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UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

**FORM 6-K**

REPORT OF FOREIGN PRIVATE ISSUER PURSUANT TO RULE 13a-16 OR 15d-16 UNDER THE SECURITIES EXCHANGE ACT OF 1934

November 8, 2023

Commission File Number: 001-39363

**IMMATICS N.V.**

Paul-Ehrlich-Straße 15  
72076 Tübingen, Federal Republic of Germany  
(Address of principal executive office)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F:

Form 20-F



Form 40-F



**INFORMATION CONTAINED IN THIS REPORT ON FORM 6-K**

On November 8, 2023, Immatics N.V. (the “Company” or “Immatics”) provided interim data from its ongoing Phase 1 trial with ACTengine® IMA203 GEN1, with a focus on IMA203 GEN1 in melanoma at the recently defined recommended Phase 2 dose (“RP2D”), and IMA203CD8 GEN2 TCR-T both as monotherapy in patients with recurrent and/or refractory solid cancers. The data cutoff was September 30, 2023.

**IMA203 GEN1 in Melanoma Patients Treated as RP2D**

- 16 PRAME-positive patients with cutaneous, uveal or melanoma of unknown primary origin were infused with IMA203 GEN1 at the RP2D (1-10x10<sup>9</sup> total TCR-T cells) across Phase 1a or Phase 1b Cohort A.
- **Safety Data:**
  - o All 16 patients experienced expected cytopenia (Grade 1-4) associated with lymphodepletion as expected. Patients had mostly mild-moderate cytokine release syndrome (“CRS”), of which 10 patients (63%) had Grade 1 CRS, and 5 patients (31%) had Grade 2 CRS, and 1 patient (6%) had Grade 3 CRS.
  - o One non-serious, mild (Grade 1) immune effector cell associated neurotoxicity syndrome (“ICANS”) was observed.
  - o No dose-dependent increase of CRS, no dose-limiting toxicity, and no IMA203-related death was observed.
  - o The most common Grade ≥3 treatment-emergent adverse events (“TEAEs”) observed across all dose levels (N=49) and at the RP2D (N=28) for all patients are set forth in the tables below:

TEAEs by maximum severity for all patients in Phase 1a dose escalation and Cohort A dose expansion (N=49) <sup>1</sup>					
Adverse event (System organ class, Preferred term)	≥ Grade 3		Adverse event (System organ class, Preferred term)	≥ Grade 3	
	No.	%		No.	%
<b>Patients with any adverse event</b>	<b>49</b>	<b>100.0</b>	<b>table continued...</b>		
<b>Adverse Events of Special Interest</b>	<b>2</b>	<b>4.1</b>	<b>General disorders and administration site conditions</b>	<b>4</b>	<b>8.2</b>
Cytokine release syndrome	2	4.1	Condition aggravated <sup>4</sup>	1	2.0
ICANS <sup>2</sup>	0	0.0	Fatigue	1	2.0
<b>Blood and lymphatic system disorders</b>	<b>48</b>	<b>98.0</b>	Pyrexia	1	2.0
Neutropenia	36	73.5	Swelling face	1	2.0
Lymphopenia	27	55.1	<b>Metabolism and nutrition disorders</b>	<b>4</b>	<b>8.2</b>
Leukopenia	26	53.1	Hypokalaemia	3	6.1
Anaemia	24	49.0	Failure to thrive	1	2.0
Thrombocytopenia	17	34.7	Hypophosphataemia	1	2.0
Cytopenia	1	2.0	<b>Gastrointestinal disorders</b>	<b>2</b>	<b>4.1</b>
Leukocytosis	1	2.0	Abdominal pain	1	2.0
Lymphocytosis	1	2.0	Diarrhoea	1	2.0
<b>Investigations</b>	<b>9</b>	<b>18.4</b>	Vomiting	1	2.0
Neutrophil count decreased	4	8.2	<b>Injury, poisoning and procedural complications</b>	<b>2</b>	<b>4.1</b>
Alanine aminotransferase increased	2	4.1	Humerus fracture	1	2.0
Aspartate aminotransferase increased	2	4.1	Infusion related reaction	1	2.0
White blood cell count decreased	2	4.1	<b>Renal and urinary disorders</b>	<b>2</b>	<b>4.1</b>
Blood alkaline phosphatase increased	1	2.0	Acute kidney injury	1	2.0
Blood creatinine increased	1	2.0	Proteinuria	1	2.0
Blood fibrinogen decreased	1	2.0	<b>Skin and subcutaneous tissue disorders</b>	<b>2</b>	<b>4.1</b>
<b>Infections and infestations</b>	<b>7</b>	<b>14.3</b>	Rash maculo-papular	2	4.1
Appendicitis	1	2.0	<b>Cardiac disorders</b>	<b>1</b>	<b>2.0</b>
COVID-19	1	2.0	Atrial fibrillation <sup>3</sup>	1	2.0
Enterococcal infection	1	2.0	<b>Endocrine disorders</b>	<b>1</b>	<b>2.0</b>
Infection	1	2.0	Inappropriate antidiuretic hormone secretion	1	2.0
Orchitis	1	2.0	<b>Eye disorders</b>	<b>1</b>	<b>2.0</b>
Sepsis <sup>5</sup>	1	2.0	Ulcerative keratitis	1	2.0
Septic shock <sup>4</sup>	1	2.0	<b>Hepatobiliary disorders</b>	<b>1</b>	<b>2.0</b>
Urinary tract infection	1	2.0	Cholangitis	1	2.0
<b>Respiratory, thoracic and mediastinal disorders</b>	<b>6</b>	<b>12.2</b>	<b>Immune system disorders</b>	<b>1</b>	<b>2.0</b>
Hypoxia	3	6.1	Contrast media allergy	1	2.0
Bronchial obstruction	1	2.0	<b>Musculoskeletal and connective tissue disorders</b>	<b>1</b>	<b>2.0</b>
Laryngeal inflammation	1	2.0	Muscle spasms	1	2.0
Pleural effusion	1	2.0	<b>Nervous system disorders</b>	<b>1</b>	<b>2.0</b>
Respiratory failure	1	2.0	Headache	1	2.0
<b>Vascular disorders</b>	<b>6</b>	<b>12.2</b>	<b>Reproductive system and breast disorders</b>	<b>1</b>	<b>2.0</b>
Hypertension	4	8.2	Vaginal haemorrhage	1	2.0
Hypotension	2	4.1			

All treatment-emergent adverse events (TEAEs) with ≥ Grade 3 regardless of relatedness to study treatment that occurred in at least 1 patient (except for ICANS, where only Grade 1-2 occurred; listed for completeness due to being an adverse event of special interest) are presented. Adverse events were coded using the Medical Dictionary for Regulatory Activities. Grades were determined according to National Cancer Institute Common Terminology Criteria of Adverse Events, version 5.0. Grades for CRS and ICANS were determined according to CARTOX criteria (Neelapu et al., 2018). Patients are counted only once per adverse event and severity classification. Based on interim data extracted from open clinical database (30-Sep-2023); <sup>1</sup> Two patients with disease progression after first IMA203 infusion received exploratory second IMA203 infusion. They had these ≥ Grade 3 TEAEs only after second infusion, which are included in the table: First patient: Abdominal pain, Cytokine release syndrome, Diarrhoea, Hypokalaemia, Proteinuria; Second patient: Humerus fracture, Muscle spasms, Neutropenia, Thrombocytopenia; <sup>2</sup> ICANS: Immune effector cell-associated neurotoxicity syndrome; <sup>3</sup> DLT: Dose limiting toxicity in phase 1a at DL2 reported on March 17, 2021; <sup>4</sup> Fatal Adverse events were not considered related to any study drug; <sup>5</sup> Patient died from sepsis of unknown origin and did not receive IMA203 TCR-T cells.

TEAEs by maximum severity for all patients in Ph1a dose escalation DL4 and Ph1b Cohort A dose expansion (RP2D, N=28)<sup>1</sup>

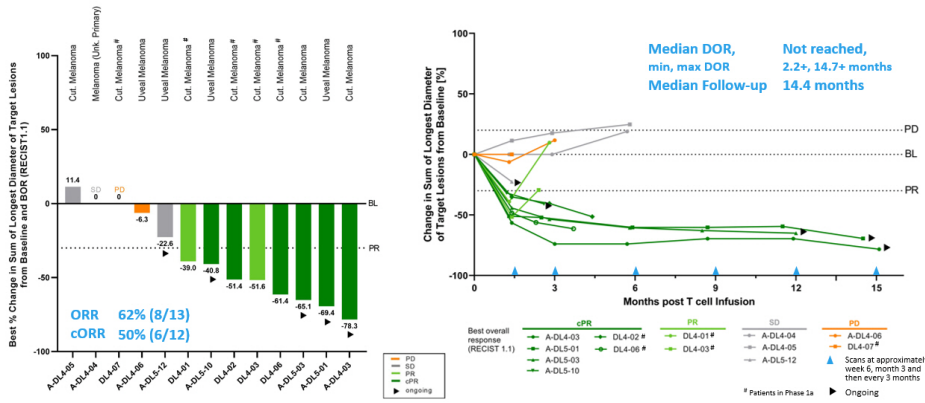
Adverse event (System organ class, Preferred term)	≥ Grade 3		Adverse event (System organ class, Preferred term)	≥ Grade 3	
	No.	%		No.	%
<b>Patients with any adverse event</b>	<b>28</b>	<b>100.0</b>	<b>table continued...</b>		
<b>Adverse Events of Special Interest</b>	<b>1</b>	<b>3.6</b>	<b>General disorders and administration site conditions</b>	<b>1</b>	<b>3.6</b>
Cytokine release syndrome	1	3.6	Pyrexia	1	3.6
ICANS <sup>2</sup>	0	0.0	<b>Hepatobiliary disorders</b>	<b>1</b>	<b>3.6</b>
<b>Blood and lymphatic system disorders</b>	<b>27</b>	<b>96.4</b>	Cholangitis	1	3.6
Neutropenia	18	64.3	<b>Injury, poisoning and procedural complications</b>	<b>1</b>	<b>3.6</b>
Anaemia	14	50.0	Humerus fracture	1	3.6
Leukopenia	13	46.4	<b>Musculoskeletal and connective tissue disorders</b>	<b>1</b>	<b>3.6</b>
Lymphopenia	11	39.3	Muscle spasms	1	3.6
Thrombocytopenia	9	32.1	<b>Nervous system disorders</b>	<b>1</b>	<b>3.6</b>
Leukocytosis	1	3.6	Headache	1	3.6
Lymphocytosis	1	3.6	<b>Skin and subcutaneous tissue disorders</b>	<b>1</b>	<b>3.6</b>
<b>Investigations</b>	<b>7</b>	<b>25.0</b>	Rash maculo-papular	1	3.6
Neutrophil count decreased	4	14.3			
Alanine aminotransferase increased	2	7.1			
Aspartate aminotransferase increased	2	7.1			
White blood cell count decreased	2	7.1			
Blood alkaline phosphatase increased	1	3.6			
<b>Infections and infestations</b>	<b>3</b>	<b>10.7</b>			
Infection	1	3.6			
Septic shock <sup>3</sup>	1	3.6			
Urinary tract infection	1	3.6			
<b>Respiratory, thoracic and mediastinal disorders</b>	<b>3</b>	<b>10.7</b>			
Hypoxia	2	7.1			
Laryngeal inflammation	1	3.6			
<b>Vascular disorders</b>	<b>3</b>	<b>10.7</b>			
Hypotension	2	7.1			
Hypertension	1	3.6			
<b>Metabolism and nutrition disorders</b>	<b>2</b>	<b>7.1</b>			
Failure to thrive	1	3.6			
Hypokalaemia	1	3.6			
Hypophosphataemia	1	3.6			
<b>Eye disorders</b>	<b>1</b>	<b>3.6</b>			
Ulcerative keratitis	1	3.6			

All treatment-emergent adverse events (TEAEs) with ≥ Grade 3 regardless of relatedness to study treatment that occurred in at least 1 patient (except for ICANS, where only Grade 1-2 occurred; listed for completeness due to being an adverse event of special interest) are presented. Adverse events were coded using the Medical Dictionary for Regulatory Activities. Grades were determined according to National Cancer Institute Common Terminology Criteria of Adverse Events, version 5.0. Grades for CRS and ICANS were determined according to CARTOX criteria (Neelapu et al., 2018). Patients are counted only once per adverse event and severity classification. Based on interim data extracted from open clinical database (30-Sep-2023); <sup>1</sup> One patient in Phase 1a DL4 with disease progression after first IMA203 infusion received exploratory second IMA203 infusion and had these ≥ Grade 3 TEAEs only after second infusion, which are included in the table: Humerus fracture, Muscle spasms, Neutropenia, Thrombocytopenia; <sup>2</sup> ICANS: Immune effector cell-associated neurotoxicity syndrome; <sup>3</sup> Fatal Adverse events were not considered related to any study drug

#### Clinical Activity:

- o 13 out of 16 melanoma patients infused at RP2D were evaluable for efficacy analysis based on at least one tumor response assessment being available post treatment. These patients received a median total infused dose of 1.73x10<sup>9</sup> IMA203 TCR-T cells (range 1.07-5.12x10<sup>9</sup> TCR-T cells).
- o Most patients were heavily pre-treated with a median of 4 lines of systemic therapies, thereof a median of 2 lines of checkpoint inhibitors. All 8 cutaneous melanoma patients were checkpoint inhibitor-refractory and 5 of 8 cutaneous melanoma patients were BRAF inhibitor-pretreated.
- o 50% (6/12) cORR and 62% (8/13) initial objective response rate (“ORR”) (according to RECIST 1.1).
- o Durability of responses ongoing beyond 12 months in one patient and 15 months in two patients after treatment.

- o Median duration of response (“mDOR”) was not reached (min. 2.2+ months, max. 14.7+ months) at a median follow-up (“mFU”) of 14.4 months.
- o The best overall response and response over time for melanoma patients in Phase 1a and Phase 1b Cohort A at the RP2D are set forth in the charts below:



Initial ORR: Objective response rate according to RECIST 1.1 at any post infusion scan; Confirmed ORR (cORR): Confirmed objective response rate according to RECIST 1.1 for patients with at least two available post infusion scans or patients with progressive disease (PD) at any prior timepoint, patients with ongoing unconfirmed PR not included in cORR calculation; Duration of response (DOR) in confirmed responders is defined as time from first documented response until disease progression/death. Patients with ongoing response will be censored at date of data cut-off. Median DOR is analyzed by using the Kaplan-Meier method; Median Follow-up is analyzed by using the reverse Kaplan-Meier method; PD: Progressive Disease; SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response; BL: Baseline; BOR: Best Overall Response; DOR: Duration of Response.

**IMA203CD8 GEN2**

- 12 PRAME-positive patients were infused with IMA203CD8 GEN2 across DL3 (0.2-0.48x10<sup>9</sup> TCR-T cells/m<sup>2</sup> BSA), DL4a (0.481-0.8x10<sup>9</sup> TCR-T cells/m<sup>2</sup> BSA) and DL4b (0.801-1.2x10<sup>9</sup> TCR-T cells/m<sup>2</sup>) in Cohort C with a median total infused dose of 1.17x10<sup>9</sup> IMA203CD8 TCR-T cells (range 0.64-2.05x10<sup>9</sup> TCR-T cells).
- All patients were heavily pre-treated with a median of 3 lines of systemic therapies.
- **Safety Data:**
  - o All patients experienced cytopenia (Grade 1-4) associated with lymphodepletion as expected. 11 out of 12 patients (92%) experienced a CRS, of which 8 patients (67%) had Grade 1 or 2 CRS, 2 patients (17%) had Grade 3 CRS, and 1 patient (8%) had a Grade 4 CRS. The latter patient also had a reported Grade 4 neurotoxicity.
  - o No ICANS or neurotoxicity was reported for the other patients.
  - o No IMA203CD8-related deaths were observed.
  - o DLTs were reported for 2 of 4 patients treated at DL4b. No DLT was reported for 4 patients treated at DL3 or 4 patients treated at DL4a. The DL4a dose cohort is ongoing.
  - o The most common Grade ≥3 TEAEs observed are set forth in the table below:



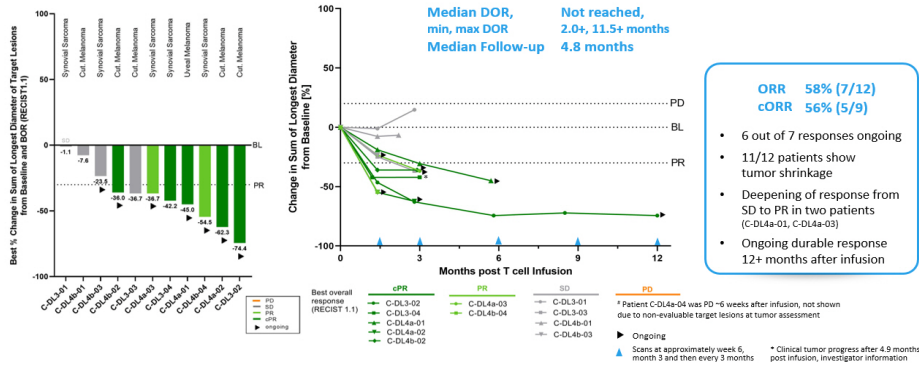
TEAEs by maximum severity for all patients in Cohort C (N=12)

Adverse event (System organ class, preferred term)	≥ Grade 3	
	No.	%
<b>Patients with any adverse event</b>	<b>12</b>	<b>100.0</b>
<b>Adverse events of special interest</b>	<b>3</b>	<b>25.0</b>
Cytokine release syndrome <sup>1</sup>	3	25.0
Immune effector cell-associated neurotoxicity syndrome	0	0.0
<b>Blood and lymphatic system disorders</b>	<b>11</b>	<b>91.7</b>
Neutropenia	9	75.0
Anaemia	8	66.7
Lymphopenia	8	66.7
Thrombocytopenia	4	33.3
Leukopenia	2	16.7
<b>Investigations</b>	<b>4</b>	<b>33.3</b>
Aspartate aminotransferase increased	2	16.7
Neutrophil count decreased	2	16.7
Alanine aminotransferase increased	1	8.3
Blood alkaline phosphatase increased	1	8.3
Blood bilirubin increased	1	8.3
Gamma-glutamyltransferase increased	1	8.3
<b>Metabolism and nutrition disorders</b>	<b>2</b>	<b>16.7</b>
Hypermagnesaemia	1	8.3
Hypoalbuminaemia	1	8.3
Hypophosphataemia	1	8.3
<b>Nervous system disorders</b>	<b>2</b>	<b>16.7</b>
Neurotoxicity <sup>2</sup>	1	8.3
Syncope	1	8.3
<b>Immune system disorders</b>	<b>1</b>	<b>8.3</b>
Haemophagocytic lymphohistiocytosis <sup>2</sup>	1	8.3
<b>Infections and infestations</b>	<b>1</b>	<b>8.3</b>
Infection	1	8.3

All treatment-emergent adverse events (TEAEs) with ≥ Grade 3 regardless of relatedness to study treatment that occurred in at least 1 patient (except for ICANS, where no event was documented; listed for completeness due to being an adverse event of special interest) are presented. Adverse events were coded using the Medical Dictionary for Regulatory Activities. Grades were determined according to National Cancer Institute Common Terminology Criteria of Adverse Events, version 5.0. Grades for CRS and ICANS were determined according to CARTOX criteria (Neelapu et al., 2018). Patients are counted only once per adverse event and severity classification. Based on interim data extracted from open clinical database (30-Sep-2023); <sup>1</sup> DLT: Dose limiting toxicity in patient DL4b-04. <sup>2</sup> DLTs in patient DL4b-01.

*Clinical Activity:*

- o Initial clinical activity was observed with a cORR of 56% (5/9) and initial ORR of 58% (7/12) (RECIST 1.1).
- o 6 of 7 responses (including two unconfirmed responses with no subsequent scan available at data cut-off) were ongoing at data cut-off with longest response at >12 months after infusion.
- o mDOR was not reached (min. 2.0+ months, max. 11.5+ months) at a mFU of 4.8 months.
- o Reduction of tumor size was observed in 11 out of 12 patients, with a deepening of response from initially stable disease (“SD”) to partial response (“PR”) observed in two patients.
- o The best overall response and response over time for IMA203CD8 GEN2 are set forth in the charts below:



Initial ORR: Objective response rate according to RECIST 1.1 at any post infusion scan; Confirmed ORR (cORR): Confirmed objective response rate according to RECIST 1.1 for patients with at least two available post infusion scans or patients with progressive disease (PD) at any prior timepoint, patients with ongoing unconfirmed PR not included in cORR calculation; PD: Progressive Disease; SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response; BL: Baseline; BOR: Best Overall Response; CPI: Checkpoint Inhibitor .

- o Translational data showed enhanced pharmacology of IMA203CD8 GEN2: trend towards responses at lower T cell dose and higher tumor burden compared to IMA203 GEN1, IMA203CD8 GEN2 achieved higher peak expansion (Cmax) when normalized to infused dose and T cells showed higher, initial activation levels without exhaustion over time.

**Development Path for IMA203 GEN1 and IMA203CD8 GEN2 Monotherapies**

The goal of Immatics’ development strategy is to make its cell therapies targeting PRAME available to the broadest possible solid cancer patient population with an initial focus on the US market. To achieve this, Immatics has announced a three-step development strategy for leveraging the full breadth of PRAME, a target that is highly expressed in various solid cancers.

1. Focus on IMA203 GEN1 in cutaneous melanoma (potentially bundled with uveal melanoma), targeted to enter a registration-enabling Phase 2 clinical trial in 2024. Discussions with FDA to align on patient population, clinical trial design and CMC aspects are ongoing under the RMAT designation achieved for IMA203 GEN1 in multiple cancer types including cutaneous and uveal melanoma. There are up to 3,300 HLA-A\*02 and PRAME-positive cutaneous and uveal melanoma last-line patients per year in the US. A next update on the clinical development plan is expected in the first quarter of 2024.
2. In parallel, commence dedicated dose expansion cohorts for signal finding in ovarian and uterine cancer, preferentially with IMA203CD8 GEN2. Enrollment of patients with these cancer types is already ongoing. There are up to 9,000 HLA-A\*02 and PRAME-positive ovarian and uterine last-line cancer patients per year in the US.
3. The development of a broader tumor-agnostic label in PRAME+ solid cancers, including in NSCLC, triple-negative breast cancer, and others. This could leverage the full potential of PRAME across multiple solid cancer types.

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In connection with the foregoing, the Company issued a press release, a copy of which is attached hereto as Exhibit 99.1, and provided a presentation, a copy of which is attached hereto as Exhibit 99.2, and made available an updated corporate presentation, a copy of which is attached hereto as Exhibit 99.3.

Certain statements in this report 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 and outcome 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 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, Immatix 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 report 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 report 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.

#### INCORPORATION BY REFERENCE

This Report on Form 6-K (other than Exhibits 99.1, 99.2 and 99.3 hereto) shall be deemed to be incorporated by reference into the registration statements on Form F-3 (Registration Nos. 333-258351, 333-240260 and 333-274218) of Immatix N.V. and to be a part thereof from the date on which this report is filed, to the extent not superseded by documents or reports subsequently filed or furnished.

#### EXHIBIT INDEX

<b>Exhibit No.</b>	<b>Description</b>
<a href="#"><u>99.1</u></a>	<a href="#"><u>Press release dated November 8, 2023</u></a>
<a href="#"><u>99.2</u></a>	<a href="#"><u>Presentation dated November 8, 2023</u></a>
<a href="#"><u>99.3</u></a>	<a href="#"><u>Corporate presentation dated November 8, 2023</u></a>

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**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: November 8, 2023

**IMMATICS N.V.**

By: /s/ Harpreet Singh  
Name: Harpreet Singh  
Title: Chief Executive Officer

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## PRESS RELEASE

### Immatics Reports Interim Clinical Data from ACTengine® IMA203 and IMA203CD8 TCR-T Monotherapies Targeting PRAME in an Ongoing Phase 1 Trial

Company to host [conference call and webcast](#) today, November 8, at 8:30 am EST/2:30 pm CET

*IMA203 data with focus on melanoma patients presented at the International Congress of the Society for Melanoma Research today, November 8*

- IMA203 GEN1 TCR cell therapy targeting PRAME – update on Phase 1a and Cohort A
  - o Continues to be well tolerated
  - o 50% confirmed objective response rate (cORR) in melanoma patients treated at recommended Phase 2 dose; durability with some ongoing responses at >15 months and median duration of response not reached at a median follow-up of 14.4 months
  - o Targeted to enter registration-enabling Phase 2 trial in melanoma in 2024; discussions with FDA ongoing based on recently obtained RMAT designation
- IMA203CD8 GEN2 TCR cell therapy targeting PRAME – first clinical data from Cohort C
  - o Manageable tolerability, dose escalation ongoing
  - o Initial clinical activity with 56% (5/9) cORR and 58% ORR (7/12) observed during dose escalation dose levels 3 and 4; 6 out of 7 responses ongoing with longest response at >12 months
  - o Enhanced pharmacology and differentiated response pattern
- Signal finding in non-melanoma indications started, including ovarian cancer, uterine cancer, NSCLC, triple-negative breast cancer, preferentially with IMA203CD8 GEN2
- Cash and cash equivalents over \$500 million and cash reach well into 2026; updates across the entire clinical portfolio of Cell Therapy and two TCR Bispecifics programs planned throughout 2024

**Houston, Texas and Tuebingen, Germany, November 8, 2023** – [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 interim data from the ongoing Phase 1 trial with ACTengine® IMA203 in patients with recurrent and/or refractory solid cancers. The update is focused on IMA203 GEN1 in melanoma at the recently defined recommended Phase 2 dose (RP2D) and the first clinical data for IMA203CD8 GEN2.

Treatment with IMA203 GEN1 monotherapy in Phase 1a and Phase 1b Cohort A at RP2D demonstrated durable objective responses in melanoma patients with one patient exceeding 12 months and two patients exceeding 15 months post infusion and a 50% (6/12) confirmed objective response rate (cORR). In line with previous results, IMA203 GEN1 monotherapy was well tolerated at total doses up to  $10 \times 10^9$  TCR-T cells infused.

In addition, the first data on the company's second-generation product candidate IMA203CD8 demonstrated 56% (5/9) cORR with enhanced pharmacology and a differentiated response pattern compared to IMA203 GEN1. The company plans to develop IMA203 GEN1 in melanoma and to pursue development of IMA203 in ovarian cancer, uterine cancer, NSCLC, triple-negative breast cancer and other tumor types preferentially with IMA203CD8 GEN2.

The melanoma-focused data on IMA203 GEN1 will be presented today by Martin Wermke, MD, Professor at the University Hospital Dresden and Coordinating Investigator of the ACTengine<sup>®</sup> IMA203 TCR-T trial, at the 20<sup>th</sup> International Congress of the Society for Melanoma Research in Philadelphia, PA, taking place November 6<sup>th</sup>-9<sup>th</sup>, 2023.

In addition, Dr. Wermke together with Cedrik Britten, MD, Chief Medical Officer at Immatics will provide the complete data update during a [conference call and webcast](#) today, November 8 at 8:30 am EST/2:30 pm CET. The presentation is available on [Immatics' website](#) – covering the complete data set including Phase 1a, Phase 1b Cohort A and the deprioritized Cohort B (IMA203 GEN1 combined with nivolumab).

“A cancer diagnosis can be the start of a daunting journey characterized by devastating setbacks when conventional therapies fail. I believe that the updated data on IMA203 GEN1 shows meaningful benefit and long-term durability in melanoma patients,” said Martin Wermke, MD, Coordinating Investigator of the ACTengine<sup>®</sup> IMA203 TCR-T trial. “With the maturation of the clinical data set, it becomes progressively evident to me that targeting PRAME with Immatics' IMA203 TCR-T approach has the potential to provide a durable benefit for advanced-stage checkpoint- and BRAF-inhibitor refractory melanoma patients.”

“Today, we are excited to report on the continued clinical progress for our ACTengine<sup>®</sup> IMA203 TCR-T cell therapies, which we believe have demonstrated meaningful clinical benefit for last-line solid cancer patients treated with IMA203 or its second-generation product candidate IMA203CD8. We now plan to progress IMA203 into a registration-enabling Phase 2 trial in melanoma as quickly as possible, while we believe that our second-generation approach is exhibiting unique patterns in pharmacology guiding our development efforts towards other

tumor types such as ovarian, uterine, lung and triple-negative breast cancer," commented Dr. Cedrik Britten, Chief Medical Officer at Immatics. "We plan to provide an update on the clinical development plan for IMA203 in the first quarter of 2024 as well as updates across the entire clinical TCR cell therapy and bispecifics portfolio throughout 2024."

#### **Clinical data on anti-tumor activity and safety**

***IMA203 GEN1 in melanoma patients treated at RP2D: IMA203 GEN1 demonstrates a high rate of objective responses with ongoing durability of more than 15 months after treatment***

- At data cut-off on September 30, 2023, a total of 16 PRAME-positive patients with cutaneous, uveal or melanoma of unknown primary origin were infused with IMA203 GEN1 at the recommended Phase 2 dose (RP2D,  $1-10 \times 10^9$  total TCR-T cells) across Phase 1a or Phase 1b Cohort A.
- IMA203 GEN1 monotherapy continues to be well tolerated. All 16 patients experienced cytopenia (Grade 1-4) associated with lymphodepletion as expected. Patients had mostly mild-moderate cytokine release syndrome (CRS), of which 10 patients (63%) had Grade 1, and 5 patients (31%) Grade 2 and 1 patient (6%) Grade 3 CRS. One non-serious, mild (Grade 1) immune effector cell associated neurotoxicity syndrome (ICANS) was observed. No dose-dependent increase of CRS, no dose-limiting toxicities (DLTs) and no IMA203-related death was observed. The safety profile for non-melanoma patients treated with IMA203 GEN1 was generally consistent with safety in the melanoma subset and is provided in the appendix of the presentation.
- 13 out of 16 infused patients were evaluable for efficacy analysis based on at least one tumor response assessment being available post treatment. These patients received a median total infused dose of  $1.73 \times 10^9$  IMA203 TCR-T cells (range  $1.07-5.12 \times 10^9$  TCR-T cells).
- Most patients were heavily pre-treated with a median of 4 lines of systemic therapies, thereof a median of 2 lines of checkpoint inhibitors; all 8 cutaneous melanoma patients were checkpoint inhibitor-refractory and 5 of 8 were BRAF inhibitor-pretreated.
- 50% (6/12) confirmed objective response rate (cORR) and 62% (8/13) initial ORR (RECIST 1.1).
- Durability of responses ongoing beyond 12 months in one patient and 15 months in two patients after treatment.
- Median duration of response (mDOR) was not reached (min 2.2+ months, max 14.7+ months) at a median follow-up (mFU) of 14.4 months.
- RP2D has been defined at  $1-10 \times 10^9$  total TCR-T cells.
- Cell product manufacturing:
  - o 7-day manufacturing process plus 7-day release testing
  - o Manufacturing success rate: >95% to reach RP2D

- Immatics has recently received Regenerative Medicine Advanced Therapy (RMAT) designation from the FDA for IMA203 GEN1 in multiple PRAME-expressing cancers, including cutaneous and uveal melanoma, and is now targeting a registration-enabling Phase 2 trial in cutaneous melanoma potentially bundled with uveal melanoma in 2024. Discussions with FDA to align on patient populations, trial design and CMC aspects concerning the planned Phase 2 trial are ongoing.

***IMA203CD8 GEN2 in Cohort C:*** First clinical data set on IMA203CD8 shows an enhanced pharmacology profile with a differentiated response pattern compared to IMA203 GEN1

- At data cut-off on September 30, 2023, a total of 12 PRAME-positive patients were infused with IMA203CD8 GEN2 across DL3 (0.2-0.48x10<sup>9</sup> TCR-T cells/m<sup>2</sup> BSA), DL4a (0.481-0.8x10<sup>9</sup> TCR-T cells/m<sup>2</sup> BSA) and DL4b (0.801-1.2x10<sup>9</sup> TCR-T cells/m<sup>2</sup>) in Cohort C with a median total infused dose of 1.17x10<sup>9</sup> IMA203CD8 TCR-T cells (range 0.64-2.05x10<sup>9</sup> TCR-T cells).
- All patients were heavily pre-treated with a median of 3 lines of systemic therapies.
- All patients experienced cytopenia (Grade 1-4) associated with lymphodepletion as expected. 11 out of 12 patients (92%) experienced a cytokine release syndrome (CRS), of which 8 patients (67%) had Grade 1 or 2 CRS, 2 patients (17%) had Grade 3 CRS and 1 patient (8%) had a Grade 4 CRS. The latter patient also had a reported Grade 4 neurotoxicity. No ICANS or neurotoxicity was reported for the other patients. No IMA203CD8-related deaths were observed. Dose-limiting toxicities (DLTs) were reported for 2 of 4 patients treated at DL4b. No DLT was reported for all 4 patients treated at DL3, or all 4 patients treated at DL4a. DL4a dose cohort is ongoing.
- Initial clinical activity was observed with a cORR of 56% (5/9) and initial ORR of 58% (7/12) (RECIST 1.1).
- 6 of 7 responses (including two unconfirmed responses with no subsequent scan available at data cut-off) were ongoing at data cut-off with longest response at >12 months after infusion.
- mDOR was not reached (min 2.0+ months, max 11.5+ months) at a mFU of 4.8 months.
- Reduction of tumor size was observed in 11 out of 12 patients, with a deepening of response from initially stable disease (SD) to partial response (PR) observed in two patients.
- Translational data showed enhanced pharmacology of IMA203CD8 GEN2: trend towards responses at lower T cell dose and higher tumor burden compared to IMA203 GEN1; IMA203CD8 GEN2 achieved higher peak expansion (Cmax) when normalized to infused dose and T cells showed higher initial activation levels without exhaustion over time.



