Updated Positive Results from Two Trials of Cobimetinib in Combination with Vemurafenib for the Treatment of Patients with Advanced Melanoma Presented at 2015 ASCO Annual Meeting

May 30, 2015

- Updated results from coBRIM phase 3 pivotal trial show median progression-free survival of one year for patients with BRAF V600 mutation-positive advanced melanoma –

- Additional data from phase 1b BRIM7 study showed 61 percent of patients who had not been previously treated with a BRAF inhibitor were alive after two years -

- Cobimetinib for use in combination with vemurafenib is the subject of pending U.S. and European regulatory applications, with U.S. PDUFA date of August 11, 2015 -

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--May 30, 2015-- Exelixis Inc. (NASDAQ:EXEL) today announced updated positive results for cobimetinib, an Exelixis-discovered investigational compound, in combination with vemurafenib for the treatment of patients with previously untreated BRAF V600 mutation-positive advanced melanoma. Updated data from coBRIM (Abstract #9006), the phase 3 pivotal trial conducted by Exelixis' collaborator Genentech, a member of the Roche Group, showed the combination helped patients with previously untreated BRAF V600 mutation-positive advanced melanoma live a median of one year (12.3 months) without disease progression or death, compared to 7.2 months with vemurafenib alone (hazard ratio [HR] = 0.58, 95% confidence interval [CI] 0.46-0.72). Data from a second trial, the phase 1b BRIM7 study (Abstract #9020), showed that treatment with the combination resulted in a median overall survival of more than two years (28.5 months) for patients without prior BRAF inhibitor treatment. Both data sets will be presented at the 2015 Annual Meeting of the American Society of Clinical Oncology (ASCO), which is being held this week in Chicago, Illinois.

"The updated results for the combination of cobimetinib and vemurafenib, including a median progression-free survival of one year in patients with previously untreated BRAF V600 mutation-positive advanced melanoma, are encouraging," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "The data underscore the potential for the combination to become a meaningful new treatment option for patients with this type of melanoma. We congratulate Genentech and Roche on two well-run trials, and we look forward to working with them to bring the combination to physicians and patients in the event of potential regulatory approval later this year."

The updated results from coBRIM also showed higher response rates with cobimetinib and vemurafenib compared to vemurafenib alone. Objective response rate, a secondary endpoint of the trial, was 70% (16% compete response [CR], 54% partial response [PR]) with the combination compared to 50% (11% CR, 40% PR) with vemurafenib alone. The CR rate with the combination has increased from 10% to 16% with further follow-up as some patients who had an initial PR achieved a CR after more than one year of treatment. The safety profile of the combination was consistent with data previously reported. The most common adverse events in the combination arm include diarrhea, rash, nausea, fever, sun sensitivity, liver lab abnormalities, elevated creatine phosphokinase (CPK, an enzyme released by muscles) and vomiting.

Follow-up data from BRIM7, the phase 1b study that provided the rationale for the coBRIM pivotal trial, demonstrated that the combination of cobimetinib and vemurafenib resulted in a median overall survival of 28.5 months, with 61% of BRAF inhibitor-naive patients remaining alive after two years. The safety profile from the BRIM7 trial was consistent with previous analyses, and the incidence of serous retinopathy, cardiomyopathy and cutaneous squamous cell carcinoma were similar to those previously reported.

The coBRIM data will be presented in an oral session today by Dr. James Larkin, FRCP, of The Royal Marsden Hospital, London, UK (Abstract #9006, May 30, 3:15-3:27 pm CDT), while the BRIM7 data will be presented in a poster session by Dr. Anna Pavlick, New York University Medical Center (Abstract #9020, June 1, 1:15-4:45 pm CDT).

The cobimetinib New Drug Application for BRAF V600 mutation-positive advanced melanoma was granted priority review by the U.S. Food and Drug Administration (FDA) and a decision is expected by August 11, 2015. The European Medicines Agency is expected to make a decision on Roche's marketing authorization application for cobimetinib before the end of this year.

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. Investigator-assessed PFS is the primary endpoint. Secondary endpoints include PFS by independent review committee, overall response rate, overall survival, duration of response and other safety, pharmacokinetic and quality of life measures.

The most common adverse events reported in patients taking cobimetinib in combination with vemurafenib (≥ 20%) were diarrhea, rash, nausea, fever, sun sensitivity, liver lab abnormalities, elevated creatine phosphokinase (CPK, an enzyme released by muscles) and vomiting. Serous retinopathy (collection of fluid under the retina) was observed at a higher frequency in the combination arm (26% vs. 3%) with most of these events either Grade 1

or 2, asymptomatic, and temporary in nature. Some adverse events, including cutaneous squamous cell carcinomas and keratoacanthomas, were reported less frequently in the combination arm.

About the BRIM7 Study

BRIM7 is a Phase 1b study of 129 patients evaluating the safety and tolerability of cobimetinib in combination with vemurafenib in people with BRAF V600 mutation-positive unresectable or metastatic melanoma who had either not been previously treated with a BRAF inhibitor or had shown disease progression following treatment with a BRAF inhibitor. The primary endpoint of the BRIM7 study focused on safety, tolerability, and the identification of an optimal dose. The secondary outcome measures focused on efficacy. Patients in the dose-escalation stage of the study received cobimetinib 60, 80 or 100 mg once daily given on a schedule of 14 days on/14 days off; 21 days on/7 days off; or continuously for 28 days, and vemurafenib 720 or 960 mg twice daily continuously. Following the dose-escalation stage, two dose levels were selected for further investigation: cobimetinib 60 mg once daily for 21 days on/7 days off and vemurafenib (720 mg or 960 mg twice daily).

The most common adverse events were mild to moderate in severity, and the overall frequency of adverse events with an extended median follow-up of up to 21 months have remained consistent without new safety signals.

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 collaboration 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 a BRAF inhibitor and a MEK inhibitor 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: the continued development and clinical, therapeutic and commercial potential of cobimetinib for use in combination with vemurafenib; future potential regulatory approvals of cobimetinib; data presentations for the coBRIM phase 3 pivotal trial and the phase 1b BRIM7 study; Exelixis' co-promotion efforts with Genentech in the event of regulatory approval; 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 on sales of cobimetinib products outside the United States; and projections and assumptions regarding melanoma. Words such as "will," "encouraging," "potential," "look forward," "expected," "entitled," "eligible," "projected," "may," "committed," "focusing," 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 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; the general sufficiency of Exelixis' capital and other resources; 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 April 30, 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.

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