

PRESS RELEASE

Immatics Announces First Cancer Patient Treated with Second-Generation ACTengine® TCR-T Candidate IMA203CD8 Targeting PRAME

- IMA203CD8 is a 2nd-generation product candidate co-expressing Immatics' proprietary CD8 $\alpha\beta$ co-receptor engaging functional CD4 and CD8 T cells directed against PRAME
- Preclinical data with IMA203CD8 showed enhanced potency and prolonged anti-tumor activity mediated by activated TCR-engineered CD4 T cells
- The IMA203CD8 Phase 1b expansion study is the third cohort of Immatics' multi-cohort strategy to achieve durable high response rates with TCR-T cells targeting PRAME-positive, hard-to-treat solid tumors
- First three patients to be treated at dose level 3 with the intention to advance directly to the recommended Phase 2 dose

Houston, Texas and Tuebingen, Germany, August 23, 2022 – [Immatics N.V.](#) (NASDAQ: IMTX, “Immatics”), a clinical-stage biopharmaceutical company active in the discovery and development of T cell-redirecting cancer immunotherapies, today announced the treatment of the first patient in its Phase 1b expansion cohort C (NCT03686124) evaluating IMA203CD8, the company’s 2nd generation TCR-T monotherapy approach where a proprietary CD8 $\alpha\beta$ co-receptor is added to PRAME-specific IMA203 T cells. The CD8 co-receptor plays an important role during T cell antigen recognition and T cell activation, enabling the effective engagement of CD8 and CD4 T cells in the anti-tumor response. The 2nd generation TCR-T IMA203CD8 aims to further enhance depth and durability of anti-tumor responses and clinical outcomes of TCR-T targeting PRAME in patients with solid cancers. PRAME is highly prevalent across several indications thereby supporting the program’s potential to reach a broad patient population.

“IMA203CD8’s unique mode of action has been validated by preclinical data presented at SITC last year, which demonstrated sustained suppression of tumor growth in serial killing experiments. With the initiation of the IMA203CD8 cohort, we can now test to what extent the interplay of engineered CD8 and CD4 T cells enhances anti-tumor activity in the clinical setting,” said Dr. Cedrik Britten, M.D., Chief Medical Officer at Immatics. “Today’s milestone brings us closer to our goal of achieving long-lasting responses for a broad range of cancer patients having solid tumors that express PRAME.”

The importance of CD4 T cells for the duration of responses has been demonstrated by Immatics in [preclinical assays](#) where IMA203CD8 showed enhanced potency and prolonged anti-tumor activity compared to IMA203 alone. These findings are in line with a growing body of literature from CD19 CAR-T cells in hematological cancers that suggest a relevant role of engineered CD4 T cells in maintaining durable anti-tumor responses over a long period. Immatics' proprietary lentiviral vector enables CD4 and CD8 T cells to be engineered with the PRAME-specific IMA203 TCR and a CD8 $\alpha\beta$ construct. In the preclinical studies, this approach showed functional superiority over multiple other CD8 constructs in conjunction with the PRAME-specific IMA203 TCR. Immatics has successfully developed a proprietary 4-in-1 vector that includes both IMA203 TCR α and TCR β as well as CD8 α and CD8 β chains while maintaining a high transduction rate, circumventing the challenges associated with increasing the lentiviral vector payload.

The IMA203CD8 Phase 1b dose expansion cohort is expected to enroll up to 24 patients with different types of solid tumors across several clinical trial sites in the U.S. and in Germany. Following personalized manufacturing and lymphodepletion, patients will receive a single dose of IMA203CD8. Initially, 3 patients will be treated at a dose level 3 (DL3, up to 0.48 billion total transduced T cells per m² body surface area) before patient treatment at the provisional recommended Phase 2 dose, DL4 (up to 1.2 billion total transduced cells per m² body surface area). The primary objective of this Phase 1b cohort is to evaluate the safety profile of IMA203CD8. Secondary objectives include evaluating initial anti-tumor and biological activity.

The 2nd generation TCR-T IMA203CD8 is part of Immatics' strategy to realize the full clinical potential of IMA203 TCR-T targeting PRAME. This strategy includes three Phase 1b expansion cohorts, which have all been initiated during the first half of 2022 and build on the promising early clinical results during the company's Phase 1a trial. Interim data showed a 50% objective response rate (8/16 patients) across several solid tumor indications including melanoma, head and neck cancer, uveal melanoma and synovial sarcoma.

