

## **Ipsen to present new data from its oncology portfolio at the 2018 European Society for Medical Oncology (ESMO) congress**

**Paris (France), 12 October 2018** – Ipsen (Euronext: IPN; ADR: IPSEY) today announced that cabozantinib (Cabometyx<sup>®</sup>), irinotecan liposome injection (Onivyde<sup>®</sup>), lanreotide (Somatuline<sup>®</sup>) and the combination of lanreotide and telotristat (Xermelo<sup>®</sup>) are the subject of 12 presentations at the 2018 European Society for Medical Oncology (ESMO) annual congress. The meeting takes place in Munich, Germany, October 19-23, 2018.

*“Ipsen has had a momentous 12 months since ESMO 2017, particularly with the positive regulatory milestones achieved for Cabometyx<sup>®</sup> in renal cell and hepatocellular carcinoma, and for Xermelo<sup>®</sup> in neuroendocrine tumours. Our story continues with a strong presence at ESMO 2018 with 12 posters presenting meaningful data for patients with hepatocellular carcinoma, renal cell carcinoma, medullary thyroid cancer, pancreatic cancer and neuroendocrine tumours,”* said **Alexandre Lebeaut M.D, Executive Vice President, Research & Development and Chief Scientific Officer, Ipsen.**

*“Our oncology products, notably Cabometyx<sup>®</sup>, Onivyde<sup>®</sup>, Somatuline<sup>®</sup> and Xermelo<sup>®</sup> have been evaluated by scientific teams around the world; either directly by investigators, by our partners, or by Ipsen, and results from some of these investigations will be shared at ESMO 2018. We are committed in our efforts against cancer, and through our interactions at ESMO will continue to advance innovation for patient care in oncology”,* added **Dr Lebeaut.**

### **Cabozantinib (Cabometyx<sup>®</sup>) will be featured in 5 posters:**

Poster session, Sunday October 21<sup>st</sup>, 13:15 - 14:15, Hall A3

#### *CELESTIAL study*

- [Poster 702P] Outcomes by baseline alpha-fetoprotein (AFP) levels in the phase 3 CELESTIAL trial of cabozantinib (C) versus placebo (P) in previously treated advanced hepatocellular carcinoma (HCC) (Kelley et al.)

Presenting author: R.K. Kelley [Sponsor: Exelixis]

- [Poster 703P] Assessment of disease burden in the phase 3 CELESTIAL trial of cabozantinib (C) versus placebo (P) in advanced hepatocellular carcinoma (HCC) (Blanc et al.)

Presenting author: JF Blanc [Sponsor: Exelixis]

- [Poster 704P] Outcomes by prior transarterial chemoembolization (TACE) in the phase 3 CELESTIAL trial of cabozantinib (C) versus placebo (P) in patients (pts) with advanced hepatocellular carcinoma (HCC) (Yau et al.)

Presenting author: T Yau [Sponsor: Exelixis]

Poster session, Monday October 22<sup>nd</sup>, 13:15 - 14:15, Hall A3

*COSMIC-021 study (Cabozantinib + atezolizumab)*

- [Poster 872P] Phase 1b study (COSMIC-021) of cabozantinib in combination with atezolizumab in solid tumors: Results of the dose escalation stage in patients with treatment-naïve advanced RCC (Agarwal et al.)

Presenting author: N Agarwal [Sponsor: Exelixis]

Poster session, Sunday October 21<sup>st</sup>, 13:15 - 14:15, Hall A3

*EXAMINER study*

- [Poster 129TiP] A noninferiority trial of cabozantinib (C) comparing 140 mg vs 60 mg orally per day to evaluate the efficacy and safety in patients (pts) with progressive, metastatic medullary thyroid cancer (MTC) (Krajewska et al.)

Presenting author: J Krajewska [Sponsor: Exelixis]

Poster session, Sunday October 21<sup>st</sup>, 13:15 - 14:15, Hall A3

**Irinotecan liposome injection (Onivyde®) will be featured in 4 presentations:**

- [Poster 749P] The prognostic value of the Modified Glasgow Prognostic Score (mGPS) in predicting overall survival (OS) in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) receiving liposomal irinotecan (nal-IRI)+5-fluorouracil and leucovorin (5-FU/LV). (Chen, et al.)

Presenting author: L-T Chen [Sponsor: Ipsen]

- [Poster 734P] Impact of dose reduction or dose delay on the efficacy of liposomal irinotecan (nal-IRI)+5-fluorouracil/leucovorin (5-FU/LV): Survival analysis from NAPOLI-1. (Chen, et al.)

