

## **Ipsen and its partner Exelixis announce independent radiology committee review confirms results from Phase 2 CABOSUN trial of cabozantinib versus sunitinib in previously untreated advanced renal cell carcinoma**

**IRC confirms cabozantinib significantly improved progression-free survival compared to sunitinib**

**E.U. regulatory submission remains on track for Q3 2017**

**Paris (France), 19 June 2017** – Ipsen (Euronext: IPN; ADR: IPSEY) and its partner Exelixis (NASDAQ:EXEL) today announced that the analysis of the review by a blinded independent radiology review committee (IRC) has confirmed the primary efficacy endpoint results of investigator-assessed progression-free survival (PFS) from the CABOSUN randomized Phase 2 trial of cabozantinib as compared with sunitinib in patients with previously untreated advanced renal cell carcinoma (RCC) with intermediate- or poor-risk disease per the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC). Per the IRC analysis, cabozantinib demonstrated a clinically meaningful and statistically significant reduction in the rate of disease progression or death as measured by PFS. Ipsen remains on track to submit the regulatory dossier for cabozantinib as a treatment for first-line advanced renal cell carcinoma in Europe in the third quarter of 2017.

CABOSUN was conducted by The Alliance for Clinical Trials in Oncology as part of Exelixis' agreement with the National Cancer Institute's Cancer Therapy Evaluation Program (NCI-CTEP). Exelixis and the Alliance cooperative group plan to submit these results for presentation at an upcoming international medical meeting.

**David Meek, Ipsen's Chief Executive Officer** stated: *"Following the European commission approval of cabozantinib in second line advanced RCC, cabozantinib has demonstrated clinical benefit in patients with advanced RCC in the first-line setting. With our partner Exelixis, we are very pleased that CABOSUN's primary endpoint of a statistically significant improvement of progression-free survival has been confirmed by the independent radiology review committee in patients with previously untreated advanced intermediate- or poor-risk RCC. We intend to file these important data with European regulatory authorities in the third quarter of 2017."*

### **About the CABOSUN Study**

*On May 23, 2016, Exelixis announced that CABOSUN met its primary endpoint, demonstrating a statistically significant and clinically meaningful improvement in PFS compared with sunitinib in patients with advanced intermediate- or poor-risk RCC as determined by investigator assessment. CABOSUN was conducted by The Alliance for Clinical Trials in Oncology as part of Exelixis' collaboration with the NCI-CTEP. These results were first presented by Dr. Toni Choueiri at the meeting of the European Society for Medical Oncology (ESMO) 2016, and published in the Journal of Clinical Oncology (Choueiri, JCO, 2016).<sup>1</sup>*

*CABOSUN was a randomized, open-label, active-controlled phase 2 trial that enrolled 157 patients with advanced RCC determined to be intermediate- or poor-risk by the IMDC criteria. Patients were randomized 1:1 to receive cabozantinib (60 mg once daily) or sunitinib (50 mg once daily, four weeks on followed by two weeks off). The primary endpoint was PFS. Secondary endpoints included overall survival and objective response rate. Eligible patients were required to have locally advanced or metastatic clear-cell RCC, ECOG performance status 0-2, and had to be intermediate or poor risk per the IMDC criteria (Heng, JCO, 2009).<sup>2</sup> Prior systemic treatment for RCC was not permitted.*

### **About Advanced Renal Cell Carcinoma**

*The American Cancer Society's 2017 statistics cite kidney cancer as among the top ten most commonly diagnosed forms of cancer among both men and women in the U.S.<sup>3</sup> Clear cell RCC is the most common type of kidney cancer in adults.<sup>4</sup> If detected in its early stages, the five-year survival rate for RCC is high; for patients with advanced or late-stage metastatic RCC, however, the five-year survival rate is only 12 percent, with no identified cure for the disease.<sup>5</sup> Approximately 30,000 patients in the U.S. and 68,000 globally require treatment.<sup>6</sup>*

*The majority of clear cell RCC tumors have lower than normal levels of a protein called von Hippel-Lindau, which leads to higher levels of MET, AXL and VEGF.<sup>7,8</sup> These proteins promote tumor angiogenesis (blood vessel growth), growth, invasiveness and metastasis.<sup>9-12</sup> MET and AXL may provide escape pathways that drive resistance to VEGF receptor inhibitors.<sup>8,9</sup>*

### **About CABOMETRYX™ (cabozantinib)**

*CABOMETRYX is the tablet formulation of cabozantinib. Its targets include MET, AXL and VEGFR-1, -2 and -3. 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. CABOMETRYX is available in 20 mg, 40 mg or 60 mg doses. The recommended dose is 60 mg orally, once daily.*

*On April 25, 2016, the FDA approved CABOMETRYX tablets for the treatment of patients with advanced renal cell carcinoma who have received prior anti-angiogenic therapy. On September 9, 2016, the European Commission approved CABOMETRYX tablets for the treatment of advanced renal cell carcinoma in adults who have received prior vascular endothelial growth factor (VEGF)-targeted therapy in the European Union, Norway and Iceland.*

### **About Ipsen**

*Ipsen is a global specialty-driven pharmaceutical group with total sales close to €1.6 billion in 2016. Ipsen sells more than 20 drugs in more than 115 countries, with a direct commercial presence in more than 30 countries. Ipsen's ambition is to become a leader in specialty healthcare solutions for targeted debilitating diseases. Its fields of expertise cover oncology, neurosciences and endocrinology (adult & pediatric). Ipsen's commitment to oncology is exemplified through its growing portfolio of key therapies improving the care of patients suffering from prostate cancer, neuroendocrine tumors, renal cell carcinoma and pancreatic cancer. Ipsen also has a significant presence in primary care. Moreover, the Group has an active policy of partnerships. Ipsen's R&D is focused on its innovative and differentiated technological platforms, peptides and toxins, located in the heart of the leading biotechnological and life sciences hubs (Les Ulis/Paris-Saclay, France; Slough/Oxford, UK; Cambridge, US). In 2016, R&D expenditures exceeded €200 million. The Group has more than 4,900 employees worldwide. Ipsen's shares are traded on segment A of Euronext Paris (stock code: IPN, ISIN code: FR0010259150) and are eligible to the "Service de Règlement Différé" ("SRD"). The Group is part of the SBF 120 index. Ipsen has implemented a Sponsored Level I American Depositary Receipt (ADR) program, which trades on the over-the-counter market in the United States under the symbol IPSEY. For more information on Ipsen, visit [www.ipsen.com](http://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](http://www.ipsen.com)).*

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