Press Release

IQIRVO® late-breaking data raises ambitions in PBC with more than 85% of patients on treatment achieving ALP normalization

- Results from the ELSPIRE study will be presented as late-breaking data at The Liver Meeting® 2026 and simultaneously published in AASLD's flagship journal, *HEPATOLOGY*
- At Week 52, 85.3% of patients receiving IQIRVO® achieved normalization of ALP compared with 23.3% receiving placebo and was generally well tolerated
- Findings add to growing evidence supporting ALP normalization as an achievable treatment goal in PBC

PARIS, FRANCE, 5 NOVEMBER 2026 – Ipsen (Euronext: IPN; ADR: IPSEY) announced today late-breaking data from the ELSPIRE Phase III study in people living with primary biliary cholangitis (PBC) and alkaline phosphatase (ALP) levels between 1- 1.67× upper limit of normal (ULN). At Week 52, 85.3% of patients receiving IQIRVO® achieved normalization of ALP, a biochemical measure of disease activity, compared with 23.3% receiving placebo ($p<0.0001$). The findings will be presented as late-breaking data at the American Association for the Study of Liver Diseases (AASLD) The Liver Meeting® 2026 and simultaneously published in *HEPATOLOGY*[1]. In addition, these data with an expanded patient population, are being shared with regulatory authorities.

"ELSPIRE challenges us to think more ambitiously about what can be achieved for people living with PBC," said Kris V. Kowdley, MD, AGAF, FAASLD, FACG, FACP, Liver Institute Northwest, Velocity Clinical Research and Washington State University. "The ALP threshold of 1.67×ULN has traditionally been used in PBC clinical trials to define adequate treatment response. However, patients below this threshold can still have active disease. With the majority of patients treated with IQIRVO achieving ALP normalization, these data support consideration of normal ALP as an achievable treatment goal for patients with an incomplete response to first-line ursodeoxycholic acid treatment."

In ELSPIRE, IQIRVO also showed:

- A rapid and sustained reduction in ALP, with an adjusted mean reduction of 36.5% from baseline versus 4.2% with placebo at Week 52 ($p<0.0001$).
- 84.5% of patients achieved ALP normalization together with a ≥15% reduction from baseline, compared with 20.0% receiving placebo ($p<0.0001$).
- At Week 52, IQIRVO reduced total bilirubin versus placebo, with an adjusted 15-percentage-point difference in change from baseline ($p=0.0260$)
- 64.3% of patients on IQIRVO achieved complete biochemical response (normal total bilirubin, ALP, AST, ALT, albumin and INR) versus 16.7% on placebo ($p<0.0001$) at Week 52
- A greater reduction from baseline in GGT was seen in patients receiving IQIRVO versus placebo at Week 52 (adjusted mean difference of 36.3 U/L, $p=0.0002$).

IQIRVO was well tolerated in this trial, with no new safety signals observed. Most treatment emergent adverse events (TEAEs) were mild or moderate, no serious TEAEs were related to IQIRVO, and treatment discontinuation due to TEAEs was low.

"The ELSPIRE data show that patients with PBC can achieve ALP normalization with IQIRVO, including patients whose ALP may previously have been considered relatively well controlled," said Sandra Silvestri, MD, PhD, Chief Medical Officer, Ipsen. "Normalization should be our goal. These data give us clear evidence to raise our ambition for patients with PBC."

In a second late-breaking presentation, six-month results from the ongoing global Phase IV ELFINITY study with IQIRVO provide evidence from routine clinical practice on ALP normalization and symptom improvements in fatigue and pruritus, among patients with moderate-to-severe symptoms at baseline. For fatigue, 42.3% of relevant patients achieved a clinically meaningful improvement using PBC-40 Fatigue and 38.5% using PROMIS Fatigue Short Form 13a. Patients with moderate-to-severe pruritus at baseline showed clinically meaningful improvements in itch severity and burden across multiple measures (WI-NRS, 5D-itch and PBC-40 Itch).

PBC is a rare, progressive autoimmune liver disease that can lead to fibrosis, cirrhosis and liver failure. Historically, inadequate treatment response has commonly been defined as ALP ≥1.67× ULN, and registrational clinical trials have therefore largely focused on patients at or above this threshold. However, ALP above ULN is associated with active disease and reduced transplant-free survival, while ALP normalization is associated with better complication-free survival.[2,3] ELSPIRE was designed specifically to evaluate IQIRVO in patients with ALP 1 to 1.67× ULN, a population not previously studied in registrational trials of IQIRVO.

"With all of the recent advances in PBC management, it's encouraging that we are now at a point where to effectively treat PBC, we can set a goal for not only lowering key liver function test levels, but we can aim to bring measures of disease, like ALP, into a normal range," said Carol Roberts, President of PBCers, a patient advocacy organization.

"For those of us living with PBC, protecting our liver health and addressing the symptoms that affect our daily lives are equally important. We want care teams to hear us when we talk about fatigue and itching, and to make those concerns part of our care. Meaningful progress means helping us live better while managing our disease," said L. Marie Asad, Founder and President of PBC Awareness, NFP.

