

PRESS RELEASE

Immatics Announces Updated Phase 1b Clinical Data on ACTengine® IMA203 TCR-T Targeting PRAME in Melanoma Patients and Provides Update on Upcoming SUPRAME Phase 3 Trial

Company to host [conference call and webcast](#) today, October 10, at 9:00 am EDT/3:00 pm CEST

- Company announces updated Phase 1b clinical data on ACTengine® IMA203 targeting PRAME in 28 heavily pretreated metastatic melanoma patients with substantially enhanced maturity compared to the last data update in May 2024 and provides the first report on progression-free survival (PFS) and overall survival (OS)
- Based on the Phase 1b data, the Company will proceed directly to a registration-enabling Phase 3 trial
- Regulatory pathway and clinical trial design for IMA203 finalized following FDA Type D meetings and meeting with the Paul Ehrlich Institute (PEI); RP2D and CMC package confirmed
- IMA203 continues to maintain a favorable tolerability profile in patients in Phase 1a and Phase 1b treated across all dose levels
- IMA203 demonstrates a confirmed objective response rate of 54% with median duration of response of 12.1 months in Phase 1b
- Median PFS is 6 months, comparing favorably to the IMA203 Phase 1a dose escalation median PFS of 2.6 months; patients with deep responses show median PFS of more than one year; median OS not reached
- Phase 3 trial, “SUPRAME,” will enroll 360 patients with unresectable or metastatic melanoma post treatment with a checkpoint inhibitor (2L+) and will randomize patients 1:1 for treatment with IMA203 or investigator’s choice
- Primary endpoint for full approval will be median PFS, which constitutes the fastest pathway to registration in this patient population

- SUPRAME Phase 3 trial is on track to commence in December 2024; enrollment forecasted to be completed in 2026 with a pre-specified interim analysis planned for early 2026
- Conference call and webcast can be accessed [here](#)

Houston, Texas and Tuebingen, Germany, October 10, 2024 – [Immatics N.V.](#) (NASDAQ: IMTX, “Immatics” or the “Company”), a clinical-stage biopharmaceutical company active in the discovery and development of T cell-redirecting cancer immunotherapies, today announced updated Phase 1b clinical data on ACTengine® IMA203 TCR-T targeting PRAME in melanoma patients and provided an update on SUPRAME, the upcoming Phase 3 trial to evaluate IMA203 in metastatic melanoma patients.

The data from the ongoing Phase 1b trial will be presented on Friday, October 11, 2024, by Martin Wermke, M.D., during Plenary Session 1, Developmental Immunotherapy (Cellular Immunotherapy, Vaccines, & New Checkpoints) at the Society for Melanoma Research Congress 2024. The IMA203 data slides are accessible in the [‘Events & Presentations’](#) section of the Investor & Media section of the Company’s website. The conference presentation will include additional patient cases.

“Observing significant tumor shrinkage and durable responses combined with meaningful progression-free survival and overall survival outcomes after a single treatment with ACTengine® IMA203 in this patient population that have all exhausted multiple lines of systemic treatments illustrates the impact IMA203 can have on metastatic melanoma patients,” said Martin Wermke, M.D., Coordinating Investigator of the ACTengine® IMA203 TCR-T trial. “These results now affirm the therapeutic potential of IMA203 and provide a strong rationale for the expedited late-stage clinical development of this product candidate.”

“We are enthusiastic about the clinical data as they confirm our conviction in the durability and long-term efficacy of ACTengine® IMA203, demonstrated by the favorable median progression-free survival for patients in the dose expansion cohort. I would like to highlight that a subgroup of 12 out of 26 patients showed more than 50% reduction of tumor lesions and a median PFS of 13.4 months,” said Cedrik Britten, M.D., Chief Medical Officer at Immatics. “We believe the presentation of this data set in conjunction with our recent meeting with the FDA, which has resulted in a pivotal trial design with progression-free survival as the primary endpoint for full approval, positions us to advance the development of IMA203 in the second-line or later metastatic melanoma setting.”

Patient Population and Clinical Data Summary - ACTengine® IMA203 Monotherapy Phase 1b Trial

Patient population: *Heavily pretreated metastatic melanoma patients*

As of August 23, 2024, 28 heavily pretreated patients with metastatic melanoma were treated at the recommended Phase 2 dose (RP2D, 1 to 10 billion total TCR-T cells) with IMA203 during the Phase 1b dose expansion part of the clinical trial. The treated patient population is composed of patients with a median of 2 lines of prior systemic treatments, consisting of cutaneous melanoma patients (N=13), uveal melanoma patients (N=12), mucosal melanoma patients (N=2) and a patient with melanoma of unknown primary (N=1).

