Exelixis Announces FDA Approval of CABOMETYX™ (Cabozantinib) Tablets for Patients with Advanced Renal Cell Carcinoma Who Have Received Prior Anti-Angiogenic Therapy

April 25, 2016

– CABOMETYX is the first therapy to demonstrate improved overall survival, progression-free survival and objective response rate in a large, randomized phase 3 trial of patients with advanced kidney cancer –

– Exelixis to hold conference call/webcast at 4:00 EDT / 1:00 PDT to discuss approval –

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Apr. 25, 2016-- Exelixis, Inc. (NASDAQ:EXEL) today announced that the U.S. Food and Drug Administration (FDA) has approved CABOMETYX™ (cabozantinib) tablets for the treatment of patients with advanced renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy. RCC is the most common form of kidney cancer in adults. CABOMETYX, which was granted Fast Track and Breakthrough Therapy designations by the FDA, is the first therapy to demonstrate in a phase 3 trial for patients with advanced RCC, robust and clinically meaningful improvements in all three key efficacy parameters — overall survival, progression-free survival and objective response rate.

This Smart News Release features multimedia. View the full release here: http://www.businesswire.com/news/home/20160425006329/en/

Renal Cell Carcinoma Fact Sheet

"With today's announcement, patients with previously treated advanced kidney cancer now have a new option, the first and only approved product demonstrated to help patients live longer while also delaying the progression of their cancer," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "We are proud to bring new hope to this community, who are looking for more therapies that can help extend lives. Exelixis is committed to making CABOMETYX available to patients in need within the next couple weeks."

"The efficacy profile demonstrated by CABOMETYX in the METEOR trial, now complemented by the overall survival benefit, is highly compelling," said Toni Choueiri, MD, Clinical Director, Lank Center for Genitourinary Oncology, Dana-Farber Cancer Institute. "CABOMETYX is distinct from other approved treatment options, as it targets multiple tyrosine kinases involved in the development of RCC, including MET, AXL and three VEGF receptors. At the same time, physicians are very familiar with this class of drug and how to use dose adjustments to balance safety and efficacy. The approval of CABOMETYX is wonderful news for physicians who are looking for a new option for their previously treated patients with advanced kidney cancer."

The approval of CABOMETYX is based on results of the phase 3 METEOR trial, which met its primary endpoint of improving progression-free survival. Compared with everolimus, a standard of care therapy for second-line RCC, CABOMETYX was associated with a 42 percent reduction in the rate of disease progression or death. Median progression-free survival for cabozantinib was 7.4 months versus 3.8 months for everolimus (HR=0.58, 95% CI 0.45-0.74, P<0.0001). CABOMETYX also significantly improved the objective response rate compared with everolimus. These data were presented at the European Cancer Congress in September 2015 and published in *The New England Journal of Medicine*.

As announced in February 2016, CABOMETYX also demonstrated a statistically significant and clinically meaningful increase in overall survival in the METEOR trial. Compared with everolimus, CABOMETYX was associated with a 34 percent reduction in the rate of death. Median overall survival was 21.4 months for patients receiving CABOMETYX versus 16.5 months for those receiving everolimus (HR=0.66, 95% CI 0.53-0.83, P=0.0003).

The most common (frequency ≥25 percent) adverse reactions in CABOMETYX-treated patients include diarrhea, fatigue, nausea, decreased appetite, hand-foot syndrome, high blood pressure, vomiting, weight loss, and constipation. Dose reduction rates were 60 percent for CABOMETYX and 24 percent for everolimus. The rate of treatment discontinuation due to adverse reactions was low (10 percent in each arm) and consistent with that previously reported for everolimus.

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

Conference Call/Webcast at 4:00 EDT / 1:00 PDT Today

Exelixis management will discuss the CABOMETYX U.S. regulatory approval during a conference call beginning at 4:00 p.m. EDT/1:00 p.m. PDT today, April 25, 2016. To listen to a live webcast of the conference call, visit the Event Calendar page under Investors & Media at www.exelixis.com. Alternatively, participants may dial (855) 793-2457 (domestic) or (631) 485-4921 (international) and provide the conference call passcode 94229895 to join by phone.

