UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 6-K

REPORT OF FOREIGN PRIVATE ISSUER PURSUANT TO RULE 13a-16 OR 15d-16 UNDER THE SECURITIES EXCHANGE ACT OF 1934

November 10, 2022

Commission File Number: 001-39363

IMMATICS N.V.

Paul-Ehrlich-Straße 15
72076 Tübingen, Federal Republic of Germany
(Address of principal executive office)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F:

Form 20-F ☒ Form 40-F ☐

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INFORMATION CONTAINED IN THIS REPORT ON FORM 6-K

On November 10, 2022, Immatics N.V. (the "Company" or "Immatics") made available two posters, which are attached as Exhibit 99.1 and 99.2 to this Report on Form 6-K.

EXHIBIT INDEX

Exhibit No.	Description
99.1	Next-Generation TCR Bispecifics (TCER) Targeting Peptide-HLA Antigens for the Treatment of Patients with Solid Tumors
99.2	The PRAME Opportunity – High Peptide Copy Numbers, Homogenous Expression and High Prevalence to Address a Broad Patient Population across Different Solid Cancers with TCR-based Therapeutics

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

IMMATICS N.V.

Date: November 10, 2022

By: /s/ Harpreet Singh
Name: Harpreet Singh
Title: Chief Executive Officer

Next-Generation TCR Bispecifics (TCER) Targeting Peptide-HLA Antigens for the Treatment of Patients with Solid Tumors

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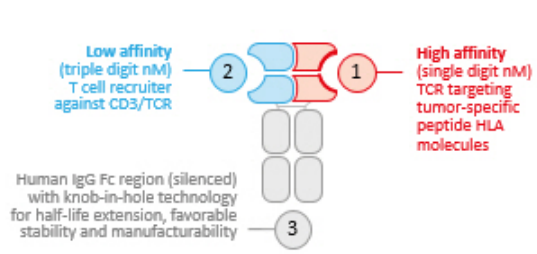
1 Immatics Biotechnologies GmbH, Tuebingen, Germany, 2 Immatics N.V., Tuebingen, Germany

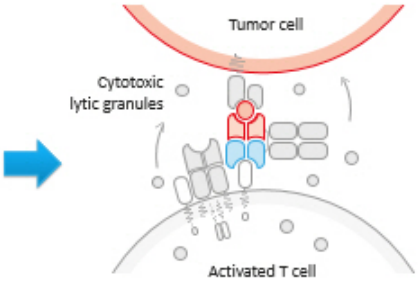
Background – Overcoming Challenges of T cell Engaging Bispecifics

T cell engaging bispecifics have emerged as a promising therapeutic opportunity for patients with solid cancers. However, challenges related to target specificity and drug safety remain and many efforts are being made to generate optimized molecules with improved pharmacodynamics while reducing T cell engager-associated toxicities. We have developed a pipeline of bispecific T cell engaging receptor (TCER) molecules comprising a T cell receptor (TCR) for giving access to intracellular tumor antigens presented as peptide-HLA molecules. The next-generation design of TCER is established through a novel, low-affinity T cell recruiting antibody aiming at conferring a favorable drug safety profile while enabling a highly potent anti-tumor response. TCER molecules are further equipped with an effector function-silenced Fc region for prolongation of serum half-life.

The Next-generation of TCR Bispecifics – TCER

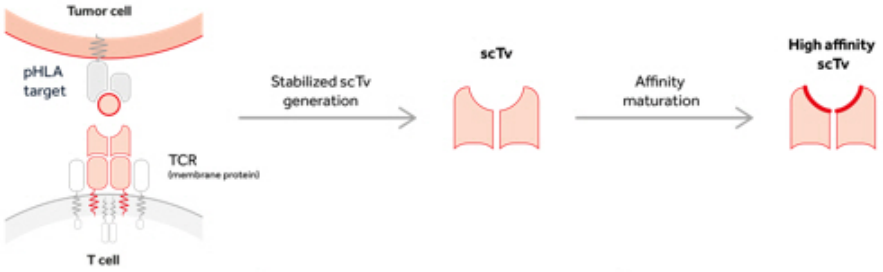


Proprietary TCER format consisting of three distinct elements designed for optimal efficacy and minimal toxicity risk in patients



