

Ipsen announces 13 posters and 1 oral presentation at the 2018 ASCO Gastrointestinal Symposium

Ipsen to co-host financial community briefing to discuss data presented at the 2018 American Society of Clinical Oncology Gastrointestinal Cancers Symposium

Paris (France), 15 January 2018 – Ipsen (Euronext: IPN; ADR: IPSEY) today announced that irinotecan liposome injection (Onivyde[®]), cabozantinib (Cabometyx[®]), lanreotide (Somatuline[®] Autogel[®] / Depot[®]), and telotristat ethyl (Xermelo[®]) are the subject of 11 posters, along with 2 others focusing on patients living with neuroendocrine tumors, at the 2018 American Society of Clinical Oncology's Gastrointestinal Cancers Symposium (ASCO-GI), January 18-20, 2018 in San Francisco (CA, USA). **In addition, cabozantinib (Cabometyx[®]) will be featured in one oral abstract session:**

Oral Abstract Session B - CANCERS OF THE PANCREAS, SMALL BOWEL, AND HEPATOBILIARY TRACT Friday, January 19: 2:15 PM-3:45 PM

- Abstract 207:
Cabozantinib (C) versus placebo (P) in patients (pts) with advanced hepatocellular carcinoma (HCC) who have received prior sorafenib: results from the randomized phase 3 CELESTIAL trial.
First Author: Ghassan Abou-Alfa, MD

"Ipsen has a strong presence in oncology at ASCO-GI 2018 with 13 posters dealing with clinical outcomes in pancreatic cancer, advanced hepatocellular carcinoma, neuroendocrine tumors and carcinoid syndrome. We and Exelixis, our partner, are excited to announce that the results of the pivotal Phase 3 CELESTIAL Trial of Cabozantinib in Previously Treated Advanced Hepatocellular Carcinoma will be shared for the first time with the medical community as a late breaking presentation, on January 19th," said **Alexandre Lebeaut, MD, Executive Vice-President, R&D, Chief Scientific Officer, Ipsen.**

2 poster sessions (poster session B and poster session C) with 7 abstracts/posters featuring nal-IRI / liposomal irinotecan (ONIVYDE[®]) :

Poster Session B - CANCERS OF THE PANCREAS, SMALL BOWEL, AND HEPATOBILIARY TRACT

Poster Display Session, Friday, January 19: 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

- BOARD F20 - (Abstract 335)

Deposition characteristics and resulting DNA damage patterns of liposomal irinotecan (nal-IRI) in pancreatic cancer xenografts.

First Author: Shannon Leonard

- BOARD H16 - (Abstract 379)

Subgroup analysis by baseline pain intensity (BPI) and analgesic use (BAU) in NAPOLI-1: A phase III study of liposomal irinotecan (nal IRI)±5-fluorouracil/ leucovorin (5-FU/LV) in patients (pts) with metastatic pancreatic ductal adenocarcinoma (mPDAC) previously treated with gemcitabine-based therapy.

First Author: Teresa Macarulla, MD, PhD

- BOARD J2 - (Abstract 388)

Dose modifications of liposomal irinotecan (nal-IRI) + 5-fluorouracil/leucovorin (5-FU/LV) in NAPOLI-1: Impact on efficacy.

First Author: Andrea Wang-Gillam, MD, PhD

- BOARD K3 - (Abstract 410)

Subgroup analysis by baseline (BL) weight-associated parameters: A phase III study of liposomal irinotecan (nal IRI)±5 fluorouracil/leucovorin (5 FU/LV) in patients (pts) with metastatic pancreatic ductal adenocarcinoma (mPDAC) previously treated with gemcitabine-based (gem) therapy.

First Author: Teresa Macarulla, MD, PhD

- BOARD M6 - (Abstract 459)

Nomogram for predicting overall survival (OS) in patients (pts) treated with liposomal irinotecan (nal-IRI) ± 5-fluorouracil/leucovorin (5-FU/LV) in metastatic pancreatic ductal adenocarcinoma (mPDAC) previously treated with gemcitabine-based therapy in NAPOLI-1.

