PRESS RELEASE

Ipsen announces CELESTIAL phase 3 pivotal trial results in the *New England Journal of Medicine*

– Trial results formed the basis of regulatory filings in the U.S. and European Union for CABOMETYX® for previously treated advanced hepatocellular carcinoma (HCC) –

Paris (France), 04 July 2018 – Ipsen (Euronext: IPN; ADR: IPSEY) today announced that *The New England Journal of Medicine* (*NEJM*) published results from the CELESTIAL phase 3 pivotal trial of cabozantinib in patients with previously treated advanced hepatocellular carcinoma (HCC).[1] The data, originally presented at the 2018 American Society of Clinical Oncology's Gastrointestinal Cancers Symposium (ASCO-GI) in January, demonstrate that cabozantinib provided a statistically significant and clinically meaningful improvement in overall survival (OS) versus placebo.

"Patients with this form of advanced liver cancer have very limited treatment options once their disease progresses following treatment with sorafenib," said Ghassan K. Abou-Alfa, M.D., Memorial Sloan Kettering Cancer Center, New York and lead investigator on CELESTIAL. *"These results suggest that, if approved, cabozantinib could become an important addition to the treatment landscape that may help slow disease progression and, critically, improve survival for these patients."*

"Patients with advanced HCC have a very poor prognosis and limited treatment options. Given the worldwide prevalence of advanced HCC, there is a continued urgency to bring new treatment options to these patients", added Lorenza Rimassa M.D., Deputy Director, Medical Oncology Unit, Humanitas Cancer Center Humanitas Research Hospital, Milan. *"The clinically significant benefits in both overall survival and progression-free survival shown in the CELESTIAL trial, in patients previously treated with up to two treatment lines, suggest that cabozantinib could become (when approved) an important addition to the treatment landscape for this patient population."*

Ipsen received validation by the European Medicines Agency in March 2018 for its application for variation to the Cabometyx® marketing authorization to include the new indication for patients with previously treated advanced HCC. Ipsen's partner Exelixis announced in May 2018 that the U.S. Food and Drug Administration (FDA) accepted the company's supplemental New Drug Application (sNDA) for Cabometyx® (cabozantinib) tablets as a treatment for patients with previously treated HCC. The filing has been assigned a Prescription Drug User Fee Act action date of January 14, 2019.

"*This publication of CELESTIAL phase 3 data in the NEJM this week further validates the medical importance of these results for the treatment of patients with advanced liver cancer"* said Alexandre Lebeaut, Executive Vice President Research & Development, Chief Scientific Officer, Ipsen. *"Together with our partner Exelixis we relentlessly contribute to expanding the clinical benefits of cabozantinib across solid tumors to address unmet medical needs".*

Median OS in CELESTIAL 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 patients in the cabozantinib group compared with 33 percent of patients in 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. 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.

About CELESTIAL

CELESTIAL is a randomized, double-blind, placebo-controlled global phase 3 study of cabozantinib versus placebo in patients with advanced hepatocellular carcinoma (HCC) who have been previously treated with sorafenib. The study was conducted at more than 100 sites globally in 19 countries. The trial was designed to enroll 760 patients with advanced hepatocellular carcinoma (HCC) who previously received sorafenib and may have received up to two prior systemic cancer therapies for hepatocellular carcinoma (HCC) and had adequate liver function. Enrollment of the trial was completed in September 2017, and 773 patients were ultimately randomized. 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.

The primary endpoint for the trial is OS, and secondary endpoints include objective response rate and progression-free survival. 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 hepatocellular carcinoma (HCC), the CELESTIAL trial statistics for the primary endpoint of OS 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 50 percent and 75 percent of the planned 621 events.
CELESTIAL trial met its primary endpoint of overall survival (OS), with cabozantinib providing a statistically significant and clinically meaningful improvement in median OS compared to placebo in patients with advanced HCC. The independent data monitoring committee for the study recommended that the trial should be stopped for efficacy following review of the second planned interim analysis. The safety data in the study were consistent with the established profile of cabozantinib.

About HCC
Hepatocellular carcinoma (HCC) is the most common form of liver cancer in adults.[2] The disease originates in cells called hepatocytes found in the liver. With approximately 800'000 new cases diagnosed each year, hepatocellular carcinoma (HCC) is the sixth most common cancer and the second-leading cause of cancer deaths worldwide.[3,4] 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.[5] Without treatment, patients with the disease in advanced stage usually survive between 4 and 8 months.[6]

About CABOMETYX® (cabozantinib)
Cabometyx® is an oral small molecule inhibitor of receptors, including VEGFR, MET, AXL and RET. 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 renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy and on September 9, 2016, the European Commission approved Cabometyx® tablets for the treatment of advanced renal cell carcinoma (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.

On December 19, 2017, Exelixis received approval from the FDA for Cabometyx® for the expanded indication of treatment of first-line advanced RCC .

On May 17, 2018, Ipsen announced that the European Commission approved Cabometyx® for the first-line treatment of adults with intermediate- or poor- risk advanced renal cell carcinomain the European Union, Norway and Iceland.

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

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, Neuroscience 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 over €1.9 billion in 2017, 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 5,400 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.

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 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 2016 Registration Document available on its website (www.ipsen.com).

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