



PRESS RELEASE



Results from Ipsen's ELATIVE® pivotal Phase III trial of elafibranor in PBC presented as late breaking data at AASLD congress and published in New England Journal of Medicine

- ELATIVE® Phase III trial confirms potential for investigational elafibranor as a novel, first-in-class, dual PPAR α,δ agonist for patients with primary biliary cholangitis.
- Elafibranor demonstrates significant improvements in biomarkers of disease progression versus placebo, including significant treatment benefit with improvement in biochemical response and alkaline phosphatase (ALP) normalization, along with patient-reported outcomes data suggesting a possible improvement in pruritus.
- Elafibranor was generally well-tolerated with a well-documented safety profile consistent with previous trials.

PARIS, FRANCE, 13 November, 2023 – Ipsen (Euronext: IPN; ADR: IPSEY) and GENFIT (Nasdaq and Euronext: GNFT) today announced full results from the pivotal Phase III ELATIVE® trial, which are being presented in a late-breaking oral session (Abstract #484, Monday, 13 November at 16.45 EST) at the American Association for the Study of Liver Disease (AASLD) and simultaneously published in the [New England Journal of Medicine](#) (NEJM). This trial evaluated the efficacy and safety of investigational elafibranor, an oral, dual PPAR α,δ agonist, as a potential novel class of treatment for patients with the rare, autoimmune cholestatic liver disease, primary biliary cholangitis (PBC).

Results show statistically significant improvements in biomarkers of disease progression across key endpoints with a significant treatment benefit achieved in the primary composite endpoint, demonstrating a 47% placebo-adjusted difference ($P < 0.001$) between patients on elafibranor 80mg (51%) compared with patients on placebo (4%) achieving a biochemical response. In the trial, a biochemical response is defined as alkaline phosphatase (ALP) $< 1.67 \times$ upper limit of normal (ULN), an ALP decrease ≥ 15 percent and total bilirubin (TB) \leq 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.

Only patients receiving elafibranor achieved normalization of ALP (upper limit of normal 104 U/L in females and 129 U/L in males) at Week 52 (15% vs 0% placebo, $P = 0.002$), a key secondary endpoint of the trial. The significant biochemical effect of elafibranor measured by ALP reduction was further supported by data demonstrating reductions from baseline in ALP levels were rapid, seen as early as Week 4 in the elafibranor group, and were sustained through Week 52, with a decrease in ALP of 41% on elafibranor compared with placebo.

“When managing PBC our first goal is to effectively control the disease progression which can lead to liver failure. The results from ELATIVE provide compelling evidence that elafibranor has the potential to

achieve this goal, with evidence of a highly significant treatment benefit that is associated with improved clinical outcomes,” said Dr Christopher Bowlus, Professor of Gastroenterology and Hepatology, University of California Davis, U.S. “In addition, our patients need relief from the significant symptom burden of PBC, particularly those with moderate to severe itch. Data from ELATIVE demonstrated the possibility of improved pruritus for patients taking elafibranor compared with those on placebo. Taken together, these data suggest elafibranor could offer an effective new treatment opportunity for PBC management.”

ELATIVE investigated the effect of treatment with elafibranor on pruritus (severe itch) across three separate patient-reported outcome measures. On the key secondary endpoint using the PBC Worst Itch NRS score, the reduction of pruritus observed for elafibranor versus placebo was not statistically significant (LS mean, -1.93 versus -1.15; difference, -0.78; 95% CI, -1.99 to 0.42; P=0.20). Two other secondary patient-reported outcome measures were used to assess itch, and greater reductions in pruritus were observed with elafibranor compared with placebo at Week 52, according to the itch domain of PBC-40 quality of life questionnaire (LS mean difference -2.3; 95% CI, -4.0 to -0.7) and 5-D Itch total score (LS mean difference, -3.0; 95% CI, -5.5 to -0.5).

“We believe these data suggest that elafibranor could be a paradigm-changing treatment meeting the unmet need for an effective second-line option,” said Christelle Huguet, EVP and Head of Research and Development, Ipsen. “These data from ELATIVE have provided a better understanding of how we can effectively manage both disease progression and the symptom burden still experienced by many people living with PBC. It would not have been possible for us to investigate the potential for new innovative treatments without the involvement of the patients and their wider families and caregivers, to whom we are immensely grateful. We are also enormously grateful to the study investigators, who have supported us and provided us with the benefit of their expertise in designing and running this study.”

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. Currently, there are no approved treatments available that can effectively manage both disease progression and life-impacting symptoms.

“Living with PBC can be very challenging for many people. The fear of the disease progressing hangs over you, and you have to manage as best you can with the daily symptom burden, symptoms that can sometimes be so debilitating it takes every ounce of strength to get through another day,” explained Mo Christie, Head of Patient Services, PBC Foundation, UK. “As someone who is living with PBC, I appreciate the need for clinicians, other patients, and families to understand the condition and the impact that coming to terms with living with an incurable condition can have on a person’s life. The impact can be enormous, so it is vitally important to all aspects of our lives that we can access knowledge, care and effective medicines, when we see our clinicians.”

