GSK presents promising new data for bepirovirsen, an investigational treatment for chronic hepatitis B

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- Interim analysis from the B-Clear phase IIb trial shows bepirovirsen's potential to suppress both the surface antigen and the virus of hepatitis B, leading to the possibility of functional cure

- Phase III trial evaluating bepirovirsen as a monotherapy is anticipated to start in the first half of 2023

- Exploring potential combination treatments to further reduce the global burden of chronic hepatitis B

GSK plc today announced promising interim results from the B-Clear phase IIb trial showing that bepirovirsen, an investigational antisense oligonucleotide treatment for hepatitis B, reduced levels of hepatitis B surface antigen (HBsAg) and hepatitis B virus (HBV) DNA after 24 weeks' treatment in people with chronic hepatitis B (CHB).

These interim analysis data were presented today in an oral late-breaker session at the European Association for the Study of the Liver's International Liver Congress 2022 in London, UK. The final results from the study will be submitted for presentation at a scientific congress later this year, and for publication in a peer-reviewed journal.

Chris Corsico, SVP, Development, GSK, said:

> Chronic hepatitis B affects nearly 300 million people with approximately 900,000 patients dying each year from its associated complications. These encouraging data support

> further investigation of bepirovirsen, both as monotherapy and in combination, as a potentially transformative new treatment option for patients with chronic hepatitis B.

Current treatment options have limited success in leading to functional cure, where the virus is not eliminated from the body but is at low levels that are undetectable in blood and can be controlled by the immune system without medication. The mainstay of therapy includes nucleoside/nucleotide analogues (NA) which are often taken for life because they suppress but rarely clear the virus. Bepirovirsen's unique mechanism of action works to reduce HBV replication, suppress HBsAg and stimulate the immune system. Bepirovirsen has the potential to lead to functional cure in patients with CHB.

Professor Man-Fung Yuen, Principal Investigator and Chief of Division of Gastroenterology and Hepatology, Queen Mary Hospital, The University of Hong Kong, said:

> The data presented today are a promising step forward for the millions of people living with chronic hepatitis B worldwide. Specifically, the reduction in hepatitis B surface antigen and HBV DNA to below the lower limit of quantification has the potential to be clinically meaningful and lead to functional cure. This could help people living with CHB and healthcare providers manage the long-term consequences of CHB which include the social burden as well as the risk of developing life-threatening liver complications.

GSK is also exploring combinations of bepirovirsen and other therapeutic modalities in the following trials. Combination treatments could increase functional cure rates in more patients, thereby further reducing the global disease burden of CHB. Trials include:

- Phase IIb trial of bepirovirsen in sequential combination with pegylated interferon (PegIFN) treatment

- Phase II trial of bepirovirsen in combination with GSK's chronic hepatitis B targeted immunotherapy

About the B-Clear phase IIb trial

The B-Clear phase IIb study is investigating the efficacy and safety of 12 or 24 weeks treatment with bepirovirsen in people with CHB on

stable NA treatment or not on NA treatment at study start. The primary endpoints are the proportion of patients achieving HBsAg levels below the Lower Limit of Quantification (LLOQ), and HBV DNA levels below LLOQ sustained for 24 weeks without rescue medication after end of treatment with bepirovirsen.

The study consists of two parallel cohorts, one for patients receiving NA treatment and the other for patients who were not on NA. Patients from each arm were randomised to 1 of 4 treatment arms within each cohort, with treatment administered weekly with or without loading doses (LD) on days 4 and 11:

- Bepirovirsen 300 mg with LD for 24 weeks;

- Bepirovirsen 300 mg with LD for 12 weeks then 150 mg for 12 weeks;

- Bepirovirsen 300 mg with LD for 12 weeks then placebo for 12 weeks;

- Placebo with LD for 12 weeks then bepirovirsen 300 mg without LD for 12 weeks.

In both cohorts, virologic responses were observed at the end of treatment:

- For those patients receiving NA treatment (n=227), 24 weeks treatment of 300 mg bepirovirsen resulted in HBsAg

- For patients not on NA (n=230), 24 weeks treatment of 300 mg bepirovirsen resulted in HBsAg

- The durability of these responses is being assessed.

Treatment-related serious adverse events (SAEs) were observed in

Hepatitis B is a viral infection of the liver, caused by the hepatitis B virus, that can cause both acute and chronic liver disease. 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. It is estimated that there are 296 million people globally with CHB. As of 2019, 30.4 million people were aware of their infection, while 6.6 million of the people diagnosed were on treatment.

Viral suppression is the current goal for treatment of CHB. However, viral replicative activity may return upon cessation of treatment, requiring lifelong therapy to prevent viral rebound. The concept of functional cure of CHB aims to eliminate the virus from circulating in the blood and prevent any disease activity in the liver. As only a limited number of patients currently treated for CHB achieve HBsAg loss, considered the hallmark for achieving functional cure, development of therapeutic approaches to reach functional cure are needed.

About bepirovirsen (GSK3228836)

Bepirovirsen is an investigational antisense oligonucleotide (ASO) designed to specifically recognise the RNA that the hepatitis B virus uses to replicate itself in the infected liver cells (hepatocytes) and make the viral antigens (proteins) which facilitate chronicity of the disease by helping to avoid clearance by the immune system. The ASO recruits the liver's own enzymes to eliminate the RNA by digesting it to an inactive form. The subsequent reduction in the levels of the RNA results in a decrease in both the virus and the production of viral antigen (HBsAg) by the hepatocytes, which can be measured by a drop in the HBV DNA and antigen levels in the circulating blood. Bepirovirsen has an additional property of stimulating immune responses via Toll-like receptor 8 (TLR8) which may help the immune system to achieve durable clearance of the virus from circulating blood.

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.

GSK is a science-led global healthcare company. For further information please visit http://www.gsk.com/en-gb/company/

Cautionary statement regarding forward-looking statements

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any impacts of the COVID-19 pandemic.

World Health Organisation, Hepatitis B Key Facts, June 2022

World Health Organization. Global Hepatitis Report, 2017

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