# Immatics Corporate Presentation

November 18, 2024

*Delivering the Power of T cells to Cancer Patients*

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# Building a Leading TCR Therapeutics Company

### Two Clinical-Stage Modalities

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

### Clinical PoC for Cell Therapy

High confirmed objective response rate and durable responses in melanoma; registration-enabling Phase 3 trial to commence in December 2024

### Differentiated Platforms

Unique technologies to identify true cancer targets and right TCRs

### Therapeutic Opportunity

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

# 2024 ACTengine® and TCER® Clinical Milestones

**ACTengine®**
**IMA203 / IMA203CD8 (PRAME)**

- Targeted randomized Phase 3 trial for ACTengine® IMA203 in 2L+ melanoma in 2024
- Clinical data update from Phase 1b dose expansion trial at SMR Conference on Oct 11, 2024; IMA203CD8 (GEN2) update at SITC Conference on Nov 9, 2024

**TCER® IMA401**
**(MAGEA4/8)**

First clinical data update from dose escalation in ongoing Phase 1 trial at ESMO on Sep 16, 2024

**TCER® IMA402**
**(PRAME)**

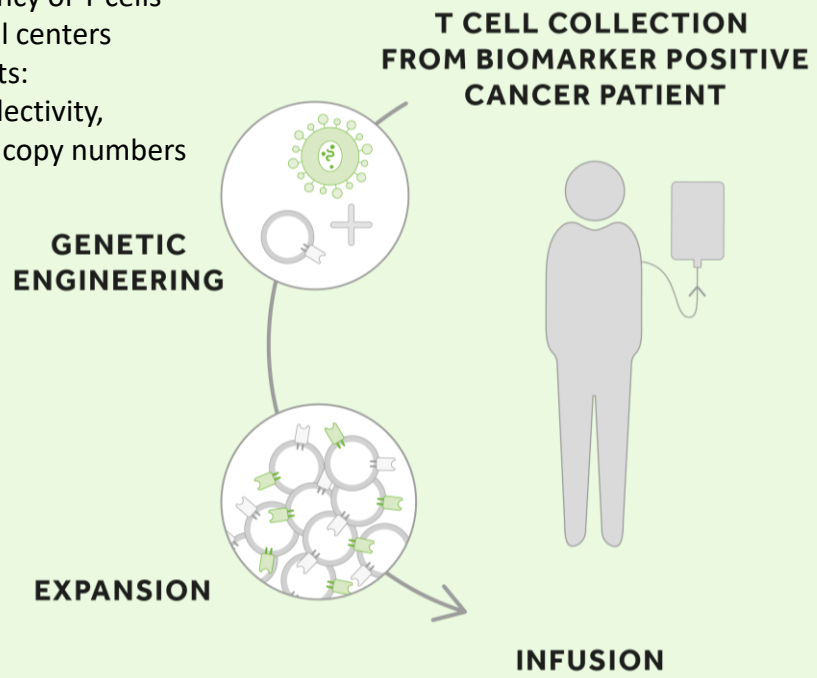
First clinical data update from dose escalation in ongoing Phase 1/2 trial with initial focus on early doses and melanoma on Nov 18, 2024

Planned focus indications: melanoma, ovarian cancer, uterine cancer, lung cancer, and others

# Two Distinct TCR-based Therapeutic Modalities in Clinical Development

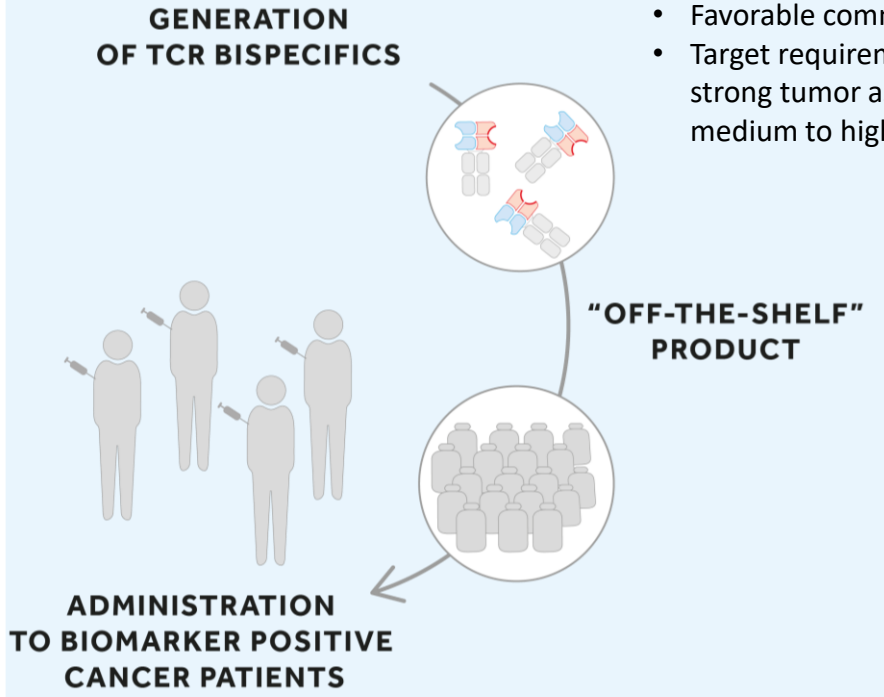
## Autologous TCR-T (ACTengine®)

- Strong clinical activity in patients with high tumor burden[1]
- Single dose
- Proprietary manufacturing process for enhanced potency of T cells
- Specialized medical centers
- Target requirements: stringent tumor selectivity, low, medium, high copy numbers




## TCR Bispecifics (TCER®)

- Off-the-shelf biologic for immediate treatment
- Repeat dosing
- All hospitals and out-patient, opportunity for larger patient reach
- Favorable commercial characteristics
- Target requirements: strong tumor association, medium to high copy numbers




**Differentiated positioning of ACTengine® vs. TCER® based on patient population and medical need**



[1] Interim data update from the ACTengine® IMA203 and IMA203CD8 monotherapies (published November 8, 2024)

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

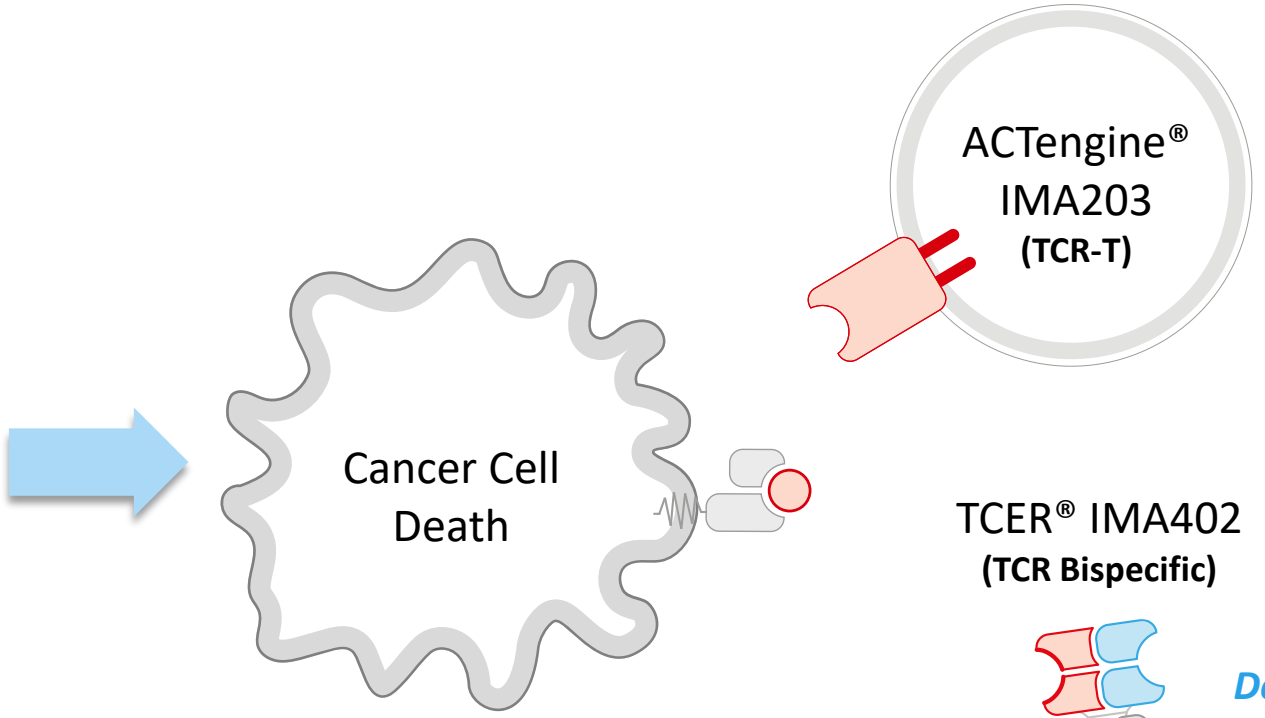
| Modality | Product Candidate | Target | Preclinical | Phase 1a[1] | Phase 1b[1] | Phase 2 | Phase 3 |
|---|---|---|---|---|---|---|---|
| **Autologous ACT** | ACTengine® IMA203 | PRAME | | | | | |
| | ACTengine® IMA203CD8 | PRAME | | | | | |
| | ACTengine® IMA204 | COL6A3 | | | | | |
| | Multiple programs | Undisclosed | | | | | |
| | ACTengine® IMA203 + mRNA cancer vaccine | PRAME | | | | | |
| **Allogeneic ACT** γδ T cells | ACTallo® IMA30x | Undisclosed | | | | | |
| | Multiple programs | Undisclosed | | | | | |
| **Bispecifics** | TCER® IMA401 | MAGEA4/8 | | | | | |
| | TCER® IMA402 | PRAME | | | | | |
| | TCER® IMA40x | Undisclosed | | | | | |
| | Multiple programs[3] | Undisclosed | | | | | |

[1] Phase 1a: Dose escalation, Phase 1b: Dose expansion; [2] Immatics' proprietary ACTallo® platform utilizing Editas' CRISPR gene editing technology;
[3] mRNA-enabled *in vivo* expressed TCER® molecules

# Realizing the Full Multi-Cancer Opportunity of PRAME

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

| Indication | % PRAME positive patients[1] |
|---|---|
| Uterine Carcinosarcoma | 100% |
| Sarcoma Subtypes | up to 100% |
| Uterine Carcinoma | 95% |
| Cut. Melanoma | 95% |
| Uveal Melanoma[2] | 90% |
| Ovarian Carcinoma | 85% |
| Squamous NSCLC | 70% |
| TNBC | 65% |
| Small Cell Lung Cancer | 45% |
| Kidney Carcinoma | up to 40% |
| Cholangiocarcinoma | 35% |
| Adeno NSCLC | 25% |
| Breast Carcinoma | 25% |
| HNSCC | 25% |
| Esophageal Carcinoma | 25% |
| HCC | 20% |
| Bladder Carcinoma | 20% |




*Phase 1b dose expansion ongoing*

*Phase 3 trial in preparation*

*Dose escalation of Phase 1/2 trial ongoing*

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

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

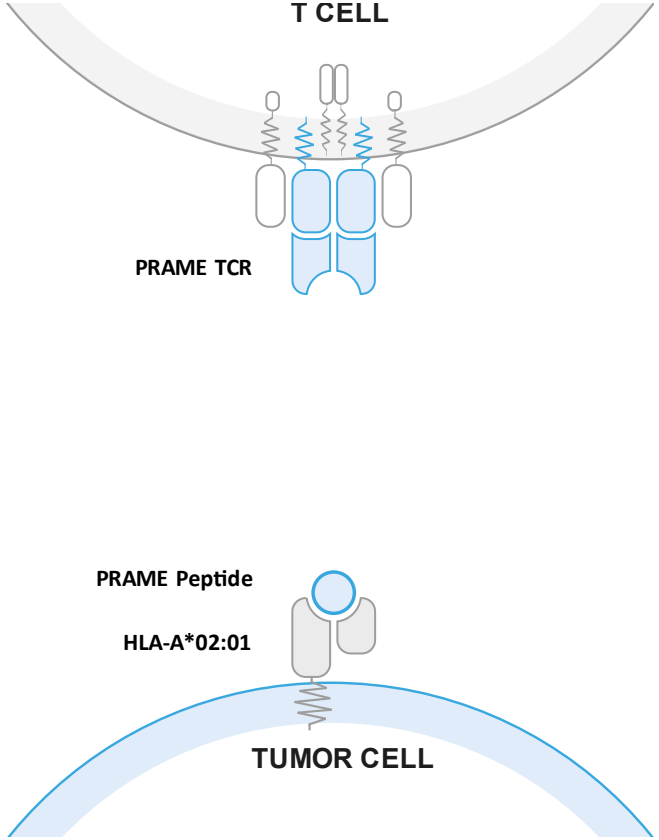


[1] PRAME target prevalence is based on TCGA (for SCLC: in-house) RNAseq data combined with a proprietary mass spec-guided RNA expression threshold; [2] Uveal melanoma target prevalence is based on IMADetect® qPCR testing of screening biopsies from clinical trial patients (n=61); NSCLC: Non-small cell lung cancer, TNBC: Triple-negative breast cancer, HNSCC: Head and neck squamous cell carcinoma; HCC: Hepatocellular carcinoma

# ACTengine® IMA203 – TCR-T Targeting PRAME

# The Multi-Cancer Opportunity of PRAME

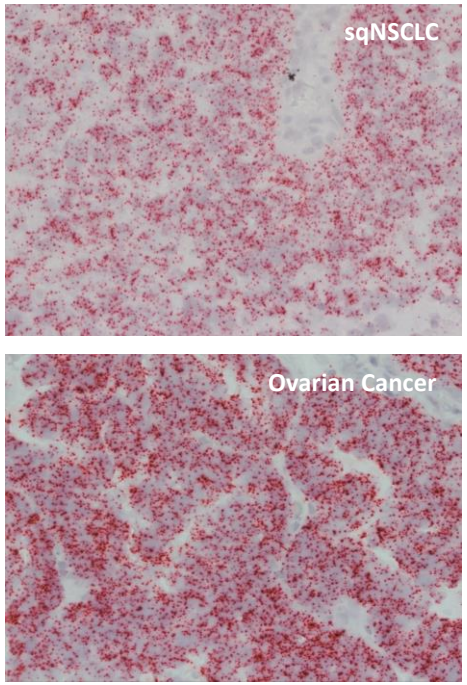
## One of the Most Promising Solid Tumor Targets for TCR-based Therapies Known To Date




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

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

PRAME RNA detection in tumor samples (ISH)






ISH: in situ hybridization, sqNSCLC: squamous non-small cell lung cancer

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

## ~39,000 Patients per Year in the US only

| Selected Indications | Incidence | R/R Incidence | PRAME Positive | Patient Population (Based on R/R Incidence; PRAME and HLA-A*02:01+) |
|---|---|---|---|---|
| Cut. Melanoma | 99,800 | 7,700 | 95% | 2,999 |
| Uveal Melanoma | 1,500 | 800 | 89% | 292 |
| Ovarian Carcinoma | 19,900 | 12,800 | 84% | 4,408 |
| Uterine Carcinoma | 62,700 | 10,700 | 97% | 4,255 |
| Uterine Carcinosarcoma | 3,300 | 1,900 | 100% | 779 |
| Squamous NSCLC | 57,000 | 34,600 | 68% | 9,646 |
| Small Cell Lung Cancer | 31,900 | 19,400 | 45% | 3,579 |
| Adeno NSCLC | 91,200 | 55,300 | 25% | 5,668 |
| HNSCC | 66,500 | 15,100 | 27% | 1,672 |
| Breast Carcinoma | 290,600 | 43,800 | 26% TNBC: 63% | 4,669 |
| Synovial Sarcoma | 1,000 | 400 | 100% | 164 |
| Cholangiocarcinoma | 8,000 | 7,000 | 33% | 947 |

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

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

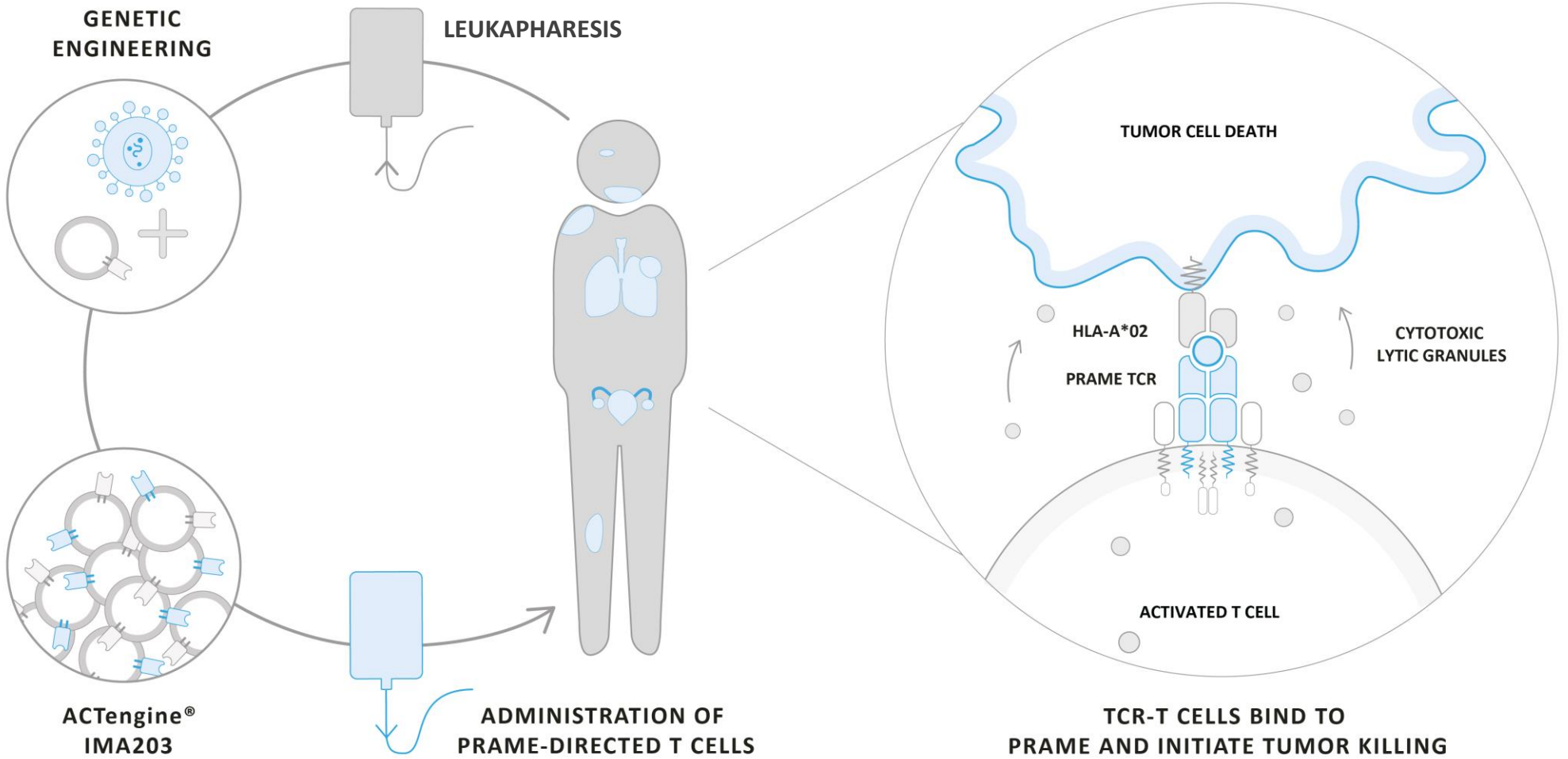
- Expand beyond US population
- Expand into other indications such as kidney, esophageal, bladder, other liver cancers, other sarcoma subtypes through indication-specific or indication-agonistic label expansion
- Move into earlier lines of therapy (R/R Incidence → Incidence)
- Inclusion of patients with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



Incidences based on public estimates and Immatics internal model; Relapsed/refractory (R/R) or last-line patient population approximated by annual mortality; Estimated 41% HLA-A*02:01 positive population in the US; PRAME target prevalence is based on TCGA (for SCLC: in-house) RNAseq data combined with a proprietary mass spec-guided RNA expression threshold; Uveal melanoma target prevalence is based on IMADetect® qPCR testing of screening biopsies from clinical trial patients (n=61)

# ACTengine® IMA203 Targeting PRAME – Mechanism of Action

## Immatics' Leading TCR-T Approach



# ACTengine® IMA203 TCR-T Product Manufacturing

## Differentiated Manufacturing Process and Setup

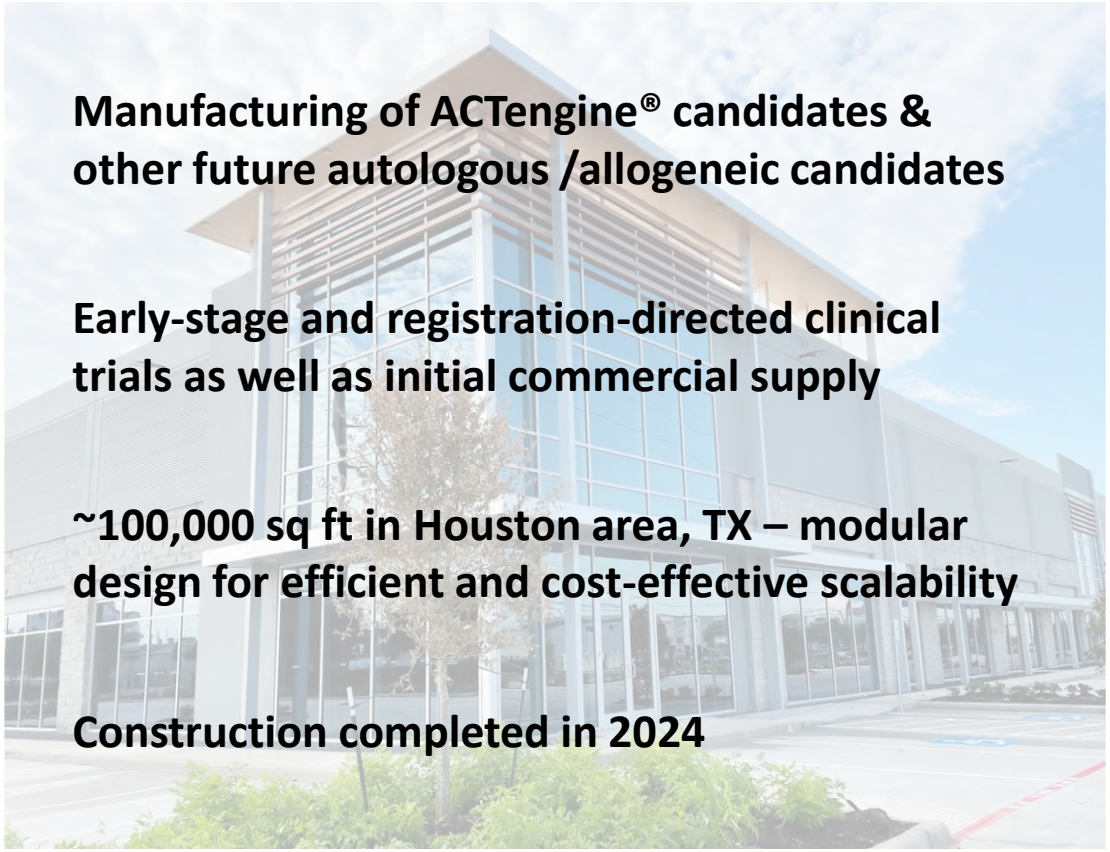
### Proprietary Manufacturing Process

**SHORT** — 1-week manufacturing process followed by 1-week QC release testing

**ROBUST** — High manufacturing success rate of >95% to reach IMA203 target dose*

**SIMPLE** — Lean and cost-efficient process

### State-of-the-art Research & GMP Manufacturing Facility



Manufacturing of ACTengine® candidates & other future autologous /allogeneic candidates

Early-stage and registration-directed clinical trials as well as initial commercial supply

~100,000 sq ft in Houston area, TX – modular design for efficient and cost-effective scalability

Construction completed in 2024

IMA203

*IMA203: RP2D 1-10x$10^9$ total TCR-T cells

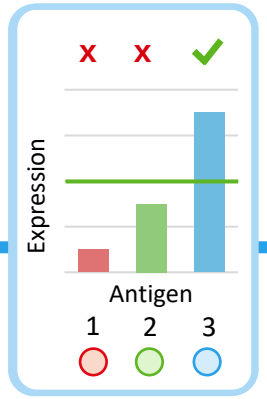
# ACTengine® IMA203 TCR-T Monotherapy – Patient Flow

**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

**Leukapheresis**




**Target Profiling**
IMADetect® mRNA assay using
Immatics' MS-guided threshold;
Biopsy or archived tissue

**Patient screening data from Immatics' clinical trials:**

| | |
|---|---|
| Cut. Melanoma | 95% (138/146) |
| Uveal Melanoma | 89% (54/61) |
| Uterine Carcinoma | 93% (14/15) |
| Ovarian Carcinoma | 81% (48/59) |

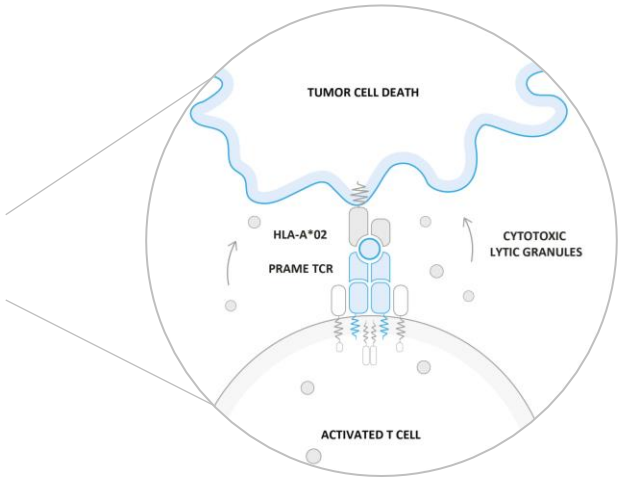
**Manufacturing**
by Immatics

**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**






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

# ACTengine® IMA203 TCR-T Trial in Melanoma

## Heavily Pretreated Patient Population

**Total Safety Population[1] (N=70)**

**Phase 1a Dose Escalation**
Dose Level 1-4
(total safety pop. N=28)

**Phase 1b Dose Expansion**
Dose Level 4/5
(total safety pop. N=42)

**RP2D defined at**
1-10x$10^9$ TCR-T cells (DL4/5)

**Melanoma Efficacy Population[2] (N=28)**

**Melanoma Patients in Phase 1b Dose Expansion**

| | Total Safety Population[1] | Melanoma Dose Escalation Population | Melanoma Efficacy Population[2] |
|---|---|---|---|
| | All Comers (Phase 1a and Phase 1b) | Melanoma (Phase 1a) | Melanoma (Phase 1b, at RP2D) |
| **Number of patients** | **Total N=70**<br>Melanoma N=41<br>Other N=29 | **Total N=11**<br>Cutaneous melanoma N=8<br>Uveal melanoma N=2<br>Mucosal melanoma N=1 | **Total N=28**<br>Cutaneous melanoma N=13<br>Uveal melanoma N=12<br>Melanoma of unknown primary N=1<br>Mucosal melanoma N=2 |
| **Prior lines of systemic treatment** (median, min, max) | 3 (0, 9) | 4 (2, 7) | 2 (0, 6) |
| **Thereof CPI** (melanoma only) (median, min, max) | 2 (0, 4) | 2 (1, 4) | 1* (0, 4) |
| **LDH at baseline** >1 x ULN [% of patients] | 64.3 | 81.8 | 60.7 |
| **Baseline tumor burden** Median Target lesion sum of diameter [mm] (min, max) | 117.8 (15.0, 309.8) | 117.5 (37.0, 211.0) | 107.5 (15.0, 309.8) |
| **Liver/brain lesions at baseline** [% of patients] | 65.7 | 63.6 | 82.1 |
| **Dose level** | DL1-5 | EC1/DL3/4 | DL4/5 |
| **Total infused dose** TCR-T cells [x$10^9$] | 2.09 (0.08, 10.2) | 0.586 (0.10, 2.09) | 4.1 (1.3, 10.2) |

IMA203

[1] See patient flow in appendix. [2] All infused patients; *Cutaneous melanoma patients had a median of 2 prior lines of checkpoints, see appendix; RP2D: recommended phase 2 dose; CPI: Checkpoint inhibitors; EC1: 0.06-0.12x$10^9$ TCR-T cells/$m^2$ BSA; DL3: 0.2-0.48x$10^9$ TCR-T cells/$m^2$ BSA, DL4: 0.2-1.2x$10^9$ TCR-T cells/$m^2$ BSA, DL5: 1.201 - 4.7x$10^9$ TCR-T cells/$m^2$ BSA

# Most Frequent Adverse Events of IMA203 Across All Dose Levels in Phase 1a/b

## N=70 Patients in Total Safety Population[1]

- Most frequent adverse events were **expected cytopenias (Grade 1-4)** associated with lymphodepletion in all patients
- **Mostly mild to moderate cytokine release syndrome (CRS)**
  - 37% (26/70) Grade 1
  - 46% (32/70) Grade 2
  - 11% (8/70) Grade 3[2]
- **Infrequent ICANS (6% Grade 1, 4% Grade 2, 4% Grade 3)**
- **No IMA203-related deaths**
- Full IMA203 monotherapy tolerability profile is available in appendix
- Tolerability in the melanoma subset is generally consistent with the full IMA203 monotherapy tolerability profile

**Favorable tolerability profile for IMA203 monotherapy at recommended phase 2 dose ($1x10^9$ to $10x10^9$ TCR-T cells)**



[1] See patient flow in appendix; [2] One grade 3 CRS only after exploratory second infusion; CRS and ICANS graded by CARTOX criteria (Neelapu *et al*., 2019); ICANS: Immune Effector Cell-Associated Neurotoxicity Syndrome.

