TSCAN THERAPEUTICS

Unleash Immunity

Investor Presentation
May 2023

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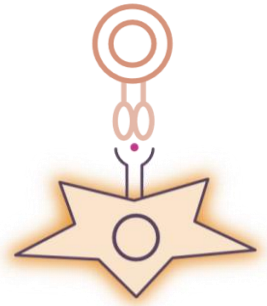
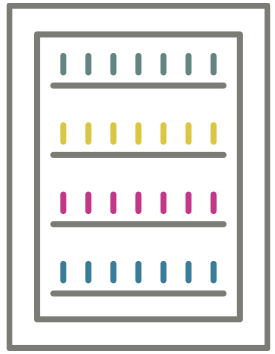
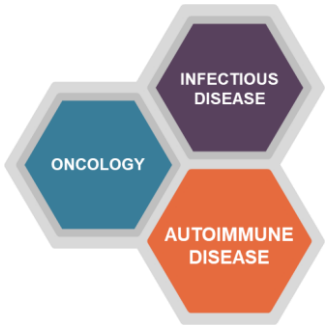
TScan: A fully integrated, next-generation TCR-T cell company





Transformative platform enables rapid **Discovery of Targets and TCRs** for engineered T cell therapy



Heme Program to prevent relapse following allogeneic HCT

- First patient dosed; Phase 1 multi-site trial currently enrolling

Solid Tumor Program to deliver **Enhanced Multiplexed TCR-T**

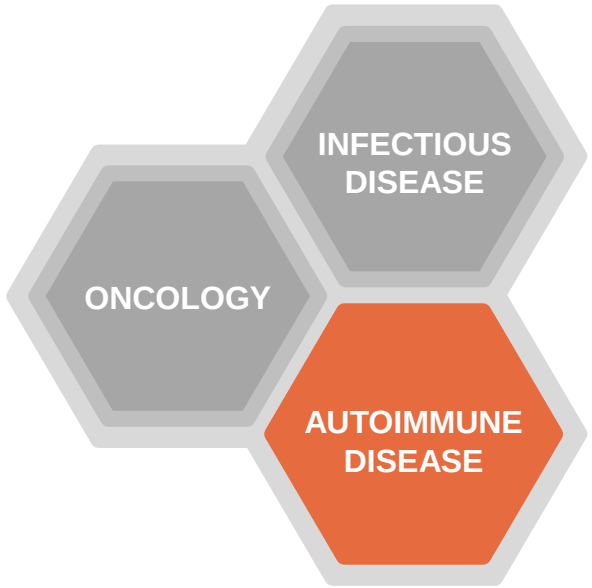
- First three INDs cleared in January 2023; four more planned this year

In-house GMP Manufacturing using non-viral vectors

- Seamless transition through development
- Large cargo size enables multiple enhancements (CD8α/β, DN-TGFβRII)

Cash of $95.6 MM (Q1 2023) Along with Amgen Proceeds ($30 MM) Extends Runway into Q3 2024

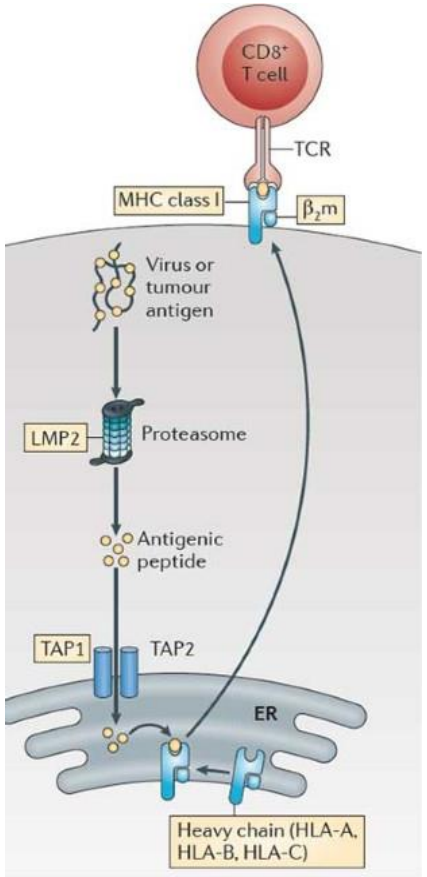
Amgen partnership builds value in autoimmune disease



- Multi-year collaboration uses TargetScan to identify targets recognized by CD4+ T cells in patients with Crohn's disease; option to expand collaboration in ulcerative colitis
- Amgen developing modalities to create novel therapeutics using identified antigens
- Financials include:
  - *$30 million upfront payment*
  - *Success-based development and commercial milestone payments of over $500 million*
  - *Covers one HLA type; opt-in for additional HLAs for additional economics*
  - *Tiered royalties*

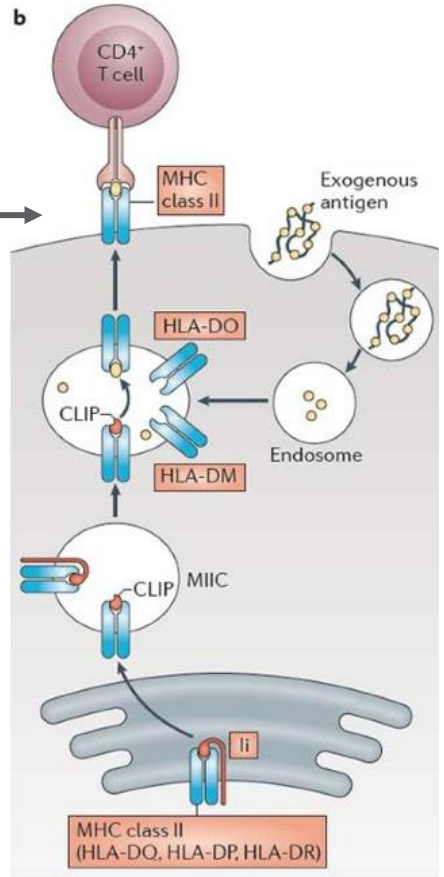
Extends cash runway into 3Q 2024

TargetScan screening extended to class II HLAs to identify targets of CD4+ T cells mediating many autoimmune diseases



Class I HLAs present antigens to CD8+ T-cells relevant for TScan oncology program and select autoimmune diseases

Class II HLAs present antigens to CD4+ effector and regulatory T cells mediating many additional autoimmune diseases

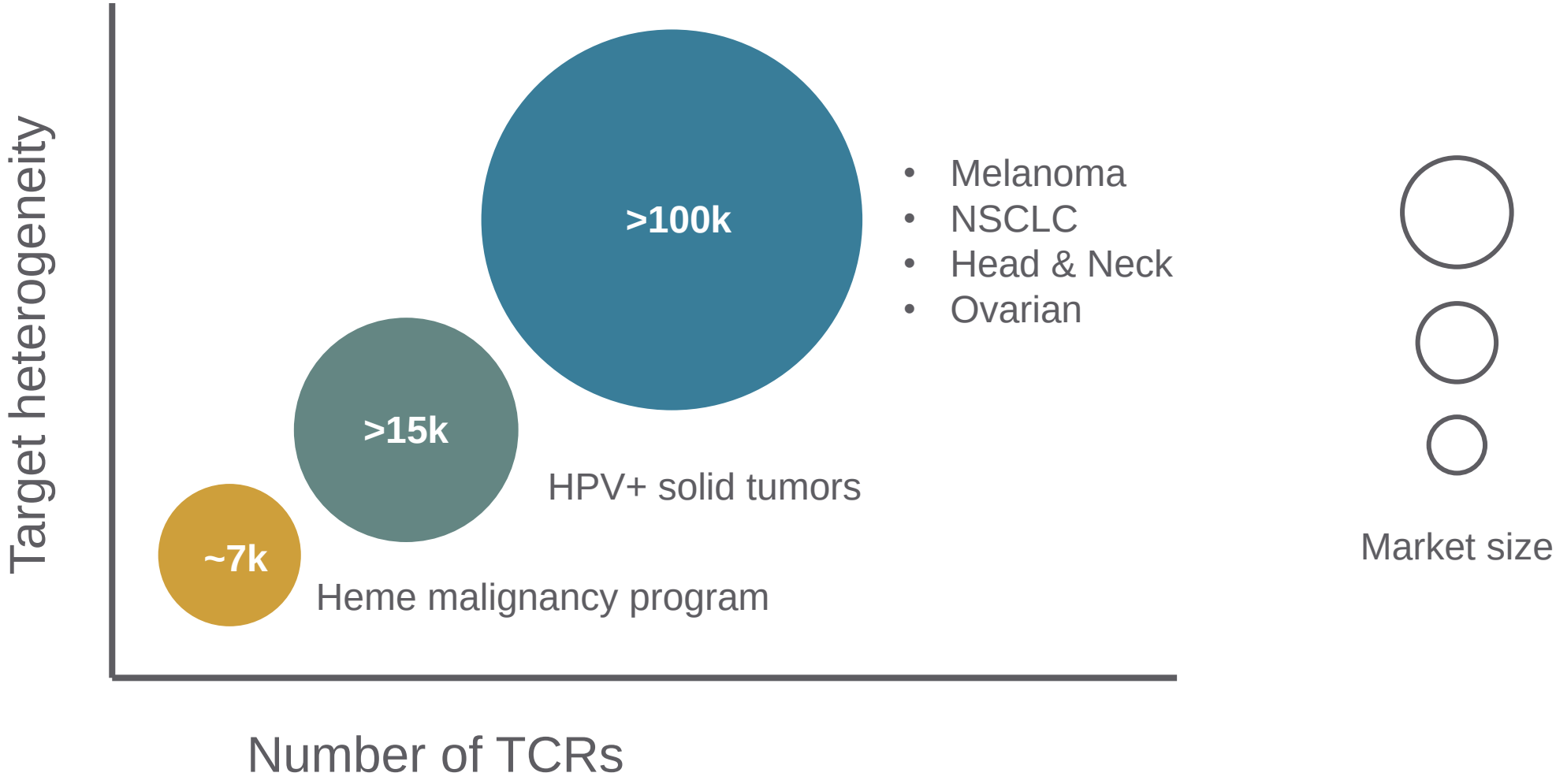


Kobayashi *et al*, *Nat Rev Immunol*, 2012

TScan has initiated tissue collection and novel target discovery for other T cell-mediated autoimmune diseases such as:

Ankylosing spondylitis, celiac disease, multiple sclerosis (MS), psoriasis, scleroderma, vitiligo and others

TScan's oncology programs sequentially build value

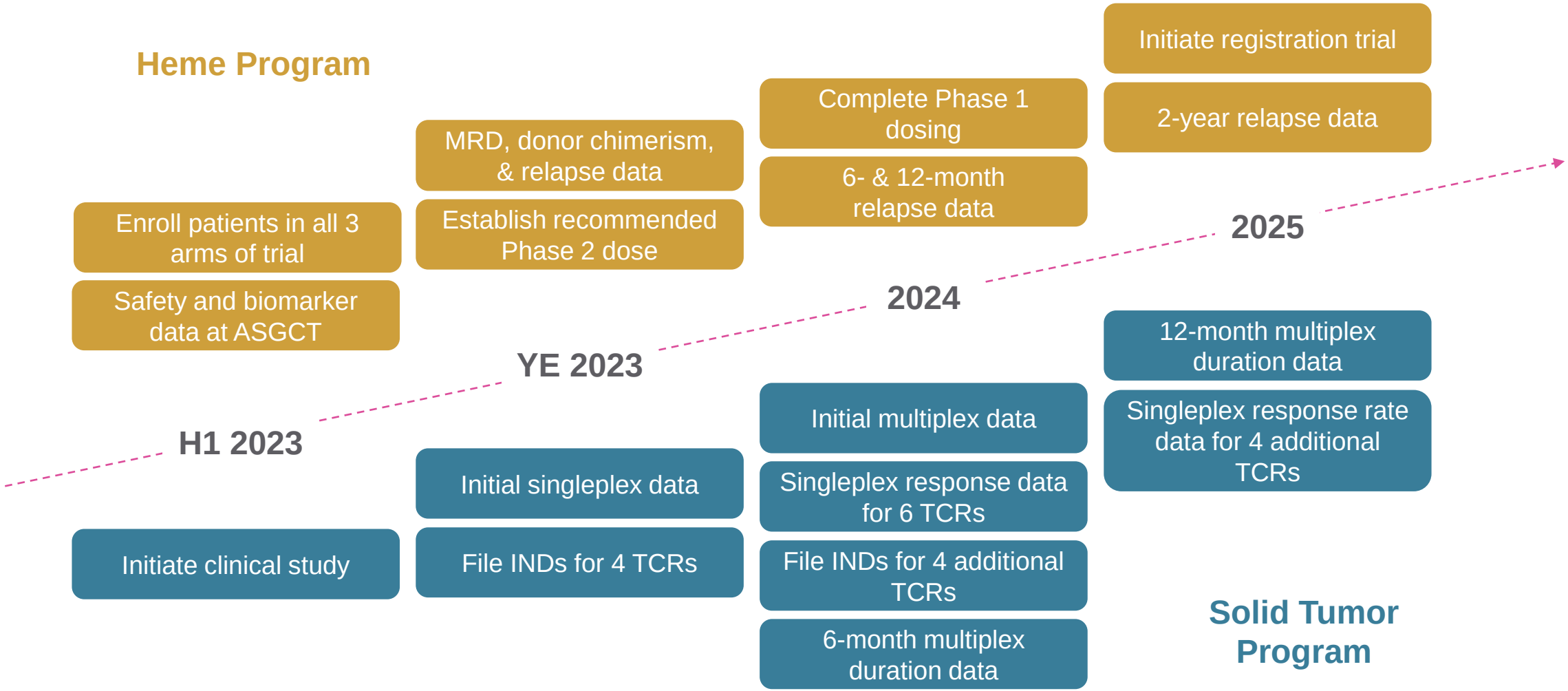


Platform delivers broad proprietary pipeline

PROGRAMS (TARGET)	HLA Type	Indications	Discovery	Lead Optimization	IND-Enabling	Phase 1	Phase 2/3
Hematologic Malignancies							
TSC-100 (HA-1)	HLA-A*02:01	AML, MDS, ALL					
TSC-101 (HA-2)	HLA-A*02:01						
Solid Tumors							
TSC-200 (HPV16)	HLA-A*02:01 HLA-B*07:02 HLA-C*07:02	Head & Neck, Cervical, NSCLC, Melanoma, Ovarian					
TSC-201 (undisclosed)	HLA-B*07:02 HLA-A*02:01 HLA-A*24:02						
TSC-202 (undisclosed)	HLA-A*02:01						
TSC-203 (PRAME)	HLA-A*02:01 HLA-B*07:02						
TSC-204 (MAGE-A1)	HLA-A*02:01 HLA-C*07:02 HLA-A*01:01 HLA-A*03:01 HLA-B*07:02						
TSC-205 (undisclosed)	HLA-A*02:01						

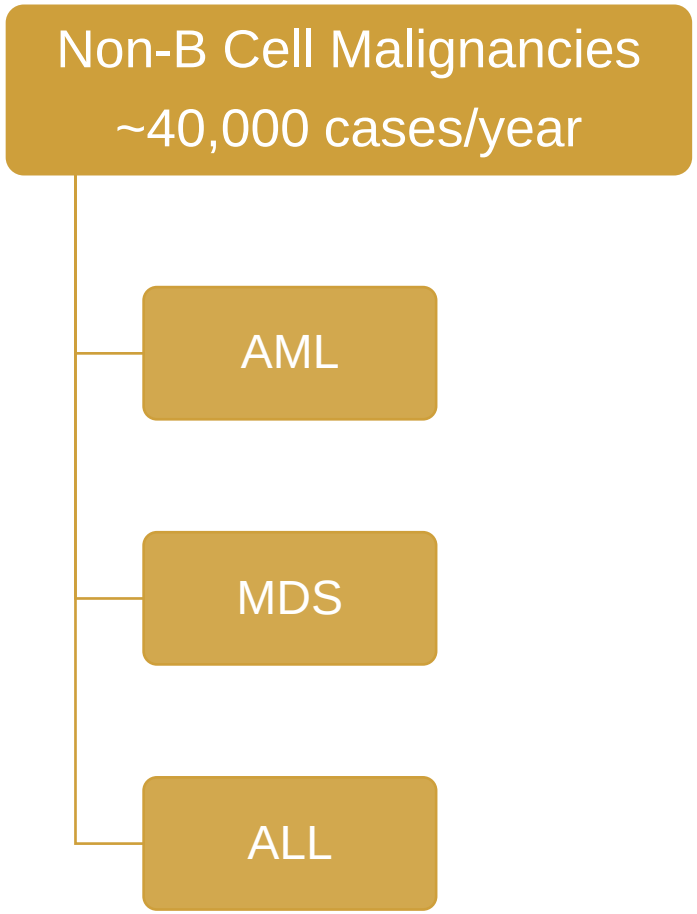
*Primary solid tumor IND, **T-Plex**, supports simultaneous use of multiple TCRs*

Steady value-generating data flow across clinical programs



Clinical Programs:
Hematologic Malignancies

TCR-T uniquely addresses myeloid leukemias

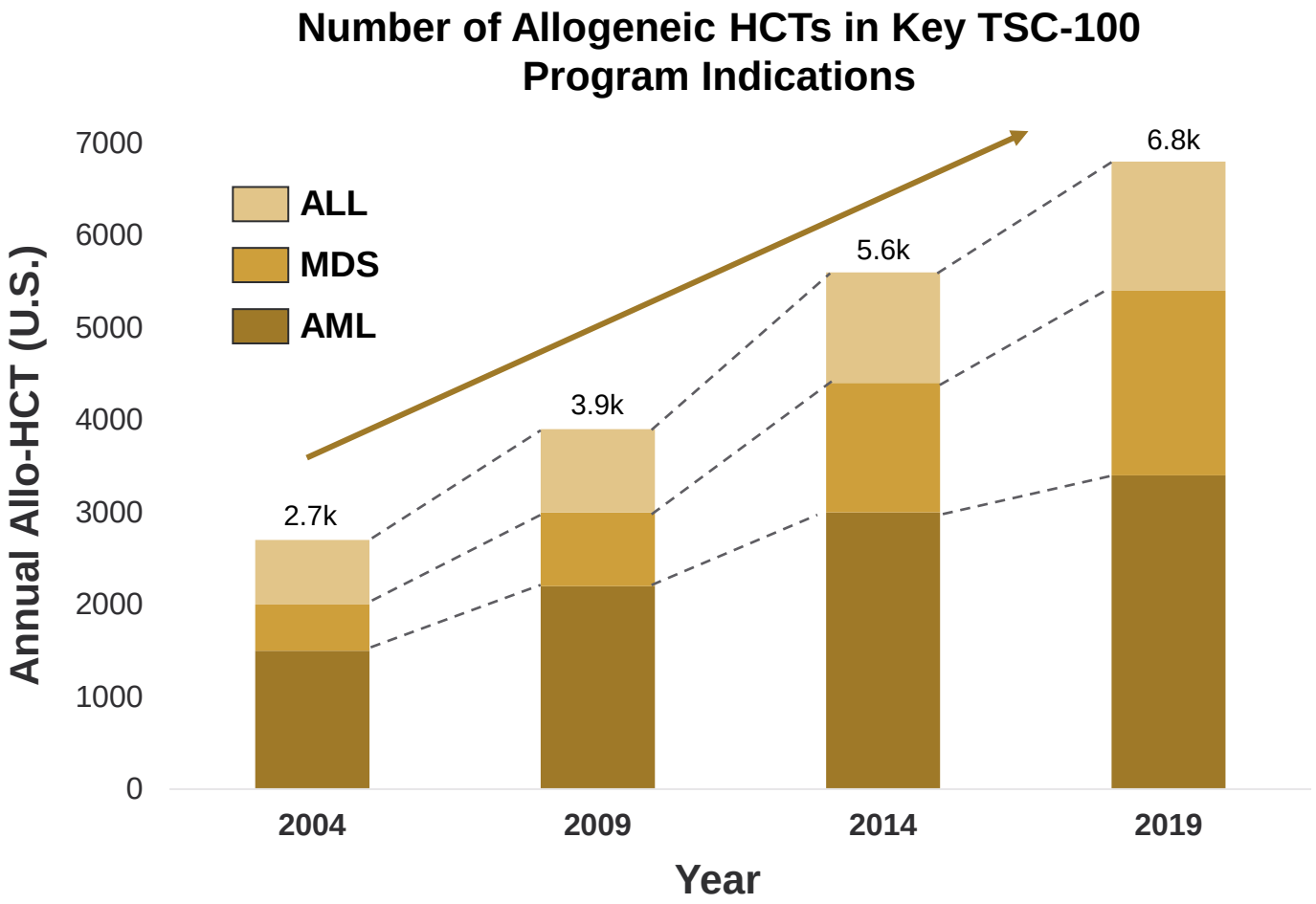


- Not addressable by CAR-T therapy
- Transplant is considered curative for many and is expected to remain standard of care
- ~40% of patients relapse post-transplant with few treatment options (~90% mortality within 1 year of relapse)

TScan program is designed to prevent relapse in patients undergoing HCT

Source: Independent KOL market research conducted June 2020.