First Author: Andrea Wang-Gillam, MD, PhD

- BOARD M7 - (Abstract 460)

Subgroup analysis by measurable metastatic lesion (ML) number and selected lesion locations (LL) at baseline (BL) in NAPOLI 1: A phase III study of liposomal irinotecan (nal-IRI)±5 fluorouracil/leucovorin (5 FU/LV) in patients (pts) with metastatic pancreatic ductal adenocarcinoma (mPDAC) previously treated with gemcitabine-based therapy.

First Author: Jens Siveke, Prof. Dr. med.

Poster Session C - CANCERS OF THE COLON, RECTUM, AND ANUS

Poster Session Display, Saturday, January 20: 7:00 AM-7:55 AM and 11:30 AM-1:00 PM

- BOARD G24 - (Abstract 711)

Influence of liposomal irinotecan (nal-IRI) and non-liposomal irinotecan, alone and in combination, on tumor growth and angiogenesis in colorectal cancer (CRC) models.
First Author: Annette Larsen, DVM, PhD

Cabozantinib (Cabometyx®) is featured in 2 sessions:

Oral Abstract Session B - CANCERS OF THE PANCREAS, SMALL BOWEL, AND HEPATOBILIARY TRACT Friday, January 19: 2:15 PM-3:45 PM

- Abstract 207:
Cabozantinib (C) versus placebo (P) in patients (pts) with advanced hepatocellular carcinoma (HCC) who have received prior sorafenib: results from the randomized phase 3 CELESTIAL trial.
First Author: Ghassan Abou-Alfa, MD

Poster Session B - CANCERS OF THE PANCREAS, SMALL BOWEL, AND HEPATOBILIARY TRACT

Poster Session Display, Friday, January 19: 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

- BOARD A4 - (Abstract 207)
Cabozantinib (C) versus placebo (P) in patients (pts) with advanced hepatocellular carcinoma (HCC) who have received prior sorafenib: results from the randomized phase 3 CELESTIAL trial.
First Author: Ghassan Abou-Alfa, MD

Lanreotide (Somatuline® Autogel® / Depot®) is featured in 1 poster session:

Poster Session B - CANCERS OF THE PANCREAS, SMALL BOWEL, AND HEPATOBILIARY TRACT

Poster Session Display, Friday, January 19: 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

- BOARD G8 - (Abstract 347)
Lanreotide for the prolonged control of carcinoid syndrome (CS) in somatostatin analog (SSA)-naïve or experienced patients.
First Author: Edward Wolin, MD

Neuroendocrine tumors clinical research is featured in 1 poster session:

Poster Session B - CANCERS OF THE PANCREAS, SMALL BOWEL, AND HEPATOBILIARY TRACT

Poster Session Display, Friday, January 19: 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

- BOARD G20 - (Abstract 359)
Living with neuroendocrine tumors: Assessing quality of life (QoL) through a mobile application.
First Author: Jared Adams, MD, PhD



- BOARD E8 - (Abstract 299)
Physical, emotional, and informational challenges of patients living with neuroendocrine tumors in the United States: Understanding their unmet needs.
First Author: Grace Goldstein

Telotristat ethyl (Xermelo®) is featured in 1 poster session

Poster Session B - CANCERS OF THE PANCREAS, SMALL BOWEL, AND HEPATOBILIARY TRACT

Poster session, Friday, January 19: 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

- BOARD J9 - (Abstract 395)
Time to sustained improvement in bowel movement frequency with telotristat ethyl: Analysis of the phase III TELECAST study.
First Author: Joseph Dillon

Nota bene: Approved indications for products vary by country and not all indications are available in every country. The product safety and efficacy profiles have not yet been established outside the approved indications.

ABOUT ONIVYDE®

ONIVYDE® is an encapsulated formulation of irinotecan. This long-circulating liposomal form is designed to increase length of tumor exposure to both irinotecan and its active metabolite, SN- 38.

On April 3, 2017, Ipsen completed the acquisition from Merrimack Pharmaceuticals of ONIVYDE® (irinotecan liposome injection) for the treatment of patients with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy, in combination with fluorouracil and leucovorin. Ipsen gained exclusive commercialization rights for the current and potential future indications for ONIVYDE® in the U.S., as well as the current licensing agreements with Shire for commercialization rights ex-U.S. and PharmaEngine for Taiwan.

