ACTengine® IMA203 / IMA203CD8 TCR-T Monotherapy Targeting PRAME

– Phase 1 Interim Data Update

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Delivering the Power of T cells to Cancer Patients

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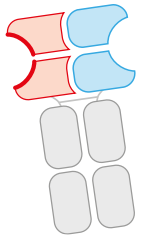
Realizing the Full Multi-Cancer Opportunity of PRAME

ACTengine® IMA203 (TCR Cell Therapy) and TCER® IMA402 (TCR Bispecific)

	Indication	% PRAME positive patients[1]
	Uterine Carcinoma	97%
	Uterine Carcinosarcoma	100%
	Sarcoma Subtypes	up to 100%
Focus today	Cut. Melanoma	≥95%
Focus today	Uveal Melanoma[2]	≥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

TCER® IMA402
(TCR Bispecific)



Dose escalation of Phase 1/2 trial ongoing

[1] PRAME target prevalence is based on TCGA (for SCLC: in-house) RNAseq data combined with a proprietary mass spec-guided RNA expression threshold; [2] 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

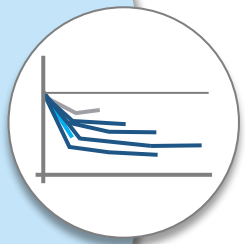
ACTengine® IMA203 / IMA203CD8 TCR-T Monotherapy

Two Assets with Distinct Opportunities and Near-Term Catalysts

GEN1: IMA203 in Melanoma at RP2D

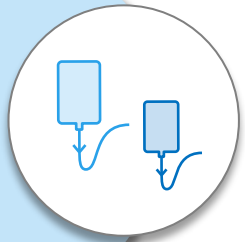
Clinical Data

- **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 1-10x10^9 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

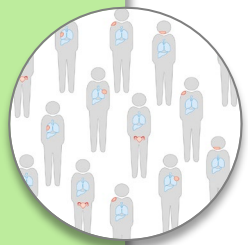
GEN2: IMA203CD8 in Solid Tumors

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

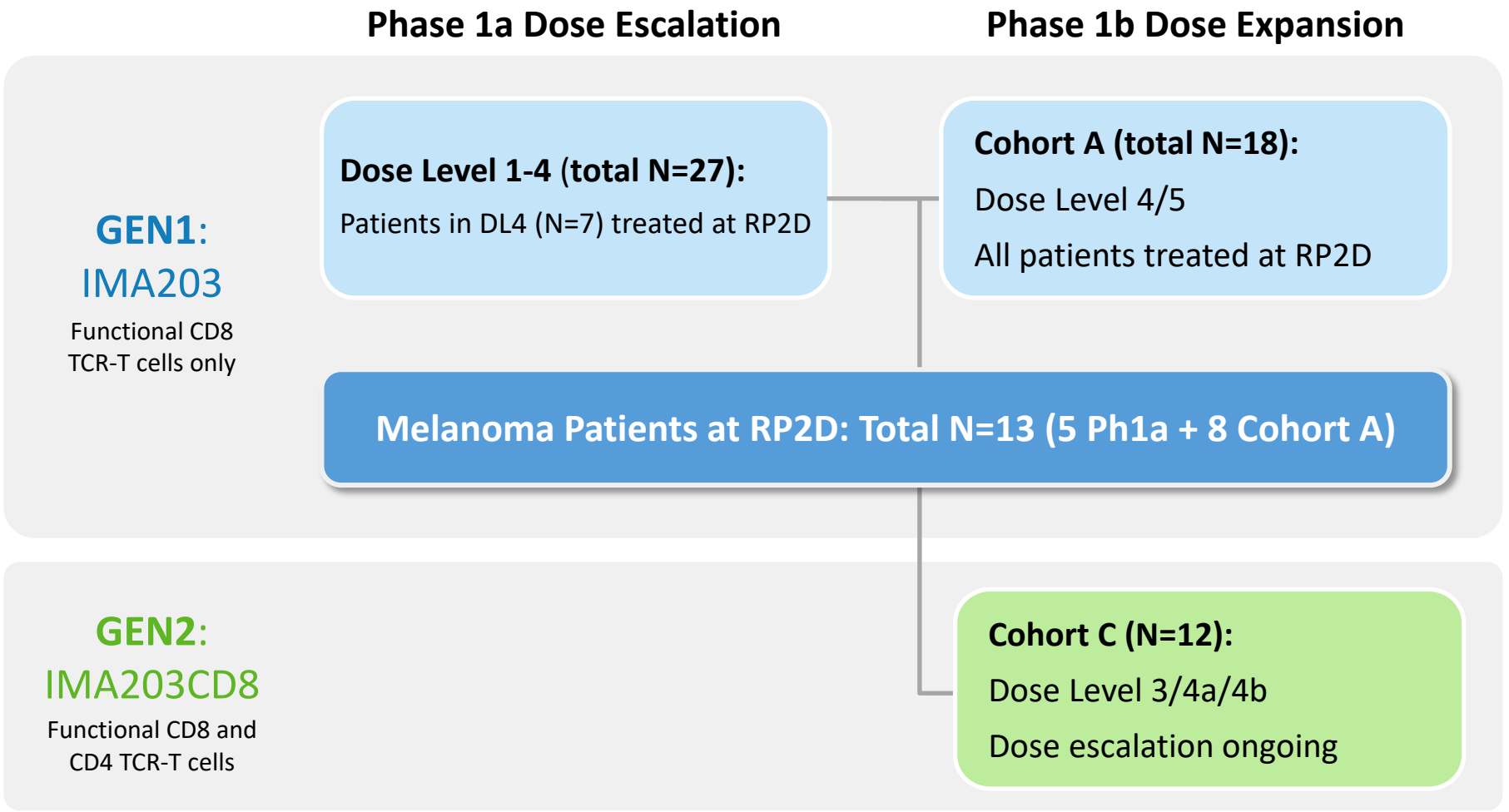
- Complete dose escalation
- Signal finding in non-melanoma indications, such as ovarian cancer, uterine cancer, NSCLC, triple-negative breast cancer and others



mDOR: median Duration of Response; mFU: median Follow-up; RP2D: Recommended Phase 2 Dose

ACTengine® IMA203 / IMA203CD8 TCR-T Trial in Advanced Solid Tumors

Overview



Today's update focuses on

13 melanoma patients treated at RP2D with IMA203 GEN1

and

12 all comers patients treated with IMA203CD8 GEN2

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

Efficacy population shown: patients treated with IMA203 (Cohort A) or IMA203CD8 (Cohort C) and with at least one available tumor response assessment post infusion;
RP2D: Recommended Phase 2 Dose of 1-10x10^9 total TCR-T cells; IMA203 DL4: 0.2-1.2x10^9 TCR-T cells/m^2 BSA, IMA203 DL5: 1.201 x 4.7x10^9 TCR-T cells/m^2 BSA;
IMA203CD8 DL3: 0.2-0.48x10^9 TCR-T cells/m^2 BSA, IMA203CD8 DL4a: 0.481-0.8x10^9 TCR-T cells/m^2 BSA, IMA203CD8 DL4b: 0.801-1.2x10^9 TCR-T cells/m^2

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
Efficacy population*	N=27 Thereof N=7 at RP2D	N=18 at RP2D	N=13 at RP2D	N=12
Prior lines of systemic treatment (median, min, max)	4 (1, 8)	3 (0, 10)	4 (0, 7)	3 (1, 5)
LDH at baseline >1 x ULN [% of patients]	66.7	50.0	53.8	50.0
Baseline tumor burden 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)
Dose level	DL1-4	DL4/5	DL4/5	DL3/DL4a/DL4b
ORR	48% (13/27)	50% (9/18)	62% (8/13)	58% (7/12)
cORR	**19% (5/27)**	**47% (8/17)**	**50% (6/12)**	**56% (5/9)**
mDOR [months]	**4.4 (2.4, 23.0)**	**Not reached**	**Not reached**	**Not reached**
mFU [months]	**Not defined#**	**10.8**	**14.4**	**4.8**

* 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 2nd Generation

Summary & Next Development Steps

IMA203 GEN1 in All Melanoma Patients at RP2D – Most Frequent Adverse Events

N=16 Patients in Safety Population[1]

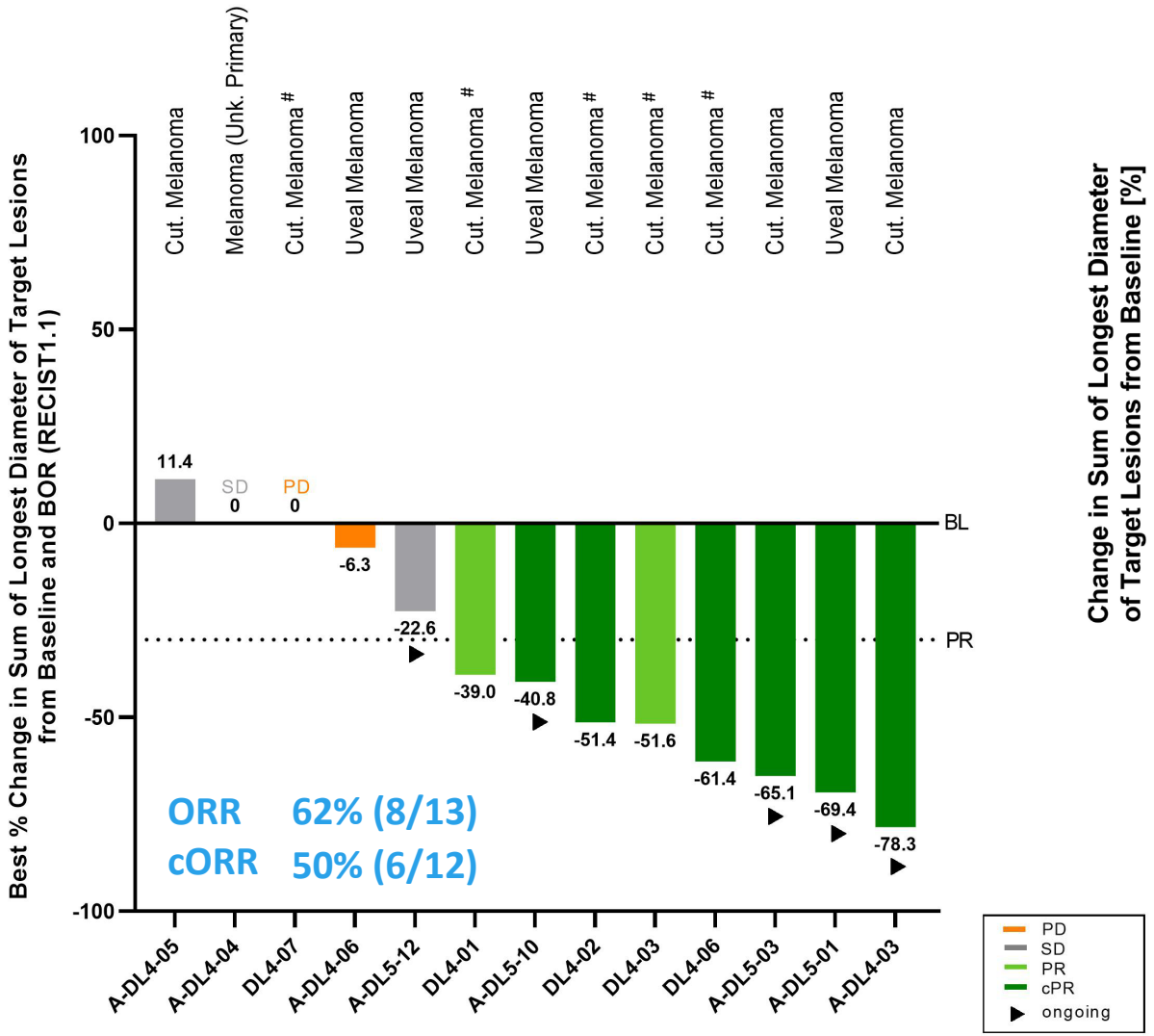
- **Expected cytopenia (Grade 1-4)** associated with lymphodepletion in all patients
- **Mostly mild to moderate cytokine release syndrome (CRS)**
  - 63% (10/16) with Grade 1 CRS
  - 31% (5/16) with Grade 2 CRS
  - 6% (1/16) with Grade 3 CRS (Phase 1a patient; recovered to Grade 2 after 3 days, no need for vasopressors and/or ventilation)
  - No dose-dependent increase of CRS
- **One non-serious, mild (Grade 1) ICANS[2] 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

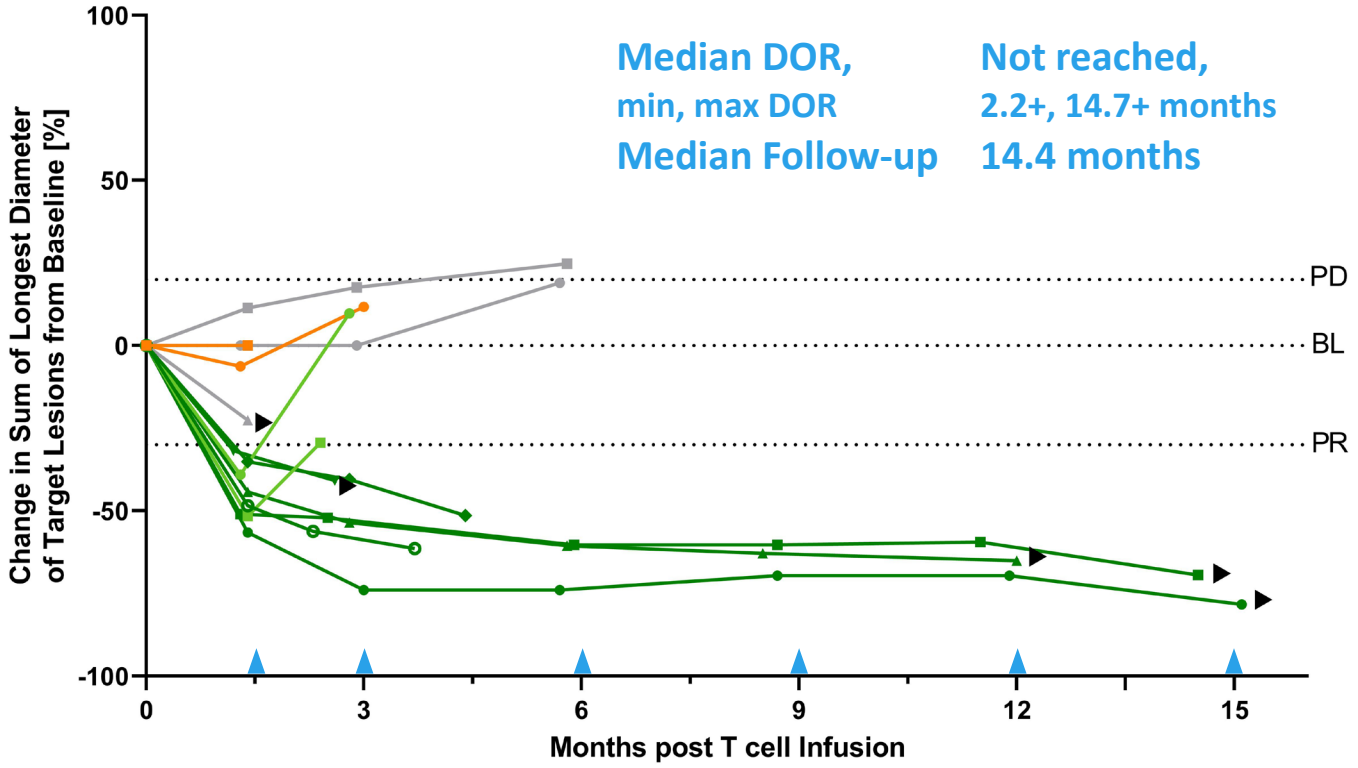
IMA203 GEN1 monotherapy continues to be well tolerated at total doses between 1-10x10^9 TCR-T cells (RP2D)

