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# A Phase 1 Trial of IMA203CD8, a PRAME-directed TCR T-cell Therapy in PRAME-positive Solid Tumors

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# Declaration of Interests

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***Employment or leadership position: None***

***Consultancy / advisory activities: None***

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***Patents, copyrights, licensing rights or royalties: None***

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***Other financial relationships: None***

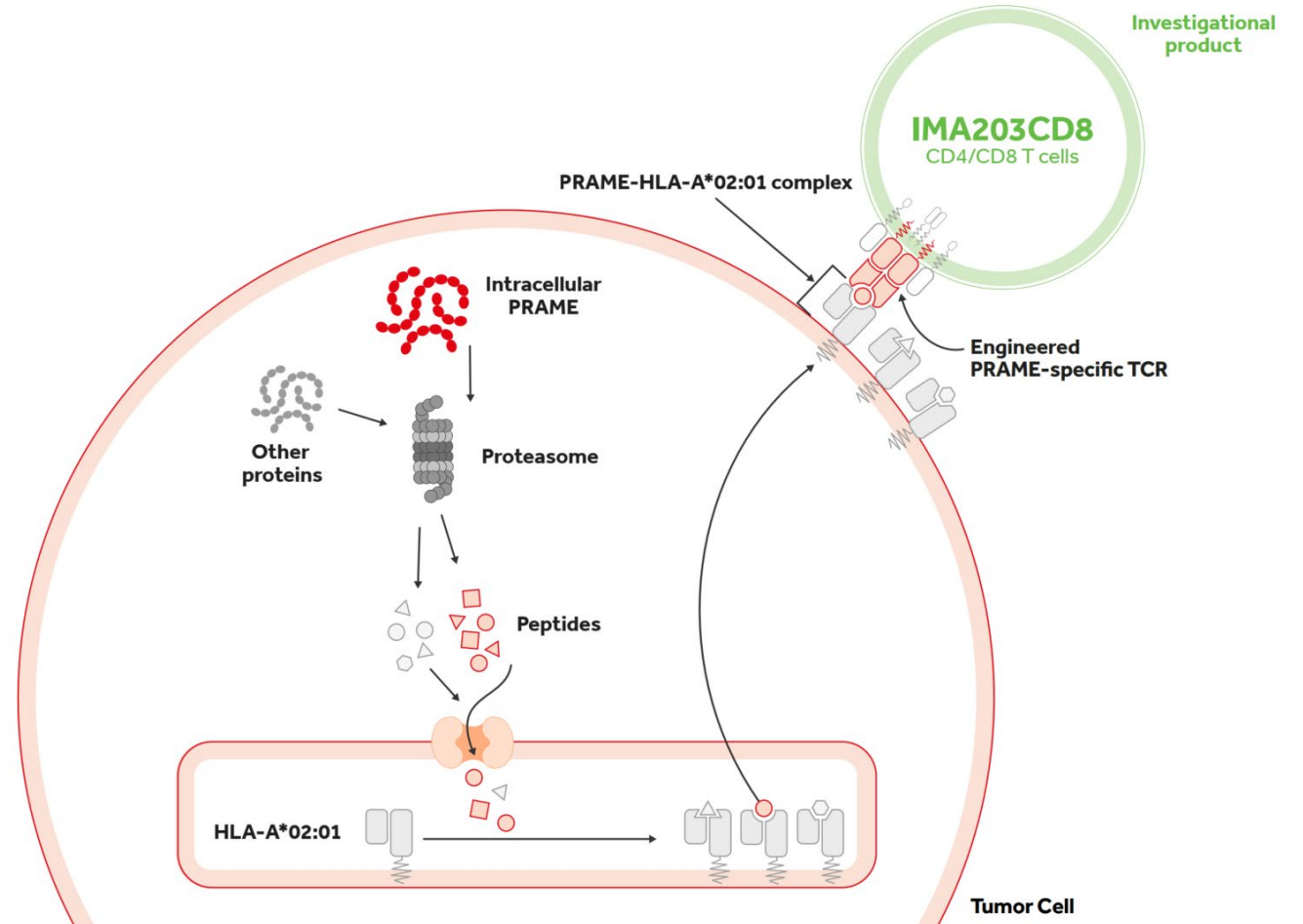
***Non-financial interests: None***

# IMA203CD8: Precision Targeting of PRAME Across Tumor Types with Both CD8<sup>+</sup> and CD4<sup>+</sup> T Cells

## PRAME is expressed in >50 cancers

Indication	% PRAME+ Patients <sup>1</sup>
<b>Cutaneous melanoma</b>	<b>95%</b>
Uterine carcinoma	95%
Uterine carcinosarcoma	95%
<b>Synovial sarcoma</b>	<b>95%</b>
<b>Uveal melanoma<sup>2</sup></b>	<b>90%</b>
Mucosal melanoma	90%
<b>Ovarian carcinoma (clear cell, endometrioid)</b>	<b>85%</b>
Squamous cell NSCLC	70%
Triple-negative breast carcinoma	65%
Small cell lung cancer	45%
Esophageal small cell carcinoma	45%
Renal papillary cell carcinoma	40%
Cholangiocarcinoma	35%
HER2-enriched breast carcinoma	30%
Adenocarcinoma NSCLC	25%
Head & neck squamous cell carcinoma	25%
Hepatocellular carcinoma	20%
Bladder carcinoma	20%

