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YEARS

Exelixis Announces Results from Subgroup Analysis of CABINET Phase 3 Pivotal Trial Evaluating CABOMETYX® (cabozantinib) in Advanced Lung and Thymic Neuroendocrine Tumors at ESMO 2025

October 18, 2025

– CABOMETYX reduced the risk of disease progression or death by 81% versus placebo in patients with advanced lung or thymic neuroendocrine tumors (NET) –
– The lungs are the second most common NET site of origin, yet limited treatment options are available¹ –

ALAMEDA, Calif.--(BUSINESS WIRE)--Oct. 18, 2025-- [Exelixis, Inc.](#) (Nasdaq: EXEL) today announced results from a subgroup analysis of the CABINET phase 3 pivotal trial evaluating CABOMETYX® (cabozantinib) versus placebo in patients with previously treated advanced neuroendocrine tumors (NET) originating in the lungs or thymus. These data will be presented at the 2025 European Society for Medical Oncology Congress (ESMO) during the Monday Poster Session: Neuroendocrine Tumours on October 20, 2025, from 12:00 – 12:45 p.m. CEST.

"The regulatory approvals of cabozantinib in the United States and European Union earlier this year provide a much-needed targeted treatment option for patients with previously treated advanced NET," said Jennifer Chan, M.D., M.P.H., study chair for the CABINET trial, Clinical Director of the Gastrointestinal Cancer Center and Director of the Program in Carcinoid and Neuroendocrine Tumors at Dana-Farber Cancer Institute. "These subgroup results showing that cabozantinib achieved a meaningful progression-free survival benefit in patients with lung or thymic NET are encouraging, as these subtypes of the disease can be particularly challenging to treat."

In the phase 3 CABINET study, patients with locally advanced or metastatic pancreatic NET (pNET) or extra-pancreatic NET (epNET) were randomized 2:1 in separate cohorts to receive CABOMETYX 60 mg daily versus placebo. Patients with epNET had tumors arising in the gastrointestinal (GI) tract, lung, rare sites including the thymus and unknown primary sites. Of the 203 patients in the epNET cohort, 49 had lung or thymic NET. With a median follow-up for progression-free survival (PFS) of 5.5 months, CABOMETYX reduced the risk of disease progression or death by 81% versus placebo (stratified hazard ratio: 0.19; 95% confidence interval: 0.06-0.54; one-sided stratified log-rank P=0.0003). Median PFS was 8.2 months with CABOMETYX compared to 2.7 months with placebo. Confirmed objective response rates were 6% versus 0%, respectively.

"These subgroup data build upon the strong overall findings from the CABINET trial and reinforce the benefits of CABOMETYX for a heterogeneous NET patient population," said Dana T. Aftab, Ph.D., Executive Vice President, Research & Development, Exelixis. "Lung and thymic NET are forms of cancer with limited treatment options, and we are pleased CABOMETYX helps address an unmet need for these patients. We are committed to continuing to serve the NET patient community with our ongoing STELLAR-311 pivotal trial examining zanzalintinib as a potential first-line oral targeted therapy versus everolimus for patients with locally advanced or metastatic NET."

The safety profile of CABOMETYX observed in patients with lung or thymic NET was consistent with its known safety profile; no new safety signals were identified. The most frequent grade 3/4 adverse events attributed to CABOMETYX included fatigue (24%), hypertension (18%), diarrhea (9%) and palmar plantar erythrodysesthesia (9%).

In March 2025, the U.S. Food and Drug Administration [approved](#) CABOMETYX for the treatment of 1) adult and pediatric patients 12 years of age and older with previously treated, unresectable, locally advanced or metastatic, well-differentiated pNET; and 2) adult and pediatric patients 12 years of age and older with previously treated, unresectable, locally advanced or metastatic, well-differentiated epNET, based on results from the CABINET study. In July 2025, the European Commission [approved](#) CABOMETYX for the treatment of adult patients with unresectable or metastatic, well-differentiated pNET and epNET who have progressed following at least one prior systemic therapy other than somatostatin analogues.