Growing unmet transplant need in myeloid leukemias



~7,000 patients annually in the U.S. undergo allogeneic transplant (HCT)

HCT use has been increasing ~6% per year on average for the past 15 years

Addressable market limited by requirement for remission

Market will grow as pre-transplant novel agents bring more patients into remission

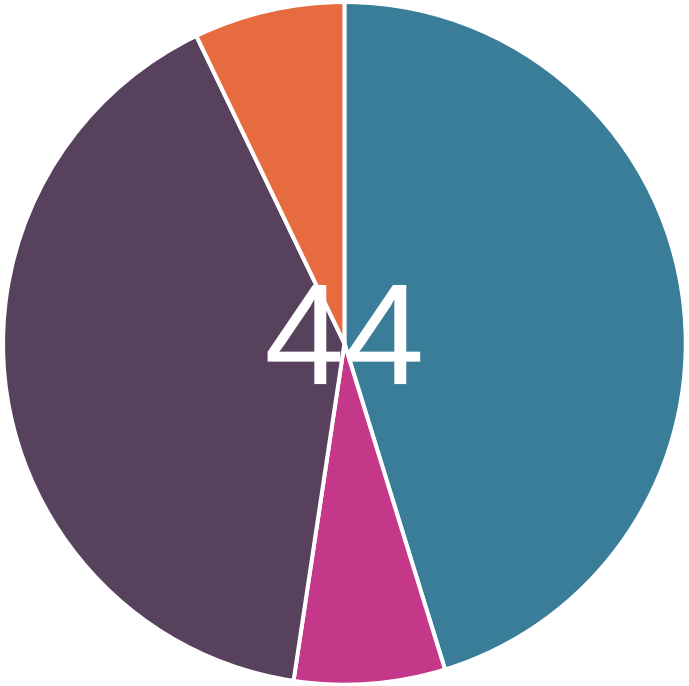
If TScan is successful, HCT will expand to majority of patients not in remission

Source: CIBMTR and independent market research conducted in July 2021.

Most cell therapy trials in AML are in the pre-transplant setting, where success increases our addressable market

Pre-Transplant

Number of clinical programs



Limitations

- **Most will be bridging to HCT** (e.g., NKarta)
- Success increases addressable market for TScan

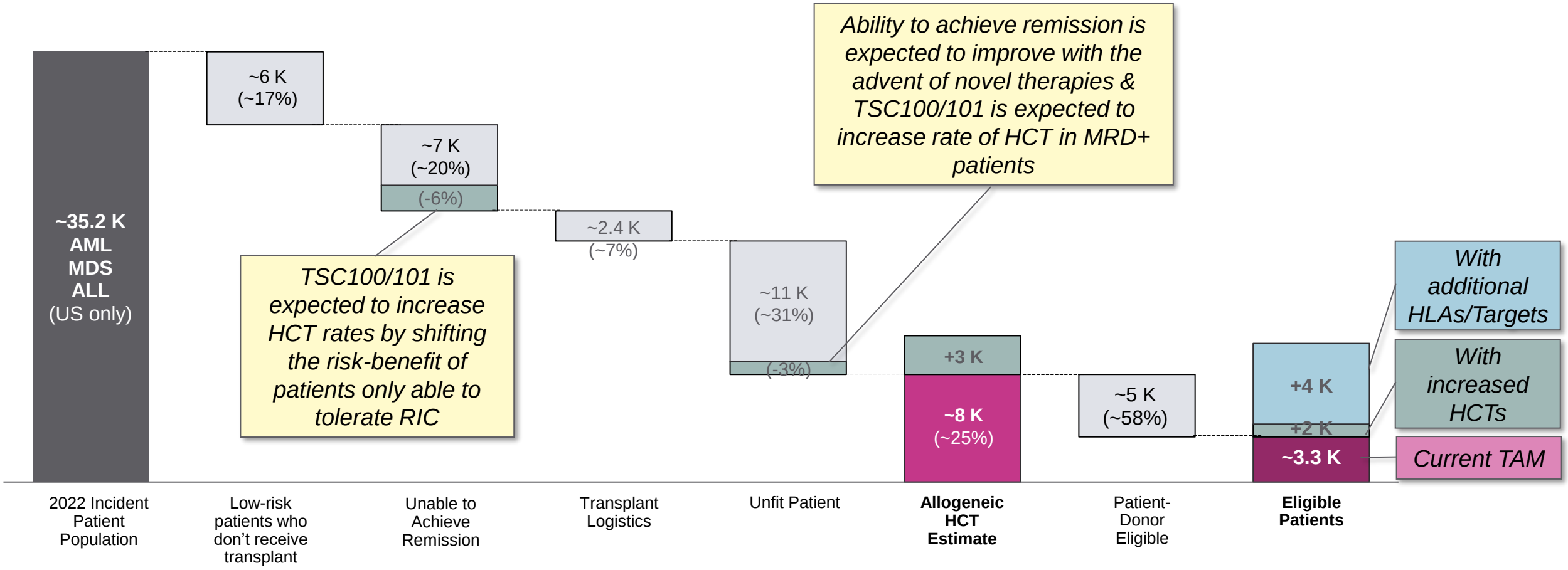
Peri/Post-Transplant

Transplant Add-On	Relapse Prevention	Post-HCT Relapse Tx
2	TScan  5	1
• GvHD prevention	• 1ary competition: gene-edited HSCs (Vor) • 2ary competition: ex vivo-expanded T cells, NK cells	• HighPass Bio (no longer active)

Key:

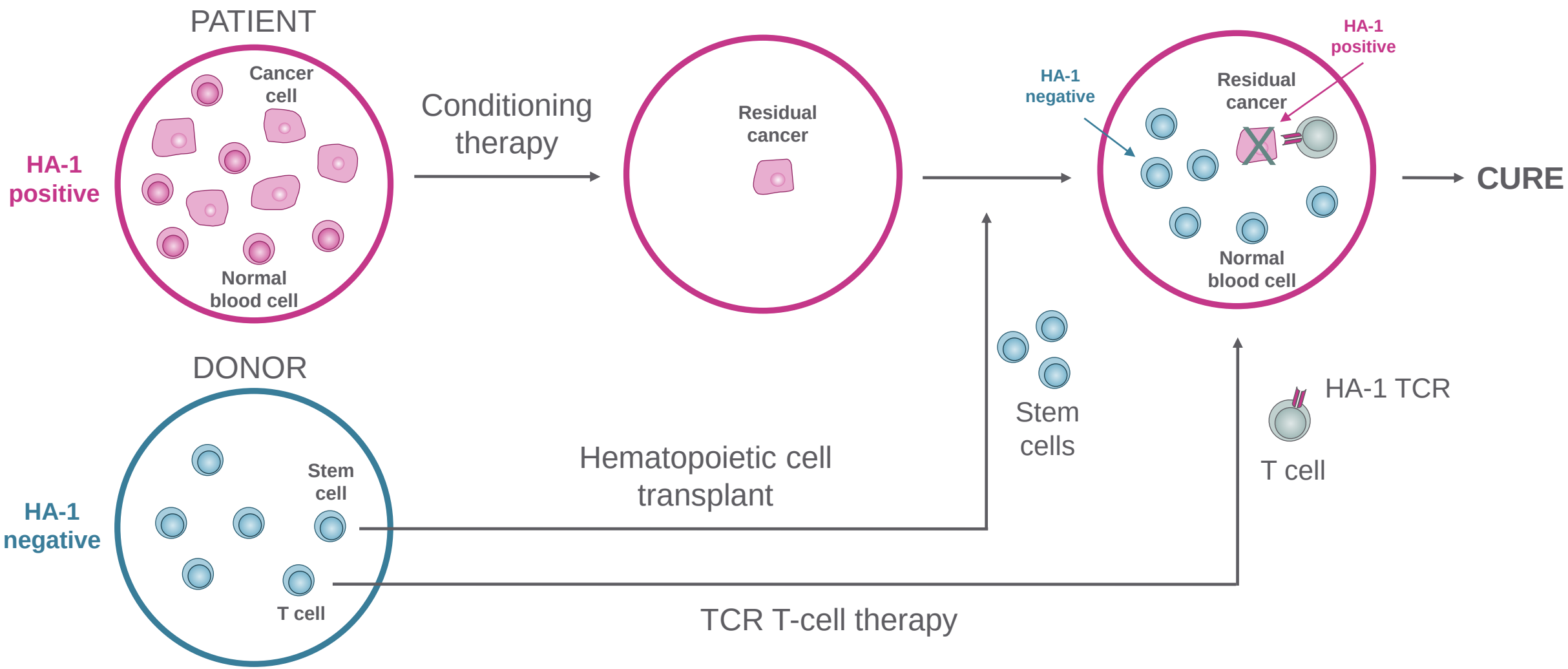
- TCR-T
- eHSC/CAR-T
- Sel Exp
- γδT/NK
- Vaccine
- Treg

Current US addressable market for heme program of 3,000+ patients could more than double with additional HLAs and changes in transplant practice



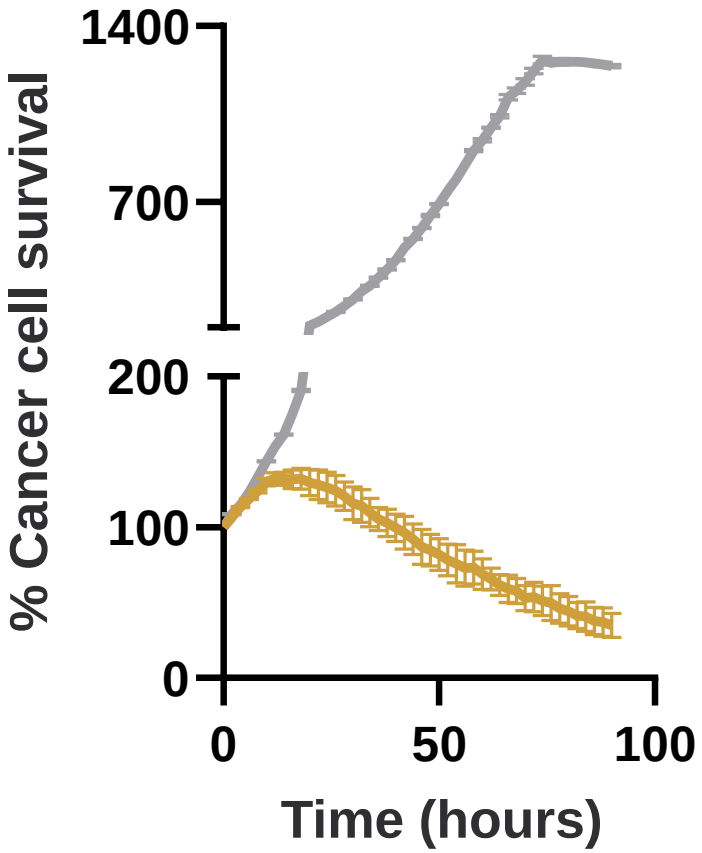
HCT: Hematopoietic Cell Transplant.
Source: SEER, CIBMTR, ClearView Analysis.

Eliminate residual cancer by targeting blood-specific antigens present in the patient but not the donor

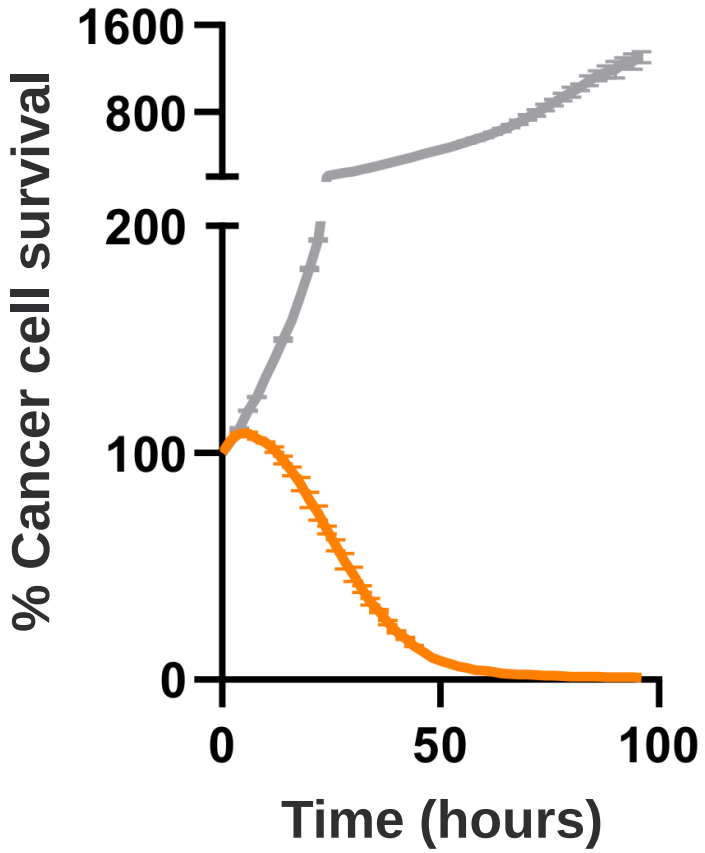


TSC-100 and TSC-101 address 40% of patients undergoing allogeneic HCT

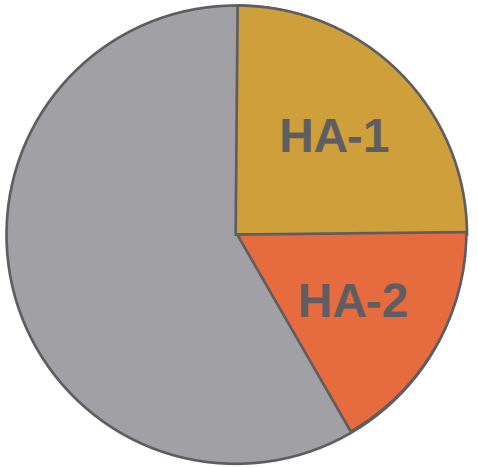
TSC-100
(HA-1 TCR-T)



TSC-101
(HA-2 TCR-T)

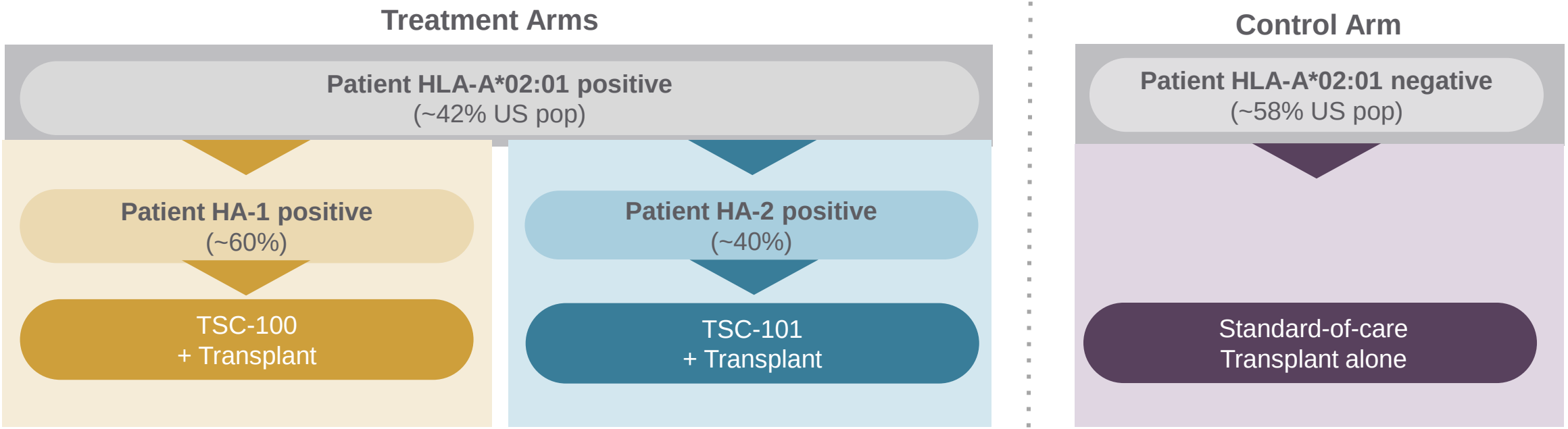


HA-1- or HA-2-positive
40% of allo-HCT



Hematologic malignancy program multi-arm Phase 1 clinical trial open for enrollment

Inclusion Criteria: Reduced Intensity Conditioning; Haploidentical donor transplant



Endpoints

Primary

- Safety, feasibility
- DLTs

Secondary

- Relapse rates:
  - 6 months ~22%
  - 12 months ~33%
  - 24 months ~42%

Exploratory

- Donor chimerism rates, kinetics
- Minimal residual disease (MRD)

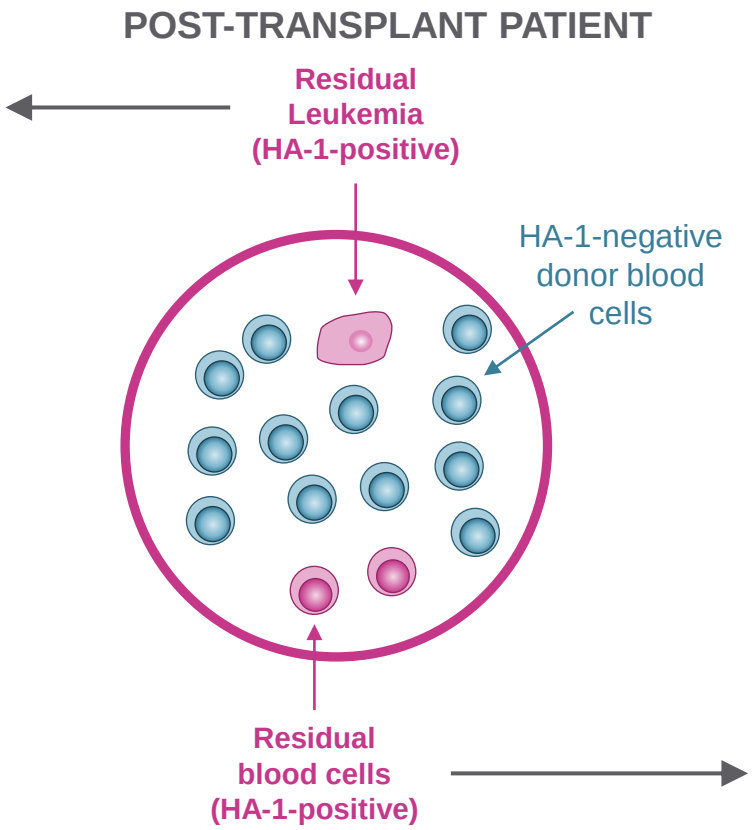
Key biomarkers measure residual leukemia or residual patient-derived blood cells as surrogates of efficacy

Minimal Residual Disease (MRD)

Conventional
- MRD by flow cytometry
- Sensitivity ~0.1%
- Performed at local sites

High sensitivity
- MRD by NGS
- Sensitivity ~0.01%
- Performed at Columbia University

MRD+ patients post-transplant (~30%) have ~90% chance of relapse[1,2].