Presenting author: L-T Chen [Sponsor: Ipsen]

- [Poster 735P] Real-world dosing patterns of patients (pts) with metastatic pancreatic cancer (mPC) treated with liposomal irinotecan (nal-IRI) in US oncology clinics. (Ahn, et al.)

Presenting author: D Ahn [Sponsor: Ipsen]

- [Poster 733P] NAPOLI-1 Phase 3 trial outcomes by prior surgery, and disease stage, in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC). (Macarulla, et al.)

Presenting author: T Macarulla [Sponsor: Shire]

Poster session, Sunday October 21<sup>st</sup>, 13:15 - 14:15, Hall A3

**Lanreotide (Somatuline®) will be featured in 2 presentations:**

*PRELUDE (TGR)*

- [Poster 1331P] Tumour growth rate (TGR) when using lanreotide Autogel® (LAN) before, during and after peptide receptor radionuclide therapy (PRRT) in advanced neuroendocrine tumours (NETs). (Prasad, et al.)

Presenting author: V Prasad [Sponsor: Ipsen]

Poster session, Sunday October 21<sup>st</sup>, 13:15 - 14:15, Hall A3

*CLARINET (diabetes)*

- [Poster 1319P] Post-hoc analysis of CLARINET phase III study to investigate the influence of diabetic status on progression-free survival (PFS) of patients with neuroendocrine tumours (NETs) treated with lanreotide (LAN) or placebo (PBO). (Pusceddu, et al.)

Presenting author: V Pusceddu [Sponsor: Ipsen]

Poster session, Sunday October 21<sup>st</sup>, 13:15 - 14:15, Hall A3

**Lanreotide (Somatuline®) & telotristat (Xermelo®) will be featured in 1 presentation:**

*TELESTAR & TELECAST (LAN patients)*

- [Poster 1314P] Efficacy and safety of telotristat ethyl (TE) in combination with lanreotide (LAN) in patients with a neuroendocrine tumour and carcinoid syndrome (CS) diarrhoea (CSD): Meta-analysis of phase 3 double-blind placebo (PBO)-controlled TELESTAR and TELECAST studies. (Hörsch, et al.)

Presenting author: D Hörsch [Sponsor: Ipsen]

**ABOUT CABOMETRYX® (cabozantinib)**

Cabometryx® is an oral small molecule inhibitor of receptors, including VEGFR, MET, AXL and RET. In preclinical models, cabozantinib has been shown to inhibit the activity of these receptors, which are involved in normal cellular function and pathologic processes such as tumor angiogenesis, invasiveness, metastasis and drug resistance.

In February of 2016, Exelixis and Ipsen jointly announced an exclusive licensing agreement for the commercialization and further development of cabozantinib indications outside of the United States, Canada and Japan. This agreement was amended in December of 2016 to include commercialization rights for Ipsen in Canada.

On April 25, 2016, the FDA approved Cabometryx® tablets for the treatment of patients with advanced RCC who have received prior anti-angiogenic therapy and on September 9, 2016, the European Commission approved Cabometryx® tablets for the treatment of advanced RCC in adults who have received prior vascular endothelial growth factor (VEGF)-targeted therapy in the European Union, Norway and Iceland. Cabometryx® is also approved in Australia, Canada, South Korea and Switzerland. Cabometryx® is available in 20 mg, 40 mg or 60 mg doses. The recommended dose is 60 mg orally, once daily.

On December 19, 2017, Exelixis received approval from the FDA for Cabometryx® for the expanded indication of treatment of first-line advanced RCC.

On May 17, 2018, Ipsen announced that the European Commission approved Cabometryx® for the first-line treatment of adults with intermediate- or poor- risk advanced renal cell carcinoma in the European Union, Norway and Iceland.

Cabozantinib is not yet approved for the treatment of hepatocellular carcinoma.

**Indications:** CABOMETRYX® is indicated for the treatment of advanced renal cell carcinoma (RCC) in treatment-naïve adults with intermediate or poor risk or in adults following prior vascular endothelial growth factor (VEGF)-targeted therapy

**Dosage and Administration:** The recommended dose of CABOMETRYX® 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 CABOMETRYX® therapy. For dose modification, please refer to full SmPC. CABOMETRYX® 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:**

Monitor closely for toxicity during first 8 weeks of therapy. Events that generally have early onset include hypocalcaemia, hypokalaemia, thrombocytopenia, hypertension, palmar-plantar erythrodysesthesia syndrome (PPES), proteinuria, and gastrointestinal (GI) events. Perforations and fistulas: serious gastrointestinal perforations and fistulas, sometimes fatal, have been observed with cabozantinib. Patients with inflammatory bowel disease, GI tumour infiltration or complications from prior GI surgery should be evaluated prior to therapy and monitored; if perforation and unmanageable fistula occur, discontinue cabozantinib.

