Targeting of Tumor-specific Peptide Antigens with Bispecific T Cell-Engaging Receptor (TCER®) Molecules

PEGS: The Essential Protein Engineering & Cell Therapy Summit 2021

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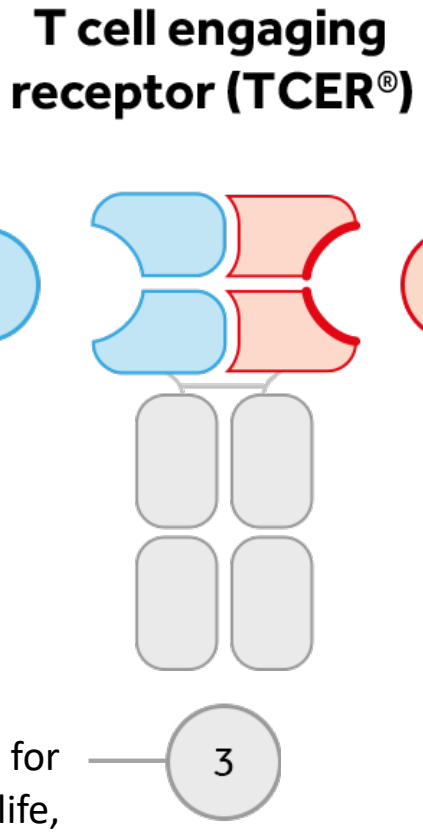
TCER® – Immatics' TCR Bispecifics

Proprietary TCER® Format Consisting of Three Distinct Elements



Antibody domains for recruitment of T cells

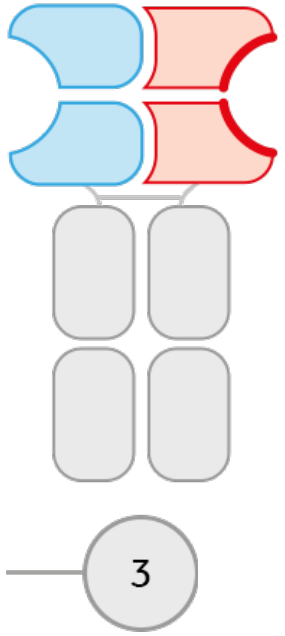
stability- and affinity-engineered TCR domains for targeting tumor-specific peptides presented by HLA molecules

Human IgG Fc region (silenced) for conferring preferential serum half-life, stability and manufacturability

TCER® – Immatics' TCR Bispecifics

Unlock Immunotherapies for Solid Cancers with Targets beyond the Cancer Cell Surface

T cell engaging receptor (TCER®)



Antibody domains for recruitment of T cells

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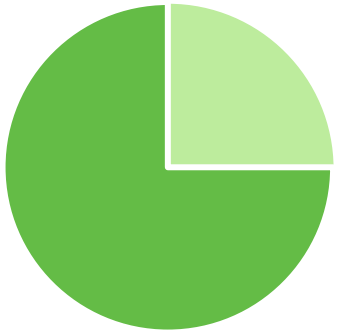
Human IgG Fc region (silenced) for conferring preferential serum half-life, stability and manufacturability

