Exelixis Announces Results from a Phase 2 Investigator-Sponsored Trial of Cabozantinib in the First-Line Treatment of Metastatic Radioiodine-Refractory Differentiated Thyroid Carcinoma

February 13, 2018

– 54 percent objective response rate and 43 percent stable disease observed among 35 evaluable patients –

– Exelixis plans to initiate a pivotal phase 3 trial later this year –

– Results to be presented during an oral session on February 16 at the 2018 Multidisciplinary Head and Neck Cancers Symposium –

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Feb. 13, 2018-- Exelixis, Inc. (NASDAQ:EXEL) today announced results from a phase 2 investigator-sponsored trial (IST) of cabozantinib for the first-line treatment of metastatic radioiodine (RAI)-refractory differentiated thyroid carcinoma (DTC). The results were the subject of a news briefing that took place earlier today and will be presented during an oral session on February 16 starting at 1:30 p.m. MT at the 2018 Multidisciplinary Head and Neck Cancers Symposium, which is being held in Scottsdale, Arizona, February 15–17, 2018.

Patients with metastatic, RAI-refractory DTC were enrolled in this single-arm, open-label trial, and were administered oral cabozantinib 60 mg once daily. The primary endpoint of the trial is objective response rate. Among the 35 patients who were evaluable for response, partial response was achieved by 54 percent of patients (n=19), and stable disease was reported in 43 percent of patients (n=15) per RECIST 1.1. All but one evaluated patient experienced a decrease in tumor target lesions. Secondary endpoints of the trial include progression-free survival (PFS), time to progression (TTP), duration of response (DOR) and clinical benefit rate (CBR) defined as the number of patients achieving an objective response or stable disease for at least 6 months. The CBR at six months was 80 percent (n=28). With a median follow up for the study of 35 weeks the median PFS has not been reached. The median TTP among those patients who progressed was 35 weeks.

“While many patients with differentiated thyroid cancer can be treated successfully with radioiodine, there are very few options for those patients whose tumors have become resistant to treatment,” said Marcia Brose, M.D., Ph.D., Associate Professor of Otorhinolaryngology: Head and Neck Surgery and Director of the Center for Rare Cancers at the Abramson Cancer Center of the University of Pennsylvania, and principal investigator of the trial. “These findings suggest that cabozantinib, which showed encouraging efficacy and a manageable safety profile in this phase 2 trial, may be a promising treatment option for this patient population and warrants further evaluation.”

“We are dedicated to supporting investigator-sponsored trials focused on evaluating cabozantinib in a range of tumor types to help inform our ongoing development program whose main goal is to provide improved treatment options to patients in need,” said Gisela Schwab, M.D., President, Product Development and Medical Affairs and Chief Medical Officer, Exelixis. “Based on these promising results and data from other studies of cabozantinib in previously treated DTC, Exelixis plans to initiate a pivotal phase 3 study with cabozantinib in patients with advanced DTC later this year.”

The most common treatment-related adverse events included hyperglycemia (80 percent), diarrhea (77 percent), malaise/fatigue (74 percent), and weight loss (71 percent). The majority of these adverse events were grade 1 or 2. The most comment grade 3-5 adverse events occurring in more than one patient included hypertension (14 percent), increased lipase (9 percent), pulmonary embolism (6 percent), and hyponatremia (6 percent).

About the Trial

The IST is being conducted by the Center for Rare Cancers and Personalized Therapy at the Abramson Cancer Center of the University of Pennsylvania. Enrollment for the trial was completed in August 2017. Dr. Marcia Brose, Associate Professor of Otorhinolaryngology: Head and Neck Surgery, Perelman School of Medicine of the University of Pennsylvania is the principal investigator. The median age of patients is 65 years (range 45 to 84) and 17 patients (49 percent) are male. Of the patients in the trial, 23 (66 percent) had papillary thyroid cancer, 3 (9 percent) had follicular (Hürthle cell) thyroid cancer and 9 (26 percent) had poorly differentiated histology. Patients are administered oral cabozantinib 60 mg once daily as long as they continue to derive clinical benefit or until unacceptable drug-related toxicity. Sixteen patients remain on the trial as of February 6, 2018.

