PRESS RELEASE

Ipsen and Exelixis announce phase 3 trial results of cabozantinib demonstrating significant overall survival benefit in patients with previously treated advanced hepatocellular carcinoma

Pivotal phase 3 CELESTIAL trial results, including additional subset analyses, to be presented during oral session on Friday, January 19 at the 2018 American Society of Clinical Oncology's Gastrointestinal Cancers Symposium (ASCO GI)

In line with and in collaboration with our partner Exelixis, Ipsen expects to file in the first half of 2018 a variation of the initial application to the EMA and other relevant regulatory agencies

Paris (France), 16 January 2018 – Ipsen (Euronext:IPN; ADR:IPSEY) and Exelixis, Inc. (NASDAQ:EXEL) today announced detailed results of the pivotal phase 3 CELESTIAL trial in patients with previously treated advanced hepatocellular carcinoma (HCC), which will be presented in a late-breaking oral session at the 2018 ASCO-GI Symposium being held in San Francisco, January 18-20, 2018. In CELESTIAL, cabozantinib provided a statistically significant and clinically meaningful improvement versus placebo in overall survival (OS), the trial's primary endpoint, at the planned second interim analysis (prespecified critical p value ≤ 0.021) for the population of second- and third-line patients enrolled in this study. Median OS was 10.2 months with cabozantinib versus 8.0 months with placebo (HR 0.76, 95 percent CI 0.63-0.92; p=0.0049). Median progression-free survival (PFS) was more than doubled, at 5.2 months with cabozantinib and 1.9 months with placebo (HR 0.44, 95 percent CI 0.36-0.52; p<0.0001). Objective response rates per RECIST 1.1 were 4 percent with cabozantinib and 0.4 percent with placebo (p=0.0086). Disease control (partial response or stable disease) was achieved by 64 percent of the cabozantinib group compared with 33 percent of the placebo group.

In a subgroup analysis of patients whose only prior therapy for advanced HCC was sorafenib (70 percent of patients in the study), median OS was 11.3 months with cabozantinib versus 7.2 months with placebo (HR 0.70, 95 percent CI 0.55-0.88). Median PFS in the subgroup was 5.5 months with cabozantinib versus 1.9 months with placebo (HR 0.40, 95 percent CI 0.32-0.50). Adverse events were consistent with the known safety profile of cabozantinib.

Ghassan K. Abou-Alfa, M.D., Memorial Sloan Kettering Cancer Center, New York and lead investigator on CELESTIAL, will present detailed findings, including analyses of OS and PFS in various patient subgroups, during Oral Abstract Session B: Cancers of the Pancreas, Small Bowel, and Hepatobiliary Tract, which begins at 2:15 p.m. PT on Friday, January 19, 2018.

"Patients with advanced hepatocellular carcinoma often have a poor prognosis and limited treatment options following prior systemic therapy," said **Dr. Abou-Alfa**. *"The clinically significant benefits in both overall survival and progression-free survival shown in the CELESTIAL trial suggest that, if approved, cabozantinib could become an important addition to the treatment landscape for these patients."*

"We are excited by the potential benefit cabozantinib may offer to patients with previously treated advanced hepatocellular carcinoma," said **Gisela Schwab, M.D., President, Product Development and Medical Affairs and Chief Medical Officer, Exelixis**. *"Given the worldwide prevalence of advanced hepatocellular carcinoma, there is a continued urgency to bring new treatment options to this patient population. We look forward to submitting our supplemental New Drug Application to the FDA for cabozantinib in the first quarter of 2018, and to further advancing our mission to help cancer patients recover stronger and live longer."*

Alexandre Lebeaut, M.D., Executive Vice-President, R&D, Chief Scientific Officer, Ipsen, said: *" Patients diagnosed with advanced hepatocellular carcinoma urgently need new treatment options. The positive results of the pivotal phase 3 CELESTIAL trial are encouraging for both physicians and patients, and we have committed to file in the first half of 2018 a variation of the initial application to the EMA and other relevant regulatory agencies. "*

The most common (≥10 percent) grade 3 or 4 adverse events in the cabozantinib group compared to the placebo group were palmar-plantar erythrodysesthesia (17 percent vs. 0 percent), hypertension (16 percent vs. 2 percent), increased aspartate aminotransferase (12 percent vs. 7 percent), fatigue (10 percent vs. 4 percent), and diarrhea (10 percent vs. 2 percent). Treatment-related grade 5 adverse events occurred in six patients in the cabozantinib group (hepatic failure, esophagobronchial fistula, portal vein thrombosis, upper gastrointestinal hemorrhage, pulmonary embolism and hepatorenal syndrome) and in one patient in the placebo group (hepatic failure). Sixteen percent of patients in the cabozantinib arm and three percent of patients in the placebo arm discontinued treatment due to treatment-related adverse events.