- Cohort A – IMA203 as monotherapy at the provisional, recommended Phase 2 dose (RP2D) plus exploration of a higher dose level DL5 (up to 4.7 billion transduced CD8 T cells per m² body surface area)
- Cohort B – IMA203 in combination with an immune checkpoint inhibitor, Opdivo® (nivolumab)
- Cohort C – IMA203CD8, a 2nd generation monotherapy in which IMA203 is co-transduced with a CD8 co-receptor

Each Phase 1b expansion cohort is designed to evaluate the observed objective response rate, demonstrate durability of response and provide the basis for entering registration trials. The next



data readout for the IMA203 monotherapy cohort at RP2D is expected during 2H 2022 and an initial data readout for Cohort B and Cohort C is planned for YE2022.

About IMA203CD8 and target PRAME

ACTEngine® IMA203CD8 T cells are directed against an HLA-A*02-presented peptide derived from preferentially expressed antigen in melanoma (PRAME), a protein frequently expressed in a large variety of solid cancers thereby supporting the programs' potential to address a broad cancer patient population. Immatics' PRAME peptide is present at a high copy number per tumor cell and is homogenously and specifically expressed in tumor tissue. The peptide has been identified and characterized by Immatics' proprietary mass spectrometry-based target discovery platform XPRESIDENT®. Through its proprietary TCR discovery and engineering platform XCEPTOR®, Immatics has generated a highly specific T cell receptor (TCR) against this target which is engineered into CD8 and CD4 T cells alongside a proprietary CD8αβ co-receptor for its 2nd generation TCR-based cell therapy approach, ACTEngine® IMA203CD8. In preclinical studies, Immatics' proprietary CD8αβ construct showed functional superiority over multiple other CD8 constructs in conjunction with the PRAME-specific IMA203 TCR.

About ACTEngine®

ACTEngine® is a personalized cell therapy approach for patients with advanced solid tumors. The patient's own T cells are genetically engineered to express a novel, proprietary TCR directed against a defined cancer target. The modified T cells are then reinfused into the patient to attack the tumor. The approach is also known as TCR-engineered cell therapy (TCR-T). All Immatics' ACTEngine® product candidates can be rapidly manufactured utilizing a proprietary manufacturing process designed to enhance T cell engraftment and persistence *in vivo*.

The ACTEngine® T cell products are manufactured at the Evelyn H. Griffin Stem Cell Therapeutics Research Laboratory in collaboration with UTHealth.

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About Immatics

Immatics combines the discovery of true targets for cancer immunotherapies with the development of the right T cell receptors with the goal of enabling a robust and specific T cell response against these targets. This deep know-how is the foundation for our pipeline of Adoptive Cell Therapies and TCR Bispecifics as well as our partnerships with global leaders in the pharmaceutical industry. We are committed to delivering the power of T cells and to unlocking new avenues for patients in their fight against cancer.

For regular updates about Immatics, visit www.immatics.com. You can also follow us on [Instagram](#), [Twitter](#) and [LinkedIn](#).

Forward-Looking Statements:

Certain statements in this press release may be considered forward-looking statements. Forward-looking statements generally relate to future events or Immatics' future financial or operating performance. For example, statements concerning the timing of product candidates and Immatics' focus on partnerships to advance its strategy are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "may", "should", "expect", "intend", "will", "estimate", "anticipate", "believe", "predict", "potential" or "continue", or the negatives of these terms or variations of them or similar terminology. Such forward-looking statements are subject to risks, uncertainties, and other factors which could cause actual results to differ materially from those expressed or implied by such forward looking statements. These forward-looking statements are based upon estimates and assumptions that, while considered reasonable by Immatics and its management, are inherently uncertain. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Factors that may cause actual results to differ materially from current expectations include, but are not limited to, various factors beyond management's control including general economic conditions and other risks, uncertainties and factors set forth in filings with the SEC. Nothing in this presentation should be regarded as a representation by any person that the forward-looking statements set forth herein will be achieved or that any of the contemplated results of such forward-looking statements will be achieved. You should not place undue reliance on forward-looking statements, which speak only as of the date they are made. Immatics undertakes no duty to update these forward-looking statements. All the scientific and clinical data presented within this press release are – by definition prior to completion of the clinical trial and a clinical study report – preliminary in nature and subject to further quality checks including customary source data verification.

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