Exelixis Announces Presentation of Final Phase 1b Data for Cobimetinib in Combination with Vemurafenib at EADO Congress 2014

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- Data from BRIM7, ongoing phase 1b trial in patients with locally advanced/unresectable or metastatic melanoma with the BRAF^{V600} mutation -

- 87% confirmed Overall Response Rate, 13.7-month median Progression Free Survival and 83% 1 year survival estimate for the combination in BRAFi-naive patients observed in exploratory analyses of anti-tumor activity -

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--May 7, 2014-- Exelixis, Inc. (NASDAQ:EXEL) today announced final results from BRIM7, an ongoing phase 1b clinical trial conducted by Roche and Genentech, Exelixis' collaborator and a member of the Roche Group (SIX: RO, ROG; OTCQX: RHHBY), of the BRAF inhibitor (BRAFi) vemurafenib in combination with the MEK inhibitor cobimetinib in patients with locally advanced/unresectable or metastatic melanoma carrying a BRAF^{V600} mutation. Antoni Ribas, M.D., Ph.D., a professor in the department of medicine at Jonsson Comprehensive Cancer Center at the University of California, Los Angeles, presented the data during a plenary session today at the 10th European Association of Dermato-Oncology (EADO) Congress. The meeting is taking place from May 7-10, 2014, in Vilnius, Lithuania.

“Building on the previous data from the BRIM7 trial, these final results provide encouraging signs of clinical activity in BRAFi-naïve patients with the combination of cobimetinib and vemurafenib,” said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. “We are pleased with the progress Roche has made in investigating cobimetinib, an Exelixis-discovered compound, in this patient population. People with this disease still urgently need improved treatment options, and we look forward to the top-line data from coBRIM, the ongoing phase 3 pivotal trial, anticipated later this year.”

Study Design

The phase 1b dose escalation study was designed to evaluate the safety and tolerability of cobimetinib in combination with vemurafenib. The dose escalation stage of the trial comprised 10 dosing cohorts of 3-6 patients and evaluated three different dosing schedules of cobimetinib in combination with twice daily administration of vemurafenib. After the maximum tolerated dose (MTD) was defined, two dose cohorts were expanded and additional patients with BRAF-mutated melanoma who were either BRAFi-naïve or vemurafenib-progressing patients were accrued.

Study Results

As of October 1st, 2013, 129 patients had been treated, comprising 66 patients who had previously progressed while receiving vemurafenib and 63 patients who were BRAFi-naïve. Of the 63 BRAFi-naïve patients, 43 (68%) were previously untreated and 20 (32%) had been treated with agents other than a BRAFi. The majority of the patients had Stage IV, M1c melanoma at the time of enrollment (vemurafenib-progressors 82%, BRAFi-naïve 70%). The median duration of follow-up in vemurafenib-progressor and BRAFi-naïve patients was 6.3 and 12.7 months, respectively.

The final results of the exploratory secondary endpoints of BRIM7 showed anti-tumor activity for the combination of cobimetinib and vemurafenib. In BRAFi-naïve patients (n=63), an 87% confirmed overall response rate (ORR) was achieved, including 10% complete responses and 78% partial responses. An additional 10% of patients achieved stable disease. The majority of tumor responses were observed within the first six weeks following initiation of treatment. The median progression free survival (PFS) for BRAFi-naïve patients was 13.7 months. Results for vemurafenib-progressor patients (n=66) showed a 15% confirmed ORR, 42% stable disease rate, and median PFS of 2.8 months. The median overall survival (OS) for BRAFi-naïve patients had not been reached, with a 1 year survival estimate of 83%. For the vemurafenib-progressor patients the median OS was 8.3 months with an estimated 1 year survival of 32%.

Safety

The most common adverse events (AEs) regardless of attribution to study treatment in the 129 patients treated to date were non-acneiform rash, diarrhea, fatigue, photosensitivity/sunburn, liver laboratory abnormalities and nausea. The most common (all Grade; ≥ Grade 3) AEs in BRAFi-naïve patients were non-acneiform rash (87%; 14%) diarrhea (83%; 8%), fatigue (70%; 10%) photosensitivity/sunburn (67%; 3%), liver laboratory abnormality (67%, 19%) and nausea (57%; 3%). The most common (all Grade; ≥ Grade 3) AEs in vemurafenib-progressor patients were diarrhea (47%; 3%), nausea (33%; 3%), non-acneiform rash (33%; 2%), fatigue (27%; 2%) and liver laboratory abnormality (33%; 6%). Most adverse events were mild to moderate in severity. Permanent discontinuation of vemurafenib, cobimetinib or the combination due to AEs was infrequent, and occurred in 5% (vemurafenib), 2% (cobimetinib) and 2% (combination) of the vemurafenib progressing patients and 6% (vemurafenib), 5% (cobimetinib) and 3% (combination) of the BRAFi-naïve patients.

About the Phase 3 Pivotal Trial coBRIM

coBRIM is the multicenter, randomized, double-blind, placebo-controlled phase 3 clinical trial evaluating the combination of vemurafenib with cobimetinib versus vemurafenib in previously untreated BRAF^{V600} mutation positive patients with unresectable locally advanced or metastatic melanoma. The trial is fully enrolled and data are expected to be available in 2014.

About Cobimetinib

Cobimetinib (formerly GDC-0973/XL518) is an inhibitor of MEK, a serine/threonine kinase that is a component of the RAS/RAF/MEK/ERK pathway. This pathway mediates signaling downstream of growth factor receptors, and is prominently activated in a wide variety of human tumors. In preclinical studies, oral dosing of cobimetinib resulted in sustained inhibition of MEK in RAS or BRAF mutant tumor models. Cobimetinib is being developed by Roche and Genentech, a member of the Roche Group, under a collaboration with Exelixis.

About the 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 end of phase 1, at which point Genentech exercised its option to further develop the compound.

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 net sales of the product outside the United States. In December 2012, Exelixis announced that it exercised its option to co-promote cobimetinib in the United States.

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, Inc. (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 and therapeutic potential of cobimetinib; anticipated developments with respect to coBRIM, including the expected availability of top-line data therefrom; the designs, plans and goals for BRIM7 and coBRIM; 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 net sales of cobimetinib products outside the United States. Words such as “provide,” “encouraging,” “investigating,” “look forward,” “anticipated,” “designed,” “expected,” “available,” “entitled,” “share,” “will,” “potential,” 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 to demonstrate safety and efficacy in clinical testing; the availability of data at the expected times; the clinical, therapeutic and commercial value of cobimetinib; Exelixis' dependence on its relationship with Genentech/Roche and Exelixis’ ability to maintain its rights under the collaboration; the uncertainty of regulatory approval processes; 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 May 1, 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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