Press release

Intended for international media and investor audiences only

Ipsen's Iqirvo® (elafibranor) approved in the European Union as first new treatment for primary biliary cholangitis in nearly a decade

- ***European Commission grants conditional marketing authorization for Iqirvo® (elafibranor), first-in-class new treatment for primary biliary cholangitis (PBC), a rare liver disease***
- ***Approval follows positive CHMP opinion based on ELATIVE phase III trial data, which demonstrated significant efficacy over placebo and was well-tolerated with an acceptable safety profile***
- ***This new European approval reinforces Ipsen's commitment to advancing medical innovations to treat people living with rare cholestatic liver diseases***

PARIS, FRANCE, 20 September 2024 - Ipsen (Euronext: IPN; ADR: IPSEY) announced today that the European Commission has conditionally approved Iqirvo® (elafibranor) 80mg tablets for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA or as a monotherapy in patients unable to tolerate UDCA. Iqirvo is a first-in-class, oral, peroxisome proliferator-activated receptor (PPAR) agonist, that exerts an effect on the proteins PPARα and PPARδ, thought to be key regulators of bile acid, inflammation and fibrosis.

"We are delighted that Iqirvo is approved in the E.U. as an effective new option for the treatment of people living with PBC. This is a rare liver disease, predominantly found in women, which hasn't seen new innovation for nearly a decade. This is despite up to half of patients being intolerant or unresponsive to current therapies," said Sandra Silvestri, Chief Medical Officer, Ipsen. "For those patients with PBC that may be at risk of disease progression and who continue to suffer from debilitating symptoms of the disease, we are delighted to be able to offer an effective treatment choice."

Approval of Iqirvo was based on data from the phase III ELATIVE[1] trial, which demonstrated a statistically significant treatment benefit with a 47% placebo-adjusted difference (P<0.001) between patients on Iqirvo 80mg (51%) compared with patients on placebo (4%) achieving a biochemical response. A greater decrease in PBC Worst Itch-NRS score from baseline was also observed for patients on Iqirvo versus placebo, but this was not statistically significant. Treatment with Iqirvo was associated with an improvement in pruritus (itch) as evidenced by a greater reduction in PBC-40 itch and 5-D itch total scores compared to placebo. Similar percentages of patients in the Iqirvo group and the placebo group experienced adverse events, treatment-related adverse events, severe or serious adverse events or adverse events leading to discontinuation.

"It is a positive development in the treatment and management of PBC that we have a new, efficacious and well-tolerated treatment for our patients living with the condition," said Dr Marco Carbone, Professor of Gastroenterology, University of Milano-Bicocca and Consultant Hepatologist, the Niguarda Liver Transplant Centre, Milan. "PBC is a progressive liver disease that can lead to liver failure and in some people the need for liver transplantation. So, this new medicine, that has demonstrated its potential in managing disease progression, as well as reducing itch, a symptom that can have a detrimental effect on patients' quality of life, is positive news for doctors and their patients."

"PBC is a very personal disease which affects everyone differently. Some people may be more symptomatic with extreme fatigue or severe itch. For others there are no symptoms, but their biomarker levels are poor, suggesting the disease is not being controlled. This means that an individualized approach to management and treatment is needed for each patient," said Patient Advocate, Mrs Sindee Weinbaum from European Liver Patients' Association. "Patients need to be able to partner with their doctors and

have constructive conversations about what they personally need to manage the PBC they are living with. So, it is great news to have a new treatment choice for the many people who are living with PBC that is not under control."

ENDS

About PBC

PBC is a rare, autoimmune, cholestatic liver disease, affecting approximately nine women for every one man. A build-up of bile and toxins (cholestasis) and chronic inflammation causes irreversible fibrosis (scarring) of the liver and destruction of the bile ducts. It is a life-long condition that can worsen over time if not effectively treated, leading to liver transplant and in some cases, premature death. PBC impacts patient's daily lives through debilitating symptoms including most commonly pruritus and fatigue.

