

## **Ipsen announces the acceptance by the European Medicines Agency of the marketing authorization application for telotristat etiprate to treat carcinoid syndrome caused by neuroendocrine tumors, in combination with somatostatin analogues**

**Paris (France), July 18, 2016** — Ipsen (Euronext: IPN; ADR: IPSEY) today announced that the European Medicines Agency (EMA), the European regulatory authority, has accepted the submission of filing for telotristat etiprate as an adjunct to somatostatin analogue therapy for the long-term treatment of carcinoid syndrome to improve symptom control in adult patients with metastatic neuroendocrine tumors.

In addition to this European submission, Ipsen will pursue a worldwide regulatory plan for marketing authorization submissions in the territories where it operates. As such the Marketing Authorization Application was submitted to SwissMedic (the Swiss Regulatory Agency) on July 5<sup>th</sup> 2016. In October 2014, Ipsen and Lexicon announced that they had entered into an exclusive licensing agreement for Ipsen to commercialize telotristat etiprate in all territories excluding the United States and Japan, where Lexicon retains the rights. Lexicon filed a New Drug Application in the United States on 30 March 2016 and was granted priority review on 31 May 2016 by the U.S. Food and Drug Administration (FDA).

Regulatory submission is supported by the results of TELESTAR, a pivotal, placebo-controlled phase 3 clinical trial and TELECAST, the phase 3 companion study to TELESTAR. Results from TELESTAR demonstrated a statistically significant ( $p < 0.001$ ) reduction from baseline in the average number of daily bowel movements over the first 12-week study period in both treatment arms (250 mg tid and 500 mg tid) compared with placebo, thereby meeting the study's primary endpoint. A statistically significant ( $p < 0.001$ ) reduction in urinary 5-hydroxyindoleacetic acid (the main metabolite of serotonin) was also observed at week 12 compared with placebo in both treatment arms. The most common adverse reactions associated with the use of telotristat etiprate were nausea, abdominal pain, fatigue and gamma-glutamyl transferase increased in the pooled placebo-controlled data of the two phase 3 clinical trials, TELESTAR and TELECAST.

**David Meek, Chief Executive Officer of Ipsen**, said: *"Ipsen is a global leader in neuroendocrine tumors, and is committed to improve patient outcomes from diagnosis to each stage of the disease including symptomatic treatment of carcinoid syndrome. We look forward to working with the EMA so that as many patients as possible can benefit from telotristat etiprate"*.

### **About carcinoid syndrome**

Well-differentiated neuroendocrine tumor (NET) is a relatively rare tumor type that arises from cells of the neuroendocrine system. Carcinoid syndrome (CS) occurs when well-differentiated NETs secrete large amounts of serotonin and other vasoactive products into the systemic circulation. Classically, symptoms associated with CS include cutaneous flushing, diarrhea, wheezing, abdominal pain, and in the long-term, valvular heart disease.

Somatostatin analogues (SSA) are the cornerstone of therapy for the relief of CS and tumor control. SSA inhibit the release of serotonin by NETs and have become first-line therapy for CS. However, SSA may not adequately control symptoms for all patients.

Due to the severe morbidity of CS and the lack of established treatment options, the population of patients with CS needing further control in addition to their SSA therapy is one with a high unmet medical need.

### **About telotristat etiprate**

Telotristat etiprate is a novel, orally administered, inhibitor of the enzyme tryptophan hydroxylase (TPH). Through inhibition of TPH, the rate-limiting step in the synthesis of serotonin, the compound was designed to reduce the production of serotonin within neuroendocrine tumors. Carcinoid syndrome occurs when well differentiated neuroendocrine tumors secrete large amounts of serotonin and other vasoactive products into the systemic circulation. Telotristat etiprate has been developed as an adjunct to SSA therapy for the long term treatment of CS to improve symptom control in adult patients with metastatic NETs.

Telotristat etiprate received priority review status and orphan drug designation from the FDA in the United States, and has received orphan drug designation from the EMA.

### **About Ipsen**

Ipsen is a global specialty-driven pharmaceutical group with total sales exceeding €1.4 billion in 2015. 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, bladder cancer and neuro-endocrine tumors. 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 2015, R&D expenditures neared €193 million. The Group has more than 4,600 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).

## **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 2015 Registration Document available on its website ([www.ipsen.com](http://www.ipsen.com)).

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