Exelixis Announces Cabozantinib Significantly Improved Progression-Free Survival in COSMIC-311 Phase 3 Pivotal Trial in Patients with Previously Treated Radioiodine-Refractory Differentiated Thyroid Cancer

December 21, 2020

– Cabozantinib reduced the risk of disease progression or death by 78%; hazard ratio = 0.22, (p<0.0001) compared to placebo –

– Exelixis will discuss the trial results and regulatory filing plans with the U.S. Food and Drug Administration (FDA) –

ALAMEDA, Calif.--(BUSINESS WIRE)--Dec. 21, 2020-- Exelixis, Inc. (NASDAQ: EXEL) today announced that COSMIC-311, the phase 3 pivotal trial evaluating cabozantinib (CABOMETYX®) versus placebo in patients with radioiodine-refractory differentiated thyroid cancer who have progressed after up to two prior vascular endothelial growth factor receptor (VEGFR)-targeted therapies, met the co-primary endpoint of demonstrating significant improvement in progression-free survival. Cabozantinib reduced the risk of disease progression or death by 78% with a hazard ratio of 0.22 (96% CI 0.13 – 0.36; p<0.0001) at this planned interim analysis. The safety profile was consistent with that previously observed for cabozantinib.

“Considering the poor prognosis and lack of progress in the treatment of differentiated thyroid cancer following anti-VEGFR therapy, a significant improvement in progression-free survival is a long-awaited clinical advance,” said Marcia S. Brose, M.D., Ph.D., Full Professor of Otorhinolaryngology: Head and Neck Surgery and Director of the Center for Rare Cancers and Personalized Therapy at the Abramson Cancer Center of the University of Pennsylvania, and principal investigator of the trial. “These encouraging results from COSMIC-311 suggest cabozantinib has the potential to become an important new option for these patients. We look forward to sharing the detailed data from the trial at an upcoming medical meeting.”

Given these results, the independent data monitoring committee for the study recommended to stop enrollment and unblind sites and patients. Exelixis intends to discuss the study results, proposed changes to the study conduct, as well as plans for a regulatory filing with the U.S. FDA in the near term.

“We are very pleased that at this early interim analysis of COSMIC-311, cabozantinib has demonstrated a clinically meaningful and statistically significant improvement in progression-free survival for patients with differentiated thyroid cancer who are in need of additional treatment options after prior therapy,” said Gisela Schwab, M.D., President, Product Development and Medical Affairs and Chief Medical Officer, Exelixis. “We are thankful to the patients, physicians and site staff who are participating in this trial during the COVID-19 pandemic. We intend to discuss the findings with regulatory authorities and look forward to sharing the detailed final COSMIC-311 results when they become available.”

COSMIC-311 is a multicenter, randomized, double-blind, placebo-controlled phase 3 pivotal trial that aimed to enroll approximately 300 patients at 150 sites globally. Patients were randomized in a 2:1 ratio to receive either cabozantinib 60 mg or placebo once daily. Detailed results will be submitted for presentation at a future medical conference. More information about this trial is available at ClinicalTrials.gov.

About Differentiated Thyroid Cancer

Approximately 53,000 new cases of thyroid cancer will be diagnosed in the U.S. in 2020.[1] Nearly three out of four of these cases will be in women, and the disease is more commonly diagnosed at a younger age compared to most other adult cancers.[1] While cancerous thyroid tumors include differentiated, medullary and anaplastic forms, differentiated thyroid tumors make up about 90 percent of cases.[1] These include papillary, follicular and Hürthle cell cancer.[1] Differentiated thyroid cancer is typically treated with surgery followed by ablation of the remaining thyroid tissue with radioiodine, but approximately 5% to 15% of cases are resistant to radioiodine treatment. [2,3] For these patients, life expectancy is only three to six years from the time metastatic lesions are detected.[4,5,6]

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. In 2016, Exelixis granted Ipsen exclusive rights for the commercialization and further clinical development of cabozantinib outside of the United States and Japan. In 2017, Exelixis granted exclusive rights to Takeda Pharmaceutical Company Limited for the commercialization and further clinical development of cabozantinib for all future indications in Japan. Exelixis holds the exclusive rights to develop and commercialize cabozantinib in the United States.

CABOMETYX is not indicated for radioiodine-refractory differentiated thyroid cancer.

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. In November 2020, the company was named to *Fortune*'s 100 Fastest-Growing Companies list for the first time, ranking 17th overall and the third-highest biopharmaceutical company. 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 for cabozantinib to become an important new option for patients with differentiated thyroid cancer following anti-VEGFR therapy; Exelixis' plans to discuss the study results, proposed

changes to the study conduct, as well as plans for a regulatory filing with the U.S. FDA in the near term; Exelixis' plans to present detailed final COSMIC-311 results, when they become available, at a future medical conference; 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. 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; complexities and the unpredictability of the regulatory review and approval processes in the U.S. and elsewhere; Exelixis' continuing compliance with applicable legal and regulatory requirements; the potential failure of cabozantinib to demonstrate continued safety and efficacy in clinical testing; uncertainties inherent in the product development process; the continuing COVID-19 pandemic and its impact on Exelixis' research and development operations; the costs of conducting clinical 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 November 5, 2020, 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, except as required by law.

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[1] American Cancer Society. About Thyroid Cancer. Available at: https://www.cancer.org/cancer/thyroid-cancer/about.html. Accessed December 2020.

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[5] Pacini F, et al. 2012. Radioactive iodine-refractory differentiated thyroid cancer: unmet needs and future directions. *Expert Rev Endocrinol Metab*. 7:541–554.

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