Exelixis Announces Positive Results from Phase 2 Investigator-Sponsored Trial of Cabozantinib in RET-Rearranged Non-Small Cell Lung Cancers

May 31, 2015

-- Study met its primary endpoint with a 38% objective response rate

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--May 31, 2015-- Exelixis Inc. (NASDAQ:EXEL) today announced positive results from a two-stage phase 2 investigator-sponsored trial (IST) evaluating cabozantinib in patients with advanced RET-rearranged lung cancers. Data were reported for the first stage, which enrolled 16 patients. The objective response rate (ORR) was 38% (6/16), with a median duration of response of 8 months. Although the trial is still accruing, it has already met its primary endpoint, exceeding the predefined targeted number of five objective responses. Alexander Drilon, M.D. of New York's Memorial Sloan Kettering Cancer Center (MSKCC) will present the data (Abstract #8007) today during an oral abstract session at the 2015 Annual Meeting of the American Society of Clinical Oncology in Chicago, Illinois.

"Constitutive activation of receptor tyrosine kinases by mutation or rearrangement is an oncogenic event in a substantial proportion of patients with non-small cell lung cancer (NSCLC), and includes the activation of RET by gene rearrangement in about 1-2% of patients with adenocarcinoma histology," said Dr. Drilon, the study's principal investigator. "Cabozantinib is an active therapy in RET-rearranged lung cancers, as demonstrated by the durable objective responses observed in the first stage of this study. While this trial continues to accrue patients to complete its second stage, it has already met its primary endpoint. Further investigation is clearly warranted."

Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis, commented on the results: "Exelixis is committed to working with independent investigators, and with our collaborators at the National Cancer Institute's Cancer Therapy Evaluation Program, to fully evaluate cabozantinib's potential in a variety of disease settings beyond our company-sponsored pivotal trials in renal and liver cancers. The data in RET-rearranged NSCLC are compelling, and we look forward to discussing with our collaborators potential next steps for cabozantinib in this setting."

Study Design

This single-institution, open-label phase 2 trial evaluates cabozantinib in patients with advanced RET-rearranged NSCLC, including the KIF5B-RET fusion, the most common rearrangement. Eligible patients must have stage IV lung cancer (with RET rearrangement confirmed by break apart fluorescence in situ hybridization and/or next generation sequencing), Karnofsky Performance Status greater than 70 percent, and measurable disease per RECIST 1.1. Patients receive 60 mg daily cabozantinib in 28-day cycles until disease progression or unacceptable toxicity.

The trial is designed to enroll a maximum of 25 patients in two stages. The first stage of the trial, the subject of today's data presentation, enrolled 16 patients, and one partial response was required to expand the trial into its second stage that will enroll an additional nine patients.

The primary endpoint of the trial is ORR, with five partial responses (PRs) required to meet the endpoint. Secondary endpoints include response rate at 12 weeks, progression-free survival (PFS), overall survival (OS), and toxicity.

Study Results

At the time of data cut-off, 20 patients had been treated and 18 were evaluable. Data were presented for the 16 patients enrolled in the first stage of the trial. The median age for patients in the first stage of the trial was 59 (range 38-80 years), and 62 percent (10/16) of these were female. All patients in the first stage had adenocarcinoma, the median number of prior lines of chemotherapy was 1, and 31% of patients had received ≥ 2 lines of prior chemotherapy.

Sixteen patients from the first stage of the trial were evaluable for tumor response. ORR, the primary endpoint of the trial, was 38%, with six confirmed PRs recorded. The median duration of response was 8 months (range 5.5-26 months) including one patient with a confirmed partial response who remained on treatment more than 25 months. One patient with a best response of stable disease remained on cabozantinib treatment for more than 21 months. ORR at 12 weeks, a secondary endpoint, was 36%, with five confirmed PRs recorded among the 14 patients evaluable at 12 weeks.

PFS and OS are secondary endpoints. The median PFS was 7 months (95% CI 5-NA). The median OS was 10 months (95% CI 8-NA) with a median follow-up of 24 months.

Grade 3 adverse events deemed related to study drug by the investigators were thrombocytopenia (19%), increased lipase (13%), increased AST, hypophosphatemia, fatigue, oral mucositis, palmar plantar erthrodysesthesia, hypertension, and retroperitoneal hematoma (all 6%). Half of the patients (8/16) experienced one dose reduction to 40 mg during the course of therapy, with 19% (3/16) reducing to 20 mg daily. One patient discontinued therapy secondary to a grade 3 retroperitoneal hemorrhage, and there was one death unrelated to drug (grade 5 respiratory failure [post-thoracentesis]).

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 highly 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: future data presentations for the phase 2 IST evaluating cabozantinib in patients with advanced RET-rearranged lung cancers; potential future evaluation of cabozantinib in NSCLC; the continued development and clinical, therapeutic and commercial potential of, and opportunities for, cabozantinib in a variety of disease settings; and Exelixis' commitment to working with independent investigators and collaborators at the National Cancer Institute's Cancer Therapy Evaluation Program to evaluate such potential and discuss the potential next steps for cabozantinib in NSCLC. Words such as "will," "continues," "further," "committed," "potential," "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 collaborators 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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