## Mechanism of action of IMA203CD8



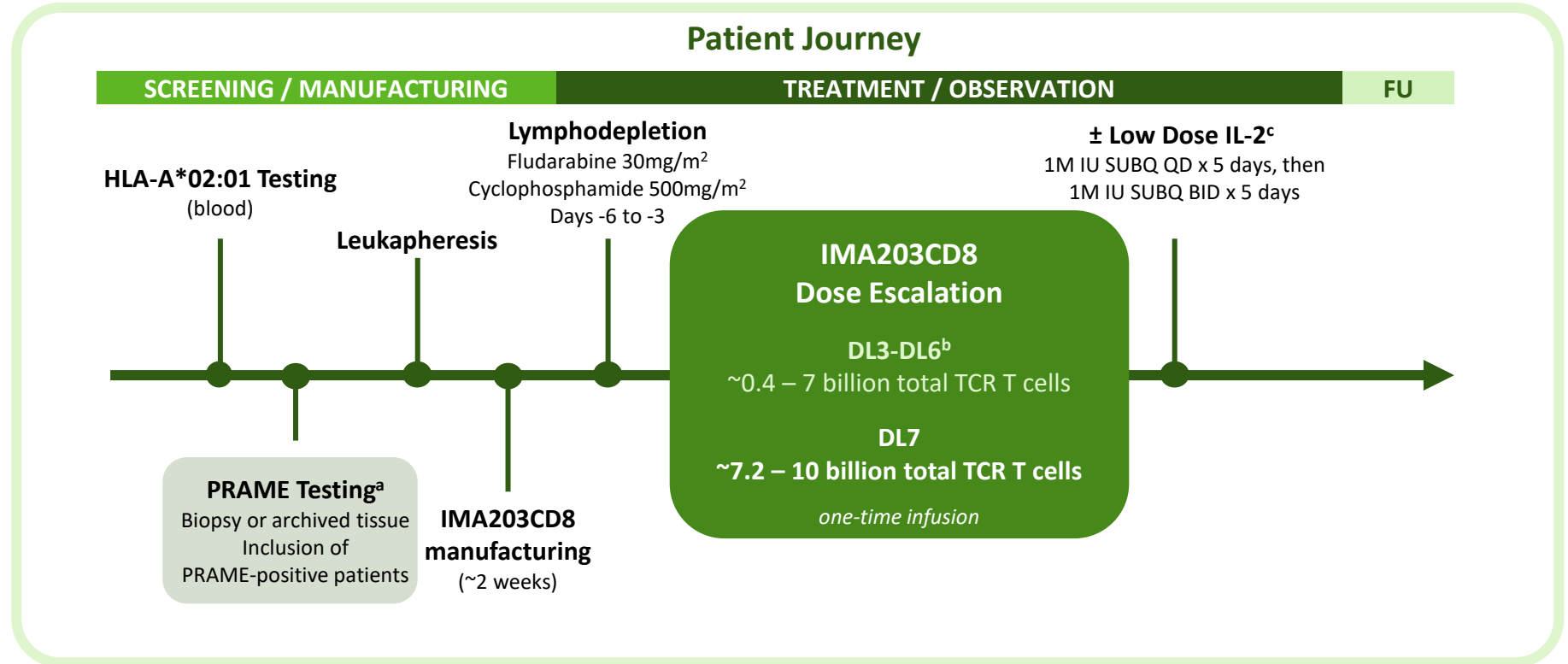
<sup>1</sup> Data on file: PRAME target prevalence is based on a proprietary mass spec-guided initial expression threshold applied to RNAseq and/or IHC data (approximate values; values between 95-100% shown as 95%), presumed optimized proprietary threshold considered for further development to address more patients; <sup>2</sup> PRAME target prevalence in uveal melanoma based on IMADetect<sup>®</sup> qPCR testing of screening biopsies from 61 clinical trial patients demonstrates substantial higher prevalence of ~90% compared to prevalence based on TCGA data of 50%, TCGA: early & late-stage primary tumor samples, Immatics clinical trials: primarily late-stage/metastatic tumor samples; HER2: Human epidermal growth factor receptor 2; HLA: human leukocyte antigen; NSCLC: non-small cell lung cancer; PRAME: preferentially expressed antigen in melanoma; TCR: T-cell receptor.

# Study Schema: IMA203CD8 in Solid Tumors Expressing PRAME

## Ongoing Phase 1a Dose Escalation Study

### Key Eligibility Criteria

- Adults with advanced and/or metastatic solid tumors
- ECOG PS 0-1
- HLA-A\*02:01 positive
- PRAME positive
- Patients having received or not been eligible for all available SOC treatment
- Adequate organ function
- No active brain metastasis



### Key Objectives

#### Primary:

- Safety/tolerability

#### Secondary:

- Efficacy
- Pharmacokinetics

<sup>a</sup> PRAME Testing no longer required for indications with high PRAME prevalence <sup>b</sup> Based on initial safety data observed with anzu-cel (IMA203), dose escalation for IMA203CD8 was initiated at DL3. Total TCR T cells calculated from defined number of TCR T cells/m<sup>2</sup> body surface area (BSA) per dose level x 1.8 m<sup>2</sup> BSA (BSA of average patient); <sup>c</sup> Each dose level ≥ DL4c is evaluated ±IL-2: start without IL-2; if considered tolerable, either add IL-2 at the same dose, or escalate to the next dose without IL-2; outpatient IL-2 administration at investigator's discretion. BID: twice daily; DL: dose level; ECOG PS: Eastern Cooperative Oncology Group Performance Status; FU: follow-up; IL: interleukin; IU: international unit; QD: daily; SOC: standard-of-care; SUBQ: subcutaneous; TCR: T-cell receptor. ClinicalTrials.gov: NCT03686124, Accessed Oct 28, 2025.

# Demographics: Baseline Characteristics

	Safety Population <sup>1</sup>	Efficacy-evaluable Population <sup>2</sup>			
	All Indications N=78	Melanoma <sup>3</sup> n=42	Ovarian Carcinoma n=11	Synovial Sarcoma n=11	Other <sup>4</sup> n=5
Age, median (range)	60 (20, 85)	62 (23, 85)	60 (35, 75)	40 (20, 66)	54 (38, 71)
Female, n (%)	46 (59)	21 (50)	11 (100)	4 (36)	3 (60)
ECOG PS 1, n (%)	36 (46)	22 (52)	8 (73)	2 (18)	2 (40)
LDH ≥1 x ULN, n (%)	37 (47)	22 (52)	5 (45)	4 (36)	4 (80)
<b>Tumor burden<sup>5</sup></b> Target lesion sum of diameter [cm], median (range)	9.4 (1.1, 43.4)	8.8 (1.5, 43.4)	9.6 (3.4, 21.6)	9.4 (1.2, 41.1)	6.4 (3.9, 12.3)
<b>Number of tumor lesions<sup>5</sup></b> Median (range)	5 (1, 25)	4 (1, 25)	5 (2, 25)	7 (1, 15)	6 (5, 14)
Liver metastasis <sup>5</sup> , n (%)	33 (45)	24 (57)	4 (36)	1 (9)	1 (20)
Brain metastasis <sup>5</sup> , n (%)	4 (5)	4 (10)	0 (0)	0 (0)	0 (0)
Platinum-resistant <sup>5</sup> , n (%)	-	-	5 (45)	-	-

## Patient Population with Limited Treatment Options

<sup>1</sup> All patients who started lymphodepletion; <sup>2</sup> All patients who received IMA203CD8 infusion and had at least one post-baseline scan or progressive disease; <sup>3</sup> Includes cutaneous melanoma (n=22), uveal melanoma (n=14), mucosal melanoma (n=3), acral melanoma (n=1) and melanoma of unknown primary (n=2); <sup>4</sup> Includes uterine cancer, lung adenocarcinoma, NSCLC and TNBC; <sup>5</sup> For N=74 with available assessment of baseline tumor burden (not available for n=1 cutaneous melanoma, n=2 ovarian carcinoma, n=1 synovial sarcoma in safety population); ECOG: Eastern Cooperative Oncology Group Performance Status; LDH: lactate dehydrogenase; NSCLC: non-small cell lung cancer; TNBC: triple-negative breast cancer; ULN: upper limit of normal.

# Demographics: Treatment Experience

Prior Therapy	Safety Population <sup>1</sup>	Efficacy-evaluable Population <sup>2</sup>			
	All Indications N=78	Melanoma <sup>3</sup> n=42	Ovarian Carcinoma n=11	Synovial Sarcoma n=11	Other <sup>4</sup> n=5
<b>Treatment, n (%)</b>					
Radiation	47 (60)	27 (64)	3 (27)	8 (73)	5 (100)
Systemic treatment	77 (99)	41 (98)	11 (100)	11 (100)	5 (100)
<b>Lines of systemic treatment</b>					
Median, (range)	3 (0, 8)	3 (0, 8)	4 (1, 7)	2 (1, 5)	3 (2, 5)
≥3, n (%)	50 (64)	26 (62)	10 (91)	5 (45)	3 (60)
Immune checkpoint inhibitors, n (%)	46 (59)	37 (88)	1 (9)	0 (0)	5 (100)
Chemotherapy, n (%)	52 (67)	18 (43)	10 (91)	11 (100)	5 (100)
Platinum-based regimen, n (%)	27 (35)	5 (12)	10 (91)	0 (0)	5 (100)
Targeted therapies (i.e., ADCs, TKIs), n (%)	15 (19)	8 (19)	4 (36)	0 (0)	0 (0)
TCR-based therapies, n (%)	18 (23)	15 (36)	0 (0)	1 (9)	0 (0)
On Study	All Indications N=78	Melanoma <sup>3</sup> n=42	Ovarian Carcinoma n=11	Synovial Sarcoma n=11	Other <sup>4</sup> n=5
<b>Total infused dose</b>					
TCR T cells [x10 <sup>9</sup> ], median (range)	1.6 (0.4, 12.5)	1.6 (0.4, 11.7)	2.3 (1.4, 7.1)	1.6 (0.9, 2.1)	1.6 (1.3, 2.1)
CD4 subset	0.9 (0.1, 7.4)	1.0 (0.1, 5.7)	1.3 (0.7, 4.0)	0.6 (0.2, 1.1)	0.7 (0.2, 1.2)
CD8 subset	0.7 (0.2, 8.3)	0.6 (0.2, 0.8)	0.8 (0.4, 3.0)	0.8 (0.5, 1.6)	0.9 (0.7, 1.4)