TCER binds to target, recruits and activates T cells and initiates tumor cell killing

Discovery and Affinity Maturation of TCRs Required for TCER Generation

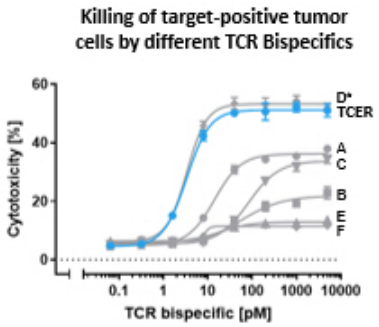


- **XCEPTOR** for TCR Discovery, Engineering & Validation
- Generation of **multiple TCR candidates per target**
- Unique XPRESIDENT-guided **on- and off-target toxicity screening**

- TCR variable domains (scTv format) are **stabilized and optimized** for facilitated production in mammalian cells
- This enables combination with various bispecific platforms

- Low binding affinity of natural TCRs is **increased by at least 1,000-fold** while retaining high specificity
- XPRESIDENT's immunopeptidome database is essential for **specificity-controlled affinity maturation**

TCER Format Exhibits Highest Potency Combined with Specificity in Targeting pHLA Antigens



*high potency of 2+1 format D was caused by pronounced unspecific reactivity against T2

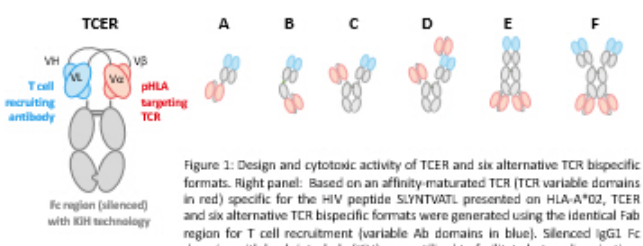


Figure 1: Design and cytotoxic activity of TCER and six alternative TCR bispecific formats. Right panel: Based on an affinity-maturated TCR (TCR variable domains in red) specific for the HIV peptide SLYNTVATL presented on HLA-A*02, TCER and six alternative TCR bispecific formats were generated using the identical Fab region for T cell recruitment (variable Ab domains in blue). Silenced IgG1 Fc domains with knob-into-hole (KIH) were utilized to facilitate heterodimerization. Left panel: PBMC-mediated cytotoxicity of TCR bispecific formats against HLA-A*02–positive T2 cells loaded with HIV peptide. Cytotoxicity was calculated based on LDH release during 24h coculture of PBMC and T2. LDH content of T2 cells alone was used as 100% cytotoxicity reference leading to underestimated cytotoxicity values due to T2 cell proliferation.

Novel, Low-Affinity Recruiter Designed to Improve Efficacy/Toxicity Profile of TCER

TCER molecules are designed with a high affinity TCR and a low affinity T cell recruiting Ab to optimize biodistribution*. The design also intends to selectively induce T cell activation at the tumor site but not in the periphery and thereby reducing immune-related toxicities, like cytokine release syndrome, and to reach sufficiently high drug doses for achieving meaningful clinical responses. * Refer to literature data for other low-affinity recruiters (e.g. Harber *et al.*, 2021, Nature; Trinklein *et al.*, 2019, mAbs)

Superior tumor control using a novel, low-affinity recruiter with high T cell activation capacity

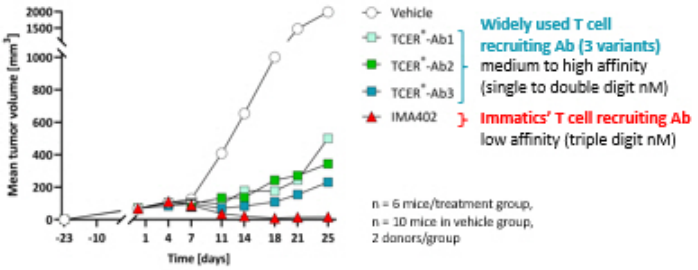


Figure 2. *In vivo* efficacy assessment of TCER molecules incorporating identical tumor-targeting TCR domains, but different T cell recruiting Ab domains in Hs695T (melanoma) cell line xenograft model in NOG mice. Weekly intravenous injections of 0.025 mg/kg body weight of PRAME-specific TCER molecules for three weeks starting at study day 1 after intravenous transfusion of human PBMC. PRAME TCER IMA402 utilizes a novel, low affinity recruiter (triple digit nM affinity) binding both CD3 and TCR. Analogous TCER molecules TCER-Ab1, -Ab2 and -Ab3 utilize medium to high affinity recruiters (TCER-Ab1: 39 nM, TCER-Ab2: 9 nM, TCER-Ab3: 31 nM) binding CD3 only.