[1] Three cutaneous melanoma patients treated with IMA203 and pending post infusion scan included in safety population, but not efficacy population;
[2] 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





Median DOR, **Not reached,**
min, max DOR **2.2+, 14.7+ months**
Median Follow-up **14.4 months**

Best overall response (RECIST 1.1)

cPR	PR	SD	PD
A-DL4-03	DL4-01 #	A-DL4-04	A-DL4-06
A-DL5-01	DL4-03 #	A-DL4-05	DL4-07 #
A-DL5-03		A-DL5-12	
A-DL5-10			
DL4-02 #			
DL4-06 #			

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

Patients in Phase 1a

Ongoing

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;

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)
- Leukapharesis 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[1]	**~300** HLA-A*02:01 and PRAME-positive uveal melanoma patients annually in the US[2]

CPI: Checkpoint inhibitor; [1] 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); [2] 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% (IMADetect® qPCR testing of screening biopsies from clinical trial patients (n=33))

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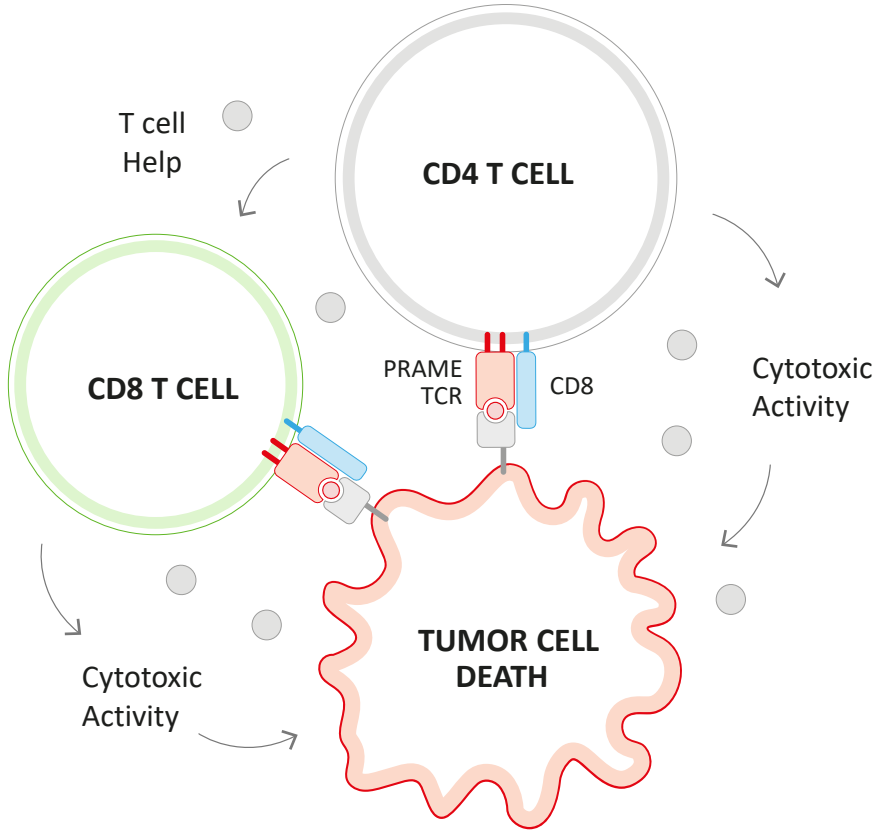
IMA203CD8 GEN2 Monotherapy
Cohort C – First Data Set on 2nd Generation

Summary & Next Development Steps

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

Differentiated Pharmacology Compared to 1st-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 CD8αβ 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[1]
- Data from CD19 CAR-T-treated leukaemia patients suggest a relevant role of engineered CD4 T cells in long-term durability[2]

[1] Internal data not shown here, published in Bajwa *et al.* 2021, Journal for Immunotherapy of Cancer; [2] Melenhorst *et al.* 2022 Nature, Bai *et al.* 202,2 Science Advances

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

Manageable Tolerability in 12 Patients Treated with IMA203CD8 at 3 Escalating Dose Levels[1]

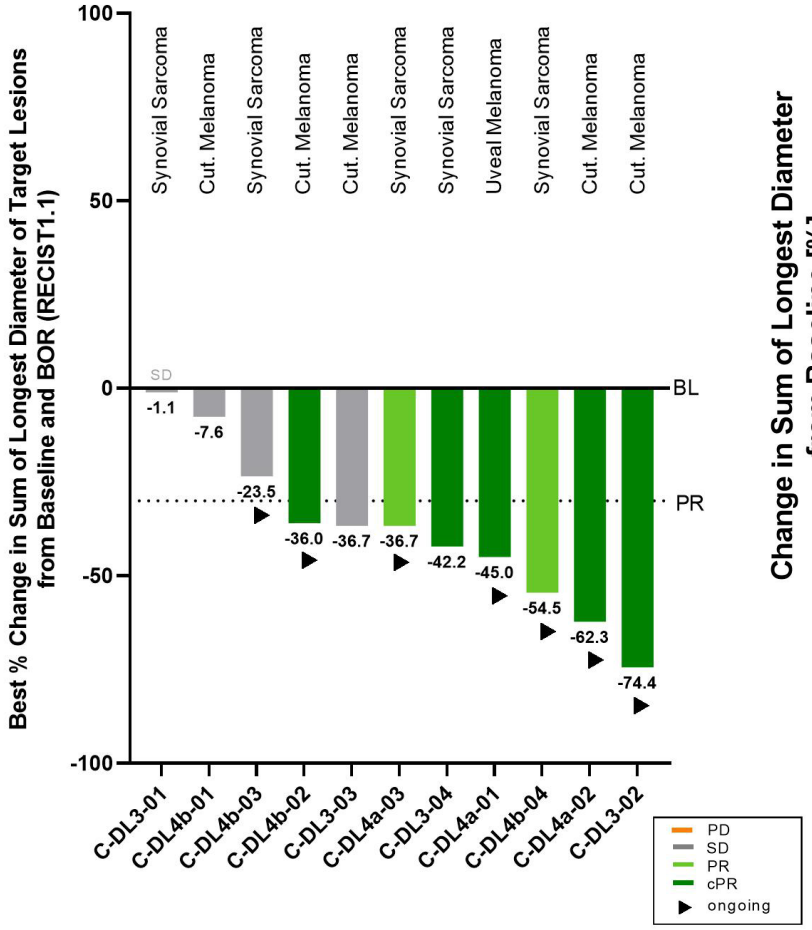
- **Expected cytopenia (Grade 1-4)** associated with lymphodepletion in all patients
- Cytokine release syndrome (CRS) in 92% (11/12) of patients:
  Trend towards **more severe CRS at higher doses, in all cases well manageable**
  - 67% (8/12) with Grade 1 or 2 CRS (4 in DL3, 3 in DL4a, 1 in DL4b)
  - 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[2] 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**

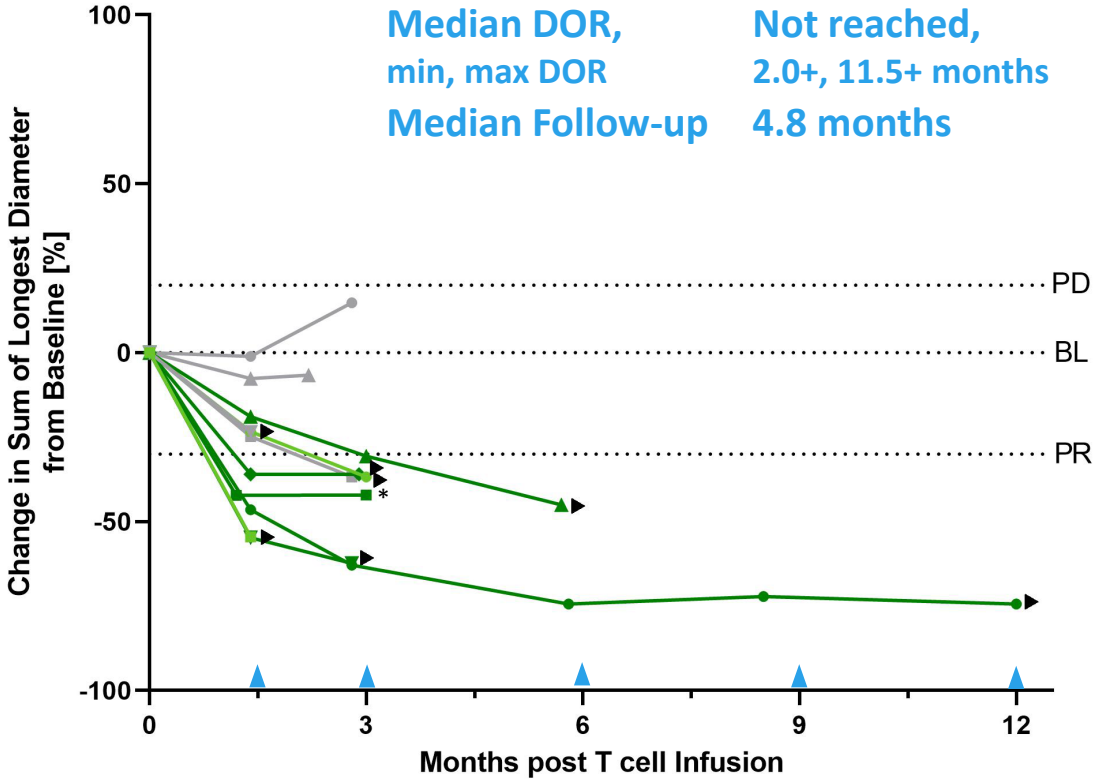
IMA203CD8 GEN2 monotherapy shows a manageable tolerability profile

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





Median DOR, **Not reached,**
min, max DOR **2.0+, 11.5+ months**
Median Follow-up **4.8 months**

ORR **58% (7/12)**
cORR **56% (5/9)**

- 6 out of 7 responses ongoing
- 11/12 patients show tumor shrinkage
- Deepening of response from SD to PR in two patients (C-DL4a-01, C-DL4a-03)
- Ongoing durable response 12+ months after infusion

Best overall response (RECIST 1.1)

cPR	PR	SD	PD
C-DL3-02	C-DL4a-03	C-DL3-01	
C-DL3-04	C-DL4b-04	C-DL3-03	
C-DL4a-01		C-DL4b-01	
C-DL4a-02		C-DL4b-03	
C-DL4b-02			

[#] Patient C-DL4a-04 was PD ~6 weeks after infusion, not shown due to non-evaluable target lesions at tumor assessment

▶ Ongoing

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

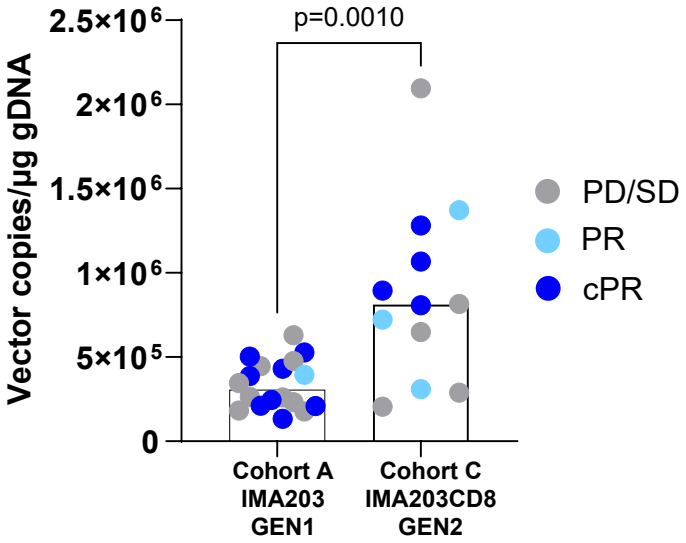
* Clinical tumor progress after 4.9 months post infusion, investigator information

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

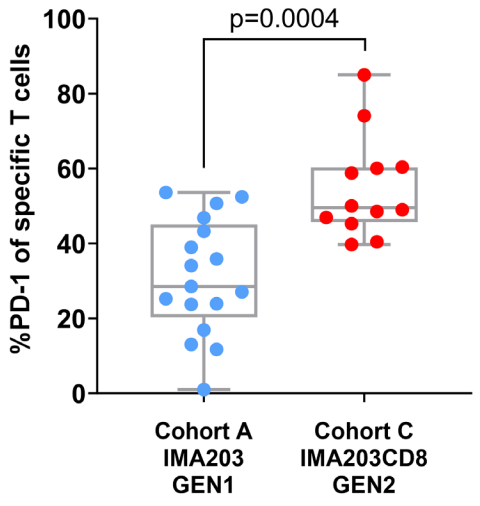
IMA203CD8 GEN2: Translational Data Shows Enhanced Pharmacology

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

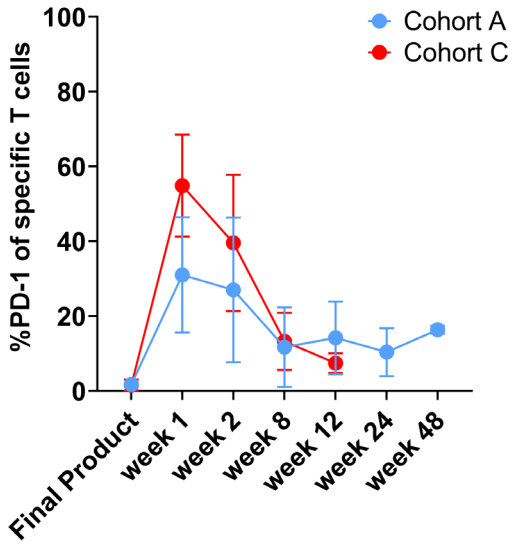
Higher peak expansion (C_{max}) of IMA203CD8 T cells when normalized to infused dose



