

PRESS RELEASE**New Data Uncover Deeper Insight into Tebentafusp (IMCgp100) Clinical Activity in Patients with Advanced Melanoma, Including Uveal**

(Oxfordshire, UK, Pennsylvania and Maryland, US, 11 November 2019) Immunocore Limited, a leading T cell receptor (TCR) biotechnology company, presented new findings from its Phase 1/2 tebentafusp (IMCgp100) clinical trial programme demonstrating a correlation between treatment-induced immune response and improvement in overall survival and tumour shrinkage, in patients with advanced uveal and cutaneous melanoma. The new analyses from two clinical trials (IMCgp100-101, IMCgp100-102) were presented at the Society for Immunotherapy of Cancer (SITC) Annual Meeting in National Harbor, Maryland.

“We are gaining valuable insights from our clinical data to further our understanding of the mechanism of action of our bispecific, soluble TCR,” **said Bahija Jallal, Chief Executive Officer of Immunocore.** “Advancing the science underlying TCR recognition of antigens supports our efforts to further develop our platform and maximize its value on behalf of patients.”

Tebentafusp is an investigational novel bispecific protein comprised of a soluble T cell receptor fused to an anti-CD3 immune-effector function. It is engineered to specifically target gp100, a lineage antigen expressed in melanocytes and melanoma, and is the first molecule developed using Immunocore’s ImmTAC technology platform designed to redirect and activate T cells to recognise and kill tumour cells. Pivotal tebentafusp clinical trials are currently underway in metastatic uveal melanoma (UM), a rare form of eye cancer.

“When using a therapy designed to induce an immune response, it’s not unexpected to see inflammatory events like rash or cytokine response syndrome,” **said Alexander N. Shoushtari, M.D., study investigator and medical oncologist at Memorial Sloan Kettering Cancer Center in New York.** “While these were general low-grade events that resolved with treatment and time, it was interesting to see their potential connection to overall survival and other clinical outcomes. These findings are encouraging and will help to inform future research and treatment protocols.”

SITC Presentation Highlights:**Induction of serum CXCL10 by tebentafusp, a gp100-CD3 bispecific fusion protein, was associated with survival in uveal melanoma in a Phase 1/2 study**

The goal of this analysis was to increase understanding of the biological effects of tebentafusp and association between rash seen with treatment, CXCL10 and clinical outcomes in UM. Researchers focused on the initial 42 patient cohort enrolled in IMCgp100-102, a Phase 1/2 study in patients with HLA-A2+ positive advanced UM. Patients were treated using a weekly intra-patient dose-escalation regimen and the occurrence of rash within 21 days following treatment initiation was evaluated as a predictor of overall survival.

The findings showed a transient increase in peripheral cytokines after treatment with tebentafusp, reaching maximal changes at 8-24 hours post treatment, with CXCL10 having the greatest increment between 12-24 hours. Patients treated with tebentafusp experienced induced type 1/2 IFN pathways and neutrophil, eosinophil signatures and reduced CD4, CD8 and NK cell signatures in the blood.

Tebentafusp-treated patients with rash and those with a greater increase in serum CXCL10 following the first treatment dose appeared to be associated with improved overall survival. In a multivariate Cox proportional hazards model, both rash ($p < 0.001$) and CXCL10 induction ($p = 0.01$) were independent predictors of survival.

Cytokine release syndrome following treatment with tebentafusp, a novel bispecific TCR-anti-CD3 directed against gp100, in patients with advanced melanoma

The goal of this analysis was to better understand the incidence, severity and resolution of cytokine release syndrome (CRS) following tebentafusp treatment, an adverse event commonly associated with CD3-bispecifics, and its association with clinical outcomes in advanced melanoma. Researchers analysed data from IMCgp100-101, a Phase 1 first-in-human clinical trial assessing the safety and tolerability of tebentafusp in 84 HLA-A2+ patients with metastatic melanoma ($n = 61$ cutaneous, $n = 19$ uveal, $n = 4$ other) resistant to standard treatment regimens or for which no standard treatments exist. This post-hoc analysis evaluated adverse events, serious adverse events, vital signs, and concomitant medications reported by investigators to identify episodes of CRS.

