Exelixis Announces Positive Results from METEOR Phase 3 Pivotal Trial of Cabozantinib in Advanced Renal Cell Carcinoma Presented at European Cancer Congress 2015

September 25, 2015

– Cabozantinib met the primary endpoint of improving progression-free survival as compared to everolimus –

– Cabozantinib showed a strong trend towards improving overall survival as compared to everolimus at an interim analysis –

– Results will be presented during ECC 2015 Presidential Session I and have been published in The New England Journal of Medicine –

– U.S. and EU regulatory filings anticipated by end of 2015 and early 2016, respectively –

– Exelixis to host investor/analyst webcast from Vienna to discuss the data on Sat., Sept. 26 –

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Sep. 25, 2015-- Exelixis, Inc. (NASDAQ:EXEL) today announced positive results from METEOR, the phase 3 pivotal trial comparing cabozantinib to everolimus in 658 patients with renal cell carcinoma (RCC) who have experienced disease progression following treatment with a VEGF receptor tyrosine kinase inhibitor (TKI). In July 2015, Exelixis disclosed that the trial met its primary endpoint, demonstrating a statistically significant increase in progression-free survival for patients in the cabozantinib arm. Principal investigator Toni K. Choueiri, M.D. will present detailed data from the late-breaking METEOR abstract (#4-LBA) on Saturday, September 26, during the Presidential Session I at the European Cancer Congress (ECC) 2015, which is being held September 25-29 in Vienna. The METEOR data and an accompanying editorial were also published today in *The New England Journal of Medicine.*

As announced in July, the METEOR trial met its primary endpoint of demonstrating a statistically significant increase in progression-free survival (PFS) for cabozantinib as compared to everolimus, as determined by an independent radiology committee. Per the trial protocol, the primary analysis was conducted among the first 375 patients randomized to ensure sufficient follow up and a PFS profile that would not be primarily weighted toward early events. The median PFS was 7.4 months for the cabozantinib arm versus 3.8 months for the everolimus arm, corresponding to a 42% reduction in the rate of disease progression or death for cabozantinib as compared to the everolimus arm (hazard ratio [HR]=0.58, 95% confidence interval [CI] 0.45-0.75, p<0.001). Cabozantinib effects were favorable across patient stratification subgroups including the number of prior VEGF receptor TKI therapies and commonly applied RCC risk criteria developed by Motzer *et al*.

In a post-hoc subset analysis of patients who had received sunitinib, the most commonly used first-line therapy, as their only prior VEGF receptor TKI, the median PFS for cabozantinib-treated patients (n=76) was 9.1 months versus 3.7 months for everolimus-treated patients (n=77). This corresponds to a 59% reduction in the rate of disease progression or death for patients treated with cabozantinib (HR=0.41, 95% CI 0.28-0.61).

“In the METEOR trial, cabozantinib significantly improved progression-free survival as compared to everolimus, a commonly-used standard of care, in both the full study population for the primary endpoint analysis as well as in the subgroup of patients previously treated with sunitinib only. Cabozantinib was also associated with a safety profile similar to other VEGF receptor TKIs used to treat renal cell carcinoma,” 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. “Uniquely, treatment with cabozantinib resulted in a strong trend towards improving overall survival, which is unprecedented as compared with other studies to date evaluating TKIs. The totality of the data support cabozantinib as a potential new treatment option for RCC patients whose disease has progressed following VEGF receptor-targeting therapy.”

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. As previously announced, a pre-specified interim analysis triggered by the primary analysis for PFS showed a strong trend in OS favoring cabozantinib (HR=0.67, 95% CI 0.51-0.89, p=0.005) At the time of the interim analysis, the p-value of 0.0019 to achieve statistical significance was not reached, and the trial will continue to the final analysis of OS anticipated in 2016. Objective response rate, another secondary endpoint, was significantly higher with cabozantinib (21%) as compared with everolimus (5%; p < 0.001). Treatment discontinuations for adverse events unrelated to progressive disease were 9% and 10% for cabozantinib and everolimus, respectively.

“These results from the METEOR trial suggest that cabozantinib has the potential to become a new and differentiated treatment option for patients with renal cell carcinoma who have progressed following VEGF receptor tyrosine kinase therapy, the most commonly-utilized treatment in the first-line setting,” said Michael M. Morrissey, Ph.D., Exelixis’ president and chief executive officer. “Exelixis is working quickly to share the data with regulators in the United States and European Union. We are on track to complete our U.S. NDA filing by the end of this year, where cabozantinib has received Breakthrough Therapy Designation, and expect a European filing to follow in early 2016. We look forward to advancing these regulatory processes in hopes of bringing cabozantinib to the renal cell carcinoma community as soon as possible.”