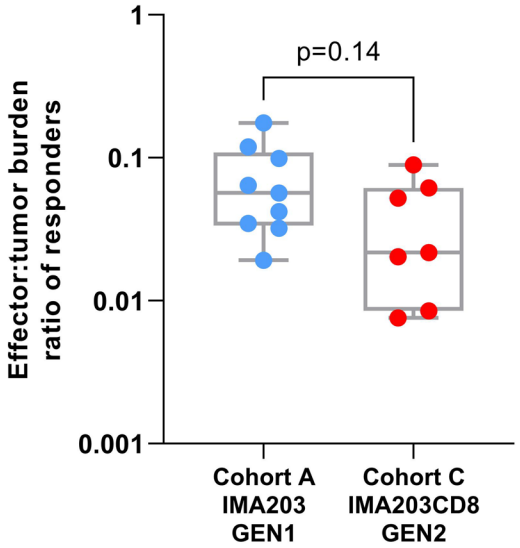
Higher activation levels in IMA203CD8 T cells at week 1…



…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

%PD-1 of specific T cells at week1: for patient A-DL5-05 data not available for week 1

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ACTengine® IMA203 / IMA203CD8 TCR-T Monotherapy Targeting PRAME

Summary of GEN1 and GEN2 Clinical Data and Planned Next 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 1-10x10^9 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

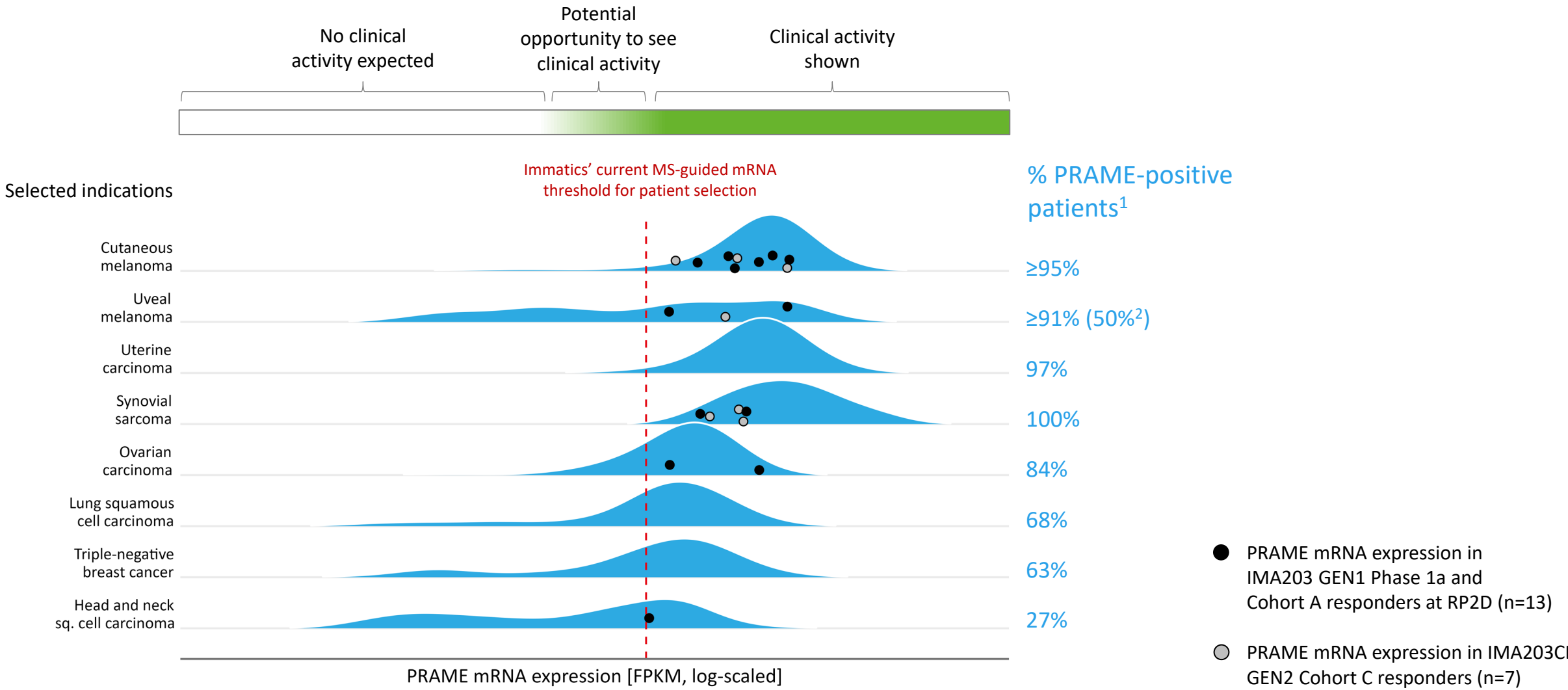
- Enhanced primary and secondary pharmacology when compared to GEN1
- Manageable tolerability (2 DLTs at DL4b, dose escalation ongoing)
- Initial clinical activity observed with differentiated response pattern
  - 56% (5/9) cORR
  - 6 out of 7 responses ongoing at data cut-off, durable response at 12+ 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; [1] PRAME target prevalence is based on TCGA RNAseq data combined with a proprietary MS-guided RNA expression threshold; [2] 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 91% compared to prevalence based on TCGA data of 50%, TCGA: early & late-stage primary tumor samples, Immatics clinical trials: late-stage/metastatic tumor samples, Role of PRAME in metastasis of uveal melanoma: Field *et al.* 2016 Clinical Cancer Research; MS: mass spectrometry

ACTengine® IMA203 / IMA203CD8 TCR-T Monotherapy Targeting PRAME

Leveraging the Full Breath of PRAME in Three Steps

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 Inflections Points

ACTengine®
IMA203 / IMA203CD8 (PRAME)

IMA203 GEN1
- Update on clinical development plan in 1Q 2024
- Targeted registration-enabling Phase 2 trial for ACTengine® IMA203 GEN1 in melanoma

IMA203CD8 GEN2
- Interim data update with longer follow-up planned

TCER® IMA401
(MAGEA4/8)

Bristol Myers Squibb™

First clinical data update from dose escalation in ongoing Phase 1 trial planned

TCER® IMA402
(PRAME)

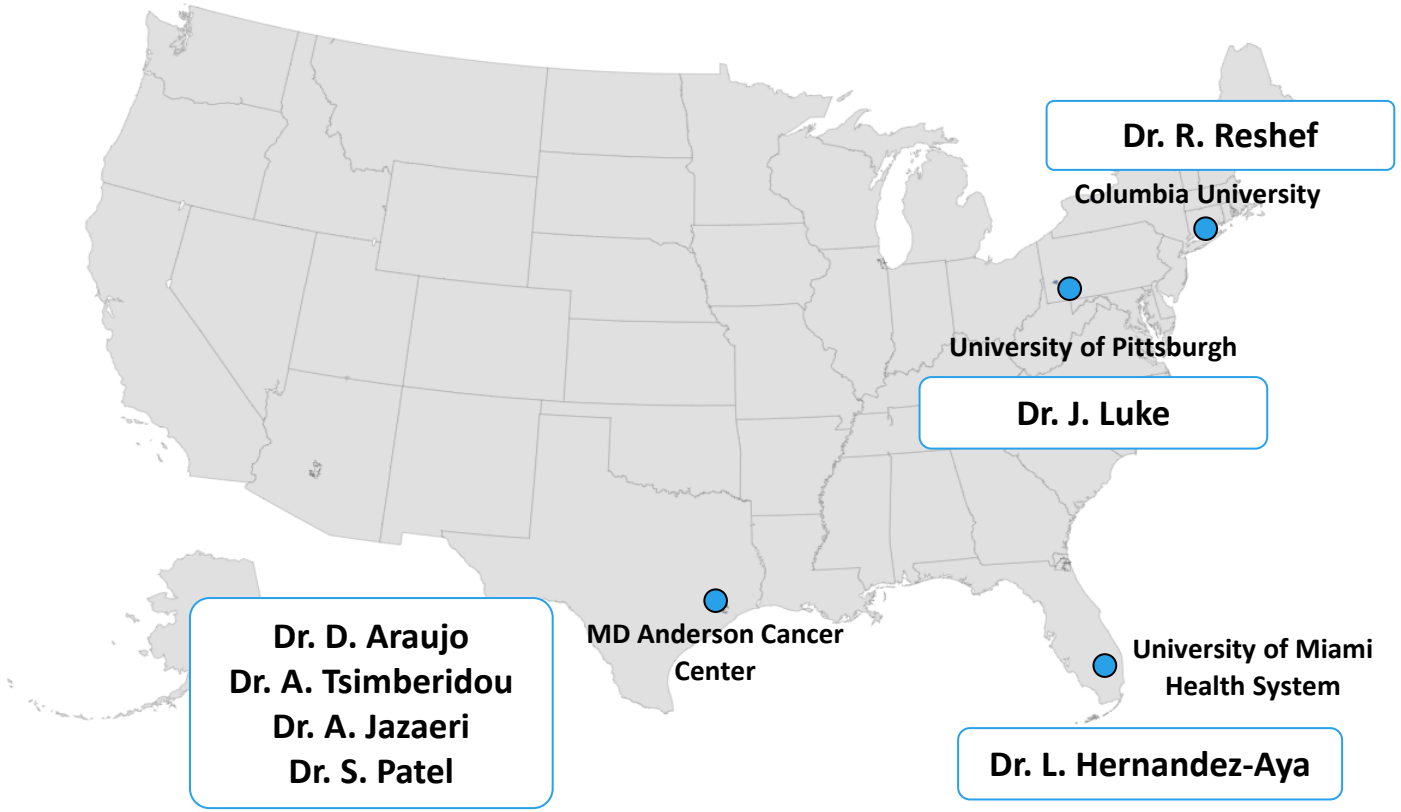
First clinical data update from dose escalation in ongoing Phase 1/2 trial planned

Initial focus indications: Ovarian cancer, uterine cancer, lung cancer, melanoma and others

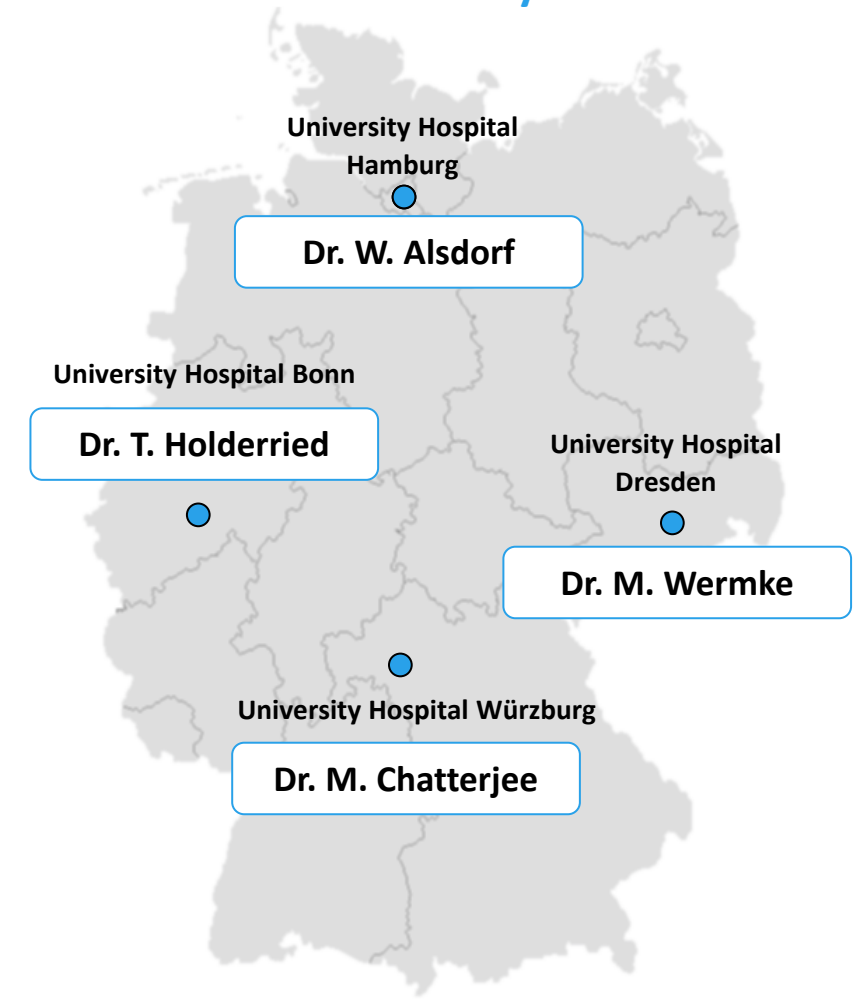
Updates planned across the entire clinical portfolio throughout 2024

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

Q&A

www.immatics.com

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

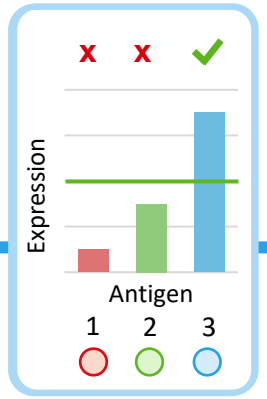
ACTengine® IMA203/IMA203CD8 TCR-T Monotherapy – Patient Flow

Screening & Manufacturing Phase | **Treatment & Observation Phase** | **Long Term Follow-up**

Safety and efficacy monitoring for 12 months

HLA-A*02 Testing
Blood sample;
Central lab

Target Profiling
IMADetect®
Biopsy or archived tissue



Leukapheresis

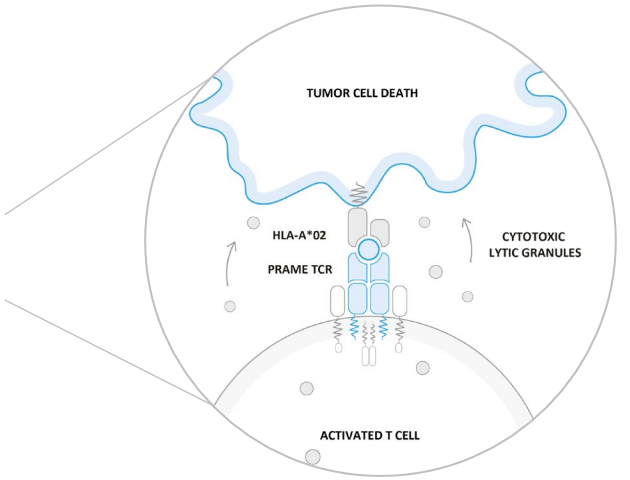
Manufacturing
by Immatics

Short process time of 14 days
7-day manufacturing process
applying CD8/CD4 T cell selection
7-day QC release testing