# Tolerability Profile of IMA203 Across All Dose Levels in Phase 1a/b

## All ≥Grade 3 Adverse Events (N=70[1])

**TEAEs by maximum severity for all patients in Phase 1a and Phase 1b (N=70[1])**

| Adverse event (**System organ class**, Preferred term) | ≥ Grade 3 No. | ≥ Grade 3 % |
|---|---|---|
| **Patients with any adverse event** | 70 | 100.0 |
| **Adverse Events of Special Interest** | **9** | **12.9** |
| Cytokine release syndrome | 8 | 11.4 |
| ICANS[2] | 3 | 4.3 |
| **Blood and lymphatic system disorders** | **70** | **100.0** |
| Neutropenia | 62 | 88.6 |
| Lymphopenia | 39 | 55.7 |
| Leukopenia | 38 | 54.3 |
| Anaemia | 36 | 51.4 |
| Thrombocytopenia | 24 | 34.3 |
| Febrile neutropenia | 2 | 2.9 |
| Cytopenia | 1 | 1.4 |
| Leukocytosis | 1 | 1.4 |
| **Infections and infestations** | **10** | **14.3** |
| Urinary tract infection | 2 | 2.9 |
| Appendicitis | 1 | 1.4 |
| COVID-19 | 1 | 1.4 |
| Cytomegalovirus infection reactivation | 1 | 1.4 |
| Enterococcal infection | 1 | 1.4 |
| Human herpesvirus 6 encephalitis | 1 | 1.4 |
| Infection | 1 | 1.4 |
| Orchitis | 1 | 1.4 |
| Sepsis[3,4] | 1 | 1.4 |
| Septic shock[3] | 1 | 1.4 |
| **Investigations** | **10** | **14.3** |
| Alanine aminotransferase increased | 6 | 8.6 |
| Aspartate aminotransferase increased | 5 | 7.1 |
| Blood creatinine increased | 2 | 2.9 |
| Blood alkaline phosphatase increased | 1 | 1.4 |
| Blood bilirubin increased | 1 | 1.4 |
| Blood fibrinogen decreased | 1 | 1.4 |
| Lymphocyte count increased | 1 | 1.4 |
| **Respiratory, thoracic and mediastinal disorders** | **10** | **14.3** |
| Hypoxia | 4 | 5.7 |
| Pleural effusion | 2 | 2.9 |
| Bronchial obstruction | 1 | 1.4 |
| Dyspnoea | 1 | 1.4 |
| Epistaxis | 1 | 1.4 |
| Laryngeal inflammation | 1 | 1.4 |
| Respiratory failure | 1 | 1.4 |

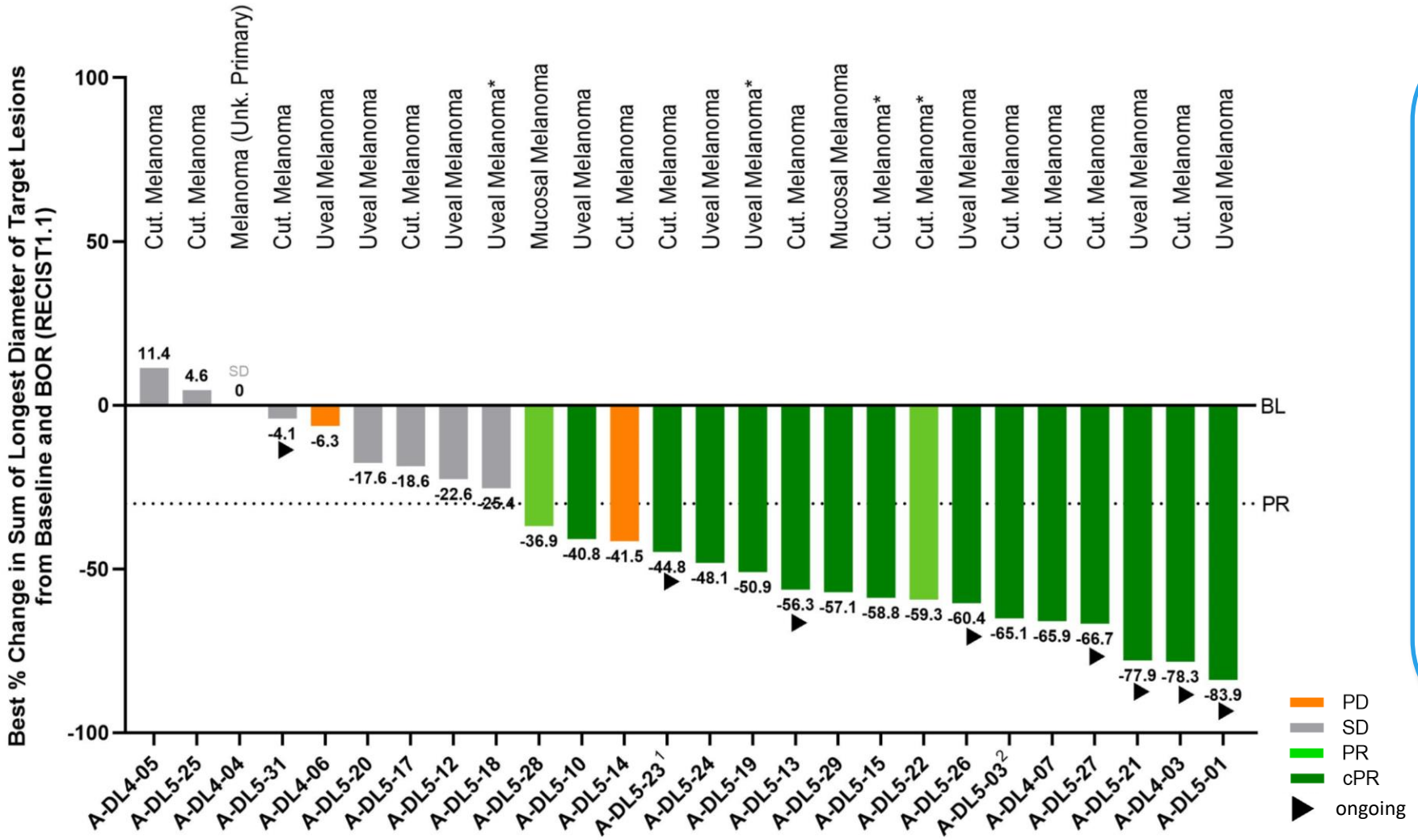
| Adverse event (**System organ class**, Preferred term) | ≥ Grade 3 No. | ≥ Grade 3 % |
|---|---|---|
| table continued… | | |
| **Metabolism and nutrition disorders** | **7** | **10.0** |
| Hypokalaemia | 3 | 4.3 |
| Hyponatraemia | 3 | 4.3 |
| Hypophosphataemia | 2 | 2.9 |
| Dehydration | 1 | 1.4 |
| Failure to thrive | 1 | 1.4 |
| **Vascular disorders** | **7** | **10.0** |
| Hypertension | 6 | 8.6 |
| Hypotension | 1 | 1.4 |
| **Renal and urinary disorders** | **6** | **8.6** |
| Acute kidney injury | 4 | 5.7 |
| Nephritis | 1 | 1.4 |
| Proteinuria | 1 | 1.4 |
| **Gastrointestinal disorders** | **5** | **7.1** |
| Abdominal pain | 3 | 4.3 |
| Diarrhoea | 1 | 1.4 |
| Ileus | 1 | 1.4 |
| Vomiting | 1 | 1.4 |
| **General disorders and administration site conditions** | **4** | **5.7** |
| Fatigue | 1 | 1.4 |
| General physical health deterioration[3] | 1 | 1.4 |
| Pyrexia | 1 | 1.4 |
| Swelling face | 1 | 1.4 |
| **Skin and subcutaneous tissue disorders** | **4** | **5.7** |
| Rash maculo-papular | 3 | 4.3 |
| Eczema | 1 | 1.4 |
| **Cardiac disorders** | **3** | **4.3** |
| Atrial fibrillation[5] | 3 | 4.3 |
| **Eye disorders** | **2** | **2.9** |
| Periorbital oedema | 1 | 1.4 |
| Ulcerative keratitis | 1 | 1.4 |
| **Injury, poisoning and procedural complications** | **2** | **2.9** |
| Humerus fracture | 1 | 1.4 |
| Infusion related reaction | 1 | 1.4 |
| **Musculoskeletal and connective tissue disorders** | **2** | **2.9** |
| Back pain | 1 | 1.4 |
| Muscle spasms | 1 | 1.4 |

| Adverse event (**System organ class**, Preferred term) | ≥ Grade 3 No. | ≥ Grade 3 % |
|---|---|---|
| table continued… | | |
| **Nervous system disorders** | **2** | **2.9** |
| Headache | 1 | 1.4 |
| Posterior reversible encephalopathy syndrome | 1 | 1.4 |
| **Endocrine disorders** | **1** | **1.4** |
| Inappropriate antidiuretic hormone secretion | 1 | 1.4 |
| **Hepatobiliary disorders** | **1** | **1.4** |
| Cholangitis | 1 | 1.4 |
| **Immune system disorders** | **1** | **1.4** |
| Haemophagocytic lymphohistiocytosis | 1 | 1.4 |
| **Reproductive system and breast disorders** | **1** | **1.4** |
| Vaginal haemorrhage | 1 | 1.4 |

All treatment-emergent adverse events (TEAEs) with ≥ Grade 3 regardless of relatedness to study treatment. 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 Cytokine release syndrome and ICANS were determined according to CARTOX criteria (Neelapu et al., 2019). Patients are counted only once per adverse event and severity classification. Based on interim data extracted from open clinical database (23-Aug-2024); [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] Fatal Adverse events were not considered related to any study drug; [4] Patient died from sepsis of unknown origin and did not receive IMA203 TCR-T cells; [5] DLT: Dose limiting toxicity in phase 1a at DL2 reported on March 17, 2021.

# Best Overall Response for IMA203 in Melanoma

## Objective Responses in Heavily Pretreated Patients in Phase 1b (N=28[#])



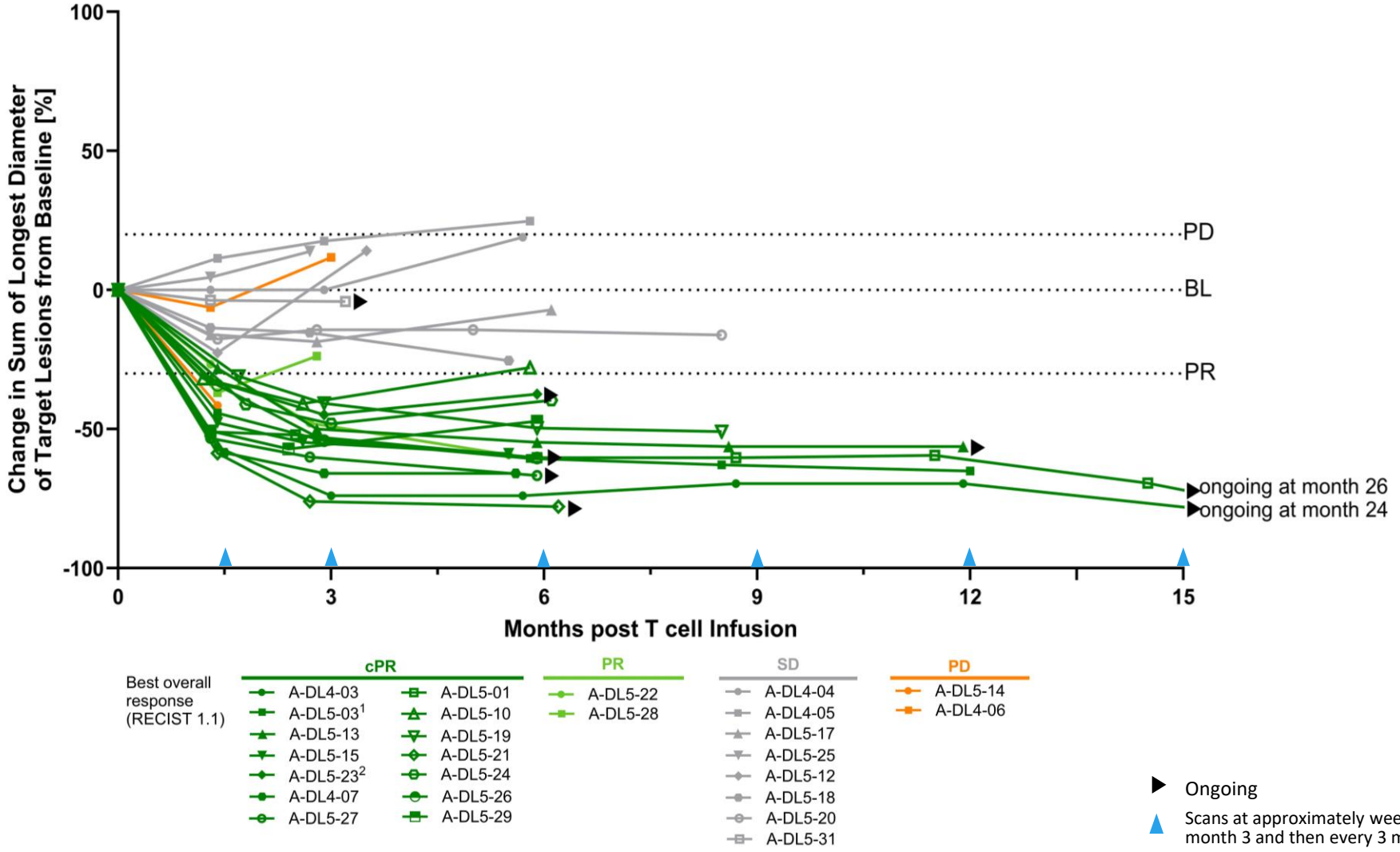

| | |
|---|---|
| **cORR** | **54% (14/26)** |
| **median DOR** | **12.1 months** |
| (min, max) | (4.2, 25.5+ months) |
| mFU | 9.3 months |
| 7/14 confirmed responses ongoing | |
| **median PFS** | **6.0 months** |
| (min, max) | (0.3+, 26.8+ months) |
| **median OS** | **Not reached** |
| (min, max) | (0.3+, 26.8+ months) |
| mFU | 8.6 months |
| ORR | 62% (16/26) |
| Tumor shrinkage** | 88% (23/26) |
| DCR (at week 6) | 92% (24/26) |



[#]First tumor assessment post infusion pending for two melanoma patients at data-cut; *Maximum change of target lesions and RECIST1.1 response at different timepoints. **Tumor shrinkage of target lesions; [1]Patient A-DL5-23 is off study at data cut-off; [2]Patient out of study due to PD (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 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; Overall survival (OS) and progression-free survival (PFS) censored at data-cut; BL: Baseline PD: Progressive Disease; SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response; DCR: Disease control rate, mFU: median follow-up

# Response Over Time of IMA203 in Melanoma

## Durable Responses 2 Years+ after Treatment in Heavily Pretreated Patients in Phase 1b (N=28#)




| | |
|---|---|
| **cORR** | **54% (14/26)** |
| **median DOR** | **12.1 months** |
| (min, max) | (4.2, 25.5+ months) |
| mFU | 9.3 months |
| 7/14 confirmed responses ongoing | |
| **median PFS** | **6.0 months** |
| (min, max) | (0.3+, 26.8+ months) |
| **median OS** | **Not reached** |
| (min, max) | (0.3+, 26.8+ months) |
| mFU | 8.6 months |
| ORR | 62% (16/26) |
| Tumor shrinkage** | 88% (23/26) |
| DCR (at week 6) | 92% (24/26) |

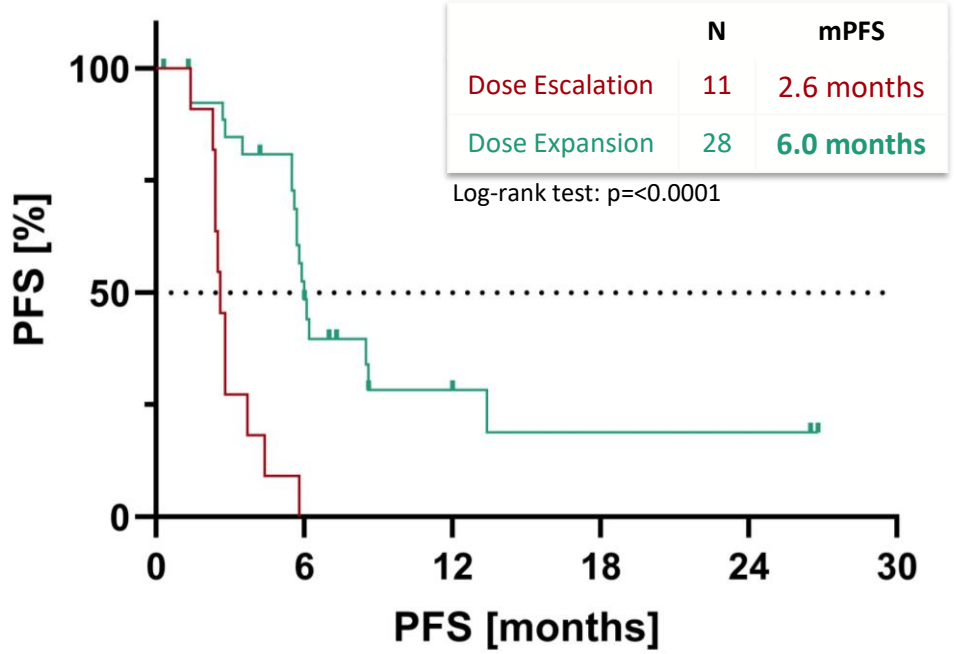
IMA203

#First tumor assessment post infusion pending for two melanoma patients at data-cut; *Tumor shrinkage of target lesions; [1]Patient out of study due to PD (external assessment) [2]Patient A-DL5-23 is off study 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 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; Overall survival (OS) and progression-free survival (PFS) censored at data-cut; BL: Baseline PD: Progressive Disease; SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response; DCR: Disease control rate, mFU: median follow-up

# Significant Shift in PFS and OS Between Dose Escalation & Dose Expansion

## PFS of 6 Months and OS Not Reached in Melanoma Efficacy Population

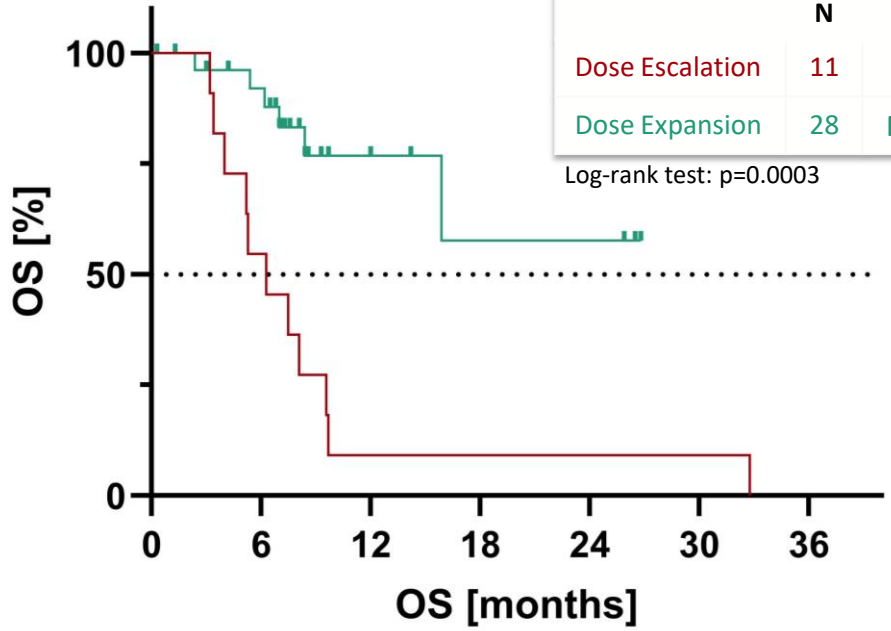
### Progression Free Survival




| | N | mPFS |
|---|---|---|
| Dose Escalation | 11 | 2.6 months |
| Dose Expansion | 28 | **6.0 months** |

Log-rank test: p=<0.0001

### Overall Survival




| | N | mOS |
|---|---|---|
| Dose Escalation | 11 | 6.3 months |
| Dose Expansion | 28 | **Not reached** |

Log-rank test: p=0.0003

- Significant shift in PFS and OS between melanoma patients treated during the dose escalation and dose expansion phase
- PFS in dose escalation is comparable to reported data in 2L+ cut. melanoma population*
- OS in dose escalation is shorter than reported OS for 2L+ cut. melanoma population*
- All patients in the dose escalation group died and 20/28 patients are alive in dose expansion



Overall survival (OS) and progression-free survival (PFS) censored at data-cut; * These data are derived from different clinical trials at different points in time with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

# IMA203 Phase 1b in Melanoma: Overview of Studies

## PFS and OS Data in 2L+ Melanoma Cohorts

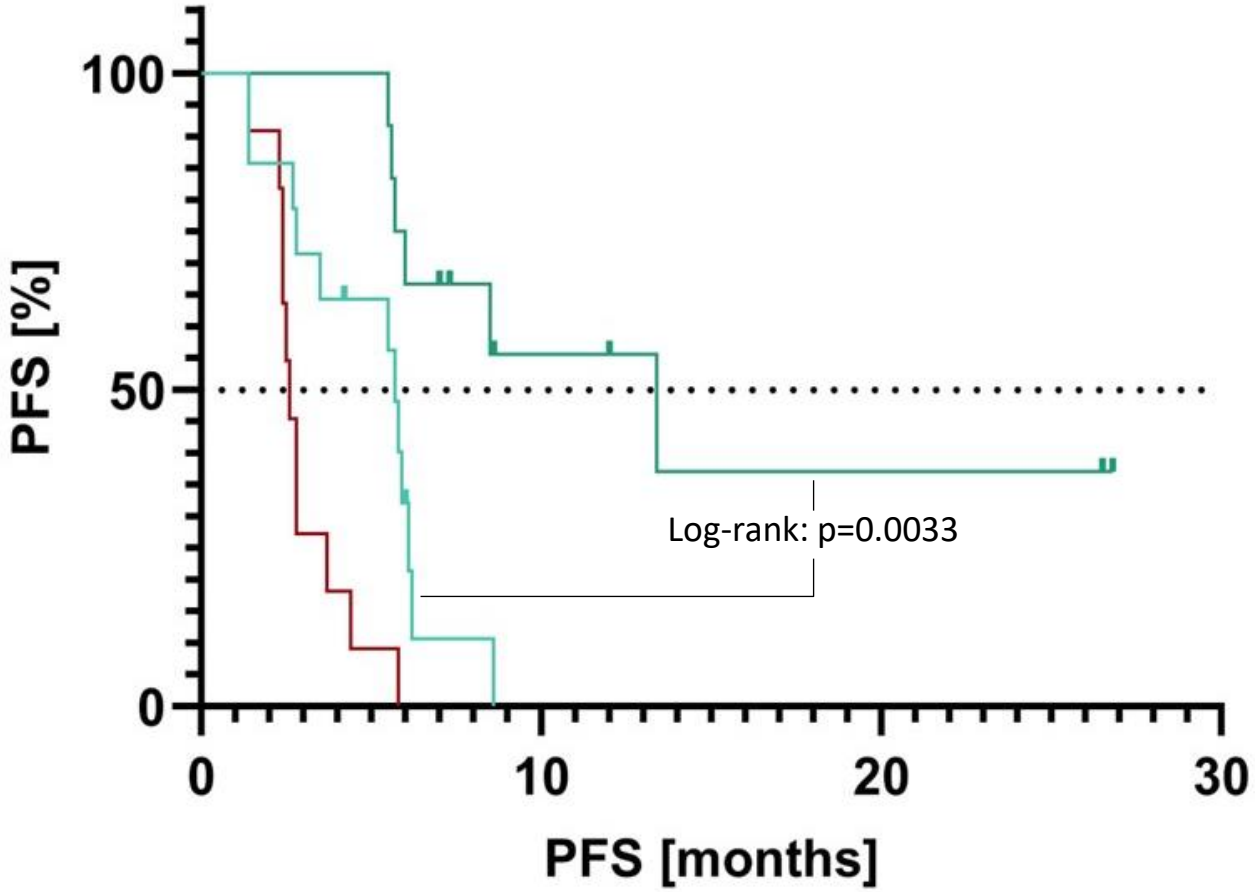
| Drug Product | Phase | N | 2L+ melanoma patient population | Prior lines of therapies | mPFS (months) | mOS (months) |
|---|---|---|---|---|---|---|
| **IMA203 in Melanoma** | 1b (Dose Expansion) | 28 | 46% cutaneous<br>43% uveal<br>11% other | 4% n=0, 18% n=1, 32% n=2, 29% n=3:, 4% n=4, 11% n=5, 4% n=6<br>86% received prior CPI (median of 1 prior line of CPI in overall population, median of 2 prior lines of CPI in cut. melanoma)<br>Median of 2 prior lines, median of 2 prior lines in cut. melanoma | **6.0** | **not reached** |
| **IMA203 in Melanoma** | 1a (Dose Escalation) | 11 | 73% cutaneous<br>18% uveal<br>9% other | 0% n=1, 27% n=2, 73% n>2 prior lines<br>100% received prior CPI (median of 2 prior lines of CPI, median of 2.5 prior lines of CPI in cut. melanoma)<br>Median of 4 prior lines, median of 4.5 prior lines in cut. melanoma | **2.6** | **6.3** |
| **IMA201/202/203 combined in Melanoma** | 1a (Dose Escalation) | 19 | 63% cutaneous<br>11% uveal<br>26% other | 0% n=1, 16% n=2, 84% n>2 prior lines<br>100% received prior CPI (median 3 prior lines of CPI)<br>Median of 4 prior lines, median of 4.5 prior lines in cut. melanoma | **2.5** | **5.3** |
| **Lifileucel (C-144-01, Cohort 2+4)[1]** | 2 | 153 | 54% cutaneous<br>0% uveal<br>45% other | median of 3 prior lines (min/max: 1/9)<br>100% received prior CPI | **4.1** | **13.9** |
| **Tilsotolimod + Ipilimumab (ILLUMINATE-301)[2]** | 3 | 238 | 85% cutaneous<br>0% uveal<br>15% other | 57% n=1, 27% n=2, 12% n>2 prior lines<br>99% received prior CPI | **2.9** | **11.6** |
| **Nivolumab + Relatlimab (RELATIVITY-020, D1 Cohort)[3]** | 1/2 | 354 | 68% cutaneous<br>0% uveal<br>32% other | 46% n=1, 35% n=2, 19% n≥3 prior lines<br>99% received prior CPI | **2.1** | **14.7** |

***These data are derived from different clinical trials at different points in time with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.***


[1] Chesney et al., 2022; [2] Diab et al., 2024; [3] Ascierto et al., 2023.

# Enhanced PFS in Phase 1b Melanoma Patients with Deep Responses

## N=26#




| | N | mPFS |
|---|---|---|
| Dose Escalation IMA203 | 11 | **2.6 months** |
| Dose Expansion IMA203 <50% tumor size reduction (including tumor size increase) | 14* | **5.7 months** |
| Dose Expansion IMA203 ≥50% tumor size reduction | 12 | **13.4 months** |

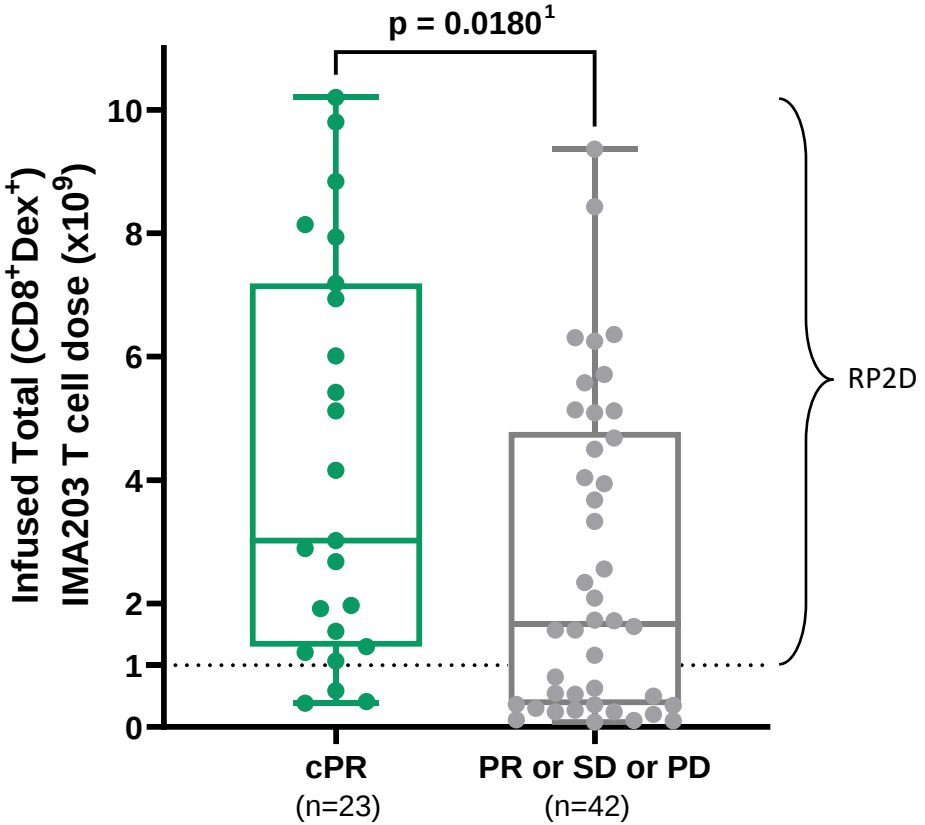
- Approx. half of all patients have a deep response (>50% tumor reduction)
- This subgroup of patients has highly medically meaningful mPFS of more than 1 year
- Patients with <50% tumor reduction (including tumor size increase) still observe a more than 2x longer mPFS as compared to patients treated in dose escalation with suboptimal doses

IMA203

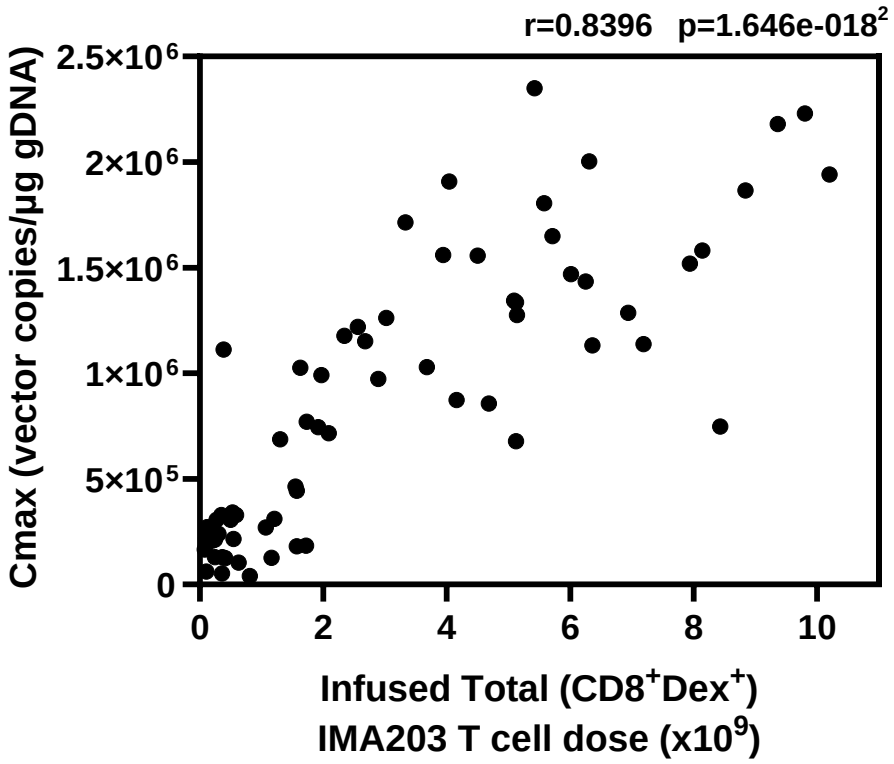
# Excluding two patients that were infused but did not have their first tumor assessment post baseline at data-cut;
*Includes one patient with ongoing SD 4.4 months after infusion with tumor reduction <50%

