GSK enters agreement to obtain exclusive license for JNJ-3989 to expand the development of bepirovirsen

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For media and investors only

- GSK’s bepirovirsen both alone and in combination with nucleos(t)ide analogue therapy has shown functional cure in patients with chronic hepatitis B

- Addition of JNJ-3989 when administered sequentially with bepirovirsen may have the potential to further increase functional cure rates

- Transaction underscores GSK’s leadership in the treatment and prevention of infectious diseases and commitment to the development of oligonucleotide therapeutics

GSK plc (LSE/NYSE: GSK) and Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) today announced that they have reached an agreement with Janssen Pharmaceuticals, Inc. (Janssen), a Johnson & Johnson company, to transfer exclusive worldwide rights to further develop and commercialise JNJ-3989 to GSK. JNJ-3989 (formerly ARO-HBV) was initially in-licensed by Janssen from Arrowhead in 2018.

JNJ-3989 is an investigational hepatitis B virus-targeted small interfering ribonucleic acid (siRNA) therapeutic that GSK intends to evaluate in a sequential regimen with bepirovirsen, GSK’s investigational antisense oligonucleotide, for the treatment of adult non-cirrhotic patients with chronic hepatitis B (CHB) on nucleos(t)ide analogue (NA) therapy.

There is high unmet need in CHB with an estimated 300 million people living with the disease and a less than 3-7% functional cure rate with

current treatment options.1,2 Patients reach functional cure when the hepatitis B virus and viral proteins are at levels low enough to be undetectable in blood and can be controlled by the immune system without medication.

Bepirovirsen is the only single agent in phase III development that has shown clinically meaningful functional cure response for patients with CHB receiving oral NAs, following positive results demonstrated in the B-Clear and B-Sure clinical trials.3,4 B-Clear identified sub-groups of patients most likely to benefit from treatment with bepirovirsen, and also solidified bepirovirsen as a potential backbone therapy in future sequential regimens to pursue functional cure in additional patients with CHB.

Tony Wood, Chief Scientific Officer, GSK, said:

> We are excited to build on promising results already demonstrated with bepirovirsen to investigate a novel sequential regimen with JNJ-3989. We believe this approach could redefine the treatment paradigm for chronic hepatitis B by helping even more patients achieve functional cure.

Chris Anzalone, Ph.D., President and CEO of Arrowhead said:

> GSK has a global reach, a clear commitment to help those living with chronic hepatitis B, and a promising strategy for clinical studies designed to improve functional cure rates. We have great confidence in the team at GSK and look forward to seeing this program progress towards the goal of potentially helping the millions of patients with chronic hepatitis B worldwide without adequate treatment options. We would also like to thank our colleagues at Janssen for the great progress they made with JNJ-3989, the investigational siRNA therapeutic that Arrowhead discovered and initially developed.

JNJ-3989 has the potential to move immediately into a phase II sequential regimen trial with bepirovirsen beginning in 2024, further strengthening GSK’s late-stage pipeline of specialty medicines. This transaction is aligned with GSK’s leadership in the treatment and prevention of infectious diseases and commitment to the development of oligonucleotide therapeutics.

This transaction builds on GSK’s relationship with Arrowhead,

following the 2021 exclusive license of GSK4532990 (ARO-HSD), an investigational oligonucleotide therapeutic targeting HSD17B13 as a potential treatment for patients with alcohol-related and nonalcohol related liver diseases. The exclusive license granted GSK rights to further develop and commercialise GSK4532990 outside of Greater China.

Upon closing of the transaction, GSK will assume rights and obligations of the existing license agreement between Janssen and Arrowhead, including all remaining financial obligations owed to Arrowhead for JNJ-3989 under the original agreement. GSK will be responsible for upfront and potential milestone-based payments to both Janssen and Arrowhead totalling approximately $1 billion. Janssen will continue to be responsible for the ongoing clinical trials of JNJ-3989 at its expense and GSK will be solely responsible for all future development and commercialisation activities. Additionally, Arrowhead will receive tiered royalties on net sales pursuant to the original agreement.

This transaction is subject to customary conditions, including applicable regulatory agency clearances under the Hart-Scott-Rodino Act in the US.

Hepatitis B is a viral infection of the liver, caused by the hepatitis B virus, that can cause both acute and chronic liver disease.5 Chronic hepatitis B (CHB) is a long-lasting infection and occurs when the body’s immune system is unable to fight off the virus and it persists in the blood and liver.6 CHB is a major global health issue, affecting nearly 300 million people across the world, although only about 10% of these people have a diagnosis and only 5% receive treatment.1 Even when treated, CHB can progress to liver complications including cirrhosis and liver cancer, which results in almost a million deaths per year.1,6

JNJ-3989 is a liver-targeted siRNA antiviral therapeutic for subcutaneous injection designed to treat chronic hepatitis B virus infection via a ribonucleic acid interference (RNAi) mechanism.

About bepirovirsen (GSK3228836)

Bepirovirsen is a triple-action investigational antisense oligonucleotide (ASO), currently being evaluated in the B-Well phase III clinical trial programme for the treatment of CHB. Bepirovirsen is designed to

recognise and destroy the genetic components (i.e. RNA) of the hepatitis B virus that can lead to chronic disease, potentially allowing a person's immune system to regain control. Bepirovirsen inhibits the replication of viral DNA in the body, suppresses the level of hepatitis B surface antigen (HBsAg) in the blood, and stimulates the immune system to increase the chances of a durable and sustained response.

Bepirovirsen (previously known as 'ISIS 505358 or IONIS-HBVRX') was discovered by and jointly developed with Ionis Pharmaceuticals. Bepirovirsen is one of the ASO HBV programme assets in-licensed by GSK from Ionis Pharmaceuticals in August 2019.

About Arrowhead Pharmaceuticals

Arrowhead Pharmaceuticals develops medicines that treat intractable diseases by silencing the genes that cause them. Using a broad portfolio of RNA chemistries and efficient modes of delivery, Arrowhead therapies trigger the RNA interference mechanism to induce rapid, deep, and durable knockdown of target genes. RNA interference, or RNAi, is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. Arrowhead's RNAi-based therapeutics leverage this natural pathway of gene silencing.

For more information, please visit www.arrowheadpharma.com, or follow us on Twitter @ArrowheadPharma. To be added to the Company's email list and receive news directly, please visit http://ir.arrowheadpharma.com/email-alerts.

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.

Cautionary statement regarding forward-looking statements

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 under Item 3.D 'Risk factors" in the company's Annual Report on Form 20-F for 2022, and Q2 Results for 2023.

World Health Organization. Global Hepatitis Report, 2017. Lok AS et al. Antiviral therapy for chronic hepatitis B viral infection in adults: A systematic review and meta-analysis. Hepatology. 2016;63:284-306. Yuen M-F, Lim S-G, Plesniak R, et al. Efficacy and safety of bepirovirsen in chronic hepatitis B infection. N Engl J Med. 2022;387(21):1957–68. Gadano et al. EASL 2023 Abstract 4132. World Health Organisation, Hepatitis B Key Facts, July 2023. Polaris estimate. https://cdafound.org/polaris-regions-dashboard/. Last accessed 28 Sept 2023.

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