Exelixis Announces Initiation of CONTACT-03 Phase 3 Pivotal Trial of Cabozantinib in Combination With Atezolizumab in Previously Treated Metastatic Renal Cell Carcinoma

July 20, 2020

– CONTACT-03 is the third of three phase 3 pivotal trials that are part of a clinical collaboration with Roche –

ALAMEDA, Calif.--(BUSINESS WIRE)--Jul. 20, 2020-- Exelixis, Inc. (NASDAQ: EXEL) today announced the initiation of CONTACT-03, a global phase 3 pivotal trial of cabozantinib (CABOMETYX®) in combination with atezolizumab (TECENTRIQ®) in patients with inoperable, locally advanced or metastatic renal cell carcinoma (RCC) who progressed during or following treatment with an immune checkpoint inhibitor as the immediate preceding therapy. CONTACT-03 is part of a clinical trial collaboration between Exelixis and Roche that includes two additional phase 3 pivotal trials – CONTACT-01 in patients with metastatic non-small cell lung cancer (NSCLC) who have been previously treated with an immune checkpoint inhibitor and platinum-containing chemotherapy and CONTACT-02 in patients with metastatic castration-resistant prostate cancer (CRPC) who have been previously treated with one novel hormonal therapy – both initiated in June 2020.

“The treatment landscape for metastatic kidney cancer is rapidly evolving as the use of immune checkpoint inhibitor-based regimens move to earlier lines of therapy,” said Gisela Schwab, M.D., President, Product Development and Medical Affairs and Chief Medical Officer, Exelixis. “More data are needed to better understand the sequential use of treatments for this patient community, and we look forward to learning more about the potential role of the combination of cabozantinib and atezolizumab following checkpoint inhibitor therapy in this pivotal trial with our partner Roche.”

CONTACT-03 is a global, multicenter, randomized, phase 3, open-label study that aims to enroll approximately 500 patients. Patients will be randomized 1:1 to the experimental arm of cabozantinib in combination with atezolizumab or the control arm of cabozantinib alone. The co-primary endpoints of the trial are progression-free survival per Response Evaluation Criteria in Solid Tumors (RECIST) v. 1.1 as assessed by independent review and overall survival. Secondary endpoints include progression-free survival, objective response rate and duration of response as assessed by the investigators. The CONTACT-03 trial is sponsored by Roche and co-funded by Exelixis.

The design of CONTACT-03 was informed by the ongoing COSMIC-021 trial — a phase 1b study of cabozantinib in combination with atezolizumab in multiple advanced solid tumors including RCC, NSCLC and CRPC. More information about CONTACT-03 is available at ClinicalTrials.gov (NCT04338269).

About RCC

The American Cancer Society’s 2020 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%.[2] Approximately 32,000 patients in the U.S. and 71,000 worldwide will require systemic treatment for advanced kidney cancer in 2020.[3]

About 70% of RCC cases are known as “clear cell” carcinomas, based on histology. [4] The majority of clear cell RCC tumors have below-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.[7,8,9,10] MET and AXL may provide escape pathways that drive resistance to VEGF receptor inhibitors.[6,7]

About CABOMETYX® (cabozantinib)
In the U.S., CABOMETYX tablets are approved for the treatment of patients with advanced RCC and for the treatment of patients with HCC who have been previously treated with sorafenib. CABOMETYX tablets have also received regulatory approvals in the European Union and additional countries and regions worldwide.

CABOMETYX in combination with atezolizumab is not indicated for metastatic renal cell carcinoma.

About Exelixis’ Collaboration with Ipsen
On February 29, 2016, Exelixis and Ipsen jointly announced an exclusive collaboration agreement for the further development and commercialization of cabozantinib outside of the United States, Canada and Japan. On December 21, 2016, this agreement was amended to include commercialization rights for Ipsen in Canada. Under the parties’ collaboration agreement, if Ipsen opts to participate in funding this phase 3 trial, or future studies, it will have access to the respective study results to support potential future regulatory submissions in their territory.

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 this phase 3 trial, or future studies, it 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.

Important Safety Information

Warnings and Precautions

Hemorrhage: Severe and fatal hemorrhages occurred with CABOMETYX. The incidence of Grade 3 to 5 hemorrhagic events was 5% in

CABOMETYX patients in RCC and HCC studies. Discontinue CABOMETYX for Grade 3 or 4 hemorrhage. Do not administer CABOMETYX to patients who have a recent history of hemorrhage, including hemoptysis, hematemesis, or melena.

Perforations and Fistulas: Gastrointestinal (GI) perforations, including fatal cases, occurred in 1% of CABOMETYX patients. Fistulas, including fatal cases, occurred in 1% of CABOMETYX patients. Monitor patients for signs and symptoms of perforations and fistulas, including abscess and sepsis. Discontinue CABOMETYX in patients who experience a Grade 4 fistula or a GI perforation.

Thrombotic Events: CABOMETYX increased the risk of thrombotic events. Venous thromboembolism occurred in 7% (including 4% pulmonary embolism) and arterial thromboembolism in 2% of CABOMETYX patients. Fatal thrombotic events occurred in CABOMETYX patients. Discontinue CABOMETYX in patients who develop an acute myocardial infarction or serious arterial or venous thromboembolic event requiring medical intervention.

Hypertension and Hypertensive Crisis: CABOMETYX can cause hypertension, including hypertensive crisis. Hypertension occurred in 36% (17% Grade 3 and <1% Grade 4) of CABOMETYX patients. Do not initiate CABOMETYX in patients with uncontrolled hypertension. Monitor blood pressure regularly during CABOMETYX treatment. Withhold CABOMETYX for hypertension that is not adequately controlled with medical management; when controlled, resume at a reduced dose. Discontinue CABOMETYX for severe hypertension that cannot be controlled with anti-hypertensive therapy or for hypertensive crisis.

