

ACTengine® IMA203 TCR-T Monotherapy Targeting PRAME

– Phase 1b Cohort A Interim Data Update

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Update on IMA203 TCR-T Monotherapy – Phase 1b Cohort A

Delivering a Meaningful Benefit to Patients with an Unmet Need



Martin Wermke, MD

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



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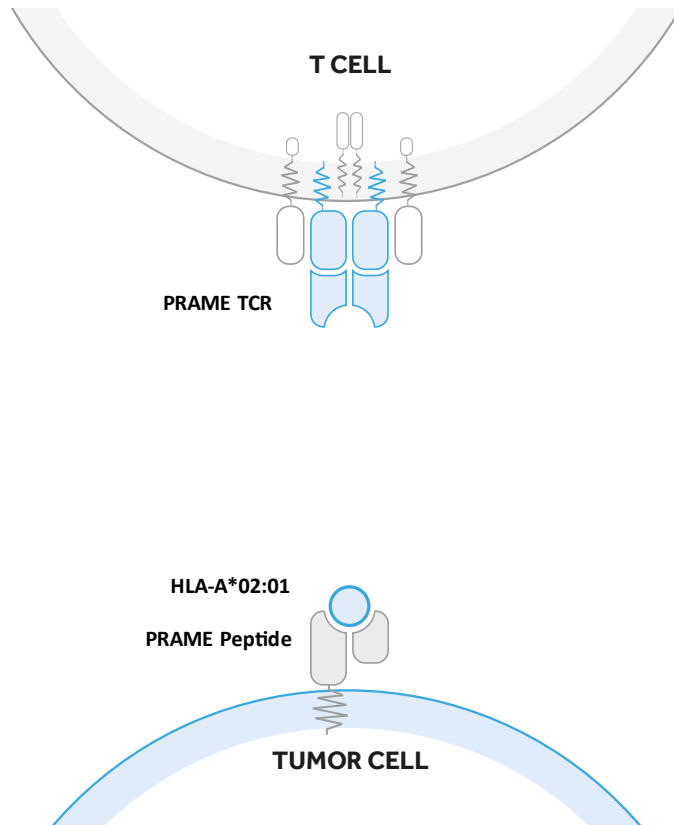
Chief Executive Officer
Immatics

The Multi-Cancer Opportunity of PRAME

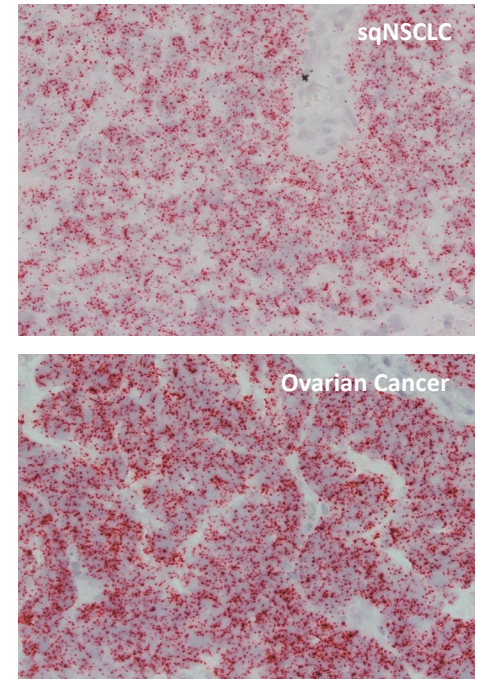
One of the Most Promising Solid Tumor Targets for TCR-based Therapies Known To Date

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)



Unlocking Novel Treatments for Patients with Solid Cancers

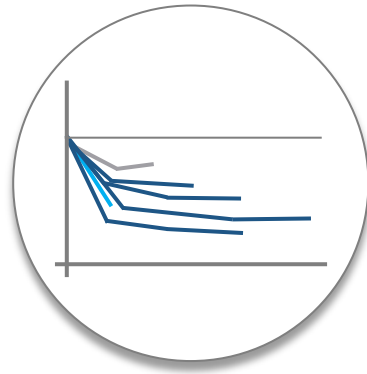
Key Pillars of Developing a Successful TCR-T Product Candidate



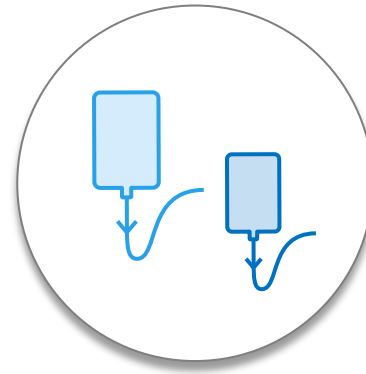
Safety



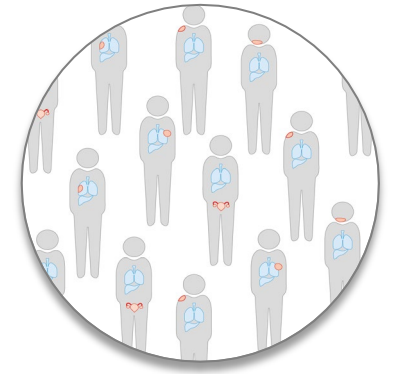
Anti-Tumor Activity



Durability



Product Quality



Broad Reach

Key Pillars of Developing a Successful TCR-T Product Candidate

Summary of Today's Update on IMA203 TCR-T Phase 1b Cohort A



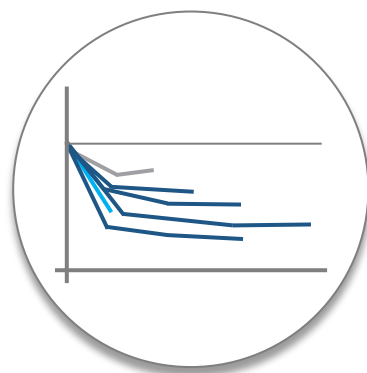
Safety

Manageable tolerability
at doses as high as
~ 9×10^9 TCR-T cells



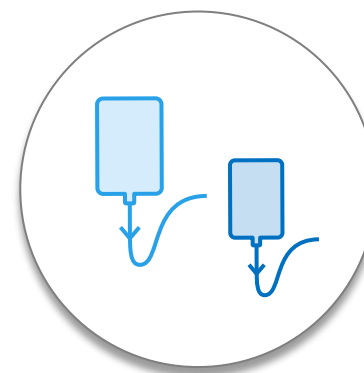
Anti-Tumor Activity

High rate of
objective responses:
64% (7/11) ORR¹
67% (6/9) cORR²



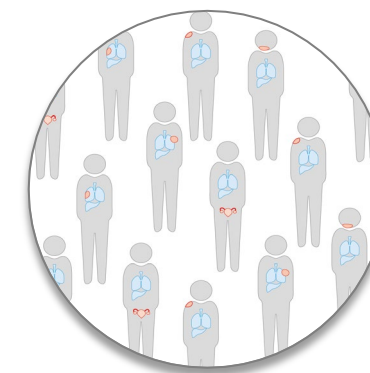
Durability

Ongoing durable
responses at 9+ months
mDOR: Not reached
min 1.3+, max 8.8+
mFU: 8.5 months



Product Quality

Rapid manufacturing
time of 7 days
(+ 7-day release testing),
manufacturing
success rate of 94%