**Overview of patient characteristics and anti-tumor activity across IMA203 clinical trial cohorts**

	IMA203 GEN1			IMA203CD8 GEN2
	All Comers (N=45)		Melanoma Subgroup (N=13 out of 45)	All Comers (N=12)
	Phase 1a	Cohort A	Phase 1a + Cohort A	Cohort C
<b>Efficacy population*</b>	N=27 Thereof N=7 at RP2D	N=18 at RP2D	N=13 at RP2D	N=12
<b>Dose level</b>	DL1-4	DL4/5	DL4/5	DL3/DL4a/DL4b
<b>ORR</b>	48% (13/27)	50% (9/18)	62% (8/13)	58% (7/12)
<b>cORR</b>	19% (5/27)	47% (8/17)	<b>50%</b> <b>(6/12)</b>	<b>56%</b> <b>(5/9)</b>
<b>mDOR [months]</b>	4.4 (2.4, 23.0)	Not reached	<b>Not reached</b>	<b>Not reached</b>
<b>mFU [months]</b>	Not defined <sup>#</sup>	10.8	<b>14.4</b>	<b>4.8</b>

\* Patients with at least one available tumor response assessment post infusion; <sup>#</sup> All patients were PD at data cut-off; Initial ORR: Objective response rate according to RECIST 1.1 at any post infusion scan; Confirmed ORR (cORR): Confirmed objective response rate according to RECIST 1.1 for patients with at least two available post infusion scans or patients with progressive disease (PD) at any prior timepoint, patients with ongoing unconfirmed PR not included in cORR calculation; Duration of response (DOR) in confirmed responders is defined as time from first documented response until disease progression/death. Patients with ongoing response will be censored at date of data cut-off. Median DOR (mDOR) is analyzed by using the Kaplan-Meier method; Median Follow-up (mFU) is analyzed by using the reverse Kaplan-Meier method.

The full data analysis including IMA203 GEN1 in Phase 1a and Cohort A as well as deprioritized Cohort B (IMA203 in combination with a checkpoint inhibitor), is available as part of the presentation on the [company's website](#).

**Development path for IMA203 GEN1 and IMA203CD8 GEN2 monotherapies**

The goal of Immatics' development strategy is to make its cell therapies targeting PRAME available to the broadest possible solid cancer patient population with an initial focus on the US market. To achieve this, Immatics has announced a three-step development strategy for leveraging the full breadth of PRAME, a target that is highly expressed in various solid cancers.

1. Focus on IMA203 GEN1 in cutaneous melanoma (potentially bundled with uveal melanoma), targeted to enter a registration-enabling Phase 2 clinical trial in 2024. Discussions with FDA to align on patient population, clinical trial design and CMC aspects are ongoing under the RMAT designation achieved for IMA203 GEN1 in multiple cancer types including cutaneous and uveal melanoma. There are up to 3,300 HLA-A\*02 and PRAME-positive cutaneous and

veal melanoma last-line patients per year in the US. A next update on the clinical development plan is expected in the first quarter of 2024.

2. In parallel, commence dedicated dose expansion cohorts for signal finding in ovarian and uterine cancer, preferentially with IMA203CD8 GEN2. Enrollment of patients with these cancer types is already ongoing. There are up to 9,000 HLA-A\*02 and PRAME-positive ovarian and uterine last-line cancer patients per year in the US.
3. The development of a broader tumor-agnostic label in PRAME+ solid cancers, including in NSCLC, triple-negative breast cancer, and others. This could leverage the full potential of PRAME across multiple solid cancer types.

#### **Immatics conference call and webcast**

Immatics will host a [conference call and webcast](#) today, November 8, 2023, at 8:30 am EST/2:30 pm CET to discuss the clinical data. The presentation can be accessed directly through this [link](#). 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 IMA203 and target PRAME**

ACTengine® IMA203 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 program's potential to address a broad cancer patient population. Immatics' PRAME peptide is present at a high copy number per tumor cell and is homogeneously 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 for its TCR-based cell therapy approach, ACTengine® IMA203.

ACTengine® IMA203 TCR-T is currently being evaluated in Phase 1 Cohort A IMA203 GEN1 monotherapy, and Cohort C IMA203CD8 GEN2 monotherapy, where IMA203 engineered T cells are co-transduced with a CD8αβ co-receptor. As previously reported, Cohort B IMA203 in combination with an immune checkpoint inhibitor has been deprioritized.

#### **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<sup>®</sup> product candidates are manufactured utilizing a proprietary manufacturing process designed to enhance T cell engraftment and persistence *in vivo*.

The ACTengine<sup>®</sup> T cell products are manufactured at the Evelyn H. Griffin Stem Cell Therapeutics Research Laboratory in collaboration with UTHealth.

- END -

#### **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](http://www.immatics.com) as a means of disclosing material non-public information. For regular updates, you can also follow us on [Twitter](#), [Instagram](#) and [LinkedIn](#).

#### **Forward-Looking Statements:**

Certain statements in this presentation 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 and outcome 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, estimated market opportunities of product candidates, 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, 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

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# ACTengine® IMA203 / IMA203CD8 TCR-T Monotherapy Targeting PRAME

## – Phase 1 Interim Data Update

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**Martin Wermke**, Professor at the University Hospital Dresden and Coordinating Investigator of the ACTengine® IMA203 TCR-T trial

**Cedrik Britten**, Chief Medical Officer, Immatics

**Harpreet Singh**, Chief Executive Officer, Immatics

November 8, 2023



Additional oral presentation by **Martin Wermke** at the Society for Melanoma Research Congress on November 08, 2023

Data cut-off Sep 30, 2023

*Delivering the Power of T cells to Cancer Patients*

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# Realizing the Full Multi-Cancer Opportunity of PRAME

## ACTEngine® IMA203 (TCR Cell Therapy) and TCER® IMA402 (TCR Bispecific)

**Focus today**

Indication	% PRAME positive patients <sup>1</sup>
Uterine Carcinoma	97%
Uterine Carcinosarcoma	100%
Sarcoma Subtypes	up to 100%
Cut. Melanoma	≥95%
Uveal Melanoma <sup>2</sup>	≥91%
Ovarian Carcinoma	84%
Squamous NSCLC	68%
TNBC	63%
Small Cell Lung Cancer	45%
Kidney Carcinoma	up to 40%
Cholangiocarcinoma	33%
HNSCC	27%
Esophageal Carcinoma	27%
Breast Carcinoma	26%
Adeno NSCLC	25%
HCC	18%
Bladder Carcinoma	18%



**Focus today**

**ACTEngine® IMA203 (TCR Cell Therapy)**

*Phase 1b dose expansion ongoing*

**TCER® IMA402 (TCR Bispecific)**

*Dose escalation of Phase 1/2 trial ongoing*

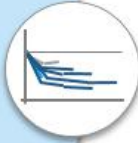
<sup>1</sup>PRAME target prevalence is based on TCGA (for SCLC, in-house) RNAseq data combined with a proprietary mass spec-guided RNA expression threshold; <sup>2</sup>Uveal melanoma target prevalence is based on IMADetect® qPCR testing of screening biopsies from clinical trial patients (n=33). NSCLC: Non-small cell lung cancer, TNBC: Triple-negative breast cancer, HNSCC: Head and neck squamous cell carcinoma; HCC: Hepatocellular carcinoma



### GEN1: IMA203 in Melanoma at RP2D

#### Clinical Data

- Well tolerated
- 50% (6/12) confirmed objective response rate (cORR)
- Durability with ongoing responses at 15+ months; mDOR not reached at mFU of 14.4 months



#### Cell Product Manufacturing

- 7-day manufacturing process, plus 7-day release testing
- RP2D defined at  $1-10 \times 10^9$  total TCR-T cells
- Manufacturing success rate: >95%



#### Development Path

- FDA RMAT designation for multiple PRAME+ cancers including cutaneous & uveal melanoma
- IMA203 GEN1 in melanoma targeted to enter registration-enabling Phase 2 trial in 2024
- Update on clinical development plan in 1Q 2024



### GEN2: IMA203CD8 in Solid Tumors

#### Initial Clinical Data

- Manageable tolerability
- 56% (5/9) confirmed objective response rate (cORR)
- Durable response at 12+ months; mDOR not reached at mFU of 4.8 months
- 6 out of 7 responses ongoing at data cut-off
- Enhanced pharmacology with differentiated response pattern



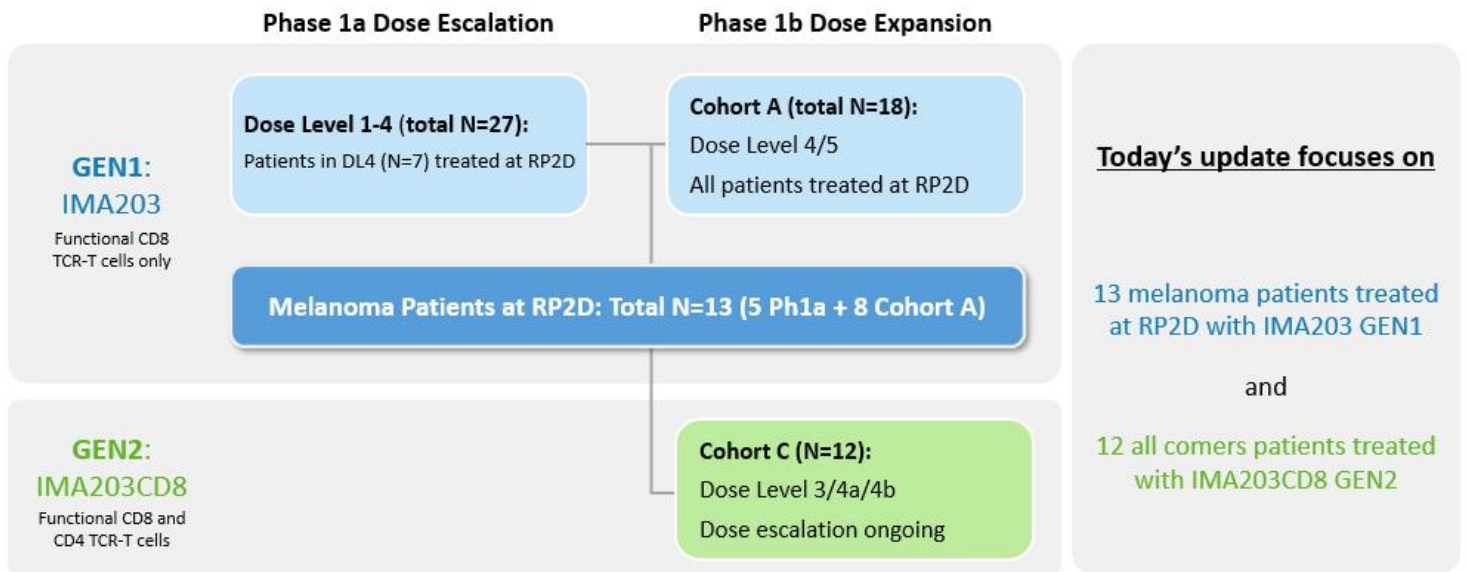
#### Development Path

- Complete dose escalation
- Signal finding in non-melanoma indications, such as ovarian cancer, uterine cancer, NSCLC, triple-negative breast cancer and others





Overview



Phase 1a and Cohort A data set in appendix; Cohort B deprioritized, detailed analysis in appendix

# Overview of Patient Characteristics and Responses

## Heavily Pretreated Patient Population across Clinical Trial Cohorts

	IMA203 GEN1			IMA203CD8 GEN2
	All Comers (N=45)		Melanoma Subgroup (N=13 of 45)	All Comers (N=12)
	Phase 1a	Cohort A	Phase 1a + Cohort A	Cohort C
<b>Efficacy population*</b>	N=27 Thereof N=7 at RP2D	N=18 at RP2D	N=13 at RP2D	N=12
<b>Prior lines of systemic treatment</b> (median, min, max)	4 (1, 8)	3 (0, 10)	4 (0, 7)	3 (1, 5)
<b>LDH at baseline</b> >1 x ULN [% of patients]	66.7	50.0	53.8	50.0
<b>Baseline tumor burden</b> Median target lesion sum of diameter [mm] (min, max)	133.0 (29, 219.7)	58.9 (21, 207.3)	52.0 (21.0, 178.7)	79.8 (20.0, 182.0)
<b>Dose level</b>	DL1-4	DL4/5	DL4/5	DL3/DL4a/DL4b
<b>ORR</b>	48% (13/27)	50% (9/18)	62% (8/13)	58% (7/12)
<b>cORR</b>	<b>19%</b> (5/27)	<b>47%</b> (8/17)	<b>50%</b> (6/12)	<b>56%</b> (5/9)
<b>mDOR [months]</b>	4.4 (2.4, 23.0)	<b>Not reached</b>	<b>Not reached</b>	<b>Not reached</b>
<b>mFU [months]</b>	<b>Not defined*</b>	<b>10.8</b>	<b>14.4</b>	<b>4.8</b>

\* Patients with at least one available tumor response assessment post infusion; † All patients were PD at data cut-off; Initial ORR: Objective response rate according to RECIST 1.1 at any post infusion scan; Confirmed ORR (cORR): Confirmed objective response rate according to RECIST 1.1 for patients with at least two available post infusion scans or patients with progressive disease (PD) at any prior timepoint; patients with ongoing unconfirmed PR not included in cORR calculation; Duration of response (DOR): In confirmed responders is defined as time from first documented response until disease progression/death. Patients with ongoing response will be censored at date of data cut-off; Median DOR is analyzed by using the Kaplan-Meier method; Median Follow-up is analyzed by using the reverse Kaplan-Meier method; DOR: Duration of Response; FU: Follow-up

# ACTengine® IMA203 TCR-T Interim Update

Delivering a Meaningful Benefit to Patients with an Unmet Medical Need



## IMA203 GEN1 Monotherapy

Phase 1a & Cohort A – Focus on Melanoma at RP2D

## IMA203CD8 GEN2 Monotherapy

Cohort C – First Data Set on 2<sup>nd</sup> Generation

## Summary & Next Development Steps

## IMA203 GEN1 in All Melanoma Patients at RP2D – Most Frequent Adverse Events N=16 Patients in Safety Population<sup>1</sup>



- **Expected cytopenia (Grade 1-4)** associated with lymphodepletion in all patients
- **Mostly mild to moderate cytokine release syndrome (CRS)**
  - 63% (10/16) with Grade 1 CRS
  - 31% (5/16) with Grade 2 CRS
  - 6% (1/16) with Grade 3 CRS (Phase 1a patient; recovered to Grade 2 after 3 days, no need for vasopressors and/or ventilation)
  - No dose-dependent increase of CRS
- **One non-serious, mild (Grade 1) ICANS<sup>2</sup> in DL5**
- **No dose-limiting toxicity**
- **No IMA203-related deaths**
- For full IMA203 GEN1 monotherapy safety profile (generally consistent with safety in melanoma subset), see appendix

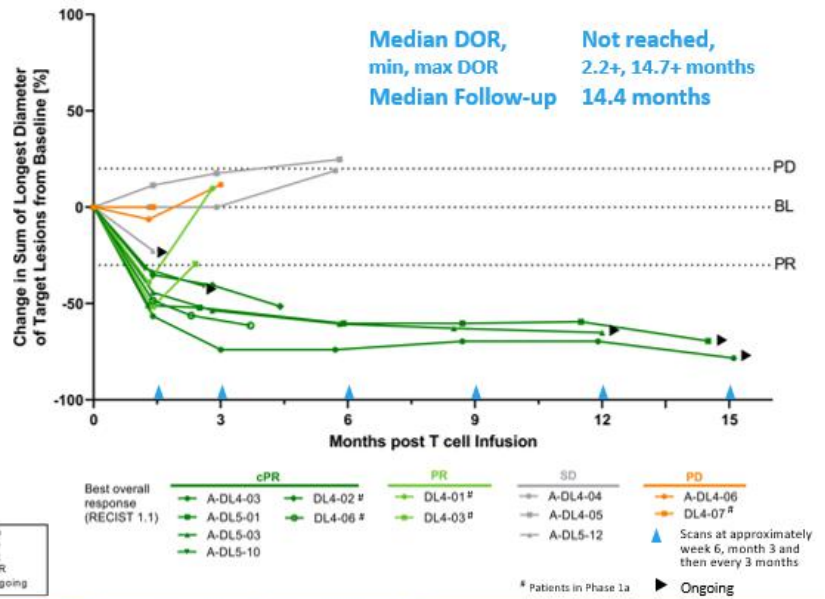
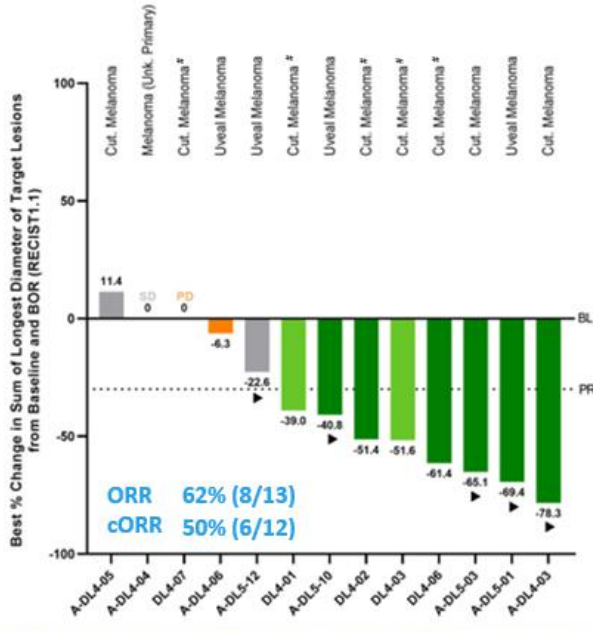
**IMA203 GEN1 monotherapy continues to be well tolerated  
at total doses between 1-10x10<sup>9</sup> TCR-T cells (RP2D)**

<sup>1</sup> Three cutaneous melanoma patients treated with IMA203 and pending post infusion scan included in safety population, but not efficacy population;  
<sup>2</sup> ICANS: Immune Effector Cell-Associated Neurotoxicity Syndrome; CRS and ICANS graded by CARTOX criteria (Neelapu *et al.*, 2018)

# IMA203 GEN1 in All Melanoma Patients at RP2D (N=13) – BOR and Response over Time



## Durable Responses 15+ Months after Treatment



Initial ORR: Objective response rate according to RECIST 1.1 at any post infusion scan; Confirmed ORR (cORR): Confirmed objective response rate according to RECIST 1.1 for patients with at least two available post infusion scans or patients with progressive disease (PD) at any prior timepoint; patients with ongoing unconfirmed PR not included in cORR calculation; Duration of response (DOR) in confirmed responders is defined as time from first documented response until disease progression/death. Patients with ongoing response will be removed at date of data cut-off; Median DOR is analyzed by using the Kaplan-Meier method; Median Follow-up is analyzed by using the Reverse Kaplan-Meier method; PD: Progressive Disease; SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response; BL: Baseline; BOR: Best Overall Response; DOR: Duration of Response

# IMA203 GEN1 in Melanoma Targeted to Enter Registration-Enabling Phase 2 Trial in 2024



## Clinically and Commercially Attractive Features of IMA203

≥95% of cutaneous melanoma patients are PRAME-positive
Well tolerated Mostly mild to moderate CRS, infrequent & mild ICANS
Promising anti-tumor activity (cORR, mDOR)
Leukapheresis as source for cell product, no surgery required
Short manufacturing time of 7 days plus 7 days of QC release testing
Low dose IL-2 post IMA203 infusion with better tolerability profile than high dose IL-2

## High Medical Need in Cutaneous and Uveal Melanoma

	Cutaneous Melanoma	Uveal Melanoma
Patient Population	2L+ CPI-refractory, BRAF/MEK inhibitor-refractory if BRAF mutation+	2L+ Kimmtrak-refractory, CPI/chemotherapy-refractory
IMA203 Opportunity	~3,000 HLA-A*02:01 and PRAME-positive cutaneous melanoma patients annually in the US <sup>1</sup>	~300 HLA-A*02:01 and PRAME-positive uveal melanoma patients annually in the US <sup>2</sup>

CPI: Checkpoint inhibitor; <sup>1</sup> Based on annual mortality of ~7,700 cutaneous melanoma patients in the US, HLA-A\*02:01 prevalence of 41% in the US and PRAME prevalence of 95% (TCGA RNAseq data combined with proprietary MS-guided RNA expression threshold); <sup>2</sup> Based on annual mortality of ~800 uveal melanoma patients in the US, HLA-A\*02:01 prevalence of 41% in the US and PRAME prevalence of 93% (IMADetect® qPCR testing of screening biopsies from clinical trial patients (n=33))

# ACTengine® IMA203 TCR-T Interim Update

Delivering a Meaningful Benefit to Patients with an Unmet Medical Need



**IMA203 GEN1 Monotherapy**

Phase 1a & Cohort A – Focus on Melanoma at RP2D

**IMA203CD8 GEN2 Monotherapy**

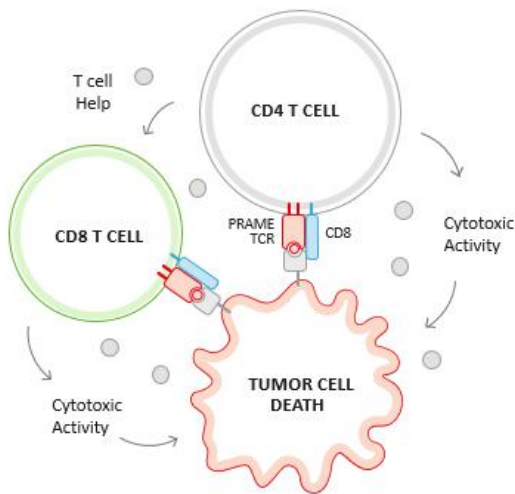
Cohort C – First Data Set on 2<sup>nd</sup> Generation

**Summary & Next Development Steps**



# IMA203CD8 GEN2 – IMA203 TCR-T Monotherapy Leveraging CD8 and CD4 cells

Differentiated Pharmacology Compared to 1<sup>st</sup>-Generation TCR-only Approaches



- IMA203CD8 GEN2 designed to broaden the clinical potential of IMA203 TCR-T monotherapy by adding functional CD4 T cells via co-transduction of CD8 $\alpha\beta$  alongside PRAME TCR
- Activated CD4 T cells aid activity of other immune cells by releasing cytokines and acquire cytotoxic functions
- Functional CD4 T cells mediate longer anti-tumor activity than CD8 T cells and potentiate the anti-tumor activity of the cell product in preclinical studies<sup>1</sup>
- Data from CD19 CAR-T-treated leukaemia patients suggest a relevant role of engineered CD4 T cells in long-term durability<sup>2</sup>



## IMA203CD8 GEN2 in Cohort C (N=12) – Most Frequent Adverse Events

### Manageable Tolerability in 12 Patients Treated with IMA203CD8 at 3 Escalating Dose Levels<sup>1</sup>

- **Expected cytopenia (Grade 1-4)** associated with lymphodepletion in all patients
- Cytokine release syndrome (CRS) in 92% (11/12) of patients:  
Trend towards **more severe CRS at higher doses, in all cases well manageable**
  - 67% (8/12) with Grade 1 or 2 CRS (4 in DL3, 3 in DL4a, 1 in DL4b)
  - 17% (2/12) with Grade 3 CRS (2 in DL4b; patient C-DL4b-04, see also description below)
  - 8% (1/12) with Grade 4 CRS (1 in DL4b, patient C-DL4b-01, see also description below)
- **One patient with neurotoxicity (see below), no ICANS<sup>2</sup> or neurotoxicity reported for the other patients**
- **Dose-limiting toxicities (DLTs) at Dose Level 4b** were observed in 2 of 4 patients
  - 1) In patient C-DL4b-01 treated with highest possible dose at DL4b, high biological activity (*in vivo* T cell expansion) observed; patient developed Grade 4 neurotoxicity and Grade 4 CRS on day 6 after infusion, combined with Grade 3 Hemophagocytic Lymphohistiocytosis (HLH)
  - 2) Patient C-DL4b-04 treated at DL4b developed Grade 3 CRS with transient Grade 3 liver enzyme (ALT) increase that resolved to Grade 2 within 10 days; no need for vasopressors or ventilation at any time
- **No high-grade CRS, no neurotoxicity and no DLTs were reported for 4 patients treated at DL3 and 4 patients treated at DL4a**
- **No IMA203CD8-related deaths**
- **Expanded DL4a dose cohort ongoing**

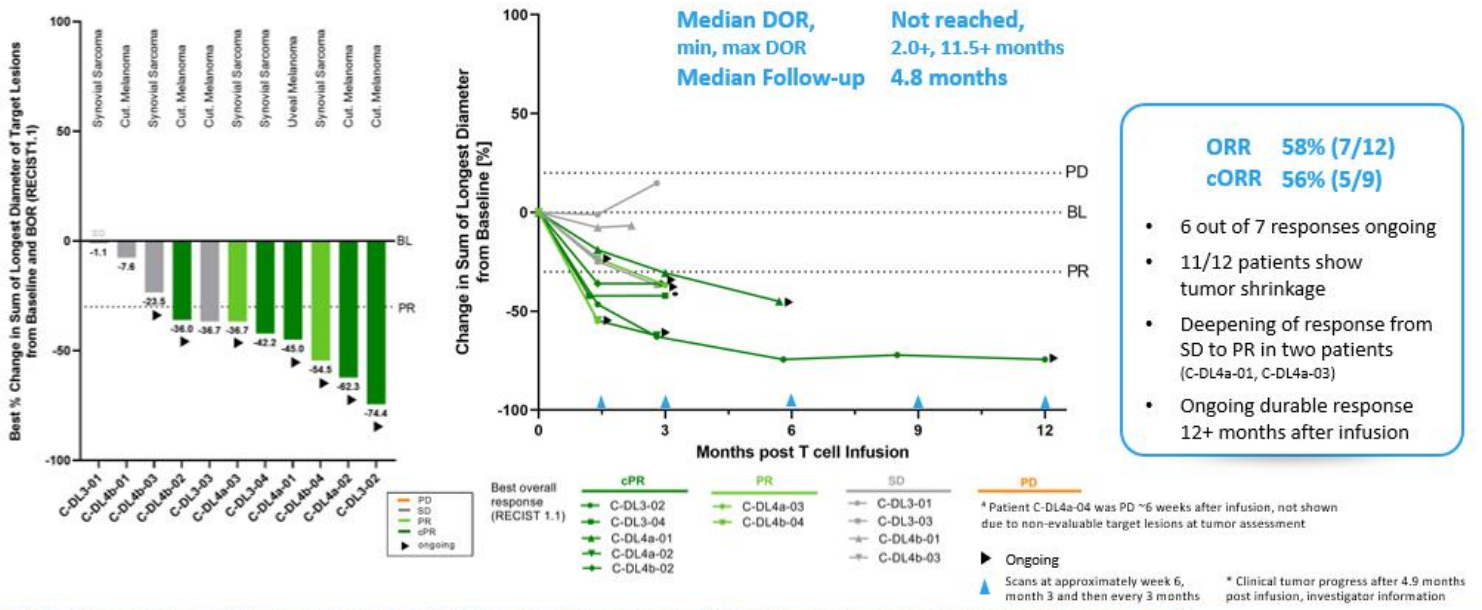
### IMA203CD8 GEN2 monotherapy shows a manageable tolerability profile

<sup>1</sup> N=4 DL3, N=4 DL4a, N=4 DL4b, DL3: 0.2-0.48x10<sup>9</sup> TCR-T cells/m<sup>2</sup> BSA, DL4 is split into a DL4a (0.481-0.8x10<sup>9</sup> TCR-T cells/m<sup>2</sup> BSA) and DL4b (0.801-1.2x10<sup>9</sup> TCR-T cells/m<sup>2</sup> BSA);

<sup>2</sup> ICANS: Immune Effector Cell-Associated Neurotoxicity Syndrome; CRS and ICANS graded by CARTOX criteria (Neelapu *et al.*, 2018)

# IMA203CD8 GEN2 in Cohort C (N=12#) – BOR and Response over Time

## Deepening of Response from SD to PR in 2 Patients, 6 Responses Ongoing



# IMA203CD8 GEN2: Translational Data Shows Enhanced Pharmacology



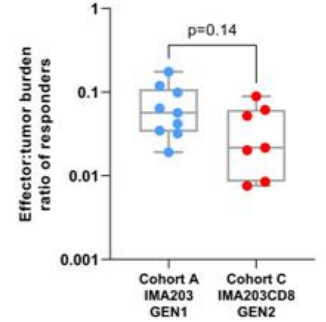
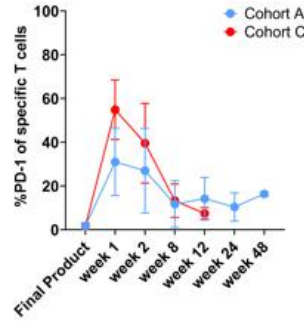
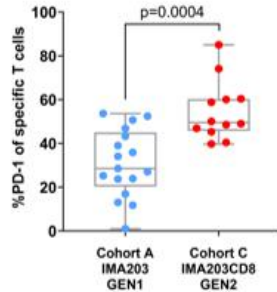
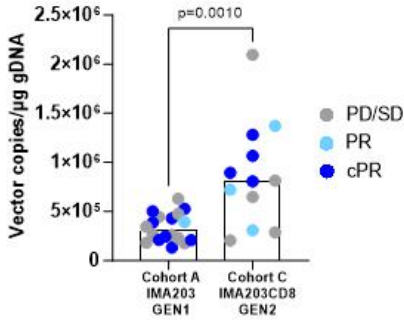
## Cohort A IMA203 GEN1 (All Patients at RP2D) vs Cohort C IMA203CD8 GEN2

Higher peak expansion ( $C_{max}$ ) of IMA203CD8 T cells when normalized to infused dose

Higher activation levels in IMA203CD8 T cells at week 1...

