IMMUNOCORE

# European Commission Approves KIMMTRAK® (tebentafusp) for the treatment of unresectable or metastatic uveal melanoma

April 4, 2022

***PRESS RELEASE***

**European Commission Approves KIMMTRAK® (tebentafusp) for the treatment of unresectable or metastatic uveal melanoma**

*KIMMTRAK is the first and only treatment approved in the E.U. to treat patients with unresectable or metastatic uveal melanoma*

*KIMMTRAK demonstrated statistically and clinically meaningful overall survival (OS) benefit, hazard ratio of 0.51, with median OS of almost 22 months*

(OXFORDSHIRE, England & CONSHOHOCKEN, Penn. & ROCKVILLE, Md., US, 4 April 2022) Immunocore Holdings plc (Nasdaq: IMCR) ("Immunocore" or the "Company"), 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 today announces that the European Commission (EC) has approved KIMMTRAK® (tebentafusp) for the treatment of HLA-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma (mUM). KIMMTRAK is a novel bispecific protein comprised of a soluble T cell receptor fused to an anti-CD3 immune-effector function.

*"The approval of KIMMTRAK by the European Commission is a historic step as the first ever TCR therapy to be approved in the E.U.," said* **Bahija Jallal, Chief Executive Officer of Immunocore***. "KIMMTRAK, a bispecific T-cell engager, is the first therapy to demonstrate a survival benefit in patients with unresectable or metastatic uveal melanoma. We are excited about what today's approval means for patients and their caregivers and we are working closely with national health authorities to make KIMMTRAK available as quickly as possible."*

The EC approval follows a positive opinion by the Committee for Medicinal Products for Human Use (CHMP) in February 2022. The CHMP recommendation of KIMMTRAK is based on the results of Immunocore's Phase 3 IMCgp100-202 clinical trial, which were published in the September 23, 2021 issue of the *New England Journal of Medicine*.

Data from the trial, the largest Phase 3 trial undertaken in mUM, showed that KIMMTRAK demonstrated unprecedented median OS benefit as a first-line treatment. The OS Hazard Ratio (HR) in the intent-to-treat population favoured KIMMTRAK, HR=0.51 (95% CI: 0.37, 0.71); p< 0.0001, over investigator's choice of treatment (82% pembrolizumab; 13% ipilimumab; 6% dacarbazine). In this study IMCgp100-202, 43% of patients received treatment beyond progression with tebentafusp with no new safety signals identified. Median duration of tebentafusp treatment beyond progression was 8 weeks. Of the total tebentafusp infusions during the study, 21.5% was administered after progression.

*"For years, metastatic uveal melanoma patients have had no treatment choice that is active – today's approval offers them new hope and a chance at longer survival," commented* **Dr. Sophie Piperno-Neumann, Medical Oncologist at the Institute Curie.** *"As a treating physician, it is heart-warming to finally be able to offer a licensed medicine to eligible patients. KIMMTRAK represents a paradigm shift in the treatment of unresectable or metastatic uveal melanoma."*

In the randomised Phase 3 trial of KIMMTRAK (tebentafusp), treatment-related adverse reactions were generally manageable and consistent with the proposed mechanism of action. Among the patients treated with KIMMTRAK, the most common Grade 3 or higher adverse events were rash (18%), pyrexia (4%), and pruritus (5%). In the 245 patients treated with KIMMTRAK, Grade 3 cytokine release syndrome (CRS) occurred in <1% of patients and were generally well-managed. There were no Grade 4 or higher CRS events observed in the Phase 3 clinical trial.

**Dr. Jessica Hassel, Head of Dermatooncology at Heidelberg University Hospital, said** *"The approval of tebentafusp by the EMA is a great step forward in the treatment of metastatic uveal melanoma. Being the first agent with a proven survival benefit, this approval provides hope to patients with uveal melanoma. And for us treating physicians, it is a significant advancement to be able to offer these patients an effective treatment with good tolerability."*

With EC approval, KIMMTRAK has received marketing authorisation in all E.U. member states, and following completion of related national procedures, also in Iceland, Liechtenstein, and Norway. The United Kingdom's Medicines and Healthcare Regulatory Agency (MHRA), Health Canada, and the Australian Government Department of Health Therapeutic Goods Administration (TGA) have each accepted the submission of the Company's Marketing Authorisation Application.

In January 2022, the United States Food and Drug Administration (FDA) approved KIMMTRAK® (tebentafusp-tebn) for the treatment of HLA-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma (mUM).

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**About Uveal Melanoma**

Uveal melanoma is a rare and aggressive form of melanoma, which affects the eye. Although it is the most common primary intraocular malignancy in adults, the diagnosis is rare, and up to 50% of people with uveal melanoma will eventually develop metastatic disease. Unresectable or metastatic uveal melanoma typically has a poor prognosis and had no approved treatment until KIMMTRAK.