# Dose Response Relationship

## IMA203 T Cell Dose is Associated with Clinical Activity and IMA203 T Cell Exposure (N=65 out of 68*)




### IMA203 T Cell Dose is Associated with Clinical Activity



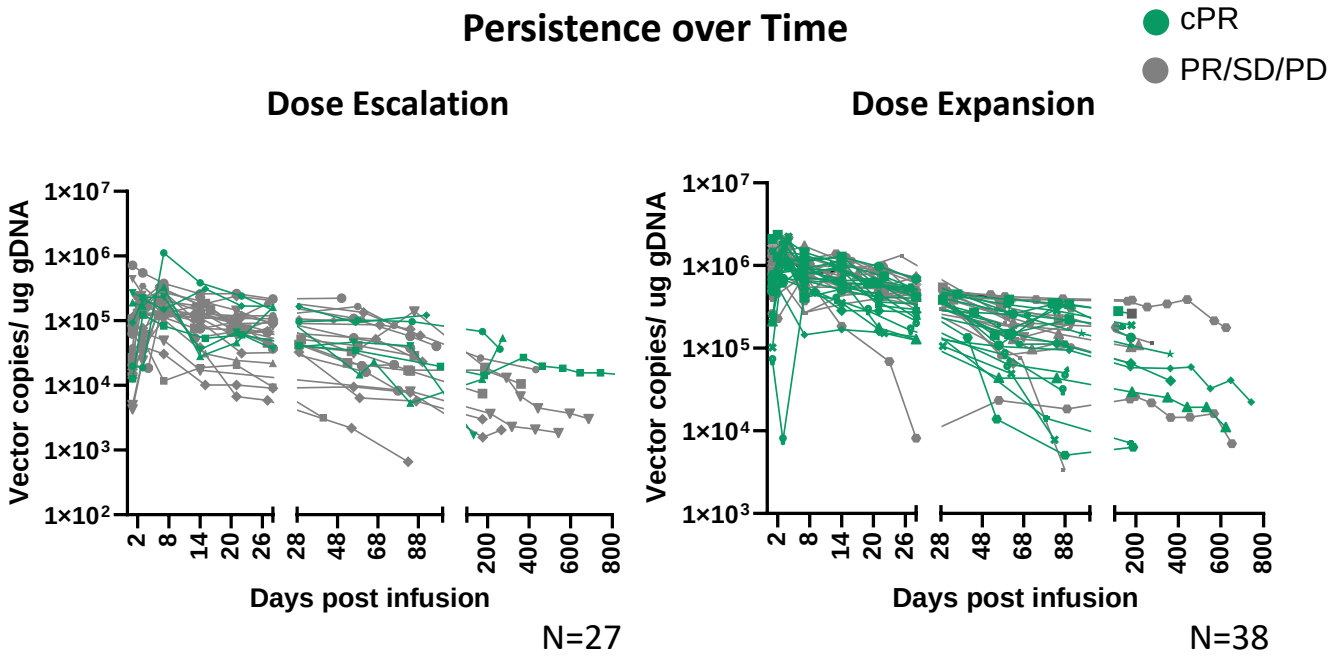

### IMA203 T Cell Dose Correlates with T Cell Exposure

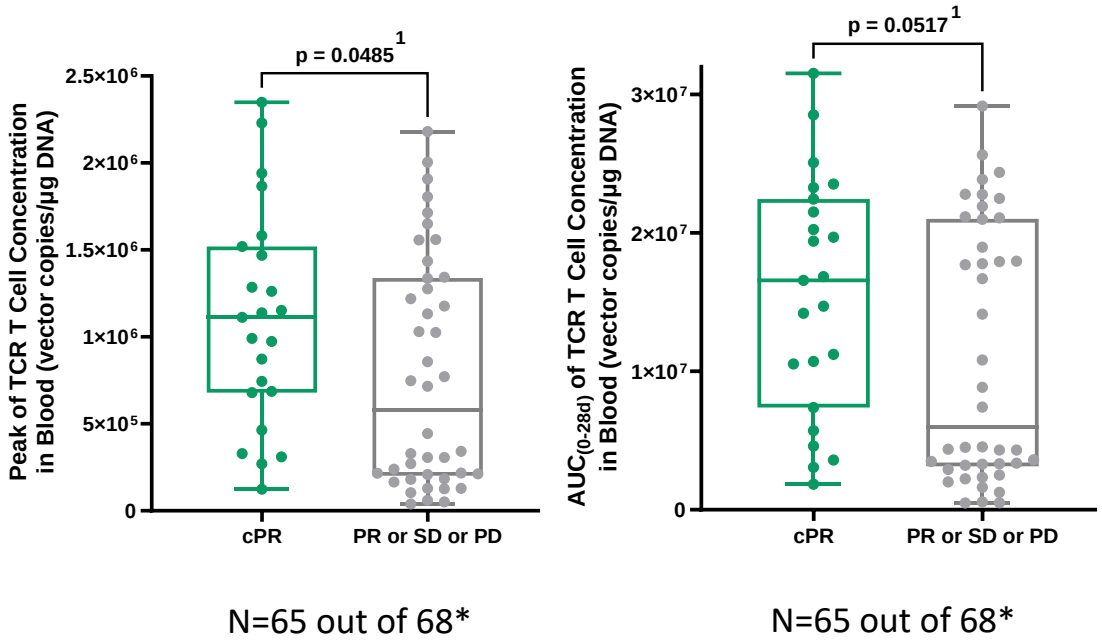


[1]Mann-Whitney U test, [2]Spearman Correlation; * no data available yet for patients recently treated;
PD: Progressive Disease; SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response; , RP2D: recommended phase 2 dose

# Exposure Response Relationship

## IMA203 T Cell Persistence Over Time and T Cell Exposure is Associated with Clinical Response




**Rapid T cell engraftment ($C_{max}$) in all patients with over two years of persistence**

**Higher $C_{max}$ and persistence in patients treated at higher doses in dose expansion versus dose escalation**

**IMA203 T cell exposure ($C_{max}$ & $AUC_{(0-28d)}$) is associated with clinical responses**



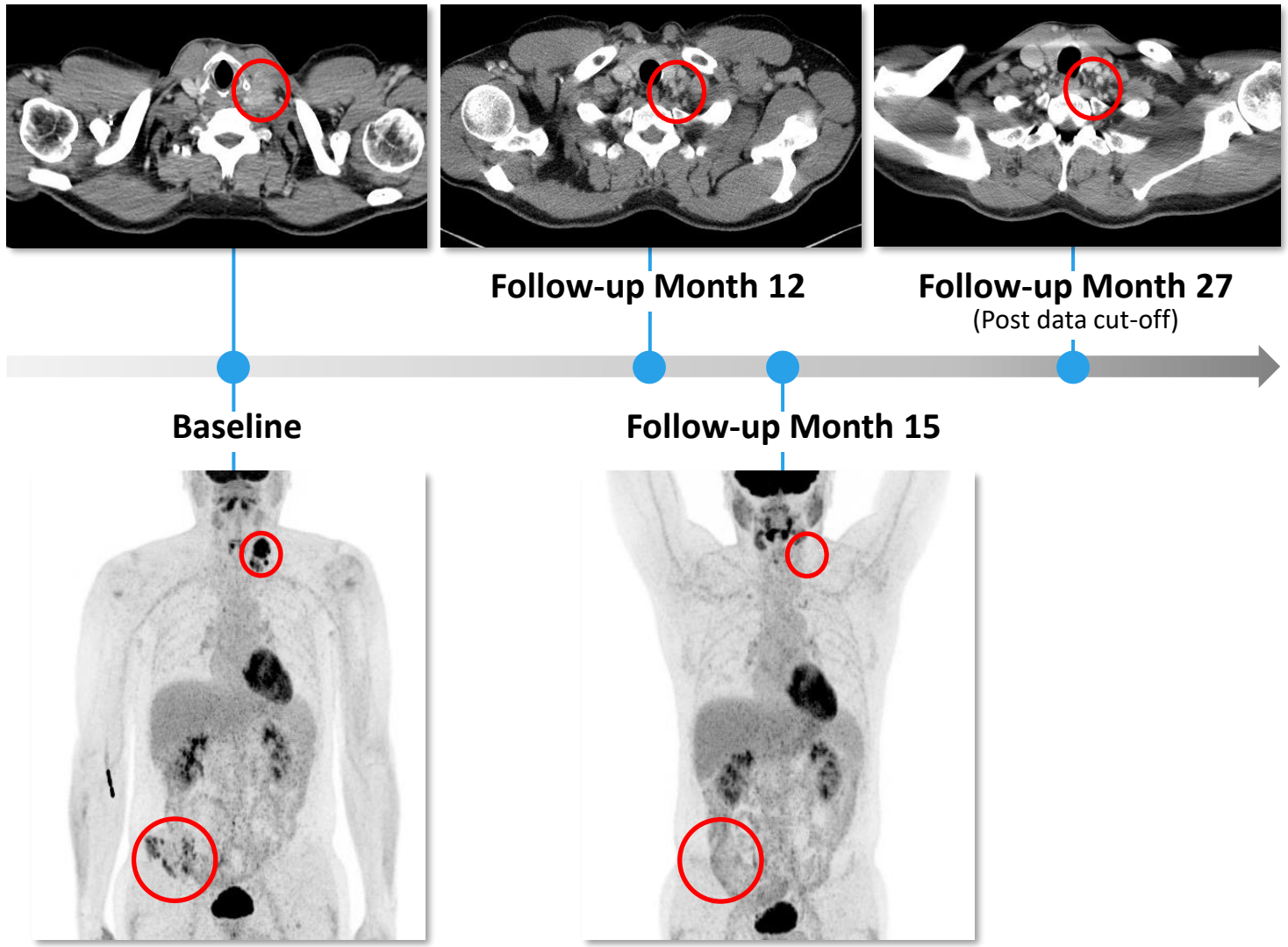
[1] Mann-Whitney U test; * no data available yet for patients recently treated;
PD: Progressive Disease; SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response, AUC: Area under curve

# Patient Case A-DL4-03 : Cutaneous Melanoma

## PET-based Complete Response 15 Months Post Infusion and Ongoing Response at 24 Months

**51-year-old male patient with complete remission according to PET imaging after 15 months and ongoing beyond two years post infusion at data cut**

- 5 prior systemic treatment lines:
  - Dabrafenib + Trametinib
  - Pembrolizumab
  - Dabrafenib + Trametinib + Vemurafenib + Cobimetinib
  - Tebentafusp
  - Encorafenib + Binimetinib
- 13 years of cancer history
- 23 mm target lesion in cervical lymph node and non-target lesions in pelvic bone and lung
- Patient received ~$1.3x10^9$ IMA203 TCR-T cells
- Ongoing PR at 24 months post infusion with -78.3% reduction according to RECIST1.1
- Metabolic complete response reported based on investigator-initiated PET imaging at baseline and month 15 post infusion

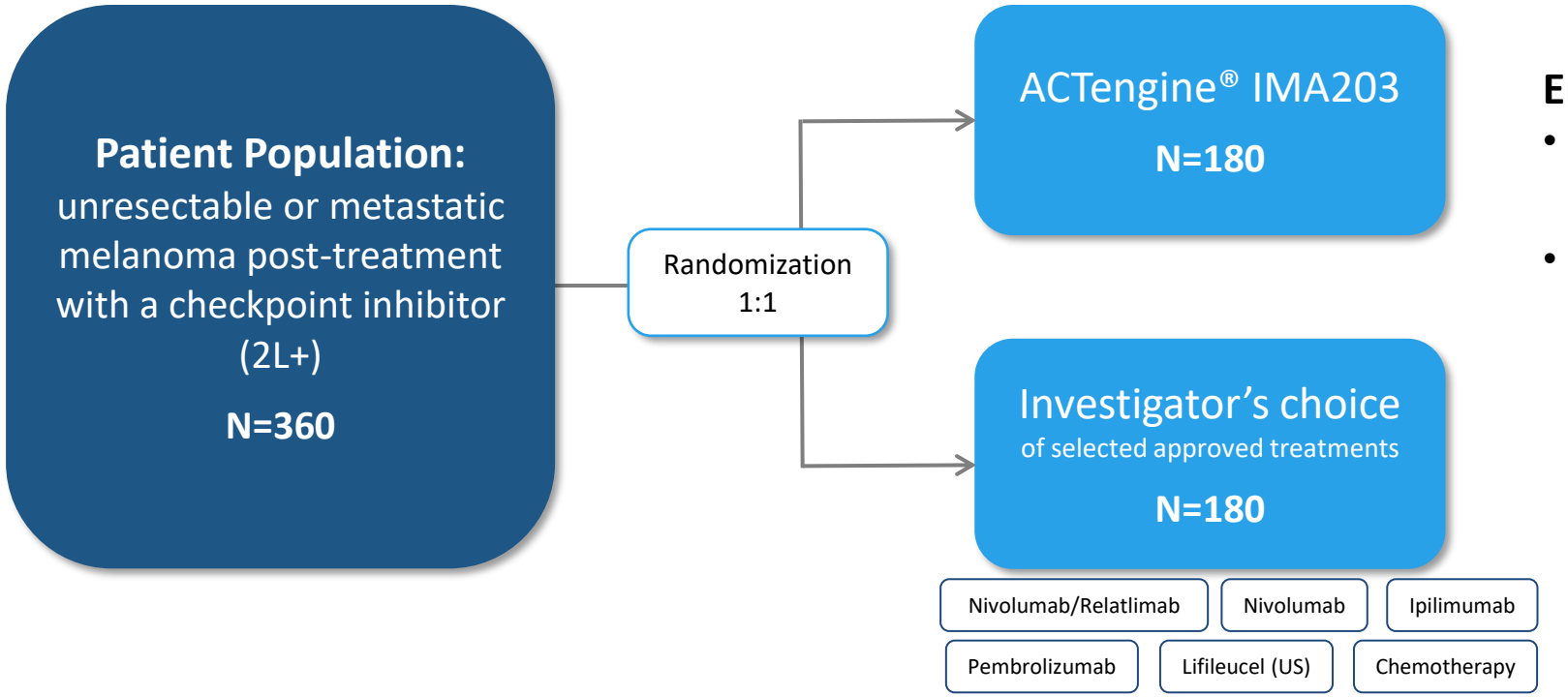




Images courtesy of treating physician (Dr. Martin Wermke, University of Dresden)

# SUPRAME: Registration-enabling Randomized Phase 3 Trial

## Trial Design Following Recent Type D Meeting with FDA and SA Meeting with PEI[1]




### Endpoints

- **Primary Endpoint**
  - **PFS**
- **Secondary Endpoints**
  - Safety
  - ORR + DOR
  - No OS detriment
  - Patient-reported outcomes (EORTC QLQ-C30, EQ-5D-5L)

### Next Steps

- SUPRAME Phase 3 trial is projected to commence in **December 2024**
- Pre-specified interim analysis planned after approx. 200 patients enrolled
- Full enrollment anticipated by late **2026**


mPFS: median progression-free survival, ORR: objective response rate; [1] Scientific Advice Meeting with Paul-Ehrlich-Institute, the German regulatory authority

# Combining Immatics' TCR-T Therapy with Moderna's mRNA Cancer Vaccine – Patient Flow

## IMA203 Targeting PRAME Together with PRAME mRNA-based Cancer Vaccine

**Screening & Manufacturing Phase**

**Treatment & Observation Phase (1 year)**

**Follow-up (2 years)**

Safety and efficacy monitoring for 12 months

**HLA-A*02 testing**
Blood sample;
Central lab

**Tumor tissue collection**

**Leukapheresis**

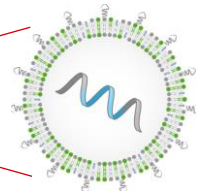
**Manufacturing**
by Immatics

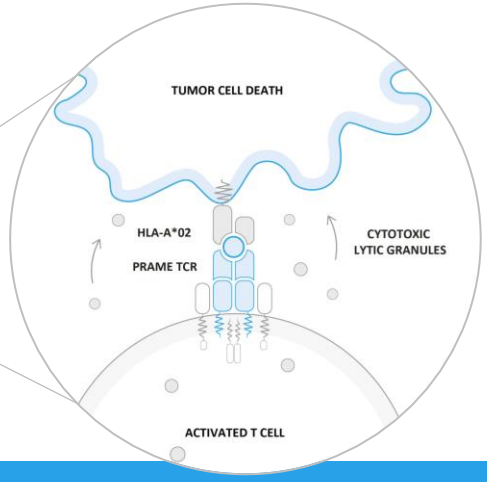
**Short process time of 14 days**
7-day manufacturing process applying CD8/CD4 T cell selection
7-day QC release testing

**Lymphodepletion***

**Infusion of ACTengine®**
**IMA203 TCR-T Product**

**mRNA/LNP**
Up to 13 administrations given q2-4 weeks over 52 weeks





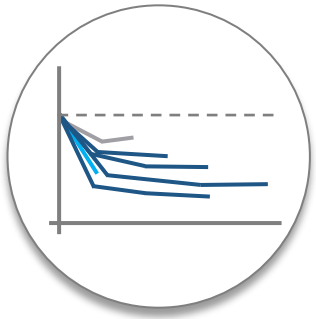

* 30 mg/m² Fludarabine and 500 mg/m² Cyclophosphamide for 4 days; ** 1m IU daily days 1-5 and twice daily days 6-10

# ACTengine® IMA203 TCR-T Monotherapy Targeting PRAME in Melanoma

## Summary of Clinical Data

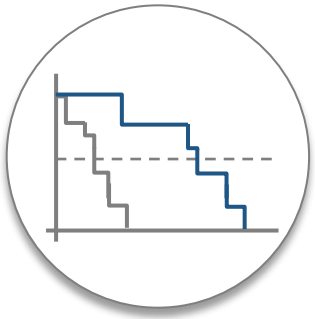
### Tolerability

Favorable tolerability profile:
mostly mild to moderate CRS;
infrequent ICANS
(5.7% Gr1, 4.3% Gr2, 4.3% Gr3);
no treatment related deaths



### Anti-Tumor Activity & Durability

54% (14/26) cORR and 92% (24/26) DCR;
12.1 months mDOR and ongoing responses for over two years

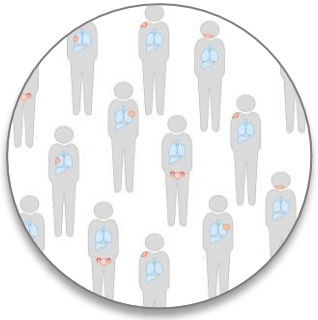


### PFS & OS

PFS of 6 months and OS not reached (mFU 8.6 months)

### Biological Data

T cell dose and exposure are significantly associated with clinical response



### Broad Reach

FDA RMAT designation received in multiple PRAME expressing cancers including cutaneous and uveal melanoma

SUPRAME Phase 3 trial in cutaneous melanoma patients is projected to commence in **December 2024**

# IMA203 in Melanoma Targeted to Enter Randomized Phase 3 Trial in 2L+ Melanoma in 2024

## Clinically and Commercially Attractive Features of IMA203

- ≥95% of cutaneous melanoma patients are PRAME-positive
- Favorable tolerability profile
  mostly mild to moderate CRS, infrequent ICANS (6% Gr1, 4% Gr2, 4% Gr3), no treatment related deaths
- Promising anti-tumor activity (cORR, mDOR, PFS)
- 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 Unmet Medical Need in Cutaneous and Uveal Melanoma

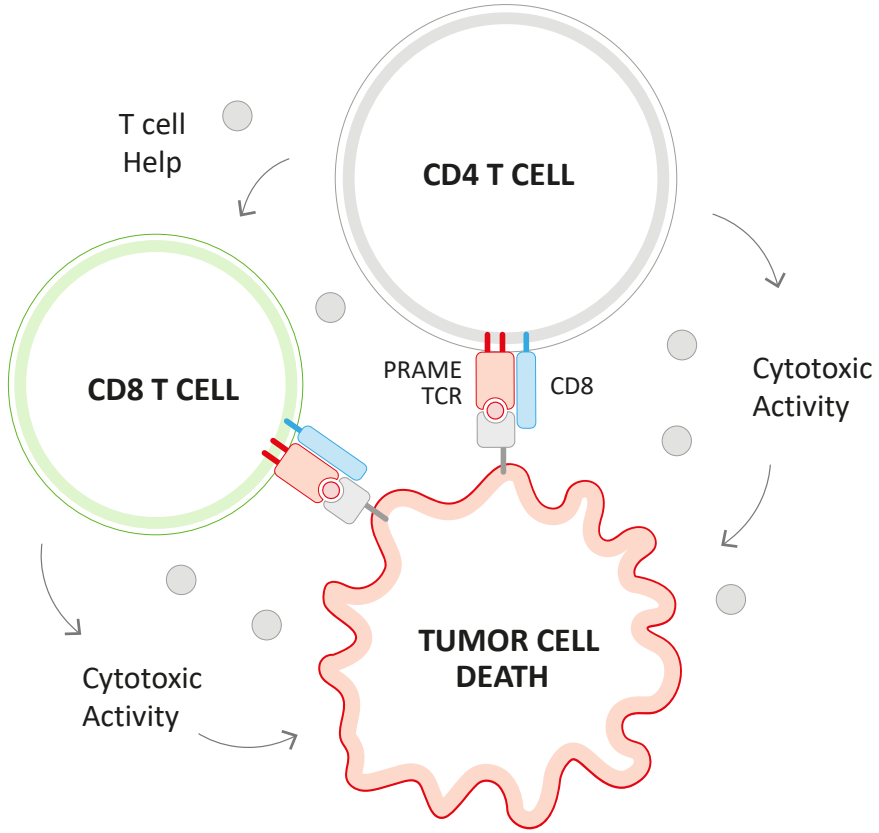
| | Cutaneous Melanoma | Uveal Melanoma |
|---|---|---|
| Patient Population | **2L+** CPI-refractory, BRAF/MEK inhibitor-refractory if BRAF mutation+ | **2L+** Kimmtrak-refractory, CPI/chemotherapy-refractory |
| IMA203 Opportunity | **~3,000** HLA-A*02:01 and PRAME-positive cutaneous melanoma patients 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 89% (IMADetect® qPCR testing of screening biopsies from clinical trial patients (n=33))

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

## Differentiated Pharmacology Compared to 1st-Generation TCR-only Approaches



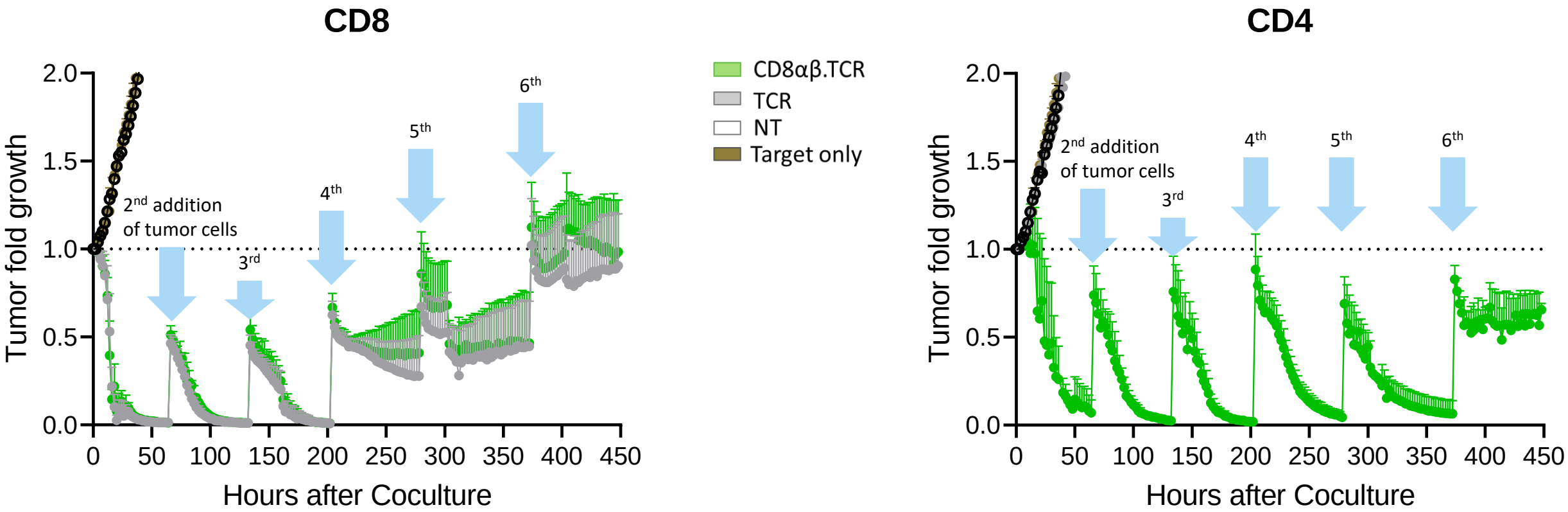

- IMA203CD8 (GEN2) designed to broaden the clinical potential of IMA203 TCR-T monotherapy by adding functional CD4 T cells via co-transduction of CD8αβ alongside PRAME TCR
- Activated CD4 T cells aid activity of other immune cells by releasing cytokines and acquire cytotoxic functions
- Functional CD4 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.* 2022 Science Advances

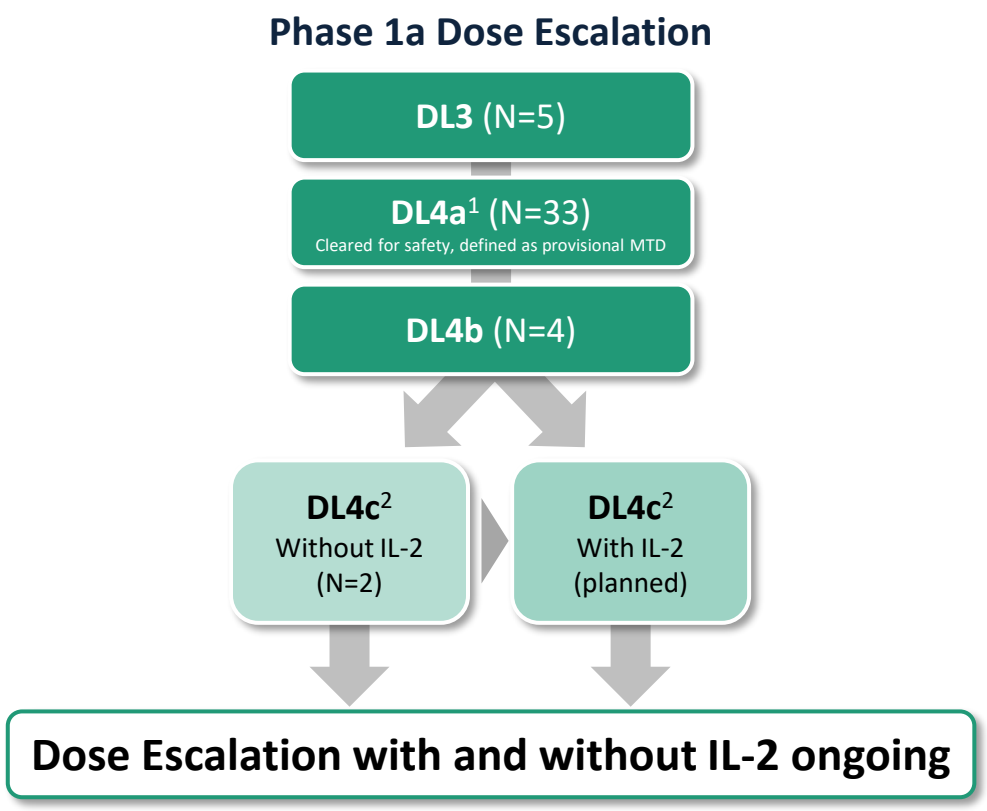
# IMA203CD8 (GEN2) – Preclinical Assessment of Anti-Tumor Efficacy

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



# IMA203CD8 (GEN2) – Overview of Patient Characteristics

## Data cut-off Sep 30, 2024




| | Total Safety Population | Efficacy Population |
|---|---|---|
| **Number of patients** | N=44[3] | N=41[4] |
| **Prior lines of systemic treatment** (median, min, max) | 3 (0, 8) | 3 (0, 8) |
| **LDH at baseline** >1 x ULN [% of patients] | 47.7 | 43.9 |
| **Baseline tumor burden** Median target lesion sum of diameter [mm] (min, max) | 84.5 (12.4, 434.4) | 83.0 (12.4, 434.4) |
| **With liver/brain lesions at baseline** [% of patients] | 45.5 | 43.9 |
| **Infused dose levels** TCR-T cells/$m^2$ BSA [$x10^9$] | DL3: 0.2-0.48<br>DL4a: 0.481-0.8<br>DL4b: 0.801-1.2<br>DL4c[2]: 0.801-1.2 | DL3: 0.2-0.48<br>DL4a: 0.481-0.8<br>DL4b: 0.801-1.2<br>DL4c[2]: 0.801-1.2 |
| **Total infused dose** TCR-T cells [$x10^9$] (median, min, max) | 1.48 (0.44, 2.05) | 1.47 (0.44, 2.05) |



[1] DL4a cleared in Dec 2023; [2] DLTs at DL4b triggered modifications of the eligibility criteria, adapted patient population is treated with DL4c; [3] All patients who started lymphodepletion. [4] All infused patients with at least one tumor assessment postbaseline.

