

## **Ipsen provides update on E.U. Marketing Authorization Application for Bylvay® for cholestatic pruritus in patients with Alagille syndrome**

- Positive opinion from Committee for Medicinal Products for Human Use (CHMP) based on Bylvay Phase III ASSERT clinical-trial data in Alagille syndrome (ALGS)
- Negative opinion from Committee for Orphan Medicinal Products (COMP) recommending not to maintain orphan drug designation for treatment of ALGS
- Ipsen to appeal negative COMP opinion, which might delay final European Commission decision
- Approval already granted by U.S. FDA in June 2023 for the treatment of cholestatic pruritus in patients with ALGS aged 12 months and older

**PARIS, FRANCE, 21 July 2023** – Ipsen (Euronext: IPN: ADR: IPSEY) today announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has issued a positive opinion recommending the approval of Bylvay® (odevixibat) for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) aged six months or older.

“We are pleased with today’s CHMP positive opinion which is supported by the data from our Phase III ASSERT trial,” said Howard Mayer, Executive Vice President and Head of Research and Development for Ipsen. “These children endure a very poor quality of life. The severe itching, known as pruritus, caused by the back-up of bile acids in the liver and bloodstream of individuals living with Alagille syndrome, sometimes results in scratching so hard it leads to broken skin. We are committed to bringing a much-needed additional drug treatment option to Alagille patients and families in the E.U.”

The Committee for Orphan Medicinal Products (COMP), a scientific committee of the EMA, has concurrently issued a negative opinion for the maintenance of Bylvay’s orphan drug designation in ALGS. This negative COMP opinion prevents the retention of orphan-drug status in Bylvay’s marketing authorization in ALGS and might delay a final European Commission decision. Ipsen plans to submit an appeal in respect of the COMP opinion.

Bylvay, is an orphan medicine already approved in the E.U. for the treatment of progressive familial intrahepatic cholestasis (PFIC) in patients aged six months or older. In November 2022, a variation application to the current market authorization of was submitted. The application sought approval in the E.U. for a second orphan indication for Bylvay, the treatment of pruritus in patients with ALGS. In 2012, Bylvay received orphan designation for the treatment of ALGS in the E.U., which supported the development of Bylvay through preclinical and clinical stages.

The CHMP and COMP reviewed data from the Bylvay clinical-trial program, including ASSERT, a double-blind, randomized, placebo-controlled Phase III, multi-center efficacy and safety trial conducted in ALGS. Positive data from ASSERT presented at the 2023 European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) congress, demonstrated that Bylvay provided highly statistically significant and clinically meaningful improvements in pruritus, starting as early as one week after initiation

of treatment and were sustained over the 24 weeks of the trial. More than 90% of patients were pruritus responders ( $\geq$  one point change at any time during 24 weeks). The overall incidence of treatment-emergent adverse events was similar to placebo. No patients discontinued the trial, and 96% of patients rolled over into the open-label extension trial.

Bylvay was approved in 2021 in the U.S. as the first medicine-treatment option for patients three months of age and older living with cholestatic pruritus due to PFIC, and for the treatment of PFIC in patients aged six months or older in the E.U. In June 2023, Bylvay was also approved in the U.S. for the treatment of cholestatic pruritus in patients from 12 months of age with ALGS.

Bylvay has received orphan exclusivity for the treatment of PFIC, and orphan drug designations for the treatment of ALGS and biliary atresia, in the U.S. and the E.U. In a potential future third indication, the rare pediatric cholestatic liver disease, biliary atresia, Bylvay is in late-stage development with the Phase III BOLD trial.

## ENDS

### About Bylvay® (odevixibat)

Bylvay is a potent, once-daily, non-systemic ileal bile acid transport inhibitor (IBATi) that acts locally in the small intestine and has minimal systemic exposure. It is approved in the U.S. for the treatment of pruritus in patients three months of age and older with PFIC, where it has orphan exclusivity. Bylvay was first launched as a treatment option for patients with PFIC in the U.S. in 2021, where it is supported by a program designed to assist with access to treatment and patient support. Bylvay is also approved in the E.U. for the treatment of PFIC in patients aged six months or older. It has launched in over nine countries and has secured public reimbursement across several major markets including Germany, Italy, the U.K., France and Belgium. In June 2023, Bylvay was also approved in the U.S. for the treatment of cholestatic pruritus in patients from 12 months of age with Alagille syndrome.