Target-unrelated cytokine release in human whole blood is reduced with low-affinity recruiter

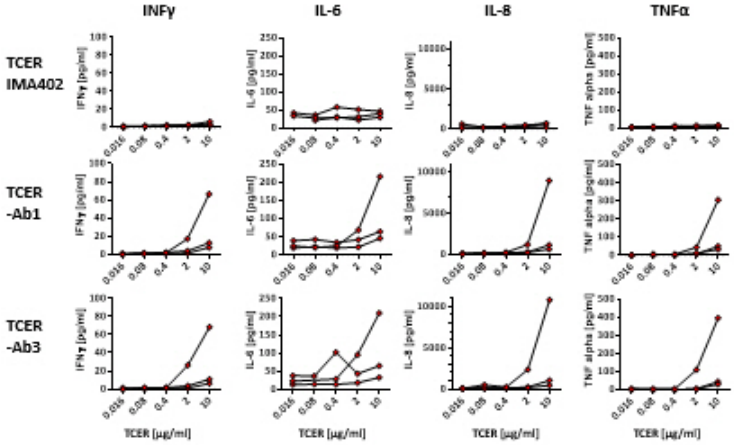


Figure 3. Whole blood cytokine release assay to assess the risk of different recruiters to induce cytokines in absence of target. Recruiter arm-driven non-specific activation of T cells was assessed by measuring TCER-mediated cytokine release in whole blood of 3 HLA-A*02-positive donors and human endothelial cells (HUVEC) after incubation with PRAME TCER IMA402, TCER-Ab1 or TCER-Ab3 for 48h. N = 16 cytokines tested, individual values for 4 exemplary cytokines shown. Higher background of IL-6 is due to the presence of HUVEC. TCER-Ab2 was not tested.

Preclinical Data Package for TCER Programs

- Tumor cell lines presenting target pHLA at endogenous levels
- Tumor cell-mediated cytokine release and proliferation of T cells
- Tumor xenografts in mice
- Pharmacokinetic and -dynamic

- XPRESIDENT data package
- Absolute quantification of target pHLA copies (AbsQuant)
- Homogeneity of target pHLA presentation within tumors

- Normal tissue cell types and iPSC-derived normal cells (n≥20)
- Target-negative tumor cell lines
- Alloreactivity screening
- Cytokine release from whole blood
- XPRESIDENT-guided off-target screening based on similarity to target peptide sequence and TCR binding motif

- Yield and purity of material produced by CHO cells
- Freeze-thaw and storage stress stability
- Sequence liabilities
- N-glycan profiling of TCR domains

Pharmacodynamic and Pharmacokinetic of PRAME TCER (IMA402)

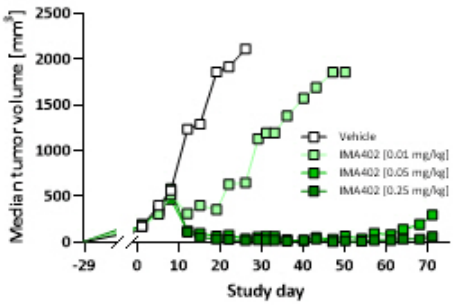


Figure 4. *In vivo* efficacy of IMA402 in large (≈ 195 mm³ average tumor volume) melanoma cell line-derived tumors in MHC I/II knock-out NSG mice over a prolonged observation period of 71 days. Weekly intravenous injections of IMA402 starting at study day 1 after intravenous transfusion of human PBMC. Treatment was discontinued when complete response was noted. Median values for n = 6 mice/group, 2 donors/group.

