PRESS RELEASE

Ipsen announces 18 posters to be presented at the 15th Annual ENETS Conference

Paris (France), 6 March 2018 – Ipsen (Euronext: IPN; ADR: IPSEY) today announced that lanreotide (Somatuline®), cabozantinib (Cabometyx®), and telotristat ethyl (Xermelo®), alongside research on real-world NET treatment, nuclear medicine and imaging, and the patient experience will be highlighted in 18 posters at the 15th Annual ENETS (European Neuroendocrine Tumor Society) Conference, to be held from March 7th to March 9th in Barcelona, Spain. The posters will be presented during two poster sessions: March 8th from 15:20 pm to 16:05 pm (CET) and March 9th from 10:40 am to 11:30 am (CET).

“Ipsen remains committed to advancing research and education in order to better understand and continuously improve treatment options for patients with neuroendocrine tumors (NETs). Our goal is to optimize the treatment outcomes and quality of life of patients with NETs. We are pleased to present encouraging scientific and clinical data from our portfolio in neuroendocrine tumors and carcinoid syndrome” said Sotirios Stergiopoulos, MD, Senior Vice-President, Head of Global Medical Affairs (GMA) and Chief Medical Officer (CMO), Ipsen.

The presentations upcoming on Cabometyx®, Xermelo®, Somatuline® and 68Ga-OPS-202 are based on the results of investigational research studies.

**Lanreotide (Somatuline®) is featured in 4 posters:**

- **Poster H19 - Category: Medical Treatment - Chemotherapy Somatostatin Analogues, Interferon**
  Title: Disease control in progressive pancreatic and intestinal neuroendocrine tumours by combined treatment with lanreotide autogel and temozolomide: the SONNET study

- **Poster J09 - Category: Medical Treatment - Others Not Specified**
  Title: Observational study of perception of information and quality of life in patients with neuroendocrine tumor starting lanreotide – Study design
  Authors: V. Hautefeuille, F. Bonnetain, D. Gueguen, A. Houchard, P. Hammel

- **Poster - H14 Category: Medical Treatment - Chemotherapy Somatostatin Analogues, Interferon**
  Title: Somatostatin Analog (SSA) Usage in Neuroendocrine Tumors (NETs): A Retrospective Database Analysis with Supplemental Chart Review

- **Poster - K01 - Category: Nuclear Medicine Imaging and Therapy (PRRT)**
  Title: Influence of Lanreotide on Uptake of [68Ga]-DOTATATE in Patients with NETs
  Authors: E.A. Aalbersberg, B.J. de Wi - van der Veen, L.J. Saveur, G.D. Valk, M.E.T. Tesselaar, M.P.M. Stokkel
  Investigator-lead study
Cabozantinib (Cabometyx®) is featured in 1 poster:

- Poster I05 - Category: Medical Treatment - Targeted Therapies
  Title: Phase II trial of cabozantinib in patients with carcinoid and pancreatic neuroendocrine tumors
  Investigator-lead study

Telotristat (Xermelo®) is featured in 1 poster:

- Poster J06 Category: Medical Treatment - Others, Not Specified
  TIMELESTAR/TELECAST time to sustained BM improvement - "[Lexicon-lead study]" - Telotristat
  Title: Time to Sustained Improvement in Bowel Movement Frequency with Telotristat Ethyl: Analyses of Two Phase 3 Studies in Carcinoid Syndrome
  Lexicon-lead study

$^{68}$Ga-OPS202 is featured in 1 poster:

- Poster K25 - Category: Nuclear Medicine Imaging and Therapy (PRRT)
  Title: Study to Evaluate the Optimal Dose of $^{68}$Ga-OPS202 as a PET Imaging Agent in Patients with GEP-NET
  Authors: I. Virgolini, A. Brouwers, A. Haug, H. Grønbæk, A. Kjær, D. Novac, A. Ang, C. Miller, J. Kaufmann, J. Czernin

6 posters present Real World Data:

- Poster D53 - Category: Epidemiology/Natural History/Prognosis – Registries, Nationwide and Regional Surveys
  Title: Prevalence of Carcinoid Syndrome in the European Union: Systematic Review
  Authors: G. Nayroles, A. Bergamasco, J. Mouchet, Y. Moride

