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Exelixis and Ipsen Announce Detailed Results from Phase 3 COSMIC-311 Pivotal Trial of Cabozantinib in Patients with Previously Treated Radioactive Iodine-Refractory Differentiated Thyroid Cancer Presented at ASCO 2021

– New findings demonstrate the significant progression-free survival benefit seen in the intent-to-treat population was also consistent across subgroups –

– Results from COSMIC-311 served as basis for Exelixis' recent supplemental New Drug Application to U.S. Food and Drug Administration –

***– Data are in press to be published in* The Lancet Oncology –**

ALAMEDA, Calif. & PARIS – June 7, 2021 – Exelixis, Inc. (NASDAQ: EXEL) and Ipsen (Euronext:IPN; ADR:IPSEY) today announced detailed results from the phase 3 COSMIC-311 pivotal trial of cabozantinib (CABOMETYX®) in patients with previously treated radioactive iodine-refractory differentiated thyroid cancer (DTC). Results from the trial, which met the co-primary endpoint of significant improvement in progression-free survival (PFS) assessed by blinded independent radiology committee (BIRC), are in press to be published in *The Lancet Oncology* and have been submitted to the U.S. Food and Drug Administration (FDA). The data are being presented during the Oral Abstract Session: Head and Neck Cancer at 11:45 a.m. PT on Monday, June 7 at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting (abstract #6001).

"Following disease progression on anti-VEGFR therapy, patients with radioactive iodine-refractory differentiated thyroid cancer currently have no standard of care available to them, making the positive results of the COSMIC-311 trial an important clinical advance for this community in need of additional treatment options," said Marcia S. Brose, M.D., Ph.D., Full Professor of Otorhinolaryngology: Head and Neck Surgery and Director of the Center for Rare Cancers and Personalized Therapy at the Abramson

Cancer Center of the University of Pennsylvania, and principal investigator of COSMIC-311. "The significant improvement in progression-free survival and favorable trend for overall survival suggest cabozantinib could be an important new option for these patients."

Results from COSMIC-311 served as the basis for the supplemental New Drug Application that Exelixis has submitted to the FDA, seeking an expanded indication for CABOMETYX for patients 12 and older with DTC that has progressed following prior therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).

As previously announced, at a planned interim analysis, cabozantinib demonstrated a significant reduction in the risk of disease progression or death of 78% versus placebo (hazard ratio [HR]: 0.22; 96% confidence interval [CI]: 0.13-0.36; P<0.0001) in the intent-to-treat (ITT) population. At a median follow-up of 6.2 months, median PFS was not reached (96% CI: 5.7 months – not estimable) in patients treated with cabozantinib and was 1.9 months (96% CI: 1.8-3.6 months) for placebo. The data presented at the 2021 ASCO Annual Meeting demonstrate that HRs for PFS consistently favored cabozantinib over placebo for prespecified subgroups, including age ≤65 vs. >65; prior treatment with lenvatinib (yes vs. no), and number of prior vascular endothelial growth factor receptor (VEGFR)-targeting therapies (1 vs. 2).

The results for the co-primary endpoint of objective response rate in the first 100 randomized patients after six months favored cabozantinib at 15% versus 0% for placebo, although this difference was not statistically significant (P=0.028). In the ITT population, a reduction in target lesion size was found in 76% of patients receiving cabozantinib versus 29% of patients receiving placebo; median overall survival was not reached in either treatment arm but favored cabozantinib (HR: 0.54; 95% CI: 0.27-1.11).

The safety profile was consistent with that previously observed for cabozantinib and adverse events (AEs) were managed with dose modifications. The discontinuation rate due to treatment-emergent AEs was 5% for cabozantinib versus 0% for placebo. The most common (≥5%) all-causality grade 3 or 4 AEs with cabozantinib were palmar-plantar erythrodysesthesia (10%), hypertension (9%), fatigue (8%), diarrhea (7%) and hypocalcemia (7%). There were no treatment-related deaths per investigator.

In February 2021, the U.S. FDA granted Breakthrough Therapy Designation to cabozantinib as a potential treatment for patients with DTC that has progressed following prior therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).

