Exelixis-Discovered Compounds to Be Featured in 10 Presentations at ESMO 2017 Congress

August 1, 2017

- CABOSUN overall survival results and independent radiology review committee analysis of progression-free survival data to be presented during poster discussion session on September 10 -

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Aug. 1, 2017-- Exelixis, Inc. (NASDAQ:EXEL) today announced that data from clinical trials of cabozantinib and cobimetinib will be the subject of 10 presentations at the European Society for Medical Oncology (ESMO) 2017 Congress in Madrid, September 8 – 12, 2017.

Progression-free survival by independent radiology review and updated overall survival results from CABOSUN, a randomized phase 2 clinical trial of cabozantinib compared with sunitinib in patients with previously untreated advanced renal cell carcinoma (RCC), will be presented as a late-breaking abstract in the Genitourinary Tumours, Non-Prostate poster discussion session on Sunday, September 10. Final data from the phase 1 study of cabozantinib in combination with nivolumab with or without ipilimumab for the treatment of metastatic urothelial carcinoma and other genitourinary malignancies will be presented in the Genitourinary Tumours, Non-Prostate oral presentation session on Saturday, September 9. Additionally, poster presentations will detail the evaluation of cabozantinib in RCC and advanced penile squamous cell carcinoma, and of cobimetinib in combination studies in metastatic melanoma.

"We look forward to this year's ESMO Congress where new data from the CABOSUN trial of cabozantinib in patients with previously untreated advanced renal cell carcinoma will be presented, as well as the final analysis from the study exploring cabozantinib in combination with nivolumab and ipilimumab in genitourinary tumors, including metastatic urothelial carcinoma," said Michael M. Morrissey, Ph.D., President and Chief Executive Officer of Exelixis. "The slate of data featuring Exelixis-discovered compounds demonstrates our commitment to advancing our ongoing clinical research program to help improve care and outcomes for patients with cancer."

Cabozantinib to be featured in eight presentations

The full schedule of cabozantinib presentations expected at the meeting is as follows:

Oral Presentation

[846O] "Final results of a phase I study of cabozantinib (Cabo) plus nivolumab (Nivo) and CaboNivo plus Ipilimumab (Ipi) in patients (pts) with metastatic urothelial carcinoma (mUC) and other genitourinary (GU) malignancies"
Dr. Rosa Nadal, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, Baltimore, Maryland, USA
Session: Genitourinary Tumours, Non-Prostate
Oral presentation Saturday, September 9, 9:15 – 10:45 a.m. CEST, Madrid Auditorium
Note: This is a National Cancer Institute Cancer Therapy Evaluation Program (NCI-CTEP) study.

Poster Discussion

[LBA38] "Progression-free survival (PFS) by independent review and updated overall survival (OS) results from Alliance A031203 trial (CABOSUN): cabozantinib versus sunitinib as initial targeted therapy for patients (pts) with metastatic renal cell carcinoma (mRCC)"
Dr. Toni Choueiri, Lank Center for Genitourinary Oncology, Dana-Farber Cancer Institute, Boston, Massachusetts, USA
Session: Genitourinary Tumours, Non-Prostate
Poster presented Sunday, September 10, 2:45 – 4:15 p.m. CEST, Cordoba Auditorium
Note: This is an NCI-CTEP study.

Poster Presentations

[872P] "Outcomes based on plasma biomarkers in METEOR, a randomized phase 3 trial of cabozantinib (C) vs everolimus (E) in advanced renal cell carcinoma (RCC)"
Dr. Thomas Powles, Barts Cancer Institute, Cancer Research UK Experimental Cancer Medicine Centre, Queen Mary University of London, Royal Free NHS Trust, London, England
Session: Genitourinary Tumours, Non-Prostate
Poster presented Sunday, September 10, 1:15 – 2:15 p.m. CEST, Hall 8

[876P] "Efficacy of cabozantinib (C) after PD-1/PD-L1 checkpoint inhibitors in metastatic renal cell carcinoma (mRCC): the Gustave Roussy experience"
Dr. Lisa Derosa, Gustave Roussy Institute of Oncology, Villejuif, France
Session: Genitourinary Tumours, Non-Prostate
Poster presented Sunday, September 10, 1:15 – 2:15 p.m. CEST, Hall 8

[891P] "Outcomes of patients with metastatic renal cell carcinoma (mRCC) who were treated with second-line (2L) vascular endothelial growth factor receptor tyrosine kinase inhibitors (VEGFR-TKI) after first-line (1L) immune checkpoint inhibitor (ICI) therapy"

Dr. A.Y. Shah, Department of Genitourinary Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA
Session: Genitourinary Tumours, Non-Prostate
Poster presented Sunday, September 10, 1:15 – 2:15 p.m. CEST, Hall 8

