Press release

Late-breaking exploratory data highlights the impact of IQIRVO® (elafibranor) on fatigue and provides mechanistic insights into anti-inflammatory and symptom-related effects in patients with primary biliary cholangitis

- ***Additional late-breaking data suggests up to twice as many patients treated with IQIRVO® achieved a clinically meaningful improvement in fatigue compared to placebo after 52 weeks of treatment***
- ***IQIRVO dual PPARα/δ activation impacts inflammation and fibrosis***
- ***PPARα activation linked to fatigue improvement in primary biliary cholangitis***

PARIS, FRANCE, 7 May 2025 Today, Ipsen (Euronext: IPN; ADR: IPSEY) announced new data from two late-breaking presentations on IQIRVO® (elafibranor) during the European Association for the Study of the Liver congress.

Additional analyses from the ELATIVE® study (LBP-027) suggest that patients with primary biliary cholangitis (PBC) treated with IQIRVO had greater improvements in fatigue compared to placebo after 52 weeks, as measured by both the PROMIS Fatigue Short Form 7a questionnaire (42.9% IQIRVO versus 31.3% placebo) and PBC-40 fatigue domain (22.6% IQIRVO versus 15.4% placebo). Among patients with moderate-to-severe fatigue at baseline, more than twice as many patients treated with IQIRVO (66.7%) achieved clinically meaningful improvements compared to placebo (31.3%). Importantly, the data suggest that the positive effect of IQIRVO on fatigue occurs independently of its effect on pruritus.[1]

"For so many patients living with PBC, fatigue is a debilitating symptom that can impact their ability to perform daily tasks or participate in social activities," said Dr David Jones, Professor of Liver Immunology for the Faculty of Medical Science at Newcastle University. "As a physician treating people with PBC, these new data are providing important insights into how the action of IQIRVO could impact fatigue."

These findings are supported by additional late-breaking exploratory data (LBP-025) from a comprehensive proteomic analysis with longitudinal samples from patients in ELATIVE® evaluated using Olink® technology covering more than 5,500 proteins. Over 20 proteins involved in disease biology mapping to pathways involved in inflammation and immune response, bile acids and lipid homeostasis, fibrosis, and key PBC symptomatic domains, including pruritus and fatigue, had changes in expression in patients treated with IQIRVO with biochemical response at Week 52. Effects observed on fatigue-associated proteomic signatures appeared to be associated with PPARα activation.[2]

"These mechanistic data reinforce the value of IQIRVO as an important treatment option for people with PBC," said Sandra Silvestri, MD, EVP and Chief Medical Officer, Ipsen. "Today, we have a clearer understanding of the molecular action of PBC. We believe the more we learn about a disease, the more effective we can be in developing treatments for patients that address both the disease and debilitating symptoms."

PBC is a rare, autoimmune liver disease where a build-up of bile and toxins and chronic inflammation causes irreversible fibrosis of the liver and destruction of the bile ducts. Impacting approximately 100,000

people in the US and 165,000 people in Europe, the majority being women, PBC is a lifelong condition that can worsen over time if not effectively treated and may lead to liver transplant and in some cases, premature death.

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. 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 was granted U.S. FDA accelerated approval in June 2024, EU conditional approval by the European Commission (EC) in September 2024 and UK Medicines and Healthcare products Regulatory Agency (MHRA) approval in October 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. The FDA, EC and MHRA approvals are contingent on the further verification of clinical benefit. IQIRVO is currently in regulatory processes with other authorities. 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 is a multi-center, randomized, double-blind, placebo-controlled Phase III clinical trial, with an open-label long-term extension (NCT04526665). ELATIVE is evaluating 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 would continue to receive UDCA in combination with elafibranor or placebo, while patients unable to tolerate UDCA would receive 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 of ELATIVE remains ongoing.

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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 fueled 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.

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References

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