"We're excited to offer a more detailed picture of results from the COSMIC-311 trial following the previous announcements that the trial met its co-primary endpoint of PFS, and that we received Breakthrough Therapy Designation for cabozantinib earlier this year," said Gisela Schwab, M.D., President, Product Development and Medical Affairs and Chief Medical Officer, Exelixis. "The submission of our regulatory application for CABOMETYX to the FDA is an important step toward our goal of addressing an urgent treatment need for this patient community as soon as possible."

"The results from the COSMIC-311 phase 3 trial have been highly anticipated, with the current survival time for people living with this uncommon form of differentiated thyroid cancer at just three to five years from the time metastatic lesions are detected," said Howard Mayer, M.D., Executive Vice President and Head of Research and Development, Ipsen. "We're delighted to share these data at ASCO together with Exelixis, highlighting our continued commitment to exploring the potential of cabozantinib across a range of hard-to-treat cancers. We look forward to working with regulatory authorities in our territories with the aim of bringing a meaningful new treatment option to a patient population in critical need."

About COSMIC-311
COSMIC-311 is a global, multicenter, randomized, double-blind, placebo-controlled phase 3 pivotal trial that aimed to enroll approximately 300 patients at 150 sites globally. Patients were randomized in a 2:1 ratio to receive either cabozantinib 60 mg or placebo once daily. The co-primary endpoints are PFS and ORR, both assessed by BIRC. Patients randomized to placebo were eligible to cross over to open label cabozantinib upon BIRC-confirmed disease progression. Exelixis is sponsoring COSMIC-311, and Ipsen is co-funding the trial. More information about this trial is available at ClinicalTrials.gov.

About Differentiated Thyroid Cancer
Approximately 44,000 new cases of thyroid cancer will be diagnosed in the U.S. in 2021.[1] Nearly three out of four of these cases will be in women, and the disease is more commonly diagnosed at a younger age compared to most other adult cancers.[2] While cancerous thyroid tumors include differentiated, medullary and anaplastic forms, differentiated thyroid tumors make up about 90 percent of cases.[2] These include papillary, follicular and Hürthle cell cancer.[2] Differentiated thyroid cancer is typically treated with surgery followed by ablation of the remaining thyroid tissue with radioiodine, but approximately 5% to 15% of cases are resistant to radioiodine treatment. [2,3] For these patients, life expectancy is only three to five years from the time metastatic lesions are detected.[4,5,6]

About CABOMETYX® (cabozantinib)
In the U.S., CABOMETYX tablets are approved for the treatment of patients with advanced RCC; for the treatment of patients with HCC who have been previously treated with sorafenib; and for patients with advanced RCC as a first-line treatment in combination with nivolumab. CABOMETYX tablets have also received regulatory approvals in the European Union and additional countries and regions worldwide. In 2016, Exelixis granted Ipsen exclusive rights for the commercialization and further clinical development of cabozantinib outside of the United States and Japan. In 2017, Exelixis granted exclusive rights to Takeda Pharmaceutical Company Limited for the commercialization and further clinical development of cabozantinib for all future indications in Japan. Exelixis holds the exclusive rights to develop and commercialize cabozantinib in the United States.

CABOMETYX is not indicated for the treatment of differentiated thyroid cancer.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage: Severe and fatal hemorrhages occurred with CABOMETYX. The incidence of Grade 3 to 5 hemorrhagic events was 5% in CABOMETYX patients in RCC and HCC studies. Discontinue CABOMETYX for Grade 3 or 4 hemorrhage. Do not administer CABOMETYX to patients who have a recent history of hemorrhage, including hemoptysis, hematemesis, or melena.

Perforations and Fistulas: Fistulas, including fatal cases, occurred in 1% of CABOMETYX patients. Gastrointestinal (GI) perforations, including fatal cases, occurred in 1% of CABOMETYX patients. Monitor patients for signs and symptoms of fistulas and perforations, including abscess and sepsis. Discontinue CABOMETYX in patients who experience a Grade 4 fistula or a GI perforation.