# Tolerability Data – IMA203CD8 (GEN2)

## All ≥Grade 3 Adverse Events (N=44)

**TEAEs by maximum severity for all patients (N=44)**

| Adverse event (**System organ class**, preferred term) | ≥ Grade 3 No. | ≥ Grade 3 % |
|---|---|---|
| **Patients with any adverse event** | **44** | **100.0** |
| **Adverse events of special interest** | **7** | **15.9** |
| Cytokine release syndrome[1] | 6 | 13.6 |
| Immune effector cell-associated neurotoxicity syndrome | 1 | 2.3 |
| **Blood and lymphatic system disorders** | **44** | **100.0** |
| Neutropenia | 40 | 90.9 |
| Anaemia | 25 | 56.8 |
| Lymphopenia | 25 | 56.8 |
| Thrombocytopenia | 15 | 34.1 |
| Leukopenia | 11 | 25.0 |
| Febrile neutropenia | 2 | 4.5 |
| **Investigations** | **9** | **20.5** |
| Alanine aminotransferase increased | 5 | 11.4 |
| Aspartate aminotransferase increased | 5 | 11.4 |
| Blood creatinine increased | 2 | 4.5 |
| Blood alkaline phosphatase increased | 1 | 2.3 |
| Blood bilirubin increased | 1 | 2.3 |
| Gamma-glutamyltransferase increased | 1 | 2.3 |
| **Metabolism and nutrition disorders** | **6** | **13.6** |
| Hypophosphataemia | 2 | 4.5 |
| Acidosis | 1 | 2.3 |
| Decreased appetite | 1 | 2.3 |
| Hyperglycaemia | 1 | 2.3 |
| Hypermagnesaemia | 1 | 2.3 |
| Hypoalbuminaemia | 1 | 2.3 |
| **General disorders and administration site conditions** | **5** | **11.4** |
| Fatigue | 5 | 11.4 |
| Oedema peripheral | 1 | 2.3 |
| **Musculoskeletal and connective tissue disorders** | **5** | **11.4** |
| Bone pain | 3 | 6.8 |
| Myalgia | 2 | 4.5 |
| Back pain | 2 | 4.5 |
| Arthralgia | 1 | 2.3 |

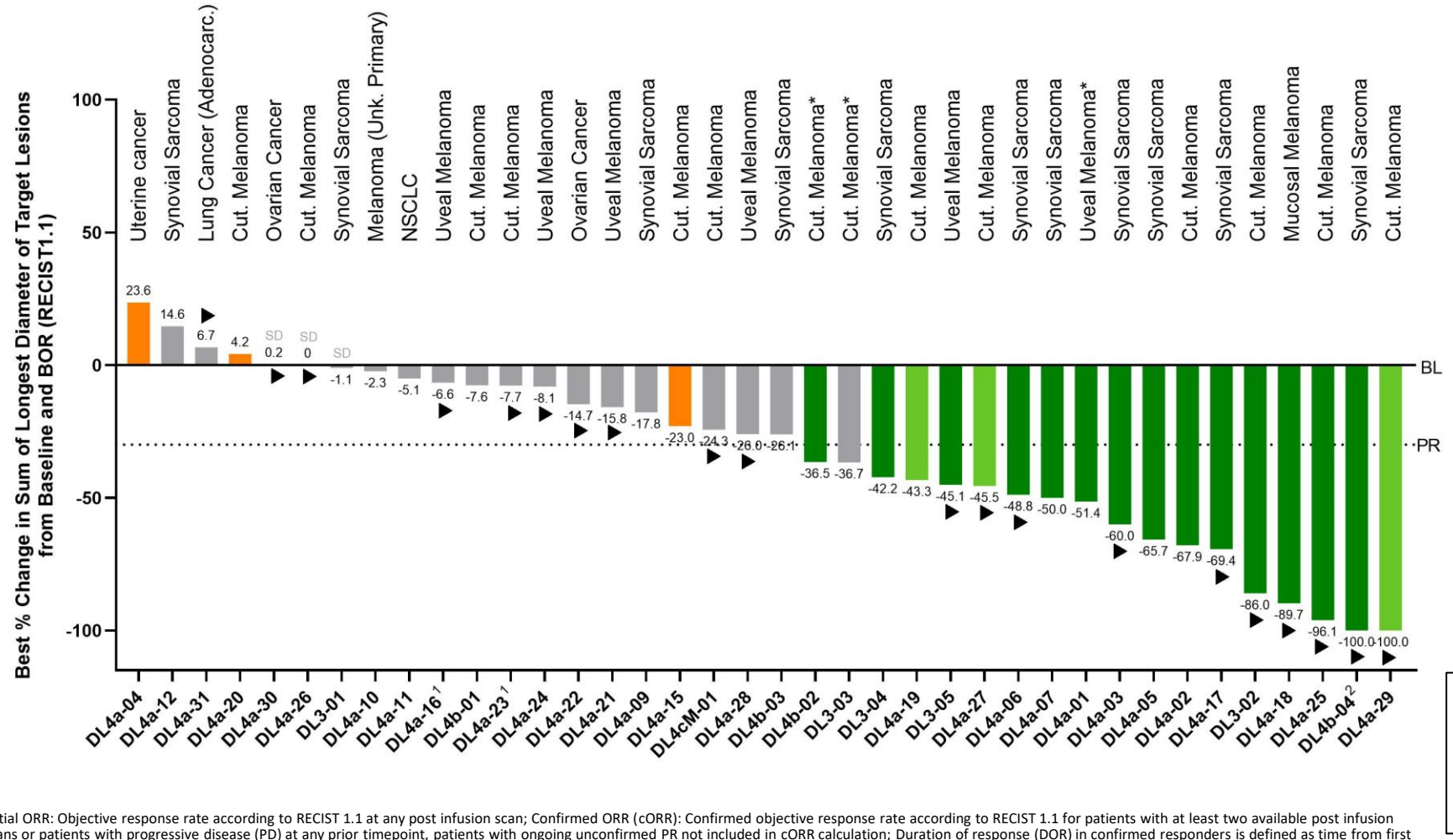
| Adverse event (**System organ class**, preferred term) | ≥ Grade 3 No. | ≥ Grade 3 % |
|---|---|---|
| … table continued | | |
| **Immune system disorders** | **4** | **9.1** |
| Haemophagocytic lymphohistiocytosis[2] | 4 | 9.1 |
| **Infections and infestations** | **4** | **9.1** |
| Pneumonia | 2 | 4.5 |
| Infection | 1 | 2.3 |
| Sepsis[3] | 1 | 2.3 |
| Systemic candida | 1 | 2.3 |
| **Gastrointestinal disorders** | **3** | **6.8** |
| Diarrhoea | 2 | 4.5 |
| Abdominal pain | 1 | 2.3 |
| **Skin and subcutaneous tissue disorders** | **3** | **6.8** |
| Rash | 2 | 4.5 |
| Alopecia | 1 | 2.3 |
| Rash maculo-papular | 1 | 2.3 |
| **Vascular disorders** | **3** | **6.8** |
| Hypertension | 3 | 6.8 |
| **Nervous system disorders** | **2** | **4.5** |
| Neurotoxicity[2] | 1 | 2.3 |
| Syncope | 1 | 2.3 |
| **Renal and urinary disorders** | **2** | **4.5** |
| Acute kidney injury | 1 | 2.3 |
| Urinary tract obstruction | 1 | 2.3 |
| **Hepatobiliary disorders** | **1** | **2.3** |
| Hepatic function abnormal | 1 | 2.3 |
| **Reproductive system and breast disorders** | **1** | **2.3** |
| Pelvic pain | 1 | 2.3 |

All treatment-emergent adverse events (TEAEs) with ≥ Grade 3 regardless of relatedness to study treatment that occurred in at least 1 patient are presented; [1]DLT: Dose limiting toxicity in patient DL4b-04. [2]DLTs in patient DL4b-01; [3]The patient's immediate cause of death was considered to be fatal sepsis, aggravated by the immunosuppression, a high-grade Immune Effector Cell-Associated Hemophagocytic Lymphohistiocytosis-Like Syndrome (IEC-HS), and the fast-progressing disease. Event was reported in Annual Report 2023.

- **Overall manageable tolerability profile**
- Expected cytopenia
- Mostly mild to moderate CRS:
  - 36% (16/44) Grade 1
  - 48% (21/44) Grade 2
  - 11% (5/44) Grade 3
  - 2% (1/44) Grade 4
- DLTs in 2 patients at DL4b as previously reported by the Company:
  - Patient DL4b-01: high *in vivo* T cell expansion, Grade 4 neurotoxicity, Grade 4 CRS, Grade 3 HLH
  - Patient DL4b-04: Grade 3 CRS defined by Grade 3 ALT resolved to Grade 2 within 10 days; no need for vasopressors or ventilation
- One possibly-related Grade 5 adverse event as previously reported by the Company:
  - Cause of death: fatal sepsis - aggravated by immunosuppression, IEC-HS, fast-progressing disease
- Consecutive modification I/E criteria + IL2 scheme
- **Dose escalation ongoing** based upon manageable tolerability in patients at DL4a

# IMA203CD8 (GEN2) (N=41) – Best Overall Response in Dose Escalation

## Data cut-off Sep 30, 2024




| | |
|---|---|
| **cORR** | **41% (14/34)** |
| **median DOR** | **9.2 months** |
| (min, max) | **2.0+, 23.5+** |
| mFU | **13.1 months** |

**10/17 responses ongoing including 3 confirmed responses at 1+ year**

**Deep responses with ≥50% tumor size reduction in 11/17 responders incl. 2 patients with complete response of target lesions**

| | |
|---|---|
| ORR | 41% (17/41) |
| Tumor shrinkage[3] | 84% (32/38) |
| DCR[4] (at week 6) | 85% (34/40) |

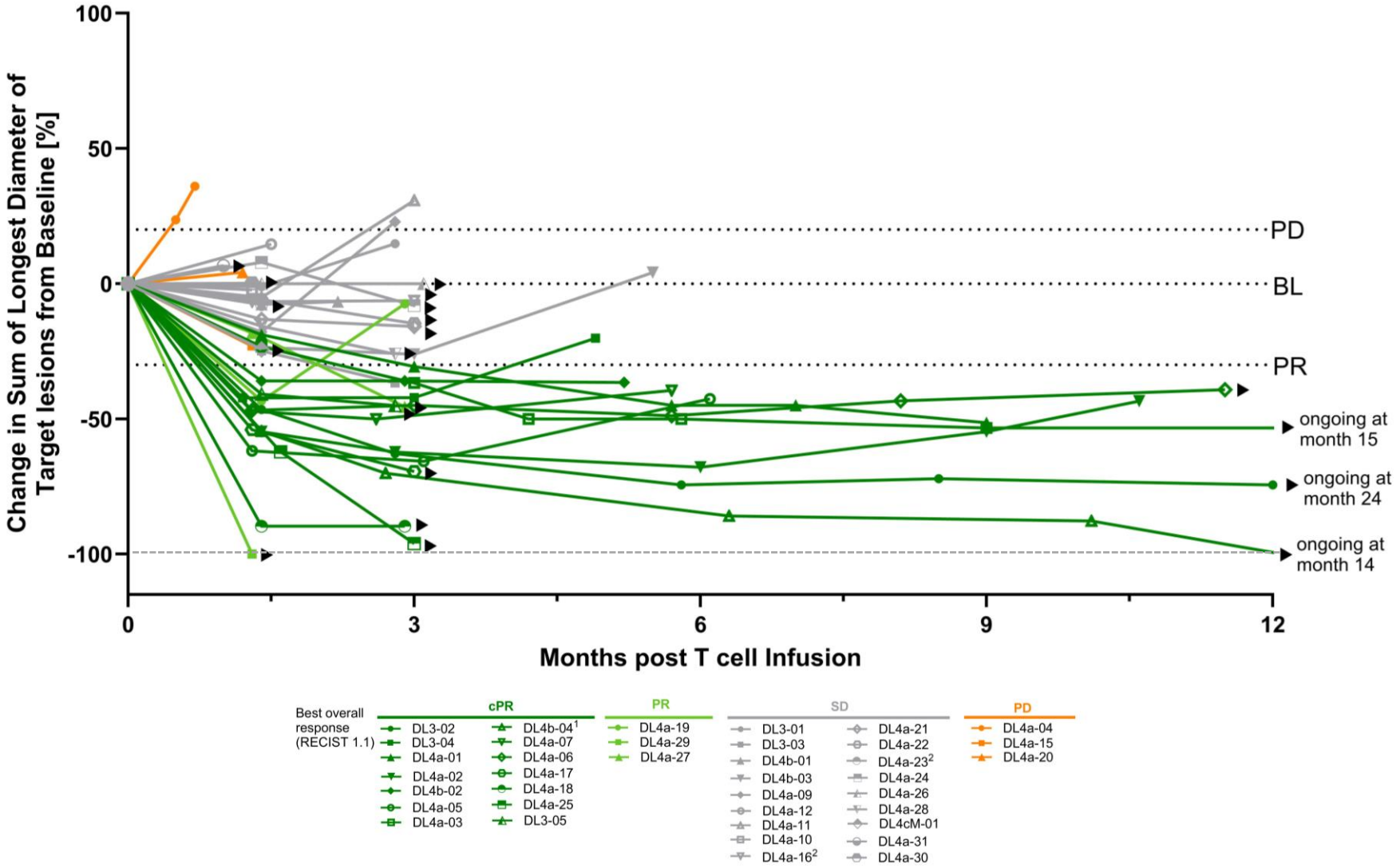
Initial ORR: Objective response rate according to RECIST 1.1 at any post infusion scan; Confirmed ORR (cORR): Confirmed objective response rate according to RECIST 1.1 for patients with at least two available post infusion scans or patients with progressive disease (PD) at any prior timepoint, patients 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



*Maximum change of target lesions and RECIST1.1 response at different timepoints; [1]Patients off study at data-cut; [2]Metabolic CR according to PET-CT; [3] three patients excluded from tumor shrinkage analysis and figures due to lack of post-treatment assessment; [4] One patient had an early tumor assessment, outside the first assessment visit window and is not included in DCR calculation.

# IMA203CD8 (GEN2) (N=41) – Response over Time in Dose Escalation

## Data cut-off Sep 30, 2024




| | |
|---|---|
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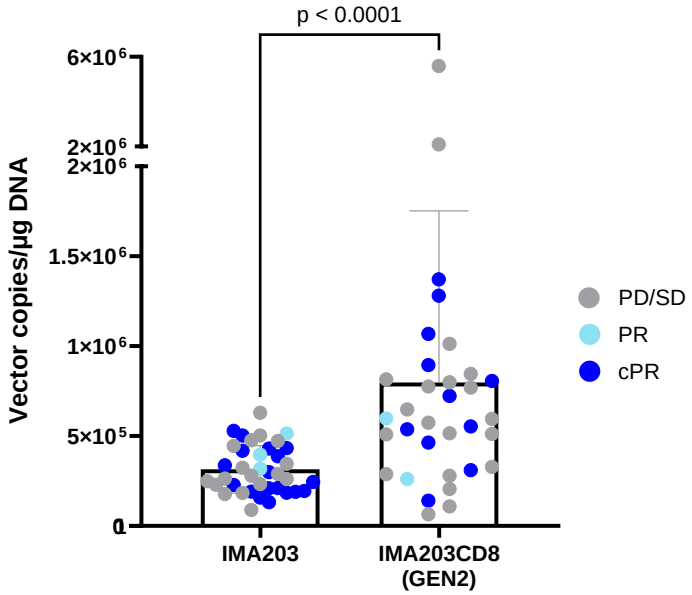
[1] Metabolic CR according to PET-CT [2] Patients off study at data-cut; [3] three patients excluded from tumor shrinkage analysis and figures due to lack of post-treatment assessment; [4] One patient had an early tumor assessment, outside the first assessment visit window and is not included in DCR calculation.

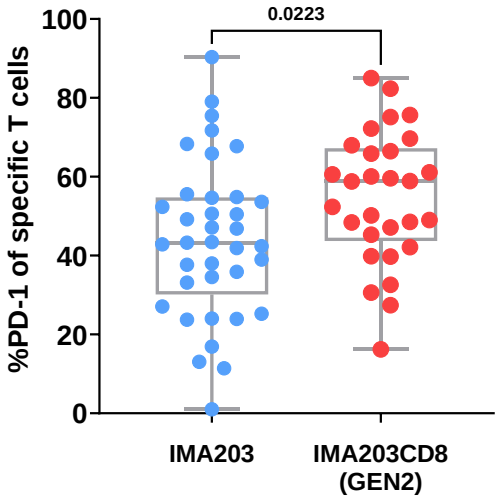
# IMA203CD8 (GEN2): Translational Data Shows Enhanced Pharmacology

## IMA203 Phase 1b vs IMA203CD8 (GEN2)

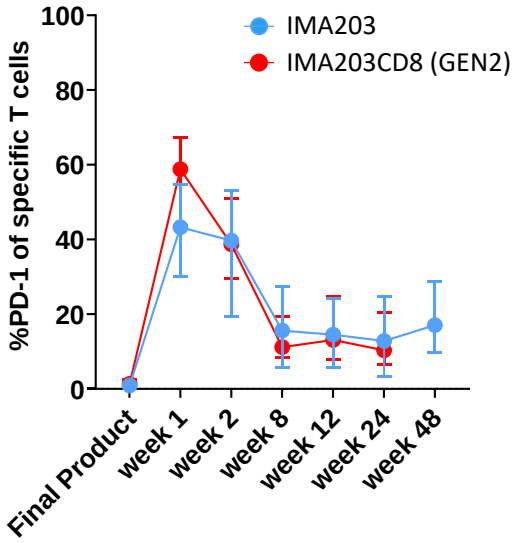
Higher peak expansion ($C_{max}$) of IMA203CD8 T cells when normalized to infused dose



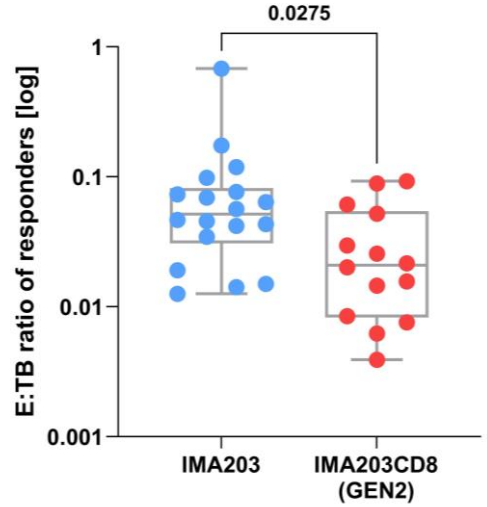

Higher activation levels in IMA203CD8 T cells at week 1…




…without exhaustion over time

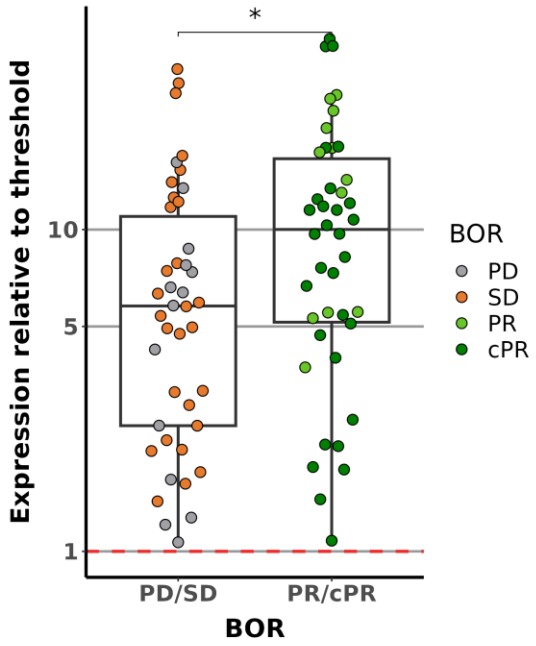



Trend towards responses at lower cell dose and higher tumor burden with IMA203CD8

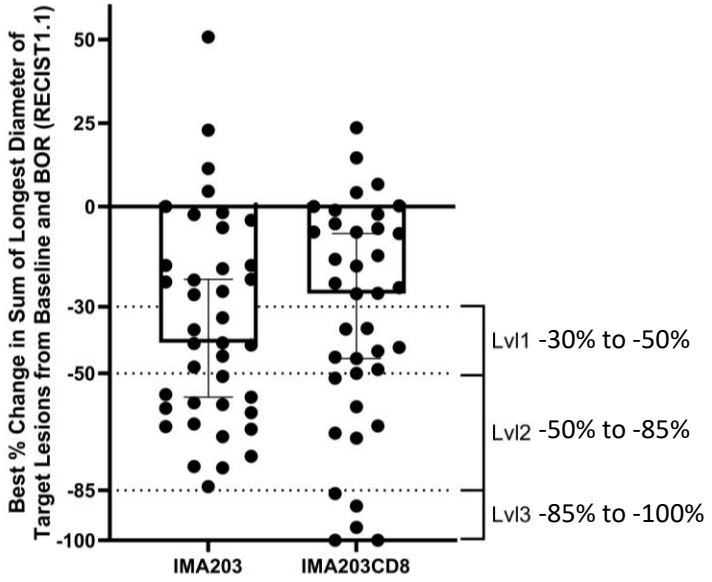


# Opportunity of IMA203CD8 in Medium-Level PRAME Expressing Indications

PRAME expression level associates with clinical activity in IMA203 and IMA203CD8 treated patients

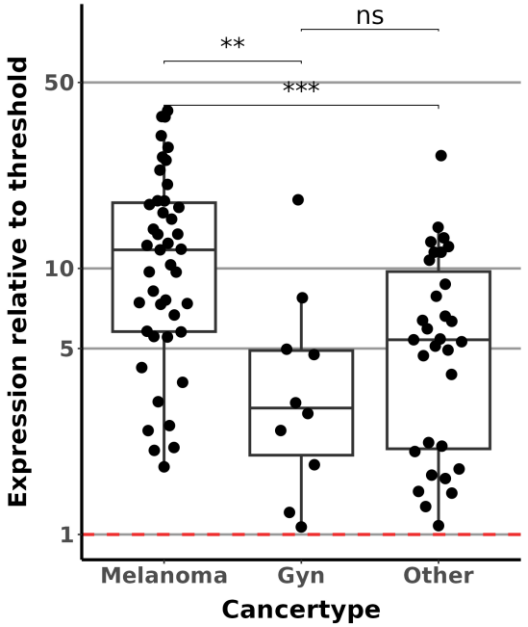



Both IMA203 and IMA203CD8 achieve deep responses despite IMA203CD8 patients receiving lower doses




| | | |
|---|---|---|
| Number of patients | N=39* | N=38 |
| Total infused dose TCR-T cells [x$10^9$] | **5.09** (1.0, 10.2) | **1.48** (0.443, 2.05) |

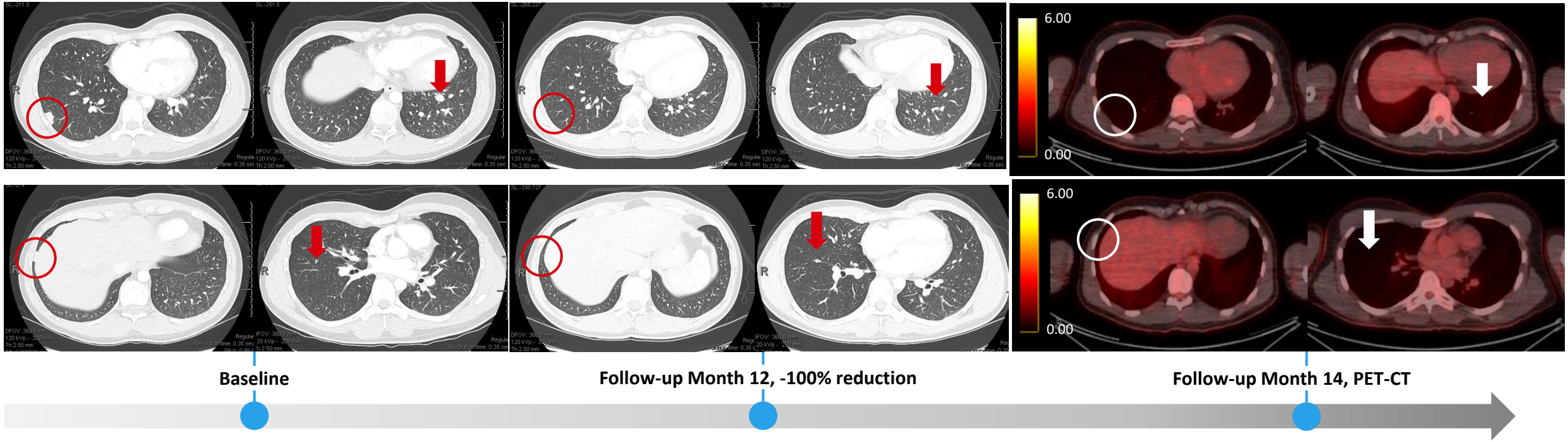
Enhanced pharmacology of IMA203CD8, with potential for higher dosing, opens avenues to explore its full potential in patients with medium-level PRAME expression






* Patients treated at RP2D during Ph1b with evaluable post baseline assessments at data-cut off IMA203: Aug 23, 2024

# Patient Case DL4b-04: Synovial Sarcoma




## 24-year-old male patient with complete remission according to PET imaging after 14 months post infusion

- 1 prior systemic treatment line: Doxorubicin + Ifosfamide + Mesna
- 3 years of cancer history
- At BL: 33.4 mm TL sum in lung, NTL in lymph nodes and lung
- Received ~$2.05x10^9$ IMA203CD8 TCR-T cells
- Metabolic CR on investigator-initiated PET month 14 post infusion
- Ongoing PR at 14+ months post infusion with -100% reduction according to RECIST 1.1


Images courtesy of treating physician (Dr. Dejka Araujo, University of Texas, MD Anderson Cancer Center)
Data cut-off Sep 30, 2024

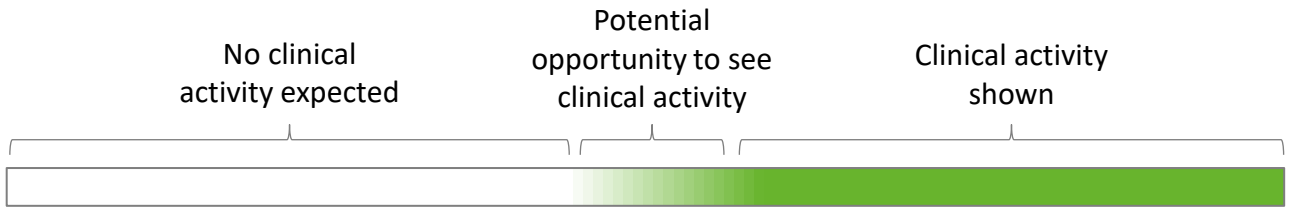
# ACTengine® IMA203CD8 (GEN2) TCR-T Monotherapy Targeting PRAME

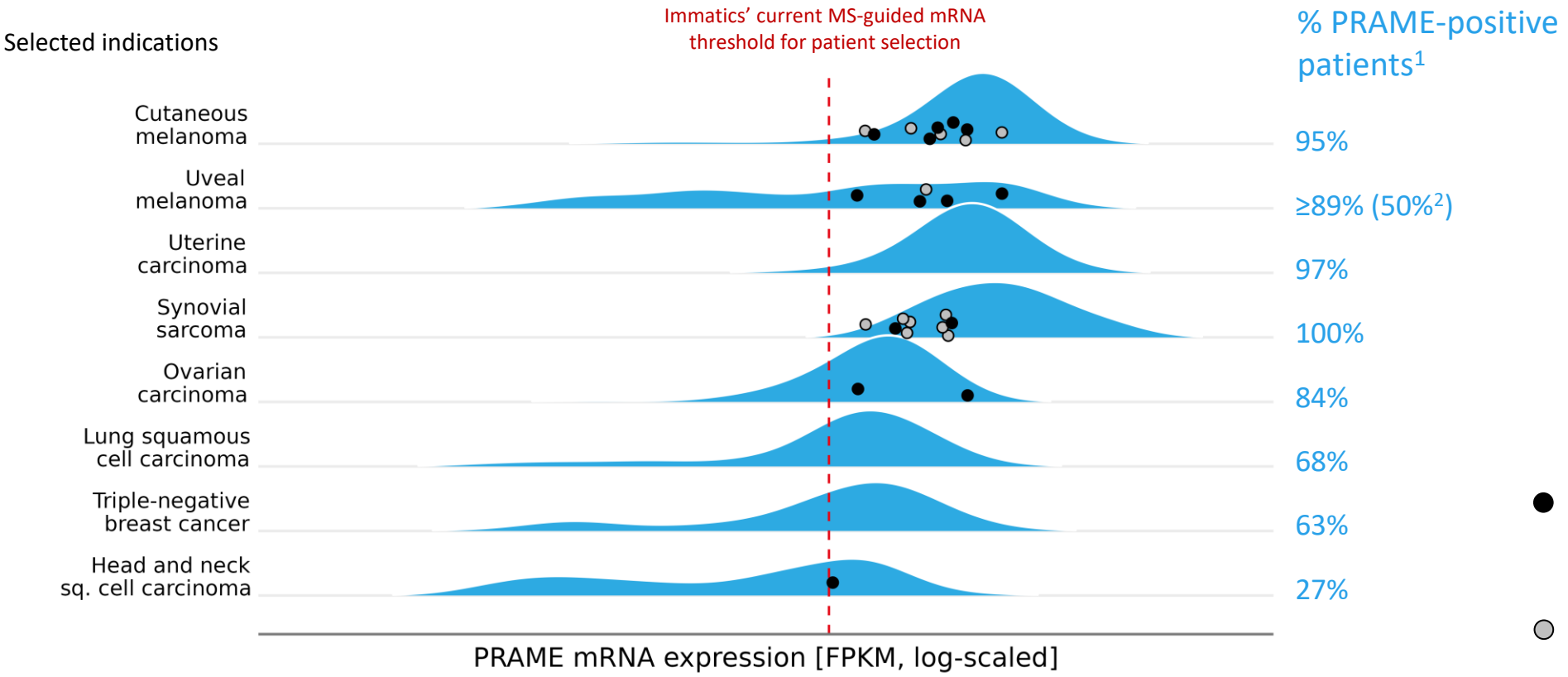
## Summary of IMA203CD8 Clinical Data and Planned Next Steps

- Manageable tolerability with most frequent ≥Grade 3 AEs being expected cytopenia
  - DLTs in 2 patients at DL4b triggered dosing adjustment to DL4a
  - Manageable tolerability in patients at DL4a combined with modifications of the eligibility criteria and IL-2 scheme allows further exploration of higher doses
- Deep and durable objective responses already observed at low doses (median: 1.48 x$10^9$ T cells)
  - 41% (14/34) cORR and tumor shrinkage in 84% (32/38) of patients including two patients with complete response of target lesions
  - 9.2 months median DOR with 3 confirmed responses ongoing at 1+ year
- Opportunity of IMA203CD8 in medium-level PRAME expressing indications
  - Association of PRAME expression with clinical activity in IMA203 and IMA203CD8 treated patients
  - Deep responses with IMA203CD8, even though applied dose still lower than IMA203
- **Dose escalation with and without post-infusion low-dose IL-2 is ongoing** to investigate the full clinical potential of IMA203CD8 in hard-to-treat solid tumors such as ovarian cancer, endometrial cancers and triple-negative breast cancer

# Potential of IMA203 in Additional Solid Cancer Indications

## Based on PRAME Expression in IMA203 and IMA203CD8 (GEN2) Responders




● PRAME mRNA expression in IMA203 (GEN1) (n=14)
Data cut-off Aug 23, 2024

○ PRAME mRNA expression in IMA203CD8 (GEN2) responders (n=13)
Data cut-off Sep 30, 2024

IMA203

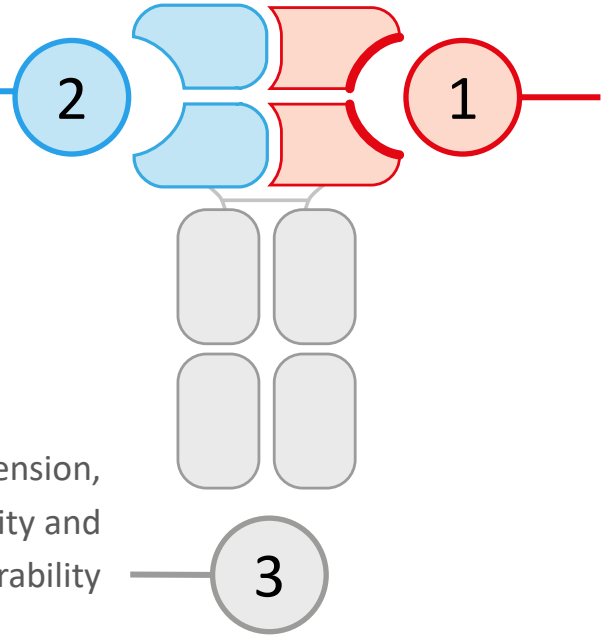
PRAME target expression distribution (blue histogram) based on TCGA RNAseq data, patient data (black dots) based on IMADetect® qPCR testing of screening biopsies; [1] PRAME target prevalence is based on TCGA RNAseq data combined with a proprietary MS-guided RNA expression threshold; [2] PRAME target prevalence in uveal melanoma based on IMADetect® qPCR testing of screening biopsies from clinical trial patients (n=61) demonstrates substantial higher prevalence of 89% 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