Elafibranor was well tolerated in the trial. Similar percentages of patients in the treatment group and the placebo group experienced adverse events, treatment-related adverse events, severe or serious adverse events or adverse events leading to discontinuation. Adverse events occurring in >10% of patients and more frequently on elafibranor versus placebo included abdominal pain, diarrhea, nausea, and vomiting. Elafibranor has a well-documented safety profile across a broad patient population and is consistent with cumulative safety data from past elafibranor trials in other indications, including NASH.

Data from ELATIVE are being used to support submissions for elafibranor as a treatment for PBC with regulatory authorities worldwide.

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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.

Elafibranor

Elafibranor is a novel, oral, once-daily, dual peroxisome activated receptor (PPAR) alpha/delta (α,δ) agonist, currently under investigation as a treatment for patients with PBC, a rare liver disease. Concurrent α,δ activation targets inflammation, cholestasis and fibrosis in PBC. In 2019, elafibranor was granted a Breakthrough Therapy Designation by the FDA in adults with PBC who have an inadequate response to UDCA. Elafibranor has not received approval by regulatory authorities anywhere in the world.

Ipsen

Ipsen is a global, mid-sized biopharmaceutical company focused on transformative medicines in Oncology, Rare Disease and Neuroscience. With total sales of €3.0bn in FY 2022, 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 has around 5,300 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 [ipсен.com](https://www.ipсен.com)

GENFIT

GENFIT is a late-stage biopharmaceutical company dedicated to improving the lives of patients with rare and life-threatening liver diseases characterized by high unmet medical needs. GENFIT is a pioneer in liver disease research and development with a rich history and strong scientific heritage spanning more than two decades. Today, GENFIT has a growing and diversified pipeline with programs at various development stages. The Company's area of focus is Acute on Chronic Liver Failure (ACLF). Its ACLF franchise consists of five assets in development: VS-01, NTZ, SRT-015, CLM-022 and VS-02-HE. These are all based on differentiated mechanisms of action leveraging complementary pathways. Other assets target other life-threatening disease indications such as cholangiocarcinoma (CCA) and Urea Cycle Disorders (UCD)/Organic Acidemias (OA). GENFIT's track record in bringing early-stage assets with high potential to late development and pre-commercialization stages is highlighted in the successful 52-week Phase 3 ELATIVE® trial evaluating elafibranor in PBC. Beyond therapeutics, GENFIT's pipeline also includes a diagnostic franchise focused on MASH (previously known as NASH) and ammonia. GENFIT has facilities in Lille and Paris (France), Zurich (Switzerland) and Cambridge, MA (USA). GENFIT is a publicly traded company listed on the Nasdaq Global Select Market and on compartment B of Euronext's regulated market in Paris (Nasdaq and Euronext: GNFT). In 2021, IPSEN became one of GENFIT's largest shareholders and holds 8% of the company's share capital. For more information, visit www.genfit.com

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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 latest Universal Registration Document, available on [ipsen.com](https://www.ipsen.com).

GENFIT's forward-looking statements

This press release contains certain forward-looking statements, including those within the meaning of the Private Securities Litigation Reform Act of 1995 with respect to GENFIT, including, but not limited to statements about the potential of elafibranor as a safe and effective second-line treatment for PBC, the opportunity to manage the disease progression and the potential of elafibranor to improve pruritus, reduce cholestatic injury and improve liver function. The use of certain words, including "believe", "potential," "expect", "target", "may" and "will" and similar expressions, is intended to identify forward-looking statements. Although the Company believes its expectations are based on the current expectations and reasonable assumptions of the Company's management, these forward-looking statements are subject to numerous known and unknown risks and uncertainties, which could cause actual results to differ materially from those expressed in, or implied or projected by, the forward-looking statements. These risks and uncertainties include, among other things, the uncertainties inherent in research and development, including in relation to safety of drug candidates, cost of, progression of, and results from, our ongoing and planned clinical trials, review and approvals by regulatory authorities in the United States, Europe and worldwide, of our drug and diagnostic candidates, potential commercial success of elafibranor if approved, exchange rate fluctuations, our continued ability to raise capital to fund our development, as well as those risks and uncertainties discussed or identified in the Company's public filings with the AMF, including those listed in Chapter 2 "Main Risks and Uncertainties" of the Company's 2022 Universal Registration Document filed with the AMF on April 18, 2023, which is available on the Company's website (www.genfit.com) and on the website of the AMF (www.amf-france.org) and public filings and reports filed with the U.S. Securities and Exchange Commission ("SEC") including the Company's 2022 Annual Report on Form 20-F filed with the SEC on April 18, 2023 and subsequent filings and reports filed with the AMF or SEC, including the Half-Year Business and Financial Report at June 30, 2023 or otherwise made public, by the Company. In addition, even if the Company's results, performance, financial condition and liquidity, and the development of the industry in which it operates are consistent with such forward-looking statements, they may not be predictive of results or developments in future periods. These forward-looking statements speak only as of the date of publication of this document. Other than as required by applicable law, the Company does not undertake any obligation to update or revise any forward-looking information or statements, whether as a result of new information, future events or otherwise.