Thrombotic Events: CABOMETYX increased the risk of thrombotic events. Venous thromboembolism occurred in 7% (including 4% pulmonary embolism) and arterial thromboembolism in 2% of CABOMETYX patients. Fatal thrombotic events occurred in CABOMETYX patients. Discontinue CABOMETYX in patients who develop an acute myocardial infarction or serious arterial or venous thromboembolic events that require medical intervention.

– more –

Hypertension and Hypertensive Crisis: CABOMETYX can cause hypertension, including hypertensive crisis. Hypertension was reported in 36% (17% Grade 3 and <1% Grade 4) of CABOMETYX patients. Do not initiate CABOMETYX in patients with uncontrolled hypertension. Monitor blood pressure regularly during CABOMETYX treatment. Withhold CABOMETYX for hypertension that is not adequately controlled with medical management; when controlled, resume at a reduced dose. Discontinue CABOMETYX for severe hypertension that cannot be controlled with anti-hypertensive therapy or for hypertensive crisis.

Diarrhea: Diarrhea occurred in 63% of CABOMETYX patients. Grade 3 diarrhea occurred in 11% of CABOMETYX patients. Withhold CABOMETYX until improvement to Grade 1 and resume at a reduced dose for intolerable Grade 2 diarrhea, Grade 3 diarrhea that cannot be managed with standard antidiarrheal treatments, or Grade 4 diarrhea.

Palmar-Plantar Erythrodysesthesia (PPE): PPE occurred in 44% of CABOMETYX patients. Grade 3 PPE occurred in 13% of CABOMETYX patients. Withhold CABOMETYX until improvement to Grade 1 and resume at a reduced dose for intolerable Grade 2 PPE or Grade 3 PPE.

Hepatotoxicity: CABOMETYX in combination with nivolumab can cause hepatic toxicity with higher frequencies of Grades 3 and 4 ALT and AST elevations compared to CABOMETYX alone.

Monitor liver enzymes before initiation of and periodically throughout treatment. Consider more frequent monitoring of liver enzymes than when the drugs are administered as single agents. For elevated liver enzymes, interrupt CABOMETYX and nivolumab and consider administering corticosteroids.

With the combination of CABOMETYX and nivolumab, Grades 3 and 4 increased ALT or AST were seen in 11% of patients. ALT or AST >3 times ULN (Grade ≥2) was reported in 83 patients, of whom 23 (28%) received systemic corticosteroids; ALT or AST resolved to Grades 0-1 in 74 (89%). Among the 44 patients with Grade ≥2 increased ALT or AST who were rechallenged with either CABOMETYX (n=9) or nivolumab (n=11) as a single agent or with both (n=24), recurrence of Grade ≥2 increased ALT or AST was observed in 2 patients receiving CABOMETYX, 2 patients receiving nivolumab, and 7 patients receiving both CABOMETYX and nivolumab.

Adrenal Insufficiency: CABOMETYX in combination with nivolumab can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold CABOMETYX and/or nivolumab depending on severity.

Adrenal insufficiency occurred in 4.7% (15/320) of patients with RCC who received CABOMETYX with nivolumab, including Grade 3 (2.2%), and Grade 2 (1.9%) adverse reactions. Adrenal insufficiency led to permanent discontinuation of CABOMETYX and nivolumab in 0.9% and withholding of CABOMETYX and nivolumab in 2.8% of patients with RCC.

Approximately 80% (12/15) of patients with adrenal insufficiency received hormone replacement therapy, including systemic corticosteroids. Adrenal insufficiency resolved in 27% (n=4) of the 15 patients. Of the 9 patients in whom CABOMETYX with nivolumab was withheld for adrenal insufficiency, 6 reinstated treatment after symptom improvement; of these, all (n=6) received hormone replacement therapy and 2 had recurrence of adrenal insufficiency.

Proteinuria: Proteinuria was observed in 7% of CABOMETYX patients. Monitor urine protein regularly during CABOMETYX treatment. Discontinue CABOMETYX in patients who develop nephrotic syndrome.

