

## **Ipsen presents new analyses utilizing modern data mining approaches at ISPOR Europe 2019**

Presentations showcase insights in advanced renal cell carcinoma, gastroenteropancreatic neuroendocrine tumors and acromegaly

**Paris (France), 31 October 2019** – Ipsen (Euronext: IPN; ADR: IPSEY) today announced that results from a network meta-analysis (NMA) in advanced renal cell carcinoma (aRCC), and a UK-focused budget impact study assessing long-acting somatostatin analogues (LA-SSAs) for the treatment of acromegaly and gastroenteropancreatic neuroendocrine tumors (GEP NET) will be presented at the International Society of Pharmacoeconomics and Outcomes Research (ISPOR) Europe 2019 Annual Conference. ISPOR takes place in Copenhagen, Denmark from 2 – 6 November 2019.

Key studies to be presented at ISPOR Europe 2019:

- **An assessment** of the budget impact of LA-SSAs in the treatment of acromegaly and GEP NET, considering attributes related to the drug delivery of LA-SSAs in the UK.
- **An NMA** analyzing cabozantinib versus standard-of-care comparators in progression free survival (PFS) and overall survival (OS) in the first-line treatment of advanced renal cell carcinoma.

“We’re excited to be sharing two interesting sets of results – namely a comparison of first-line therapies and budget impact of a treatment approach for acromegaly and gastroenteropancreatic neuroendocrine tumors,” said Ulf Staginnus, Senior Vice President, Head Global Market Access and Pricing, Ipsen. “With more than 5,000 global healthcare leaders, seeking robust health solutions and new insights, ISPOR Europe 2019 is the perfect stage to share these results.”

The delivery attributes of both LA-SSAs were considered in the UK-focused study assessing the budget impact of the LA-SSAs, lanreotide versus octreotide in the treatment of acromegaly and GEP-NET. Model inputs (including drug acquisition and administration costs) were based on publicly available sources. The analysis compared the current and hypothetical market share scenarios from three perspectives in the UK: the National Health Service (NHS), a regional clinical commissioning group (CCG), and a local institution (hospital). Results suggested that increasing the use of lanreotide to a hypothetical 80% market share for lanreotide in the UK would reduce overall LA-SSAs patient treatment expenses by £2.9 million annually in the UK (a reduction of 3.6% from the current budget estimate of £80.6 million).

In the area of treatment provision in aRCC, Ipsen used an NMA to respond to the challenge presented to healthcare professionals by the introduction of targeted therapies in the last year with no way to objectively compare them. While randomized trials are the gold standard for comparative effectiveness research, they are not always available for clinically and economically important treatment comparisons. In this case, the NMA may offer some helpful insights as it suggests that cabozantinib significantly increases progression free survival (PFS) in intermediate and poor-risk patients when compared with standards-of-care and concludes that cabozantinib may be considered as an efficient treatment option in first-line aRCC.

“Modern quantitative data reviews of available agents offer additional insights into existing healthcare,” said Bartek Bednarz, Senior Vice-President, Global Product and Portfolio Strategy, Ipsen. “The network meta-analysis (NMA) for cabozantinib and budget impact model for somatostatin analogues shared at ISPOR Europe 2019 are just part of Ipsen’s ongoing commitment to demonstrating benefit for payers and improving options for patients with high unmet needs.”

Follow Ipsen on Twitter via @IpsenGroup and keep up to date with ISPOR Europe 2019 Conference news and updates by using the hashtag #ISPOREurope.

#### Overview of key Ipsen presentations at ISPOR Europe 2019:

Medicine	Abstract title	Abstract number/timing (CEST)
Cabometyx® (cabozantinib)	Cabozantinib versus standard-of-care comparators: a network meta-analysis of progression free survival and overall survival in the first-line treatment of advanced renal cell carcinoma	PCN42; Board D5 RESEARCH POSTER SESSION 2 CANCER Monday, November 4, 2019 Display Hours: 15:30 - 19:00
Somatuline® Autogel® (lanreotide autogel/depot)	Budget impact analysis of somatostatin analogues in the treatment of GEP-NET and acromegaly in the UK	PDG23; Board J3 RESEARCH POSTER SESSION 4 DRUGS & GENERICS Tuesday, November 5, 2019 Display Hours: 15:45 - 19:00
N/A	Retrospective Gesetzliche Krankenversicherung (statutory health insurance) (GKV) research study on the initial treatment of bladder carcinoma (BCA) by transurethral bladder resection (TURB) - a comparative analysis of costs and urological follow-	PCN502; Board W12 RESEARCH POSTER SESSION 2 CANCER Monday, November 4, 2019 Display Hours: 15:30 - 19:00

	up therapies using standard white light- (WL-) vs. Blue light- (WL-)TURB	
N/A	Assessing the human and economic burden of short stature: a systematic literature review	PMU142; Board V19 RESEARCH POSTER SESSION 4 MULTIPLE DISEASES Tuesday, November 5, 2019 Display Hours: 15:45 - 19:00

## ABOUT IPSEN PRODUCTS

This press release mentions investigational uses of Ipsen products. Product indications and approvals for use vary by jurisdiction; please see SmPC/PI for full indications and safety information, including Boxed Warnings.

