# Exelixis Announces Results from the COMET-1 Phase 3 Pivotal Trial of Cabozantinib in Men with Metastatic Castration-Resistant Prostate Cancer

September 1, 2014

*Conference Call on Tuesday, September 2, 2014 at 8:30 a.m. EDT*

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Sep. 1, 2014-- Exelixis, Inc. (NASDAQ:EXEL) today announced top-line results from the final analysis of COMET-1, the phase 3 pivotal trial of cabozantinib in men with metastatic castration-resistant prostate cancer (mCRPC) whose disease progressed after treatment with docetaxel as well as abiraterone and/or enzalutamide. The trial did not meet its primary endpoint of demonstrating a statistically significant increase in overall survival (OS) for patients treated with cabozantinib as compared to prednisone. The median OS for the cabozantinib arm of the trial was 11.0 months versus 9.8 months for the prednisone arm (hazard ratio 0.90; 95% confidence interval 0.76 – 1.06; p value 0.212).

The COMET-1 results are the subject of ongoing analyses. Exelixis will submit additional data, including secondary and exploratory endpoints, for presentation at a future medical conference. Besides OS, the exploratory endpoint of progression-free survival (PFS) as assessed by the investigators is the only time-to-event-based endpoint for which data are available. Median PFS was 5.5 months for the cabozantinib arm of the trial versus 2.8 months for the prednisone arm (hazard ratio 0.50; 95% confidence interval 0.42 – 0.60; p value <0.0001). Safety data were consistent with those observed in earlier-stage trials of cabozantinib in mCRPC.

As a result of the outcome of COMET-1, Exelixis will initiate a significant workforce reduction to enable the company to focus its financial resources on the late-stage clinical trials of cabozantinib in metastatic renal cell carcinoma (the METEOR trial) and advanced hepatocellular carcinoma (the CELESTIAL trial). The company will reduce its workforce by approximately 70 percent, or approximately 160 employees, resulting in approximately 70 remaining employees.

Exelixis anticipates the one-time restructuring charge associated with the workforce reduction to be approximately $6 million - $8 million, with the majority to be completed by the end of the fourth quarter of 2014. As a result of this and other cost-saving measures contemplated, the company anticipates that it has sufficient cash to support its operations through the release of top-line results of the METEOR trial next year. More financial details will be provided by the company in its third quarter 2014 financial report.

“We are very disappointed that COMET-1 did not meet its primary endpoint of extending overall survival in men with mCRPC,” said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. “We are grateful to the patients, physicians, nurses, caregivers, and other study team members who participated in the trial. We remain focused on the development program for cabozantinib beyond mCRPC, including the ongoing METEOR and CELESTIAL phase 3 pivotal trials, from which we expect top-line data in 2015 and 2017, respectively.”

Dr. Morrissey continued, “We have thoughtfully prepared for this scenario and the resulting very difficult decisions. The workforce reduction we have announced today is necessary to significantly reduce our corporate operating expenses. I would like to personally express my deep appreciation to the talented and dedicated Exelixis employees who will be impacted by these actions, both for their commitment to Exelixis and for their tremendous contributions to patients with cancer.”

Based on the outcome of COMET-1, Exelixis has deprioritized the clinical development of cabozantinib in mCRPC. Enrollment in COMET-2, which is the second pivotal trial in mCRPC and evaluates pain palliation, has been halted. The company expects top-line data before the end of this year. Based on the outcome of COMET-2, Exelixis will discuss with regulatory authorities the potential regulatory path, if any, of cabozantinib in mCRPC. Other company-sponsored studies in mCRPC, including a randomized phase 2 study of cabozantinib in combination with abiraterone, will also be halted.

**Investor Conference Call and Webcast**

Exelixis management will discuss the COMET-1 top-line results and the resulting corporate initiatives during a conference call beginning at 8:30 a.m. EDT/ 5:30 a.m. PDT tomorrow, Tuesday, September 2, 2014. To join the call, participants may dial 877-546-5020 (domestic) or 857-244-7552 (international) and use passcode 60161764. To listen to a live webcast of the conference call, please visit the Event Calendar page under Investors & Media at www.exelixis.com.

An archived replay of the conference call will be available on the Event Calendar page under Investors & Media at www.exelixis.com and via phone until 11:59 p.m. EDT on October 2, 2014. Access numbers for the phone replay are: 888-286-8010 (domestic) and 617-801-6888 (international); the passcode is 69796111.

**About the COMET-1 Phase 3 Pivotal Trial**

COMET-1 was a randomized, double-blind, controlled trial that enrolled 960 patients with mCRPC who had previously been treated with and progressed after treatment with docetaxel, abiraterone and/or enzalutamide. The primary endpoint of the trial was OS, and the secondary endpoint was bone scan response as assessed by an independent radiology committee. All patients in the trial had bone metastases, and there was no limit to the number or type of prior treatments. Patients were randomized 2:1 to receive cabozantinib (60 mg daily) or prednisone (5 mg twice daily). The trial

was event-driven and had 90% power to detect a 25% reduction in the risk of death (HR = 0.75) at the time of final analysis, which required 578 events.

**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: the continued development and clinical, therapeutic and commercial potential of, and opportunities for, cabozantinib; the results and implications of completed, partial, and ongoing clinical data analyses; future data presentations; future discussions with regulatory authorities; anticipated developments and timing with respect to Exelixis' ongoing phase 3 pivotal trials of cabozantinib; plans to focus financial resources, to halt company-sponsored studies in mCRPC; and plans to initiate a workforce reduction, including the objectives and anticipated timing thereof. Words such as "will," "enable," "focus," "anticipates," "expect," "ensure," "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, 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 study; the clinical, therapeutic and commercial value of cabozantinib; 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; expenses and charges resulting from the referenced workforce reduction; 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 July 31, 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.

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