- Poster J05 - Category: Medical Treatment
  Title: On-going Evaluation of the Use of Resources and the Costs (UR/C) Associated with Controlled or Uncontrolled Carcinoid Syndrome (CS) in Patients (pts) with Neuroendocrine Tumours (NETs), RECOSY Study
  Authors: A. Custodio, A. Carmona-Bayonas, C. Villabona, M. Pérez, G. de la Cruz, P. Jiménez-Fonseca
o Poster D05 - Category: Medical Treatment - Epidemiology Natural History/Prognosis - Registries, Nationwide and Regional Surveys
Title: Direct cost of metastatic gastroenteropancreatic neuroendocrine tumours (GEP-NET) Grade 1 or 2 (G1/G2) in relation to time since diagnosis shows growing importance of somatostatin analogues (SSA)

o Poster D06 - Category: Epidemiology/Natural History/Prognosis - Registries, Nationwide and Regional Surveys
Title: Long-acting Somatostatin Analogue (LA-SSA) Treatment Durations in Patients Diagnosed with Metastatic Gastroenteropancreatic Neuroendocrine Tumours (GEP-NET) Grade 1 or 2 (G1/G2) in Sweden

o Poster D77 Category: Epidemiology/Natural History/Prognosis - Registries, Nationwide and Regional Surveys
Title: Long-acting Somatostatin Analogue (LA-SSA) Treatment Patterns in Patients Diagnosed with Metastatic Gastroenteropancreatic Neuroendocrine Tumours (GEP-NET) Grade 1 or 2 (G1/G2) in Sweden

o Poster H09 - Category: Medical Treatment - Chemotherapy Somatostayin Analogues, Interferon
Title: Therapeutic sequences in patients with G1-G2 neuroendocrine tumors (NETs): an observational, multicentre, prospective/retrospective study
Investigator-lead study

2 posters present data on NET and carcinoid syndrome:

o Poster J13 - Category: Medical Treatment, Others Not Specified
Title: Patient and Clinician Perspectives on Symptom Priorities across the Spectrum of Neuroendocrine Tumors (NETs)
Investigator-lead study
Poster D20 - Category: Epidemiology/Natural History/Prognosis - Registries, Nationwide and Regional Surveys
Title: Carcinoid syndrome open questions – Evaluations from a real life setting
Authors: R. Fijalkowski, A. Singh, R. Baum, H. Kulkarni, K. Niepsch, D. Kaemmerer, M. Hommann, D. Hoersch
Investigator-lead study

Patient experience and quality of life is featured in 2 posters:

Poster D59 - Category: Epidemiology/Natural History/Prognosis - Registries, Nationwide and Regional Surveys
Title: Patient survey devoted to characterizing experience and expectations of patients with Neuroendocrine Tumors (NET)
Authors: M. Sarabi, D. Gueguen, E. Baudin

Poster J08 - Category: Medical treatment, Others Not Specified
Title: Clinical Utility (CU) Evaluation of the Health-Related Quality-Of-Life (HRQoL) QLQ-GINET21 Questionnaire (QNR) in the Treatment of Patients (pts) with Gastrointestinal (GI) Neuroendocrine Tumours (NETs). QUALINETS Study
Authors: J. Gallego, O. Reig, J. Sastre, I. García, A. Segura, J. Capdevila, A. Carmona, I. Sevilla, T. Alonso, G. Crespo, L. García, D. Arnau, G. de la Cruz, M. Benavent

Predicting response to SSAs:

Poster F08 - Category: Biomarkers
Title: Plasma Protein hK14 Strongly Predict Pronounced Chromogranin A Response in Small Intestinal Neuroendocrine Tumor Patients After Somatostatin Analog Treatment: The Nordic EXPLAIN Biomarker Study

ABOUT SOMATULINE®
Somatuline® Autogel® / Depot® is made of the active substance lanreotide, which is a somatostatin analogue that inhibits the secretion of growth hormone and certain hormones secreted by the digestive system.
The main indications of Somatuline® and Somatuline® Autogel® are the following:
- Treatment of acromegaly when circulating levels of growth hormone and/or Insulin-like Growth Factor-1 remain abnormal after surgery and/or radiotherapy, or in patients who otherwise require medical treatment.
- Treatment of symptoms associated with carcinoid syndrome related to neuroendocrine tumors (ex-US).
- Anti-proliferative treatment of gastroenteropancreatic neuroendocrine tumors.
IMPORTANT SAFETY INFORMATION - UNITED STATES

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 ≥ 60 beats per minute (bpm) treated with Somatuline DEPOT in the GEPNETs 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® Depot by accessing the following link.

ABOUT CABOMETYX®

CABOMETYX® 20mg, 40mg and 60mg film-coated tablets

Active ingredient: Cabozantinib (S)-malate 20mg, 40mg and 60mg

Other components: Lactose
**Indications:** CABOMETYX® is indicated for the treatment of advanced renal cell carcinoma (RCC) in adults following prior vascular endothelial growth factor (VEGF)-targeted therapy.

