, non-randomized phase 1 trial will enroll a maximum of 66 patients. The trial is divided into two parts: a dose-escalation phase and an expansion cohort phase. The dose-escalation phase will enroll patients with metastatic genitourinary solid tumors including renal cell carcinoma, urothelial cancer and castration-resistant prostate cancer who have progressed following treatment with at least one standard therapy. Up to 24 patients will be treated with the combination of cabozantinib plus nivolumab (CaboNivo), and up to 18 patients will receive the combination of cabozantinib, nivolumab, and ipilimumab (CaboNivoIpi). The starting dose of cabozantinib will be 40 mg daily for each combination and can increase up to 60 mg daily. Depending upon the cohort, dose levels for nivolumab will range from 1 to 3 mg/kg administered on an every two or every three week schedule, and ipilimumab will be administered at a dose level of 1 mg/kg every three weeks for a maximum of 4 doses.

Once the RP2Ds are determined for the combinations of CaboNivo and CaboNivoIpi, the trial will enroll expansion cohorts of up to 12 eligible patients for each combination, for up to 24 patients total in the expansion cohort. To be eligible for the expansion cohort, patients must have histologically confirmed metastatic, progressive urothelial cancer of the bladder, urethra, ureter, or renal pelvis. Patients in the expansion cohort will be evaluated for objective response rate, PFS and OS: all secondary endpoints of the trial.

"There is a strong rationale for combining cabozantinib with immunoncology agents, including clinical evidence of the compound's ability to create a more immune-permissive environment, as well as preclinical data that suggest cabozantinib increases T-cell infiltration into tumors," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "In addition to bladder cancer, we believe that data on the tolerability and activity of the therapy combinations studied in this trial could have relevance in other disease settings, including non-small cell lung cancer and kidney cancer."

Dr. Morrissey continued: "Our collaboration with NCI-CTEP allows researchers to evaluate cabozantinib's potential in diverse cancers while Exelixis focuses its internal resources on late-stage development, including the METEOR phase 3 pivotal trial in metastatic renal cell cancer expected to read out early this quarter. We look forward to following the progress of Dr. Apolo's trial, which is one of more than 45 studies of cabozantinib either planned or ongoing under the CTEP collaboration and our investigator-sponsored trial program."

More information about this trial will be available at ClinicalTrials.gov shortly.

About Cabozantinib

Cabozantinib inhibits the activity of tyrosine kinases including MET, VEGFRs and RET. 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 (MTC).

The European Commission granted COMETRIQ conditional approval for the treatment of adult patients with progressive, unresectable locally advanced or metastatic MTC. Similar to another drug approved in this setting, the approved indication states that for patients in whom Rearranged during Transfection (RET) mutation status is not known or is negative, a possible lower benefit should be taken into account before individual treatment decisions.

Important Safety Information, including Boxed WARNINGS

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 Syndrome (PPES) 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.
- Avoid administration of COMETRIQ with agents that are strong CYP3A4 inducers or inhibitors.
- 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.

Please see full U.S. prescribing information, including Boxed WARNINGS, at www.COMETRIQ.com/downloads/Cometriq_Full_Prescribing_Information.pdf. Please refer to the full European Summary of Product Characteristics for full European Union prescribing information, including contraindication, special warnings and precautions for use at www.sobi.com once posted.

About Exelixis

Exelixis, Inc. is a biopharmaceutical company committed to developing small molecule therapies for the treatment of cancer. Exelixis is focusing its development and commercialization efforts primarily on COMETRIQ® (cabozantinib), its wholly-owned inhibitor of multiple receptor tyrosine kinases. Another Exelixis-discovered compound, cobimetinib, a selective inhibitor of MEK, is being evaluated by Roche and Genentech (a member of the Roche Group) in a broad development program under a collaboration with Exelixis. 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 combining cabozantinib with immunocology agents in a variety of disease settings; the evaluation of cabozantinib's potential in diverse cancers under Exelixis' collaboration with NCI-CTEP while Exelixis focuses its internal resources on the late-stage development of cabozantinib; and anticipated developments and timing with respect to Exelixis' ongoing phase 3 pivotal trials of cabozantinib and trials of cabozantinib either planned or ongoing under Exelixis' NCI-CTEP collaboration and its investigator sponsored trial program. Words such as "will," "rationale," "believe," "could," "potential," "focus," "expected," "look forward," "planned," or other similar expressions, identify forward-looking statements, but the absence of these words does not necessarily mean that a statement is not forward-looking. In addition, any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements. These forward-looking statements are based upon Exelixis' current plans, assumptions, beliefs, expectations, estimates and projections. Forward-looking statements involve risks and uncertainties. Exelixis' actual results and the timing of events could differ materially from those anticipated in the 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; the clinical, therapeutic and commercial value of cabozantinib; the uncertain timing and level of expenses associated with the development of cabozantinib; Exelixis' ability and the ability of its collaborators to conduct clinical trials of cabozantinib sufficient to achieve a positive completion; the availability of data at the expected times; market competition; changes in economic and business conditions; and other factors discussed under the caption "Risk Factors" in Exelixis' quarterly report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on April 30, 2015 and in Exelixis' other filings with the SEC. The forward-looking statements made in this press release speak only as of the date of this press release. 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.

View source version on businesswire.com: http://www.businesswire.com/news/home/20150713005613/en/

Source: Exelixis, Inc.

Exelixis, Inc.
Susan Hubbard, 650-837-8194
Investor Relations and

Corporate Communications
shubbard@exelixis.com