Osteonecrosis of the Jaw (ONJ): ONJ occurred in <1% of CABOMETYX patients. ONJ can manifest as jaw pain, osteomyelitis, osteitis, bone erosion, tooth or periodontal infection, toothache, gingival ulceration or erosion, persistent jaw pain, or slow healing of the mouth or jaw after dental surgery. Perform an oral examination prior to CABOMETYX initiation and periodically during treatment. Advise patients regarding good oral hygiene practices. Withhold CABOMETYX for at least 3 weeks prior to scheduled dental surgery or invasive dental procedures, if possible. Withhold CABOMETYX for development of ONJ until complete resolution.

Impaired Wound Healing: Wound complications occurred with CABOMETYX. Withhold CABOMETYX for at least 3 weeks prior to elective surgery. Do not administer CABOMETYX for at least 2 weeks after major surgery and until adequate wound healing is observed. The safety of resumption of CABOMETYX after resolution of wound healing complications has not been established.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS): RPLS, a syndrome of subcortical vasogenic edema diagnosed by characteristic findings on MRI, can occur with CABOMETYX. Evaluate for RPLS in patients presenting with seizures, headache, visual disturbances, confusion, or altered mental function. Discontinue CABOMETYX in patients who develop RPLS.

Embryo-Fetal Toxicity: CABOMETYX can cause fetal harm. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Verify the pregnancy status of females of reproductive potential prior to initiating CABOMETYX and advise them to use effective contraception during treatment and for 4 months after the last dose.

ADVERSE REACTIONS

The most common (≥20%) adverse reactions are:

CABOMETYX as a single agent: diarrhea, fatigue, decreased appetite, PPE, nausea, hypertension, vomiting, weight decreased, constipation, and dysphonia.

CABOMETYX in combination with nivolumab: diarrhea, fatigue, hepatotoxicity, PPE, stomatitis, rash, hypertension, hypothyroidism, musculoskeletal pain, decreased appetite, nausea, dysgeusia, abdominal pain, cough, and upper respiratory tract infection.

DRUG INTERACTIONS

Strong CYP3A4 Inhibitors: If coadministration with strong CYP3A4 inhibitors cannot be avoided, reduce the CABOMETYX dosage. Avoid grapefruit or grapefruit juice.

Strong CYP3A4 Inducers: If coadministration with strong CYP3A4 inducers cannot be avoided, increase the CABOMETYX dosage. Avoid St. John's wort.

USE IN SPECIFIC POPULATIONS

Lactation: Advise women not to breastfeed during CABOMETYX treatment and for 4 months after the final dose.

Hepatic Impairment: In patients with moderate hepatic impairment, reduce the CABOMETYX dosage. Avoid CABOMETYX in patients with severe hepatic impairment.

Please see accompanying full Prescribing Information
https://www.cabometyx.com/downloads/CABOMETYXUSPI.pdf**.**

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.FDA.gov/medwatch or call 1-800-FDA-1088.

For detailed recommendations on the use of CABOMETYX in the European Union, please see the Summary of Product Characteristics.

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 the Standard & Poor's (S&P) MidCap 400 index, which measures the performance of profitable mid-sized companies. In November 2020, the company was named to *Fortune*'s 100 Fastest-Growing Companies list for the first time, ranking 17th overall and the third-highest biopharmaceutical company. For more information about Exelixis, please visit www.exelixis.com, follow @ExelixisInc on Twitter or like Exelixis, Inc. on Facebook.

About Ipsen
Ipsen is a global mid-size biopharmaceutical company with a focus on transformative medicines in Oncology, Rare Disease and Neuroscience. Ipsen also has a well-established Consumer Healthcare business. With total sales over €2.5 billion in 2020, Ipsen sells more than 20 drugs in over 110 countries, with a direct commercial presence in more than 30 countries. Ipsen's R&D is focused on its innovative and differentiated technological platforms located in the heart of the leading biotechnological and life sciences hubs (Paris-Saclay, France; Oxford, UK; Cambridge, US; Shanghai, China). The Group has about 5,700 employees worldwide. Ipsen is listed in Paris (Euronext: IPN) and in the United States through a Sponsored Level I American Depositary Receipt program (ADR: IPSEY). For more information on Ipsen, visit www.ipsen.com.