View full U.S. prescribing information here: [ipsen.com](https://www.ipsen.com)

View full E.U. prescribing information here: [Bylvay, INN-odevixibat \(europa.eu\)](https://www.europa.eu)

### Important Safety Information

- PFIC: The most common adverse reactions are diarrhea, liver test abnormalities, vomiting, abdominal pain, and fat-soluble vitamin deficiency.
- ALGS: The most common adverse reactions are diarrhea, abdominal pain, hematoma, and weight decrease.
- Liver Test Abnormalities: Patients should obtain baseline liver tests and monitor during treatment. Dose reduction or treatment interruption may be required if abnormalities occur. For persistent or recurrent liver test abnormalities, consider treatment discontinuation.
- Diarrhea: Treat dehydration. Treatment interruption or discontinuation may be required for persistent diarrhea.
- Fat-Soluble Vitamin (FSV) Deficiency: Patient should obtain baseline vitamin levels and monitor during treatment. Supplement if deficiency is observed. If FSV deficiency persists or worsens despite FSV supplementation, discontinue treatment.

## ALGS

ALGS is an inherited rare, genetic disorder that can affect multiple organ systems in the body including the liver, heart, skeleton, eyes and kidneys. Liver damage may result from having fewer than normal, narrowed or malformed bile ducts, which leads to toxic bile acid build-up, which in turn can cause scarring and progressive liver disease. Approximately 95% of patients with the condition present with chronic cholestasis, usually within the first three months of life and as many as 88% also present with severe, intractable pruritus. The estimated global incidence of ALGS is 3 in 100,000 live births. Currently in the U.S., it is estimated that there are 1,300 patients who may be eligible for IBATi treatment.

### **ASSERT Phase III clinical trial data**

ASSERT is a double-blind, randomized, placebo-controlled trial designed to evaluate the safety and efficacy of 120 µg /kg/day Bylvay for 24 weeks in relieving pruritus in patients with ALGS with 32 sites across North America, Europe, Middle East, and Asia Pacific. The trial enrolled patients aged 0 to 17 years of age with a genetically confirmed diagnosis of ALGS. In the primary analysis, the study met the primary endpoint showing highly statistically significant improvement in pruritus as measured by the PRUCISION Observer-Reported Outcome scratching score (0-4 point scale), from baseline at month 6 (weeks 21 to 24), compared to the placebo arm (p=0.002). More than 90% of patients were pruritus responders (≥ 1 point change at any time during 24 weeks). The study also met the key secondary endpoint showing a highly statistically significant reduction in serum bile acid concentration from baseline to the average of weeks 20 and 24 (compared to the placebo arm p=0.001). Statistically significant improvements in multiple sleep parameters were observed as early as week 1-4 compared to patients on placebo with continued improvement through week 24. In the study, there were no patient discontinuations and 96% of patients rolled over into the open-label extension study. Bylvay had an overall adverse event incidence similar to placebo and a low incidence of drug-related diarrhea (11.4% vs. 5.9% placebo).

### **About 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 5,400 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)

On March 3<sup>rd</sup>, 2023, Ipsen completed the acquisition of Albireo Pharma Inc, a leading innovator in bile-acid modulators to treat rare liver conditions, and the marketing authorization holder of Bylvay.

### **For further information:**

#### **Ipsen Contacts**

#### **Investors**

##### **Craig Marks**

Vice President, Investor Relations  
+44 (0)7584 349 193

##### **Nicolas Bogler**

Investor Relations Manager  
+33 6 52 19 98 92

#### **Media**

**Jennifer Moore**

Senior Director, Global Corporate  
Communications  
+1 (347) 401-8583

**Ioana Piscociu**

Senior Manager  
Global Media Relations  
+33 6 69 09 12 96

**Amy Wolf**

VP, Head of Corporate Brand Strategy &  
Communications  
+41 79 576 07 23

**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).

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