Exelixis Announces Acceptance of New Drug Application for Cobimetinib in Combination with Vemurafenib for Treatment of Patients with BRAF V600 Mutation-Positive Advanced Melanoma

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- FDA Grants Priority Review, Assigns Action Date of August 11, 2015 -

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Feb. 19, 2015-- Exelixis, Inc. (NASDAQ:EXEL) announced today that the U.S. Food and Drug Administration (FDA) has accepted for review Genentech's New Drug Application (NDA) for cobimetinib in combination with vemurafenib for patients with unresectable or metastatic melanoma harboring a BRAF V600 mutation. Cobimetinib is a specific MEK inhibitor that was discovered by Exelixis and is now the subject of a worldwide co-development agreement between Exelixis and Genentech, a member of the Roche Group.

FDA has granted Priority Review to the NDA and assigned a Prescription Drug User Fee Act (PDUFA) action date of August 11, 2015. A Priority Review designation is granted to medicines that the FDA determines have the potential to provide significant improvements in the treatment, prevention or diagnosis of a disease.

"The FDA's acceptance of the cobimetinib NDA brings us one step closer to a potential new treatment option for patients with advanced BRAF V600 mutation-positive melanoma, a form of the disease for which new approaches are needed," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "We applaud Genentech on this regulatory progress, and we look forward to working with them, as well as with Roche, to commercialize and co-promote the combination in the event that it is approved."

The NDA is based on data from coBRIM, a phase 3 pivotal trial conducted by Genentech. Roche also submitted a Marketing Authorization Application (MAA) to the European Medicines Agency for the combination of cobimetinib and vemurafenib in 2014.

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. At the time of the primary analysis, median follow up was 7.4 months for the combination arm and 7.2 months for the control arm.

As presented during the Presidential Symposium at the European Society for Medical Oncology 2014 Congress, coBRIM met its primary endpoint, 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; $p < 0.0001$). The safety profile of the combination was consistent with that observed in a previous study of the combination. The most common Grade 3 or higher adverse events in the combination arm included liver laboratory abnormalities, elevated creatine phosphokinase and diarrhea. The most common adverse events seen in the combination arm included diarrhea, nausea, rash, photosensitivity and laboratory value abnormalities.

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 in connection with 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, 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 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: potential regulatory approval for cobimetinib and the timing thereof; Exelixis' future U.S. co-promotion efforts for cobimetinib in the United States; 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 "potential," "brings," "progress," "projected," "if," "entitled," "will," "eligible," and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Exelixis' (and its partner Genentech's) 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 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 4, 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.

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