Exelixis Announces Positive Top-Line Results from METEOR, the Phase 3 Pivotal Trial of Cabozantinib versus Everolimus in Patients with Metastatic Renal Cell Carcinoma

July 20, 2015

- Study Met Primary Endpoint of Significantly Improving Progression-Free Survival -

- Cabozantinib Reduced the Risk of Disease Progression or Death by 42%; Hazard Ratio = 0.58, (p < 0.0001) Compared to Everolimus -

- Overall Survival Interim Analysis Showed a Trend Favoring Cabozantinib; Hazard Ratio = 0.67, (p = 0.005) Compared to Everolimus -

- Exelixis to Complete U.S. and EU Regulatory Filings in Early 2016 -

- Conference Call at 8:30 AM EDT / 5:30 AM PDT Today -

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jul. 20, 2015-- Exelixis, Inc. (NASDAQ:EXEL) today announced positive top-line results from the primary analysis of METEOR, the phase 3 pivotal trial comparing cabozantinib to everolimus in 658 patients with metastatic renal cell carcinoma (RCC) who have experienced disease progression following treatment with a VEGF receptor tyrosine kinase inhibitor (TKI).

The trial met its primary endpoint of demonstrating a statistically significant increase in progression-free survival (PFS) in the first 375 randomized patients as determined by an independent radiology committee (IRC). Cabozantinib reduced the risk of disease progression or death by 42 percent compared to the everolimus arm (hazard ratio [HR]=0.58, 95 percent CI 0.45-0.75, p<0.0001).

Data pertaining to overall survival (OS) in the entire study population of 658 patients, a secondary endpoint of the trial, were immature at the data cutoff. A prespecified interim analysis, triggered by the primary analysis for PFS, showed a trend in OS favoring cabozantinib (HR = 0.67, unadjusted 95 percent CI 0.51 - 0.89; p=0.005). At the time of the interim analysis, the pre-specified p-value of 0.0019 to achieve statistical significance was not reached. The trial will continue to the final analysis of OS anticipated in 2016.

METEOR's primary analysis included a review of serious adverse event (SAE) data. Based on this analysis, the frequency of SAEs of any Grade regardless of causality was approximately balanced between study arms. The rate of treatment discontinuation due to adverse events was low (10%) in both study arms.

Detailed results of the trial will be submitted for presentation at an upcoming medical conference.

In April 2015, cabozantinib received Fast Track designation by the U.S. Food and Drug Administration (FDA) for the potential treatment of advanced RCC patients who have received one prior therapy. Based on the outcome of METEOR, Exelixis plans to complete regulatory filings in the United States and European Union in early 2016.

"We are eager to offer new treatment options for patients with metastatic RCC, particularly in the second-line setting where the most commonly utilized therapies have demonstrated a uniformly modest progression-free survival benefit," said Toni K. Choueiri, M.D., clinical director of the Lank Center for Genitourinary Oncology at Dana-Farber Cancer Institute, and METEOR's principal investigator. "The magnitude of the improvement in PFS observed with cabozantinib compared to everolimus in the METEOR trial is an exciting and important development — it suggests an opportunity to improve care and outcomes for patients with metastatic RCC."

"The positive top-line results from METEOR represent strong progress for the kidney cancer community and for Exelixis, bringing us one step closer to our shared goal of delivering a new and meaningfully differentiated therapeutic option for the many metastatic RCC patients in need," said Michael M. Morrissey, Ph.D., the company's president and chief executive officer. "With these data now in hand, Exelixis' highest corporate priority becomes the submission of U.S. and EU regulatory filings, which we intend to complete in early 2016."

Dr. Morrissey continued, "Delivering these top-line results for METEOR is one of multiple clinical development and regulatory milestones that we have planned for this year. These milestones collectively have the potential to significantly enhance the opportunities before us and bring value to the multiple stakeholders we serve. We look forward to sharing the detailed results of METEOR with the oncology community at an upcoming medical conference, and we thank all of the patients, families, investigators, and clinical staff who made the trial possible."

Conference Call and Webcast

Exelixis' management will host a conference call to discuss the METEOR results beginning at 8:30 a.m. EDT/ 5:30 a.m. PDT today, July 20, 2015. To join the call, participants may dial 877-358-0169 (domestic) or 706-679-2029 (international) and provide the conference call passcode 90168151 to join by phone. To listen to a live webcast of the conference call, visit the Event Calendar page under Investors & Media at www.exelixis.com.

An archived replay of the webcast will be available on the Event Calendar page under Investors & Media at www.exelixis.com for at least thirty days. An audio-only phone replay will be available until 11:59 p.m. EDT on July 22, 2015. Access numbers for the phone replay are: 855-859-2056 (domestic) and 404-537-3406 (international); the passcode is 90168151.

