Exelixis Announces Positive Results from Phase 3 Pivotal Trial of Cobimetinib in Combination with Vemurafenib in Patients with BRAF V600 Mutation-Positive Advanced Melanoma

September 29, 2014

- Combination reduced the risk of disease worsening by half compared to Vemurafenib alone -

- CoBRIM results will be presented today during the Presidential Symposium at the European Society for Medical Oncology (ESMO) and published in the New England Journal of Medicine -

- Partner Roche has submitted EU Marketing Authorization Application;
U.S. filing anticipated later this year -

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Sep. 29, 2014-- Exelixis Inc. (NASDAQ:EXEL) today announced the positive results from coBRIM, the phase 3 pivotal trial conducted by Exelixis' collaborator Genentech, a member of the Roche Group, evaluating cobimetinib, a specific MEK inhibitor discovered by Exelixis, in combination with vemurafenib in previously untreated patients with unresectable locally advanced or metastatic melanoma harboring a BRAF V600 mutation.

The trial met its primary endpoint of demonstrating a statistically significant increase in investigator-determined progression-free survival (PFS). The median PFS was 9.9 months for the combination of cobimetinib and vemurafenib versus 6.2 months for vemurafenib alone (hazard ratio [HR]=0.51, 95 percent CI 0.39-0.68; p<0.0001), demonstrating the combination reduced the risk of the disease worsening by half (49 percent). The median PFS by independent review committee (IRC), a secondary endpoint, was 11.3 months for the combination arm compared to 6.0 months for the control arm (HR=0.60, 95 percent CI 0.45-0.79; p=0.0003). Objective response rate (ORR), another secondary endpoint, was 68% for the combination versus 45% for vemurafenib alone (p<0.0001). Overall survival data are not yet mature (HR=0.65, 95 percent CI 0.42-1.00; p=0.046), and at the interim analysis the p-value did not cross the prespecified boundary for significance. The safety profile of the combination was consistent with that observed in a previous study.

The coBRIM data will be presented at ESMO 2014 today, Monday, September 29, during the Presidential Symposium by Professor Grant McArthur, Peter MacCallum Cancer Centre, Australia (Abstract #LBA5_PR, Monday, September 29, 2014, 4:00-5:20 p.m. CEST) and are also part of the official press program. Additionally, the study was published online today in the *New England Journal of Medicine.*

Roche has submitted a Marketing Authorization Application (MAA) to the European Medicines Agency, and Genentech plans to submit a New Drug Application (NDA) to the U.S. Food and Drug Administration later this year.

"Today's presentation of data from the coBRIM trial underscore the potential for the combination of cobimetinib, an Exelixis-discovered compound, and vemurafenib to provide significant clinical benefit for patients with previously untreated BRAF V600 mutation-positive advanced melanoma," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "Our partner Genentech sponsored a rigorous and well-run trial, and the results, including a significant increase in PFS and a high objective response rate, are compelling. The regulatory filing process is underway with the submission of the EU filing of the MAA. We look forward to the U.S. filing later this year and then ultimately, if approved, to supporting cobimetinib's commercialization through our longstanding collaboration that includes a co-promotion component in the United States."

About the coBRIM study

The coBRIM trial is an international, randomized, double-blind, placebo-controlled Phase III study evaluating the safety and efficacy of 60 mg once daily of cobimetinib in combination with 960 mg twice daily of vemurafenib, compared to 960 mg twice daily of vemurafenib alone. In the study, 495 patients with BRAF V600 mutation-positive unresectable locally advanced or metastatic melanoma (detected by the cobas® 4800 BRAF Mutation Test) and previously untreated for advanced disease, were randomized to receive vemurafenib every day on a 28-day cycle plus either cobimetinib or placebo for days 1-21. Treatment was continued until disease progression, unacceptable toxicity or withdrawal of consent. Median follow up was 7.4 months for the combination arm and 7.2 months for the control arm.

There was a higher overall frequency of Grade 3 or higher adverse events in the combination arm (65 vs. 59 percent), with close to half of these due to lab abnormalities. Common adverse events of any grade that occurred in more than 20 percent of patients and were observed at a higher frequency in the combination arm compared to the vemurafenib arm included diarrhea (57 vs. 28 percent), nausea (39 vs. 24 percent), photosensitivity (28 vs. 16 percent), lab abnormalities (increased alanine aminotransferase [24 vs. 18 percent], increased aspartate aminotransferase [22 vs. 13 percent], increased creatine phosphokinase [an enzyme released by muscles, 30 vs. 3 percent]), and vomiting (21 vs. 12 percent). Common adverse events observed at a lower frequency in the combination arm included hair loss (14 vs. 29 percent), thickening of the outer layer of the skin (10 vs. 29 percent), and joint pain (33 vs. 40 percent). Most instances of each common adverse event were grade 1 or 2 in severity.