## ABOUT CABOMETYX® (cabozantinib)

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

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

Other components: Lactose

**Indications:** Treatment of advanced renal cell carcinoma (RCC) in treatment-naïve adults with intermediate or poor risk or adults following prior vascular endothelial growth factor (VEGF)-targeted therapy and in adults as monotherapy for the treatment of hepatocellular carcinoma (HCC) who have previously been treated with sorafenib.

In the U.S., CABOMETYX® tablets are approved for the treatment of patients with advanced RCC and for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

CABOMETYX® tablets are also approved in: the European Union, Norway, Iceland, Australia, Switzerland, South Korea, Canada, Brazil, Taiwan, Chile, Russia, Ukraine, Serbia, Turkey, Israel, Lebanon, Jordan, UAE, Saudia Arabia, Hong Kong, Singapore and Macau for the treatment of advanced RCC in adults who have received prior VEGF-targeted therapy; in the European Union, Norway, Iceland, Australia, Canada, Brazil, Taiwan, Chile, Russia, Serbia, Turkey, Israel, Jordan, UAE, Saudia Arabia, Hong Kong and Singapore for previously untreated intermediate- or poor-risk advanced RCC; and in the European Union, Norway, Iceland, Australia, Jordan, UAE, Saudia Arabia, Hong Kong and Singapore for HCC in adults who have previously been treated with sorafenib.

**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:

Monitor closely for toxicity during first 8 weeks of therapy. Events that generally have early onset include hypocalcemia, hypokalemia, 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 tumor infiltration or complications from prior GI surgery should be evaluated prior to therapy and monitored; persistent or recurring diarrhea while on treatment may be a risk factor for the development of anal fistula, if perforation and unmanageable fistula occur, discontinue cabozantinib.

**Thromboembolic events:** Events of venous thromboembolism sometimes fatal, have been observed, use with caution in patients with a history of or risk factors for thromboembolism; discontinue if acute myocardial infarction or other significant arterial thromboembolic complication occurs.

**Hemorrhage:** severe hemorrhages, sometimes fatal, have been observed, not recommended for patients that have or are at risk of severe hemorrhage.

**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:** monitor urine protein, 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.

**Hepatic effects:** abnormal liver function tests have frequently been observed, monitor during treatment for symptoms of hepatic encephalopathy, not recommended in severe hepatic impairment.

**Laboratory tests:** electrolyte abnormalities have been observed, monitor during treatment.

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

**Drug interactions:** Cabozantinib is a CYP3A4 substrate. Potent CYP3A4 inhibitors may result in an increase in cabozantinib plasma exposure (e.g. ketoconazole, 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: CABOMETRYX® 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.

#### **Adverse reactions:**

The most common serious adverse reactions are diarrhea, hypertension, dehydration, hyponatraemia, nausea, decreased appetite, embolism, fatigue, hypomagnesaemia, PPES, hepatic encephalopathy and asthenia. Very common (>1/10): anemia, hypothyroidism, decreased appetite, hypomagnesemia, hypokalaemia, dysgeusia, headache, dizziness, hypertension, hemorrhage, dysphonia, dyspnoea, cough, diarrhea, nausea, vomiting, stomatitis, constipation, abdominal pain, dyspepsia, PPES, rash, pain in extremity, fatigue, mucosal inflammation, asthenia, peripheral oedema, weight decreased, serum ALT increased, AST increased. Common (>1/100 to <1/10): abscess, thrombocytopenia, neutropenia, dehydration, hypoalbuminemia, hypophosphatemia, hyponatremia, hypocalcemia, hyperkalemia, hyperbilirubinemia, hyperglycemia, hypoglycemia, peripheral sensory neuropathy, tinnitus, venous thrombosis, arterial thrombosis, pulmonary embolism, gastrointestinal perforation, fistula, gastroesophageal reflux disease, hemorrhoids, oral pain, dry mouth, hepatic encephalopathy, pruritus, alopecia, dry skin, dermatitis acneiform, hair colour change, muscle spasms, arthralgia, proteinuria, blood ALP increased, GGT increased, blood creatinine increased, amylase increased, lipase increased, blood cholesterol increased, white blood cell count decreased. Uncommon (>1/1000 to <1/100): lymphopenia, convulsion, pancreatitis, glossodynia, hepatitis cholestatic, osteonecrosis of the jaw, blood triglycerides increased, wound complications. Frequency not known: cerebrovascular accident, myocardial infarction. Selected adverse reactions: GI perforation, hepatic encephalopathy, diarrhea, fistulas, hemorrhage, RPLS. Prescribers should consult the SmPC in relation to other adverse reactions. Overdose: no specific treatment, in the event of suspected overdose, cabozantinib should be withheld and supportive care instituted.