653 patients were evaluable for safety. Median duration of exposure was 7.6 months for cabozantinib and 4.4 months for everolimus. Investigators employed dose reductions to manage adverse events (AE), and 60% of patients on the cabozantinib arm and 25% of patients on the everolimus arm had dose reductions. The median average daily dose was 44 mg for cabozantinib and 9 mg for everolimus. The incidence of adverse events (any grade), regardless of causality, was 100% with cabozantinib and more than 99% with everolimus. Serious adverse events occurred in 40% of cabozantinib patients and 43% of everolimus patients. The most common AEs regardless of causality, grade 3 or higher, for cabozantinib were: hypertension (15%), diarrhea (11%), fatigue (9%), and hand-foot syndrome (8%). The most common AEs regardless of causality, grade 3 or higher, for

everolimus were: anemia (16%), fatigue (7%), hyperglycemia (5%), and dyspnea (4%). Grade 5 adverse events occurred in 6.6% of patients in the cabozantinib arm and in 7.8% of patients in the everolimus arm, and were primarily related to disease progression. Treatment-related grade 5 events occurred in one patient (0.3%; death not otherwise specified) in the cabozantinib arm and 2 patients (0.6%; aspergillus infection and aspiration pneumonia) in the everolimus arm.

Cabozantinib is currently marketed in capsule form under the brand name COMETRIQ® in the United States for the treatment of progressive, metastatic medullary thyroid cancer (MTC), and in the European Union for the treatment of adult patients with progressive, unresectable locally advanced or metastatic MTC. COMETRIQ is not indicated for patients with advanced RCC or any other form of the disease. In the METEOR trial, and all other cancer trials currently underway, Exelixis is investigating a tablet formulation of cabozantinib distinct from the COMETRIQ capsule form.

Webcast for the Investment Community

Exelixis will host a live webcast on Saturday, September 26, 2015, following the METEOR presentation at ECC 2015. The webcast will begin at 12:30 p.m. EDT / 9:30 a.m. PDT (18:30 local Vienna time). During the webcast, Exelixis management and Dr. Toni Choueiri, principal investigator of the METEOR trial, will review and provide context for the data presented at the Congress.

To access the webcast link, log onto www.exelixis.com and proceed to the Event Calendar page under Investors & Media. Please connect to the company's website at least 15 minutes prior to the webcast to ensure adequate time for any software download that may be required to listen to the webcast. Alternatively, you may access the webcast at this address: http://edge.media-server.com/m/p/c7qgq2ma/lan/en.

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 September 28, 2015. Access numbers for the phone replay are: (855) 859-2056 (domestic) and (404) 537-3406 (international); the passcode is 47549145.

About Advanced 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 advanced 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, 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 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 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 capsules) 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 cabozantinib, its wholly-owned inhibitor of multiple receptor tyrosine kinases. Another Exelixis-discovered compound, cobimetinib, a selective inhibitor of MEK, received its first regulatory approval in Switzerland and 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 Statements

This press release contains forward-looking statements that are subject to risk and uncertainty, including, without limitation, cabozantinib's potential as a new and differentiated treatment option for RCC patients whose disease has progressed following VEGF receptor-targeting therapy; that the METEOR trial will continue to the final analysis of OS in 2016; and that Exelixis will complete our U.S. NDA filing by the end of 2015 and our EU filing in early 2016. Words such as "will," "potential", "suggest", "expect", "look forward," "hope", and "as soon as possible" 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, and projections. Actual results and the timing of events could differ materially from those anticipated in the forward-looking statements, which include, without limitation: risks related to the clinical, therapeutic and commercial potential of cabozantinib; risks related to 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; risks related to 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 August 11, 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.*

View source version on businesswire.com: http://www.businesswire.com/news/home/20150925005838/en/

Source: Exelixis, Inc.

Investor Contact:
Exelixis, Inc.
Susan Hubbard, 650-837-8194
Investor Relations and
Corporate Communications
shubbard@exelixis.com
or
Media Contact:

For Exelixis, Inc.
Hal Mackins, 415-994-0040
hal@torchcommunications.com