Press Release

Bylvay® (odevixibat) approved in Japan for rare liver disease PFIC

- Bylvay® is the first once-daily ileal bile acid transport inhibitor to be approved as a treatment for pruritus associated with progressive familial intrahepatic cholestasis (PFIC) in Japan, offering a non-surgical treatment option for infants, young children and adults
- PFIC is a rare and life-threatening liver disease that affects an estimated 100 children and infants in Japan.[1]

Paris, France – 19 September 2025 – Ipsen (Euronext: IPN; ADR: IPSEY) announced today that Japan's Ministry of Health, Labour and Welfare (MHLW) has granted regulatory approval for Bylvay® (odevixibat) for the treatment of pruritus associated with progressive familial intrahepatic cholestasis (PFIC). PFIC is a group of rare genetic disorders in which bile acid accumulates in the liver, leading to progressive liver damage and potentially liver failure. The condition severely impacts quality of life through debilitating symptoms such as severe itching (pruritus), caused by the bile accumulation in the liver and bloodstream, which can cause skin mutilation, sleep disruption, irritability, and impaired cognitive and social development.

"Children with PFIC often endure relentless itching that affects their daily quality of life. This includes regular, nightly sleep disturbance, which can have a negative impact on the whole family," said Sandra Silvestri, MD, PhD, Executive Vice President, Chief Medical Officer, Ipsen. "The approval of Bylvay as a once-daily oral therapy represents a welcomed new option in how we approach this disease and offers new hope for patients and families in Japan living with the devastating impact of PFIC."

Bylvay is a potent, once-daily, oral, ileal bile acid transport inhibitor (IBATi) that reduces reabsorption of bile acid back to the liver. In PEDFIC, the largest global Phase III trial conducted in PFIC, children treated with Bylvay showed significant improvements in serum bile acid and pruritus severity. The treatment was generally well-tolerated, with no drug-related serious adverse events and a low incidence of gastrointestinal events.

"Early diagnosis and intervention are critical in PFIC to manage symptoms and preserve liver function," said Dr. Hiroki Kondou, Associate Professor, Department of Pediatrics, Kindai University Nara Hospital. "This approval of Bylvay provides patients and caregivers with a new treatment option that has the potential to reduce itching, and thereby improve sleep quality, while potentially supporting the preservation of liver."

The approval from the MHLW was based on data from a Phase III, open-label study conducted in Japan, which evaluated the efficacy and safety of odevixibat in pediatric patients with PFIC types 1 and 2. The study confirmed improvements in serum bile acid levels and pruritus consistent with the global Phase III PEDFIC results. The Phase III clinical development plan for Bylvay in Japan was managed by Jadeite Medicines Inc and as part of the strategic collaboration, the new drug application for this indication was transferred to Ipsen headquartered in Tokyo, Japan. Ipsen will also be responsible for commercialization of Bylvay in Japan.

About PFIC

Progressive familial intrahepatic cholestasis (PFIC) is a group of rare genetic disorders in which bile acids build up in the liver, causing damage to the liver which may result in liver failure.[2,3] There are several PFIC subtypes of which three are the most distinct : PFIC1 and PFIC2 typically manifest in the early stages of life – infancy or early childhood, while PFIC3 can have possible onset between infancy and adolescence.[3,4] PFIC impacts males and females equally, at a rate ranging from 1 per 50,000 to 1 per 100,000[5] births. While some late presentations of PFIC can present in adulthood, it typically manifests and is most aggressive in infants and young children.[6] PFIC impacts patient's daily lives through debilitating symptoms including severe itching (pruritus) which can result in skin mutilation, loss of sleep, irritability, poor attention, and impaired school function.[4]

About Bylvay (odevixibat)

Bylvay is a potent, once-daily ileal bile acid transport inhibitor (IBATi) that acts locally in the small intestine with minimal absorption into the rest of the body (minimal systemic exposure). Bylvay was approved in June 2021 in the EU as the first drug treatment option for all types of progressive familial intrahepatic cholestasis (PFIC) in patients aged 6 months or older, and in the US as the first drug treatment option for patients 3 months of age and older living with cholestatic pruritus due to PFIC. Bylvay has received orphan exclusivity for the treatment of PFIC in the EU and in the US In June 2023 Bylvay was approved in the U.S. for the treatment of cholestatic pruritus in patients from 12 months of age with ALGS and received orphan exclusivity for ALGS. In 2024 under the brand name Kayfanda (odevixibat), an approval under exceptional circumstances was granted by the European Commission for the treatment of cholestatic pruritus in Alagille syndrome (ALGS) in patients aged 6 months or older. Odevixibat is also in late-stage development in an ongoing Phase III clinical trial (BOLD) for the treatment of biliary atresia.