# TCER® – TCR Bispecifics

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

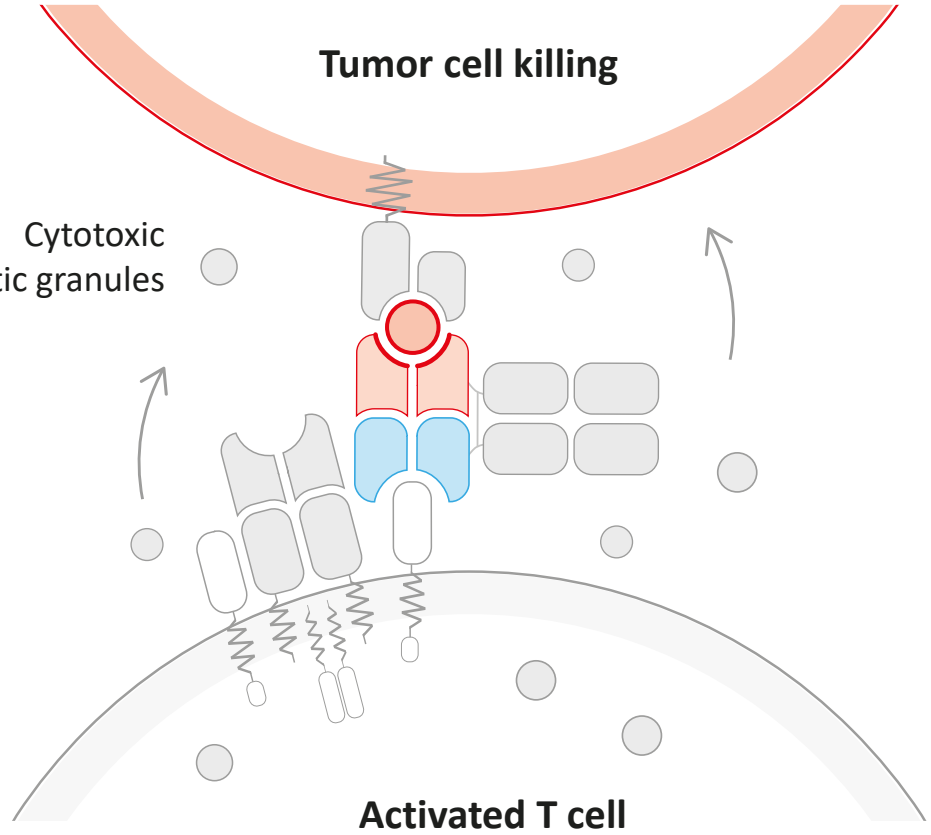
## Proprietary TCER® Format Consisting of Three Distinct Elements

**Low-affinity**
T cell recruiter
against CD3/TCR



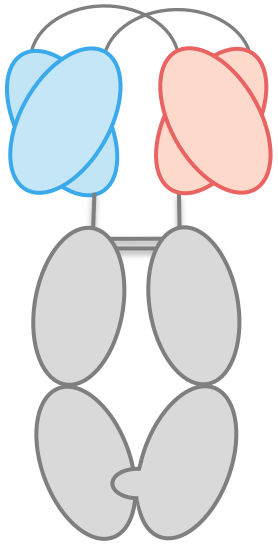

**High-affinity** TCR domains targeting **XPRESIDENT®-selected** tumor-specific peptide-HLA molecules

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




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

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



1 **pHLA targeting TCR**

- ✓ **High-affinity** (single digit nM) TCR targeting **XPRESIDENT®-selected** tumor-specific peptide-HLA molecules
- ✓ Broad therapeutic window through **XPRESIDENT®-guided** affinity maturation (>1000x)[1]
- ✓ **Complete tumor eradication** in mouse xenograft models at low doses

2 **T cell recruiting antibody**

- ✓ **Low-affinity** (triple digit nM) T cell recruiter against both **TCR & CD3**
- ✓ **Optimized biodistribution** aiming for enrichment at tumor site and **prevention of CRS**[2]
- ✓ **Superior anti-tumor activity** in mouse models as compared to widely used CD3 recruiters

3 **Next-generation TCER® format**

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

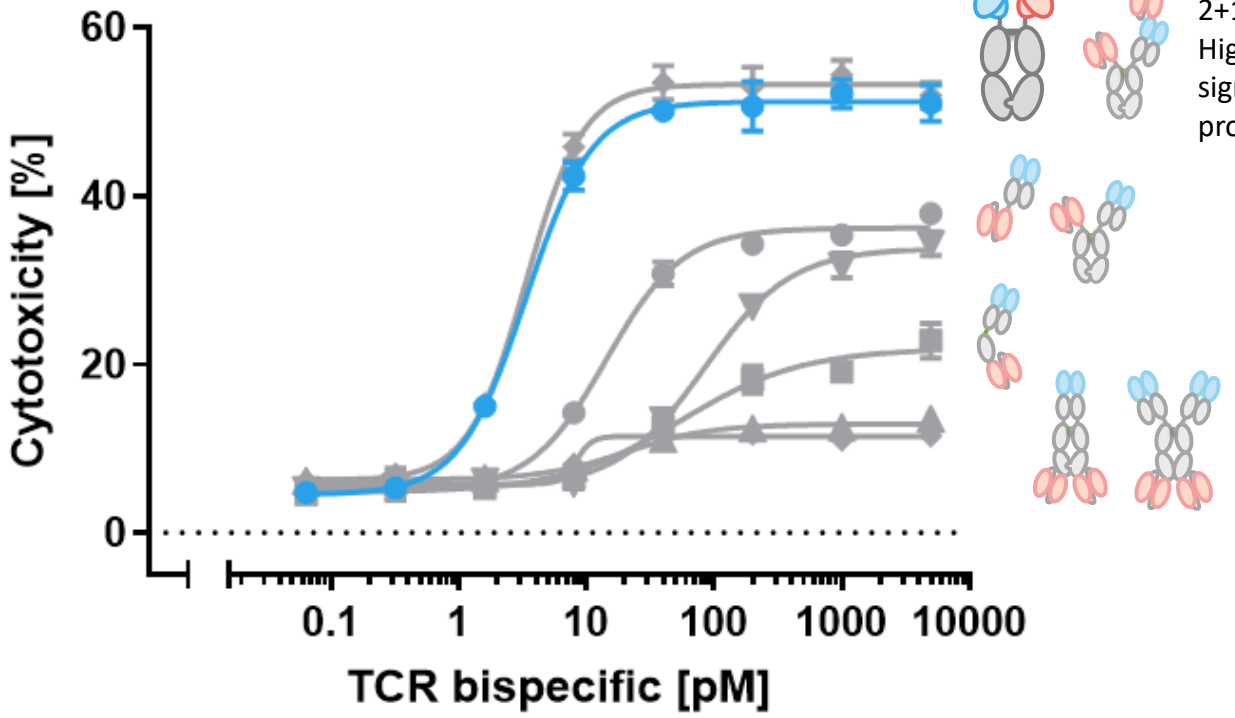
**Our TCER® format is designed to maximize efficacy while minimizing toxicities in patients**



[1] As compared to natural TCR; [2] Based on literature data for other low-affinity recruiters (e.g. Harber *et al.*, 2021, Nature; Trinklein *et al.*, 2019, mAbs);
[3] Production in mammalian cells (CHO cells); [4] Based on preclinical testing

# Potency of Our Proprietary TCR Bispecific Format TCER®

**Killing of target-positive cells by different TCR Bispecifics[1]**




**TCER®**



2+1 TCR bispecific format:
High potency was linked to a significantly reduced specificity profile[2]

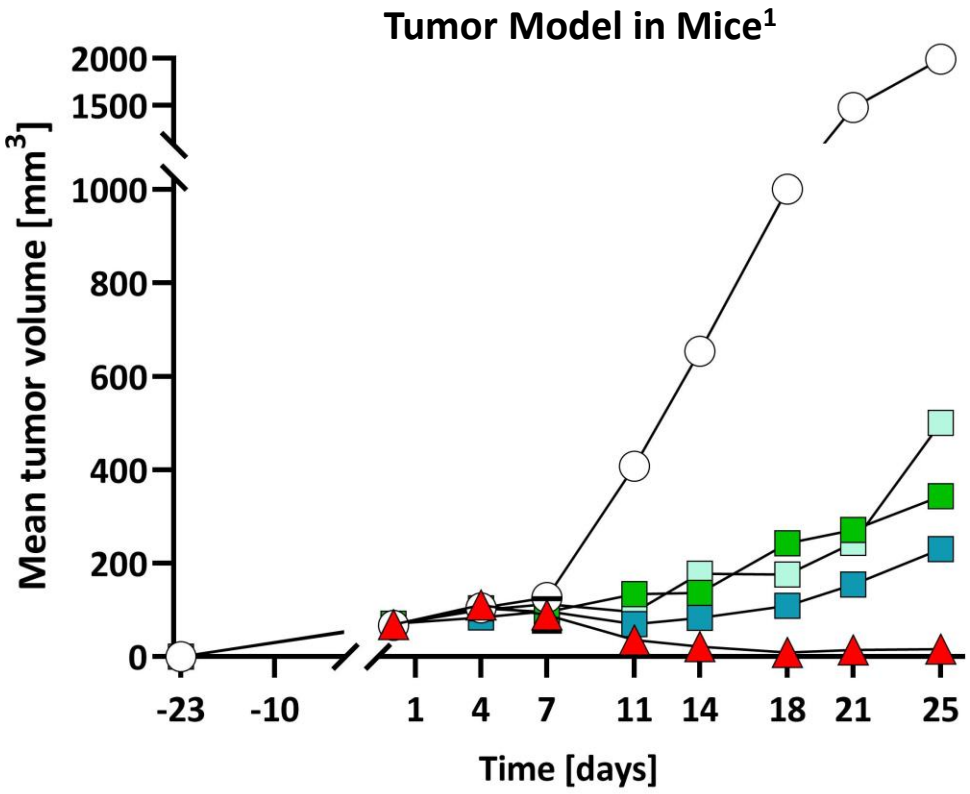
- Seven different TCR Bispecific formats were evaluated with a pHLA targeting TCR and the identical T cell recruiting antibody
- TCER® format had higher combination of potency and specificity[2] than six alternative TCR Bispecific format designs evaluated

**Flexible Plug-and-play platform: TCER® format successfully validated for different TCRs & different T cell recruiting antibodies**


[1]Data presented at SITC 2022; [2]Preclinical data on specificity not shown

# TCER® Format Is Designed for Optimized Efficacy and Safety

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




Vehicle

TCER®-Ab1

TCER®-Ab2

TCER®-Ab3

**Widely used T cell recruiting Ab (3 variants)**
medium to high affinity
(single to double digit nM)

IMA402

**Immatics' T cell recruiting Ab**
low affinity (triple digit nM)

n = 6 mice/treatment group,
n = 10 mice in vehicle group,
2 donors/group
**Dose: 0.025 mg/kg**

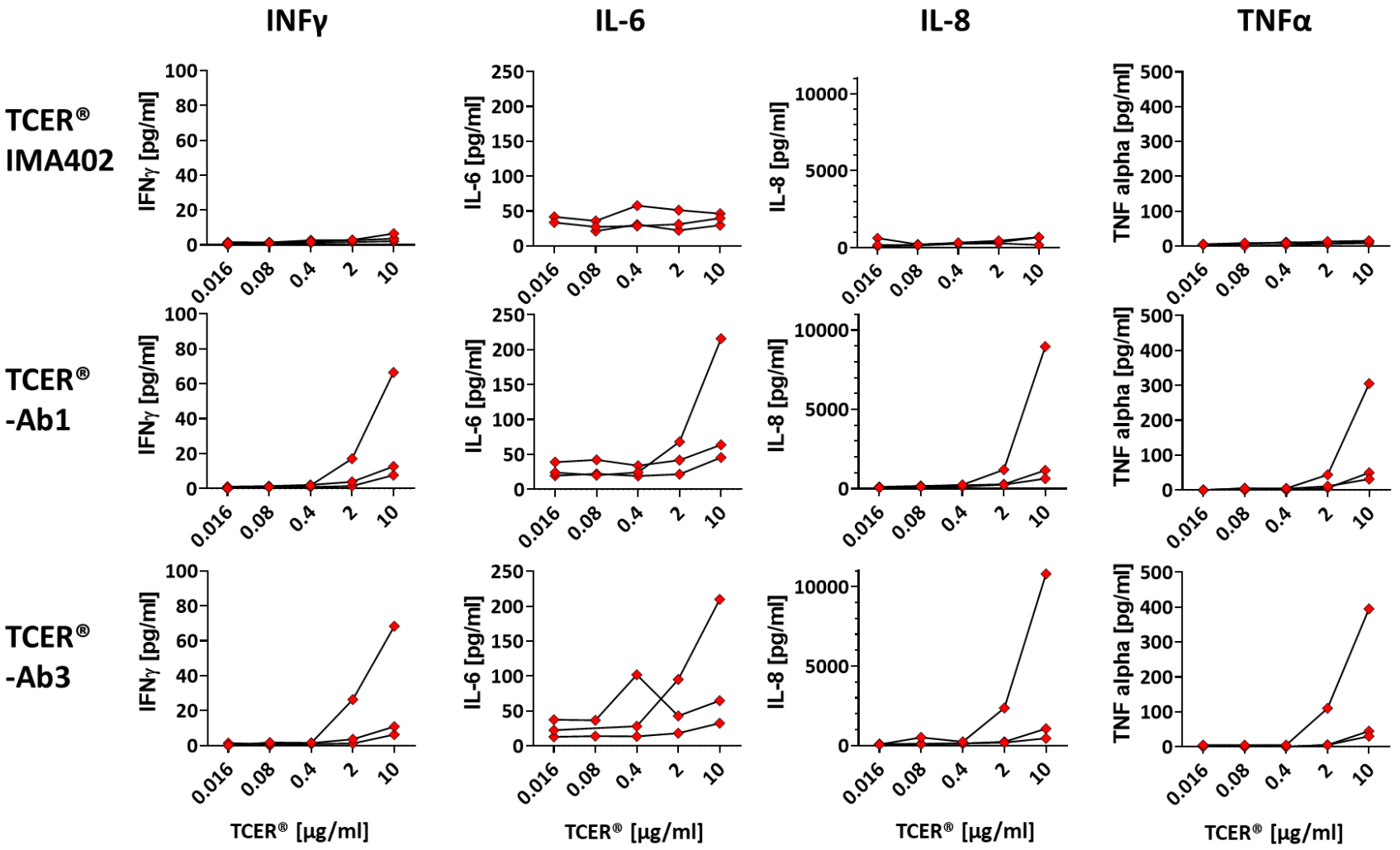
Proprietary, **low-affinity T cell recruiting region** demonstrates superior tumor control compared to analogous TCER® molecules designed with higher-affinity variants of a widely used recruiter



[1] Hs695T xenograft model in NOG mice, tumor volume of group means shown

# TCER® Format Is Designed for Optimized Efficacy and Safety

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




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

# Our TCER® Portfolio

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

CLINICAL

**IMA401**

- MAGEA4/8 peptide presented by HLA-A*02:01
- Dose escalation ongoing, first clinical data presented at ESMO 2024

**IMA402**

- PRAME peptide presented by HLA-A*02:01
- Start of clinical trial in Aug 2023, first clinical data published in November 2024

PRECLINICAL

**IMA40x**

Several innovative programs

- Undisclosed peptides presented by HLA-A*02:01 and other HLA-types
- TCER® engineering and preclinical testing ongoing

Potential for addressing different indications and large patient populations with novel, off-the-shelf TCR Bispecifics

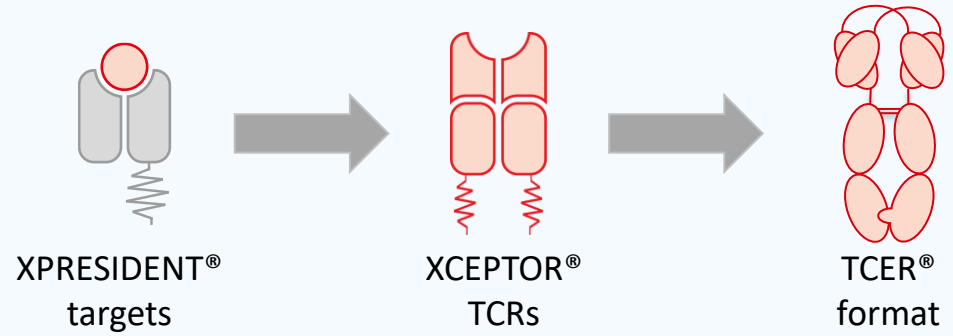
The current collaboration with Moderna includes the development of mRNA-enabled *in vivo* expressed TCER® molecules

# *In Vivo* Expressed TCER® Molecules Targeting Cancer-specific pHLA Targets

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

### Immatics

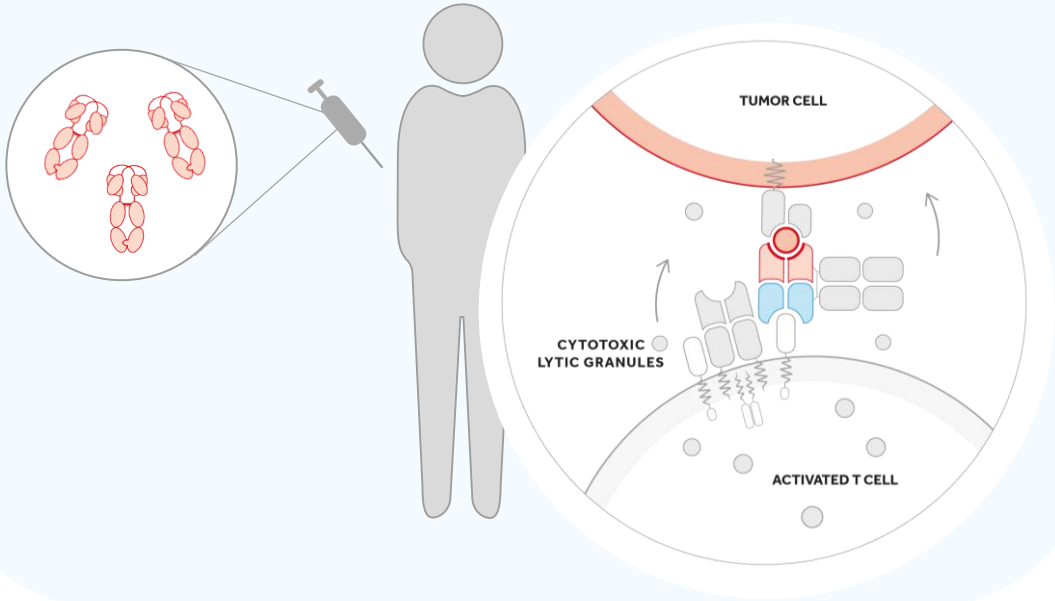
Proprietary cancer targets & TCR Bispecifics format



XPRESIDENT® targets

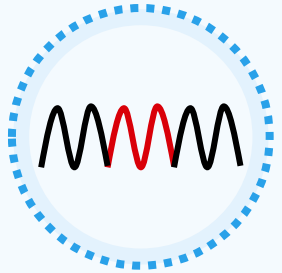
XCEPTOR® TCRs

TCER® format

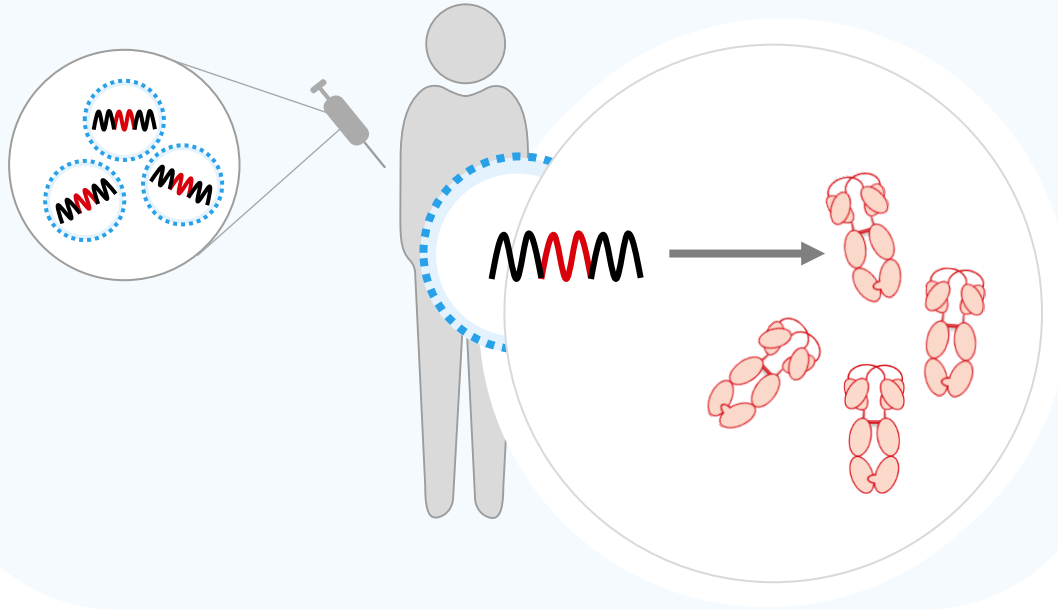



### Moderna

Delivery of TCER® biologics through mRNA



mRNA-encoded TCER® molecule

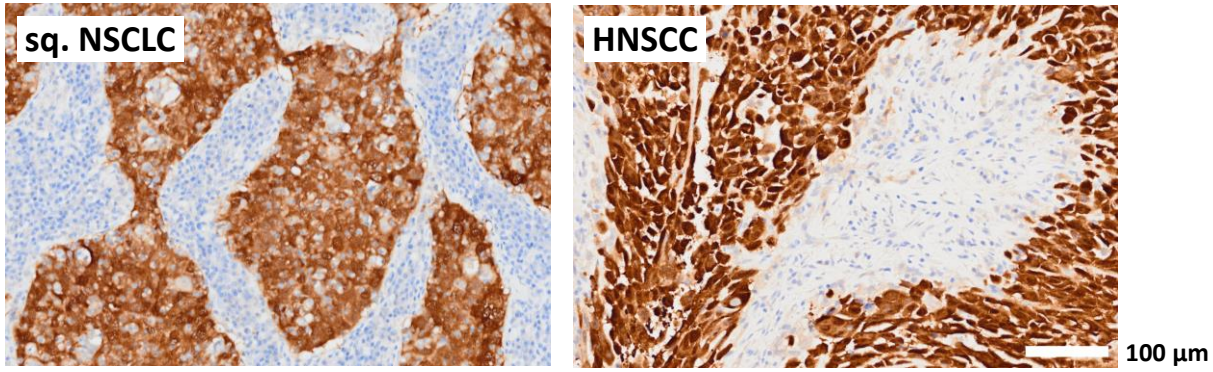


# TCER® IMA401 Targeting MAGEA4/8

# TCER® IMA401 Targeting MAGEA4/8

## Higher Target Density of MAGEA4/8 Peptide

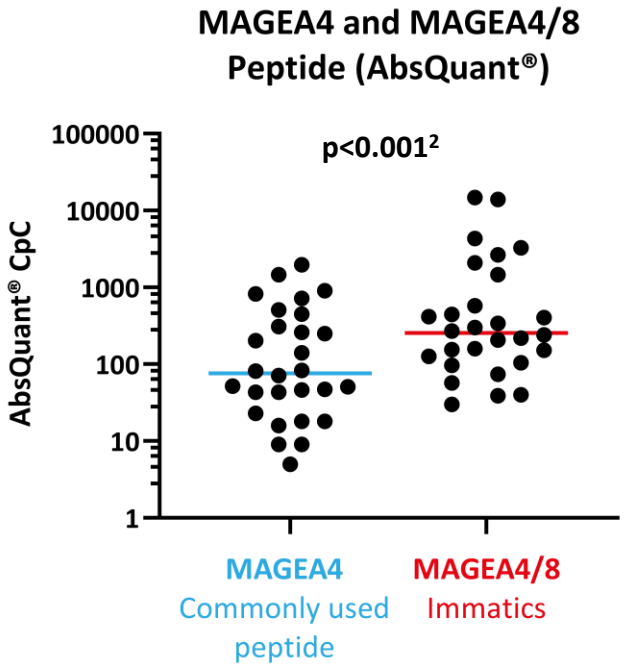
### MAGEA4 protein detection in tumor samples (IHC)




### MAGEA4/8 target prevalence in selected cancer indications

| Indications | Target prevalence[1] [%] | Number of addressable patients* |
|---|---|---|
| Squamous non-small cell lung carcinoma | 52% | 22k |
| Head and neck squamous cell carcinoma | 36% | 7k |
| Bladder carcinoma | 29% | 9k |
| Ovarian carcinoma | 23% | 4k |
| Esophageal carcinoma | 23% | 3k |
| Small cell lung cancer | 21% | 4k |
| Triple-negative breast cancer | 20% | 2k |
| Gastric adenocarcinoma | 14% | 3k |
| Cutaneous melanoma | 18% | 2k |
| Non-small cell lung adenocarcinoma | 9% | 6k |

*1L+ Unresectable or Metastatic Addressable Patient Populations (US, UK, EU4 in 2025), total MAGE A4/A8+ and HLA-A*02+




MAGEA4/8 target is presented at >5-fold higher target density[3] than a commonly used MAGEA4 target peptide



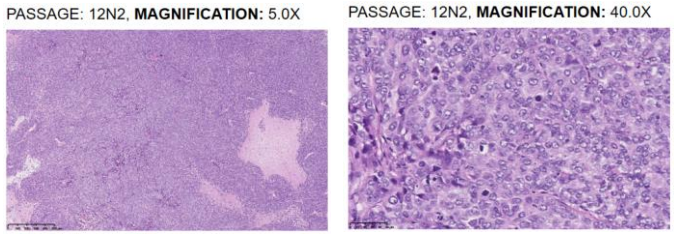
[1]MAGEA4/8 target prevalences are based on TCGA and in-house data combined with a XPRESIDENT®-determined target individual MS-based mRNA expression threshold; qPCR-threshold for patient screening; [2]Students paired T test; [3]Copy number per tumor cell (CpC) measured on a paired-sample basis by AbsQuant®, i.e. comparing MAGEA4 vs. MAGEA4/8 peptide presentation on same sample

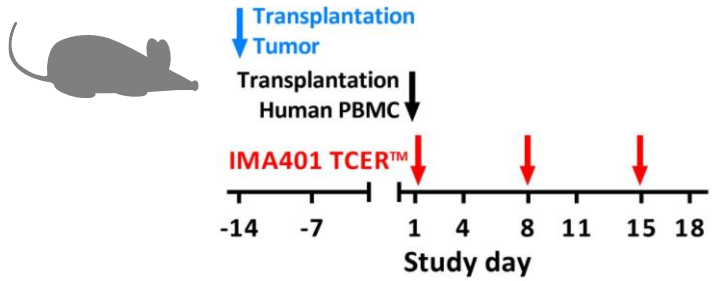
# TCER® IMA401 (MAGEA4/8) – Assessment of Anti-Tumor Activity *in vivo*

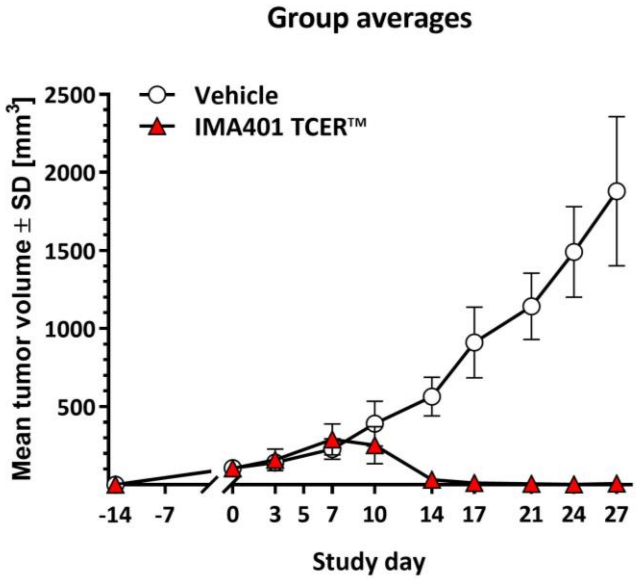
## Patient-Derived Tumor Model

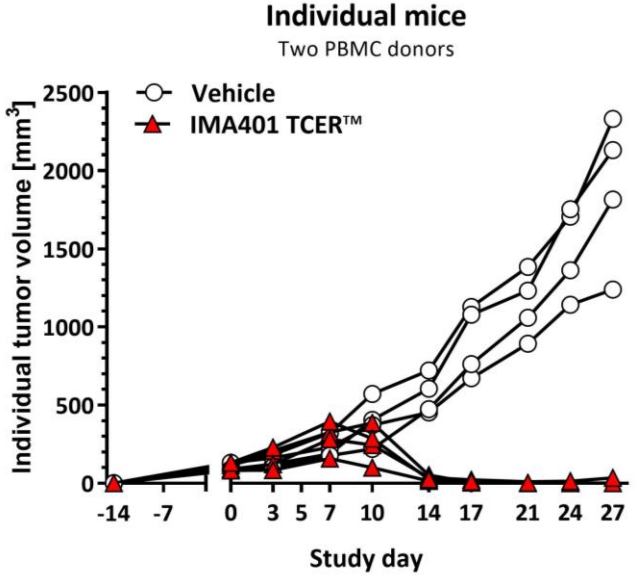
**NSCLC adenocarcinoma:**

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



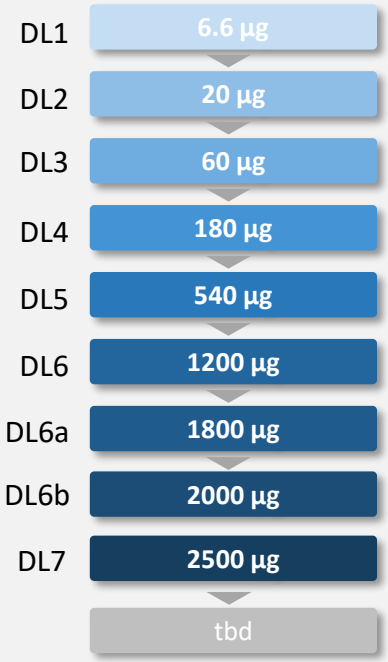




- TCER® IMA401 shows **high anti-tumor activity in Patient-derived xenograft model** of non-small cell lung adenocarcinoma
- **Remission observed in all mice (3 out of 4 mice with complete remission)**

# Trial Design – IMA401-101 Phase 1a Dose Escalation

## First-in-Human Basket Trial Targeting the MAGEA4/8 Peptide in Solid Tumors




### Total safety population (N=35)

- MABEL-based starting dose
- Dose escalation based on cohorts of 1-6 patients using adaptive design (BLRM model)
- Four initial q1w step dosings[1] up to target dose, q2w after reaching target dose[2]

- MTD not yet determined
- Dose escalation ongoing to optimize dosing intervals and schedule

### Objectives

**Primary:**

- Determine MTD and/or RP2D

**Secondary:**

- Tolerability
- Pharmacokinetics
- Initial anti-tumor activity

### Key Eligibility Criteria

- Recurrent and/or refractory **solid tumors**
- HLA-A*02:01 positive
- MAGEA4/8-positive as confirmed by mRNA-based assay[3]
- ECOG status 0-2
- Received or not eligible for all available indicated standard of care treatments



[1]Step dosing with 300 µg and 600 µg introduced at DL6; Low-dose dexamethasone pre-medication used at higher dose levels as used with other approved bispecific products has been implemented as preventive measure for continued dose escalation; Patients can increase their dose to previously cleared dose levels; [2]q2w: once every two weeks, weekly (q1w) dosing was applied up to DL5; [3]IMADetect®: proprietary mRNA-based assay using Immatics' MS-guided threshold; BLRM: Bayesian logistic regression model; MTD: Maximum tolerated dose.

