GSK

Stock exchange announcement

For media and investors only

Issued: 19 November 2024, London UK

Linerixibat shows positive Phase III results in cholestatic pruritus (relentless itch) in primary biliary cholangitis (PBC)

- Primary endpoint met with a statistically significant improvement in itch over 24 weeks compared with placebo
- Linerixibat has the potential to be the first global therapy indicated to treat itch in PBC
- Cholestatic pruritus is one of the most common symptoms of PBC, an autoimmune disease that can lead to liver failure

GSK plc (LSE/NYSE: GSK) today announced positive headline results of GLISTEN, the ongoing global phase III clinical trial evaluating linerixibat, an investigational targeted inhibitor of the ileal bile acid transporter (IBAT), in adults with cholestatic pruritus (relentless itch) associated with primary biliary cholangitis (PBC), a rare autoimmune liver disease.

GLISTEN met its primary endpoint, with linerixibat resulting in an improvement in itch, as demonstrated by a statistically significant reduction from baseline in monthly itch score over 24 weeks versus placebo. The trial recruited PBC patients with moderate to severe itch, who were receiving stable doses of guideline-suggested therapies for pruritus, or were treatment naïve, or had been previously treated. The preliminary safety results are generally consistent with those seen in prior studies of linerixibat. Further analysis of these data is ongoing.

Kaivan Khavandi, SVP & Global Head, Respiratory/Immunology R&D, GSK, said: “Linerixibat has the potential to be the first global therapy specifically developed to treat itch in PBC. These positive data suggest that it could have a place in supporting patients whose quality of life is significantly affected in multiple ways by persistent itching.”

People who have been diagnosed with PBC will reach 510,000 globally by 2030, and more than 240,000 people will experience relentless itch requiring treatment, representing a significant unmet need. [1,2,3,4] Current guideline suggested therapies available for cholestatic pruritus are inadequate, with known limited impact on itch, and poor tolerability. [5,6] PBC is a rare disease of the bile ducts that primarily affects women and can cause liver damage and possible liver failure if untreated. One of the most common symptoms is constant, relentless itching or skin-crawling sensations, as well as fatigue that is often made worse by itching at night. The disease currently has no cure.

Carol Roberts, President, The PBCers Organization, said: “The itch associated with PBC for many patients is unrelenting and often severe but is a symptom that is frequently overlooked or dismissed. It has a significant impact on quality of life and mental health for people with PBC. The potential of a treatment option that addresses a root cause of itch answers a previously unmet need for people with PBC."

The full results of GLISTEN will be presented at a future scientific congress. Linerixibat is currently not approved anywhere in the world; it has been granted Orphan Drug Designation in both the US and EU.

About cholestatic pruritus in primary biliary cholangitis

In primary biliary cholangitis (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 and is experienced by up to 90% of people living with PBC.[4] The first line treatment for PBC controls disease in approximately 70% of patients, but does not reduce the severity or impact of the pruritus.[7] Cholestatic pruritus is a serious condition that can be

debilitating, with patients experiencing sleep disturbance, fatigue, impaired quality of life and even sometimes requiring liver transplantation in the absence of liver failure.[4]

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

About the GLISTEN trial
GLISTEN is an ongoing double-blind, randomised, placebo-controlled, phase III trial (NCT04950127; GSK study 212620) conducted in PBC patients with cholestatic pruritus. The primary analysis evaluated the efficacy (including impact on sleep) and safety of linerixibat compared with placebo. Participants with moderate to severe itch were enrolled. The trial includes multiple arms where participants receive either linerixibat or placebo and have the potential to cross over at one point in the study. Primary and secondary outcome measures were assessed using the Numerical Rating Scale (NRS) for worst itch and itch-related sleep interference, and the PBC-40 questionnaire for quality of life. Stable use of guideline suggested anti-itch therapy was permitted. A small number of participants remain ongoing in an exploratory portion of the trial.

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.

GSK enquiries

Media:	Tim Foley	+44 (0) 20 8047 5502	(London)
	Sarah Clements	+44 (0) 20 8047 5502	(London)
	Kathleen Quinn	+1 202 603 5003	(Washington DC)
	Lyndsay Meyer	+1 202 302 4595	(Washington DC)
Investor Relations:	Annabel Brownrigg-Gleeson	+44 (0) 7901 101944	(London)
	James Dodwell	+44 (0) 20 8047 2406	(London)
	Mick Readey	+44 (0) 7990 339653	(London)
	Camilla Campbell	+44 (0) 7803 050238	(London)
	Steph Mountifield	+44 (0) 7796 707505	(London)
	Jeff McLaughlin	+1 215 751 7002	(Philadelphia)
	Frannie DeFranco	+1 215 751 4855	(Philadelphia)

Registered in England & Wales:
No. 3888792

Registered Office:
79 New Oxford Street
London
WC1A 1DG

Stock exchange announcement

For media and investors only

References
1 Lu M et al. *Clin Gastroenterol Hepatol.* 2018 Aug;16(8):1342-1350
2 Sebode M et al. *Z Gastroenterol.* 2020 May;58(5):431-438
3 Tanaka A et al. *Hepatol Res*. 2019 Aug;49(8):881-889
4 Gungabissoon U, et al.. *BMJ Open Gastroenterol* 2024; 11(1)
5 Hegade VS, et al. *Clin Gastroenterol Hepatol*. 2019 Jun;17(7):1379-1387
6 Mayo MJ et al. *Dig Dis Sci*. 2023 Mar;68(3):995-1005
7 Carbone M, et al. *Lancet Gastroenterol Hepatol*. 2018 Jul 13;3(9):626–634