## Heavily Pre-treated Patients Treated with IMA203CD8 at Escalating Doses

<sup>1</sup> All patients who started lymphodepletion; <sup>2</sup> All patients who received IMA203CD8 infusion and had at least one post-baseline scan or progressive disease; <sup>3</sup> Includes cutaneous melanoma (n=22), uveal melanoma (n=14), mucosal melanoma (n=3), acral melanoma (n=1) and melanoma of unknown primary (n=2); <sup>4</sup> Includes uterine cancer, lung adenocarcinoma, NSCLC and TNBC.

Total TCR T cells calculated from defined number of TCR T cells/m<sup>2</sup> body surface area (BSA) per dose level x 1.8 m<sup>2</sup> BSA (BSA of average patient).

ADC: antibody drug conjugate; NSCLC: non-small cell lung cancer; TCR: T-cell receptor; TNBC: triple-negative breast cancer; TKI: tyrosine kinase inhibitor.

# IMA203CD8: Tolerability in Advanced Solid Tumors

## Overall Manageable Tolerability Profile

### TEAEs in ≥20% of patients

Preferred term, n (%)	N=78 <sup>a</sup>	
	Any grade	Grade ≥3
Neutropenia	67 (86)	66 (85)
Anaemia	61 (78)	40 (51)
Thrombocytopenia	55 (71)	25 (32)
Nausea	50 (64)	0
Lymphopenia	36 (46)	35 (45)
Fatigue	30 (39)	6 (8)
ALT/AST increased	30 (39)	9 (12)
Rash/Rash maculo-papular	26 (33)	3 (4)
Constipation	25 (32)	0
Hypokalaemia	24 (31)	0
Leukopenia	20 (26)	18 (23)
Vomiting	20 (26)	0
Abdominal pain	17 (22)	2 (3)
Diarrhoea	17 (22)	3 (4)
Pyrexia	17 (22)	0
Hyponatraemia	17 (22)	1 (1)
Headache	16 (21)	0

### Adverse events of special interest

N=78 <sup>a</sup>	
<b>CRS, any grade, n (%)</b>	<b>74 (95)</b>
Grade 1	27 (35)
Grade 2	39 (50)
Grade 3	7 (9)
Grade 4	1 (1)
<b>HLH, any grade, n (%)</b>	<b>7 (9)</b>
Grade 1	0
Grade 2	4 (5)
Grade 3	2 (3)
Grade 4	1 (1)
<b>ICANS, any grade, n (%)</b>	<b>6 (8)</b>
Grade 1	4 (5)
Grade 2	1 (1)
Grade 3	1 (1)

All TEAEs occurring in at least 16 patients (≥20%) are presented. 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, for patients enrolled under protocol v11.0 and higher according to Neelapu et al, 2019).

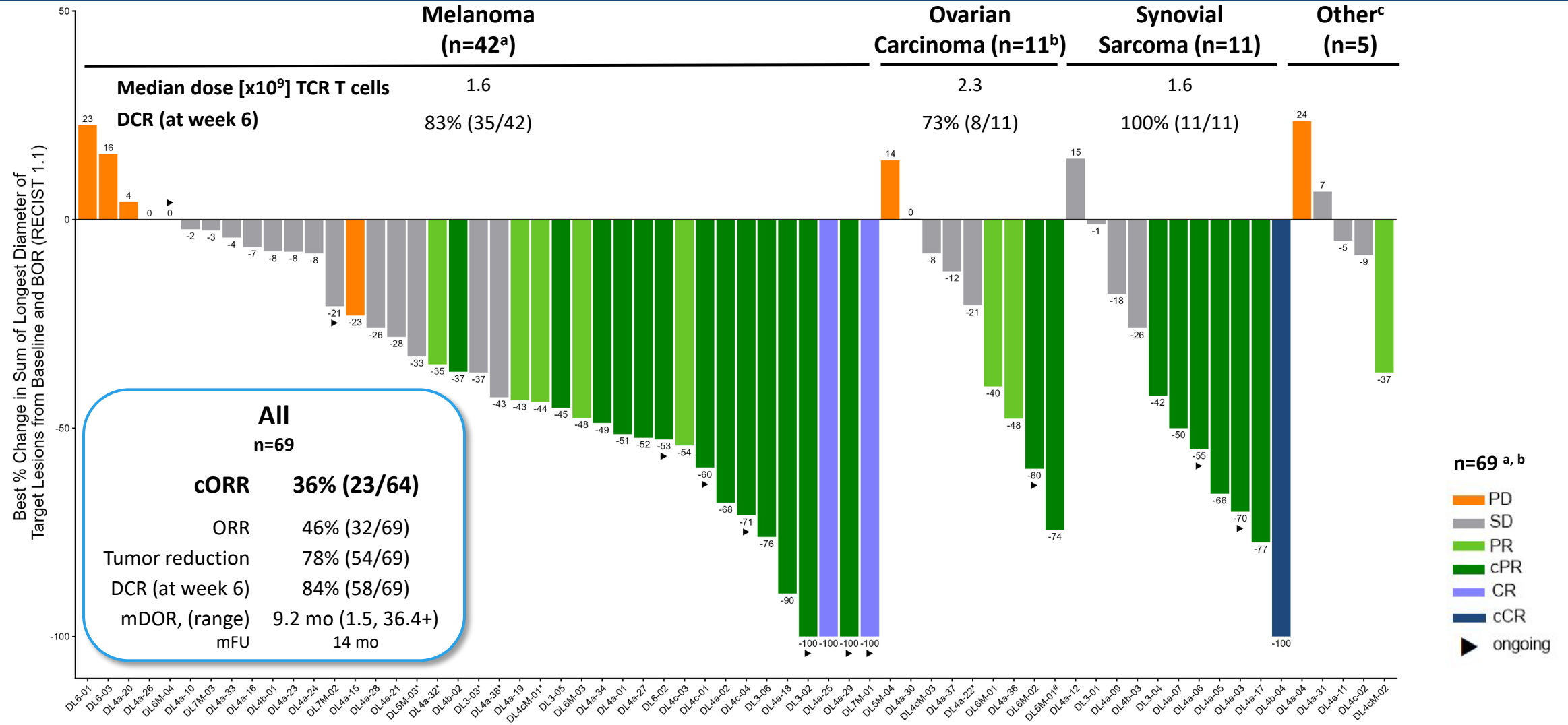
- Most frequent TEAEs were cytopenias associated with lymphodepletion
- CRS: mostly Grade 1-2
- DLTs in 2 patients at DL4b:
  - Patient DL4b-01: high in vivo TCR T-cell expansion, Grade 4 neurotoxicity, Grade 4 CRS, Grade 3 HLH
  - Patient DL4b-04: Grade 3 CRS defined by Grade 3 ALT elevation which resolved to Grade 2 within 10 days; no need for vasopressors or ventilation
- No IMA203CD8-related Grade 5 events<sup>b</sup>