Lymphodepletion*

Low dose IL-2**

Infusion of ACTengine®
IMA203 TCR-T Product



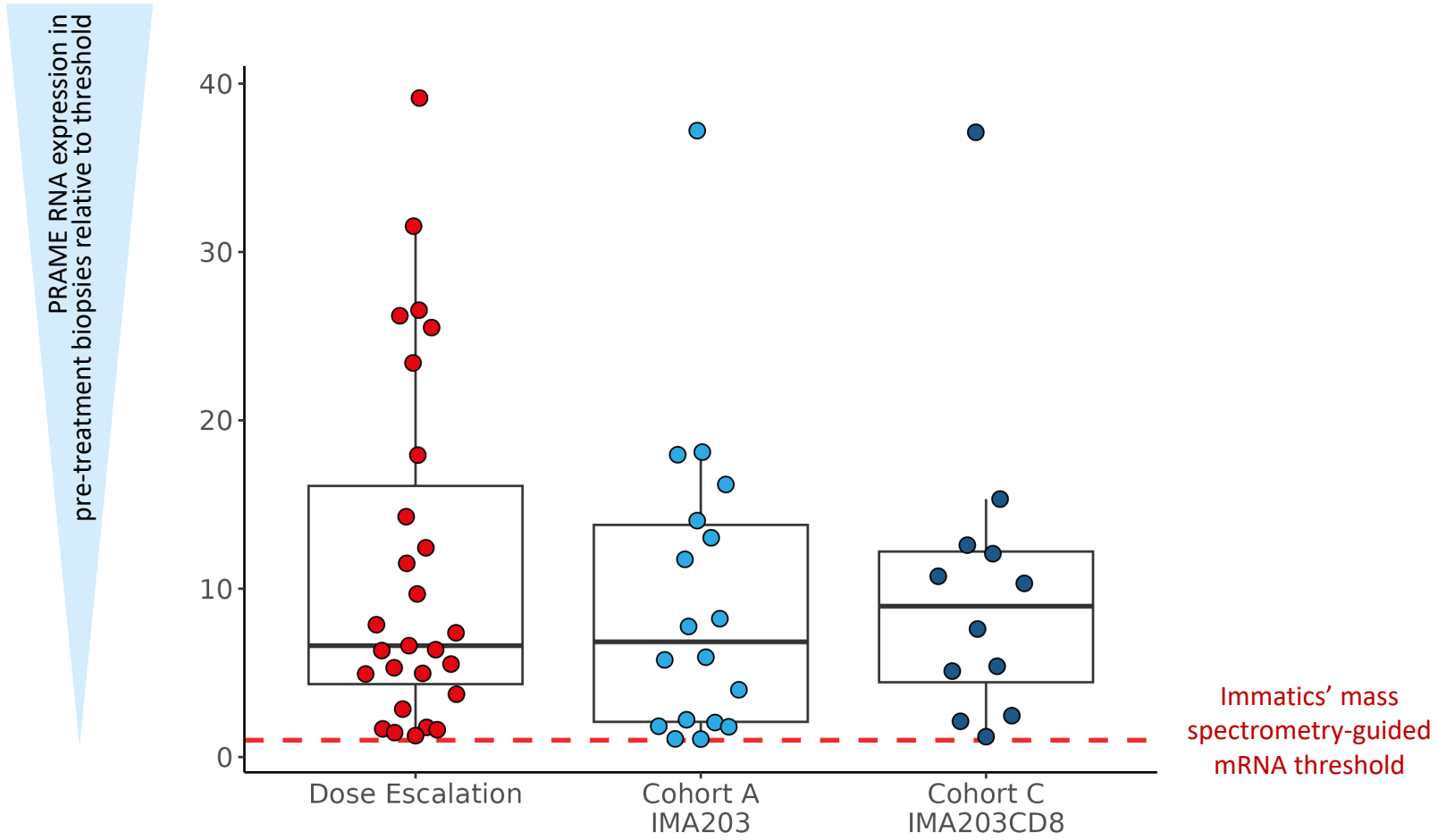
Patient screening data from Immatics' clinical trials:

Cut. Melanoma	95% (58/61)
Uveal Melanoma	91% (30/33)
Uterine Carcinoma	89% (8/9)
Ovarian Carcinoma	82% (23/28)

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

PRAME Expression in Pre-Treatment Tumor Biopsies

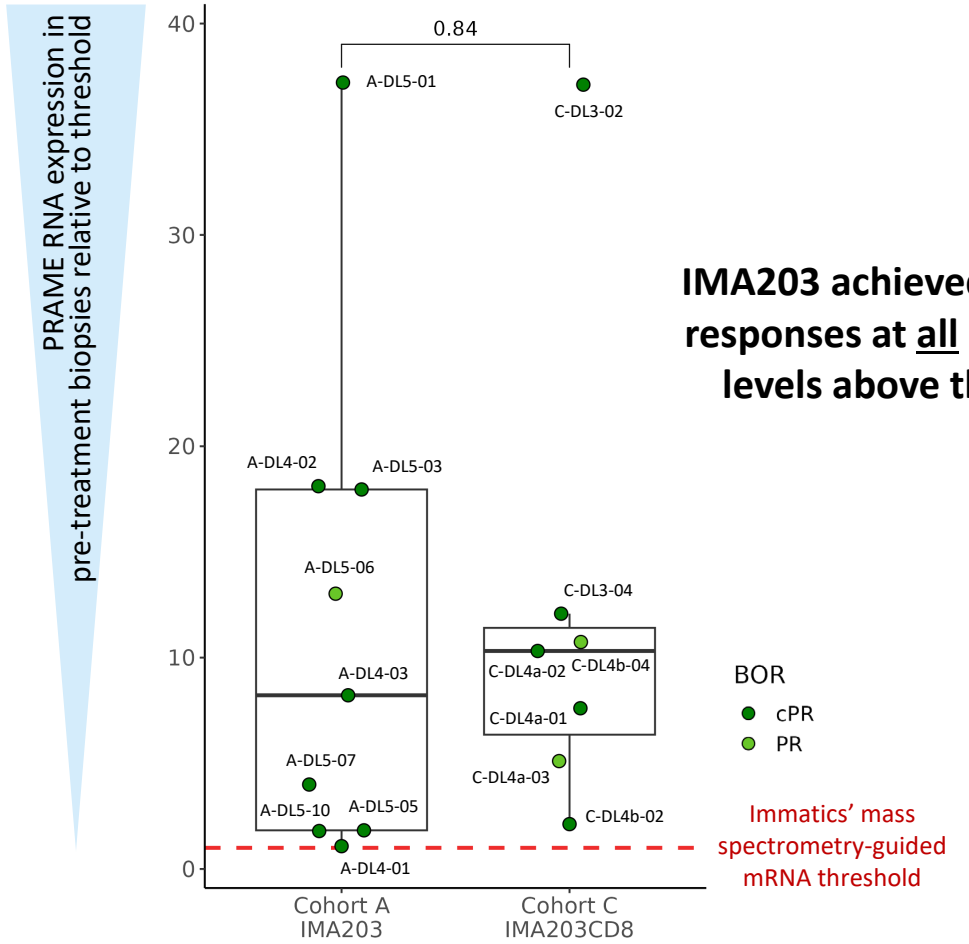
Comparable PRAME Expression Levels in Patients Treated in Phase 1a Dose Escalation, Cohort A and C



PRAME Expression in Pre-Treatment Tumor Biopsies

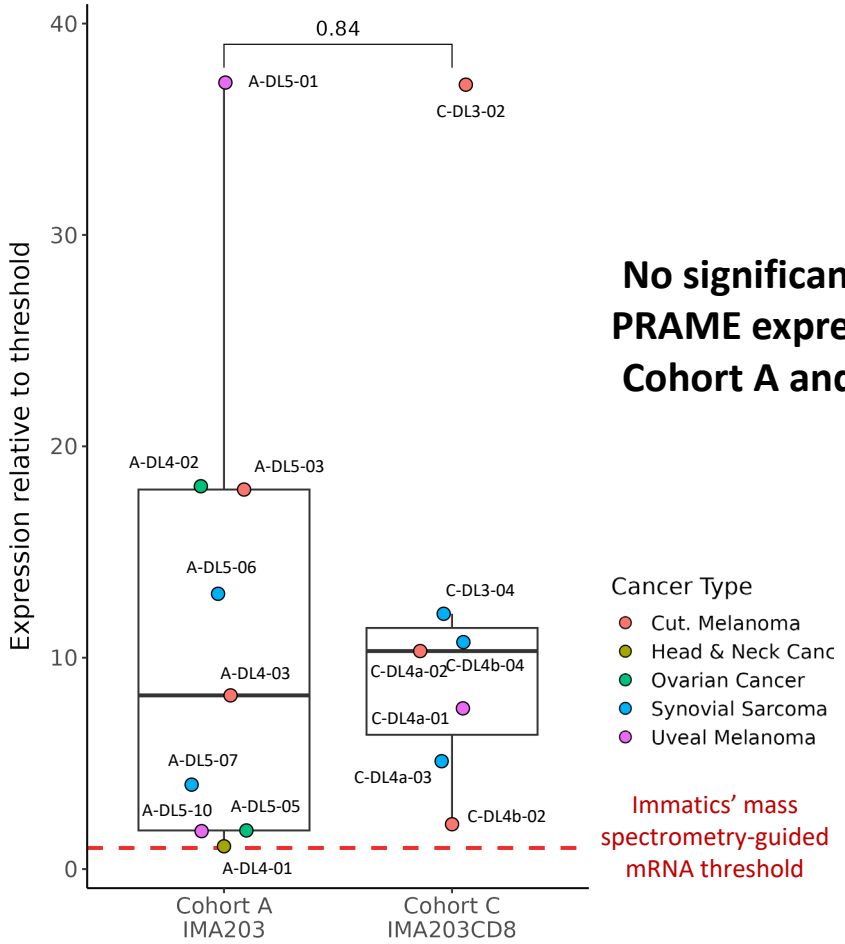
Responders in Cohort A IMA203 GEN1 and Cohort C IMA203CD8 GEN2

Best Overall Response



IMA203 achieved objective responses at <u>all</u> expression levels above threshold

Indication



No significant difference in PRAME expression between Cohort A and C responders

Mann-Whitney U test

Appendix – Additional Data

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IMA203 GEN1 – Melanoma as First Indication for Pivotal Development

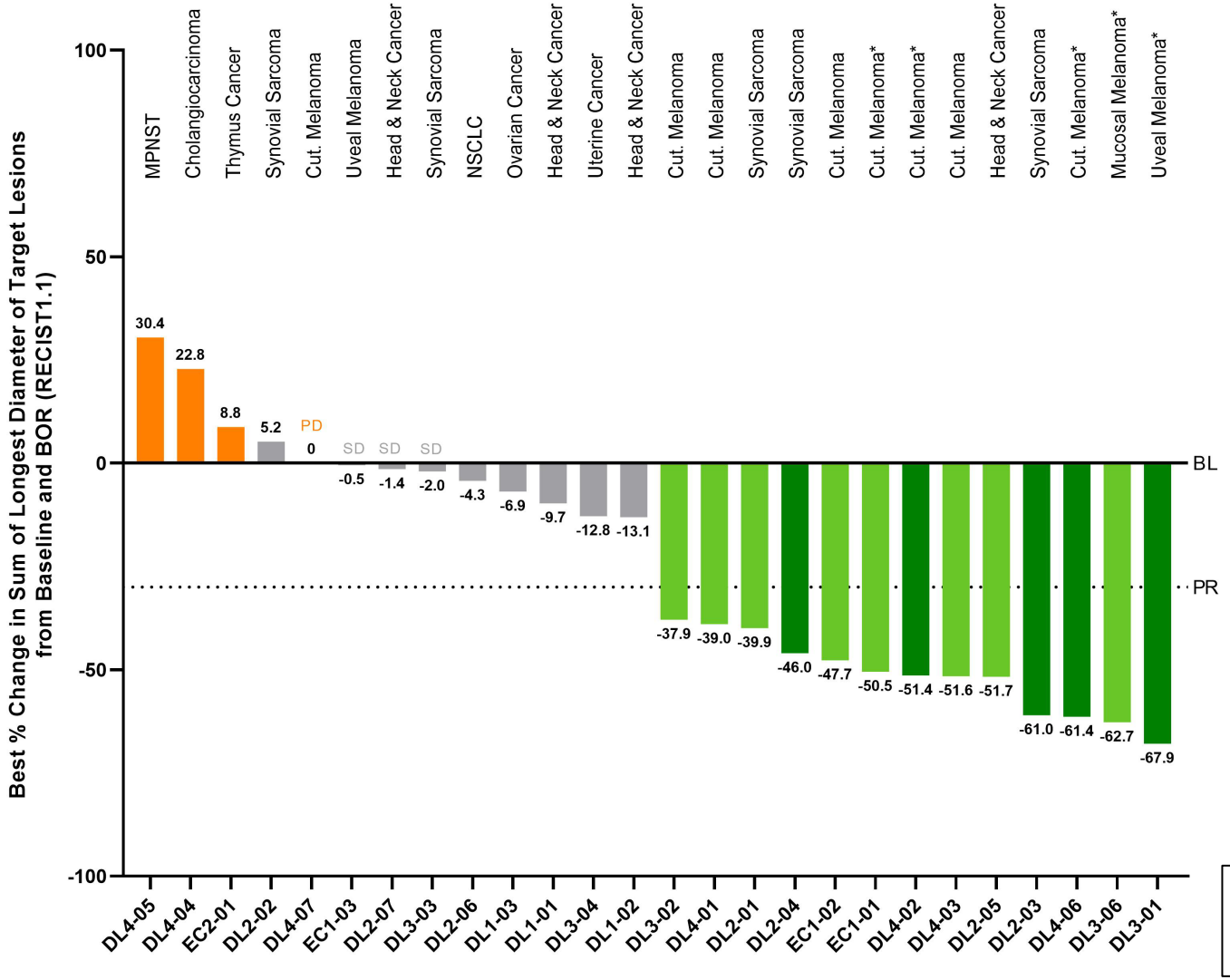
Patient Numbers*	ALL	Melanoma	Ovarian Cancer	Synovial Sarcoma	H&N Cancer	Others
Phase 1a RP2D	7	5	0	0	0	2
Cohort A RP2D	18	8	4	3	1	2

