



PRESS RELEASE

ESMO 2020: Phase II CLARINET FORTE results show increasing dose frequencies of Somatuline® Autogel® (lanreotide) allows patients with NETs to delay treatment escalation by up to 8.3 months

- Increasing the dose frequency of lanreotide from monthly to bi-monthly achieved a progression-free survival of 8.3 months in patients with progressive midgut neuroendocrine tumors (NETs) and 5.6 months in patients with progressive pancreatic NETs
- These results show no new safety signals associated with this increased dose regimen, potentially delaying the need for additional, more toxic second-line therapies
- The incidence of NETs is increasing, and are now among the fastest growing class of cancers worldwide, accounting for around 2% of all cancers¹

PARIS, FRANCE, 18 September 2020 – Ipsen (Euronext: IPN; ADR: IPSEY) today announced the release of first efficacy and safety data from the CLARINET FORTE study, with the abstract to be presented as a mini-oral presentation at the 2020 European Society for Medical Oncology (ESMO) Congress, taking place virtually from 19-21 September 2020. The prospective single-arm, open-label, exploratory, international Phase II study investigated the efficacy and safety of increasing the dose frequency of Somatuline® Autogel® (lanreotide) in patients with pancreatic or midgut NETs with centrally-assessed progression within the last two years while on a standard lanreotide regimen for ≥ 24 weeks. An extension of progression-free survival (PFS) rates and encouraging disease-control rates (DCR) were recorded in both tumor types, with no new safety signals.

“These results support a clinically meaningful benefit to a population of patients with high unmet medical need by potentially delaying escalation to more toxic treatments. This means patients with progressive NETs are able to remain on a more tolerable first-line standard of care for longer,” said Professor Marianne Pavel, Friedrich-Alexander University of Erlangen, Germany, Senior Physician and Chair of Endocrinology, and lead investigator of the study.

Lanreotide is a synthetic form of a natural hormone called somatostatin and is used to control and treat the growth of some advanced tumors of the midgut and the pancreas called gastroenteropancreatic NETs or GEP-NETs. Previous studies have shown efficacy in tumor control for the 28-day regimen of lanreotide 120 mg, and positive effects on relief of clinical symptoms.²

Currently, patients with progressive disease after treatment with lanreotide (120 mg every 28 days) have limited treatment options and receive less well-tolerated systemic chemotherapy or molecular targeted therapies. As lanreotide has a favorable tolerability profile, an increased dosing frequency might delay the need for such therapies and could potentially maintain patients’ quality of life for longer.

The CLARINET FORTE study found that increasing the dose frequency of lanreotide from a first line standard dose of 120 mg every 28 days, to an increased dose of 120 mg every 14 days, a median PFS of 8.3 months (95% confidence interval [CI]: 5.5–8.3) was achieved in patients with progressive midgut NETs (n=51) and 5.6 months (95% CI: 5.5–8.3) in patients with progressive pancreatic NETs (n=48). Post-hoc subgroup analysis in the pancreatic NETs cohort showed median PFS of 8.0 months (95% CI: 5.6–8.3) in patients with Ki67 $\leq 10\%$ (n=43).

“The CLARINET FORTE study is another example of Ipsen’s commitment to delivering scientific and medical advances that translate into patient outcomes. Progressive pancreatic or midgut NETs are among the fastest growing class of cancers worldwide, so we are delighted that these data presented at ESMO may mean that for these patients, the need for aggressive second-line therapies could be delayed for longer whilst also benefitting from continued progression-free survival,” said Professor Steven Hildemann, Executive Vice President, Chief Medical Officer, Head of Global Medical Affairs and Patient Safety, Ipsen.

The study found no new safety signals associated with this increased dose regimen. The increased lanreotide dosing frequency was well-tolerated, with treatment-related adverse events (TRAEs) remaining consistent with previous clinical studies and occurring in 37.5% and 51.0% of patients in the pancreatic NETs and midgut NETs cohorts, respectively; only one TRAE was Grade ≥ 3 (pancreatic NETs: fatigue [n=1], Grade 3). The most common ($\geq 10\%$) classes of TRAEs were gastrointestinal disorders (pancreatic NETs, 25.0%; midgut NETs, 37.3%) and general disorders/administration-site conditions (midgut NETs, 13.7%).

Together, these efficacy and safety results may represent an important therapeutic approach for patients living with pancreatic or midgut NETs. The full data will be presented as an on-demand mini-oral presentation on Friday 18 September at the ESMO Virtual Congress 2020.

To complement the format of the ESMO Virtual Congress 2020, Ipsen's new virtual congress platform includes a virtual press office <https://events.ipсен.com/esmo-press/> to support media in accessing further information. Highlights include insights around our data and contributions to the ESMO 2020 scientific program, our mission to advance oncology research and our commitment to address patients' unmet needs. Registration for a digital media briefing for selected ESMO data is available [here](#).

Follow Ipsen on Twitter via @IpsenGroup and keep up to date with ESMO Virtual Congress 2020 news and updates by using the hashtag #ESMO20.

