FDA Approves COTELLIC™ (Cobimetinib) for use in Combination with Vemurafenib to Treat Advanced Melanoma

November 10, 2015

-- Exelixis and Genentech to Co-Promote COTELLIC in the United States;

COTELLIC is expected to be available in the U.S. within two weeks –

--U.S. Profit Share Arrangement Will Provide Exelixis a Second Source of Product Revenue --

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Nov. 10, 2015-- Exelixis, Inc. (Nasdaq:EXEL) today announced that the U.S. Food and Drug Administration (FDA) has approved COTELLIC™(cobimetinib) as a treatment for patients with BRAF V600E or V600K mutation-positive unresectable or metastatic melanoma in combination with vemurafenib. COTELLIC and vemurafenib are not used to treat melanoma with a normal BRAF gene. COTELLIC 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. This is the second regulatory approval for COTELLIC, which was first approved in Switzerland in late August 2015.

Genentech sponsored the COTELLIC U.S. New Drug Application (NDA), having led the compound's development since midway through the initial phase 1 clinical trial. Genentech filed its NDA in December 2014; the FDA accepted the filing and granted it Priority Review in February 2015. Separately, Roche filed a Marketing Authorization Application (MAA) with the European Medicines Agency in late 2014, and the Committee for Medicinal Products for Human Use issued a positive opinion for the MAA in September 2015. Roche anticipates a decision from the European Commission by year-end.

"The approval of COTELLIC for use in combination with vemurafenib is an important milestone for the melanoma community, and also for Exelixis, as it is the second medicine discovered in our laboratories to receive regulatory approval in the United States," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "We look forward to working with Genentech and Roche to bring this important new treatment option for BRAF V600E and V600K mutation-positive advanced melanoma to patients, physicians, and caregivers."

The COTELLIC approval is based on data from the phase 3 coBRIM study, which showed COTELLIC plus vemurafenib reduced the risk of disease worsening or death (progression-free survival; PFS) by about half in people who received the combination (HR=0.56, 95 percent CI 0.45-0.70; p<0.001), with a median PFS of 12.3 months for COTELLIC plus vemurafenib compared to 7.2 months with vemurafenib alone. An interim analysis also showed the combination of COTELLIC and vemurafenib helped people live significantly longer (overall survival) than vemurafenib alone (HR=0.63, 95 percent CI 0.47-0.85; p=0.0019). The objective response rate (tumor shrinkage) was higher with COTELLIC plus vemurafenib compared to vemurafenib alone (70 vs. 50 percent; p<0.001), as was the complete response rate (complete tumor shrinkage, 16 vs. 10 percent).

Possible serious side effects with COTELLIC include risk of skin cancers, increased risk of bleeding, heart problems that can lead to inadequate pumping of the blood by the heart, rash, eye problems, abnormal liver test or liver injury, increased levels of an enzyme in the blood, and photosensitivity. The most common side effects of COTELLIC include diarrhea, sunburn or sun sensitivity, nausea, fever and vomiting. COTELLIC can also cause changes in blood test results.

The final overall survival analysis from the coBRIM trial will be presented at the Society for Melanoma Research 2015 International Congress, which will be held in San Francisco from November 18-21.

In November 2013, Exelixis exercised its option under the 2006 collaboration agreement to co-promote COTELLIC in the United States; accordingly, Exelixis will field 25% of the sales force, closely coordinating its efforts with Genentech. 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. The company is also eligible to receive royalties on any sales of the product outside the country, including in Switzerland, where COTELLIC was first approved, and in the European Union, where Roche anticipates a regulatory decision by year-end.

Dr. Morrissey continued: "The approval of COTELLIC represents a major achievement for Exelixis and for all of the employees, past and present, who contributed to the program since its inception. As we enter the commercialization phase of our partnership with Genentech and Roche, our agreement enables Exelixis to participate meaningfully in the product's introduction and ongoing sales. In the United States, our team is fully prepared to co-promote COTELLIC. Outside of the country, we are eligible to receive royalties on sales. 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 COTELLIC discovery and clinical development."