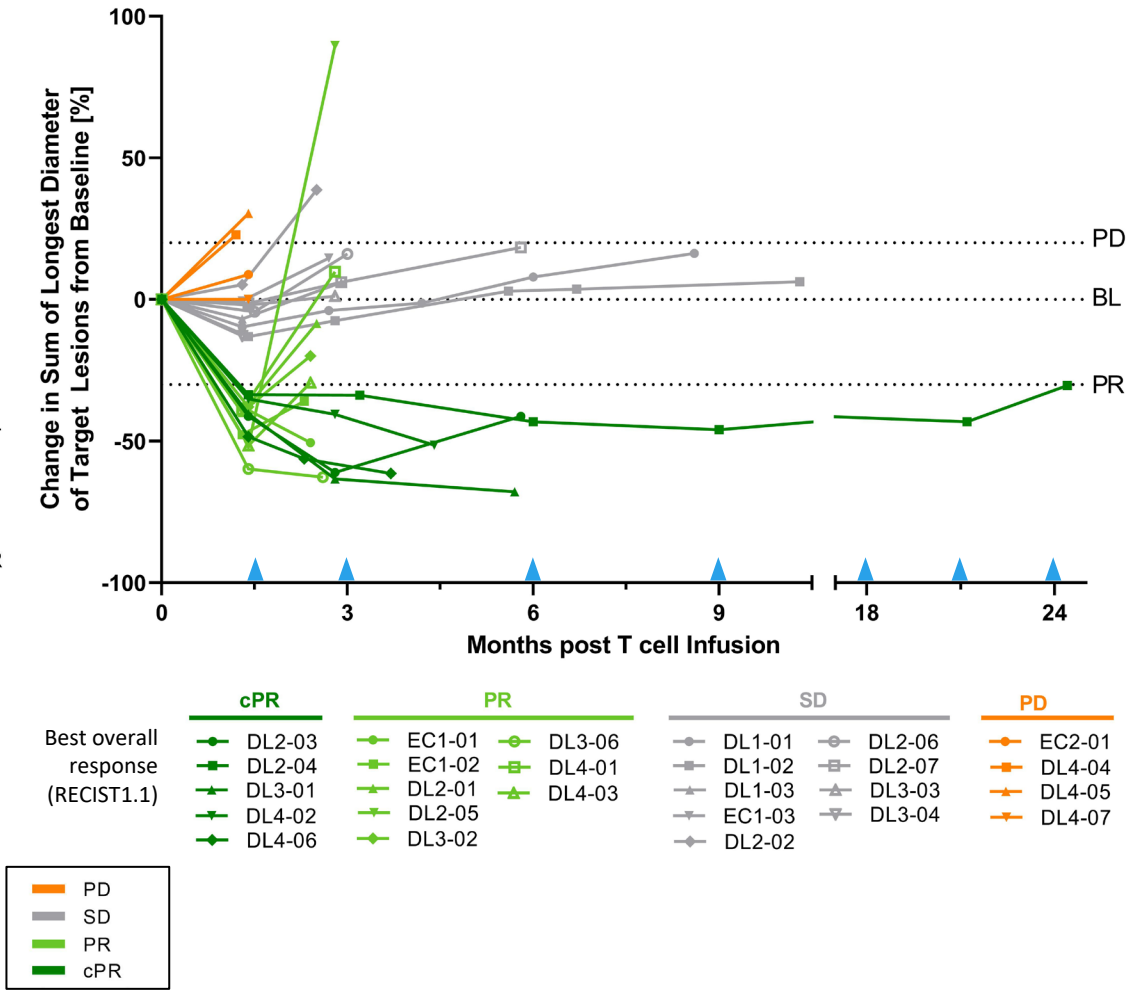
Patient characteristics	All comers Cohort A	Melanoma pts Ph1a & Cohort A at RP2D	Ovarian cancer pts Ph1a & Cohort A at RP2D
Efficacy population*	18	13	4
Prior lines of treatment Median (min, max)	3 (0, 10)	4 (0, 7)	4.5 (3, 10)
LDH at baseline >1 x ULN [% of patients]	50.0	53.9	100.0
Baseline tumor burden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

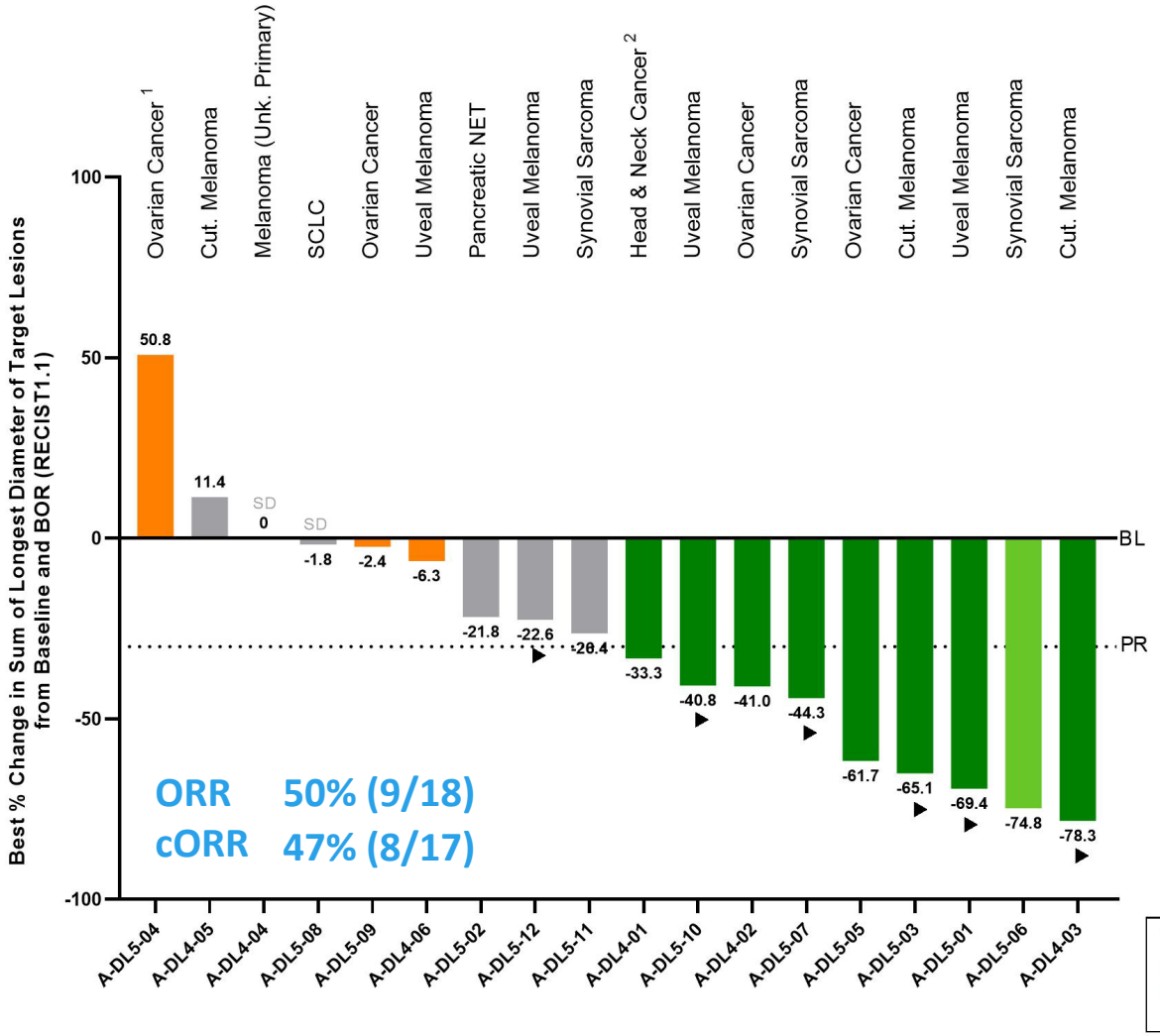




* Maximum change of target lesions and RECIST 1.1 BOR at different timepoints; # Synovial sarcoma patient (DL3) PD at week 6 not shown as target lesions were not evaluable;
PD: Progressive disease; SD: Stable disease; PR: Partial response; cPR: Confirmed partial response; BL: Baseline

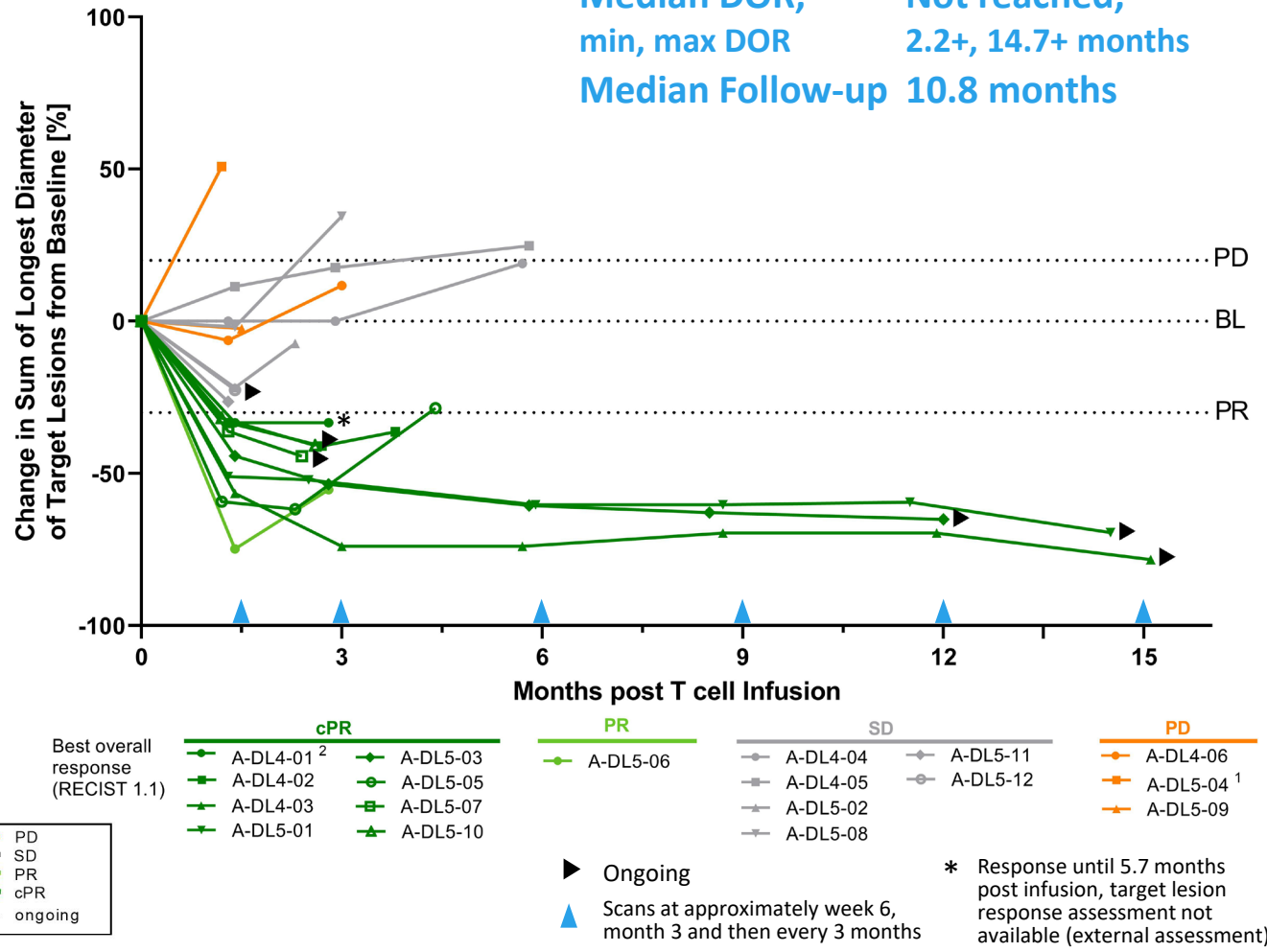
IMA203 GEN1 in Cohort A (N=18) – BOR and Response over Time

Objective Responses across Multiple Solid Cancer Types



Median DOR, min, max DOR Not reached, 2.2+, 14.7+ months

Median Follow-up 10.8 months



[1] Patient received one dose nivolumab erroneously; [2] 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 1.1 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

IMA203 GEN1 in Cohort A – Most Frequent Adverse Events

N=21 Patients in Safety Population[1]

- **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[2] in DL5**
- **No dose-limiting toxicity**
- **No IMA203-related deaths**

IMA203 GEN1 monotherapy continues to be well tolerated at total doses between 1-10x10^9 TCR-T cells (RP2D)

[1] Three cutaneous melanoma patients treated with IMA203, and pending post infusion scan included in safety population, but not efficacy population;
[2] 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)[1]

Adverse event (**System organ class**, Preferred term)	≥ Grade 3 No.	≥ Grade 3 %
Patients with any adverse event	49	100.0
Adverse Events of Special Interest	2	4.1
Cytokine release syndrome	2	4.1
ICANS[2]	0	0.0
Blood and lymphatic system disorders	**48**	**98.0**
Neutropenia	36	73.5
Lymphopenia	27	55.1
Leukopenia	26	53.1
Anaemia	24	49.0
Thrombocytopenia	17	34.7
Cytopenia	1	2.0
Leukocytosis	1	2.0
Lymphocytosis	1	2.0
Investigations	**9**	**18.4**
Neutrophil count decreased	4	8.2
Alanine aminotransferase increased	2	4.1
Aspartate aminotransferase increased	2	4.1
White blood cell count decreased	2	4.1
Blood alkaline phosphatase increased	1	2.0
Blood creatinine increased	1	2.0
Blood fibrinogen decreased	1	2.0
Infections and infestations	**7**	**14.3**
Appendicitis	1	2.0
COVID-19	1	2.0
Enterococcal infection	1	2.0
Infection	1	2.0
Orchitis	1	2.0
Sepsis[4,5]	1	2.0
Septic shock[4]	1	2.0
Urinary tract infection	1	2.0
Respiratory, thoracic and mediastinal disorders	**6**	**12.2**
Hypoxia	3	6.1
Bronchial obstruction	1	2.0
Laryngeal inflammation	1	2.0
Pleural effusion	1	2.0
Respiratory failure	1	2.0
Vascular disorders	**6**	**12.2**
Hypertension	4	8.2
Hypotension	2	4.1

Adverse event (**System organ class**, Preferred term)	≥ Grade 3 No.	≥ Grade 3 %
table continued…		
General disorders and administration site conditions	**4**	**8.2**
Condition aggravated[4]	1	2.0
Fatigue	1	2.0
Pyrexia	1	2.0
Swelling face	1	2.0
Metabolism and nutrition disorders	**4**	**8.2**
Hypokalaemia	3	6.1
Failure to thrive	1	2.0
Hypophosphataemia	1	2.0
Gastrointestinal disorders	**2**	**4.1**
Abdominal pain	1	2.0
Diarrhoea	1	2.0
Vomiting	1	2.0
Injury, poisoning and procedural complications	**2**	**4.1**
Humerus fracture	1	2.0
Infusion related reaction	1	2.0
Renal and urinary disorders	2	4.1
Acute kidney injury	1	2.0
Proteinuria	1	2.0
Skin and subcutaneous tissue disorders	**2**	**4.1**
Rash maculo-papular	2	4.1
Cardiac disorders	**1**	**2.0**
Atrial fibrillation[3]	1	2.0
Endocrine disorders	1	**2.0**
Inappropriate antidiuretic hormone secretion	1	2.0
Eye disorders	**1**	**2.0**
Ulcerative keratitis	1	2.0
Hepatobiliary disorders	**1**	**2.0**
Cholangitis	1	2.0
Immune system disorders	**1**	**2.0**
Contrast media allergy	1	2.0
Musculoskeletal and connective tissue disorders	**1**	**2.0**
Muscle spasms	1	2.0
Nervous system disorders	**1**	**2.0**
Headache	1	2.0
Reproductive system and breast disorders	**1**	**2.0**
Vaginal haemorrhage	1	2.0

- Well tolerated at doses as high as ~$10x10^9$ 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); [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.

