PRESS RELEASE

Ipsen announces results from Phase III RESILIENT trial evaluating Onivyde® in second-line monotherapy for small cell lung cancer

- At the primary analysis, the trial did not meet its primary endpoint of overall survival (OS)
- The safety profile was consistent with previously reported studies of Onivyde® (irinotecan liposomal injection)
- The clinical study results will be communicated with the regulatory agency

PARIS, FRANCE, 03 August 2022 – Ipsen (Euronext: IPN; ADR: IPSEY) announced today that the Phase III RESILIENT trial did not meet its primary endpoint of overall survival (OS) compared to topotecan. The trial is evaluating Onivyde® (irinotecan liposomal injection) versus topotecan in patients with small cell lung cancer (SCLC), who have progressed on or after platinum-based first-line therapy treatment. RESILIENT is a Phase III trial conducted in two parts; the first part read out in 2020 confirming the safety, dosing and efficacy of Onivyde; part two is evaluating the efficacy of Onivyde versus topotecan. Detailed results from the RESILIENT trial will be presented at an upcoming medical conference.

The analysis concluded that the primary endpoint OS was not met in patients treated with Onivyde versus topotecan. However, a doubling of the secondary endpoint of objective response rate (ORR) in favor of Onivyde was observed. The safety and tolerability of Onivyde was consistent with its already-known safety profile, and no new safety concerns emerged. The clinical study results will be communicated with the regulatory agency.

Howard Mayer, M.D., Executive Vice President, Head of Research and Development at Ipsen, said: "While the results from the analysis of the RESILIENT trial have not demonstrated an overall survival benefit with Onivyde in patients in second-line small cell lung cancer, we will now work with our teams to analyze the data further before decisions regarding next steps are made. These data confirm the complexities associated with treating small cell lung cancer. We wish to thank the patients, their families and healthcare teams for their participation in this clinical trial."

Onivyde is currently approved in most major markets including the U.S., Europe and Asia 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. Onivyde is not indicated as a single agent for the treatment of patients with metastatic adenocarcinoma of the pancreas. Ipsen will continue to explore the potential of Onivyde in other areas, and the final data readout of the NAPOLI-3 Phase III trial in first-line pancreatic ductal adenocarcinoma is expected in H2 2022.

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About RESILIENT

RESILIENT is a randomized, open-label Phase III trial of Onivyde (irinotecan liposome injection) versus topotecan in patients with small cell lung cancer who have progressed on or after platinum-based first-line therapy. The trial is being conducted in two parts:

- Part 1: Open-label dose-finding trial of Onivyde. 30 patients were enrolled.
  Part 1 Primary endpoints:
  - Describe the safety and tolerability of Onivyde monotherapy administered every 2 weeks
  - Determine the optimal Onivyde monotherapy dose for Part 2 of this trial
- Part 2: A randomized, efficacy study of Onviyde versus intravenous (IV) topotecan. Approximately 450 patients were enrolled in part 2.
  Part 2 objectives: To compare overall survival (OS) following treatment with Onivyde with OS following treatment with IV topotecan

The primary outcome measure is OS. Secondary outcome measures include progression-free survival, objective response rate, quality of life assessment using European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Lung Cancer 13 (EORTC QLQ-C30/LC13) dyspnea scale, quality of life assessment using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Lung Cancer 13 (EORTC QLQ-LC13) cough scale, incidence of treatment-emergent adverse events, serious adverse events and laboratory abnormalities. Safety analyses (adverse events and laboratory analyses) will be performed using the safety population, defined as all patients receiving any trial medicine.

About Onivyde (irinotecan liposome injection)
Ipsen has exclusive commercialization rights for the current and potential future indications for Onivyde in the U.S. Servier, an independent international pharmaceutical company with a strong international presence in 150 countries, is responsible for the commercialization of Onivyde outside of the U.S. and Taiwan. PharmaEngine is a commercial stage oncology company headquartered in Taipei and is responsible for the commercialization of Onivyde in Taiwan.

Indication - U.S.
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 - U.S.

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 hydrochloride.

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 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

1. Avoid the use of strong CYP3A4 inducers, if possible, and substitute non-enzyme inducing therapies ≥2 weeks prior to initiation of Onivyde
2. 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 including Boxed WARNING for Onivyde.

About Ipsen

Ipsen is a global, mid-sized biopharmaceutical company focused on transformative medicines in Oncology, Rare Disease and Neuroscience. With Specialty Care sales of €2.6bn in FY 2021, Ipsen sells medicines in over 100 countries. Alongside its external-innovation strategy, the Company's research and development efforts are focused on its innovative and differentiated technological platforms located in the heart of leading biotechnological and life-science hubs: Paris-Saclay, France; Oxford, U.K.; Cambridge, U.S.; Shanghai, China. Ipsen, excluding its Consumer HealthCare business, has around 4,500 colleagues worldwide and is listed in Paris (Euronext: IPN) and in the U.S. through a Sponsored Level I American Depositary Receipt program (ADR: IPSEY). For more information, visit ipsen.com

Ipsen's Forward-Looking Statements

The forward-looking statements, objectives and targets contained herein are based on Ipsen'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 Ipsen'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 Ipsen'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 Ipsen. 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 medicine 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. Ipsen must face or might face competition from generic medicine 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 Ipsen may fail to achieve its objectives and be forced to abandon its efforts with regards to a medicine in which it has invested significant sums. Therefore, Ipsen cannot be certain that favorable results obtained during preclinical 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 medicine concerned. There can be no guarantees a medicine will receive the necessary regulatory approvals or that the medicine 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 healthcare legislation; global trends toward healthcare cost containment; technological advances, new medicine and patents attained by competitors; challenges inherent in new-medicine development, including obtaining regulatory approval; Ipsen'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 Ipsen's patents and other protections for innovative medicines; and the exposure to litigation, including patent litigation, and/or regulatory actions. Ipsen also depends on third parties to develop and market some of its medicines which could potentially generate substantial royalties; these partners could behave in such ways which could cause damage to Ipsen's activities and financial results. Ipsen 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 Ipsen's partners could generate lower revenues than expected. Such situations could have a negative impact on Ipsen's business, financial position or performance. Ipsen 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. Ipsen'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 Ipsen's 2021 Universal Registration Document, available on ipsen.com

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