

## Endocrine Practice Publishes ELECT Phase III Trial Results in Adults with Carcinoid Syndrome

BASKING RIDGE, NJ, June 4, 2016 - Ipsen Biopharmaceuticals, Inc., an affiliate of Ipsen (Euronext: IPN; ADR: IPSEY), today announced that *Endocrine Practice* has published Phase III clinical trial results examining the efficacy and safety of Somatuline<sup>®</sup> Depot<sup>®</sup> (lanreotide) Injection 120 mg (referred to as Somatuline<sup>®</sup>) in patients with carcinoid syndrome. “Evaluation of Lanreotide Depot/Autogel Efficacy and Safety as a Carcinoid Syndrome Treatment (ELECT): A Randomized, Double-Blind, Placebo-Controlled Trial” is published online at <http://www.ncbi.nlm.nih.gov/pubmed/27214300> and will be published in an upcoming print edition.

In the 16-week, Phase III randomized, double-blind, placebo-controlled study of the efficacy and safety of Somatuline<sup>®</sup> in patients with carcinoid syndrome, 115 patients were randomized to Somatuline<sup>®</sup> 120mg or placebo every four weeks, with access to short-acting octreotide as rescue medication. The study showed the adjusted mean percentage days with rescue octreotide use (the primary endpoint) was lower in the Somatuline<sup>®</sup> group (33.7 percent) versus the placebo group (48.5 percent) ([95% CI: -26.8, -2.8] p=0.017). The odds ratio of full or partial treatment success (defined as three or fewer days of short-acting octreotide use in weeks 12 to 15) was significantly greater with Somatuline<sup>®</sup> than placebo (2.4 [95% CI: 1.1, 5.3]; p=0.036). The most common Adverse Events observed in the study were nausea, vomiting, abdominal pain, and flatulence.

“The publication of the ELECT data in *Endocrine Practice* marks another important milestone for Somatuline<sup>®</sup> in neuroendocrine tumors,” said Cynthia Schwalm, Chief Executive Officer, Ipsen Biopharmaceuticals, Inc.

Aaron I. Vinik, MD, PhD, Lead Study Author and Director, Neuroendocrine Unit, Eastern Virginia Medical School, Norfolk, VA, said, “The Phase 3 ELECT study further expands our understanding of lanreotide’s potential in patients with neuroendocrine tumors with carcinoid syndrome.”

The CLARINET trial, published in the *New England Journal of Medicine* in 2014, was the first large Phase III prospective trial to evaluate the antiproliferative effects of Somatuline<sup>®</sup> in patients with non-functioning gastroenteropancreatic neuroendocrine tumors (GEP-NETs.) The study showed that treatment with Somatuline<sup>®</sup> significantly prolonged progression-free survival in patients with GEP-NETs compared to treatment with placebo.

### About the ELECT Study

In the 16-week, double-blind, Phase-3 trial, patients with or without prior somatostatin analog (SSA) use were randomized to Somatuline<sup>®</sup> Autogel<sup>®</sup> 120mg or placebo every four weeks, with access to short-acting octreotide as rescue medication. The primary endpoint was the percentage of days in which short-acting octreotide was used, which was assessed from daily diaries using an analysis of covariance (ANCOVA) including the stratification variables, baseline

short-acting octreotide use and frequency of diarrhea/flushing. The proportions of patients experiencing treatment success was a supportive analysis. Adverse events were recorded at all visits.

## **Indication**

Somatuline® Depot (lanreotide) Injection 120 mg is indicated for the treatment of adult patients with unresectable, well- or moderately differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival.

## **Important Safety Information**

### **Contraindications:**

Somatuline is contraindicated in patients with hypersensitivity to lanreotide. Allergic reactions (including angioedema and anaphylaxis) have been reported following administration of lanreotide.

### **Warnings and Precautions:**

- **Cholelithiasis and Gallbladder Sludge:** Somatuline may reduce gallbladder motility and lead to gallstone formation. Periodic monitoring may be needed.
- **Hypoglycemia or Hyperglycemia:** Pharmacological studies show that Somatuline, like somatostatin and other somatostatin analogs, inhibits the secretion of insulin and glucagon. Blood glucose levels should be monitored when Somatuline treatment is initiated, or when the dose is altered, and antidiabetic treatment should be adjusted accordingly.
- **Cardiac Abnormalities:** Somatuline may decrease heart rate. In 81 patients with baseline heart rates of  $\geq 60$  beats per minute (bpm) treated with Somatuline in the GEP-NETs clinical trial, the incidence of heart rate  $< 60$  bpm was 23% (19/81) with Somatuline vs 16% (15/94) with placebo; 10 patients (12%) had documented heart rates  $< 60$  bpm on more than one visit. The incidence of documented episodes of heart rate  $< 50$  bpm or bradycardia reported as an adverse event was 1% in each treatment group. Initiate appropriate medical management in patients who develop symptomatic bradycardia. In patients without underlying cardiac disease, Somatuline may lead to a decrease in heart rate without necessarily reaching the threshold of bradycardia. In patients suffering from cardiac disorders prior to treatment, sinus bradycardia may occur. Care should be taken when initiating treatment in patients with bradycardia.
- **Drug Interactions:** The pharmacological gastrointestinal effects of Somatuline may reduce the intestinal absorption of concomitant drugs. Concomitant administration of Somatuline Depot may decrease the relative bioavailability of cyclosporine and may necessitate the adjustment of cyclosporine dose to maintain therapeutic levels.

## **Adverse Reactions:**

In the GEP-NET pivotal trial, the most common adverse reactions (incidence >10% and more common than placebo) in patients treated with Somatuline DEPOT vs placebo were abdominal pain (34% vs 24%), musculoskeletal pain (19% vs 13%), vomiting (19% vs 9%), headache (16% vs 11%), injection site reaction (15% vs 7%), hyperglycemia (14% vs 5%), hypertension (14% vs 5%), and cholelithiasis (14% vs 7%).

You may report suspected adverse reactions to FDA at 1-800-FDA-1088 or to Ipsen Biopharmaceuticals, Inc. at 1-888-980-2889.

Please see the full Prescribing Information for Somatuline<sup>®</sup> Depot by accessing the following [link](#).

## **About Ipsen**

Ipsen is a global specialty-driven biotechnological 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. Ipsen's commitment to oncology is exemplified through its growing portfolio of key therapies improving the care of patients. 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 expenditure totaled close to €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 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 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 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.

Somatuline DEPOT is a registered trademark of IPSEN PHARMA S.A.S.

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