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)[1]

Adverse event (System organ class, Preferred term)	≥ Grade 3 No.	≥ Grade 3 %
Patients with any adverse event	28	100.0
Adverse Events of Special Interest	**1**	**3.6**
Cytokine release syndrome	1	3.6
ICANS[2]	0	0.0
Blood and lymphatic system disorders	**27**	**96.4**
Neutropenia	18	64.3
Anaemia	14	50.0
Leukopenia	13	46.4
Lymphopenia	11	39.3
Thrombocytopenia	9	32.1
Leukocytosis	1	3.6
Lymphocytosis	1	3.6
Investigations	**7**	**25.0**
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
Infections and infestations	**3**	**10.7**
Infection	1	3.6
Septic shock[3]	1	3.6
Urinary tract infection	1	3.6
Respiratory, thoracic and mediastinal disorders	**3**	**10.7**
Hypoxia	2	7.1
Laryngeal inflammation	1	3.6
Vascular disorders	**3**	**10.7**
Hypotension	2	7.1
Hypertension	1	3.6
Metabolism and nutrition disorders	**2**	**7.1**
Failure to thrive	1	3.6
Hypokalaemia	1	3.6
Hypophosphataemia	1	3.6
Eye disorders	**1**	**3.6**
Ulcerative keratitis	1	3.6

Adverse event (System organ class, Preferred term)	≥ Grade 3 No.	≥ Grade 3 %
table continued…		
General disorders and administration site conditions	**1**	**3.6**
Pyrexia	1	3.6
Hepatobiliary disorders	**1**	**3.6**
Cholangitis	1	3.6
Injury, poisoning and procedural complications	**1**	**3.6**
Humerus fracture	1	3.6
Musculoskeletal and connective tissue disorders	**1**	**3.6**
Muscle spasms	1	3.6
Nervous system disorders	**1**	**3.6**
Headache	1	3.6
Skin and subcutaneous tissue disorders	**1**	**3.6**
Rash maculo-papular	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); [1] 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; [2] ICANS: Immune effector cell-associated neurotoxicity syndrome; [3] Fatal Adverse events were not considered related to any study drug

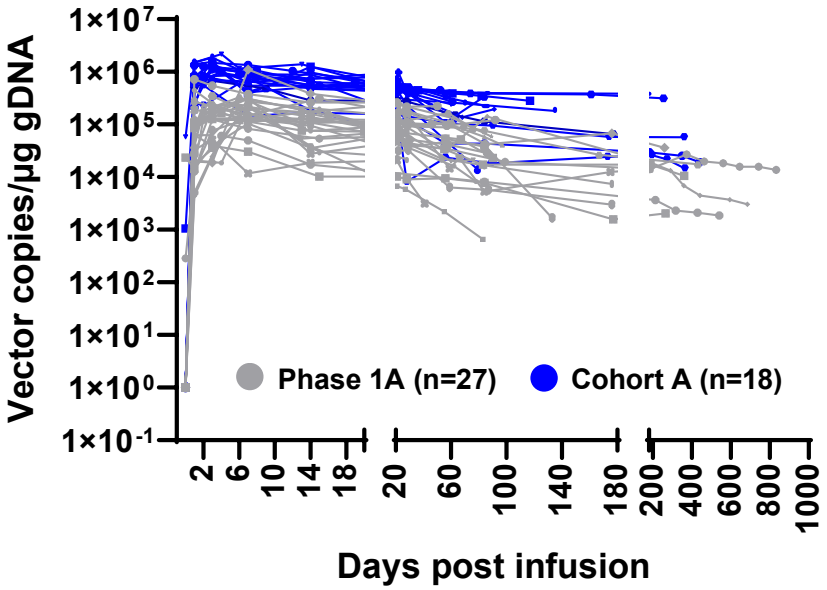
- IMA203 was well tolerated at doses as high as ~$10x10^9$ TCR-T cells
- Most frequent ≥Grade 3 AEs were expected cytopenia associated with lymphodepletion
- No IMA203-related Grade 5 AEs

Biological Data Consistent with Clinical Data – IMA203 GEN1

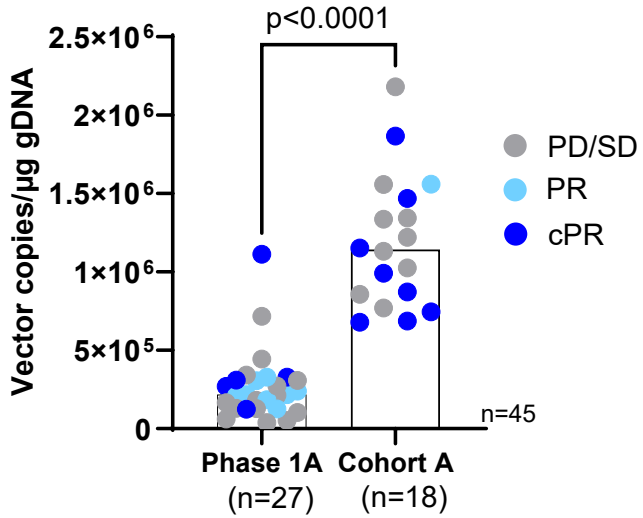
IMA203 T cell Levels and Tumor Infiltration across Patients in Phase 1a and Cohort A

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

Persistence over time

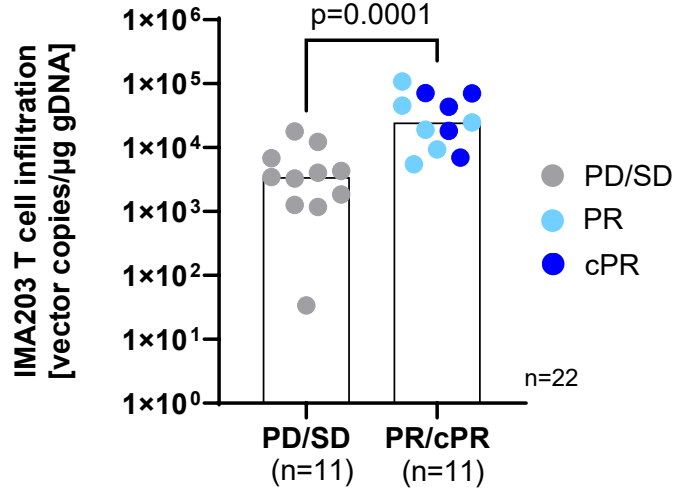


Peak expansion (C_{max})



IMA203 T cells found in all evaluable tumor tissues, level of infiltration associated with objective responses[1]

Tumor Infiltration



Mann-Whitney U test; [1] 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[1] [x10^9]	BOR	BOR (Max % change of target lesions)	Comment	Reason for Progression
Cohort A	A-DL5-01	Uveal Melanoma	1	ARRY614 + 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 Tebentafusp 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	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 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-Merit-study (experimental therapy) Nivolumab Pembrolizumab Ipilimumab + Nivolumab Decortin + Infiliximab Nivolumab + Ipilimumab + Mekinist + Infiliximab	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	Vemurafenib + Cobimetinib 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 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 Tebentafusp	4.50	SD	-22.6	Ongoing disease stabilization 2.2 months post infusion	
Phase 1a	DL4-07	Cut. Melanoma	6	Interferon alpha Pembrolizumab Ipilimumab + Nivolumab Nivolumab LXH254 + Ribociclib 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

[1] 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[1] [x10^9]	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 + Ifosphamid	6.01	**cPR**	-44.3	Ongoing response 4.4 months post infusion	
A-DL5-05	Ovarian Cancer	3	Adriamycin + Cytoxan + Taxol Carboplatin + Taxol Carboplatin + Doxil	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	Carboplatin + Taxol 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+ Atelizumab 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	Lanreotid Streptozocin + 5-Fluorouracil Everolismus	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 ZN-C3 + Gemcitabine 2020-0755 COM 701 + 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 Doxurubicin + 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 + Isofamide Pazobanib NY-ESO1-TCR T-Cells Pazobanib BRD9 PROTAC CFT8634	9.36	SD	-26.4	Clinical progression 2.0 months post infusion	Clinical progression

[1] 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

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

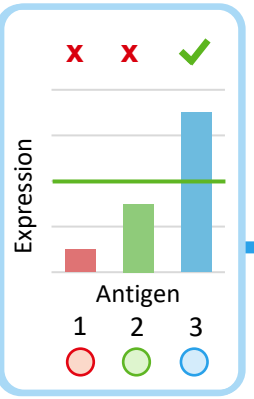
Patient Flow – Cohort B IMA203 + Nivolumab

Screening & Manufacturing Phase | **Treatment & Observation Phase** | **Long Term Follow-up**

Safety and efficacy monitoring for 12 months

HLA-A*02 Testing
Blood sample;
Central lab

Target Profiling
IMADetect®
Biopsy or archived tissue



Leukapheresis

Manufacturing
by Immatics

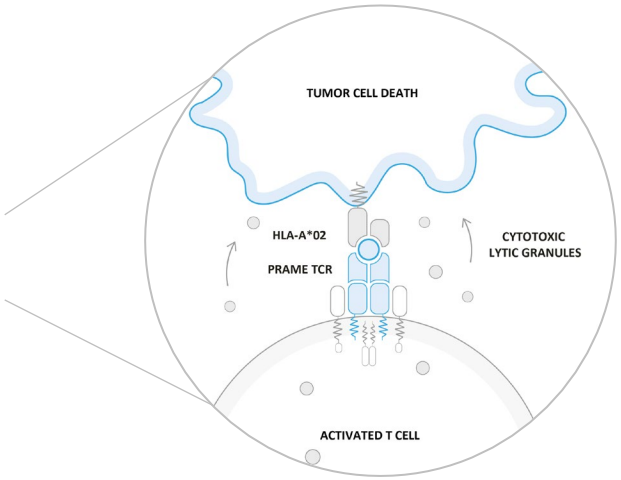
Short process time of 14 days
7-day manufacturing process
7-day QC release testing

Lymphodepletion*

Low dose IL-2**

Nivolumab***

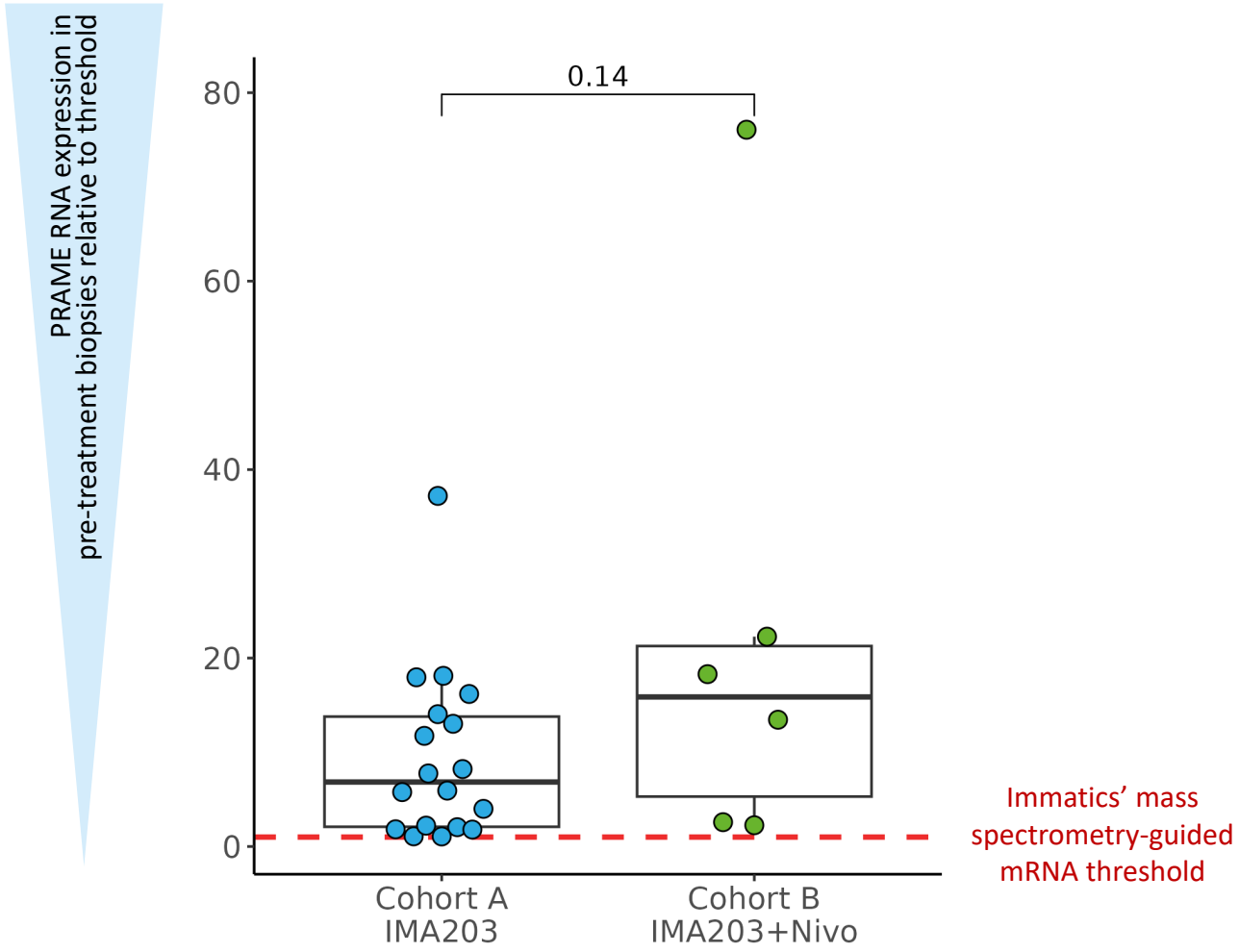
Infusion of ACTengine®
IMA203 TCR-T Product



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



Mann-Whitney U test

Patient Characteristics

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

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

*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; [1] Demonstrated to be associated with durable response: Locke *et al.* 2020 Blood Advances

Most Frequent Adverse Events – Cohort B IMA203 + Nivolumab (N=7)[1]

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[2]** 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

[1] 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;
[2] 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)[1]

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.	≥ Grade 3 %
Patients with any adverse event	**7**	**100.0**
Adverse events of special interest	**0**	**0.0**
Cytokine release syndrome	0	0.0
Immune effector cell-associated neurotoxicity syndrome	0	0.0
Blood and lymphatic system disorders	**7**	**100.0**
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
General disorders and administration site conditions	**2**	**28.6**
Pyrexia	2	28.6
Investigations	**1**	**14.8**
Aspartate aminotransferase increased	1	14.3

