

## PRESS RELEASE

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

- *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<sup>®</sup> 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  $\leq$ 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>.

- Ends -

**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 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](https://www.clinicaltrials.gov) (NCT03070392).

**About Immunocore**

Immunocore is a leading T cell receptor (TCR) biotechnology company working to create first-in-class biological therapies that have the potential to transform patients' lives. The Company's primary therapeutic focus is oncology and it also has programmes in infectious and autoimmune diseases. Immunocore has a pipeline of proprietary and partnered programmes in development and the lead tebentafusp is being investigated in pivotal clinical studies as a treatment for patients with metastatic uveal melanoma. Collaboration partners include Genentech, GlaxoSmithKline, AstraZeneca, Lilly, and the Bill and Melinda Gates Foundation. Immunocore is headquartered at Milton Park, 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](http://www.immunocore.com).

**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 can potentially enable the immune system to recognise and kill cancerous cells. ImmTAC molecules are based on soluble TCRs engineered to recognise intracellular cancer antigens with ultra-high affinity and selectively kill cancer cells via an anti-CD3 immune-redirecting effector function. Based on the demonstrated

mechanism of T cell infiltration into human tumours, the ImmTAC mechanism of action holds the potential to tackle solid “cold” low mutation rate tumours, the majority of tumours that do not adequately respond to currently available immunotherapies.

## About Uveal Melanoma

Uveal melanoma is an aggressive form of melanoma which affects the eye, with a poor prognosis and no standard of care.<sup>1</sup> 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).<sup>1,2,3,4</sup> Up to 50% of people with uveal melanoma will eventually develop metastatic disease.<sup>1</sup> When the cancer spreads beyond the eye, only approximately 40% of patients will survive for one year.<sup>1</sup>

## For more information, please contact:

### Immunocore

Louise Conlon, External Affairs and Brand Communications Manager

T: +44 (0) 1235 438600

E: [info@immunocore.com](mailto:info@immunocore.com)

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

### Syneos Health Communications (Tebentafusp/IMCgp100)

Stephanie Bukantz

T: +973 477 1814

E: [ImmunocorePR@syneoshealth.com](mailto:ImmunocorePR@syneoshealth.com)

---

<sup>1</sup> 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.

<sup>2</sup> Pandiani C, Béranger GE, Leclerc J, Ballotti R, Bertolotto C. Focus on cutaneous and uveal melanoma specificities. *Genes Dev.* 2017;31(8):724-743.

<sup>3</sup> Jovanovic P, Mihajlovic M, Djordjevic-Jocic J, Vlajkovic S, Cekic S, Stefanovic V. Ocular melanoma: an overview of the current status. *Int J Clin Exp Pathol.* 2013;6(7):1230-1244.

<sup>4</sup> About ocular melanoma. Ocular Melanoma Foundation website. [www.ocularmelanoma.org/about-om.htm](http://www.ocularmelanoma.org/about-om.htm). Accessed May 2019.