



Exelixis Provides Update on Phase 3 CONTACT-01 Trial Evaluating Cabozantinib in Combination with Atezolizumab in Patients with Metastatic Non-Small Cell Lung Cancer Previously Treated with Immunotherapy and Chemotherapy

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ALAMEDA, Calif.--(BUSINESS WIRE)--Dec. 8, 2022-- [Exelixis, Inc.](https://www.exelixis.com) (Nasdaq: EXEL) today announced that the CONTACT-01 study did not meet its primary endpoint of overall survival at the final analysis. CONTACT-01 is a phase 3 trial evaluating cabozantinib (CABOMETYX[®]) in combination with atezolizumab (TECENTRIQ[®]) versus docetaxel in patients with metastatic non-small cell lung cancer (NSCLC) without actionable mutations who experienced disease progression on or after treatment with an immune checkpoint inhibitor and platinum-containing chemotherapy.

The safety profile of the combination of cabozantinib and atezolizumab observed in the trial was consistent with the known safety profiles for each single agent, and no new safety signals were identified. Detailed findings from CONTACT-01 will be submitted for presentation at a future medical meeting.

About CONTACT-01

CONTACT-01 is a global, multicenter, randomized, phase 3, open-label study that enrolled 366 patients who were randomized 1:1 to the experimental arm of cabozantinib in combination with atezolizumab and the control arm of docetaxel. The study enrolled patients with both squamous and non-squamous NSCLC who progressed during or following anti-PD-1/PD-L1 therapy administered either concurrently or sequentially with chemotherapy. The primary endpoint of the trial was overall survival. Secondary endpoints included progression-free survival, objective response rate and duration of response. Results from cohort 7 of the phase 1b COSMIC-021 trial informed the CONTACT-01 trial design. CONTACT-01 was sponsored by Roche and co-funded by Exelixis. Both Ipsen and Takeda Pharmaceutical Company Limited (Takeda) opted in to participate in the trial and are contributing to the funding for this study under the terms of the companies' respective collaboration agreements with Exelixis. More information about the trial is available at [ClinicalTrials.gov](https://clinicaltrials.gov).

About NSCLC

Lung cancer is a leading cause of cancer death globally.¹ Every year, almost 1.8 million people die from the disease.¹ In the U.S., lung cancer is the second most common type of cancer, with more than 236,000 new cases expected to be diagnosed in 2022.² The majority (84%) of lung cancer cases are NSCLC.³ The overall five-year survival rate for patients with NSCLC is 26%, but that rate falls to just 7% for those with advanced or metastatic disease.⁴ More than half of lung cancer cases are diagnosed when metastatic.⁵

Cancer immunotherapy alone or in combination with platinum-containing chemotherapy is a standard of care treatment in first- and second-line NSCLC.⁶ However, people who progress after this initial therapy have limited treatment options and survival outcomes remain poor.^{5,6,7}

About CABOMETYX[®] (cabozantinib)

In the U.S., CABOMETYX tablets are approved for the treatment of patients with advanced renal cell carcinoma (RCC); for the treatment of patients with hepatocellular carcinoma who have been previously treated with sorafenib; for patients with advanced RCC as a first-line treatment in combination with nivolumab; and for adult and pediatric patients 12 years of age and older with locally advanced or metastatic differentiated thyroid cancer that has progressed following prior VEGFR-targeted therapy and who are radioactive iodine-refractory or ineligible. 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 U.S. and Japan. In 2017, Exelixis granted exclusive rights to Takeda 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 U.S.

CABOMETYX in combination with atezolizumab is not indicated as a treatment for NSCLC.

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

Perforations and Fistulas: Fistulas, including fatal cases, occurred in 1% of CABOMETYX patients. Gastrointestinal (GI) perforations, including fatal cases, occurred in 1% of CABOMETYX patients. Monitor patients for signs and symptoms of fistulas and perforations, 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 events that require medical intervention.

Hypertension and Hypertensive Crisis: CABOMETYX can cause hypertension, including hypertensive crisis. Hypertension was reported in 37% (16% 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. Permanently discontinue CABOMETYX for severe hypertension that cannot be controlled with anti-hypertensive therapy or for hypertensive crisis.

Diarrhea: Diarrhea occurred in 62% of CABOMETYX patients. Grade 3 diarrhea occurred in 10% of CABOMETYX patients. Monitor and manage patients using antidiarrheals as indicated. Withhold CABOMETYX until improvement to \leq Grade 1, resume at a reduced dose.

Palmar-Plantar Erythrodysesthesia (PPE): PPE occurred in 45% 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.

Hepatotoxicity: CABOMETYX in combination with nivolumab can cause hepatic toxicity with higher frequencies of Grades 3 and 4 ALT and AST elevations compared to CABOMETYX alone. Monitor liver enzymes before initiation of and periodically throughout treatment. Consider more frequent monitoring of liver enzymes than when the drugs are administered as single agents. For elevated liver enzymes, interrupt CABOMETYX and nivolumab and consider administering corticosteroids.

With the combination of CABOMETYX and nivolumab, Grades 3 and 4 increased ALT or AST were seen in 11% of patients. ALT or AST $>$ 3 times ULN (Grade \geq 2) was reported in 83 patients, of whom 23 (28%) received systemic corticosteroids; ALT or AST resolved to Grades 0-1 in 74 (89%). Among the 44 patients with Grade \geq 2 increased ALT or AST who were rechallenged with either CABOMETYX (n=9) or nivolumab (n=11) as a single agent or with both (n=24), recurrence of Grade \geq 2 increased ALT or AST was observed in 2 patients receiving CABOMETYX, 2 patients receiving nivolumab, and 7 patients receiving both CABOMETYX and nivolumab. Withhold and resume at a reduced dose based on severity.