# Baseline Characteristics

## Heavily Pre-treated Patients with a Broad Range of Tumor Types

| Characteristic | Safety Population N=35 | Efficacy-evaluable Population[1] N=29 | Patients with relevant IMA401 doses and MAGEA4/8$^{high}$ levels[2] N=17 |
|---|---|---|---|
| **Age** | | | |
| Median (min, max) | 62 (19, 82) | 63 (35, 82) | 64 (35, 82) |
| **ECOG performance status** | | | |
| 0 - n [%] | 10 [28.6] | 6 [20.7] | 3 [17.6] |
| 1 - n [%] | 23 [65.7] | 21 [72.4] | 12 [70.6] |
| 2 - n [%] | 2 [5.7] | 2 [6.9] | 2 [11.8] |
| **Prior lines of systemic treatment** | | | |
| Median (min, max) | 4 (2, 8) | 3 (2, 8) | 4 (2, 8) |
| **LDH at baseline** | | | |
| ≤ 1xULN [%] | 51.4 | 55.2 | 41.2 |
| 1-2xULN [%] | 40.0 | 41.4 | 58.8 |
| > 2xULN [%] | 8.6 | 3.4 | 0.0 |
| **Baseline tumor burden** | | | |
| Median target lesion sum of diameter [mm] (min, max) | 74 (15, 202.8) | 80 (15, 202.8) | 84 (18, 202.8) |
| **Number of organs with metastases** | | | |
| Median (min, max) | 3 (1, 6) | 3 (1, 6) | 3 (1, 6) |
| **Liver/ Brain Lesions** | | | |
| [% of patients] | 40.0 | 41.4 | 47.1 |

[1]Efficacy Analysis Set (EAS) prospectively defined in the study protocol: patients who received at least four IMA401 infusions and had at least one post-baseline efficacy assessment or clinical progression. Three patients did not receive all four infusions due to clinical progression and three patients awaiting their first scans as of the data cut-off date are not included in the EAS; [2]Patients in this analysis had received IMA401 infusions at ≥1 mg and showed MAGEA4/8 target expression higher than the MAGEA4/8 qPCR threshold. LDH: Lactate dehydrogenase; ULN: Upper limit of normal.

# IMA401 Demonstrates Manageable Tolerability in N=35 Patients

## Most Frequent Related AEs were Lymphopenia, CRS and Neutropenia

| Treatment-related AEs[1], n [%] | All Grades | ≥ Grade 3 |
|---|---|---|
| Lymphopenia | 12 [34] | 11 [31] |
| Cytokine release syndrome | 11 [31] | 0 |
| Neutropenia | 8 [23] | 5 [14] |
| Facial pain | 6 [17] | 2 [6] |
| Anaemia | 5 [14] | 4 [11] |
| Thrombocytopenia | 5 [14] | 2 [6] |
| Headache | 5 [14] | 1 [3] |
| Hypertension | 4 [11] | 2 [6] |
| Leukopenia | 4 [11] | 2 [6] |
| Fatigue | 4 [11] | 0 |
| Nausea | 3 [9] | 0 |
| Hypoxia | 2 [6] | 1 [3] |
| Aspartate aminotransferase increased | 1 [3] | 1[3] |
| Febrile neutropenia | 1 [3] | 1[3] |
| Pneumonia | 1 [3] | 1[3] |
| Sinus tachycardia | 1 [3] | 1[3] |

| TEAEs, n [%] | All Grades | ≥ Grade 3 |
|---|---|---|
| Any | 32 [91] | 26 [74] |
| Treatment-related | 28 [80] | 19 [54] |

- Overall **manageable tolerability** profile
- **Most frequent/relevant related AEs** were
  - transient lymphopenia,
  - mild to moderate CRS (23% Grade 1, 9% Grade 2, **no Grade ≥ 3**), majority at first dose
  - neutropenia[2] occurred mostly at initial target dose and fully resolved in all cases except one (see below)
  - one possibly related death (pneumonia in the context of lung tumor progression and concurrent neutropenia) as previously reported[3]
- **MTD not reached** based on the BLRM



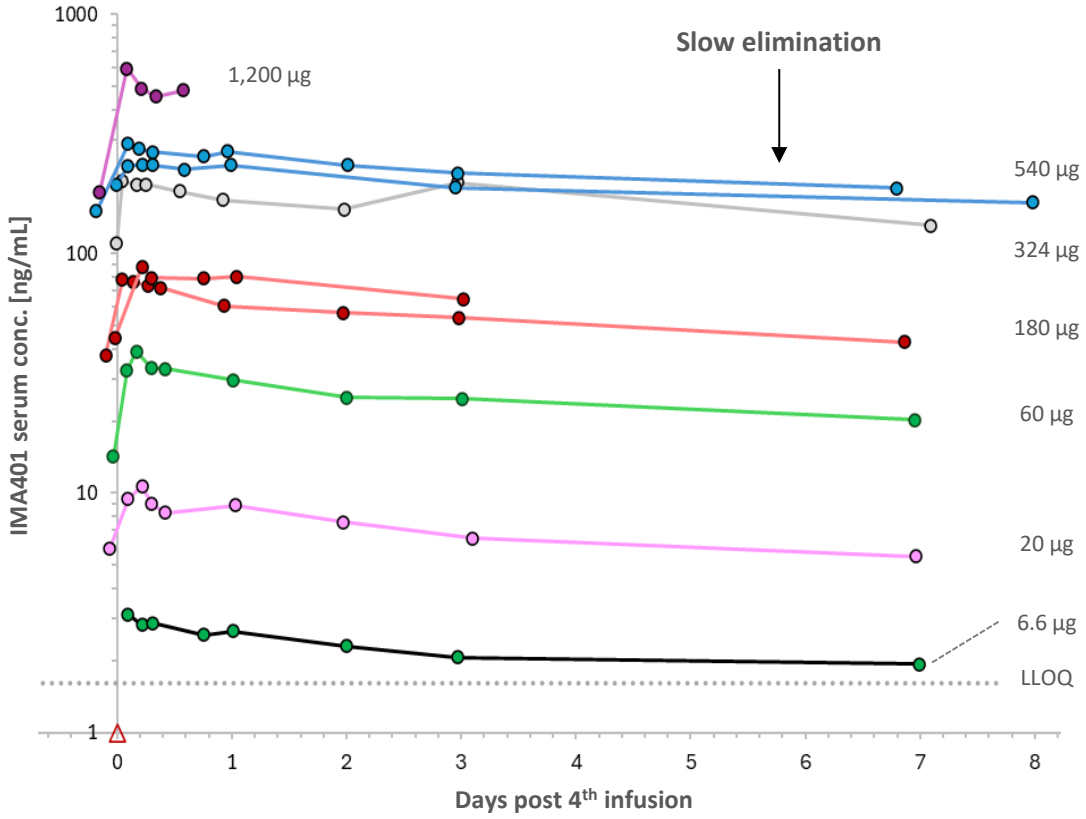
[1]All treatment-emergent adverse events (TEAEs) at least possibly related to IMA401 infusion with grade 1-2 occurring in at least 9% of patients and all events with grade 3-5; [2]with three dose-limiting events at 2.5 mg (DLT), neutropenia observed in patients with and without dexamethasone pre-medication; [3]reported in Annual Report 2023, patient did not receive dexamethasone pre-medication; CRS: Cytokine Release Syndrome; BLRM: Bayesian logistic regression model; MTD: Maximum tolerated dose.

# IMA401 Pharmacokinetics

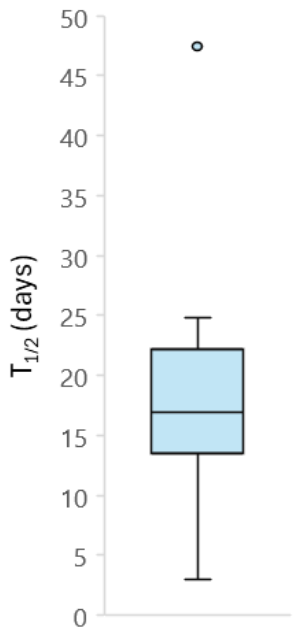
## TCER® Format Shows Extended Half-Life in Solid Cancer Patients

**PK profiles**

(1 week profiles after 4th IMA401 infusion)




**Median half-life: 16.9 days (N=16)[1]**




**Observed $T_{1/2}$ > 2 weeks**

- Confirms "antibody-like" half-life predicted by preclinical *in-vivo* data[2]
- Supports exploring increased dosing intervals of up to q4w and pursuing alignment with typically applied CPI dosing regimens

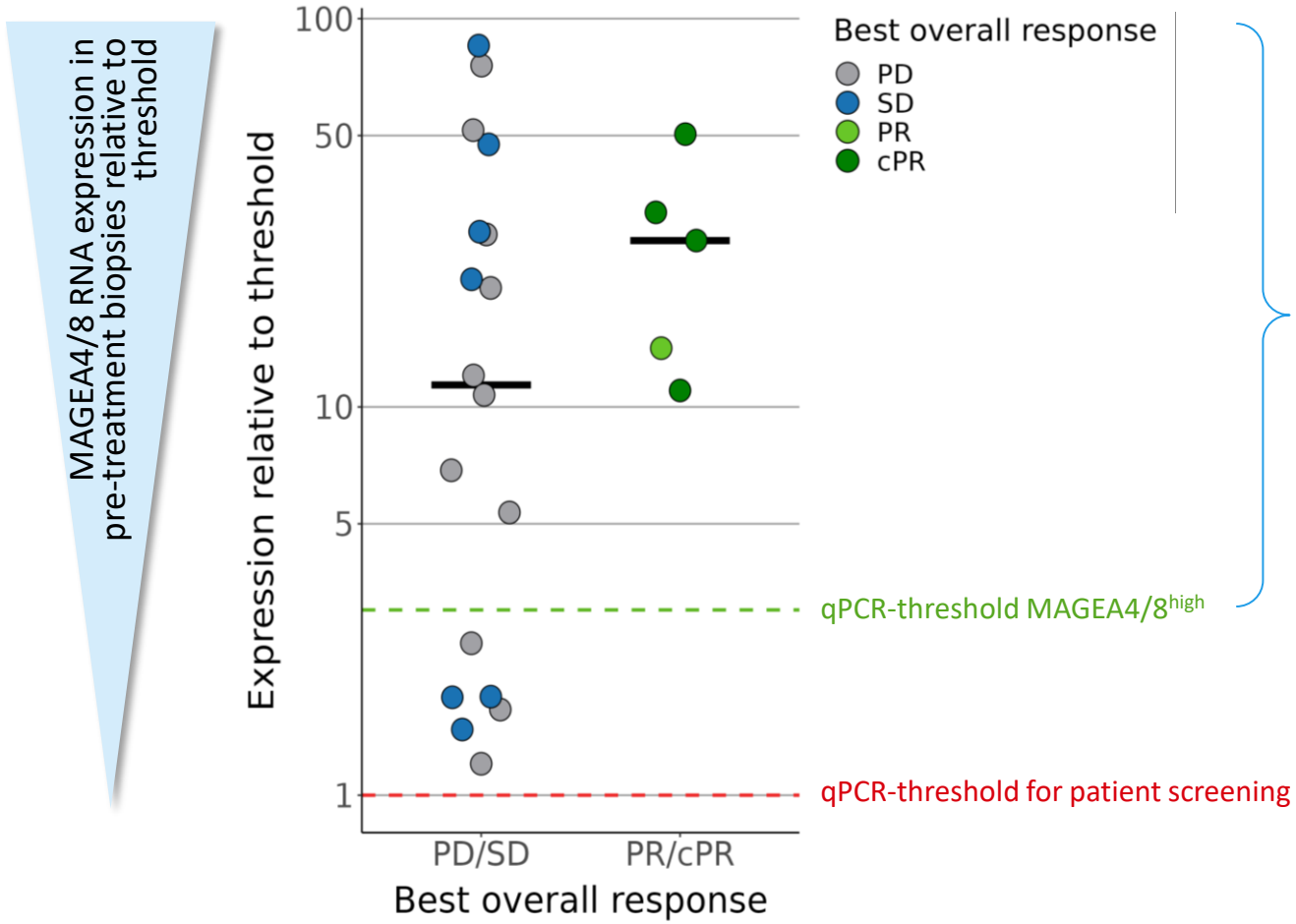
IMA401

[1]Half-lifes derived from 2nd PK profiles close to steady-state. Calculated by non-compartmental analysis (NCA) using Phoenix WinNonlin (Certara); Interquartile range (25%-75% percentile): 13.5-22.2 days; [2]Data presented at European Antibody Congress 2020; Zinn et al., *Nature Cancer*, 2023: https://doi.org/10.1038/s43018-023-00516-z; LLOQ: lower limit of quantification; q4w: once every four weeks. CPI: Checkpoint inhibitor

Data cut-off Jul 23, 2024

# Objective Responses are Associated with Target Expression

## Exploratory Analysis in Patients with MAGEA4/8$^{high}$ Expression at Relevant IMA401 Doses (DL6-7; N=17)



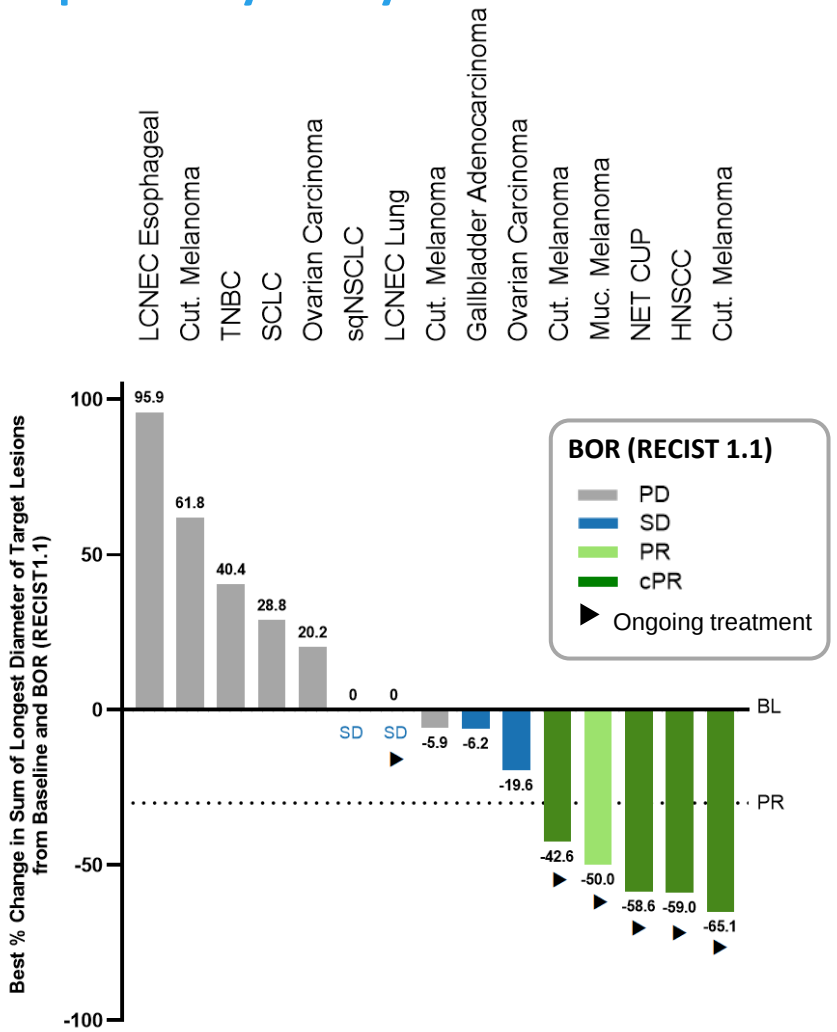

**N=17 patients with relevant IMA401 doses and MAGEA4/8$^{high}$ levels[1]**

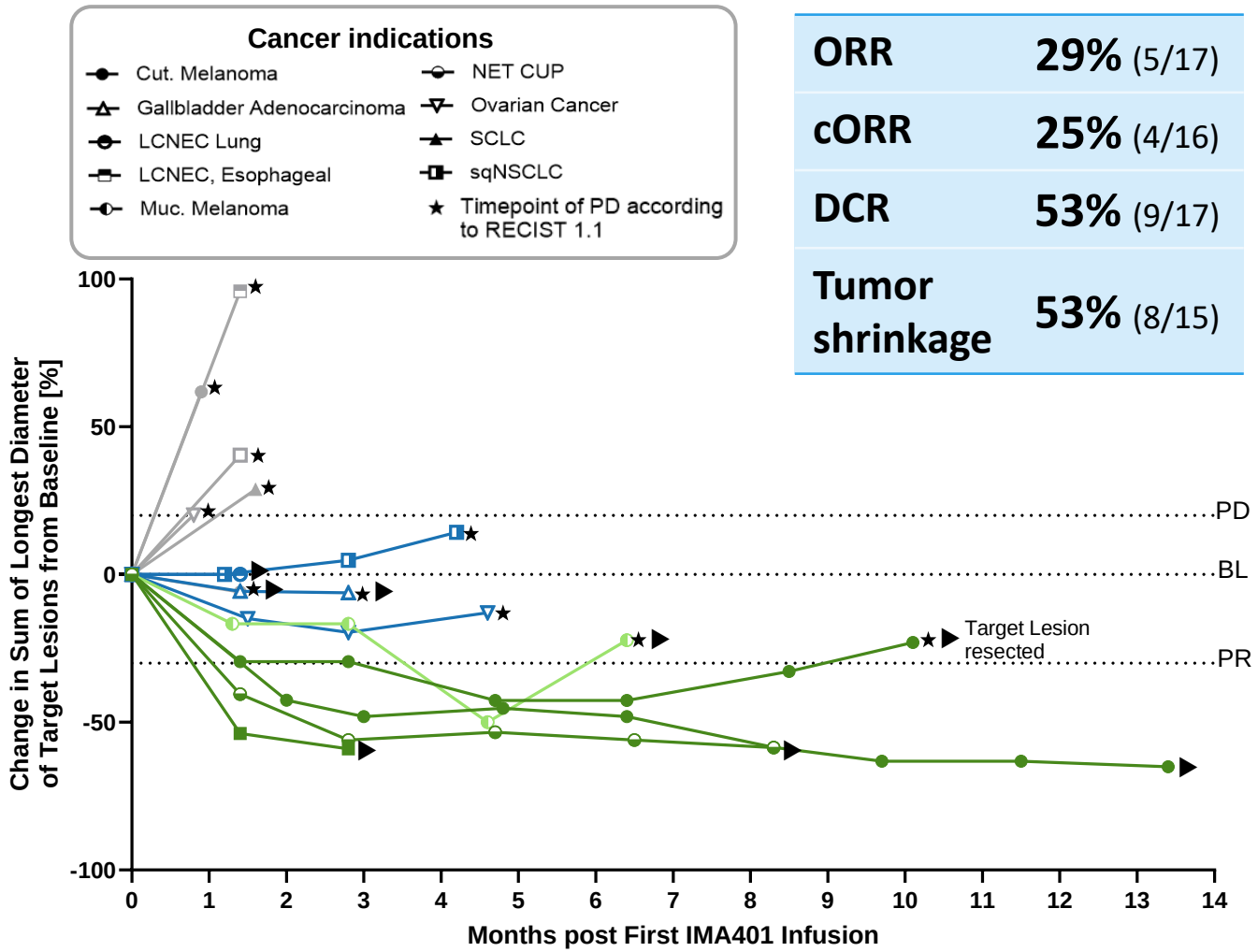


[1]Patients in this analysis had received IMA401 infusions at ≥1 mg and showed MAGEA4/8 target expression above indicated MAGEA4/A8$^{high}$ qPCR threshold (n=17);
PD: Progressive disease; PR: Partial response; cPR: confirmed Partial response; SD: Stable disease.

# IMA401 Demonstrates Initial Anti-Tumor Activity in Multiple Tumor Types

## Exploratory Analysis in Patients with MAGEA4/8$^{high}$ Expression at Relevant IMA401 Doses (DL6-7; N=17*)




| | |
|---|---|
| **ORR** | **29%** (5/17) |
| **cORR** | **25%** (4/16) |
| **DCR** | **53%** (9/17) |
| **Tumor shrinkage** | **53%** (8/15) |

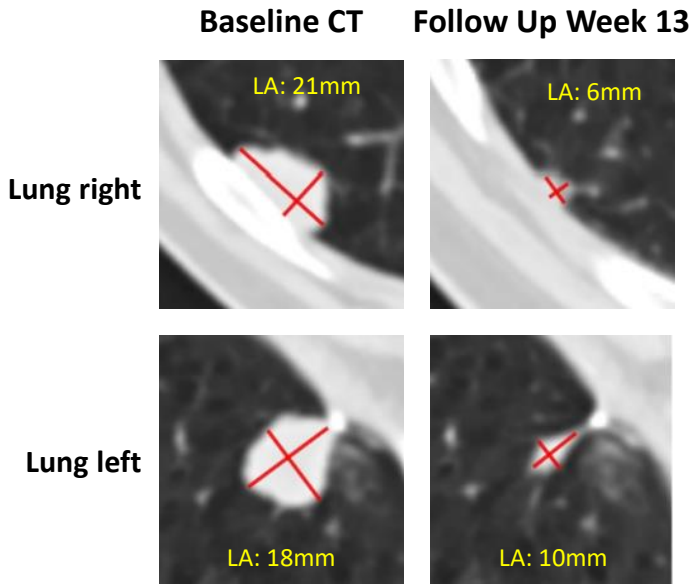
Cancer Indications: Cut.: Cutaneous; HNSCC: Head & Neck Squamous Cell Carcinoma; LCNEC: Large Cell Neuroendocrine Carcinoma; Muc.: Mucosal; NET CUP: Neurodendocrine Tumor, Cancer of Unknown Primary; SCLC: Small Cell Lung Cancer; sqNSCLC: Squamous Non-small Cell Lung Cancer; TNBC: Triple Negative Breast Cancer.



*Patients in this analysis are part of the efficacy analysis set with at least one post-treatment tumor assessment and had received IMA401 infusions at ≥1 mg and showed MAGEA4/8 target expression higher than the MAGEA4/8 qPCR threshold (n=17); 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; two patients not included in tumor shrinkage calculation or shown in the figures as they had clinical progression and post-treatment tumor assessment is not available; PR: Partial Response; cPR: Confirmed Partial Response; SD: Stable Disease.

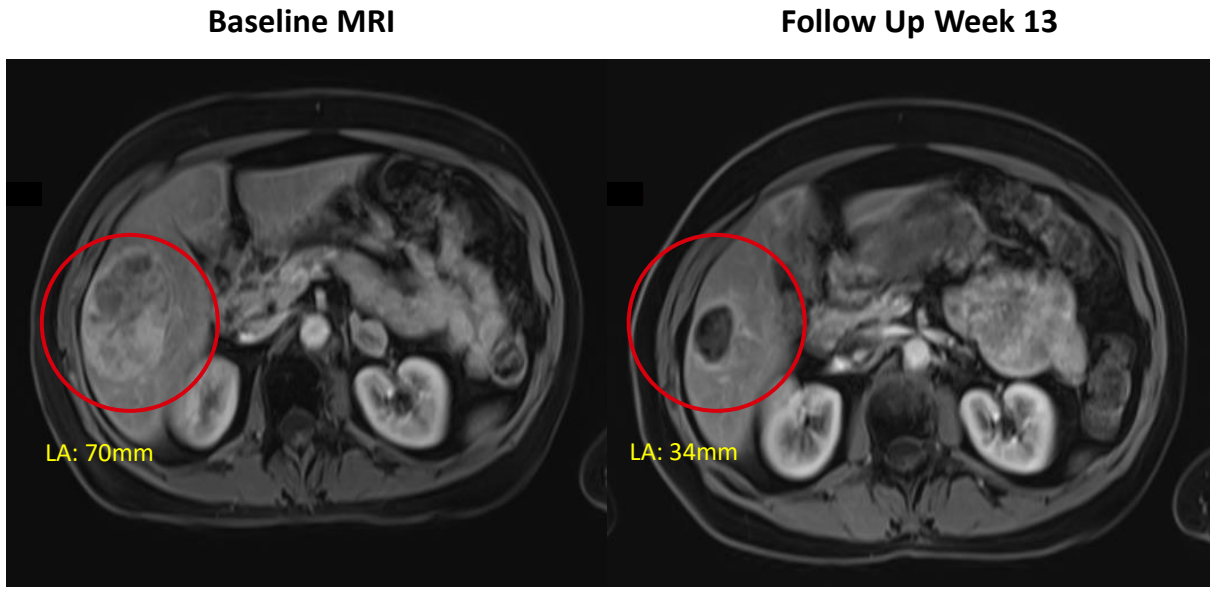
# Clinical Activity in Heavily Pre-Treated Cancer Patients

## 63-year-old male, HNSCC, MAGEA4/8$^{high}$




| Patient Characteristics | Outcomes |
|---|---|
| HNSCC, Hypopharynx | cPR -59% reduction |
| Lesions in lung | cPR ongoing at week 12 post-treatment start |
| 3 prior lines of therapy: Platinum chemotherapy, anti-PD-1/chemotherapy, anti-EGFR/chemotherapy | |

## 60-year-old female, NET CUP, MAGEA4/8$^{high}$




| Patient Characteristics | Outcomes |
|---|---|
| NET CUP | cPR -56% reduction (BOR: -58.6%) |
| Lesions in liver, lung, bone, pancreas, adrenal gland, lymph nodes | cPR ongoing at week 36 post-treatment start |
| 4 prior lines of therapy: Two lines of radiopharmaceuticals, chemotherapy, mTOR inhibitor | |



CT and MRI scans courtesy of treating physicians (Dr. Manik Chatterjee, University Hospital Wuerzburg and Dr. Max-Felix Häring, Eberhard Karls University Tuebingen); HNSCC: Head and neck squamous cell carcinoma; NET CUP: Neuroendocrine tumor-cancer of unknown primary; LA: Long axis; cPR: confirmed Partial response; BOR: Best overall response

# First-in-human Data of IMA401 TCER® Targeting MAGEA4/8

## Presentation at ESMO on September 16, 2024

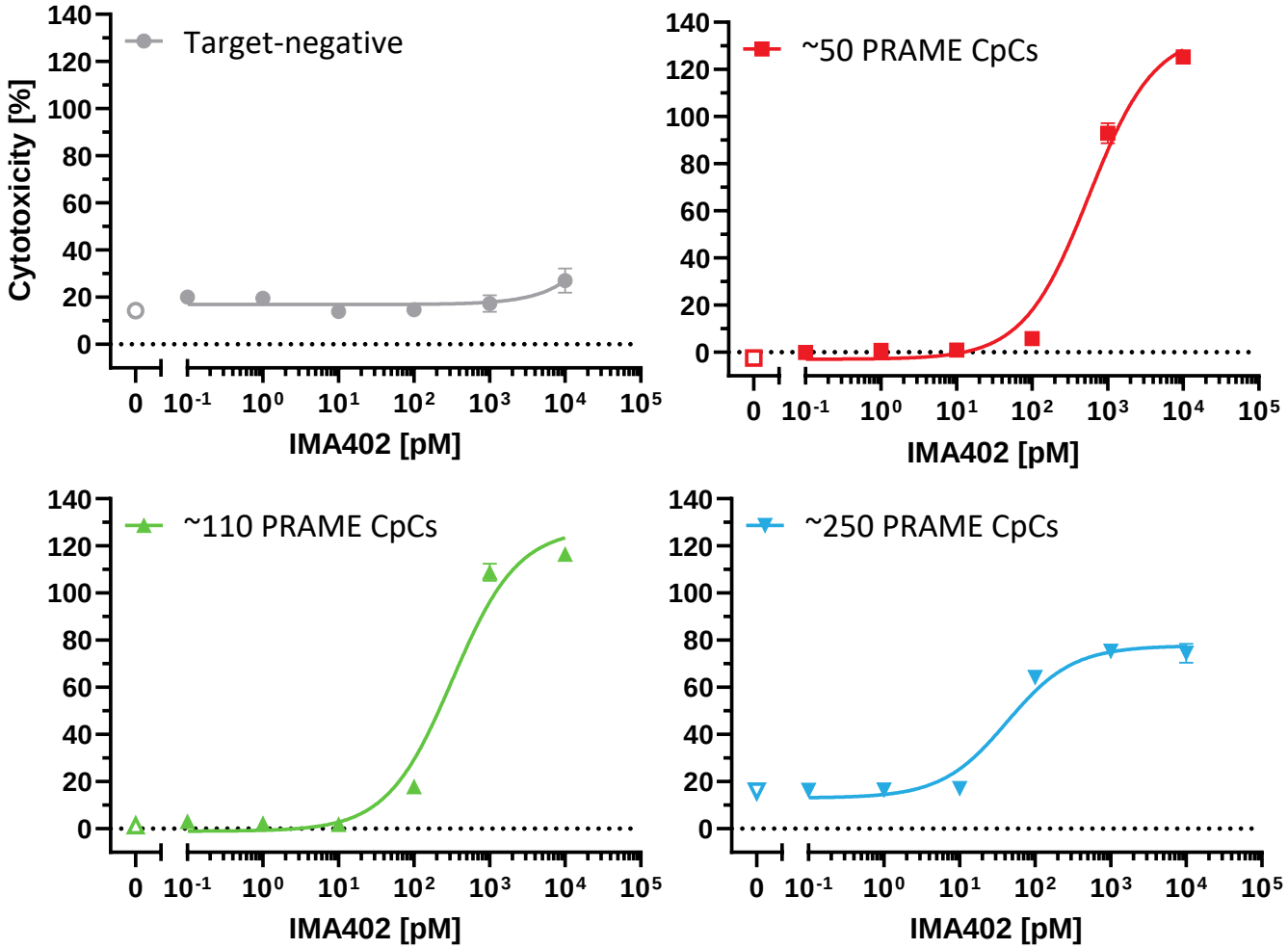
- **Tolerability**: Most common treatment-related AEs are low-grade CRS, transient lymphopenia and neutropenia
- **Pharmacokinetics**: Median terminal half-life of 16.9 days supporting potential further flexibility in future dosing schedules incl. combination with CPI and increased dosing intervals up to q4w
- **Initial anti-tumor activity in heavily pre-treated patients**
  - Objective responses in HNSCC, neuroendocrine tumor of unknown origin, cutaneous and mucosal melanoma including durable ongoing PRs of up to 13+ months
  - Deep responses (tumor shrinkage of ≥ 50%) in four patients including deepening of responses over time
  - Objective responses are associated with target expression and IMA401 dose: ORR 29%, cORR 25%, and tumor shrinkage in 53% of patients with relevant IMA401 doses and MAGEA4/8$^{high}$ target levels
- **Dose escalation ongoing**