[901P] "Safety and efficacy of cabozantinib for metastatic renal cell carcinoma (mRCC): real world data from an Italian Expanded Access Program (EAP)"
Dr. G. Procopio, Department of Medical Oncology, Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, Italy
Session: Genitourinary Tumours, Non-Prostate
Poster presented Sunday, September 10, 1:15 – 2:15 p.m. CEST, Hall 8

[912P] "Cabozantinib for the treatment of patients with metastatic variant histology renal cell carcinoma (vhRCC): a retrospective study"
Dr. M.T. Campbell, Department of Genitourinary Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA
Session: Genitourinary Tumours, Non-Prostate
Poster presented Sunday, September 10, 1:15 – 2:15 p.m. CEST, Hall 8

[927TiP] "Cabozantinib in patients with advanced penile squamous cell carcinoma (PSCC): the open-label, single-arm, single-center, phase 2, CaboPen trial"
Dr. A. Necchi, Experimental Oncology and Molecular Medicine, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy
Session: Genitourinary Tumours, Non-Prostate
Poster presented Sunday, September 10, 1:15 – 2:15 p.m. CEST, Hall 8

Cobimetinib to be featured in two presentations

Also at the congress, Exelixis' collaborator Genentech, a member of the Roche Group, will present data on cobimetinib, an Exelixis-discovered compound, in metastatic melanoma. The full schedule of cobimetinib presentations expected at the meeting is as follows:

Poster Discussion

[1225PD] "Prognostic impact of early complete metabolic response on FDG-PET, in BRAF V600 mutant metastatic melanoma patients treated with combination vemurafenib & cobimetinib"
Dr. Wen Xu, Peter MacCallum Cancer Centre, Melbourne, Australia
Session: Melanoma and Other Skin Tumours
Poster presented Monday, September 11, 11:00 a.m. – 12:15 p.m. CEST, Pamplona Auditorium

Poster Presentation

[1241P] "Impact of duration of response (DOR) on overall survival (OS) in patients with metastatic melanoma treated with dacarbazine (DTIC), vemurafenib (V), or cobimetinib plus vemurafenib (C+V): a pooled analysis"
Dr. Karl Lewis, University of Colorado Cancer Center, Aurora, Colorado, USA
Session: Melanoma and Other Skin Tumours
Poster presented Sunday, September 10, 1:15 – 2:15 p.m. CEST, Hall 8

About the CABOSUN Study

On May 23, 2016, Exelixis announced that CABOSUN met its primary endpoint, demonstrating a statistically significant and clinically meaningful improvement in PFS compared with sunitinib in patients with advanced intermediate- or poor-risk RCC as determined by investigator assessment. CABOSUN was conducted by The Alliance for Clinical Trials in Oncology as part of Exelixis' collaboration with the NCI-CTEP. These results were first presented by Dr. Toni Choueiri at the ESMO 2016 Congress, and published in the *Journal of Clinical Oncology* (Choueiri, *JCO*, 2016).[1] In June 2017, a blinded independent radiology review committee confirmed that cabozantinib provided a clinically meaningful and statistically significant improvement in the primary efficacy endpoint of investigator-assessed PFS.

CABOSUN was a randomized, open-label, active-controlled phase 2 trial that enrolled 157 patients with advanced RCC determined to be intermediate- or poor-risk by the IMDC criteria. Patients were randomized 1:1 to receive cabozantinib (60 mg once daily) or sunitinib (50 mg once daily, 4 weeks on followed by 2 weeks off). The primary endpoint was PFS. Secondary endpoints included overall survival and objective response rate. Eligible patients were required to have locally advanced or metastatic clear-cell RCC, ECOG performance status 0-2 and had to be intermediate or poor risk per the IMDC criteria (Heng, *JCO*, 2009).[2] Prior systemic treatment for RCC was not permitted.

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

About Genitourinary Cancers

Genitourinary cancers are those that affect the urinary tract, bladder, kidneys, ureter, prostate, testicles, penis or adrenal glands — parts of the body involved in reproduction and excretion — and include renal cell carcinoma (RCC) and urothelial carcinoma.[3]

The American Cancer Society's 2017 statistics cite kidney cancer as among the top ten most commonly diagnosed forms of cancer among both men and women in the U.S.[4] Clear cell RCC is the most common type of kidney cancer in adults.[5] 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.[6] Approximately 30,000 patients in the U.S. and 68,000 globally require treatment, and an estimated 14,000 patients in the U.S. each year are in need of a first-line treatment for advanced kidney cancer.[7]