About NETs

Neuroendocrine tumors, or NETs, are a group of uncommon tumors that develop in the cells of the neuroendocrine system, throughout the body.^{3,4} NETs occur in both men and women, in general aged 50 to 60 years old, although they can affect anyone of any age.¹

The three main areas where NETs are found in the body are the gastrointestinal tract, the pancreas and the lungs.^{3,5}

- Gastrointestinal NETs are found in the gastrointestinal tract or digestive system and are the most common type of NETs.⁵
- Pancreatic NETs are formed in the islet cells of the pancreas and include several uncommon types of NETs.⁵
- Lung NETs are less common, accounting for about one quarter of NETs.⁵

The symptoms of NETs are often not distinct and difficult to identify, and can take between five to seven years to fully diagnose.⁶ The number of people being newly diagnosed with NETs overall is believed to be rising.¹ This is mainly due to increased awareness of the condition and diagnostic testing.¹ NETs are now among the fastest growing class of cancers worldwide, accounting for around 2% of all cancers.¹

About CLARINET FORTE

CLARINET FORTE is a prospective single-arm, open-label, exploratory, international Phase II study to explore the efficacy and safety of an increased Somatuline® Autogel® (lanreotide) dosing interval (120 mg every 14 days) in patients with metastatic or locally advanced unresectable pancreatic NETs or midgut NETs, with centrally-accessed progression within the last two years while on a standard lanreotide regimen (120 mg every 28 days) for more than 24 weeks.⁷

About Somatuline® (lanreotide)

Somatuline® Autogel®/Depot is made of the active substance lanreotide, which is a long-acting somatostatin analogue that inhibits the secretion of growth hormone and certain hormones secreted by the digestive system. The main indications of lanreotide are:⁸

- The treatment of individuals with acromegaly when the circulating levels of Growth Hormone (GH) and/or Insulin-like Growth Factor-1 (IGF-1) remain abnormal after surgery and/or radiotherapy, or in patients who otherwise require medical treatment.
- The treatment of grade 1 and a subset of grade 2 (Ki-67 index up to 10%) gastroenteropancreatic neuroendocrine tumors (GEP-NETs) of midgut, pancreatic or unknown origin where hindgut sites of origin have been excluded, in adult patients with unresectable locally advanced or metastatic disease.
- The treatment of symptoms associated with neuroendocrine (particularly carcinoid) tumors.

The detailed recommendations for the use of lanreotide are described in the Summary of Product Characteristics (SmPC), available [here](#).

About Ipsen

Ipsen is a global specialty-driven biopharmaceutical group focused on innovation and Specialty Care. The Group develops and commercializes innovative medicines in three key therapeutic areas – Oncology, Neuroscience and Rare Diseases. Its commitment to Oncology is exemplified through its growing portfolio of key therapies for prostate cancer, neuroendocrine tumors, renal cell carcinoma and pancreatic cancer. Ipsen also has a well-established Consumer Healthcare business. With total sales over €2.5 billion in 2019, Ipsen sells more than 20 drugs in over 115 countries, with a direct commercial presence in more than 30 countries. Ipsen's R&D is focused on its innovative and differentiated technological platforms located in the heart of the leading biotechnological and life sciences hubs (Paris-Saclay, France; Oxford, UK; Cambridge, U.S.). The Group has about 5,800 employees worldwide. Ipsen is listed in Paris (Euronext: IPN) and in the United States through a Sponsored Level I American Depositary Receipt program (ADR: IPSEY). For more information on Ipsen, visit www.ipsen.com.

Ipsen's 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, and the outcome of this study or other studies. 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 preclinical 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 2019 Universal Registration Document available on its website (www.ipsen.com).

For further information:

Media

Fanny Allaire
Global Communications Director
+33 (0) 6 08 91 92 55
fanny.allaire@ipsen.com

Financial

Myriam Koutchinsky
Investor Relations Manager
+33 (0)1 58 33 51 04
myriam.koutchinsky@ipsen.com

References

1. How Common are NETs? LivingWithNETs. Accessed: August 2020. Available: <https://www.livingwithnets.com/about-neuroendocrine-tumours-nets/learn-about-nets/how-common-are-neuroendocrine-tumours-nets/>.
2. Caron, P et al. Tumor Shrinkage With Lanreotide Autogel 120 mg as Primary Therapy in Acromegaly: Results of a Prospective Multicenter Clinical Trial. *The Journal of Clinical Endocrinology & Metabolism*. 2013; 99:4. DOI: <https://doi.org/10.1210/jc.2013-3318>.
3. Neuroendocrine Tumour (NETs). Macmillan. Accessed: August 2020. Available: <https://www.macmillan.org.uk/cancer-information-and-support/neuroendocrine-tumours-nets>.
4. Zekri et al. (2019). Neuroendocrine tumor of the kidney: Diagnostic challenge and successful therapy. *Urology Annals*. 2019; 11:4, DOI: https://doi.org/10.4103/UA.UA_169_18.
5. Types of NETs. LivingWithNETs. Accessed: August 2020. Available: <https://www.livingwithnets.com/about-neuroendocrine-tumours-nets/learn-about-nets/types-of-neuroendocrine-tumours-nets/>.
6. Symptoms of NETs. LivingWithNETs. Accessed: August 2020. Available: <https://www.livingwithnets.com/about-neuroendocrine-tumours-nets/learn-about-nets/symptoms-of-neuroendocrine-tumours-nets/>.
7. Pavel M et al. Efficacy and safety of lanreotide autogel (LAN) 120 mg every 14 days in progressive pancreatic or midgut neuroendocrine tumours (NETs): CLARINET FORTE study results. Abstract presented at ESMO Virtual Congress 2020, 19–21 September.
8. EMC. Somatuline Autogel (lanreotide acetate) SmPC. December 2019. Available: <https://www.medicines.org.uk/emc/product/4808/smpc>