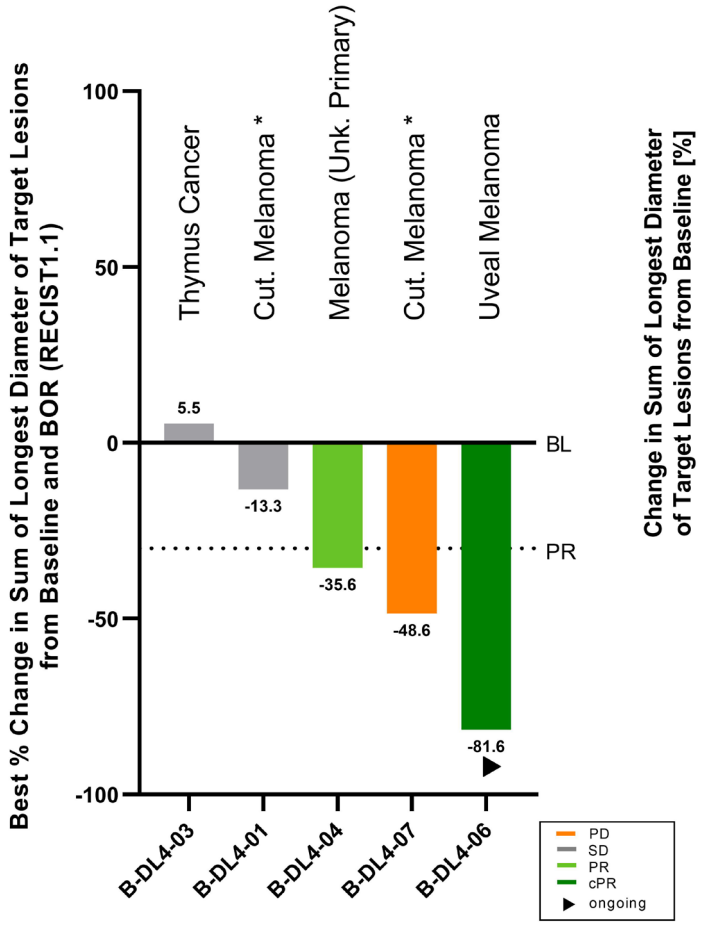
All treatment-emergent adverse events (TEAEs) with ≥ Grade 3 regardless of relatedness to study treatment that occurred in at least 1 patient (except for ICANS and CRS, where only lower grades occurred; listed for completeness due to being adverse events of special interest) are presented. Adverse events 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)

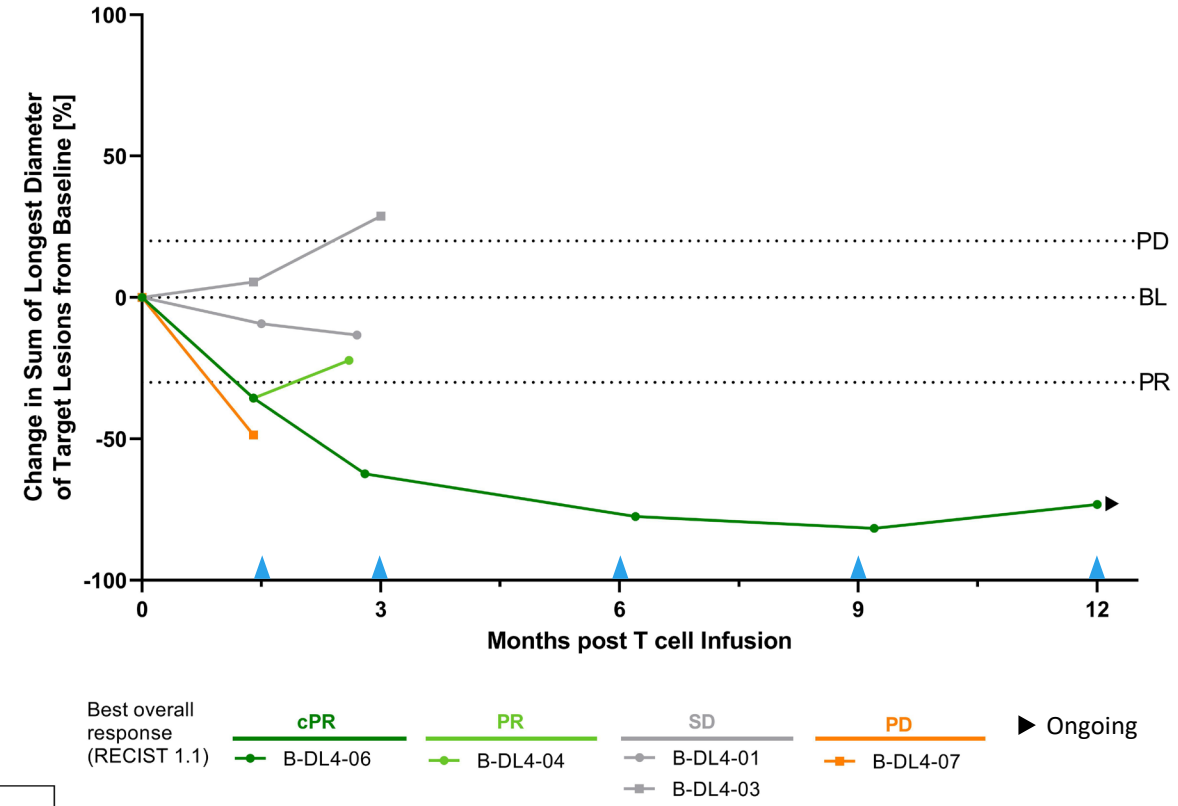
- IMA203 TCR-T in combination with nivolumab was well tolerated
- No unexpected or additive toxicities compared to IMA203 TCR-T monotherapy
- Most frequent ≥Grade 3 AEs were expected cytopenia associated with lymphodepletion
- No IMA203-related Grade 5 AEs

[1] 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





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

Pt B-DL4-05 not shown due to clinical progression prior to 1st post infusion scan, response assessment not available, considered as non-responder for ORR and cORR

ORR[1]	33% (2/6)
cORR[2]	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

[1] Initial ORR: Objective response rate according to RECIST 1.1 at any post infusion scan; [2] 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.

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

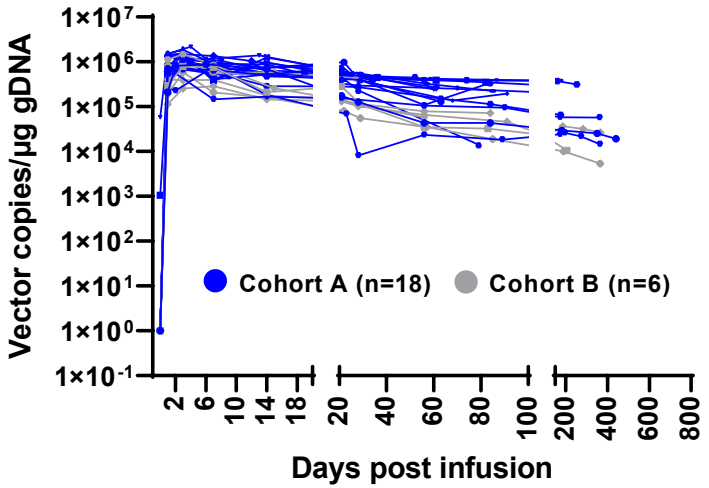
Patient ID	Indication	No of prior treatment lines	Prior treatments	Total infused dose TCR-T cells [x10^9]	BOR	BOR (Max % change of target lesions)	Comment	Reason for Progression
B-DL4-06	Uveal Melanoma	0	NA	2.22	**cPR**	-81.2	Ongoing response 12 months post infusion	On trial
B-DL4-04	Melanoma (Unk. Primary) Patient case	6	Nivolumab/NKTR-214, Nivolumab/Ipilimumab, Encorafenib/Binimetinib, CLXH254C12210 (Panrafi+ERKI) Encorafenib/Binimetinib/Pembrolizumab, Carboplatin/Paclitaxel	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	Dabrafenib/Trametinib, Nivolumab/Ipilimumab, Nivolumab 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, Encorafinib/Binimetinib	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	Adriamycine/Ifosfamide/Vincristine, Ifosfamide/Doxorubicin, Ifosfamide/Doxorubicin, Etoposide/Topotecan/Carboplatin/Cyclophosphamide Trofosfamide/Etoposide/Idarubicine Doxorubicin/Ifosfamide, Carboplatin/Topotecan, Vincristine	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.

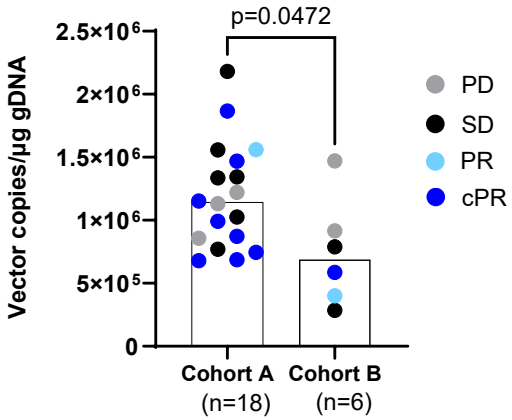
IMA203 T cell Levels – Molecular Immunomonitoring

Cohort A IMA203 vs. Cohort B IMA203 + Nivolumab

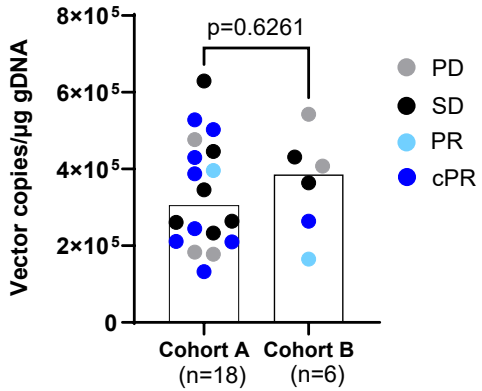
Persistence over time



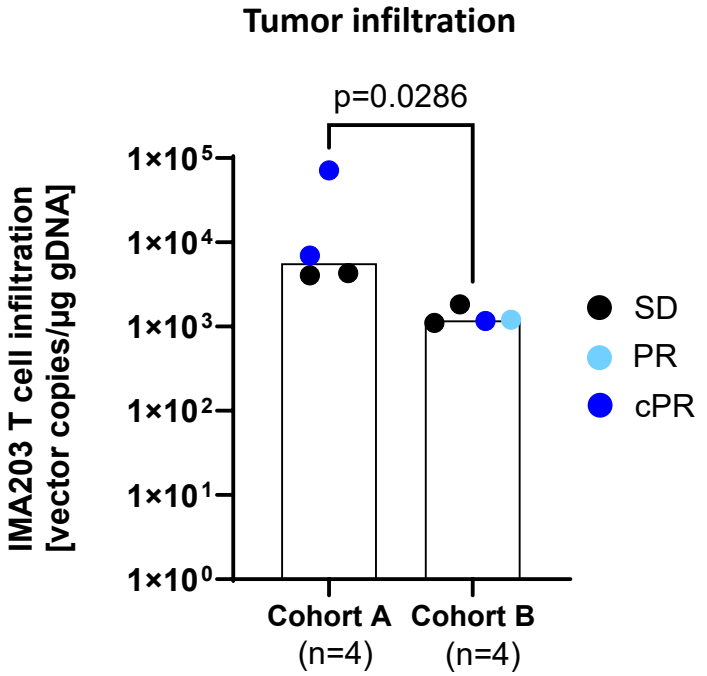
Peak expansion (C_{max})



Peak expansion (C_{max}) normalized to cell dose



Tumor infiltration



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

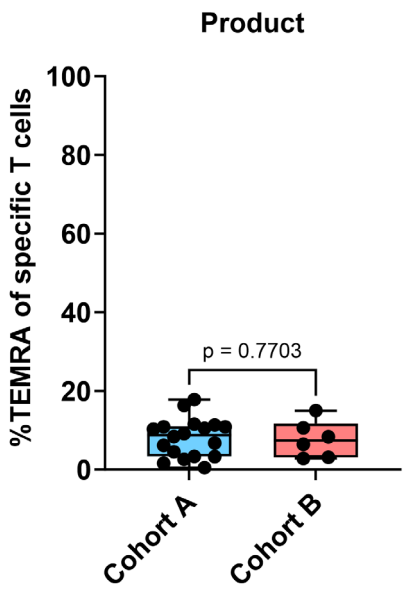
Statistical test: Mann-Whitney U

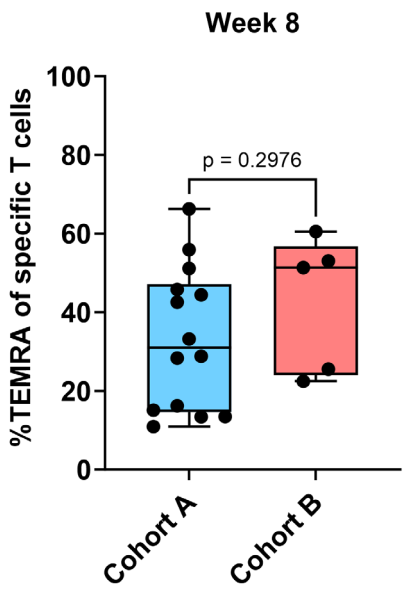
IMA203 T cell Activation and Differentiation

