Exelixis Announces Results from the COMET-2 Pivotal Phase 3 Trial of Cabozantinib in Men With Metastatic Castration-Resistant Prostate Cancer

December 1, 2014

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Dec. 1, 2014-- Exelixis, Inc. (NASDAQ:EXEL) today announced top-line results from the final analysis of COMET-2, a randomized, double-blind, controlled trial of cabozantinib in men with metastatic castration-resistant prostate cancer (mCRPC) who are suffering from moderate to severe pain despite optimized narcotic medication, and whose disease has progressed following treatment with docetaxel as well as abiraterone and/or enzalutamide. The trial did not meet its primary endpoint of alleviation of bone pain, as determined by comparing the percentage of patients in the two treatment arms who achieved a pain response at Week 6 that was confirmed at Week 12 without increase in narcotic medication. Fifteen percent of patients in the cabozantinib arm reported a pain response, compared to 17 percent of patients in the control arm receiving mitoxantrone/ prednisone. The difference in pain response between the arms was not statistically significant. The safety profile of cabozantinib in the trial was consistent with that observed in previous studies in mCRPC.

“Following the COMET-1 top-line results announced in September, we deprioritized the cabozantinib development program in mCRPC; at that time, we also initiated a significant workforce reduction in order to focus our development efforts and financial resources on the pivotal phase 3 studies of cabozantinib in metastatic renal cell carcinoma (RCC) and advanced hepatocellular carcinoma (HCC),” said Michael Morrissey, Ph.D., president and chief executive officer of Exelixis. “With target enrollment in the METEOR study in RCC recently achieved, we anticipate top-line results in the second quarter of 2015. We also look forward to Roche and Genentech’s continued regulatory progress with cobimetinib for metastatic melanoma. The EU review is underway and the U.S. filing is expected before year-end, which could ultimately lead to our opportunity to co-promote cobimetinib in the U.S. if it is approved for this indication.”

Exelixis will submit the results from the COMET program for potential presentation at a future medical meeting.

About the COMET-2 Trial

COMET-2, the second phase 3 study from the COMET program, was a randomized, double-blind, controlled trial designed to enroll patients with CRPC that is metastatic to the bone, who were suffering from moderate to severe pain despite optimized narcotic medication, and whose disease had progressed following treatment with docetaxel as well as abiraterone and/or enzalutamide. One hundred and nineteen of the planned 246 patients were randomized 1:1 to receive either cabozantinib or mitoxantrone/prednisone. The primary endpoint was alleviation of bone pain, as determined by comparing the percentage of patients in the two treatment arms who achieve a pain response -- a greater than or equal to 30% decrease from baseline in the average of daily worst pain intensity according to the BPI collected over seven days -- at Week 6 that is confirmed at Week 12 without increase in narcotic medication. Secondary endpoints were bone scan response and overall survival, and other endpoints include PFS, safety, and evaluation of bone biomarkers and circulating tumor cells.

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: Exelixis' plans to focus financial resources on pivotal phase 3 studies of cabozantinib in RCC and HCC; the continued development and clinical, therapeutic and commercial potential of, and opportunities for, cabozantinib and cobimetinib; anticipated developments and timing with respect to Exelixis' pivotal phase 3 study of cabozantinib in RCC; future cobimetinib regulatory filings, regulatory progress and potential approvals; the potential for Exelixis to co-promote cobimetinib in the U.S. in metastatic melanoma; and future potential data presentations. Words such as "focus," "anticipate," "look-forward," "expected" "could," "will," "potential," 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 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 study; the availability of data at the expected times; the clinical, therapeutic and commercial value of cabozantinib and cobimetinib; Exelixis' ability to conduct clinical trials of cabozantinib sufficient to achieve a positive completion; risks and uncertainties related to regulatory review and approval processes and Exelixis' compliance with applicable legal and regulatory requirements; the general sufficiency of Exelixis' capital and other resources and the specific risk of unforeseen expenses that could diminish Exelixis' financial ability to support its operations through the release of top-line METEOR results; the uncertain timing and level of expenses associated with the development of cabozantinib; risks related to Exelixis' ability to implement the referenced workforce reduction according to plan and its impact on Exelixis' business; market competition; 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 November 4, 2014 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.

Source: Exelixis, Inc.

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