**Dosage and Administration:** The recommended dose of CABOMETYX® is 60 mg once daily. Treatment should continue until the patient is no longer clinically benefiting from therapy or until unacceptable toxicity occurs. Management of suspected adverse drug reactions may require temporary interruption and/or dose reduction of CABOMETYX® therapy. For dose modification, please refer to full SmPC. CABOMETYX® is for oral use. The tablets should be swallowed whole and not crushed. Patients should be instructed to not eat anything for at least 2 hours before through 1 hour after taking CABOMETYX®.

**Contraindications:** Hypersensitivity to the active substance or to any of the excipients listed in the SmPC.

**Special warnings and precautions for use:** As most events can occur early in the course of treatment, the physician should evaluate the patient closely during the first eight weeks of treatment to determine if dose modifications are warranted. Events that generally have early onset include hypocalcaemia, hypokalaemia, thrombocytopenia, hypertension, palmar-plantar erythrodysesthesia syndrome (PPES), proteinuria, and gastrointestinal (GI) events (abdominal pain, mucosal inflammation, constipation, diarrhoea, vomiting). Dose reductions and dose interruptions due to an AE occurred in 59.8% and 70%, respectively, of cabozantinib-treated patients in the pivotal clinical trial. Two dose reductions were required in 19.3% of patients. The median time to first dose reduction was 55 days, and to first dose interruption was 38 days.

**Perforations and fistulas:** Serious gastrointestinal perforations and fistulas, sometimes fatal, have been observed with cabozantinib. Patients who have inflammatory bowel disease (e.g., Crohn's disease, ulcerative colitis, peritonitis, diverticulitis, or appendicitis), have tumour infiltration in the GI tract, or have complications from prior GI surgery (particularly when associated with delayed or incomplete healing) should be carefully evaluated before initiating cabozantinib therapy and subsequently they should be monitored closely for symptoms of perforations and fistulas including abscesses. Persistent or recurring diarrhoea while on treatment may be a risk factor for the development of anal fistula. Cabozantinib should be discontinued in patients who experience a GI perforation or a fistula that cannot be adequately managed.

**Thromboembolic events:** Events of venous thromboembolism, including pulmonary embolism, and events of arterial thromboembolism have been observed with cabozantinib. Cabozantinib should be used with caution in patients who are at risk for, or who have a history of, these events. Cabozantinib should be discontinued in patients who develop an acute myocardial infarction or any other clinically significant arterial thromboembolic complication.

**Haemorrhage:** Severe haemorrhage has been observed with cabozantinib. Patients who have a history of severe bleeding prior to treatment initiation should be carefully evaluated before initiating cabozantinib therapy. Cabozantinib should not be administered to patients that have or are at risk for severe haemorrhage.

**Wound complications:** Wound complications have been observed with cabozantinib. Cabozantinib treatment should be stopped at least 28 days prior to scheduled surgery, including dental surgery, if possible. The decision to resume cabozantinib therapy after surgery should be based on clinical judgment of adequate wound healing. Cabozantinib should be discontinued in patients with wound healing complications requiring medical intervention.

**Hypertension:** Hypertension has been observed with cabozantinib. Blood pressure should be well-controlled prior to initiating cabozantinib. During treatment with cabozantinib, all patients should be monitored for hypertension and treated as needed with standard anti-hypertensive therapy. In the case of persistent hypertension despite use of anti-hypertensives, the cabozantinib dose should be reduced. Cabozantinib should be discontinued if hypertension is severe and persistent despite anti-hypertensive therapy and dose reduction of cabozantinib. In case of hypertensive crisis, cabozantinib should be discontinued.
Palmar-plantar erythrodysaesthesia syndrome: Palmar-plantar erythrodysaesthesia syndrome (PPES) has been observed with cabozantinib. When PPES is severe, interruption of treatment with cabozantinib should be considered. Cabozantinib should be restarted with a lower dose when PPES has been resolved to grade 1.

Proteinuria: Proteinuria has been observed with cabozantinib. Urine protein should be monitored regularly during cabozantinib treatment. Cabozantinib should be discontinued in patients who develop nephrotic syndrome.

Reversible posterior leukoencephalopathy syndrome: Reversible Posterior Leukoencephalopathy Syndrome (RPLS), also known as Posterior Reversible Encephalopathy Syndrome (PRES), has been observed with cabozantinib. This syndrome should be considered in any patient presenting with multiple symptoms, including seizures, headache, visual disturbances, confusion or altered mental function. Cabozantinib treatment should be discontinued in patients with RPLS.