Urothelial cancers encompass carcinomas of the bladder, ureter and renal pelvis at a ratio of 50:3:1, respectively.[8] Urothelial carcinoma occurs mainly in older people, with 90 percent of patients aged 55 or older.[9] Bladder cancer is the fourth most common cancer in men and accounts for about five percent of all new cases of cancer in the U.S. each year.[9] In 2013, an estimated 587,426 people were living with bladder cancer in the U.S.[10]

About CABOMETYX® (cabozantinib)

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

On April 25, 2016, the FDA approved CABOMETYX tablets for the treatment of patients with advanced RCC who have received prior anti-angiogenic therapy. In February of 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. This agreement was amended in December of 2016 to include commercialization rights for Ipsen in Canada. On September 9, 2016, the European Commission approved CABOMETYX tablets for the treatment of advanced RCC in adults who have received prior vascular endothelial growth factor (VEGF)-targeted therapy in the European Union, Norway and Iceland. Ipsen has confirmed its intent to submit the regulatory dossier for cabozantinib as a treatment for first-line advanced renal cell carcinoma in the European Union in the third quarter of 2017.

On January 30, 2017, Exelixis and Takeda Pharmaceutical Company Limited announced an exclusive licensing agreement for the commercialization and further clinical development of cabozantinib for all future indications in Japan, including RCC.

CABOMEYX is not indicated for the treatment of previously untreated advanced RCC.

U.S. 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 the Cobimetinib and Vemurafenib Combination

Cobimetinib is a reversible inhibitor that blocks the activity of MEK, a protein kinase that is part of a key pathway (the RAS-RAF-MEK-ERK pathway) that promotes cell division and survival. This pathway is frequently activated in human cancers including melanoma, where mutation of one of its components (BRAF) causes abnormal activation in about 50% of cases. Tumors with BRAF mutations may develop resistance and subsequently progress after treatment with a BRAF inhibitor. About 50% of patients with BRAF mutation positive melanoma experience a tumor response when treated with a BRAF inhibitor, however development of resistance and subsequent tumor progression limits treatment benefit. Clinical and preclinical analyses indicated that reactivation of the MEK-ERK pathway may underlie development of resistance to BRAF inhibitors in many progressing tumors, and that co-treatment with a BRAF and MEK inhibitor delays the emergence of resistance in the preclinical setting, providing the rationale for testing the combination of vemurafenib and cobimetinib in clinical trials. The U.S. Food & Drug Administration approved cobimetinib for the treatment of unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in combination with vemurafenib, in 2015. Cobimetinib is also being investigated in combination with several investigational and approved medicines, including an immunotherapy, in several tumor types, including non-small cell lung cancer, colorectal cancer, triple-negative breast cancer and melanoma.

About Exelixis

Exelixis, Inc. (Nasdaq: EXEL) is a biopharmaceutical company committed to the discovery, development and commercialization of new medicines to improve care and outcomes for people with cancer. Since its founding in 1994, three products discovered at Exelixis have progressed through clinical development, received regulatory approval, and entered the marketplace. Two are derived from cabozantinib, an inhibitor of multiple tyrosine kinases including VEGF, MET, AXL and RET receptors: CABOMETYX® tablets approved for previously treated advanced renal cell carcinoma and COMETRIQ® capsules approved for progressive, metastatic medullary thyroid cancer. The third product, COTELLIC®, is a formulation of cobimetinib, a reversible inhibitor of MEK, is marketed under a collaboration with Genentech (a member of the Roche Group), and is approved as part of a combination regimen to treat advanced melanoma. Both cabozantinib and cobimetinib have shown potential in a variety of forms of cancer and are the subjects of broad clinical development programs. 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: future data presentations from clinical trials of cabozantinib and cobimetinib at ESMO; Exelixis' commitment to advancing the company's ongoing clinical research program to help improve care and outcomes for patients with cancer; Ipsen's confirmation of its intent to submit the regulatory dossier for cabozantinib as a treatment for first-line advanced RCC in the European Union in the third quarter of 2017; and the therapeutic potential and continued development of both cabozantinib and cobimetinib. Words such as "will," "look forward," "commitment," "intent," "potential," 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 availability of data at the referenced times; Exelixis' ability to conduct clinical trials of cabozantinib sufficient to achieve a positive completion; risks related to the potential failure of cabozantinib or cobimetinib to demonstrate safety and efficacy in clinical testing; risks and uncertainties related to regulatory review and approval processes; Exelixis' dependence on its relationship with Ipsen, including, the level of Ipsen's investment in the resources necessary to successfully commercialize cabozantinib in the territories where it is approved; Exelixis' dependence on its relationship with Genentech with respect to the development of cobimetinib; Exelixis' dependence on third-party vendors; 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 May 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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