Exelixis Announces Positive Results from Phase 2 CABOSUN Trial of Cabozantinib Versus Sunitinib in Previously Untreated Advanced Renal Cell Carcinoma Presented at ESMO 2016

October 10, 2016

– Cabozantinib met the primary endpoint of improving progression-free survival as compared to sunitinib, decreasing the rate of disease progression or death by 31 percent –

– Objective response rate significantly improved: 46 percent for cabozantinib versus 18 percent for sunitinib –

– Exelixis to host investor and media webcast from Copenhagen to discuss the data on Monday, October 10 –

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Oct. 10, 2016-- Exelixis, Inc. (NASDAQ:EXEL) today announced detailed results from the CABOSUN randomized phase 2 trial of cabozantinib in patients with previously untreated advanced renal cell carcinoma (RCC) with intermediate- or poor-risk disease per the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC). Principal investigator Toni K. Choueiri, M.D. will present detailed data from late-breaking CABOSUN abstract [#LBA30_PR] today in the Presidential Symposium 3 session, starting at 16:30 CEST (local Copenhagen time) / 10:30 a.m. EDT / 7:30 a.m. PDT at the European Society for Medical Oncology (ESMO) 2016, which is being held October 7 – 11, 2016 in Copenhagen.

CABOSUN was 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).

In CABOSUN, with a median follow-up of 20.8 months, cabozantinib demonstrated a clinically meaningful and statistically significant 31 percent reduction in the rate of disease progression or death [HR 0.69, 95% CI (0.48-0.99), one-sided P=0.012]. The median progression-free survival (PFS) for cabozantinib was 8.2 months versus 5.6 months for sunitinib, corresponding to a 2.6 months (46 percent) improvement favoring cabozantinib over sunitinib. PFS benefits were independent of IMDC risk group (intermediate or poor risk) and presence or absence of bone metastases at baseline. The results for sunitinib were in line with a previously published retrospective analysis of 1,174 intermediate- and poor-risk RCC patients from the IMDC database, which documented a median PFS of 5.6 months with a first-line targeted therapy, mainly sunitinib, in this patient population.[1]

Objective response rate (ORR) was also significantly improved, at 46 percent (95% CI 34% – 57%) for cabozantinib versus 18 percent (95% CI 10% to 28%) for sunitinib. With a median follow up of 22.8 months, median overall survival was 30.3 months for cabozantinib versus 21.8 months for sunitinib [HR 0.80, 95% CI (0.50 - 1.26)].

"The results presented today support the potential of cabozantinib to become a new therapeutic option for previously untreated patients following their diagnosis with advanced kidney cancer," said Toni K. Choueiri, M.D., Director, Lank Center for Genitourinary Oncology, Dana-Farber Cancer Institute and chair of the CABOSUN study. "Not only has cabozantinib surpassed sunitinib, the current standard of care, in progression-free survival and objective response rate, cabozantinib's effects on progression-free survival were also consistently favorable across patient stratification subgroups including IMDC intermediate versus poor-risk groups and presence or absence of bone metastases."

"We at the Alliance for Clinical Trials in Oncology are pleased that CABOSUN has successfully demonstrated that cabozantinib has the potential to benefit patients with advanced renal cell carcinoma as a first-line therapy," said Michael J. Morris, M.D., Associate Member at Memorial Sloan Kettering Cancer Center, and Chair of the Alliance Genitourinary Committee. "We are grateful to everyone who has participated in the trial, especially the physicians, patients and their families."

Based on these results, Exelixis plans to submit a Supplemental New Drug Application (sNDA) for cabozantinib as a treatment of first-line advanced renal cell carcinoma, and is working with the Alliance to transfer the complete CABOSUN clinical database to Exelixis.

"The past year has seen a tremendous level of progress in the treatment of kidney cancer, and we are excited to be at the forefront of bringing these advancements to patients," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "Patients in the first-line setting with either intermediate- or poor-risk disease progress rapidly with sunitinib, a current standard of care; therefore, there is a clear need for new options that provide improved clinical benefit in this difficult to treat patient population. To that end, based on the CABOSUN results, we are planning to submit a supplemental New Drug Application in the United States for cabozantinib as a first-line treatment for advanced renal cell carcinoma."

CABOSUN enrolled 157 patients with previously untreated advanced RCC: 80.9 percent of patients were intermediate risk per IMDC criteria and 19.1 percent were poor risk, 36.3 percent of patients had bone metastases, 46 percent of patients had ECOG Performance Status (PS) 0, 41 percent had ECOG PS 1, and 13 percent had ECOG PS 2. All patients were included in the efficacy analyses that followed the intent-to-treat principle. Tumor assessments were performed by the investigators following RECIST criteria. At the time of the analysis of the primary endpoint of PFS, the median duration of treatment in CABOSUN was 6.9 months with cabozantinib and 2.8 months with sunitinib; 13 patients continued on cabozantinib treatment versus 2 patients on sunitinib treatment. Dose reductions occurred for 58 percent and 49 percent of patients, respectively. Discontinuation rate due to an adverse event was 20 percent with cabozantinib and 21 percent with sunitinib.

