Press release

Intended for international media and investor audiences only

Ipsen's Kayfanda® (odevixibat) approved in European Union for cholestatic pruritus in Alagille Syndrome, a rare liver disease

- ***Kayfanda® (odevixibat) approved as new treatment choice for cholestatic pruritus in children from six months with the rare liver condition, Alagille Syndrome***
- ***E.U. marketing authorization for Kayfanda based on data from ASSERT the only Phase III trial completed in patients with Alagille Syndrome***
- ***Kayfanda approval for use in the E.U. further expands Ipsen's rare cholestatic liver disease portfolio***

PARIS, FRANCE, 23 September, 2024 Ipsen (Euronext: IPN; ADR: IPSEY) today announced that the European Commission has approved Kayfanda® (odevixibat) under exceptional circumstances for the treatment of cholestatic pruritus in Alagille Syndrome (ALGS) in patients aged 6 months or older. Kayfanda is a once-daily non-systemic ileal bile acid transport (IBAT) inhibitor. Odevixibat, the active substance in Kayfanda, blocks the ileal bile acid transporter (IBAT), which ultimately results in a decrease in serum bile acids that can form in the liver.

"Patients living with Alagille syndrome often endure a very poor quality of life as a result of the intolerable itch, which is one of the most significant symptoms of this condition," said Christelle Huguet, Executive Vice President and Head of Research and Development, Ipsen. "Today's decision is therefore very welcome. We will now continue in our ongoing efforts to make this new treatment option available for use with patients living in the E.U."

Approval of Kayfanda, known in ALGS as Bylvay® outside of the E.U., was based on the ASSERT Phase III clinical trial data.[1] ASSERT is the world's first and only Phase III trial completed in patients with ALGS. These data demonstrated statistically significant and clinically meaningful improvements from baseline to month 6 in scratching severity for patients on Kayfanda versus placebo. This was observed rapidly and maintained over the period of the study. A statistically significant reduction in serum bile acid concentration at the end of treatment was also demonstrated for patients on Kayfanda versus placebo, with improvements in multiple observer-reported sleep parameters. The overall incidence of treatment emergent adverse events with Kayfanda was similar to placebo, with a low drug-related diarrhea rate in patients with ALGS.

"ALGS is a distressing condition, which often presents in the first few months of life. One of the most common symptoms reported, as a result of the condition, is severe pruritus, with children scratching to the point of bleeding and the itch causing sleep disturbances for the child and their carers," said Professor Henkjan Verkade, Pediatric Gastroenterology and Hepatology, Department of Pediatrics, University of Groningen, Beatrix Children's Hospital and University Medical Center Groningen, Netherlands. "To have a new treatment option that has been shown to reduce the itch and improve sleep is a very positive development for the ALGS community."

ALGS is an inherited rare, genetic disorder that can affect multiple organs 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 a build-up of toxic bile acid, known as cholestasis and this in turn can cause fibrosis and progressive liver disease. Approximately 95% of patients with the condition present with chronic cholestasis, usually within the first few 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.

Ipsen has also received E.U. approval for Iqirvo® (elafibranor) for Primary Biliary Cholangitis, another important treatment in the company's leading rare cholestatic liver disease portfolio.

Kayfanda is known in ALGS as Bylvay® outside of the European Union (E.U.). Under the brand name of Bylvay it was approved in the E.U. as the first drug treatment option for all types of progressive familial intrahepatic cholestasis (PFIC) in patients aged 6 months or older. The medicine is also currently being studied in a Phase III trial, BOLD, in Biliary Atresia with data anticipated in 2026.

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About Kayfanda® (odevixibat)

Kaydanda® (odevixibat) is a once-daily non-systemic ileal bile acid transport (IBAT) inhibitor approved under exceptional circumstances in the E.U. for the treatment of cholestatic pruritus in Alagille syndrome (ALGS) in patients aged 6 months or older. Odevixibat was approved in June 2021 in the E.U. under the brand name Bylvay®, 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 U.S. under the brand name Bylvay®, 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 E.U. and in the U.S. 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.

About ASSERT

ASSERT is a double-blind, randomized, placebo-controlled trial designed to evaluate the safety and efficacy of 120 µg /kg/day odevixibat 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 weeks 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. Odevixibat had an overall adverse event incidence similar to placebo and a low incidence of drug-related diarrhea (11.4% vs. 5.9% placebo). [1]

Full results of the ASSERT study have been published in the Lancet, Gastroenterology & Hepatology in April 2024,

Important safety information and recommendations for the use of Kayfanda will be detailed in the Summary of Product Characteristics (SmPC), published in the European public assessment report (EPAR) and available in all official EU languages. The full SmPC will be found at: http://www.ema.europa.eu

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 fuelled 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.

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References

1. Ovchinsky N., et al. Efficacy and safety of odevixibat in patients with Alagille syndrome (ASSRT); a phase 3, double-blind, randomized, placebo-controlled trial. Lancet Gastroenterol / Hepatol. 2024 doi.org/10.1016/S2468-1253(24)00074-8