**Dose escalation ongoing at DL7 based upon manageable tolerability**

<sup>a</sup> All patients who started lymphodepletion. Includes one patient that started lymphodepletion but did not receive IMA203CD8 cells yet. Includes one patient without AE entry at date of data cutoff. <sup>b</sup> Possibly-related Grade 5 event as previously reported was determined by the principal investigator to be unlikely related to IMA203CD8 after complete assessment. Patient died from sepsis that was aggravated by immunosuppression from Flu/Cy (possibly related), a grade 4 HLH event, the toxicity management and rapidly-progressing disease. ALT: alanine aminotransferase; AST: aspartate aminotransferase; CRS: cytokine release syndrome; Cy, cyclophosphamide; Flu, fludarabine; DL: dose level; DLT: dose-limiting toxicity; HLH: hemophagocytic lymphohistiocytosis; ICANS: immune effector cell-associated neurotoxicity syndrome; TCR: T-cell receptor; TEAE: treatment-emergent adverse event.

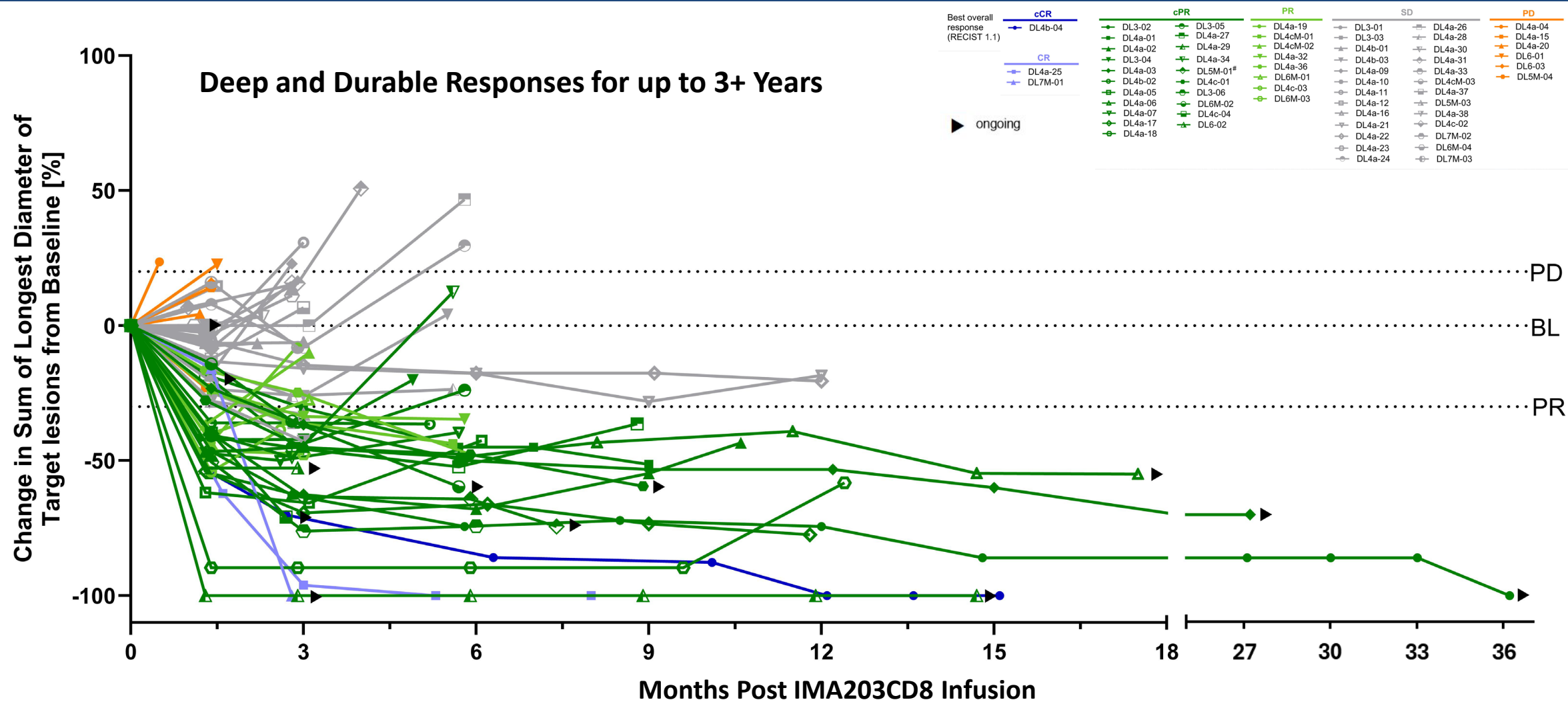
# IMA203CD8: Tumor Reduction During Dose Escalation

## All Dose Levels Across Various PRAME-expressing Indications



<sup>a</sup> Includes 3 patients without post-baseline scan not depicted in plot: n=2 deceased prior to first scan, n=1 with non-evaluable measurements of target lesions (all DL4a); <sup>b</sup> Includes 2 patients without post-baseline scan not depicted in plot: n=2 deceased prior to first scan (1 DL4a, 1 DL5); <sup>c</sup> Includes uterine cancer, lung adenocarcinoma, NSCLC and TNBC; \* best change and RECIST BOR at different timepoints; <sup>†</sup> Ongoing confirmed PR (RECIST 1.1) as of last scan at month 7.5, suspected clinical progression by clinical site at month 6 in discrepancy to RECIST response due to tumor marker increase; patient off study at month 8 and receiving further anti-tumor treatment; DCR: includes one patient with post-baseline scan at week 5; ORR: according to RECIST 1.1 at any post-baseline scan; cORR: according to RECIST 1.1 for patients with at least two available post-baseline scans (excluding patients with ongoing unconfirmed response) or patients with PD or death at any prior timepoint; patient DL4a-25 had a cPR prior to CR; BOR: best overall response; cCR: (confirmed) complete response; DCR: disease control rate; mDOR: median duration of response; mFU: median follow-up; NSCLC: non-small cell lung cancer; (c)ORR: (confirmed) objective response rate; PD: progressive disease; (c)PR: (confirmed) partial response SD: stable disease; TNBC: triple-negative breast cancer.

# IMA203CD8: Changes in Tumor Size Over Time During Dose Escalation



5 patients without post-baseline scan not depicted in plot: n=2 with melanoma deceased prior to first scan, n=1 with melanoma had non-evaluable measurements of target lesions (all DL4a), n=2 with ovarian carcinoma deceased prior to first scan (1 DL4a, 1 DL5); # Ongoing confirmed PR (RECIST 1.1) as of last scan at month 7.5, suspected clinical progression by clinical site at month 6 in discrepancy to RECIST response due to tumor marker increase; patient off study at month 8 and receiving further anti-tumor treatment. BL: baseline; (c)CR: (confirmed) complete response; PD: progressive disease; (c)PR: (confirmed) partial response; SD: stable disease.

