PRESS RELEASE

Ipsen and Servier announce initial Phase 1/2 clinical data evaluating liposomal irinotecan (ONIVYDE®) as an investigational first-line treatment for metastatic pancreatic cancer at ESMO 21st World Congress on Gastrointestinal Cancer

– Treatment emergent adverse events Grade 3 or higher were reported by 20 of 32 patients from the 50/60 dose pooled patient analysis; no patient reported Grade 3 or higher fatigue or peripheral neuropathy (primary endpoint) –

– Approximately three quarters of patients (71.9%) achieved disease control at week 16, while 34% had a response (secondary endpoint) –

Paris (France), 5 July 2019 – Ipsen (Euronext: IPN; ADR: IPSEY) and Servier announced today preliminary data from the Phase 1/2 study of the investigational use of liposomal irinotecan (ONIVYDE®) in combination with 5- fluorouracil/leucovorin (5-FU/LV) and oxaliplatin (OX) in study patients with previously untreated metastatic pancreatic ductal adenocarcinoma cancer (PDAC) at the ESMO 21st World Congress on Gastrointestinal Cancer in Barcelona, Spain, 3–6 July 2019. The results, which were presented as a short oral presentation, included preliminary safety and efficacy data from an ongoing multicenter, open-label, dose-escalation study, which aims to determine the maximum tolerated dose and the recommended dose to be used in future clinical studies.

"Pancreatic cancer is aggressive and difficult to treat. With most patients going undiagnosed until the disease has spread and the prognosis is poor, some physicians may be reluctant to consider novel treatment options," said Zev Wainberg, M.D., lead investigator and associate professor of medicine, University of California Los Angeles. "It's critical that physicians have more treatment options for their patients, particularly in the first line of therapy."

"ONIVYDE® is the first and only FDA and EMA approved second-line treatment for metastatic pancreatic cancer following gemcitabine-based therapy, and the initial data presented today provides a first look into the use of this investigational therapy earlier in the treatment sequence," said Yan Moore, M.D., Ipsen's Senior Vice President, Head of Oncology Therapeutic Area. "We look forward to further analyses of these early data, with the aim of evolving the standard of care in metastatic pancreatic cancer."

"It is vitally important to advance the research of new treatment approaches for pancreatic cancer patients, a goal Servier shares with Ipsen," said Patrick Therasse, Head of Servier Research and Development Oncology.

ONIVYDE® is a topoisomerase inhibitor indicated in combination with 5-FU/LV for metastatic pancreatic cancer after disease progression following gemcitabine-based therapy. The ongoing Phase 1/2, open-label trial (NCT02551991) was designed to assess the safety, tolerability and dose-limiting toxicities (DLTs) of the study drug, liposomal irinotecan, in combination with 5-FU/LV and OX, known as NAPOX, for the first-line treatment of study participants with metastatic pancreatic cancer. Secondary objectives were to assess clinical efficacy, defined by overall response rate (ORR), disease control rate (DCR) and best overall response (BOR). Preliminary analyses of median progression-free survival and median overall survival were not mature enough for evaluation.

As of the 19 February 2019 data cut off, a total of 56 study patients (median age = 58 (39-76) years) were enrolled and dosed at 15 sites across the US, Spain and Australia. The interim analysis was conducted after all study participants in the four dose exploration cohorts had completed their second scheduled tumor evaluation at 16 weeks. Study participants from the Part 1A–cohort B (n=7) dose exploration phase and study participants from the Part 1B–dose expansion phase (n=25) received the selected dose level of liposomal irinotecan 50 mg/m^2 [free-base equivalent; FBE], LV 400 mg/m^2, 5-FU 2400 mg/m^2, and OX 60 mg/m^2. These 32 patients made up the pooled population (PP) analysis (n=29 mPDAC; n=3 locally advanced pancreatic PDAC).

Safety Results:

- No reported Grade 3 or higher fatigue or peripheral neuropathy.
- One study participant in the Part 1A–cohort B dose exploration phase reported a DLT (febrile neutropenia).
- Treatment emergent adverse events (TEAEs) Grade 3 or higher were reported by 20 of 32 study patients in the 50/60 PP and included: neutropenia (n=9); febrile neutropenia (n=4); hypokalemia (n=4); diarrhea (n=3); nausea (n=3); anemia (n=2); vomiting (n=2).
- Four study patients in the 50/60 PP reported TEAEs leading to discontinuation (n=4/32), with 23 study patients requiring dose adjustment due to AEs.
- At data cut-off, 15/32 study patients in the 50/60 PP remained on treatment.