About COTELLIC ™in Combination with Vemurafenib

COTELLIC™ (cobimetinib) is indicated for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in combination with vemurafenib.

COTELLIC and vemurafenib are prescription medicines used in combination to treat melanoma that has spread to other parts of the body or cannot be

removed by surgery, and that has a certain type of abnormal BRAF gene. Found in approximately half of melanomas, mutated BRAF causes abnormal signaling inside cancer cells leading to tumor growth. Vemurafenib is designed to inhibit some mutated forms of BRAF and COTELLIC is designed to inhibit some forms of MEK. Both BRAF and MEK are proteins in a cell signaling pathway that help control cell growth and survival. When used in combination, COTELLIC and vemurafenib are thought to reduce cancer cell growth longer than with vemurafenib alone. A patient's healthcare provider will perform a test to make sure COTELLIC and vemurafenib are right for the patient. It is not known if COTELLIC and vemurafenib are safe and effective in children under 18 years of age.

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.

COTELLIC ™Important Safety Information

Before taking COTELLIC, patients should tell their doctor if they:

- have any previous or current skin problems other than melanoma
- have any medical conditions and/or are on any medications that increase your risk of bleeding
- have any heart problems
- have any eye problems
- have any liver problems
- have any muscle problems
- have any other medical conditions
- are pregnant or plan to become pregnant. COTELLIC can harm an unborn baby.
    - Patients who take COTELLIC should use effective methods of birth control during treatment, for at least two weeks after stopping COTELLIC, and for at least two months after stopping vemurafenib.
    - Patients should talk to their healthcare provider about birth control methods that may be right for them.
    - Patients should tell their healthcare provider right away if they become pregnant or think they are pregnant during treatment with COTELLIC.
- are breastfeeding or plan to breastfeed. It is not known if COTELLIC passes into breast milk, so patients should not breastfeed during treatment with COTELLIC and for two weeks after the final dose. Patients should talk to their healthcare provider about the best way to feed their baby during this time.

Patients should tell their healthcare provider about all the medicines they take, including prescription and over-the-counter medicines, vitamins and herbal supplements because some types of medicines will make COTELLIC more harmful or less effective. Patients should know the medicines they take and keep a list of them to show their healthcare provider and pharmacist when they get a new medicine.

Patients should avoid sunlight while taking COTELLIC. COTELLIC can make patients' skin sensitive to sunlight and cause them to burn more easily and get severe sunburns. To help protect against sunburn:

- When patients go outside they should wear clothes that protect their skin, including their head, face, hands, arms and legs.
- Patients should use lip balm and a broad-spectrum sunscreen with SPF 30 or higher.

COTELLIC may cause serious side effects, including:

- **Risk of skin cancers.** COTELLIC may cause skin cancers (cutaneous squamous cell carcinoma, keratoacanthoma or basal cell carcinoma).

Patients must check their skin and tell their doctor right away about any skin changes, including:

- new wart
- skin sore or reddish bump that bleeds or does not heal
- change in size or color of a mole

A patient's healthcare provider should check their skin before they start taking COTELLIC and every two months while taking COTELLIC. A patient's healthcare provider may continue to check their skin for six months after they stop taking COTELLIC.

- **Increased risk of bleeding.** COTELLIC may cause bleeding, including blood in the urine, rectal bleeding, unusual or excessive vaginal bleeding, bleeding of the gums and bleeding within the brain (cerebral hemorrhage).
  A patient should tell their healthcare provider right away if they experience any of these symptoms:
    - red or black stools that look like tar
    - blood in the urine
    - headache, dizziness or feeling weak

    - abdominal pain
    - unusual vaginal bleeding

- **Heart problems that can lead to inadequate pumping of the blood by the heart.** A patient's healthcare provider should perform tests before the patient starts taking COTELLIC and during a patient's treatment with COTELLIC to check the ability of the heart to pump blood. Signs and symptoms of a decrease in the amount of blood pumped include:
    - persistent coughing or wheezing
    - shortness of breath
    - swelling of their ankles and feet
    - tiredness
    - increased heart rate

- **Rash.** Patients should tell their healthcare provider right away if they experience any of these symptoms:
    - a rash that covers a large area of their body, blisters or peeling skin
- **Eye problems.** Patients should tell their healthcare provider right away if they experience any of these symptoms during treatment with COTELLIC:
    - blurred vision
    - distorted vision
    - partly missing vision
    - halos
    - any other vision changes

      Some of these eye problems may be a result of something called "serous retinopathy" (a build-up of fluid under the retina of the eye). A patient's healthcare provider should check their eyes if they notice any of the symptoms above.