Safety: *Favorable tolerability profile demonstrated across all dose levels in Phase 1a and Phase 1b* IMA203 monotherapy has maintained a favorable tolerability profile with no treatment-related Grade 5 adverse events in the safety population (N=70¹ Phase 1a and Phase 1b patients across all dose levels and all tumor types), even at doses up to $\sim 10 \times 10^9$ TCR-T cells.

The most frequent adverse events were expected cytopenias (Grade 1 – 4) associated with lymphodepletion as well as mostly mild to moderate cytokine release syndrome (CRS). Some patients infrequently experienced ICANS (Grade 1: 6%, Grade 2: 4%, Grade 3: 4%).

The full IMA203 monotherapy tolerability profile is also generally consistent with that observed in the Phase 1b melanoma subset.

Anti-tumor activity and durability: *Durable objective responses in melanoma patients at RP2D³*

This data update adds substantial maturity to the most recent data update from May 2024 (data cut-off on April 25, 2024). The median follow-up for the median duration of response for this analysis was 9.3 months compared to 3.5 months in May 2024.

¹ All patients who started lymphodepletion. Includes one patient who started lymphodepletion but did not receive IMA203 TCR-T cells and one patient who started lymphodepletion with T cell infusion scheduled after data-cut.

	All melanoma patients in Phase 1b (N=28^{2,3})	Cutaneous melanoma patients in Phase 1b (N=13³)
Confirmed Objective Response Rate	54% (14/26)	54% (7/13)
Objective Response Rate	62% (16/26)	62% (8/13)
Disease Control Rate	92% (24/26)	92% (12/13)
Tumor Shrinkage	88% (23/26)	85% (11/13)
Median Duration of Response	12.1 months	12.1 months
Median Progression-Free Survival	6.0 months	6.1 months
Median Overall Survival	Not reached	15.9 months

Progression-free survival (PFS) and overall survival (OS): Significant shift in PFS and OS between Phase 1a dose escalation to Phase 1b dose expansion in melanoma patients

Manufacturing improvements were implemented prior to the Phase 1b part of the trial to enhance key features of IMA203. As a result, all patients in dose expansion were treated with an updated version of IMA203 that includes a T cell enrichment process using monocyte depletion (negative selection) or CD8/CD4 positive selection.

The data presented today demonstrate a significant positive shift in median PFS and median OS between melanoma patients treated during Phase 1a and patients treated in Phase 1b.

	Phase 1b dose expansion melanoma patients (N=28)	Phase 1a dose escalation melanoma patients (N=11)
Median Progression-Free Survival	6.0 months	2.6 months
Median Overall Survival	Not reached	6.3 months

² First tumor assessment post infusion pending for additional two melanoma patients at data-cut.

³ Melanoma efficacy population excludes 5 patients treated at DL4 in Phase 1a of the trial as reported in the May 2024 update, based on different manufacturing version used that affects the T cell product. See the IMA203 data presentation slides available on the Immatics website for more detailed information and a patient population flow chart.

In addition, approximately half of all patients in the Phase 1b trial have a deep response (>50% tumor reduction). This subgroup of patients was observed to have a median PFS of more than one year, while patients with <50% tumor reduction (including patients with tumor size increase) were still observed with a more than 2 times longer median PFS compared to patients treated in dose escalation with suboptimal doses.

Translational data: *IMA203 T cell dose and T cell exposure are associated with clinical responses*

Translational data from patients across Phase 1a and Phase 1b indicate that IMA203 T cells rapidly engrafted in all patients after a single dose and show a persistence of more than two years. Three associations/correlations were observed demonstrating high consistency of dose exposure, biological data and clinical outcome in all patients treated with IMA203 for which samples were available (N=65):

1. IMA203 T cell dose is significantly associated with confirmed clinical responses ($p=0.02$),
2. IMA203 T cell dose is correlated with T cell peak level (c_{max} , $r=0.84$, $p=1.6 \times 10^{-18}$),
3. IMA203 T cell peak level (c_{max} , $p=0.05$) and T cell exposure (AUC_{0-28d} , $p=0.05$) are associated with confirmed clinical responses.

Development Path and Manufacturing for ACTengine® IMA203 Monotherapy

On September 24, 2024, Immatics completed a Type D meeting with the U.S. Food and Drug Administration (FDA) to confirm RP2D and the CMC package as well as discuss the trial design for SUPRAME, the planned registration-enabling Phase 3 randomized-controlled clinical trial for IMA203. Written post-meeting minutes from the FDA have been received.

