

PRESS RELEASE

Immunocore announces publication of preclinical data in *Hepatology* showing the potential of ImmTAV® bispecific molecules for functional cure of chronic hepatitis B

New preclinical data show potential of ImmTAV platform to facilitate specific and rapid elimination of Hepatitis B-infected cells with the goal of achieving functional cure

Lead bispecific candidate, IMC-I109V, to progress into first-in-human clinical trials for the treatment of chronic Hepatitis B

(OXFORDSHIRE, England & CONSHOHOCKEN, Penn. & ROCKVILLE, Md., US, 27 August 2020) Immunocore (or the “Company”), a pioneering, clinical-stage T cell receptor biotechnology company working to develop and commercialise a new generation of transformative medicines to address unmet needs in cancer, infection and autoimmune disease, today announces publication of a novel therapeutic approach with the potential to provide a functional cure for chronic hepatitis B, in leading peer reviewed journal *Hepatology*.

Achieving functional cure, a sustained loss of circulating HBsAg and HBV DNA, is a challenge for the field due to the persistence of cells capable of producing HBsAg and which act as a reservoir for virus production. These cells can contain integrated HBV-DNA or long-lived covalently closed circular DNA (cccDNA), both of which are difficult for direct-acting anti-viral therapies to permanently eradicate. Additionally, HBV-specific immune responses in people living with Hepatitis B are often exhausted, making it difficult for them to eliminate the infected cells.

With this in mind, the team at Immunocore is utilising its immune-mobilising monoclonal T cell receptors against virus (ImmTAV®) platform to address these challenges. These bi-specific molecules consist of a targeting arm which tightly binds viral protein fragments on the surface of infected hepatocytes, and an immune-activating arm to redirect non-exhausted T cells to eliminate infected hepatocytes, bypassing exhausted HBV-specific T cells. The team were able to generate multiple ImmTAV molecules to specifically recognise fragments of 3 different viral proteins and achieve potent T cell redirection *in vitro*.

To achieve a functional cure, sources of HBsAg (Env) must be eliminated. Therefore, ImmTAV-Env molecules were further characterised and shown to redirect a broad range of T cells subsets towards HBsAg positive cells, with T cell responses observed from both healthy and HBV-infected donors. Crucially, the redirection of T cells by ImmTAV-Env resulted in elimination of cells representative of both major sources of HBsAg, hepatocellular carcinoma (HCC) cells containing integrated HBV-DNA, and cells infected with HBV *in vitro*, causing a substantial reduction of HBeAg and specific elimination of up to 97% of cells expressing viral RNA.

Importantly, activated T cells did not attack healthy, un-infected human hepatocytes and furthermore, could be switched off by the addition of a corticosteroid. This demonstrates the feasibility of controlling the activity of the ImmTAV-Env molecule in order to safeguard against excessive cytokine release.

Collectively, these data support on-target efficacy of the lead HBV ImmTAV against HBV-infected hepatocytes. Following completion of preclinical development earlier this year, Immunocore has been granted regulatory approval to move forward with a first-in-human trial of IMC-I109V (#ACTRN12620000403932p).

“Hundreds of millions of people are chronically infected with HBV worldwide and current treatment options require lifelong adherence to be effective. There is an urgent need for new therapies to provide a functional cure, defined as absence of detectable HBV or viral proteins in the bloodstream after standard of care drugs are withdrawn,” said **David Berman, Head of Research and Development at Immunocore**. “These highly

encouraging preclinical data demonstrate the ability of our novel ImmTAV-Env molecule to redirect T cells to target and kill cells infected with HBV, representing a potential therapeutic option for patients with chronic Hepatitis B. We look forward to progressing IMC-I109V into first-in-human clinical trials.”

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About ImmTAV molecules and infectious diseases

Chronic viral infections such as Hepatitis B occur when the virus succeeds in hiding from the immune system or drives the immune system to exhaustion. Immunocore's bi-specific T cell receptor (TCR) technology platform is being investigated to offer a new approach for the treatment of chronic infections by redirecting non-exhausted immune cells to attack infected cells, even if those cells present levels of target that are too low for the natural immune system to see.

ImmTAV (Immune mobilising mTCR Against Virus) molecules are novel small protein bispecific molecules that, like ImmTAC (Immune mobilising monoclonal TCRs Against Cancer) molecules, enable the immune system to recognize and kill diseased cells, in this case, virally infected cells. ImmTAV and ImmTAC molecules resemble each other in appearance and function, although ImmTAV molecules are designed to specifically recognise and kill virally infected cells.

Immunocore aims to achieve sustained loss of circulating viral antigens and markers of viral replication for people living with chronic hepatitis B, after stopping medication. This is known as “functional cure”

About Immunocore

Immunocore is a pioneering, clinical-stage T cell receptor biotechnology company working to develop and commercialise a new generation of transformative medicines to address unmet needs in cancer, infection and autoimmune disease. The Company's most advanced programmes are in oncology and it has a rich pipeline of programmes in infectious and autoimmune diseases. Immunocore's lead programme, tebentafusp (IMCgp100), has entered pivotal clinical studies as a treatment for patients with metastatic uveal melanoma. Collaboration partners include Genentech, GlaxoSmithKline, AstraZeneca, Eli Lilly and Company, and the Bill and Melinda Gates Foundation. Immunocore is headquartered at Milton Park, Oxfordshire, UK, with offices in Conshohocken, Pennsylvania and Rockville, Maryland in the US. For more information, please visit www.immunocore.com.

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