



Exelixis Announces Results From COSMIC-021 Trial of Cabozantinib in Combination With Atezolizumab in Multiple Advanced Solid Tumor Types

May 13, 2020

– Data from three cohorts of phase 1b COSMIC-021 trial to be presented during the 2020 American Society of Clinical Oncology Virtual Scientific Program (ASCO20) –

– 27% objective response rate seen in immune checkpoint inhibitor-pretreated non-small cell lung cancer cohort 7 –

– Phase 3 pivotal trials planned for advanced non-small cell lung cancer and metastatic castration-resistant prostate cancer –

ALAMEDA, Calif.--(BUSINESS WIRE)--May 13, 2020-- [Exelixis, Inc.](#) (NASDAQ: EXEL) today announced phase 1b clinical trial results for the combination of cabozantinib (CABOMETYX®) and atezolizumab (TECENTRIQ®) in patients with locally advanced or metastatic solid tumors. The data from three expansion cohorts of the COSMIC-021 trial will be presented during the 2020 American Society of Clinical Oncology Virtual Scientific Program (ASCO20). Results from the non-small cell lung cancer (NSCLC) and the metastatic castration-resistant prostate cancer (CRPC) cohorts will be presented as posters, and results from the urothelial carcinoma (UC) cohort will be presented as a poster discussion; all three presentations will be available on demand for ASCO20 registrants beginning Friday, May 29 at 8:00 a.m. ET.

NSCLC Expansion Cohort (abstract 9610):

Initial results from the NSCLC expansion cohort (cohort 7) will be presented by Joel Neal, M.D., Ph.D., Associate Professor of Medicine – Oncology at the Stanford University School of Medicine, one of the lead trial investigators. The analysis included 30 patients who had received prior therapy with immune checkpoint inhibitors, and 87% of patients had received prior chemotherapy. Fifty percent of patients received the cabozantinib and atezolizumab combination as their second line of therapy and 50% as their third line of therapy. At the time of enrollment in the study, the best response to prior immune checkpoint inhibitor therapy was a partial response in 3 (10%) patients, stable disease in 7 (23%) patients, progressive disease in 14 (47%) patients and unknown in 5 (17%) patients.

At a median follow-up of 12.1 months, the investigator-assessed confirmed objective response rate (ORR) per Response Evaluation Criteria in Solid Tumors (RECIST) v. 1.1, the trial's primary endpoint, was 27%, and the disease control rate was 83%. Median progression-free survival (PFS) was 4.2 months (95% confidence interval [CI] 2.7–7 months) with 22 events (73%), and median duration of response for all responding patients was 5.7 months.

"Cabozantinib, in combination with immune checkpoint inhibitors, has now demonstrated promise in multiple difficult to treat tumor types," said Dr. Sumanta Pal, Clinical Professor, City of Hope, the principal investigator for the COSMIC-021 study. "The findings from the three COSMIC-021 cohorts presented at ASCO20 add to the growing body of evidence of potential synergistic effects with cabozantinib and immune checkpoint inhibitors. We are particularly encouraged by the new data emerging from the NSCLC cohort which showed a 27% confirmed overall response rate, including three patients with primary refractory disease to checkpoint inhibition. Further evaluation of cabozantinib and atezolizumab in patients with advanced tumor types, including immune checkpoint inhibitor-pretreated NSCLC, and forms of prostate and urothelial cancers, is warranted."

The most common treatment-related adverse events (AEs) were diarrhea (53%), fatigue (37%), nausea (30%), decreased appetite (23%), palmar-plantar erythrodysesthesia (20%) and vomiting (20%). One patient experienced grade 5 pneumonitis that was related to atezolizumab, and one patient (3%) discontinued due to treatment-related AEs not associated with disease progression.

"We are encouraged by these promising findings in patients with non-small cell lung cancer who had been previously treated with immune checkpoint inhibitor therapy, along with other COSMIC-021 results presented at ASCO20," said Gisela Schwab, M.D., President, Product Development and Medical Affairs and Chief Medical Officer, Exelixis. "The efficacy data and favorable safety profiles seen in the three cohorts suggest the combination of cabozantinib and atezolizumab offers promise for patients with advanced, difficult-to-treat tumor types. These findings and additional data from these cohorts will inform the design of future studies, including planned phase 3 pivotal trials for the combination of cabozantinib and atezolizumab in advanced or metastatic NSCLC and CRPC."

UC Expansion Cohort (abstract 5013):

Initial results from the UC expansion cohort (cohort 2) will be presented by Dr. Pal. The analysis included 30 patients who had been previously treated with platinum-containing chemotherapy, with a median follow-up of 19.7 months. The investigator-assessed ORR per RECIST v. 1.1 was 27%, with two complete responses; disease control rate was 63%. Median duration of response was not yet reached, and the longest ongoing response was 15.6 months. Median PFS was 5.4 months. Preliminary data did not suggest an association between PD-L1 expression and tumor response.

The most common treatment-related AEs were asthenia (37%), diarrhea (27%), decreased appetite (23%), increased transaminases (23%) and mucosal inflammation (20%). No discontinuations due to treatment-related AEs occurred.