AE: Adverse Event; CRS: Cytokine Release Syndrome; CPI: checkpoint inhibitors; q4w: once every four weeks; HNSCC: Head and neck squamous cell carcinoma; PR: Partial Response

# TCER® IMA402 Targeting PRAME

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

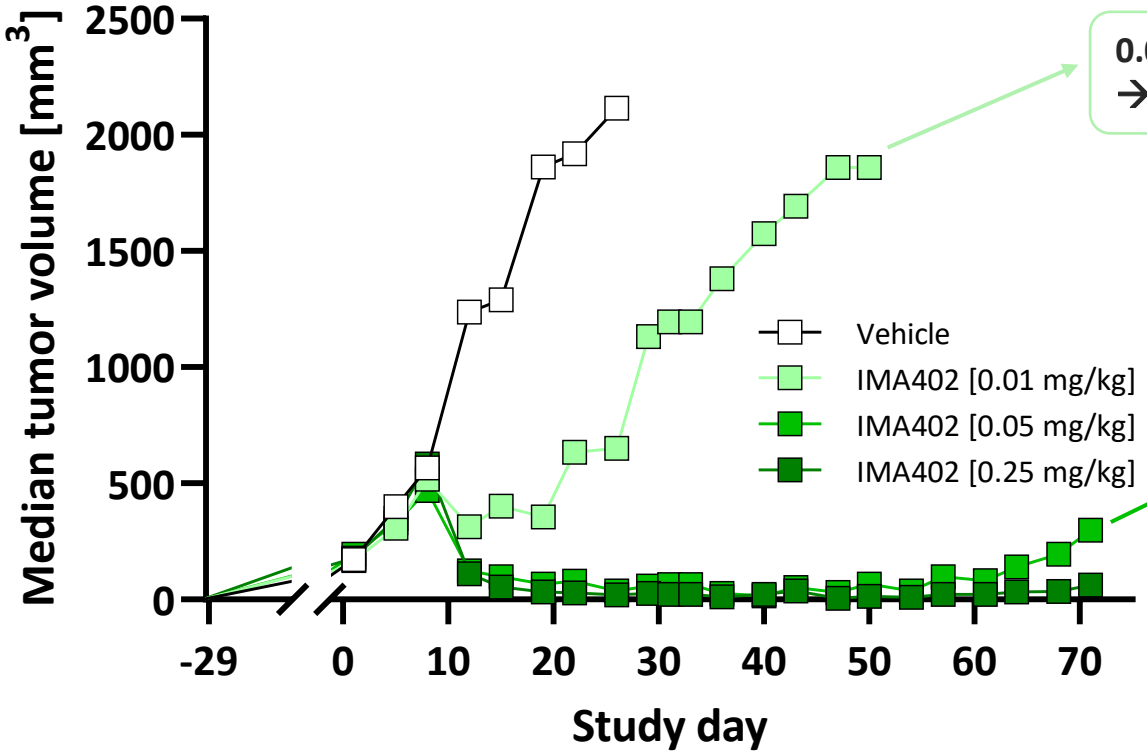
## Tumor Cell Killing at Low Physiological PRAME Peptide Levels




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

# TCER® IMA402 Achieves Dose-Dependent Durable Tumor Control *in vivo*

## Dose-response Relationship in Mouse Xenograft Model

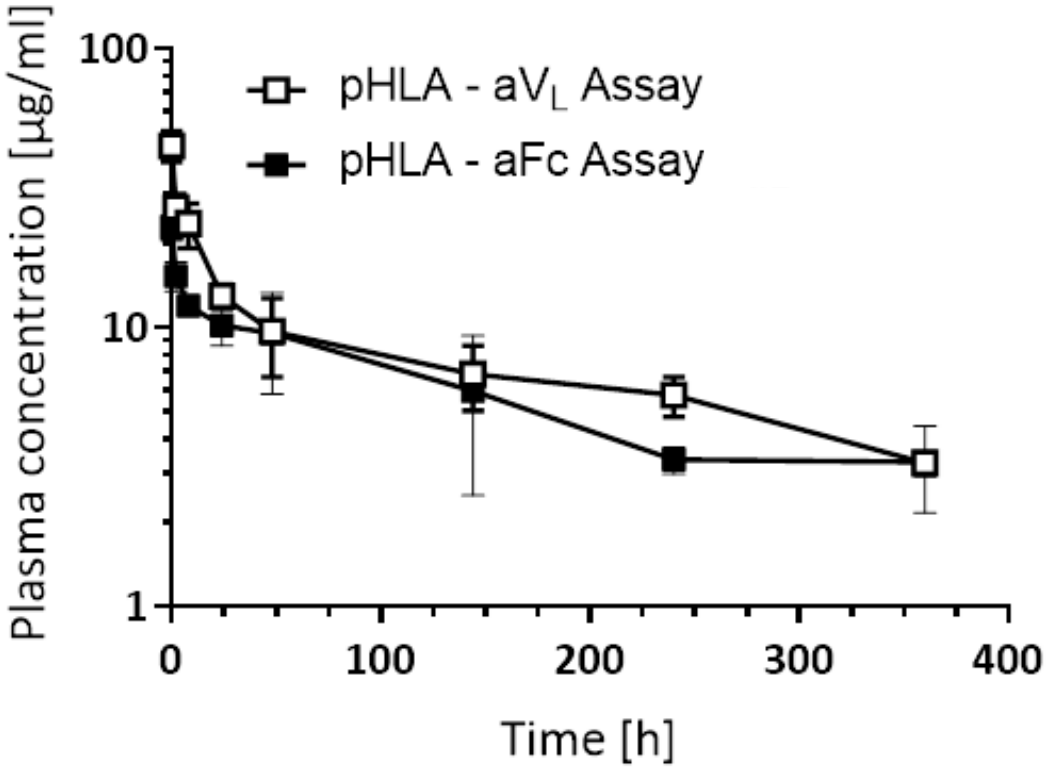



**0.01 mg/kg mouse dose**
**→ equivalent to approximately 0.6 mg human dose (~DL5)**

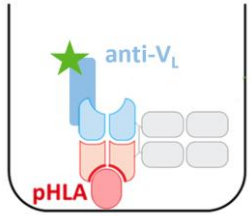
**0.05 mg/kg mouse dose**
**→ equivalent to approximately 3 mg human dose (DL7)**

**Preclinical data suggest that a dose of ≥3mg of IMA402 (DL7 in Phase 1 trial) is expected to start showing relevant efficacy in humans**

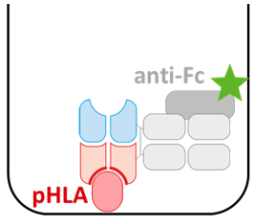
# Half-life Extended Format of IMA402 Confers Terminal Half-life of >1 Week




**pHLA – aV$_L$ Assay**




**pHLA – aFc Assay**




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

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

## Trial Overview

**Phase 1/2 clinical trial to evaluate safety, tolerability and anti-tumor activity of IMA402**

- HLA-A*02:01-positive patients with recurrent and/or refractory solid tumors with high PRAME prevalence
- Initially weekly i.v. infusions
- Potential for early adjustment of treatment interval based on PK data of half-life extended TCER® format

## Phase 1: Dose Escalation

**Adaptive design aimed at accelerating dose escalation**

**MTD/ RP2D**

- Basket trial in focus indications to accelerate signal finding
- Melanoma, ovarian cancer, lung cancer, uterine cancer and others

## Phase 2a: Dose Expansion

**Expansion cohort**

**Expansion cohort**

**Expansion cohort**

- Specific indications plus ongoing basket
- Combination therapies
- Optional dose/application optimization



MTD: maximum tolerated dose, RP2D: recommended phase 2 dose

# Baseline Characteristics
## Heavily Pre-treated Patients

| Characteristic | Safety population (N=33) | Efficacy-evaluable population[1] (N=21 excl. PRAME neg.) | | |
|---|---|---|---|---|
| | All patients dosed DL1-DL8 | PRAME-negative patients across DLs N=7 | PRAME-positive/NT patients DL1-DL6 N=12 | **DL7+ N=9** |
| **Age** Median (min, max) | 61 (28, 82) | 62 (56, 75) | 62 (28, 82) | **61 (40, 74)** |
| **ECOG performance status** | | | | |
| 0 - n [%] | 18 [54.5] | 4 [57.1] | 5 [41.7] | **7 [77.8]** |
| 1 - n [%] | 15 [45.5] | 3 [42.9] | 7 [58.3] | **2 [22.2]** |
| 2 - n [%] | 0 [0.0] | 0 [0] | 0 [0] | **0 [0.0]** |
| **Prior lines of systemic treatment** Median (min, max) | 3 (1, 5) | 3 (1, 4) | 3.5 (2, 5) | **3 (1, 5)** |
| **LDH at baseline** | | | | |
| ≤ 1xULN [%] | 15 [45.5] | 4 [57.1] | 4 [33.3] | **5 [55.6]** |
| 1-2xULN [%] | 15 [45.5] | 2 [28.6] | 7 [58.3] | **4 [44.4]** |
| > 2xULN [%] | 3 [9.1] | 1 [14.3] | 1 [8.3] | **0 [0.0]** |
| **Baseline tumor burden** Median target lesion sum of diameter [mm] (min, max) | 76.5 (24.5, 398) | 80.0 (30.1, 180) | 76.4 (46, 398) | **61.4 (24.5, 258)** |
| **Number of organs with metastases** Median (min, max) | 3 (1, 8) | 2 (1, 5) | 3 (2, 7) | **3 (1, 6)** |
| **Liver and/or Brain Lesions** [% of patients] | 54.5 | 71.4 | 41.7 | **55.6** |

[1]Efficacy Analysis Set prospectively defined in the study protocol: patients who received at least four IMA402 infusions and had at least one post-baseline efficacy assessment or clinical progression. LDH: Lactate dehydrogenase; ULN: Upper limit of normal; NT: not tested or not evaluable for PRAME expression

# IMA402 Demonstrates Favorable Tolerability in N=33 Patients

## Most Frequent Related AEs were Lymphopenia and CRS

| Treatment-related AEs[1], n [%] | All Grades | ≥ Grade 3 |
|---|---|---|
| Lymphopenia | 17 [52] | 10 [30] |
| Cytokine release syndrome | 16 [48] | 1 [3] |
| Arthralgia | 9 [27] | 0 |
| Fatigue | 9 [27] | 0 |
| Pruritus | 7 [21] | 0 |
| Rash | 7 [21] | 0 |
| Aspartate aminotransferase increased | 6 [18] | 2 [6] |
| Alanine aminotransferase increased | 5 [15] | 1 [3] |
| Pyrexia | 5 [15] | 0 |
| Anaemia | 4 [12] | 2 [6] |
| Vomiting | 4 [12] | 0 |
| C-reactive protein increased | 3 [9] | 0 |
| Headache | 3 [9] | 0 |
| Rash maculo-popular | 3 [9] | 0 |
| Neutropenia | 2 [6] | 2 [6] |
| Stomatitis | 2 [6] | 1 [3] |
| Blood creatinine increased | 1 [3] | 1 [3] |
| Electrocardiogram abnormal | 1 [3] | 1 [3] |
| Gamma-glutamyltransferase increased | 1 [3] | 1 [3] |
| Hypertension | 1 [3] | 1 [3] |
| Immune-mediated arthritis | 1 [3] | 1 [3] |
| Tumor lysis syndrome | 1 [3] | 1 [3] |
| Tumor pain | 1 [3] | 1 [3] |

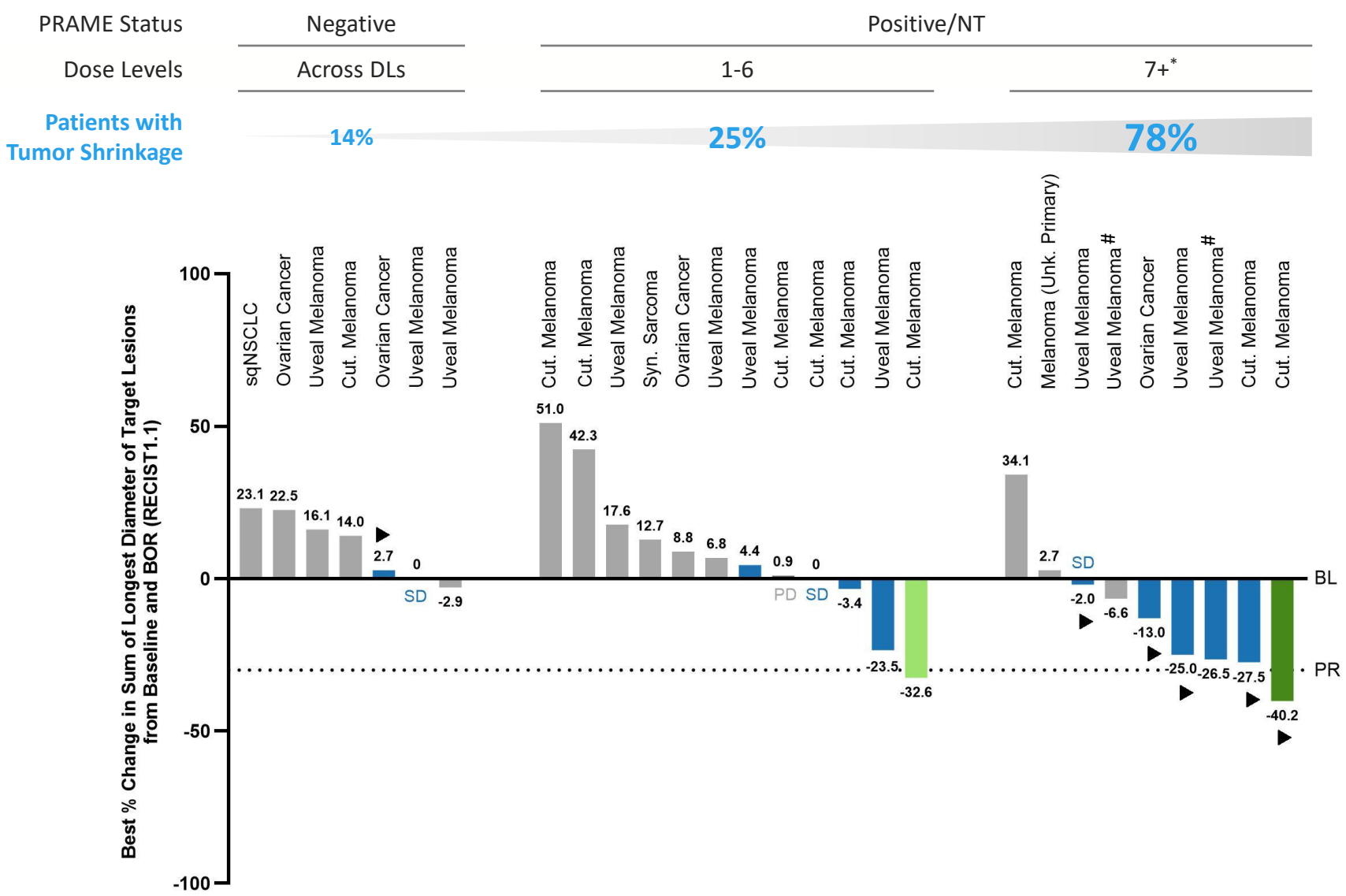
| TEAEs, n [%] | All Grades | ≥ Grade 3 |
|---|---|---|
| Any | 33 [100] | 17 [52] |
| Treatment-related | 32 [97] | 15 [45] |

- **Favorable tolerability** profile
- **Most frequent/relevant related AEs** were
  - transient lymphopenia,
  - mostly mild to moderate CRS (42% Grade 1, 3% Grade 2, 0% Grade 3, 3% Grade 4), majority at first dose
  - One DLT: Grade 4 CRS (fully resolved)
- No IMA402-related Grade 5 events
- **MTD not reached**



[1]All treatment-emergent adverse events (TEAEs) at least possibly related to IMA402 infusion with grade 1-2 occurring in at least 9% of patients and all events with grade 3-5; CRS: Cytokine release syndrome; MTD: Maximum tolerated dose.; One AE "Rash, Intermittent" was not coded at data cut-off, but added to the preferred term "Rash"

# Early Signs of Clinical Activity Associated with PRAME Expression and IMA402 Dose




**BOR (RECIST 1.1)**

- PD
- SD
- PR
- cPR
- ▶ Ongoing response / SD (RECIST1.1/ iRECIST)

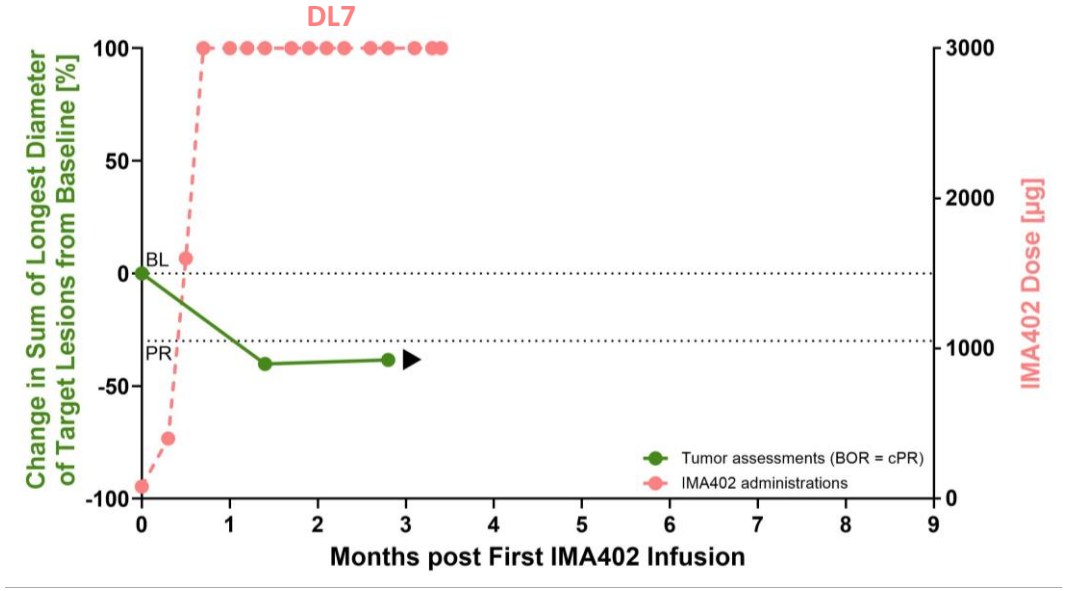
- Melanoma patient with confirmed partial response ongoing at 3 months (DL7, see next slide)
- Melanoma patient with -27.5% tumor shrinkage at first scan (DL8)
- Uveal melanoma patient with -25.0% tumor shrinkage deepening over time (started at DL4 and currently at DL7, see next slide)
- Ovarian cancer patient with -13% tumor shrinkage ongoing at 3 months (started at DL6 and currently at DL7)

* Patients who received DL7 or higher, either from start or as part of intra-patient dose-escalation; #continuing treatment; PD: Progressive Disease; SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response; BOR: Best Overall Response; BL: Baseline; NT: not tested or not evaluable for PRAME expression

# Exemplary Patient Cases Suggesting Dose-Dependent Tumor Response

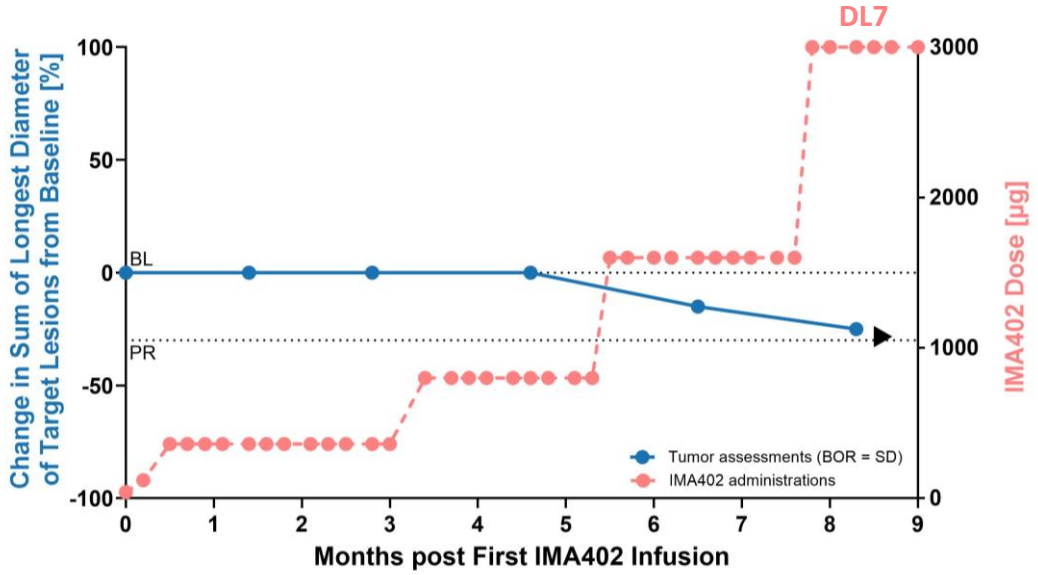
## Patients with Disease Control (RECIST1.1) at Relevant Doses (DL7+)

### Case 1




| Patient Characteristics & Outcomes |
|---|
| 52-year-old female with cutaneous melanoma |
| Lesions in lung, lymph nodes, gall bladder, fat tissue, pancreas |
| 1 prior line of therapy and maintenance with anti-PD-1 |
| Patient received DL7 from start (after step-up dosing) |
| Ongoing cPR at 3 months post treatment start with -40.2% reduction of target lesion size |

### Case 2




| Patient Characteristics & Outcomes |
|---|
| 46-year-old female with uveal melanoma |
| Lesions in liver |
| 3 prior lines of therapy with anti-PD1 and tebentatafusp |
| Patient received DL4 and went up to DL7 through intra-patient dose escalation |
| Ongoing SD at 8+ months post-treatment start with -25% reduction of target lesion size |


BOR: Best Overall Response; SD: Stable Disease; cPR: Confirmed Partial Response; arrow: Ongoing response / stable disease (RECIST 1.1/ iRECIST)

# IMA402 Phase 1 Dose Escalation Study

## Summary as of Nov 6, 2024

- **Study design and patient population**
  - BLRM-model based dose escalation with currently 33 patients treated with IMA402 at a dose range from 0.02 mg to 4 mg

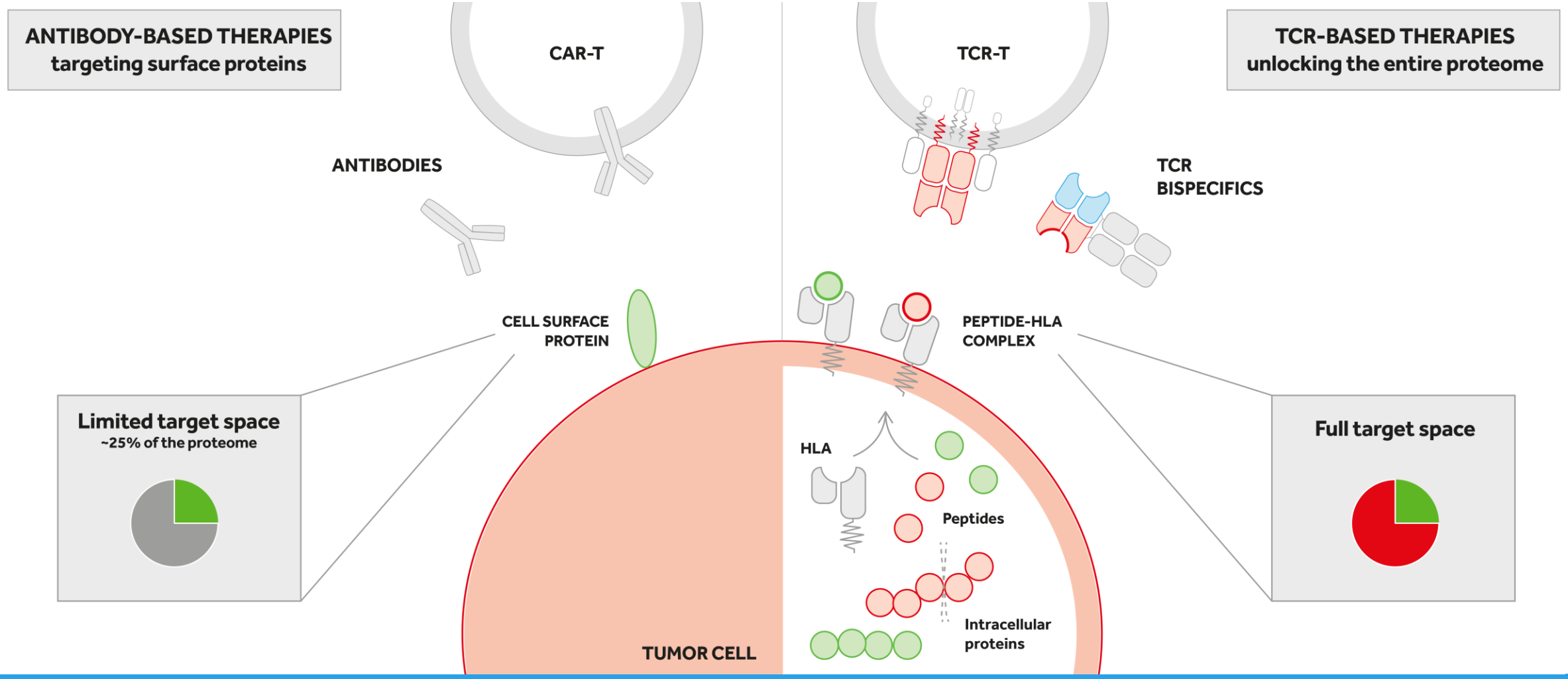
  → *preclinical in-vivo data suggested relevant anti tumor efficacy starting at ~3 mg human equivalent dose (DL7)*
  - Advanced metastatic solid cancer patients with no available treatment option, PRAME expression tested retrospectively
  - Efficacy-evaluable population: N=21 patients (per protocol and excluding PRAME-negative patients)
  - Relevant patient population: N=9 patients received ≥3 mg (DL7) via initial or escalated dose (N=8 DL7, N=1 DL8)
- **Favorable tolerability profile with CRS and transient lymphopenia being most common AE, dose escalation ongoing**
- **Early PK data indicates median half-life of ~7 days, potentially enabling bi-weekly dosing**
- **Initial signs of clinical activity, associated with PRAME expression and IMA402 dose**
  - No relevant tumor shrinkage in PRAME-*negative* patients
  - Dose-dependent clinical activity in PRAME-*positive/NT* patients with DCR of 52% across all doses
  - Tumor shrinkage in 25% of patients at low doses (DL1-6) including one unconfirmed partial response
  - **Tumor shrinkage in 78% (7/9) of patients at relevant doses (DL7+, ≥3 mg) including**
    - **1 cPR in cutaneous melanoma (-40.2% and ongoing at 3 months)**
    - **2 SD with significant tumor shrinkage in cutaneous/uveal melanoma (-27.5%/-25% and ongoing at 6+ weeks/8+ months)**
    - **1 SD in ovarian cancer (-13% and ongoing at 3 months)**

For comprehensive patient flow chart, see appendix


NT: not tested or not evaluable for PRAME expression; CRS: Cytokine release syndrome; DCR: Disease control rate

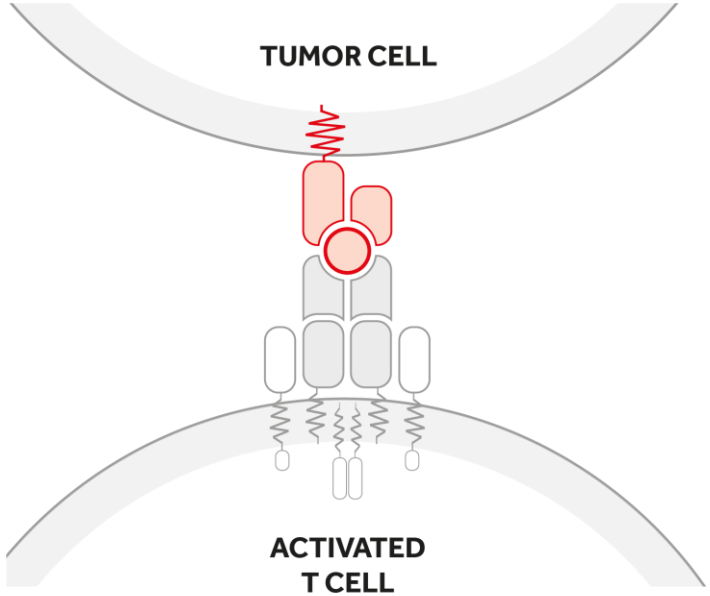
# Immatics' Proprietary Target and TCR Discovery Platforms

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



# True Cancer Targets & Matching Right TCRs

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

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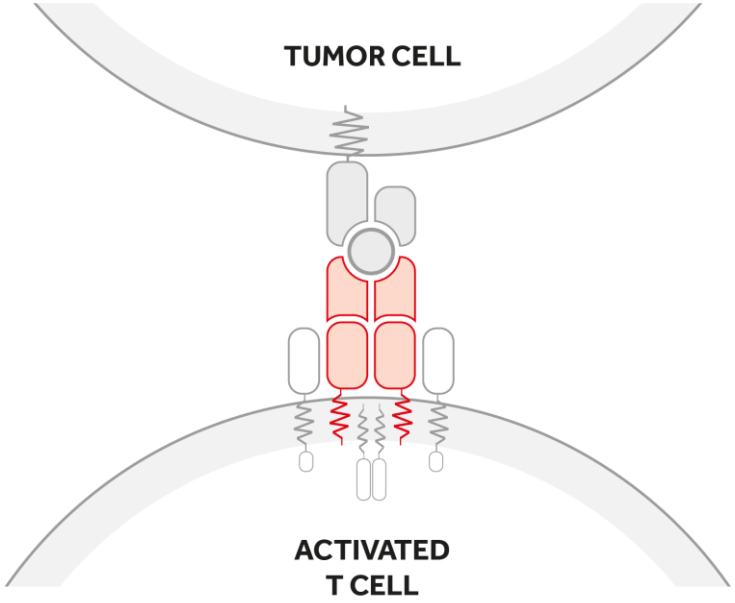



