FDA Approves COMETRIQ™ (Cabozantinib) for Treatment of Progressive, Metastatic Medullary Thyroid Cancer

November 29, 2012

-- Exelixis will host conference call at 5:00 p.m. EST / 2:00 p.m. PST today

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Nov. 29, 2012-- Exelixis, Inc. (NASDAQ: EXEL) today announced that the U.S. Food and Drug Administration (FDA) has approved COMETRIQ ™ (cabozantinib) for the treatment of progressive, metastatic medullary thyroid cancer (MTC). COMETRIQ is an inhibitor of multiple receptor tyrosine kinases involved in both normal cellular function and pathologic processes such as oncogenesis, metastasis, tumor angiogenesis, and maintenance of the tumor microenvironment. The COMETRIQ label has boxed warnings concerning risk of perforations and fistulas, and hemorrhage.

Exelixis completed its rolling New Drug Application (NDA) in May 2012, and the FDA granted Priority Review Designation to the filing, assigning a Prescription Drug User Fee Act (PDUFA) action date of November 29, 2012. The COMETRIQ approval is based on the results of EXAM, a randomized phase 3 clinical trial conducted in 330 patients with progressive, metastatic MTC, which met its primary efficacy endpoint of improving progression-free survival (PFS).

“The approval of COMETRIQ is an important milestone for patients with progressive, metastatic medullary thyroid cancer, their families, and their physicians, as well as for Exelixis,” said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. “We are grateful to the many patients who participated in the clinical development of COMETRIQ in MTC, and we are committed to making this important new therapy available as quickly as possible.”

The recommended dose of COMETRIQ is 140 mg orally, once daily (one 80 mg capsule and three 20 mg capsules). COMETRIQ should not be taken with food, and patients are advised to not eat for at least 2 hours before and at least 1 hour after taking COMETRIQ. Full prescribing information, including Boxed Warning, is available at www.exelixis.com or www.COMETRIQ.com.

“There has been little clinical progress in treating advanced MTC until the introduction of targeted therapies, and it is gratifying to give these patients a new treatment option that has been shown in clinical trials to improve progression-free survival remarkably by nearly three-fold,” said Steven I. Sherman, M.D., Naguib Samaan Distinguished Professor in Endocrinology at M.D. Anderson Cancer Center and a senior investigator in the phase 3 study. “The availability of a new therapeutic approach that has the potential to improve patient care and outcomes changes the MTC treatment landscape and provides patients and physicians with a new way to manage the disease.”

COMETRIQ Conference Call and Webcast Information

Exelixis' management will discuss the company's plans to launch COMETRIQ in MTC during a conference call beginning at 5:00 p.m. EST / 2:00 p.m. PST today, Thursday, November 29, 2012. To listen to a live webcast of the discussion, visit the Event Calendar page under Investors at www.exelixis.com or access this page directly: http://www.media-server.com/m/p/o5e857m6.

An archived replay of the webcast will be available on the Event Calendar page under Investors at www.exelixis.com and via phone until 11:59 p.m. PST on December 29, 2012. Access numbers for the phone replay are: 888-286-8010 (domestic) and 617-801-6888 (international); the passcode is 91510575.

About COMETRIQ

COMETRIQ’s safety and efficacy was assessed in an international, multi-center, randomized double-blinded controlled trial called EXAM of 330 patients with progressive, metastatic medullary thyroid carcinoma (MTC). Patients were required to have evidence of actively progressive disease within 14 months prior to study entry confirmed by an Independent Radiology Review Committee (IRRC) masked to treatment assignment (89%) or the treating physician (11%). Patients were randomized (2:1) to receive COMETRIQ 140 mg (n = 219) or placebo (n = 111) orally, once daily until disease progression determined by the treating physician or until intolerable toxicity. Randomization was stratified by age (≤65 years vs. > 65 years) and prior use of a tyrosine kinase inhibitor (TKI). No cross-over was allowed at the time of progression. The main efficacy outcome measures of PFS, objective response and response duration were based on IRRC-confirmed events using the modified RECIST criteria.

A statistically significant prolongation in PFS was demonstrated among COMETRIQ-treated patients compared to those receiving placebo [HR 0.28 (95% CI: 0.19, 0.40); p<0.0001], with median PFS times of 11.2 months and 4.0 months in the COMETRIQ and placebo arms, respectively. Partial responses were observed only among patients in the COMETRIQ arm (27% vs 0; p<0.0001). The median duration of objective responses was 14.7 months (95% CI: 11.1, 19.3) for patients treated with COMETRIQ. There was no statistically significant difference in overall survival between the treatment arms at the planned interim analysis.

COMETRIQ Mechanism of Action

COMETRIQ (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™ 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.exelixis.com or www.COMETRIQ.com.

About Exelixis

Exelixis, Inc. 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 its lead product, COMETRIQ. 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 significance of the referenced approval of COMETRIQ for patients, their families, physicians and Exelixis; the clinical, therapeutic and commercial potential of COMETRIQ; and Exelixis' plans and expectations regarding the launch, commercialization, distribution and availability of COMETRIQ. Words such as "milestone," "committed," "available," "new," "quickly as possible," "new," "option," "shown," "potential," "provides," 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 risk that unanticipated developments could delay or prevent the launch, commercialization, manufacturing, distribution and availability of COMETRIQ; the degree of market acceptance of COMETRIQ; the extent to which coverage and reimbursement for COMETRIQ will be available from third-party payors; risks and uncertainties related to Exelixis' compliance with applicable regulatory requirements, including healthcare fraud and abuse laws and post-marketing requirements; the company's dependence on third-party vendors; market competition; the uncertainty of the regulatory approval process; 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 quarter ended September 28, 2012, filed with the Securities and Exchange Commission (SEC) on November 7, 2012, 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.

Exelixis, Inc.
Charles Butler, 650-837-7277
Vice President,
Investor Relations and
Corporate Communications
cbutler@exelixis.com