PRESS RELEASE

European Commission approves Ipsen's Cabometyx® (cabozantinib) for the treatment of hepatocellular carcinoma in adults previously treated with sorafenib

Paris (France), 15 November 2018 – Ipsen (Euronext: IPN; ADR: IPSEY) today announced that the European Commission (EC) has approved Cabometyx® (cabozantinib) 20, 40, 60 mg as a monotherapy for hepatocellular carcinoma (HCC) in adults who have previously been treated with sorafenib. This approval allows for the marketing of Cabometyx® (cabozantinib) in this indication in all 28 member states of the European Union, Norway and Iceland.

"Today's EC approval for the use of Cabometyx® provides a much needed new option for HCC patients. Until now, physicians in Europe had only one approved therapy for the 2nd line treatment of this aggressive and difficult-to-treat cancer.[1,2] *We are proud to offer Cabometyx® as an innovative treatment that has been shown to extend survival in previously treated patients with HCC",* said **Harout Semerjian, Chief Commercial Officer, Ipsen**, *"This new indication reinforces Ipsen's commitment to improve patients' lives through the expansion of the clinical benefit of Cabometyx® in the treatment of solid tumors."*

Philippe Merle, M.D., Ph.D., Hepatology and Gastroenterology specialist at La Croix-Rousse Hospital, Lyon, stated: "*Patients with HCC in Europe can now benefit from a treatment that has, through the CELESTIAL trial, proven effective in prolonging life and delaying disease progression. This is a very encouraging development for liver cancer patients, and provides physicians with a new therapeutic option for this complex disease."*

The EC approval is based on the results of the global placebo-controlled CELESTIAL phase 3 pivotal trial which met its primary endpoint of overall survival (OS), with cabozantinib providing a statistically significant and clinically meaningful improvement in OS compared with placebo in patients with advanced HCC who have been previously treated with sorafenib.[3] In July 2018, CELESTIAL phase 3 pivotal trial results were published in the New England Journal of Medicine.[3]

The EC has also approved Cabometyx® for the treatment of advanced renal cell carcinoma (aRCC) both in treatment-naïve adults with intermediate or poor risk (May 2018) and in adults following prior vascular endothelial growth factor (VEGF)-targeted therapy (September 2016).

The detailed recommendations for the use of this product are described in the Summary of Product Characteristics (SmPC), available here.

About CELESTIAL
CELESTIAL is a randomized, double-blind, placebo-controlled global phase 3 study of cabozantinib versus placebo in patients with advanced 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 HCC who previously received 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, 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 (ORR) and progression-free survival (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 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.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. CELESTIAL trial met its primary endpoint, with cabozantinib providing a statistically significant and clinically meaningful improvement in OS compared to placebo in patients with advanced HCC. The safety data in the study were consistent with the established profile of cabozantinib.

About Hepatocellular Carcinoma (HCC)
Hepatocellular carcinoma is the most common form of liver cancer in adults.[4] 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.[5,6] 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.[7] Without treatment, patients with the disease in advanced stage usually survive between 4 and 8 months.[8]

About Cabometyx® (cabozantinib)
Cabometyx® is an oral small molecule inhibitor of tyrosine kinase 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.

Cabometyx® tablets are approved in the United States for the treatment of patients with advanced RCC. 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 also approved in Australia, Brazil, Canada, Hong Kong, South Korea, Switzerland, Taiwan and Ukraine. Cabometyx® is available in 20 mg, 40 mg or 60 mg doses. The recommended dose is 60 mg orally, once daily.

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 carcinoma in the European Union, Norway and Iceland.

On November 15, 2018, Ipsen announced that the European Commission approved Cabometyx® for the second-line treatment of hepatocellular carcinoma in adults who have previously been treated with sorafenib in the European Union, Norway and Iceland.

About Ipsen
Ipsen is a global 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 2017 Registration Document available on its website (www.ipsen.com).

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