Exelixis Announces Presentation of Updated Phase 1b Data for Cobimetinib (GDC-0973/XL518) in Combination with Vemurafenib at ECC 2013

September 28, 2013

- *Data from BRIM7, ongoing phase 1b trial in patients with locally advanced/unresectable or metastatic melanoma with the BRAF^{V600} mutation*
- *Although trial was primarily designed to evaluate safety, objective responses observed in 85% of BRAFi-naive patients receiving combination*

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Sep. 28, 2013-- Exelixis, Inc. (NASDAQ:EXEL) today announced updated 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 (GDC-0973/XL518) in patients with locally advanced/unresectable or metastatic melanoma carrying a BRAF^{V600} mutation. Grant McArthur, M.D., Head of the Medical Oncology Skin and Melanoma Clinical Service at the Peter MacCallum Cancer Centre in Australia, and an investigator on the trial, presented the data today at the European Cancer Congress (ECC) 2013 (Abstract #3703) which is taking place in Amsterdam, The Netherlands.

“The data presented today, while early-stage, suggest that the preliminary safety profile and activity of the investigational combination of cobimetinib and vemurafenib is promising in BRAFi-naïve patients,” said Michael Morrissey, Ph.D., president and CEO of Exelixis. “Importantly, responses in these patients generally occurred early in their course of treatment. We are pleased with the progress Roche has made in advancing cobimetinib, and believe that this Exelixis-discovered compound warrants further study in melanoma, as people with this incurable disease desperately need new options.”

Exelixis received notice from Genentech in January 2013 that the first patient was dosed in a phase 3 pivotal trial (coBRIM) evaluating vemurafenib alone or in combination with cobimetinib in previously untreated patients with malignant melanoma harboring the BRAF^{V600} mutation. This study is ongoing and currently enrolling globally. Top-line data from the trial are expected to be available next 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 for the two active treatments. Cohorts that met the protocol-specified criteria for MTD were expanded and included BRAFi-naïve or vemurafenib-progressing patients.

Study Results

As of June 21, 2013, 128 patients had been treated, comprising 65 patients who had disease progression while receiving vemurafenib and 63 patients who were BRAFi-naïve. Of the 63 BRAFi-naïve patients, 42 (67%) were previously untreated and 21 (33%) had been treated with agents other than a BRAFi. The majority of patients had Stage IV, M1c melanoma at the time of enrollment (vemurafenib-progressors = 82%, BRAFi naïve = 70%). Dose-limiting toxicities were reported in one of six patients in the dose-escalation stage receiving 960 mg of vemurafenib bid and 60 mg of cobimetinib qd on a 21/7-day schedule (Grade 3 QT interval prolongation), and in one of five patients in the dose escalation stage receiving 960 mg of vemurafenib bid and 80 mg cobimetinib qd on a 14/14-day schedule. Dose-limiting toxicities of Grade 3 mucositis and Grade 3 arthralgia were each observed in one of four patients in the dose-escalation stage receiving 960 mg vemurafenib bid and 60 mg cobimetinib qd on a 28/0-day schedule. Two cohorts receiving 60 mg of cobimetinib qd on a 21/7-day schedule with vemurafenib at either 720 mg or 960 mg bid were selected for expansion.

While the study was not designed to measure efficacy, updated results showed a partial or complete response (tumor shrinkage) in many of the patients who had not been previously treated with a BRAF inhibitor. Of the 63 BRAFi-naïve patients, 10% had a complete response, 75% had a partial response, and 13% had stable disease, for an objective response rate of 85%. Most objective responses occurred by the time of the first tumor assessment at 6 weeks. Only two of the BRAFi-naïve patients (3%) had progressive disease. Sixty-one of the 65 patients who had progressed on prior vemurafenib therapy were evaluated for tumor response by RECIST, of which 15% had a partial response, and 43% had stable disease, for an objective response rate of 15%. As of the June 21, 2013 cut-off date, with a median follow-up time of three months, 85.2% of vemurafenib-progressors had already experienced disease progression, and the median progression-free survival (PFS) was 2.8 months. At a median follow-up time of 10 months, 33.3% of BRAFi-naïve patients had experienced disease progression, and the median PFS had not yet been reached.