Thromboembolic events: use with caution in patients with a history of or risk factors for thromboembolism; discontinue if acute myocardial infarction (MI) or other significant arterial thromboembolic complication occurs.

Haemorrhage: not recommended for patients that have or are at risk of severe haemorrhage. Wound complications: treatment should be stopped at least 28 days prior to scheduled surgery (including dental).

Hypertension: monitor blood pressure (BP); reduce with persistent hypertension and discontinue should uncontrolled hypertension or hypertensive crisis occur.

Palmar-plantar erythrodysesthesia (PPES): interrupt treatment if severe PPES occurs.

Proteinuria: discontinue in patients with nephrotic syndrome. Reversible posterior leukoencephalopathy syndrome (RPLS): discontinue in patients with RPLS.

QT interval prolongation: use with caution in patients with a history of QT prolongation, those on antiarrhythmics or with pre-existing cardiac disease.

Excipients: do not use in patients with hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption.

**Interactions:** Cabozantinib is a CYP3A4 substrate. Potent CYP3A4 inhibitors may result in an increase in cabozantinib plasma exposure (e.g. ritonavir, itraconazole, erythromycin, clarithromycin, grapefruit juice). Coadministration with CYP3A4 inducers may result in decreased cabozantinib plasma exposure (e.g. rifampicin, phenytoin, carbamazepine, phenobarbital, St John's Wort). Cabozantinib may increase the plasma concentration of P-glycoprotein substrates (e.g. fexofenadine, aliskiren, ambrisentan, dabigatran etexilate, digoxin, colchicine, maraviroc, posaconazole, ranolazine, saxagliptin, sitagliptin, talinolol, tolvaptan). MRP2 inhibitors may increase cabozantinib plasma concentrations (e.g. cyclosporine, efavirenz, emtricitabine). Bile salt sequestering agents may impact absorption or reabsorption resulting in potentially decreased cabozantinib exposure. No dose adjustment when co-administered with gastric pH modifying agents. A plasma protein displacement interaction may be possible with warfarin. INR values should be monitored in such a combination.

**Women of childbearing potential/contraception in males and females:** Ensure effective measures of contraception (oral contraceptive plus a barrier method) in male and female patients and their partners during therapy and for at least 4 months after treatment.

**Pregnancy and lactation:** CABOMETYX should not be used during pregnancy unless the clinical condition of the woman requires treatment. Lactation – discontinue breast-feeding during and for at least 4 months after completing treatment.

**Drive and use machines:** Caution is recommended.

**Adverse reactions:** The most common serious adverse reactions are hypertension, diarrhoea, PPES, pulmonary embolism, fatigue and hypomagnesaemia. Very common (>1/10): anaemia, lymphopenia, neutropenia, thrombocytopenia, hypothyroidism, dehydration, decreased appetite, hyperglycaemia, hypoglycaemia, hypophosphataemia, hypoalbuminaemia, hypomagnesaemia, hyponatraemia, hypokalaemia, hyperkalaemia, hypocalcaemia, hyperbilirubinaemia, peripheral sensory neuropathy, dysgeusia, headache, 6 / 8 dizziness, hypertension, dysphonia, dyspnoea, cough, diarrhoea, nausea, vomiting, stomatitis, constipation, abdominal pain, dyspepsia, oral pain, dry mouth, PPES, dermatitis acneiform, rash, rash maculopapular, dry skin, alopecia, hair colour change, pain in extremity, muscle spasms, arthralgia, proteinuria, fatigue, mucosal inflammation, asthenia, weight decreased, serum ALT, AST, and ALP increased, blood bilirubin increased, creatinine increased, triglycerides increased, white blood cell decreased, GGT increased, amylase increased, blood cholesterol increased, lipase increased. Common (>1/100 to <1/10): abscess, tinnitus, pulmonary embolism, pancreatitis, abdominal pain upper, gastro oesophageal reflux disease, haemorrhoids, pruritus, peripheral oedema, wound complications. Uncommon (>1/1000 to <1/100): convulsion, anal fistula, hepatitis cholestatic, osteonecrosis of the jaw. Selected adverse events: GI perforation, fistulas, haemorrhage, RPLS. Prescribers should consult the SPC in relation to other adverse reactions.