About PEDFIC

PEDFIC is the largest, global, Phase III trial ever conducted in PFIC. PEDFIC 1 is a randomized (1:1:1), double-blind, placebo-controlled 24-week trial that evaluated the efficacy and tolerability of two doses of odevixibat (40 μg/kg or 120 μg/kg) in reducing pruritus and serum bile acid levels in children with PFIC. The results were published in The Lancet.[6]

Data from the Phase III PEDFIC 1 trial demonstrated the potential for Bylvay to be an effective new treatment option for PFIC.[6]

- The PEDFIC trial (n=62) met its first primary endpoint, in which pruritus symptoms were significantly improved with odevixibat, with 55% of patients on odevixibat achieving a reduction in pruritus compared to 30% on placebo.
- The trial met its second primary endpoint of serum bile acid (sBA) response, defined as the number of patients who showed a reduction (either 70% or more from baseline, or levels of 70 μmol/L or less) in sBA at Week 24. Significantly more patients achieved a sBA response with odevixibat, with 33% of patients showing a reduction in sBA levels on odevixibat compared to no patients on placebo at Week 24.
- Odevixibat was generally well-tolerated, with no drug-related serious adverse events and a low incidence of diarrhea/frequent bowel movements reported during the trial.

PEDFIC 2, an open-label extension of PEDFIC 1, is an ongoing 72-week trial that aims to evaluate the efficacy and tolerability of odevixibat 120 µg/kg once a day in patients with PFIC. Interim results were published in The Journal of Hepatology.[7]

The approval from the Japanese MHLW was based on an open-label Phase III study conducted by Jadeite Medicines in Japan. Jadeite Medicines received Orphan Drug Designation for odevixibat in Progressive Familial Intrahepatic Cholestasis (PFIC) from the Ministry of Health, Labour and Welfare of Japan in May 2023, followed by the initiation of the Phase III trial in PFIC for patients in Japan. The study evaluated the efficacy and safety of odevixibat in pediatric patients with PFIC types 1 and 2 and confirmed improvements in serum bile acid levels and pruritus consistent with the global PEDFIC results.

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 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 7766471149
Khalid Deojee khalid.deojee@ipsen.com +33 666019526

Media

Sally Bain sally.bain@ipsen.com +1 8573200517
Anne Liontas anne.liontas.ext@ipsen.com +33 0767347296

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 forwardlooking 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

1Summar,y, Ministry of Health Labour and Wellbeing, Japan: 001175135.pdf Last accessed: September, 2025

2. Baker A, *et al*. Systematic review of progressive familial intrahepatic cholestasis. *Clin Res Hepatol Gastroenterol*. 2019. 43(1):20–36.

3. Nayagam JS, *et al*. Clinical phenotype of adult-onset liver disease in patients with variants in ABCB4, ABCB11, and ATP8B1. *Hepatol Commun*. 2022. 6(10):2654-2664.

4. Agarwal S, *et al*. Progressive Familial Intrahepatic Cholestasis (PFIC) in Indian Children: Clinical Spectrum and Outcome. *J Clin Exp Hepatol*. 2016. v.6(3).

5. Davit-Spraul A, et al. Progressive familial intrahepatic cholestasis. Orphanet J Rare Dis. 2009. 4(1):1-12.

6. Thompson RJ, *et a*l. Odevixibat treatment in progressive familial intrahepatic cholestasis: a randomised, placebo-controlled, phase 3 trial. *Lancet Gastroenterol Hepatol*. 2022. 7:830–842.

7. Thompson RJ, *et al*. Interim results from an ongoing, open-label, single-arm trial of odevixibat in progressive familial intrahepatic cholestasis 2023. *JHEP Rep*. 5(8):100782.