About Differentiated Thyroid Carcinoma

Thyroid cancer is commonly diagnosed at a younger age than most other adult cancers and is the most rapidly increasing cancer in the U.S., tripling in incidence in the past three decades.[1] Approximately 54,000 new cases of thyroid cancer will be diagnosed in the U.S. in 2018.[1] Nearly three out of four of these cases will be in women.[1] Cancerous thyroid tumors include differentiated, medullary and anaplastic forms.[1]

Differentiated thyroid tumors, which make up about 90 percent of all thyroid cancers, are typically treated with surgery followed by ablation of the remaining thyroid with radioiodine.[2] Approximately 5 to 15 percent of differentiated thyroid tumors are resistant to radioiodine treatment.[3] For these patients, life expectancy is only three to six years from the time metastatic lesions are detected.[4-6]

About CABOMETYX® (cabozantinib)

CABOMETYX tablets are approved in the United States for the treatment of patients with advanced RCC. CABOMETYX tablets are also approved in the European Union, Norway, Iceland, Australia and Switzerland for the treatment of advanced RCC in adults who have received prior vascular

endothelial growth factor (VEGF)-targeted therapy. Ipsen also submitted to European Medicines Agency (EMA) the regulatory dossier for cabozantinib as a treatment for first-line advanced RCC in the European Union on August 28, 2017; on September 8, 2017, Ipsen announced that the EMA validated the application. 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, including RCC.

CABOMETYX is not indicated for the treatment of differentiated thyroid carcinoma.

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 have occurred with CABOMETYX. In two RCC studies, the incidence of Grade ≥ 3 hemorrhagic events was 3% in CABOMETYX-treated patients. Do not administer CABOMETYX to patients that have or are at risk for severe hemorrhage.
- **Gastrointestinal (GI) Perforations and Fistulas:** In RCC studies, fistulas were reported in 1% of CABOMETYX-treated patients. Fatal perforations occurred in patients treated with CABOMETYX. In RCC studies, gastrointestinal (GI) perforations were reported in 1% of CABOMETYX-treated patients. Monitor patients for symptoms of fistulas and perforations, including abscess and sepsis. Discontinue CABOMETYX in patients who experience a fistula which cannot be appropriately managed or a GI perforation.
- **Thrombotic Events:** CABOMETYX treatment results in an increased incidence of thrombotic events. In RCC studies, venous thromboembolism occurred in 9% (including 5% pulmonary embolism) and arterial thromboembolism occurred in 1% of CABOMETYX-treated patients. Fatal thrombotic events occurred in the cabozantinib clinical program. Discontinue CABOMETYX in patients who develop an acute myocardial infarction or any other arterial thromboembolic complication.
- **Hypertension and Hypertensive Crisis:** CABOMETYX treatment results in an increased incidence of treatment-emergent hypertension, including hypertensive crisis. In RCC studies, hypertension was reported in 44% (18% Grade ≥ 3) of CABOMETYX-treated patients. Monitor blood pressure prior to initiation and regularly during CABOMETYX treatment. Withhold CABOMETYX for hypertension that is not adequately controlled with medical management; when controlled, resume CABOMETYX at a reduced dose. Discontinue CABOMETYX for severe hypertension that cannot be controlled with anti-hypertensive therapy. Discontinue CABOMETYX if there is evidence of hypertensive crisis or severe hypertension despite optimal medical management.
- **Diarrhea:** In RCC studies, diarrhea occurred in 74% of patients treated with CABOMETYX. Grade 3 diarrhea occurred in 11% of patients treated with CABOMETYX. Withhold CABOMETYX in patients who develop intolerable Grade 2 diarrhea or Grade 3-4 diarrhea that cannot be managed with standard antidiarrheal treatments until improvement to Grade 1; resume CABOMETYX at a reduced dose.
- **Palmar-Plantar Erythrodysesthesia (PPE):** In RCC studies, palmar-plantar erythrodysesthesia (PPE) occurred in 42% of patients treated with CABOMETYX. Grade 3 PPE occurred in 8% of patients treated with CABOMETYX. Withhold CABOMETYX in patients who develop intolerable Grade 2 PPE or Grade 3 PPE until improvement to Grade 1; resume CABOMETYX at a reduced dose.
- **Reversible Posterior Leukoencephalopathy Syndrome (RPLS)**, a syndrome of subcortical vasogenic edema diagnosed by characteristic finding on MRI, occurred in the cabozantinib clinical program. Perform an evaluation for RPLS in any patient presenting with seizures, headache, visual disturbances, confusion or altered mental function. Discontinue CABOMETYX in patients who develop RPLS.
- **Embryo-fetal Toxicity** may be associated with CABOMETYX. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during CABOMETYX treatment and for 4 months after the last dose.
- **Adverse Reactions:** The most commonly reported (≥25%) adverse reactions are: diarrhea, fatigue, nausea, decreased appetite, hypertension, PPE, weight decreased, vomiting, dysgeusia, and stomatitis.
- **Strong CYP3A4 Inhibitors**: If concomitant use with strong CYP3A4 inhibitors cannot be avoided, reduce the CABOMETYX dosage.
- **Strong CYP3A4 Inducers:** If concomitant use with strong CYP3A4 inducers cannot be avoided, increase the CABOMETYX dosage.
- **Lactation:** Advise women not to breastfeed while taking CABOMETYX and for 4 months after the final dose.
- **Hepatic Impairment:** In patients with mild to 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 genetic systems, 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. We discovered our lead compounds, cabozantinib and cobimetinib, and advanced them into clinical development before

