Exelixis Announces Positive Results From IMspire150, the Phase 3 Trial of Atezolizumab Plus Cotellic and Vemurafenib in People With Previously Untreated BRAF V600 Mutation-Positive Advanced Melanoma

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ALAMEDA, Calif.--(BUSINESS WIRE)--Dec. 13, 2019-- Exelixis, Inc. (Nasdaq: EXEL) today announced positive results from IMspire150, the phase 3 trial of atezolizumab (TECENTRIQ®), cobimetinib (COTELLIC®) and vemurafenib (ZELBORAF®) in people with previously untreated BRAF V600 mutation-positive advanced melanoma. Genentech, Inc. (a member of the Roche Group), Exelixis' collaborator and the sponsor of the IMspire150 trial, informed the company that the study met its primary endpoint of progression-free survival (PFS). Adding atezolizumab to cobimetinib and vemurafenib helped to reduce the risk of disease worsening or death, compared to placebo plus cobimetinib and vemurafenib.

A significant and clinically meaningful improvement in PFS was demonstrated in IMspire150. The safety profile observed in the trial was consistent with the known safety profiles of the individual medicines. Results will be presented at an upcoming medical meeting and discussed with health authorities around the world, including the U.S. Food and Drug Administration and the European Medicines Agency.

About Advanced Melanoma

Melanoma is less common, but more aggressive and deadlier than other forms of skin cancer. When melanoma is diagnosed early, it is generally a curable disease, but most people with advanced melanoma have a poor prognosis. The American Cancer Society estimates there will be more than 96,000 new cases of melanoma and 7,000 melanoma deaths this year in the United States.

In recent years, there have been significant advances in treatment for advanced melanoma and people with the disease have more options. However, it continues to be a serious health issue with a high medical need and a steadily increasing incidence over the past 30 years.

About the IMspire150 study

IMspire150 is a phase 3, multi-center, double-blind, placebo-controlled randomized study in people with previously untreated BRAF V600 mutation-positive metastatic or unresectable locally advanced melanoma. The study compared the efficacy and safety of atezolizumab plus cobimetinib and vemurafenib to the combination of placebo plus cobimetinib and vemurafenib. The primary endpoint of the study was investigator-assessed PFS. Key secondary endpoints include PFS by an independent review committee, overall survival, objective response rate, duration of response and other safety and pharmacokinetic measures.

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 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 cobimetinib.

Under the terms of the collaboration, Exelixis is entitled to an initial equal share of U.S. profits and losses, which will decrease as sales increase, and shares U.S. commercialization costs. Outside of the United States, Exelixis is eligible to receive royalties on any sales.

Cobimetinib is also the subject of a clinical development program aimed at evaluating its potential in combination with investigational and approved therapies in multiple disease settings.

TECENTRIQ® (atezolizumab), COTELLIC® (cobimetinib) and ZELBORAF® (vemurafenib) are registered trademarks of Genentech, a member of the Roche Group.

COTELLIC Indication

Important: If a patient's healthcare provider prescribes ZELBORAF (vemurafenib), the patient should also read the Medication Guide that comes with ZELBORAF.

COTELLIC is a prescription medicine that is used with the medicine ZELBORAF to treat a type of skin cancer called 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.

A patient's healthcare provider will perform a test to make sure that COTELLIC is right for the patient. It is not known if COTELLIC is safe and effective in children under 18 years of age.

Important Safety Information

Before taking COTELLIC, patients should tell their healthcare provider about all of their medical conditions, including if they:

- have skin problems or history of skin problems, other than melanoma

- have bleeding problems, any medical conditions and/or on any medications that increase the risk of bleeding
- have heart problems
- have eye problems
- have liver problems
- have muscle problems
- are pregnant or plan to become pregnant. COTELLIC can harm an unborn baby.
    - Females who are able to become pregnant should use effective birth control during treatment with COTELLIC, and for two weeks after the final dose of COTELLIC.
    - 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. Patients should not breastfeed during treatment with COTELLIC and for two weeks after the final dose of COTELLIC. 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. Certain medicines may affect the blood levels of COTELLIC.

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.

How should patients take COTELLIC?

- Patients should take COTELLIC exactly as their healthcare provider tells them. Patients should not change their dose or stop taking COTELLIC unless their healthcare provider tells them to.
- Patients should take COTELLIC one time a day for 21 days, followed by seven days off treatment, to complete a 28-day treatment cycle.
- Patients can take COTELLIC with or without food.
- If a patient vomits after taking their dose of COTELLIC, they should not take an additional dose. Patients should take their next dose as scheduled.
- If a patient misses a dose of COTELLIC, they should take their next dose as scheduled.

What should patients avoid during treatment with COTELLIC?

Patients should avoid sunlight during treatment with COTELLIC. COTELLIC can make a patient's skin sensitive to sunlight. They may burn more easily and get severe sunburns. To help protect against sunburn:

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

What are the possible side effects of COTELLIC? COTELLIC may cause serious side effects, including:

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

Patients should check their skin regularly and tell their healthcare provider right away if they have 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 the patient's skin before they start taking COTELLIC, and every two months during treatment with COTELLIC. A patient's healthcare provider may continue to check the patient's skin for six months after the patient stops taking COTELLIC.

A patient's healthcare provider should also check for cancers that may not occur on the skin. Patients should tell their healthcare provider about any new symptoms that develop during treatment with COTELLIC.