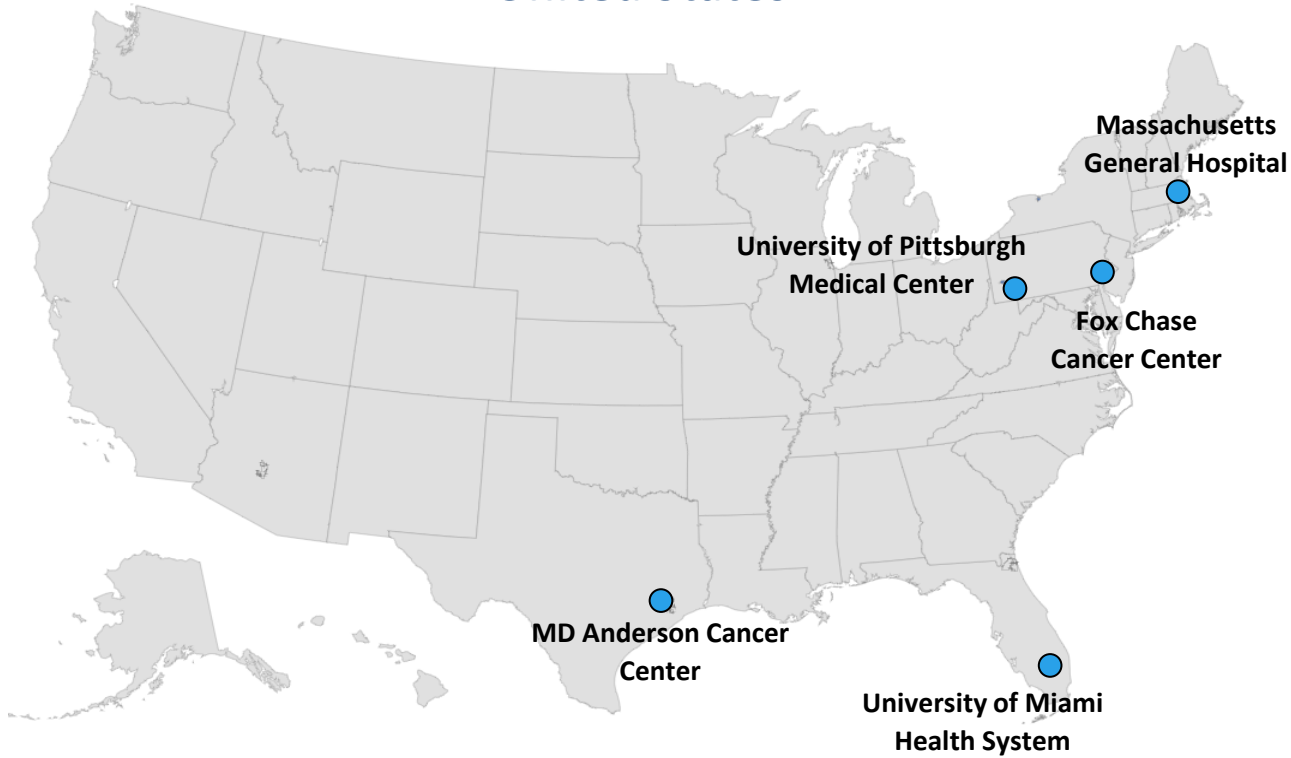
# Conclusions

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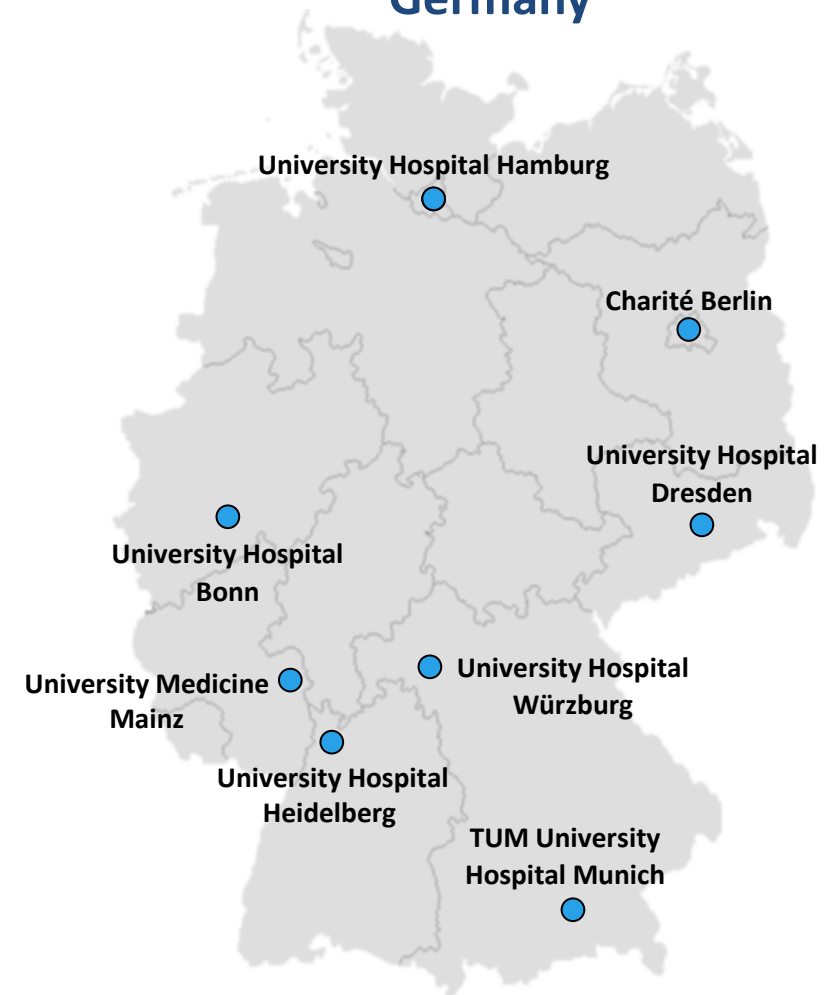
- PRAME is an intracellular cancer antigen that is targetable across multiple cancers
- IMA203CD8 PRAME-directed TCR T-cell therapy harnesses collaborative antitumor activity of both CD8 and CD4 T-cells
- One-time infusion of IMA203CD8 demonstrates tolerability at increasing dose-levels with promising systemic anti-tumor activity in advanced solid tumors beyond melanoma
- This Phase 1a study provides clinical proof-of-concept for systemic, multi-indication targeting of PRAME in patients with limited treatment options and high unmet medical need
- Dose escalation is ongoing based on an acceptable tolerability profile; efficacy evaluations, including patients treated at DL6 and DL7, are planned for 2026