entering into partnerships with leading biopharmaceutical companies in our efforts to bring these medicines to patients globally. We are steadfast in our commitment to prudently reinvest in our business to maximize the potential of our pipeline. We intend to supplement 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 recently earned a spot on Deloitte's Technology Fast 500 list, a yearly award program honoring the 500 fastest-growing companies over the past four years. For more information about Exelixis, please visit www.exelixis.com or follow @ExelixisInc on Twitter.

Exelixis Forward-Looking Statement Disclaimer

This press release contains forward-looking statements, including, without limitation, statements related to: Exelixis' plans to initiate a pivotal phase 3 trial with cabozantinib in patients with advanced DTC later this year; the future presentation of data results from a phase 2 IST of cabozantinib for the first-line treatment of metastatic radioiodine (RAI)-refractory DTC at the 2018 Multidisciplinary Head and Neck Cancers Symposium; the clinical and therapeutic potential of cabozantinib for patients with DTC; Exelixis' continued support of ISTs focused on evaluating cabozantinib in a range of tumor types; Exelixis' goal to provide improved treatment options to patients in need; and Exelixis' commitment to reinvesting in its business to maximize the potential of its pipeline, including supplementing its existing therapeutic assets through targeted business development activities and internal drug discovery. Words such as "plan," "will," "may," "focused," "goal," "potential," "future," "commitment," "intend," or other similar expressions identify forward-looking statements, but the absence of these words does not necessarily mean that a statement is not forward-looking. In addition, any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements. These forward-looking statements 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 potential failure of cabozantinib to demonstrate safety and efficacy in clinical testing; the availability of data at the referenced times; Exelixis' ability and the ability of its collaborators to conduct clinical trials of cabozantinib sufficient to achieve a positive completion; the complexities and challenges associated with regulatory review and approval processes; the level of costs associated with Exelixis' commercialization, research and development and other activities; competition in the area of business development activities and the inherent uncertainty of the drug discovery process; Exelixis' dependence on its relationships with its cabozantinib collaboration partners, including, the level of their investment in the resources necessary to successfully commercialize cabozantinib in the territories where it is approved; Exelixis' dependence on its relationship with Genentech/Roche with respect to cobimetinib and Exelixis' ability to maintain its rights under the collaboration; market acceptance of CABOMETYX, COMETRIQ, and COTELLIC and the availability of coverage and reimbursement for these products; Exelixis' dependence on third-party vendors for the development, manufacture and supply of its products; Exelixis' ability to protect the company's intellectual property rights; market competition; changes in economic and business conditions, and other factors 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, 2017, and in Exelixis' future filings with the SEC. The forward-looking statements made in this press release speak only as of the date of this press release. Exelixis expressly disclaims any duty, obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in Exelixis' expectations with regard thereto or any change in events, conditions or circumstances on which any such statements are based.

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Source: Exelixis, Inc.

Exelixis, Inc.
Investors:
Susan Hubbard, 650-837-8194
EVP, Public Affairs and Investor Relations
shubbard@exelixis.com
or
Media:
Lindsay Treadway, 650-837-7522
Director, Public Affairs and Advocacy Relations
ltreadway@exelixis.com