ONIVYDE® is approved by the U.S. FDA in combination with fluorouracil and leucovorin for the treatment of patients with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy. For full prescribing information, including Boxed WARNING, please visit www.ONIVYDE.com.

INDICATION - UNITED STATES

ONIVYDE® (irinotecan liposome injection) is indicated, in combination with fluorouracil (5-FU) and leucovorin (LV), for the treatment of patients with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy. Limitation of Use: ONIVYDE® is not indicated as a single agent for the treatment of patients with metastatic adenocarcinoma of the pancreas.

IMPORTANT SAFETY INFORMATION - UNITED STATES

BOXED WARNING: SEVERE NEUTROPENIA and SEVERE DIARRHEA

Fatal neutropenic sepsis occurred in 0.8% of patients receiving ONIVYDE®. Severe or life threatening neutropenic fever or sepsis occurred in 3% and severe or life-threatening neutropenia occurred in 20% of patients receiving ONIVYDE® in combination with fluorouracil (5-FU) and leucovorin (LV). Withhold ONIVYDE® for absolute neutrophil count below 1500/mm³ or neutropenic fever. Monitor blood cell counts periodically during treatment.



Severe diarrhea occurred in 13% of patients receiving ONIVYDE® in combination with 5- FU/LV. Do not administer ONIVYDE® to patients with bowel obstruction. Withhold ONIVYDE® for diarrhea of Grade 2-4 severity.

CONTRAINDICATION - UNITED STATES

ONIVYDE® is contraindicated in patients who have experienced a severe hypersensitivity reaction to ONIVYDE® or irinotecan HCl.

WARNINGS AND PRECAUTIONS – UNITED STATES

Severe Neutropenia

ONIVYDE® can cause severe or life-threatening neutropenia and fatal neutropenic sepsis. In a clinical study, the incidence of fatal neutropenic sepsis was 0.8% among patients receiving ONIVYDE®, occurring in 1/117 patients in the ONIVYDE®/5-FU/LV arm and 1/147 patients receiving ONIVYDE® as a single agent. Severe or life-threatening neutropenia occurred in 20% of patients receiving ONIVYDE®/5-FU/LV vs 2% of patients receiving 5-FU/LV. Grade 3/4 neutropenic fever/neutropenic sepsis occurred in 3% of patients receiving ONIVYDE®/5-FU/LV, and did not occur in patients receiving 5-FU/LV.

In patients receiving ONIVYDE®/5-FU/LV, the incidence of Grade 3/4 neutropenia was higher among Asian (18/33 [55%]) vs White patients (13/73 [18%]). Neutropenic fever/neutropenic sepsis was reported in 6% of Asian vs 1% of White patients.

Severe Diarrhea

ONIVYDE® can cause severe and life-threatening diarrhea. Do not administer ONIVYDE® to patients with bowel obstruction. Severe and life-threatening late-onset (onset > 24 hours after chemotherapy) and early-onset diarrhea (onset ≤24 hours after chemotherapy, sometimes with other symptoms of cholinergic reaction) were observed. An individual patient may experience both early- and late-onset diarrhea.

In a clinical study, Grade 3/4 diarrhea occurred in 13% of patients receiving ONIVYDE®/5-FU/LV vs 4% receiving 5-FU/LV. Grade 3/4 late-onset diarrhea occurred in 9% of patients receiving ONIVYDE®/5-FU/LV vs 4% in patients receiving 5-FU/LV; the incidences of early-onset diarrhea were 3% and no Grade 3/4 incidences, respectively. Of patients receiving ONIVYDE®/5-FU/LV, 34% received loperamide for late-onset diarrhea and 26% received atropine for early-onset diarrhea.

Interstitial Lung Disease (ILD)

Irinotecan HCl can cause severe and fatal ILD. Withhold ONIVYDE® in patients with new or progressive dyspnea, cough, and fever, pending diagnostic evaluation. Discontinue ONIVYDE® in patients with a confirmed diagnosis of ILD.