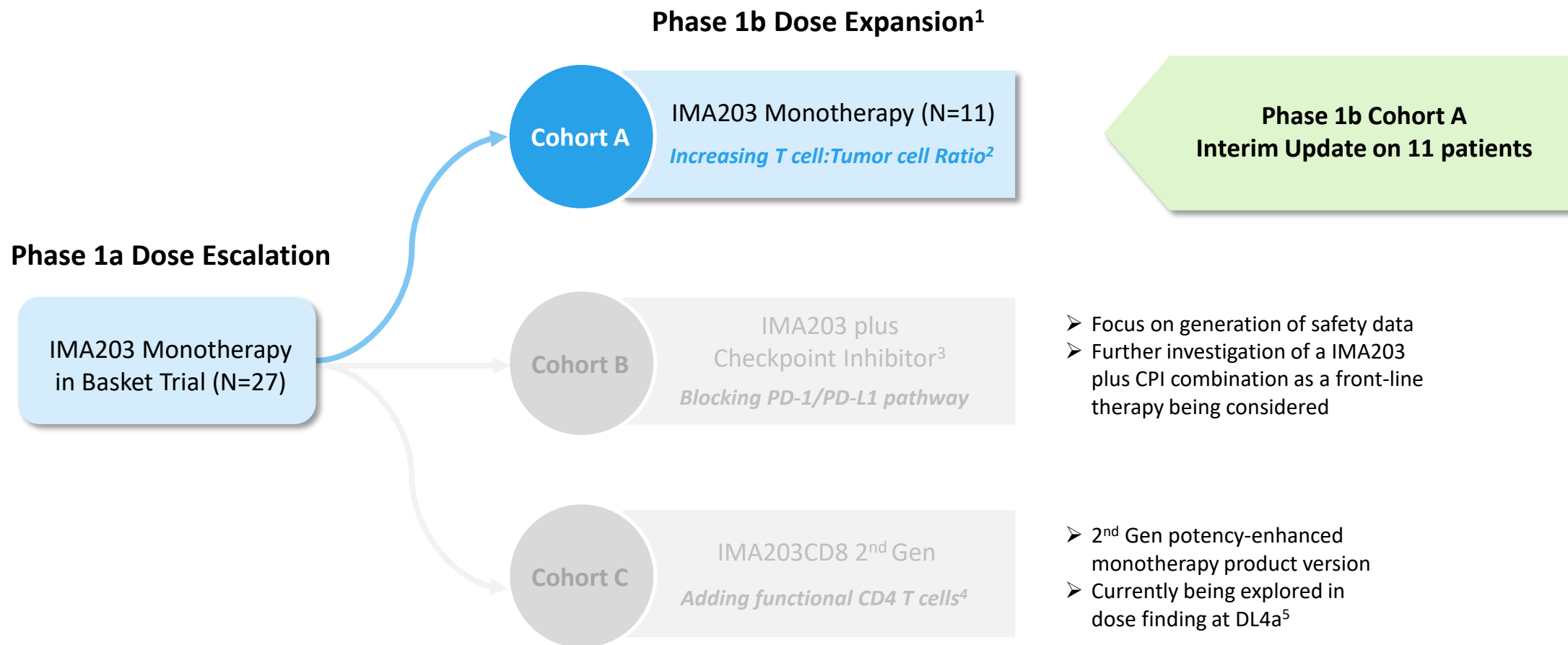


Broad Reach

Confirmed objective
responses in broad
range of solid cancer
types at low, medium
and high PRAME levels
above threshold

ACTengine® IMA203 TCR-T Phase 1 Design

Focus on IMA203 TCR-T Monotherapy Investigated in Cohort A



Data cut-off Apr 04, 2023

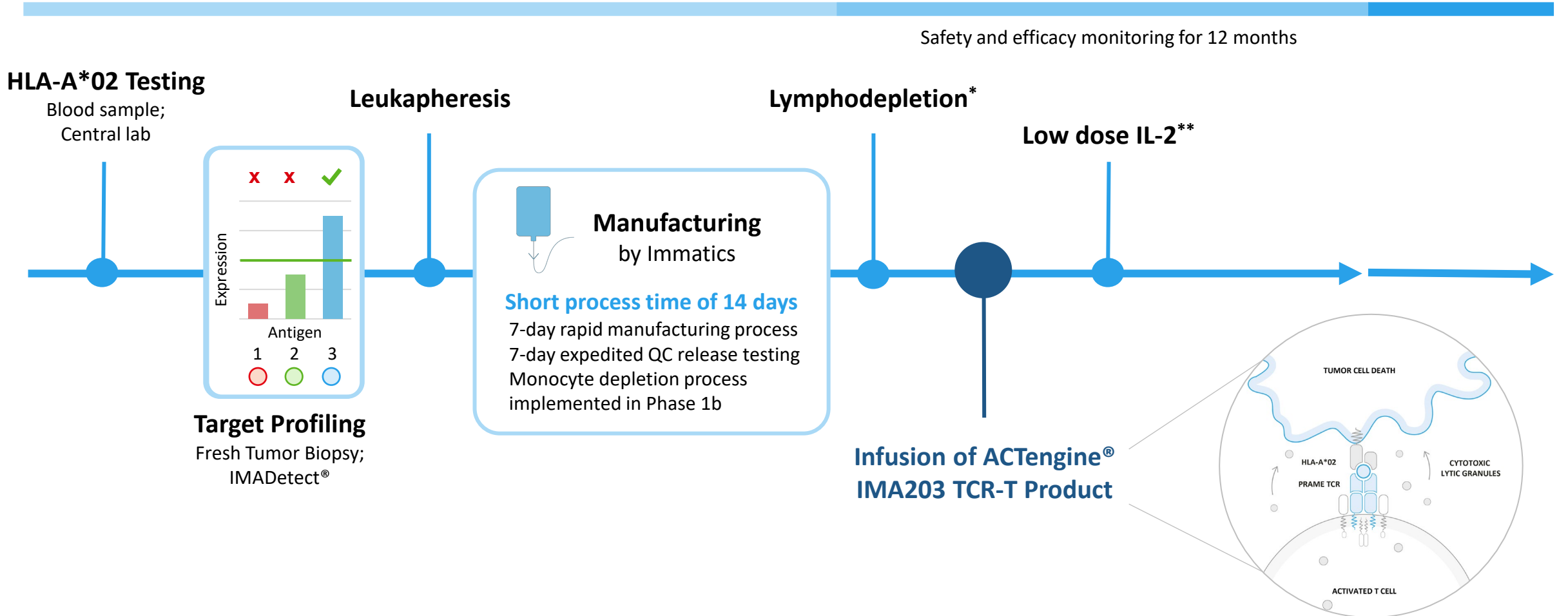
¹ Updated target dose (provisional recommended Phase 2 dose, RP2D) determined at DL4+DL5 for Cohort A and B, for Cohort C treatment of n=3 patients at DL3 completed, enrollment at DL4a ongoing before continuation at DL4b and potentially DL5; ² Demonstrated to be associated with durable response: Locke *et al.* 2020 Blood Advances; ³ Opdivo® (nivolumab): programmed death-1 (PD-1) immune checkpoint inhibitor; ⁴ Demonstrated to be important for long-term remission: Melenhorst *et al.* 2022 Nature, Bai *et al.* 2022 Science Advances; ⁵ IMA203CD8 Dose Level 4a: 0.481-0.8x10⁹ transduced viable CD8 T cells/m² BSA

ACTengine® IMA203 TCR-T Monotherapy – Patient Flow

Screening & Manufacturing Phase

Treatment & Observation Phase

Long Term Follow-up



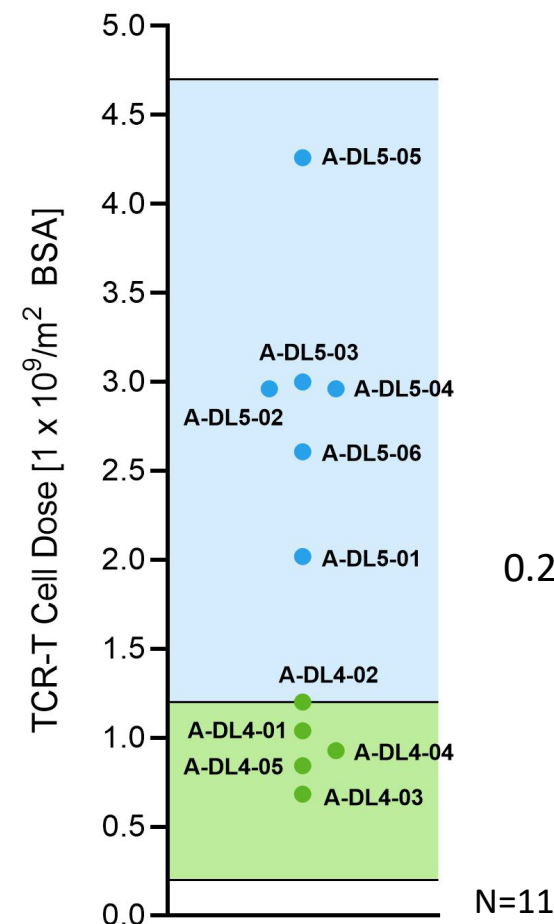
* 30 mg/m² Fludarabine and 500 mg/m² Cyclophosphamide for 4 days; ** 1m IU daily days 1-5 and twice daily days 6-10

ACTengine® IMA203 TCR-T Monotherapy – Phase 1b Cohort A

Patient and Product Characteristics

Patients in Phase 1b Cohort A (N=11) ¹	
Age Mean (min, max)	55.4 (31, 79)
Gender Male / Female [% of patients]	45.5 / 54.5
Prior lines of treatment Mean (min, max)	3.7 (1, 10)
LDH at baseline >1 x ULN [% of patients]	54.5
Baseline tumor burden Mean target lesion sum of diameter [mm] (min, max)	73.8 (21.0, 207.3)
Total infused dose Mean TCR-T cells ² infused [x10 ⁹] (min, max)	3.67 (1.30, 8.84)

Heavily pre-treated, metastatic last-line patients that have exhausted all available standard of care treatments



DL5 cleared for safety,
updated provisional RP2D
comprises DL4 + DL5:
0.2-4.7 x 10⁹ TCR-T cells/m² BSA

¹Including ovarian cancer patient A-DL5-04 who erroneously received one dose of nivolumab and is part of intent-to-treat (shown here) but not per-protocol population;

²Transduced viable CD8 T cells; ULN: Upper limit of normal; LDH: Lactate dehydrogenase; BSA: Body surface area; RP2D: Recommended Phase 2 Dose

Most Frequent Adverse Events – Phase 1b Cohort A (N=11)