Accessing the full target space

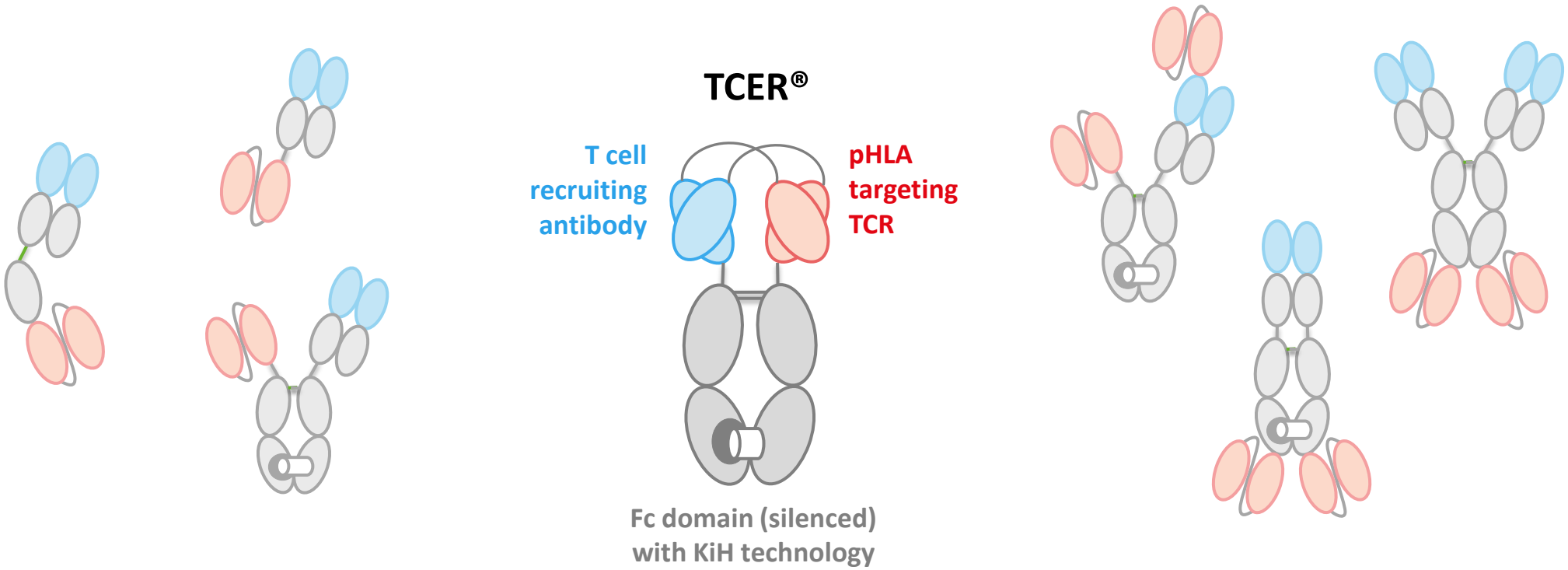


Membrane-associated proteins
Accessible for mAb, CAR-T and TCR

Intracellular proteins
Accessible for TCR

Adapted from Chandran *et al.,* 2019

TCER® – Superior Proprietary TCR Bispecific Format



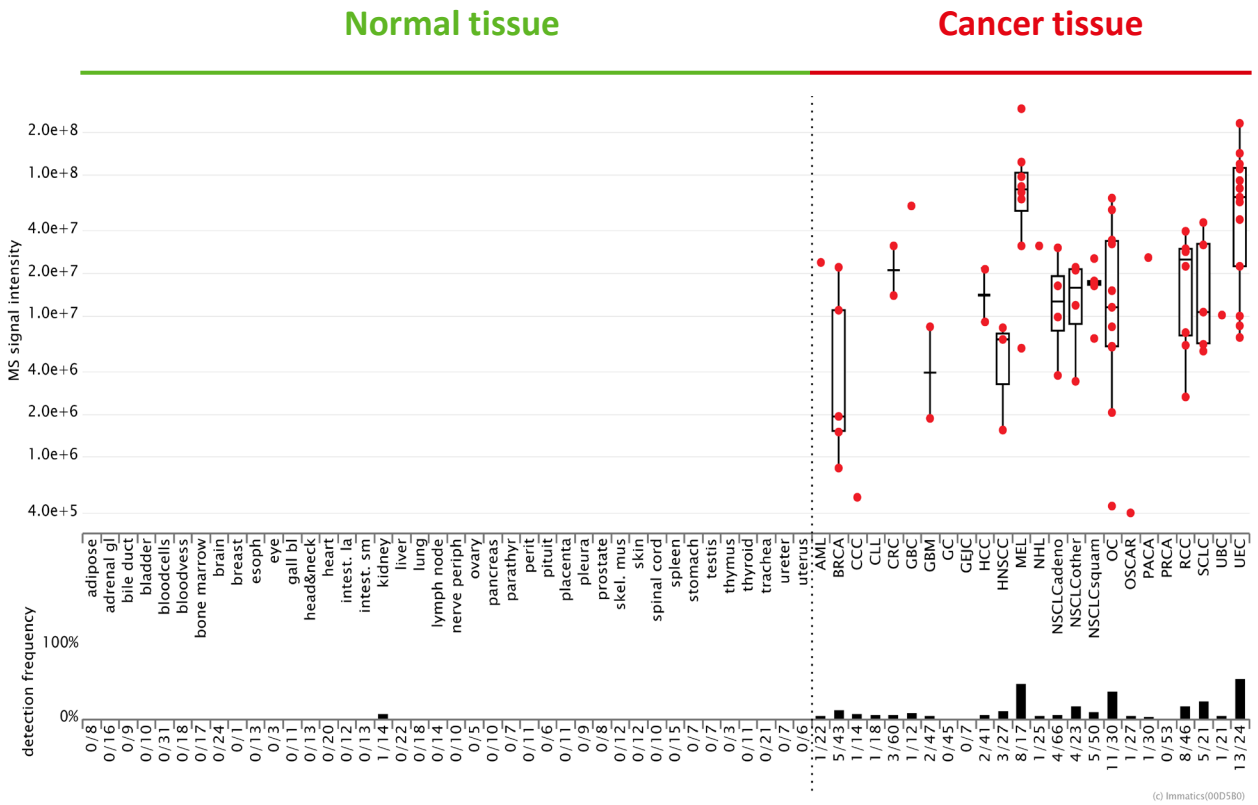
Potency and stability of proprietary TCER® format is superior to six alternative TCR Bispecific formats[1]

