Exelixis Provides Update on IMblaze370 Phase 3 Pivotal Trial of Atezolizumab and Cobimetinib in Patients With Heavily Pretreated Locally Advanced or Metastatic Colorectal Cancer

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– Study did not meet its primary endpoint of improving overall survival versus regorafenib –

– Results will be submitted for presentation at an upcoming medical meeting –

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--May 10, 2018-- Exelixis, Inc. (Nasdaq:EXEL) today announced that IMblaze370, the phase 3 pivotal trial of atezolizumab (TECENTRIQ®), an anti-PDL1 antibody discovered and developed by Genentech, a member of the Roche Group, and cobimetinib (COTELLIC®), an Exelixis-discovered MEK inhibitor, did not meet its primary endpoint. Genentech, Exelixis' collaborator and sponsor of the IMblaze370 trial, informed the company that the combination of atezolizumab and cobimetinib did not deliver an improvement in overall survival (OS) versus regorafenib. The IMblaze370 trial evaluated the combination in patients with difficult-to-treat, locally advanced or metastatic colorectal cancer (CRC) whose disease had progressed or who were intolerant to at least two systemic chemotherapy regimens.

The safety profile for the combination appeared consistent with the known safety profile of each individual medicine, and no new safety signals were identified with the combination. Genentech will further examine results from IMblaze370 and plans to present the data at an upcoming medical meeting.

"We are disappointed that the IMblaze370 trial did not reach a positive conclusion," said Michael M. Morrissey, Ph.D., President and Chief Executive Officer of Exelixis. "Metastatic colorectal cancer is an aggressive and difficult-to-treat disease, and patients and clinicians would be well served by additional treatment options. We will continue to work with Genentech on the evaluation of cobimetinib's potential in other tumor types, including in melanoma, in which there are two ongoing phase 3 pivotal trials. Separately, Exelixis remains focused on and committed to maximizing the potential of the cabozantinib franchise through our commercial activities and ongoing clinical development program evaluating the compound alone, or in combination with immune checkpoint inhibitors, across numerous tumor types."

Other ongoing late-stage clinical trials of cobimetinib include: IMspire150 TRILOGY, a fully enrolled study of cobimetinib, vemurafenib, and atezolizumab in previously untreated patients with BRAF V600-positive metastatic melanoma; and IMspire170, which is evaluating cobimetinib and atezolizumab in BRAF V600-wild type metastatic melanoma.

About the IMblaze370 Phase 3 Pivotal Trial

In early June 2016, shortly before the initial presentation of data from the phase 1b clinical trial of cobimetinib and atezolizumab at the 2016 Annual Meeting of the American Society of Clinical Oncology, Genentech initiated IMblaze370, a phase 3 pivotal trial of cobimetinib plus atezolizumab and atezolizumab monotherapy versus regorafenib in patients with locally advanced or metastatic CRC who had received at least two prior regimens of chemotherapy. The trial enrolled 363 patients who were randomized 2:1:1 to receive cobimetinib plus atezolizumab, atezolizumab alone, or regorafenib.

Patients in the combination arm received cobimetinib on days 1 to 21 plus atezolizumab on day 1 and day 15 in a 28-day cycle. Patients in the experimental monotherapy arm received atezolizumab on day 1 of each 21-day cycle. Patients in the control arm received regorafenib on days 1 to 21 in a 28-day cycle. All patients continued to receive study drug until clinical benefit was no longer observed.

The primary endpoint of IMblaze370 is OS; key secondary endpoints include progression-free survival, objective response rate, and duration of response. IMblaze370 completed enrollment in the first quarter of 2017. More information about IMblaze370 is available at www.clinicaltrials.gov.

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 now approved in multiple countries, including the U.S., European Union, Switzerland, Canada, Australia and Brazil, to treat specific forms of BRAF mutation-positive unresectable or metastatic melanoma, in combination with vemurafenib (ZELBORAF®). The trade name for cobimetinib is COTELLIC®. Cobimetinib is also the subject of a clinical development program aimed at evaluating its potential in combination with a variety of investigational and approved therapies in disease settings including metastatic melanoma, triple-negative breast cancer and colorectal carcinoma.

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

ZELBORAF.

COTELLIC Indication

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.
- 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 changes

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.

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

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 genetic systems, 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. We discovered our lead compounds, cabozantinib and cobimetinib, and advanced them into clinical development before entering into partnerships with leading biopharmaceutical companies in our efforts to bring these medicines to patients globally. We are steadfast in our commitment to prudently reinvest in our business to maximize the potential of our pipeline. We intend to supplement 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 recently earned a spot on Deloitte's Technology Fast 500 list, a yearly award program honoring the 500 fastest-growing companies over the past four years. For more information about Exelixis, please visit www.exelixis.com or follow @ExelixisInc on Twitter.

Forward-Looking Statement Disclaimer

This press release contains forward-looking statements, including, without limitation, statements related to: Genentech's intent to further examine results from IMblaze and plans to present the data at an upcoming medical meeting; Exelixis' plan to continue to work with Genentech on the evaluation of cobimetinib's potential in other tumor types; Exelixis' focus on and commitment to maximizing the potential of the cabozantinib franchise through commercial activities and ongoing clinical development program evaluating the compound alone, or in combination with immune checkpoint inhibitors, across multiple tumor types; the financial terms of Exelixis' collaboration with Genentech and eligibility to receive royalties on sales; Exelixis' commitment to reinvesting in its business to maximize the potential of its pipeline, including supplementing its existing therapeutic assets through targeted business development activities and internal drug discovery; and Exelixis' mission to deliver the next generation of Exelixis medicines and help patients recover stronger and live longer. Words such as "will," "plan," "focused," "eligible," "commitment," "intend," 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. 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: Exelixis' dependence on its relationship with Genentech/Roche with respect to cobimetinib and Exelixis' ability to maintain its rights under the collaboration; risks related to the potential failure of cobimetinib to demonstrate safety and efficacy in clinical testing; the availability of data at future medical meeting; market acceptance and the availability of coverage and reimbursement for COTELLIC; risks and uncertainties related to regulatory review and approval processes; Exelixis' ability to conduct clinical trials of its product candidates sufficient to achieve a positive completion; the level of costs associated with Exelixis' commercialization, research and development and other activities; competition in the area of business development activities and the inherent uncertainty of the drug discovery process; Exelixis' dependence on its relationships with its cabozantinib collaboration partners, including, the level of their investment in the resources necessary to successfully commercialize cabozantinib in the territories where it is approved; Exelixis' dependence on third-party vendors for the development, manufacture and supply of its products; Exelixis' ability to protect the company's intellectual property rights; 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 May 2, 2018, and in Exelixis' future 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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