Cohort A IMA203 vs. Cohort B IMA203 + Nivolumab

Terminal differentiation

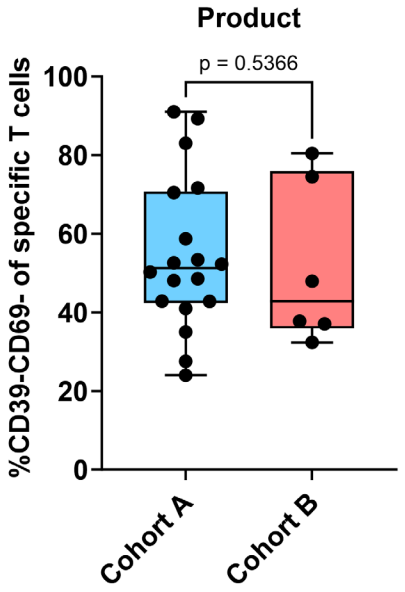
TEMRA*

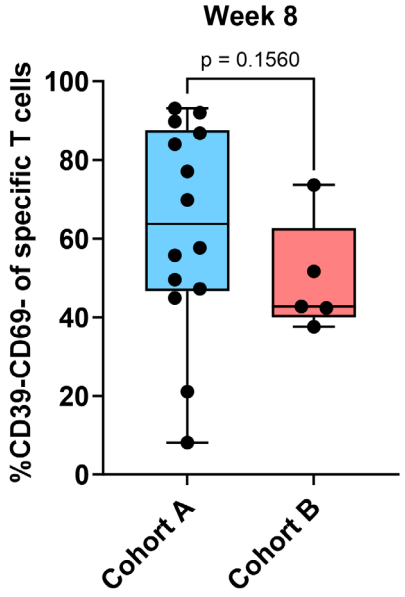




Stem-like phenotype

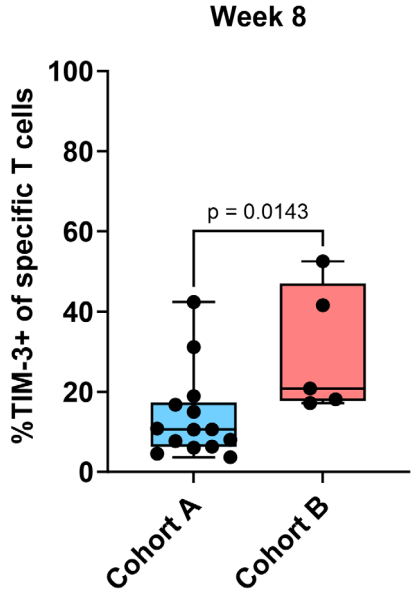
CD39- CD69-





Exhaustion surrogate receptor

TIM-3



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

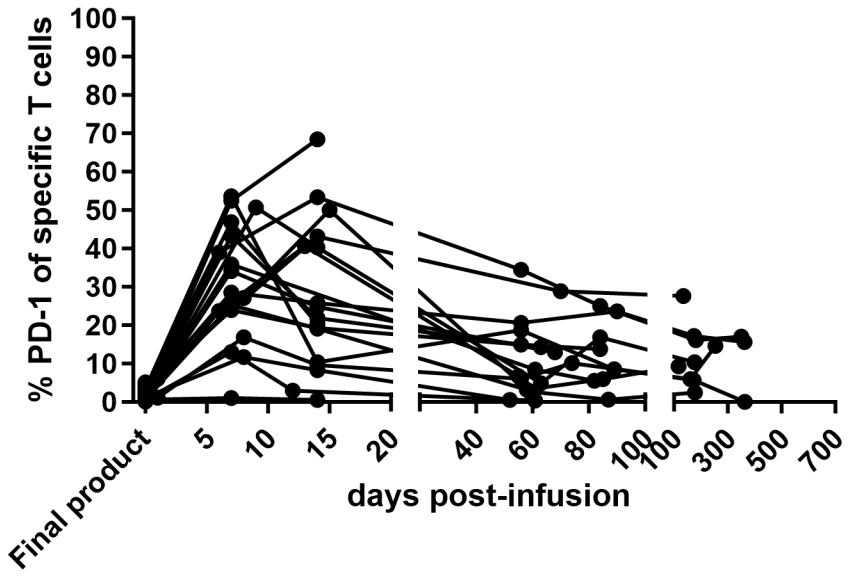
Cohort A: n=18
Cohort B: n=6

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

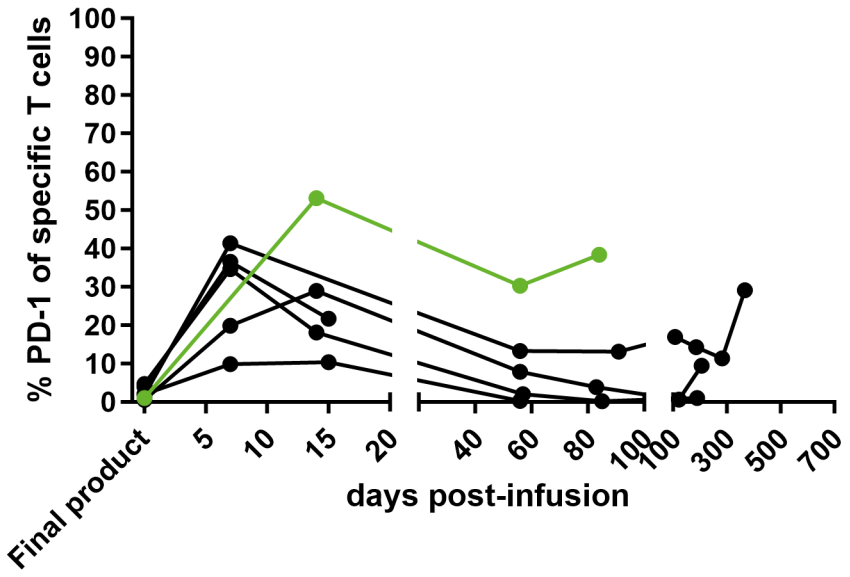
Kinetics of PD-1^{+} Frequency on IMA203 T Cells

Cohort A IMA203 vs. Cohort B IMA203 + Nivolumab

Cohort A



Cohort B



Pt. B-DL4-04 (case study)

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

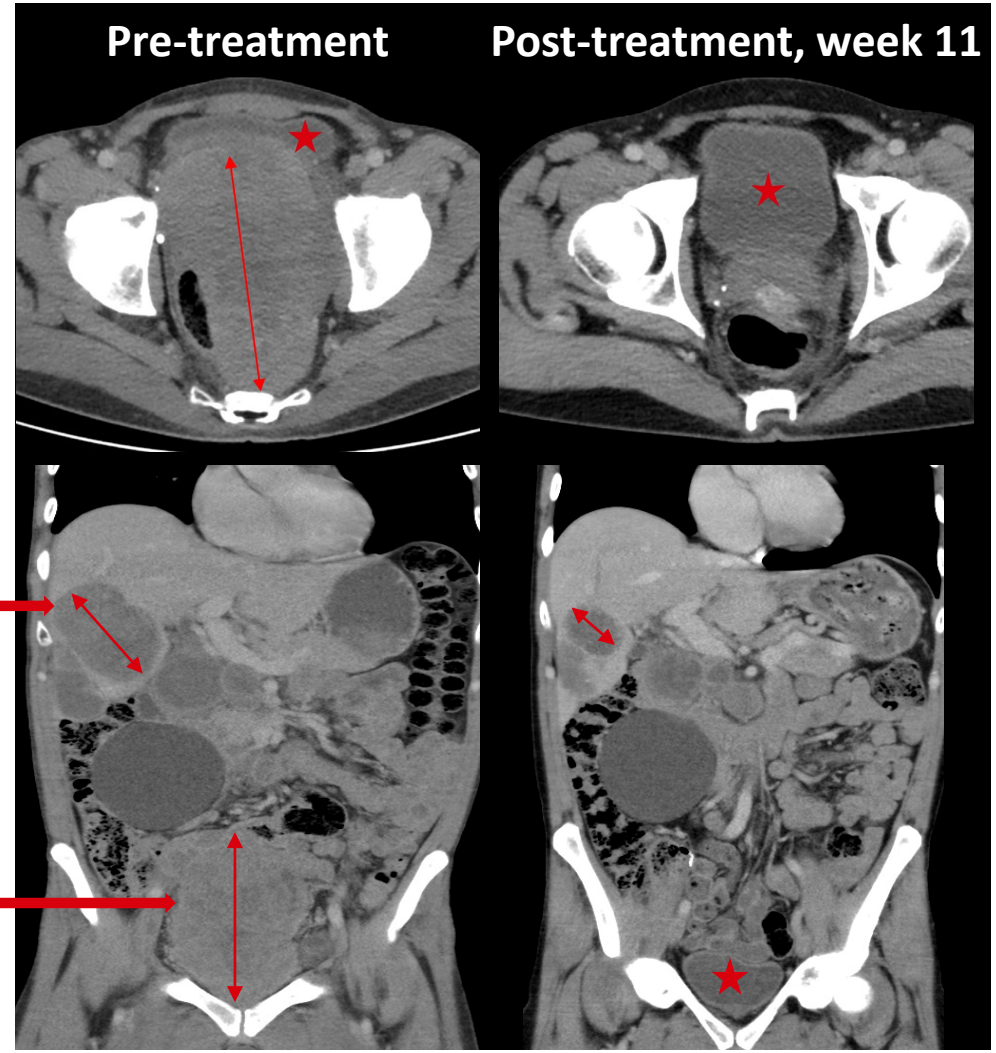
Observed Sustained Clinical Benefit in Patient despite PD at Week 11

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[1]
- ➢ Treatment provided sustained improvement of tumor-related symptoms[1]
- ➢ Patient was PD (pararenal metastases) at week 11 and switched to pembrolizumab + lenvatinib treatment[1]. As of data cut off patient is still alive ~13 months post IMA203 + nivolumab treatment[1]
- ➢ **Patient case study could indicate potential clinical benefit of IMA203 + checkpoint inhibitors in patients with PD-1/PD-L1 upregulation**



Large pelvic lesion compressing the bladder and colon prior to treatment

★ = bladder

[1] Per treating physician; CT scans courtesy of treating physician

Appendix – Additional Data

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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.	%
Patients with any adverse event	**12**	**100.0**
Adverse events of special interest	**3**	**25.0**
Cytokine release syndrome [1]	3	25.0
Immune effector cell-associated neurotoxicity syndrome	0	0.0
Blood and lymphatic system disorders	**11**	**91.7**
Neutropenia	9	75.0
Anaemia	8	66.7
Lymphopenia	8	66.7
Thrombocytopenia	4	33.3
Leukopenia	2	16.7
Investigations	**4**	**33.3**
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
Metabolism and nutrition disorders	**2**	**16.7**
Hypermagnesaemia	1	8.3
Hypoalbuminaemia	1	8.3
Hypophosphataemia	1	8.3
Nervous system disorders	**2**	**16.7**
Neurotoxicity [2]	1	8.3
Syncope	1	8.3
Immune system disorders	**1**	**8.3**
Haemophagocytic lymphohistiocytosis [2]	1	8.3
Infections and infestations	**1**	**8.3**
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); [1] DLT: Dose limiting toxicity in patient DL4b-04. [2] 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[1] [x10^9]	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	0.94	**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[2]	New lesions, target and non-target lesion progression[2]
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

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

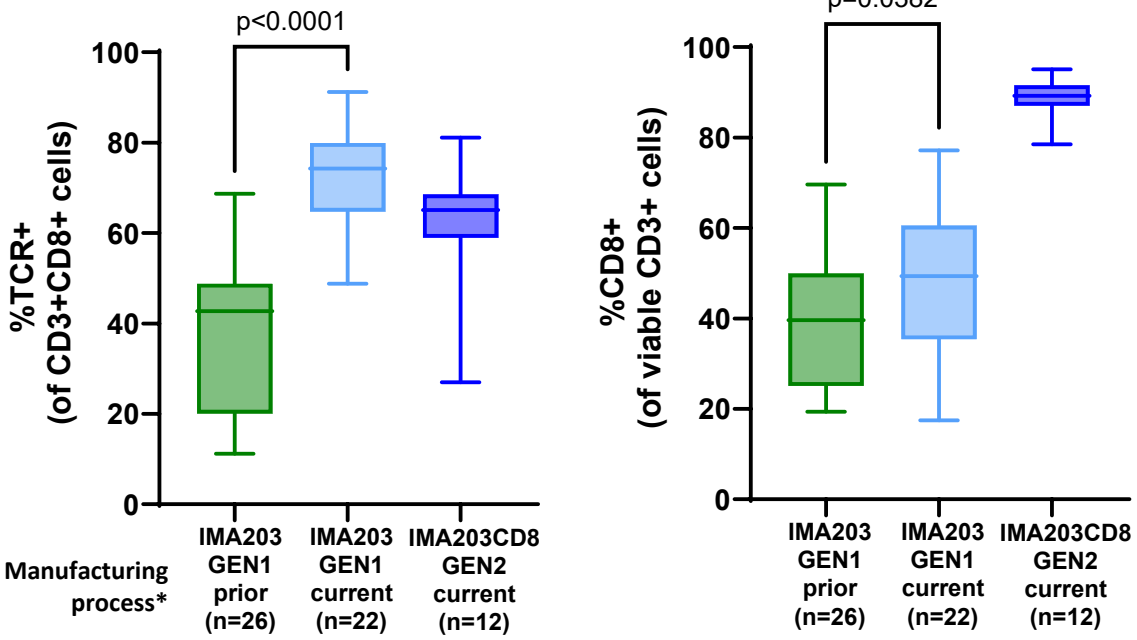
Appendix – Additional Data

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

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

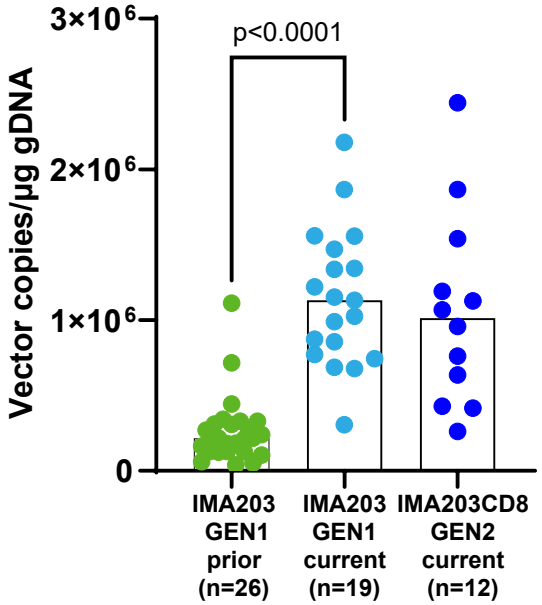
Manufacturing Improvements Implemented in Phase 1b Enhance Key Features of the Cell Product

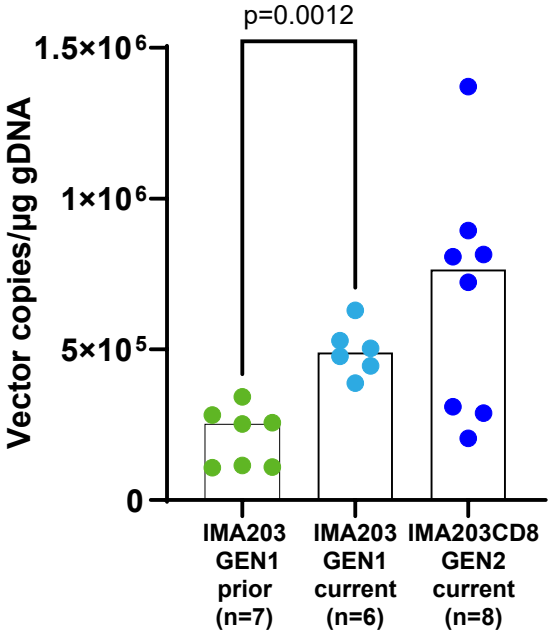
Robust TCR-T product features



Increased peak IMA203 T cell levels in patients

DL4 only, normalized to cell dose





Current manufacturing success rate of >95% to reach RP2D of 1-10x10^9 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

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