Exelixis Further Expands Prostate Cancer Cohort in Phase 1b COSMIC-021 Trial of Cabozantinib in Combination with Atezolizumab in Patients with Advanced Solid Tumors

January 7, 2020

– Based on continued encouraging efficacy and safety data, metastatic castration-resistant prostate cancer cohort further expanded to 130 patients –

– Initial data to be presented on February 13 at the 2020 American Society of Clinical Oncology's Genitourinary Cancers Symposium (ASCO GU 2020) in San Francisco, CA –

ALAMEDA, Calif.--(BUSINESS WIRE)--Jan. 7, 2020-- Exelixis, Inc. (NASDAQ: EXEL) today announced that based on continued encouraging efficacy and safety data, the company plans to further expand the metastatic castration-resistant prostate cancer (CRPC) cohort of COSMIC-021, the phase 1b trial of cabozantinib (CABOMETYX®) in combination with atezolizumab (TECENTRIQ®) in patients with locally advanced or metastatic solid tumors. The cohort, which was previously expanded from 30 to 80 patients in July 2019, will now include up to 130 patients.

"We continue to see encouraging efficacy and safety data from the prostate cancer cohort in COSMIC-021," said Gisela Schwab, M.D., President, Product Development and Medical Affairs and Chief Medical Officer, Exelixis. "Expanding this cohort by an additional 50 patients will allow us to further document how the combination of cabozantinib and atezolizumab may benefit this patient population as we assess our potential regulatory plans for the combination and prepare to initiate a phase 3 pivotal trial. We look forward to the presentation of initial data from this cohort of CRPC patients at ASCO GU 2020 in February."

Based on preliminary encouraging activity, as determined by response assessment per Response Evaluation Criteria in Solid Tumors (version 1.1) (RECISTv1.1), and safety data of patients enrolled in the metastatic CRPC cohort, 50 additional patients with metastatic CRPC (130 total) who have histologically or cytologically confirmed adenocarcinoma of the prostate are being enrolled in the trial.

Initial data from the CRPC cohort in COSMIC-021 will be presented at ASCO GU 2020 in San Francisco on Thursday, February 13th during Poster Session A: Prostate Cancer at 11:30 a.m. – 1:00 p.m. PT and again at 5:30 – 6:30 p.m. PT.

COSMIC-021 includes 24 cohorts and aims to enroll up to 1,732 patients with advanced or metastatic solid tumors including CRPC, renal cell carcinoma (RCC), hepatocellular carcinoma (HCC), non-small cell lung cancer (NSCLC), colorectal cancer, ovarian cancer, and urothelial carcinoma (UC), among others. The primary objective in the expansion stage of this trial is to determine the objective response rate in each cohort. More information about the currently enrolling cohorts in this trial is available at ClinicalTrials.gov. To date, early data from various cohorts of this study have informed the initiation or planned initiation of several phase 3 pivotal trials, evaluating the combination in advanced HCC, CRPC, NSCLC and RCC.

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

About the COSMIC-021 Study

COSMIC-021 is a multicenter, phase 1b, open-label study that is divided into two parts: a dose-escalation phase and an expansion cohort phase. The dose-escalation phase was designed to enroll patients either with advanced RCC with or without prior systemic therapy or with inoperable, locally advanced, metastatic or recurrent UC (including renal, pelvis, ureter, urinary bladder and urethra) after prior platinum-based therapy. Ultimately, all 12 patients enrolled in this stage of the trial were patients with advanced RCC. The dose-escalation phase of the study determined the optimal dose of cabozantinib to be 40 mg daily when given in combination with atezolizumab (1200 mg infusion once every 3 weeks). These results were presented at the European Society for Medical Oncology 2018 Congress.

In the expansion phase, the trial is enrolling 24 cohorts in 12 tumor types: RCC, UC, NSCLC, CRPC, HCC, triple-negative breast cancer, epithelial ovarian cancer, endometrial cancer, gastric or gastroesophageal junction adenocarcinoma, colorectal adenocarcinoma, head and neck cancer, and differentiated thyroid cancer. Up to 1,720 patients may enroll in this phase of the trial: each expansion cohort will initially enroll approximately 30 patients, and up to 10 cohorts may expand enrollment up to 1,000 additional patients in the expansion phase.

Four of the cohorts are exploratory: three are enrolling approximately 30 patients each with advanced UC, CRPC or NSCLC to be treated with cabozantinib as a single-agent, and one is enrolling approximately 10 patients with advanced CRPC to be treated with single-agent atezolizumab. Exploratory cohorts have the option to be expanded up to 80 patients (cabozantinib) and 30 patients (atezolizumab) total.

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.

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 occurred with CABOMETYX. The incidence of Grade 3 to 5 hemorrhagic events was 5% in CABOMETYX patients. 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 fistula that cannot be appropriately managed 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 28 days prior to scheduled dental surgery or invasive dental procedures. Withhold CABOMETYX for development of ONJ until complete resolution.
- **Wound Complications:** Wound complications were reported with CABOMETYX. Stop CABOMETYX at least 28 days prior to scheduled surgery. Resume CABOMETYX after surgery based on clinical judgment of adequate wound healing. Withhold CABOMETYX in patients with dehiscence or wound healing complications requiring medical intervention.
- **Reversible Posterior Leukoencephalopathy Syndrome (RPLS):** RPLS, a syndrome of subcortical vasogenic edema diagnosed by characteristic finding 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.
- **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.
- **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 further expand the metastatic CRPC cohort of COSMIC-021 to include up to 130 patients and Exelixis' belief that this expansion will allow Exelixis to further understand how the combination of cabozantinib and atezolizumab may benefit this patient population; Exelixis' potential regulatory plans for the combination of cabozantinib and atezolizumab in patients with metastatic CRPC and preparations to initiate a phase 3 pivotal trial; Exelixis' plans to present initial data from this cohort of metastatic CRPC patients at ASCO GU 2020; Exelixis' plans to initiate several phase 3 pivotal trials evaluating the combination of cabozantinib and atezolizumab in CRPC, NSCLC and RCC based on early data from various cohorts of COSMIC-021; 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 availability of data at the referenced times; risks and uncertainties related to regulatory review and approval processes and Exelixis' compliance with applicable legal and regulatory requirements; the potential failure of the combination of cabozantinib and atezolizumab to demonstrate safety and/or efficacy in COSMIC-021 or in future phase 3 pivotal trials; 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 October 30, 2019, 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.

Exelixis, the Exelixis logo, CABOMETYX, COMETRIQ and COTELLIC are registered U.S. trademarks. MINNEBRO is a Japanese trademark.

View source version on businesswire.com: https://www.businesswire.com/news/home/20200107005227/en/

Source: Exelixis, Inc.

Investors Contact:
Susan Hubbard
EVP, Public Affairs and
Investor Relations
Exelixis, Inc.
(650) 837-8194
shubbard@exelixis.com

Media Contact:
Lindsay Treadway
Senior Director, Public Affairs and Advocacy Relations
Exelixis, Inc.
(650) 837-7522
ltreadway@exelixis.com