# Thank You – Study Participants & Caregivers

## United States



## Germany



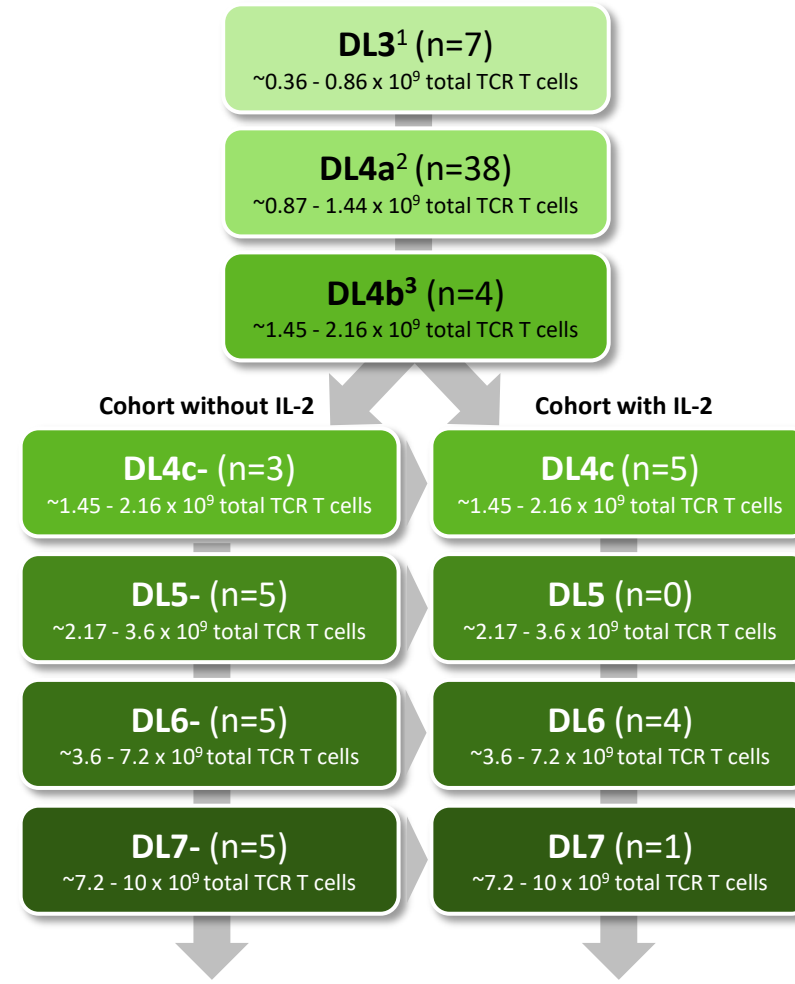
IMA203CD8 Phase 1 Study  
Sponsor: Immatics

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# Appendix

# Phase 1a Dose Escalation Study Design

## Safety Population (N=78\*)



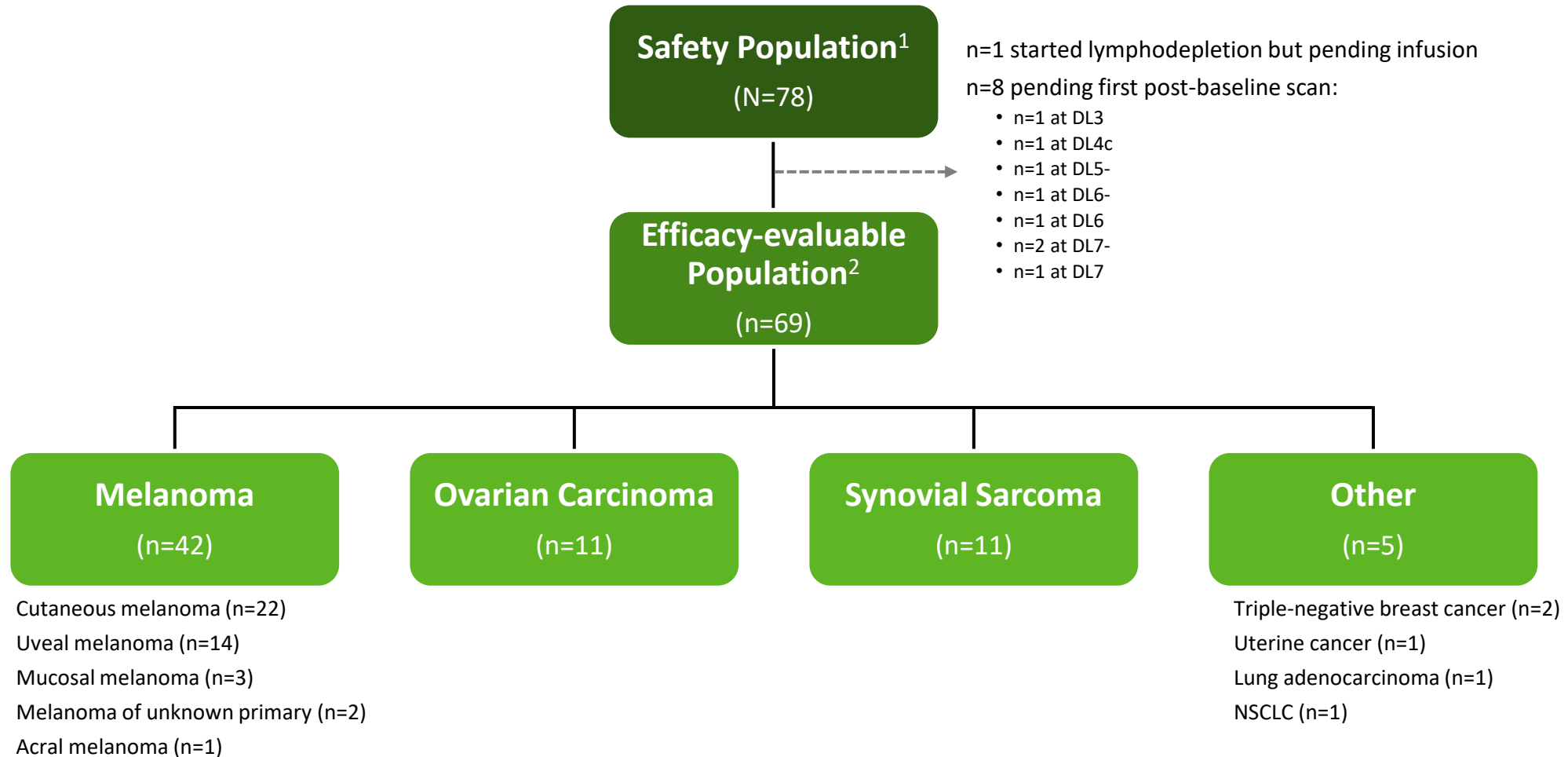
Median dose of 1.6 billion total IMA203CD8 TCR T cells  
Dose escalation at DL7 with and without IL-2 ongoing

Patients assigned to the cohort without IL-2 are indicated with an additional "M" in their patient ID depicted in waterfall and spider plots

\* Includes one patient who started lymphodepletion but pending IMA203CD8 infusion; <sup>1</sup> Based on initial safety data observed with anzu-cel (IMA203), dose escalation for IMA203CD8 was initiated at DL3; <sup>2</sup> DL4a cleared in Dec 2023; <sup>3</sup> DLTs at DL4b triggered modifications of the eligibility criteria, adapted patient population is treated with DL4c. Each dose level  $\geq$  DL4c is evaluated  $\pm$ IL-2: start without IL-2; if considered tolerable, either add IL-2 at the same dose, or escalate to the next dose without IL-2; patients depicted according to assigned cohort, two patients in cohort with IL-2 did not receive IL-2 infusions (DL4c-04, DL6-01). Total TCR T cells calculated from defined number of TCR T cells/m<sup>2</sup> body surface area (BSA) per dose level x 1.8 m<sup>2</sup> BSA (BSA of average patient). BSA: body surface area; DL: dose level; DLT: dose-limiting toxicity; MTD: maximum tolerated dose; TCR, T-cell receptor.