Diarrhea: Diarrhea occurred in 63% of CABOMETYX patients. Grade 3 diarrhea occurred in 11% of CABOMETYX patients. Withhold CABOMETYX until improvement to Grade 1 and resume at a reduced dose for intolerable Grade 2 diarrhea, Grade 3 diarrhea that cannot be managed with standard antidiarrheal treatments, or Grade 4 diarrhea.

Palmar-Plantar Erythrodysesthesia (PPE): PPE occurred in 44% of CABOMETYX patients. Grade 3 PPE occurred in 13% of CABOMETYX patients. Withhold CABOMETYX until improvement to Grade 1 and resume at a reduced dose for intolerable Grade 2 PPE or Grade 3 PPE.

Proteinuria: Proteinuria occurred in 7% of CABOMETYX patients. Monitor urine protein regularly during CABOMETYX treatment. Discontinue CABOMETYX in patients who develop nephrotic syndrome.

Osteonecrosis of the Jaw (ONJ): ONJ occurred in <1% of CABOMETYX patients. ONJ can manifest as jaw pain, osteomyelitis, osteitis, bone erosion, tooth or periodontal infection, toothache, gingival ulceration or erosion, persistent jaw pain, or slow healing of the mouth or jaw after dental surgery. Perform an oral examination prior to CABOMETYX initiation and periodically during treatment. Advise patients regarding good oral hygiene practices. Withhold CABOMETYX for at least 3 weeks prior to scheduled dental surgery or invasive dental procedures, if possible. Withhold CABOMETYX for development of ONJ until complete resolution.

Impaired Wound Healing: Wound complications occurred with CABOMETYX. Withhold CABOMETYX for at least 3 weeks prior to elective surgery. Do not administer CABOMETYX for at least 2 weeks after major surgery and until adequate wound healing is observed. The safety of resumption of CABOMETYX after resolution of wound healing complications has not been established.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS): RPLS, a syndrome of subcortical vasogenic edema diagnosed by characteristic findings on MRI, can occur with CABOMETYX. Evaluate for RPLS in patients 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. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Verify the pregnancy status of females of reproductive potential prior to initiating CABOMETYX and advise them to use effective contraception during treatment and for 4 months after the last dose.

Adverse Reactions

The most commonly reported (≥25%) adverse reactions are: diarrhea, fatigue, decreased appetite, PPE, nausea, hypertension, and vomiting.

Drug Interactions

Strong CYP3A4 Inhibitors: If coadministration with strong CYP3A4 inhibitors cannot be avoided, reduce the CABOMETYX dosage. Avoid grapefruit or grapefruit juice.

Strong CYP3A4 Inducers: If coadministration with strong CYP3A4 inducers cannot be avoided, increase the CABOMETYX dosage. Avoid St. John's wort.

USE IN SPECIFIC POPULATIONS

Lactation: Advise women not to breastfeed during CABOMETYX treatment and for 4 months after the final dose.

Hepatic Impairment: In patients with 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 system genetics, 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. Our discovery efforts have resulted in four commercially available products, CABOMETYX® (cabozantinib), COMETRIQ® (cabozantinib), COTELLIC® (cobimetinib) and MINNEBRO® (esaxerenone), and we have entered into partnerships with leading pharmaceutical companies to bring these important medicines to patients worldwide. Supported by revenues from our marketed products and collaborations, we are committed to prudently reinvesting in our business to maximize the potential of our pipeline. We are supplementing 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 is a member of the Standard & Poor's (S&P) MidCap 400 index, which measures the performance of profitable mid-sized companies. For more information about Exelixis, please visit www.exelixis.com, follow @ExelixisInc on Twitter or like Exelixis, Inc. on Facebook.

Forward-Looking Statements
This press release contains forward-looking statements, including, without limitation, statements related to: the potential role of the combination of cabozantinib and atezolizumab following checkpoint inhibitor therapy as a treatment for patients with metastatic kidney cancer; and Exelixis' plans to reinvest in its business to maximize the potential of the company's pipeline, including through targeted business development activities and internal drug discovery. Any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements and 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 continuing COVID-19 pandemic and its impact on Exelixis' research and development operations, including Exelixis' ability to initiate new clinical trials and clinical trial sites, enroll clinical trial patients, conduct trials per protocol, and conduct drug research and discovery operations and related activities; complexities and the unpredictability of the regulatory review and approval processes in the U.S. and elsewhere; Exelixis' and Roche's continuing compliance with applicable legal and regulatory requirements; the potential failure of the combination of cabozantinib and atezolizumab to demonstrate safety and/or efficacy in CONTACT-03; uncertainties inherent in the product development process; the costs of conducting clinical trials, including the ability or willingness of Exelixis' collaboration partners to invest in the resources necessary to complete the trials; Exelixis' dependence on third-party vendors for the development, manufacture and supply of cabozantinib; Exelixis' ability to protect its intellectual property rights; market competition, including the potential for competitors to obtain approval for generic versions of CABOMETYX; changes in economic and business conditions; and other factors affecting Exelixis and its development programs discussed under the caption "Risk Factors" in Exelixis' Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on May 5, 2020, and in Exelixis' future filings with the SEC. All forward-looking statements in this press release are based on information available to Exelixis as of the date of this press release, and Exelixis undertakes no obligation to update or revise any forward-looking statements contained herein, except as required by law.

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[1] American Cancer Society: Cancer Facts & Figures 2020. Available at: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2020/cancer-facts-and-figures-2020.pdf. Accessed July 2020.

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