[1] Based on comparative preclinical testing

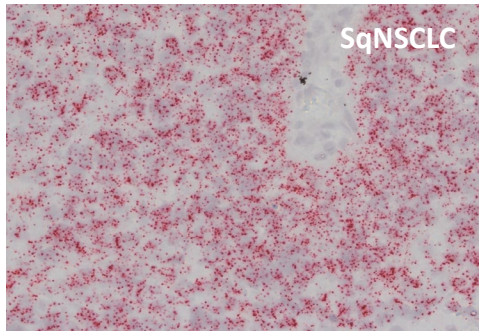
IMA402 TCER® – PRAME Target Peptide on HLA-A*02

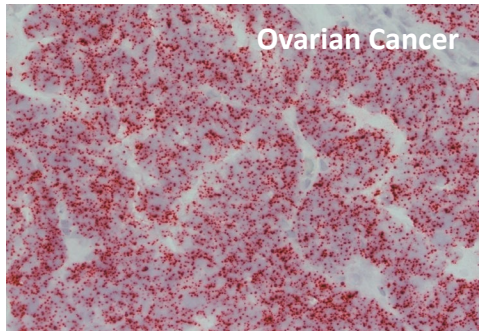
Detection of PRAME Peptide and PRAME RNA in Tumor and Normal Tissues

PRAME Peptide detection (MS)



PRAME RNA detection in tumor samples (ISH)





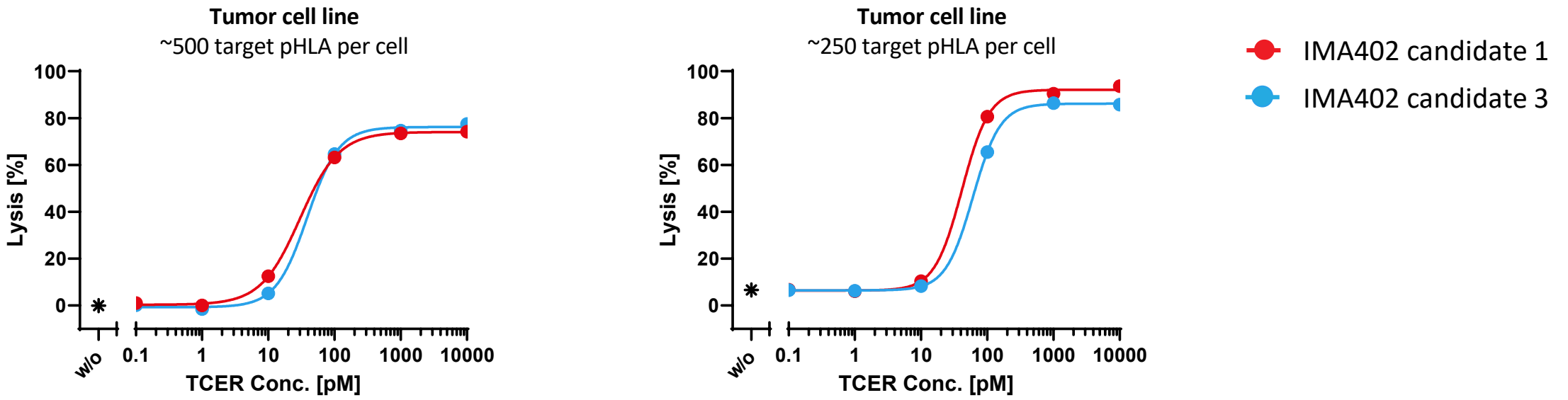
PRAME target prevalence in selected cancer indications