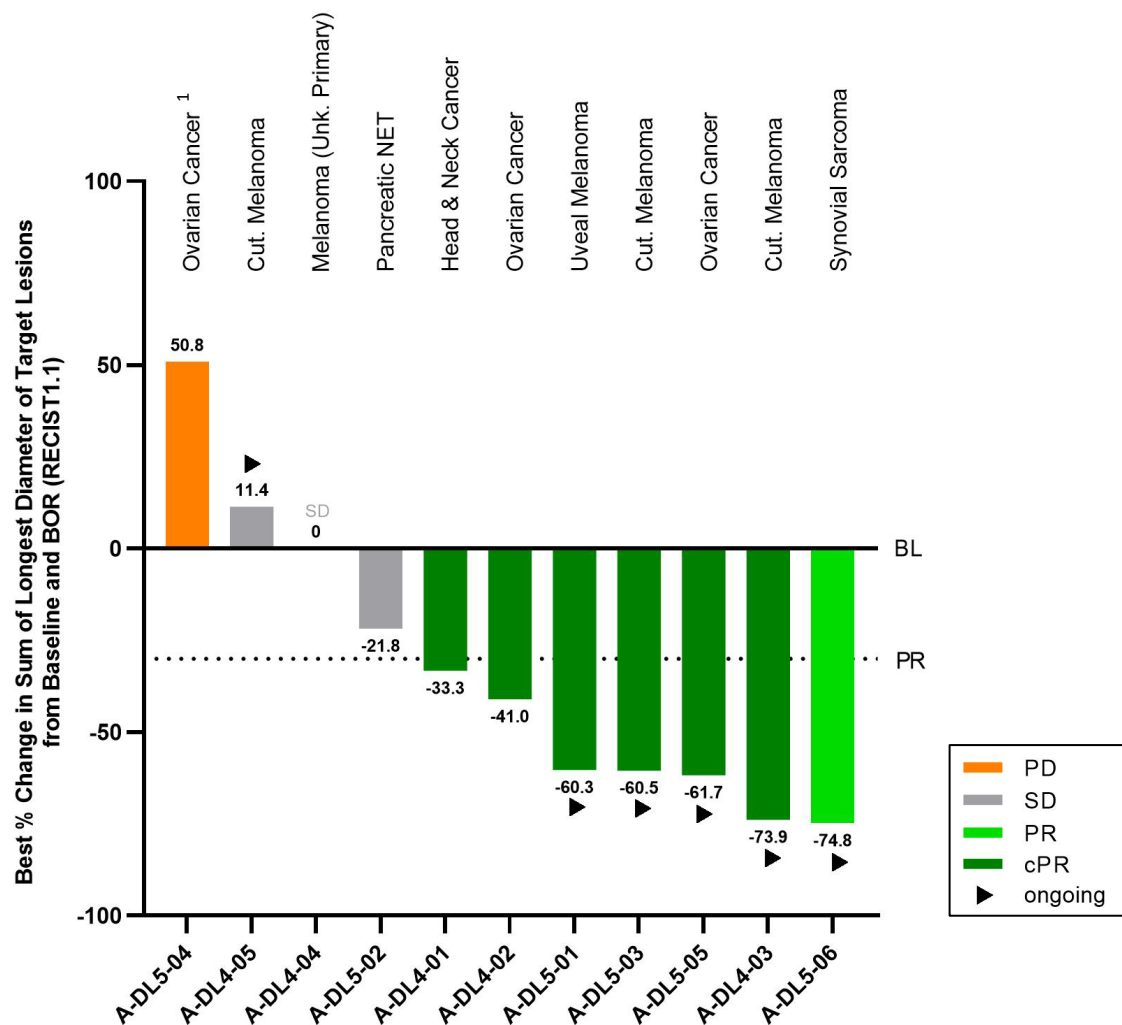
Manageable Treatment-emergent Adverse Events (TEAEs)

- **Expected cytopenia (Grade 1-4)** associated with lymphodepletion in all patients
- **Low-moderate cytokine release syndrome (CRS)** in 91% (10/11) of patients
 - 45% (5/11) of patients had Grade 1 CRS (3 in DL4, 2 in DL5)
 - 45% (5/11) of patients had Grade 2 CRS (2 in DL4, 3 in DL5)
 - No dose-dependent increase of CRS
- **No ICANS¹**
- **No Dose-limiting toxicity**
- For IMA203 TCR-T monotherapy tolerability profile including Phase 1a dose escalation, see appendix

IMA203 TCR-T monotherapy shows manageable tolerability at total doses as high as $\sim 9 \times 10^9$ TCR-T cells

Best Overall Response – Phase 1b Cohort A

Deep Objective Responses Independent of Tumor Type



ORR (at ~week 6)² 64% (7/11)

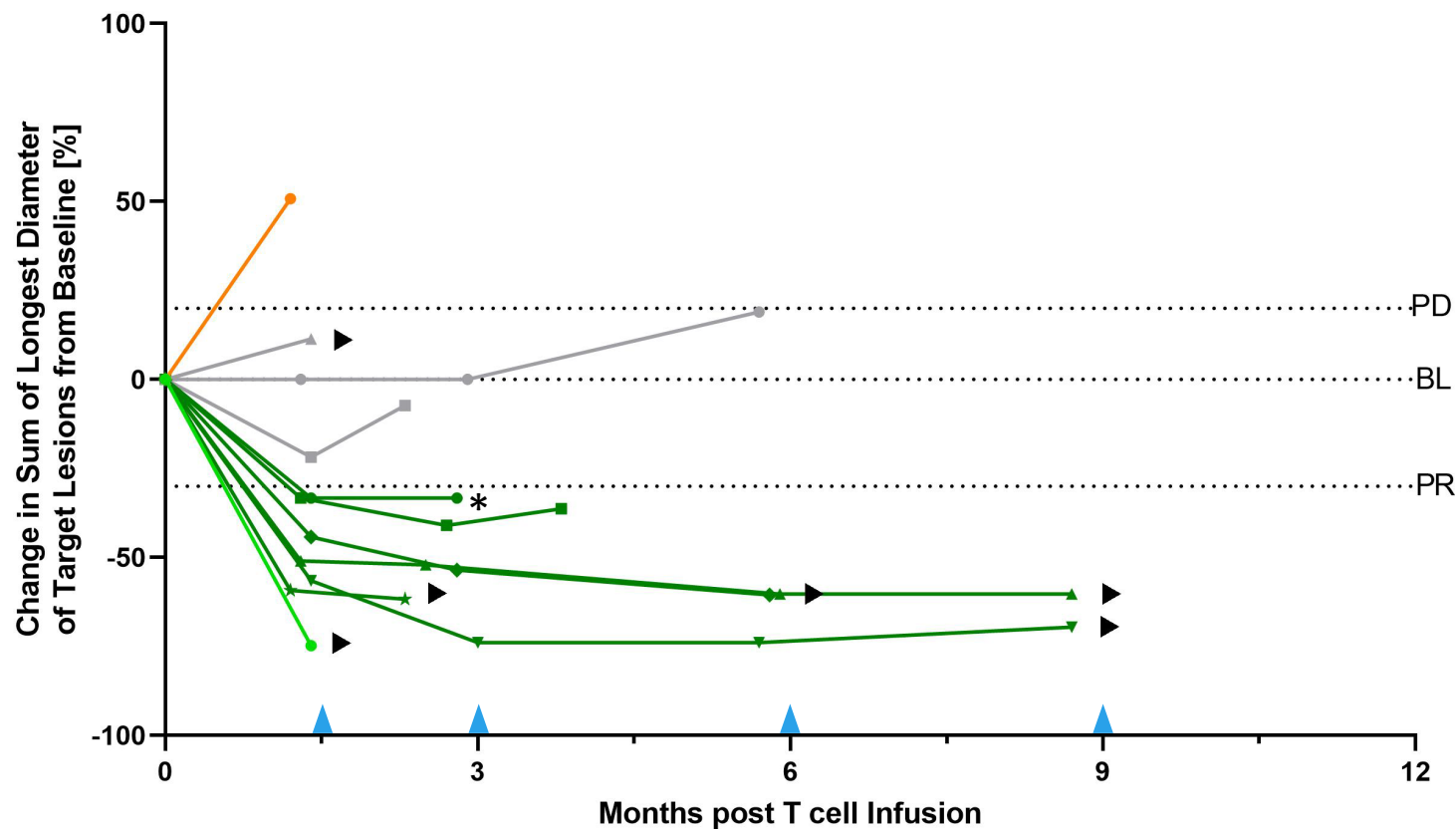
cORR (at ~month 3)³ 67% (6/9)

Deep objective responses observed across multiple, heavily pre-treated tumor types

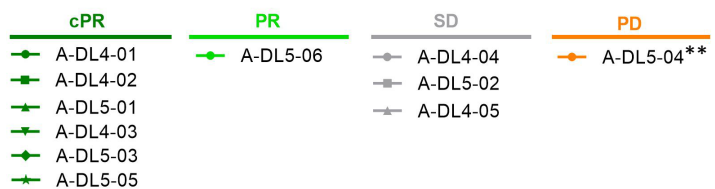
- Responses observed in cutaneous and uveal melanoma, synovial sarcoma, head and neck cancer, and ovarian cancer
- Initial responses at week 6 were confirmed in all 6 responders with available subsequent 3-month scan
- All cut. melanoma patients were CPI-refractory
- All ovarian cancer patients were platinum-resistant

