Exelixis Announces Presentation of Updated Phase 1b Results for the Combination of Cobimetinib and Atezolizumab in Metastatic Colorectal Cancer at the 2018 American Society of Clinical Oncology Gastrointestinal Cancers Symposium

January 20, 2018

– Median overall survival of 13 months in patients with microsatellite-stable (MSS) disease –

– Durable responses observed in heavily pretreated patient population –

– Top-line results for IMblaze370, the phase 3 pivotal trial of the cobimetinib-atezolizumab combination in MSS colorectal cancer are anticipated in 1H 2018 –

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jan. 20, 2018-- Exelixis, Inc. (NASDAQ:EXEL) today announced the presentation of updated results from the Genentech-sponsored phase 1b clinical trial of cobimetinib (COTELLIC®), an Exelixis-discovered MEK inhibitor, in combination with atezolizumab (TECENTRIQ®), an anti-PDL1 antibody discovered and developed by Genentech, a member of the Roche Group, in patients with metastatic colorectal cancer (CRC). Johanna Bendell, M.D., Chief Development Officer at the Sarah Cannon Research Institute/Tennessee Oncology (Nashville, Tennessee), presented the results (Abstract #560) during an oral abstract session at the 2018 American Society of Clinical Oncology Gastrointestinal Cancers Symposium this morning in San Francisco.

"The results of this study suggest the combination of cobimetinib and atezolizumab continues to be associated with encouraging tolerability and clinical activity in patients with metastatic colorectal cancer," said Michael M. Morrissey, Ph.D., President and Chief Executive Officer of Exelixis. "In addition, the combination demonstrated a median 13-month overall survival as well as durable responses in patients with microsatellite-stable tumors, which have historically been resistant to immunotherapy administered on its own. We look forward to the readout of IMblaze370, the ongoing confirmatory phase 3 pivotal trial evaluating the combination of cobimetinib and atezolizumab in the third-line treatment setting, anticipated in the first half of this year."

The ongoing phase 1b trial (NCT01988896) evaluates the combination of cobimetinib and atezolizumab in a variety of solid tumors. Following the selection of a recommended dose in the trial's dose escalation stage, expansion cohorts in metastatic CRC, non-small cell lung cancer, and melanoma began enrolling. The trial's primary endpoints are the evaluation of the safety and tolerability of the combination. Secondary endpoints include investigator-assessed objective response rate (ORR), progression-free survival (PFS) by RECIST 1.1, and overall survival (OS).

As of the September 4, 2017 data cut-off, a total of 84 patients with metastatic CRC from both stages of the trial were evaluable for safety and clinical activity. All patients were previously treated, with 79 percent (n=66) receiving 5+ prior systemic therapies. Microsatellite instability (MSI) status was locally reported and centrally confirmed by next-generation sequencing-based scoring; half of the evaluable patients (n=42) were classified as having microsatellite-stable (MSS) disease, a form of CRC for which PD1 and PD-L1 inhibitors alone have shown minimal activity. An additional 11 percent of patients (n=9) were classified as MSI-low. One patient was MSI-high, while the MSI status of the remaining 32 patients was unknown. The majority of patients (68 percent; n=57) had KRAS-mutant tumors. The median follow-up across all CRC patients was 17.0 months (range 0.5 to 33.8 months).

Preliminary Clinical Activity. Across all 84 CRC patients, median OS was 9.8 months, with 6-month and 12-month landmark OS at 65 and 43 percent, respectively. For patients with confirmed MSS disease (n=42), median OS was 13.0 months, with 6-month and 12-month landmark OS at 71 and 51 percent, respectively. Across all 84 patients, median PFS was 1.9 months, with six-month landmark PFS at 18 percent. For patients with MSS disease (n=42), median PFS was 2.5 months, with six-month landmark PFS at 27 percent.

Investigators also conducted a best overall response (BOR) analysis across all patients, although seven patients had missing or unevaluable BOR data. The ORR was eight percent (n=7). Of the seven confirmed Partial Responses (PRs), four were in patients with MSS tumors, and one was in a patient with MSI-low tumors. The remaining two PRs were in patients whose tumor MSI status was unknown. The Disease Control Rate (PR + Stable Disease [SD]) was 31 percent, comprised of the 7 PRs (8%) and 19 instances (23%) of SD. The median duration of response was 14.3 months.

Safety. Investigators reported the majority of adverse events (AEs) were manageable. There were no treatment-related grade 5 AEs, and the incidence of treatment-related grade 3 and 4 AEs was 38 percent (n=32). Rash, diarrhea, fatigue, and increased blood creatine phosphokinase were the most frequent treatment-related grade 3-4 AEs reported (five percent each).

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 ASCO Annual Meeting, Genentech initiated IMblaze370, a phase 3 pivotal trial of cobimetinib plus atezolizumab and atezolizumab monotherapy versus regorafenib in patients with previously treated, unresectable, advanced metastatic CRC. The trial targeted an enrollment of 360 patients who had received at least two prior chemotherapy regimens. The primary endpoint of IMblaze370 is OS. IMblaze370 completed enrollment in the first quarter of 2017, and Genentech has guided it expects top-line results from the trial in the first half of 2018. 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®.

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

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. 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 misses a dose of COTELLIC® or vomits after taking their dose, 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 weaknes
    - 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
- sunburn or sun sensitivity

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)

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®.

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 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: the clinical and therapeutic potential of the combination of cobimetinib and atezolizumab for patients with metastatic CRC; the expected timing for top-line results from IMblaze370 in the first half of 2018; 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 "could," "expects," "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; risks and uncertainties related to regulatory review and approval processes; the availability of data at the referenced time; market acceptance and the availability of coverage and reimbursement for COTELLIC; 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 November 1, 2017, 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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