- **Abnormal liver test or liver injury.** A patient's healthcare provider should perform blood tests before the start taking COTELLIC, and during treatment. A patient should tell their healthcare provider right away if you experience any of these symptoms:
    - yellowing of their skin or the white of their eyes
    - dark or brown (tea color) urine
    - nausea or vomiting
    - feeling tired or weak
    - loss of appetite
- **Increased levels of an enzyme in the blood.** Creatine phosphokinase (CPK) is an enzyme that is primarily found in the muscle, heart and brain. Treatment with COTELLIC may increase the level of this enzyme in your blood and be a sign of muscle damage. A patient's healthcare provider should perform a blood test before and during treatment. Increased blood levels of CPK can also be an indication of a serious condition caused by injury to the muscles (rhabdomyolysis). A patient should tell their healthcare provider right away if they experience any of these symptoms:
    - muscle aches
    - muscle spasms and weakness
    - dark, reddish urine
- **Photosensitivity**. A patient's skin may become more sensitive to sunlight while taking COTELLIC. A patient should tell their healthcare provider if they notice any of the following symptoms:
    - red, painful, itchy skin that is hot to touch
    - sun rash
    - skin irritation bumps or tiny papules
    - thicken, dry, wrinkled skin

The most common side effects of COTELLIC include:

- diarrhea
- sunburn or sun sensitivity
- nausea
- vomiting
- fever

A patient's healthcare provider will take blood tests while they are taking COTELLIC. The most common changes to blood tests include:

- increased blood levels of liver enzymes (GGT, ALT or AST)
- increased blood level of enzyme from muscle (creatine phosphokinase)
- decreased blood level of phosphate, sodium or potassium
- increased blood level of liver or bone enzyme (alkaline phosphatase)

- decreased blood level of a type of white blood cell (lymphocyte)

Patients should tell their healthcare provider if they have any side effect that bothers them or that does not go away.

These are not all the possible side effects of COTELLIC. For more information about side effects, patients should ask their healthcare provider or pharmacist. Patients should call their doctor for medical advice about side effects.

Patients should talk to their doctor for medical advice about side effects. Report side effects to FDA at (800) FDA-1088 or http://www.fda.gov/medwatch. Report side effects to Genentech at (888) 835-2555.

Please see full COTELLIC Prescribing Information and Patient Information for additional important safety information.

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. Positive results were recently announced for a phase 3 pivotal trial of cabozantinib in patients with advanced renal cell carcinoma who received at least one prior VEGF receptor tyrosine kinase inhibitor, and Exelixis expects to complete regulatory filings in the U.S. and European Union in late 2015 and early 2016, respectively. Another Exelixis-discovered compound, COTELLIC™ (cobimetinib), a selective inhibitor of MEK, received its first regulatory approvals in Switzerland and the United States, 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 website at www.exelixis.com.

Forward-Looking Statement Disclaimer

This press release contains forward-looking statements, including, without limitation, statements related to: the potential for regulatory approval for cobimetinib by the European Commission by the end of 2015; the potential for cobimetinib to advance melanoma treatment; the plan of Genentech and Exelixis to share U.S. profits and losses and U.S. sales and marketing costs for cobimetinib; Exelixis' potential receipt of royalties on sales of cobimetinib products outside the U.S.; and, Exelixis' preparedness to support U.S. co-promotion efforts for cobimetinib in the U.S. Words such as "anticipate," "look forward," "will," "entitled," "eligible," "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, 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.

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