Response over Time – Phase 1b Cohort A

Durable Partial Responses 9+ Months after IMA203 TCR-T Treatment



Best overall response (RECIST 1.1)



▶ Ongoing

* Response until 5.7 months post infusion, target lesion response assessment not available (external assessment)

▲ Scans at approximately week 6, month 3 and then every 3 months

Median DOR¹,
min, max DOR

Not reached,
1.3+, 8.8+ months

Median Follow-up²

8.5 months

Median time from IMA203 TCR-T infusion to onset of response was 1.4 months

Ongoing responses in 5 of 7 responders:

- 2 cPRs (cut. & uveal melanoma) ongoing at 9+ months
- 1 cPR (cut. melanoma) ongoing at 6+ months
- 1 cPR (ovarian cancer) ongoing at ~3 months
- 1 PR (synovial sarcoma) ongoing at 6+ weeks

Deep & Durable Responses in Heavily Pre-Treated Patients – Phase 1b Cohort A



Immatics®

Patient ID	Indication	No of prior treatment lines	Prior treatments	Total infused dose TCR-T cells ¹ [x10 ⁹]	BOR	BOR (Max % change of target lesions)	Comment
A-DL5-01	Uveal Melanoma	1	ARRY614/Nivolumab	4.16	cPR	-60.3	Ongoing response 10.1 months post infusion
A-DL4-03	Cut. Melanoma	7	Dabrafenib/Trametinib, Pembrolizumab, Dabrafenib/Trametinib, Vemurafenib/Cobimetinib, Dabrafenib/Trametinib, IMCgp-100, Encorafenib/Binimetinib	1.30	cPR	-73.9	Ongoing response 9.9 months post infusion
A-DL5-03	Cut. Melanoma	3	Interferon, Pembrolizumab, Nivolumab/Ipilimumab	5.12	cPR	-60.5	Ongoing response 6.2 months post infusion
A-DL4-01	Head & Neck Cancer	1	Carboplatin/Paclitaxel	1.92	cPR	-33.3	Response until 5.7 months post infusion
A-DL4-02	Ovarian Cancer	10	Carboplatin/Taxol, Taxol, Gemcitabine/Carboplatin, Olaparib, Letrozole, Rucaparib, UPCC 03118 (CAR-T cell directed folate receptor), Bevacizumab/Cyclophosphamide, Carboplatin, Doxorubicin	1.97	cPR	-41.0	Response until 3.8 months post infusion
A-DL5-05	Ovarian Cancer	3	Adriamycin/Cytotaxan/Taxol, Carboplatin/Taxol, Carboplatin/Doxil	8.84	cPR	-61.7	Ongoing response 2.5 months post infusion
A-DL5-06	Synovial Sarcoma	1	Adriamycin/Ifosfamide/Mesna	3.94	PR	-74.8	Initial PR at week 6, 3-month scan pending
A-DL4-04	Melanoma (Unk. Primary)	2	Nivolumab/Ipilimumab, Nivolumab	1.73	SD	0.0	Disease stabilization until 5.7 months post infusion
A-DL4-05	Cut. Melanoma	5	Nivolumab, Nivolumab (re-exposure), Nivolumab/Ipilimumab, Dabrafenib/Trametinib, Nivolumab	1.63	SD	11.4	Ongoing disease stabilization 2.1 months post infusion
A-DL5-02	Pancreatic Neuroendocrine Tumor	3	Lanreotid, Streptozocin/5-Fluorouracil, Everolimus	5.12	SD	-21.8	Disease stabilization until 2.3 months post infusion
A-DL5-04*	Ovarian Cancer	5	Paclitaxel/Carboplatin, Niraparib, Doxorubicin/Liposomal/Carboplatin, 2020-0808 ZN-C3/Gemcitabine, 2020-0755 COM 701/BMS-986207/Nivolumab	4.68	PD	50.8	Progressive disease at 1.2 months post infusion

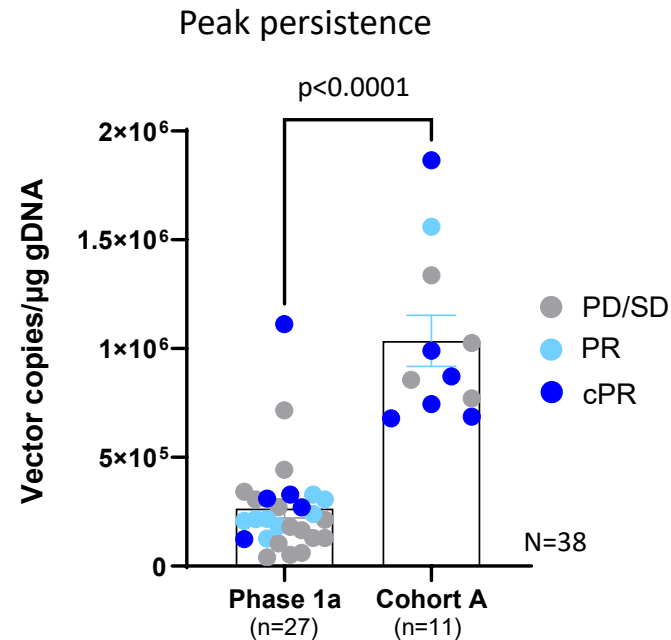
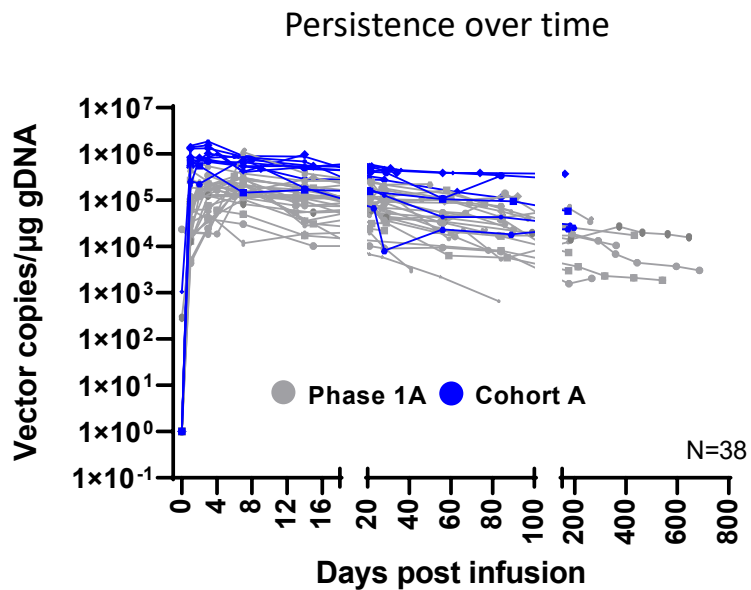
¹ Transduced viable CD8 T cells; PD: Progressive Disease; SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response; BL: Baseline; BOR: Best Overall Response

*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.

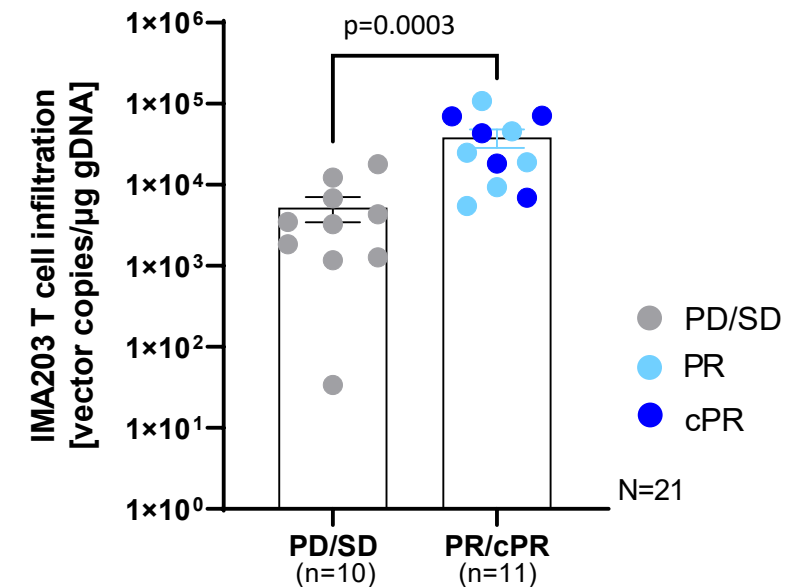
Biological Data Consistent with Clinical Data

IMA203 TCR-T Levels and Tumor Infiltration across Patients in Phase 1a and Phase 1b Cohort A

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



IMA203 T cells found in all evaluable tumor tissues, level of infiltration associated with objective responses¹