The Phase 3 trial will evaluate IMA203 targeting PRAME in 360 HLA-A*02:01-positive patients with second-line or later (2L+) unresectable or metastatic melanoma who have received prior treatment with a checkpoint inhibitor. Patients will be randomized 1:1 for IMA203 or investigator's choice of selected approved treatments in the 2L+ setting.

Based on the Company's discussions with the FDA, the primary endpoint for full approval will be median PFS. Given the expected PFS of 2-3 months⁴ in this patient population, as well as the PFS of 6 months observed in the data from the IMA203 Phase 1b trial, the Company has determined that utilizing median PFS as the primary endpoint is the fastest pathway to seeking full approval and presents a more attractive commercial positioning as compared to objective response rate (ORR). Secondary endpoints for the trial will include ORR, safety, duration of response, no overall

⁴ See the IMA203 data presentation slides available on the Immatics website for more detailed information and an overview of studies.

survival detriment and patient-reported outcomes. A pre-specified interim analysis is planned for early 2026.

The SUPRAME Phase 3 trial is planned to run globally with sites in the United States and Europe with the initial goal of seeking Biologics License Application (BLA) approval in the United States. On October 2, 2024, Immatics also completed a meeting with the Paul Ehrlich Institute (PEI), the German regulatory authority, and determined the same trial design for conducting the clinical trial in Germany.

The Phase 3 trial is on track to commence in December 2024 and patient enrollment is forecasted to be completed in 2026. The Company aims to submit a BLA in early 2027 for full approval.

Immatics' late-stage clinical cell therapy development is supported by its differentiated manufacturing related to timeline, capabilities and facilities. ACTEngine® IMA203 cell therapy products are manufactured within 7 days, followed by a 7-day QC release testing at a success rate of >95% to reach the target dose. The Company has also completed construction of a ~100,000 square foot R&D and GMP manufacturing facility with a modular design for efficient and cost-effective scalability intended to serve early-stage and registration-enabling trials, as well as commercial supply. The new site is expected to start GMP manufacturing of cell therapy products in early 2025. Meanwhile, the existing GMP facility, which is run in collaboration with UT Health, will remain active until YE 2025.

Immatics Conference Call and Webcast

Immatics will host a [conference call and webcast](#) today, October 10, 2024, at 9:00 am EDT/ 3:00 pm CEST to discuss the clinical data.

A replay of the webcast will be made available shortly after the conclusion of the call and archived on the Immatics website for at least 90 days.

About ACTEngine® IMA203 and Target PRAME

ACTEngine® IMA203 is Immatics' most advanced TCR-based autologous cell therapy that is directed against an HLA-A*02-presented (human leukocyte antigen) peptide derived from preferentially expressed antigen in melanoma (PRAME), a protein frequently expressed in a large variety of solid cancers. PRAME is homogeneously and specifically expressed in tumor tissue and Immatics' PRAME peptide is present at a high copy number per tumor cell. 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 for ACTEngine® IMA203.

ACTengine® IMA203 TCR-T is currently being evaluated as a monotherapy in a Phase 1 clinical trial in patients with solid tumors expressing PRAME, such as cutaneous melanoma. An IMA203 registration-enabling randomized controlled Phase 3 trial, “SUPRAME,” is planned to commence in December 2024.

ACTengine® IMA203 TCR-T is also currently being evaluated in Phase 1 IMA203CD8 (GEN2) monotherapy, where IMA203 engineered T cells are co-transduced with a CD8αβ co-receptor.

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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.

Immatics intends to use its website www.immatics.com as a means of disclosing material non-public information. For regular updates you can also follow us on [X](#), [Instagram](#) 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 the Company’s future financial or operating performance. For example, statements concerning timing of data read-outs for product candidates, the timing, outcome and design of clinical trials, the nature of clinical trials (including whether such clinical trials will be registration-enabling), the timing of IND or CTA filing for pre-clinical stage product candidates, the timing of BLA filings for clinical stage product candidates, estimated market opportunities of product candidates, manufacturing timetables, capacity and success rates, the Company’s focus on partnerships to advance its strategy, and other metrics are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “may”, “should”, “expect”, “plan”, “target”, “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 the Company's Annual Report on Form 20-F and other filings with the Securities and Exchange Commission (SEC). Nothing in this press release 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. The Company 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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