Exelixis Presents COMETRIQ™ (cabozantinib) Clinical Trial Data in Patients with Progressive, Metastatic Medullary Thyroid Cancer

June 2, 2013

-- 30% of patients in a phase 1 study remain progression-free for more than two years --

-- Association of RET or RAS mutational status with progression-free survival in the EXAM phase 3 pivotal trial of COMETRIQ in progressive, metastatic MTC patients --

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jun. 2, 2013-- Exelixis, Inc. (NASDAQ:EXEL) today announced the presentation of additional data from clinical trials of COMETRIQ™ (cabozantinib) in patients with progressive, metastatic medullary thyroid cancer (MTC). The data were presented this weekend at the 2013 Annual Meeting of the American Society of Clinical Oncology (ASCO). Long-term follow-up of a phase 1 trial (Abstract #6090) shows that 30% of progressive, metastatic MTC patients treated with COMETRIQ experienced disease control (DC) and have remained progression-free for more than 2 years. A separate presentation (Abstract #6000) reports data from the prospective analysis of RET mutational status and retrospective *ad hoc* analysis of RAS mutational status of patients in EXAM, Exelixis' phase 3 pivotal trial of COMETRIQ in progressive, metastatic MTC. These data show improvement in progression-free survival (PFS) with COMETRIQ treatment compared to placebo in all genetically defined subgroups, with a greater effect on PFS seen in the RET mutation positive and RET mutation unknown subgroups. The U.S. Food & Drug Administration approved COMETRIQ for the treatment of progressive, metastatic MTC in November 2012. The label allows for use of COMETRIQ in progressive, metastatic MTC without regard to mutation status.

"These data provide important insight into the clinical utility of COMETRIQ in patients with progressive, metastatic MTC, the first indication in which this tyrosine kinase inhibitor has been approved," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "The long-term follow up data provide supporting evidence indicating that COMETRIQ offers these patients an important new treatment option that can lead to durable disease control. We believe the analyses of clinical benefit from COMETRIQ treatment in progressive, metastatic MTC patients with RET and RAS gene mutations provide additional rationale for investigating the activity of COMETRIQ in other tumor types with alterations in these genes."

Ezra Cohen, M.D., Associate Professor of Medicine at the University of Chicago, Department of Medicine, Associate Director for Education at the University of Chicago Comprehensive Cancer Center, and a principal investigator on the COMETRIQ phase 1 study, presented long-term follow-up data for the cohort of MTC patients included in the study in a poster session on June 1. Of 85 patients enrolled in the phase 1 study, 37 had metastatic or locally advanced MTC. After a minimum follow-up of 52 months, 11 of the 37 patients (30%) experienced long term disease control (DC), defined as confirmed partial response (cPR) or progression free ≥ 24 months. Time from diagnosis and time since development of metastatic disease was similar between patients with or without long-term DC. The most frequent adverse events associated with COMETRIQ were diarrhea, fatigue, nausea, and decreased appetite. The adverse event profile observed after 1 year of treatment was generally consistent with that seen during any time of treatment with COMETRIQ. The median final COMETRIQ dose for patients with long-term DC was 60 mg (range: 20-140 mg), and the median number of dose reductions was 2 (range: 0-4).

"These results are encouraging for the field of medullary thyroid cancer because, for many years, patients with this disease have had limited treatment options," said Dr. Cohen. "These results show that a significant number of patients treated with cabozantinib achieved meaningful long-term disease control and were able to remain on continuous daily therapy."

Dr. Steven I. Sherman, M.D., Naguib Samaan Distinguished Professor in Endocrinology at M.D. Anderson Cancer Center and Chairman of the International Thyroid Oncology Group, presented the phase 3 mutational analysis data in an oral session on Sunday, June 2. RET and RAS mutations were assessed in patients enrolled in EXAM, a double blind, placebo-controlled, phase 3 trial of COMETRIQ in patients with progressive, metastatic MTC. The median PFS on the COMETRIQ arm was 11.2 months, compared with 4 months for the placebo arm, HR 0.28, 95% CI 0.19, 0.40, $p < 0.0001$. RET status was determined in 65% (215/330) of the patients enrolled in the phase 3 trial. Of these 215 patients, 79% had activating RET mutations and 21% had no RET mutations detected. Of 85 evaluated patients with either no RET mutations or unknown RET status, 16 were found to have a RAS gene mutation. COMETRIQ had activity across all RET and RAS mutational subgroups, and demonstrated response rates of 22-32%, consistent with the response rate of patients in the study overall (28% COMETRIQ vs. 0% placebo). Patients with RET mutations had significantly longer median PFS (60 weeks) than patients who were RET mutation-negative (25 weeks). Patients with RAS mutations had a median PFS of 47 weeks, indicating that clinical activity measured in the RET mutation-negative subgroup can be attributed partially to patients with RAS mutations.

"These data show that COMETRIQ improves PFS in all RET subgroups," said Dr. Sherman. "The extent of the benefit varies in part based on tumor genotype. Given that RET mutations are associated with most cases of hereditary MTC and about half of sporadic cases, understanding the correlation between specific RET mutations and response to COMETRIQ may be important for optimizing outcomes in patients with metastatic MTC. Recent data have shown RAS mutations in subsets of patients without RET mutations, and the data from our study show that these patients also benefit from treatment with COMETRIQ. These findings are important for improving outcomes and PFS for patients with metastatic MTC."

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 crossover 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.COMETRIQ.com.

About Exelixis

Exelixis 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 COMETRIQ™ (cabozantinib)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 continued development and clinical, therapeutic and commercial potential of, and opportunities for, COMETRIQ; the belief that the referenced data provide important insight into the clinical utility of COMETRIQ in patients with progressive, metastatic MTC; the belief that COMETRIQ offers patients an important new treatment option that can lead to durable disease control; the belief that the referenced analyses provide additional rationale for exploring the clinical utility of COMETRIQ in other tumor types with genetic alterations in the RET and RAS genes; the belief that the referenced results provide physicians and patients with additional information showing that COMETRIQ can help improve long-term disease control; the belief that understanding the correlation between specific RET mutations and response to COMETRIQ may be important for optimizing outcomes in patients with metastatic MTC; and the belief that the referenced findings are important for improving outcomes and PFS for patients with metastatic MTC. Words such as “show,” “provide,” “insight,” “supporting,” “evidence,” “offers,” “can,” “believe,” “rationale,” “investigating,” “activity,” “encouraging,” “may,” “important,” 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 availability of data at the expected times; risks related to the potential failure of COMETRIQ to demonstrate safety and efficacy in clinical testing; the uncertain timing and level of expenses associated with the development of COMETRIQ; Exelixis' ability to conduct clinical trials of COMETRIQ sufficient to achieve a positive completion; 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; the sufficiency of Exelixis' capital and other resources; the uncertainty of the regulatory approval process; market competition; 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 three months ended March 29, 2013, filed with the Securities and Exchange Commission (SEC) on May 7, 2013, 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.

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