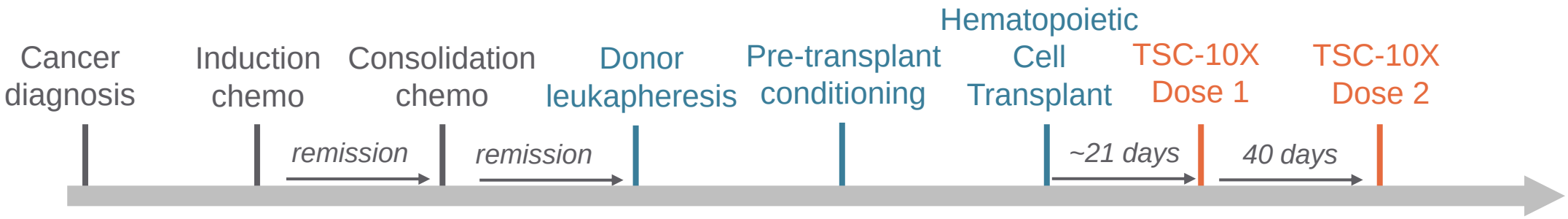
Mixed donor cell chimerism

Conventional
- STR assay
- Sensitivity ~1%
- Performed at LabCorp

High sensitivity
- NGS-based Alloheme assay
- Sensitivity ~0.03%
- Performed by CareDx

1. Craddock, J Clin Oncol 2021
2. Loke, ASH 2021

AML, MDS, and ALL transplant patients eligible for TScan trial



Hematopoietic cell transplant

- Patients must be in remission to qualify for transplant
- Reduced-intensity conditioning
  - Less toxic
- Haploidentical donors
  - Easier donor identification

TScan therapy

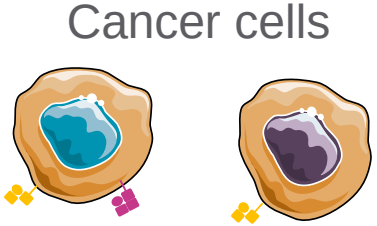
- 1-2 doses of TSC-100 or 101
  - (3 dose cohorts, 1-12 patients/ cohort)
- Endpoints:
  - Primary: safety
  - Secondary: relapse rates, DFS, OS
  - Exploratory: MRD, chimerism status

Clinical Programs:
Solid Tumor Program

TScan platform was deployed to understand, exploit, and enhance how T cells recognize and fight cancer

THE CHALLENGE

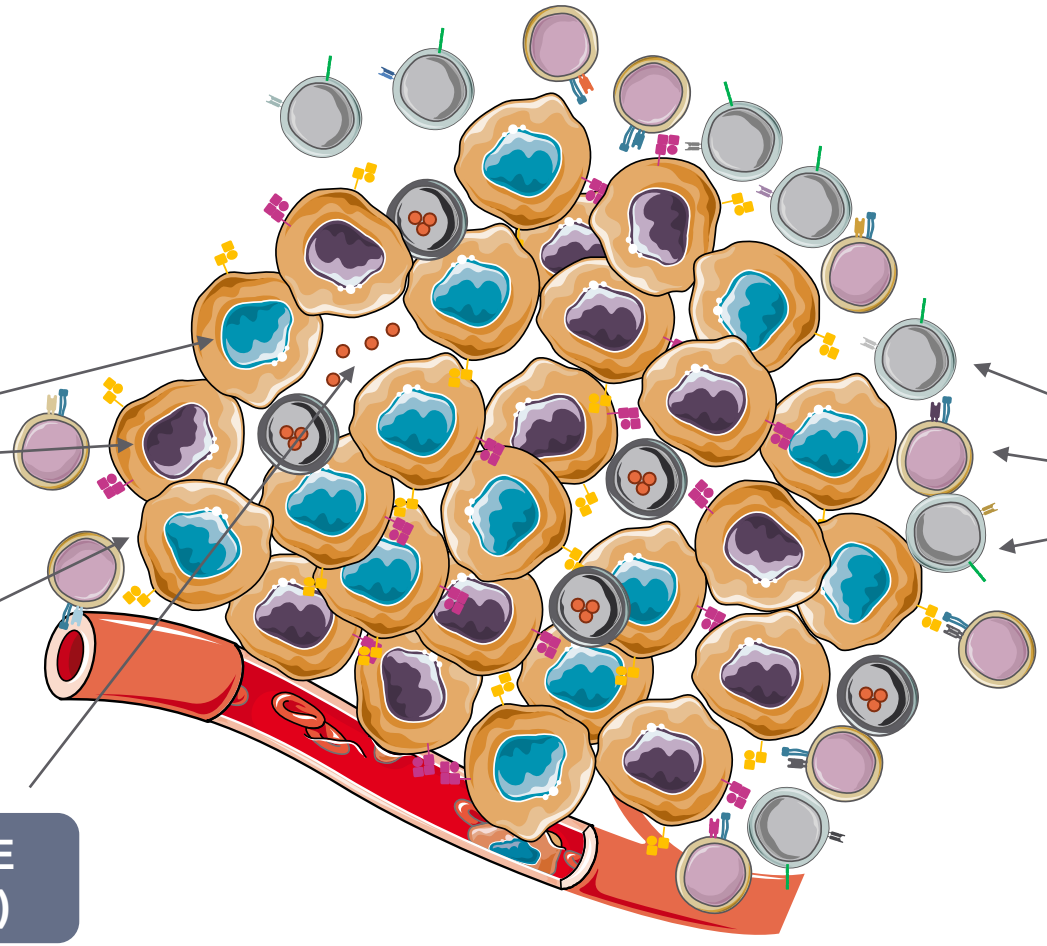
Cancer cells



Heterogeneous target expression

HLA loss

Hostile TME (e.g., TGFβ)



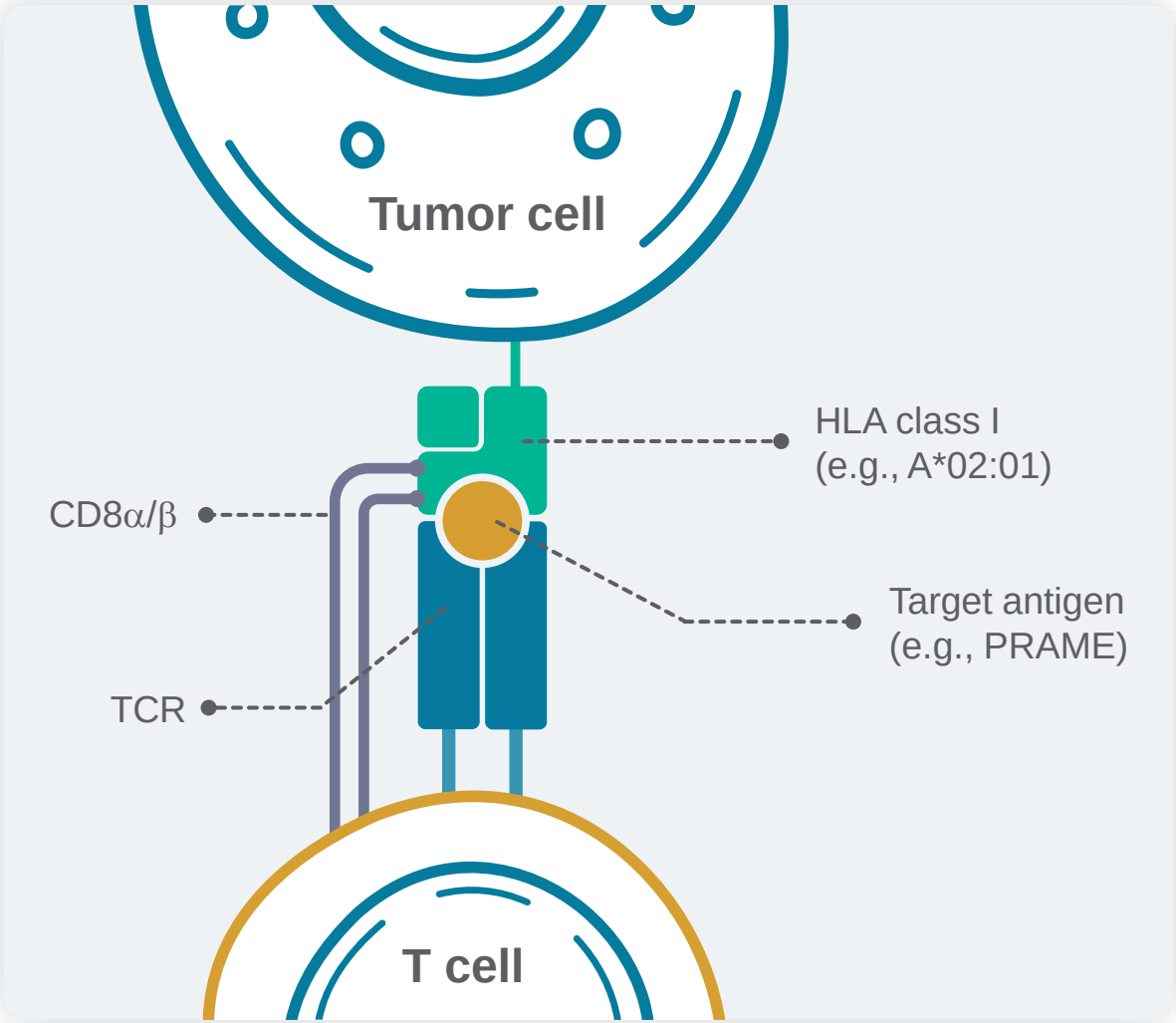
NATURE'S SOLUTION

T cells

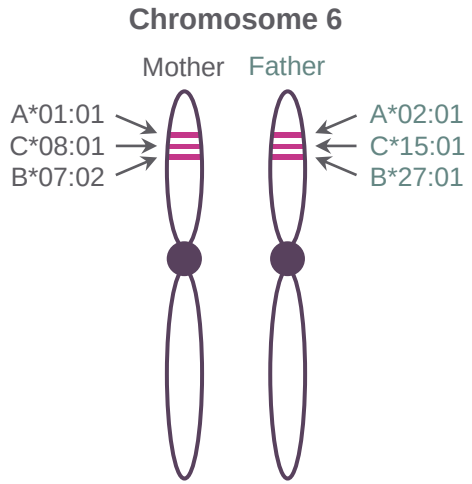
Diverse repertoire of CD4+ and CD8+ T cells

What do T cells naturally recognize and how can we use that information to design better therapeutics?

T cells are Nature's most effective way to kill cancer cells



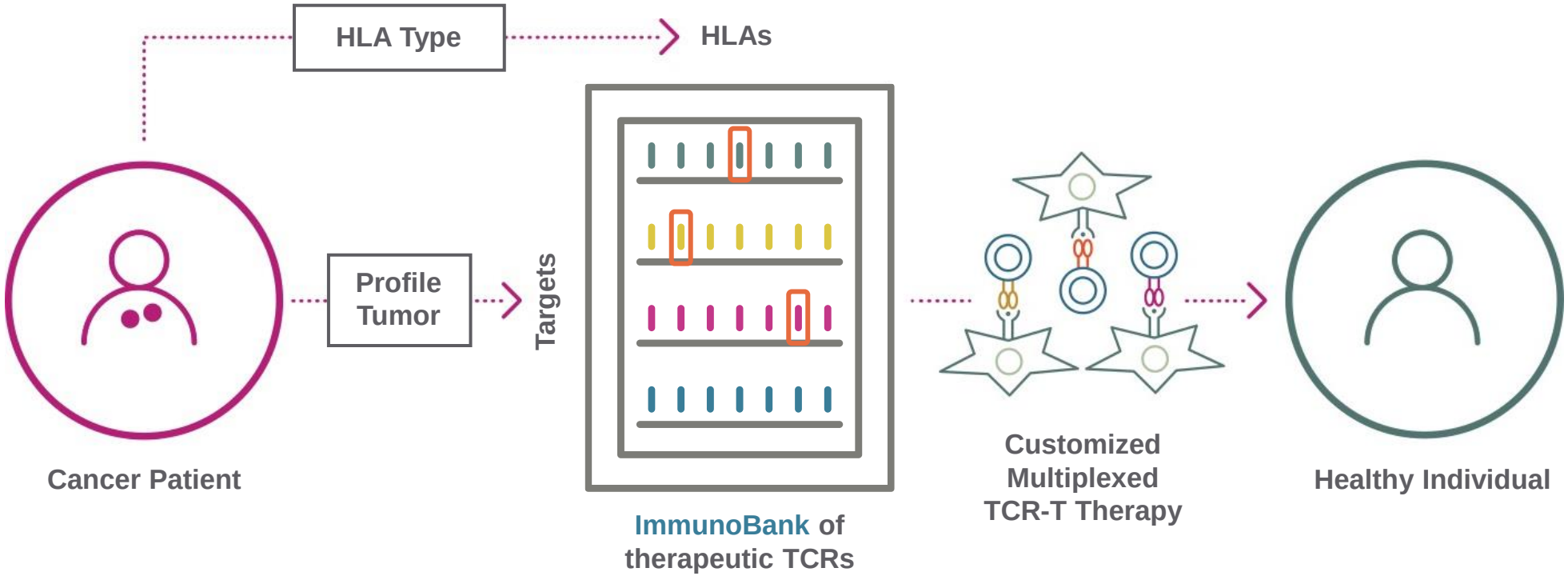
Everyone has six class I HLA alleles



~90% of people in the U.S. are positive for at least one of the top 6 class I HLAs

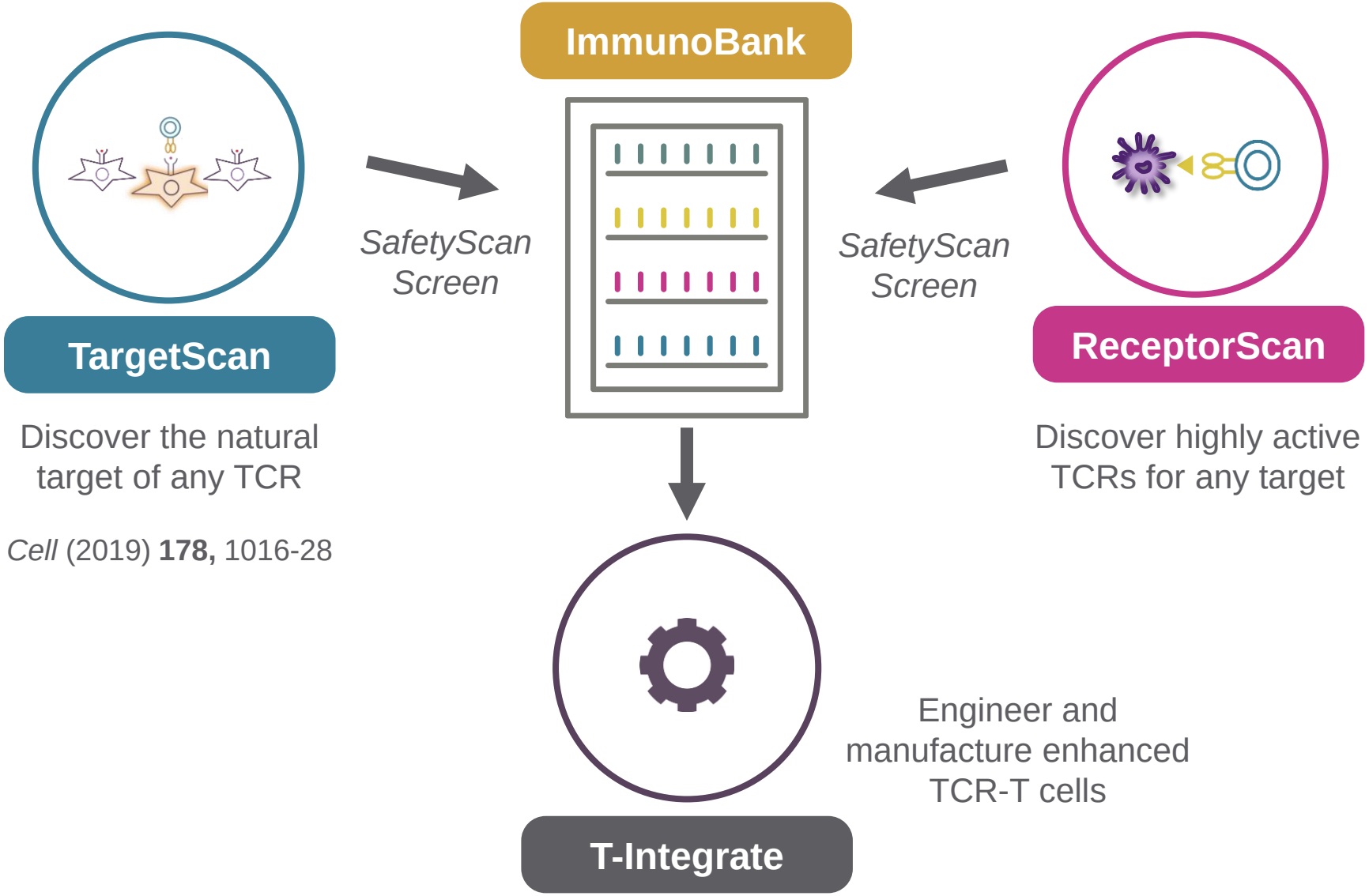
	% people positive for each HLA type		
HLA type	United States	Europe	Asia
A*02:01	42	47	19
A*01:01	24	26	14
A*03:01	22	25	7.0
B*07:02	20	21	8.1
C*07:02	24	23	24
A*24:02	17	19	37

TScan is building an ImmunoBank of TCRs to enable enhanced, multiplexed TCR-T cell therapy

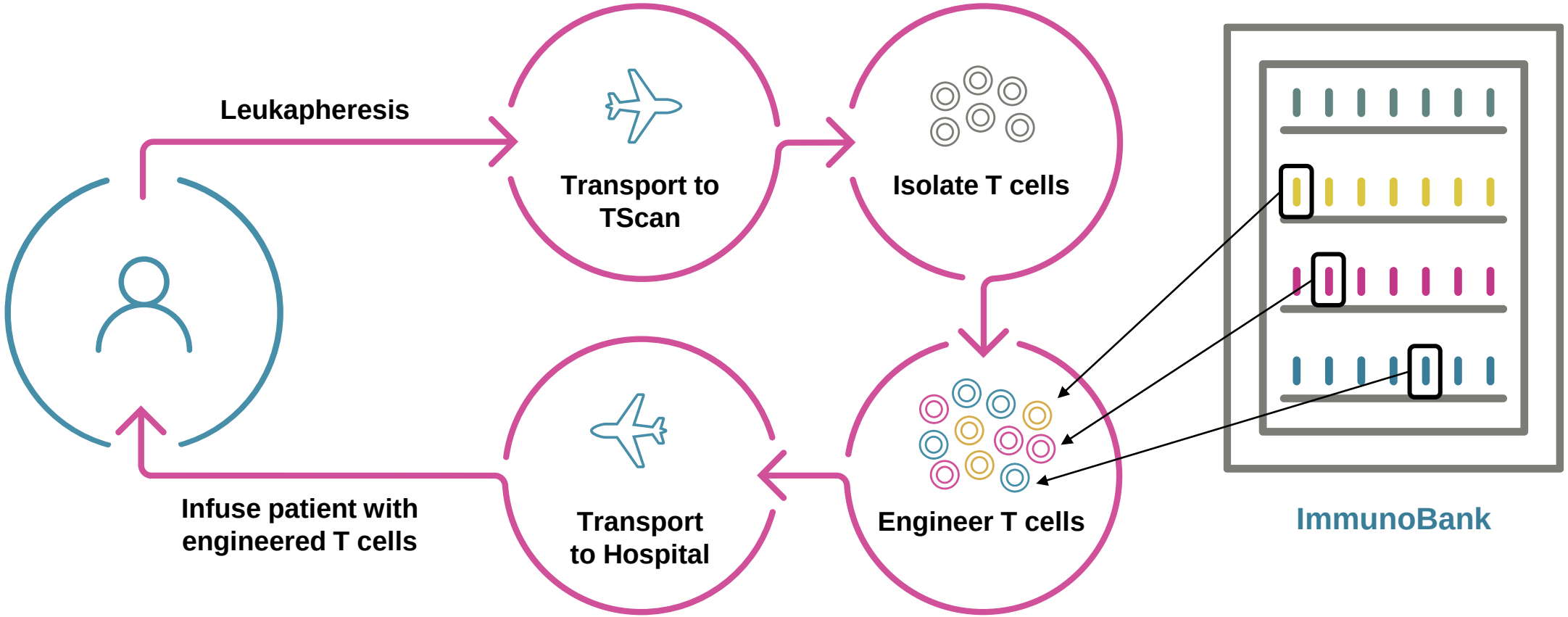


- Engineer T cells with potent, anti-cancer TCRs
- Enhance T cells to overcome the hostile tumor microenvironment
- Treat patients with multiplexed TCR-T cell therapy