...without exhaustion over time

Trend towards responses at lower cell dose and higher tumor burden with IMA203CD8



### Initial translational data indicates higher biological and clinical activity of IMA203CD8 GEN2

# ACTengine® IMA203 TCR-T Interim Update

Delivering a Meaningful Benefit to Patients with an Unmet Medical Need



**IMA203 GEN1 Monotherapy**

Phase 1a & Cohort A – Focus on Melanoma at RP2D

**IMA203CD8 GEN2 Monotherapy**

Cohort C – First Data Set on 2<sup>nd</sup> Generation

**Summary & Next Development Steps**

### IMA203 GEN1 Monotherapy in Melanoma at RP2D

- Well tolerated, mostly mild to moderate CRS, infrequent & mild ICANS
- **50% (6/12) cORR, mDOR not reached at mFU of 14.4 months**
- **Durability with ongoing responses at 15+ months in some patients**
- RP2D defined at  $1-10 \times 10^9$  total TCR-T cells
- FDA RMAT designation received in multiple PRAME expressing cancers including cutaneous and uveal melanoma

#### Next Step

Alignment with FDA on patient population, trial design, CMC targeting registration-enabling Phase 2 trial in melanoma

### IMA203CD8 GEN2 Monotherapy

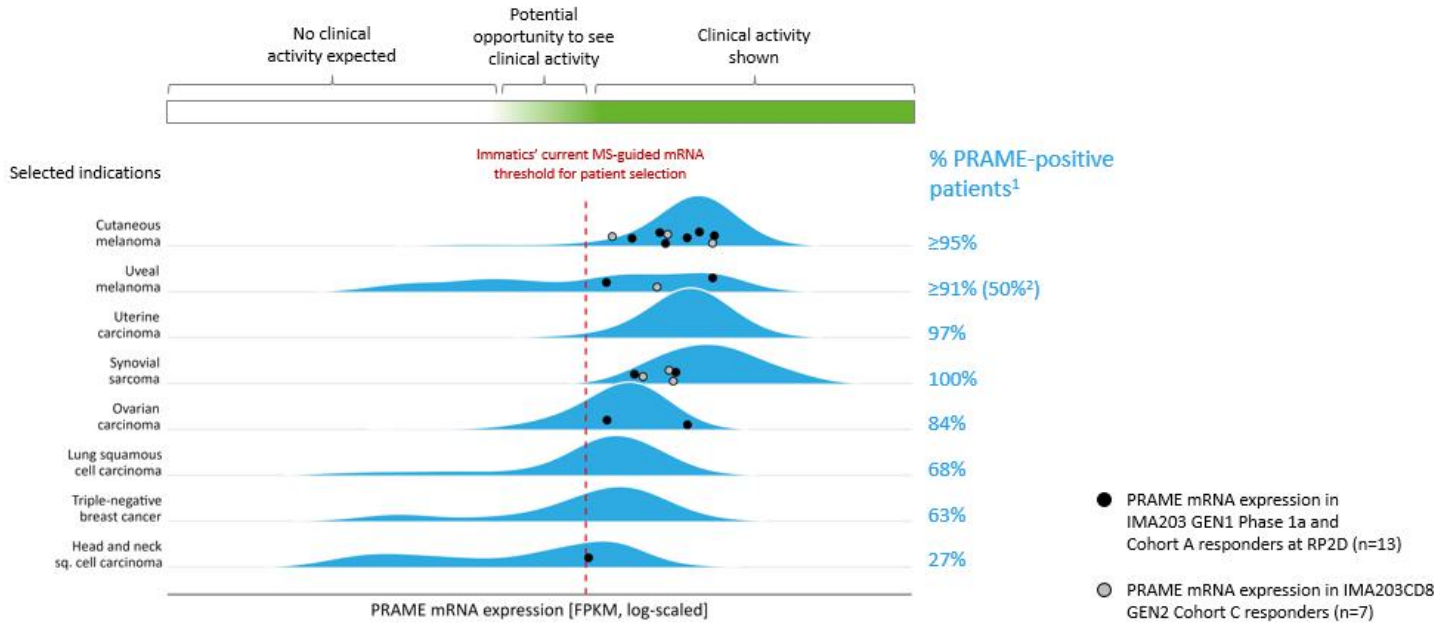
- Enhanced primary and secondary pharmacology when compared to GEN1
- Manageable tolerability (2 DLTs at DL4b, dose escalation ongoing)
- Initial clinical activity observed with differentiated response pattern
  - 56% (5/9) cORR
  - 6 out of 7 responses ongoing at data cut-off, durable response at 12+ months
  - SD converting to PR over time (N=2)
  - Enhanced biological efficacy with PRs at lower T cell:tumor cell ratio compared to IMA203 GEN1

#### Next Step

Complete dose escalation and further dose expansion with focus on non-melanoma patients

# Potential of IMA203 in Additional Solid Cancer Indications

## Based on PRAME Expression in IMA203 GEN1 and IMA203CD8 GEN2 Responders



PRAME target expression distribution (blue histogram) based on TCGA RNAseq data, patient data (black dots) based on IMADetect® qPCR testing of screening biopsies; <sup>1</sup> PRAME target prevalence is based on TCGA RNAseq data combined with a proprietary MS-guided RNA expression threshold; <sup>2</sup> PRAME target prevalence in uveal melanoma based on IMADetect® qPCR testing of screening biopsies from clinical trial patients (n=33) demonstrates substantial higher prevalence of 93% compared to prevalence based on TCGA data of 50%; TCGA: early & late-stage primary tumor samples, Immatics clinical trial: late-stage/metastatic tumor samples, Role of PRAME in metastasis of uveal melanoma: Field et al. 2016 Clinical Cancer Research; MS: mass spectrometry



### Development Strategy

#### Step 1

2024

IMA203 GEN1 in cutaneous melanoma (potentially bundled with uveal melanoma) as first tumor type targeted to enter registration-enabling trial

#### Step 2

2024

Signal finding in ovarian cancer and uterine cancer in dedicated dose expansion cohorts, preferentially with IMA203CD8 GEN2

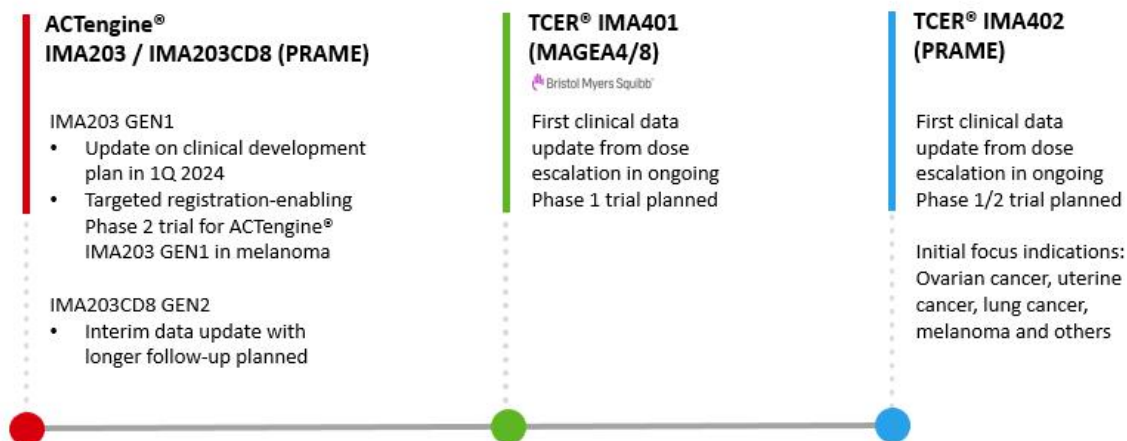
#### Step 3

Pursue tumor-agnostic label in PRAME+ solid cancers to leverage full breadth of PRAME - including NSCLC, triple-negative breast cancer and others

# Upcoming 2024 Catalysts for ACTengine® and TCER® Clinical Lead Assets



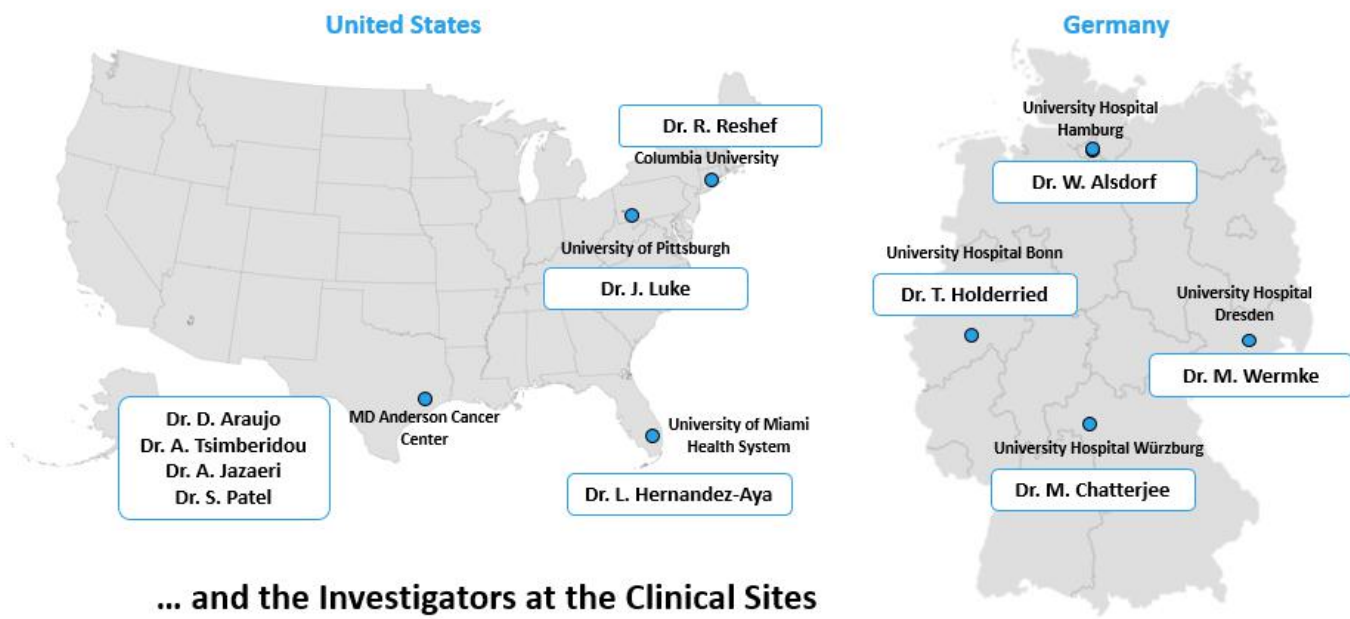
Projected Cash Runway Well into 2026 to Reach Multiple Value Inflection Points



Updates planned across the entire clinical portfolio throughout 2024



# We are Immensely Grateful to the Patients, Their Families ...



## ... and the Investigators at the Clinical Sites

# Delivering

the Power of T cells  
to Cancer Patients

## Q&A

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## Appendix – Additional Data

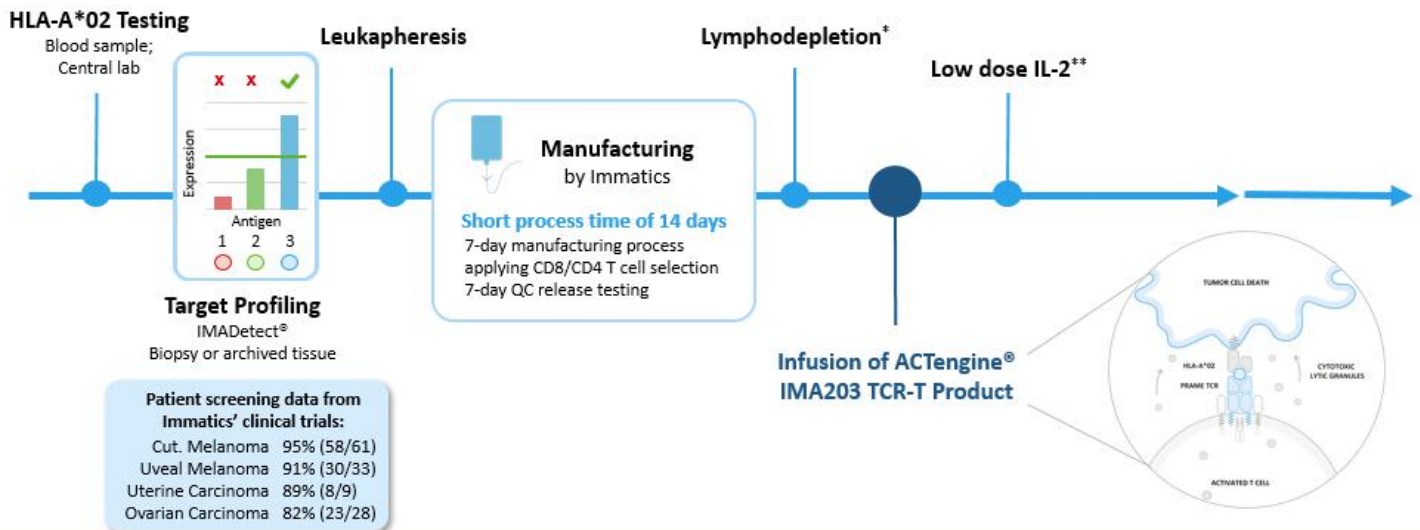
1. Patient Flow and PRAME Expression in Pre-Treatment Tumor Biopsies
  2. Dose Escalation and Cohort A IMA203 GEN1
  3. Cohort B IMA203 GEN1 + Nivolumab
  4. Cohort C IMA203 GEN2
  5. Manufacturing and *in vivo* Engraftment Data IMA203 GEN1 and IMA203CD8 GEN2
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## Screening & Manufacturing Phase

## Treatment & Observation Phase

## Long Term Follow-up

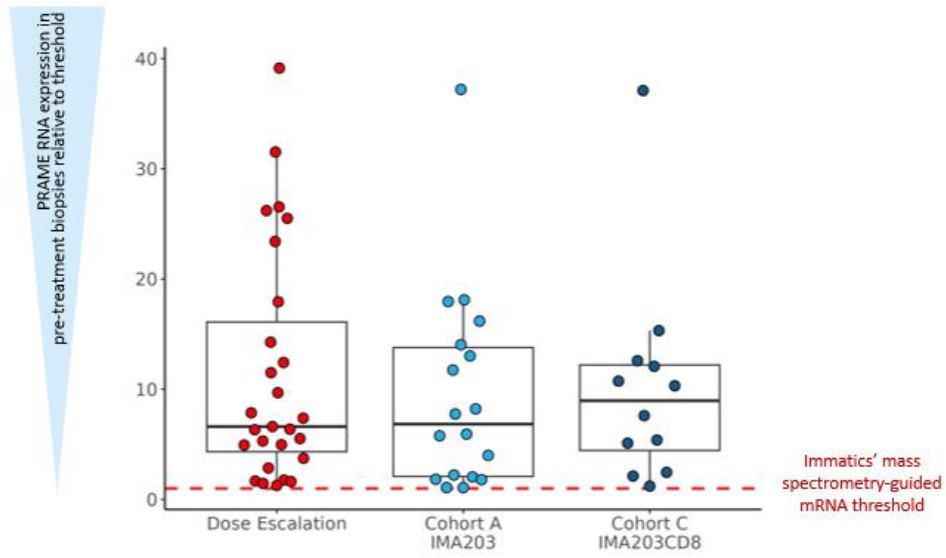
Safety and efficacy monitoring for 12 months



\* 30 mg/m<sup>2</sup> Fludarabine and 500 mg/m<sup>2</sup> Cyclophosphamide for 4 days; \*\* 1m IU daily days 1-5 and twice daily days 6-10

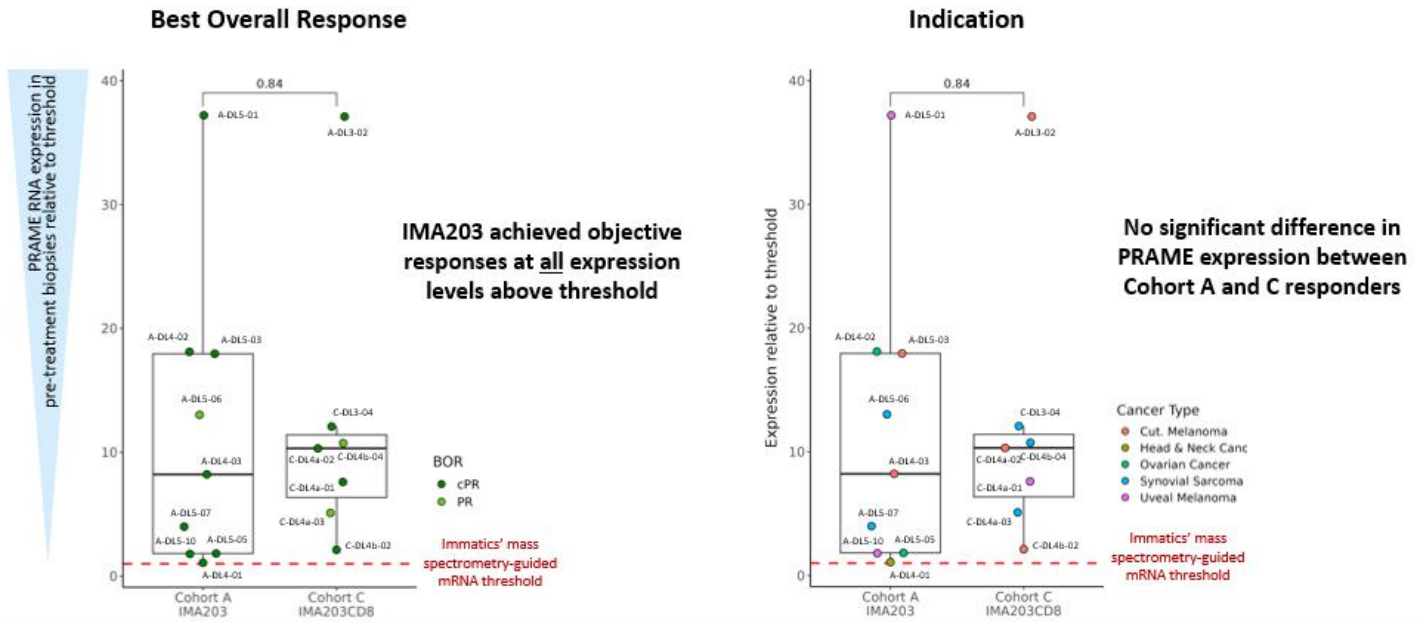
# PRAME Expression in Pre-Treatment Tumor Biopsies

Comparable PRAME Expression Levels in Patients Treated in Phase 1a Dose Escalation, Cohort A and C



# PRAME Expression in Pre-Treatment Tumor Biopsies

## Responders in Cohort A IMA203 GEN1 and Cohort C IMA203CD8 GEN2





## Appendix – Additional Data

1. Patient Flow and PRAME Expression in Pre-Treatment Tumor Biopsies
2. Dose Escalation and Cohort A IMA203 GEN1
3. Cohort B IMA203 GEN1 + Nivolumab
4. Cohort C IMA203 GEN2
5. Manufacturing and *in vivo* Engraftment Data IMA203 GEN1 and IMA203CD8 GEN2



# IMA203 GEN1 – Melanoma as First Indication for Pivotal Development

Patient Numbers*	ALL	Melanoma	Ovarian Cancer	Synovial Sarcoma	H&N Cancer	Others
Phase 1a RP2D	7	5	0	0	0	2
Cohort A RP2D	18	8	4	3	1	2

Patient characteristics	All comers Cohort A	Melanoma pts Ph1a & Cohort A at RP2D	Ovarian cancer pts Ph1a & Cohort A at RP2D
<b>Efficacy population*</b>	<b>18</b>	<b>13</b>	<b>4</b>
<b>Prior lines of treatment</b> Median (min, max)	<b>3</b> (0, 10)	<b>4</b> (0, 7)	<b>4.5</b> (3, 10)
<b>LDH at baseline</b> >1 x ULN [% of patients]	<b>50.0</b>	<b>53.9</b>	<b>100.0</b>
<b>Baseline tumor burden</b> Target lesion sum of diameter [mm] (median, min, max)	<b>58.9</b> (21.0, 207.3)	<b>52.0</b> (21.0, 178.7)	<b>108.8</b> (50.6, 207.3)

All 8 cut. melanoma patients were CPI-refractory and 5 of 8 were BRAF-inhibitor pretreated

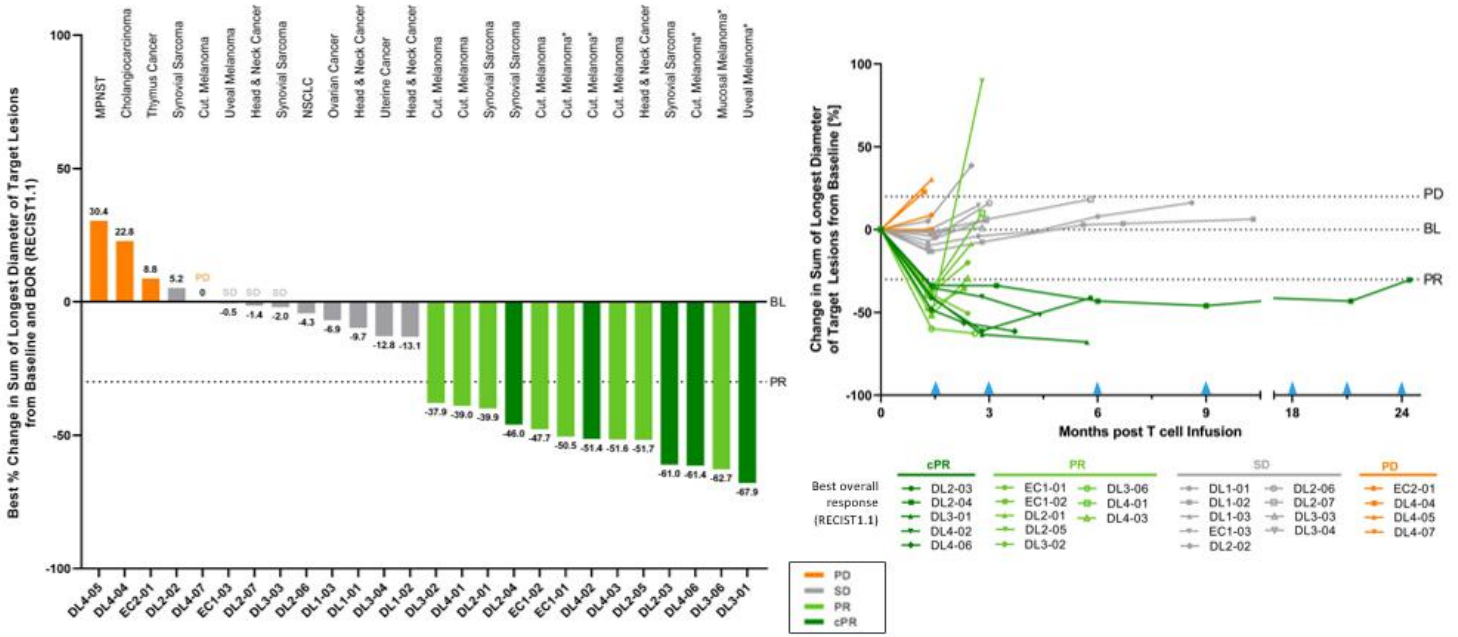
All ovarian cancer patients were platinum-resistant

- Sub-group analysis per tumor type at target dose includes data from Phase 1a plus Cohort A at RP2D
- Melanoma patient number (N=13) and characteristics allow such sub-group analysis for initial assessment of anti-tumor activity
- For other tumor types, appropriate patient numbers and characteristics have not yet been achieved

\* Patients with at least one post treatment tumor response assessment



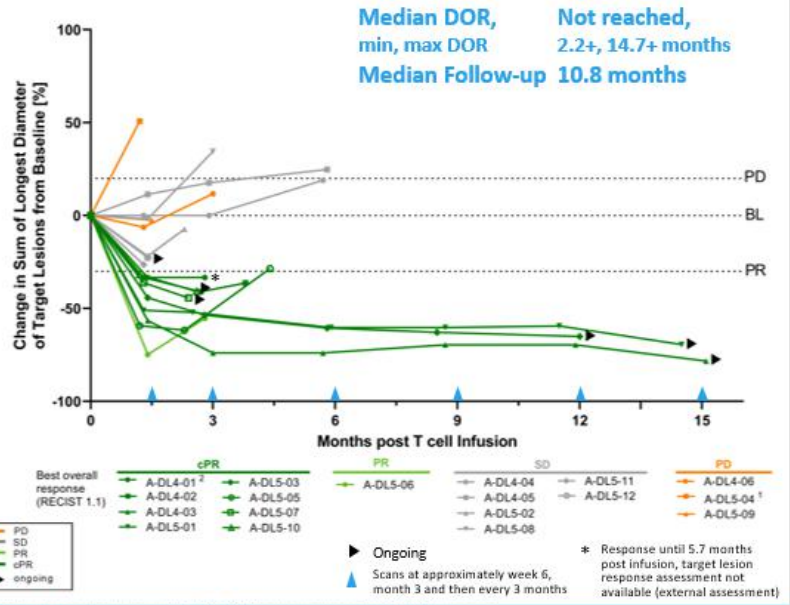
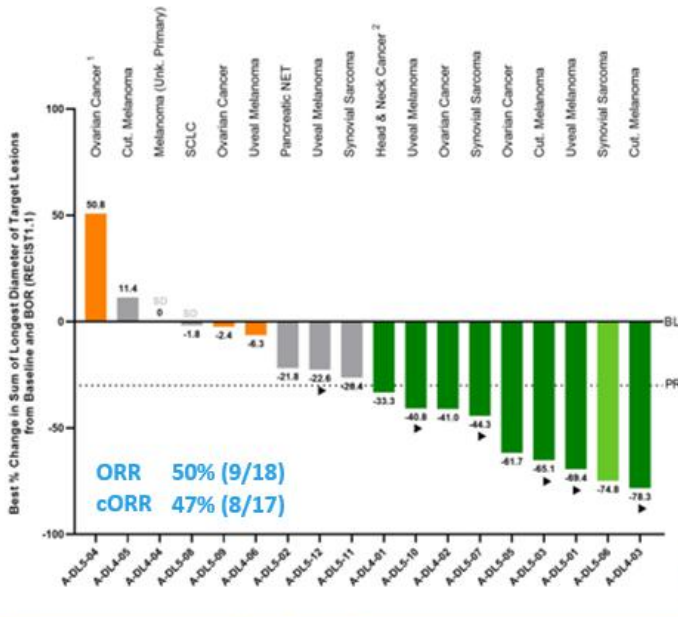
# IMA203 GEN1 in Phase 1a Dose Escalation (N=27#) – BOR and Response over Time



\* Maximum change of target lesions and RECIST 1.1 BOR at different timepoints; # Synovial sarcoma patient (DL3) PD at week 6 not shown as target lesions were not evaluable; PD: Progressive disease, SD: Stable disease, PR: Partial response; cPR: Confirmed partial response; BL: Baseline

# IMA203 GEN1 in Cohort A (N=18) – BOR and Response over Time

## Objective Responses across Multiple Solid Cancer Types



\* Patient received one dose nivolumab erroneously; † Progressive disease at month 5 due to unequivocal progression of non-target lesions, target lesions not evaluable due to external assessment; ‡ Initial ORR: Objective response rate according to RECIST 1.1 at any post infusion scan; Confirmed ORR (cORR): Confirmed objective response rate according to RECIST 1.1 for patients with at least two available post infusion scans or patients with progressive disease (PD) at any prior timepoint; patients with ongoing unconfirmed PR not included in cORR calculation; Duration of response (DOR) is confirmed responders is defined as time from first documented response until disease progression/death; Patients with ongoing response will be censored at date of data cut-off; Median DOR is analyzed by using the Kaplan-Meier method; Median Follow-up is analyzed by using the reverse Kaplan-Meier method; PD: Progressive Disease; SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response; BL: Baseline; BOR: Best Overall Response; DOR: Duration of Response

## IMA203 GEN1 in Cohort A – Most Frequent Adverse Events

N=21 Patients in Safety Population<sup>1</sup>

- **Expected cytopenia (Grade 1-4)** associated with lymphodepletion in all patients
- **Mild-moderate cytokine release syndrome (CRS) in 90% (19/21) of patients**
  - 43% (9/21) with Grade 1 CRS
  - 48% (10/21) with Grade 2 CRS
  - No dose-dependent increase of CRS
- **One non-serious, mild (Grade 1) ICANS<sup>2</sup> in DL5**
- **No dose-limiting toxicity**
- **No IMA203-related deaths**

**IMA203 GEN1 monotherapy continues to be well tolerated at total doses  
between 1-10x10<sup>9</sup> TCR-T cells (RP2D)**

<sup>1</sup> Three cutaneous melanoma patients treated with IMA203, and pending post infusion scan included in safety population, but not efficacy population;

<sup>2</sup> ICANS: Immune Effector Cell-Associated Neurotoxicity Syndrome; CRS and ICANS graded by CARTOX criteria (Neelapu *et al.*, 2018)

# Tolerability Data – IMA203 GEN1 across All Dose Levels

## Phase 1a Dose Escalation and Cohort A – All ≥Grade 3 Adverse Events (N=49)

TEAEs by maximum severity for all patients in Phase 1a dose escalation and Cohort A dose expansion (N=49)<sup>1</sup>

Adverse event (System organ class, Preferred term)	≥ Grade 3		Adverse event (System organ class, Preferred term)	≥ Grade 3	
	No.	%		No.	%
<b>Patients with any adverse event</b>	49	100.0	<b>table continued...</b>		
<b>Adverse Events of Special Interest</b>	2	4.1	<b>General disorders and administration site conditions</b>	4	8.2
Cytokine release syndrome	2	4.1	Condition aggravated <sup>1</sup>	1	2.0
ICANS <sup>2</sup>	0	0.0	Fatigue	1	2.0
<b>Blood and lymphatic system disorders</b>	48	98.0	Pyrexia	1	2.0
Neutropenia	36	73.5	Swelling face	1	2.0
Lymphopenia	27	55.1	<b>Metabolism and nutrition disorders</b>	4	8.2
Leukopenia	26	53.1	Hypokalaemia	3	6.1
Anaemia	24	49.0	Failure to thrive	1	2.0
Thrombocytopenia	17	34.7	Hypophosphataemia	1	2.0
Cytopenia	1	2.0	<b>Gastrointestinal disorders</b>	2	4.1
Leukocytosis	1	2.0	Abdominal pain	1	2.0
Lymphocytosis	1	2.0	Diarrhoea	1	2.0
<b>Investigations</b>	9	18.4	Vomiting	1	2.0
Neutrophil count decreased	4	8.2	<b>Injury, poisoning and procedural complications</b>	2	4.1
Alanine aminotransferase increased	2	4.1	Humerus fracture	1	2.0
Aspartate aminotransferase increased	2	4.1	Infusion related reaction	1	2.0
White blood cell count decreased	2	4.1	<b>Renal and urinary disorders</b>	2	4.1
Blood alkaline phosphatase increased	1	2.0	Acute kidney injury	1	2.0
Blood creatinine increased	1	2.0	Proteinuria	1	2.0
Blood fibrinogen decreased	1	2.0	<b>Skin and subcutaneous tissue disorders</b>	2	4.1
<b>Infections and infestations</b>	7	14.3	Rash maculo-papular	2	4.1
Appendicitis	1	2.0	<b>Cardiac disorders</b>	1	2.0
COVID-19	1	2.0	Atrial fibrillation <sup>3</sup>	1	2.0
Enterococcal infection	1	2.0	<b>Endocrine disorders</b>	1	2.0
Infection	1	2.0	Inappropriate antidiuretic hormone secretion	1	2.0
Orchitis	1	2.0	<b>Eye disorders</b>	1	2.0
Sepsis <sup>4,5</sup>	1	2.0	Ulcerative keratitis	1	2.0
Septic shock <sup>4</sup>	1	2.0	<b>Hepatobiliary disorders</b>	1	2.0
Urinary tract infection	1	2.0	Cholangitis	1	2.0
<b>Respiratory, thoracic and mediastinal disorders</b>	6	12.2	<b>Immune system disorders</b>	1	2.0
Hypoxia	3	6.1	Contrast media allergy	1	2.0
Bronchial obstruction	1	2.0	<b>Musculoskeletal and connective tissue disorders</b>	1	2.0
Laryngeal inflammation	1	2.0	Muscle spasms	1	2.0
Pleural effusion	1	2.0	<b>Nervous system disorders</b>	1	2.0
Respiratory failure	1	2.0	Headache	1	2.0
<b>Vascular disorders</b>	6	12.2	<b>Reproductive system and breast disorders</b>	1	2.0
Hypertension	4	8.2	Vaginal haemorrhage	1	2.0
Hypotension	2	4.1			

- Well tolerated at doses as high as ~10x10<sup>9</sup> TCR-T cells
- No AE ≥Grade 3 was observed with a frequency ≥10% when excluding expected cytopenia associated with lymphodepletion
- No IMA203-related Grade 5 Adverse Events

All treatment-emergent adverse events (TEAEs) with ≥ Grade 3 regardless of relatedness to study treatment that occurred in at least 1 patient (except for ICANS, where only Grade 1-2 occurred; listed for completeness due to being an adverse event of special interest) are presented. Adverse events were coded using the Medical Dictionary for Regulatory Activities. Grades were determined according to National Cancer Institute Common Terminology Criteria of Adverse Events, version 5.0. Grades for CRS and ICANS were determined according to CARTOX criteria (Neelapu et al., 2018). Patients are counted only once per adverse event and severity classification. Based on interim data extracted from open clinical database (30-Sep-2023); <sup>1</sup> Two patients with disease progression after first IMA203 infusion received exploratory second IMA203 infusion. They had these ≥ Grade 3 TEAEs only after second infusion, which are included in the table: First patient: Abdominal pain, Cytokine release syndrome, Diarrhoea, Hypokalaemia, Proteinuria; Second patient: Humerus fracture, Muscle spasms, Neutropenia, Thrombocytopenia; <sup>2</sup> ICANS: Immune effector cell-associated neurotoxicity syndrome; <sup>3</sup> DLT: Dose limiting toxicity in phase 1a at DL2 reported on March 17, 2021; <sup>4</sup> Fatal Adverse events were not considered related to any study drug; <sup>5</sup> Patient died from sepsis of unknown origin and did not receive IMA203 TCR-T cells.

# Tolerability Data – IMA203 GEN1 at RP2D

## Phase 1a DL4 and Cohort A – All ≥Grade 3 Adverse Events (N=28)

TEAEs by maximum severity for all patients in Ph1a dose escalation DL4 and Ph1b Cohort A dose expansion (RP2D, N=28)<sup>1</sup>

Adverse event (System organ class, Preferred term)	≥ Grade 3		Adverse event (System organ class, Preferred term)	≥ Grade 3	
	No.	%		No.	%
<b>Patients with any adverse event</b>	<b>28</b>	<b>100.0</b>	<b>Table continued...</b>		
<b>Adverse Events of Special Interest</b>	<b>1</b>	<b>3.6</b>	<b>General disorders and administration site conditions</b>	<b>1</b>	<b>3.6</b>
Cytokine release syndrome	1	3.6	Pyrexia	1	3.6
ICANS <sup>2</sup>	0	0.0	<b>Hepatobiliary disorders</b>	<b>1</b>	<b>3.6</b>
<b>Blood and lymphatic system disorders</b>	<b>27</b>	<b>96.4</b>	Cholangitis	1	3.6
Neutropenia	18	64.3	<b>Injury, poisoning and procedural complications</b>	<b>1</b>	<b>3.6</b>
Anaemia	14	50.0	Humerus fracture	1	3.6
Leukopenia	13	46.4	<b>Musculoskeletal and connective tissue disorders</b>	<b>1</b>	<b>3.6</b>
Lymphopenia	11	39.3	Muscle spasms	1	3.6
Thrombocytopenia	9	32.1	<b>Nervous system disorders</b>	<b>1</b>	<b>3.6</b>
Leukocytosis	1	3.6	Headache	1	3.6
Lymphocytosis	1	3.6	<b>Skin and subcutaneous tissue disorders</b>	<b>1</b>	<b>3.6</b>
<b>Investigations</b>	<b>7</b>	<b>25.0</b>	Rash maculo-papular	1	3.6
Neutrophil count decreased	4	14.3			
Alanine aminotransferase increased	2	7.1			
Aspartate aminotransferase increased	2	7.1			
White blood cell count decreased	2	7.1			
Blood alkaline phosphatase increased	1	3.6			
<b>Infections and infestations</b>	<b>3</b>	<b>10.7</b>			
Infection	1	3.6			
Septic shock <sup>3</sup>	1	3.6			
Urinary tract infection	1	3.6			
<b>Respiratory, thoracic and mediastinal disorders</b>	<b>3</b>	<b>10.7</b>			
Hypoxia	2	7.1			
Laryngeal inflammation	1	3.6			
<b>Vascular disorders</b>	<b>3</b>	<b>10.7</b>			
Hypotension	2	7.1			
Hypertension	1	3.6			
<b>Metabolism and nutrition disorders</b>	<b>2</b>	<b>7.1</b>			
Failure to thrive	1	3.6			
Hypokalaemia	1	3.6			
Hypophosphataemia	1	3.6			
<b>Eye disorders</b>	<b>1</b>	<b>3.6</b>			
Ulcerative keratitis	1	3.6			

All treatment-emergent adverse events (TEAEs) with ≥ Grade 3 regardless of relatedness to study treatment that occurred in at least 1 patient (except for ICANS, where only Grade 1-2 occurred; listed for completeness due to being an adverse event of special interest) are presented. Adverse events were coded using the Medical Dictionary for Regulatory Activities. Grades were determined according to National Cancer Institute Common Terminology Criteria of Adverse Events, version 5.0. Grades for CRS and ICANS were determined according to CARTOX criteria (Neelapu et al., 2018). Patients are counted only once per adverse event and severity classification. Based on interim data extracted from open clinical database (30-Sep-2023); <sup>1</sup> One patient in Phase 1a DL4 with disease progression after first IMA203 infusion received exploratory second IMA203 infusion and had these ≥ Grade 3 TEAEs only after second infusion, which are included in the table: Humerus fracture, Muscle spasms, Neutropenia, Thrombocytopenia; <sup>2</sup> ICANS: Immune effector cell-associated neurotoxicity syndrome; <sup>3</sup> Fatal Adverse events were not considered related to any study drug.