An archived replay of the webcast will be available on the Event Calendar page under Investors & Media at www.exelixis.com for one year. An audio-only phone replay will be available until 11:59 p.m. EDT on April 27, 2016. Access numbers for the phone replay are: (855) 859-2056 (domestic) and (404) 537-3406 (international); the passcode is 94229895.

About the METEOR Phase 3 Pivotal Trial

METEOR was an open-label, event-driven trial of 658 patients with advanced renal cell carcinoma who had failed at least one prior vascular endothelial growth factor (VEGF) receptor tyrosine kinase inhibitor (TKI) therapy. The primary endpoint was progression-free survival. Secondary endpoints included overall survival and objective response rate. The trial was conducted at approximately 200 sites in 26 countries, and enrollment was weighted toward Western Europe, North America, and Australia.

Patients were randomized 1:1 to receive 60 mg of CABOMETYX daily or 10 mg of everolimus daily and were stratified based on the number of prior VEGF receptor TKI therapies received and on MSKCC risk criteria. No cross-over was allowed between the study arms.

About Advanced Renal Cell Carcinoma

The American Cancer Society's 2016 statistics cite kidney cancer as among the top ten most commonly diagnosed forms of cancer among both men and women in the U.S.[1] Clear cell RCC is the most common type of kidney cancer in adults.[2] If detected in its early stages, the five-year survival rate for RCC is high; for patients with advanced or late-stage metastatic RCC, however, the five-year survival rate is only 12 percent, with no identified cure for the disease.[1] Approximately 17,000 patients in the U.S. and 37,000 globally require second-line or later treatment.[3]

The majority of clear cell RCC tumors have lower than normal levels or function of the von Hippel-Lindau protein, which leads to higher levels of MET, AXL and VEGF.[4,5] Higher than normal levels of these proteins can promote tumor angiogenesis (blood vessel growth), growth, invasiveness and metastasis.[6-9] MET and AXL may also provide escape pathways that drive resistance to VEGF receptor inhibitors.[5,6]

About CABOMETYX

CABOMETYX targets include MET, AXL and VEGFR-1, -2 and -3. In preclinical models, cabozantinib has been shown to inhibit the activity of these receptors, which are involved in normal cellular function and pathologic processes such as tumor angiogenesis, invasiveness, metastasis and drug resistance.

CABOMETYX, the tablet formulation of cabozantinib, will be available in 20 mg, 40 mg or 60 mg doses. The recommended dose is 60 mg orally, once daily.

On January 28, 2016, the European Medicines Agency (EMA) validated Exelixis' Marketing Authorization Application (MAA) for cabozantinib as a treatment for patients with advanced renal cell carcinoma who have received one prior therapy. The MAA has been granted accelerated assessment, making it eligible for a 150-day review, versus the standard 210 days. On February 29, 2016, Exelixis and Ipsen jointly announced an exclusive licensing agreement for the commercialization and further development of cabozantinib indications outside of the United States, Canada and Japan.

Important Safety Information

Hemorrhage: Severe hemorrhage occurred with CABOMETYX. The incidence of Grade ≥3 hemorrhagic events was 2.1% in CABOMETYX-treated patients and 1.6% in everolimus-treated patients. 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: Fistulas were reported in 1.2% (including 0.6% anal fistula) of CABOMETYX-treated patients and 0% of everolimus-treated patients. GI perforations were reported in 0.9% of CABOMETYX-treated patients and 0.6% of everolimus-treated patients. Fatal perforations occurred in the cabozantinib clinical program. Monitor patients for symptoms of fistulas and perforations. Discontinue CABOMETYX in patients who experience a fistula that cannot be appropriately managed or a GI perforation.

