Exelixis Announces First Regulatory Approval of Cobimetinib in Switzerland

August 27, 2015

-- The Second Product Discovered by Exelixis to Receive Regulatory Approval --

-- Additional Regulatory Applications in the U.S. and EU Currently under Review --

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Aug. 27, 2015-- Exelixis, Inc. (NASDAQ:EXEL) today announced that Swissmedic, the Swiss licensing and supervisory authority of Switzerland, has approved cobimetinib for use in combination with vemurafenib as a treatment for patients with advanced melanoma. Cobimetinib is a selective inhibitor of MEK that was discovered by Exelixis and is the subject of a worldwide collaboration agreement between Exelixis and Genentech, a member of the Roche Group. The trade name for cobimetinib in Switzerland is Cotellic™.

Roche's Swiss regulatory submission for cobimetinib was based on data from coBRIM, the phase 3 pivotal trial of cobimetinib and vemurafenib conducted in 495 patients with previously untreated unresectable, locally advanced or metastatic melanoma with a BRAF V600 mutation. The resulting approval is the first for cobimetinib worldwide, and additional regulatory applications are under review in other territories. Genentech filed its New Drug Application (NDA) for cobimetinib with the U.S. Food and Drug Administration (FDA) in December 2014 and the Prescription Drug User Fee Act date is November 11, 2015. Separately, Roche filed a Marketing Authorization Application with the European Medicines Agency in late 2014, and Roche anticipates a regulatory decision before the end of 2015.

"The Swiss regulatory approval of cobimetinib is an important advance for melanoma patients, physicians, and caregivers," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "Exelixis congratulates our partner Roche on this first approval for the product, and we look forward to additional regulatory decisions in the United States and European Union, which are anticipated later this year."

After discovering cobimetinib 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 cobimetinib. Under the terms of the collaboration, Exelixis is eligible to receive royalties on sales of cobimetinib outside the United States. If cobimeitnib is 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 in U.S. marketing and commercialization costs. In November 2013, Exelixis exercised its option to co-promote cobimetinib in the United States and, under the terms of the agreement, the company is prepared to field up to 25 percent of the U.S. sales force.

Dr. Morrissey continued: "As the second approved product to have been discovered at Exelixis, cobimetinib represents a major achievement for our company and for all of the employees, past and present, who contributed to the program since its inception. Our agreement with Genentech and Roche enables Exelixis to participate meaningfully in the product's commercialization. This includes receiving royalties on ex-U.S. sales and sharing in the profits in the U.S., where our team is fully prepared to co-promote cobimetinib with Genentech pending regulatory approval. Exelixis is excited to be working with Genentech and Roche to ensure that the commercialization phase of our cobimetinib partnership mirrors the productivity and success seen during the compound's discovery and clinical development."

About the coBRIM study

The pivotal coBRIM study is an international, randomized, double-blind, placebo-controlled, phase 3 study evaluating the safety and efficacy of the combination therapy. A total of 495 patients with unresectable, locally advanced or metastatic melanoma with a BRAF V600 mutation were randomized to receive vemurafenib once daily at the approved dosage and either cobimetinib or a placebo for 3 weeks followed by one week off cobimetinib/placebo. Treatment was continued until disease progression, unacceptable toxicity or withdrawal of consent. Investigator-assessed progression-free survival (PFS) was 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.[1]

The Swissmedic approval was based on an updated analysis of the coBRIM study data that showed that patients with previously untreated BRAF V600 mutation-positive advanced melanoma live a median of more than a year (12.3 months) without progression of their disease (progression-free survival, PFS) on combination therapy with cobimetinib and vemurafenib, and 7.2 months on vemurafenib monotherapy.[2,3] Patients responded better to treatment with cobimetinib and vemurafenib than those given vemurafenib alone. In this updated analysis, the objective response rate (ORR) of the cobimetinib and vemurafenib combination was 70 percent (compared to 50 percent for vemurafenib monotherapy).[2] With further follow-up from the primary analysis, the complete response rate was 15 percent. The safety profile of cobimetinib and vemurafenib was consistent with safety data previously reported from the phase 1b BRIM7 study. The most common adverse events in the combination arm were diarrhea, rash, nausea, fever, sun sensitivity, liver lab abnormalities, elevated creatine phosphokinase (CPK, an enzyme released by muscles) and vomiting.

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 percent of tumors. About 50 percent of patients with BRAF mutation positive melanoma experience a tumor response when treated with a BRAF inhibitor, however development of resistance and subsequent tumor progression limits treatment benefit. Clinical and preclinical analyses indicated that reactivation of the MEK-ERK pathway may underlie development of resistance to BRAF inhibitors in many progressing tumors, and that co-treatment with a BRAF and MEK inhibitor delays the emergence of resistance in the preclinical setting, providing the rationale for testing the combination of vemurafenib and cobimetinib in clinical trials. 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, colorectal cancer, triple-negative breast cancer and melanoma.

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. 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 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 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, including, without limitation, statements related to: the potential for additional regulatory approvals for cobimetinib in other territories by the end of 2015, including by the FDA in the U.S. and EMA in the EU; the potential for cobimetinib to advance melanoma treatment; Exelixis' preparedness to support U.S. co-promotion efforts for cobimetinib in the U.S.; the plan of Genentech and Exelixis to share U.S. profits and losses and U.S. marketing and commercialization costs for cobimetinib; and, Exelixis' potential receipt of royalties on sales of cobimetinib products outside the U.S. Words such as "anticipate," "look forward," "if," "entitled," "eligible," "will," "prepared," 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. 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 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.

[1] Larkin J et al., Combined Vemurafenib and Cobimetinib in BRAF-Mutated Melanoma. N Engl J Med. 2014;371(20):1867-76.

[2] 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.

[3] The NDA submitted to the FDA was based on data from the primary analysis of the coBRIM study.

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