- IMA203 was well tolerated at doses as high as ~10x10<sup>9</sup> TCR-T cells
- Most frequent ≥Grade 3 AEs were expected cytopenia associated with lymphodepletion
- No IMA203-related Grade 5 AEs

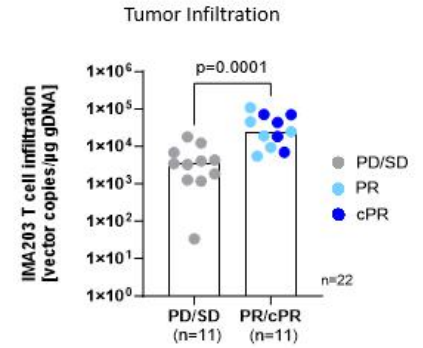
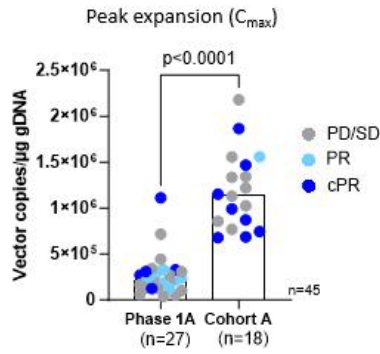
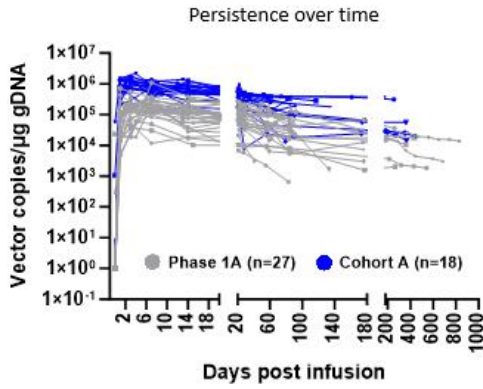


# Biological Data Consistent with Clinical Data – IMA203 GEN1

## IMA203 T cell Levels and Tumor Infiltration across Patients in Phase 1a and Cohort A

Increased levels of IMA203 T cells in the blood of patients in Cohort A following increase of cell dose and switch to T cell enrichment process

IMA203 T cells found in all evaluable tumor tissues, level of infiltration associated with objective responses<sup>1</sup>



Mann-Whitney U test; <sup>1</sup>T cell infiltration for 22 patients (11 non-responder, 11 responder) with 6-week post infusion biopsy available (1 patient with ~4-week, 3 patients with ~13-week post infusion biopsy); PD: Progressive Disease; SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response

# Melanoma Patients – Phase 1a and Cohort A IMA203 GEN1 (N=13)

Cohort	Patient ID	Indication	No of prior treatment lines	Prior treatments	Total infused dose TCR-T cells <sup>1</sup> [x10 <sup>9</sup> ]	BOR	BOR (Max % change of target lesions)	Comment	Reason for Progression
Cohort A	A-DL5-01	Uveal Melanoma	1	ARRY624 + Nivolumab	4.16	cPR	-69.4	Ongoing response 16.0 months post infusion	
Cohort A	A-DL4-03	Cut. Melanoma	7	Dabrafenib + Trametinib Pembrolizumab Dabrafenib + Trametinib Vemurafenib + Cobimetinib Dabrafenib + Trametinib Talenafusp Encorafenib + Binimetinib	1.30	cPR	-78.3	Ongoing response 15.8 months post infusion	
Cohort A	A-DL5-03	Cut. Melanoma	3	Interferon Pembrolizumab Ipilimumab + Nivolumab	5.12	cPR	-65.1	Ongoing response 12.2 months post infusion	
Cohort A	A-DL5-10	Uveal Melanoma	1	SEAGEN CD40 Agonist	2.68	cPR	-40.8	Ongoing response 3.4 months post infusion	
Phase 1a	DL4-02	Cut. Melanoma	5	Dabrafenib + Trametinib Ipilimumab + Nivolumab Nivolumab Ipilimumab + Nivolumab Vemurafenib + Cobimetinib Pembrolizumab	1.07	cPR	-51.4	Response until 4.4 months post infusion	New lesions, progressing non-target lesions
Phase 1a	DL4-06	Cut. Melanoma	4	Pembrolizumab Ipilimumab + Nivolumab Nivolumab	1.21	cPR	-61.4	Response until 3.7 months post infusion	New lesions
Phase 1a	DL4-01	Cut. Melanoma	7	Interferon NY-ESO-1, Tyrosinase, MAGE-A3, TPTE, LIP-MerB-study (experimental therapy) Nivolumab Pembrolizumab Ipilimumab + Nivolumab Decortin + Infliximab Nivolumab + Ipilimumab + Melixot + Infliximab Vemurafenib + Cobimetinib	1.16	PR	-39.0	Unconfirmed response until 2.8 months post infusion	New lesions, progressing target lesions
Phase 1a	DL4-03	Cut. Melanoma	7	Nivolumab Dabrafenib + Trametinib Ipilimumab + Nivolumab Encorafenib + Binimetinib Pembrolizumab Encorafenib + Binimetinib	1.72	PR	-51.6	Unconfirmed response until 2.4 months post infusion	Progressing target lesions
Cohort A	A-DL4-04	Melanoma (Unk. Primary)	2	Ipilimumab + Nivolumab Nivolumab	1.73	SD	0.0	Disease stabilization until 5.7 months post infusion	Non-target lesion progression and a new lesion
Cohort A	A-DL4-05	Cut. Melanoma	5	Nivolumab (re-exposure) Nivolumab + Ipilimumab Dabrafenib + Trametinib Nivolumab	1.63	SD	11.4	Disease stabilization until 5.8 months post infusion	New lesions, target lesion progression
Cohort A	A-DL5-12	Uveal Melanoma	3	Tyrosinase peptides Nivolumab + Ipilimumab + Denosumab	4.50	SD	-22.6	Ongoing disease stabilization 2.2 months post infusion	
Phase 1a	DL4-07	Cut. Melanoma	6	Talenafusp Interferon alpha Pembrolizumab Ipilimumab + Nivolumab Nivolumab LXN354 + Rilovociclib DKY709 Helios	2.09	PD	0.0	Progressive disease 1.4 months post infusion	New lesions, progressing non-target lesions
Cohort A	A-DL4-06	Uveal Melanoma	0	NA	2.56	PD	-6.3	Progressive disease 1.3 months post infusion	New target lesion

<sup>1</sup> Transduced viable CD8 T cells; PD: Progressive Disease; Efficacy population shown (Patients with at least one available tumor response assessment post infusion); SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response; BL: Baseline; BOR: Best Overall Response

# Indications beyond Melanoma – Cohort A IMA203 GEN1 (N=10)

Patient ID	Indication	No of prior treatment lines	Prior treatments	Total infused dose TCR-T cells <sup>1</sup> [x10 <sup>6</sup> ]	BOR	BOR (Max % change of target lesions)	Comment	Reason for Progression
A-DL4-01	Head & Neck Cancer	1	Paclitaxel + Carboplatin	1.92	cPR	-33.3	Response until 5.7 months post infusion	Non-target lesion progression
A-DL5-07	Synovial Sarcoma	2	Melphalan + TNF alpha Doxorubicin + Ifosfamid	6.01	cPR	-44.3	Ongoing response 4.4 months post infusion	
A-DL5-05	Ovarian Cancer	3	Adriamycin + Cytosan + Taxol Carboplatin + Doxil Carboplatin + Taxol	8.84	cPR	-61.7	Response until 4.4 months post infusion	New lesions, target and non-target lesion progression
A-DL4-02	Ovarian Cancer	10	Taxol Gemcitabine + Carboplatin Olaparib Letrozole Rubaparib UPCC 03118 Bevacizumab + Cyclophosphamide Carboplatin Doxorubicin	1.97	cPR	-41.0	Response until 3.8 months post infusion	Non-target lesion progression
A-DL5-06	Synovial Sarcoma	1	Adriamycin + Ifosfamide + Trabectedin	3.94	PR	-74.8	Response until 2.8 months post infusion	Target and non-target lesion progression
A-DL5-08	Small Cell Lung Cancer (SCLC)	4	Cisplatin + Etoposid Carboplatin + Etoposid+ Ateluzumab Topotecan Paclitaxel	5.09	SD	-1.8	Disease stabilization until 3.0 months post infusion	New lesions, target lesion progression
A-DL5-02	Pancreatic NET	3	Lanreotide Streptozocin + 5-Fluorouracil Everolimus	5.12	SD	-21.8	Disease stabilization until 2.3 months post infusion	Non-target lesion progression
A-DL5-04*	Ovarian Cancer	5	Paclitaxel + Carboplatin Niraparib Doxorubicin + Liposomal + Carboplatin 2020-0808 2N C3 + Gemcitabine 2020-0755 COM 7D1 + BMS-986207 + Nivolumab	4.68	PD	50.8	Progressive disease at 1.2 months post infusion	New lesions, target- and non-target lesion progression
A-DL5-09	Ovarian Cancer	4	Paclitaxel + Carboplatin Bevacizumab Doxorubicin + Carboplatin AVB-001 Cell Infusion	6.36	PD	-2.4	Progressive disease at 1.5 months post infusion	New target lesion
A-DL5-11	Synovial Sarcoma	5	Adriamycin + Ifosfamide Pazobanib NY-ESO1-TCR T-Cells Pazobanib BRD9 PROTAC CFT8634	9.36	SD	-26.4	Clinical progression 2.0 months post infusion	Clinical progression

<sup>1</sup> Transduced viable CD8 T cells; PD: Progressive Disease; \*Ovarian cancer patient A-DL5-04 erroneously received one dose of nivolumab and is part of intent-to-treat population (shown here) but not per-protocol population. SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response; BL: Baseline; BOR: Best Overall Response





## Appendix – Additional Data

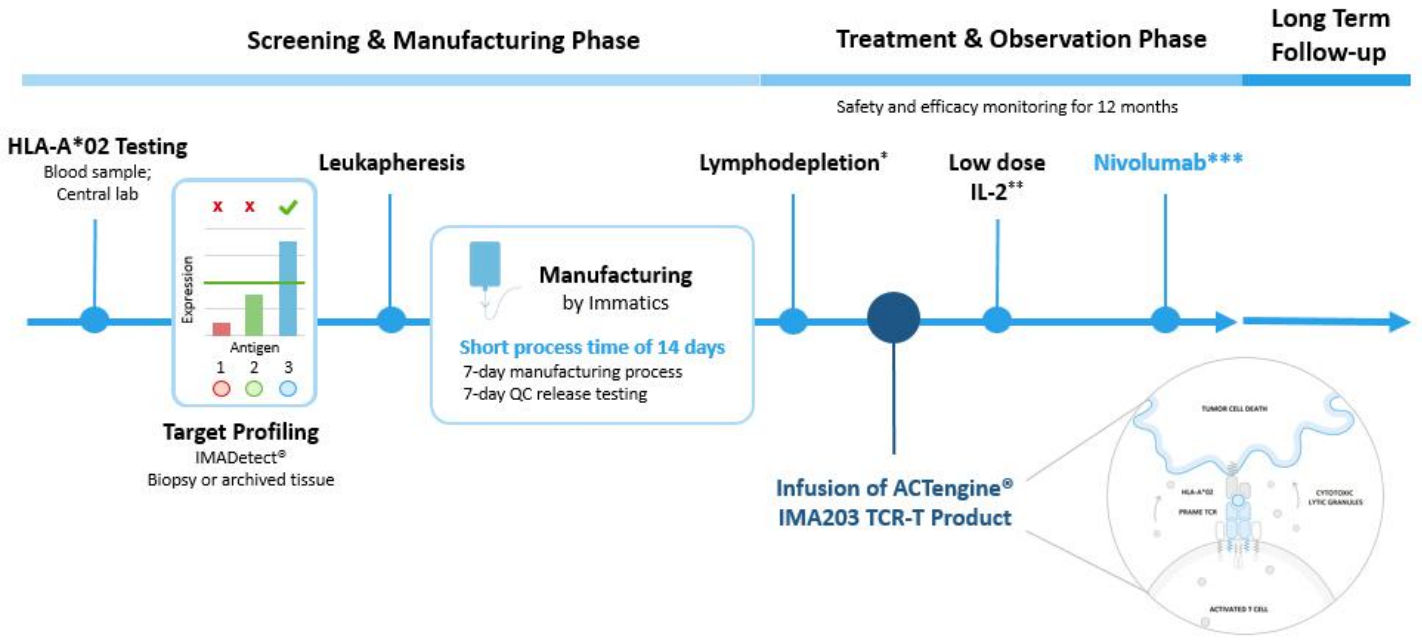
1. Patient Flow and PRAME Expression in Pre-Treatment Tumor Biopsies
  2. Dose Escalation and Cohort A IMA203 GEN1
  3. Cohort B IMA203 GEN1 + Nivolumab
  4. Cohort C IMA203 GEN2
  5. Manufacturing and *in vivo* Engraftment Data IMA203 GEN1 and IMA203CD8 GEN2
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## Cohort B: ACTengine® IMA203 TCR-T + Nivolumab

### Summary

- IMA203 TCR-T combined with nivolumab was **well tolerated** with no unexpected adverse events or additive toxicities
- The combination therapy showed **clinical activity** with one durable objective response exceeding 12 months post infusion and tumor shrinkage in 4 of 6 evaluable patients
- **No synergistic anti-tumor effects** were observed:
  - Clinical activity in combination cohort was lower compared to IMA203 monotherapy (Cohort A), but comparison is confounded by more unfavorable patient characteristics and lower applied median cell dose in IMA203 + nivolumab combination cohort
  - Trend towards lower T cell infiltration as well as increased terminal differentiation and signs of exhaustion of IMA203 T cells in combination with nivolumab
  - Data set is too small and heterogenous to draw firm conclusions
- Patient case study could indicate **potential for clinical benefit of IMA203 TCR-T treatment in combination with checkpoint inhibitors in patients with PD-1/PD-L1 upregulation**
- **IMA203 in combination with nivolumab deprioritized due to**
  - high monotherapy activity in Cohort A IMA203 and Cohort C IMA203CD8
  - lack of synergistic anti-tumor effects

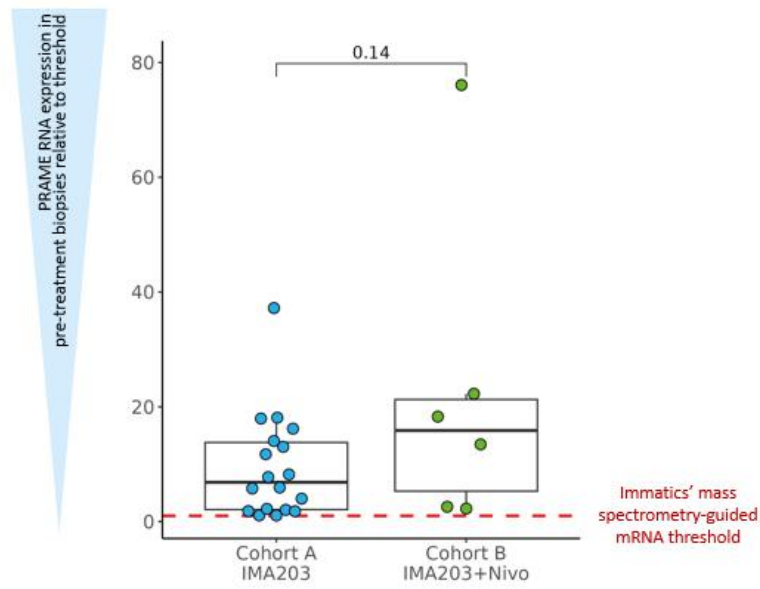
# Patient Flow – Cohort B IMA203 + Nivolumab



<sup>†</sup> 30 mg/m<sup>2</sup> Fludarabine and 500 mg/m<sup>2</sup> Cyclophosphamide for 4 days; <sup>\*\*</sup> 1m IU daily days 1-5 and twice daily days 6-10; <sup>\*\*\*</sup> Nivolumab at Day 14, or Day 21 post IMA203 infusion. Two weeks after the first infusion of nivolumab and thereafter approximately every 4 weeks, patients receive nivolumab for up to 1 year

# PRAME Expression in Pre-Treatment Tumor Biopsies

## Comparable PRAME Expression Levels in Patients Treated in Cohort A and B



## Patient Characteristics

### Dose Escalation vs. Cohort A IMA203 vs. Cohort B IMA203 + Nivolumab

	Phase 1a	Phase 1b	
	Dose Escalation	Dose Expansion	
	All pts*	Cohort A IMA203 <sup>†</sup>	Cohort B IMA203+Nivo <sup>**</sup>
<b>Patients treated</b>	<b>27</b>	<b>18</b>	<b>6</b>
<b>Age</b> Median (min, max)	<b>55.0</b> (18, 72)	<b>52.5</b> (31, 79)	<b>51.5</b> (38, 63)
<b>Prior lines of treatment</b> Median (min, max)	<b>4.0</b> (1,8)	<b>3.0</b> (0, 10)	<b>5.5</b> (0, 8)
<b>LDH at baseline</b> >1 x ULN [% of patients]	<b>66.7</b>	<b>50.0</b>	<b>66.7</b>
<b>Baseline tumor burden</b> Target lesion sum of diameter [mm] Median (min, max)	<b>133.0</b> (29.0, 219.7)	<b>58.9</b> (21.0, 207.3)	<b>117.3</b> (37.0, 280.2)
<b>Dose Level</b>	<b>DL1-4</b>	<b>DL4/5</b>	<b>DL4</b>
<b>Total infused dose</b> Median transduced viable CD8 T cells infused [x10 <sup>9</sup> ] (min, max)	<b>0.41</b> (0.08, 2.09)	<b>4.33</b> (1.30, 9.36)	<b>2.24</b> (0.66, 2.71)

- Heavily pre-treated, metastatic last-line patients that have exhausted all available SOC treatments
- Patients in IMA203+Nivo cohort had more prior lines of treatment and higher tumor burden while receiving lower cell numbers compared to IMA203 monotherapy cohort (i.e. lower E:T ratio in IMA203+Nivo cohort)<sup>1</sup>

\*Efficacy population in Phase 1a and Cohort A: patients with at least one available tumor response assessment post infusion; \*\*Efficacy per-protocol population Cohort B: patients received IMA203 + nivolumab and have at least one available tumor response assessment post infusion or reported clinical PD; <sup>†</sup>Demonstrated to be associated with durable response: Locke et al. 2020 Blood Advances

## Most Frequent Adverse Events – Cohort B IMA203 + Nivolumab (N=7)<sup>1</sup> Manageable Treatment-Emergent Adverse Events (TEAEs)

- **Expected cytopenia (Grade 1-4)** associated with lymphodepletion in all patients
- **Low-moderate (Grade 1-2) cytokine release syndrome (CRS)** in 100% (7/7) of patients
  - 57% (4/7) of patients had Grade 1 CRS
  - 43% (3/7) of patients had Grade 2 CRS
- **Low-grade ICANS<sup>2</sup>** in 14% (1/7) of patients
- **No events indicating immune-mediated adverse reactions in association with nivolumab**
- **No hints that combination with nivolumab increased number or severity of observed TEAEs**

**IMA203 TCR-T in combination with nivolumab was well tolerated,  
no unexpected or additive toxicities compared to IMA203 TCR-T monotherapy**

<sup>1</sup> One patient treated with IMA203 + nivolumab withdrew consent 1.1 months post infusion (prior to first scan) and is included safety per-protocol population, but not efficacy per-protocol population.  
<sup>2</sup> ICANS: Immune Effector Cell-Associated Neurotoxicity Syndrome; CRS and ICANS graded by CARTOX criteria (Neelapu et al., 2018)

# Detailed Tolerability Data – Cohort B IMA203 + Nivolumab (N=7)<sup>1</sup>

## All ≥Grade 3 Adverse Events (N=7)

TEAEs by maximum severity for all patients in Cohort B IMA203 + Nivolumab (N=7)

Adverse event (System organ class, preferred term)	≥ Grade 3	
	No.	%
<b>Patients with any adverse event</b>	<b>7</b>	<b>100.0</b>
<b>Adverse events of special interest</b>	<b>0</b>	<b>0.0</b>
Cytokine release syndrome	0	0.0
Immune effector cell-associated neurotoxicity syndrome	0	0.0
<b>Blood and lymphatic system disorders</b>	<b>7</b>	<b>100.0</b>
Neutropenia	7	100.0
Anaemia	6	85.7
Lymphopenia	6	85.7
Thrombocytopenia	3	42.9
Leukopenia	2	28.6
Febrile neutropenia	1	14.3
<b>General disorders and administration site conditions</b>	<b>2</b>	<b>28.6</b>
Pyrexia	2	28.6
<b>Investigations</b>	<b>1</b>	<b>14.8</b>
Aspartate aminotransferase increased	1	14.3

- IMA203 TCR-T in combination with nivolumab was well tolerated
- No unexpected or additive toxicities compared to IMA203 TCR-T monotherapy
- Most frequent ≥Grade 3 AEs were expected cytopenia associated with lymphodepletion
- No IMA203-related Grade 5 AEs

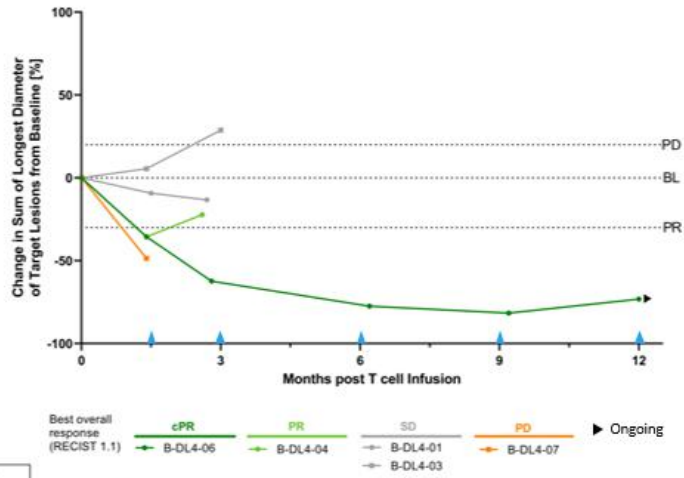
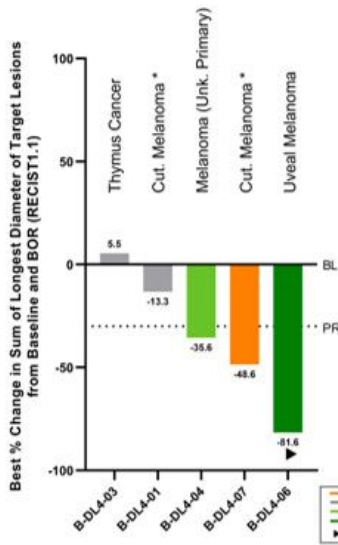
All treatment-emergent adverse events (TEAEs) with ≥ Grade 3 regardless of relatedness to study treatment that occurred in at least 1 patient (except for ICANS and CRS, where only lower grades occurred; listed for completeness due to being adverse events of special interest) are presented. Adverse events were coded using the Medical Dictionary for Regulatory Activities. Grades were determined according to National Cancer Institute Common Terminology Criteria of Adverse Events, version 5.0. Grades for CRS and ICANS were determined according to CARTOX criteria (Neelapu et al., 2018). Patients are counted only once per adverse event and severity classification. Based on interim data extracted from open clinical database (30-Sep-2023)

<sup>1</sup> One patient treated with IMA203 + nivolumab withdrew consent 1.1 months post infusion (prior to first scan) and is included safety per-protocol population, but not efficacy per-protocol population;



# Best Overall Response & Durability – Cohort B IMA203 + Nivolumab (N=6)

## Ongoing Durable Response 12+ Months post Treatment



**ORR<sup>1</sup> 33% (2/6)**  
**cORR<sup>2</sup> 17% (1/6)**

- Tumor shrinkage in 4 of 6 patients
- Ongoing long-term durable response 12+ months post treatment in melanoma patient
- All cut. melanoma patients were CPI-refractory
- Tumor burden of patient B-DL4-04 was among the highest we ever treated with tumor regression in multiple lesions observed (see patient case)
- Patient B-DL4-07 with significant reduction of target lesions but progression of non-target lesion in the brain, thus PD in BOR analysis

▲ Scans at approximately week 6, month 3 and then every 6 months  
 Pt B-DL4-05 not shown due to clinical progression prior to 1<sup>st</sup> post infusion scan, response assessment not available, considered as non-responder for ORR and cORR

<sup>1</sup> Initial ORR: Objective response rate according to RECIST 1.1 at any post infusion scan; <sup>2</sup> Confirmed ORR (cORR): Confirmed objective response rate according to RECIST 1.1 for patients with at least two available post infusion scans or patients with progressive disease (PD) at any prior timepoint, patients with ongoing unconfirmed PR not included in cORR calculation; PD: Progressive Disease; SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response; BL: Baseline; BOR: Best Overall Response; CPI: Checkpoint Inhibitor. \* Maximum change of target lesions at time of tumor progression. Data cut-off Sep 30, 2023 44



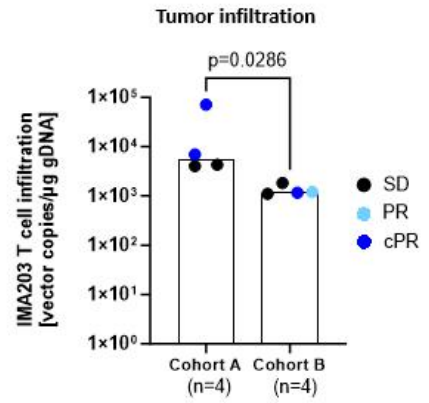
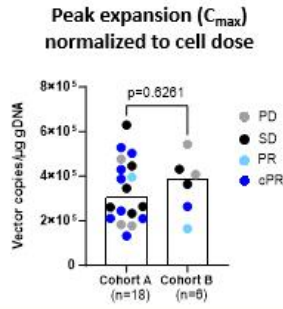
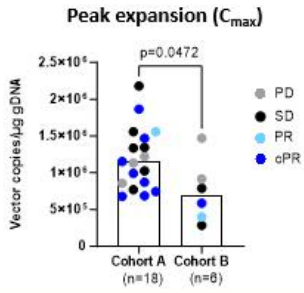
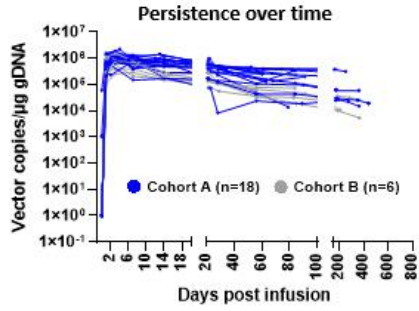
## Particularly Hard-to-Treat Patient Population – Cohort B IMA203 + Nivolumab

Patient ID	Indication	No of prior treatment lines	Prior treatments	Total infused dose TCR-T cells [x10 <sup>9</sup> ]	BOR	BOR (Max % change of target lesions)	Comment	Reason for Progression
B-DL4-06	Uveal Melanoma	0	NA	2.22	cPR	-81.2	Ongoing response 12 months post infusion	On trial
B-DL4-04	Melanoma (Unk. Primary)	6	Nivolumab/NCTN-214, Nivolumab/ipilimumab, Encorafenib/Binimetinib, CLX254C32210 (Pamrafli+ERK1) Encorafenib/Binimetinib/Pembrolizumab, Carboplatin/Paclitaxel, Dabrafenib/Trametinib, Nivolumab/ipilimumab, Encorafenib/Binimetinib Nivolumab/ipilimumab, Nivolumab	2.42	PR	-35.6	Unconfirmed response until 2.6 months post infusion	Unequivocal progression of non-target lesion in the adrenal gland
B-DL4-01	Cut. Melanoma	6	Nivolumab/ipilimumab, Encorafenib/Binimetinib Nivolumab/ipilimumab, Nivolumab	2.17	SD	-13.3*	Disease stabilization until 2.7 months post infusion	Unequivocal progression of non-target lesion in the lung and new lung lesion
B-DL4-03	Thymus cancer	2	Carboplatin/Paclitaxel, Doxorubicin/Cisplatin/Cyclophosphamide	0.66	SD	5.5	Disease stabilization until 3.0 months post infusion	Target Lesion progression
B-DL4-07	Cut. Melanoma	5	Pembrolizumab, Dabrafenib/Trametinib, Nivolumab/ipilimumab, Nivolumab, Encorafenib/Binimetinib Acirnamycine/ Ifosfamide/Vincristine, Ifosfamide/Doxorubicin, Etoposide/Topotecan/Carboplatin/Cyclophosphamide Trofosfamide/Etoposide/Idarubicine Doxorubicin/Ifosfamide, Carboplatin/Topotecan, Vincristine	2.71	PD	-48.6*	Progressive disease at 1.4 months post infusion	Unequivocal progression of non-target lesion in the brain
B-DL4-05	Rhabdomyosarcoma	8	Vincristin/ Ifosfamid/ Doxorubicin, Epirubicin/ Ifosfamid, Gemcitabin/ Docetaxel, Pazopanib, Trabectedin	2.25	PD	NA	Clinical progression at 0.9 months post infusion (prior to first scan)	Clinical progression (persistent rise in LDH, growing lymph node)
B-DL4-02	Fibrosarcoma	5	Vincristin/ Ifosfamid/ Doxorubicin, Epirubicin/ Ifosfamid, Gemcitabin/ Docetaxel, Pazopanib, Trabectedin	1.07	NA	NA	Withdrawal of consent 1.1 months post infusion (prior to first scan); safety population	NA

\* Maximum change of target lesions at time of tumor progression.

# IMA203 T cell Levels – Molecular Immunomonitoring

## Cohort A IMA203 vs. Cohort B IMA203 + Nivolumab



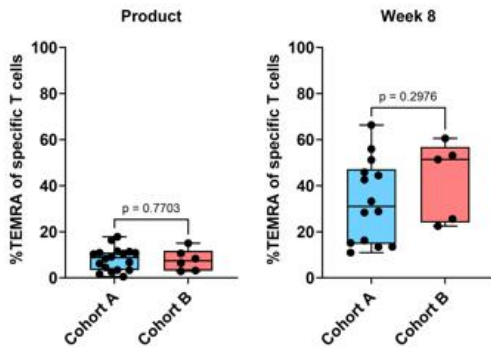
Comparable cell dose-dependent engraftment and peripheral blood kinetics of IMA203 T cells in Cohort A and C while lower tumor infiltration in combination with nivolumab

# IMA203 T cell Activation and Differentiation

## Cohort A IMA203 vs. Cohort B IMA203 + Nivolumab

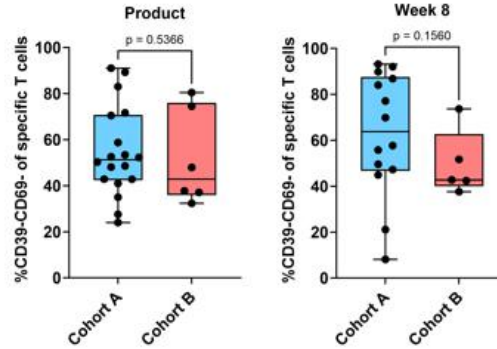
### Terminal differentiation

#### TEMRA\*



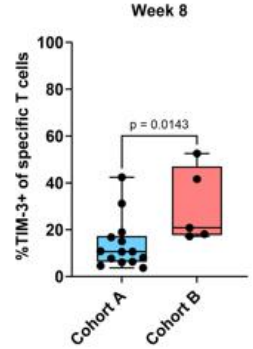
### Stem-like phenotype

#### CD39- CD69-



### Exhaustion surrogate receptor

#### TIM-3



Trend towards increased terminal differentiation of IMA203 T cells and exhaustion surrogate receptor expression in combination with nivolumab

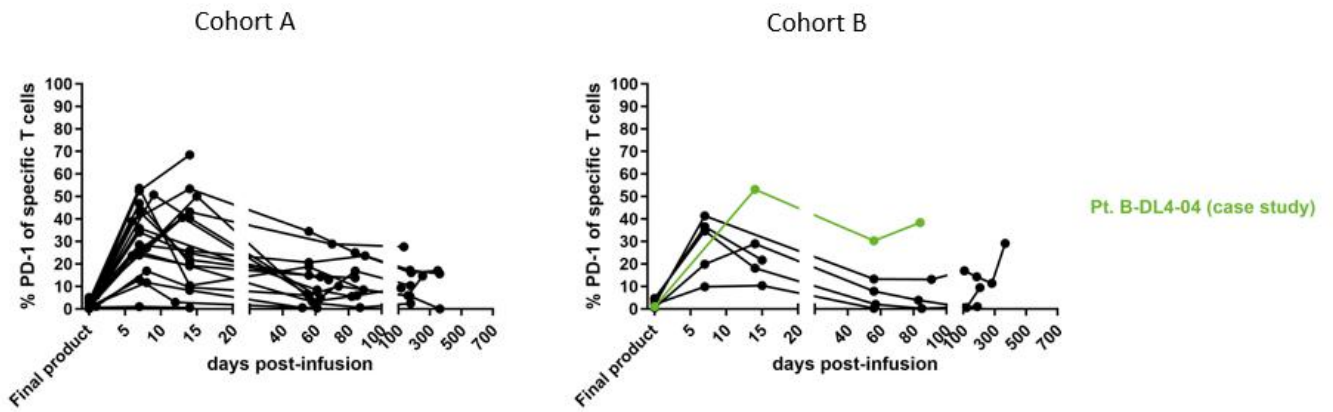
Cohort A: n=18  
Cohort B: n=6

Statistical Test: Mann Whitney; \*TEMRA (CCR7- CD45RA+), CD39-CD69-, and TIM-3: for patients B-DL4-05, A-DL5-04, A-DL5-09, A-DL5-10, and A-DL5-12 data not available for week 8

Data cut-off Sep 30, 2023 47

# Kinetics of PD-1<sup>+</sup> Frequency on IMA203 T Cells

Cohort A IMA203 vs. Cohort B IMA203 + Nivolumab



Sustained PD-1 expression on IMA203 T cells after initial activation observed in few patients

Cohort A: n=18  
Cohort B: n=6

\*Patient B-DL4-04 did not have available samples for analysis of week 1 and month 6

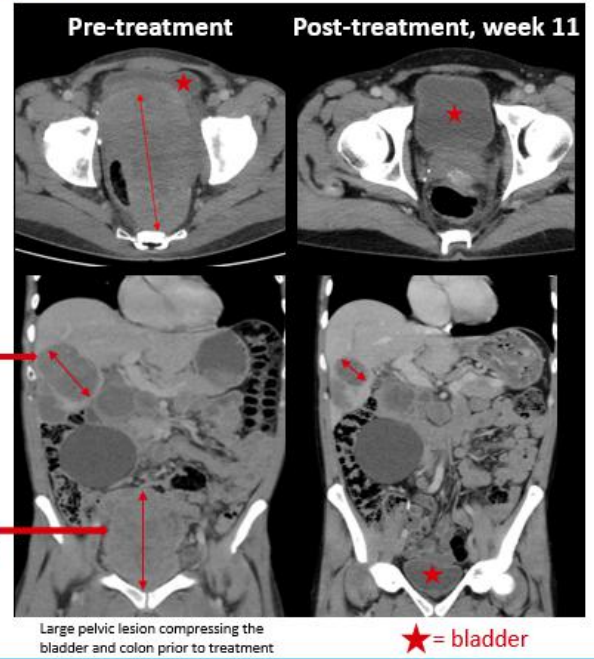
# Patient Case B-DL4-04: Tumor Reduction in Multiple Large Metastatic Lesions

## Observed Sustained Clinical Benefit in Patient despite PD at Week 11

Clinical benefit observed despite formally being a patient with early PD after unconfirmed PR according to RECIST 1.1

50-year-old male patient with highly refractory malignant melanoma (unknown primary, BRAFV600E mutation) and lesions in multiple organs entering IMA203 Cohort B

- 6 prior lines of systemic therapies, LDH at baseline 2.9xULN
  - 5 target lesions (liver, lung, left adrenal gland, 2 lymph nodes)
  - 280.2 mm target lesion sum → among the patients with highest tumor burden we have treated so far
  - 4 non-target lesions (liver, lung, right adrenal gland, large pelvic tumor bulk)
- Tumor regression in multiple lesions after IMA203 + nivolumab treatment, pelvic tumor bulk reduced from 11.5 cm to ~3.5 cm<sup>2</sup>
  - Treatment provided sustained improvement of tumor-related symptoms<sup>1</sup>
  - Patient was PD (pararenal metastases) at week 11 and switched to pembrolizumab + lenvatinib treatment<sup>1</sup>. As of data cut off patient is still alive ~13 months post IMA203 + nivolumab treatment<sup>1</sup>
  - **Patient case study could indicate potential clinical benefit of IMA203 + checkpoint inhibitors in patients with PD-1/PD-L1 upregulation**



<sup>1</sup> Per treating physician; CT scans courtesy of treating physician



## Appendix – Additional Data

1. Patient Flow and PRAME Expression in Pre-Treatment Tumor Biopsies
  2. Dose Escalation and Cohort A IMA203 GEN1
  3. Cohort B IMA203 GEN1 + Nivolumab
  4. Cohort C IMA203 GEN2
  5. Manufacturing and *in vivo* Engraftment Data IMA203 GEN1 and IMA203CD8 GEN2
- 
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# Tolerability Data – Cohort C IMA203CD8 GEN2

## All ≥Grade 3 Adverse Events (N=12)

TEAEs by maximum severity for all patients in Cohort C (N=12)

Adverse event (System organ class, preferred term)	≥ Grade 3	
	No.	%
<b>Patients with any adverse event</b>	<b>12</b>	<b>100.0</b>
<b>Adverse events of special interest</b>	<b>3</b>	<b>25.0</b>
Cytokine release syndrome <sup>1</sup>	3	25.0
Immune effector cell-associated neurotoxicity syndrome	0	0.0
<b>Blood and lymphatic system disorders</b>	<b>11</b>	<b>91.7</b>
Neutropenia	9	75.0
Anaemia	8	66.7
Lymphopenia	8	66.7
Thrombocytopenia	4	33.3
Leukopenia	2	16.7
<b>Investigations</b>	<b>4</b>	<b>33.3</b>
Aspartate aminotransferase increased	2	16.7
Neutrophil count decreased	2	16.7
Alanine aminotransferase increased	1	8.3
Blood alkaline phosphatase increased	1	8.3
Blood bilirubin increased	1	8.3
Gamma-glutamyltransferase increased	1	8.3
<b>Metabolism and nutrition disorders</b>	<b>2</b>	<b>16.7</b>
Hypermagnesaemia	1	8.3
Hypoalbuminaemia	1	8.3
Hypophosphataemia	1	8.3
<b>Nervous system disorders</b>	<b>2</b>	<b>16.7</b>
Neurotoxicity <sup>2</sup>	1	8.3
Syncope	1	8.3
<b>Immune system disorders</b>	<b>1</b>	<b>8.3</b>
Haemophagocytic lymphohistiocytosis <sup>2</sup>	1	8.3
<b>Infections and infestations</b>	<b>1</b>	<b>8.3</b>
Infection	1	8.3

- Manageable tolerability
- Most frequent ≥Grade 3 AEs were expected cytopenia associated with lymphodepletion
- No IMA203CD8-related Grade 5 Adverse Events
- Dose escalation ongoing

All treatment-emergent adverse events (TEAEs) with ≥ Grade 3 regardless of relatedness to study treatment that occurred in at least 1 patient (except for ICANS, where no event was documented; listed for completeness due to being an adverse event of special interest) are presented. Adverse events were coded using the Medical Dictionary for Regulatory Activities. Grades were determined according to National Cancer Institute Common Terminology Criteria of Adverse Events, version 5.0. Grades for CRS and ICANS were determined according to CARTOX criteria (Neelapu et al., 2018). Patients are counted only once per adverse event and severity classification. Based on interim data extracted from open clinical database (30-Sep-2023). <sup>1</sup> DLT: Dose limiting toxicity in patient DL4B-04. <sup>2</sup> DLTs in patient DL4B-01.

