

## **Ipsen announces at ASCO GI that ELECT<sup>®</sup> clinical trial of Somatuline<sup>®</sup> in the control of symptoms in GEP-NET<sup>1</sup> patients with carcinoid syndrome met its primary endpoint**

- **Results of ELECT<sup>®</sup> phase III study showed that treatment with Somatuline<sup>®</sup> resulted in a statistically significant reduction in the number of days of rescue medication use versus placebo during the 16-week double-blind phase of the study**
- **Safety data generated are consistent with known safety profile of Somatuline<sup>®</sup>**

**Paris (France), 17 January 2014** – Ipsen (Euronext: IPN; ADR: IPSEY) today announced that the results of the ELECT<sup>®</sup> phase III clinical study with Somatuline<sup>®</sup> Autogel<sup>®</sup> / Somatuline<sup>®</sup> Depot<sup>®</sup> (lanreotide) Injection (hereafter referred to as Somatuline<sup>®</sup>) will be presented on Friday 17 January 2014 at the Gastrointestinal Cancers Symposium, San Francisco, CA, USA.

Results of the ELECT<sup>®</sup> phase III study (poster 268) showed that treatment with Somatuline<sup>®</sup> 120 mg versus placebo resulted in a statistically significant reduction in the number of days in which immediate release octreotide was used as rescue medication, representing a mean difference of -14.8% (95%CI: -26.8, -2.8; p = 0.017). Somatuline<sup>®</sup> significantly improved the rates of complete/partial treatment success versus placebo (odds ratio = 2.4; 95%CI: 1.1, 5.3; p = 0.036).

Safety data collected during ELECT<sup>®</sup> study was consistent with known safety profile of Somatuline<sup>®</sup>.

Somatuline<sup>®</sup> is approved for the treatment of symptoms associated with carcinoid syndrome in patients with neuroendocrine tumors in many markets worldwide; it is marketed as Somatuline<sup>®</sup> Autogel<sup>®</sup>, but not in the US, where it is marketed as Somatuline<sup>®</sup> Depot<sup>®</sup> for acromegaly only. As such, data arising from the ELECT<sup>®</sup> study can be considered as an investigational use of Somatuline<sup>®</sup> Depot<sup>®</sup> in the United States.

**Claude Bertrand, Executive Vice-President, Research & Development and Chief Scientific Officer of Ipsen** stated: *“The results observed in the multinational ELECT<sup>®</sup> study add to the body of*

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<sup>1</sup> Gastroenteropancreatic neuroendocrine tumors



*evidence evaluating the efficacy and safety of Somatuline<sup>®</sup> in the control of symptoms in GEP-NET patients with carcinoid syndrome. Along with the recently reported CLARINET<sup>®</sup> results demonstrating the antiproliferative effect of Somatuline<sup>®</sup>, ELECT results represent new data to document the efficacy and safety of Somatuline<sup>®</sup> in gastroenteropancreatic neuroendocrine tumors.”*

**Edward M. Wolin, MD, Co-Director, Carcinoid and Neuroendocrine Tumor Program Medical Oncology, Samuel Oschin Cancer Center, Cedars-Sinai (USA)** stated: *“In the ELECT<sup>®</sup> study, rescue medication with immediate release formulation of octreotide was allowed for all patients in the Somatuline<sup>®</sup> and placebo arms when needed to control their symptoms. This study demonstrated a decreased use of octreotide as rescue medication in patients treated with Somatuline<sup>®</sup> 120mg when compared to those receiving placebo (both naïve to treatment or previously treated with a somatostatin analogue).”*

During the Gastrointestinal Cancers Symposium, Ipsen also presented the results of SYMNET observational study assessing the effect of Somatuline<sup>®</sup> on the control of symptoms (diarrhea and flushing) in patients with NET and carcinoid syndrome (poster 273).

### **About ELECT<sup>®</sup>**

ELECT<sup>®</sup> (A double-blind, randomized placebo controlled Clinical Trial investigating the efficacy and safety of Somatuline<sup>®</sup> Depot (lanreotide) injection in the treatment of carcinoid syndrome) is a 48-week phase III study in patients with a history of carcinoid syndrome. The study consisted of a 16-week, double-blind, randomized (to either Somatuline<sup>®</sup> Depot<sup>®</sup> 120 mg every 4 weeks or placebo), placebo-controlled phase followed by an initial 32-week open-label phase. Throughout the study the patients were allowed to use rescue medication in the form of subcutaneous somatostatin analogues (octreotide) as needed to control their symptoms. The primary endpoint was the percentage of days subcutaneous octreotide was required to control symptoms associated with carcinoid syndrome, as rescue medication during the 16-week double-blind phase of the study. Secondary endpoints included frequency of diarrhea and flushing, usage of other rescue medication, Quality of Life, tumor markers and safety. The trial is registered on ClinicalTrials.gov (NCT00774930).

ELECT<sup>®</sup> results were presented in poster number 268 titled “ELECT: A phase III study of efficacy and safety of Somatuline<sup>®</sup> Autogel<sup>®</sup>/ Depot<sup>®</sup> treatment for carcinoid syndrome in patients with neuroendocrine tumors (NETs).” A total of 115 patients were randomized in the study (n=59 for Somatuline<sup>®</sup> and n=56 in the placebo group).