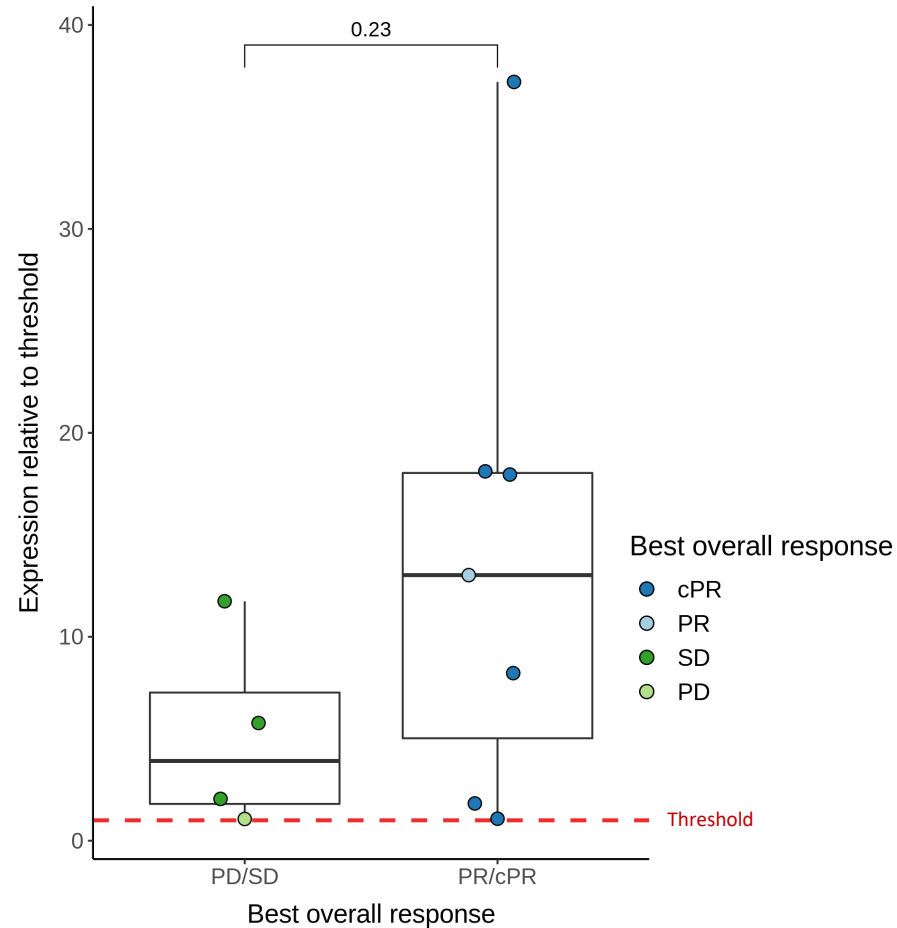
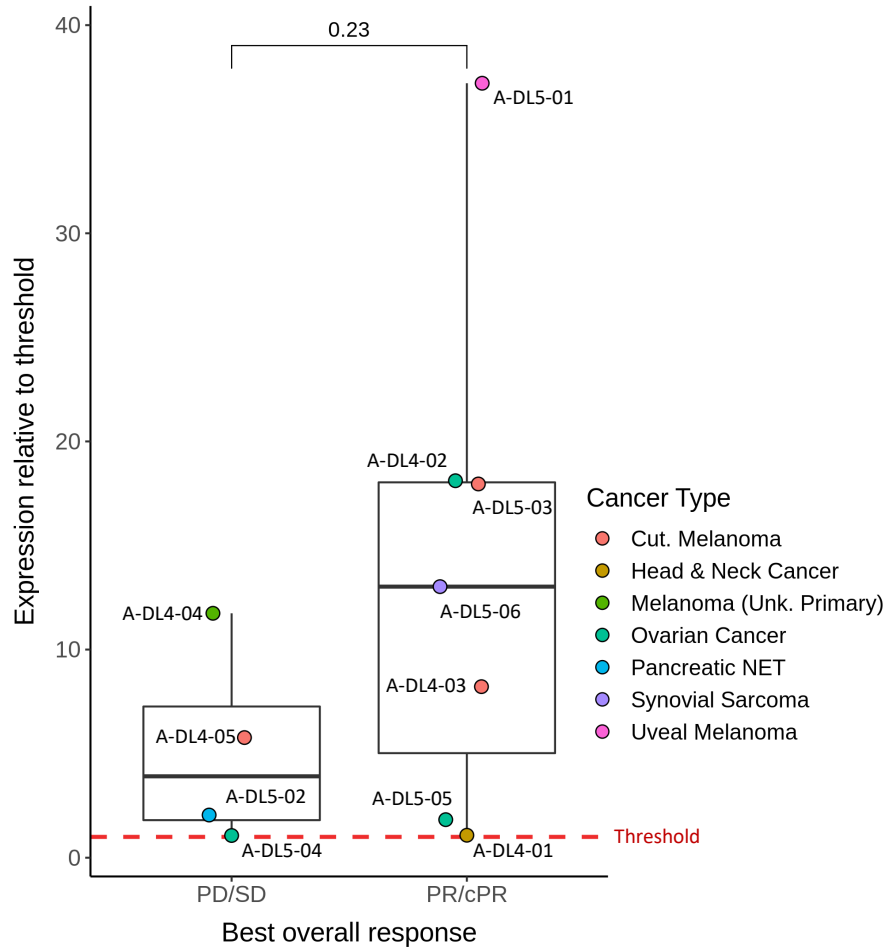




Responses above Immatics' PRAME RNA Threshold Independent of Tumor Type

Highlighting Tumor Types (left) and Type of Best Overall Response (right) – Phase 1b Cohort A

PRAME RNA expression in pre-treatment biopsies relative to threshold

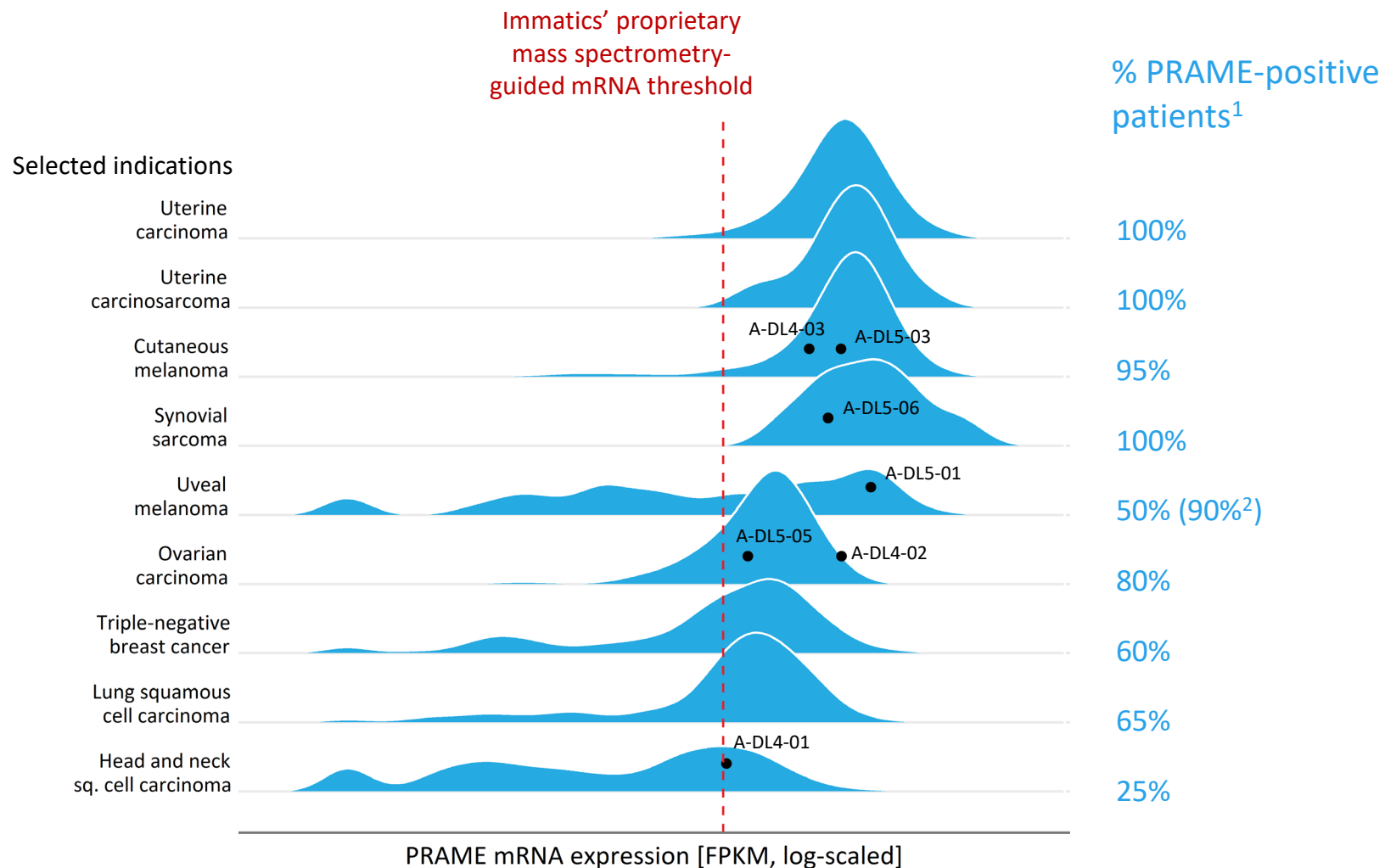


IMA203 achieved objective responses at all expression levels above Immatics' mass spectrometry-guided RNA threshold