About CABINET (Alliance A021602)

CABINET (Randomized, Double-Blinded, Phase III Study of **CAB**ozantinib versus Placebo In Patients with Advanced **NE**uroendocrine Tumors After Progression on Prior Therapy) is sponsored by the National Cancer Institute (NCI), part of the National Institutes of Health, and is being led and conducted by the NCI-funded Alliance for Clinical Trials in Oncology with participation from the NCI-funded National Clinical Trials Network, as part of Exelixis' collaboration through a Cooperative Research and Development Agreement with the NCI's Cancer Therapy Evaluation Program.

CABINET is a multicenter, randomized, double-blinded, placebo-controlled phase 3 pivotal trial that enrolled a total of 298 patients in two separate cohorts (pNET and epNET) in the U.S. at the time of the final analysis. Patients were randomized 2:1 to cabozantinib (60 mg) or placebo; each cohort was randomized separately and had its own statistical analysis plan. The trial was stopped early after an interim analysis showed superior efficacy associated with cabozantinib as compared to placebo in each of the two cohorts. Patients with epNET had primary tumors arising in the GI tract, lung, unknown primary sites and other organs. Patients must have had measurable disease per RECIST 1.1 criteria and must have experienced disease progression or intolerance after at least one U.S. FDA-approved line of prior systemic therapy other than somatostatin analogs. The primary endpoint in each cohort was PFS per RECIST 1.1 by blinded independent central review. Secondary endpoints included overall survival, objective response rate and safety. More information about this trial is available at [ClinicalTrials.gov](#).

About NET

NET are cancers that begin in the specialized cells of the body's neuroendocrine system.² These cells have traits of both hormone-producing endocrine cells and nerve cells.² It is estimated that 161,000 to 192,000 people in the U.S. are living with unresectable, locally advanced or metastatic NET.³ The number of people diagnosed with NET has been increasing in recent decades.⁴ Functional NET release peptide hormones that can cause debilitating symptoms, like diarrhea, hypertension and flushing, while symptoms of non-functional NET are related primarily to tumor growth.^{5, 6, 7, 8, 9} Most NET take years to develop and grow slowly, but eventually all patients with advanced or metastatic NET will develop refractory and progressing disease.^{10, 11}

NET can start in the pancreas (pNET), where they tend to be more aggressive, with a five-year survival rate of only 19% for advanced disease.^{2,12} NET can also develop in any part of the body, but most commonly start in the GI tract or in the lungs, where they have historically been referred to as carcinoid tumors and are more recently called epNET.² The five-year survival rate for advanced GI NET is 68%.¹³ For advanced NET patients, treatment options include somatostatin analogs, chemotherapy, molecular targeted therapy and peptide-receptor radionuclide therapy.¹⁴

Approximately 2,000-4,500 people will be newly diagnosed with lung NET in the U.S. each year.¹⁵ The five-year survival rate for advanced lung NET is 49%.¹⁶ Thymic NET are rare, typically aggressive tumors with a worse prognosis compared to that of lung NET.¹⁷

About CABOMETYX® (cabozantinib)

In the U.S., CABOMETYX tablets are approved as monotherapy for the treatment of patients with advanced renal cell carcinoma (RCC) and in combination with nivolumab as a first-line treatment for patients with advanced RCC; for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib; for adult and pediatric patients 12 years of age and older with locally advanced or metastatic differentiated thyroid cancer (DTC) that has progressed following prior VEGFR-targeted therapy and who are radioactive iodine-refractory or ineligible; for the treatment of adult and pediatric patients 12 years of age and older with previously treated, unresectable, locally advanced or metastatic, well-differentiated pNET; and adult and pediatric patients 12 years of age and older with previously treated, unresectable, locally advanced or metastatic, well-differentiated epNET. CABOMETYX tablets have also received regulatory approvals in over 65 countries outside the U.S. and Japan, including the EU. In 2016, Exelixis granted Ipsen Pharma SAS 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 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 U.S.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage: CABOMETYX can cause severe and fatal hemorrhages. The incidence of Grade 3-5 hemorrhagic events was 5% in CABOMETYX patients in RCC, HCC, and DTC studies. Discontinue CABOMETYX for Grade 3-4 hemorrhage and before surgery. Do not administer to patients who have a recent history of hemorrhage, including hemoptysis, hematemesis, or melena.

