Exelixis Announces Phase 3 CELESTIAL Trial Results of Cabozantinib in Previously Treated Advanced Hepatocellular Carcinoma to be Presented at 2018 Gastrointestinal Cancers Symposium

November 21, 2017

– Accepted as a late-breaking oral presentation at the 2018 American Society of Clinical Oncology's Gastrointestinal Cancers Symposium (ASCO-GI), January 18-20, 2018 –

– Exelixis to submit supplemental New Drug Application to U.S. Food and Drug Administration (FDA) in the first quarter of 2018 –

– Cabozantinib previously granted orphan drug designation for the treatment of hepatocellular carcinoma (HCC) by FDA –

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Nov. 21, 2017-- Exelixis, Inc. (NASDAQ:EXEL) today announced that the phase 3 CELESTIAL trial results have been accepted as a late-breaking presentation at the 2018 ASCO-GI Symposium, which is being held January 18–20, 2018 in San Francisco. Detailed results from CELESTIAL, the randomized, double-blind, placebo-controlled study of cabozantinib versus placebo in patients with advanced HCC who have received prior treatment with sorafenib, will be presented during Oral Abstract Session B: Cancers of the Pancreas, Small Bowel, and Hepatobiliary Tract, which begins at 2:15 p.m. PT on Friday, January 19, 2018.

Oral Presentation

Abstract 207: Cabozantinib (C) versus placebo (P) in patients (pts) with advanced hepatocellular carcinoma (HCC) who have received prior sorafenib: results from the randomized phase 3 CELESTIAL trial.

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On October 16, 2017, Exelixis announced that the CELESTIAL trial met its primary endpoint of overall survival (OS), with cabozantinib providing a statistically significant and clinically meaningful improvement in OS compared with placebo in patients with advanced HCC. The independent data monitoring committee for the study recommended that the trial be stopped for efficacy following review of the second planned interim analysis.

About the CELESTIAL Study

CELESTIAL is a randomized, double-blind, placebo-controlled study of cabozantinib in patients with advanced HCC conducted at more than 100 sites globally in 19 countries. The trial was designed to enroll 760 patients with advanced HCC who received prior sorafenib and may have received up to two prior systemic cancer therapies for HCC and had adequate liver function. Enrollment of the trial was completed in September 2017. Patients were randomized 2:1 to receive 60 mg of cabozantinib once daily or placebo and were stratified based on etiology of the disease (hepatitis C, hepatitis B or other), geographic region (Asia versus other regions) and presence of extrahepatic spread and/or macrovascular invasion (yes or no). No cross-over was allowed between the study arms.

The primary endpoint for the trial is OS, and secondary endpoints include objective response rate and progression-free survival. Exploratory endpoints include patient-reported outcomes, biomarkers and safety.

Based on available clinical trial data from various published trials conducted in the second-line setting of advanced HCC, the CELESTIAL trial statistics for the primary endpoint of OS assumed a median OS of 8.2 months for the placebo arm. A total of 621 events provide the study with 90 percent power to detect a 32 percent increase in median OS (HR = 0.76) at the final analysis. Two interim analyses were planned and conducted at 50 percent and 75 percent of the planned 621 events.

About HCC

Liver cancer is the third-leading cause of death worldwide, and hepatocellular carcinoma (HCC) is the most common form, making up about three-fourths of the nearly 41,000 cases that will be diagnosed in 2017 in the U.S.[1,2] Without treatment, patients with advanced disease usually survive less than 6 months, and it is estimated that 29,000 people will die due to liver cancer in the U.S.[3] Worldwide, nearly 800,000 new cases are diagnosed annually, and the disease accounts for more than 700,000 deaths each year.[4]

About CABOMETYX® (cabozantinib)

CABOMETYX tablets are approved in the United States for the treatment of patients with advanced RCC who have received prior anti-angiogenic therapy. CABOMETYX tablets are also approved in the European Union, Norway and Iceland for the treatment of advanced RCC in adults who have received prior vascular endothelial growth factor (VEGF)-targeted therapy. 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 advanced HCC.

Please see Important Safety Information below and full U.S. prescribing information at https://cabometyx.com/downloads/cabometyxuspi.pdf.

