Exelixis Announces European Commission Approval of COTELLIC™ (Cobimetinib) for Use in Combination with Vemurafenib in Advanced BRAF V600 Mutation-Positive Melanoma

November 25, 2015

-- COTELLIC's third regulatory approval, following Switzerland (August 2015) and the United States (November 2015) --

-- Exelixis eligible to receive royalties on ex-U.S. sales, including EU, per worldwide collaboration agreement with Roche and Genentech --

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Nov. 25, 2015-- Exelixis, Inc. (NASDAQ:EXEL) today announced that the European Commission (EC) has approved COTELLIC™ (cobimetinib) for use in combination with vemurafenib for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation. COTELLIC was discovered by Exelixis and is now the subject of a collaboration between Exelixis and Genentech, a member of the Roche Group. Roche sponsored COTELLIC's EU Marketing Authorization Application, which received a positive opinion from the European Medicines Agency's Committee for Medicinal Products for Human Use in September 2015.

"The approval of COTELLIC by the European Commission for use in combination with vemurafenib is an important milestone in the development of new treatments that can help patients with advanced melanoma," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "We look forward to continuing to execute on our collaboration agreement for COTELLIC."

The approval in the EU is based primarily on results of the phase 3 coBRIM study, which showed that people with previously untreated BRAF V600 mutation-positive advanced melanoma who were being treated with the MEK inhibitor COTELLIC in combination with vemurafenib lived a median of one year (12.3 months) without their disease worsening or death (progression-free survival; PFS) compared to 7.2 months with vemurafenib alone (hazard ratio [HR]=0.58, 95 percent confidence interval [CI] 0.46-0.72).[1]

The objective response rate with the combination was 70 percent (16 percent complete response [CR], 54 percent partial response [PR]) compared to 50 percent (11 percent CR, 40 percent PR) in the vemurafenib arm.[1] Possible serious side effects with COTELLIC include risk of skin cancers, increased risk of bleeding, heart problems that can lead to inadequate pumping of the blood by the heart, rash, eye problems, abnormal liver test or liver injury, increased levels of an enzyme in the blood, and photosensitivity. The most common side effects of COTELLIC include diarrhea, sunburn or sun sensitivity, nausea, fever and vomiting. COTELLIC can also cause changes in blood test results.

Additional data were presented in November 2015 at the Society for Melanoma Research congress demonstrating that the combination of COTELLIC plus vemurafenib met its secondary endpoint of improving OS compared to vemurafenib alone. Roche and Genentech have guided that these data will be submitted to the European Medicines Agency for consideration and inclusion in the label.

After discovering COTELLIC internally, Exelixis advanced the product to investigational new drug (IND) status. In late 2006, the company entered into its worldwide collaboration with Genentech, under which Exelixis received initial upfront and milestone payments for signing the agreement and submitting the IND. Following the determination of the maximum tolerated dose in phase 1 by Exelixis, Genentech exercised its option to further develop COTELLIC. Under the collaboration agreement, Exelixis is eligible to receive low double-digit royalties on sales of COTELLIC outside the United States. 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 in U.S. marketing and commercialization costs. In November 2013, Exelixis exercised its option to co-promote COTELLIC in the United States and will field 25 percent of the U.S. sales force.

COTELLIC in combination with vemurafenib is now approved in the EU and Switzerland for the treatment of people with BRAF V600 mutation-positive advanced melanoma. The combination is approved in the United States for the treatment of patients with BRAF V600E or V600K mutation-positive unresectable or metastatic melanoma. Further country approvals are anticipated in 2016.

About COTELLIC™ in Combination with Vemurafenib

COTELLIC and vemurafenib are prescription medicines used in combination to treat melanoma that has spread to other parts of the body or cannot be removed by surgery, and that has a certain type of abnormal "BRAF" gene. Found in approximately half of melanomas, mutated BRAF causes abnormal signaling inside cancer cells leading to tumor growth. Vemurafenib is designed to inhibit some mutated forms of BRAF and COTELLIC is designed to inhibit some forms of MEK. Both BRAF and MEK are proteins in a cell signaling pathway that help control cell growth and survival. When used in combination, COTELLIC and vemurafenib are thought to reduce cancer cell growth longer than with vemurafenib alone. A patient's healthcare provider will perform a test to make sure COTELLIC and vemurafenib are right for the patient. It is not known if COTELLIC and vemurafenib are safe and effective in children under 18 years of age.

About the coBRIM Trial

coBRIM is an international, randomized, double-blind, placebo-controlled phase 3 study evaluating the safety and efficacy of 60 mg once daily of cobimetinib plus 960 mg twice daily of vemurafenib compared to 960 mg twice daily of vemurafenib plus placebo. 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 on days 1-21.

Treatment was continued until disease progression, unacceptable toxicity or withdrawal of consent. Investigator-assessed PFS is the primary endpoint. Secondary endpoints include PFS by independent review committee, objective response rate, overall survival, duration of response and other safety, pharmacokinetic and quality of life measures.

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. In recent years, there have been significant advances in treatment for metastatic melanoma and people with the disease have more options. However, it continues to be a serious health issue with a high unmet need and a steadily increasing incidence over the past 30 years. It is projected 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.

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. Positive results were recently announced for a phase 3 pivotal trial of cabozantinib in patients with advanced renal cell carcinoma who received at least one prior VEGF receptor tyrosine kinase inhibitor, and Exelixis expects to complete regulatory filings in the U.S. and European Union in late 2015 and early 2016, respectively. 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 Statements

This press release contains forward-looking statements, including, without limitation, statements related to: Exelixis' and Roche's continued execution on goals of the parties' collaboration agreement; the potential for cobimetinib to advance melanoma treatment; the plan of Genentech and Exelixis to share U.S. profits and losses and U.S. sales and marketing costs for cobimetinib; Exelixis' potential receipt of royalties on sales of cobimetinib products outside the U.S.; and, Exelixis' preparedness to support U.S. co-promotion efforts for cobimetinib in the U.S. Words such as "can," "look forward," "will," "entitled," "eligible," "prepared," and 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, 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. Exelixis' actual results and the timing of events could differ materially from those anticipated in the forward-looking statements as a result of risks and uncertainties, which include, without limitation: risks related to: the clinical, therapeutic and commercial value of cobimetinib; 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; 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 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.

[1] Larkin J et al., Update of progression-free survival and correlative biomarker analysis from coBRIM: cobimetinib plus vemurafenib in advanced BRAF-mutated melanoma. Abstract presented at ASCO, Chicago, IL, USA, 29 May – 2 June 2015; abstract #9006.

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