Perforations and Fistulas: Fistulas, including fatal cases, and gastrointestinal (GI) perforations, including fatal cases, each occurred in 1% of CABOMETYX patients. Monitor for signs and symptoms, and discontinue CABOMETYX in patients with Grade 4 fistulas or GI perforation.

Thrombotic Events: CABOMETYX can cause arterial or venous thromboembolic event. Venous thromboembolism occurred in 7% (including 4% pulmonary embolism) and arterial thromboembolism in 2% of CABOMETYX patients. Fatal thrombotic events have occurred. Discontinue CABOMETYX in patients who develop an acute myocardial infarction or serious arterial or venous thromboembolic events.

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. In CABINET (n=195), hypertension occurred in 65% (26% Grade 3) 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; when controlled, resume at a reduced dose. Permanently discontinue CABOMETYX for severe hypertension that cannot be controlled with antihypertensive therapy or for hypertensive crisis.

Diarrhea: CABOMETYX can cause diarrhea and it occurred in 62% (10% Grade 3) of treated 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): CABOMETYX can cause PPE and it occurred in 45% of treated patients (13% Grade 3). Withhold CABOMETYX until PPE resolves or decreases to Grade 1 and resume at a reduced dose for intolerable Grade 2 PPE or Grade 3 PPE.

Hepatotoxicity: CABOMETYX in combination with nivolumab in RCC can cause hepatic toxicity with higher frequencies of Grades 3 and 4 ALT and AST elevations compared to CABOMETYX alone. With the combination of CABOMETYX and nivolumab, Grades 3 and 4 increased ALT or AST were seen in 11% of patients. Monitor liver enzymes before initiation of treatment and periodically. Consider more frequent monitoring as compared to when the drugs are administered as single agents. Consider withholding CABOMETYX and/or nivolumab, initiating corticosteroid therapy, and/or permanently discontinuing the combination for severe or life-threatening hepatotoxicity.

Adrenal Insufficiency: CABOMETYX in combination with nivolumab can cause primary or secondary adrenal insufficiency. 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. Withhold CABOMETYX and/or nivolumab and resume CABOMETYX at a reduced dose depending on severity.

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): CABOMETYX can cause ONJ and it occurred in <1% of treated patients. 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. Withhold CABOMETYX for development of ONJ until complete resolution; resume at a reduced dose.

Impaired Wound Healing: CABOMETYX can cause impaired wound healing. Withhold CABOMETYX for at least 3 weeks prior to elective surgery. Do not administer 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): CABOMETYX can cause RPLS. Perform evaluation for RPLS and diagnose by characteristic finding on MRI any patient presenting with seizures, headache, visual disturbances, confusion, or altered mental function. Discontinue CABOMETYX in patients who develop RPLS.

Thyroid Dysfunction: CABOMETYX can cause thyroid dysfunction, primarily hypothyroidism, and it occurred in 19% of treated patients (0.4% Grade 3). Assess for signs of thyroid dysfunction prior to the initiation of CABOMETYX and monitor for signs and symptoms during treatment.

Hypocalcemia: CABOMETYX can cause hypocalcemia, with the highest incidence in DTC patients. Based on the safety population, hypocalcemia occurred in 13% of CABOMETYX patients (2% Grade 3 and 1% Grade 4).

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

Embryo-Fetal Toxicity: CABOMETYX can cause fetal harm. Advise pregnant women of the potential risk to a fetus and advise females of reproductive potential to use effective contraception during treatment with CABOMETYX 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, and constipation.

CABOMETYX 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 CABOMETYX dosage. Avoid grapefruit or grapefruit juice.