The findings show that patients treated with tebentafusp experienced a low incidence of severe CRS. Despite no corticosteroid pre-treatment, CRS occurrence was generally low grade, reversible with standard management (i.e., IVF and short course corticosteroids), decreased in frequency and severity after the initial doses, and infrequently led to the discontinuation of treatment. The most frequent CRS adverse events were mild-to-moderate fever, fatigue, nausea, hypotension and headache. Patients with a $< 1^\circ\text{C}$ increase in body temperature eight hours following treatment were less likely to develop subsequent moderate or higher-grade CRS. Consistent with tebentafusp's hypothesized mode of action, transient increases in peripheral cytokines occurred within hours of treatment administration, and tended to be greater in patients with higher grade CRS. The incidence of CRS following the first dose of tebentafusp appeared to be associated with the greatest reductions in tumour size.

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About ImmTAC® Molecules

Immunocore's proprietary T cell receptor (TCR) technology generates a novel class of bispecific biologics called ImmTAC (Immune mobilising monoclonal TCRs Against Cancer) molecules that are designed to redirect the immune system to recognise and kill cancerous cells. ImmTAC molecules are soluble TCRs engineered to recognise 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 tumours, the ImmTAC mechanism of action holds the potential to treat hematologic and solid tumours, regardless of mutational burden or immune infiltration, including immune "cold" low mutation rate tumours.

About Tebentafusp

Tebentafusp is a novel bispecific protein comprised of a soluble T cell receptor fused to an anti-CD3 immune-effector function. Tebentafusp specifically targets gp100, a lineage antigen expressed in melanocytes and melanoma, and is the first molecule developed using Immunocore's ImmTAC technology platform designed to redirect and activate T cells to recognise and kill tumour cells. Tebentafusp has Fast Track Designation and Orphan Drug Designation in the US and Promising Innovative Medicine designation under the UK Early Access to Medicines Scheme for metastatic uveal melanoma.

For more information about enrolling tebentafusp clinical trials for metastatic uveal melanoma, please visit ClinicalTrials.gov (NCT03070392).

About Uveal Melanoma

Uveal melanoma is a rare and aggressive form of melanoma, which affects the eye. Metastatic uveal melanoma typically has a poor prognosis and has no currently accepted optimal management or treatment.^{1,2} Although it is the most common primary intraocular malignancy in adults, the diagnosis is rare, with approximately 8,000 new patients diagnosed globally each year (1,600-2,000 cases/year in the US).^{3,4,5} Up to 50% of people with uveal melanoma will eventually develop metastatic disease.^{1,2} When the cancer spreads beyond the eye, only approximately half of patients will survive for one year.⁶

About Immunocore

Immunocore is a leading T cell receptor (TCR) biotechnology company working to create first-in-class biological therapies to address unmet patient needs in oncology as well as infectious and autoimmune diseases. Immunocore has a pipeline of proprietary and partnered programmes in development. Collaboration partners include Genentech, GlaxoSmithKline, AstraZeneca, Lilly, and the Bill and Melinda Gates Foundation. Immunocore is headquartered in Oxfordshire, UK, with offices in Conshohocken, PA and Rockville, MD, US. The Company is privately held by a broad international investor base. For more information, please visit www.immunocore.com.

Dr. Shoushtari serves on Immunocore's scientific advisory board.

For more information, please contact:

Immunocore

Louise Conlon, External Affairs and Brand Communications Manager

T: +44 (0) 1235 438600

E: info@immunocore.com

Follow on Twitter: [@Immunocore](https://twitter.com/Immunocore)

Syneos Health Communications

Stephanie Bukantz

T: +973 477 1814

E: ImmunocorePR@syneoshealth.com

¹ Damato BE, Dukes J, Goodall H, Carvajal RD. Tebentafusp: T cell redirection for the treatment of metastatic uveal melanoma. *Cancers*. 2019;11(7):971.

² Carvajal, RD, Schwartz, GK, Tezel, T, *et al.*, 2017. Metastatic disease from uveal melanoma: treatment options and future prospects. *British Journal of Ophthalmology*, 101(1), 38-44.

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⁵ About ocular melanoma. Ocular Melanoma Foundation website. www.ocularmelanoma.org/about-om.htm. Accessed September 2019.

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