CRPC Expansion Cohort (abstract 5564):

An interim analysis from the metastatic CRPC expansion cohort (cohort 6) was previously presented at the 2020 American Society of Clinical Oncology's Genitourinary Cancers Symposium and was now updated with additional biomarker results that will be presented by Neeraj Agarwal, M.D., Professor, Huntsman Cancer Center, University of Utah, and an investigator of the trial. This analysis of 44 patients who had been previously treated with enzalutamide and/or abiraterone found an ORR per RECIST v. 1.1 of 32% and a disease control rate of 80% at a median follow up of 15.8 months. Preliminary data from the analysis did not suggest an association between PD-L1 expression and antitumor activity, suggesting patients with

or without PD-L1 may respond to treatment with the combination of cabozantinib plus atezolizumab. Comparison of baseline and circulating immune cell counts after 21 days showed a total increase in circulating T cells (CTLs) and a decrease in immunosuppressive cells. Subpopulations of CTLs also increased with the largest accumulation observed for prolonged activated CTLs.

Additional safety and efficacy findings from this analysis were [previously presented](#) at the 2020 American Society of Clinical Oncology's Genitourinary Cancers Symposium.

Based on regulatory feedback from the U.S. Food & Drug Administration (FDA), and if supported by the clinical data, Exelixis intends to file with the FDA for accelerated approval in a metastatic CRPC indication as early as 2021.

More information about COSMIC-021 is available at [ClinicalTrials.gov](https://clinicaltrials.gov) (NCT03170960).

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 renal cell carcinoma (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, hepatocellular carcinoma (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 further expand enrollment resulting in up to 1,000 patients across such potential additional expansion cohorts.

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.

Exelixis is the study sponsor of COSMIC-021. Ipsen has opted in to participate in the trial and is contributing to the funding for this study under the terms of the companies' collaboration agreement. Roche is providing atezolizumab for the trial.

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,³ and more options are needed for these patients.

About UC

Urothelial cancers encompass carcinomas of the bladder, ureter and renal pelvis at a ratio of 50:3:1, respectively.⁴ Bladder cancer occurs mainly in older people, with 90 percent of patients aged 55 or older.⁵ With more than 81,000 new cases expected to be diagnosed in 2020, bladder cancer accounts for about five percent of all new cases of cancer in the U.S. each year.⁶ It is the fourth most common cancer in men.⁷

About CRPC

According to the American Cancer Society, in 2020, approximately 192,000 new cases of prostate cancer will be diagnosed and 33,000 people will die from the disease.⁷ Prostate cancer that has spread beyond the prostate and does not respond to androgen-suppression therapies — a common treatment for prostate cancer — is known as metastatic CRPC.⁸ Researchers estimate that in 2020, 43,000 people with prostate cancer will progress to metastatic CRPC, which has a median survival of less than two years.^{9,10,11}

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.

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 ($\geq 25\%$) 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.](https://www.facebook.com/ExelixisInc) on Facebook.

Forward-Looking Statements

This press release contains forward-looking statements, including, without limitation, statements related to: Exelixis' expectation that data from the NSCLC, metastatic CRPC and UC cohorts of the COSMIC-021 trial will be presented at ASCO20; the potential synergistic effects with cabozantinib and immune checkpoint inhibitors; Exelixis' plans to initiate phase 3 pivotal trials in advanced or metastatic NSCLC and CRPC; Exelixis' intention to file with the FDA for accelerated approval of the combination of cabozantinib and atezolizumab in a metastatic CRPC indication as early as 2021, based on regulatory feedback from the FDA and if supported by the clinical data; 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; 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' 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 future 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 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.

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

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

¹ American Cancer Society. About Lung Cancer. <https://www.cancer.org/content/dam/CRC/PDF/Public/8703.00.pdf>. Accessed May 2020.

² American Society of Clinical Oncology. [Cancer.Net](https://www.cancer.net). Lung Cancer - Non-Small Cell: Statistics.

<https://www.cancer.net/cancer-types/lung-cancer-non-small-cell/statistics>. Accessed May 2020.

³ National Cancer Institute. SEER Stat Fact Sheets: Lung and Bronchus Cancer. <https://seer.cancer.gov/statfacts/html/lungb.html>. Accessed May 2020.

⁴ Hurwitz, M. et al. Urothelial and Kidney Cancers. Cancer Management. <http://www.cancernetwork.com/cancer-management/urothelial-and-kidney-cancers>. Accessed May 2020.

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⁶ National Cancer Institute. SEER Stat Fact Sheets: Bladder Cancer. <https://seer.cancer.gov/statfacts/html/uribn.html>. Accessed May 2020.

⁷ 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 May 2020.

⁸ American Society of Clinical Oncology. [Cancer.Net](https://www.cancer.net). Treatment of Metastatic Castration-Resistant Prostate Cancer. September 8, 2014. Available at: <https://www.cancer.net/research-and-advocacy/asco-care-and-treatment-recommendations-patients/treatment-metastatic-castration-resistant-prostate-cancer>. Accessed May 2020.

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¹⁰ American Urological Association. Prostate Cancer: Castration Resistant Guideline. 2018. Available at: <https://www.auanet.org/guidelines/prostate-cancer-castration-resistant-guideline>. Accessed May 2020.

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