Platform enables discovery and manufacturing of a broad range of enhanced TCR-T cell therapy candidates



In-house non-viral manufacturing delivers customized, enhanced TCR-T cells to patients



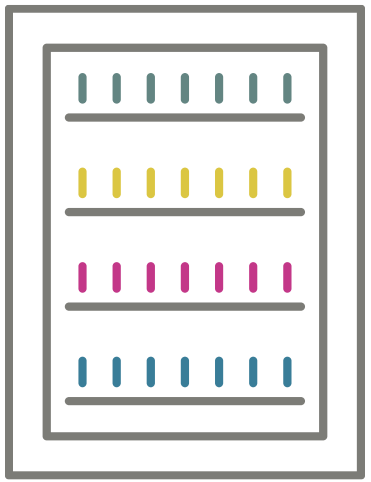
Transposon/transposase system enables lower COGs, faster development times, and larger cargo size for enhanced TCR-T cells

TScan solution is to develop *enhanced, multiplexed* TCR-T

TScan's solution for increasing duration of response

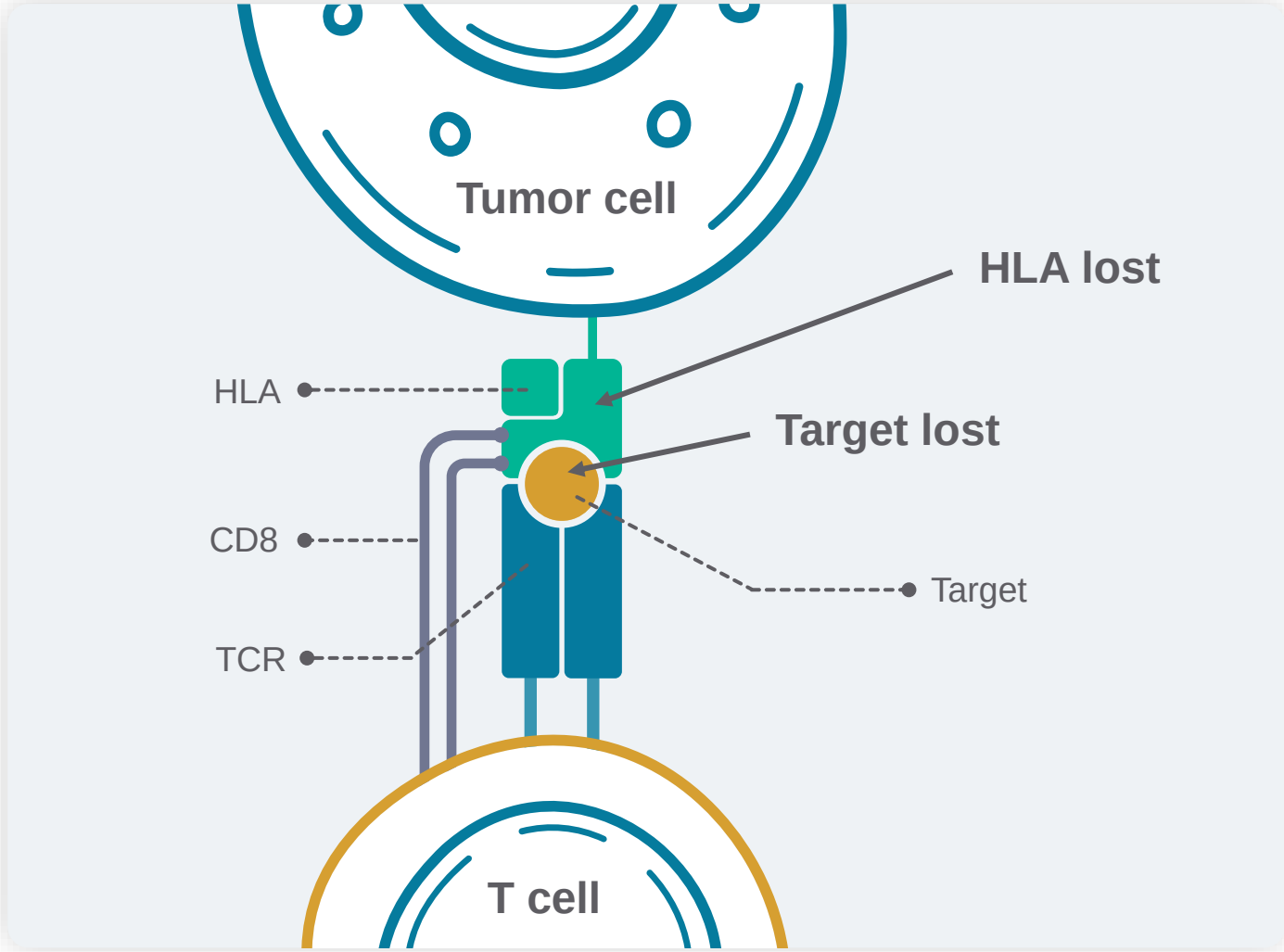
- **Prevent relapse**
  - 1 **Multiplexed TCR-T**
- **Prospectively select patients**
  - 2 Target and HLA LOH
- **Increase response rates**
  - 3 CD8α/β
- **Enhance persistence**
  - 4 DN-TGFβRII

ImmunoBank



Target or HLA loss leads to TCR-T resistance in solid tumors

1 **Prevent relapse**

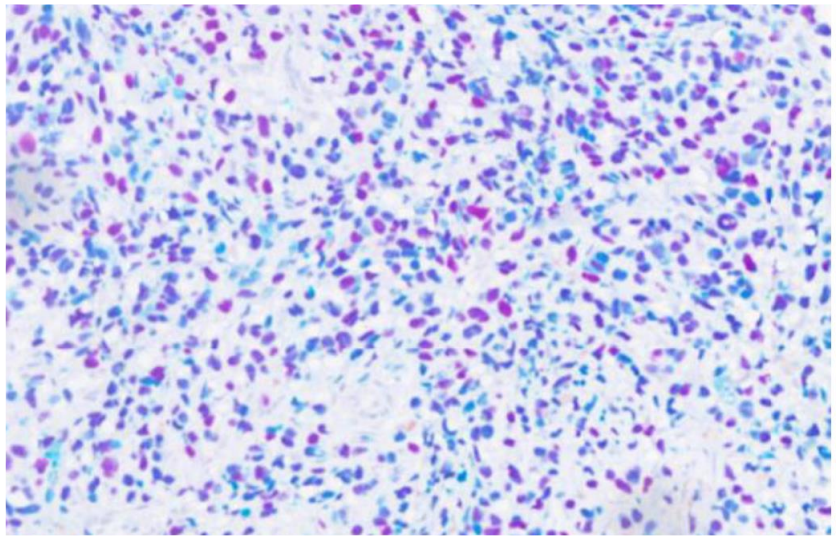


If the target is missing or lost, the patient is likely to experience a partial response followed by a rapid relapse

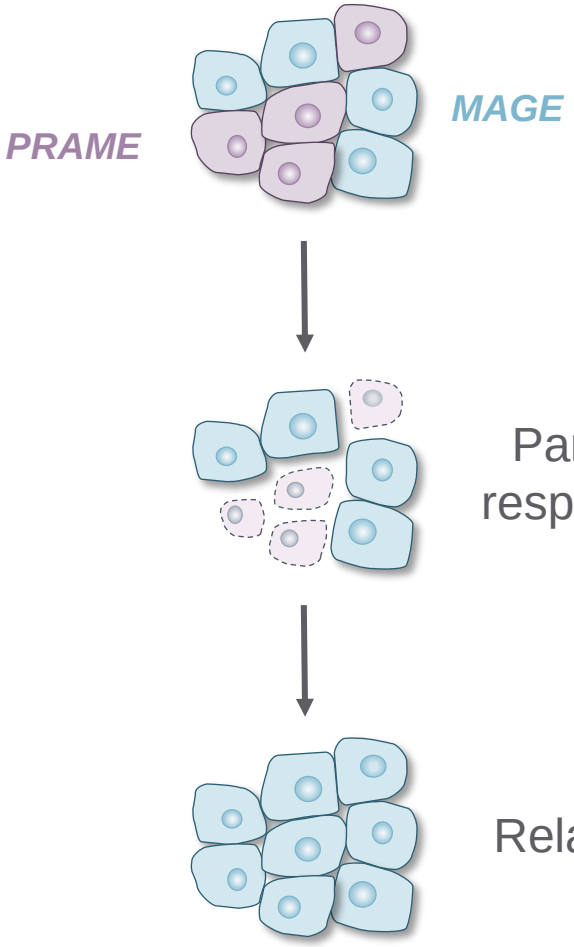
Tumor exhibiting target heterogeneity

PRAME

MAGE

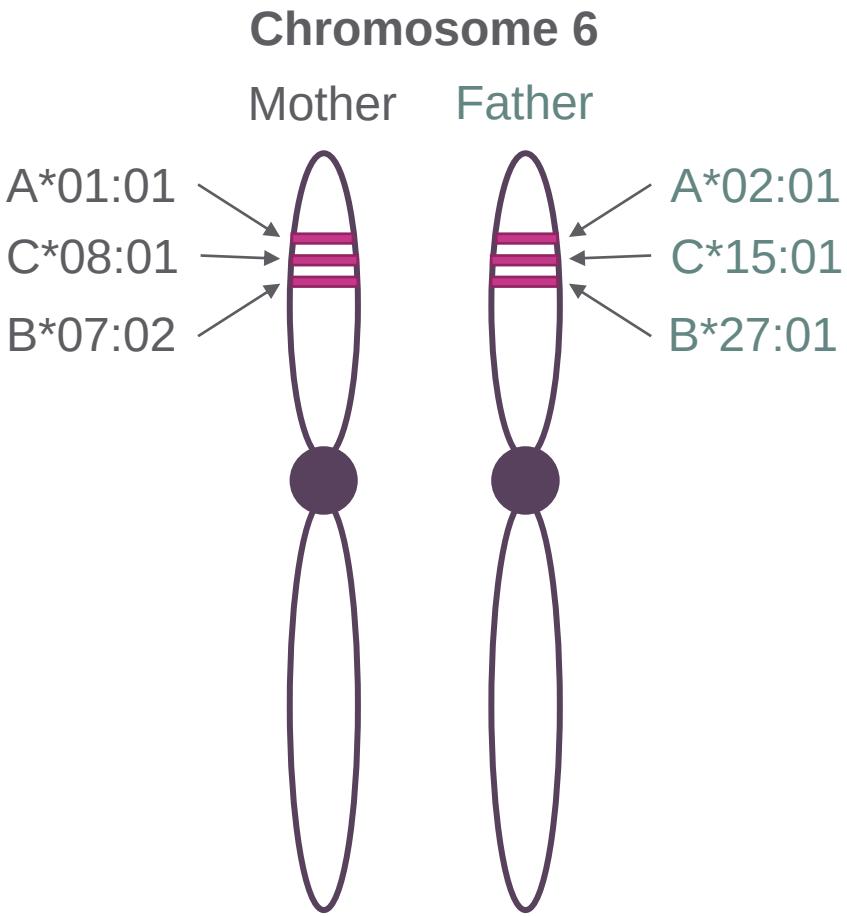


SOLID TUMOR

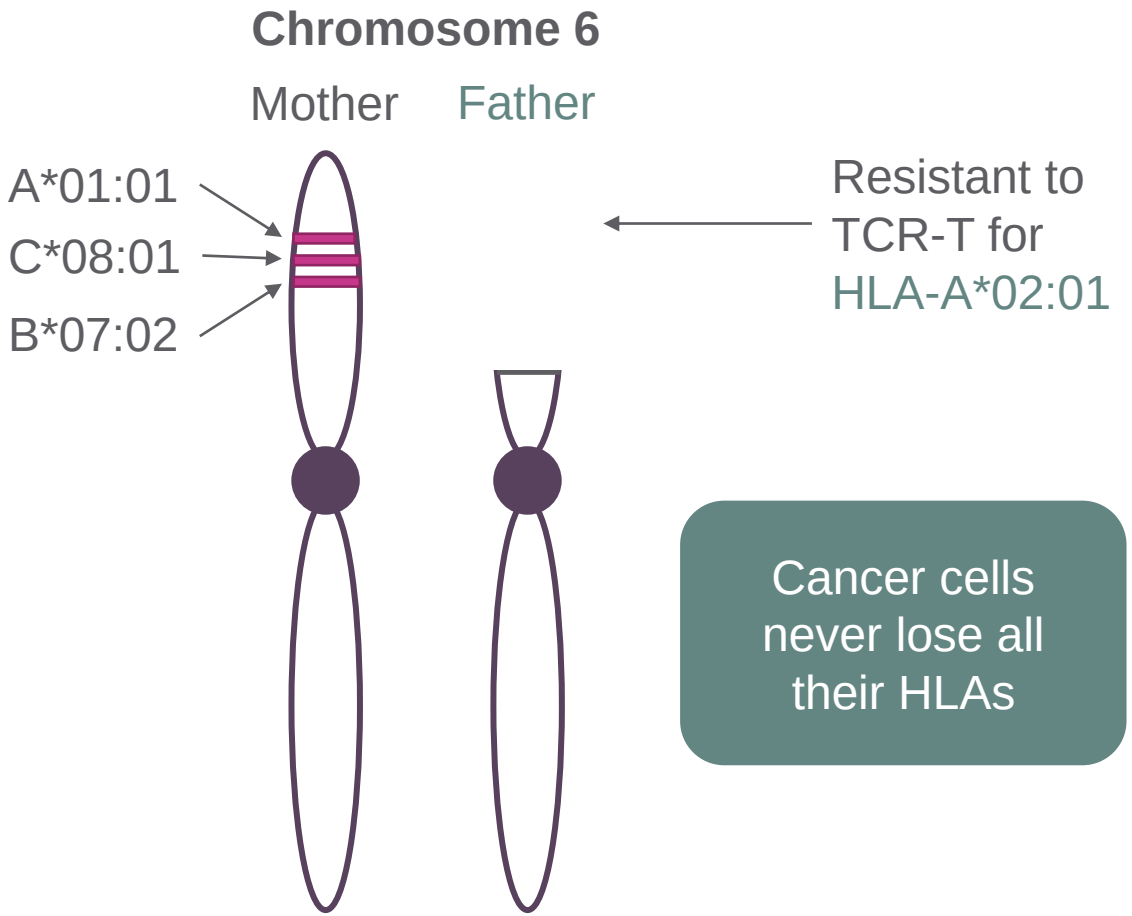


Cancer cells often lose half their HLA genes, becoming resistant to singleplexed TCR-T therapy

Normal cells



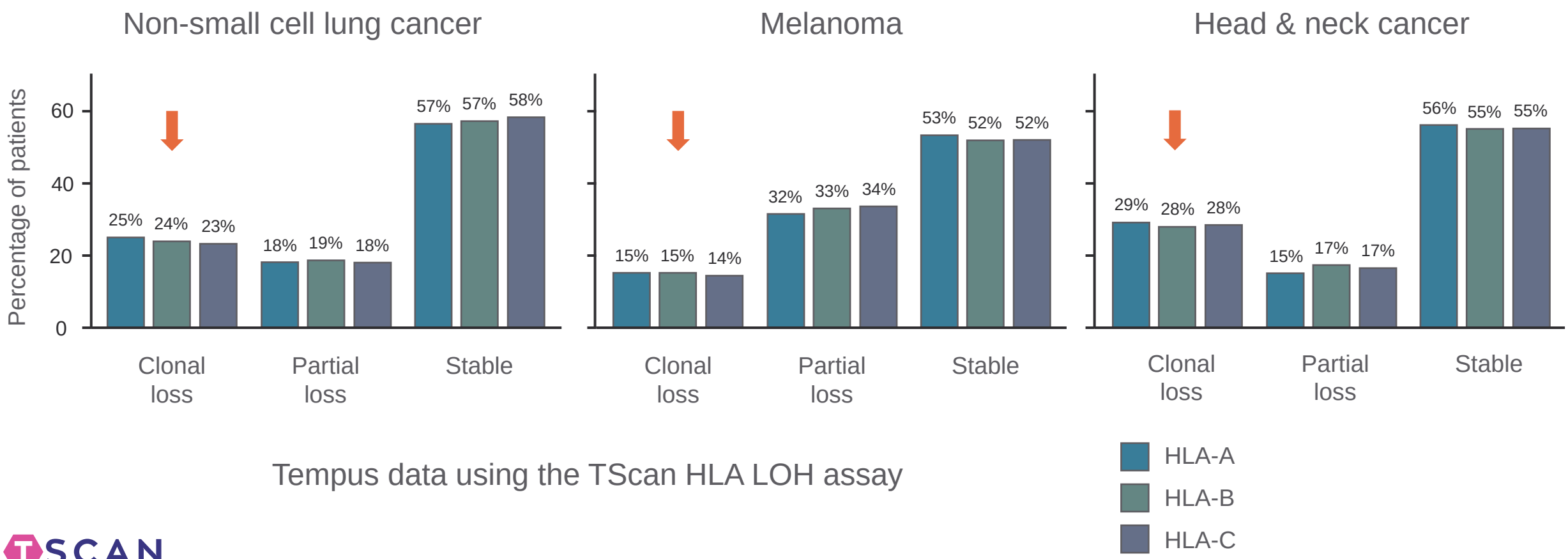
Cancer cells



Cancer cells never lose all their HLAs

HLA loss of heterozygosity (LOH) is a prevalent and overlooked mechanism of resistance to immunotherapy

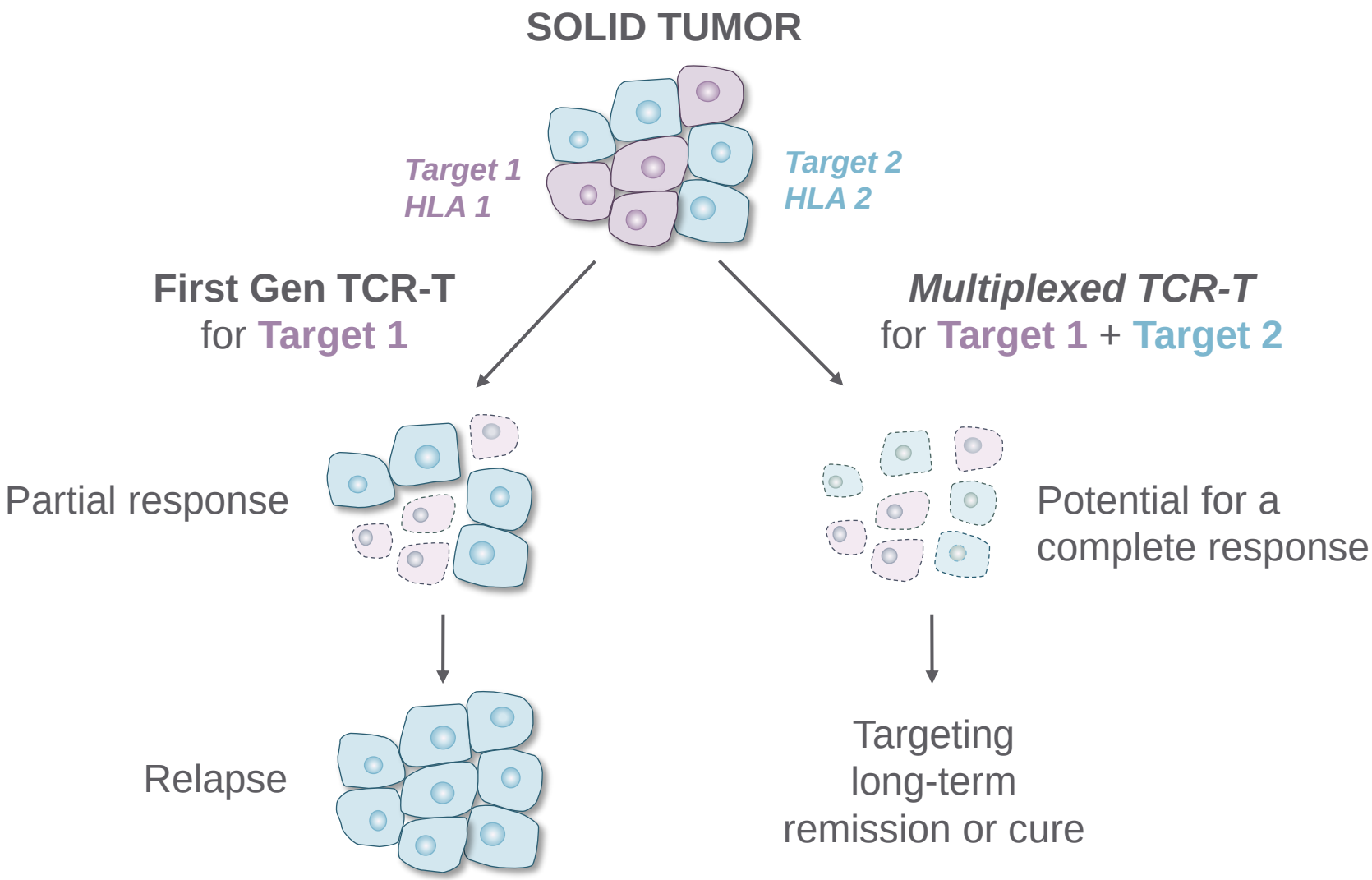
- ***15-30% of solid tumors*** exhibit clonal HLA loss
- These patients **CANNOT** respond to singleplexed TCR-T



