Exelixis Announces Results from Randomized Phase 2 Trial CABOSUN Demonstrate Cabozantinib Significantly Improved Progression-Free Survival versus Sunitinib in Previously Untreated Advanced Renal Cell Carcinoma

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– Exelixis to consult with regulatory authorities to determine next steps in development and submission strategy for cabozantinib in first-line renal cell carcinoma –

SAN FRANCISCO--(BUSINESS WIRE)--May 23, 2016-- Exelixis, Inc. (NASDAQ:EXEL) today announced positive top-line results from the CABOSUN randomized phase 2 trial of cabozantinib in patients with previously untreated advanced renal cell carcinoma (RCC). The trial met its primary endpoint, demonstrating a statistically significant and clinically meaningful improvement in progression-free survival (PFS) for cabozantinib compared with sunitinib in patients with advanced intermediate- or poor-risk RCC. The safety data in the cabozantinib-treated arm of the study were consistent with those observed in previous studies in patients with advanced RCC. CABOSUN is being conducted by The Alliance for Clinical Trials in Oncology as part of Exelixis' collaboration with the National Cancer Institute's Cancer Therapy Evaluation Program (NCI-CTEP). The final results from CABOSUN will be submitted for presentation at a future medical conference.

"The positive outcome of CABOSUN is extremely exciting, as it marks the very first time that a therapy has shown a progression-free survival benefit over standard of care first-line treatment sunitinib for patients with previously untreated advanced renal cell carcinoma," said Toni K. Choueiri, M.D., Clinical Director, Lank Center for Genitourinary Oncology, Dana-Farber Cancer Institute and chair of the CABOSUN study. "Based on these findings, cabozantinib may have the potential to become a new gold standard for previously untreated patients following their diagnosis with advanced kidney cancer."

"All of us at the Alliance for Clinical Trials in Oncology are very gratified to have successfully demonstrated the potential of first-line cabozantinib to benefit patients with renal cell carcinoma in the CABOSUN study. This trial exemplifies how NCI-sponsored studies can be efficient, accrue rapidly, and yield results highly relevant to the field," said Michael J. Morris, M.D., medical oncologist at Memorial Sloan Kettering Cancer Center, and Chair of the Alliance Genitourinary (GU) Committee.

Exelixis will share the results of CABOSUN with regulatory authorities to discuss potential next steps in the development and submission strategy for cabozantinib as a treatment of first-line advanced renal cell carcinoma. Exelixis is also working closely with clinical advisors on the development plan for cabozantinib in future clinical trials in other genitourinary malignancies.

"Demonstrating an improvement in progression-free survival with cabozantinib compared to sunitinib as a first-line treatment represents an important milestone for patients with previously untreated RCC," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "We are thrilled to be a part of the many recent advances in the treatment of advanced kidney cancer and would like to thank the patients, physicians, nurses, caregivers, the Alliance cooperative group and NCI-CTEP who made this clinical trial possible. We look forward to pursuing next steps in the development of cabozantinib in the first-line treatment of patients with advanced RCC and other GU malignancies."

About the CABOSUN Study

CABOSUN is a randomized, open-label, active-controlled phase 2 trial that was designed to enroll 150 patients with advanced RCC determined to be intermediate- or poor-risk by the International Metastatic RCC Database Consortium (IMDC) criteria. Patients were randomized 1:1 to receive cabozantinib (60 mg once daily) or sunitinib (50 mg once daily, 4 weeks on followed by 2 weeks off). The randomization was stratified by the IMDC risk strata (intermediate or poor risk) and presence of bone metastasis (yes, no). Enrollment was completed in March 2015. The primary endpoint was PFS, defined as time from randomization to disease progression or death, whichever occurs first. Positive PFS results have formed the basis for previous regulatory approvals of treatments in the first-line setting, including sunitinib. Secondary endpoints included overall survival and objective response rate. Eligible patients were required to have locally advanced or metastatic clear-cell RCC, ECOG performance status 0-2, and had to be intermediate or poor risk, per the IMDC Criteria (Heng JCO 2009). Prior systemic treatment for RCC was not permitted. With 123 events (disease progression or death), the log-rank statistic has 85 percent power (with a one-sided type I error rate=0.12) to detect a hazard ratio of 0.67. Between July 9, 2013 and April 6, 2015, 157 patients were randomized: 79 patients on the cabozantinib arm and 78 patients on the sunitinib arm.

Please see Important Safety Information below and full U.S. prescribing information at https://cabometyx.com/downloads/cabometyxuspi.pdf.

