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GLISTEN phase III trial results show linerixibat significantly improves cholestatic pruritus (relentless itch) in primary biliary cholangitis (PBC)

- Primary and key secondary endpoints met, demonstrating a rapid, significant and sustained improvement in cholestatic pruritus and itch-related sleep interference versus placebo
- Cholestatic pruritus presents in the majority of PBC patients, with debilitating impacts on quality of life including sleep disturbance
- Late-breaking results presented at the European Association for the Study of the Liver (EASL) Congress 2025

GSK plc (LSE/NYSE: GSK) today announced positive results from the GLISTEN phase III trial evaluating linerixibat, an investigational targeted inhibitor of the ileal bile acid transporter (IBAT), in adults with cholestatic pruritus and PBC, a rare autoimmune liver disease. The full data were presented in a late-breaker oral presentation at the EASL Congress 2025.

GLISTEN met the primary endpoint of change from baseline in monthly itch score and showed linerixibat (n=119) significantly improved itch versus placebo (n=119) over 24-weeks, as measured on a 0-10 numerical rating scale (NRS) for the worst itch (WI-NRS) (least squares [LS] mean difference [95% CI]: -0.72 [-1.15, -0.28], p=0.001). Monthly itch score evaluated the worst weekly itch of each month over the 24-week treatment period. This finding supports linerixibat's potential to address a major symptom of PBC, relentless itch.

The trial also met key secondary endpoints including itch score at week 2 and itch-related sleep interference NRS over 24 weeks demonstrating:

- Improvement in itch was rapid with a significant improvement over placebo at week 2 (LS mean difference [95% CI]: -0.71 [-1.07, -0.34], p<0.001) and sustained throughout the trial.
- Significant improvement in itch-related sleep interference, which impacts patient quality of life, over 24 weeks of treatment with linerixibat compared with placebo (LS mean difference [95% CI]: -0.53 [-0.98, -0.07], p=0.024).
- More patients in the linerixibat group had clinically meaningful itch improvement (WI-NRS ≥3-point reduction) with 56% versus 43% in the placebo group at week 24 (treatment difference 13% [95% CI 0%-27%], nominal p=0.043).

Kaivan Khavandi, SVP, Global Head, Respiratory, Immunology & Inflammation R&D, GSK, said: "Relentless itch is present in the majority of patients with PBC and is a symptom that affects sleep, mental health, and quality of life. With linerixibat, we are one step closer to addressing the high unmet need of itch and its related sleep interference that are critically important to patients but historically under-treated."

The safety profile of linerixibat was consistent with previous studies and the mechanism of IBAT inhibition, with gastrointestinal side-effects more common in the active treatment group. The most common adverse event, diarrhoea, was mostly mild in intensity; discontinuation due to diarrhoea was 4% in the linerixibat group versus <1% in the placebo group.

Gideon Hirschfield, Lily and Terry Horner Chair in Autoimmune Liver Disease Research, Director of the Autoimmune and Rare Liver Disease Programme at University Health Network, Toronto and lead author of

the GLISTEN study, said: “Currently there are very limited therapies for pruritus in PBC and previous attempts to develop new therapies have been unsuccessful. As an investigator who also sees many patients with PBC, and who has worked with this molecule from the early phase II studies, the clear improvements in itch and its related sleep interference seen in GLISTEN are meaningful and clinically important.”

Linerixibat is currently not approved anywhere in the world.

About cholestatic pruritus in PBC
In PBC, a cholestatic liver disease, bile flow from the liver is disrupted. The resulting excess bile acids in circulation are thought to play a causal role in cholestatic pruritus, an internal itch that cannot be relieved by scratching. Pruritus can occur at any stage of PBC disease or biochemical control, and is experienced in varying degrees of severity by up to 90% of people living with PBC.[1] The first line treatment for PBC controls disease in approximately 70% of patients,[2] but does not reduce the severity or impact of the pruritus.[3] Cholestatic pruritus is a serious condition that can be debilitating, with patients experiencing sleep disturbance, fatigue, impaired quality of life[3] and even sometimes requiring liver transplantation in the absence of liver failure.[4]

About linerixibat (GSK2330672)
Linerixibat is an IBAT inhibitor, a targeted oral agent with potential to treat cholestatic pruritus (itch) associated with the rare autoimmune liver disease known as PBC. By inhibiting bile acid re-uptake, linerixibat reduces multiple mediators of pruritus in circulation. The US Food and Drug Administration and the European Medicines Agency have granted orphan drug designation for linerixibat in the treatment of cholestatic pruritus in patients with PBC.

About the GLISTEN trial
GLISTEN is a double-blind, randomised, placebo-controlled, phase III trial (NCT04950127; GSK study 212620) conducted in 238 PBC patients with cholestatic pruritus initially enrolled equally into active and placebo arms (n=119 each). The primary analysis evaluated the efficacy and safety of linerixibat compared with placebo. Participants with moderate to severe itch were enrolled. Participants initially received either linerixibat or placebo and had the potential to cross over in a part B of the trial. Primary and secondary outcome measures were assessed using a 0-10 NRS for worst itch and itch-related sleep interference. Stable use of guideline suggested anti-itch therapy was permitted. The trial was the first truly global PBC study completed in 19 countries including the Americas, Europe, China and Japan.

About GSK research in hepatology
GSK is currently investigating multiple potential treatments for patients with liver disease. In addition to PBC, we are also investigating potential treatments for chronic hepatitis B, alcohol-related liver disease (ALD), and metabolic dysfunction-associated steatohepatitis (MASH).

About GSK
GSK is a global biopharma company with a purpose to unite science, technology, and talent to get ahead of disease together. Find out more at gsk.com.

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GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Such factors include, but are not limited to, those described in the "Risk Factors" section in GSK's Annual Report on Form 20-F for 2024, and GSK's Q1 Results for 2025.

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Footnotes
[I] The term nominal significance refers to results with a p-value <0.05 where there was no control for multiple comparisons or where the test was performed after a break in the multiplicity hierarchy.

References
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