**True Targets** via XPRESIDENT® technology platform

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

**Right TCRs** via XCEPTOR® technology platform

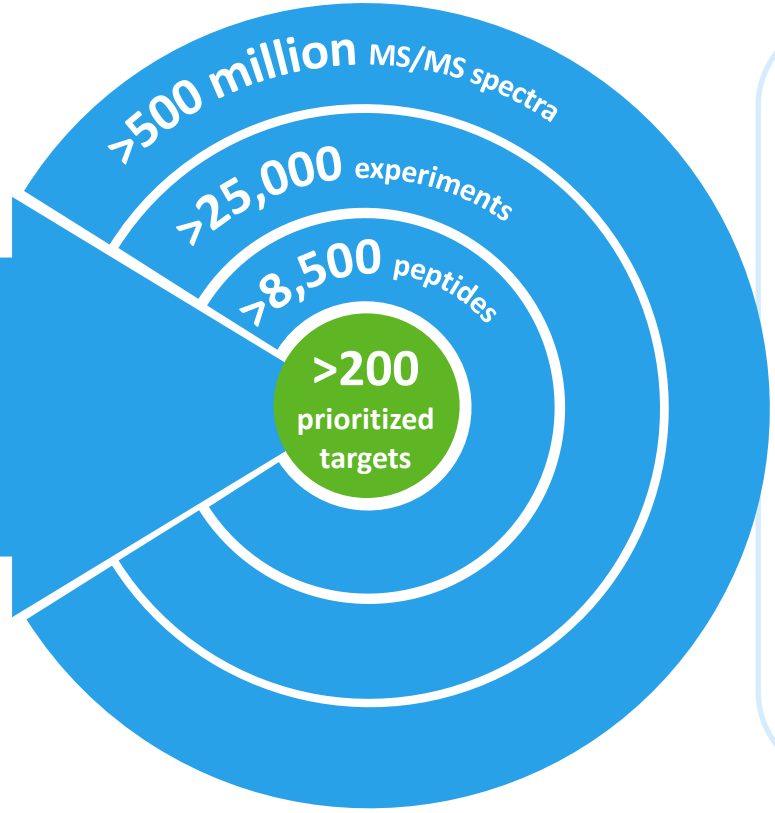
- recognize the target peptide with high affinity and specificity
- show selective killing of tumor cells
- are developed to be suitable for two different therapeutic modalities, Cell Therapies and TCR Bispecifics

# Pool of 200 Prioritized Targets as Foundation for Future Value Generation

## XPRESIDENT® Target Platform

pHLA Database
based on primary tissues

**>2,500 cancer & normal** tissues analyzed by **Quantitative, Ultra-Sensitive Mass Spectrometry**




### 200 Prioritized Targets

**Grouped in 3 Target Classes:**

1. **Well known and characterized parent protein (20%)**
   e.g. MAGE family cancer testis antigens
2. **Unknown or poorly characterized parent protein (60%)**
   e.g. stroma target COL6A3 exon 6
3. **Crypto-targets/Neoantigens (20%)**
   Novel target class which includes RNA-edited peptides & non-classical neoantigens

**~50% of our prioritized targets are non-HLA-A*02 restricted, substantially broadening the potential patient reach**

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

# Potential for Large Patient Populations across Multiple Solid Cancers

## IMA203 / IMA402 PRAME

Uterine Carcinoma – 97%
Uterine Carcinosarcoma – 100%
Sarcoma Subtypes – up to 100%
Cut. Melanoma – 95%
Uveal Melanoma[1] – 89%
Ovarian Carcinoma – 84%
Squamous NSCLC – 68%
TNBC – 63%
Small Cell Lung Cancer – 45%
Kidney Carcinoma – up to 40%
Cholangiocarcinoma – 33%
HNSCC – 27%
Esophageal Carcinoma – 27%
Breast Carcinoma– 26%
Adeno NSCLC – 25%
HCC – 18%
Bladder Carcinoma – 18%

## IMA401 MAGEA4/8

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

## IMA204 COL6A3 Exon 6

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

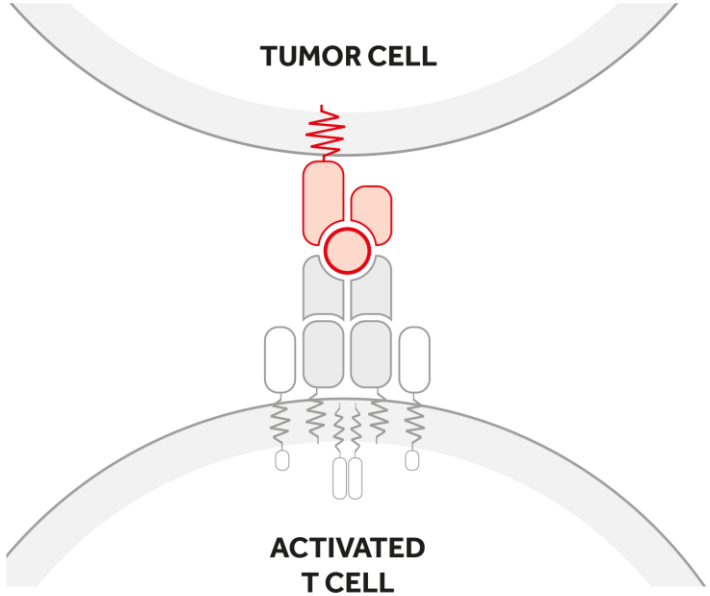
**ACTengine® and TCER® targets demonstrate high prevalence in multiple solid cancers**



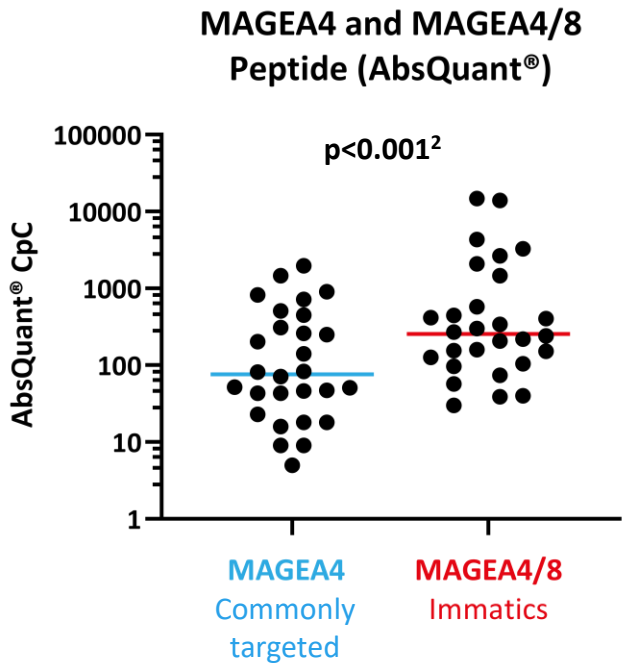
Target prevalence for selected solid cancer indications are based on TCGA (for SCLC: in-house) RNAseq data combined with a proprietary mass spec-guided RNA expression threshold;
[1] Uveal melanoma target prevalence is based on IMADetect® qPCR testing of screening biopsies from clinical trial patients (n=61)

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

## Example of MAGEA4/8 Peptide Target




**Ranking of pHLA targets**




XPRESIDENT® quantitative information on target density[1] between peptides originating from the same source protein

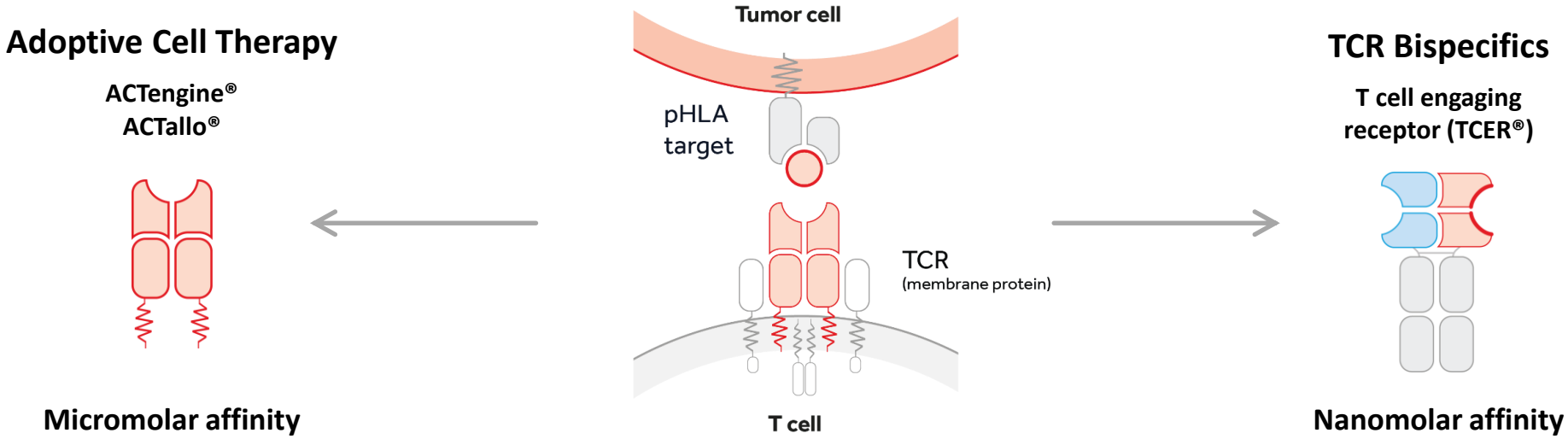
MAGEA4/8 target is presented at >5-fold higher target density[1] than a commonly targeted MAGEA4 target peptide



[1] Copy number per tumor cell (CpC) measured on a paired-sample basis by AbsQuant®, i.e. comparing MAGEA4 vs. MAGEA4/A8 peptide presentation on same sample, [2] Students paired T test

# Development of the Right TCR – XCEPTOR® Technology

## TCR Discovery and Engineering for ACT and TCR Bispecifics



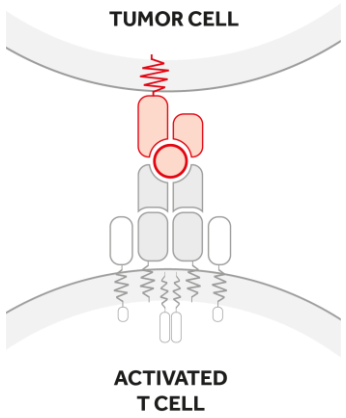
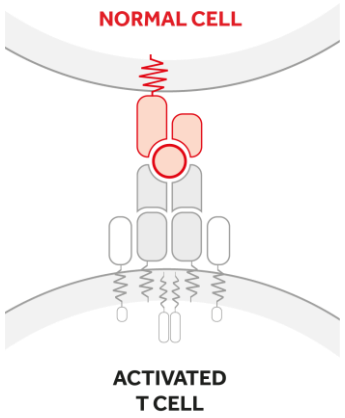
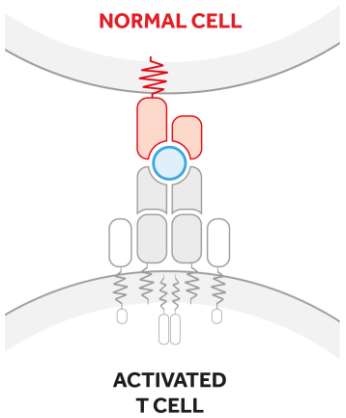
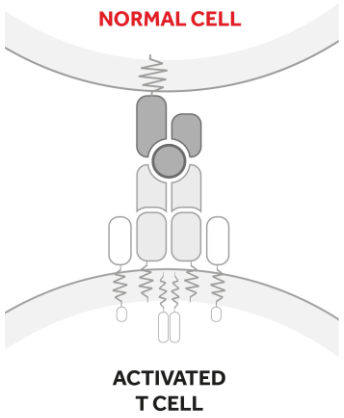

- Fast, efficient and highly sensitive discovery of highly specific, natural TCRs
- Protein engineering capabilities to design and maturate TCRs with increased affinity while retaining specificity
- Early de-selection of cross-reactive TCRs by the unique interplay between Immatics' target and TCR discovery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



[1] XPRESIDENT®-guided off-target toxicity screening; [2] XPRESIDENT®-guided similar peptide counterselection

# Optimal Target Selection & TCR Specificity for Minimizing Safety Risks

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

| Target peptide presented on tumor cells | Target peptide presented on normal cells | Similar peptide presented on normal cells[1] | A different HLA is recognized on normal cells |
|---|---|---|---|
|  |  |  |  |
| Selective killing of tumor cells | On-target (off-tumor) toxicity | Off-target toxicity | Alloreactivity |



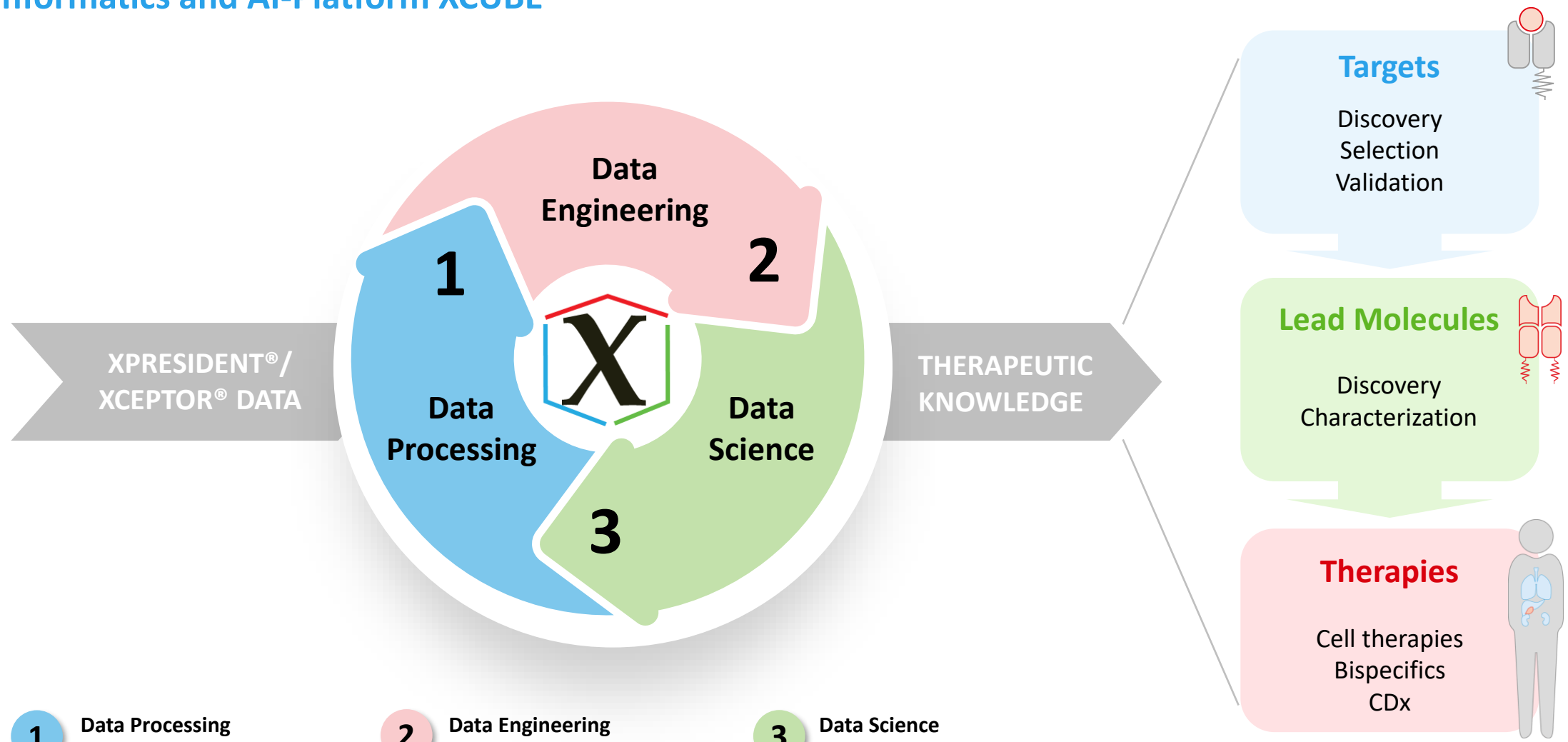
**XPRESIDENT®-guided screening** for on- and off-target toxicities of TCRs based on the extensive database of peptides presented on normal tissues



[1] Clinical fatalities have occurred in TCR-T trials using a titin cross-reactive TCR (Cameron *et al.*, Sci Transl Med)

# “AI Is Where the Data Is®”

## Bioinformatics and AI-Platform XCUBE™




**1 Data Processing**
Processing of mass-spec & next-gen sequencing data

**2 Data Engineering**
Development of data warehouses & user interfaces

**3 Data Science**
Development of statistical & machine learning models

# Immatics' Robust Intellectual Property Portfolio

## Protection Strategy of Key Assets in Major Markets and Beyond

**Differentiated** technologies, platforms and assays for **Target Research, TCR** and **TCER® development**

**Technologies**

**>200** prioritized pHLA targets

**Targets**

**TCRs**

TCRs with **high affinity** and **specificity profile**

**Half-life extended Bispecifics** with proprietary TCER® format

**TCER®**

Treatment of **indications and patient groups**

**Therapeutic Uses**

**Cell Therapy**

**ACTengine®** manufacturing & off-the-shelf **ACTallo®** platform

**Clinical Candidates**

**Clinical ACTengine® and TCER® candidates:** IMA203, IMA203CD8, IMA402, IMA401

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

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

## Key Features

### TARGET

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

Naturally and specifically presented on tumors at high target density[1]: **100-700 copies/cell**

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

### TCR

High-affinity, specific TCR targeting COL6A3 exon 6

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

High functional avidity[2]: **~0.01ng/ml**

Identified and characterized by XCEPTOR® TCR discovery and engineering platform

### PRECLINICAL DATA

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

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

Complete tumor eradication in *in vivo* mouse models

### PATIENT POPULATION[3]

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

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



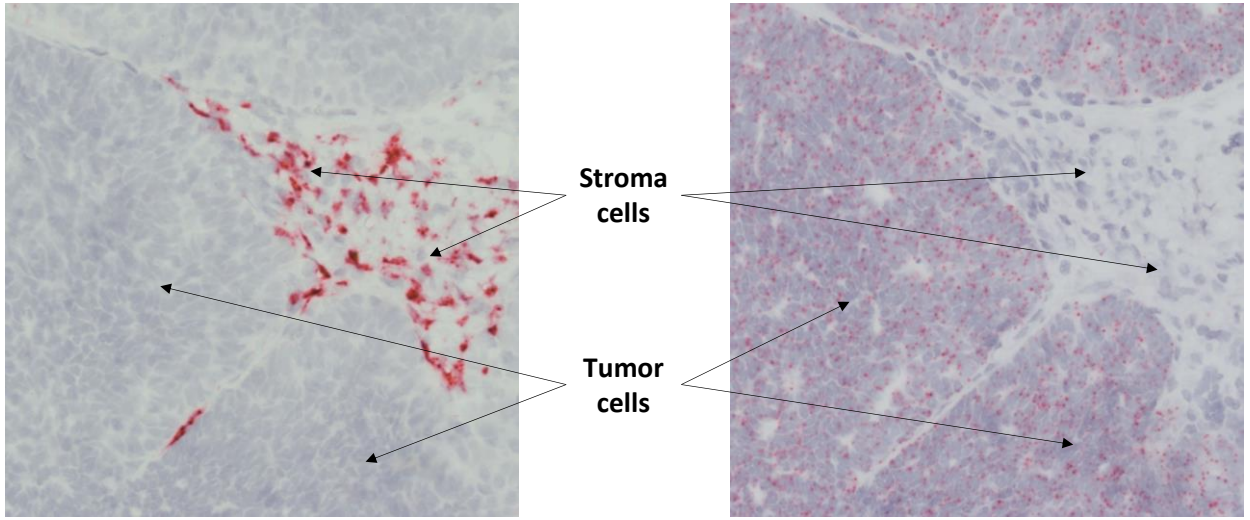
[1] Target density: peptide copy number per tumor cell, approximate range representing the majority of tumor samples analyzed; [2] Functional avidity: EC50 half maximal effective concentration;
[3] Solid cancer indications with 20% or more target expression, Target prevalence for selected cancer indications based on mRNA expression (TCGA and Immatics inhouse data)

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

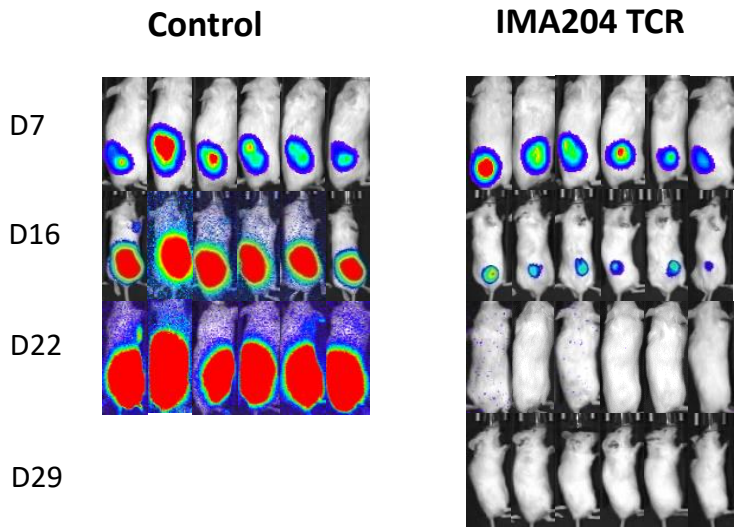
## Complete Tumor Eradication *in vitro & in vivo*[1] by Affinity-enhanced IMA204 TCR

**Stroma Target (COL6A3 exon 6)**
in Ovarian Cancer sample

**Example of a Tumor Target**
in same Ovarian Cancer sample




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




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

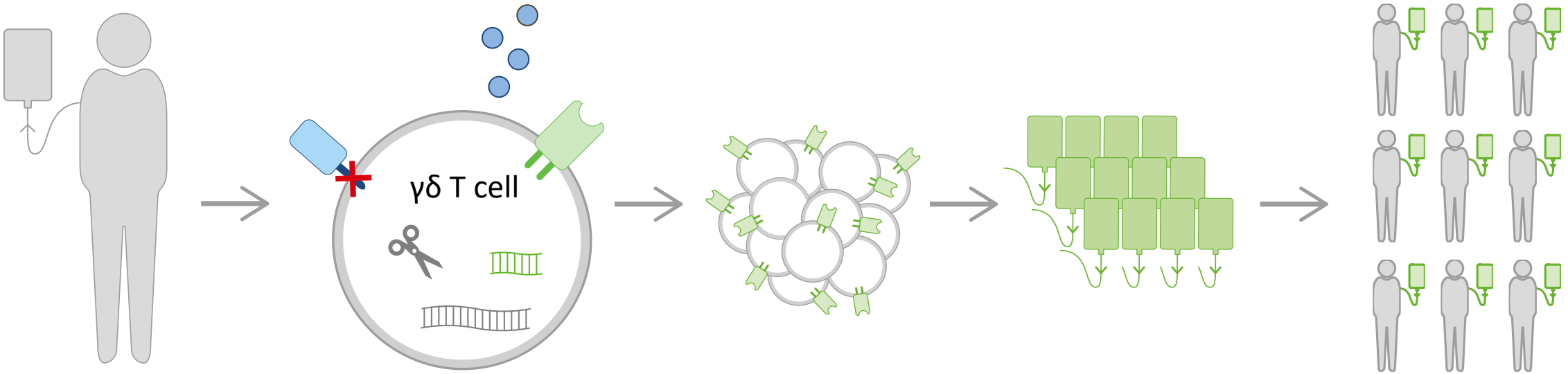
**Affinity maturated CD8-independent, next-generation TCR engages both CD4 and CD8 T cells without the need of CD8 co-transduction**



[1] *In vivo* data in collaboration with Jim Riley, University of Pennsylvania, control: non-transduced T cells. TCR avidity and specificity data not shown, available in IMA204 presentation on Immatics website.

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

# ACTallo® – Immatics' Allogeneic Cell Therapy Approach




- **Off-the-shelf cell therapy**, no need for personalized manufacturing → reduced logistics and time to application
- **Potential for hundreds of doses** from one single donor leukapheresis → lower cost of goods
- **Use of healthy donor material** provides standardized quality and quantity of starting material

- Strategic collaborations combining Immatics' proprietary ACTallo® platform with Bristol Myers Squibb's next-gen technologies and Editas Medicine's CRISPR gene editing technology to develop next-gen allogeneic γδ TCR-T/CAR-T programs

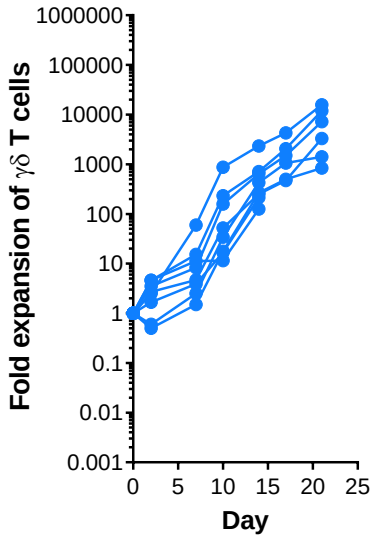
# Why γδ T cells?

## γδ T cells Are Well Suited for an Off-the-shelf Cell Therapy Approach

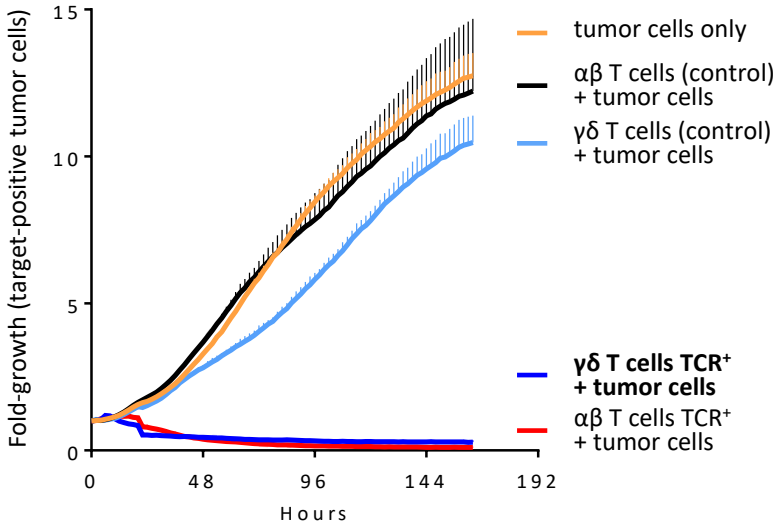
### γδ T cells

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

Expansion




*In vitro* anti-tumor activity



# Corporate Information

# Experienced Global Leadership Team Across Europe and the US

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

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

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

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

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

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

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

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

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

# Strong, Focused and Highly Integrated Trans-Atlantic Organization

**Tübingen, Germany**
**~255 FTEs**
Target & TCR discovery and TCR Bispecifics development

**Munich, Germany**
**~85 FTEs**
Various operating functions

**Houston, Texas**
**~205 FTEs**
Cell therapy development & manufacturing

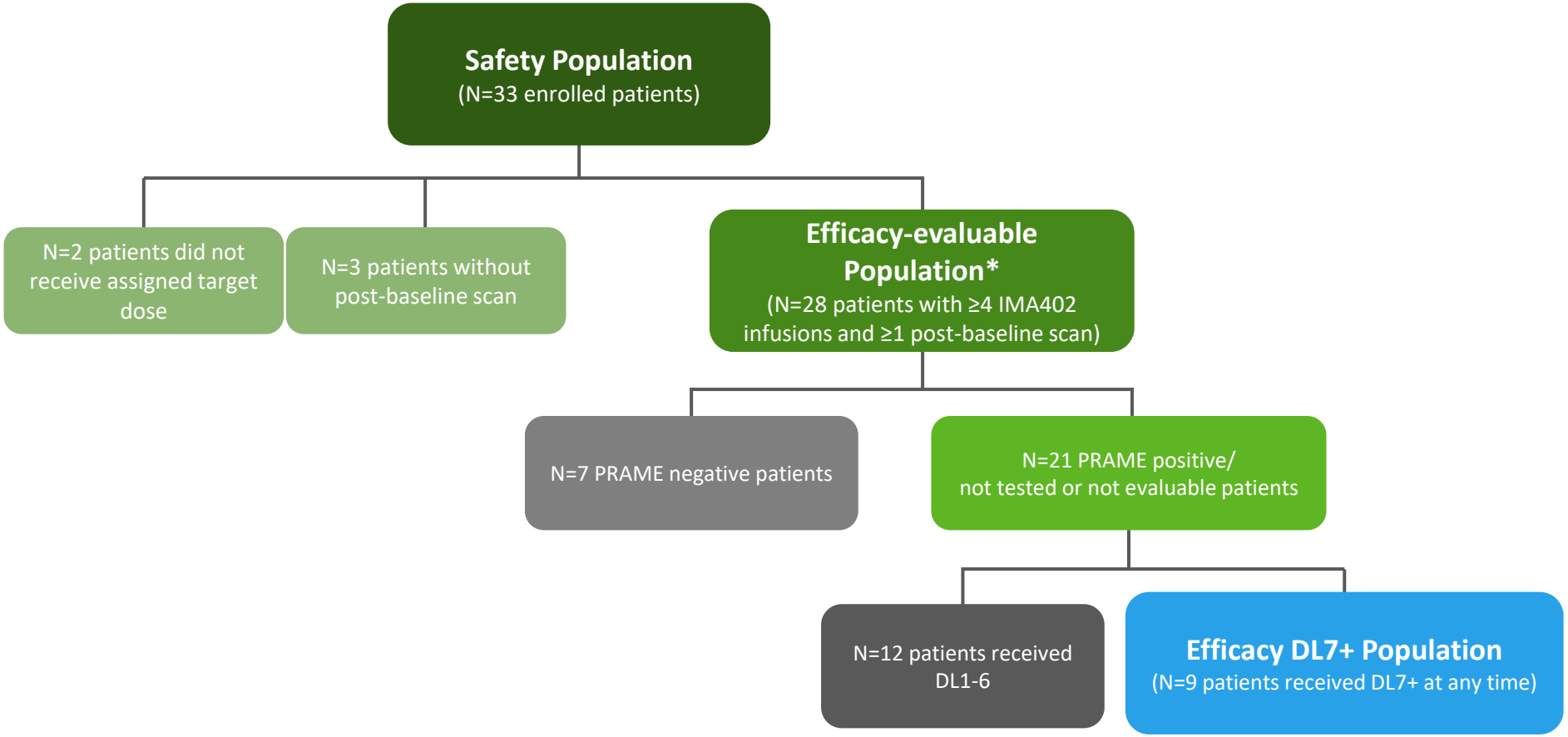
# Delivering

## the Power of T cells to Cancer Patients

## Appendix

www.immatics.com

# IMA402 Phase 1a Patient Population Flow Chart






* Efficacy Analysis Set prospectively defined in the study protocol: patients who received at least four IMA402 infusions and had at least one post-baseline efficacy assessment or clinical progression.