Severe Hypersensitivity Reactions

Irinotecan HCl can cause severe hypersensitivity reactions, including anaphylactic reactions. Permanently discontinue ONIVYDE® in patients who experience a severe hypersensitivity reaction.

Embryo-Fetal Toxicity

Based on animal data with irinotecan HCl and the mechanism of action of ONIVYDE®, ONIVYDE® can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during and for 1 month after ONIVYDE® treatment.

ADVERSE REACTIONS – UNITED STATES

- The most common (≥20%) adverse reactions in which patients receiving ONIVYDE®/5- FU/LV experienced a ≥5% higher incidence of any Grade vs the 5-FU/LV arm, were diarrhea (any 59%, 26%; severe 13%, 4%) (early diarrhea [any 30%, 15%; severe 3%, 0%], late diarrhea [any 43%, 17%; severe 9%, 4%]), fatigue/asthenia (any 56%, 43%; severe 21%, 10%), vomiting (any 52%, 26%; severe 11%,

3%), nausea (any 51%, 34%; severe 8%, 4%), decreased appetite (any 44%, 32%; severe 4%, 2%), stomatitis (any 32%, 12%; severe 4%, 1%), pyrexia (any 23%, 11%; severe 2%, 1%).

- Of less common (< 20%) adverse reactions, patients receiving ONIVYDE®/5-FU/LV who experienced Grade 3/4 adverse reactions at a ≥2% higher incidence of Grade 3/4 toxicity vs the 5-FU/LV arm, respectively, were sepsis (3%, 1%), neutropenic fever/neutropenic sepsis (3%, 0%), gastroenteritis (3%, 0%), intravenous catheter-related infection (3%, 0%), weight loss (2%, 0%), and dehydration (4%, 2%).
- The laboratory abnormalities in which patients receiving ONIVYDE®/5-FU/LV experienced a ≥5% higher incidence vs the 5-FU/LV arm, were anemia (any 97%, 86%; severe 6%, 5%), lymphopenia (any 81%, 75%; severe 27%, 17%), neutropenia (any 52%, 6%; severe 20%, 2%), thrombocytopenia (any 41%, 33%; severe 2%, 0%), increased alanine aminotransferase (any 51%, 37%; severe 6%, 1%), hypoalbuminemia (any 43%, 30%; severe 2%, 0%), hypomagnesemia (any 35%, 21%; severe 0%, 0%), hypokalemia (any 32%, 19%; severe 2%, 2%), hypocalcemia (any 32%, 20%; severe 1%, 0%), hypophosphatemia (any 29%, 18%; severe 4%, 1%), hyponatremia (any 27%, 12%; severe 5%, 3%), increased creatinine (any 18%, 13%; severe 0%, 0%).
- ONIVYDE® can cause cholinergic reactions manifesting as rhinitis, increased salivation, flushing, bradycardia, miosis, lacrimation, diaphoresis, and intestinal hyperperistalsis with abdominal cramping and early-onset diarrhea. Grade 1/2 cholinergic symptoms other than early diarrhea occurred in 12 (4.5%) ONIVYDE®-treated patients.
- Infusion reactions, consisting of rash, urticaria, periorbital edema, or pruritus, occurring on the day of ONIVYDE® administration were reported in 3% of patients receiving ONIVYDE® or ONIVYDE®/5-FU/LV.
- The most common serious adverse reactions (≥2%) of ONIVYDE® were diarrhea, vomiting, neutropenic fever or neutropenic sepsis, nausea, pyrexia, sepsis, dehydration, septic shock, pneumonia, acute renal failure, and thrombocytopenia.

DRUG INTERACTIONS – UNITED STATES

Avoid the use of strong CYP3A4 inducers, if possible, and substitute non-enzyme-inducing therapies ≥2 weeks prior to initiation of ONIVYDE®. Avoid the use of strong CYP3A4 or UGT1A1 inhibitors, if possible, and discontinue strong CYP3A4 inhibitors ≥1 week prior to starting therapy.

USE IN SPECIFIC POPULATIONS – UNITED STATES

Pregnancy and Reproductive Potential

Advise pregnant women of the potential risk to a fetus. Advise males with female partners of reproductive potential to use effective contraception during and for 4 months after ONIVYDE® treatment.