About Iqirvo (elafibranor)

Iqirvo (pronounced EYE-KER-VO) is an oral, once-daily, peroxisome proliferator-activated receptor (PPAR) agonist, which exerts an effect on PPARα and PPARδ. Activation of PPARα and PPARδ decreases bile toxicity and improves cholestasis by modulating bile acid synthesis, detoxification and transporters. Activation of PPARα and PPARδ also has anti-inflammatory effects by acting on different pathways. The benefits of Iqirvo are its ability to reduce alkaline phosphatase and bilirubin levels in adults with PBC. Iqirvo is therefore expected to have clinical benefits such as delayed development of liver fibrosis, cirrhosis, liver transplant and death.[1] In 2019, Iqirvo was granted Breakthrough Therapy Designation by the U.S Food and Drug Administration (FDA) in adults with PBC who have an inadequate response to ursodeoxycholic acid (UDCA) the existing first-line therapy for PBC. Iqirvo has been granted accelerated approval in the US in June 2024 and conditional approval in EU in September 2024 for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults who have an inadequate response to UDCA, or as monotherapy in patients unable to tolerate UDCA. These approvals are contingent on the further verification of clinical benefit. Iqirvo is currently in regulatory processes with other authorities including the UK Medicines and Healthcare products Regulatory Agency (MHRA). Iqirvo (elafibranor) was developed by GENFIT. Ipsen licensed the exclusive worldwide rights (except China, Hong Kong, Taiwan and Macau) to elafibranor from GENFIT in 2021.

About ELATIVE

ELATIVE was a multi-center, randomized, double-blind, placebo-controlled Phase III clinical trial (NCT04526665). ELATIVE evaluated the efficacy and safety of elafibranor 80mg once daily versus placebo for the treatment of patients with PBC with an inadequate response or intolerance to ursodeoxycholic acid (UDCA), the existing first-line therapy for PBC. The trial enrolled 161 patients who were randomized 2:1 to receive elafibranor 80mg once daily or placebo. Patients with an inadequate response to UDCA continued to receive UDCA in combination with elafibranor or placebo, while patients unable to tolerate UDCA received only elafibranor or placebo. Patients continued their assigned treatment after Week 52 until all patients had completed their treatment or for a maximum of 104 weeks. The open-label long-term extension study of ELATIVE remains ongoing, where patients with PBC may receive elafibranor for up to 5 years. In the trial, the composite endpoint biochemical response is defined as alkaline phosphatase (ALP) <1.67 x upper limit of normal (ULN), an ALP decrease ≥ 15 percent and total bilirubin (TB) ≤ ULN at 52 weeks. ALP and bilirubin are important predictors of PBC disease progression. Reductions in levels of both can indicate reduced cholestatic injury and improved liver function. Full results of the ELATIVE 52-week study have been published in the New England Journal of Medicine (NEJM).

Important safety information and recommendations for the use of Iqirvo will be detailed in the Summary of Product Characteristics (SmPC), published in the European public assessment report (EPAR) and available in all official EU languages. The full SmPC will be found at: Iqirvo, INN-elafibranor (europa.eu)

About Ipsen

We are a global biopharmaceutical company with a focus on bringing transformative medicines to patients in three therapeutic areas: Oncology, Rare Disease and Neuroscience.

Our pipeline is fuelled by external innovation and supported by nearly 100 years of development experience and global hubs in the U.S., France and the U.K. Our teams in more than 40 countries and our partnerships around the world enable us to bring medicines to patients in more than 80 countries.

Ipsen 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 contacts

Investors

- **Craig Marks | + 44 (0)7584 34 91 93 | craig.marks@ipsen.com**
- **Nicolas Bogler | + 33 6 52 19 98 92 | nicolas.bogler@ipsen.com**

Media

- **Anna Gibbins | + 44 7717 80 19 00| anna.gibbins@ipsen.com**

Disclaimers and/or 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 latest Universal Registration Document, available on ipsen.com.

References

1. Kowdley. K.V, et al. Efficacy and Safety of Elafibranor in Primary Biliary Cholangitis. NEJM. 2023. DOI: 10.1056/NEJMoa2306185