Thrombotic Events: CABOMETYX treatment results in an increased incidence of thrombotic events. Venous thromboembolism was reported in 7.3% of CABOMETYX-treated patients and 2.5% of everolimus-treated patients. Pulmonary embolism occurred in 3.9% of CABOMETYX-treated patients and 0.3% of everolimus-treated patients. Events of arterial thromboembolism were reported in 0.9% of CABOMETYX-treated patients and 0.3% of everolimus-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. Hypertension was reported in 37% (15% Grade ≥3) of CABOMETYX-treated patients and 7.1% (3.1% Grade ≥3) of everolimus-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: Diarrhea occurred in 74% of patients treated with CABOMETYX and in 28% of patients treated with everolimus. Grade 3 diarrhea occurred in 11% of CABOMETYX-treated patients and in 2% of everolimus-treated patients. 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. Dose modification due to diarrhea occurred in 26% of patients.

Palmar-Plantar Erythrodysesthesia Syndrome (PPES): Palmar-plantar erythrodysesthesia syndrome (PPES) occurred in 42% of patients treated with CABOMETYX and in 6% of patients treated with everolimus. Grade 3 PPES occurred in 8.2% of CABOMETYX-treated patients and in <1% of everolimus-treated patients. 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. Dose modification due to PPES occurred in 16% of patients.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS): 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: CABOMETYX can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. 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 commonly reported (≥25%) adverse reactions are: diarrhea, fatigue, nausea, decreased appetite, PPES, hypertension, vomiting, weight decreased, and constipation.

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 a lactating woman not to breastfeed during treatment with CABOMETYX and for 4 months after the final dose.

Reproductive Potential: Contraception—Advise females of reproductive potential to use effective contraception during treatment with CABOMETYX and for 4 months after the final dose. **Infertility —**CABOMETYX may impair fertility in females and males of reproductive potential.

Hepatic Impairment: Reduce the CABOMETYX dose in patients with mild (Child-Pugh score [C-P] A) or moderate (C-P B) hepatic impairment. CABOMETYX is not recommended for use in patients with severe hepatic impairment.

Please see full Prescribing Information at https://cabometyx.com/downloads/cabometyxuspi.pdf.

About Exelixis

Exelixis, Inc. (Nasdaq: EXEL) is a biopharmaceutical company committed to the discovery, development and commercialization of new medicines with the potential to improve care and outcomes for people with cancer. Since its founding in 1994, three medicines discovered at Exelixis have progressed through clinical development to receive regulatory approval. Currently, Exelixis is focused on advancing cabozantinib, an inhibitor of multiple tyrosine kinases including MET, AXL and VEGF receptors, which has shown clinical anti-tumor activity in more than 20 forms of cancer and is the subject of a broad clinical development program. Two separate formulations of cabozantinib have received regulatory approval to treat certain forms of kidney and thyroid cancer and are marketed for those purposes as CABOMETYX™ tablets (U.S.) and COMETRIQ® capsules (U.S. and EU), respectively. Another Exelixis-discovered compound, COTELLIC™ (cobimetinib), a selective inhibitor of MEK, has been approved in major territories including the United States and European Union, and is being evaluated for further potential indications by Roche and Genentech (a member of the Roche Group) under a collaboration with Exelixis. For more information on 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: the therapeutic potential of CABOMETYX; Exelixis' commitment to making CABOMETYX available to patients within the next couple weeks and the doses in which CABOMETYX will be available; the eligibility for an expedited review of Exelixis' MAA for cabozantinib in advanced RCC by the EMA; Exelixis' commitment to developing small molecule therapies for the treatment of cancer; and Exelixis' primary focus on the development and commercialization of cabozantinib. Words such as "committed," "will," "eligible," "focusing," 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 degree of market acceptance of CABOMETYX and the availability of coverage and reimbursement for CABOMETYX; Exelixis' ability to judge the proper size and level of experience of the commercialization teams required to support the launch of cabozantinib for advanced RCC in the U.S.; Exelixis' dependence on third-party vendors; risks and uncertainties related to regulatory review and approval processes and Exelixis' compliance with applicable legal and regulatory requirements; Exelixis' ability to conduct clinical trials of cabozantinib sufficient to achieve a positive completion; and other factors discussed under the caption "Risk Factors" in Exelixis' annual report on Form 10-K filed with the Securities and Exchange Commission (SEC) on February 29, 2016, and in Exelixis' other 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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