Lactation

Advise nursing women not to breastfeed during and for 1 month after ONIVYDE® treatment.

Pediatric

Safety and effectiveness of ONIVYDE® have not been established in pediatric patients.

DOSAGE AND ADMINISTRATION - UNITED STATES

The recommended dose of ONIVYDE® is 70 mg/m² intravenous (IV) infusion over 90 minutes every 2 weeks, administered prior to LV and 5-FU. The recommended starting dose of ONIVYDE® in patients known to be homozygous for the UGT1A1*28 allele is 50 mg/m² administered by IV infusion over 90 minutes. There is no



recommended dose of ONIVYDE® for patients with serum bilirubin above the upper limit of normal. Premedicate with a corticosteroid and an anti-emetic 30 minutes prior to ONIVYDE®. Withhold ONIVYDE® for Grade 3/4 adverse reactions. Resume ONIVYDE® with reduced dose once adverse reaction recovered to ≤Grade 1. Discontinue ONIVYDE® in patients who experience a severe hypersensitivity reaction and in patients with a confirmed diagnosis of ILD.

Do not substitute ONIVYDE® for other drugs containing irinotecan HCl.

Please see full U.S. [Prescribing Information](#) for ONIVYDE®.

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, palmarplantar 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 erythrodysesthesia syndrome: Palmar-plantar erythrodysesthesia 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 breast-feeding 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 erythrodysesthesia syndrome (PPES) (42%), hypertension (37%), vomiting (32%), weight decreased (31%), and constipation (25%). Other very common adverse reactions: anemia, hypophosphataemia, hypoalbuminaemia, hypomagnesaemia, hyponatraemia, hypokalaemia, 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 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 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 the Investor Briefing

Ipsen and its partner Exelixis will host a live briefing event for the financial community to discuss data presented at the 2018 American Society of Clinical Oncology Gastrointestinal Cancers Symposium (ASCO-GI). The webcast event will be held following the closing of the ASCO-GI day's sessions on Friday, January 19, 2018,



beginning at 9:30 p.m. EST / 6:30 p.m. PST (local San Francisco time). During the briefing, Exelixis and Ipsen management, along with an invited guest, will discuss and provide context for the cabozantinib clinical data presented earlier that day at the Symposium. Ipsen previously announced that detailed results from the CELESTIAL trial will be the subject of a late-breaking oral presentation at ASCO-GI. CELESTIAL is a randomized, double-blind, placebo-controlled study of cabozantinib versus placebo in patients with advanced hepatocellular carcinoma who have received prior treatment with sorafenib.

To access the webcast link, log onto www.exelixis.com and proceed to the News & Events / Event Calendar page under the Investors & Media heading. Please connect to the company's website at least 15 minutes prior to the presentation to ensure adequate time for any software download that may be required to listen to the webcast. Alternatively, please call 855-793-2457 (domestic) or 631-485-4921 (international) and provide the conference call passcode 2478857 to join by phone. A webcast replay will be archived on www.exelixis.com for one year. A telephone replay will also be available until 11:59 p.m. EST on January 26, 2018. Access numbers for the telephone replay are: 855-859-2056 (domestic) and 404-537-3406 (international); the passcode is 2478857.

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 close to €1.6 billion in 2016, 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 5,100 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.ipсен.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 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 2016 Registration Document available on its website (www.ipsen.com).

For further information:

Media

Ian Weatherhead

Vice President, Corporate External Communications
Tel.: +44 (0) 1753 627733
E-mail: ian.weatherhead@ipsen.com

Brigitte Le Guennec

Senior Manager, Global External Communications
Tel.: +33 (0)1 58 33 51 17
E-mail : brigitte.le.guennec@ipsen.com

Financial Community

Eugenia Litz

Vice-President Investor Relations
Tel.: +44 (0) 1753 627721
E-mail: eugenia.litz@ipsen.com

Côme de La Tour du Pin

Investor Relations Executive
Tel.: +33 (0)1 58 33 53 31
E-mail: come.de.la.tour.du.pin@ipsen.com