About the METEOR Phase 3 Pivotal Trial

METEOR is an open-label, event-driven trial with the primary endpoint of progression-free survival (PFS). The target enrollment for METEOR was 650 patients, and 658 patients were ultimately randomized. 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 cabozantinib daily or 10 mg of everolimus daily, and were stratified based on the number of prior VEGF receptor TKI therapies received, and on commonly applied RCC risk criteria developed by Motzer *et al*. No cross-over was allowed between the study arms.

The trial protocol specified that the primary analysis of PFS would be conducted among the first 375 patients randomized. This design was employed to ensure sufficient follow up and a PFS profile that would not be primarily weighted toward early events. Such disproportionate weighting of events was a potential risk if the entire study population required for the secondary endpoint analysis of OS had also served as the population for the primary analysis of PFS. The analysis of PFS was event-driven, and was designed to observe 259 events, providing 90% power to detect a HR of 0.67 (assuming a median PFS of 5 months for the everolimus arm and 7.5 months for the cabozantinib arm). Enrollment of the first 375 patients was completed in June 2014 and the median follow-up for these patients was 13.4 months at the time of the data cut off for the primary analysis for PFS.

Secondary endpoints for METEOR include OS and objective response rate. The secondary endpoint of OS assumes a median of 15 months for the everolimus arm and 20 months for the cabozantinib arm. The study was designed to observe 408 deaths in the entire intent-to-treat population of 650 planned patients, providing 80% power to detect a HR of 0.75. An interim analysis of OS at the 2-sided 0.0019 level per the Lan-DeMets O'Brien-Fleming alpha-spending function was planned at the time of the primary analysis for PFS, if the trial met the primary PFS endpoint.

About Metastatic Renal Cell Carcinoma

The American Cancer Society's 2015 statistics cite kidney cancer as among the top ten most commonly diagnosed forms of cancer among both men and women in the United States.[1] Clear cell renal cell carcinoma 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; however, the five-year survival rate for patients with advanced or late-stage metastatic RCC is under 10 percent, with no identified cure for the disease.[3]

Treatments for metastatic RCC had historically been limited to cytokine therapy (e.g., interleukin-2 and interferon) until the introduction of targeted therapies into the RCC setting a decade ago. In the second and later-line setting, which encompasses approximately 17,000 drug-eligible patients in the U.S. and 37,000 globally,[4] two therapies have been approved for the treatment of patients who have received prior VEGF receptor TKIs. However, despite the availability of several therapeutic options, currently approved agents have shown little differentiation in terms of efficacy and have demonstrated only modest PFS benefit in patients refractory to sunitinib, a commonly-used first-line therapy.

The majority of clear cell RCC tumors exhibit down-regulation of von Hippel-Lindau (VHL) protein function, either due to gene inactivation or epigenetic silencing, resulting in a stabilization of the hypoxia-inducible transcription factors (HIFs) and consequent up-regulation of VEGF, MET, and AXL.[5] The up-regulation of VEGF may contribute to the angiogenic nature of clear cell RCC, and expression of MET or AXL may be associated with tumor cell viability, a more invasive tumor phenotype, and reduced overall survival. [6] Up-regulation of MET and AXL in clear cell RCC has also been shown to occur in response to treatment with VEGF receptor TKIs in preclinical models, indicating a potential role for MET and AXL in the development of resistance to these therapies.[7]

About Cabozantinib

Cabozantinib inhibits the activity of tyrosine kinases including MET, VEGF receptors, AXL, and RET. These receptor tyrosine kinases are involved in both normal cellular function and in pathologic processes such as oncogenesis, metastasis, tumor angiogenesis, and maintenance of the tumor microenvironment.

COMETRIQ® (cabozantinib) is currently approved by the U.S. Food and Drug Administration for the treatment of progressive, metastatic medullary thyroid cancer (MTC).

The European Commission granted COMETRIQ conditional approval for the treatment of adult patients with progressive, unresectable locally advanced or metastatic MTC. Similar to another drug approved in this setting, the approved indication states that for patients in whom Rearranged during Transfection (RET) mutation status is not known or is negative, a possible lower benefit should be taken into account before individual treatment decisions.

