Exelixis Announces Further Expansion to Clinical Research Protocol for Phase 1b COSMIC-021 Trial of Cabozantinib in Combination with Anti-PD-L1 Immunotherapy in Patients with Locally Advanced or Metastatic Solid Tumors

June 1, 2018

– Ten new trial cohorts added to expansion phase of combination trial, bringing the total number of cohorts to 18 –

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jun. 1, 2018-- Exelixis, Inc. (Nasdaq:EXEL) today announced an amendment to the protocol for COSMIC-021, the phase 1b trial of cabozantinib (CABOMETYX®) in combination with atezolizumab (TECENTRIQ®) in patients with locally advanced or metastatic solid tumors to add 10 new expansion cohorts to the trial. The primary objective in the expansion stage of this trial remains to determine the objective response rate in each cohort.

The 10 new expansion cohorts will evaluate the combination of cabozantinib and atezolizumab in patients with:

- non-small cell lung cancer (NSCLC) with an EGFR mutation who have progressed following treatment with an EGFR-targeting tyrosine kinase inhibitor for metastatic disease
- renal cell carcinoma (RCC) with non-clear cell histology who have not had prior systemic anticancer therapy for inoperable, locally advanced, recurrent or metastatic disease
- triple-negative breast cancer who have progressed following treatment with at least one prior systemic therapy for inoperable, locally advanced, recurrent or metastatic disease
- epithelial ovarian cancer who have platinum-resistant or refractory disease
- endometrial cancer who have progressed following treatment with at least one prior systemic therapy for inoperable, locally advanced, recurrent or metastatic disease
- advanced hepatocellular carcinoma (HCC) who have a Child-Pugh score of A and have not had prior systemic anticancer therapy for inoperable, locally advanced, recurrent or metastatic disease
- gastric or gastroesophageal junction adenocarcinoma who have progressed following treatment with platinum-containing or fluoropyrimidine-containing chemotherapy for inoperable locally advanced, recurrent or metastatic disease
- colorectal adenocarcinoma who have progressed following treatment with systemic chemotherapy that contained fluoropyrimidine in combination with oxaliplatin or irinotecan for metastatic disease
- head and neck cancer of squamous cell histology who have progressed following treatment with platinum-containing chemotherapy for inoperable locally advanced, recurrent or metastatic disease
- differentiated thyroid cancer who are radio-refractory or deemed ineligible for treatment with iodine-131

“We look forward to expanding this phase 1b COSMIC-021 clinical trial of cabozantinib in combination with atezolizumab in a number of additional tumor types, which include patient populations in significant need of new therapies that may improve response rates, slow disease progression and improve treatment outcomes,” said Gisela Schwab, M.D., President, Product Development and Medical Affairs and Chief Medical Officer, Exelixis. “We look forward to advancing this trial and to generating data that will inform late stage trials of cabozantinib in combination with immune checkpoint inhibitors.”

In January 2018, the protocol was amended to include the following eight expansion cohorts, which are actively enrolling patients with:

- RCC with clear cell histology who have not had prior systemic anticancer therapy
- urothelial carcinoma (UC) who have progressed on or after platinum-containing chemotherapy
- UC who are ineligible for cisplatin-based chemotherapy and have not received prior systemic chemotherapy for inoperable, locally advanced or metastatic disease
- UC who are eligible for cisplatin-based chemotherapy and have not received prior systemic chemotherapy for inoperable, locally advanced or metastatic disease
- advanced non-squamous NSCLC without a defined tumor genetic alteration (EGFR, ALK, ROS1, or BRAF) who have not received prior therapy with an immune checkpoint inhibitor
- NSCLC without a defined tumor genetic alteration who have progressed following treatment with an immune checkpoint inhibitor
- UC who have progressed following treatment with an immune checkpoint inhibitor
- castration-resistant prostate cancer (CRPC) who have previously received enzalutamide and/or abiraterone acetate and

experienced radiographic disease progression in soft tissue

The dose-escalation phase of the study determined the optimal dose of cabozantinib as 40 mg daily when given in combination with atezolizumab (1200 mg infusion once every 3 weeks). Each expansion cohort of this multicenter phase 1b, open-label study will initially enroll approximately 30 patients. Up to 80 may enroll in the cohorts of patients with UC or NSCLC who have been previously treated with an immune checkpoint inhibitor, with up to a total of 640 patients in the entire study.

