PRESS RELEASE

Ipsen announces clinical data to be presented at ASCO demonstrating its commitment to patients with cancer

Paris (France), 29 May 2018 – Ipsen (Euronext: IPN; ADR: IPSEY) today announced that cabozantinib (Cabometyx®) and irinotecan liposome injection (Onivyde®) are the subject of 8 presentations at the 2018 American Society of Clinical Oncology (ASCO) annual meeting. The meeting takes place in Chicago, Illinois, June 1-5, 2018.

Alexandre Lebeaut, Executive Vice President, R&D and Chief Scientific Officer, Ipsen stated: "*Ipsen's oncology products, notably Onivyde®, Decapeptyl® and Cabometyx®, have been evaluated by many scientific teams around the world: either directly by investigators, our partners or by Ipsen. Results from some of these investigations will be the subject of oral abstract sessions. We are committed in our efforts against cancer, and through our interactions at ASCO 2018 we will continue to advance innovation for patient care in Oncology .*"

Cabozantinib (Cabometyx®) will be presented in 7 abstracts:

Cabozantinib (Cabometyx®) will be featured in one oral poster discussion:

- [Abstract 4019] Poster 208 Discussion: Sunday, 3 June, 16:45–18:00, Hall D2
  - 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
  - Presenting author: Ghassan Abou-Alfa [Sponsor: Exelixis]

Cabozantinib (Cabometyx®) will be featured in other presentations:

- [Abstract 4556] Poster 382 – Category: Genitourinary (Nonprostate) Cancer; Saturday, 2 June, 8:00–11:30, Hall A
  - Title: Quality-adjusted time without symptoms or toxicity (Q-TWiST): Analysis of cabozantinib (Cabo) vs sunitinib (Sun) in patients with advanced renal cell carcinoma (aRCC) of intermediate or poor risk (Alliance A031203)
  - Presenting author: Ronald Chen [Sponsor: Ipsen]
- [Abstract 4598] Poster 418a – Category: Genitourinary (Nonprostate) Cancer; Saturday, 2 June, 8:00–11:30, Hall A
  - A phase 3, randomized, open-label study of nivolumab combined with cabozantinib vs sunitinib in patients with previously untreated advanced or metastatic renal cell carcinoma (RCC; CheckMate 9ER)
  - Presenting author: Toni Choueiri [Sponsor: Bristol-Myers Squibb, Exelixis & Ipsen]
- [Abstract 4601] Poster 419b – Category: Genitourinary (Nonprostate) Cancer; Saturday, 2 June, 8:00–11:30, Hall A

- CANTATA: A randomized phase 2 study of CB-839 in combination with cabozantinib vs. placebo with cabozantinib in patients with advanced/metastatic renal cell carcinoma
- Presenting author: Nizar Tannir [Sponsor: Calithera Biosciences, Inc]

- [Abstract 4088] Poster 277 – Category: Gastrointestinal (Noncolorectal) Cancer; Sunday, 3 June, 8:00–11:30, Hall A
  - Outcomes based on receipt of sorafenib (S) as the only prior systemic therapy in the phase 3 CELESTIAL trial of cabozantinib (C) versus placebo (P) in advanced hepatocellular carcinoma (HCC)
  - Presenting author: Robin Kelley [Sponsor: Exelixis]
- [Abstract 4090] Poster 279 – Category: Gastrointestinal (Noncolorectal) Cancer; Sunday, 3 June, 8:00–11:30, Hall A
  - Outcomes based on age in the phase 3 CELESTIAL trial of cabozantinib (C) versus placebo (P) in patients (pts) with advanced hepatocellular carcinoma (HCC)
  - Presenting author: Lorenza Rimassa [Sponsor: Exelixis]
- [Abstract TPS 4157] Poster 333a – Category: Gastrointestinal (Noncolorectal) Cancer; Sunday, 3 June, 8:00–11:30, Hall A
  - A phase II trial of cabozantinib and erlotinib for patients with EGFR and c-MET co-expressing metastatic pancreatic adenocarcinoma
  - Presenting author: Olumide Gbolahan [Sponsor: Exelixis]

nal-IRI / liposomal irinotecan (ONIVYDE®) will be featured in 1 poster:

- [Abstract 4111] Poster 300 – Category: Gastrointestinal (Noncolorectal) Cancer; Sunday, 3 June, 8:00–11:30, Hall A
  - A phase 1/2, open-label dose-escalation study of liposomal irinotecan (nal-IRI) plus 5- fluorouracil/leucovorin (5-FU/LV) and oxaliplatin (OX) in patients with previously untreated metastatic pancreatic cancer (mPAC).
  - Presenting author: Andrew Dean [Sponsor: Ipsen]

ABOUT ONIVYDE® (irinotecan liposome injection)
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 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 (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 WARNINGS: 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 5-FU and LV. Withhold ONIVYDE for absolute neutrophil count below 1500/mm^3 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 ≥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

- **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 CABOMETYX® (UK)

CABOMETYX® 20mg, 40mg and 60mg film-coated unscored 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 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 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 hypocalcaemia, hypokalaemia, thrombocytopenia, hypertension, palmar-plantar erythrodysaesthesia 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 erythrodysaesthesia (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 antiarrythmics 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). Co-administration 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,

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

ONIVYDE is a registered trademark of Ipsen Biopharm Limited.

CABOMETYX® (cabozantinib), XERMELO® (telotristat ethyl) and DECAPEPTYL® (triptorelin) are not marketed by Ipsen in the United States. The approved indications may vary by country.
CABOMETYX® is marketed by Exelixis, Inc. in the United States. Ipsen has exclusive rights for the commercialization and further clinical development of CABOMETYX® 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.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 2017 Registration Document available on its website (www.ipsen.com).

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