# Patients Treated in Cohort C IMA203CD8

Patient ID	Indication	No of prior treatment lines	Prior treatments	Total infused dose TCR-T cells <sup>1</sup> (x10 <sup>9</sup> )	BOR	BOR (Max % change of target lesions)	Comment	Reason for Progression
C-DL3-02	Cut. Melanoma	3	Ipilimumab + Nivolumab Nivolumab Binimetinib	0.93	cPR	-74.4	Ongoing response 12.8 months post infusion	
C-DL4a-01	Uveal Melanoma	4	Transarterial chemo-embolization right liver Ipilimumab + Nivolumab Pembrolizumab Tebentafusp	0.54	cPR	-45.0	Ongoing response (after initial SD) 7.8 months post infusion	
C-DL4a-02	Cut. Melanoma	3	Interferon Pembrolizumab Ipilimumab + Nivolumab	1.07	cPR	-62.3	Ongoing response 5.3 months post infusion	
C-DL3-04	Synovial Sarcoma	3	Adriamycin + Ifosfamide Doxorubicin + Dacarbazine Pazopanib	1.00	cPR	-42.2	Response until 4.9 months post infusion <sup>2</sup>	New lesions, target and non-target lesion progression <sup>2</sup>
C-DL4b-02	Cut. Melanoma	3	Pembrolizumab Ipilimumab + Nivolumab Nivolumab	1.78	cPR	-36.0	Ongoing response 3.4 months post infusion	
C-DL4a-03	Synovial Sarcoma	2	Doxorubicin Ifosfamid	1.56	PR	-36.7	Ongoing unconfirmed response (after initial SD) 4.8 months post infusion	
C-DL4b-04	Synovial Sarcoma	1	Doxorubicin + Ifosfamide + Mesna	2.05	PR	-54.5	Ongoing unconfirmed response 2.4 months post infusion	
C-DL3-01	Synovial Sarcoma	5	Doxorubicin + Ifosfamid Doxorubicin + Ifosfamid Doxorubicin Trabectedin Ifosfamid	0.89	SD	-1.1	Disease stabilization until 2.8 months post infusion	New lesions, target and non-target lesion progression
C-DL3-03	Cut. Melanoma	3	Ipilimumab + Nivolumab Dabrafenib + Trametinib Pembrolizumab + Dabrafenib + Trametinib	0.64	SD	-36.7	Disease stabilization until 2.8 months post infusion	New target lesion
C-DL4b-01	Cut. Melanoma	4	CMP-100 + Nivolumab Encorafenib + Binimetinib Ipilimumab + Nivolumab Encorafenib + Binimetinib	1.89	SD	-7.6	Disease stabilization until 2.2 months post infusion	Non-target lesion progression
C-DL4b-03	Synovial Sarcoma	3	Doxorubicin + Ifosfamide Votrient Pazopanib	1.49	SD	-23.5	Ongoing disease stabilization 2.9 months post infusion	
C-DL4a-04	Uterine Cancer	2	Carboplatin + Paclitaxel Pembrolizumab + Lenvatinib	1.27	PD	NA	Progressive disease 1.7 months post infusion	New lesions, target and non-target lesion progression

<sup>1</sup> Transduced viable CD8 T cells; <sup>2</sup> Investigator information; PD: Progressive Disease; SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response; BL: Baseline; BOR: Best Overall Response





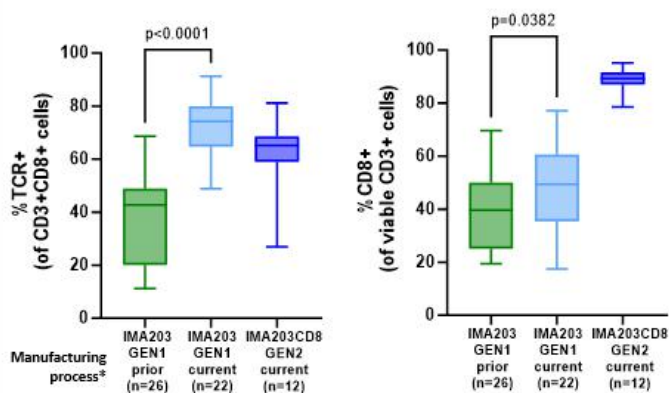
## Appendix – Additional Data

1. Patient Flow and PRAME Expression in Pre-Treatment Tumor Biopsies
  2. Dose Escalation and Cohort A IMA203GEN1
  3. Cohort B IMA203 GEN1 + Nivolumab
  4. Cohort C IMA203 GEN2
  5. **Manufacturing and *in vivo* Engraftment Data IMA203 GEN1 and IMA203CD8 GEN2**
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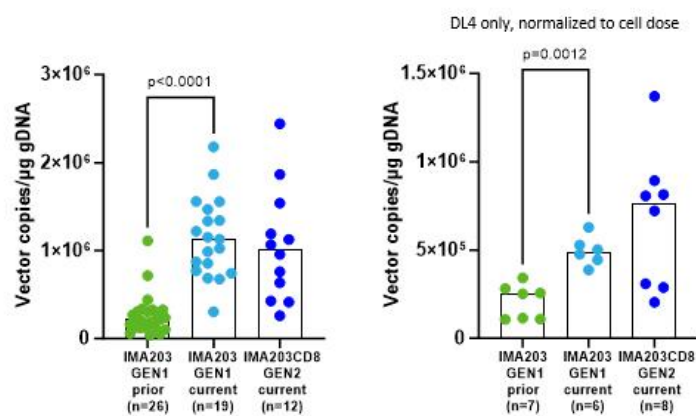
# Favorable TCR-T Product Characteristics and High TCR-T Levels in Patients

## Manufacturing Improvements Implemented in Phase 1b Enhance Key Features of the Cell Product

### Robust TCR-T product features



### Increased peak IMA203 T cell levels in patients



**Current manufacturing success rate of >95% to reach RP2D of  $1-10 \times 10^9$  TCR-T cells for IMA203**

\*Current: T cell enrichment process using monocyte depletion (negative selection) or CD8/CD4 positive selection; prior: manufacturing process without specific T cell enrichment

# Delivering

the Power of T cells  
to Cancer Patients



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# Immatics Corporate Presentation

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November 08, 2023



*Delivering the Power of T cells to Cancer Patients*

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## Two Clinical-Stage Modalities

Pipeline of TCR-T and TCR Bispecific product candidates in clinical & preclinical development



## Clinical PoC for Cell Therapy

Anti-tumor activity and durability of response across multiple solid tumors in early TCR-T clinical development



## Differentiated Platforms

Unique technologies to identify true cancer targets and right TCRs



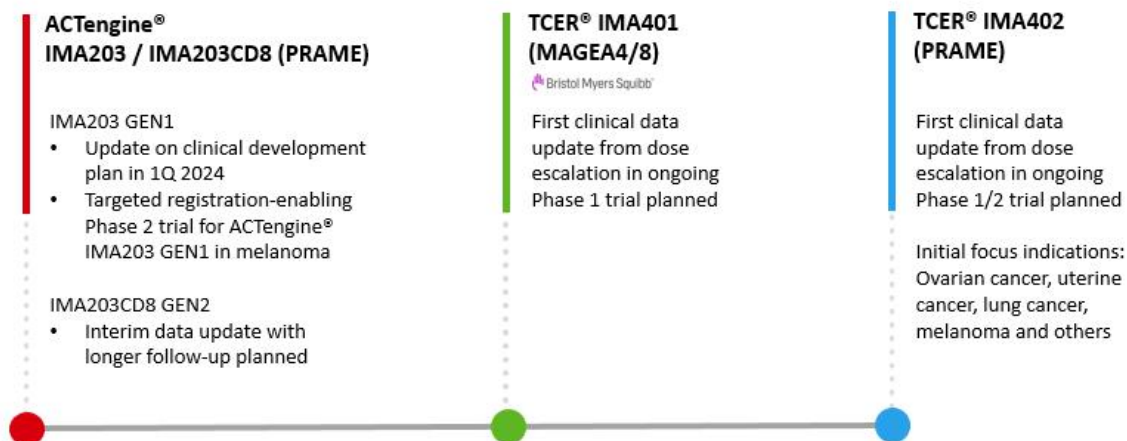
## Therapeutic Opportunity

Potential for addressing large patient populations with high prevalence targets in solid tumors

# Upcoming 2024 Catalysts for ACTengine® and TCER® Clinical Lead Assets

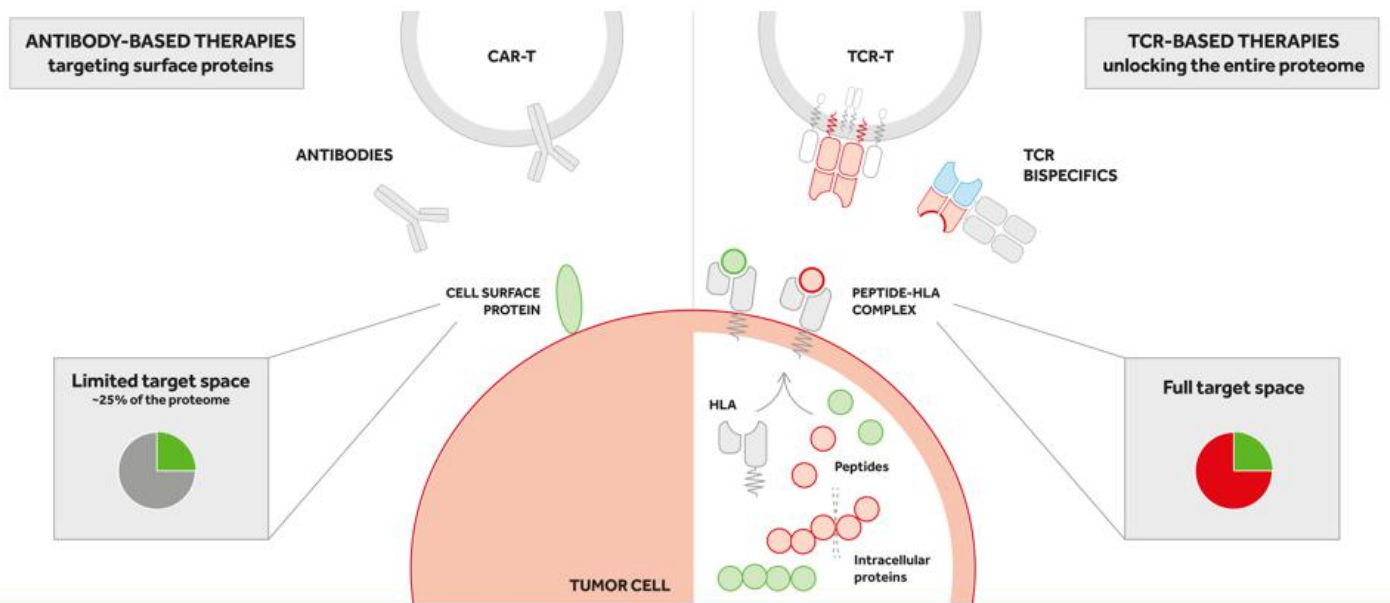


Projected Cash Runway Well into 2026 to Reach Multiple Value Inflection Points

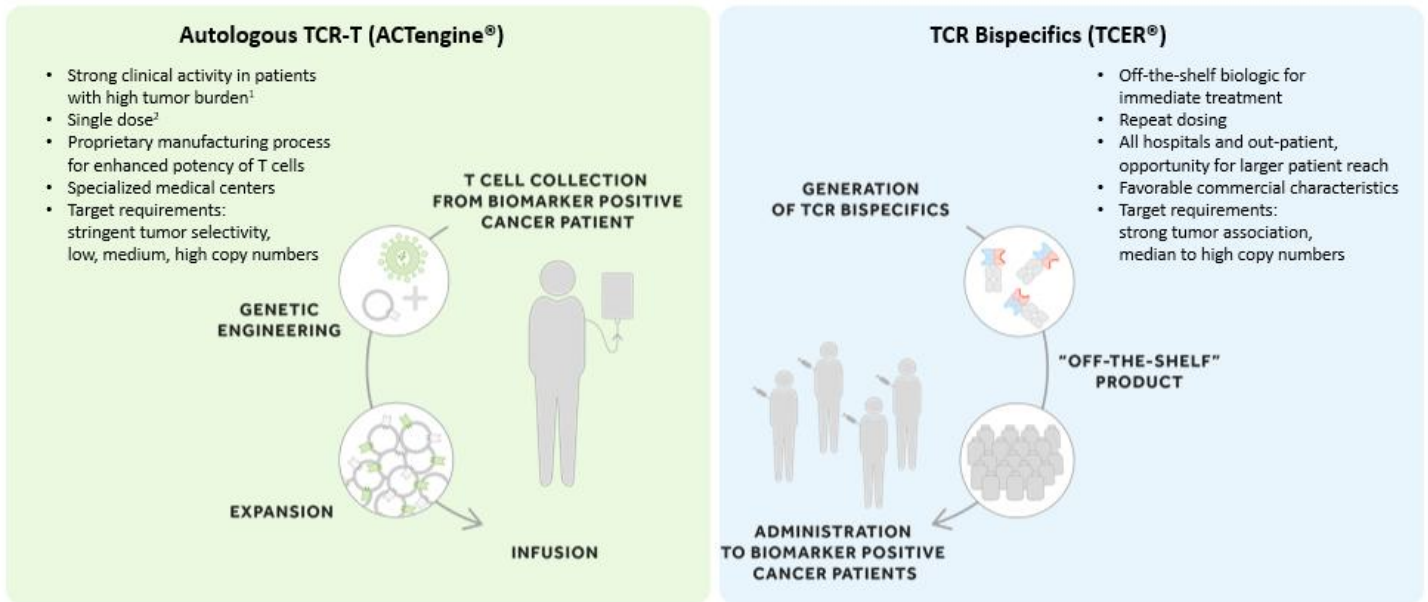


Updates planned across the entire clinical portfolio throughout 2024

# Our TCR-based Approaches Leverage the Full Target Space beyond the Cancer Cell Surface







## Differentiated positioning of ACTEngine® vs. TCER® based on patient population and medical need

# Our Pipeline of TCR-based Adoptive Cell Therapies and Bispecifics



**Intro** <sup>1</sup> Phase 1a: Dose escalation, Phase 1b: Dose expansion; <sup>2</sup> Immatics' proprietary ACTallo® platform utilizing Editas' CRISPR gene editing technology; <sup>3</sup> mRNA-enabled *in vivo* expressed TCER® molecules; IMA203 Cohort B (IMA203 in combination with an immune checkpoint inhibitor) has previously been deprioritized

# Immatics & Moderna – A Strategic Multi-Platform R&D Collaboration

## Combining Immatics' Target and TCR Platforms with Moderna's mRNA Technology



### TCER<sup>®</sup> mRNA Approach

Development of mRNA-enabled *in vivo* expressed half-life extended TCER<sup>®</sup> molecules targeting cancer-specific HLA-presented peptides

Option for global P&L sharing for most advanced TCER<sup>®</sup> program

### mRNA Cancer Vaccines

Development of mRNA cancer vaccines by leveraging Moderna's mRNA technology and Immatics' target discovery platform XPRESIDENT<sup>®</sup> and bioinformatics and AI platform XCUBE<sup>™</sup>

### TCR-T + mRNA Vaccine Combo

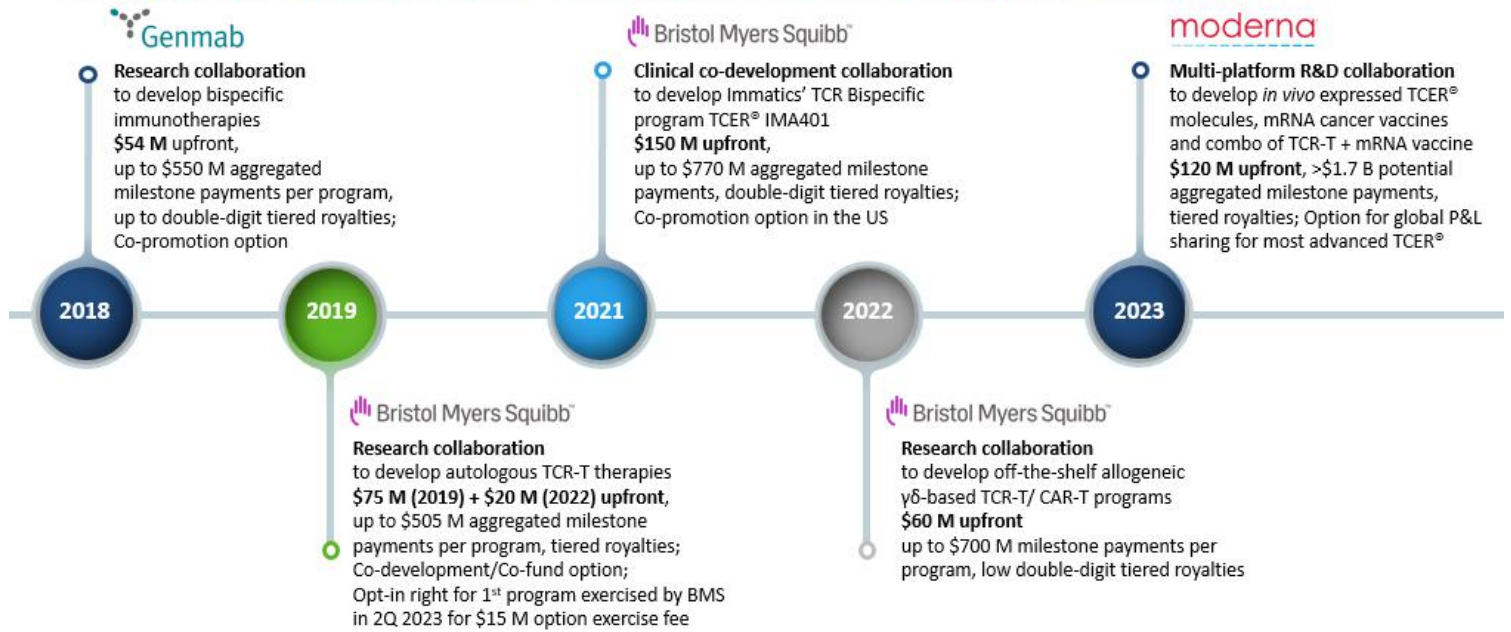
Evaluation of Immatics' IMA203 TCR-T therapy targeting PRAME in combination with Moderna's PRAME mRNA-based cancer vaccine<sup>1</sup>

### Economics

- \$120 million upfront cash payment plus research funding
- >\$1.7 billion potential development, regulatory & commercial milestones
- Potential for tiered royalties on global net sales of TCER<sup>®</sup> products and certain cancer vaccine products commercialized under the agreement

# Strategic Collaborations

Synergistic Expertise that Can Foster Transformative Innovations across Various Modalities



## IMA203 / IMA402 PRAME

Uterine Carcinoma – 97%  
 Uterine Carcinosarcoma – 100%  
 Sarcoma Subtypes – up to 100%  
 Cut. Melanoma  $\geq$  95%  
 Uveal Melanoma<sup>1</sup>  $\geq$  91%  
 Ovarian Carcinoma – 84%  
 Squamous NSCLC – 68%  
 TNBC – 63%  
 Small Cell Lung Cancer – 45%  
 Kidney Carcinoma – up to 40%  
 Cholangiocarcinoma – 33%  
 HNSCC – 27%  
 Esophageal Carcinoma – 27%  
 Breast Carcinoma – 26%  
 Adeno NSCLC – 25%  
 HCC – 18%  
 Bladder Carcinoma – 18%

## IMA401 MAGEA4/8

Squamous NSCLC – 52%  
 Sarcoma Subtypes – up to 60%  
 HNSCC – 36%  
 Bladder Carcinoma – 29%  
 Uterine Carcinosarcoma – 29%  
 Esophageal Carcinoma – 23%  
 Ovarian Carcinoma – 23%  
 Melanoma – 18%

## IMA204 COL6A3 Exon 6

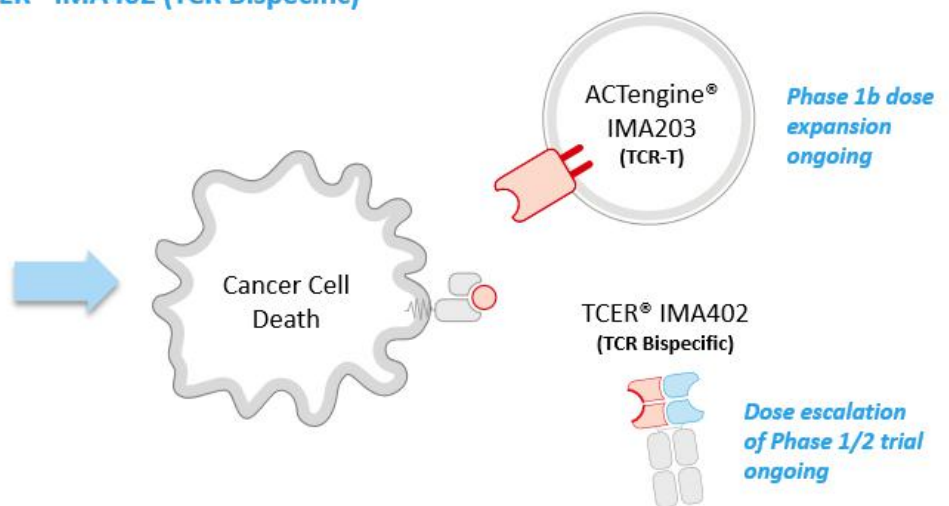
Pancreatic Carcinoma – 76%  
 Breast Carcinoma – 77%  
 Stomach Carcinoma – 67%  
 Sarcoma – 63%  
 Colorectal Carcinoma – 60%  
 Esophageal Carcinoma – 60%  
 Squamous NSCLC – 55%  
 Adeno NSCLC – 57%  
 HNSCC – 56%  
 Uterine Carcinosarcoma – 50%  
 Mesothelioma – 44%  
 Cholangiocarcinoma – 36%  
 Melanoma – 35%  
 Bladder Carcinoma – 34%  
 Ovarian Carcinoma – 31%

**ACTengine® and TCER® targets demonstrate high prevalence in multiple solid cancers**

# Realizing the Full Multi-Cancer Opportunity of PRAME

## ACTengine® IMA203 (TCR-T) and TCER® IMA402 (TCR Bispecific)

Indication	% PRAME positive patients <sup>1</sup>
Uterine Carcinoma	97%
Uterine Carcinosarcoma	100%
Sarcoma Subtypes	up to 100%
Cut. Melanoma	≥95%
Uveal Melanoma <sup>2</sup>	≥91%
Ovarian Carcinoma	84%
Squamous NSCLC	68%
TNBC	63%
Small Cell Lung Cancer	45%
Kidney Carcinoma	up to 40%
Cholangiocarcinoma	33%
HNSCC	27%
Esophageal Carcinoma	27%
Breast Carcinoma	26%
Adeno NSCLC	25%
HCC	18%
Bladder Carcinoma	18%



PRAME is one of the most promising and most prevalent, clinically validated solid tumor targets known to date

**Leverage the full potential of targeting PRAME by continued evaluation of the best suited therapeutic modality (ACTengine® vs. TCER® or both) for each cancer type**



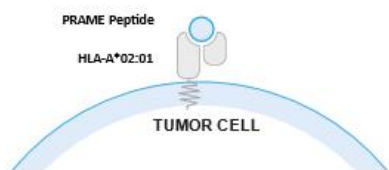
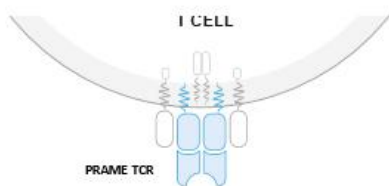


## ACTengine® IMA203 – TCR-T Targeting PRAME



# The Multi-Cancer Opportunity of PRAME

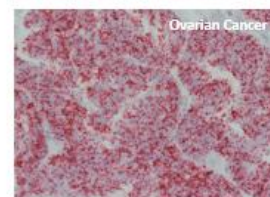
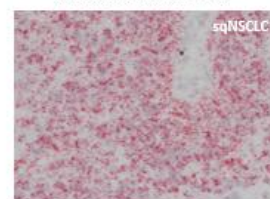
One of the Most Promising Solid Tumor Targets for TCR-based Therapies Known To Date



**PRAME fulfills all properties of an ideal target for TCR-based therapies**

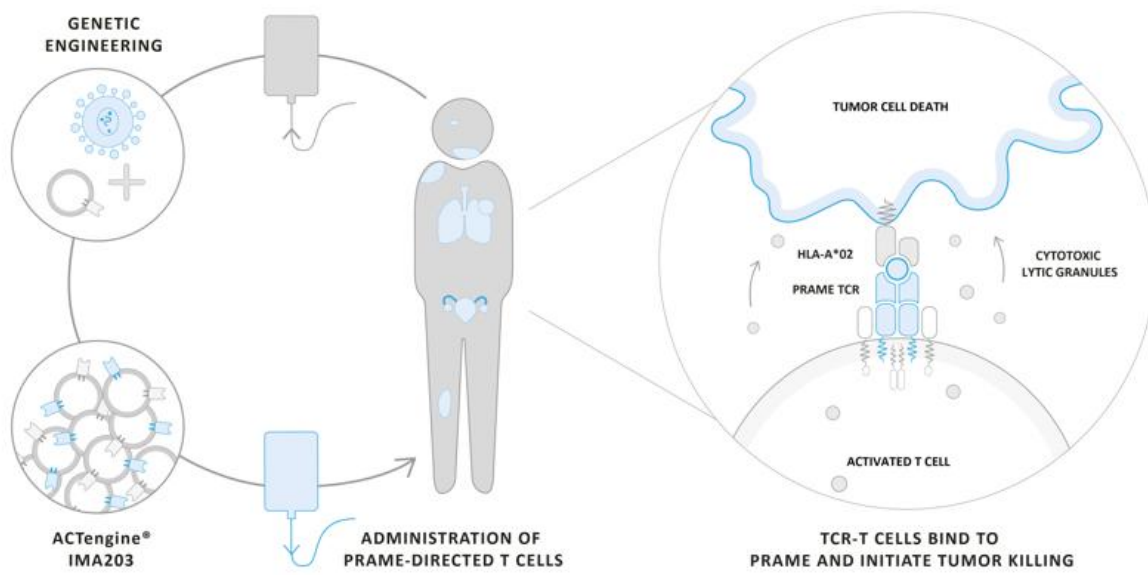
- ✓ High prevalence
- ✓ High target density
- ✓ Homogeneous expression
- ✓ “Clean” expression profile
- ✓ Clinical proof-of-concept

PRAME RNA detection in tumor samples (ISH)



# ACTengine® IMA203 Targeting PRAME – Mechanism of Action

Immatic's Leading TCR-T Approach

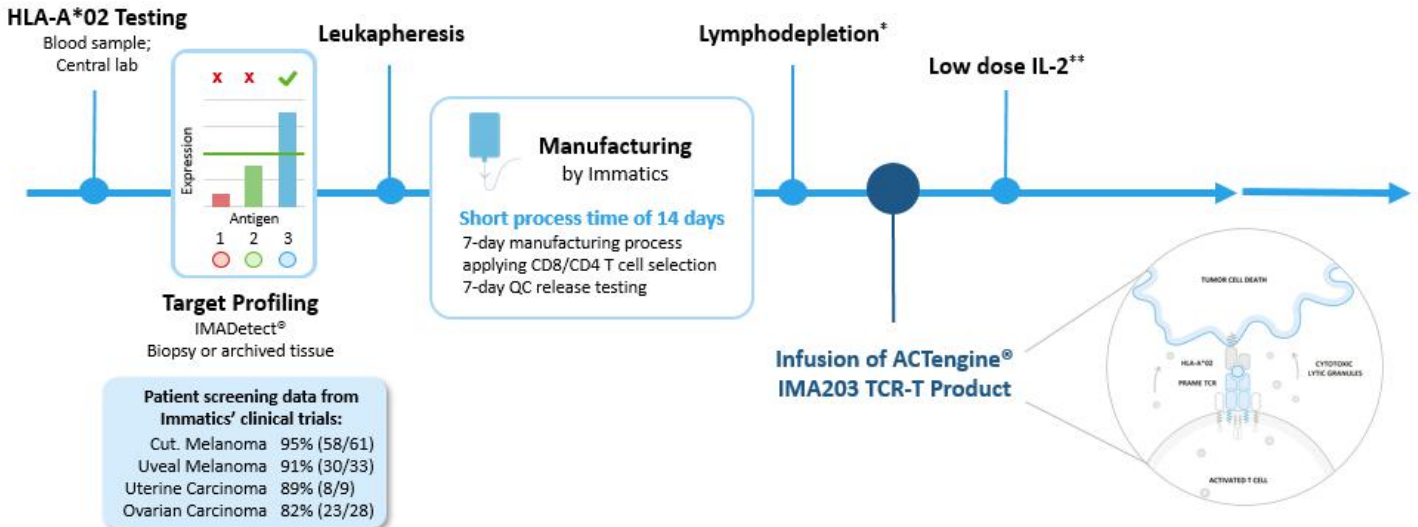


## Screening & Manufacturing Phase

## Treatment & Observation Phase

## Long Term Follow-up

Safety and efficacy monitoring for 12 months



Patient Numbers*	ALL	Melanoma	Ovarian Cancer	Synovial Sarcoma	H&N Cancer	Others
Phase 1a RP2D	7	5	0	0	0	2
Cohort A RP2D	18	8	4	3	1	2