Prolongation of QT interval
Cabozantinib should be used with caution in patients with a history of QT interval prolongation, patients who are taking antiarrhythmics, or patients with relevant pre-existing cardiac disease, bradycardia, or electrolyte disturbances. When using cabozantinib, periodic monitoring with on-treatment ECGs and electrolytes (serum calcium, potassium, and magnesium) should be considered.

Interactions: CYP3A4 inducers and inhibitors: Cabozantinib is a CYP3A4 substrate. Concurrent administration of cabozantinib with the strong CYP3A4 inhibitor ketoconazole resulted in an increase in cabozantinib plasma exposure. Caution is required when administering cabozantinib with agents that are strong CYP3A4 inhibitors. Concurrent administration of cabozantinib with the strong CYP3A4 inducer rifampicin resulted in a decrease in cabozantinib plasma exposure. Therefore, chronic administration of agents that are strong CYP3A4 inducers with cabozantinib should be avoided. P-glycoprotein substrates: Cabozantinib was an inhibitor but not a substrate, of P-glycoprotein (P-gp) transport activities in a bi-directional assay system using MDCK-MDR1 cells. Therefore, cabozantinib may have the potential to increase plasma concentrations of co-administered substrates of P-gp. Subjects should be cautioned regarding taking a P-gp substrate while receiving Cabozantinib. MRP2 inhibitors: Administration of MRP2 inhibitors may result in increases in cabozantinib plasma concentrations. Therefore, concomitant use of MRP2 inhibitors should be approached with caution. Bile salt-sequestering agents: Bile salt-sequestering agents may interact with cabozantinib and may impact absorption (or reabsorption) resulting in potentially decreased exposure. The clinical significance of these potential interactions is unknown. Excipient related warnings: Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Pregnancy and lactation: Avoid pregnancy, use effective methods of contraception and discontinue breastfeeding during treatment with cabozantinib, and for at least 4 months after completing therapy.

Drive and use machines: Caution is recommended

Undesirable effects:
The most common serious adverse reactions associated with cabozantinib are abdominal pain (3%), pleural effusion (3%), diarrhoea (2%), and nausea (2%). The most frequent adverse reactions of any grade (experienced by at least 25% of patients) included diarrhoea (74%), fatigue (56%), nausea (50%), decreased appetite (46%), palmar-plantar erythrodysaesthesia syndrome (PPES) (42%), hypertension (37%), vomiting (32%), weight decreased (31%), and constipation (25%). Other very common adverse reactions: anemia, hypophosphataemia, hyperaluminaemia, hypomagnesaemia, hypophosphataemia, hyperkalaemia, hypocalcaemia, hyperbilirubinemia, dysgeusia, headache, dizziness, dysphonia, dyspnea, cough, stomatitis, abdominal pain, dyspepsia, rash, dry skin, muscle spasms, arthralgia, proteinuria, mucosal inflammation, serum ALT, AST, and ALP increased, creatinine increased, triglycerides increased, hyperglycaemia,
hypoglycaemia, lymphopenia, neutropenia, thrombocytopenia, GGT increased, amylase increased, blood cholesterol increased, lipase increased.

For all common and uncommon adverse reactions, please refer to full SmPC. For more information, see the regularly updated registered product information on the European Medicine Agency www.ema.europa.eu

ABOUT XERMELO® (TELOTRISTAT ETHYL)
Xermelo® 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, Xermelo® was designed to reduce the production of serotonin within neuroendocrine tumors.

On 22 October 2014, Ipsen and Lexicon announced that they had entered into an exclusive licensing agreement for Ipsen to commercialize Xermelo® (telotristat ethyl) in all territories excluding the United States and Japan, where Lexicon retains the rights. On 28 February 2017, Lexicon received U.S. Food and Drug Administration (FDA) approval for Xermelo® as a first and only orally administered therapy for the treatment of carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy.

General safety information about Xermelo®
In clinical trials, over 230 patients with carcinoid syndrome were treated with Xermelo®. The placebo-controlled safety analyses were focused on the integrated data from the 12-week placebo-controlled double-blind periods from the two phase 3 randomized clinical trials. For this safety analysis, 71 patients received placebo and 70 patients received Xermelo® 250 mg three times daily. The most commonly reported adverse reactions in patients treated with telotristat ethyl were abdominal pain (26%), gamma-glutamyl transferase increased (11%) and fatigue (10%). They were generally of mild or moderate intensity. The most frequently reported adverse reaction leading to discontinuation of telotristat ethyl was abdominal pain in 7.1% of patients (5/70).

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, Neurosciences 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 €1.9 billion in 2017, 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, US). The Group has about 5,400 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 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 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. The risks and uncertainties set out are not exhaustive and the reader is advised to refer to the Group's 2016 Registration Document available on its website (www.ipsen.com).

For further information:

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