



## Exelixis Announces First 100 Patients Enrolled in Phase 3 COSMIC-311 Pivotal Trial of Cabozantinib in Relapsed Radioiodine-Refractory Differentiated Thyroid Cancer

February 25, 2020

*– Analysis for the co-primary endpoint of objective response rate and an interim analysis of progression-free survival expected in the second half of 2020 –*

ALAMEDA, Calif.--(BUSINESS WIRE)--Feb. 25, 2020-- [Exelixis, Inc.](#) (NASDAQ: EXEL) today announced enrollment of the first 100 patients in COSMIC-311, a phase 3 pivotal trial evaluating cabozantinib (CABOMETYX<sup>®</sup>) versus placebo in patients with radioactive iodine-refractory differentiated thyroid cancer who have progressed after up to two vascular endothelial growth factor (VEGF) receptor-targeted therapies.

"Given the encouraging clinical activity observed for cabozantinib in phase 1 and 2 trials in differentiated thyroid cancer, and the poor prognosis for patients who have progressed after prior VEGF receptor-targeting therapy, it is exciting to reach this milestone for COSMIC-311," said Gisela Schwab, M.D., President, Product Development and Medical Affairs and Chief Medical Officer, Exelixis. "This brings us one step closer to a first analysis that will help us better understand cabozantinib's potential in treating patients with this intractable form of thyroid cancer. We look forward to sharing those initial results later this year."

COSMIC-311 is a multicenter, randomized, double-blind, placebo-controlled phase 3 pivotal trial that aims to enroll approximately 300 patients at 150 sites globally. Patients will be randomized in a 2:1 ratio to receive either cabozantinib 60 mg or placebo once daily. Exelixis expects to conduct an analysis in the first 100 patients for the co-primary endpoint of objective response rate, and an interim analysis of progression-free survival in the second half of 2020. Additionally, total enrollment of 300 patients is expected to be reached in the second half of 2020.

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.<sup>1</sup> 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.<sup>1</sup> While cancerous thyroid tumors include differentiated, medullary and anaplastic forms, differentiated thyroid tumors make up about 90 percent of cases.<sup>1</sup> These include papillary, follicular and Hürthle cell cancer.<sup>1</sup> Differentiated thyroid cancer is typically treated with surgery followed by ablation of the remaining thyroid with radioiodine, but approximately 5% to 15% of cases are resistant to radioiodine treatment.<sup>2,3</sup> For these patients, life expectancy is only three to six years from the time metastatic lesions are detected.<sup>4,5,6</sup>

### About CABOMETYX<sup>®</sup> (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.

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 ( $\geq 25\%$ ) 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<sup>®</sup> (cabozantinib), COMETRIQ<sup>®</sup> (cabozantinib), COTELLIC<sup>®</sup> (cobimetinib) and MINNEBRO<sup>®</sup> (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](http://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: the therapeutic potential of cabozantinib as a treatment for patients with radioactive iodine-refractory differentiated thyroid cancer; Exelixis' plans to conduct an analysis in the first 100 patients enrolled in COSMIC-311 for the co-primary endpoint of objective response rate, and an interim analysis of progression-free survival in the second half of 2020; Exelixis' expectation that total enrollment of 300 patients in COSMIC-311 will be reached in the second half of 2020; 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: risks and uncertainties related to regulatory review and approval processes and Exelixis' compliance with applicable legal and regulatory requirements; the potential failure of cabozantinib to demonstrate safety and/or efficacy in COSMIC-311; uncertainties inherent in the product development process, including evolving regulatory requirements, slower than

anticipated patient enrollment or inability to identify a sufficient number of clinical trial sites; 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 October 30, 2019, and in Exelixis' future filings with the SEC, including, without limitation, Exelixis' Annual Report on Form 10-K expected to be filed with the SEC on February 25, 2020. 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.*

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- <sup>1</sup> American Cancer Society. About Thyroid Cancer. Available at: <https://www.cancer.org/cancer/thyroid-cancer/about.html>. Accessed February 2020.
- <sup>2</sup> Cooper DS, et al. 2009. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid*. 19:1167–1214.
- <sup>3</sup> Worden F. 2014. Treatment strategies for radioactive iodine-refractory differentiated thyroid cancer. *Ther Adv Med Oncol*. 6:267–279.
- <sup>4</sup> Xing M, Haugen BR, Schlumberger M. 2013. Progress in molecular-based management of differentiated thyroid cancer. *Lancet*. 381:1058–1069.
- <sup>5</sup> Pacini F, et al. 2012. Radioactive iodine-refractory differentiated thyroid cancer: unmet needs and future directions. *Expert Rev Endocrinol Metab*. 7:541–554.
- <sup>6</sup> Durante C, et al. 2006. Long-term outcome of 444 patients with distant metastases from papillary and follicular thyroid carcinoma: benefits and limits of radioiodine therapy. *J Clin Endocrinol Metab*. 91:2892–2899.

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