Strong or Moderate CYP3A4 Inducers: If coadministration with strong or moderate 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. Avoid CABOMETYX in patients with severe hepatic impairment.

Pediatric Use: Physéal widening has been observed in children with open growth plates when treated with CABOMETYX. Physéal and longitudinal growth monitoring is recommended in children (12 years and older) with open growth plates. Consider interrupting or discontinuing CABOMETYX if abnormalities occur. The safety and effectiveness of CABOMETYX in pediatric patients less than 12 years of age have not been established.

Please see accompanying full Prescribing Information <https://www.cabometryx.com/downloads/CABOMETYXUSPI.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

Exelixis is a globally ambitious oncology company innovating next-generation medicines and regimens at the forefront of cancer care. Powered by drug discovery and development excellence, we are rapidly evolving our product portfolio to target an expanding range of tumor types and indications with our clinically differentiated pipeline of small molecules and biotherapeutics. This comprehensive approach harnesses decades of robust investment in our science and partnerships to advance our investigational programs and extend the impact of our flagship commercial product, CABOMETYX® (cabozantinib). Exelixis is driven by a bold scientific pursuit to create transformational treatments that give more patients hope for the future. For information about the company and its mission to help cancer patients recover stronger and live longer, visit www.exelixis.com, follow @ExelixisInc on X (Twitter), like Exelixis, Inc. on Facebook and follow Exelixis on LinkedIn.

Forward-Looking Statements

This press release contains forward-looking statements, including, without limitation, statements related to: the presentation of detailed results from the CABINET trial at the 2025 ESMO; the therapeutic potential of cabozantinib as a treatment across a wide range of patients with neuroendocrine tumors and the potential of cabozantinib to become a much-needed option for those with lung and thymic NET; and Exelixis' scientific pursuit to create transformational treatments that give more patients hope for the future. 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; 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 safety and/or efficacy in future clinical testing; unexpected concerns that may arise as a result of the occurrence of adverse safety events or additional data analyses of clinical trials evaluating cabozantinib; 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 detailed from time to time under the caption "Risk Factors" in Exelixis' most recent Annual Report on Form 10-K and subsequent Quarterly Reports on Form 10-Q, and in Exelixis' future filings with the Securities and Exchange Commission. 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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² Neuroendocrine Tumors. Cleveland Clinic website. Available at: <https://my.clevelandclinic.org/health/diseases/22006-neuroendocrine-tumors-net>. Accessed October 2025.

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⁵ Pancreatic Neuroendocrine Tumors (Islet Cell Tumors) Treatment (PDQ®)—Patient Version. NCI website. Available at: <https://www.cancer.gov/types/pancreatic/patient/pnet-treatment-pdq>. Accessed October 2025.

⁶ What Is a Pancreatic Neuroendocrine Tumor? ACS website. Available at: <https://www.cancer.org/cancer/types/pancreatic-neuroendocrine-tumor/about/what-is-pnet.html>. Accessed October 2025.

⁷ Carcinoid Syndrome. Cleveland Clinic website. Available at: <https://my.clevelandclinic.org/health/diseases/22103-carcinoid-syndrome>. Accessed October 2025.

⁸ Signs and Symptoms of Gastrointestinal Carcinoid Tumors. ACS website. Available at: <https://www.cancer.org/cancer/types/gastrointestinal-carcinoid-tumor/detection-diagnosis-staging/signs-symptoms.html>. Accessed October 2025.

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¹² Survival Rates for Pancreatic Neuroendocrine Tumor. ACS website. Available at: <https://www.cancer.org/cancer/types/pancreatic-neuroendocrine-tumor/detection-diagnosis-staging/survival-rates.html>. Accessed October 2025.

¹³ Survival Rates for Gastrointestinal Carcinoid Tumors. ACS website. Available at: <https://www.cancer.org/cancer/types/gastrointestinal-carcinoid-tumor/detection-diagnosis-staging/survival-rates.html>. Accessed October 2025.

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