Exelixis Announces Presentation of Positive Overall Survival Results for COTELLIC™ in Combination with Vemurafenib in Advanced BRAF V600 Mutation-Positive Melanoma at Society for Melanoma Research 2015 International Congress

November 21, 2015

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Nov. 21, 2015-- Exelixis, Inc. (NASDAQ:EXEL) today announced the presentation of positive overall survival (OS) results from coBRIM, the phase 3 pivotal trial evaluating COTELLIC ™(cobimetinib) in patients with previously untreated resectable, locally advanced or metastatic melanoma carrying a BRAF V600E or V600K mutation, in combination with vemurafenib. Dr. Victoria Atkinson, Medical Oncologist at Princess Alexandra Hospital, Queensland, Australia, presented the data during a late-breaking abstract oral presentation this afternoon at the Society for Melanoma Research (SMR) 2015 International Congress, which is being held November 18-21 in San Francisco. COTELLIC is a selective inhibitor of MEK that was discovered by Exelixis and is now the subject of a worldwide collaboration agreement between Exelixis and Genentech, a member of the Roche Group.

In October 2015, Exelixis announced the coBRIM trial met its OS secondary endpoint, demonstrating a statistically significant increase in OS for the combination of COTELLIC and vemurafenib compared to vemurafenib monotherapy. Today's presentation was the first to include detailed data on the endpoint. The median OS was 22.3 months for the combination of COTELLIC and vemurafenib versus 17.4 months for vemurafenib alone, corresponding to a 30% reduction in the rate of death for the combination as compared to vemurafenib alone (hazard ratio [HR]=0.70, 95% confidence interval [CI] 0.55-0.90, p= 0.005). Ongoing study monitoring did not identify any new safety signals.

"The overall survival benefit for COTELLIC and vemurafenib observed in the coBRIM trial further underscores the positive impact that the combination of these two therapies can have on the treatment of advanced BRAF V600 mutation-positive melanoma," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis.

On November 10, 2015, the U.S. Food and Drug Administration (FDA) approved COTELLIC as a treatment for patients with BRAF V600E or V600K mutation-positive unresectable or metastatic melanoma, in combination with vemurafenib. COTELLIC was first approved in Switzerland in late August 2015. The COTELLIC approvals are based on data from coBRIM, the phase 3 pivotal trial conducted by Genentech in 495 patients with previously untreated unresectable, locally advanced or metastatic melanoma carrying a BRAF V600 mutation (detected by the cobas® 4800 BRAF Mutation Test). Genentech sponsored the U.S. New Drug Application and Roche sponsored the Swiss regulatory application. Roche also 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 recommendation on the MAA in September 2015. Roche anticipates a decision from the European Commission by year-end.

About the COTELLIC Development Collaboration

Exelixis discovered COTELLIC internally and advanced the compound to investigational new drug (IND) status. In late 2006, Exelixis entered into a worldwide collaboration agreement with Genentech, under which Exelixis received initial upfront and milestone payments for signing the agreement and submitting the IND. Following the determination of the maximum tolerated dose in phase 1 by Exelixis, Genentech exercised its option to further develop COTELLIC.

Under the terms of collaboration, 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. In November 2013, Exelixis exercised its option to co-promote COTELLIC in the United States and, under the terms of the agreement, the company is fielding 25 percent of the U.S. sales force, closely coordinating its efforts with Genentech. Outside of the United States, Exelixis is eligible to receive royalties on any sales.

About COTELLIC ™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 the coBRIM Trial

CoBRIM is an international, randomized, double-blind, placebo-controlled phase 3 study evaluating the safety and efficacy of 60 mg once daily of cobimetinib plus 960 mg twice daily of vemurafenib compared to 960 mg twice daily of vemurafenib plus placebo. 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 on 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, objective response rate, overall survival, duration of response and other safety, pharmacokinetic and quality of life measures.

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 (gamma glutamyltransferase [GGT], alanine aminotransferase [ALT] or aspartate aminotransferase [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 cobimetinib to advance the treatment of advanced BRAF V600 mutation-positive melanoma; the potential for regulatory approval for cobimetinib by the European Commission by the end of 2015; the plan of Genentech and Exelixis to share U.S. profits and losses and U.S. sales and marketing costs for cobimetinib; and, Exelixis' potential receipt of royalties on sales of cobimetinib products outside the U.S. Words such as "can," "anticipate," "entitled," "eligible," "will," 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 November 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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Source: Exelixis, Inc.

Investors Contact:
Exelixis, Inc.
Susan Hubbard, 650-837-8194
Investor Relations and Corporate Communications
shubbard@exelixis.com
or
Media Contact:
For Exelixis, Inc.
Hal Mackins, 415-994-0040
hal@torchcommunications.com