Safety

The most common adverse events (AEs) regardless of attribution to study treatment in the 128 patients treated to date were: non-acneiform rash (35% [2% ≥ Grade 3] for vemurafenib-progressors; and 89% [13% ≥ Grade 3] for BRAFi-naïve), diarrhea (48% [3%]; 81% [8%]), photosensitivity/sunburn (48% [3%]; 70% [0%])), fatigue (28% [2%]; 67% [10%]), nausea (32% [3%]; 56% [3%]), arthralgia (11% [2%]; 48% [11%]), CPK elevation (15% [2%]; 43% [3%]), fever (14% [0%]; 43% [2%]), peripheral edema (20% [0%]; 41% [0%]), vomiting (19% [2%]; 37% [0%]), and acneiform rash (12% [2%]; 33% [3%]). Selected AEs were: choreoretinopathy (2% [0]; 9% [0%]), cardiomyopathy [0% [0%]; 2% [2%]), and squamous cell carcinoma/keratocanthoma (8% [6%]; 10% [5%]).

Temporary interruptions in vemurafenib, cobimetinib, or the combination of both agents were reported in 20%, 20%, and 19% of the 65 vemurafenib-progressor patients, respectively. Dose reductions were reported in 5% 3%, and 3% of vemurafenib-progressor patients, respectively, and permanent discontinuation was reported for vemurafenib (3%) only. Among the 63 BRAFi-naïve patients, temporary interruptions in vemurafenib, cobimetinib, or

the combination of both agents were reported in 67%, 49%, and 46%, and dose reductions were reported in 19%, 16% and 2% of patients, respectively. Permanent discontinuation of cobimetinib was reported for one BRAFi-naïve patient (2%). None of the 128 patients receiving the combination of vemurafenib and cobimetinib discontinued treatment due to an adverse event to date.

About Cobimetinib (GDC-0973/XL518)

Cobimetinib 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 Genentech, a member of the Roche Group under a collaboration agreement with Exelixis.

About the Collaboration

Exelixis discovered cobimetinib (GDC-0973/XL518) 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 any sales of the product outside the United States. Exelixis has the option to co-promote in the United States.

About Exelixis

Exelixis is a biotechnology company committed to developing small molecule therapies for the treatment of cancer. Exelixis is focusing its proprietary resources and development efforts exclusively on COMETRIQ® (cabozantinib). Exelixis has also established a portfolio of other novel compounds that it believes have the potential to address serious unmet medical needs, many of which are being advanced by partners as part of collaborations. 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 (GDC-0973/XL518); the potential benefit of the investigational combination of cobimetinib and vemurafenib to BRAFi-naïve patients; the belief that cobimetinib warrants further study in melanoma; developments with respect to coBRIM, including the expected availability of top-line data therefrom; the designs, plans and goals for BRIM7; the plan of Genentech and Exelixis to share U.S. profits and losses for cobimetinib and U.S. marketing and commercialization costs for cobimetinib; Exelixis' potential receipt of royalties for cobimetinib products sales outside the United States; and Exelixis' option to co-promote in the United States. Words such as "ongoing," "suggest," "promising," "believe," "warrants," "further," "new," "currently," "enrolling," "expected," "available," "designed," "entitled," "share," "will," "potential," and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Exelixis' current plans, assumptions, beliefs and expectations. Forward-looking statements involve risks and uncertainties. Exelixis' actual results and the timing of events could differ materially from those anticipated in such 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; and changes in economic and business conditions. These and other risk factors are discussed under "Risk Factors" and elsewhere in Exelixis' quarterly report on Form 10-Q for the three months ended June 28, 2013, filed with the Securities and Exchange Commission (SEC) on August 6, 2013, and Exelixis' other filings with the SEC. 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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