Other select adverse events that were lower in the combination arm included cutaneous squamous cell carcinomas (3 vs. 11 percent; all grades) and keratoacanthomas (<1 vs. 8 percent; all grades). Serous retinopathy (collection of fluid under the retina) was observed at a higher frequency in the combination arm (20 vs. <1 percent) with most of these events either Grade 1 or 2 and temporary in nature. Specific adverse events leading to withdrawal from treatment were similar in both study arms, as was the overall discontinuation rate from treatment (13 vs. 12 percent).

About the Cobimetinib Development Collaboration

Exelixis discovered cobimetinib internally and advanced the compound to investigational new drug (IND) status. In late 2006, Exelixis entered into a worldwide co-development agreement with Genentech, under which Exelixis received initial upfront and milestone payments for signing the agreement and submitting the IND. Exelixis was responsible for development of cobimetinib through the determination of the maximum tolerated dose in phase 1, at which point Genentech exercised its option to further develop the compound.

In November 2013, Exelixis exercised its option to co-promote cobimetinib, if approved, in the United States. Exelixis is entitled to an initial equal share of U.S. profits and losses, which will decrease as sales increase, and will share equally in the U.S. marketing and commercialization costs. Exelixis is eligible to receive royalties on any sales of the product outside the United States.

About the Cobimetinib and Vemurafenib Combination

Cobimetinib is a selective 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 tumors. Tumors with BRAF mutations may develop resistance and subsequently progress after treatment with a BRAF inhibitor. In preclinical melanoma models, co-treatment with vemurafenib and the MEK inhibitor cobimetinib may delay the emergence of resistant tumors. In addition to the combination with vemurafenib in melanoma, cobimetinib is also being investigated in combination with several investigational medicines, including an immunotherapy, in several tumor types, including non-small cell lung cancer and colorectal cancer.

About Melanoma and its BRAF V600 Mutation-Positive Form

Melanoma is the less common, but more serious category of skin cancer that starts in the skin’s pigment producing cells known as melanocytes. According to the American Cancer Society, approximately five percent of skin cancer diagnoses are melanoma, but melanoma accounts for a large majority of skin cancer deaths. Cases of melanoma have been increasing for at least 30 years, and in 2014 it is estimated that in the United States more than 76,100 people will be diagnosed with melanoma and more than 9,700 people will die from the disease. It is thought that approximately half of all melanomas, and eight percent of solid tumors, contain a mutation of the BRAF protein. BRAF is a key component of the RAS-RAF-MEK-ERK pathway involved in normal cell growth and survival. However, mutations that keep the BRAF protein in an active state may cause excessive signaling in the pathway, leading to uncontrolled cell growth and survival. The BRAF V600 mutation-positive form of melanoma is associated with high-risk characteristics of the disease, including early onset, the absence of chronic skin damage, and decreased survival.

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 highly 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 Statements

This press release contains forward-looking statements, including, without limitation, statements related to: the continued development and clinical, therapeutic and commercial potential of cobimetinib in combination with vemurafenib and other investigational medicines; coBRIM data presentations; future regulatory filings and potential approvals; Exelixis’ future U.S. co-promotion efforts with Genentech; the plan of Genentech and Exelixis to share U.S. profits and losses for cobimetinib and U.S. marketing and commercialization costs for cobimetinib; and Exelixis' potential receipt of royalties on sales of cobimetinib products outside the United States. Words such as “will,” “anticipated,” “plans,” “underscore,” “potential,” “compelling,” “underway,” “look forward,” “entitled,” “share,” “estimated,” “eligible,” 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. Exelixis' 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: risks related to the potential failure of cobimetinib or cabozantinib to demonstrate safety and efficacy in clinical testing; the availability of data at the expected times; the clinical, therapeutic and commercial value of cobimetinib and cabozantinib; Exelixis' dependence on its relationship with Genentech/Roche with respect to cobimetinib and Exelixis’ ability to maintain its rights under the collaboration; 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 and the specific risk of unforeseen expenses that could diminish Exelixis’ financial ability to support its operations through the release of top-line results from METEOR, Exelixis’ phase 3 pivotal trial of cabozantinib in metastatic renal cell cancer; the uncertain timing and level of expenses associated with the development of cabozantinib; risks related to Exelixis’ ability to implement its previously announced workforce reduction according to plan and its impact on Exelixis’ business; charges, expenses and cash expenditures resulting from the referenced workforce reduction; 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 July 31, 2014 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.

Source: Exelixis, Inc.

Exelixis, Inc.
Susan Hubbard, 650-837-8194

Investor Relations and
Corporate Communications
shubbard@exelixis.com