Indications	Target prevalence [%]
Uterine carcinoma	100
Melanoma	95
Ovarian carcinoma	80
Squamous non-small cell lung carcinoma	65
Uveal melanoma	50
Cholangiocarcinoma	35
Diffuse large B-cell lymphoma	30
Breast carcinoma	25
Head & neck squamous cell carcinoma	25
plus several further indications	

PRAME target prevalences are based on TCGA data combined with a XPRESIDENT®-determined target individual MS-based mRNA expression threshold

IMA402 TCER® – *In Vitro* Efficacy Assessment

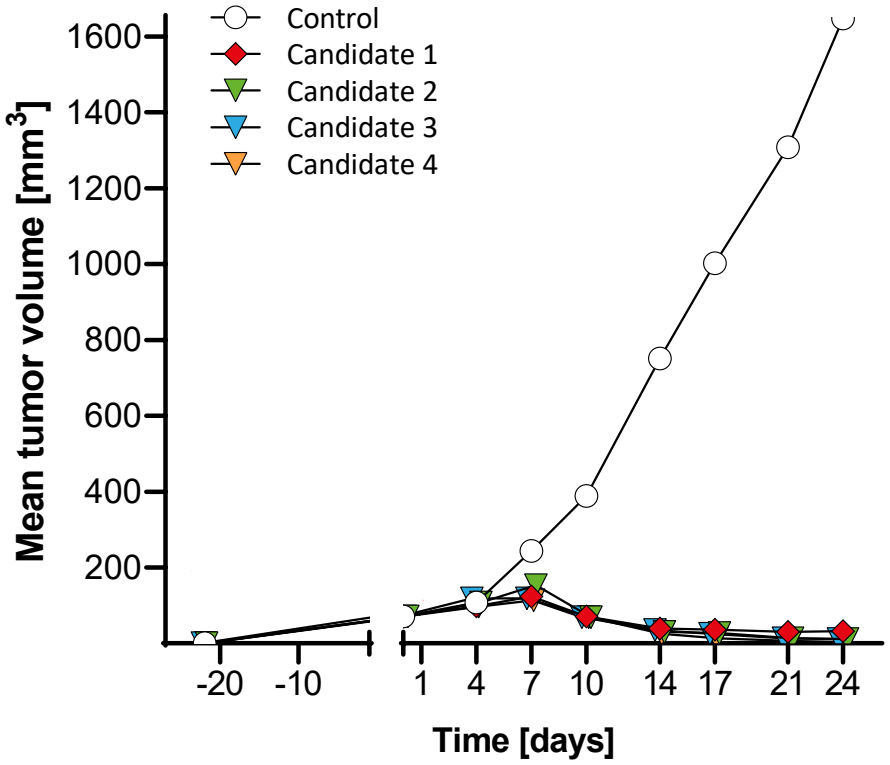
PBMC-mediated Cytotoxicity Against Tumor Cells



IMA402 TCER® candidates **induce killing of tumor cell lines presenting PRAME** target peptide-HLA at similar copy numbers than detected in patient cancer tissue (100 – 1000 copies per cell)

IMA402 TCER® – *In Vivo* Efficacy Assessment

Anti-Tumor Activity of Four IMA402 Candidates in Subcutaneous Tumor Xenograft in Mice