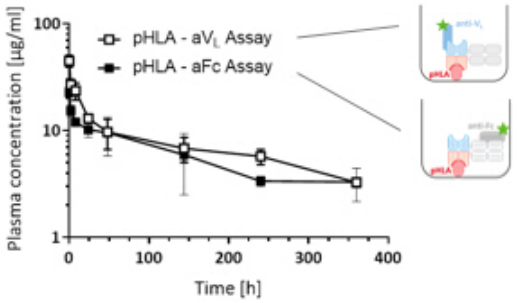


Figure 5. Pharmacokinetic analysis of IMA402 in mice. NOG mice received a single intravenous injection of IMA402 (2 mg/kg). TCER plasma concentrations at different time points were determined by ELISA detecting binding of IMA402 to the PRAME target via pHLA. The integrity of the molecule was confirmed via aV$_L$ or aFc detection. Terminal half-life ($t_{1/2}$) was calculated via linear regression of time points between 24 h and 360 h (n=3 per timepoint, mean ± SD).

Manufacturing of PRAME TCER (IMA402)

CMC data support antibody-like manufacturability and developability

- Manufacturing in Chinese Hamster Ovary (CHO) cells able to process natural TCR glycosylation
- High titer (>3.5 g/L) and good stability allowing liquid formulation
- Manufacturing process development completed
- Manufacturing advantages of TCER format: no formation of typical but unwanted Hole-Hole and Knob-Knob side products

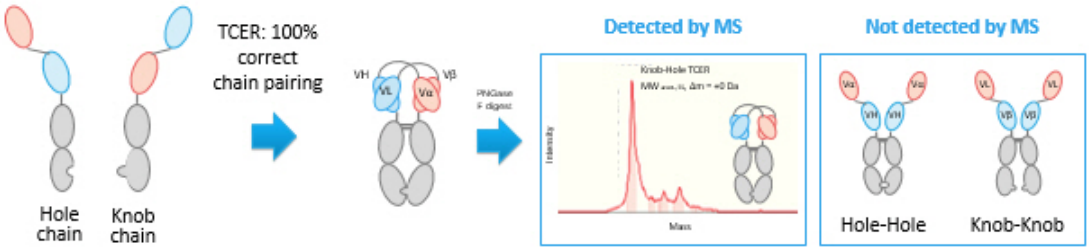


Figure 6. Theoretical product-related impurities such as hole-hole and knob-knob homodimers, are considered inactive due to absence of variable IgG or TCR domains. Total mass analysis by mass spectrometry (MS) of transiently and CHO stably expressed IMA402 has demonstrated lack of hole-hole and knob-knob homodimers in both Protein-L and Protein-A captured TCER fractions. IMA402 was analyzed by MS after complete deglycosylation with PNGase F. With a 100% correct chain pairing of the TCER knob and hole chains, IMA402 can be captured with standard Protein-A chromatography, and no specific downstream processing steps are needed for the removal of these product-related impurities.

Conclusion

T cell engaging receptor (TCER) – a Next-generation TCR Bispecific Format

- Comparison of seven different TCR bispecific formats revealed highest anti-tumor potency for TCER format together with a 2+1 format that failed specificity requirements
- High affinity TCR domains targeting peptide-HLA tumor antigens are generated by specificity-controlled affinity maturation
- Novel, low affinity Ab domains developed for T cell recruitment aim to improve efficacy while minimizing toxicity of TCER molecules as demonstrated in tumor xenograft models in mice and by cytokine release in human whole blood
- IgG Fc region incorporated into TCER format for the extension of serum half-life and improved manufacturability
- Comprehensive preclinical data package including *in vivo* tumor models are generated for each TCER program

PRAME TCER IMA402 with encouraging preclinical and CMC data

- *In vivo* studies in mice demonstrate dose-dependent anti-tumor activity of IMA402 and that sufficiently high drug doses are key to achieving sustained anti-tumor response over prolonged time period
- IMA402 demonstrates a serum half-life of ≈ 8 days in mice suggesting a favorable dosing regimen and prolonged drug exposure at therapeutic levels when compared to TCR bispecifics lacking half-life extension
- TCER IMA402 is manufactured by utilizing standard processes of mAb production resulting in high titer, protein quality and stability while unwanted side products are absent, a unique feature of our TCER format

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immatics

The PRAME Opportunity – High Peptide Copy Numbers, Homogenous Expression and High Prevalence to Address a Broad Patient Population across Different Solid Cancers with TCR-based Therapeutics

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Abstract ID: 713

PRAME – Promising Opportunity for TCR-based Therapies

Several peptide-HLA targets for T cell receptor (TCR)-based immunotherapies are currently being evaluated in the field, however, many are limited by their overall low prevalence, low copy numbers or relevant expression in healthy tissues. A T cell target with nearly ideal properties has high, homogenous and prevalent expression across multiple cancers in the absence of significant safety/toxicity liabilities. Here, we describe the in-depth characterization of an HLA-A*02:01-presented peptide derived from the cancer germline antigen preferentially expressed antigen in melanoma (PRAME) that opens an avenue of new opportunities for patients with solid cancers which we aim to leverage by two distinct TCR-based therapeutic modalities, TCR-engineered T cells (ACTengine IMA203) and TCR Bispecifics (TCER IMA402).

Proprietary Technologies to Analyze PRAME on Every Cellular Level

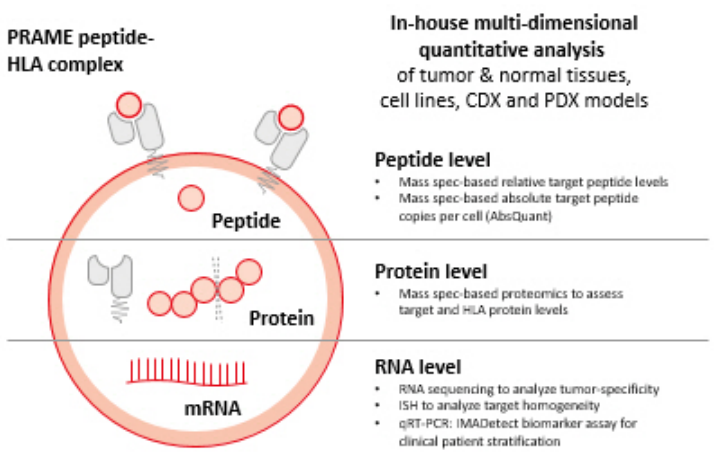


Figure 1. Immatics' XPRESIDENT-based multi-dimensional analysis of PRAME.

- HLA-A*02:01-presented PRAME peptide for development of TCR-based therapies selected among >30 possible PRAME-derived HLA-A*02:01 peptides
- Mass spectrometry (MS) and matched RNAseq data from healthy normal and tumor samples were processed and organized into a large quantitative immuno-peptidomics database using proprietary immunoinformatics platform XCUBE
- Based on matched RNAseq and MS data, we defined an RNA threshold which corresponds to actual peptide presentation (Fritsche *et al.*, 2018). This MS-guided RNA threshold is used for
  - clinical patient stratification
  - prevalence estimation

