IMMUNOCORE

New Biomarker Research Builds Further Understanding of Tebentafusp (IMCgp100) Mechanism of Action, Link to Clinical Activity in Advanced Melanoma

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- *New analyses from first-in-human clinical trial presented at the 2019 ASCO Annual Meeting*
- *Pivotal trials in metastatic uveal melanoma are ongoing*

(Oxfordshire, UK and Pennsylvania and Maryland, US, 3 June 2019) Monotherapy treatment with the first-in-class ImmTAC® molecule tebentafusp (IMCgp100) induced an immunologically potent response in patients with advanced uveal and cutaneous melanoma, according to new data presented today by Immunocore Limited at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting. The biomarker research provides additional insight into the mechanism of action of tebentafusp in patients with advanced melanoma and demonstrates the potential association with clinical outcomes.

"We are pleased to share new biomarker data from our tebentafusp clinical trial programme, which add to the growing body of evidence supporting the investigational agent's clinical activity and reinforce the potential applicability of our ImmTAC technology," **said Bahija Jallal, Chief Executive Officer of Immunocore**. "We recognise the immediate need for new treatment options for people living with metastatic uveal melanoma and are working to advance tebentafusp as quickly and safely as possible."

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 T cells to recognise and kill tumour cells. Pivotal tebentafusp clinical trials are currently underway in metastatic uveal melanoma, a rare form of eye cancer.

"Biomarker research is critical to informing the development of new immunotherapy agents, particularly in difficult-to-treat cancers like uveal melanoma," **said Mark R Middleton, MD, lead study investigator and Head of the Department of Oncology at the University of Oxford**. "These data build a deeper understanding of how the immune system responds to tebentafusp and provide insights needed to inform future enhancements."

ASCO Presentations

Researchers analysed data from the 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.

Pharmacodynamic Effect of IMCgp100 (TCR–CD3 bispecific) on Peripheral Cytokines and Association with Overall Survival in Patients with Advanced Melanoma

The goal of this analysis was to understand the biological effects of tebentafusp and an association with anti-tumour activity. The findings showed an association between a greater increase in serum CXCL10, a chemokine for T cells expressing CXCR3 receptor, and a greater transient reduction in peripheral CXCR3+CD8+ T cells, tumour shrinkage and longer overall survival (OS). A greater reduction in peripheral CXCR3+ CD8+ T cells also appeared to be associated with tumour shrinkage and longer OS, and changes in tumour biopsies were consistent with T cell infiltration and immune activation.

Relationship Between Clinical Efficacy and AEs of IMCgp100, a Novel Bispecific TCR–anti-CD3, in Patients with Advanced Melanoma

In this analysis, adverse events (AEs) were consistent with tebentafusp's proposed mechanism of action with most AEs relating to on-target (gp100) off-tumour activity (e.g., rash, pruritus), or were cytokine mediated (e.g., pyrexia, hypotension). There appears to be an association between the timing of onset and resolution of these AEs and certain cytokines in the blood. AEs were generally manageable with standard clinical interventions. An association was also observed between OS and LDH ≤ULN and any-grade rash occurring within 21 days.

"Further understanding of the potential association of mechanism of action with safety and activity is important in the success of novel immune therapies," **said Omid Hamid, MD, study investigator and Chief of Translational Research and Immunotherapy at The Angeles Clinic**. "These data support the continued investigation of tebentafusp in cutaneous melanoma in addition to the pivotal trials in metastatic uveal melanoma already underway."

More information about the tebentafusp clinical trials can be found at https://www.clinicaltrials.gov.

Please click on the link below to download the full Press Release: