

ACTengine® IMA203 TCR-T Targeting PRAME

– Monotherapy Interim Data Update

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Delivering the Power of T cells to Cancer Patients

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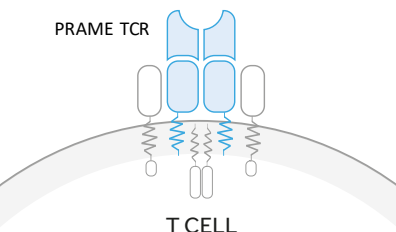
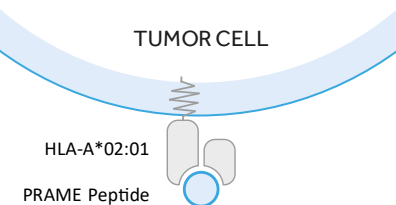
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Multi-Tumor Target PRAME

Promising Opportunity for TCR-based Therapies

PRAME Peptide Target

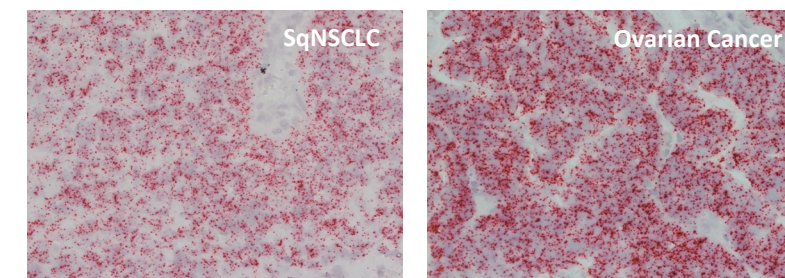
- HLA-A*02:01-presented peptide identified by XPRESIDENT® quant. mass spectrometry
- Presented at high target density in tumor tissue (100-1000 copies/cell)
- Homogenously expressed
- Highly cancer-specific, not expressed in normal tissue at relevant levels
- Highly prevalent across many solid cancers
- Potential to reach a large cancer patient population



IMA203 T cell Receptor (TCR):

- Affinity-improved TCR by enhanced TCR chain pairing
- High functional avidity: EC50 ~5 ng/ml
- Off-target toxicity screening against normal tissue peptides selected from our immunopeptidome database to retain specificity

PRAME RNA detection in tumor samples (ISH)



Patient screening data from Immatics' clinical trials support high prevalence of PRAME:

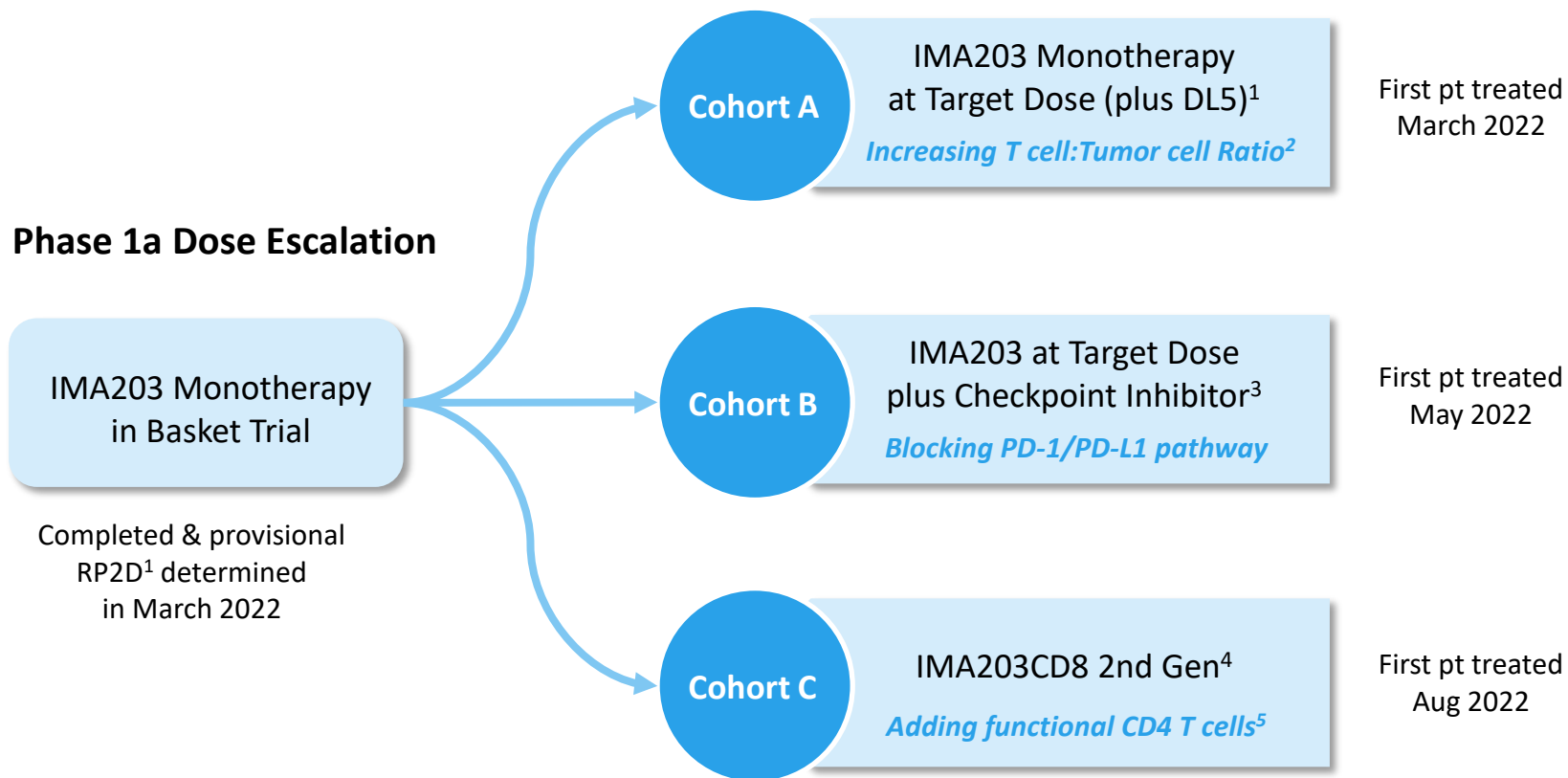
Uterine Carcinoma	90%
Cut. Melanoma	95%
Uveal Melanoma ²	90%
Ovarian Carcinoma	70%

Indication	% PRAME positive patients ¹
Uterine Carcinoma	100%
Uterine Carcinosarcoma	100%
Sarcoma Subtypes	up to 100%
Cut. Melanoma	95%
Uveal Melanoma ²	50%
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%

IMA203 TCR-T Phase 1 Design

Three Phase 1b Expansion Cohorts to Establish Durable Objective Responses

Phase 1b Dose Expansion

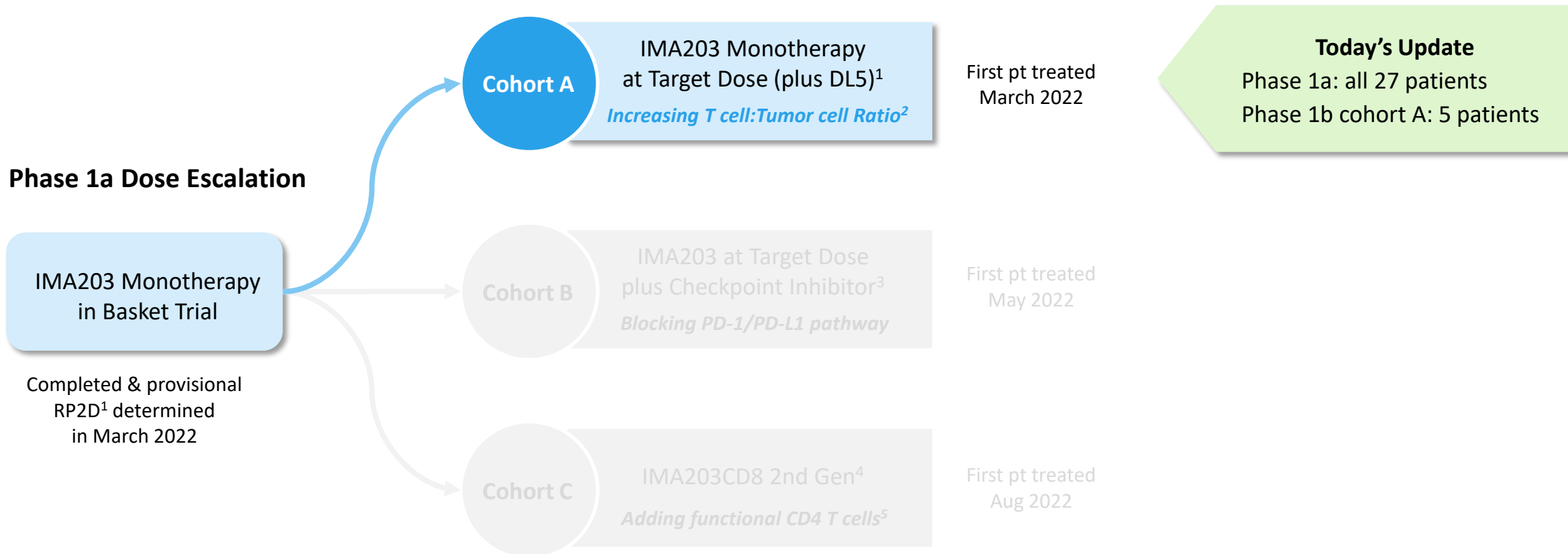


Each expansion cohort is designed to establish safety, evaluate the observed objective response rate, demonstrate durability & provide the trigger for registration trials

IMA203 TCR-T Phase 1 Design

Interim Clinical Data Update Focused on Phase 1a and Expansion Cohort A

Phase 1b Dose Expansion

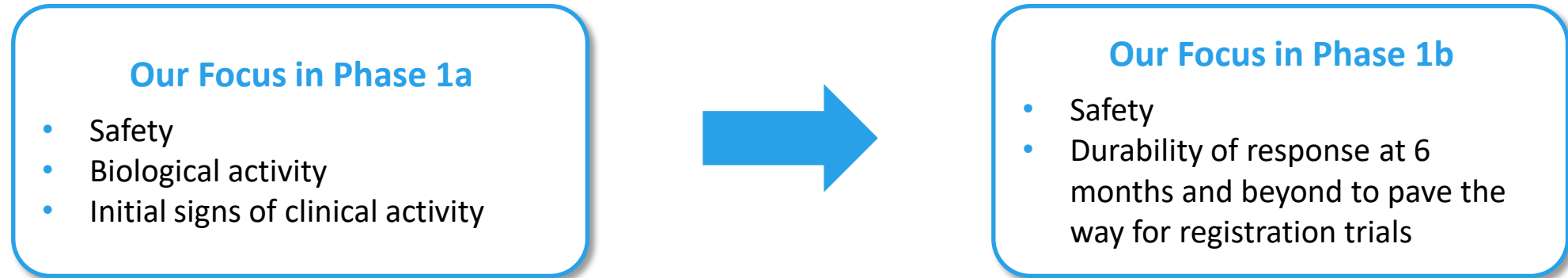


Data cut-off – 06-Sept-2022

¹ RP2D (target dose) determined at DL4, exploration of higher dose (DL5) ongoing; 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 Treatment of n=3 patients in DL3 prior to patient treatment at provisional RP2D (DL4); ⁵ Demonstrated to be important for long-term remission: Melenhorst *et al.* 2022 Nature, Bai *et al.* 2022 Science Advances

Moving from Phase 1a to Phase 1b

Continuous Improvement of Key Aspects that May Influence Clinical Outcome



We continue to improve key determinants as we move from Phase 1a into Phase 1b

1. **Higher T cell dose:** Only RP2D or exploratory DL5
2. **Enhanced cell product:** Implementation of manufacturing enhancements (e.g. monocyte depletion, see appendix) focusing on robustness, quality, and speed of product release
3. **“Real life” patients:** Working with more disease area experts to reduce the fraction of very heavily pre-treated patients with extreme disease burden who have exhausted standard of care and have undergone multiple clinical trials

ACTengine® IMA203 – Interim Monotherapy Update

Phase 1a

Dose Escalation Data from 27 Patients

- Acceptable & manageable treatment-emergent adverse events (TEAEs)
- DL4 defined as provisional RP2D
- 48% (13/27) initial ORR¹ across all doses and multiple solid cancers
- Limited number of confirmed responses



Phase 1b Cohort A

Initial Data from 5 Patients

- Acceptable & manageable TEAEs
- Patients treated at RP2D (DL4) and exploratory DL5
- 80% (4/5) initial ORR¹ in patients with 4 different solid tumors
- 80% (4/5) confirmed ORR²: Confirmation of all objective responses after ~3 months; all responses ongoing



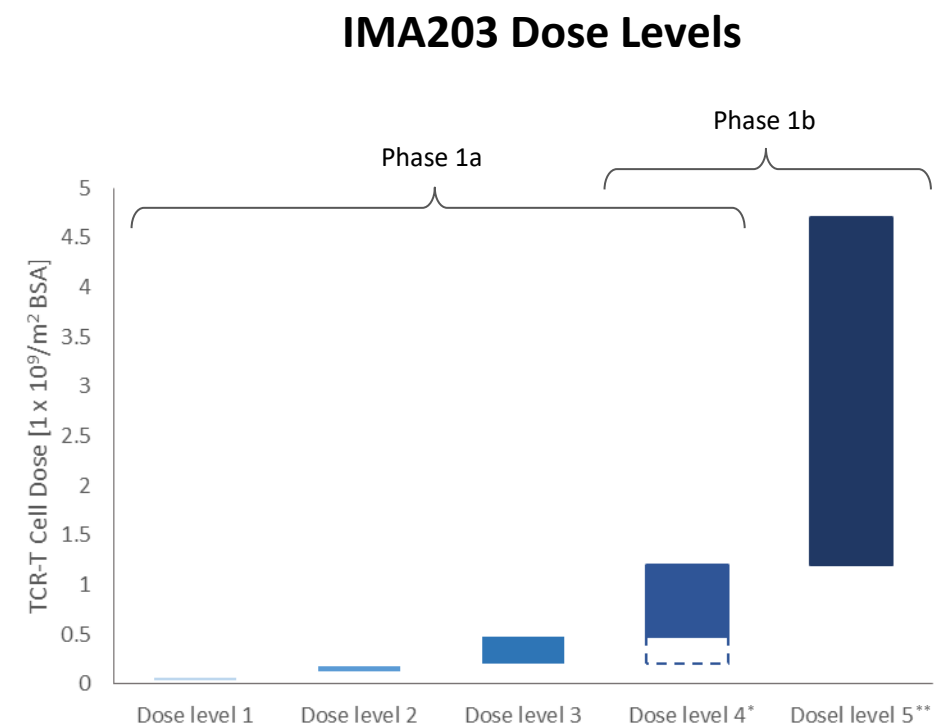
Key Take Aways

IMA203 Monotherapy

- Favorable tolerability profile
- Confirmed responses in multiple heavily pre-treated solid tumor types (*cut. melanoma, uveal melanoma, head and neck cancer, ovarian cancer, synovial sarcoma*)
- Positively evolving durability profile for IMA203
 - above 1 bn TCR-T cells (DL4/5)* in phase 1a and phase 1b: **50% (6/12) confirmed ORR²**
 - in phase 1b patients only: **80% (4/5) confirmed ORR²**

ACTengine® IMA203 Monotherapy – Patient and Product Characteristics

	Phase 1a Dose Escalation		Phase 1b (Cohort A) Dose Expansion
	All pts (DL1-4)	DL4 pts only	All pts (DL4/DL5)
Patients treated	27	7	5
Prior lines of treatment Mean (min, max)	4.2 (1, 8)	4.6 (1, 7)	4.0 (1, 10)
LDH at baseline >1 x ULN [% of patients]	66.7	85.7	40.0
Baseline tumor burden Mean target lesion sum of diameter [mm] (min, max)	130.3 (29.0, 219.7)	115.8 (37.0, 197.6)	55.2 (21.0, 102.9)
Dose Mean transduced viable CD8 T cells infused [$\times 10^9$] (min, max)	0.65 (0.08, 2.09)	1.48 (1.07, 2.09)	2.22 (1.30, 4.16)
Manufacturing Process	Prior versions ¹		Current version



32 heavily pre-treated patients, thereof **12 patients at target dose or above**, were infused with IMA203 TCR-T cells targeting PRAME

DL4 was defined as provisional RP2D for Phase 1b, exploration of higher DL5 ongoing

IMA203 Tolerability Profile – Most Frequent Adverse Events

Acceptable and Manageable Treatment-emergent Adverse Events (TEAEs)

- **Expected cytopenia (Grade 1-4)** associated with lymphodepletion in all patients
- **Cytokine release syndrome (CRS)**: 31 of 32 (97%) patients infused with IMA203 experienced CRS of any Grade
 - 29 patients had Grade 1 or 2 CRS
 - 2 patients had Grade 3 CRS (both in phase 1a); recovered to Grade \leq 2 after 3 and 4 days, respectively
- **Low-moderate ICANS¹**: 5 of 32 (16%) patients infused with IMA203 experienced Grade 1 or 2 ICANS (all in phase 1a)
- **No dose-dependent increase of CRS and ICANS**
- **No additional DLT²**

Frequency of Observed Objective Responses

Improved ORR and Confirmed ORR at Higher Dose and in Phase 1b Cohort A

	Phase 1a		Phase 1a + Phase 1b	Phase 1b only
	All pts (DL1-4)	DL4 pts only ¹	DL4/DL5 pts only ¹	All pts (DL4/DL5) ¹
Patients Treated	27	7	12	5
ORR (~6 weeks)²	48% (13/27)	57% (4/7)	67% (8/12)	80% (4/5)
cORR (~12 weeks)³	19% (5/27)	29% (2/7)	50% (6/12)*	80% (4/5)*

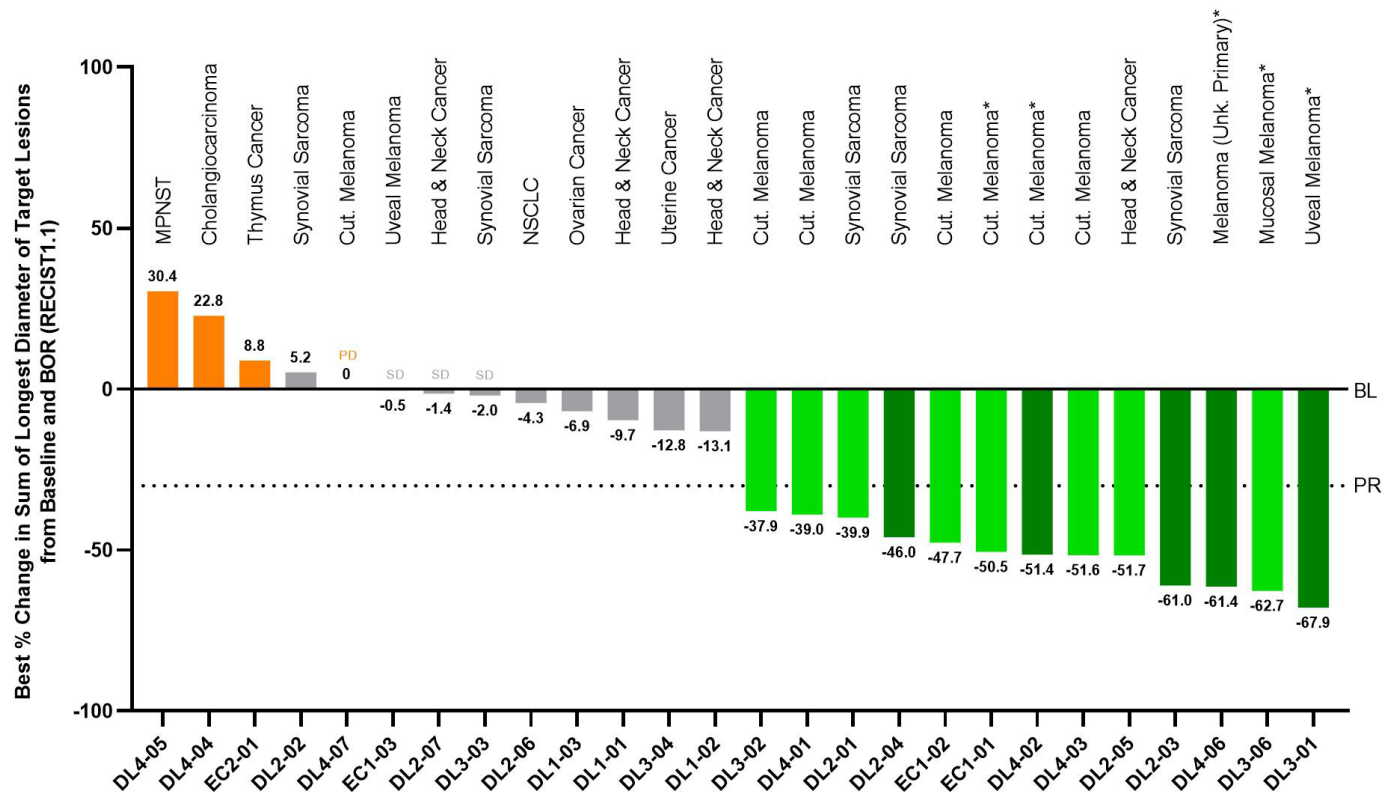
- Higher ORR and confirmed ORR observed at doses above 1 billion TCR-T cells (DL4, DL5)
- Early trends towards higher ORR and confirmed ORR observed in Phase 1b vs. Phase 1a patients

Best Overall Response

IMA203 Continues to Deliver Objective Responses in Major Solid Tumor Types

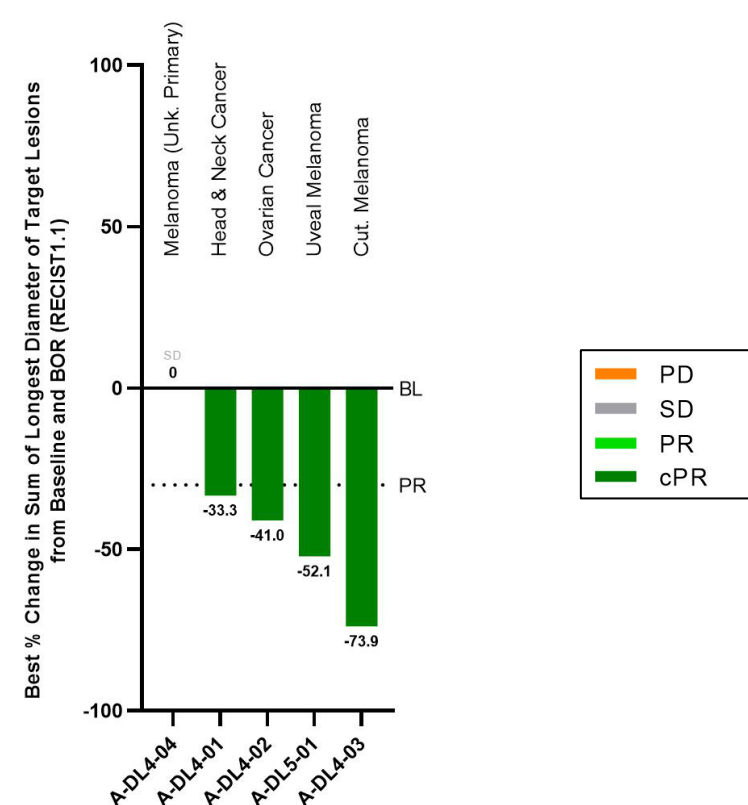
Phase 1a (Dose Escalation)

N=27#



Phase 1b (Cohort A)

N=5



Confirmed objective responses across a broad spectrum of different tumor types such as cutaneous melanoma, uveal melanoma, head and neck cancer, ovarian cancer, synovial sarcoma

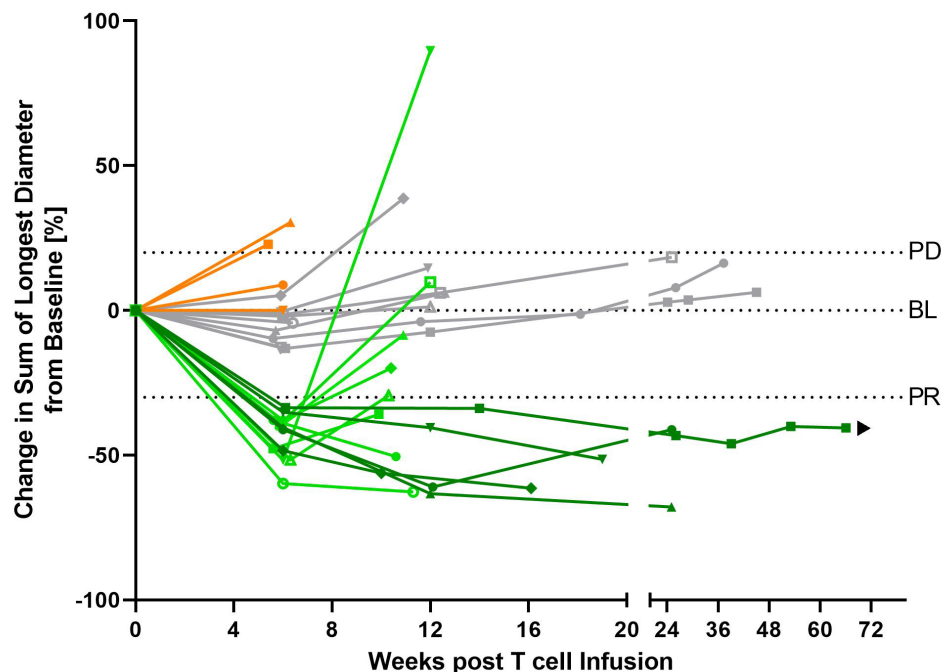
Data cut-off – 06-Sept-2022

Responses over Time

Encouraging Early Signs for Improved Durability at Higher Dose and in Phase 1b Patients

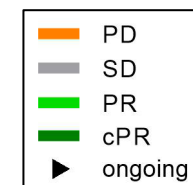
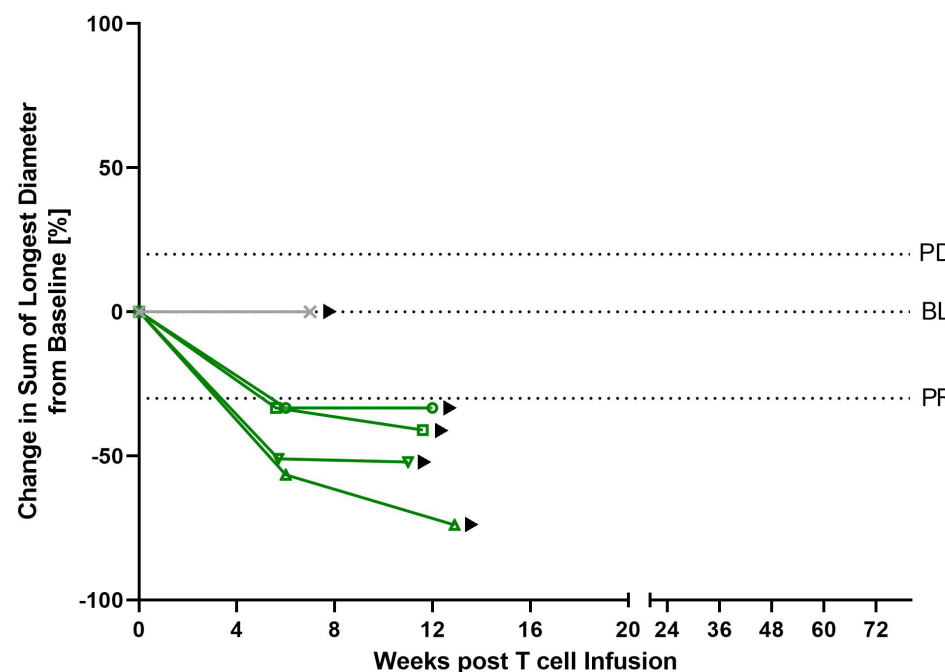
Phase 1a (Dose Escalation)

N=27#



Phase 1b (Cohort A)

N=5



Best overall response (RECIST1.1)

cPR		PR		SD		PD	
DL2-03	DL3-06	DL1-01	DL2-06	DL1-01	DL2-06	DL4-04	DL4-05
DL2-04	DL4-01	DL1-02	DL2-07	DL1-02	DL2-07	DL4-04	DL4-05
DL3-01	DL4-03	DL1-03	DL3-03	DL1-03	DL3-03	DL4-04	DL4-07
DL4-02	DL4-03	EC1-03	DL3-04	EC1-03	DL3-04	DL4-04	DL4-07
DL4-06	DL3-02	DL2-02		DL2-02			

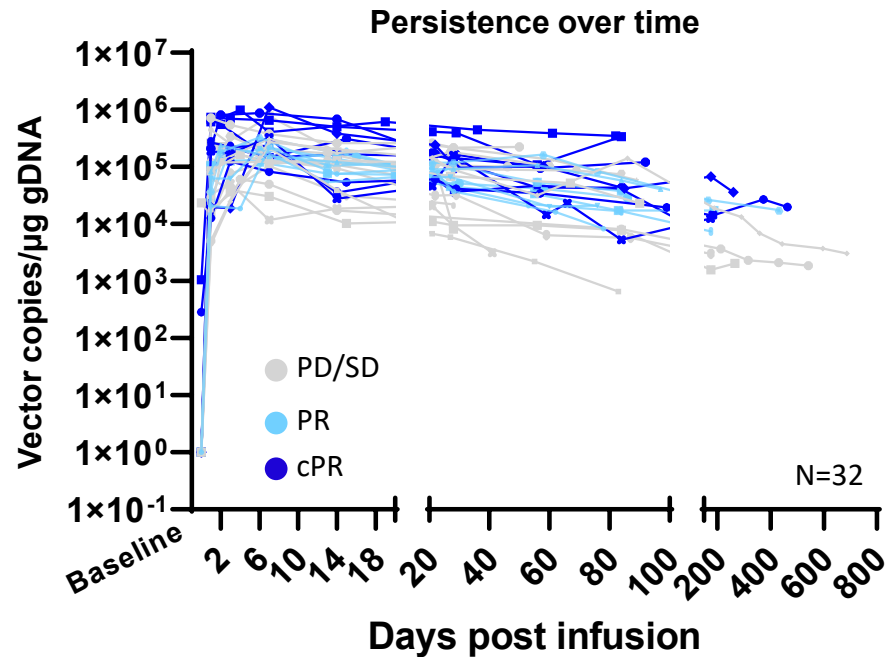
cPR	SD
A-DL4-01	A-DL4-04
A-DL4-02	
A-DL4-03	
A-DL5-01	

Data cut-off – 06-Sept-2022

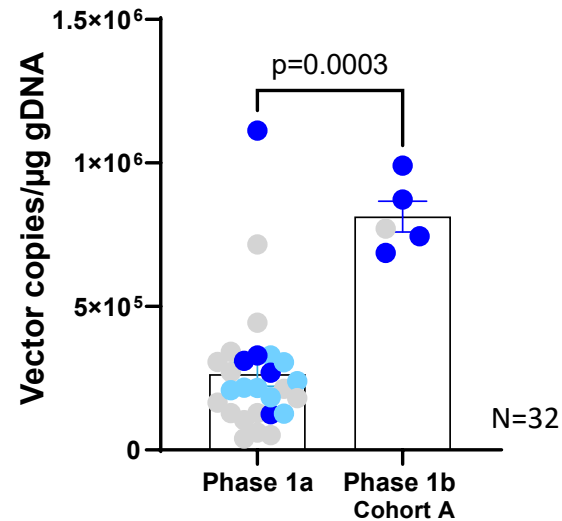
Translational Data Consistent with Clinical Outcomes

Supporting Proposed Mechanism of Action for IMA203

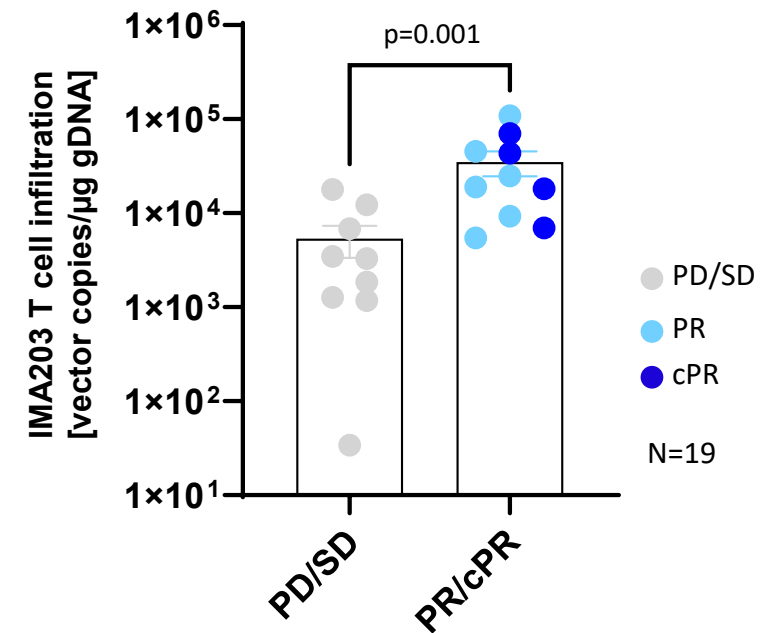
High IMA203 T cell engraftment and persistence in peripheral blood



Peak frequency

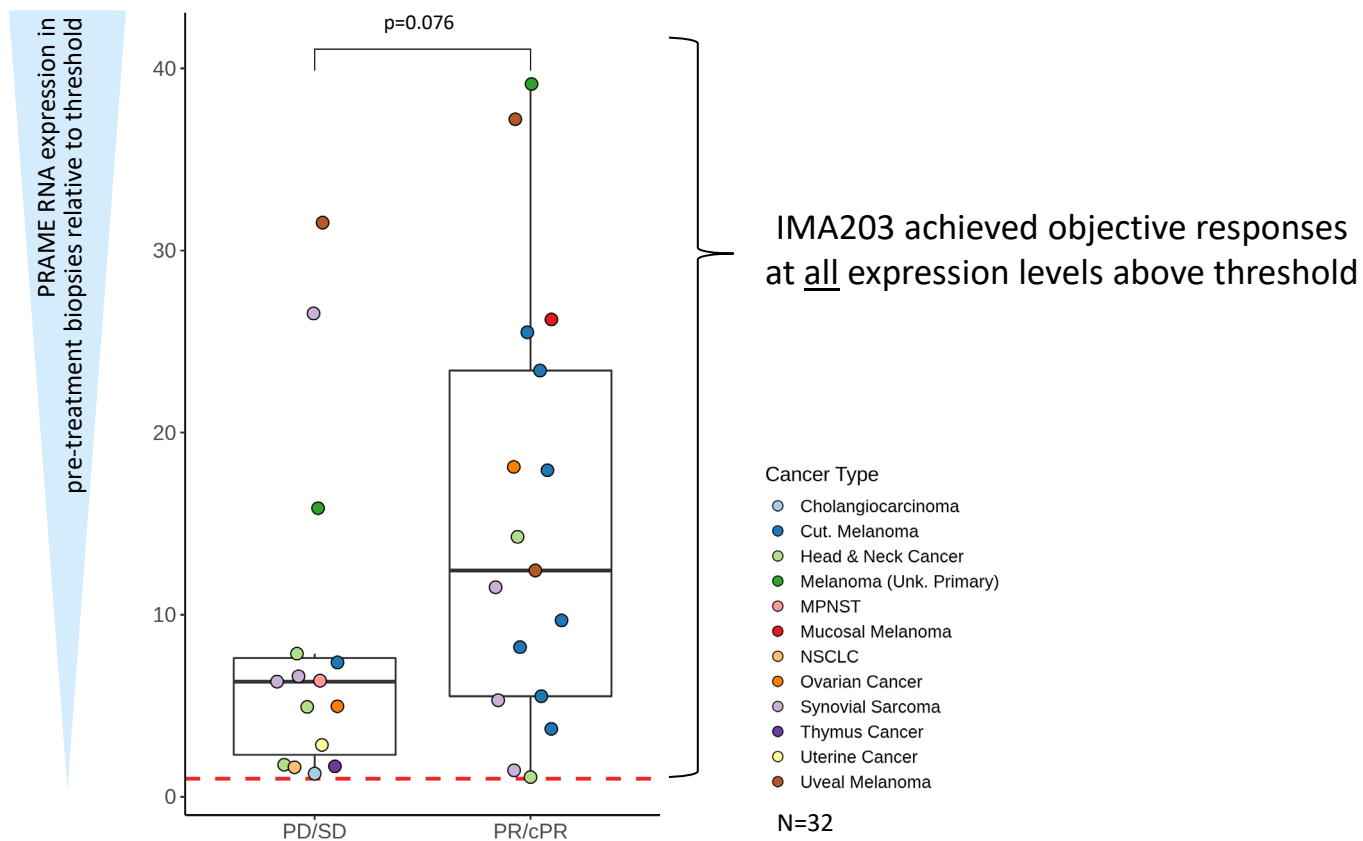


IMA203 T cell infiltration into tumor correlates with objective responses¹



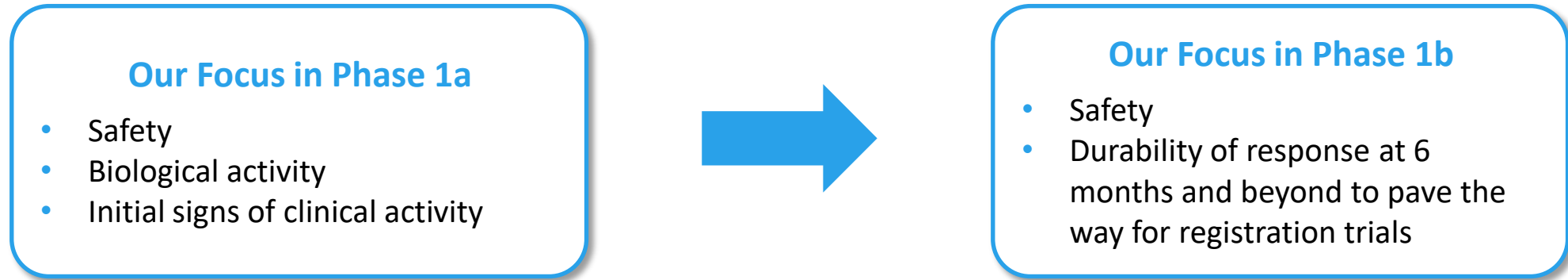
PRAME Expression in Tumors from Screened Patients

Clinical Validation of Immatics' Mass Spectrometry-guided RNA Threshold for PRAME



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

Moving from Phase 1a to Phase 1b



We continue to improve key determinants as we move from Phase 1a into Phase 1b

1. **Higher T cell dose:** Only RP2D or exploratory DL5
2. **Enhanced cell product:** Implementation of manufacturing enhancements (e.g. monocyte depletion, see appendix) focusing on robustness, quality, and speed of product release
3. **“Real life” patients:** Working with more disease area experts to reduce the fraction of very heavily pre-treated patients with extreme disease burden who have exhausted standard of care and have undergone multiple clinical trials
4. **Transition to indication-specific development strategy:** Based on PRAME prevalence, patient population size and observed responses

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

~39,000 Patients per Year in the US only

Selected Indications

Initial indications of interest based on PRAME prevalence, patient population size and observed clinical responses

Cut. Melanoma
 Uveal Melanoma
 Ovarian Carcinoma
 Uterine Carcinoma
 Uterine Carcinosarcoma
 Synovial Sarcoma
 Squamous NSCLC
 Small Cell Lung Cancer
 Cholangiocarcinoma
 Adeno NSCLC
 Breast Carcinoma
 HNSCC

Incidence	R/R Incidence	PRAME Positive
99,800	7,700	95%
1,500	800	90%
19,900	12,800	80%
62,700	10,700	100%
3,300	1,900	100%
1,000	400	100%
57,000	34,600	65%
31,900	19,400	55%
8,000	7,000	35%
91,200	55,300	25%
290,600	43,800	25% TNBC: 60%
66,500	15,100	25%

Patient Population

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

2,999
 295
 4,198
 4,387
 779
 164
 9,221
 4,375
 1,005
 5,668
 4,490
 1,548

TOTAL ~39,000
annually in the US

Multiple opportunities to broaden patient reach and patient benefit:

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

IMA203 Monotherapy – Conclusions

ACTengine® IMA203 Targeting PRAME Offers a Unique Opportunity for Solid Cancer Patients

IMA203 monotherapy Phase 1a and Phase 1b cohort A summary:

- IMA203 continues to be well tolerated with manageable safety profile
- Confirmed responses across a broad spectrum of different solid tumor types in heavily pre-treated patients
- Positively evolving durability profile for patients treated with higher doses and in phase 1b
- Clinical validation of PRAME biomarker threshold and associated prevalences
- **We have clinically validated PRAME as one of the largest known T cell targets for solid cancers to date**

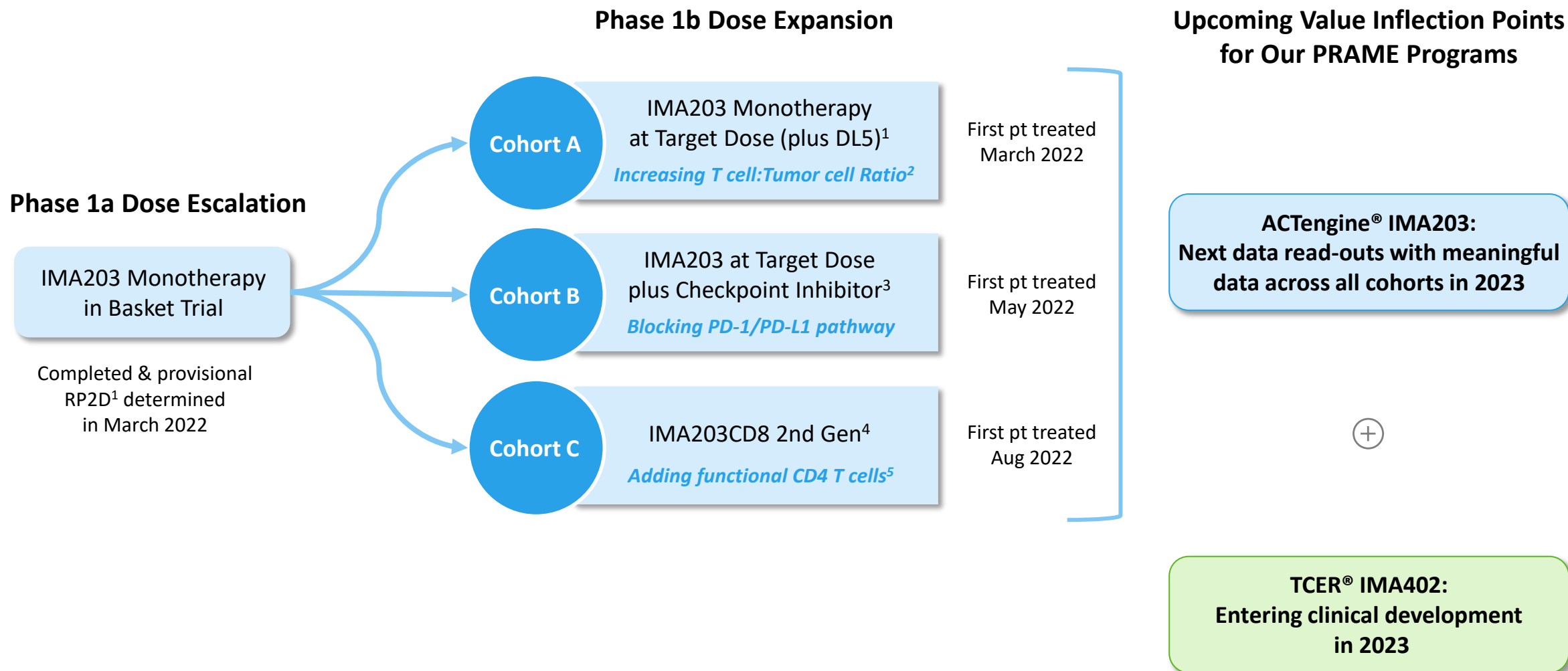
IMA203 development strategy:

- Transition to indication-specific development strategy
- Three Phase 1b expansion cohorts ongoing each designed to establish safety, evaluate the observed objective response rate, demonstrate durability & provide the trigger for registration trials

Data highlight the clinical potential of IMA203 TCR-T to achieve meaningful benefit for a large patient population

Comprehensive PRAME Strategy

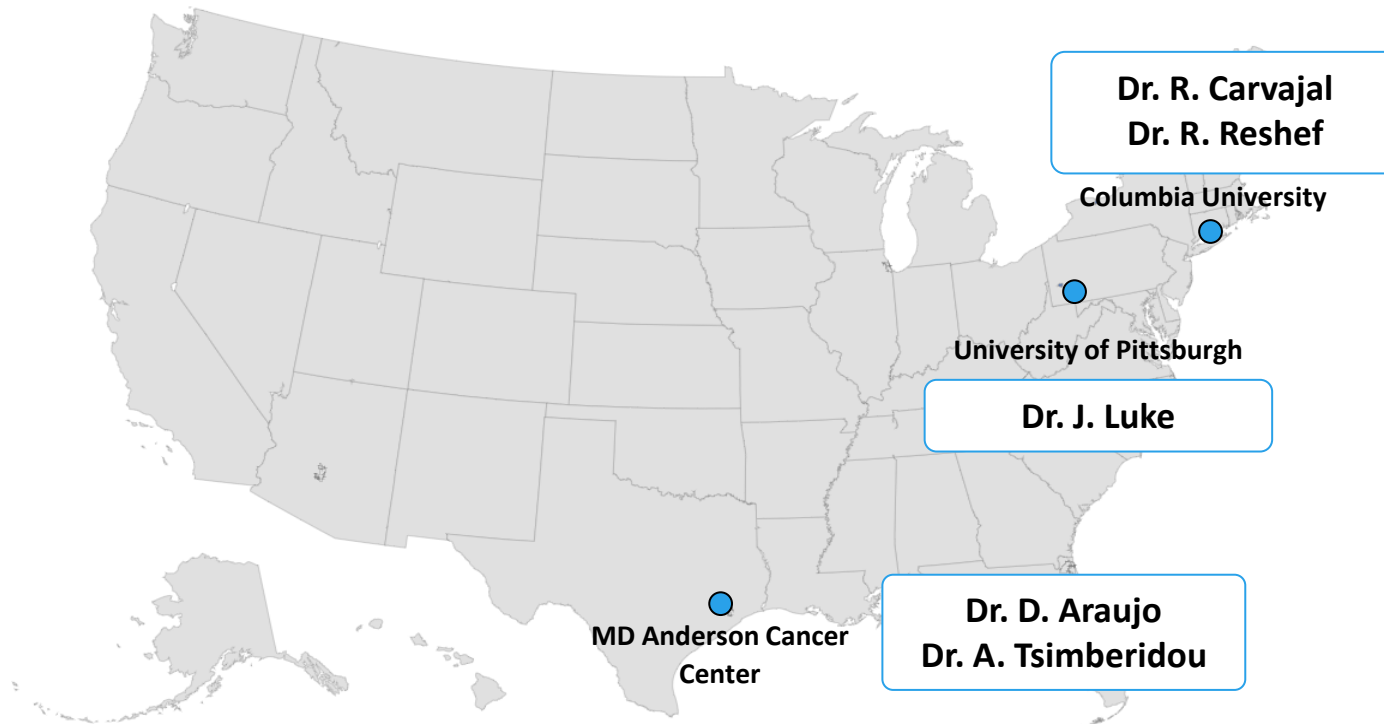
To Deliver Meaningful Clinical Benefit to Patients with PRAME-positive Cancers



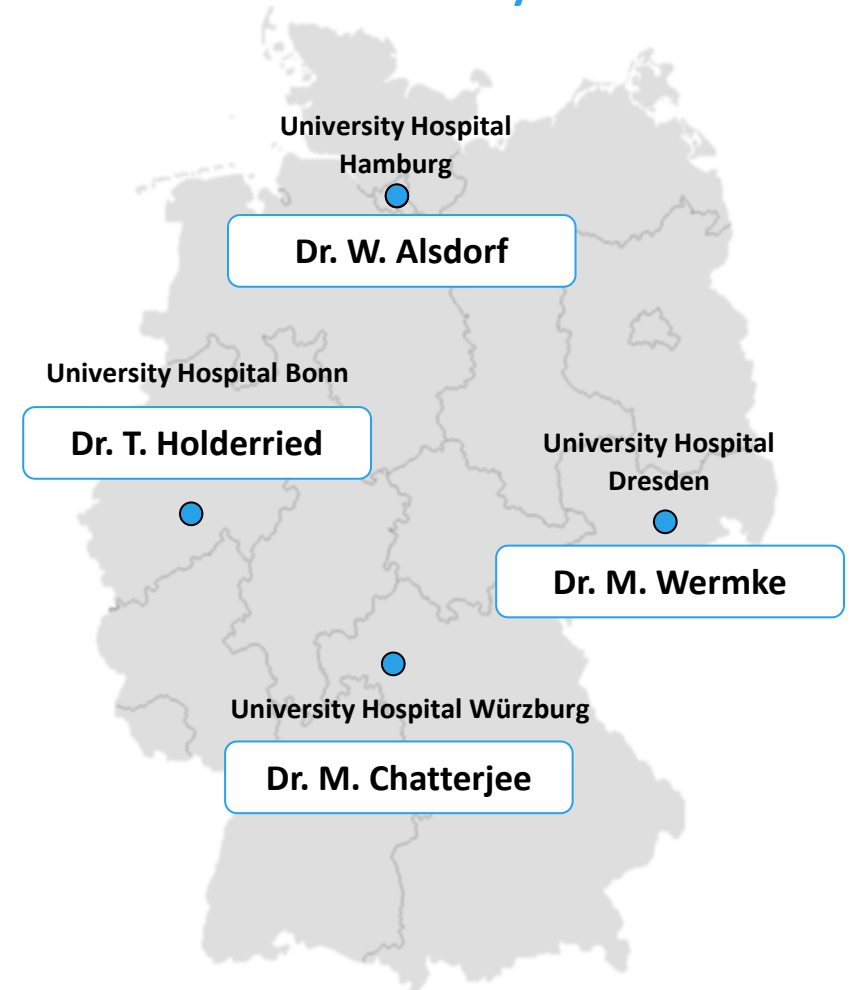
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We are Immensely Grateful to the Patients, Their Families ...

United States



Germany



... and the Investigators at the Clinical Sites

Delivering

the Power of T cells
to Cancer Patients



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ACTengine® IMA203 Product Manufacturing

Targeting Higher Robustness, Favorable Product Attributes, Faster Turn Around Time

Accelerated Product Release



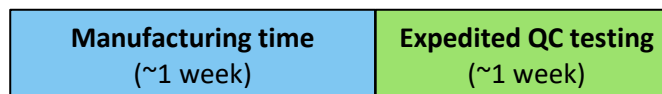
Leukapheresis



ACTengine® clinical programs: ~3 weeks



Faster ACTengine®: expected ~2 weeks

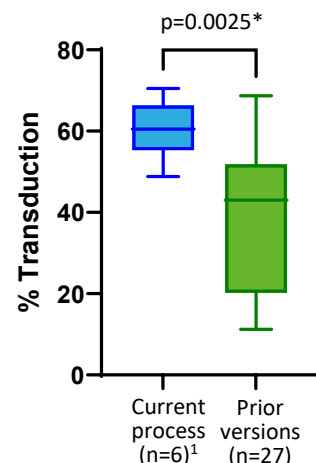
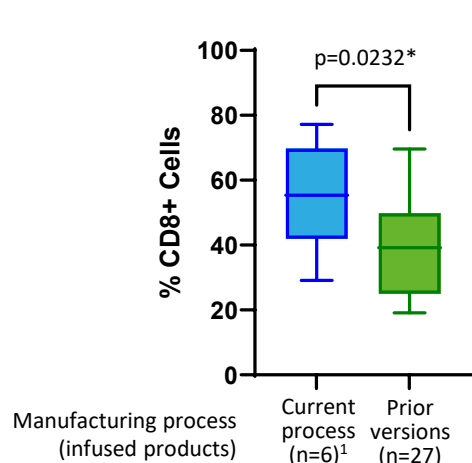


Implementation planned



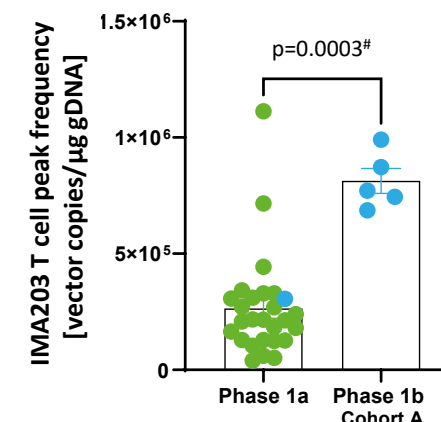
Infusion-Ready

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



All Phase 1b cell products were manufactured with the current, optimized process including manufacturing improvements such as

- ✓ Monocyte depletion
- ✓ Serum-free transduction



Significantly higher peak frequencies in Phase 1b patients infused with current, optimized product version

- Current process
- Prior versions

¹ Includes 5 IMA203 products infused into Phase 1b cohort A patients, and 1 product infused into Phase 1a patient at DL3; * Unpaired t test; # Mann-Whitney U test, 1 patient in Phase 1a at DL3 received ~0.5 x 10⁹ total transduced viable CD8 T cells manufactured with current process

IMA203 Tolerability Profile – All ≥Grade 3 Adverse Events

TEAEs by maximum severity (N=33)^{1*}

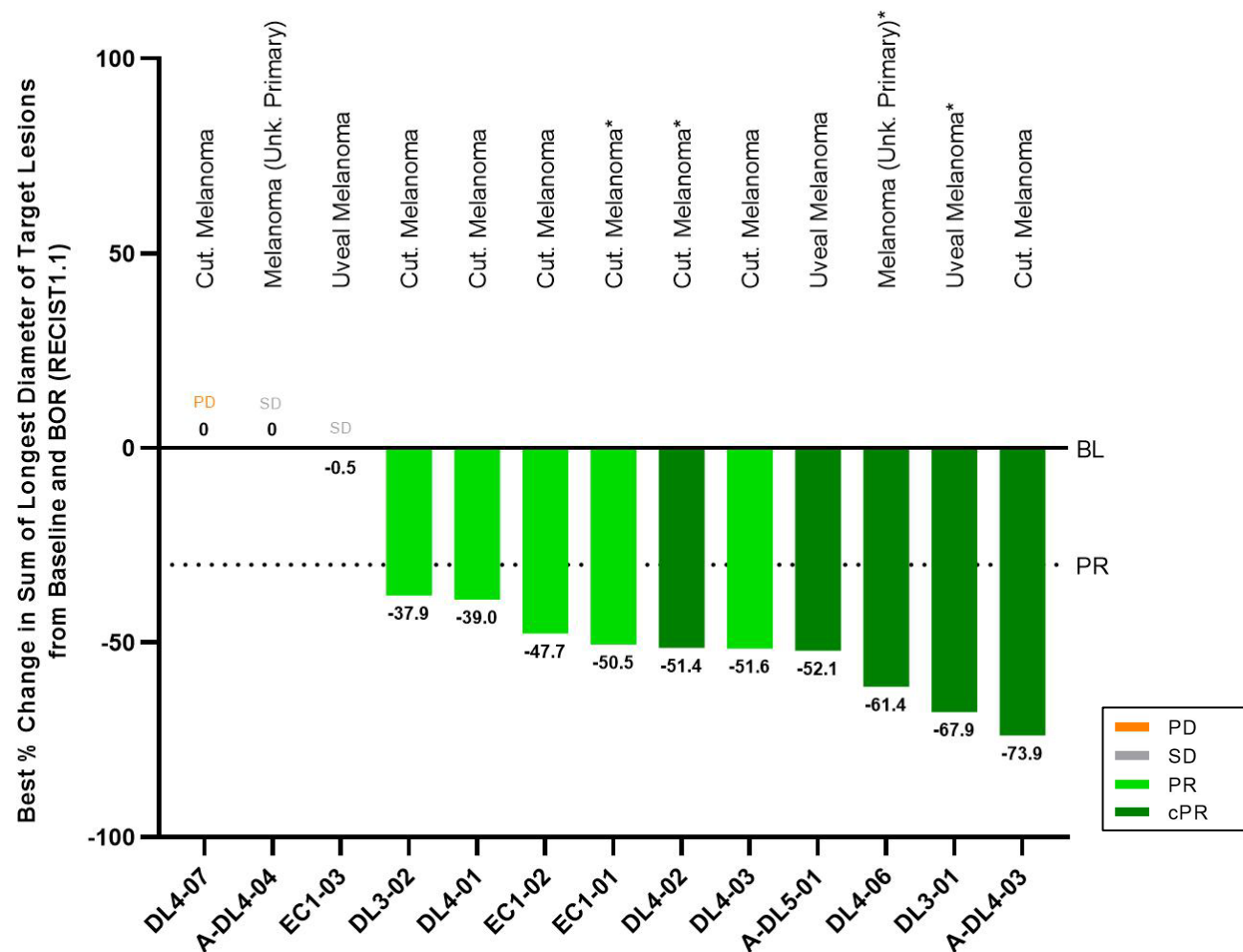
Adverse event	≥ Grade 3		Adverse event	≥ Grade 3	
	No.	%		No.	%
Patients with any adverse event	33	100.0	table continued...		
Adverse Events of Special Interest			Investigations		
Cytokine release syndrome	2	6.1	Blood alkaline phosphatase increased	1	3.0
ICANS ²	0	0.0	Blood creatinine increased	1	3.0
Blood and lymphatic system disorders			Blood fibrinogen decreased	1	3.0
Neutropenia	27	81.8	Metabolism and nutrition disorders		
Lymphopenia	22	66.7	Hypokalaemia	2	6.1
Leukopenia	20	60.6	Failure to thrive	1	3.0
Anaemia	17	51.5	Vascular disorders		
Thrombocytopenia	13	39.4	Hypertension	2	6.1
Cytopenia	1	3.0	Hypotension	1	3.0
Leukocytosis	1	3.0	Injury, poisoning and procedural complications		
Lymphocytosis	1	3.0	Fracture	1	3.0
Infections and infestations			Infusion related reaction	1	3.0
Appendicitis	1	3.0	Renal and urinary disorders		
COVID-19	1	3.0	Acute kidney injury	1	3.0
Enterococcal infection	1	3.0	Proteinuria	1	3.0
Orchitis	1	3.0	Cardiac disorders		
Sepsis ^{4,5}	1	3.0	Atrial fibrillation ³	1	3.0
Septic shock ⁴	1	3.0	Endocrine disorders		
Respiratory, thoracic and mediastinal disorders			Inappropriate antidiuretic hormone secretion	1	3.0
Hypoxia	2	6.1	Eye disorders		
Bronchial obstruction	1	3.0	Ulcerative keratitis	1	3.0
Laryngeal inflammation	1	3.0	Hepatobiliary disorders		
Pleural effusion	1	3.0	Cholangitis	1	3.0
Respiratory failure	1	3.0	Immune system disorders		
General disorders and administration site conditions			Contrast media allergy	1	3.0
Condition aggravated ⁴	1	3.0	Musculoskeletal and connective tissue disorders		
Fatigue	1	3.0	Muscle spasms	1	3.0
Pyrexia	1	3.0	Reproductive system and breast disorders		
Swelling face	1	3.0	Vaginal haemorrhage	1	3.0
Gastrointestinal disorders			Skin and subcutaneous tissue disorders		
Abdominal pain	1	3.0	Rash maculo-papular	1	3.0
Diarrhoea	1	3.0			
Vomiting	1	3.0			

- IMA203 was well tolerated
- No ≥Grade 3 Adverse Events in ≥ 10% of patients except for expected events associated with lymphodepletion
- No IMA203-related Grade 5 Adverse Events

¹ All treatment-emergent adverse events (TEAEs) with ≥ Grade 3 regardless of relatedness to study treatment that occurred in at least 1 patient (except for ICANS, where only Grade 1-2 occurred; listed for completeness due to being an adverse event of special interest) are presented. Adverse events were coded using the Medical Dictionary for Regulatory Activities. Grades were determined according to National Cancer Institute Common Terminology Criteria of Adverse Events, version 5.0. Grades for CRS and ICANS were determined according to CARTOX criteria (Neelapu *et al.*, 2018). Patients are counted only once per adverse event and severity classification. Based on interim data extracted from open clinical database (06-Sep-2022); 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 in N=3 patients were not considered related to any study drug; ⁵ Patient did not receive IMA203 TCR-T cells; * 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, Diarrhoea, Cytokine release syndrome, Hypokalaemia, Proteinuria; Second patient: Fracture, Muscle spasms, Neutropenia, Thrombocytopenia.

Focus on Melanoma Patients

High ORR and cORR in Heavily Pre-Treated Patients with High Tumor Burden



Patient Characteristics (n=13)

Prior lines of treatment Mean (min, max)	4.5 (1, 7)
Previous lines of CPI Mean (Min, Max)	2.5 (1, 4)
LDH at baseline >1 x ULN [% of patients]	69%

Particular hard-to-treat patient population enrolled so far

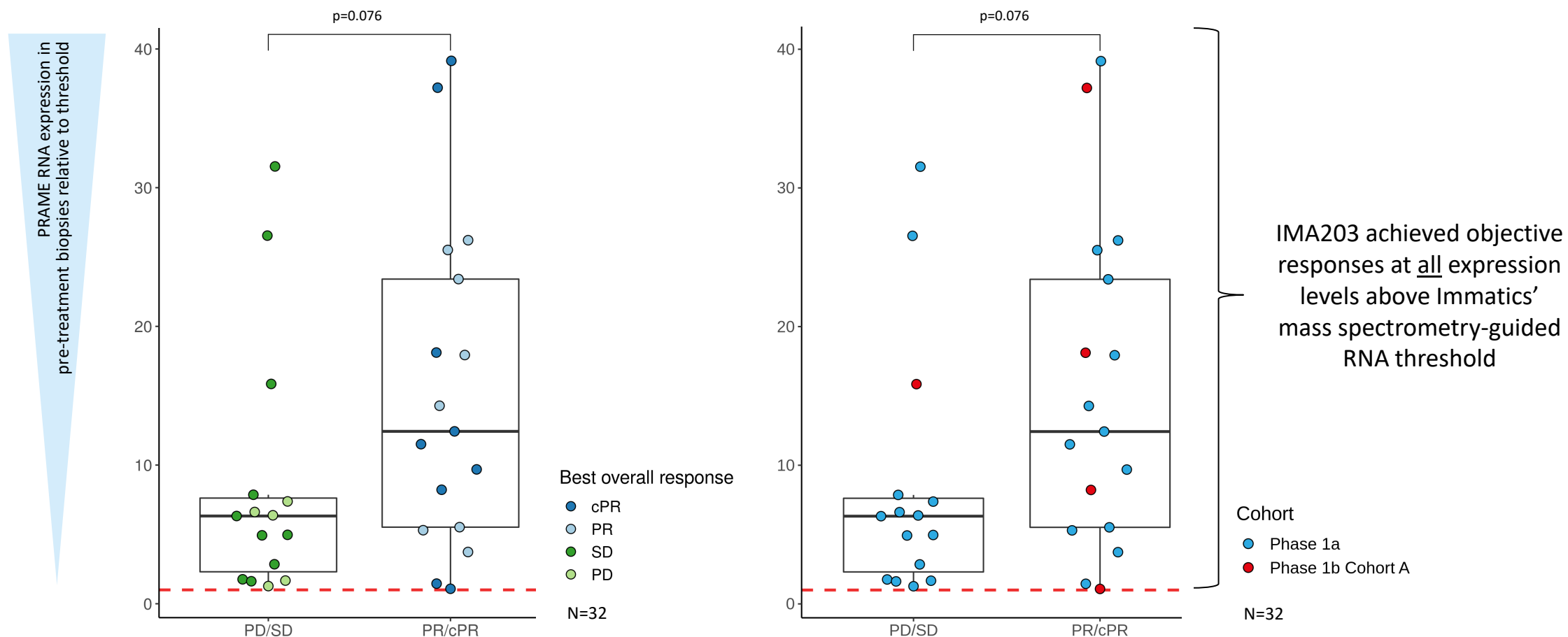
Melanoma Subtype	ORR (~6 weeks) ¹	cORR (~12 weeks) ²
Melanoma (DL4/DL5) ³	6/8 (75%)	4/8 (50%) [#]
Melanoma (all DL)	10/13 (77%)	5/13 (38%) [#]
Cutaneous Melanoma	7/8 (88%)	2/8 (25%)
Uveal Melanoma	2/3 (67%)	2/3 (67%)
Unknown Primary	1/2 (50%)	1/2 (50%) [#]

Data cut-off – 06-Sept-2022

* Maximum change of target lesions and RECIST1.1 response at different timepoints; ¹ ORR: Objective response rate (partial responses) according to RECIST 1.1 at first scan post infusion (~6 weeks); ² Confirmed ORR (cORR): Confirmed objective response rate (confirmed partial responses) according to RECIST 1.1 at second scan post infusion (~12 weeks); ³ All patients received >1x10⁹ total transduced viable CD8 T cells; [#] 1 patient with SD at ~6-week scan with pending ~12-week scan considered as non-responder for cORR; CPI: checkpoint inhibitor

PRAME Expression in Tumors from Screened Patients

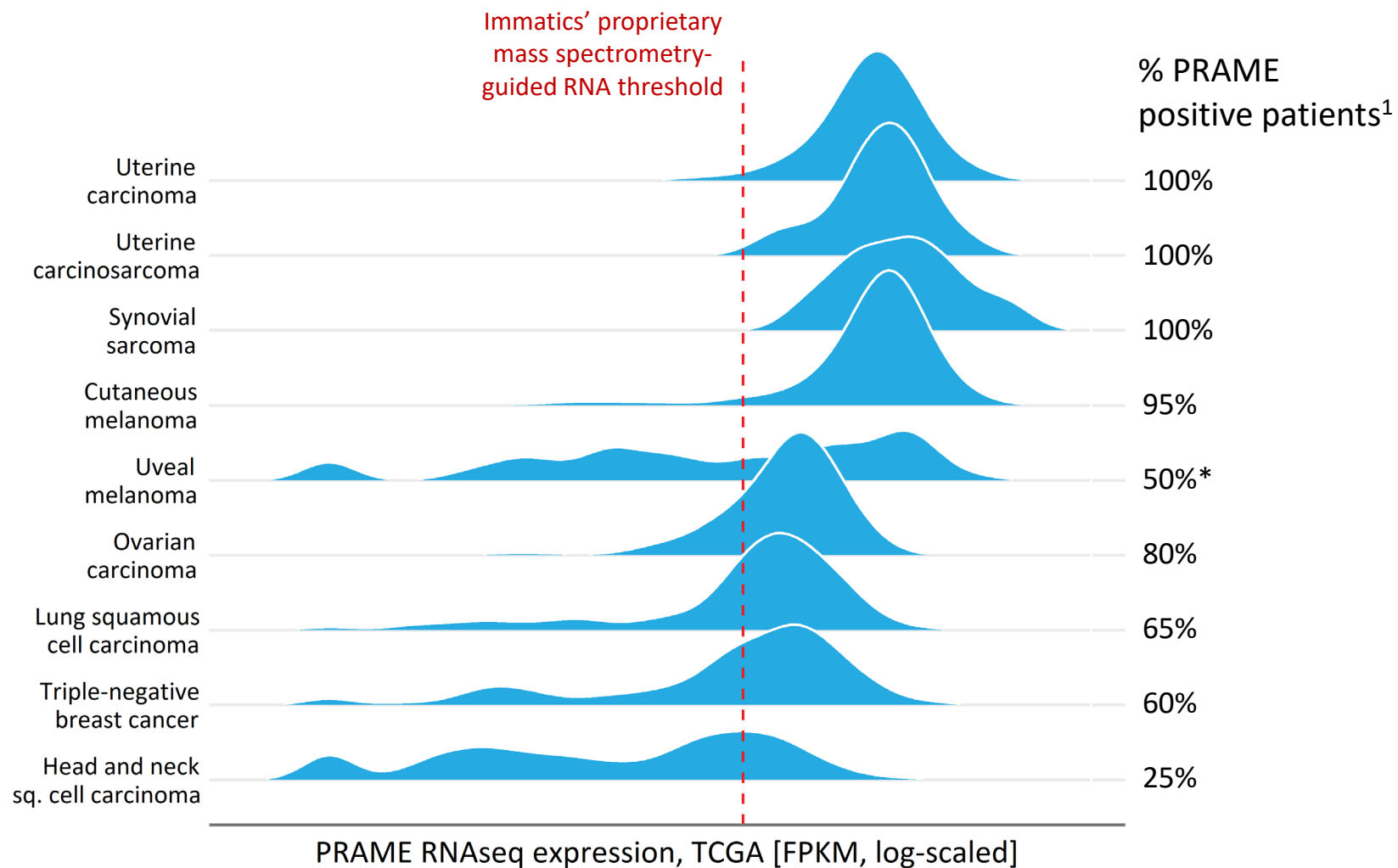
Highlighting Type of Best Overall Response (left) and Study Cohort (right)



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

PRAME Expression – RNAseq Data

Combined with Immatics' Mass Spectrometry-guided RNA Threshold for Prevalence Prediction



¹ PRAME target prevalence is based on TCGA RNAseq data combined with a proprietary mass spectrometry-guided RNA expression threshold; * PRAME target prevalence in uveal melanoma based on IMADetect® qPCR testing of screening biopsies from clinical trial patients (n=21) demonstrates substantial higher prevalence of 90%, 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