Bringing Two Distinct TCR-based Modalities to Cancer Patients by Targeting PRAME

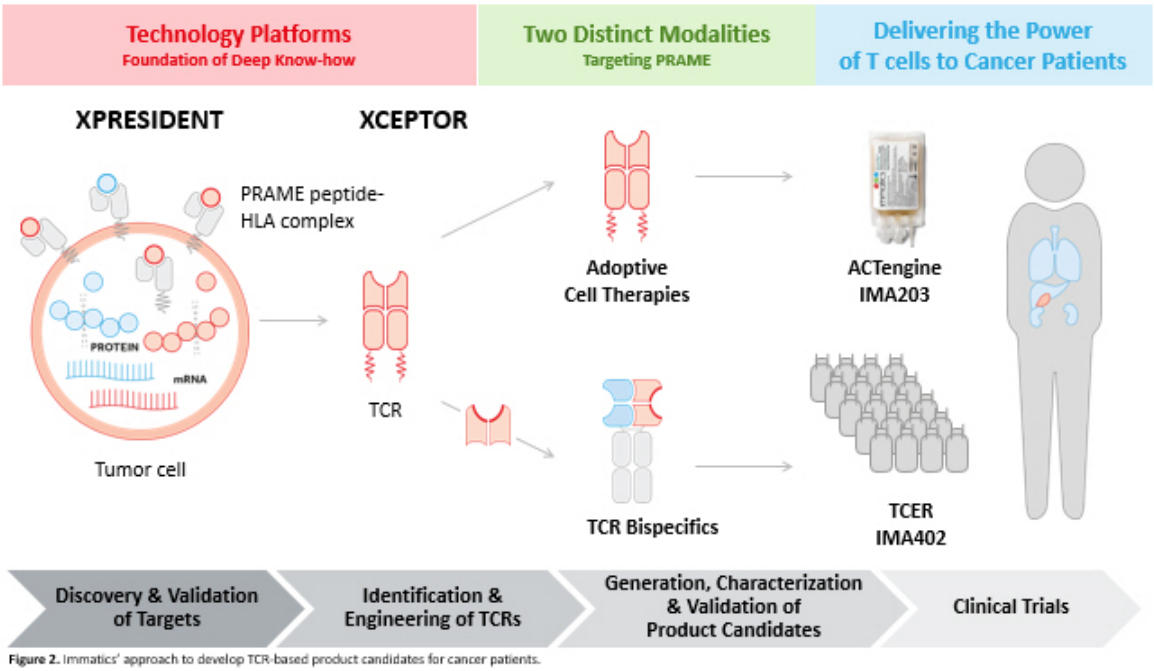


Figure 2. Immatics' approach to develop TCR-based product candidates for cancer patients.

PRAME Expression is Highly Cancer-Associated

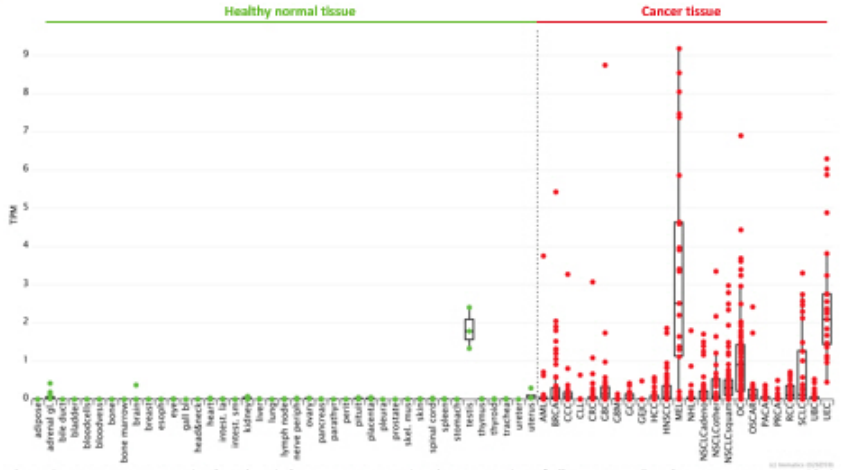


Figure 3. PRAME exon expression based on in-house RNA sequencing data. Expression of all exons encoding the PRAME target peptide in normal tissues from various organs and in different hematologic and solid cancer types. Each dot represents the maximum TPM value across all peptide-encoding exons in one sample. Box-and-whisker plots represent TPM values of multiple samples per organ or tumor entity. TPM: transcripts per million.

- PRAME RNA expression is elevated across multiple different solid tumor types
- Stable PRAME RNA expression across early and late tumor stages and tumor subtypes
- Minimal expression in some normal tissues except testis, not translating into relevant peptide presentation (see Figure 4)

PRAME Peptide Is Presented across Multiple Tumors

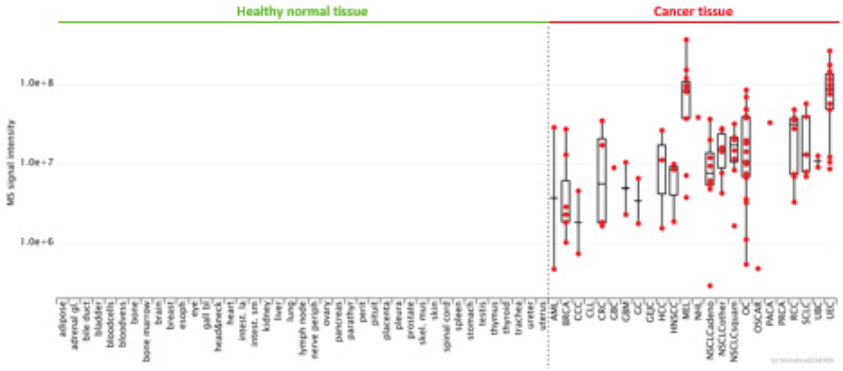


Figure 4. HLA*02:01-presented PRAME relative presentation levels on HLA-A*02 positive normal and tumor tissues quantified via MS. Each dot represents the median PRAME pHLA-derived MS intensity as an indicator for target abundance in one sample. Box-and-whisker plots represent signal intensities of multiple samples per organ or tumor entity.

