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Immunocore announces initial Phase 1 safety and pharmacodynamic activity data with first soluble TCR therapy for people living with HIV

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Data from the single ascending dose part of the Phase 1 trial shows IMC-M113V is well tolerated

Expected markers of T cell activation observed in half of participants at 15-mcg dose; plasma viral load remained suppressed throughout dosing and follow-up

The multiple ascending dose part of the trial is enrolling participants to identify safety and anti-viral activity

(OXFORDSHIRE, England & CONSHOHOCKEN, Penn. & ROCKVILLE, Md., US, 22 February, 2023) Immunocore Holdings plc (Nasdaq: IMCR), a commercial-stage biotechnology company pioneering the development of a novel class of T cell receptor (TCR) bispecific immunotherapies designed to treat a broad range of diseases, including cancer, autoimmune and infectious diseases, has presented at the Conference on Retroviruses and Opportunistic Infection (CROI) the first safety and activity data with IMC-M113V, a bispecific soluble TCR therapy built on Immunocore's ImmTAX® technology which is being developed for the treatment of people living with HIV (PLWH).

IMC-M113V is an immunotherapeutic approach designed to specifically eliminate CD4+ cells that are persistently infected with HIV ('reservoirs'). IMC-M113V targets a peptide derived from the Gag protein that is presented by HLA*A02 on the surface of HIV infected cells. Reduction in the number of these cells is one way to potentially achieve a state of viral suppression in the absence of anti-retroviral medications, or a 'functional cure.'

"IMC-M113V, which is designed to redirect T cells to eliminate HIV-infected cells, was well tolerated at doses where we observed biomarkers of T cell engagement," said **David Berman, Head of R&D of Immunocore**. "We are now enrolling people living with HIV in the multiple ascending dose part of the trial where we will evaluate the active dosing schedules that could lead to functional cure."

Dr Linos Vandekerckhove, Laboratory director, HIV Cure Research Center, University Hospital Ghent, Belgium, said: "HIV continues to be a huge global health challenge. Although people living with HIV can control their disease with antiretroviral therapies, lifelong treatment is needed as reservoirs of HIV infected cells persist. If a functional cure could be found this could significantly transform treatment of this chronic infectious disease and decrease stigma of HIV."

Initial Phase 1 trial data

In the single ascending dose part of the trial, three dose levels of IMC-M113V, given as a single IV infusion, were evaluated: a starting dose of 1.6 mcg, based on the minimum anticipated biological effect level (n=1), 5 mcg (n=1) and 15 mcg (n=10). All doses were well tolerated. There were no serious adverse events, significant changes in hematology or chemistry, nor cytokine release syndrome or neurotoxicity.

Plasma viral load remained suppressed throughout dosing and follow-up. In addition, transient, dose-dependent increases in serum IL6 occurred 8-24 hours post-infusion. Five out of the ten participants who received the 15-mcg dose showed a >4-fold rise in IL6, which had been prespecified as indicative of pharmacodynamic activity based on prior experience from clinical trials with KIMMTRAK (tebentafusp), the Company's first ImmTAX therapy now approved for the treatment of metastatic or unresectable uveal melanoma.

Enrollment underway in next part of the trial

The Company has started enrolling people living with HIV in the multiple ascending dose (MAD) part of the trial, to identify a safe and tolerable dosing schedule that could lead to reduction in the viral reservoir and control of HIV after stopping antiretroviral therapies (ART), or functional cure. The MAD trial will enroll up to 28 participants.

About the STRIVE (Soluble T cell Receptors In Virus Eradication) trial

The STRIVE trial (IMC-M113V-101) is a first-in-human, open-label Phase 1/2 trial, designed to identify a safe and biologically active dose in HLA-A*02:01 positive PLWH receiving suppressive ART for ≤7 years. The trial's secondary objectives are to characterize pharmacokinetic (PK) and pharmacodynamic (PD) profiles, including serum cytokines (IL2, IL6, IL8, IL10, IFNγ, TNFα, and IP10) pre- and ≤24 hours post-dosing. A ≥4-fold rise in IL6 was prespecified as indicative of PD activity.

People living with HIV can remain healthy with antiretroviral therapies, but they must continue to take medication for life as virus reservoirs remain. IMC-M113V is an immunotherapeutic approach designed to specifically eliminate CD4+ cells that are persistently infected with HIV ('reservoirs'). IMC-M113V targets a peptide derived from the Gag protein that is presented by HLA-A*02 on the surface of HIV infected cells.

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About ImmTAV molecules and infectious diseases
ImmTAV (Immune mobilising monoclonal TCRs Against Virus) molecules are novel bispecific molecules that, like ImmTAC (Immune mobilising monoclonal TCRs Against Cancer) molecules, are designed to enable the immune system to recognize and eliminate virally infected cells.

Immunocore is advancing clinical candidates to cure patients with HIV and hepatitis B virus (HBV). The Company aims to achieve sustained control of HIV after patients stop anti-retroviral therapy (ART), without the risk of virological relapse or onward transmission. This is known as 'functional cure'. For the treatment of HBV, the Company aims to achieve sustained loss of circulating viral antigens and markers of viral replication after stopping medication for people living with chronic HBV.

