Exelixis Announces Initiation of CONTACT-01 Phase 3 Pivotal Trial of Cabozantinib in Combination With Atezolizumab in Previously Treated Metastatic Non-small Cell Lung Cancer

June 11, 2020

– Initiation follows positive results from cohort 7 of phase 1b COSMIC-021 trial –

– CONTACT-01 is the first of three phase 3 pivotal trials that are part of a previously announced clinical collaboration with Roche –

ALAMEDA, Calif.--(BUSINESS WIRE)--Jun. 11, 2020-- Exelixis, Inc. (NASDAQ: EXEL) today announced the initiation of CONTACT-01, a global phase 3 pivotal trial of cabozantinib (CABOMETYX®) in combination with atezolizumab (TECENTRIQ®) in patients with metastatic non-small cell lung cancer (NSCLC) who have been previously treated with an immune checkpoint inhibitor (ICI) and platinum-containing chemotherapy. Two additional phase 3 pivotal trials in metastatic castration-resistant prostate cancer (CRPC; CONTACT-02) and renal cell carcinoma (RCC; CONTACT-03) are planned as part of the clinical trial collaboration between Exelixis and Roche.

“Survival rates for patients with metastatic non-small cell lung cancer are low, and since more than half of these patients are diagnosed at an advanced stage, the patient community is in need of new treatment options, especially for those who progress following immunotherapy and chemotherapy,” said Gisela Schwab, M.D., President, Product Development and Medical Affairs and Chief Medical Officer, Exelixis. “We were pleased to see the positive results from cohort 7 of the COSMIC-021 trial further supporting the growing body of preclinical and clinical evidence that cabozantinib may promote a more immune-permissive environment potentially resulting in additive or synergistic effects with immune checkpoint inhibitors such as atezolizumab. We look forward to forthcoming findings for the combination in this disease in CONTACT-01, as well as in other difficult-to-treat cancers in planned phase 3 studies.”

Results from the ongoing COSMIC-021 trial — a phase 1b study of cabozantinib and atezolizumab in multiple advanced solid tumors including NSCLC, CRPC and RCC — informed the design of this phase 3 pivotal trial. Initial results from the COSMIC-021 cohort of patients with advanced NSCLC who progressed after treatment with an ICI were presented at the 2020 American Society of Clinical Oncology Virtual Scientific Program.

CONTACT-01 is a global, multicenter, randomized, phase 3, open-label study that aims to enroll approximately 350 patients. Patients will be randomized 1:1 to the experimental arm of cabozantinib in combination with atezolizumab and the control arm of docetaxel. The primary endpoint of the trial is overall survival. Secondary endpoints include progression-free survival, objective response rate and duration of response. The trial is sponsored by Roche and co-funded by Exelixis.

About NSCLC

Lung cancer is the second most common type of cancer in the U.S., with more than 220,000 new cases expected to be diagnosed in 2020.[1] The disease is the leading cause of cancer-related mortality in both men and women, causing 25% of all cancer-related deaths.[1] The majority (84%) of lung cancer cases are NSCLC, which mainly comprise adenocarcinoma, squamous cell carcinoma and large cell carcinoma.[1] The five-year survival rate for patients with NSCLC is 24%, but that rate falls to just 6% for those with advanced or metastatic disease.[2] More than half of lung cancer cases are diagnosed at an advanced stage, and more options are needed for these patients.[3]

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 previously treated metastatic non-small cell lung cancer.

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. Under the parties’ collaboration agreement, if Ipsen opts to participate in funding this phase 3 trial, or future studies, Ipsen 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, 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.

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: Exelixis' plans to initiate two additional phase 3 pivotal trials in metastatic CRPC and RCC as part of the clinical trial collaboration between Exelixis and Roche; the potential for cabozantinib to promote a more immune-permissive environment, which could result in additive or synergistic effects with immune checkpoint inhibitors such as atezolizumab; 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-01; 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.

[1]American Cancer Society. About Lung Cancer. https://www.cancer.org/content/dam/CRC/PDF/Public/8703.00.pdf. Accessed June 2020.

[2]American Society of Clinical Oncology. Cancer.Net. Lung Cancer - Non-Small Cell: Statistics. https://www.cancer.net/cancer-types/lung-cancer-non-small-cell/statistics. Accessed June 2020.

[3]National Cancer Institute. SEER Stat Fact Sheets: Lung and Bronchus Cancer. https://seer.cancer.gov/statfacts/html/lungb.html. Accessed June 2020.

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