PRESS RELEASE

# Ipsen Announces U.S. FDA Approval for Newly Designed Pre-Filled Syringe for Somatuline® Depot (lanreotide)

*– New Syringe Designed to Help Enhance Injection Experience –*

**Cambridge, Mass., June 24, 2019 –** Ipsen Biopharmaceuticals, an affiliate of Ipsen (Euronext: IPN; ADR: IPSEY), announced today that the United States Food and Drug Administration (FDA) has approved a new pre-filled syringe for Somatuline® Depot (lanreotide).[1] The syringe includes updated features, such as larger flanges, designed to help make it easier for healthcare providers to administer the injection.[1] The indications remain the same as those for the previous pre-filled syringe and include 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; treatment of adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy; and the long-term treatment of patients with acromegaly who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option. Please see Important Safety Information below and accompanying full Prescribing Information.

"The conditions of GEP-NETs and acromegaly can be associated with a number of uncomfortable and unpleasant symptoms, and innovation aimed at improving the injection process is a step forward," **said Daphne Adelman, Clinical Nurse Specialist, Northwestern University, Chicago, and one of the authors of the study**.

Ipsen conducted five separate but complementary studies in partnership with patients, their caregivers, nurses and other healthcare professionals to better understand the current use of the existing Somatuline® Depot pre-filled syringe and to evaluate ways to improve the features of the device.[1] The result of this collaboration is a redesigned delivery system intended to make it easy to grip the syringe and administer the injection. The new syringe features a needle shield removal system, more stable plunger and thermoform tray that has recessed areas designed to help prevent accidental plunger depression.[1] The built-in safety system, which may help to prevent needle stick injury by locking in place following the administration, has not been changed.[1]

"We consistently look for opportunities to respond to the needs of the communities we serve, and this approval would not have been possible without the direct involvement of nurses and the patients with GEP-NETs and acromegaly whom they treat," **said Bradley Bailey, SVP, and Franchise Head Oncology/Endocrinology Business Unit at Ipsen. "**We listened and collaborated to enhance the existing pre-filled syringe, making it sturdier for healthcare providers when administering treatment, with the intention of improving the injection process. We look forward to bringing this innovation to healthcare providers for their patients soon."

The new pre-filled syringe is for deep subcutaneous injection and is intended for administration by a healthcare professional. Healthcare providers can expect to receive the new syringe during Q3 2019. The device is approved for use in the U.S., EU and additional ex-U.S. markets.

**ABOUT NETs**

A neuroendocrine tumor (NET) begins in the hormone-producing cells of the body's neuroendocrine system, which is made of cells that are a combination of hormone-producing endocrine cells and nerve cells.[2] NETs are a group of uncommon tumors occurring in both men and women aged 50 to 60 years old although they can affect anyone of any age.[2]

The three main areas where NETs are found in the body are the gastrointestinal tract, the pancreas and the lungs.[2]

- Gastrointestinal NETs (GEP-NETs) are found in the gastrointestinal tract or digestive system and are the most common type of NETs.[2]
- Pancreatic NETs (pNETs) are formed in the islet cells of the pancreas and include several uncommon types of NETs.[2]
- Lung NETs are less common than other types, accounting for about one quarter of NETs.[2]

The symptoms of NETs are often not distinct and difficult to identify, and average time from initial onset of symptoms to proper diagnosis can take more than 5 years.[3] Although NETs affect only a small percentage of the general population at any one time, the number of people being newly diagnosed with NETs overall is believed to be rising.[2] This is mainly due to increased awareness of the condition and diagnostic testing.[2] NETs are now the fastest growing class of cancers worldwide, accounting for around 2% of all cancers at any time.[2]

**ABOUT ACROMEGALY**

Acromegaly is an uncommon hormonal or endocrine disorder with slowly developing, but eventually distinct clinical symptoms.[4] In the U.S., approximately 3,500 new cases of acromegaly are diagnosed each year.[5]

It is usually caused by having too much growth hormone in the body which, over time, results in some characteristic symptoms and signs, such as heavy or prominent facial features with a prominent jaw line and enlarged hands and feet.[4]

**ABOUT SOMATULINE® DEPOT**

SOMATULINE® DEPOT (lanreotide) is a somatostatin analog indicated for:

- the long-term treatment of patients with acromegaly who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option; the goal of treatment in acromegaly is to reduce growth hormone (GH) and insulin growth factor-1 (IGF-1) levels to normal;
- 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; and
- the treatment of adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy.

