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

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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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