Tempus data using the TScan HLA LOH assay

Multiplexed TCR-T is designed to prevent relapse due to either target or HLA loss

1 **Prevent relapse**



Patients will be prospectively selected and TCRs assigned based on target expression and HLA loss

2 **Prospectively select patients**

Germline

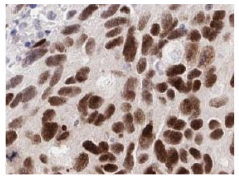
HLA testing

HLA in ImmunoBank

Tumor

Target testing

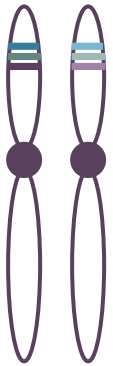
IHC / ISH



Neogenomics

HLA LOH

HLA loss

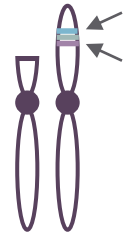


Tempus

Archival sample <6mo OR fresh biopsy

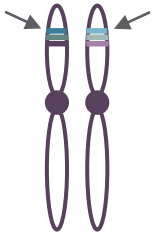
TCR-T selection

HLA loss detected



Target HLAs on intact haplotype

No HLA loss

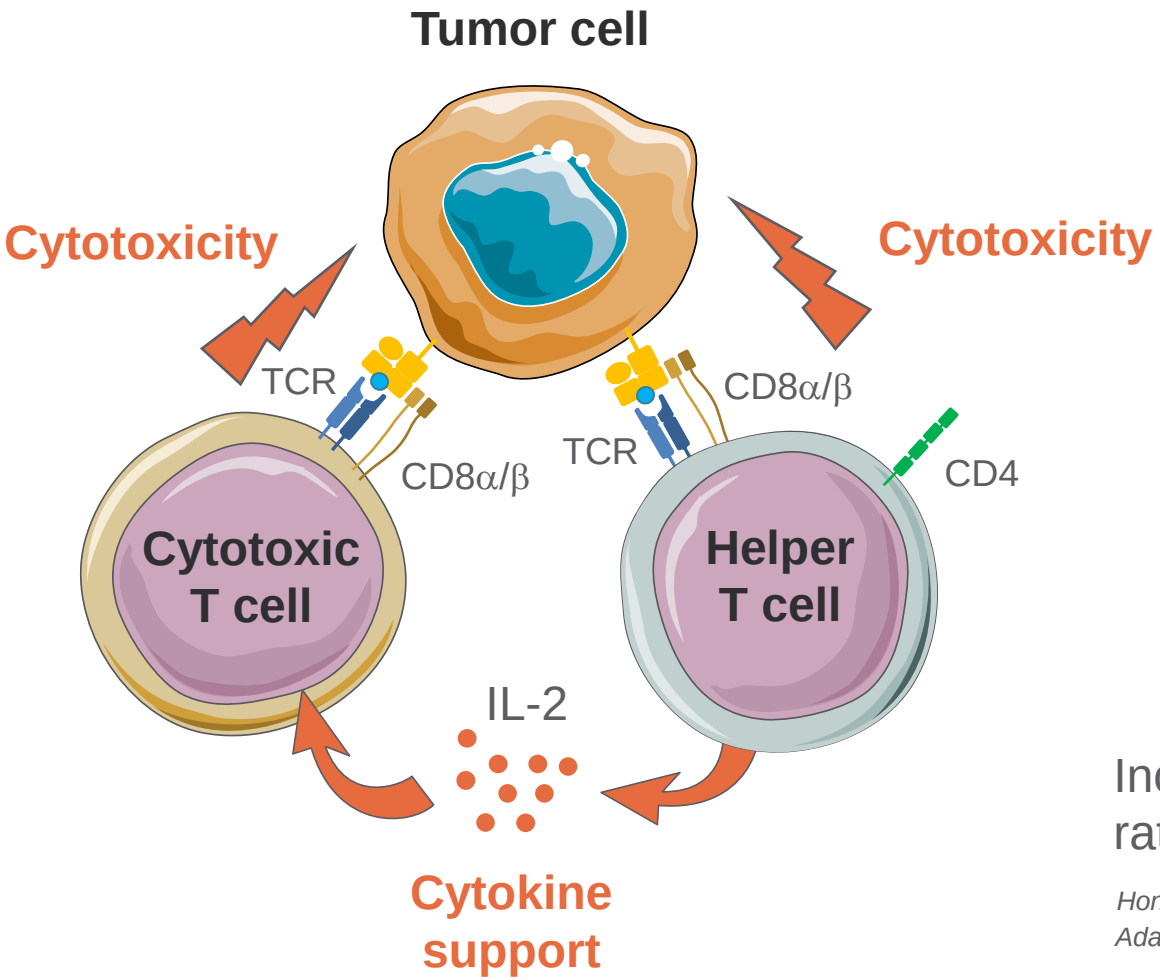


Target HLAs on opposite haplotypes

Engineered helper T cells provide support for cytotoxic T cells and directly contribute to cytotoxicity

3 **Increase response rate**

CD8 α/β



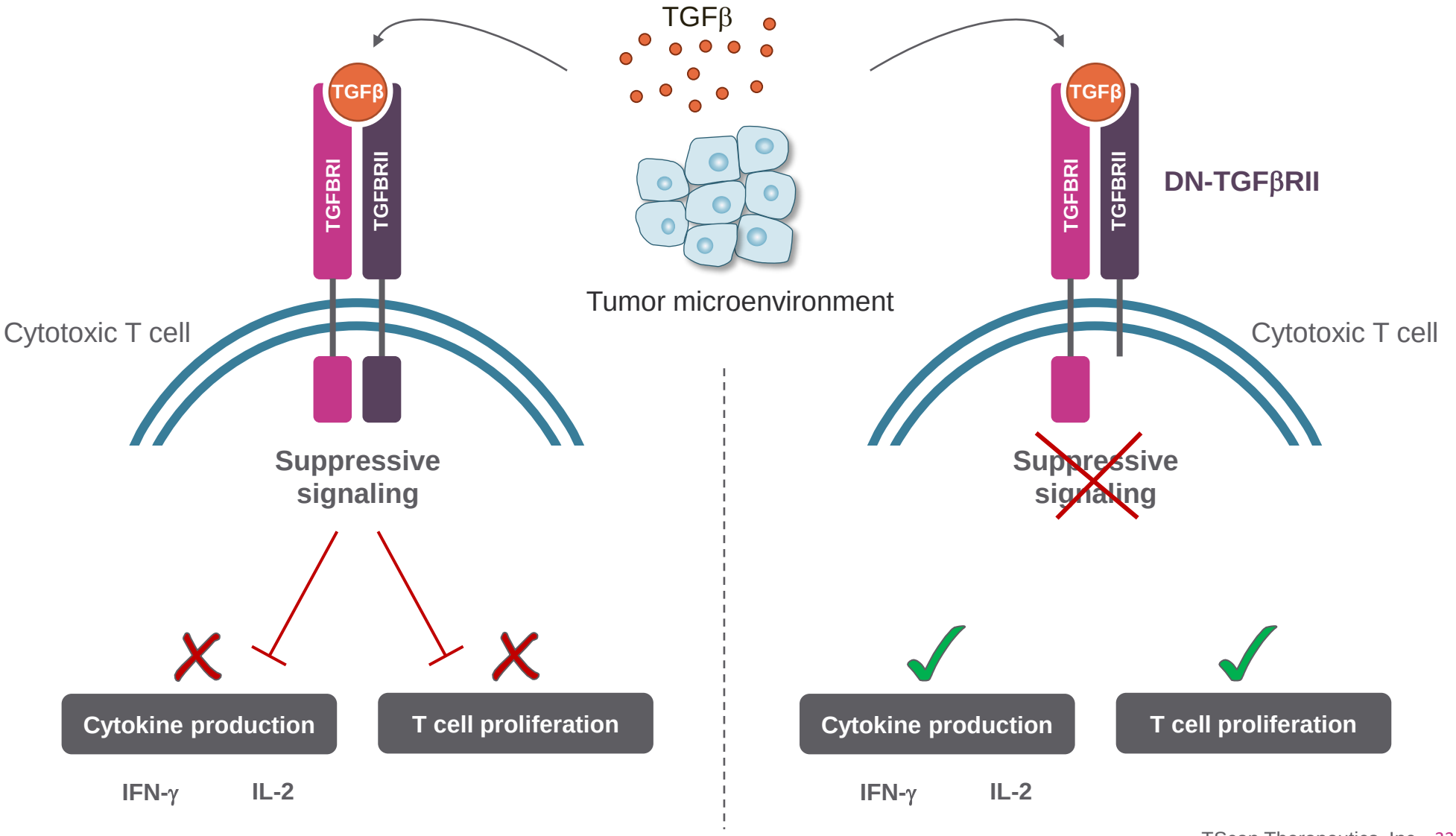
Increases TCR-T response rates up to 4-fold in clinic

Hong, ASCO 2020
Adaptimmune Company Presentation, November 2022

TGFβ is a key immune suppressor in the hostile tumor microenvironment

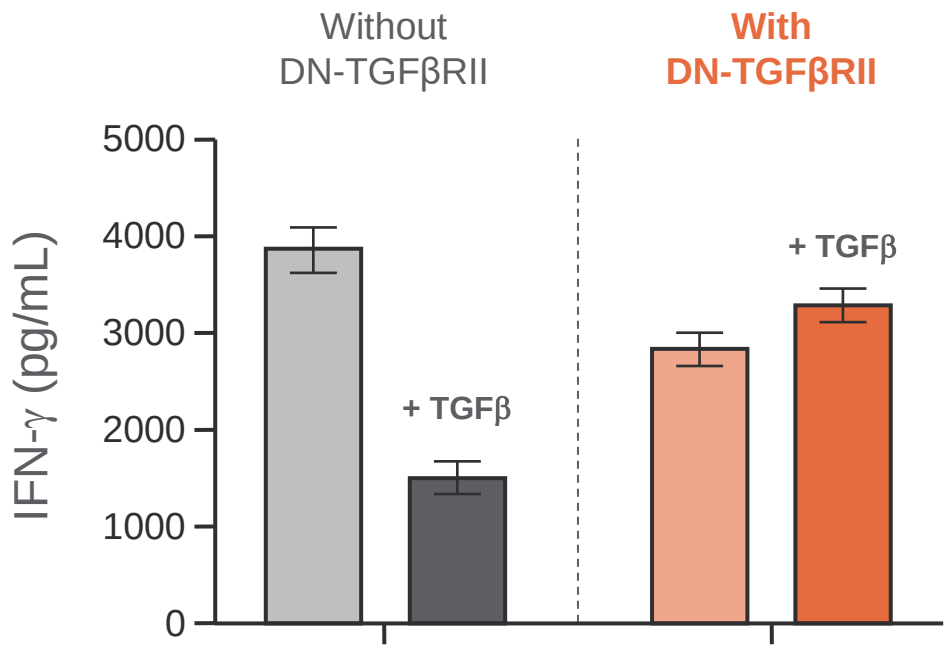
4 **Enhance persistence**

DN-TGFβRII

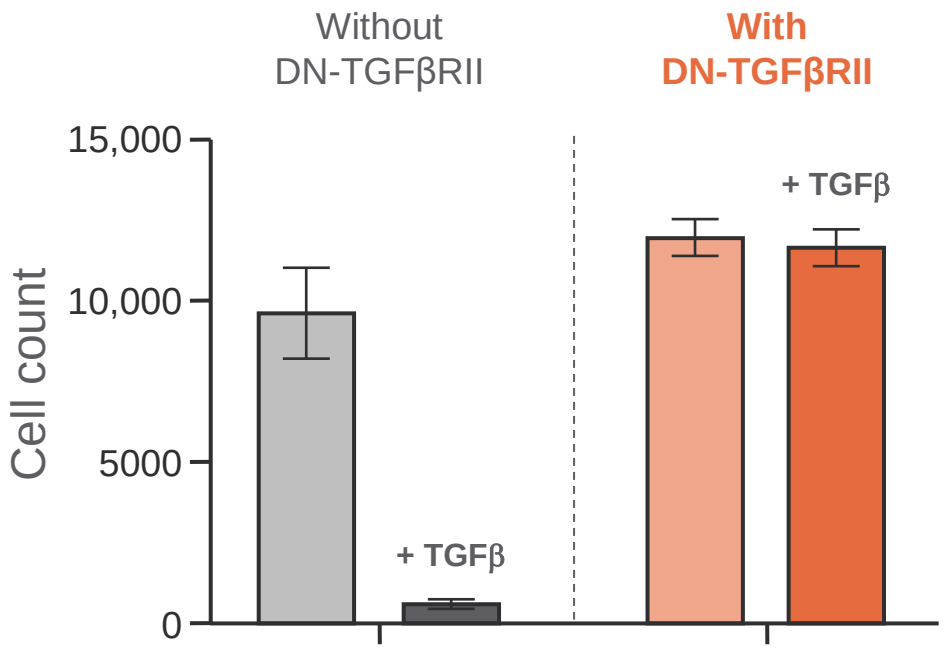


Adding DN-TGFβRII to TCR-T cells enables proliferation in the presence of TGFβ

Cytokine production



Proliferation

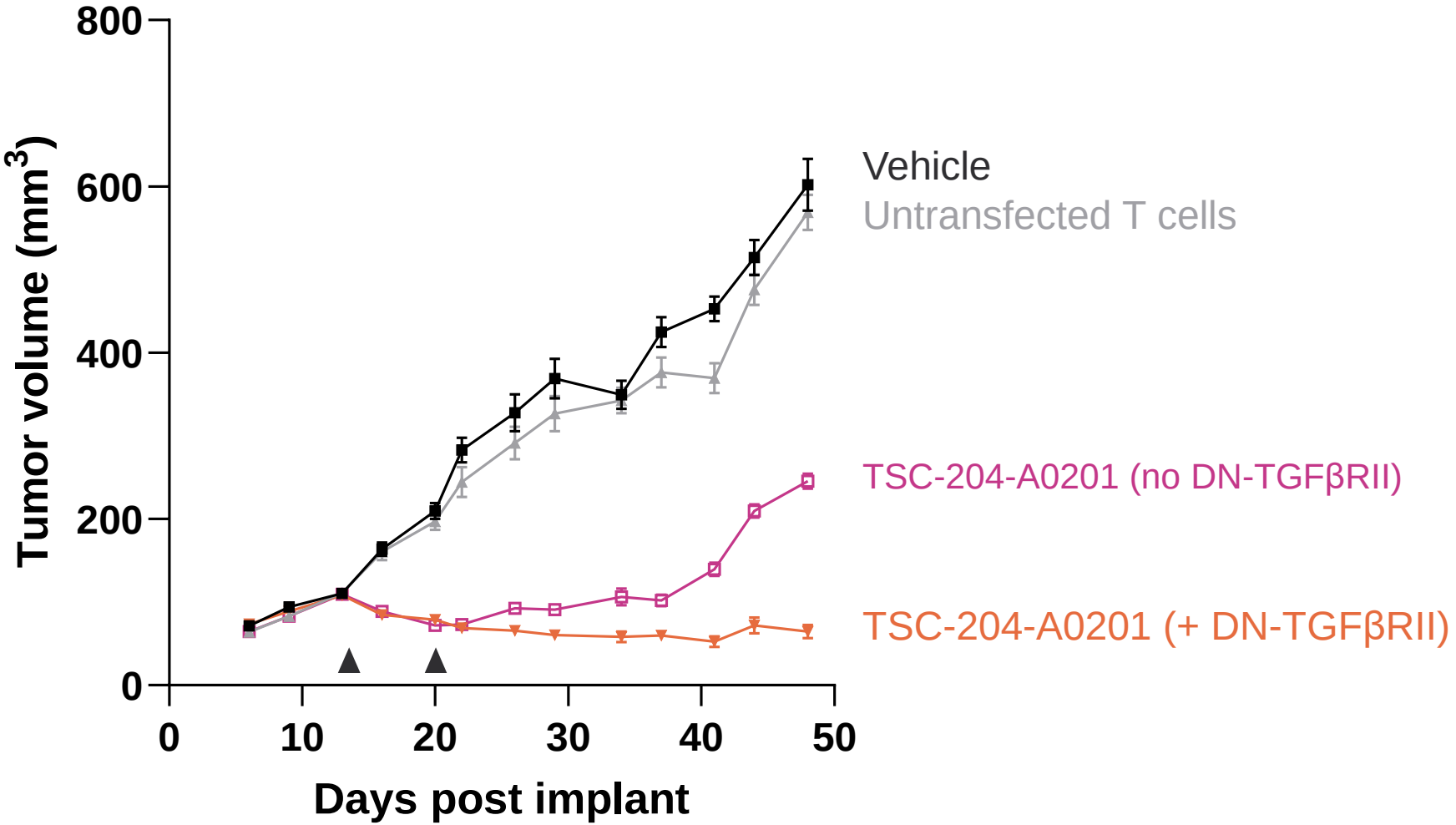


T-cells: TSC-204-A0201 (MAGE-A1)
Tumor cells: Hs936T (melanoma)

Expansion up to 100-fold and persistence up to 4 years in clinical trials

J Clin Oncol (2018) **36**, 1128-1139.

DN-TGFβRII enhances duration of activity *in vivo*

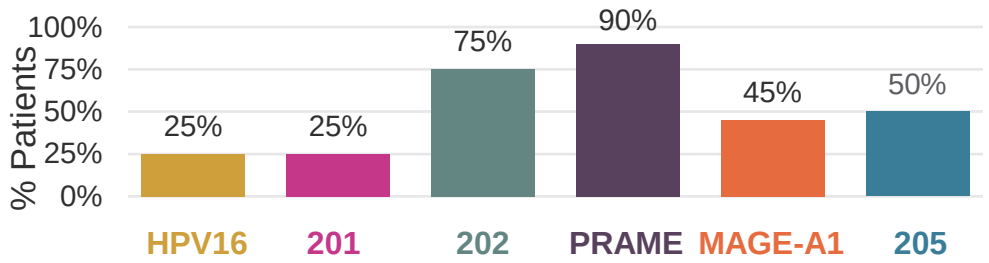


Building the ImmunoBank

ImmunoBank is being built with targets that exhibit high prevalence in immune-rich cancers

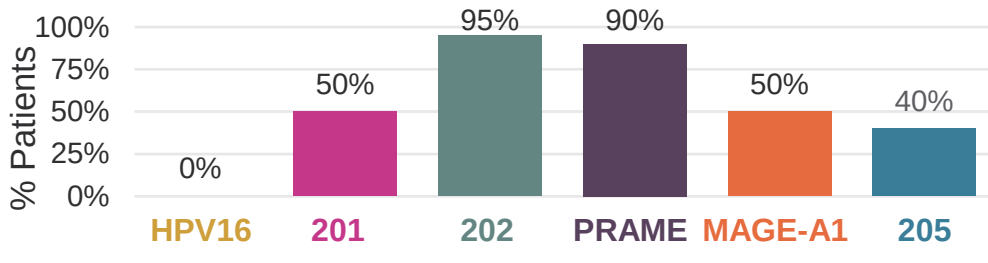
Head & Neck

65 K Incident Patients in U.S.



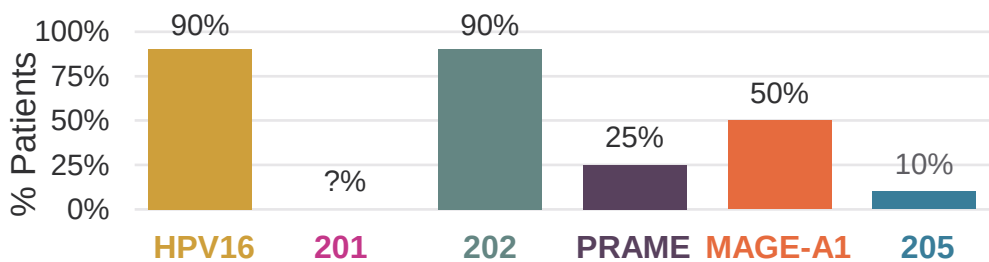
Melanoma

106 K Incident Patients in U.S.



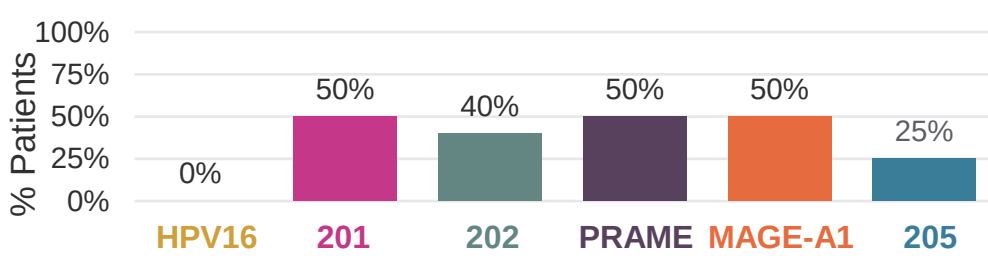
Cervical (Uterine cervix)

15 K Incident Patients in U.S.

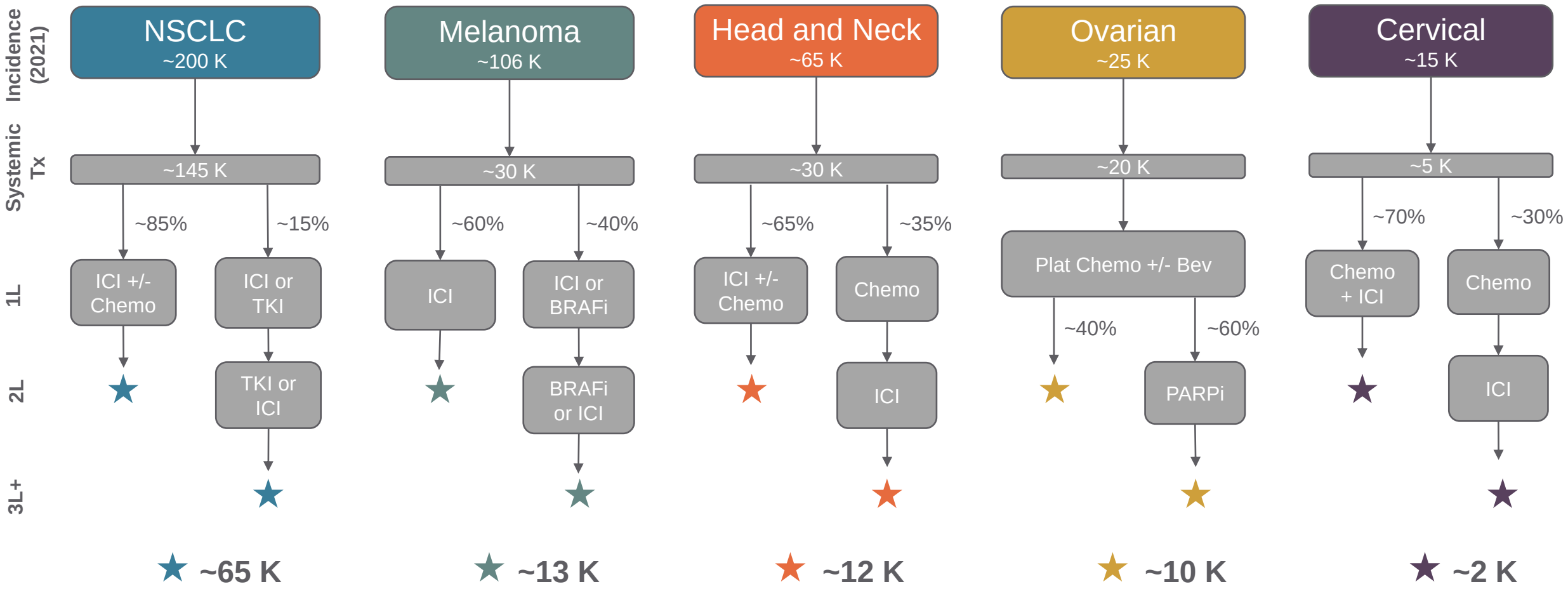


NSCLC

200 K Incident Patients in U.S.



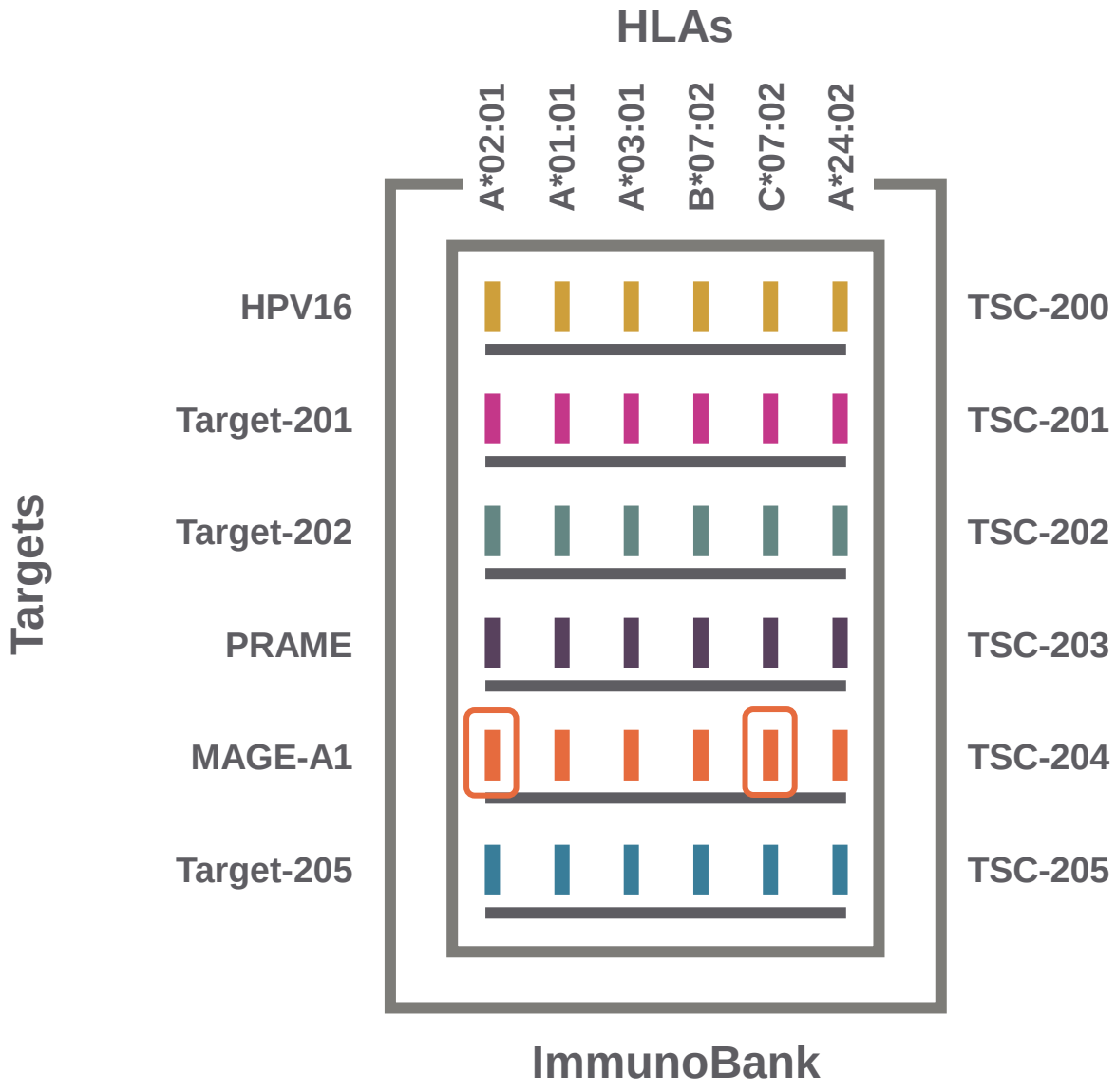
Prioritized indications provide significant market opportunity

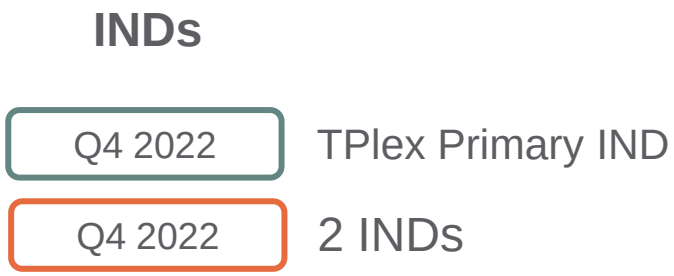


~102 K currently addressable patient population in selected indications in the US

ICI: Immune Checkpoint Inhibitors; TKI: Tyrosine Kinase Inhibitors/Targeted Therapies
Sources: SEER, Kantar Report, Chao et al.

Program initiated with three INDs filed in 2022

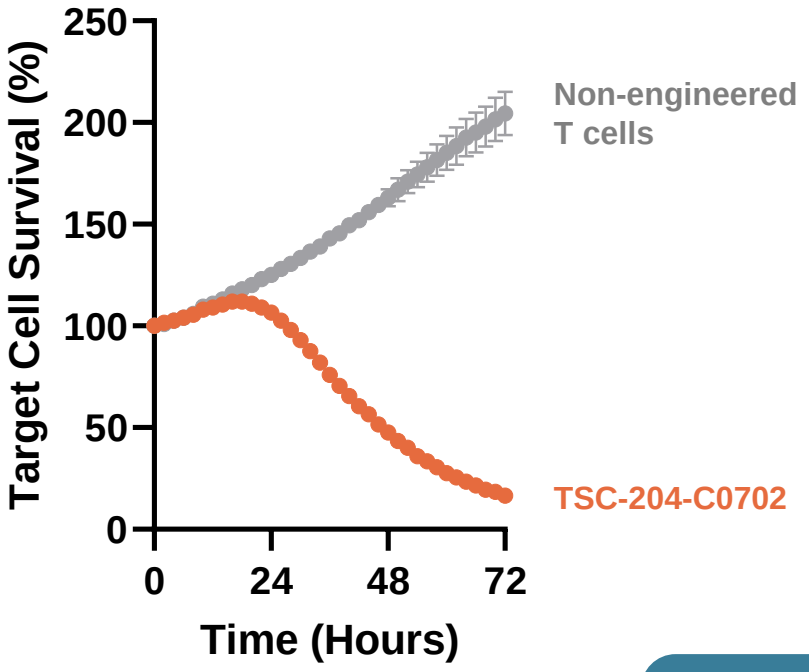




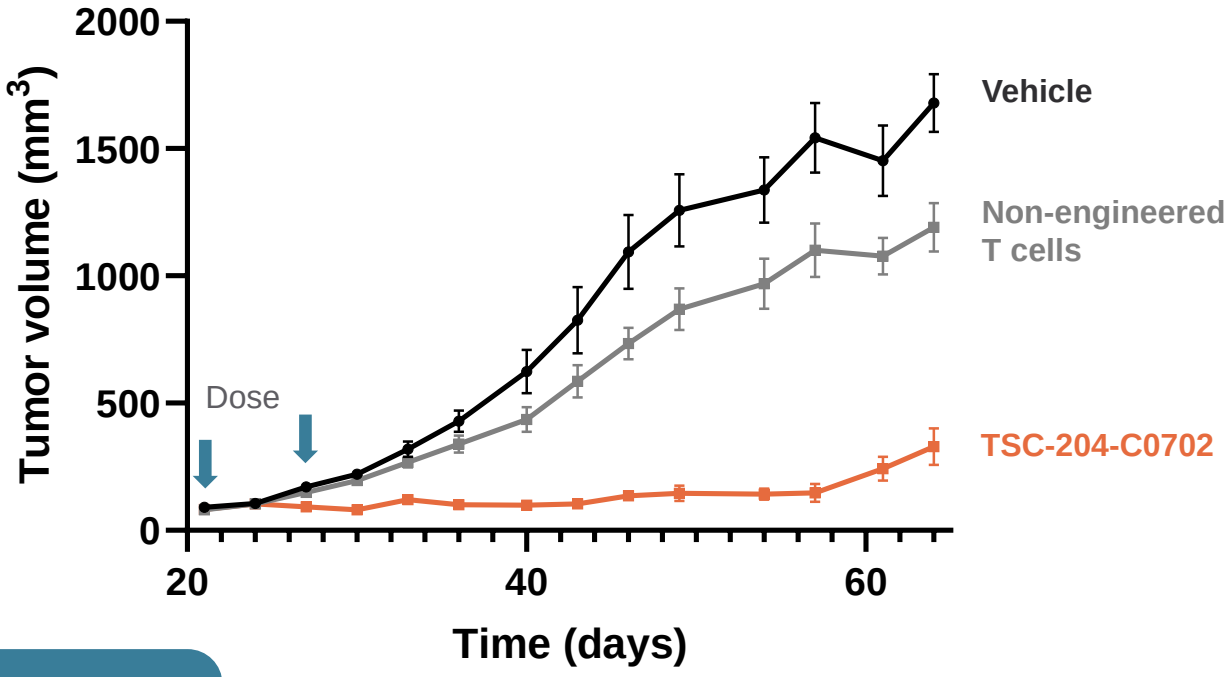
TSC-204-C0702 recognizes a *novel target* on MAGE-A1 discovered from a patient using TargetScan

Discovered from a patient with head & neck cancer responding to immunotherapy

HS936T
MAGE-A1⁺ melanoma



U266B1
MAGE-A1⁺ mouse model



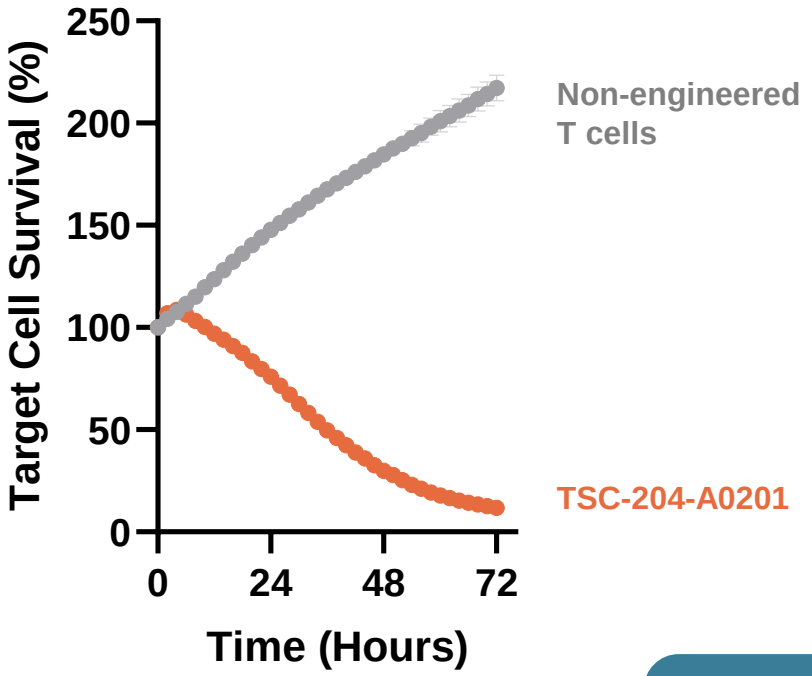
Published in *Cell*

Luoma AM *et al.* (2022) *Cell*, **185**, 2918-2935.e29

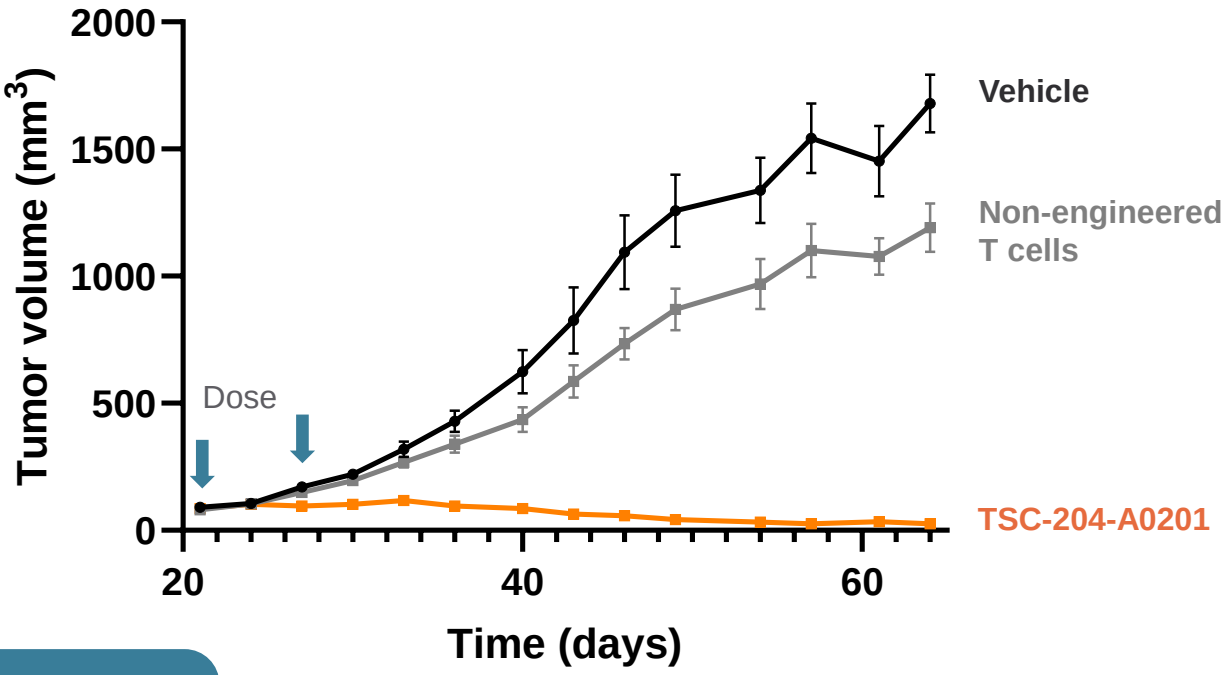
HLA coverage of MAGE-A1 was extended to A*02:01 by discovering TSC-204-A0201 using ReceptorScan

Discovered from a healthy donor using **ReceptorScan**

NCI H1702
MAGE-A1⁺ melanoma

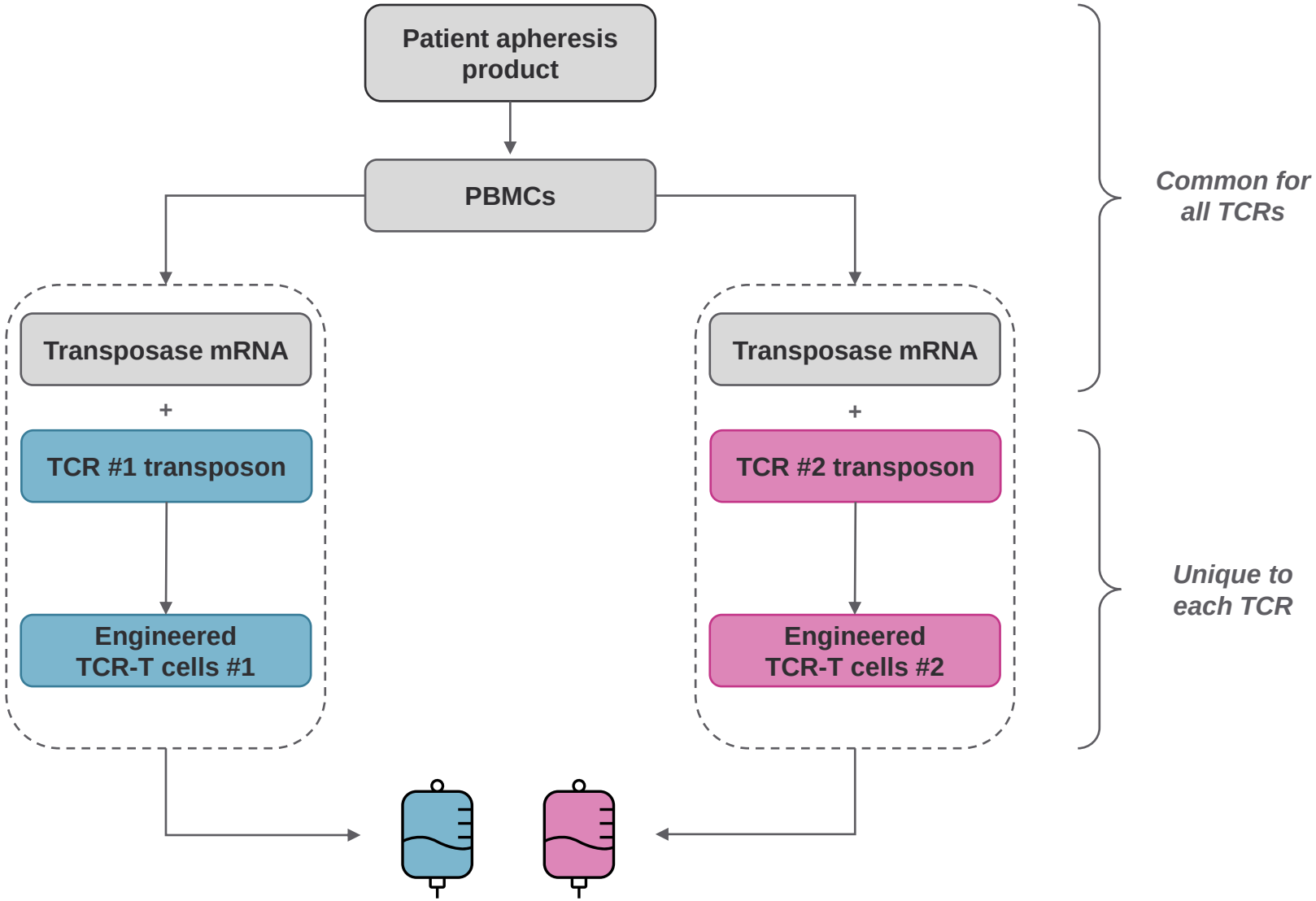


U266B1
MAGE-A1⁺ mouse model

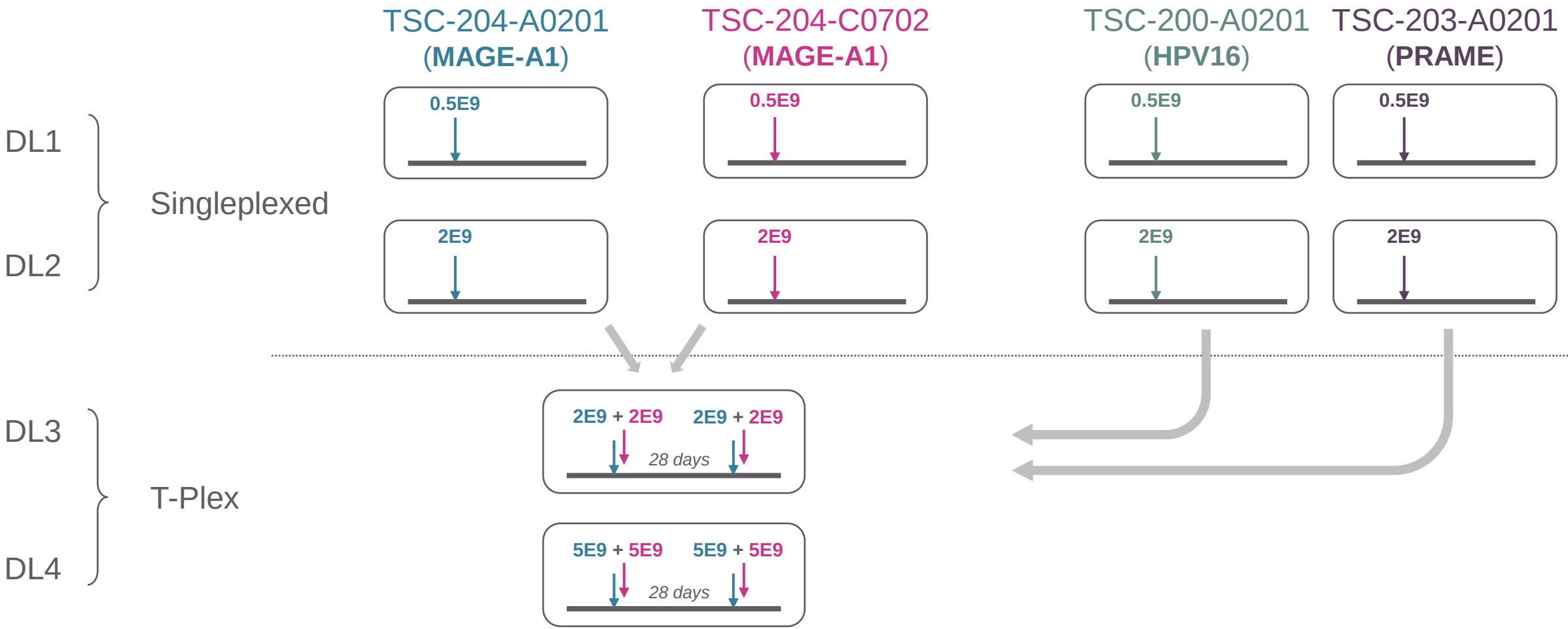


Disclosed at
SITC Annual Meeting
2022

Process enables facile manufacturing for multiplexed TCR-T

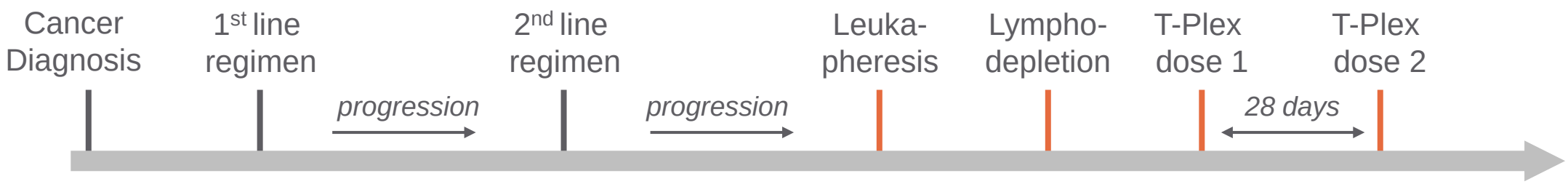


Dose escalation scheme provides a rapid path to testing and expanding multiplexed TCR-T in Phase 1



Screening protocol pre-identifies patients for treatment

Patient journey



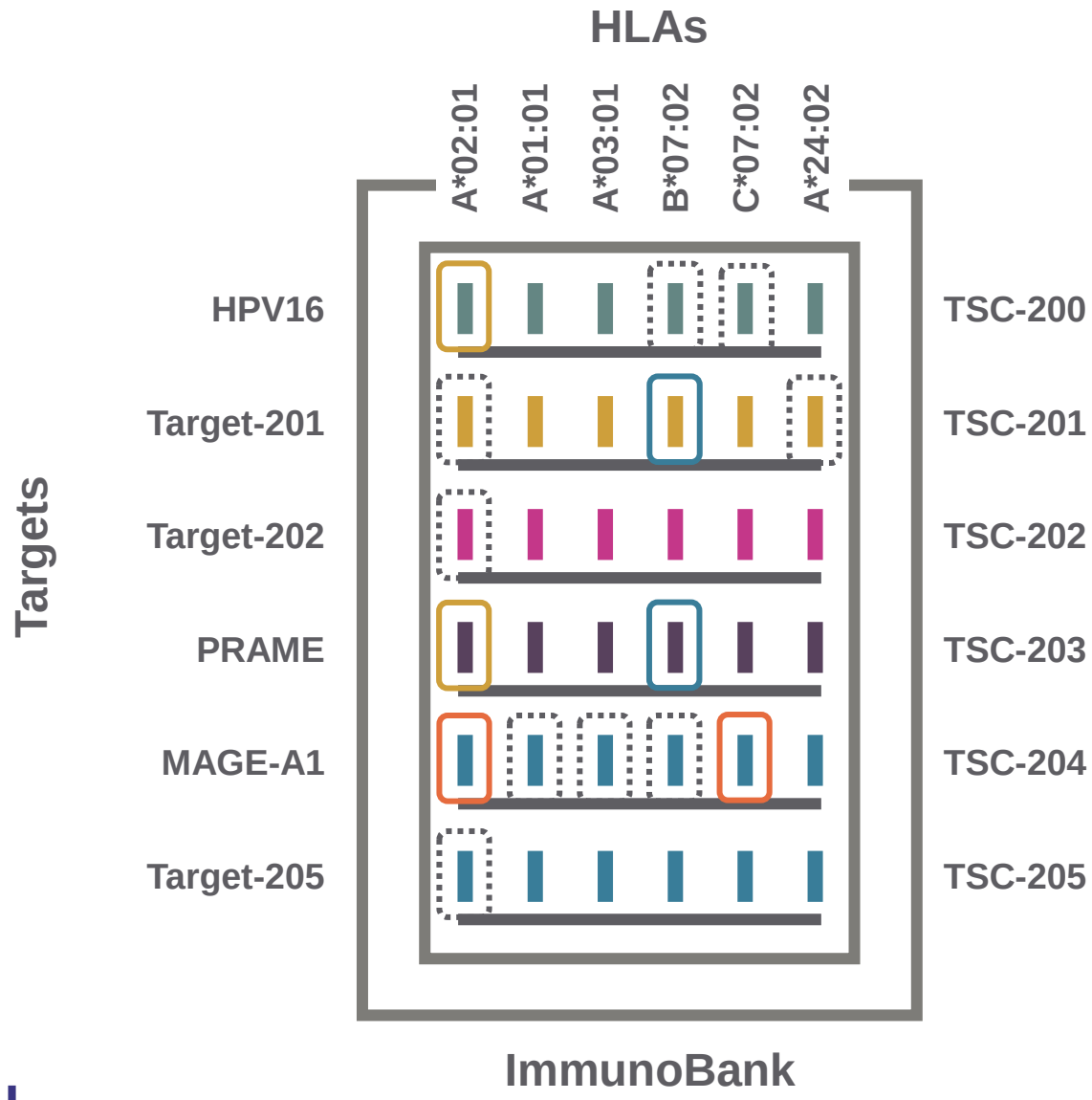
Screening protocol

- Pre-screens patients for trial eligibility
- Germline HLA testing
- Archival tumor sample
  - Tumor IHC
  - HLA LOH testing

Treatment protocol

- Vein-to-vein time 25 days
- No IL-2 given
- Endpoints
  - Primary: Safety
  - Secondary: ORR, DOR
  - Exploratory: T-cell persistence

Multiplexed TCR-T is enabled by a growing ImmunoBank



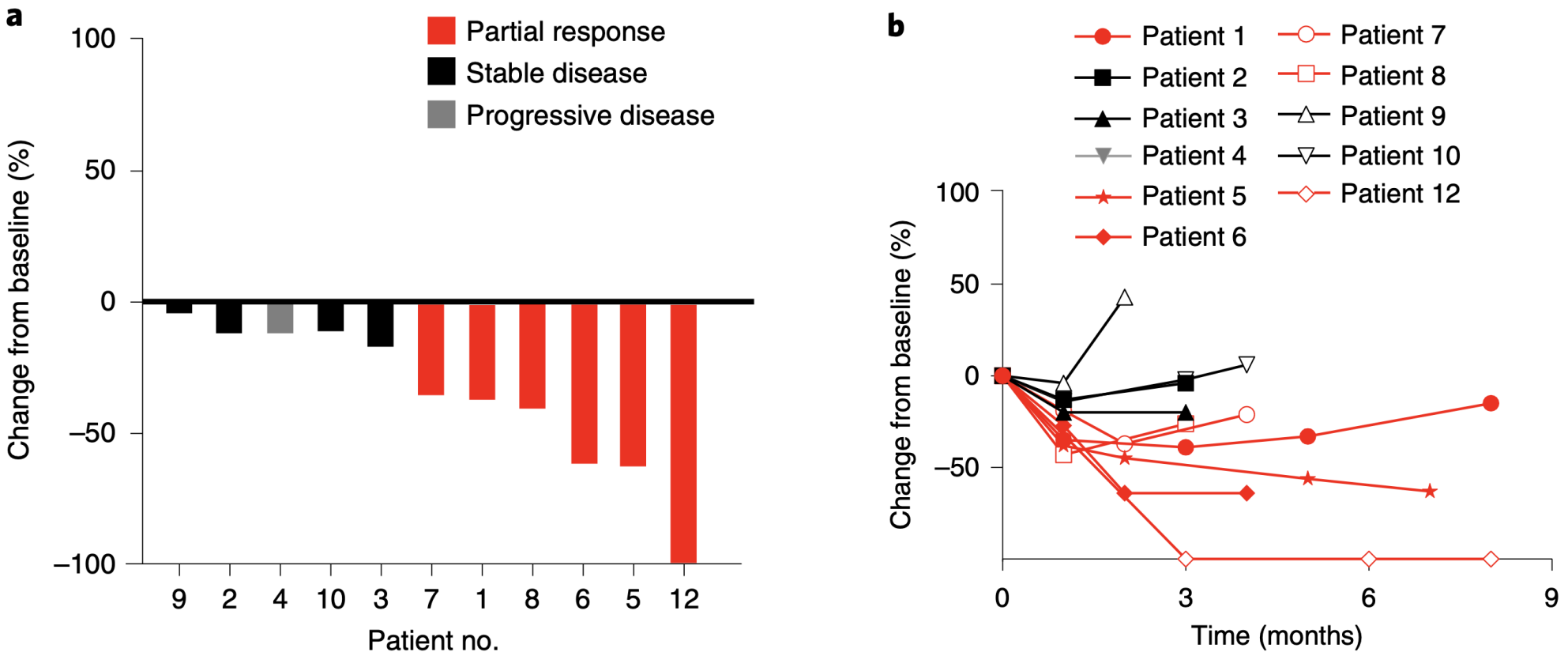
INDs

Q4 2022	TPlex Primary IND
Q4 2022	2 INDs
H1 2023	2 INDs
H2 2023	2 INDs
Discovery	4+ INDs, 2024

INDs for 6 TCRs by the end of 2023

INDs for 10+ TCRs by the end of 2024

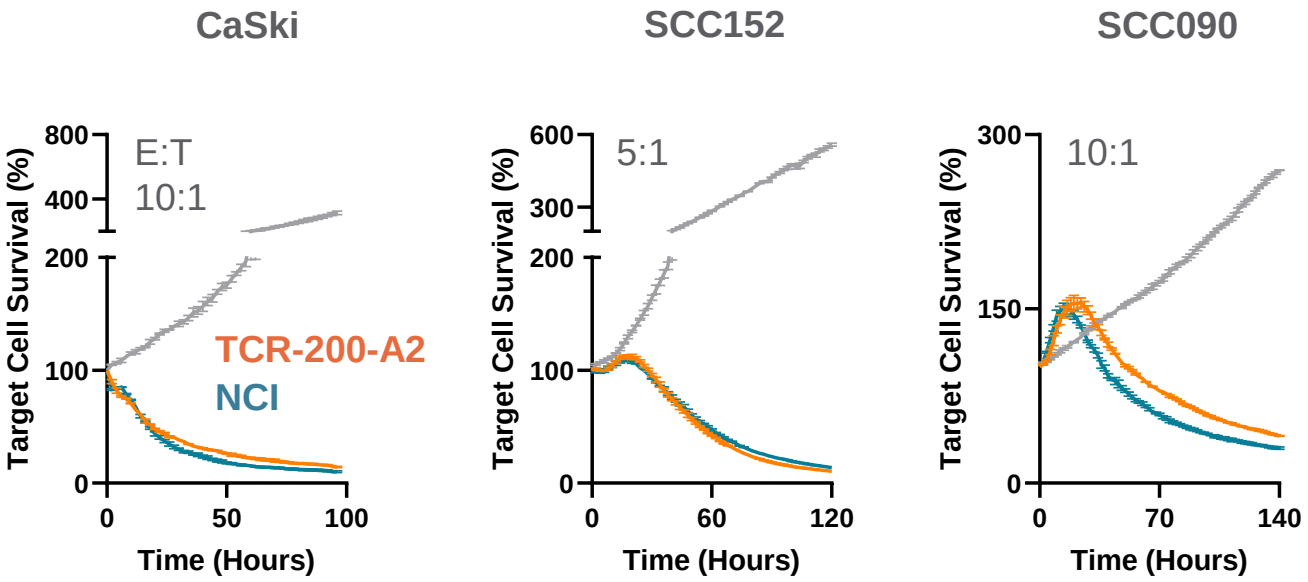
To date, the most impressive TCR-T results in solid tumors were achieved by targeting E7 of HPV16



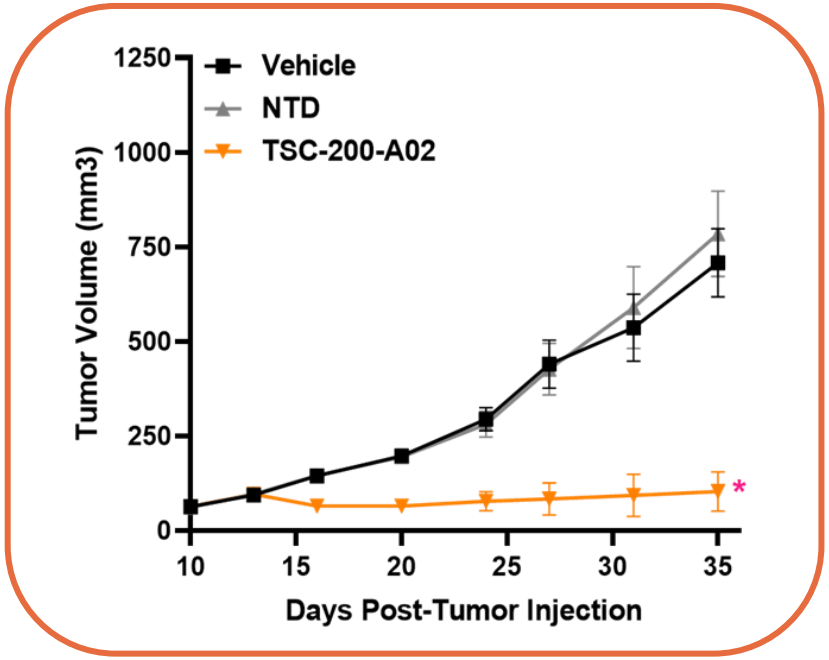
Nagarsheth NB, …, Hinrichs CS (2021) *Nature Medicine*, **27**, 419-425.