## IMPORTANT SAFETY INFORMATION

**Contraindications**

- SOMATULINE DEPOT 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 DEPOT may reduce gallbladder motility and lead to gallstone formation.
  - Periodic monitoring may be needed.
  - If complications of cholelithiasis are suspected, discontinue SOMATULINE DEPOT and treat appropriately
- **Hypoglycemia or Hyperglycemia**
  - Patients treated with SOMATULINE DEPOT may experience hypoglycemia or hyperglycemia.
  - Blood glucose levels should be monitored when SOMATULINE DEPOT treatment is initiated, or when the dose is altered, and antidiabetic treatment should be adjusted accordingly.
- **Cardiovascular Abnormalities**

  - SOMATULINE DEPOT may decrease heart rate.
  - In cardiac studies with acromegalic patients, the most common cardiac adverse reactions were sinus bradycardia, bradycardia, and hypertension.
  - In patients without underlying cardiac disease, SOMATULINE DEPOT 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.
- **Thyroid Function Abnormalities**
  - Slight decreases in thyroid function have been seen during treatment with lanreotide in acromegalic patients.
  - Thyroid function tests are recommended where clinically appropriate.
- **Monitoring/Laboratory Tests:** In acromegaly, serum GH and IGF-1 levels are useful markers of the disease and effectiveness of treatment.

**Adverse Reactions**

- **Acromegaly:** Adverse reactions in >5% of patients who received SOMATULINE DEPOT were diarrhea (37%), cholelithiasis (20%), abdominal pain (19%), nausea (11%), injection-site reactions (9%), constipation (8%), flatulence (7%), vomiting (7%), arthralgia (7%), headache (7%), and loose stools (6%).
- **GEP-NETs:** Adverse reactions >10% of patients who received SOMATULINE DEPOT were abdominal pain (34%), musculoskeletal pain (19%), vomiting (19%), headache (16%), injection site reaction (15%), hyperglycemia (14%), hypertension (14%), and cholelithiasis (14%).
- **Carcinoid Syndrome:** Adverse reactions occurring in the carcinoid syndrome trial were generally similar to those in the GEP-NET trial. Adverse reactions occurring in ≥5% of patients who received SOMATULINE DEPOT and at least 5% greater than placebo were headache (12%), dizziness (7%), and muscle spasm (5%).

**Drug Interactions:** SOMATULINE DEPOT may decrease the absorption of cyclosporine (dosage adjustment may be needed); increase the absorption of bromocriptine; and require dosage adjustment for bradycardia-inducing drugs (e.g., beta-blockers).

**Special Populations**

- **Lactation:** Advise women not to breastfeed during treatment and for 6 months after the last dose.
- **Moderate to Severe Renal and Hepatic Impairment:** See full prescribing information for dosage adjustment in patients with acromegaly.

**To report SUSPECTED ADVERSE REACTIONS,** contact Ipsen Biopharmaceuticals, Inc. at 1-855-463-5127 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**Please click here for the full Prescribing Information and Patient Information.**

**ABOUT IPSEN IN NORTH AMERICA**

Ipsen (Euronext: IPN; ADR: IPSEY) is a global biopharmaceutical company focused on innovation and specialty care. The company develops and commercializes innovative medicines in three key therapeutic areas – Oncology, Neuroscience and Rare Diseases. At Ipsen, we focus our resources, investments and energy on discovering, developing and commercializing new therapeutic options to provide hope for patients whose lives are challenged by difficult-to-treat diseases. Ipsen's North American operations are located in Cambridge, Massachusetts, one of the company's three global hubs. Based in the heart of Kendall Square, our fully integrated biopharmaceutical business includes Commercial, Research & Development, Manufacturing, and Global External Innovation and Partnering. Combined with our Canadian headquarters in Mississauga, Ontario, and other locations, Ipsen employs approximately 600 people in North America. For more information please visit www.ipsenus.com or www.ipsen.ca. Connect with us on Twitter and LinkedIn.

**Forward-Looking Statement**

This press release contains forward-looking information within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. Any statements contained herein which do not describe historical facts, including, among others, statements regarding the newly designed pre-filled syringe now approved in the U.S., and the prevalence and burden of GEP-NETs, Carcinoid Syndrome, and Acromegaly are forward-looking statements which involve risks and uncertainties that could cause actual results to differ materially from those discussed in such 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 healthcare 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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