Exelixis Forward-Looking Statements
This press release contains forward-looking statements, including, without limitation, statements related to: the presentation of data from the COSMIC-311 pivotal trial at ASCO 2021 and forthcoming publication of such data in *The Lancet Oncology*; the therapeutic potential of CABOMETYX for patients with radioactive iodine-refractory DTC; Exelixis' and Ipsen's commitment to exploring the potential of cabozantinib across a range of hard-to-treat cancers; 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 the referenced times; complexities and the unpredictability of the regulatory review and approval processes in the U.S. and elsewhere; Exelixis' continuing compliance with applicable legal and regulatory requirements; the potential failure of cabozantinib to demonstrate safety and/or efficacy in future trials; unexpected concerns that may arise as a result of the occurrence of adverse safety events or additional data analyses of clinical trials evaluating CABOMETYX; Exelixis' dependence on third-party vendors for the development, manufacture and supply of cabozantinib; Exelixis' ability to protect its intellectual property rights; market competition, including the potential for competitors to obtain approval for generic versions of CABOMETYX; changes in economic and business conditions, including as a result of the COVID-19 pandemic; and other factors affecting Exelixis and its development programs discussed under the caption "Risk Factors" in Exelixis' Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on May 6, 2021, 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, except as required by law.

Ipsen—Cautionary Note Regarding Forward-Looking Statements

The forward-looking statements, objectives and targets contained herein are based on the Group's management strategy, current views and assumptions. Such statements involve known and unknown risks and uncertainties that may cause actual results, performance or events to differ materially from those anticipated herein. All of the above risks could affect the Group's future ability to achieve its financial targets, which were set assuming reasonable macroeconomic conditions based on the information available today. Use of the words "believes", "anticipates" and "expects" and similar expressions are intended to identify forward-looking statements, including the Group's expectations regarding future events, including regulatory filings and determinations. Moreover, the targets described in this document were prepared without taking into account external growth assumptions and potential future acquisitions, which may alter these parameters. These objectives are based on data and assumptions regarded as reasonable by the Group. These targets depend on conditions or facts likely to happen in the future, and not exclusively on historical data. Actual results may depart significantly from these targets given the occurrence of certain risks and uncertainties, notably the fact that a promising product in early development phase or clinical trial may end up never being launched on the market or reaching its commercial targets, notably for regulatory or competition reasons and also taking into consideration assessment delays of certain clinical trials in light of the ongoing COVID-19 pandemic. The Group must face or might face competition from generic products that might translate into a loss of market share. Furthermore, the Research and Development process involves several stages each of which involves the substantial risk that the Group may fail to achieve its objectives and be forced to abandon its efforts with regards to a product in which it has invested significant sums. Therefore, the Group cannot be certain that favorable results obtained during pre-clinical trials will be confirmed subsequently during clinical trials, or that the results of clinical trials will be sufficient to demonstrate the safe and effective nature of the product concerned. There can be no guarantees a product will receive the necessary regulatory approvals or that the product will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements. Other risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the Group's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the

Group's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions. The Group also depends on third parties to develop and market some of its products which could potentially generate substantial royalties; these partners could behave in such ways which could cause damage to the Group's activities and financial results. The Group cannot be certain that its partners will fulfil their obligations. It might be unable to obtain any benefit from those agreements. A default by any of the Group's partners could generate lower revenues than expected. Such situations could have a negative impact on the Group's business, financial position or performance. The Group expressly disclaims any obligation or undertaking to update or revise any forward-looking statements, targets or estimates contained in this press release to reflect any change in events, conditions, assumptions or circumstances on which any such statements are based, unless so required by applicable law. The Group's business is subject to the risk factors outlined in its registration documents filed with the French Autorité des Marchés Financiers. The risks and uncertainties set out are not exhaustive and the reader is advised to refer to the Group's 2018 Registration Document available on its website (www.ipsen.com).

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