IMA203 has the potential to provide clinical benefit for all PRAME biomarker-positive cancer patients

Potential of IMA203 in Additional Solid Cancer Indications

Based on PRAME Expression in IMA203 TCR-T Responders – Phase 1b Cohort A



ACTengine® IMA203 TCR-T Monotherapy Targeting PRAME

Summary of Phase 1b Cohort A Interim Data Update

- **Manageable tolerability** with no high-grade CRS, no ICANS in 11 patients in Cohort A¹
- **Objective responses observed in heavily pre-treated last-line solid cancer patients** including checkpoint-refractory cutaneous melanoma, platinum-resistant ovarian cancer, uveal melanoma, head and neck cancer, synovial sarcoma
- **High objective response rate (ORR):**
 - 64% (7/11) ORR (at ~week 6)
 - 67% (6/9) cORR (at ~month 3)
- **Ongoing durable responses:**
 - Median duration of response not reached at a median follow-up time of 8.5 months
 - Ongoing PRs 9+ months after IMA203 TCR-T treatment
- **Objective responses independent of tumor type at low, medium and high PRAME levels above threshold**
- **Manufacturing success rate of 94%** to reach current RP2D, **rapid 7-day manufacturing process (+7-day release testing)**

**Increased confidence in the success and broad potential of targeting PRAME
and our product candidate IMA203 TCR-T**

Immatics' ACTengine® IMA203 TCR-T Development Strategy

Two Pillared Strategy

FAST & FOCUSED

Objective: Deliver best-in-class therapy in 1-2 last-line solid cancer types as fast as possible

- Focus on indications with PRAME prevalence above 80% with available clinical PoC, such as cut. melanoma (potentially bundled with uveal melanoma) and ovarian cancer
- Highly modular and scalable manufacturing facility expected to be operational in 2024 to support efforts to maximize speed to market
- Planned start of a first Phase 2 trial in 1H 2024 – targeted to be already registration-directed

GO BROAD

Objective: Expand development to other cancer types

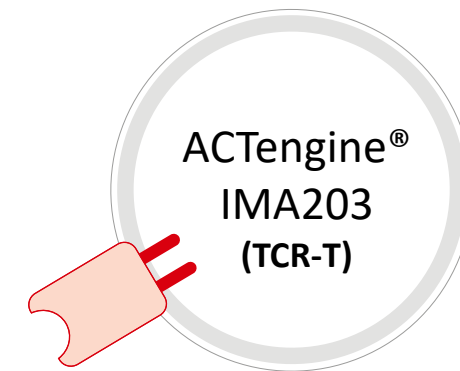
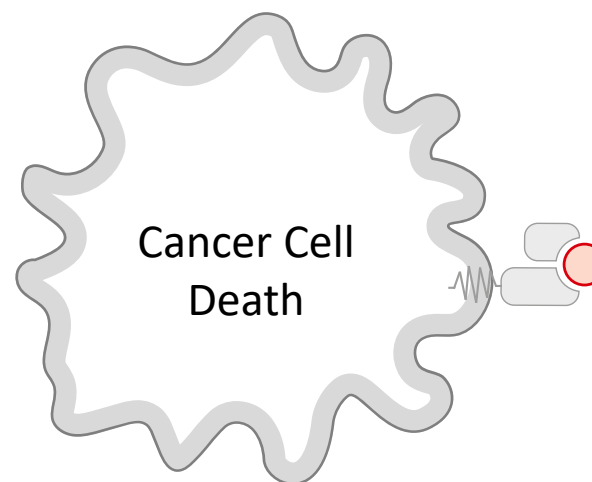
- Signal finding in other cancer types with a broad patient reach, such as uterine cancer, lung cancer, breast cancer, head and neck cancer

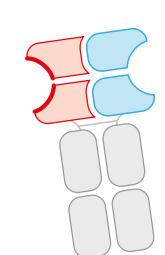
Update on all three IMA203 Phase 1b cohorts and clinical development path towards registration-directed trials and potential commercialization for PRAME TCR-T monotherapy is planned for 4Q 2023

Realizing the Full Multi-Cancer Opportunity of PRAME

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

Indication	% PRAME positive patients ¹
Uterine Carcinoma	100%
Uterine Carcinosarcoma	100%
Sarcoma Subtypes	up to 100%
Cut. Melanoma	95%
Uveal Melanoma ²	90%
Ovarian Carcinoma	80%
Squamous NSCLC	65%
TNBC	60%
Small Cell Lung Cancer	55%
Kidney Carcinoma	up to 45%
Cholangiocarcinoma	35%
Adeno NSCLC	25%
Breast Carcinoma	25%
HNSCC	25%
Esophageal Carcinoma	20%
HCC	20%
Bladder Carcinoma	20%



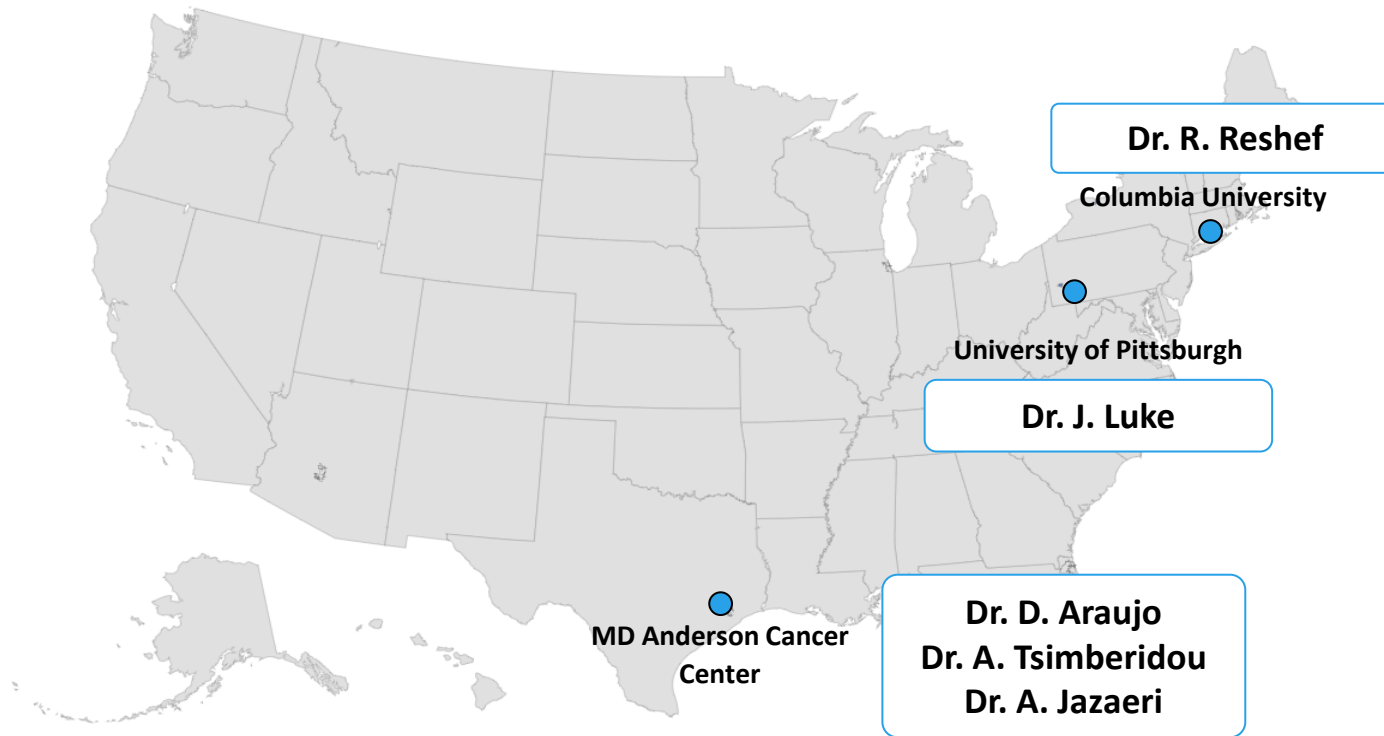
- 
- TCER® IMA402 (TCR Bispecific)**
- ✓ CTA submitted
 - ✓ Start of clinical trial planned in 2H 2023
 - ✓ First clinical data 2024