More information about the currently enrolling cohorts in this trial is available at ClinicalTrials.gov.

TECENTRIQ® (atezolizumab) is a registered trademark of Genentech, a member of the Roche Group.

About Exelixis' Collaboration with Ipsen

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. On December 21, 2016, this agreement was amended to include commercialization rights for Ipsen in Canada. Ipsen has opted to participate in the funding of the previously announced COSMIC-021 phase 1b trial cohorts in patients with locally advanced or metastatic UC, RCC, CRPC and NSCLC. They may also participate in these expansion trial cohorts and in future studies at their choosing and, in such cases, would have access to the results to support potential future regulatory submissions.

About Exelixis' Collaboration with Takeda

On January 30, 2017, Exelixis and Takeda jointly announced an exclusive licensing agreement for the commercialization and further development of cabozantinib indications in Japan. Under the parties' collaboration agreement, if Takeda opts to participate in funding the COSMIC-021 phase 1b trial, or future studies, Takeda will have access to the respective study results to support potential future regulatory submissions in their territory.

Exelixis holds the exclusive rights to develop and commercialize cabozantinib in the United States.

About CABOMETYX® (cabozantinib)

CABOMETYX tablets are approved in the United States for the treatment of patients with advanced RCC. CABOMETYX tablets are also approved in the European Union, Norway, Iceland, Australia, Switzerland and South Korea for the treatment of advanced RCC in adults who have received prior VEGF-targeted therapy, and in the European Union for previously untreated intermediate- or poor-risk advanced RCC. On May 29, 2018, Exelixis announced that the U.S. Food and Drug Administration (FDA) accepted for filing the company's supplemental New Drug Application (sNDA) for CABOMETYX tablets as a treatment for patients with previously treated advanced HCC. On March 28, 2018, Ipsen announced that the European Medicines Agency validated its application for a new indication for cabozantinib as a treatment for previously treated advanced HCC in the European Union.

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

U.S. Important Safety Information

- **Hemorrhage:** Severe and fatal hemorrhages have occurred with CABOMETYX. In two RCC studies, the incidence of Grade ≥ 3 hemorrhagic events was 3% in CABOMETYX-treated patients. Do not administer CABOMETYX to patients that have or are at risk for severe hemorrhage.
- **Gastrointestinal (GI) Perforations and Fistulas:** In RCC studies, fistulas were reported in 1% of CABOMETYX-treated patients. Fatal perforations occurred in patients treated with CABOMETYX. In RCC studies, gastrointestinal (GI) perforations were reported in 1% of CABOMETYX-treated patients. Monitor patients for symptoms of fistulas and perforations, including abscess and sepsis. Discontinue CABOMETYX in patients who experience a fistula which cannot be appropriately managed or a GI perforation.
- **Thrombotic Events:** CABOMETYX treatment results in an increased incidence of thrombotic events. In RCC studies, venous thromboembolism occurred in 9% (including 5% pulmonary embolism) and arterial thromboembolism occurred in 1% of CABOMETYX-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, including hypertensive crisis. In RCC studies, hypertension was reported in 44% (18% Grade ≥ 3) of CABOMETYX-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:** In RCC studies, diarrhea occurred in 74% of patients treated with CABOMETYX. Grade 3 diarrhea occurred in 11% of patients treated with CABOMETYX. 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.
- **Palmar-Plantar Erythrodysesthesia (PPE):** In RCC studies, palmar-plantar erythrodysesthesia (PPE) occurred in 42% of patients treated with CABOMETYX. Grade 3 PPE occurred in 8% of patients treated with CABOMETYX. Withhold CABOMETYX in patients who develop intolerable Grade 2 PPE or Grade 3 PPE until improvement to Grade 1; resume CABOMETYX at a reduced dose.

