Exelixis Announces Positive Results From Subgroup Analyses of the METEOR Phase 3 Pivotal Trial of Cabozantinib in Advanced Renal Cell Carcinoma to be Presented at ASCO 2016 Genitourinary Cancers Symposium

January 4, 2016

-- Data further underscore clinical benefit of cabozantinib across subgroups of patients with advanced renal cell carcinoma --

-- METEOR data are the foundation for the U.S. NDA filing submitted last month, EU filing planned for early 2016 --

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jan. 4, 2016-- Exelixis, Inc. (NASDAQ:EXEL) today announced the presentation of positive data from subgroup analyses of 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). Cabozantinib treatment resulted in benefits in progression-free survival (PFS), the trial's primary endpoint, and objective response rate (ORR), a secondary endpoint, across various prespecified and post-hoc analysis subgroups. Importantly, observed benefits were independent of the location and number of organ metastases, tumor burden, the type, duration and number of prior VEGF receptor TKI therapies, and prior PD-1/PD-L1 therapy.

Bernard Escudier, M.D., chair of the Genitourinary Oncology Committee at the Institut Gustave Roussy (Villejuif, France) and an investigator on the METEOR trial, summarized the results during a press briefing in advance of the American Society of Clinical Oncology 2016 Genitourinary Cancers Symposium (ASCO GU), which is being held January 7-9, 2016 in San Francisco. Dr. Escudier will formally present the data (Abstract #499) at ASCO GU during an oral presentation session starting at 2:45 p.m. PT on Saturday, January 9, 2016.

"In the METEOR trial, cabozantinib was previously associated with statistically significant improvements in progression-free survival and objective response rate as compared to everolimus, a standard of care in the second-line renal cell carcinoma treatment setting," said Dr. Escudier. "This latest data set demonstrates that these benefits are favorable across a variety of prespecified and post-hoc subgroups, including patients who have received prior therapy with immune checkpoint inhibitors. In addition, cabozantinib was active in patients with low and high tumor burden, including patients with both bone and visceral metastases. Collectively, the data from METEOR suggest that cabozantinib could become an important addition to the renal cell carcinoma treatment landscape if approved."

As previously announced, the METEOR trial met its primary endpoint of demonstrating a statistically significant increase in 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 for this population 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 everolimus (hazard ratio [HR]=0.58, 95% confidence interval [CI] 0.45-0.75, p<0.001). These data were later presented at the European Cancer Congress (ECC) in September 2015 and concurrently published in *The New England Journal of Medicine*.

The ASCO GU presentation will be the first to include PFS data from the METEOR trial's entire 658-patient study population. As assessed by independent radiology committee, the median PFS across all enrolled patients was 7.4 months for the cabozantinib arm versus 3.9 months for the everolimus arm, corresponding to a 48% reduction in the rate of disease progression or death for cabozantinib as compared to everolimus (HR = 0.52, 95% CI 0.43-0.64, p<0.001).

Updated ORR results from the full 658-patient study population will also be presented at ASCO GU for the first time. As assessed by independent radiology committee, the ORR across all 658 patients was 17% for cabozantinib and 3% for everolimus. The median duration of response for cabozantinib was not reached (95% CI 7.2 months; not reached), as compared to 7.4 months (95% CI 1.9 months; not reached) for everolimus. As previously reported at the ECC in September 2015, the ORR for the first 375 patients enrolled was 21% for cabozantinib and 5% for everolimus.

Cabozantinib's effects on PFS and ORR were favorable across patient subgroups including: ECOG performance status; commonly applied RCC risk criteria developed by Motzer et al.; organ involvement, including bone and overall tumor burden; extent and type of prior VEGF receptor TKI therapy; and prior PD-1/PD-L1 therapy. For patients without prior PD-1/PD-L1 therapy, median PFS was 7.4 months for cabozantinib and 3.9 months for everolimus (HR = 0.54, 95% CI 0.44-0.66). For patients who had received prior PD-1/PD-L1 therapy, the median PFS for cabozantinib was not reached, and the median PFS for everolimus was 4.1 months (HR = 0.22, 95% CI 0.07-0.65).

"These new METEOR subgroup analyses further underscore the potential for cabozantinib to significantly impact the treatment of renal cell carcinoma, an aggressive cancer for which patients and physicians need new options," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "These data were included in our New Drug Application with the U.S. Food and Drug Administration, filed last month, and we intend to include them in our upcoming European Union Marketing Authorization Application, which we expect to submit shortly. Additionally, in 2016 we await the final analysis for METEOR's overall survival secondary endpoint."

As previously reported, 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 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.

Safety data from the trial were consistent with what was previously presented and published.

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 RCC. 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. The tablet formulation of cabozantinib is the subject of Exelixis' New Drug Application with the U.S. Food and Drug Administration for advanced RCC.

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 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; 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]

Until the introduction of targeted therapies into the RCC setting a decade ago, treatments for metastatic RCC had historically been limited to cytokine therapy (e.g., interleukin-2 and interferon). In the second and later-line settings, which encompass approximately 17,000 drug-eligible patients in the U.S. and 37,000 globally,[4] two small-molecule therapies and an immune checkpoint inhibitor have been approved for the treatment of patients with advanced RCC who have received prior systemic therapy. The currently approved small-molecule agents have shown little differentiation in terms of efficacy and have demonstrated only modest progression-free survival 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.

Cabozantinib, marketed under the brand name COMETRIQ®, 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, COTELLIC™ (cobimetinib), a selective inhibitor of MEK, has been approved in Switzerland, the United States, and the European Union, 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 website at www.exelixis.com.

Forward-Looking Statement Disclaimer

This press release contains forward-looking statements, including, without limitation, statements related to: a future data presentation from subgroup analyses of METEOR, including PFS data and ORR results from the full 658-patient study population; the potential impact of cabozantinib on the renal cell carcinoma treatment landscape, if approved; Exelixis' intention to include results from the subgroup analysis of METEOR in its upcoming European Union Marketing Authorization Application, which it expects to submit shortly; and that the METEOR trial will continue to the final analysis of OS which is anticipated in 2016. Words such as "planned," "will," "could," "potential," "intend," "expect," "continue" "anticipated," 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: availability of clinical trial data at the referenced times; the clinical, therapeutic and commercial potential of cabozantinib; 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; 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 10, 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.

[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.*

View source version on businesswire.com: http://www.businesswire.com/news/home/20160104006510/en/

Source: Exelixis, Inc.

Investors 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