For more information, see the regularly updated registered product information on the European Medicine Agency [www.ema.europa.eu](http://www.ema.europa.eu)

## **ABOUT ONIVYDE® (US: irinotecan liposome injection ; ex-US : liposomal irinotecan)**

ONIVYDE is an encapsulated formulation of irinotecan available as a 43 mg/10 mL single dose vial. 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 and gained exclusive commercialization rights for the current and potential future indications for ONIVYDE in the US. Servier is responsible for the development and commercialization of ONIVYDE outside of the U.S. and Taiwan under an exclusive licensing agreement with Ipsen Biopharm Ltd.

ONIVYDE is approved by the U.S. FDA 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 Warnings – United States**

#### **Boxed Warnings: Severe Neutropenia and Severe Diarrhea**

- Fatal neutropenic sepsis occurred in 0.8% of patients receiving ONIVYDE. Severe or lifethreatening neutropenic fever or sepsis occurred in 3% and severe or life-threatening neutropenia occurred in 20% of patients receiving ONIVYDE in combination with 5-FU and LV. Withhold ONIVYDE for absolute neutrophil count below 1500/mm<sup>3</sup> 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. Administer loperamide for late diarrhea of any severity. Administer atropine, if not contraindicated, for early diarrhea of any severity

#### **Contraindication**

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

#### **Warnings and Precautions**

- **Severe Neutropenia:** See Boxed WARNING. 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:** See Boxed WARNING. Severe and life-threatening late-onset (onset >24 hours after chemotherapy [9%]) and early-onset diarrhea (onset ≤24 hours after chemotherapy [3%], sometimes with other symptoms of cholinergic reaction) were observed
- **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:** ONIVYDE can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during and for 1 month after ONIVYDE treatment

#### **Adverse Reactions**

- The most common adverse reactions (≥20%) were diarrhea (59%), fatigue/asthenia (56%), vomiting (52%), nausea (51%), decreased appetite (44%), stomatitis (32%), and pyrexia (23%)
- The most common Grade 3/4 adverse reactions (≥10%) were diarrhea (13%), fatigue/asthenia (21%), and vomiting (11%)
- Adverse reactions led to permanent discontinuation of ONIVYDE in 11% of patients receiving ONIVYDE/5-FU/LV; The most frequent adverse reactions resulting in discontinuation of ONIVYDE were diarrhea, vomiting, and sepsis
- Dose reductions of ONIVYDE for adverse reactions occurred in 33% of patients receiving ONIVYDE/5-FU/LV; the most frequent adverse reactions requiring dose reductions were neutropenia, diarrhea, nausea, and anemia
- ONIVYDE was withheld or delayed for adverse reactions in 62% of patients receiving ONIVYDE/5-FU/LV; the most frequent adverse reactions requiring interruption or delays were neutropenia, diarrhea, fatigue, vomiting, and thrombocytopenia
- The most common laboratory abnormalities (≥20%) were anemia (97%), lymphopenia (81%), neutropenia (52%), increased ALT (51%), hypoalbuminemia (43%), thrombocytopenia (41%), hypomagnesemia (35%), hypokalemia (32%), hypocalcemia (32%), hypophosphatemia (29%), and hyponatremia (27%)

#### **Drug interactions**

Avoid the use of strong CYP3A4 inducers, if possible, and substitute non-enzyme inducing therapies  $\geq 2$  weeks prior to initiation of ONIVYDE

- Avoid the use of strong CYP3A4 or UGT1A1 inhibitors, if possible, and discontinue strong CYP3A4 inhibitors  $\geq 1$  week prior to starting therapy

#### **Use in Specific Populations**

- **Pregnancy and Reproductive Potential:** See WARNINGS & PRECAUTIONS. Advise males with female partners of reproductive potential to use condoms during and for 4 months after ONIVYDE treatment
- **Lactation:** Advise nursing women not to breastfeed during and for 1 month after ONIVYDE treatment

**Please see full U.S. Prescribing Information for ONIVYDE®.**

#### **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 (exUS).
- 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  $\geq 60$  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).

#### **Trademarks:**

ONIVYDE is a registered trademark of Ipsen Biopharm Limited.

CABOMETRYX® (cabozantinib) and XERMELO® (telotristat ethyl) are not marketed by Ipsen in the United States. The approved indications may vary by country. CABOMETRYX® is marketed by Exelixis, Inc. in the United States. Ipsen has exclusive rights for the commercialization and further clinical development of CABOMETRYX® outside of the United States and Japan.

#### **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 €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.ipсен.com](http://www.ipсен.com).

#### **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 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 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 2017 Registration Document available on its website ([www.ipsen.com](http://www.ipsen.com)).

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