Important Safety Information, including Boxed WARNINGS

WARNING: PERFORATIONS AND FISTULAS, and HEMORRHAGE

- **Serious and sometimes fatal gastrointestinal perforations and fistulas occur in COMETRIQ-treated patients.**
- **Severe and sometimes fatal hemorrhage occurs in COMETRIQ-treated patients.**
- COMETRIQ treatment results in an increase in thrombotic events, such as heart attacks.
- Wound complications have been reported with COMETRIQ.
- COMETRIQ treatment results in an increase in hypertension.
- Osteonecrosis of the jaw has been observed in COMETRIQ-treated patients.
- Palmar-Plantar Erythrodysesthesia Syndrome (PPES) occurs in patients treated with COMETRIQ.
- The kidneys can be adversely affected by COMETRIQ. Proteinuria and nephrotic syndrome have been reported in patients receiving COMETRIQ.
- Reversible Posterior Leukoencephalopathy Syndrome has been observed with COMETRIQ.
- Avoid administration of COMETRIQ with agents that are strong CYP3A4 inducers or inhibitors.
- COMETRIQ is not recommended for use in patients with moderate or severe hepatic impairment.
- COMETRIQ can cause fetal harm when administered to a pregnant woman.

Adverse Reactions – The most commonly reported adverse drug reactions (≥25%) are diarrhea, stomatitis, palmar-plantar erythrodysesthesia syndrome (PPES), decreased weight, decreased appetite, nausea, fatigue, oral pain, hair color changes, dysgeusia, hypertension, abdominal pain, and constipation. The most common laboratory abnormalities (≥25%) are increased AST, increased ALT, lymphopenia, increased alkaline phosphatase, hypocalcemia, neutropenia, thrombocytopenia, hypophosphatemia, and hyperbilirubinemia.

Please see full U.S. prescribing information, including Boxed WARNINGS, at www.COMETRIQ.com/downloads/Cometriq_Full_Prescribing_Information.pdf

Please refer to the full European Summary of Product Characteristics for full European Union prescribing information, including contraindication, special warnings and precautions for use at www.sobi.com once posted.

About Exelixis

Exelixis, Inc. is a biopharmaceutical company committed to developing small molecule therapies for the treatment of cancer. Exelixis is focusing its development and commercialization efforts primarily on COMETRIQ® (cabozantinib), its wholly-owned inhibitor of multiple receptor tyrosine kinases. Another Exelixis-discovered compound, cobimetinib, a selective inhibitor of MEK, is being evaluated by Roche and Genentech (a member of the Roche Group) in a broad development program under a collaboration with Exelixis. For more information, please visit the company's web site at www.exelixis.com.

Forward-Looking Statement Disclaimer

The statements in this press release that Exelixis plans to complete U.S. and EU regulatory filings in early 2016, that the trial will continue to the final analysis of OS which is anticipated in early 2016, that detailed results of the trial will be submitted for presentation at an upcoming medical conference, that the results of the trial suggest an opportunity to improve care and outcomes for patients with metastatic RCC, regarding the potential that delivering upon top-line results for METEOR and other planned clinical development and regulatory milestones for this year will significantly enhance the opportunities before Exelixis and bring value to the multiple stakeholders Exelixis serves, are forward-looking statements that are subject to risk and uncertainty. 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 clinical, therapeutic and commercial value of cabozantinib; the availability of data at the expected times; risks related to the potential failure of cabozantinib to demonstrate safety and efficacy in clinical study; Exelixis' ability to conduct clinical trials of cabozantinib sufficient to achieve a positive completion; risks and uncertainties related to regulatory review and approval processes and Exelixis' compliance with applicable legal and regulatory requirements; the general sufficiency of Exelixis' capital and other resources; the uncertain timing and level of expenses associated with the development of cabozantinib; 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 April 30, 2015, 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.

Exelixis, the Exelixis logo, and COMETRIQ are registered U.S. trademarks.

[1] *Cancer Facts & Figures 2015. American Cancer Society. Available at*

http://www.cancer.org/acs/groups/content/@editorial/documents/document/acspc-044552.pdf

[2] *Jonasch et al., BMJ (2014) vol. 349, g4797.*

[3] *http://www.cancer.org/cancer/kidneycancer/detailedguide/kidney-cancer-adult-survival-rates*

[4] *ACS Cancer Facts and Figures 2015; Heng et al., Ann Oncol (2012) vol. 23 no. 6; internal data on file; Motzer et al., N Engl J Med (2007) vol. 356 no. 2; NCIN (UK) report, April 2014, Available at http://www.ncin.org.uk/view?rid=2676.*

[5] *Harschman and Choueiri, Cancer J. 2013 v19 316-323; Rankin et al., PNAS, 2014.*

[6] *Bommy-Reddi et al., PNAS, 2008; Gibney et al., Ann. Oncol. 2013 v24 343-349; Koochekpour et al., Mol. Cell. Biol. 1999, v19 5902-5912; Rankin et al., PNAS, 2014.*

[7] *Ciamporcero et al., MolCancerTher, 2014; Rankin et al., PNAS, 2014.*

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