Patient characteristics	All comers Cohort A	Melanoma pts Ph1a & Cohort A at RP2D	Ovarian cancer pts Ph1a & Cohort A at RP2D
<b>Efficacy population*</b>	<b>18</b>	<b>13</b>	<b>4</b>
<b>Prior lines of treatment</b> Median (min, max)	<b>3</b> (0, 10)	<b>4</b> (0, 7)	<b>4.5</b> (3, 10)
<b>LDH at baseline</b> >1 x ULN [% of patients]	<b>50.0</b>	<b>53.9</b>	<b>100.0</b>
<b>Baseline tumor burden</b> Target lesion sum of diameter [mm] (median, min, max)	<b>58.9</b> (21.0, 207.3)	<b>52.0</b> (21.0, 178.7)	<b>108.8</b> (50.6, 207.3)

All 8 cut. melanoma patients were CPI-refractory and 5 of 8 were BRAF-inhibitor pretreated

All ovarian cancer patients were platinum-resistant

- Sub-group analysis per tumor type at target dose includes data from Phase 1a plus Cohort A at RP2D
- Melanoma patient number (N=13) and characteristics allow such sub-group analysis for initial assessment of anti-tumor activity
- For other tumor types, appropriate patient numbers and characteristics have not yet been achieved

### GEN1: IMA203 in Melanoma at RP2D

#### Clinical Data

- Well tolerated
- 50% (6/12) confirmed objective response rate (cORR)
- Durability with ongoing responses at 15+ months; mDOR not reached at mFU of 14.4 months



#### Cell Product Manufacturing

- 7-day manufacturing process, plus 7-day release testing
- RP2D defined at  $1-10 \times 10^9$  total TCR-T cells
- Manufacturing success rate: >95%



#### Development Path

- FDA RMAT designation for multiple PRAME+ cancers including cutaneous & uveal melanoma
- **IMA203 GEN1 in melanoma targeted to enter registration-enabling Phase 2 trial in 2024**
- Update on clinical development plan in 1Q 2024



### GEN2: IMA203CD8 in Solid Tumors

#### Initial Clinical Data

- Manageable tolerability
- 56% (5/9) confirmed objective response rate (cORR)
- Durable response at 12+ months; mDOR not reached at mFU of 4.8 months
- 6 out of 7 responses ongoing at data cut-off
- **Enhanced pharmacology with differentiated response pattern**

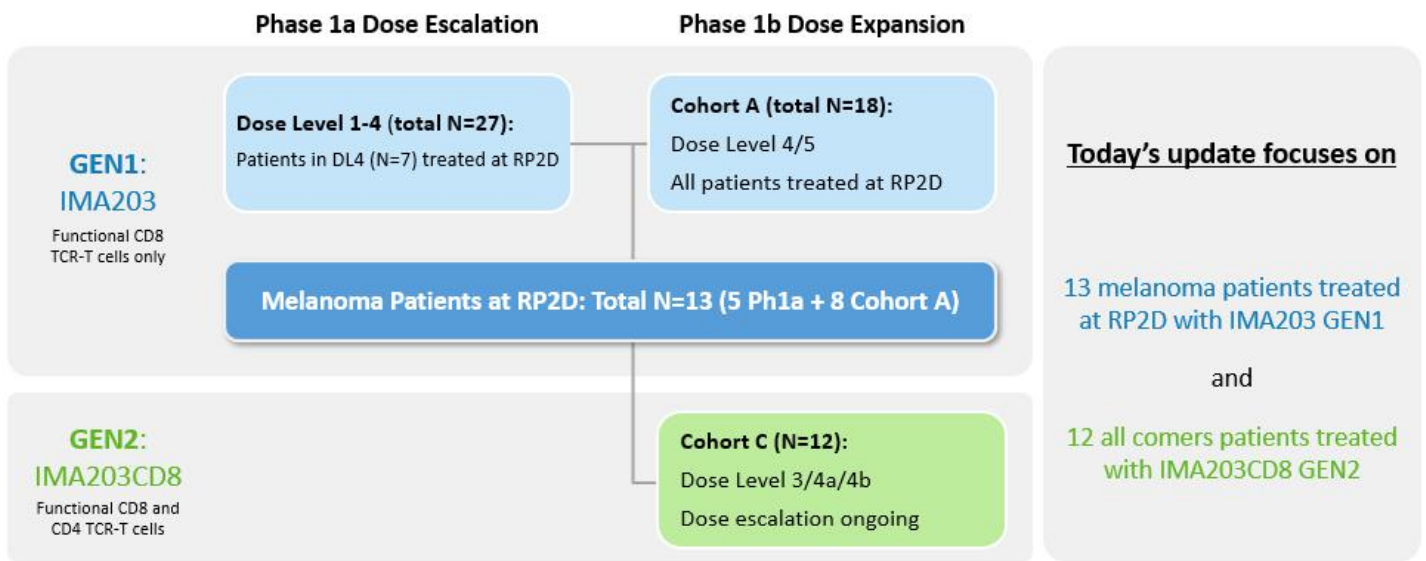


#### Development Path

- Complete dose escalation
- Signal finding in non-melanoma indications, such as ovarian cancer, uterine cancer, NSCLC, triple-negative breast cancer and others



Overview



Phase 1a and Cohort A data set in appendix; Cohort B deprioritized



# Overview of Patient Characteristics and Responses

## Heavily Pretreated Patient Population across Clinical Trial Cohorts

	IMA203 GEN1			IMA203CD8 GEN2
	All Comers (N=45)		Melanoma Subgroup (N=13 of 45)	All Comers (N=12)
	Phase 1a	Cohort A	Phase 1a + Cohort A	Cohort C
<b>Efficacy population*</b>	N=27 Thereof N=7 at RP2D	N=18 at RP2D	N=13 at RP2D	N=12
<b>Prior lines of systemic treatment</b> (median, min, max)	4 (1, 8)	3 (0, 10)	4 (0, 7)	3 (1, 5)
<b>LDH at baseline</b> >1 x ULN [% of patients]	66.7	50.0	53.8	50.0
<b>Baseline tumor burden</b> Median target lesion sum of diameter [mm] (min, max)	133.0 (29, 219.7)	58.9 (21, 207.3)	52.0 (21.0, 178.7)	79.8 (20.0, 182.0)
<b>Dose level</b>	DL1-4	DL4/5	DL4/5	DL3/DL4a/DL4b
<b>ORR</b>	48% (13/27)	50% (9/18)	62% (8/13)	58% (7/12)
<b>cORR</b>	<b>19%</b> (5/27)	<b>47%</b> (8/17)	<b>50%</b> (6/12)	<b>56%</b> (5/9)
<b>mDOR [months]</b>	4.4 (2.4, 23.0)	<b>Not reached</b>	<b>Not reached</b>	<b>Not reached</b>
<b>mFU [months]</b>	<b>Not defined*</b>	<b>10.8</b>	<b>14.4</b>	<b>4.8</b>

**IMA203** \* Patients with at least one available tumor response assessment post infusion; \*\* All patients were PD at data cut-off; Initial ORR: Objective response rate according to RECIST 1.1 at any post infusion scan; Confirmed ORR (cORR): Confirmed objective response rate according to RECIST 1.1 for patients with at least two available post infusion scans or patients with progressive disease (PD) at any prior timepoint; patients with ongoing second-line PD not included in cORR calculation; Duration of response (DOR) in confirmed responders is defined as time from first documented response until disease progression/death. Patients with ongoing response will be censored at date of data cut-off. Median DOR is analyzed by using the Kaplan-Meier method; Median Follow-up is analyzed by using the reverse Kaplan-Meier method; DOR: Durations of Response; FU: Follow-up



## IMA203 GEN1 Monotherapy

Phase 1a & Cohort A – Focus on Melanoma at RP2D

## IMA203CD8 GEN2 Monotherapy

Cohort C – First Data Set on 2<sup>nd</sup> Generation

## Summary & Next Development Steps

## IMA203 GEN1 in All Melanoma Patients at RP2D – Most Frequent Adverse Events N=16 Patients in Safety Population<sup>1</sup>



- **Expected cytopenia (Grade 1-4)** associated with lymphodepletion in all patients
- **Mostly mild to moderate cytokine release syndrome (CRS)**
  - 63% (10/16) with Grade 1 CRS
  - 31% (5/16) with Grade 2 CRS
  - 6% (1/16) with Grade 3 CRS (Phase 1a patient; recovered to Grade 2 after 3 days, no need for vasopressors and/or ventilation)
  - No dose-dependent increase of CRS
- **One non-serious, mild (Grade 1) ICANS<sup>2</sup> in DL5**
- **No dose-limiting toxicity**
- **No IMA203-related deaths**
- full IMA203 GEN1 monotherapy safety profile (generally consistent with safety in melanoma subset), see next slide

**IMA203 GEN1 monotherapy continues to be well tolerated  
at total doses between 1-10x10<sup>9</sup> TCR-T cells (RP2D)**

# IMA203 GEN1 across All Dose Levels – Tolerability Data

## Phase 1a Dose Escalation and Cohort A – All ≥Grade 3 Adverse Events (N=49)

TEAEs by maximum severity for all patients in Phase 1a dose escalation and Cohort A dose expansion (N=49)<sup>1</sup>

Adverse event (System organ class, Preferred term)	≥ Grade 3		Adverse event (System organ class, Preferred term)	≥ Grade 3	
	No.	%		No.	%
<b>Patients with any adverse event</b>	<b>49</b>	<b>100.0</b>	<b>Table continued...</b>		
<b>Adverse Events of Special Interest</b>	<b>2</b>	<b>4.1</b>	<b>General disorders and administration site conditions</b>	<b>4</b>	<b>8.2</b>
Cytokine release syndrome	2	4.1	Condition aggravated <sup>1</sup>	1	2.0
ICANS <sup>2</sup>	0	0.0	Fatigue	1	2.0
<b>Blood and lymphatic system disorders</b>	<b>48</b>	<b>98.0</b>	Pyrexia	1	2.0
Neutropenia	36	73.5	Swelling face	1	2.0
Lymphopenia	27	55.1	<b>Metabolism and nutrition disorders</b>	<b>4</b>	<b>8.2</b>
Leukopenia	26	53.1	Hypokalaemia	3	6.1
Anaemia	24	49.0	Failure to thrive	1	2.0
Thrombocytopenia	17	34.7	Hypophosphataemia	1	2.0
Cytopenia	1	2.0	<b>Gastrointestinal disorders</b>	<b>2</b>	<b>4.1</b>
Leukocytosis	1	2.0	Abdominal pain	1	2.0
Lymphocytosis	1	2.0	Diarrhoea	1	2.0
<b>Investigations</b>	<b>9</b>	<b>18.4</b>	Vomiting	1	2.0
Neutrophil count decreased	4	8.2	<b>Injury, poisoning and procedural complications</b>	<b>2</b>	<b>4.1</b>
Alanine aminotransferase increased	2	4.1	Humerus fracture	1	2.0
Aspartate aminotransferase increased	2	4.1	Infusion related reaction	1	2.0
White blood cell count decreased	2	4.1	<b>Renal and urinary disorders</b>	<b>2</b>	<b>4.1</b>
Blood alkaline phosphatase increased	1	2.0	Acute kidney injury	1	2.0
Blood creatinine increased	1	2.0	Proteinuria	1	2.0
Blood fibrinogen decreased	1	2.0	<b>Skin and subcutaneous tissue disorders</b>	<b>2</b>	<b>4.1</b>
<b>Infections and infestations</b>	<b>7</b>	<b>14.3</b>	Rash maculo-papular	2	4.1
Appendicitis	1	2.0	<b>Cardiac disorders</b>	<b>1</b>	<b>2.0</b>
COVID-19	1	2.0	Atrial fibrillation <sup>3</sup>	1	2.0
Enterococcal infection	1	2.0	<b>Endocrine disorders</b>	<b>1</b>	<b>2.0</b>
Infection	1	2.0	Inappropriate antidiuretic hormone secretion	1	2.0
Orchitis	1	2.0	<b>Eye disorders</b>	<b>1</b>	<b>2.0</b>
Sepsis <sup>4,5</sup>	1	2.0	Ulcerative keratitis	1	2.0
Septic shock <sup>4</sup>	1	2.0	<b>Hepatobiliary disorders</b>	<b>1</b>	<b>2.0</b>
Urinary tract infection	1	2.0	Cholangitis	1	2.0
<b>Respiratory, thoracic and mediastinal disorders</b>	<b>6</b>	<b>12.2</b>	<b>Immune system disorders</b>	<b>1</b>	<b>2.0</b>
Hypoxia	3	6.1	Contrast media allergy	1	2.0
Bronchial obstruction	1	2.0	<b>Musculoskeletal and connective tissue disorders</b>	<b>1</b>	<b>2.0</b>
Laryngeal inflammation	1	2.0	Muscle spasms	1	2.0
Pleural effusion	1	2.0	<b>Nervous system disorders</b>	<b>1</b>	<b>2.0</b>
Respiratory failure	1	2.0	Headache	1	2.0
<b>Vascular disorders</b>	<b>6</b>	<b>12.2</b>	<b>Reproductive system and breast disorders</b>	<b>1</b>	<b>2.0</b>
Hypertension	4	8.2	Vaginal haemorrhage	1	2.0
Hypotension	2	4.1			

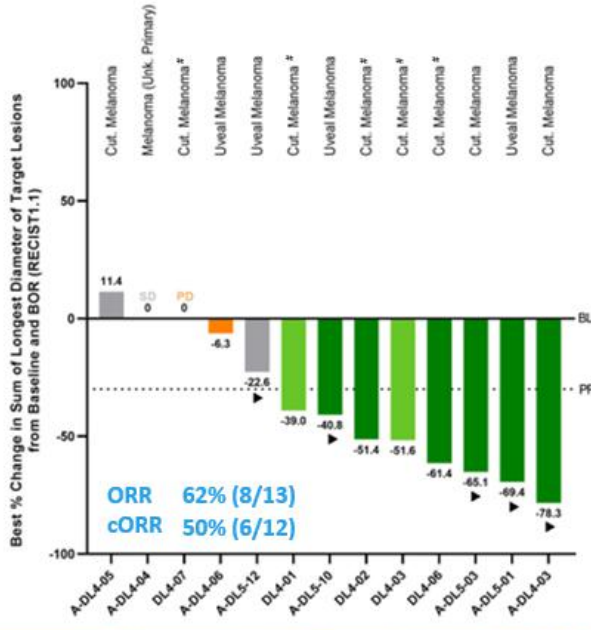
- Well tolerated at doses as high as ~10x10<sup>9</sup> TCR-T cells
- No AE ≥Grade 3 was observed with a frequency ≥10% when excluding expected cytopenia associated with lymphodepletion
- No IMA203-related Grade 5 Adverse Events

All treatment-emergent adverse events (TEAEs) with ≥ Grade 3 regardless of relatedness to study treatment that occurred in at least 1 patient (except for ICANS, where only Grade 1-2 occurred; listed for completeness due to being an adverse event of special interest) are presented. Adverse events were coded using the Medical Dictionary for Regulatory Activities. Grades were determined according to National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0. Grades for CRS and ICANS were determined according to CARTOX criteria (Neelapu et al., 2018). Patients are counted only once per adverse event and severity classification. Based on interim data extracted from open clinical database (30-Sep-2023); <sup>1</sup> Two patients with disease progression after first IMA203 infusion received exploratory second IMA203 infusion. They had these ≥ Grade 3 TEAEs only after second infusion, which are included in the table. First patient: Abdominal pain, Cytokine release syndrome, Diarrhoea, Hypokalaemia, Proteinuria; Second patient: Humerus fracture, Muscle spasms, Neutropenia, Thrombocytopenia; <sup>2</sup> ICANS: immune effector cell-associated neurotoxicity syndrome; <sup>3</sup> DLT: Dose limiting toxicity in phase 1a at DL2 reported on March 17, 2021; <sup>4</sup> Fatal Adverse events were not considered related to any study drug; <sup>5</sup> Patient died from sepsis of unknown origin and did not receive IMA203 TCR-T cells.

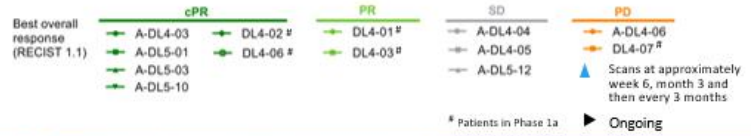
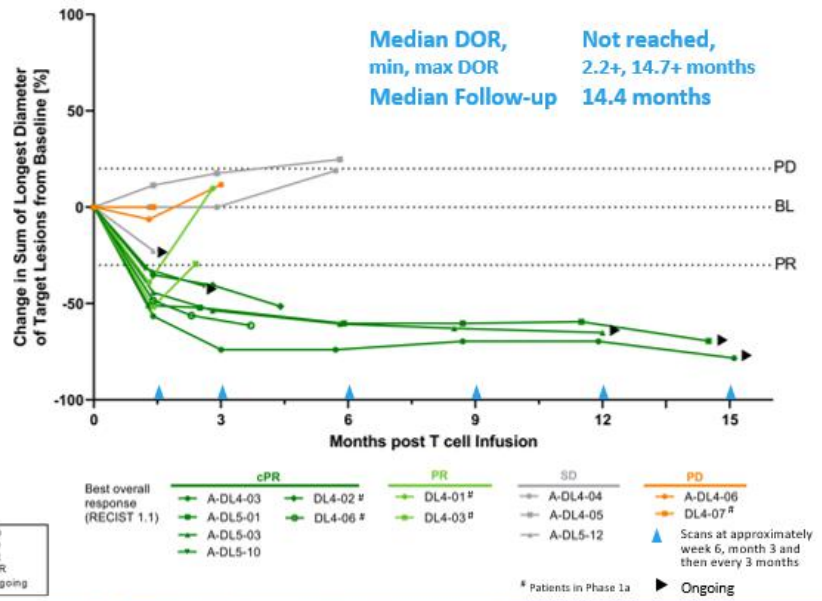
# IMA203 GEN1 in All Melanoma Patients at RP2D (N=13) – BOR and Response over Time



## Durable Responses 15+ Months after Treatment



ORR 62% (8/13)  
cORR 50% (6/12)



# IMA203 GEN1 in Melanoma Targeted to Enter Registration-Enabling Phase 2 Trial in 2024



## Clinically and Commercially Attractive Features of IMA203

≥95% of cutaneous melanoma patients are PRAME-positive
Well tolerated Mostly mild to moderate CRS, infrequent & mild ICANS
Promising anti-tumor activity (cORR, mDOR)
Leukapheresis as source for cell product, no surgery required
Short manufacturing time of 7 days plus 7 days of QC release testing
Low dose IL-2 post IMA203 infusion with better tolerability profile than high dose IL-2

## High Medical Need in Cutaneous and Uveal Melanoma

	Cutaneous Melanoma	Uveal Melanoma
Patient Population	2L+ CPI-refractory, BRAF/MEK inhibitor-refractory if BRAF mutation+	2L+ Kimmtrak-refractory, CPI/chemotherapy-refractory
IMA203 Opportunity	~3,000 HLA-A*02:01 and PRAME-positive cutaneous melanoma patients annually in the US <sup>1</sup>	~300 HLA-A*02:01 and PRAME-positive uveal melanoma patients annually in the US <sup>2</sup>

**IMA203** CPI: Checkpoint inhibitor; <sup>1</sup> Based on annual mortality of ~7,700 cutaneous melanoma patients in the US, HLA-A\*02:01 prevalence of 41% in the US and PRAME prevalence of 95% (TCGA RNAseq data combined with proprietary MS-guided RNA expression threshold); <sup>2</sup> Based on annual mortality of ~800 uveal melanoma patients in the US, HLA-A\*02:01 prevalence of 41% in the US and PRAME prevalence of 91% (IMA203 qPCR testing of screening biopsies from clinical trial patients (n=33)) Data cut-off Sep 30, 2023 24

# ACTengine® IMA203 TCR-T Interim Update

Delivering a Meaningful Benefit to Patients with an Unmet Medical Need



**IMA203 GEN1 Monotherapy**

Phase 1a & Cohort A – Focus on Melanoma at RP2D

**IMA203CD8 GEN2 Monotherapy**

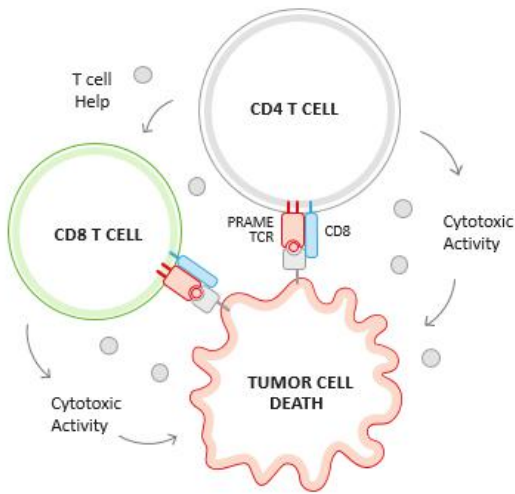
Cohort C – First Data Set on 2<sup>nd</sup> Generation

**Summary & Next Development Steps**



# IMA203CD8 GEN2 – IMA203 TCR-T Monotherapy Leveraging CD8 and CD4 cells

## Differentiated Pharmacology Compared to 1<sup>st</sup>-Generation TCR-only Approaches

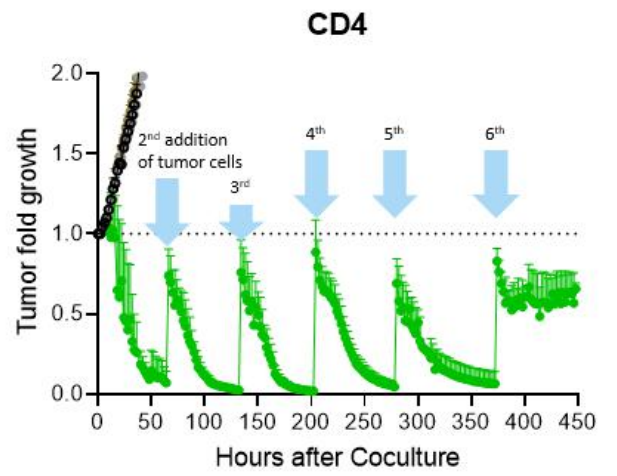
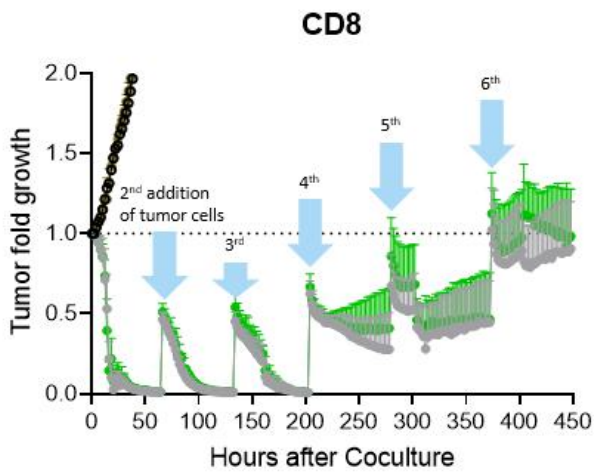


- IMA203CD8 GEN2 designed to broaden the clinical potential of IMA203 TCR-T monotherapy by adding functional CD4 T cells via co-transduction of CD8 $\alpha\beta$  alongside PRAME TCR
- Activated CD4 T cells aid activity of other immune cells by releasing cytokines and acquire cytotoxic functions
- Functional CD4 T cells mediate longer anti-tumor activity than CD8 T cells and potentiate the anti-tumor activity of the cell product in preclinical studies<sup>1</sup>
- Data from CD19 CAR-T-treated leukaemia patients suggest a relevant role of engineered CD4 T cells in long-term durability<sup>2</sup>



# IMA203CD8 GEN2 – Preclinical Assessment of Anti-Tumor Efficacy

## Functional CD4 T cells Mediate Longer Anti-Tumor Activity than CD8 T cells *in vitro*



# IMA203CD8 GEN2 in Cohort C (N=12) – Most Frequent Adverse Events

## Manageable Tolerability in 12 Patients Treated with IMA203CD8 at 3 Escalating Dose Levels<sup>1</sup>

- **Expected cytopenia (Grade 1-4)** associated with lymphodepletion in all patients
- Cytokine release syndrome (CRS) in 92% (11/12) of patients:  
Trend towards **more severe CRS at higher doses, in all cases well manageable**
  - 67% (8/12) with Grade 1 or 2 CRS (4 in DL3, 3 in DL4a, 1 in DL4b)
  - 17% (2/12) with Grade 3 CRS (2 in DL4b; patient C-DL4b-04, see also description below)
  - 8% (1/12) with Grade 4 CRS (1 in DL4b, patient C-DL4b-01, see also description below)
- **One patient with neurotoxicity (see below), no ICANS<sup>2</sup> or neurotoxicity reported for the other patients**
- **Dose-limiting toxicities (DLTs) at Dose Level 4b** were observed in 2 of 4 patients
  - 1) In patient C-DL4b-01 treated with highest possible dose at DL4b, high biological activity (*in vivo* T cell expansion) observed; patient developed Grade 4 neurotoxicity and Grade 4 CRS on day 6 after infusion, combined with Grade 3 Hemophagocytic Lymphohistiocytosis (HLH)
  - 2) Patient C-DL4b-04 treated at DL4b developed Grade 3 CRS with transient Grade 3 liver enzyme (ALT) increase that resolved to Grade 2 within 10 days; no need for vasopressors or ventilation at any time
- **No high-grade CRS, no neurotoxicity and no DLTs were reported for 4 patients treated at DL3 and 4 patients treated at DL4a**
- **No IMA203CD8-related deaths**
- **Expanded DL4a dose cohort ongoing**

### IMA203CD8 GEN2 monotherapy shows a manageable tolerability profile

## Tolerability Data – Cohort C IMA203CD8 GEN2

### All ≥Grade 3 Adverse Events (N=12)

TEAEs by maximum severity for all patients in Cohort C (N=12)

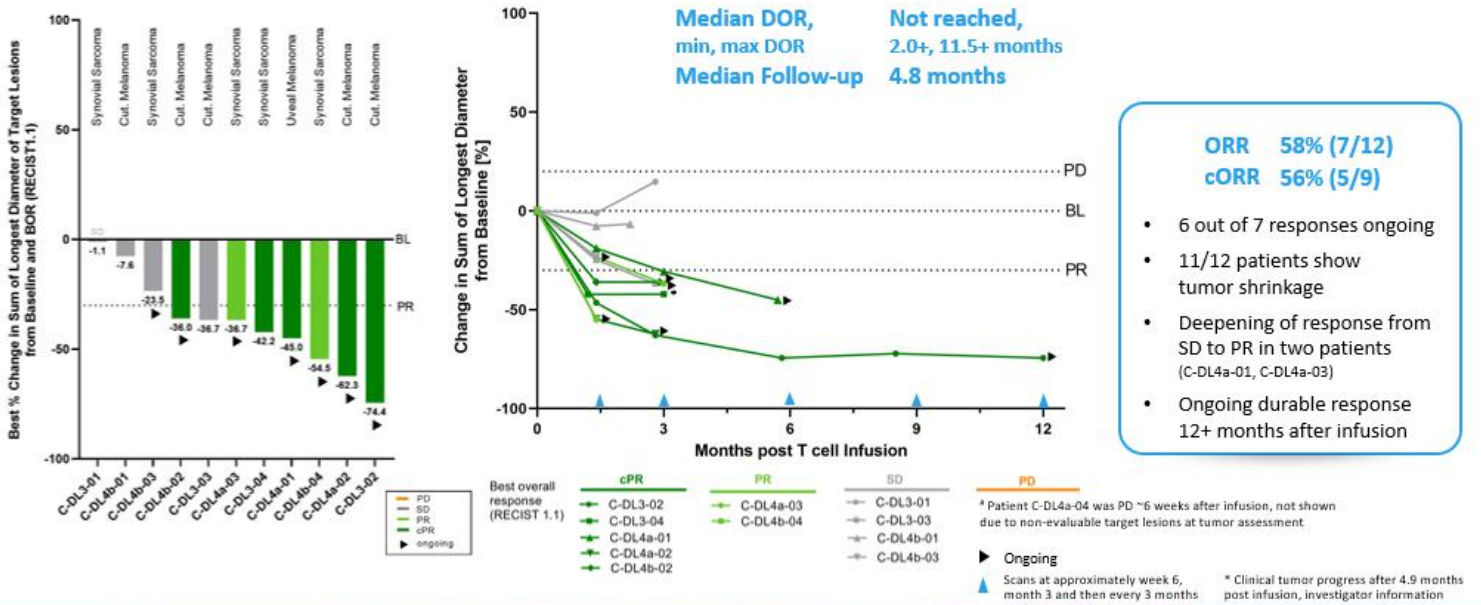
Adverse event (System organ class, preferred term)	≥ Grade 3	
	No.	%
<b>Patients with any adverse event</b>	<b>12</b>	<b>100.0</b>
<b>Adverse events of special interest</b>	<b>3</b>	<b>25.0</b>
Cytokine release syndrome <sup>1</sup>	3	25.0
Immune effector cell-associated neurotoxicity syndrome	0	0.0
<b>Blood and lymphatic system disorders</b>	<b>11</b>	<b>91.7</b>
Neutropenia	9	75.0
Anaemia	8	66.7
Lymphopenia	8	66.7
Thrombocytopenia	4	33.3
Leukopenia	2	16.7
<b>Investigations</b>	<b>4</b>	<b>33.3</b>
Aspartate aminotransferase increased	2	16.7
Neutrophil count decreased	2	16.7
Alanine aminotransferase increased	1	8.3
Blood alkaline phosphatase increased	1	8.3
Blood bilirubin increased	1	8.3
Gamma-glutamyltransferase increased	1	8.3
<b>Metabolism and nutrition disorders</b>	<b>2</b>	<b>16.7</b>
Hypermagnesaemia	1	8.3
Hypoalbuminaemia	1	8.3
Hypophosphataemia	1	8.3
<b>Nervous system disorders</b>	<b>2</b>	<b>16.7</b>
Neurotoxicity <sup>2</sup>	1	8.3
Syncope	1	8.3
<b>Immune system disorders</b>	<b>1</b>	<b>8.3</b>
Haemophagocytic lymphohistiocytosis <sup>2</sup>	1	8.3
<b>Infections and infestations</b>	<b>1</b>	<b>8.3</b>
Infection	1	8.3

- Manageable tolerability
- Most frequent ≥Grade 3 AEs were expected cytopenia associated with lymphodepletion
- No IMA203CD8-related Grade 5 Adverse Events
- Dose escalation ongoing

All treatment-emergent adverse events (TEAEs) with ≥ Grade 3 regardless of relatedness to study treatment that occurred in at least 1 patient (except for ICANS, where no event was documented; listed for completeness due to being an adverse event of special interest) are presented. Adverse events were coded using the Medical Dictionary for Regulatory Activities. Grades were determined according to National Cancer Institute Common Terminology Criteria of Adverse Events, version 5.0. Grades for CRS and ICANS were determined according to CARTOX criteria (Neelapu et al., 2018). Patients are counted only once per adverse event and severity classification. Based on interim data extracted from open clinical database (30-Sep-2023). <sup>1</sup> DLT: Dose limiting toxicity in patient DL4b-04. <sup>2</sup> DLTs in patient DL4b-01.

# IMA203CD8 GEN2 in Cohort C (N=12#) – BOR and Response over Time

## Deepening of Response from SD to PR in 2 Patients, 6 Responses Ongoing



# IMA203CD8 GEN2: Translational Data Shows Enhanced Pharmacology

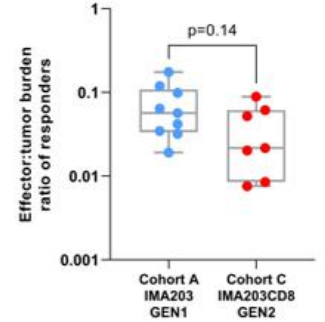
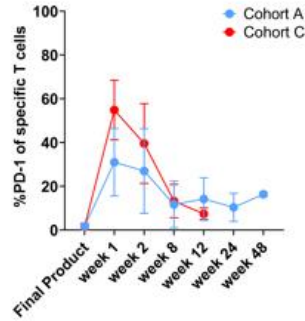
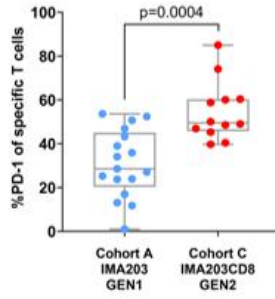
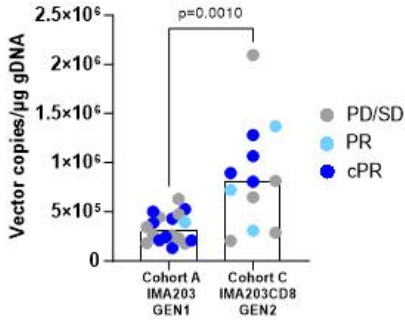
## Cohort A IMA203 GEN1 (All Patients at RP2D) vs Cohort C IMA203CD8 GEN2

Higher peak expansion ( $C_{max}$ ) of IMA203CD8 T cells when normalized to infused dose

Higher activation levels in IMA203CD8 T cells at week 1...