Adrenal Insufficiency: CABOMETYX in combination with nivolumab can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold CABOMETYX and/or nivolumab and resume CABOMETYX at a reduced dose depending on severity.

Adrenal insufficiency occurred in 4.7% (15/320) of patients with RCC who received CABOMETYX with nivolumab, including Grade 3 (2.2%), and Grade 2 (1.9%) adverse reactions. Adrenal insufficiency led to permanent discontinuation of CABOMETYX and nivolumab in 0.9% and withholding of CABOMETYX and nivolumab in 2.8% of patients with RCC.

Approximately 80% (12/15) of patients with adrenal insufficiency received hormone replacement therapy, including systemic corticosteroids. Adrenal insufficiency resolved in 27% (n=4) of the 15 patients. Of the 9 patients in whom CABOMETYX with nivolumab was withheld for adrenal insufficiency, 6 reinstated treatment after symptom improvement; of these, all (n=6) received hormone replacement therapy and 2 had recurrence of adrenal insufficiency.

Proteinuria: Proteinuria was observed in 8% of CABOMETYX patients. Monitor urine protein regularly during CABOMETYX treatment. For Grade 2 or 3 proteinuria, withhold CABOMETYX until improvement to \leq Grade 1 proteinuria, resume CABOMETYX at a reduced dose. 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, resume at a reduced dose.

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. 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.

Thyroid Dysfunction: Thyroid dysfunction, primarily hypothyroidism, has been observed with CABOMETYX. Based on the safety population, thyroid dysfunction occurred in 19% of patients treated with CABOMETYX, including Grade 3 in 0.4% of patients.

Patients should be assessed for signs of thyroid dysfunction prior to the initiation of CABOMETYX and monitored for signs and symptoms of thyroid dysfunction during CABOMETYX treatment. Thyroid function testing and management of dysfunction should be performed as clinically indicated.

Hypocalcemia: CABOMETYX can cause hypocalcemia. Based on the safety population, hypocalcemia occurred in 13% of patients treated with CABOMETYX, including Grade 3 in 2% and Grade 4 in 1% of patients. Laboratory abnormality data were not collected in CABOSUN.

In COSMIC-311, hypocalcemia occurred in 36% of patients treated with CABOMETYX, including Grade 3 in 6% and Grade 4 in 3% of patients.

Monitor blood calcium levels and replace calcium as necessary during treatment. Withhold and resume at reduced dose upon recovery or permanently discontinue CABOMETYX depending on severity.

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 common (\geq 20%) adverse reactions are:

CABOMETYX as a single agent: diarrhea, fatigue, PPE, decreased appetite, hypertension, nausea, vomiting, weight decreased, constipation.

CABOMETRYX in combination with nivolumab: diarrhea, fatigue, hepatotoxicity, PPE, stomatitis, rash, hypertension, hypothyroidism, musculoskeletal pain, decreased appetite, nausea, dysgeusia, abdominal pain, cough, and upper respiratory tract infection.

DRUG INTERACTIONS

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

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

USE IN SPECIFIC POPULATIONS

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

Hepatic Impairment: In patients with moderate hepatic impairment, reduce the CABOMETRYX dosage. Avoid CABOMETRYX in patients with severe hepatic impairment.

Please see accompanying full Prescribing Information <https://www.cabometryx.com/downloads/CABOMETRYXUSPI.pdf>.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.FDA.gov/medwatch or call 1-800-FDA-1088.

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, CABOMETRYX[®] (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.

Exelixis Forward-Looking Statements

This press release contains forward-looking statements, including, without limitation, statements related to Exelixis' plans to submit detailed findings from CONTACT-01 at a future medical meeting 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: Exelixis' continuing compliance with applicable legal and regulatory requirements; Exelixis' ability to protect its intellectual property rights; market competition; 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 1, 2022, 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 Lung. Global Cancer Observatory website. Available at: <https://gco.iarc.fr/today/data/factsheets/cancers/15-Lung-fact-sheet.pdf>. Accessed December 2022.

² Key Statistics for Lung Cancer. American Cancer Society website. Available at: <https://www.cancer.org/cancer/lung-cancer/about/key-statistics.html>. Accessed December 2022.

³ What is Lung Cancer? American Cancer Society website. Available at: <https://www.cancer.org/cancer/lung-cancer/about/what-is.html>. Accessed December 2022.

⁴ Lung Cancer – Non-small Cell: Statistics. [Cancer.Net](https://www.cancer.net) website. Available at: <https://www.cancer.net/cancer-types/lung-cancer-non-small-cell/statistics>. Accessed December 2022.

⁵ Cancer Stat Facts: Lung and Bronchus Cancer. SEER website. Available at: <https://seer.cancer.gov/statfacts/html/lungb.html>. Accessed December 2022.

⁶ Non-Small Cell Lung Cancer Treatment (PDQ[®])—Health Professional Version. NCI website. Available at: https://www.cancer.gov/types/lung/hp/non-small-cell-lung-treatment-pdq#_48457. Accessed December 2022.

⁷ Treatment Choices for Non-Small Cell Lung Cancer, by Stage. ACS website. Available at: <https://www.cancer.org/cancer/lung-cancer/treating-non-small-cell/by-stage.html>. Accessed December 2022.

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