- **Reversible Posterior Leukoencephalopathy Syndrome (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** may be associated with CABOMETYX. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during CABOMETYX treatment and for 4 months after the last dose.
- **Adverse Reactions:** The most commonly reported (≥25%) adverse reactions are: diarrhea, fatigue, nausea, decreased appetite, hypertension, PPE, weight decreased, vomiting, dysgeusia, and stomatitis.
- **Strong CYP3A4 Inhibitors**: If concomitant use with strong CYP3A4 inhibitors cannot be avoided, reduce the CABOMETYX dosage.
- **Strong CYP3A4 Inducers:** If concomitant use with strong CYP3A4 inducers cannot be avoided, increase the CABOMETYX dosage.
- **Lactation:** Advise women not to breastfeed while taking CABOMETYX and for 4 months after the final dose.
- **Hepatic Impairment:** In patients with mild to moderate hepatic impairment, reduce the CABOMETYX dosage. CABOMETYX is not recommended for use in patients with severe hepatic impairment.

Please see accompanying full Prescribing Information https://cabometyx.com/downloads/CABOMETYXUSPI.pdf.

About Exelixis

Founded in 1994, Exelixis, Inc. (Nasdaq: EXEL) is a commercially successful, oncology-focused biotechnology company that strives to accelerate the discovery, development and commercialization of new medicines for difficult-to-treat cancers. Following early work in model genetic systems, we established a broad drug discovery and development platform that has served as the foundation for our continued efforts to bring new cancer therapies to patients in need. We discovered our lead compounds, cabozantinib and cobimetinib, and advanced them into clinical development before entering into partnerships with leading biopharmaceutical companies in our efforts to bring these medicines to patients globally. We are steadfast in our commitment to prudently reinvest in our business to maximize the potential of our pipeline. We intend to supplement our existing therapeutic assets with targeted business development activities and internal drug discovery – all to deliver the next generation of Exelixis medicines and help patients recover stronger and live longer. Exelixis recently earned a spot on Deloitte's Technology Fast 500 list, a yearly award program honoring the 500 fastest-growing companies over the past four years. For more information about Exelixis, please visit www.exelixis.com, follow @ExelixisInc on Twitter or like Exelixis, Inc. on Facebook.

Exelixis Forward-Looking Statement Disclaimer

This press release contains forward-looking statements, including, without limitation, statements related to: the clinical and therapeutic potential of cabozantinib in combination with atezolizumab in patients with locally advanced or metastatic solid tumors; the potential for COSMIC-021 to generate data that will inform late stage trials of cabozantinib in combination with immune checkpoint inhibitors; the potential for Ipsen's and Takeda's participation in future cabozantinib studies under their respective collaborations and to have access to the results to support potential future regulatory submissions in their territories; Exelixis' commitment to reinvesting in its business to maximize the potential of its pipeline, including supplementing its existing therapeutic assets through targeted business development activities and internal drug discovery; and Exelixis' mission to deliver the next generation of Exelixis medicines and help patients recover stronger and live longer. Words such as "look forward," "may," "will," "commitment," "potential," "intend," 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' ability and the ability of its collaborators to conduct clinical trials of cabozantinib and cobimetinib both alone and in combination with other therapies sufficient to achieve a positive completion; risks related to the potential failure of cabozantinib and cobimetinib both alone and in combination with other therapies, 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 level of costs associated with Exelixis' commercialization, research and development and other activities; competition in the area of business development activities and the inherent uncertainty of the drug discovery process; Exelixis' dependence on its relationships with its cabozantinib collaboration partners, including, the level of their investment in the resources necessary to successfully commercialize partnered products in the territories where they are approved; market acceptance of CABOMETYX, COMETRIQ, and COTELLIC and the availability of coverage and reimbursement for these products; Exelixis' dependence on third-party vendors for the development, manufacture and supply of its products; Exelixis' ability to protect the company's intellectual property rights; market competition, including the potential for competitors to obtain approval for generic versions of Exelixis' marketed products; 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 May 2, 2018, 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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