...without exhaustion over time

Trend towards responses at lower cell dose and higher tumor burden with IMA203CD8



### Initial translational data indicates higher biological and clinical activity of IMA203CD8 GEN2

# ACTengine® IMA203 TCR-T Interim Update

Delivering a Meaningful Benefit to Patients with an Unmet Medical Need



**IMA203 GEN1 Monotherapy**

Phase 1a & Cohort A – Focus on Melanoma at RP2D

**IMA203CD8 GEN2 Monotherapy**

Cohort C – First Data Set on 2<sup>nd</sup> Generation

**Summary & Next Development Steps**



### IMA203 GEN1 Monotherapy in Melanoma at RP2D

- Well tolerated, mostly mild to moderate CRS, infrequent & mild ICANS
- **50% (6/12) cORR, mDOR not reached at mFU of 14.4 months**
- **Durability with ongoing responses at 15+ months in some patients**
- RP2D defined at  $1-10 \times 10^9$  total TCR-T cells
- FDA RMAT designation received in multiple PRAME expressing cancers including cutaneous and uveal melanoma

#### Next Step

Alignment with FDA on patient population, trial design, CMC targeting registration-enabling Phase 2 trial in melanoma

### IMA203CD8 GEN2 Monotherapy

- Enhanced primary and secondary pharmacology when compared to GEN1
- Manageable tolerability (2 DLTs at DL4b, dose escalation ongoing)
- Initial clinical activity observed with differentiated response pattern
  - 56% (5/9) cORR
  - 6 out of 7 responses ongoing at data cut-off, durable response at 12+ months
  - SD converting to PR over time (N=2)
  - Enhanced biological efficacy with PRs at lower T cell:tumor cell ratio compared to IMA203 GEN1

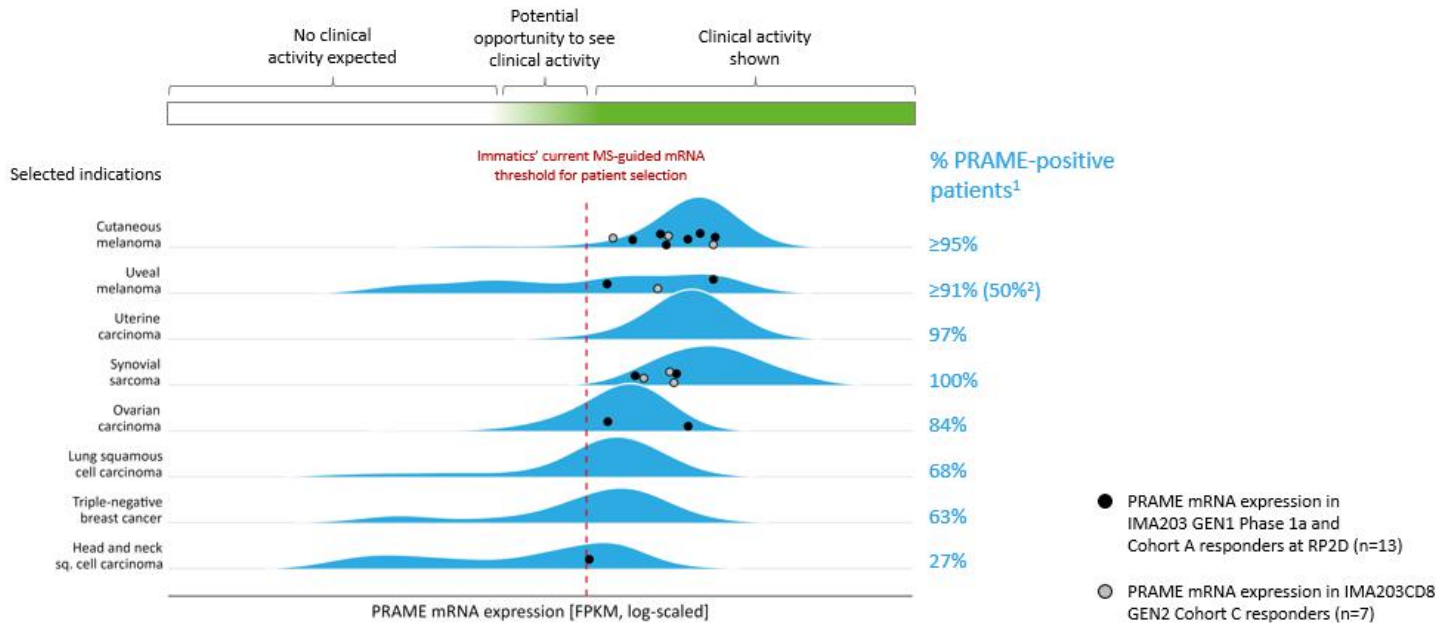
#### Next Step

Complete dose escalation and further dose expansion with focus on non-melanoma patients



# Potential of IMA203 in Additional Solid Cancer Indications

## Based on PRAME Expression in IMA203 GEN1 and IMA203CD8 GEN2 Responders



## Development Strategy

### Step 1 2024

IMA203 GEN1 in cutaneous melanoma (potentially bundled with uveal melanoma) as first tumor type targeted to enter registration-enabling trial

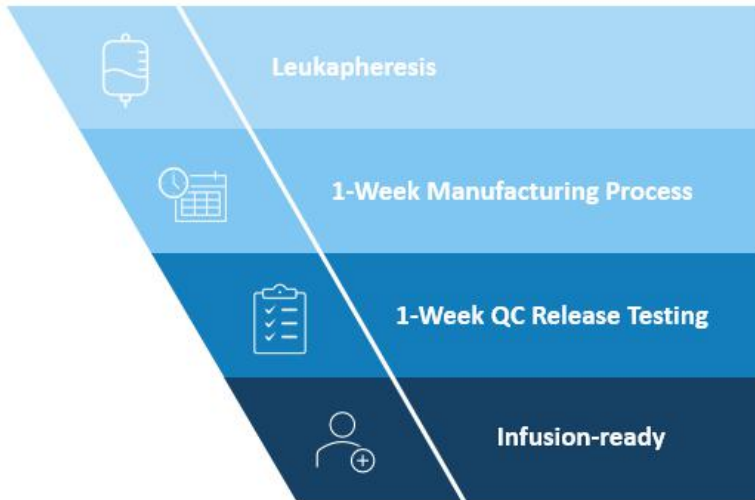
### Step 2 2024

Signal finding in ovarian cancer and uterine cancer in dedicated dose expansion cohorts, preferentially with IMA203CD8 GEN2

### Step 3

Pursue tumor-agnostic label in PRAME+ solid cancers to leverage full breadth of PRAME - including NSCLC, triple-negative breast cancer and others

**Short manufacturing turnaround time**



**State-of-the-art research & GMP manufacturing facility**



# IMA203 TCR-T Has the Potential to Reach a Large Patient Population

~39,000 Patients per Year in the US only



## Selected Indications

	Incidence	R/R Incidence	PRAME Positive
Cut. Melanoma	99,800	7,700	95%
Uveal Melanoma	1,500	800	91%
Ovarian Carcinoma	19,900	12,800	84%
Uterine Carcinoma	62,700	10,700	97%
Uterine Carcinosarcoma	3,300	1,900	100%
Squamous NSCLC	57,000	34,600	68%
Small Cell Lung Cancer	31,900	19,400	45%
Adeno NSCLC	91,200	55,300	25%
HNSCC	66,500	15,100	27%
Breast Carcinoma	290,600	43,800	26% TNBC: 63%
Synovial Sarcoma	1,000	400	100%
Cholangiocarcinoma	8,000	7,000	33%

## Patient Population

Based on R/R Incidence, PRAME and HLA-A\*02:01+

2,999
298
4,408
4,255
779
9,646
3,579
5,668
1,672
4,669
164
947

**TOTAL ~39,000  
annually in the US**

### Multiple opportunities to broaden patient reach and patient benefit:

- Expand beyond US population
- Expand into other indications such as kidney, esophageal, bladder, other liver cancers, other sarcoma subtypes through indication-specific or indication-agonistic label expansion
- Move into earlier lines of therapy (R/R Incidence → Incidence)
- Inclusion of patients with lower PRAME-threshold



**ACTengine® IMA204 – TCR-T Targeting COL6A3 Exon 6**

# ACTengine® IMA204 First-in-Class TCR-T Targeting Tumor Stroma

## Key Features

### TARGET

HLA-A\*02-presented peptide derived from **COL6A3 exon 6**

Naturally and specifically presented on tumors at high target density<sup>1</sup>:  
**100-700 copies/cell**

Novel **tumor stroma target** identified and validated by XPRESIDENT® quant. mass spectrometry platform

### TCR

High-affinity, specific TCR targeting COL6A3 exon 6

**Affinity-maturated, CD8-independent TCR**

High functional avidity<sup>2</sup>:  
**~0.01ng/ml**

Identified and characterized by XCEPTOR® TCR discovery and engineering platform

### PRECLINICAL DATA

CD8-independent, next-generation TCR engages both, CD8 and CD4 T cells

*In vitro* anti-tumor activity against target-positive cell lines in CD8 and CD4 T cells

Complete tumor eradication in *in vivo* mouse models

### PATIENT POPULATION<sup>3</sup>

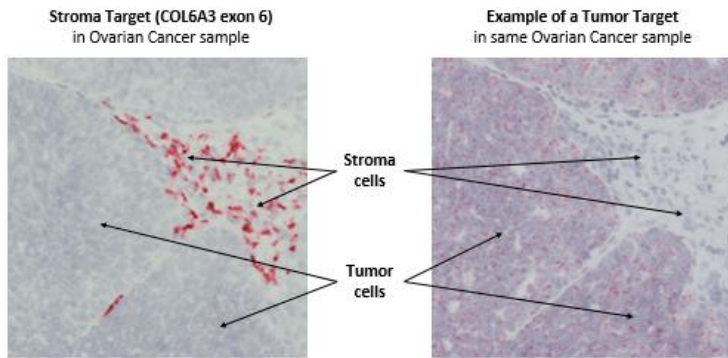
Pancreatic Carcinoma – 76%  
Breast Carcinoma – 77%  
Stomach Carcinoma – 67%  
Sarcoma – 63%  
Colorectal Carcinoma – 60%  
Esophageal Carcinoma – 60%  
Squamous NSCLC – 55%  
Adeno NSCLC – 57%  
HNSCC – 56%  
Uterine Carcinosarcoma – 50%  
Mesothelioma – 44%  
Cholangiocarcinoma – 36%  
Melanoma – 35%  
Bladder Carcinoma – 34%  
Ovarian Carcinoma – 31%

IMA204 provides a promising therapeutic opportunity for a broad patient population as monotherapy or in combination with TCR-T cells directed against tumor targets

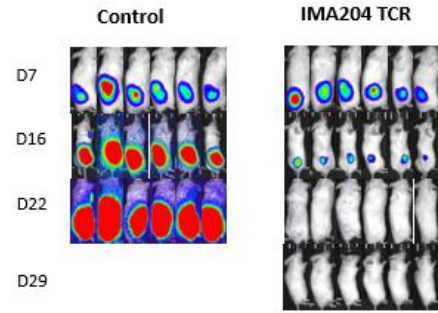


# ACTengine® IMA204 – High Affinity, CD8-independent TCR

## Complete Tumor Eradication *in vitro* & *in vivo*<sup>1</sup> by Affinity-enhanced IMA204 TCR



COL6A3 exon 6 prevalently expressed at high target density in tumor stroma across many solid cancers



CD8-independent TCR leads to tumor eradication in all mice treated

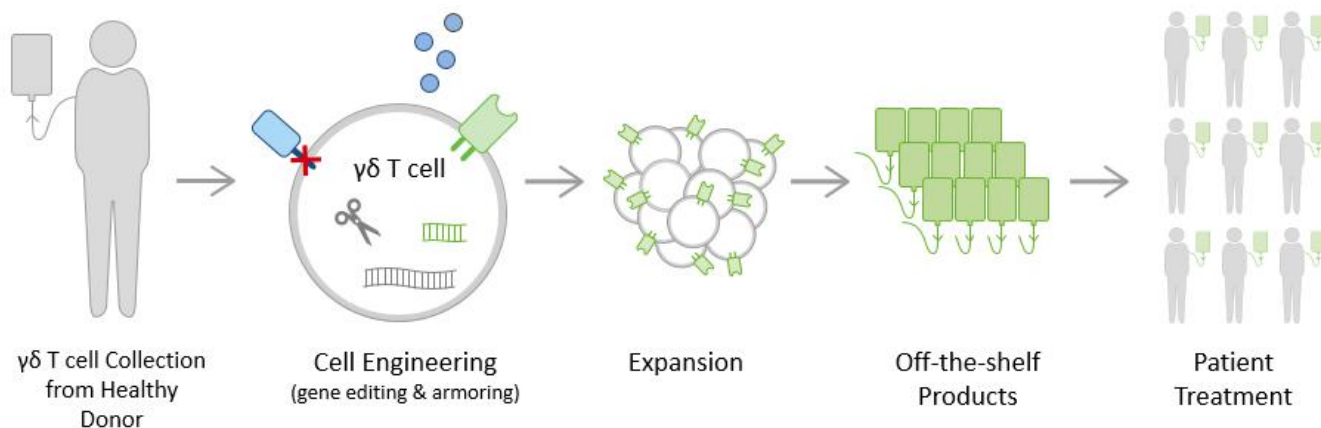
Affinity matured CD8-independent, next-generation TCR engages both CD4 and CD8 T cells without the need of CD8 co-transduction





**ACTallo® – Our Next-generation Off-the-shelf TCR-T**

## ACTallo® – Immatics' Allogeneic Cell Therapy Approach



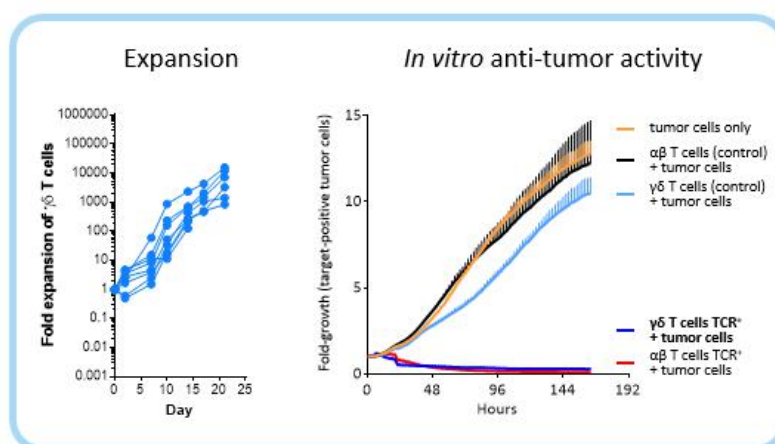
- **Off-the-shelf cell therapy**, no need for personalized manufacturing → reduced logistics and time to application
- **Potential for hundreds of doses** from one single donor leukapheresis → lower cost of goods
- **Use of healthy donor material** provides standardized quality and quantity of starting material
- Strategic collaborations combining Immatics' proprietary ACTallo® platform with Bristol Myers Squibb's next-gen technologies and Editas Medicine's CRISPR gene editing technology to develop next-gen allogeneic γδ TCR-T/CAR-T programs

## Why $\gamma\delta$ T cells?

### $\gamma\delta$ T cells Are Well Suited for an Off-the-shelf Cell Therapy Approach

#### $\gamma\delta$ T cells

- ✓ are abundant in the peripheral blood
- ✓ show intrinsic anti-tumor activity
- ✓ naturally infiltrate solid tumors & correlate with favorable prognosis
- ✓ are HLA-independent, thus do not cause graft-vs-host disease in allogeneic setting
- ✓ can be expanded to high numbers in a cGMP-compatible manner
- ✓ can be effectively redirected using  $\alpha\beta$  TCR or CAR constructs



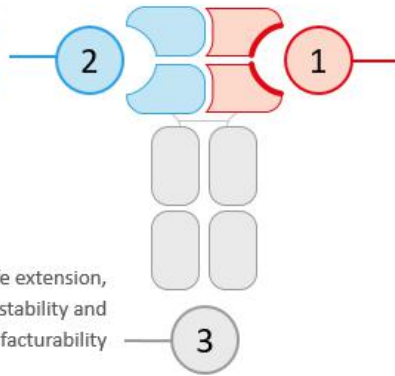


## TCER<sup>®</sup> – TCR Bispecifics

# TCER® – Immatics' Next-generation, Half-Life Extended Bispecifics

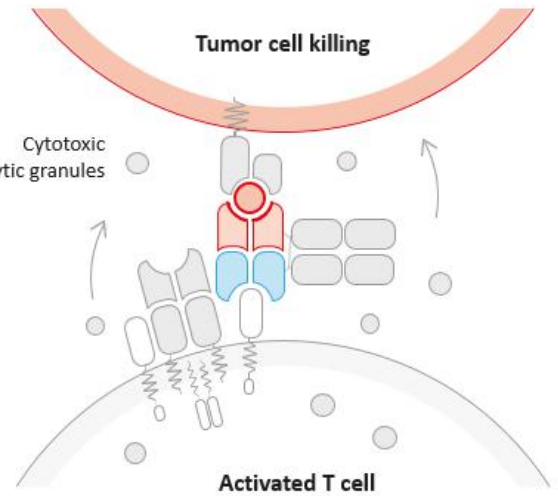
## Proprietary TCER® Format Consisting of Three Distinct Elements

Low-affinity  
T cell recruiter  
against CD3/TCR

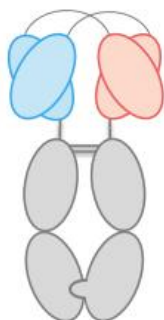


High-affinity TCR  
domains targeting  
XPRESIDENT®-selected  
tumor-specific peptide-  
HLA molecules

Fc part for half-life extension,  
favorable stability and  
manufacturability



Next-gen, half-life extended TCER® format designed to  
→ safely apply high drug doses for activity in a broad range of tumors  
→ achieve optimized scheduling



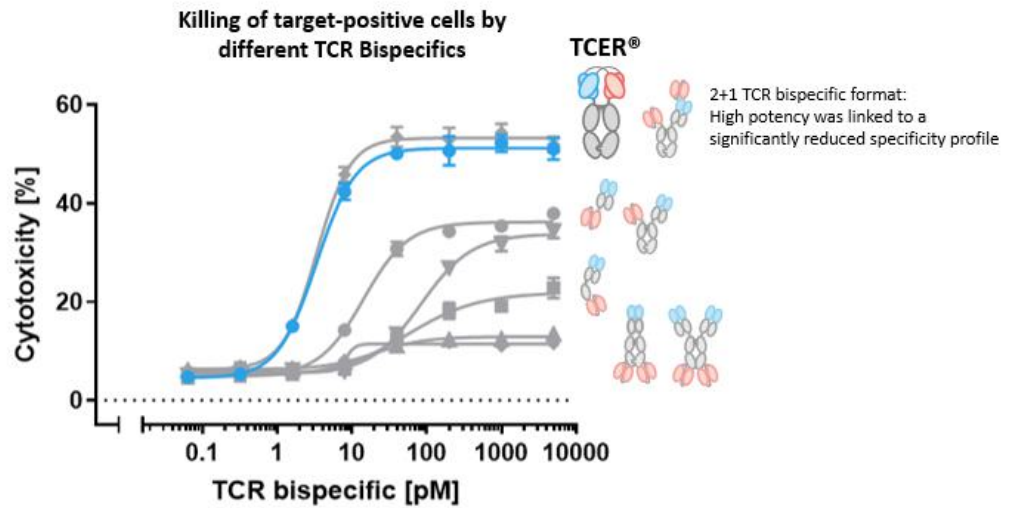
- 1 pHLA targeting TCR**

  - ✓ **High-affinity** (single digit nM) TCR targeting **XPRESIDENT®-selected** tumor-specific peptide-HLA molecules
  - ✓ Broad therapeutic window through **XPRESIDENT®-guided** affinity maturation (>1000x)<sup>1</sup>
  - ✓ **Complete tumor eradication** in mouse xenograft models at low doses
- 2 T cell recruiting antibody**

  - ✓ **Low-affinity** (triple digit nM) T cell recruiter against both **TCR & CD3**
  - ✓ **Optimized biodistribution** aiming for enrichment at tumor site and **prevention of CRS**<sup>2</sup>
  - ✓ **Superior anti-tumor activity** in mouse models as compared to widely used CD3 recruiters
- 3 Next-generation TCER® format**

  - ✓ Off-the-shelf biologic with antibody-like manufacturability<sup>3</sup> and low cost of goods
  - ✓ Superior anti-tumor activity<sup>4</sup> compared to six alternative bispecific formats
  - ✓ Half-life of several days expected in humans

**Our TCER® format is designed to maximize efficacy while minimizing toxicities in patients**

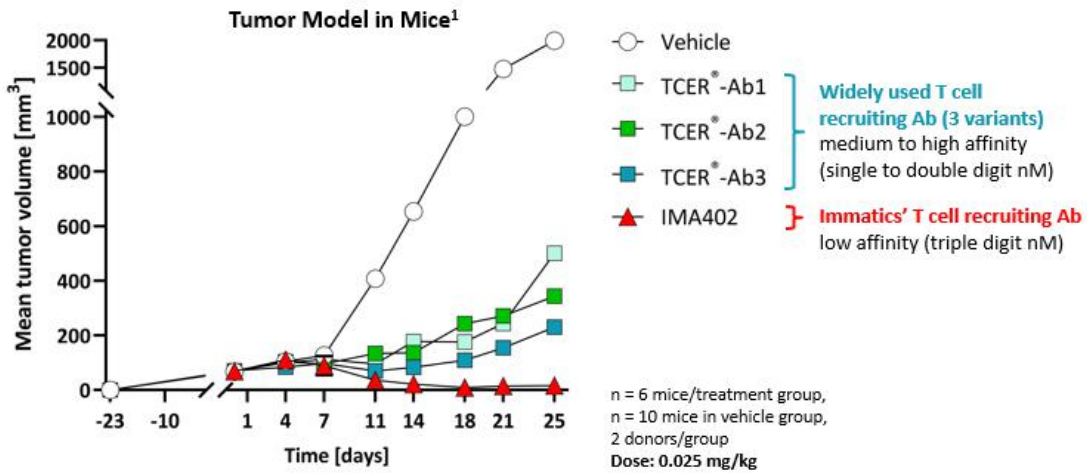


- Seven different TCR Bispecific formats were evaluated with a pHLA targeting TCR and the identical T cell recruiting antibody
  - TCER<sup>®</sup> format had higher combination of potency and specificity<sup>1</sup> than six alternative TCR Bispecific format designs evaluated
- Flexible Plug-and-play platform: TCER<sup>®</sup> format successfully validated for different TCRs & different T cell recruiting antibodies**



# TCER<sup>®</sup> Format Is Designed for Optimized Efficacy and Safety

## Superior Tumor Control Using a Novel, Low-Affinity Recruiter

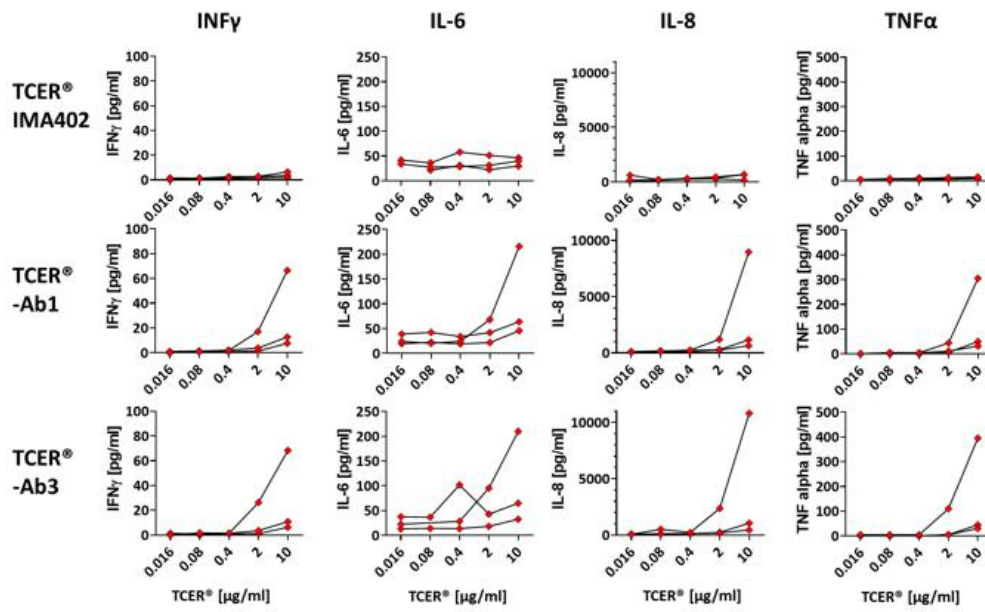


Proprietary, **low-affinity T cell recruiting region** demonstrates superior tumor control compared to analogous TCER<sup>®</sup> molecules designed with higher-affinity variants of a widely used recruiter

# TCER® Format Is Designed for Optimized Efficacy and Safety



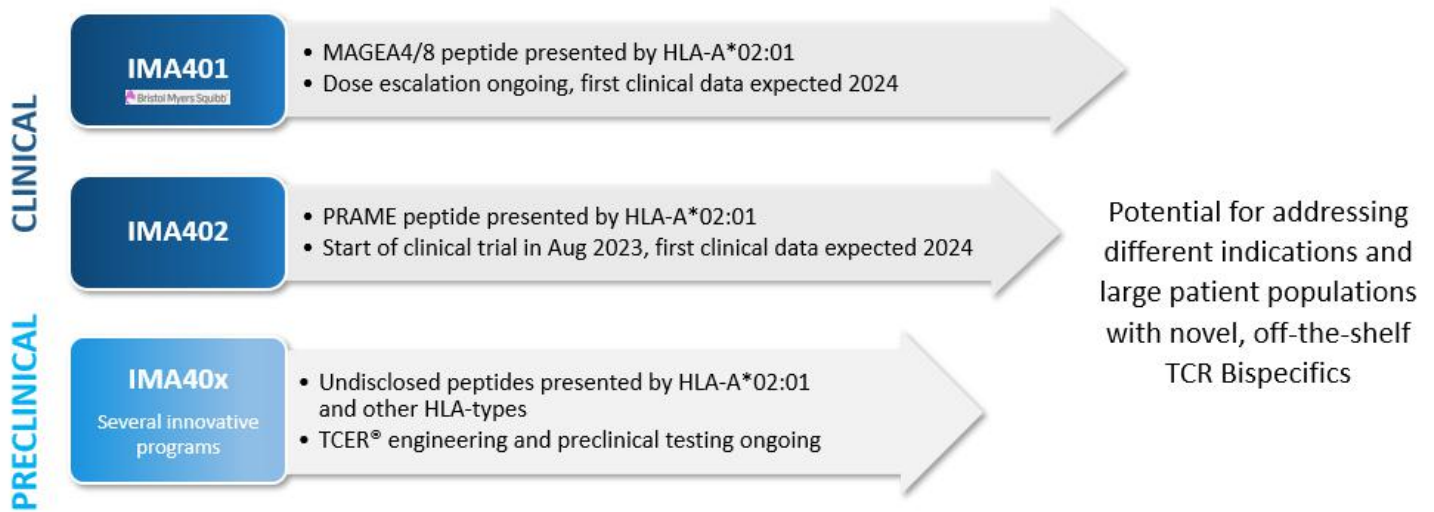
Reduced Target-Unrelated Recruiter-Mediated Cytokine Release using a Low-Affinity Recruiter



Whole blood cytokine release assay  
 N=3 HLA-A\*02-positive donors  
 N=16 cytokines tested,  
 4 exemplary cytokines shown

## Our TCER® Portfolio

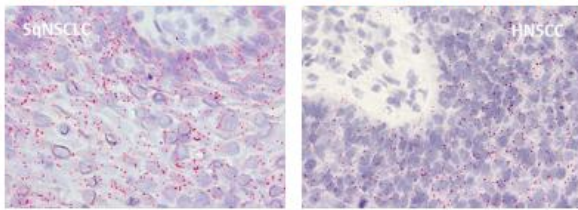
### Broad Pipeline of Next-Gen Half-Life Extended TCR Bispecifics



# TCER® IMA401 Targeting MAGEA4/8

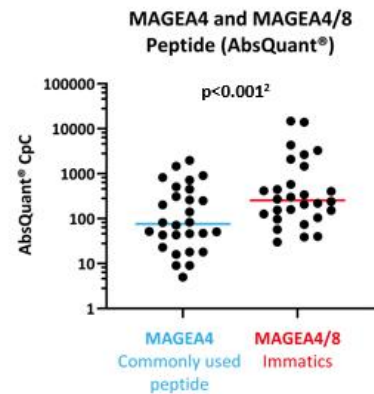
Homogeneous Expression, Broad Prevalence and High Copy Number Target

## MAGEA4 RNA detection in tumor samples (ISH)



## MAGEA4/8 target prevalence in selected cancer indications

Indications	Target prevalence [%]
Squamous non-small cell lung carcinoma	52%
Head and neck squamous cell carcinoma	36%
Bladder carcinoma	29%
Uterine carcinosarcoma	29%
Esophageal carcinoma	23%
Ovarian carcinoma	23%
Melanoma	18%
<i>plus several further indications</i>	



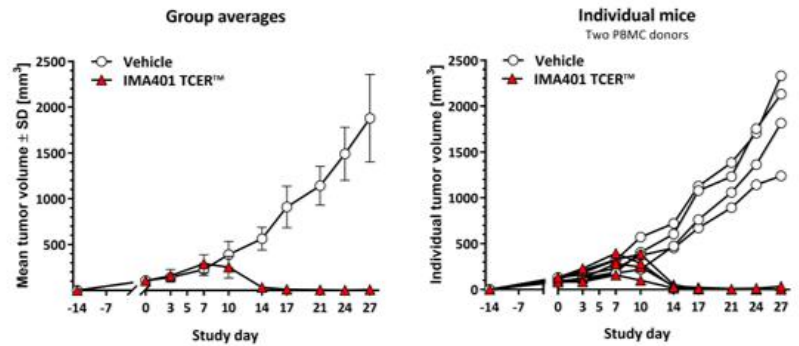
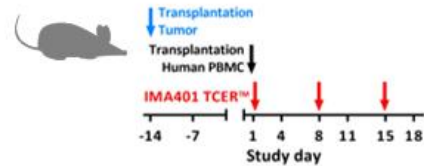
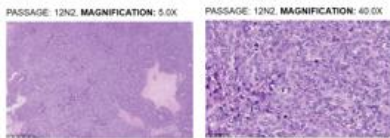
MAGEA4/8 target is presented at >5-fold higher target density<sup>1</sup> than a commonly used MAGEA4 target peptide

# TCER® IMA401 (MAGEA4/8) – Assessment of Anti-Tumor Activity *in vitro*

## Patient-Derived Tumor Model

### NSCLC adenocarcinoma:

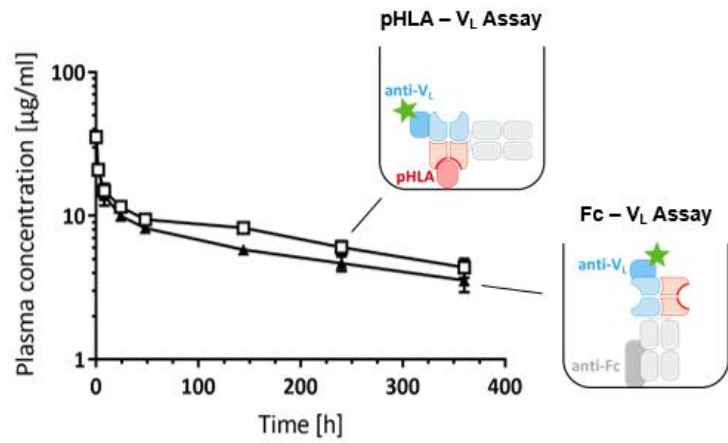
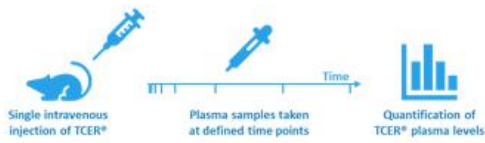
- Male, Caucasian, age 58, no therapy prior to surgery
- Site of origin: lung, differentiation poor
- Date of surgery: 1987, Freiburg Medical Center
- Volume doubling time: 7.3 day
- Histology:
  - Stroma content, 4%
  - Vascularization, high
  - Grading, undifferentiated



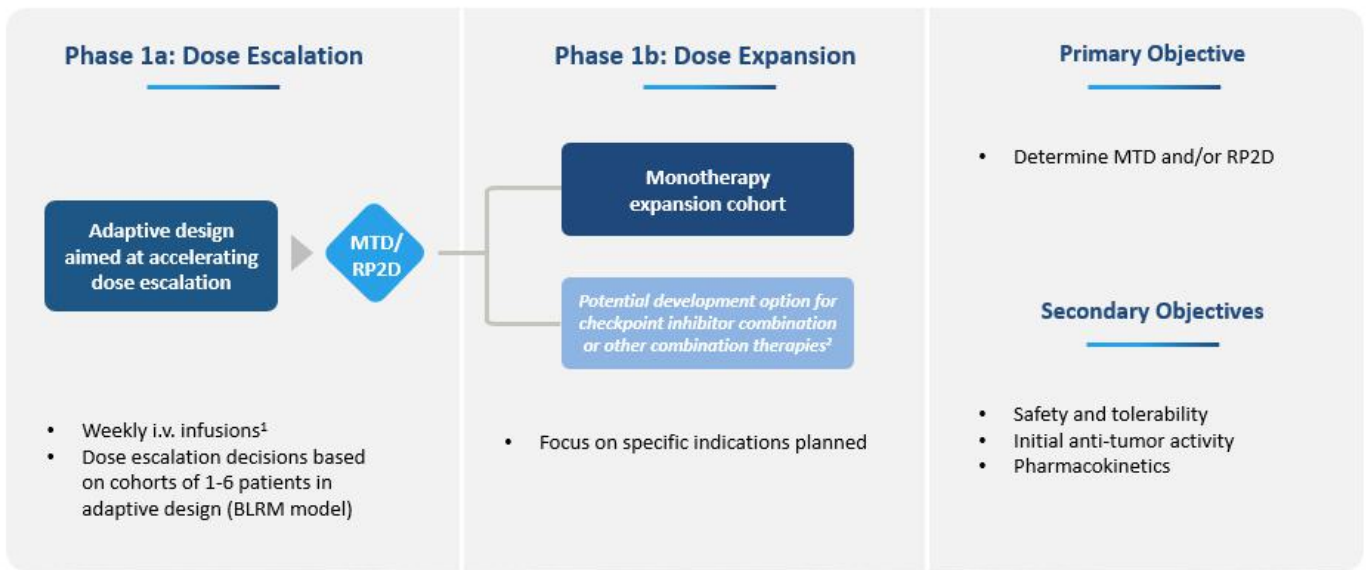
- TCER® IMA401 shows **high anti-tumor activity in Patient-derived xenograft model** of non-small cell lung adenocarcinoma
- **Remission observed in all mice (3 out of 4 mice with complete remission)**