Webcast for the Financial Community

Ipsen and its partner Exelixis will host a live briefing event for the financial community to discuss data presented at the 2018 American Society of Clinical Oncology Gastrointestinal Cancers Symposium (ASCO-GI). The webcast event will be held following the closing of the ASCO-GI day's sessions on Friday, January 19, 2018, beginning at 9:30 p.m. EST / 6:30 p.m. PST (local San Francisco time). During the briefing, Exelixis and Ipsen management, along with an invited guest, will discuss and provide context for the cabozantinib clinical data presented earlier that day at the Symposium. Ipsen previously announced that detailed results from the CELESTIAL trial will be the subject of a late-breaking oral presentation at ASCO-GI. CELESTIAL is a randomized, double-blind, placebo-controlled study of cabozantinib versus placebo in patients with advanced hepatocellular carcinoma who have received prior treatment with sorafenib.

To access the webcast link, log onto www.exelixis.com and proceed to the News & Events / Event Calendar page under the Investors & Media heading. Please connect to the company's website at least 15 minutes prior to the presentation to ensure adequate time for any software download that may be required to listen to the webcast. Alternatively, please call 855-793-2457 (domestic) or 631-485-4921 (international) and provide the conference call passcode 2478857 to join by phone. A webcast replay will be archived on www.exelixis.com for one year. A telephone replay will also be

available until 11:59 p.m. EST on January 26, 2018. Access numbers for the telephone replay are: 855-859-2056 (domestic) and 404-537-3406 (international); the passcode is 2478857.

About the CELESTIAL Study

CELESTIAL is a randomized, double-blind, placebo-controlled study of cabozantinib in patients with advanced HCC conducted at more than 100 sites globally in 19 countries. The trial was designed to enroll 760 patients with advanced HCC who received prior sorafenib and may have received up to two prior systemic cancer therapies for HCC and had adequate liver function. Enrollment of the trial was completed in September 2017. Patients were randomized 2:1 to receive 60 mg of cabozantinib once daily or placebo and were stratified based on etiology of the disease (hepatitis C, hepatitis B or other), geographic region (Asia versus other regions) and presence of extrahepatic spread and/or macrovascular invasion (yes or no). No cross-over was allowed between the study arms during the blinded treatment phase of the study.

The primary endpoint for the trial is OS, and secondary endpoints include objective response rate and PFS. Exploratory endpoints include patient-reported outcomes, biomarkers and safety.

Based on available clinical trial data from various published trials conducted in the second-line setting of advanced HCC, the CELESTIAL trial design assumed a median OS of 8.2 months for the placebo arm. A total of 621 events provide the study with 90 percent power to detect a 32 percent increase in median OS (HR = 0.76) at the final analysis. Two interim analyses were planned and conducted at approximately 50 percent and 75 percent of the planned 621 events. At the first interim analysis conducted by the independent data monitoring committee the observed hazard ratio was 0.71 and the p-value was 0.0041, which did not cross the stopping boundary for the first interim analysis ($p \leq 0.0037$).

On October 16, 2017, Ipsen announced that the independent data monitoring committee recommended that the trial be stopped for efficacy following review of the second planned interim analysis, as the trial had met its primary endpoint of OS (prespecified critical p value ≤ 0.021).

About HCC

Hepatocellular Carcinoma (HCC) is the most common form of liver cancer in adults.[1] The disease originates in cells called hepatocytes found in the liver. With approximately 800'000 new cases diagnosed each year, HCC is the sixth most common cancer and the second-leading cause of cancer deaths worldwide.[2,3] According to the GLOBOCAN data, it is estimated that across the European Union (EU-28) nearly 60'000 new patients will be diagnosed with liver cancer in 2020.[4] Without treatment, patients with the disease in advanced stage usually survive between 4 and 8 months.[5]

About CABOMETYX® (cabozantinib)

Cabometyx® is an oral small molecule inhibitor of receptors, including VEGFR, MET and AXL. In preclinical models, cabozantinib has been shown to inhibit the activity of these receptors, which are involved in normal cellular function and pathologic processes such as tumor angiogenesis, invasiveness, metastasis and drug resistance.

In February of 2016, Exelixis and Ipsen jointly announced an exclusive licensing agreement for the commercialization and further development of cabozantinib indications outside of the United States, Canada and Japan. This agreement was amended in December of 2016 to include commercialization rights for Ipsen

in Canada. On April 25, 2016, the FDA approved Cabometyx® tablets for the treatment of patients with advanced RCC who have received prior anti-angiogenic therapy and on September 9, 2016, the European Commission approved Cabometyx® tablets for the treatment of advanced RCC in adults who have received prior vascular endothelial growth factor (VEGF)-targeted therapy in the European Union, Norway and Iceland. Cabometyx® is available in 20 mg, 40 mg or 60 mg doses. The recommended dose is 60 mg orally, once daily.