Efficacy Results:

- BOR (Best Overall Response) was: one complete response (CR; study participant diagnosed with locally advanced Stage III disease), 10 partial responses (PR) in 31.3% (10/32) and 15 stable diseases (SD) in 46.9% (15/32) (sum of CR+PR+SD = 81.3%).
- 71.9% (23/32) of study patients in the 50/60 PP achieved disease control at 16 weeks.
- Overall, 34% of study patients had a response.

ABOUT ONIVYDE® (irinotecan liposome injection)

ONIVYDE® is an encapsulated formulation of irinotecan available as a 43 mg/10 mL single dose vial. This liposomal form is designed to increase length of tumor exposure to both irinotecan and its active metabolite, SN-38.

Ipsen has 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.

ONIVYDE® is approved by the FDA and the EMA 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/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. 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

Special 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 the Phase 1/2 Study

The Phase 1/2, open-label, comparative trial is designed to assess the safety, tolerability and dose-limiting toxicities of irinotecan liposomal injection (ONIVYDE®) in combination with 5- fluorouracil/leucovorin (5-FU/LV) and oxaliplatin (OX) as a first-line treatment for metastatic pancreatic ductal adenocarcinoma cancer patients. The study has enrolled 56 patients at 15 sites across the United States, Spain and Australia. It is being conducted in two parts:

- Part 1a: a safety run-in as initial dose exploration
- Part 1b: dose expansion of the nal-IRI + 5FU/LV + oxaliplatin regimen

The study's primary endpoint is safety and tolerability. Secondary assessments of clinical efficacy include overall response rate, disease control rate and best overall response. For more information visit clinicaltrials.gov and use identifier NCT02551991.

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 Depositary Receipt program (ADR: IPSEY). For more information on Ipsen, visit www.ipsen.com.

About Servier
Servier is an international pharmaceutical company governed by a non-profit foundation, with its headquarters in France (Suresnes). With a strong international presence in 149 countries and a turnover of 4.2 billion euros in 2018, Servier employs 22,000 people worldwide. Entirely independent, the Group reinvests 25% of its turnover (excluding generics) in research and development and uses all its profits for development. Corporate growth is driven by Servier's constant search for innovation in five areas of excellence: cardiovascular, immune-inflammatory and neurodegenerative diseases, cancer and diabetes, as well as by its activities in high-quality generic drugs. Servier also offers eHealth solutions beyond drug development.
Becoming a key player in oncology is part of Servier's long-term strategy. Currently, there are twelve molecular entities in clinical development in this area, targeting gastro-intestinal and lung cancers and other solid tumors, as well as different types of leukemia and lymphomas. This portfolio of innovative cancer treatments is being developed with partners worldwide, and covers different cancer hallmarks and modalities, including cytotoxics, proapoptotics, immune targeted therapies, to deliver life-changing medicines to patients.

More information: www.servier.com

Ipsen's 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, and the outcome of this study or other studies. 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).

For further information:

Christian Marcoux, M.Sc.
Global Corporate Communications
+33 (0) 1 58 33 67 94
christian.marcoux@ipsen.com

Kelly Blaney
Global Corporate Communications
+44 (0) 7903 402275
kelly.blaney@ipsen.com

Maryann Quinn
Director, Product Communications
+1-857-529-1151
maryann.quinn@ipsen.com

Financial Community
Eugenia Litz
Vice President, Investor Relations
+44 (0) 1753 627721
eugenia.litz@ipsen.com

Myriam Koutchinsky
Investor Relations Manager
+33 (0)1 58 33 51 04
myriam.koutchinsky@ipsen.com

Servier media relations
Sonia MARQUES: media@servier.com – Tel.: +33 (0)1 55 72 40 21 / + 33 (0)7 84 28 76 13
Jean-Clément VERGEAU: media@servier.com – Tel.: +33 (0)1 55 72 46 16 / +33 (0)6 79 56 75 96