# TCER® IMA401 (MAGEA4/8) – Pharmacokinetics

## PK Analysis in NOG Mice



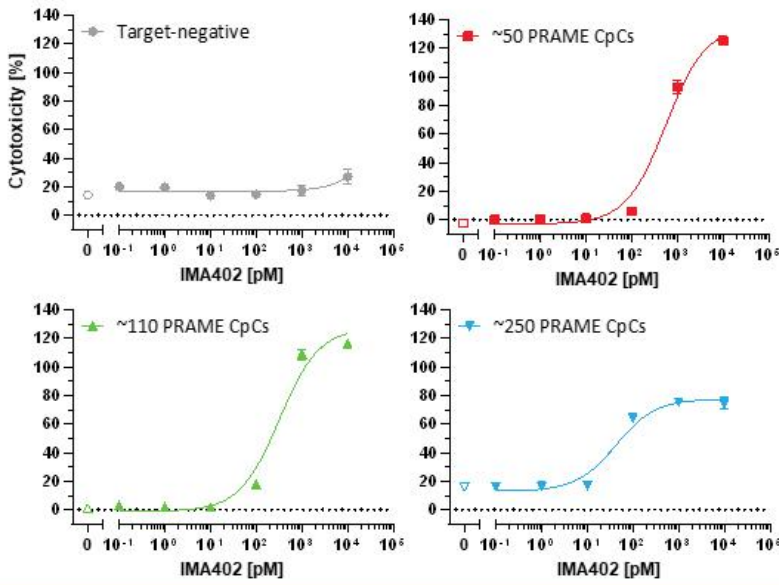
- Two different PK assays established to ensure functional integrity of protein domains
- **Terminal half-life in mice: 10-11 days**



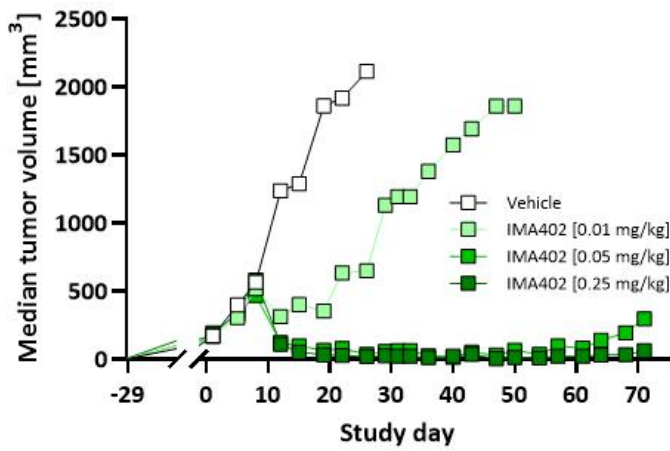


# TCER® IMA402 Targeting PRAME – Efficacy Assessment *in vitro*

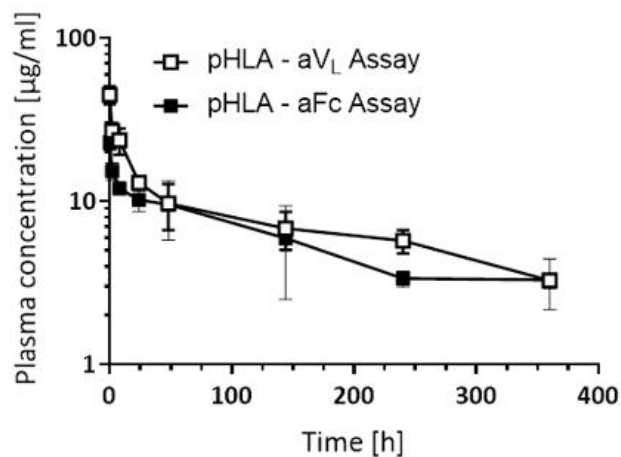
## Tumor Cell Killing at Low Physiological PRAME Peptide Levels



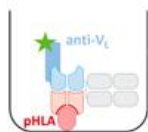
- TCER® IMA402 induces killing of tumor cells with PRAME target copies as low as 50 CpCs
- Physiological PRAME levels detected in majority of cancer tissues from patients are 100 – 1000 CpCs
- Preclinical activity profile enables targeting of a broad variety of tumor indications, such as lung cancer, breast cancer, ovarian cancer, uterine cancer, melanoma and others



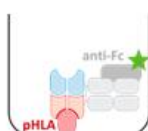
- Dose-dependent efficacy of IMA402 in cell line-derived *in vivo* mouse model
- Durable shrinkage of large tumors including complete responses over prolonged period
- Sufficiently high drug doses are key to achieving desired anti-tumor effect



pHLA – aV<sub>L</sub> Assay



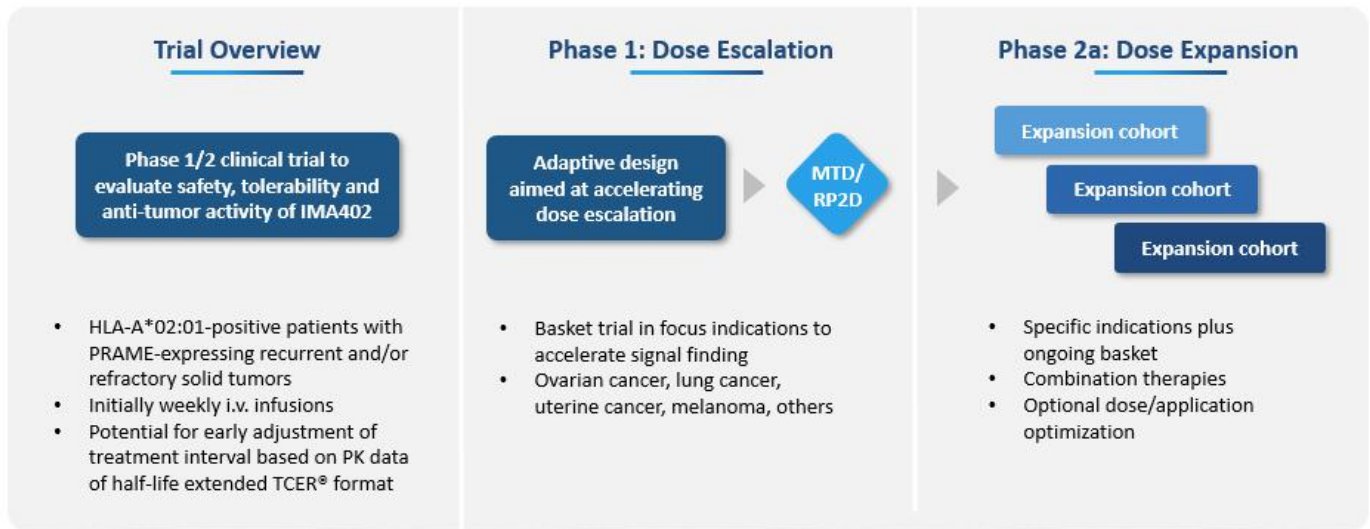
pHLA – aFc Assay



- IMA402 shows a terminal serum half-life of  $\approx$  8 days in mice
- IMA402 will be initially dosed weekly in the clinical trial
- Dosing frequency may be adapted based on clinical data

# Phase 1/2 Clinical Trial to Evaluate TCER® IMA402 Targeting PRAME

First Clinical Data Planned in 2024





## Immatics' Proprietary Target and TCR Discovery Platforms

# True Cancer Targets & Matching Right TCRs

Goal to Maximize Anti-Tumor Activity and Minimize Safety Risks of TCR-based Immunotherapies

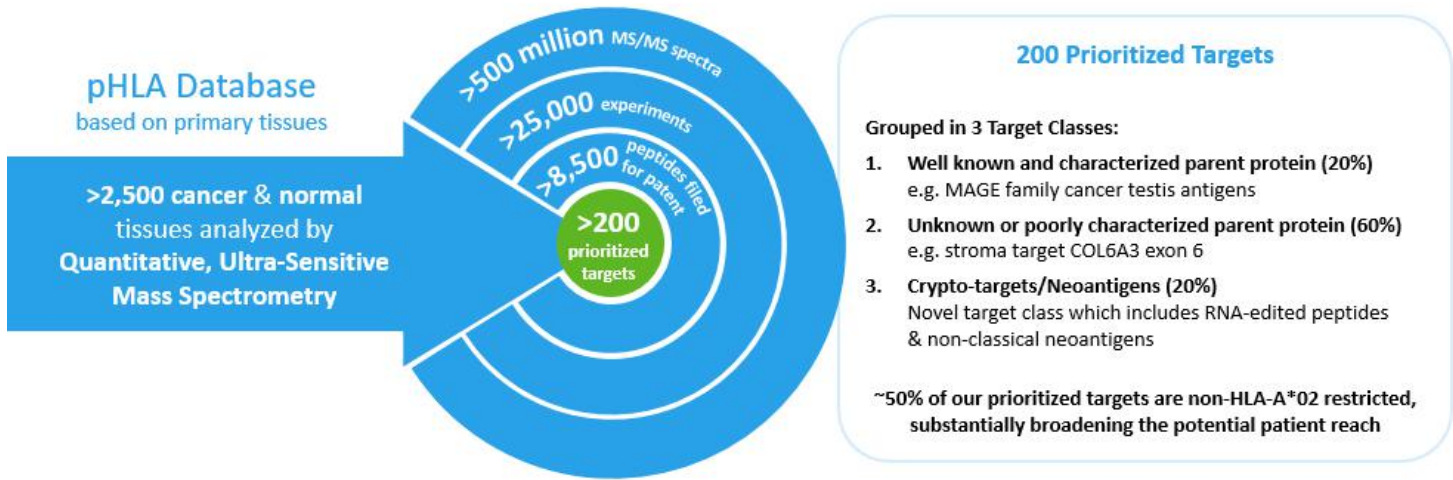


## True Targets via XPRESIDENT® technology platform

- are naturally presented on tumor tissues as identified by mass-spec
- are absent or presented at only low levels on normal tissues
- are presented at high copy numbers to trigger a pharmacological response

## Right TCRs via XCEPTOR® technology platform

- recognize the target peptide with high affinity and specificity
- show selective killing of tumor cells
- are developed to be suitable for two different therapeutic modalities, Cell Therapies and TCR Bispecifics

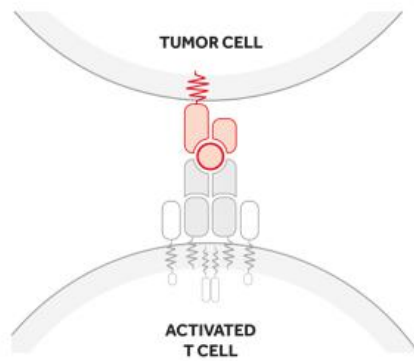


This large data set is leveraged by our bioinformatics & AI-platform XCUBE™ – „AI is where the data is“

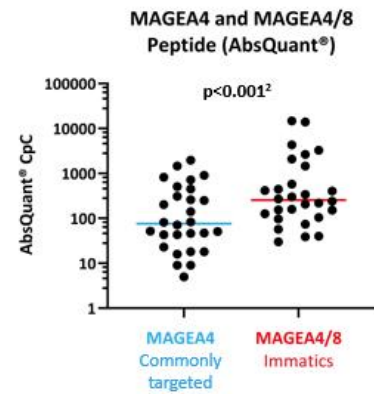


# Immatics' Unique Capability – Identification of the most Relevant Target

## Example of MAGEA4/8 Peptide Target



Ranking of pHLA targets

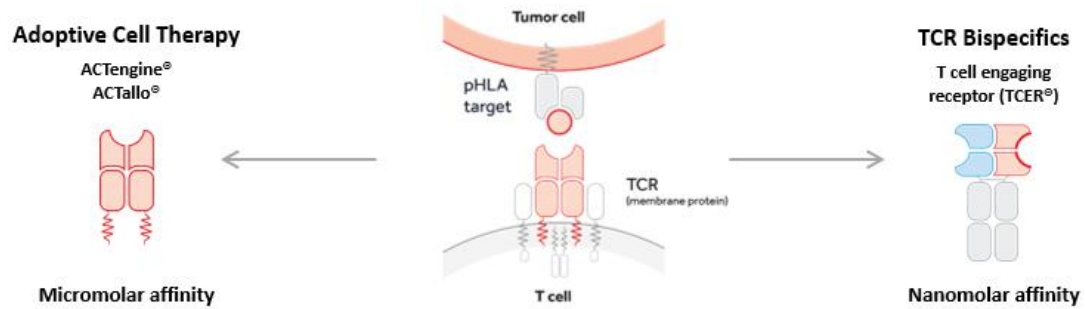


XPRESIDENT® quantitative information on target density<sup>1</sup> between peptides originating from the same source protein

MAGEA4/8 target is presented at >5-fold higher target density<sup>1</sup> than a commonly targeted MAGEA4 target peptide

# Development of the Right TCR – XCEPTOR® Technology

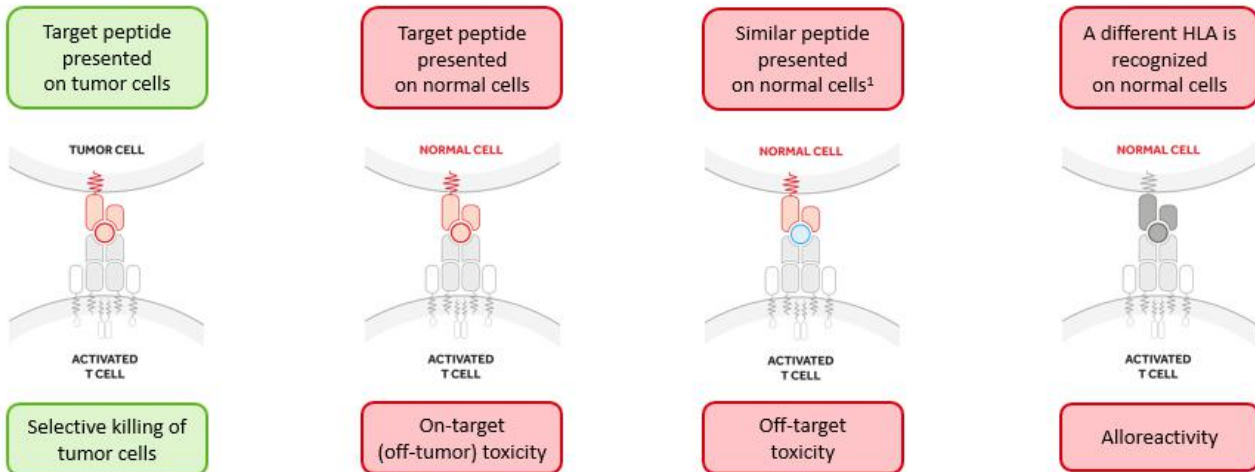
## TCR Discovery and Engineering for ACT and TCR Bispecifics



- Fast, efficient and highly sensitive discovery of highly specific, natural TCRs
- Protein engineering capabilities to design and mature TCRs with increased affinity while retaining specificity
- Early de-selection of cross-reactive TCRs by the unique interplay between Immatics' target and TCR discovery platforms XPRESIDENT® and XCEPTOR® during TCR discovery<sup>1</sup> and TCR maturation<sup>2</sup> (empowered by our bioinformatics & AI-platform XCUBE™)

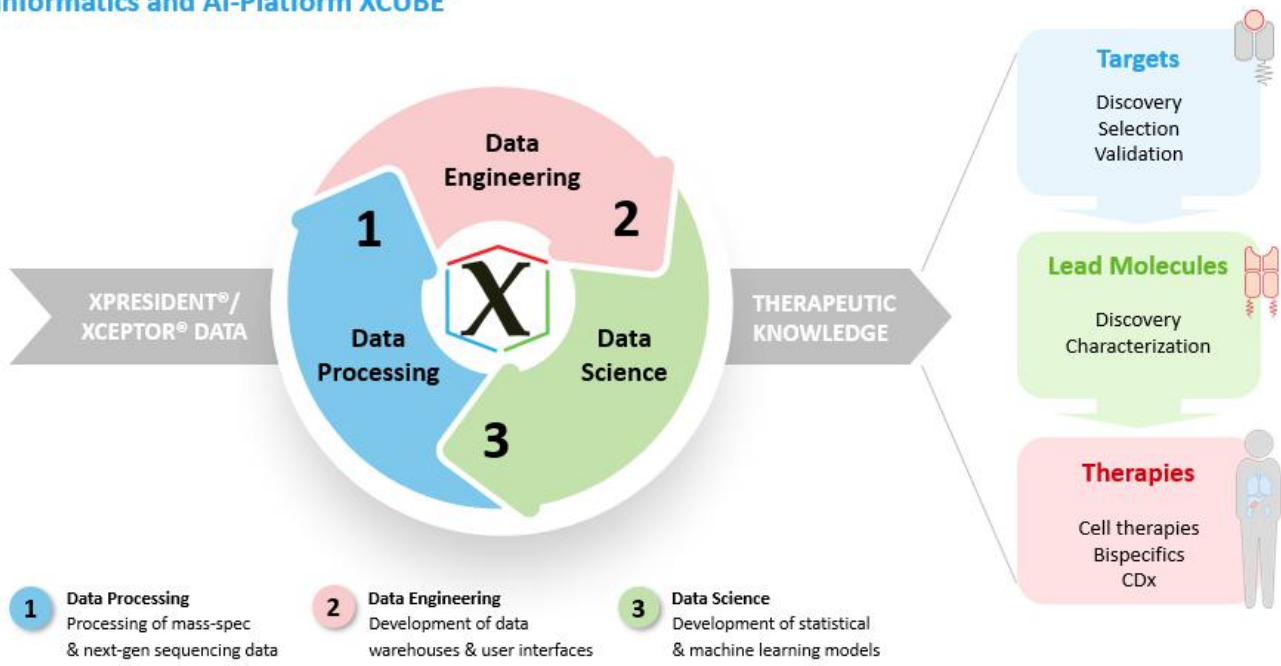
# Optimal Target Selection & TCR Specificity for Minimizing Safety Risks

Unique Interplay between Technology Platforms Allows Early De-risking for Clinical Development



**XPRESIDENT<sup>®</sup>-guided screening** for on- and off-target toxicities of TCRs based on the extensive database of peptides presented on normal tissues

**“AI Is Where the Data Is®”**  
Bioinformatics and AI-Platform XCUBE™

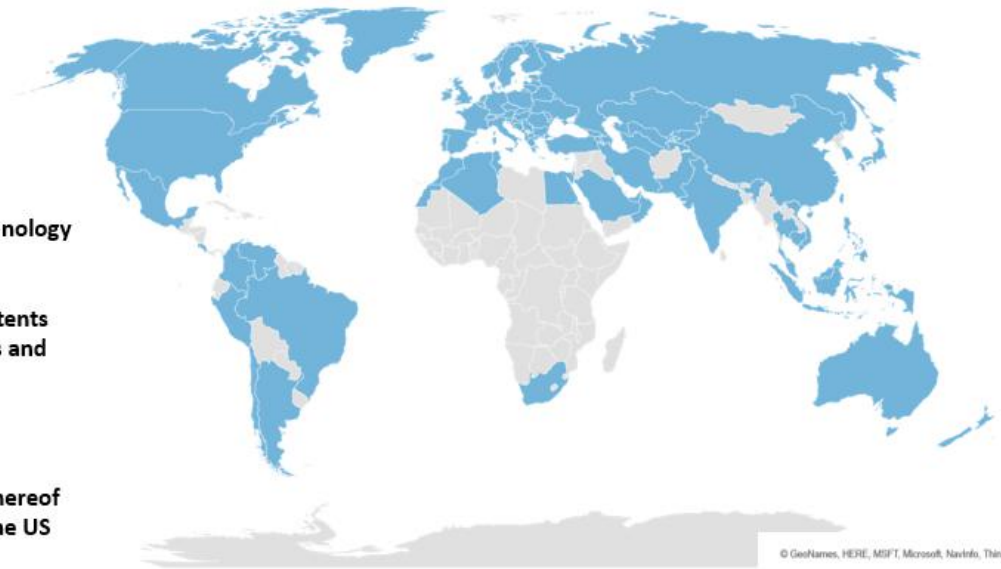


## Robust IP Portfolio

### Immatics' Patent Estate – Territorial Coverage

#### Cancer targets, TCRs and technology protected by:

- 5,800 applications and patents filed in all major countries and regions
- >115 patent families
- >2,400 granted patents, thereof >550 granted patents in the US





## Corporate Information & Milestones

## Experienced Global Leadership Team Across Europe and the US



**Harpreet Singh**  
Chief Executive Officer  
Co-Founder  
>20 yrs biotech experience



**Arnd Christ**  
Chief Financial Officer  
>20 yrs biotech experience  
(InflixR, Medigene, NovImmune,  
Probiodrug)



**Carsten Reinhardt**  
Chief Development Officer  
>20 yrs pharma & biotech experience  
(Micromet, Roche, Fresenius)



**Cedrik Britten**  
Chief Medical Officer  
15 yrs pharma & biotech experience  
(GSK, BioNTech)



**Rainer Kramer**  
Chief Business Officer  
25 yrs pharma & biotech experience  
(Amgen, MorphoSys, Jerini,  
Shire, Signature Dx)



**Steffen Walter**  
Chief Operating Officer  
Co-Founder Immatics US  
>15 yrs biotech experience



**Toni Weinschenk**  
Chief Innovation Officer  
Co-Founder  
>15 yrs biotech experience



**Edward Sturchio**  
General Counsel  
>15 yrs pharma & biotech experience  
(Abeona Therapeutics, AAA,  
Novartis, Merck, Schering)



**Jordan Silverstein**  
Head of Strategy  
>10 yrs biotech experience  
(InflixR, AAA)



# Strong, Focused and Highly Integrated Trans-Atlantic Organization



# Delivering

the Power of T cells  
to Cancer Patients

## Appendix

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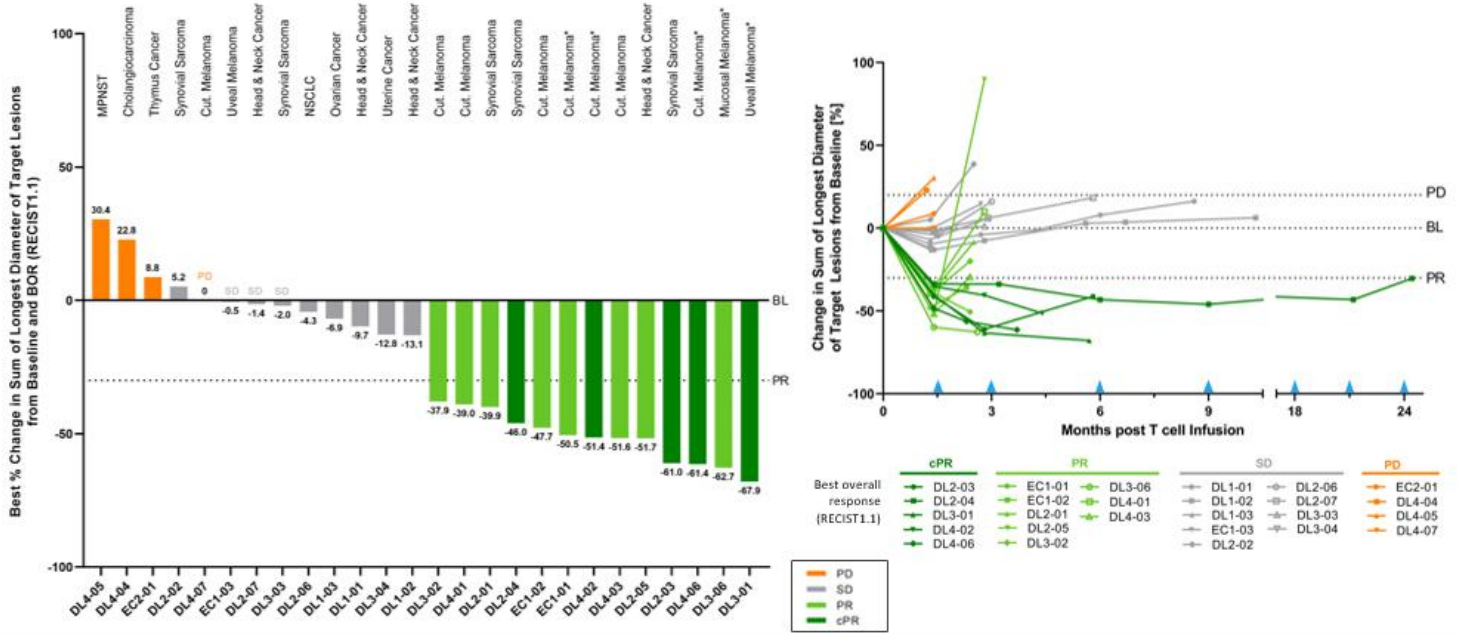


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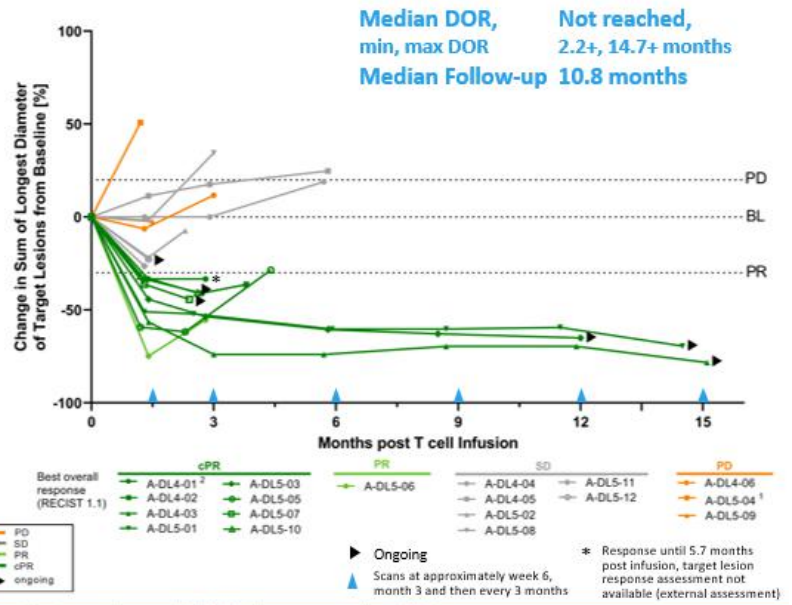
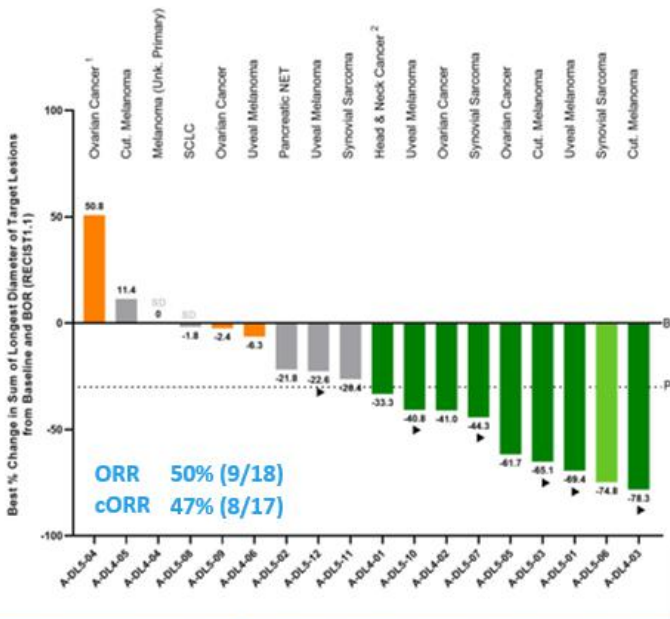
# IMA203 GEN1 in Phase 1a Dose Escalation (N=27#) – BOR and Response over Time



\* Maximum change of target lesions and RECIST 1.1 BOR at different timepoints; # Synovial sarcoma patient [DL3] PD at week 6 not shown as target lesions were not evaluable; PD: Progressive disease; SD: Stable disease; PR: Partial response; cPR: Confirmed partial response; BL: Baseline. Data cut-off Sep 30, 2023 71

# IMA203 GEN1 in Cohort A (N=18) – BOR and Response over Time

## Objective Responses across Multiple Solid Cancer Types



<sup>1</sup> Patient received one dose nivolumab erroneously; <sup>2</sup> Progressive disease at month 6 due to unequivocal progression of non-target lesions, target lesions not evaluable due to external assessment; Initial ORR: Objective response rate according to RECIST 1.3 at any post infusion scan; Confirmed ORR (cORR): Confirmed objective response rate according to RECIST 1.1 for patients with at least two available post infusion scans or patients with progressive disease (PD) at any prior timepoint, patients with ongoing unconfirmed PR not included in cORR calculation; Duration of response (DOR) is confirmed responders is defined as time from first documented response until disease progression/death; Patients with ongoing response will be censored at date of data cut-off; Median DOR is analyzed by using the Kaplan-Meier method; Median Follow-up is analyzed by using the reverse Kaplan-Meier method; PD: Progressive Disease; SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response; BL: Baseline; BOR: Best Overall Response; DOR: Duration of Response

Data cut-off Sep 30, 2023 72

## IMA203 GEN1 in Cohort A – Most Frequent Adverse Events

N=21 Patients in Safety Population<sup>1</sup>

- **Expected cytopenia (Grade 1-4)** associated with lymphodepletion in all patients
- **Mild-moderate cytokine release syndrome (CRS) in 90% (19/21) of patients**
  - 43% (9/21) with Grade 1 CRS
  - 48% (10/21) with Grade 2 CRS
  - No dose-dependent increase of CRS
- **One non-serious, mild (Grade 1) ICANS<sup>2</sup> in DL5**
- **No dose-limiting toxicity**
- **No IMA203-related deaths**

**IMA203 GEN1 monotherapy continues to be well tolerated at total doses  
between 1-10x10<sup>9</sup> TCR-T cells (RP2D)**

<sup>1</sup> Three cutaneous melanoma patients treated with IMA203, and pending post infusion scan included in safety population, but not efficacy population;

<sup>2</sup> ICANS: Immune Effector Cell-Associated Neurotoxicity Syndrome; CRS and ICANS graded by CARTOX criteria (Neelapu et al., 2018)

# IMA203 GEN1 at RP2D – Tolerability Data

## Phase 1a DL4 and Cohort A – All ≥Grade 3 Adverse Events (N=28)

TEAEs by maximum severity for all patients in Ph1a dose escalation DL4 and Ph1b Cohort A dose expansion (RP2D, N=28)<sup>1</sup>

Adverse event (System organ class, Preferred term)	≥ Grade 3		Adverse event (System organ class, Preferred term)	≥ Grade 3	
	No.	%		No.	%
<b>Patients with any adverse event</b>	<b>28</b>	<b>100.0</b>	<b>table continued...</b>		
<b>Adverse Events of Special Interest</b>	<b>1</b>	<b>3.6</b>	<b>General disorders and administration site conditions</b>	<b>1</b>	<b>3.6</b>
Cytokine release syndrome	1	3.6	Pyrexia	1	3.6
ICANS <sup>2</sup>	0	0.0	<b>Hepatobiliary disorders</b>	<b>1</b>	<b>3.6</b>
<b>Blood and lymphatic system disorders</b>	<b>27</b>	<b>96.4</b>	Cholangitis	1	3.6
Neutropenia	18	64.3	<b>Injury, poisoning and procedural complications</b>	<b>1</b>	<b>3.6</b>
Anaemia	14	50.0	Humerus fracture	1	3.6
Leukopenia	13	46.4	<b>Musculoskeletal and connective tissue disorders</b>	<b>1</b>	<b>3.6</b>
Lymphopenia	11	39.3	Muscle spasms	1	3.6
Thrombocytopenia	9	32.1	<b>Nervous system disorders</b>	<b>1</b>	<b>3.6</b>
Leukocytosis	1	3.6	Headache	1	3.6
Lymphocytosis	1	3.6	<b>Skin and subcutaneous tissue disorders</b>	<b>1</b>	<b>3.6</b>
<b>Investigations</b>	<b>7</b>	<b>25.0</b>	Rash maculo-papular	1	3.6
Neutrophil count decreased	4	14.3			
Alanine aminotransferase increased	2	7.1			
Aspartate aminotransferase increased	2	7.1			
White blood cell count decreased	2	7.1			
Blood alkaline phosphatase increased	1	3.6			
<b>Infections and infestations</b>	<b>3</b>	<b>10.7</b>			
Infection	1	3.6			
Septic shock <sup>3</sup>	1	3.6			
Urinary tract infection	1	3.6			
<b>Respiratory, thoracic and mediastinal disorders</b>	<b>3</b>	<b>10.7</b>			
Hypoxia	2	7.1			
Laryngeal inflammation	1	3.6			
<b>Vascular disorders</b>	<b>3</b>	<b>10.7</b>			
Hypotension	2	7.1			
Hypertension	1	3.6			
<b>Metabolism and nutrition disorders</b>	<b>2</b>	<b>7.1</b>			
Failure to thrive	1	3.6			
Hypokalaemia	1	3.6			
Hypophosphataemia	1	3.6			
<b>Eye disorders</b>	<b>1</b>	<b>3.6</b>			
Ulcerative keratitis	1	3.6			

All treatment-emergent adverse events (TEAEs) with ≥ Grade 3 regardless of relatedness to study treatment that occurred in at least 1 patient (except for ICANS, where only Grade 1-2 occurred; listed for completeness due to being an adverse event of special interest) are presented. Adverse events were coded using the Medical Dictionary for Regulatory Activities. Grades were determined according to National Cancer Institute Common Terminology Criteria of Adverse Events, version 5.0. Grades for CRS and ICANS were determined according to CARTOX criteria (Neelapu et al., 2018). Patients are counted only once per adverse event and severity classification. Based on interim data extracted from open clinical database (30-Sep-2023). <sup>1</sup> One patient in Phase 1a DL4 with disease progression after first IMA203 infusion received exploratory second IMA203 infusion and had these ≥ Grade 3 TEAEs only after second infusion, which are included in the table. <sup>2</sup> ICANS: Humeral fracture, Muscle spasms, Neutropenia, Thrombocytopenia; <sup>3</sup> Fatal Adverse events were not considered related to any study drug

- IMA203 was well tolerated at doses as high as ~10x10<sup>9</sup> TCR-T cells
- Most frequent ≥Grade 3 AEs were expected cytopenia associated with lymphodepletion
- No IMA203-related Grade 5 AEs



# Delivering

the Power of T cells  
to Cancer Patients



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