One hundred and fifty patients were evaluable for safety. Ninety-nine percent of patients on both arms experienced at least one adverse event. The most common all causality grade 3 or 4 adverse events observed in more than 5 percent of patients were hypertension (28 percent), diarrhea (10

percent), palmar-plantar erythrodysesthesia (8 percent), and fatigue (6 percent) in the cabozantinib arm, and hypertension (22 percent), fatigue (15 percent), diarrhea and thrombocytopenia (both 11 percent), and oral mucositis (6 percent) in the sunitinib arm. Treatment-related grade 5 events occurred in three patients in the cabozantinib arm (acute kidney injury, sepsis and jejunal perforation) and two patients in the sunitinib arm (sepsis and vascular disorder).

About the CABOSUN Study

On May 23, 2016, Exelixis announced that CABOSUN met its primary endpoint, demonstrating a statistically significant and clinically meaningful improvement in PFS compared with sunitinib in patients with advanced intermediate- or poor-risk 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).

CABOSUN was a randomized, open-label, active-controlled phase 2 trial that enrolled 157 patients with advanced RCC determined to be intermediate- or poor-risk by the 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 primary endpoint was PFS. 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.

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

Webcast for the Financial Community and Media

Exelixis and its partner Ipsen will jointly host a live webcast today, Monday, October 10. The webcast will begin at 19:00 CEST (local Copenhagen time) / 1:00 p.m. EDT / 10:00 a.m. PDT. During the webcast, Exelixis and Ipsen management and invited guest speakers will review and provide context of the results from the CABOSUN study, along with the other data sets on cabozantinib presented at the conference.

To access the webcast link, log onto www.exelixis.com and proceed to the Event Calendar page under Investors & Media. Please connect to the company's website at least 15 minutes prior to the webcast to ensure adequate time for any software download that may be required to view the program. To listen to an audio-only version of the program by phone, please dial 855-299-5224 (domestic) or 631-267-4890 (international/toll dial) and use passcode 234-026-024. An archived replay of the webcast will be available on the Event Calendar page under Investors & Media at www.exelixis.com after the event concludes.

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.[2] Clear cell RCC is the most common type of kidney cancer in adults.[3] 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.[4]

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.[5,6] These proteins promote tumor angiogenesis (blood vessel growth), growth, invasiveness and metastasis.[7-10] MET and AXL may provide escape pathways that drive resistance to VEGF receptor inhibitors.[6,7]

About CABOMETYX™ (cabozantinib)

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

On April 25, 2016, the FDA approved CABOMETYX tablets for the treatment of patients with advanced renal cell carcinoma who have received prior anti-angiogenic therapy. On September 9, 2016, the European Commission approved CABOMETYX tablets for the treatment of advanced renal cell carcinoma in adults who have received prior vascular endothelial growth factor (VEGF)-targeted therapy in the European Union, Norway and Iceland. 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.

U.S. 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 EU) 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 presentation of detailed data from CABOSUN at ESMO; the potential of cabozantinib to become a new therapeutic option for previously untreated patients following their diagnosis with advanced kidney cancer; the potential of cabozantinib to benefit patients with advanced RCC as a first-line therapy; Exelixis' plans to submit a sNDA in the United States for cabozantinib as a treatment for first-line advanced RCC; Exelixis' commitment to the discovery, development and commercialization of new medicines with the potential to improve care and outcomes for people with cancer; Exelixis' focus on advancing cabozantinib; and the continued development of cobimetinib. Words such as "will," "potential," "plans," "committed," "focused," 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: the availability of data at the referenced times; Exelixis' ability and the ability of its collaborators to conduct clinical trials of cabozantinib sufficient to achieve a positive completion; risks related to the potential failure of cabozantinib to demonstrate safety and efficacy in clinical testing; risks and uncertainties related to regulatory review and approval processes and Exelixis' compliance with applicable legal and regulatory requirements; the degree of market acceptance of CABOMETYX and the availability of coverage and reimbursement for CABOMETYX; the risk that unanticipated developments could adversely affect the commercialization of CABOMETYX; Exelixis' dependence on its relationship with Ipsen, including, the level of Ipsen's investment in the resources necessary to successfully commercialize cabozantinib in the territories where it is approved; Exelixis' dependence on its relationship with Genentech/ Roche with respect to cobimetinib and Exelixis' ability to maintain its rights under the collaboration; Exelixis' dependence on third-party vendors; Exelixis' ability to protect the company's intellectual property rights; 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 August 3, 2016, and in Exelixis' future 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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