About ImmTAC® molecules for cancer
Immunocore's proprietary T cell receptor (TCR) technology generates a novel class of bispecific biologics called ImmTAC (Immune mobilizing monoclonal TCRs Against Cancer) molecules that are designed to redirect the immune system to recognize and kill cancerous cells. ImmTAC molecules are soluble TCRs engineered to recognize intracellular cancer antigens with ultra-high affinity and selectively kill these cancer cells via an anti-CD3 immune-activating effector function. Based on the demonstrated mechanism of T cell infiltration into human tumors, the ImmTAC mechanism of action holds the potential to treat hematologic and solid tumors, regardless of mutational burden or immune infiltration, including immune "cold" low mutation rate tumors.

About Immunocore
Immunocore is a commercial-stage biotechnology company pioneering the development of a novel class of TCR bispecific immunotherapies called ImmTAX – Immune mobilizing monoclonal TCRs Against X disease – designed to treat a broad range of diseases, including cancer, autoimmune, and infectious disease. Leveraging its proprietary, flexible, off-the-shelf ImmTAX platform, Immunocore is developing a deep pipeline in multiple therapeutic areas, including five clinical stage programs in oncology and infectious disease, advanced pre-clinical programs in autoimmune disease and multiple earlier pre-clinical programs. The Company's most advanced oncology TCR therapeutic, KIMMTRAK has been approved for the treatment of HLA-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma in the United States, European Union, Canada, Australia, and the United Kingdom.

Forward Looking Statements
This press release contains "forward-looking statements" within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Words such as "may," "can," "will," "believe," "expect," "plan," "anticipate," "target" and similar expressions (as well as other words or expressions referencing future events or circumstances) are intended to identify forward-looking statements. All statements, other than statements of historical facts, included in this press release are forward-looking statements. These statements include, but are not limited to, statements regarding the ability of IMC-M113V to eliminate CD4+ cells and to be an effective treatment for patients with HIV infection; whether a reduction in the number of CD4+ cells will achieve a state of viral suppression in the absence of anti-retroviral medications; the expected clinical benefits of IMC-M113V, including its potential as a "functional cure"; the Company's plan for future development of IMC-M113V; the therapeutic potential and expected clinical benefits of Immunocore's products and product candidates, including IMC-M113V; expectations regarding the development and expansion of Immunocore's pipeline and the design, progress, timing, enrollment, scope, expansion and results of Immunocore's existing and planned clinical trials, including statements regarding the ongoing enrollment of patients in the ongoing trial of IMC-M113V; and Immunocore's ability to obtain and maintain regulatory approval for its products and product candidates; expectations regarding the potential market opportunity and potential commercial performance of Immunocore's product candidates, if approved. Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements, many of which are beyond Immunocore's control. These risks and uncertainties include, but are not limited to, the impact of worsening macroeconomic conditions and the ongoing and evolving COVID-19 pandemic on Immunocore's business, strategy, clinical trials, financial position and anticipated milestones, including Immunocore's ability to conduct ongoing and planned clinical trials; results from earlier clinical or pre-clinical studies of Immunocore's product candidates, including IMC-M113V, may not necessarily be predictive of the results from required later pre-clinical studies and future clinical trials; Immunocore's ability to obtain a clinical supply of current or future product candidates, or commercial supply of KIMMTRAK or any future approved products, including as a result of supply chain disruptions, the COVID-19 pandemic, the war in Ukraine or global geopolitical tension; Immunocore's ability to obtain and maintain regulatory approvals for its product candidates; Immunocore's ability to develop, manufacture and commercialize its product candidates; Immunocore's ability and plans in continuing to establish and expand a commercial infrastructure and to successfully launch, market and sell KIMMTRAK and any future approved products; Immunocore's ability to successfully expand the approved indications for KIMMTRAK or obtain marketing approval for KIMMTRAK in additional geographies in the future; the delay of any current or planned clinical trials, whether due to the COVID-19 pandemic, patient enrollment delays or otherwise; Immunocore's ability to successfully demonstrate the safety and efficacy of its product candidates and gain approval of its product candidates on a timely basis, if at all; competition with respect to market opportunities; unexpected safety or efficacy data observed during pre-clinical studies or clinical trials; actions of regulatory agencies, which may affect the initiation, timing and progress of Immunocore's clinical trials or future regulatory approval; Immunocore's need for and ability to obtain additional funding, on favorable terms or at all, including as a result of worsening macroeconomic conditions such as rising inflation and interest rates, volatility in the capital markets and related market uncertainty, the COVID-19 pandemic, the war in Ukraine and global geopolitical tension; Immunocore's ability to obtain, maintain and enforce intellectual property protection for KIMMTRAK or any product candidates it is developing; unexpected safety or efficacy data observed during preclinical studies or clinical trials; clinical trial site activation or enrollment rates that are lower than expected; and the success of Immunocore's current and future collaborations, partnerships or licensing arrangements. These and other risks and uncertainties are described in greater detail in the section titled "Risk Factors" in Immunocore's filings with the Securities and Exchange Commission, including Immunocore's most recent Annual Report on Form 20-F for the year ended December 31, 2021 filed with the Securities and Exchange Commission on March 3, 2022, as well as discussions of potential risks, uncertainties, and other important factors in the Company's subsequent filings with the Securities and Exchange Commission. All information in this press release is as of the date of the release, and the Company undertakes no duty to update this information, except as required by law.

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