**About KIMMTRAK®**

KIMMTRAK is a novel bispecific protein comprised of a soluble T cell receptor fused to an anti-CD3 immune-effector function. KIMMTRAK specifically targets gp100, a lineage antigen expressed in melanocytes and melanoma. This is the first molecule developed using Immunocore's ImmTAC technology platform designed to redirect and activate T cells to recognise and kill tumour cells. KIMMTRAK has been granted Breakthrough Therapy Designation, Fast Track designation and orphan drug designation by the FDA in the United States, Accelerated Assessment by the EMA, and Promising Innovative Medicine (PIM) designation under the UK Early Access to Medicines Scheme for metastatic uveal melanoma.

**About Phase 3 IMCgp100-202 Trial**

The IMCgp100-202 (NCT03070392) is a randomized pivotal trial that evaluated overall survival (OS) of KIMMTRAK (tebentafusp-tebn) compared to

investigator's choice (either pembrolizumab, ipilimumab, or dacarbazine) in HLA-A*02:01-positive adult patients with previously untreated mUM. KIMMTRAK demonstrated an unprecedented OS benefit with a Hazard Ratio (HR) in the intent-to-treat population favoring KIMMTRAK, HR=0.51 (95% CI: 0.37, 0.71); p< 0.0001, over investigator's choice (82% pembrolizumab; 13% ipilimumab; 6% dacarbazine).

**IMPORTANT U.S. SAFETY INFORMATION Regarding FDA Approval**

**Cytokine Release Syndrome (CRS), which may be serious or life-threatening, occurred in patients receiving KIMMTRAK. Monitor for at least 16 hours following first three infusions and then as clinically indicated.** Manifestations of CRS may include fever, hypotension, hypoxia, chills, nausea, vomiting, rash, elevated transaminases, fatigue, and headache. CRS occurred in 89% of patients who received KIMMTRAK with 0.8% being grade 3 or 4. Ensure immediate access to medications and resuscitative equipment to manage CRS. Ensure patients are euvolemic prior to initiating the infusions. Closely monitor patients for signs or symptoms of CRS following infusions of KIMMTRAK. Monitor fluid status, vital signs, and oxygenation level and provide appropriate therapy. Withhold or discontinue KIMMTRAK depending on persistence and severity of CRS.

**Skin Reactions**

Skin reactions, including rash, pruritus, and cutaneous edema occurred in 91% of patients treated with KIMMTRAK. Monitor patients for skin reactions. If skin reactions occur, treat with antihistamine and topical or systemic steroids based on persistence and severity of symptoms. Withhold or permanently discontinue KIMMTRAK depending on the severity of skin reactions.

**Elevated Liver Enzymes**

Elevations in liver enzymes occurred in 65% of patients treated with KIMMTRAK. Monitor alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total blood bilirubin prior to the start of and during treatment with KIMMTRAK. Withhold KIMMTRAK according to severity.

**Embryo-Fetal Toxicity**

KIMMTRAK may cause fetal harm. Advise pregnant patients of potential risk to the fetus and patients of reproductive potential to use effective contraception during treatment with KIMMTRAK and 1 week after the last dose.

The most common adverse reactions (≥30%) in patients who received KIMMTRAK were cytokine release syndrome, rash, pyrexia, pruritus, fatigue, nausea, chills, abdominal pain, edema, hypotension, dry skin, headache, and vomiting. The most common (≥50%) laboratory abnormalities were decreased lymphocyte count, increased creatinine, increased glucose, increased AST, increased ALT, decreased hemoglobin, and decreased phosphate.

Please see full Prescribing Information, including BOXED WARNING for CRS.

**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 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. Immunocore's most advanced oncology TCR therapeutic, KIMMTRAK (tebentafusp-tebn), has been approved by the U.S. FDA for the treatment of HLA-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma (mUM) having demonstrated an overall survival benefit in a randomized Phase 3 clinical trial in metastatic uveal melanoma, a cancer that has historically proven to be insensitive to other immunotherapies.

**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. 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 therapeutic potential of KIMMTRAK to be an effective treatment for patients with metastatic uveal melanoma (mUM); Immunocore's sales and marketing plans in the E.U. member states, and following completion of related national procedures, in Iceland, Liechtenstein, and Norway; the expected clinical benefits of KIMMTRAK including extended overall survival benefit; expectations regarding the ability to reach patients in a timely manner including receiving future regulatory approval in the United Kingdom, Australia and Canada; physician's feedback and physician interest in prescribing KIMMTRAK; and the benefits of the Company's global early access program as well as feedback from the participating physicians. 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 the Company's control. These risks and uncertainties include, but are not limited to, the impact of the ongoing COVID-19 pandemic and the Omicron variant on the Company's business, strategy clinical trials and financial position; Immunocore's ability to maintain regulatory approval of KIMMTRAK; its ability to execute its commercialization strategy for KIMMTRAK; its ability to develop, manufacture and commercialize its other product candidates including plans for future development of tebentafusp and other product candidates, including the timing or likelihood of expansion into additional markets or geographies; commercial supply of KIMMTRAK or any future approved products, and launching, marketing and selling of KIMMTRAK or any future approved products; Immunocore's ability and plans in continuing to establish and expand a commercial infrastructure and to successfully launch, market and sell KIMMTRAK in the United States, European Union and other territories; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials or future regulatory approval; 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; changes in expected or existing competition; Immunocore's ability to obtain, maintain and enforce intellectual property protection for KIMMTRAK or any product candidates it

is developing; 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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