Exelixis Announces Presentation of Updated Phase 2 Data for Cabozantinib in Men with Heavily-Pretreated Metastatic Castration-Resistant Prostate Cancer

June 1, 2013

-- Median Overall Survival of 10.8 months in a population where 73% of patients had 2+ prior therapies --

-- Responder analyses show that bone scan, circulating tumor cell, and pain responses are associated with longer overall survival --

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jun. 1, 2013-- Exelixis, Inc. (NASDAQ:EXEL) today announced the presentation of updated interim data from 144 docetaxel-pretreated patients with metastatic castration-resistant prostate cancer (mCRPC) and bone metastases treated with cabozantinib in an ongoing non-randomized expansion (NRE) cohort of its phase 2 randomized discontinuation trial. Median overall survival was 10.8 months in a patient population in which 73% of patients had received two or more prior therapies including docetaxel and abiraterone, enzalutamide, and/or cabazitaxel. Furthermore, a retrospective analysis of the interim data shows that early responses in bone scan, circulating tumor cell (CTC) levels, and pain are associated with longer median overall survival (OS) as compared to non-responders. These post hoc findings, particularly the bone scan response results, support the rationale for potential future prospective validation of the association of bone scan response with OS in Exelixis' ongoing phase 3 COMET trials in mCRPC. Howard I. Scher, M.D., Chief of the Genitourinary Oncology Service at Memorial Sloan-Kettering Cancer Center and a principal investigator on the study, presented the data today in a poster-discussion session at the 2013 Annual Meeting of the American Society of Clinical Oncology (ASCO) (Abstract #5026), in Chicago, Illinois.

"This clinical trial enrolled a heavily pretreated mCRPC population that has not been studied previously. These patients experienced disease progression despite treatment with docetaxel and additional therapies that included abiraterone, enzalutamide, or cabazitaxel. In this context the results are encouraging," said Dr. Scher. "Patients with such advanced disease have limited options, and the data from this cohort suggest that cabozantinib has the potential to be an important treatment option for patients with mCRPC. The preliminary data suggest that these early response indicators are associated with longer median overall survival and warrant further prospective evaluation in phase 3. The ongoing phase 3 trials will help to define the potential utility of cabozantinib in mCRPC."

The interim results presented today comprise data from 144 men with mCRPC in the NRE cohort of an ongoing phase 2 randomized discontinuation trial. All patients had disease progression in either bone or soft tissue disease within 6 months of completion of docetaxel treatment, and the protocol differed from typical CRPC studies in that it excluded patients who progressed by PSA criteria alone, who generally have a better overall prognosis. All patients also had bone metastases on bone scan and 31% had measurable soft tissue disease. Seventy three percent of patients had received at least two prior lines of therapy for mCRPC, including docetaxel in all patients. In 36% of patients, disease progression was very rapid, occurring less than one month following the last dose of taxane therapy. Clinically significant pain, defined as baseline pain score by Brief Pain Inventory (BPI) ≥ 4, was present in 47% of patients. Eighty percent of patients had a CTC count ≥ 5/7.5 mL of blood. Patients received a 100 mg or 40 mg daily dose of cabozantinib.

The median OS in the 144 patients was 10.8 months (95% confidence interval 9.1-13.0). Bone scan response (≥ 30% decrease from baseline in the Technetium-99m methylene diphosphonate bone scan lesion area determined by computer assisted detection) was observed in 65% of evaluable patients, CTC response (conversion from ≥ 5 CTC/7.5 mL of blood to < 5 CTC/7.5 mL of blood) in 32% of evaluable patients, and pain response (≥ 30% decrease from baseline in worst pain observed at 2 consecutive assessments ≥ 6 weeks apart) in 43% of evaluable patients. In univariate analyses, longer OS was associated with bone scan response at week 6, CTC response at week 6, and pain response. These findings were further examined and confirmed in sensitivity analyses after adjusting for significant baseline covariates, such as LDH, presence or absence of visceral metastasis, and bone scan lesion area (bone disease burden), which were selected from a stepwise Cox regression model.

Safety data for the NRE were presented at two medical meetings in 2012. At the ASCO Annual Meeting in June 2012, Dr. Matthew Smith of Massachusetts General Hospital presented data from 93 patients receiving a 100 mg daily dose of cabozantinib (Abstract #4513). At the European Society for Medical Oncology Congress in September 2012, Dr. Johann de Bono, of The Institute of Cancer Research, London, presented data from 51 patients receiving a 40 mg daily dose of cabozantinib (Abstract #897O). Across dose levels, the most common adverse events (AEs) of grade 3 or higher were fatigue, hypertension, and venous thrombosis. 25% of patients in the 40 mg dose cohort experienced one dose reduction due to an AE, and 84% of patients in the 100 mg dose cohort experienced at least one dose reduction due to an AE. Overall, the lower starting dose of 40 mg was better tolerated with lower rates of dose reduction and interruption.

"These data provide additional evidence that cabozantinib has clinical activity against multiple aspects of metastatic disease in this patient population," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "The overall survival results are encouraging given that the patients enrolled in the NRE cohort comprise a highly refractory and advanced mCRPC population, and are similar to those being enrolled in our ongoing phase 3 COMET trials. We believe that these data provide continued support for our clinical strategy in this indication."

About Cabozantinib

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™ (cabozantinib) is currently approved by the U.S. Food and Drug Administration for the treatment of progressive, metastatic medullary

thyroid cancer.

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, cabozantinib; the belief that the referenced post hoc findings support the rationale for potential future prospective validation of the association of bone scan response with OS in the ongoing phase 3 COMET trials; the belief that the referenced data is encouraging; the potential for cabozantinib to be an important treatment option for patients with mCRPC; the belief that the ongoing phase 3 COMET trials will help define the potential utility of cabozantinib in mCRPC; the correlation of the NRE cohort and the referenced data with the ongoing phase 3 COMET trials; and Exelixis' clinical strategy in mCRPC. Words such as “show,” “support,” “rationale,” “potential,” “future,” prospective,” “validation,” “encouraging,” “suggest,” “option,” “warrant,” “provide,” “evidence,” “being,” “believe,” “continued,” “strategy,” 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 cabozantinib to demonstrate safety and efficacy in clinical testing; the uncertain timing and level of expenses associated with the development of cabozantinib; Exelixis' ability to conduct clinical trials of cabozantinib sufficient to achieve a positive completion; the sufficiency of Exelixis' capital and other resources; 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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