About Advanced Renal Cell Carcinoma

The American Cancer Society's 2016 statistics cite kidney cancer as among the top ten most commonly diagnosed forms of cancer among both men and women in the U.S.[1] Clear cell RCC is the most common type of kidney cancer in adults.[2] If detected in its early stages, the five-year survival rate for RCC is high; for patients with advanced or late-stage metastatic RCC, however, the five-year survival rate is only 12 percent, with no identified cure for the disease.[1] Approximately 30,000 patients in the U.S. and 68,000 globally require treatment.[3]

The majority of clear cell RCC tumors have lower than normal levels of a protein called von Hippel-Lindau, which leads to higher levels of MET, AXL and VEGF.[4,5] These proteins promote tumor angiogenesis (blood vessel growth), growth, invasiveness and metastasis.[6-9] MET and AXL may provide

escape pathways that drive resistance to VEGF receptor inhibitors.[5,6]

About CABOMETYX

CABOMETYX targets include MET, AXL and VEGFR-1, -2 and -3. In preclinical models, cabozantinib has been shown to inhibit the activity of these receptors, which are involved in normal cellular function and pathologic processes such as tumor angiogenesis, invasiveness, metastasis and drug resistance.

CABOMETYX, the tablet formulation of cabozantinib, is available in 20 mg, 40 mg or 60 mg doses. The recommended dose is 60 mg orally, once daily.

On April 25, the FDA approved CABOMETYX tablets for the treatment of patients with advanced renal cell carcinoma who have received prior anti-angiogenic therapy.

On January 28, 2016, the European Medicines Agency (EMA) validated Exelixis' Marketing Authorization Application (MAA) for cabozantinib as a treatment for patients with advanced renal cell carcinoma who have received one prior therapy. The MAA has been granted accelerated assessment, making it eligible for a 150-day review, versus the standard 210 days. On February 29, 2016, Exelixis and Ipsen jointly announced an exclusive licensing agreement for the commercialization and further development of cabozantinib indications outside of the United States, Canada and Japan.

Important Safety Information

Hemorrhage: Severe hemorrhage occurred with CABOMETYX. The incidence of Grade ≥3 hemorrhagic events was 2.1% in CABOMETYX-treated patients and 1.6% in everolimus-treated patients. Fatal hemorrhages also occurred in the cabozantinib clinical program. Do not administer CABOMETYX to patients that have or are at risk for severe hemorrhage.

Gastrointestinal (GI) Perforations and Fistulas: Fistulas were reported in 1.2% (including 0.6% anal fistula) of CABOMETYX-treated patients and 0% of everolimus-treated patients. GI perforations were reported in 0.9% of CABOMETYX-treated patients and 0.6% of everolimus-treated patients. Fatal perforations occurred in the cabozantinib clinical program. Monitor patients for symptoms of fistulas and perforations. Discontinue CABOMETYX in patients who experience a fistula that cannot be appropriately managed or a GI perforation.

Thrombotic Events: CABOMETYX treatment results in an increased incidence of thrombotic events. Venous thromboembolism was reported in 7.3% of CABOMETYX-treated patients and 2.5% of everolimus-treated patients. Pulmonary embolism occurred in 3.9% of CABOMETYX-treated patients and 0.3% of everolimus-treated patients. Events of arterial thromboembolism were reported in 0.9% of CABOMETYX-treated patients and 0.3% of everolimus-treated patients. Fatal thrombotic events occurred in the cabozantinib clinical program. Discontinue CABOMETYX in patients who develop an acute myocardial infarction or any other arterial thromboembolic complication.

Hypertension and Hypertensive Crisis: CABOMETYX treatment results in an increased incidence of treatment-emergent hypertension. Hypertension was reported in 37% (15% Grade ≥3) of CABOMETYX-treated patients and 7.1% (3.1% Grade ≥3) of everolimus-treated patients. Monitor blood pressure prior to initiation and regularly during CABOMETYX treatment. Withhold CABOMETYX for hypertension that is not adequately controlled with medical management; when controlled, resume CABOMETYX at a reduced dose. Discontinue CABOMETYX for severe hypertension that cannot be controlled with anti-hypertensive therapy. Discontinue CABOMETYX if there is evidence of hypertensive crisis or severe hypertension despite optimal medical management.

Diarrhea: Diarrhea occurred in 74% of patients treated with CABOMETYX and in 28% of patients treated with everolimus. Grade 3 diarrhea occurred in 11% of CABOMETYX-treated patients and in 2% of everolimus-treated patients. Withhold CABOMETYX in patients who develop intolerable Grade 2 diarrhea or Grade 3-4 diarrhea that cannot be managed with standard antidiarrheal treatments until improvement to Grade 1; resume CABOMETYX at a reduced dose. Dose modification due to diarrhea occurred in 26% of patients.