# Patient Populations

## Various PRAME-Expressing Indications Across All Dose Levels

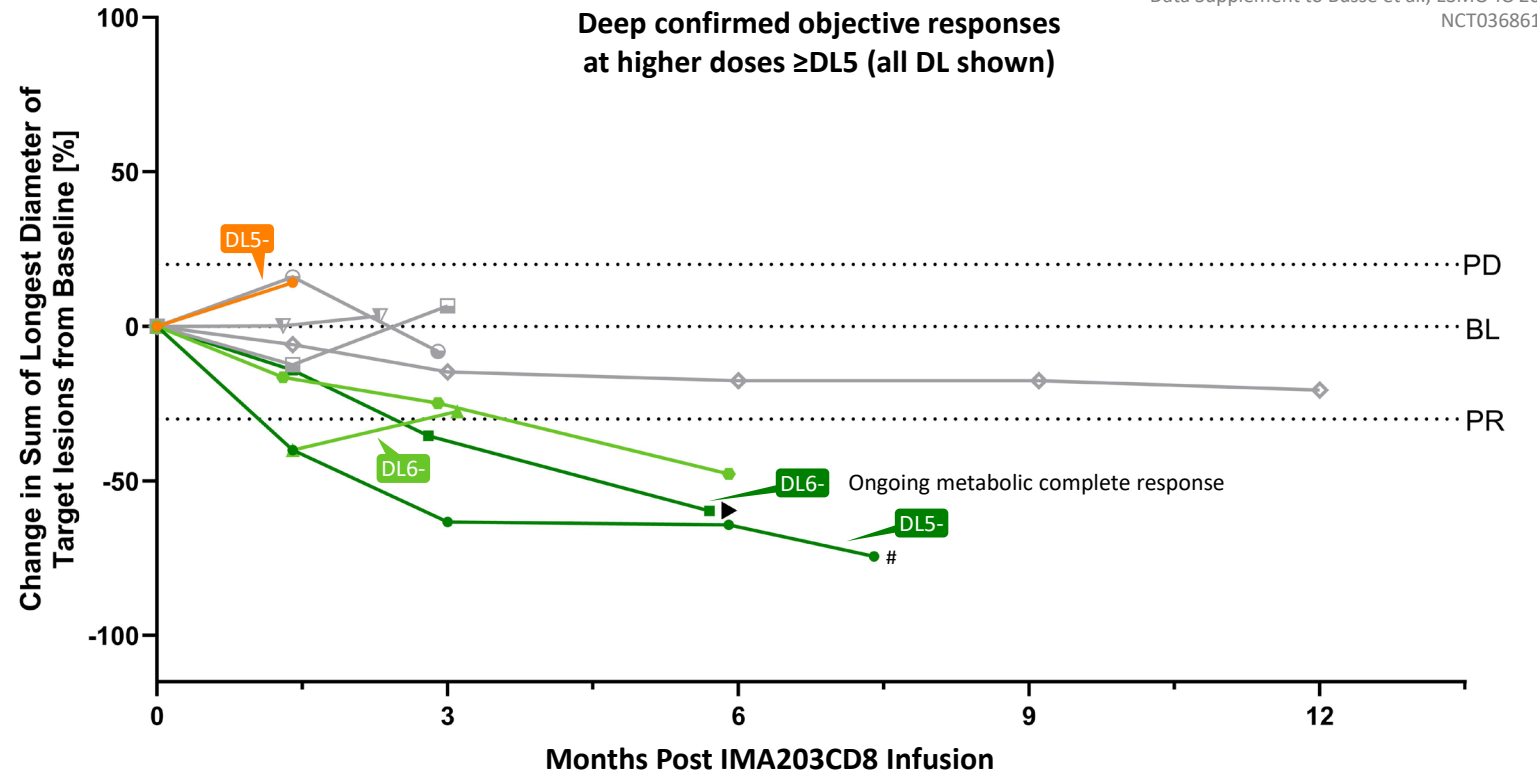
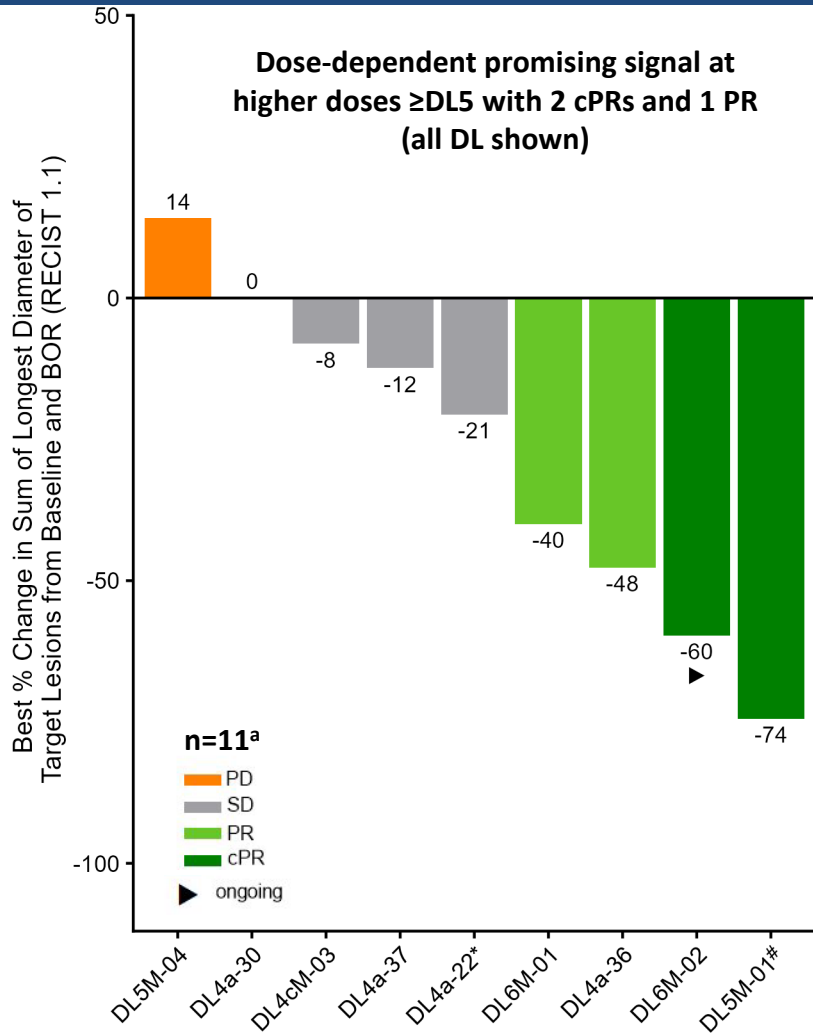


<sup>1</sup>All patients who started lymphodepletion, includes one patient without adverse event entry at date of data cutoff; <sup>2</sup>All patients who received IMA203CD8 infusion and had at least one post-baseline scan or progressive disease.  
NSCLC: non-small cell lung cancer.