- HLA-A*02:01-presented PRAME peptide can be measured directly via mass spectrometry in over 20 solid and liquid tumor entities
- PRAME RNA expression does not translate into relevant presentation on healthy normal tissues
- Quantification using Immatics' highly sensitive AbsQuant technology reveals PRAME target density of 100-1,000 copies per cell in tumor tissues

PRAME Is Homogenously Expressed across Different Solid Tumors

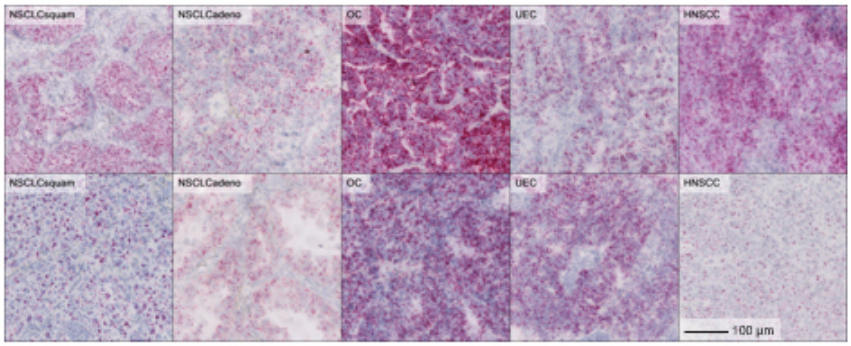
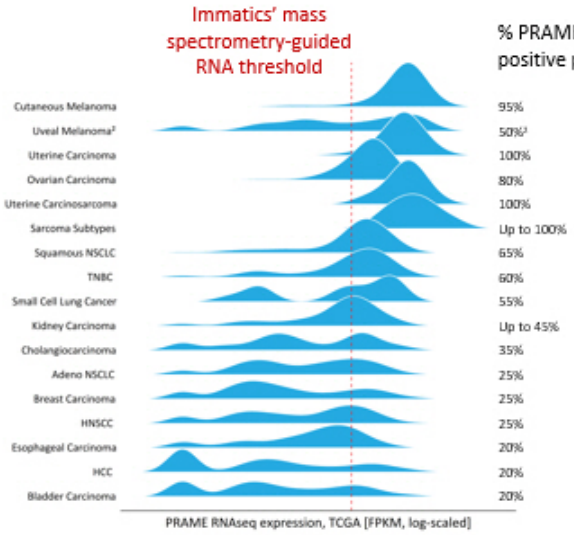


Figure 5. Spatial expression of PRAME analyzed by in situ hybridization (ISH) in various tumor types (NSCLCsquam, NSCLCadeno, OC, UEC, HNSCC). Representative images from two patients per tumor type. Positive signal intensity is visualized as red dots or clusters of red dots using Fast Red. Nuclei are stained with haematoxylin. Scale bar 100 µm.

- *In situ* hybridization was used to analyze PRAME expression homogeneity in several solid tumor samples
- Histologic analysis of PRAME RNA in different solid tumors demonstrates homogenous expression of PRAME with a high frequency of positive tumor cells

Clinical Validation of PRAME as Multi-Tumor Target for TCR-based Therapies



Patient screening data obtained via IMADetect biomarker assay in Immatics' clinical trials support high prevalence of PRAME

Clinical validation of Immatics' mass spectrometry-guided RNA threshold for PRAME: Confirmed responses were observed at high and low PRAME-expression levels above the threshold

Figure 6. PRAME target expression and prevalences in selected solid cancer types based on in-house and TCGA data (https://www.cancer.gov/tcga). [1] PRAME target expression and prevalence based on TCGA (for SCLC: in-house) RNAseq data combined with a proprietary MS-guided RNA expression threshold; [2] 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