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

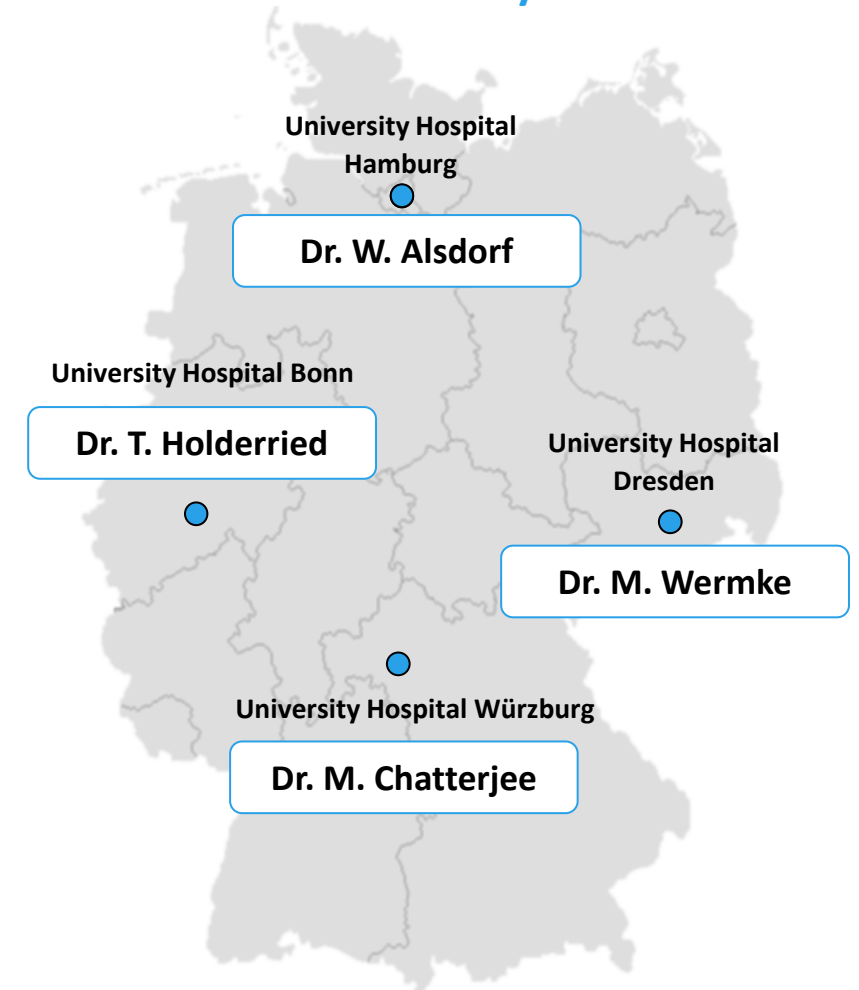
Leverage the full potential of targeting PRAME by continued evaluation of the best suited therapeutic modality (ACTengine® vs. TCER® or both) for each cancer type

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

United States



Germany



... and the Investigators at the Clinical Sites

Delivering

the Power of T cells
to Cancer Patients

Appendix

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ACTengine® IMA203 TCR-T 1st Gen Monotherapy Tolerability Data

Phase 1a and Phase 1b Cohort A – All ≥Grade 3 Adverse Events (N=39)

TEAEs by maximum severity for all patients in Ph1a dose escalation and Ph1b Cohort A dose expansion (N=39)¹

Adverse event (System organ class, Preferred term)	≥ Grade 3		Adverse event (System organ class, Preferred term)	≥ Grade 3	
	No.	%		No.	%
Patients with any adverse event	39	100.0	table continued...		
Adverse Events of Special Interest			General disorders and administration site conditions		
Cytokine release syndrome	2	5.1	Condition aggravated ⁴	1	2.6
ICANS ²	0	0.0	Fatigue	1	2.6
Blood and lymphatic system disorders			Pyrexia	1	2.6
Neutropenia	32	82.1	Swelling face	1	2.6
Lymphopenia	24	61.5	Vascular disorders		
Leukopenia	22	56.4	Hypertension	3	7.7
Anaemia	20	51.3	Hypotension	1	2.6
Thrombocytopenia	15	38.5	Metabolism and nutrition disorders		
Cytopenia	1	2.6	Hypokalaemia	2	5.1
Leukocytosis	1	2.6	Failure to thrive	1	2.6
Lymphocytosis	1	2.6	Injury, poisoning and procedural complications		
Infections and infestations			Humerus fracture	1	2.6
Appendicitis	1	2.6	Infusion related reaction	1	2.6
COVID-19	1	2.6	Renal and urinary disorders		
Enterococcal infection	1	2.6	Acute kidney injury	1	2.6
Infection	1	2.6	Proteinuria	1	2.6
Orchitis	1	2.6	Cardiac disorders		
Sepsis ^{4,5}	1	2.6	Atrial fibrillation ³	1	2.6
Septic shock ⁴	1	2.6	Endocrine disorders		
Respiratory, thoracic and mediastinal disorders			Inappropriate antidiuretic hormone secretion	1	2.6
Hypoxia	2	5.1	Eye disorders		
Bronchial obstruction	1	2.6	Ulcerative keratitis	1	2.6
Laryngeal inflammation	1	2.6	Hepatobiliary disorders		
Pleural effusion	1	2.6	Cholangitis	1	2.6
Respiratory failure	1	2.6	Immune system disorders		
Investigations			Contrast media allergy	1	2.6
Alanine aminotransferase increased	1	2.6	Musculoskeletal and connective tissue disorders		
Aspartate aminotransferase increased	1	2.6	Muscle spasms	1	2.6
Blood alkaline phosphatase increased	1	2.6	Nervous system disorders		
Blood creatinine increased	1	2.6	Headache	1	2.6
Blood fibrinogen decreased	1	2.6	Reproductive system and breast disorders		
Gastrointestinal disorders			Vaginal haemorrhage	1	2.6
Abdominal pain	1	2.6	Skin and subcutaneous tissue disorders		
Diarrhoea	1	2.6	Rash maculo-papular	1	2.6
Ileus	1	2.6			
Vomiting	1	2.6			

- IMA203 was well tolerated
- No Adverse Event ≥Grade 3 was observed with a frequency ≥10% when excluding expected cytopenias 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 (04-Apr-2023); ¹ 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; ² ICANS: Immune effector cell-associated neurotoxicity syndrome; ³ DLT: Dose limiting toxicity in phase 1a at DL2 reported on March 17, 2021; ⁴ Fatal Adverse events were not considered related to any study drug; ⁵ Patient died from sepsis of unknown origin and did not receive IMA203 TCR-T cells.

ACTengine® IMA203 TCR-T 1st Gen Monotherapy Tolerability Data

Focus on IMA203 Phase 1b Cohort A – All ≥Grade 3 Adverse Events (N=11)

TEAEs by maximum severity for all patients in Ph1b Cohort A dose expansion (N=11)

Adverse event (System organ class, Preferred term)	≥ Grade 3		Adverse event (System organ class, Preferred term)	≥ Grade 3	
	No.	%		No.	%
Patients with any adverse event	11	100.0	table continued...		
Adverse Events of Special Interest			Investigations		
Cytokine release syndrome	0	0.0	Alanine aminotransferase increased	1	9.1
ICANS ¹	0	0.0	Aspartate aminotransferase increased	1	9.1
			Blood alkaline phosphatase increased	1	9.1
Blood and lymphatic system disorders			Eye disorders		
Neutropenia	10	90.9	Ulcerative keratitis	1	9.1
Lymphopenia	6	54.5			
Leukopenia	5	45.5	Gastrointestinal disorders		
Anaemia	5	45.5	Ileus	1	9.1
Thrombocytopenia	4	36.4			
Leukocytosis	1	9.1	Infections and infestations		
Lymphocytosis	1	9.1	Infection	1	9.1
			Nervous system disorders		
			Headache	1	9.1
			Respiratory, thoracic and mediastinal disorders		
			Laryngeal inflammation	1	9.1

All treatment-emergent adverse events (TEAEs) with ≥ Grade 3 regardless of relatedness to study treatment that occurred in at least 1 patient (except for CRS and ICANS, where only Grade 1-2 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 (04-Apr-2023). ¹ ICANS: Immune effector cell-associated neurotoxicity syndrome.

- IMA203 was well tolerated
- No Adverse Event ≥Grade 3 was observed with a frequency ≥10% when excluding expected cytopenias associated with lymphodepletion
- No IMA203-related Grade 5 Adverse Events