# IMA203CD8 in Patients with Ovarian Carcinoma

## Dose Escalation at Higher Doses Ongoing to Unlock full Potential of IMA203CD8

Data Supplement to Busse et al., ESMO-IO 2025  
NCT03686124

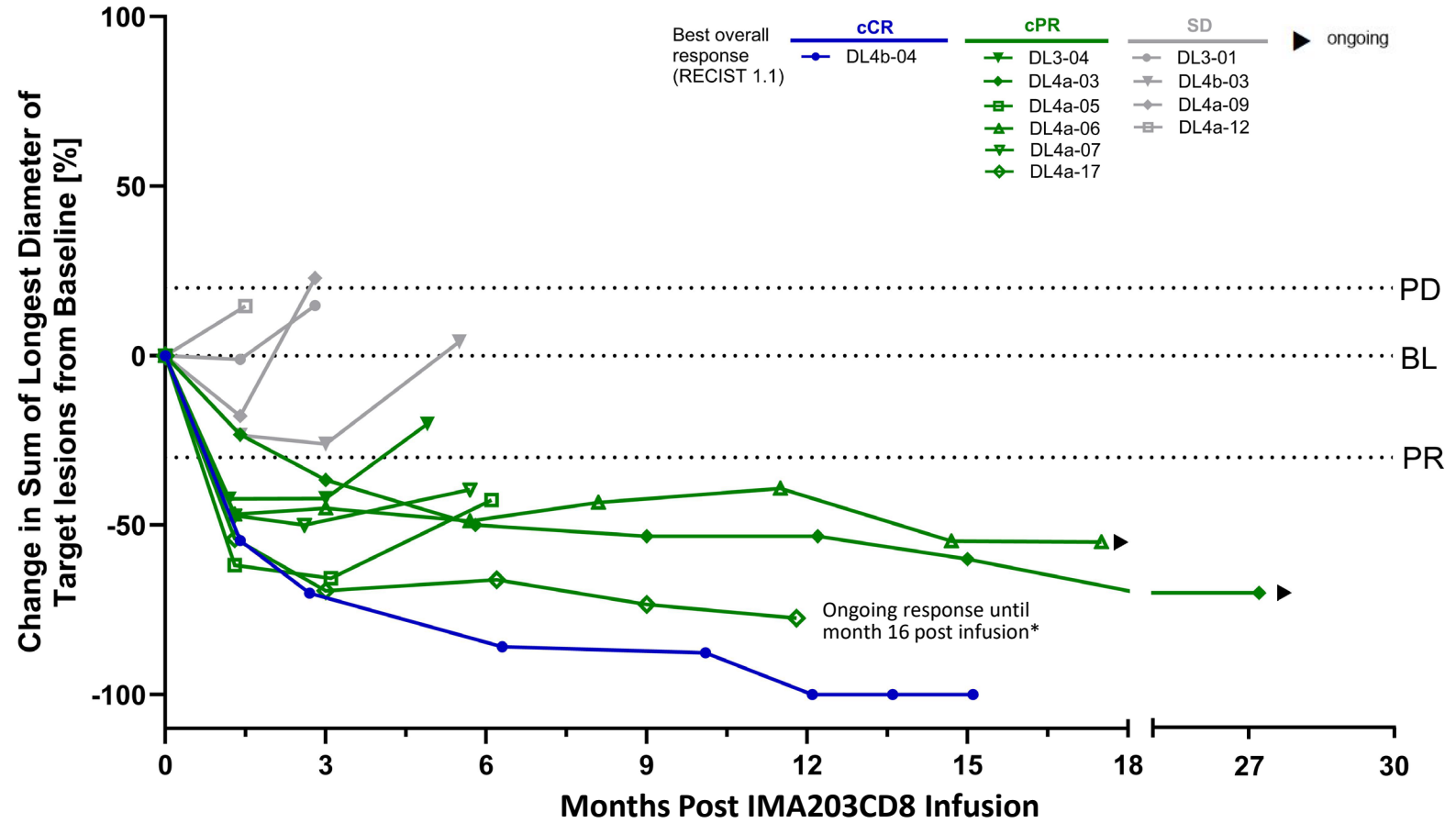
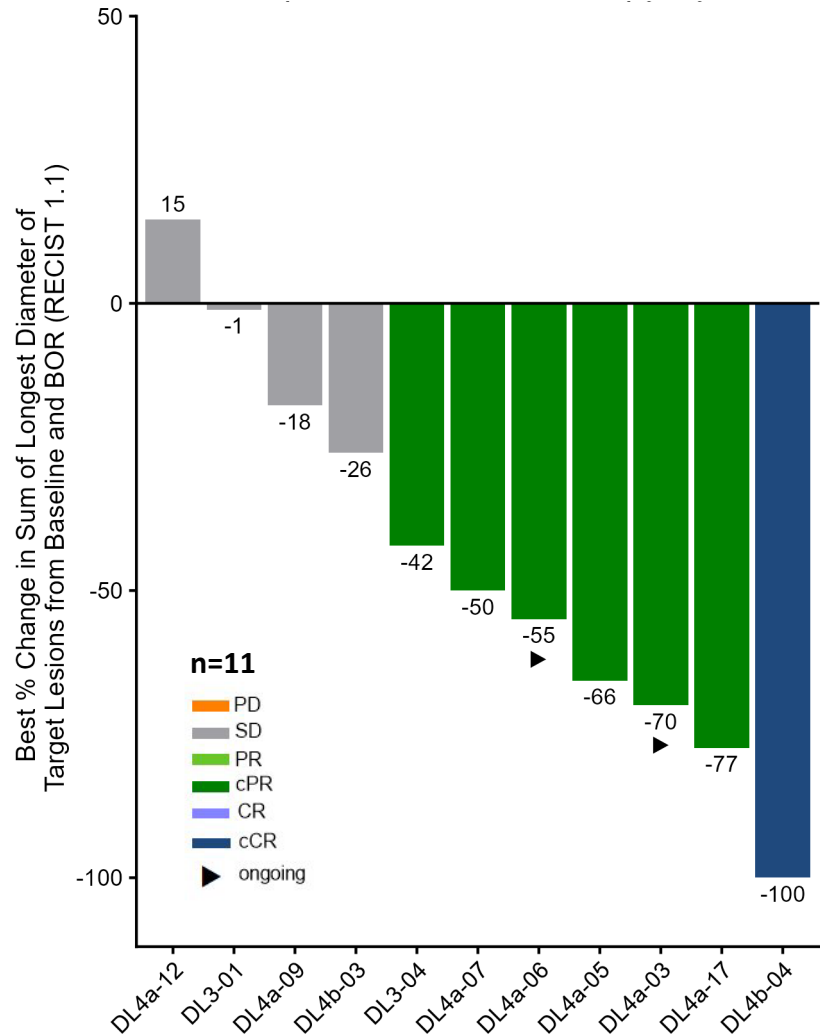


**Tolerability in ovarian carcinoma was generally consistent with full IMA203CD8 tolerability profile**

<sup>a</sup> Includes 2 patients without post-baseline scan not depicted in waterfall and spider plot: n=2 deceased prior to first scan (1 DL4a, 1 DL5); \* best change and RECIST BOR at different timepoints; # Ongoing confirmed PR (RECIST 1.1) as of last scan at month 7.5, suspected clinical progression by clinical site at month 6 in discrepancy to RECIST response due to tumor marker CA-125 increase; patient off study at month 8 and receiving new anti-tumor treatment.  
BL: baseline; BOR: best overall response; DL: dose level; PD: progressive disease; (c)PR: (confirmed) partial response; SD: stable disease.

# IMA203CD8 in Patients with Synovial Sarcoma

## Promising Clinical Activity with Deep and Durable Responses at Low Doses (DL1-DL4a)



Tolerability in synovial sarcoma was generally consistent with full IMA203CD8 tolerability profile