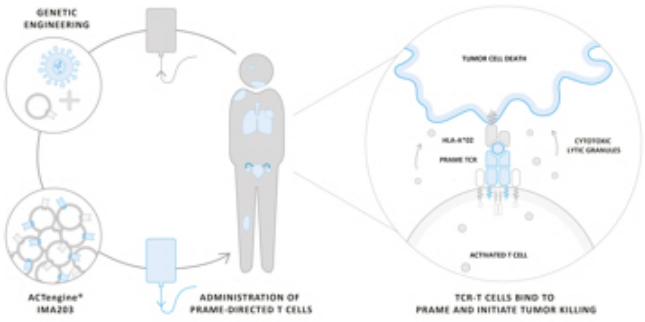


Figure 7. ACTengine IMA203 TCR-T targeting PRAME. For application as TCR-engineered T cell therapy (TCR-T) approach, the IMA203 PRAME TCR is engineered via lentiviral transduction into a patient's own T cells whose tumor has been tested positive for PRAME. The TCR-T cells are designed to bind to the PRAME pHLA target to induce a robust and specific anti-tumor response to fight the cancer.

- High clinical activity of IMA203 TCR-T: 50% (6/12) confirmed objective response rate (cORR) in patients with at least 1 billion infused TCR-T cells across Phase 1a and 1b; thereof 80% cORR (4/5) in Phase 1b patients alone with all responses ongoing at data cut-off*
- Most frequent treatment-emergent adverse events (TEAEs) were cytopenia, cytokine release syndrome, and grade 1 and 2 immune effector cell associated neurotoxicity syndrome. The TEAE profile is acceptable and adverse events were manageable
- Confirmed responses across different solid tumor types: cutaneous melanoma, ovarian cancer, head and neck cancer, uveal melanoma, and synovial sarcoma

* Immatics ACTengine® IMA203 TCR-T Targeting PRAME Monotherapy Interim clinical Data Update on Oct 10, 2022 (data cut-off Sep 6th, 2022)

Conclusions

Here, we demonstrate comprehensive target characterization and validation data supporting the favorable target properties of PRAME that can be exploited for the benefit of patients. Preclinical data of PRAME show that the target is

- highly cancer-associated,
- presented at high target density,
- homogenously expressed and
- highly prevalent across many solid cancers

underlining its potential to reach a large cancer patient population.

The data obtained during the ongoing Phase 1 trial provide clinical validation of PRAME as a highly promising T cell target for solid cancers. Confirmed clinical responses were observed at all PRAME-expression levels above threshold, indicating IMA203's potential to provide clinical benefit for all PRAME biomarker-positive cancer patients with tolerable adverse events. The predicted high PRAME prevalence across key indications has so far been supported by prevalence rates obtained during the clinical screening of patients.

Acknowledgements: We are immensely grateful to the patients and their families.

Abbreviations: adipose: adipose tissue; adrenal gl: adrenal gland; bloodvess: bloodvessel; esoph: esophagus; gall bl: gallbladder; intest. la: large intestine; intest. sm: small intestine; nerve periph: peripheral nerve; parathyr: parathyroid gland; perit: peritoneum; pituit: pituitary; skel. mus: skeletal muscle; thyroid: thyroid gland; AML: acute myeloid leukemia; BRCA: breast cancer; CCC: cholangiocellular carcinoma; CLL: chronic lymphocytic leukemia; CRC: colorectal cancer; GBC: gallbladder cancer; GBM: glioblastoma; GC: gastric cancer; GEJC: Gastro-esophageal junction cancer; HCC: hepatocellular carcinoma; HNSCC: head and neck squamous cell carcinoma; MEL: melanoma; MPNST: malignant peripheral neve sheath tumor; NHL: Non-Hodgkin lymphoma; NSCLCadeno: non- small cell lung cancer adenocarcinoma; NSCLCother: NSCLC samples that could not unambiguously be assigned to NSCLCadeno or NSCLCsquam; NSCLCsquam: squamous cell non-small cell lung cancer; ORR: objective response rate; OC: ovarian cancer; OSCAR: esophageal cancer; PACA: pancreatic cancer; PRCA: prostate cancer; RCC: renal cell carcinoma; TNBC: triple-negative breast cancer; SCLC: small cell lung cancer; UBC: urinary bladder carcinoma; UEC: uterine and endometrial cancer.

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