Exelixis Announces Positive Results from Phase 2 Trial of Cabozantinib in Patients with EGFR Wild-Type Non-Small Cell Lung Cancer

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-- Cabozantinib, as well as the combination of cabozantinib and erlotinib, significantly improved progression-free survival and overall survival compared with erlotinib alone

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--May 31, 2015-- Exelixis, Inc. (NASDAQ:EXEL) today announced positive results from a phase 2 clinical study evaluating cabozantinib as a treatment for EGFR wild-type non-small cell lung cancer (NSCLC). The trial, Study E1512, is a randomized phase 2 trial by the ECOG-ACRIN Cancer Research Group of cabozantinib and erlotinib, alone or in combination, as second- or third-line therapy in patients with metastatic EGFR wild-type NSCLC. Exelixis previously announced positive top-line results from this trial in November 2014. Data from the trial will be presented today during an oral presentation (Abstract #8003) at the 2015 Annual Meeting of the American Society of Clinical Oncology (ASCO), which is being held this week in Chicago, Illinois. Study chair Joel Neal, M.D., Ph.D., of ECOG-ACRIN's Thoracic Cancer Committee and an Assistant Professor of Medicine (Oncology) at Stanford University/Stanford Cancer Institute will present the results.

Study E1512 met its primary endpoint, demonstrating significant increases in progression-free survival (PFS) for cabozantinib and the combination of cabozantinib plus erlotinib when individually compared to the erlotinib arm. The median PFS for the combination of cabozantinib and erlotinib was 4.7 months versus 1.9 months for erlotinib alone, a more than two-fold increase that corresponds to a 65% reduction in the risk of disease worsening (hazard ratio [HR]=0.35, 80% CI 0.23-0.52, p=0.0005). The median PFS for cabozantinib monotherapy was 4.2 months versus 1.9 months for erlotinib alone, a more than doubling that corresponds to a 62% reduction in the risk of disease worsening (HR=0.38, 80% CI 0.27-0.55, p=0.0004).

Overall survival was a secondary endpoint of the trial. Median OS was 13.3 months for the combination of cabozantinib and erlotinib, and 9.2 months for cabozantinib alone, as compared to 4.1 months for erlotinib alone. These results correspond to a 56% reduction in the risk of death (HR=0.44, p=0.004) for the combination of cabozantinib plus erlotinib, and a 41% reduction in the risk of death (HR=0.59, p=0.03) for the cabozantinib monotherapy arm, respectively, when individually compared to the erlotinib arm. Objective response rate, another secondary endpoint, was 8% for the combination arm (2 partial responses [PR]), 14% (4 PRs) for the cabozantinib monotherapy arm, and 3% (1 PR) for the erlotinib arm. Stable disease as a best response was observed in 47% in the combination arm and 42% in the cabozantinib monotherapy arm, compared with 17% in the erlotinib arm.

118 patients were evaluable for safety. The most common treatment-related adverse events (AEs), grade 3 or higher, for the combination arm (n=39) were: diarrhea (27%), fatigue (15%), and syncope (8%). For the cabozantinib monotherapy arm, the most common AEs, grade 3 or higher, were: hypertension (26%), fatigue (15%), mucositis (10%) and thromboembolic events (8%). The most common AEs, grade 3 or higher, for the erlotinib arm were fatigue (12%) and diarrhea (8%). Overall, the rate of grade 3 or higher worst grade adverse events was 72% in the combination arm and 67% in the cabozantinib monotherapy arm, compared with the erlotinib arm (35%).

“Despite the availability of new therapies, lung cancer continues to pose significant clinical challenges,” said ECOG-ACRIN group co-chair Robert L. Comis, M.D. “The magnitudes of improvement in progression-free survival and overall survival delivered by the combination and single agent cabozantinib arms in this randomized phase 2 trial are encouraging, and they provide a strong rationale for further evaluation of cabozantinib in non-small cell lung cancer.”

Commenting on the results, Michael M. Morrissey, Ph.D., Exelixis’ president and chief executive officer, said: “The results from Study E1512 demonstrate cabozantinib’s ability to extend progression-free survival and overall survival in a randomized phase 2 trial in comparison with erlotinib, an active comparator. The data also speak to cabozantinib’s potential as a component of combination therapy in non-small cell lung cancer. Exelixis is committed to working with our partners at ECOG-ACRIN and the National Cancer Institute to evaluate that potential, and we look forward to discussing possible next steps, including combination trials with immunotherapies, as well as potential pivotal studies in late-line disease.”

Study E1512 enrolled 125 patients with metastatic EGFR wild-type NSCLC who had received at one or two prior chemotherapy regimens; of these, 113 patients were evaluable for efficacy and 118 patients were evaluable for safety. Patients were randomized 1:1:1 to receive erlotinib (150 mg daily), cabozantinib (60 mg daily), or the combination of erlotinib plus cabozantinib (150 mg plus 40 mg daily). Median follow up was 12.6 months. Baseline characteristics were generally well balanced between the treatment arms with the exception of a history of treated brain metastases (combination arm 25%, cabozantinib monotherapy arm 33%, and erlotinib monotherapy arm 8%) and a history of mediastinal metastases (combination arm 50%, cabozantinib monotherapy arm 56%, and erlotinib monotherapy arm 30%). The primary objective of the trial was to compare the PFS of patients on the cabozantinib and combination arms versus that of the erlotinib arm. Each comparison had 91% power to detect a PFS hazard ratio (HR) of 0.5 with a 1-sided 0.10-level test stratified on prior number of therapies and ECOG performance status.

The trial is sponsored by the U.S. National Cancer Institute (NCI) under a Cooperative Research and Development Agreement between the NCI’s Cancer Therapy Evaluation Program (CTEP) and Exelixis. The study was designed and is being conducted by the ECOG-ACRIN Cancer Research Group as part of Exelixis’ collaboration with the NCI.

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 ECOG-ACRIN

The ECOG-ACRIN Cancer Research Group is a membership-based scientific organization that designs and conducts cancer research involving adults who have or are at risk of developing cancer. ECOG-ACRIN comprises nearly 1100 member institutions and 12,000 research professionals in the United States and around the world. For more information, please visit the organization's website at www.ecog-acrin.org.

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, Inc. (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: future data presentations of for the phase 2 clinical study evaluating cabozantinib as a treatment for EGFR wild-type NSCLC; potential future evaluation of cabozantinib in NSCLC; the continued development and clinical, therapeutic and commercial potential of, and opportunities for, cabozantinib as a component of combination therapy in NSCLC; and Exelixis' commitment to working with its partners to evaluate such potential. Words such as "continues," "will," "encouraging," "further," "potential," "committed," "look forward," "next steps," 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: 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 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 partners to conduct clinical trials of cabozantinib sufficient to achieve a positive completion; 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.

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