- **Bleeding problems.** COTELLIC can cause serious bleeding problems. Patients should call their healthcare provider and get medical attention right away if they get any signs of bleeding, including:
    - red or black stools (looks like tar)
    - blood in their urine
    - headaches
    - cough up or vomit blood
    - stomach (abdominal) pain
    - unusual vaginal bleeding
    - dizziness or weakness

- **Heart problems.** A patient's healthcare provider should do tests before and during treatment to check the patient's heart function. Patients should tell their healthcare provider if they get any of these signs and symptoms of heart problems:
    - persistent coughing or wheezing
    - shortness of breath
    - swelling of their ankles and feet
    - tiredness
    - increased heart rate

- **Severe rash.** Patients should tell their healthcare provider right away if they get any of these symptoms:
    - a rash that covers a large area of their body
    - blisters
    - peeling skin

- **Eye problems.** Patients should tell their healthcare provider right away if they get any of these symptoms:
    - blurred vision
    - partly missing vision or loss of vision
    - see halos
    - any other vision change

A patient's healthcare provider should check the patient's eyes if the patient notices any of the symptoms above.

- **Liver problems.** A patient's healthcare provider should do blood tests to check the patient's liver function before and during treatment. Patients should tell their healthcare provider right away if they get 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

- **Muscle problems (rhabdomyolysis).** COTELLIC can cause muscle problems that can be severe. Treatment with COTELLIC may increase the level of an enzyme in the blood called creatine phosphokinase (CPK) and may be a sign of muscle damage. A patient's healthcare provider should do a blood test to check the patient's levels of CPK before and during treatment. Patients should tell their healthcare provider right away if they get any of these symptoms:
    - muscle aches or pain
    - muscle spasms and weakness
    - dark, reddish urine

- **Skin sensitivity to sunlight (photosensitivity)**. Skin sensitivity to sunlight during treatment with COTELLIC is common and can sometimes be severe. Patients should tell their healthcare provider if they get any of these symptoms:
    - red, painful, itchy skin that is hot to touch
    - sun rash
    - skin irritation
    - bumps or tiny papules
    - thickened, dry, wrinkled skin

See "What should patients avoid during treatment with COTELLIC?" for information on protecting the skin during treatment with COTELLIC.

The most common side effects of COTELLIC include:

- diarrhea
- nausea
- fever
- vomiting

A patient's healthcare provider will take blood tests during treatment with 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)

These are not all the possible side effects of COTELLIC. Patients should call their doctor for medical advice about side effects. Patients may report

side effects to FDA at (800) FDA-1088 or www.fda.gov/medwatch. Patients may also report side effects to Genentech at (888) 835-2555.

Please see Full COTELLIC Prescribing Information and Patient Information for additional Important Safety Information at www.COTELLIC.com.

About Exelixis

Founded in 1994, Exelixis, Inc. (Nasdaq: EXEL) is a commercially successful, oncology-focused biotechnology company that strives to accelerate the discovery, development and commercialization of new medicines for difficult-to-treat cancers. Following early work in model system genetics, we established a broad drug discovery and development platform that has served as the foundation for our continued efforts to bring new cancer therapies to patients in need. Our discovery efforts have resulted in four commercially available products, CABOMETYX® (cabozantinib), COMETRIQ® (cabozantinib), COTELLIC® (cobimetinib) and MINNEBRO® (esaxerenone), and we have entered into partnerships with leading pharmaceutical companies to bring these important medicines to patients worldwide. Supported by revenues from our marketed products and collaborations, we are committed to prudently reinvesting in our business to maximize the potential of our pipeline. We are supplementing our existing therapeutic assets with targeted business development activities and internal drug discovery — all to deliver the next generation of Exelixis medicines and help patients recover stronger and live longer. Exelixis is a member of Standard & Poor's (S&P) MidCap 400 index, which measures the performance of profitable mid-sized companies. For more information about Exelixis, please visit www.exelixis.com, follow @ExelixisInc on Twitter or like Exelixis, Inc. on Facebook.

Forward-Looking Statements

This press release contains forward-looking statements, including, without limitation, statements related to: Genentech's plans to present the IMspire150 data at an upcoming medical meeting and discuss the data with health authorities around the world, including the U.S. Food and Drug Administration and European Medicines Agency; and Exelixis' plans to reinvest in its business to maximize the potential of the company's pipeline, including through targeted business development activities and internal drug discovery. Any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements and are based upon Exelixis' current plans, assumptions, beliefs, expectations, estimates and projections. Forward-looking statements involve risks and uncertainties. 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: the availability of data at referenced times; risks and uncertainties related regulatory review and approval processes and Daiichi Sankyo's compliance with applicable legal and regulatory requirements; uncertainties inherent in the product development process; the degree of market acceptance of treatment combinations with COTELLIC in the territories where they are approved, and Genentech's ability to obtain or maintain coverage and reimbursement for this product; Exelixis' dependence on its relationship with Genentech, including Genentech's investment in the resources necessary to successfully commercialize treatment combinations with COTELLIC in the territories where they are approved; risks and uncertainties related to regulatory review and approval processes; Exelixis' and Genentech's continuing compliance with applicable legal and regulatory requirements; unexpected concerns that may arise as a result of the occurrence of adverse safety events or additional data analyses of clinical trials evaluating cobimetinib or other compounds with which it may be combined; Exelixis' dependence on third-party vendors for the manufacture and supply of cobimetinib; market competition, including the potential for competitors to obtain approval for generic versions of COTELLIC; Exelixis' and Genentech's ability to protect their respective intellectual property rights; changes in economic and business conditions; and other factors affecting Exelixis and its partnerships discussed under the caption "Risk Factors" in Exelixis' Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on October 30, 2019, and in Exelixis' future filings with the SEC. All forward-looking statements in this press release are based on information available to Exelixis as of the date of this press release, and Exelixis undertakes no obligation to update or revise any forward-looking statements contained herein.

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