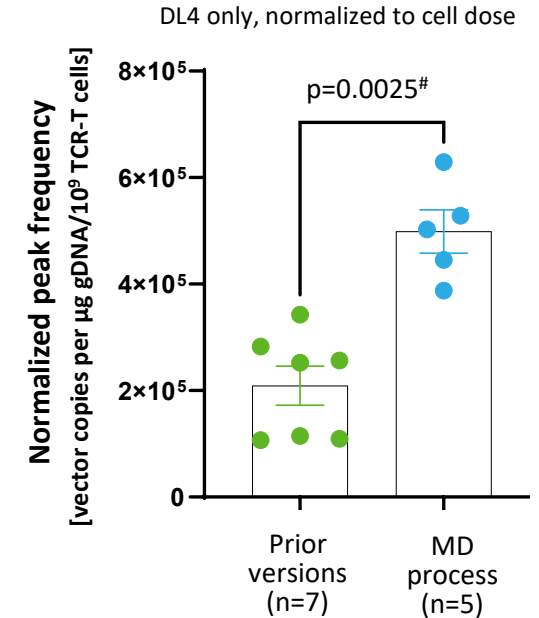
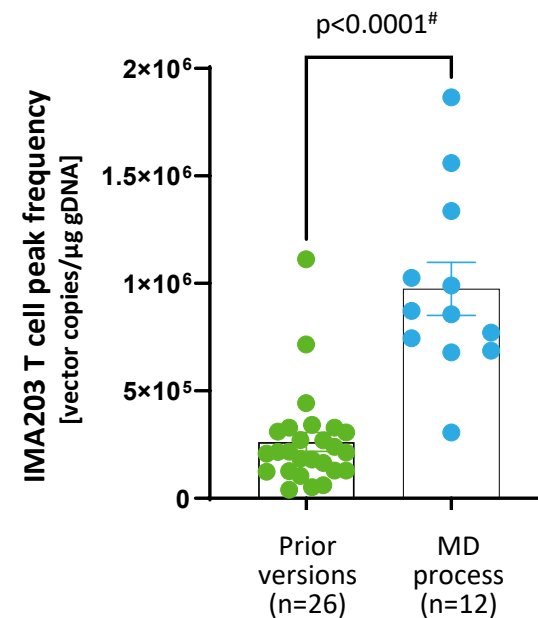
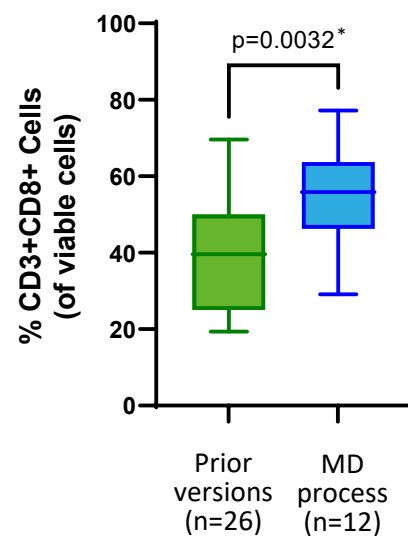
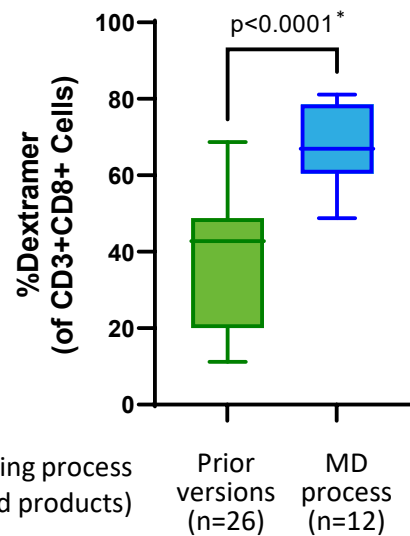
Favorable TCR-T Product Characteristics and High TCR-T Levels in Patients

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

Improved TCR-T product features



Increased peak TCR-T levels in patients



Manufacturing success rate of 94% to reach provisional RP2D**

Mean cell dose infused in 11 patients in Phase 1b Cohort A was 3.67x10⁹ TCR-T cells

Focus on Melanoma Patients Phase 1a (DL4 only) and Phase 1b Cohort A

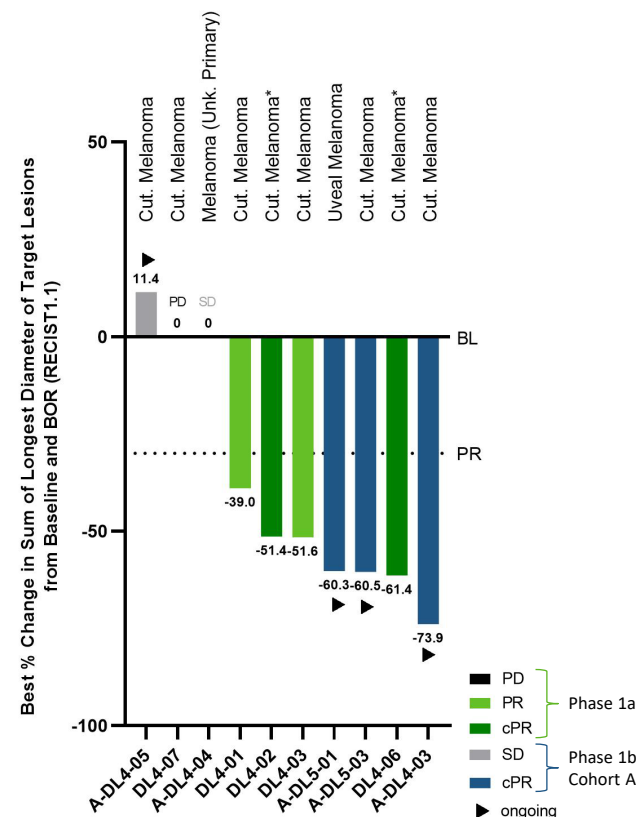
Continuous Improvement from Phase 1a to Phase 1b Cohort A

Patient Characteristics (n=10)

Prior lines of treatment Mean (min, max)	4.5 (1, 7)
Previous lines of CPI Mean (Min, Max)	2.6 (1, 4)
LDH at baseline >1 x ULN [% of patients]	60.0
Baseline tumor burden Mean target lesion sum of diameter [mm] (min, max)	66.9 (21.0, 178.7)
Total infused dose Mean TCR-T cells ¹ infused [x10 ⁹] (min, max)	2.12 (1.07, 5.12)
No. of Target- & Non-Target Lesions	60.0% with >3 lesions 40.0% with liver/brain lesions

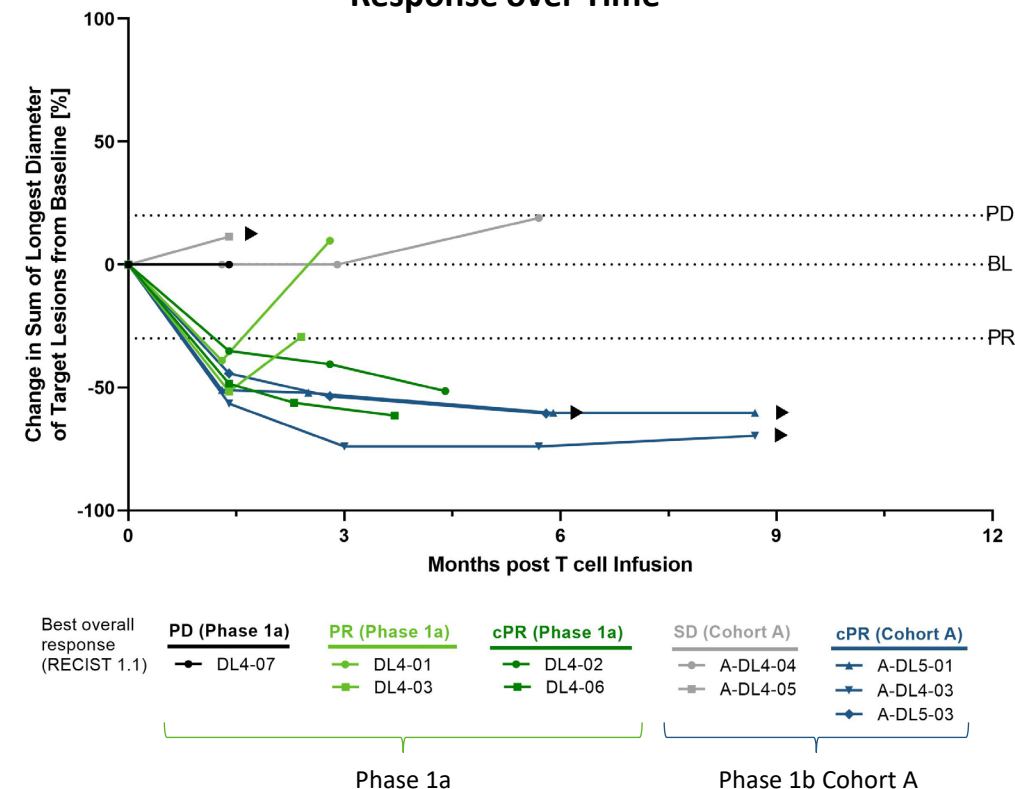
- Heavily pre-treated melanoma patients after 1-4 lines of CPI: Cutaneous (N=8), uveal (N=1) and melanoma of unk. primary (N=1)
- Phase 1a (N=5): previous manufacturing process
- Phase 1b Cohort A (N=5): new monocyte depletion process, higher dose

Best Overall Response



ORR² = 70% (7/10)
cORR³ = 56% (5/9)

Response over Time



Median DOR⁴,
min, max DOR

Not reached,
2.4, 8.8+ months

Median Follow-up⁵

8.5 months

* Maximum change of target lesions and RECIST 1.1 at different timepoints. ¹ Transduced viable CD8 T cells; ² Initial ORR: Objective response rate according to RECIST 1.1 at first scan post infusion at ~week 6; ³ Confirmed ORR (cORR): Confirmed objective response rate according to RECIST 1.1 for patients with available second scan post infusion at ~3 months or patients with progressive disease (PD) at any timepoint before this scan; ⁴ 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; ⁵ 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; BOR: Best Overall Response; BL: Baseline; CPI: Checkpoint inhibitor; LDH: Lactate dehydrogenase

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