Ipsen also submitted to European Medicines Agency (EMA) the regulatory dossier for cabozantinib as a treatment for first-line advanced RCC in the European Union on August 28, 2017; on September 8, 2017, Ipsen announced that the EMA validated the application.

Cabozantinib is not approved for the treatment of advanced hepatocellular carcinoma.

ABOUT CABOMETYX®

CABOMETYX® 20mg, 40mg and 60mg film-coated tablets

Active ingredient: Cabozantinib (S)-malate 20mg, 40mg and 60mg

Other components: Lactose

Indications: CABOMETYX® is indicated for the treatment of advanced renal cell carcinoma (RCC) in adults following prior vascular endothelial growth factor (VEGF)-targeted therapy

Dosage and Administration: The recommended dose of CABOMETYX® is 60 mg once daily. Treatment should continue until the patient is no longer clinically benefiting from therapy or until unacceptable toxicity occurs. Management of suspected adverse drug reactions may require temporary interruption and/or dose reduction of CABOMETYX® therapy. For dose modification, please refer to full SmPC. CABOMETYX® is for oral use. The tablets should be swallowed whole and not crushed. Patients should be instructed to not eat anything for at least 2 hours before through 1 hour after taking CABOMETYX®.

Contraindications: Hypersensitivity to the active substance or to any of the excipients listed in the SmPC.

Special warnings and precautions for use: As most events can occur early in the course of treatment, the physician should evaluate the patient closely during the first eight weeks of treatment to determine if dose modifications are warranted. Events that generally have early onset include hypocalcaemia, hypokalaemia, thrombocytopenia, hypertension, palmarplantar erythrodysaesthesia syndrome (PPES), proteinuria, and gastrointestinal (GI) events (abdominal pain, mucosal inflammation, constipation, diarrhoea, vomiting). Dose reductions and dose interruptions due to an AE occurred in 59.8% and 70%, respectively, of cabozantinib-treated patients in the pivotal clinical trial. Two dose reductions were required in 19.3% of patients. The median time to first dose reduction was 55 days, and to first dose interruption was 38 days.

Perforations and fistulas: Serious gastrointestinal perforations and fistulas, sometimes fatal, have been observed with cabozantinib. Patients who have inflammatory bowel disease (e.g., Crohn's disease, ulcerative colitis, peritonitis, diverticulitis, or appendicitis), have tumour infiltration in the GI tract, or have complications from prior GI surgery (particularly when associated with delayed or incomplete healing) should be carefully evaluated before initiating cabozantinib therapy and subsequently they should be monitored closely for symptoms of perforations and fistulas including abscesses. Persistent or recurring diarrhoea while on treatment may be a risk factor for the development of anal fistula. Cabozantinib should be discontinued in patients who experience a GI perforation or a fistula that cannot be adequately managed.

Thromboembolic events: Events of venous thromboembolism, including pulmonary embolism, and events of arterial thromboembolism have been observed with cabozantinib. Cabozantinib should be used with caution in patients who are at risk for, or who have a history of, these events. Cabozantinib should be discontinued in

patients who develop an acute myocardial infarction or any other clinically significant arterial thromboembolic complication.

Haemorrhage: Severe haemorrhage has been observed with cabozantinib. Patients who have a history of severe bleeding prior to treatment initiation should be carefully evaluated before initiating cabozantinib therapy. Cabozantinib should not be administered to patients that have or are at risk for severe haemorrhage.

Wound complications: Wound complications have been observed with cabozantinib. Cabozantinib treatment should be stopped at least 28 days prior to scheduled surgery, including dental surgery, if possible. The decision to resume cabozantinib therapy after surgery should be based on clinical judgment of adequate wound healing. Cabozantinib should be discontinued in patients with wound healing complications requiring medical intervention.

Hypertension: Hypertension has been observed with cabozantinib. Blood pressure should be well-controlled prior to initiating cabozantinib. During treatment with cabozantinib, all patients should be monitored for hypertension and treated as needed with standard anti-hypertensive therapy. In the case of persistent hypertension despite use of anti-hypertensives, the cabozantinib dose should be reduced. Cabozantinib should be discontinued if hypertension is severe and persistent despite anti-hypertensive therapy and dose reduction of cabozantinib. In case of hypertensive crisis, cabozantinib should be discontinued.

Palmar-plantar erythrodysaesthesia syndrome: Palmar-plantar erythrodysaesthesia syndrome (PPES) has been observed with cabozantinib. When PPES is severe, interruption of treatment with cabozantinib should be considered. Cabozantinib should be restarted with a lower dose when PPES has been resolved to grade 1.

