PRESS RELEASE

Ipsen and Servier announce initial Phase II/III clinical data evaluating investigational liposomal irinotecan (ONIVYDE®) as a second-line treatment for small cell lung cancer (SCLC) at the IASLC 2019 World Conference on Lung Cancer

– 44% of patients achieved a response and nearly half (48%) maintained disease control at week 12 (efficacy as secondary endpoint) –

– Treatment emergent adverse events Grade 3 or higher were reported by 10 of 25 patients (safety as primary endpoint) –

Paris (France), 8 September 2019 – **Ipsen** (Euronext: IPN; ADR: IPSEY) and **Servier** announced today initial safety and efficacy data from Part 1 of the Phase II/III RESILIENT study of investigational liposomal irinotecan (ONIVYDE®) in patients with small cell lung cancer (SCLC) who progressed following a first-line platinum-based regimen. The results, which included preliminary safety and efficacy data, were presented as an oral presentation at the IASLC 2019 World Conference on Lung Cancer hosted by the International Association for the Study of Lung Cancer in Barcelona, 7-10 September 2019.

The RESILIENT (NCT03088813) trial is a randomized, open-label two-part Phase II/III study assessing the safety, tolerability and efficacy of investigational liposomal irinotecan as a monotherapy for SCLC patients who have progressed on or after a first-line platinum-based regimen. The trial is being conducted in two parts. Part 1 includes dose-finding and dose-escalation analyses to determine the appropriate dose of study drug where the primary endpoints are safety and tolerability. Part 2 has just been initiated with the first patients randomized and will focus on efficacy assessments versus the current standard of care, topotecan, including progression-free survival (PFS) and overall survival (OS).

"Immunotherapies and combination therapies have proven beneficial in the first-line setting, but despite these advances, many small cell lung cancer patients rapidly relapse due to the aggressive nature of the disease," said Luis G. Paz-Ares, M.D., Ph.D., lead investigator and chief physician, Hospital Universitario 12 de Octubre, Madrid. "While the current standard of care in the second-line setting can extend survival, treatment toxicity has prevented some patients from receiving the full recommended dose. There is a clear need for more treatment options that may give more patients the chance to remain on therapy. It is positive that the RESILIENT trial will continue to investigate this."

ONIVYDE® (liposomal irinotecan) is a topoisomerase inhibitor featuring a liposomal formulation of irinotecan that is designed to prolong its circulation before conversion to its active form. This unique mechanism of delivery was evaluated in the NAPOLI-1 Phase III study, which led to the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) approval of ONIVYDE® in combination with fluorouracil (5-FU) and leucovorin (LV) for the treatment of metastatic pancreatic cancer following gemcitabine-based therapy. ONIVYDE® is not indicated as a single agent for the treatment of patients with metastatic adenocarcinoma of the pancreas.

"ONIVYDE® has been proven to help many metastatic pancreatic cancer patients whose disease has

progressed following gemcitabine-based therapy to live longer," said Yan Moore, M.D., Ipsen's Senior Vice President, Head of Oncology Therapeutic Area. "By applying this research to other hard-to-treat-cancers, like small cell lung cancer, we aim to evaluate the potential benefit investigational ONIVYDE® may bring to patients who otherwise would have limited treatment options."

"The data presented today shows that further research is warranted, and we look forward to working with Ipsen and our investigators to understand the full potential of bringing new treatment options to small cell lung cancer patients," said Patrick Therasse, M.D., Ph.D., Head of Servier Research and Development Oncology.

Part 1 of the study enrolled 30 patients (median age = 60 (48-73) years) who were treated every two weeks for >12 weeks, with tumor assessments taking place every six weeks. During the dose-finding phase, five patients received liposomal irinotecan 85mg/m2. This dose was deemed not tolerable due to dose limiting toxicity. An additional 12 patients received liposomal irinotecan 70mg/m2, which was deemed tolerable. Thirteen more patients were enrolled in the dose expansion phase of the study at this dose. As of the May 8, 2019 data cut off, a total of 25 patients had received liposomal irinotecan 70mg/m^2.

Safety Results:

- Liposomal irinotecan 70mg/m2 was generally well-tolerated with Grade 3 or higher treatment emergent adverse events (TEAEs) reported by 10 out of 25 patients.
- Diarrhea was the most common Grade 3 gastrointestinal TEAE (n=5).
- Hematologic Grade 3 or higher TEAEs included neutropenia (n=4) anemia (n=2) and thrombocytopenia (n=2).
- One reported instance of Grade 3 or higher fatigue.

Efficacy Results:

- Best overall response (partial response plus stable disease) was 72% with an objective response rate of 44%.
- 44% (11/25) of patients achieved a partial response with 68% of patients (17/25) experiencing tumor shrinkage.
- 48% of patients maintained disease control at 12-weeks (DCR12wks PR+SD).
- Data for OS and PFS are still maturing.

ABOUT ONIVYDE® (irinotecan liposome injection)

Ipsen has exclusive commercialization rights for the current and potential future indications for ONIVYDE® in the U.S. 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/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

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 RESILIENT Study
The Phase II/III, randomized, open-label, RESILIENT study is designed to assess the safety, tolerability and efficacy of investigational ONIVYDE® versus topotecan in patients with small cell lung cancer who have progressed on or after platinum-based first-line therapy. The study is enrolling up to 486 patients at 34 sites across the United States, Spain, Germany, France, Taiwan and Australia.

The study is being conducted in two parts:
- Part 1: Open-label dose-finding study of ONIVYDE®; 30 patients have been enrolled in Part 1 of the study.
- Part 2: A randomized, efficacy study of ONIVYDE® versus IV topotecan; approximately 450 patients will be enrolled in Part 2.

The study's primary endpoint is overall survival defined as the time from randomization to date of death. Secondary assessments include progression-free survival, objective response rate, proportion of patients with symptom improvement and incidence of treatment-emergent adverse events, serious adverse events and laboratory abnormalities. The rate of development of CNS metastases, and biomarkers associated with efficacy and toxicity will be explored. For more information visit clinicaltrials.gov and use identifier NCT03088813.

About Ipsen
Ipsen is a global specialty-driven biopharmaceutical company 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

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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).

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