Palmar-Plantar Erythrodysesthesia Syndrome (PPES): Palmar-plantar erythrodysesthesia syndrome (PPES) occurred in 42% of patients treated with CABOMETYX and in 6% of patients treated with everolimus. Grade 3 PPES occurred in 8.2% of CABOMETYX-treated patients and in <1% of everolimus-treated patients. Withhold CABOMETYX in patients who develop intolerable Grade 2 PPES or Grade 3 PPES until improvement to Grade 1; resume CABOMETYX at a reduced dose. Dose modification due to PPES occurred in 16% of patients.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS): RPLS, a syndrome of subcortical vasogenic edema diagnosed by characteristic finding on MRI, occurred in the cabozantinib clinical program. Perform an evaluation for RPLS in any patient presenting with seizures, headache, visual disturbances, confusion, or altered mental function. Discontinue CABOMETYX in patients who develop RPLS.

Embryo-fetal Toxicity: CABOMETYX can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with CABOMETYX and for 4 months after the last dose.

Adverse Reactions: The most commonly reported (≥25%) adverse reactions are: diarrhea, fatigue, nausea, decreased appetite, PPES, hypertension, vomiting, weight decreased, and constipation.

Drug Interactions: Strong CYP3A4 inhibitors and inducers: Reduce the dosage of CABOMETYX if concomitant use with strong CYP3A4 inhibitors cannot be avoided. Increase the dosage of CABOMETYX if concomitant use with strong CYP3A4 inducers cannot be avoided.

Lactation: Advise a lactating woman not to breastfeed during treatment with CABOMETYX and for 4 months after the final dose.

Reproductive Potential: Contraception—Advise females of reproductive potential to use effective contraception during treatment with CABOMETYX and for 4 months after the final dose. **Infertility —**CABOMETYX may impair fertility in females and males of reproductive potential.

Hepatic Impairment: Reduce the CABOMETYX dose in patients with mild (Child-Pugh score [C-P] A) or moderate (C-P B) hepatic impairment. CABOMETYX is not recommended for use in patients with severe hepatic impairment.

Please see full Prescribing Information at https://cabometyx.com/downloads/cabometyxuspi.pdf.

About Exelixis

Exelixis, Inc. (Nasdaq:EXEL) is a biopharmaceutical company committed to the discovery, development and commercialization of new medicines with the potential to improve care and outcomes for people with cancer. Since its founding in 1994, three medicines discovered at Exelixis have progressed through clinical development to receive regulatory approval. Currently, Exelixis is focused on advancing cabozantinib, an inhibitor of multiple tyrosine kinases including MET, AXL and VEGF receptors, which has shown clinical anti-tumor activity in more than 20 forms of cancer and is the subject of a broad clinical development program. Two separate formulations of cabozantinib have received regulatory approval to treat certain forms of kidney and thyroid cancer and are marketed for those purposes as CABOMETYX™ tablets (U.S.) and COMETRIQ® capsules (U.S. and EU), respectively. Another Exelixis-discovered compound, COTELLIC™ (cobimetinib), a selective inhibitor of MEK, has been approved in major territories including the United States and European Union, and is being evaluated for further potential indications by Roche and Genentech (a member of the Roche Group) under a collaboration with Exelixis. For more information on Exelixis, please visit www.exelixis.com or follow @ExelixisInc on Twitter.

Forward-Looking Statement Disclaimer

This press release contains forward-looking statements, including, without limitation, statements related to: the therapeutic potential of cabozantinib as a treatment for previously untreated patients following their diagnosis with advanced RCC; plans to present the final results from CABOSUN at a future medical conference; potential next steps in the development and submission strategy for cabozantinib as a treatment of first-line advanced RCC and other genitourinary malignancies; the eligibility of Exelixis' MAA for cabozantinib in second line advanced RCC for an expedited review by the EMA; Exelixis' commitment to developing small molecule therapies for the treatment of cancer; and Exelixis' primary focus on the development and commercialization of cabozantinib. Words such as "committed," "will," "may", "potential", "become", "pursue", "next", "look forward", "eligible," "focusing," 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. 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: Exelixis' dependence on decisions in connection with the CABOSUN study made by The Alliance for Clinical Trials in Oncology as part of Exelixis' collaboration with the NCI-CTEP; Exelixis' dependence on third-party vendors; risks and uncertainties related to regulatory application, review, and approval processes and Exelixis' compliance with applicable legal and regulatory requirements; Exelixis' ability to conduct clinical trials of cabozantinib sufficient to achieve a positive completion; and other factors discussed under the caption "Risk Factors" in Exelixis' annual report on Form 10-K filed with the Securities and Exchange Commission (SEC) on February 29, 2016, 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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