U.S. Important Safety Information

- **Severe Hemorrhage** occurred with CABOMETYX. In two RCC studies, Grade ≥3 hemorrhagic events occurred in 2.1% of CABOMETYX patients vs 1.6% with everolimus and in 5.1% of CABOMETYX patients vs 1.4% with sunitinib. Fatal hemorrhages also occurred in the cabozantinib clinical program. Do not administer CABOMETYX to patients that have or are at risk for severe hemorrhage.
- **Gastrointestinal (GI) Perforations and Fistulas** were reported with CABOMETYX. In two RCC studies, GI perforations occurred in 0.9% of CABOMETYX patients vs 0.6% with everolimus and in 2.6% of CABOMETYX patients vs 0% with sunitinib. Fatal perforations occurred in the cabozantinib clinical program. Fistulas were reported in 1.2% (including 0.6% anal fistula) of CABOMETYX patients vs 0% with everolimus. Monitor patients for symptoms of perforations and fistulas. Discontinue CABOMETYX in patients who experience a GI perforation or a fistula that cannot be appropriately managed.
- **Thrombotic Events** increased with CABOMETYX. In two RCC studies, arterial thromboembolism events were reported in 0.9% of CABOMETYX patients vs 0.3% with everolimus and 1.3% of CABOMETYX patients vs 5.6% with sunitinib. Pulmonary embolism events were reported in 3.9% of CABOMETYX patients vs 0.3% with everolimus and 9% of CABOMETYX patients vs 0% with sunitinib. Venous thromboembolism occurred in 7.3% of CABOMETYX patients vs 2.5% with everolimus. Fatal thrombotic events occurred in the cabozantinib clinical program. Discontinue CABOMETYX in patients who develop an acute myocardial infarction, cerebral infarction, or other serious arterial thromboembolic complication.
- **Hypertension and Hypertensive Crisis** occurred with CABOMETYX. In two RCC studies, treatment-emergent hypertension increased with CABOMETYX. Hypertension was reported in 37% (15% Grade ≥3) of CABOMETYX patients vs 7.1% (3.1% Grade ≥3) with everolimus and in 67% (28% Grade ≥3) of CABOMETYX patients vs 44% (21% Grade ≥3) with sunitinib. 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 hypertensive crisis or severe hypertension that cannot be controlled with antihypertensive therapy or medical management.
- **Diarrhea** occurred with CABOMETYX. In two RCC trials, diarrhea occurred in 74% (11% Grade 3) of CABOMETYX patients vs 28% (2% Grade 3) with everolimus and in 73% (10% Grade 3) of CABOMETYX patients vs 54% (11% Grade 3) with sunitinib. 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 Syndrome (PPES)** occurred with CABOMETYX. In two RCC trials, PPES occurred in 42% (8.2% Grade 3) of CABOMETYX patients vs 6% (<1% Grade 3) with everolimus and in 42% (7.7% Grade 3) of CABOMETYX patients vs 33% (4.2% Grade 3) with sunitinib. Withhold CABOMETYX in patients who develop intolerable Grade 2 PPES or Grade 3 PPES 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. 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** 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, PPES, weight decreased, vomiting, dysgeusia, and stomatitis.
- **Drug Interactions: Strong CYP3A4 inhibitors and inducers:** Reduce the dosage of CABOMETYX if concomitant use with strong CYP3A4 inhibitors cannot be avoided. Increase the dosage of CABOMETYX if concomitant use with strong CYP3A4 inducers cannot be avoided.
- **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 them 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.

Forward-Looking Statement Disclaimer

This press release contains forward-looking statements, including, without limitation, statements related to: Exelixis' plan to submit an supplemental New Drug Application to the FDA in the first quarter of 2018 for cabozantinib as a treatment for patients with advanced HCC; Exelixis' plan to present the detailed results from CELESTIAL at the 2018 ASCO-GI; 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; and Exelixis' mission to deliver the next generation of Exelixis medicines and help patients recover stronger and live longer. Words such as "to be," "will," "commitment," "potential," "plan," "mission," 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: risks and uncertainties related to regulatory review and approval processes and Exelixis' compliance with applicable legal and regulatory requirements; the availability of data at the referenced time; 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' ability and the ability of its collaborators to conduct clinical trials of cabozantinib and cobimetinib both alone and in combination with other therapies sufficient to achieve a positive completion; risks related to the potential failure of cabozantinib and cobimetinib both alone and in combination with other therapies, to demonstrate safety and efficacy in clinical testing; 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.

References:

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3. Weledji E, Orock G, Ngowe M, NsaghaD. How grim is hepatocellular carcinoma? *Annals of Medicine and Surgery*. 2014. (3):71-76.
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