Proteinuria: Proteinuria has been observed with cabozantinib. Urine protein should be monitored regularly during cabozantinib treatment. Cabozantinib should be discontinued in patients who develop nephrotic syndrome.

Reversible posterior leukoencephalopathy syndrome: Reversible Posterior Leukoencephalopathy Syndrome (RPLS), also known as Posterior Reversible Encephalopathy Syndrome (PRES), has been observed with cabozantinib. This syndrome should be considered in any patient presenting with multiple symptoms, including seizures, headache, visual disturbances, confusion or altered mental function. Cabozantinib treatment should be discontinued in patients with RPLS.

Prolongation of QT interval
Cabozantinib should be used with caution in patients with a history of QT interval prolongation, patients who are taking antiarrhythmics, or patients with relevant pre-existing cardiac disease, bradycardia, or electrolyte disturbances. When using cabozantinib, periodic monitoring with on-treatment ECGs and electrolytes (serum calcium, potassium, and magnesium) should be considered.

Interactions: CYP3A4 inducers and inhibitors: Cabozantinib is a CYP3A4 substrate. Concurrent administration of cabozantinib with the strong CYP3A4 inhibitor ketoconazole resulted in an increase in cabozantinib plasma exposure. Caution is required when administering cabozantinib with agents that are strong CYP3A4 inhibitors. Concurrent administration of cabozantinib with the strong CYP3A4 inducer rifampicin resulted in a decrease in cabozantinib plasma exposure. Therefore, chronic administration of agents that are strong CYP3A4 inducers with cabozantinib should be avoided. P-glycoprotein substrates: Cabozantinib was an inhibitor but not a substrate, of P-glycoprotein (P-gp) transport activities in a bi-directional assay system using MDCK-MDR1 cells. Therefore, cabozantinib may have the potential to increase plasma concentrations of co-administered substrates of P-gp. Subjects should be cautioned regarding taking a P-gp substrate while receiving Cabozantinib. MRP2 inhibitors: Administration of MRP2 inhibitors may result in increases in cabozantinib plasma concentrations. Therefore, concomitant use of MRP2 inhibitors should be approached with caution. Bile salt-sequestering agents: Bile salt-sequestering agents may interact with cabozantinib and may impact absorption (or reabsorption) resulting in potentially decreased exposure. The

clinical significance of these potential interactions is unknown. Excipient related warnings: Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Pregnancy and lactation: Avoid pregnancy, use effective methods of contraception and discontinue breast-feeding during treatment with cabozantinib, and for at least 4 months after completing therapy.

Drive and use machines: Caution is recommended

Undesirable effects:
The most common serious adverse reactions associated with cabozantinib are abdominal pain (3%), pleural effusion (3%), diarrhoea (2%), and nausea (2%). The most frequent adverse reactions of any grade (experienced by at least 25% of patients) included diarrhoea (74%), fatigue (56%), nausea (50%), decreased appetite (46%), palmar-plantar erythrodysaesthesia syndrome (PPES) (42%), hypertension (37%), vomiting (32%), weight decreased (31%), and constipation (25%). Other very common adverse reactions: anemia, hypophosphataemia, hypoalbuminaemia, hypomagnesaemia, hyponatraemia, hypokalaemia,hyperkalaemia, hypocalcaemia, hyperbilirubinemia, dysgeusia, headache, dizziness, dysphonia, dyspnea, cough, stomatitis, abdominal pain, dyspepsia, rash, dry skin, muscle spasms, arthralgia, proteinuria, mucosal inflammation, serum ALT, AST, and ALP increased, creatinine increased, triglycerides increased, hyperglycaemia, hypoglycaemia, lymphopenia, neutropenia, thrombocytopenia, GGT increased, amylase increased, blood cholesterol increased, lipase increased
For all common and uncommon adverse reactions, please refer to full SmPC. For more information, see the regularly updated registered product information on the European Medicine Agency www.ema.europa.eu

About Ipsen
Ipsen is a global specialty-driven biopharmaceutical group focused on innovation and specialty care. The group develops and commercializes innovative medicines in three key therapeutic areas - Oncology, Neurosciences and Rare Diseases. Its commitment to oncology is exemplified through its growing portfolio of key therapies for prostate cancer, neuroendocrine tumors, renal cell carcinoma and pancreatic cancer. Ipsen also has a well-established Consumer Healthcare business. With total sales close to €1.6 billion in 2016, Ipsen sells more than 20 drugs in over 115 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). The Group has about 5,100 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.

Ipsen Forward Looking Statement
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. 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 favourable 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 2016 Registration Document available on its website (www.ipsen.com).

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