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

CABOMETRYX® is marketed by Exelixis, Inc. in the United States. Cabometryx (r) is a registered Trademark of Exelixis, Inc. Ipsen has exclusive rights for the commercialization and further clinical development of CABOMETRYX® outside of the United States and Japan.

#### **ABOUT SOMATULINE® autogel (lanreotide)**

Somatuline® Autogel® 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:<sup>2</sup>

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

- The treatment of symptoms associated with neuroendocrine (particularly carcinoid) tumors.

### IMPORTANT SAFETY INFORMATION

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

<sup>2</sup> Somatuline® Autogel® SmPC. November 2018

Somatuline® and Autogel® are registered trademarks of Ipsen Pharma.

In the United States, Ipsen markets lanreotide as Somatuline® Depot.

### INDICATIONS

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

- the long-term treatment of patients with acromegaly who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option; the goal of treatment in acromegaly is to reduce growth hormone (GH) and insulin growth factor-1 (IGF-1) levels to normal;
- the treatment of adult patients with unresectable, well- or moderately-differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival; and
- the treatment of adults with carcinoid syndrome; when used, it reduces the frequency of shortacting somatostatin analog rescue therapy.

### IMPORTANT SAFETY INFORMATION

#### Contraindications

- SOMATULINE DEPOT is contraindicated in patients with hypersensitivity to lanreotide. Allergic reactions (including angioedema and anaphylaxis) have been reported following administration of lanreotide.

#### Warnings and Precautions

- **Cholelithiasis and Gallbladder Sludge**
  - SOMATULINE DEPOT may reduce gallbladder motility and lead to gallstone formation.
  - Periodic monitoring may be needed.
  - If complications of cholelithiasis are suspected, discontinue SOMATULINE DEPOT and treat appropriately
- **Hypoglycemia or Hyperglycemia**
  - Patients treated with SOMATULINE DEPOT may experience hypoglycemia or hyperglycemia.
  - Blood glucose levels should be monitored when SOMATULINE DEPOT treatment is initiated, or when the dose is altered, and antidiabetic treatment should be adjusted accordingly.
- **Cardiovascular Abnormalities**
  - SOMATULINE DEPOT may decrease heart rate.
  - In cardiac studies with acromegalic patients, the most common cardiac adverse reactions were sinus bradycardia, bradycardia, and hypertension.
  - In patients without underlying cardiac disease, SOMATULINE DEPOT may lead to a decrease in heart rate without necessarily reaching the threshold of bradycardia.
  - In patients suffering from cardiac disorders prior to treatment, sinus bradycardia may occur. Care should be taken when initiating treatment in patients with bradycardia.
- **Thyroid Function Abnormalities**
  - Slight decreases in thyroid function have been seen during treatment with lanreotide in acromegalic patients.
  - Thyroid function tests are recommended where clinically appropriate.
- **Monitoring/Laboratory Tests:** In acromegaly, serum GH and IGF-1 levels are useful markers of the disease and effectiveness of treatment.

#### Adverse Reactions

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

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

#### Special Populations

- **Lactation:** Advise women not to breastfeed during treatment and for 6 months after the last dose.

- Moderate to Severe Renal and Hepatic Impairment: See full prescribing information for dosage adjustment in patients with acromegaly.

**Please see full U.S. Prescribing Information, including SOMATULINE® DEPOT.**

**Somatuline Depot is a registered trademark of Ipsen Pharma S.A.S.**

#### **About Ipsen**

Ipsen is a global specialty-driven biopharmaceutical group focused on innovation and specialty care. The group develops and commercializes innovative medicines in three key therapeutic areas – Oncology, Neuroscience and Rare Diseases. Its commitment to Oncology is exemplified through its growing portfolio of key therapies for prostate cancer, neuroendocrine tumors, renal cell carcinoma and pancreatic cancer. Ipsen also has a well-established Consumer Healthcare business. With total sales over €2.2 billion in 2018, 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 5,700 employees worldwide. Ipsen is listed in Paris (Euronext: IPN) and in the United States through a Sponsored Level I American Depository Receipt program (ADR: IPSEY). For more information on Ipsen, visit [www.ipsen.com](http://www.ipsen.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 2018 Registration Document available on its website ([www.ipsen.com](http://www.ipsen.com)).

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