Treatment schedule

Transplantation
Tumor

Transplantation
Human PBMC

IMA402
Treatment start

Administration of IMA402
in defined dosage interval

-20 -10 1 4 7 10 14 17 21 24

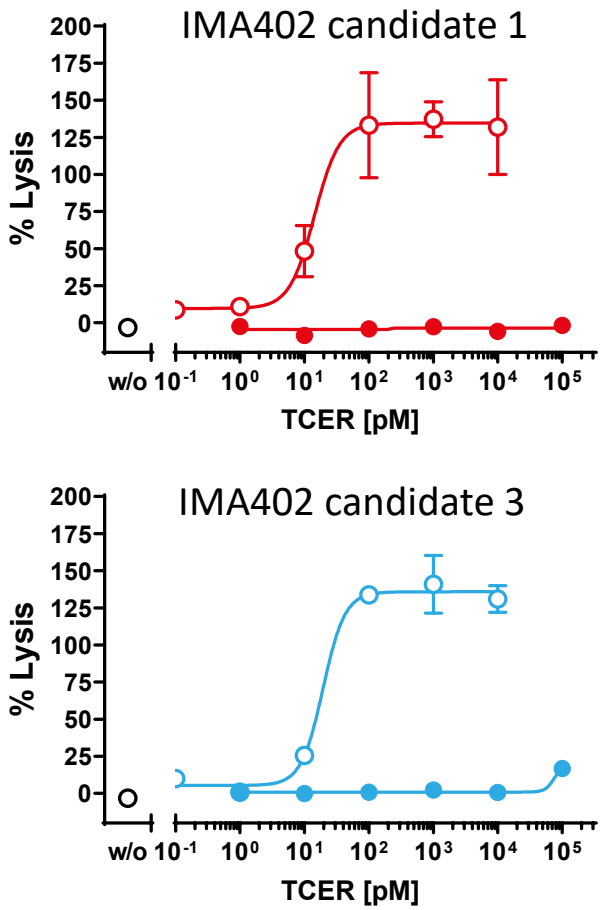
Study day

Mouse strain: NOG (8 -10 mice per group), **Tumor cell line:** ~500 target pHLA per cell, **PBMC:** 2 human donors, **Control:** Treatment with PBS (TCER® vehicle)

Anti-tumor activity of IMA402 TCER® candidates **including complete regressions in tumor xenograft model**

IMA402 TCER® – *In Vitro* Safety Assessment

PBMC-mediated Cytotoxicity Against Normal Tissue Cells

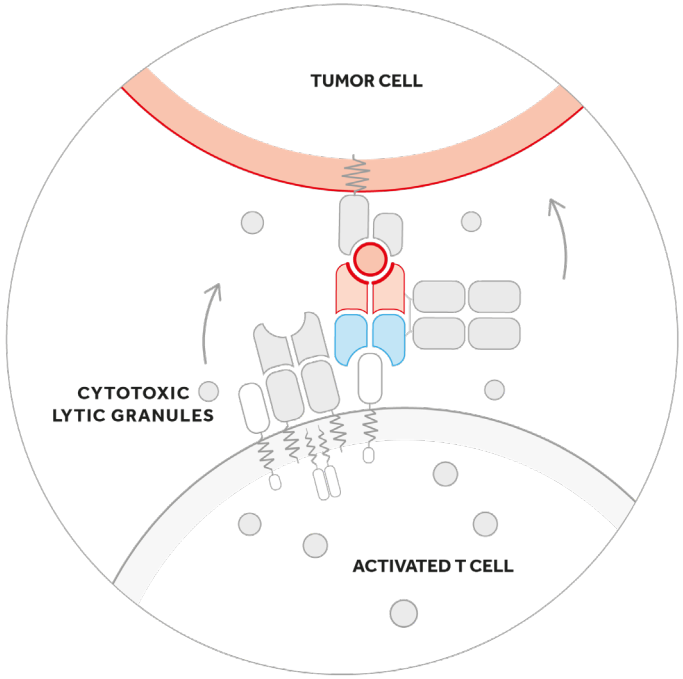


	Therapeutic window (x-fold)	
Normal tissue cell type	candidate 1	candidate 3
iPSC-derived Cardiomyocytes	≥10,000	≥1,000
iPSC-derived Astrocytes	≥10,000	≥1,000
iPSC-derived GABA neurons	≥10,000	≥10,000
Aortic Endothelial cells	≥10,000	≥1,000
Coronary Artery Smooth Muscle Cells	≥10,000	≥10,000
Cardiac Microvascular Endothelial Cells	≥10,000	≥1,000
Pulmonary Fibroblasts	≥10,000	≥1,000
Tracheal Smooth Muscle Cells	≥10,000	≥10,000
Renal Cortical Epithelial Cells	≥10,000	≥1,000
Dermal Microvascular Endothelial Cells	≥10,000	≥10,000
Mesenchymal Stem Cells from Bone Marrow	≥10,000	≥10,000

- Cytotoxicity assessed against N=11 different human normal tissue cell types
- IMA402 TCER® candidates show a **minimum of 1,000-fold therapeutic window** between tumor cell reactivity and normal tissue cell reactivity

Profile of Second TCER® Program – IMA402 Candidates Targeting PRAME

Summary



- IMA402 TCER® is directed against **PRAME**, one of the most frequently expressed intracellular cancer targets for TCR-based therapies
- Killing of PRAME-positive cancer cells with a **minimum of 1,000-fold therapeutic window**
- **Consistent tumor regression** including complete responses in *in vivo* (NOG mouse) model
- Further data support **antibody-like profiles** for manufacturability and pharmacokinetics
- **Manufacturing activities** with clinical candidates including one lead candidate have started

IMA402 is the second TCER® program having reached preclinical proof-of-concept validating Immatics' proprietary TCER® platform