Ipsen is also presenting new data from across its growing rare cholestatic liver disease portfolio, including data on its treatment for progressive familial intrahepatic cholestasis and Alagille syndrome. With two molecules approved for three different rare cholestatic liver diseases and a development pipeline, Ipsen is progressing research and development where unmet need is high, and treatments are often few or do not exist. By focusing on conditions like PBC, Primary Sclerosing Cholangitis, Progressive Familial Intrahepatic Cholestasis and Alagille syndrome, Ipsen aims to improve patient outcomes and quality of life. The company's commitment is reflected in its rigorous clinical trials, ongoing efforts to develop effective treatments and unwavering support for patients affected by these challenging and often debilitating diseases.

About the ELSPIRE Phase III trial

ELSPIRE is a Phase III randomized, double-blind, placebo-controlled study (NCT06383403) evaluating the efficacy and safety of IQIRVO in adults with PBC who have had an inadequate response or, intolerance to ursodeoxycholic acid, the existing first-line therapy for PBC. The trial enrolled 92 patients across 10 countries who had an ALP of 1 – 1.67 x ULN and were randomized 2:1 to receive IQIRVO 80 mg (n=62) once daily or placebo (n=30). The primary endpoint was ALP ≤ULN at Week 52.

Secondary endpoints included percentage change from baseline in ALP at Week 52, complete biochemical response and safety.

About the ELFINITY Phase IV trial

ELFINITY (NCT06447168) is an ongoing prospective, global, non-interventional Phase IV study assessing the real-world effectiveness and safety of IQIRVO in people with PBC. The study plans to recruit approximately 424 patients receiving IQIRVO 80 mg/day in routine clinical practice, with prospective follow-up for up to five years. At six months, 57.5% (65/113) of evaluable patients met the study's biochemical response endpoint, defined as ALP <1.67× ULN with ≥15% reduction from baseline and total bilirubin ≤ULN.

About IQIRVO® (elafibranor)

IQIRVO is an oral, once-daily, peroxisome proliferator-activated receptor (PPAR) agonist. Activation of PPARα and PPARδ decreases bile toxicity and improves cholestasis by modulating bile acid synthesis, detoxification and transporters. IQIRVO is the first approved PPAR agonist with dual α and δ activation, shown to have complementary anti-inflammatory, anti-cholestatic, anti-fibrotic effects. 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, conditional approval by the EMA in September 2024 and UK Medicines and Healthcare products Regulatory Agency (MHRA) in October 2024, for the treatment of primary biliary cholangitis in combination with ursodeoxycholic acid in adults who have an inadequate response to UDCA, or as monotherapy in patients unable to tolerate UDCA. The FDA and EMA approvals are contingent on the further verification of clinical benefit. In addition to the U.S., E.U. and UK, IQIRVO is approved in Canada, Australia, Brazil and 13 other countries and is in regulatory processes with other authorities. IQIRVO was developed by GENFIT. Ipsen licensed the exclusive worldwide rights (except China, Hong Kong, Taiwan and Macau) to elafibranor from GENFIT in 2021 and expanded the geographical scope to China, Hong Kong, Taiwan and Macau in March 2026.

About PBC

PBC is a rare, autoimmune liver disease where a build-up of bile and toxins and chronic inflammation cause fibrosis of the liver and destruction of the bile ducts.[4] With approximately 1.8 people per 100,000 diagnosed worldwide each year, 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.[5,6]

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 internal and 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 100 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

Henry Wheeler	henry.wheeler@ipsen.com	+33 7 66 47 11 49
Khalid Deojee	khalid.deojee@ipsen.com	+33 6 66 01 95 26

Media

Sally Bain	sally.bain@ipsen.com	+1 857 320 0517
Anne Liontas	anne.liontas.ext@ipsen.com	+33 7 67 34 72 96

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 and risks arising from unexpected regulatory or political changes such as changes in tax regulation and regulations on trade and tariffs, such as protectionist measures, especially in the United States; 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.

1. Kowdley. K,et al. Treatment with elafibranor to normalize alkaline phosphatase in patients with primary biliary cholangitis and incomplete response to ursodeoxycholic acid: Results from the phase III randomized controlled ELSPIRE trial. *Hepatol.* 2026 Nov https://journals.lww.com/hep/fulltext/10.1097/hep.0000000000001906~treatment-with-elafibranor-to-normalize-alkaline-phosphatase
2. Kowdley„et al. Longitudinal Relationship Between Elevated Liver Biochemical Tests and Negative Clinical Outcomes in Primary Biliary Cholangitis: A Population-Based Study. Alimentary Pharmacology & Therapeutics 2025;61:1775–1784.
3. Lammers, et al. Levels of Alkaline Phosphatase and Bilirubin Are Surrogate End Points of Outcomes of Patients With Primary Biliary Cirrhosis: An International Follow-up Study. Gastroenterology 2014;147:1338–1349.
4. Lleo, et al. Primary biliary cholangitis. The Lancet 2020:396: 1915 – 1926
5. Tan et al. Global Epidemiology of Primary Biliary Cholangitis: An Updated Systematice Review and Meta-Analysis. Clin Gastroenterol Hepatol. 2026 Mar:24(3): 621-623 doi: 10.1016/j.cgh.2025.03.025.
6. Trivella et al. Primary biliary cholangitis: Epidemiology, prognosis, and treatment. *Hepatol Commun.* 2023 Jun 2;7(6):e0179. doi: 10.1097/HC9.0000000000000179