The ELECT<sup>®</sup> study assessed the effect of monthly Somatuline<sup>®</sup> Injection 120 mg on the control of symptoms in patients with neuroendocrine tumors (NETs) associated with carcinoid syndrome. ELECT<sup>®</sup> met its primary endpoint by demonstrating that the percentage of days in which octreotide was used as rescue medication during the 16-week double blind period was significantly lower in the Somatuline<sup>®</sup> group than the placebo group [representing a mean difference of -14.8% (95%CI: -26.8, -2.8; p = 0.017). A significantly greater proportion of patients in the Somatuline<sup>®</sup> arm experienced a complete (40.7% vs. 23.2%, respectively) or a partial (6.8% vs. 5.4%, respectively) treatment success compared to placebo. As a result, Somatuline<sup>®</sup> significantly improved chances of having either a complete or a partial treatment success versus placebo (OR = 2.4; 95%CI: 1.1, 5.3; p = 0.036). “Complete success” and “partial success” were defined, respectively, as no need for, or ≤3 days of, use of octreotide as rescue medication between weeks 12 and 15. The need for >3 days of octreotide between weeks 12 and 15 was defined as treatment failure.



No significant trends in favor of Somatuline<sup>®</sup> were observed for the secondary efficacy endpoints (diarrhea events, flushing events and QoL).

Safety data generated from the study were consistent with the known safety profile of Somatuline<sup>®</sup>. The incidence of treatment emergence adverse events (AEs), including treatment related AEs, was similar between groups in all phases of the study. Treatment-emergent serious AEs were uncommon occurring in 3.4% of the Somatuline<sup>®</sup> group and 8.8% of the placebo group. One patient withdrew from each of the Somatuline<sup>®</sup> (1.8%) and placebo (1.9%) groups, respectively, due to treatment-emergent AEs. The most frequently reported treatment-related AEs were gastrointestinal in nature. Treatment-related AEs occurring at a rate of >5% and more commonly in the Somatuline<sup>®</sup> group than in the placebo group included gastrointestinal disorders (15.5% in the Somatuline<sup>®</sup> group vs. 8.8% in the placebo group), general/administration site conditions (8.6% vs. 5.3%) and nervous system disorders (6.9% vs. 1.8%).

### **About gastroenteropancreatic neuroendocrine tumors and carcinoid syndrome**

Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) constitute an heterogeneous group of tumors arising from the diffuse neuroendocrine system with location of the primary tumor in the gastric mucosa, pancreas, small and large intestine. They are rare but their incidence is increasing (approximately 2.5 to 4.5 new cases diagnosed per 100,000 persons per year). As a result of their origin, GEP-NETs when they are functioning, are capable of synthesizing and releasing a variety of hormones and neuroamines, most commonly serotonin, which, when released into the systemic circulation, can cause distinct clinical symptoms, such as the carcinoid syndrome (diarrhea, flushing, valvular heart disease, abdominal pain and cramping among others). Non-functioning GEP-NETs do not secrete hormones and can remain clinically silent, delaying the diagnosis until late presentation with symptoms like weight loss or related to mass effects such as abdominal pain.

### **About Somatuline<sup>®</sup>**

The active substance in Somatuline<sup>®</sup> is lanreotide acetate, a somatostatin analogue that inhibits the secretion of several endocrine, exocrine and paracrine functions. It has been shown effective in inhibiting the secretion of GH and certain hormones secreted by the digestive system. Somatuline<sup>®</sup> is marketed as Somatuline<sup>®</sup> Depot within the United States and as Somatuline<sup>®</sup> Autogel<sup>®</sup> in other countries where it has marketing authorization.

Somatuline<sup>®</sup> was initially developed and continues to be used for the treatment of acromegaly in many countries, including the United States, where it is indicated for the long-term treatment of patients with acromegaly who have had an inadequate response to or cannot be treated with surgery and/or radiotherapy. Somatuline<sup>®</sup> is not approved in the United States for the treatment of symptoms associated with neuroendocrine tumors, but is approved for this indication in other markets.

### **Select Important Safety Information About Somatuline<sup>®</sup> Depot<sup>®</sup>**

- **Warnings and Precautions**

- Somatuline<sup>®</sup> may reduce gallbladder motility and lead to gallstone formation. Periodic monitoring may be needed
- Patients may experience hypoglycemia or hyperglycemia. Glucose level monitoring is recommended and antidiabetic treatment adjusted accordingly
- Somatuline<sup>®</sup> may decrease heart rate. In cardiac studies, the most common cardiac adverse reactions were sinus bradycardia, bradycardia, and hypertension. Dose adjustment of coadministered drugs that decrease heart rate may be necessary



- Somatuline<sup>®</sup> may decrease bioavailability of cyclosporine. Cyclosporine dose may need to be adjusted

- **Adverse Reactions**

The most common adverse reactions (incidence >5%) were diarrhea (37%), cholelithiasis (20%), abdominal pain (19%), nausea (11%), injection-site reaction (9%), constipation (8%), flatulence (7%), headache (7%), arthralgia (7%), vomiting (7%), and loose stools (6%).

### **About Ipsen**

Ipsen is a global specialty-driven pharmaceutical company with total sales exceeding €1.2 billion in 2012. Ipsen's ambition is to become a leader in specialty healthcare solutions for targeted debilitating diseases. Its development strategy is supported by 3 franchises: neurology, endocrinology and uro-oncology. 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. In 2012, R&D expenditure totalled close to €250 million, representing more than 20% of Group sales. The Group has close to 4,900 employees worldwide. Ipsen's shares are traded on segment A of Euronext Paris (stock code: IPN, ISIN code: FR0010259150) and 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 trade on the over-the-counter market in the United States under the symbol IPSEY. For more information on Ipsen, visit [www.ipсен.com](http://www.ipсен.com).

### **Forward Looking Statements**

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 fulfill 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.

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