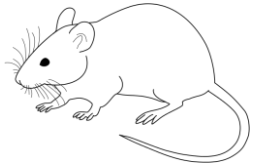
TScan's TCR-200-A02 shows comparable activity to NCI TCR

In vitro



In vivo

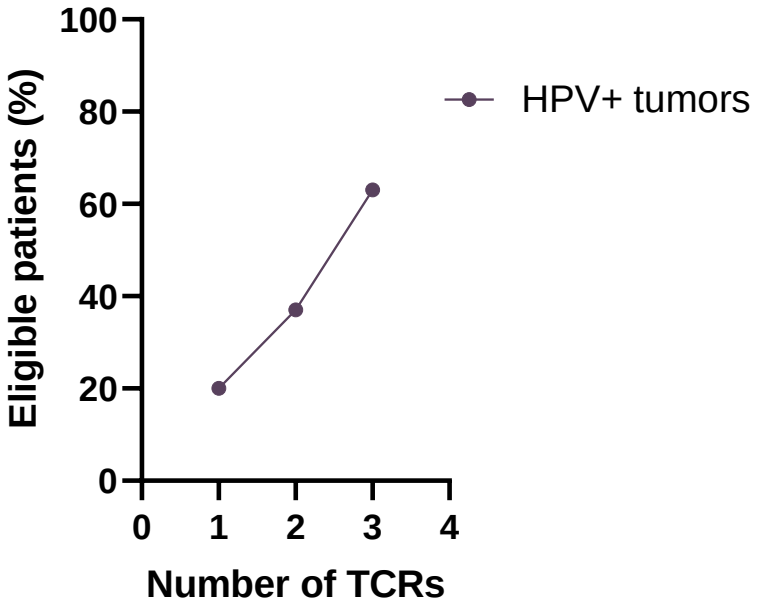




TScan data, following Nagarsheth NB, …, Hinrichs CS (2021) *Nature Medicine,* **27**, 419-425.

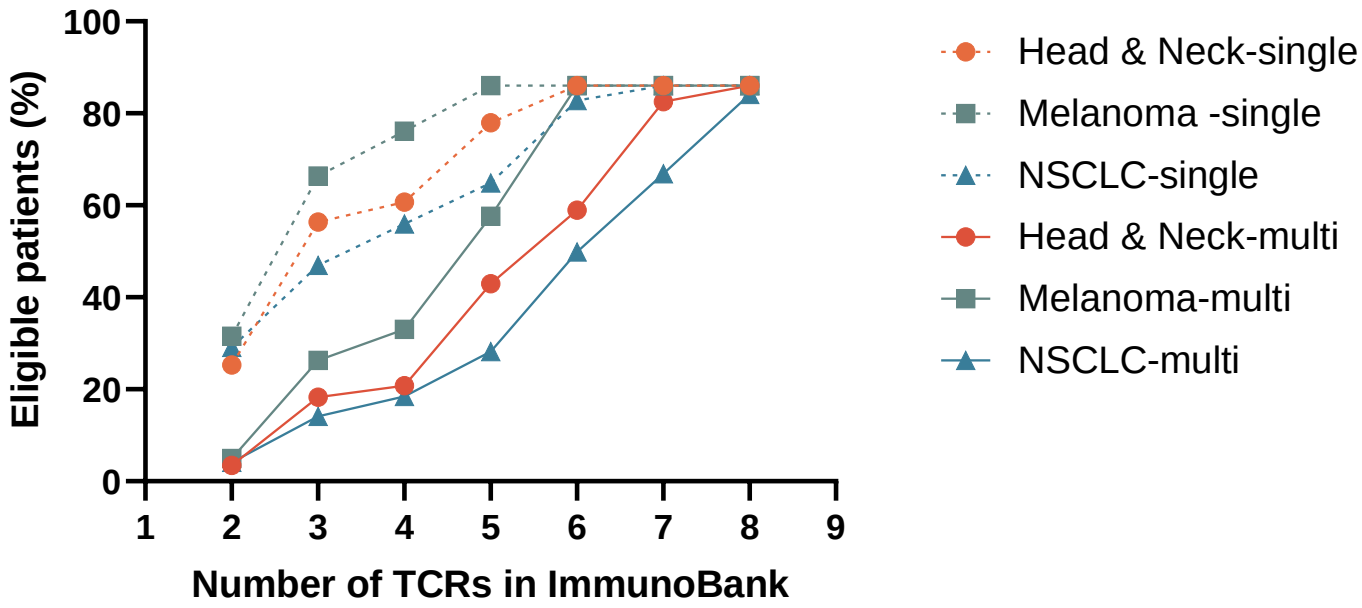
Patient eligibility is high for singleplexed dose levels, even in the early stages of building the ImmunoBank

HPV16+ cancers



Eligible patients include patients who do not require multiplexing (homozygous or hemizygous for targeted HLA type) or are eligible for at least 2 HPV16 TCRs

Other solid tumors

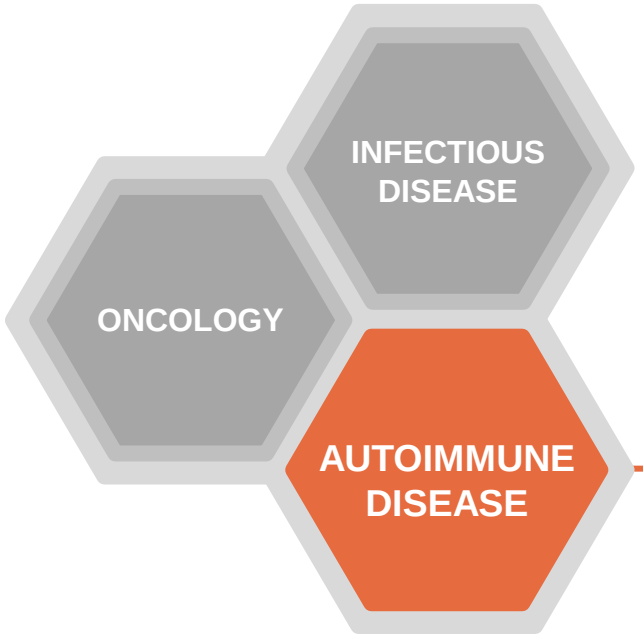


Eligible patients include patients who are positive for at least 2 TCRs in the ImmunoBank

TScan platform technologies can be deployed for target and TCR discovery across many therapeutic areas

Novel antigen and clinic-ready TCR discovery	*Shared T cell antigen ID for vaccine development or TCR-T therapeutics*	*Shared T cell antigen ID for a tolerizing product modality (e.g., TCR-Treg tx, vaccine)*
• Solid tumors and heme malignancies • Shared or neoantigens	• Viruses (COVID-19, flu, etc.) • Bacterial infections (e.g., Tb, listeria)	• T cell driven diseases (e.g., RA, IBD, scleroderma, psoriasis)

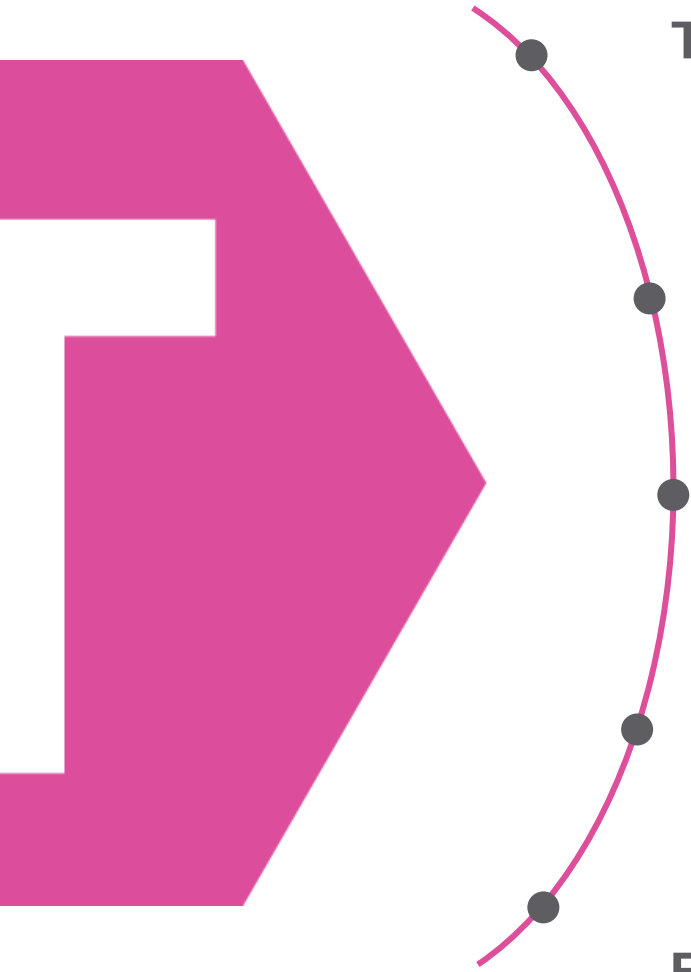
TScan's platforms can be leveraged for novel autoimmune disease target discovery for T-cell mediated diseases



Example T cell-mediated autoimmune diseases:

- Ankylosing Spondylitis
- Atopic Dermatitis
- Birdshot Uveitis
- Celiac Disease
- Crohn's Disease
- Multiple Sclerosis (MS)
- Pemphigus
- Psoriasis
- Rheumatoid Arthritis
- Scleroderma
- Sjogren's Syndrome
- Systemic Lupus Erythematosus (SLE)
- Type I Diabetes
- Ulcerative Colitis
- Vitiligo

TScan highlights



Transformative Platform Enables Rapid Discovery of TCRs for Engineered T Cell Therapy

- Recent collaboration highlights applicability outside oncology

Solid Tumor Program to Deliver Enhanced Multiplexed TCR-T

- First three INDs cleared in January 2023; four more planned by EOY

Hematologic Malignancies Program to Prevent Relapse with HCT

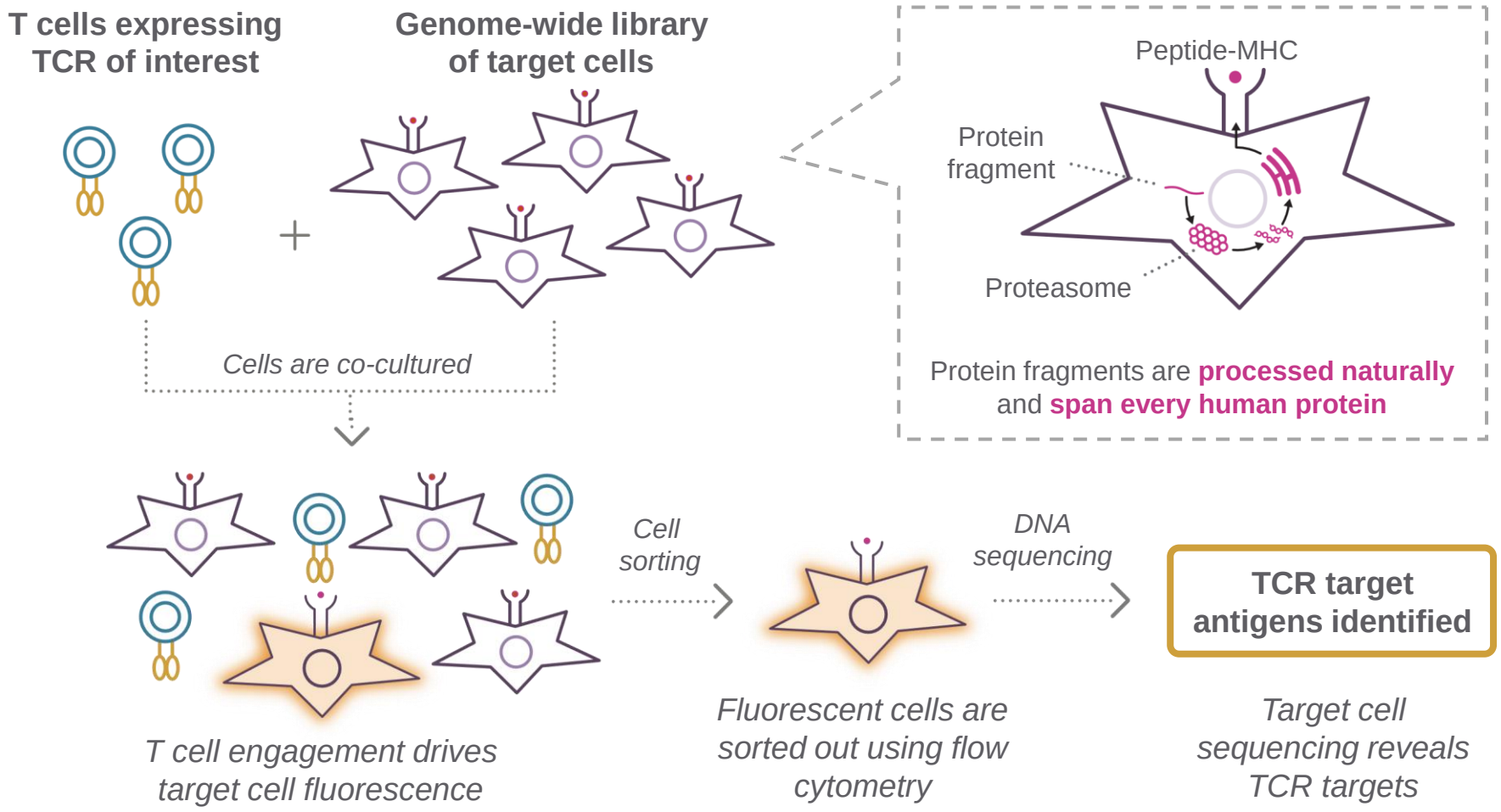
- Patients enrolled in all three arms of study; TSC-101 progressing to second dose level

In-house GMP Manufacturing Using Non-viral Vectors

Cash of $95.6 MM (Q1 2023) Along with Amgen Proceeds ($30 MM), Extends Runway into Q3 2024

TScan Platform

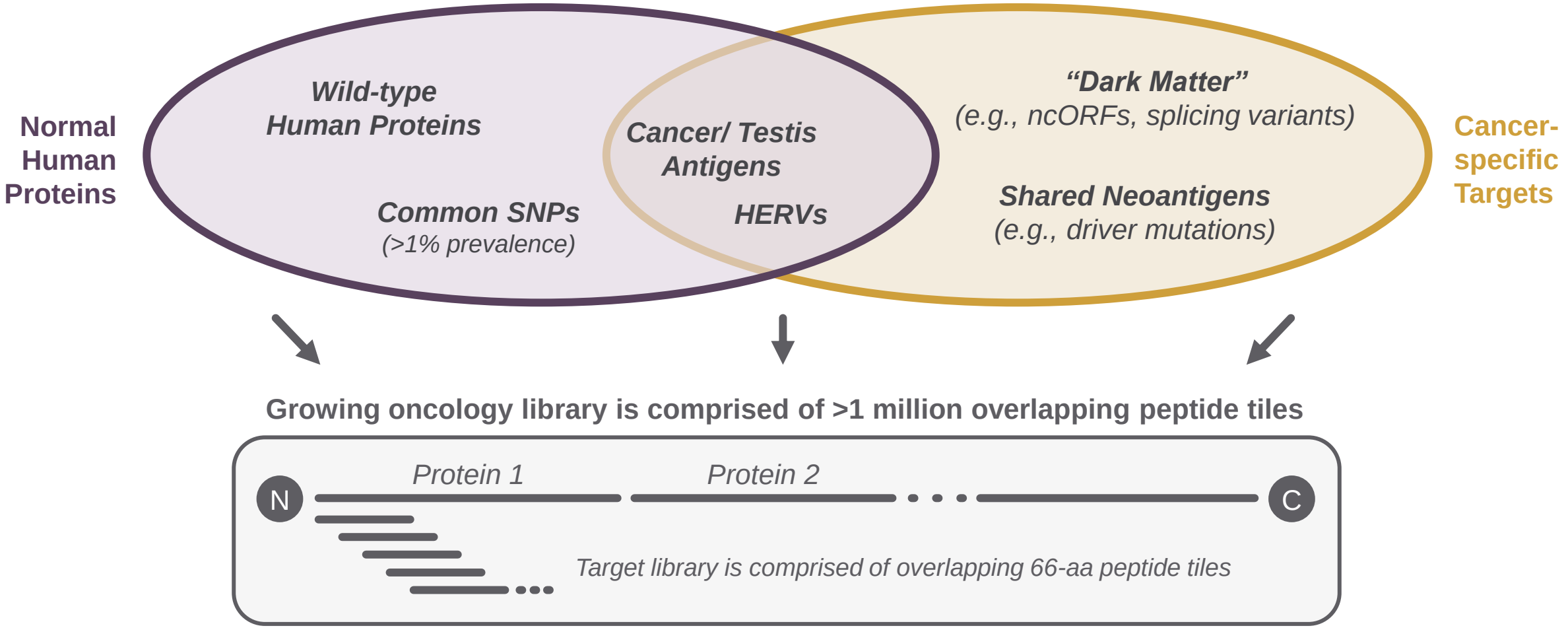
TScan's proprietary platform – TargetScan – enables ID of the natural targets of any T cell receptor (TCR) for TCR-T



TargetScan can be adapted for target discovery for both CD4+ and CD8+ T cells

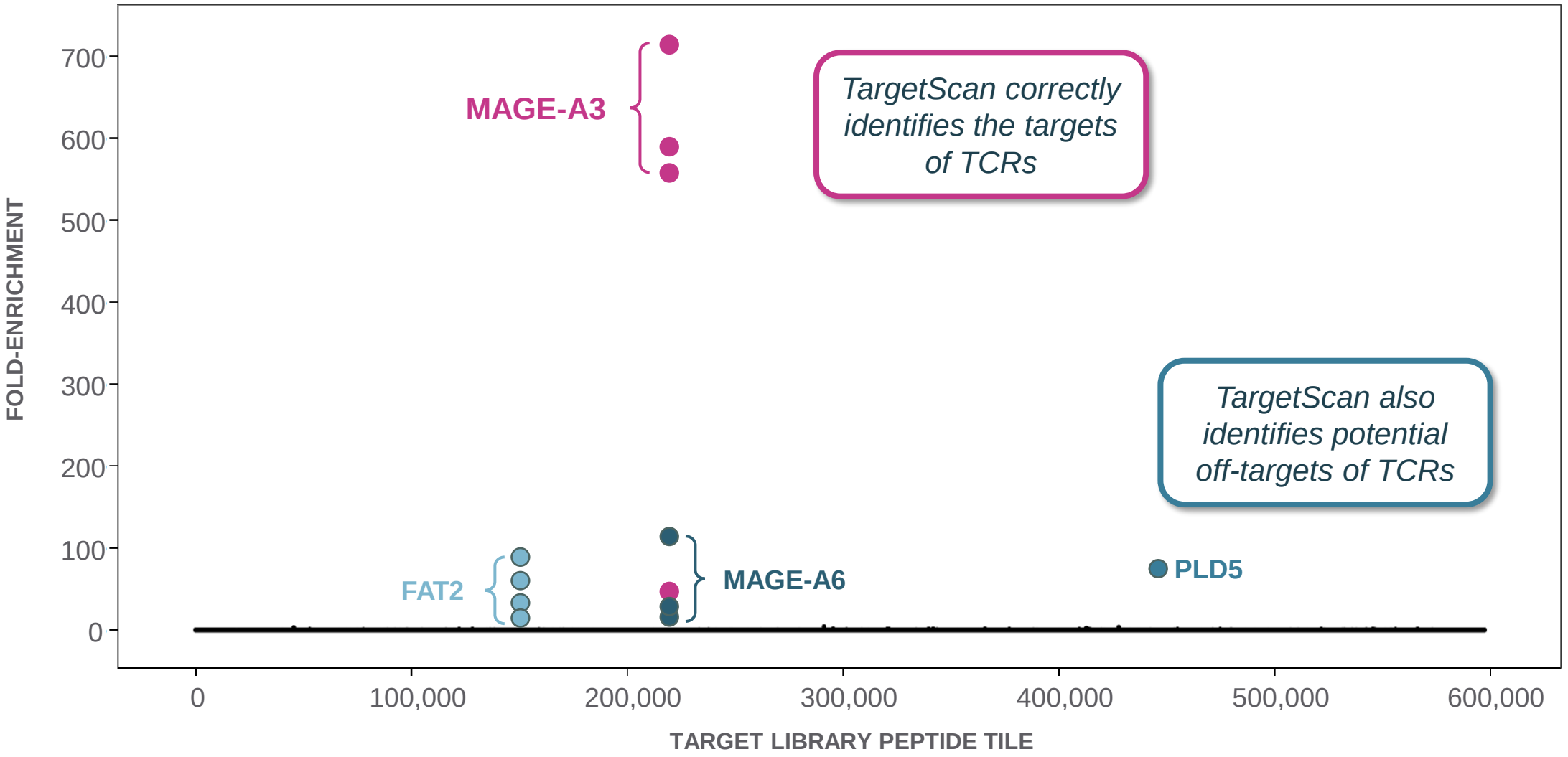
Adaptable target library enables discovery of diverse TCR targets using TargetScan

Example TScan Oncology Library *– Version 3.0*



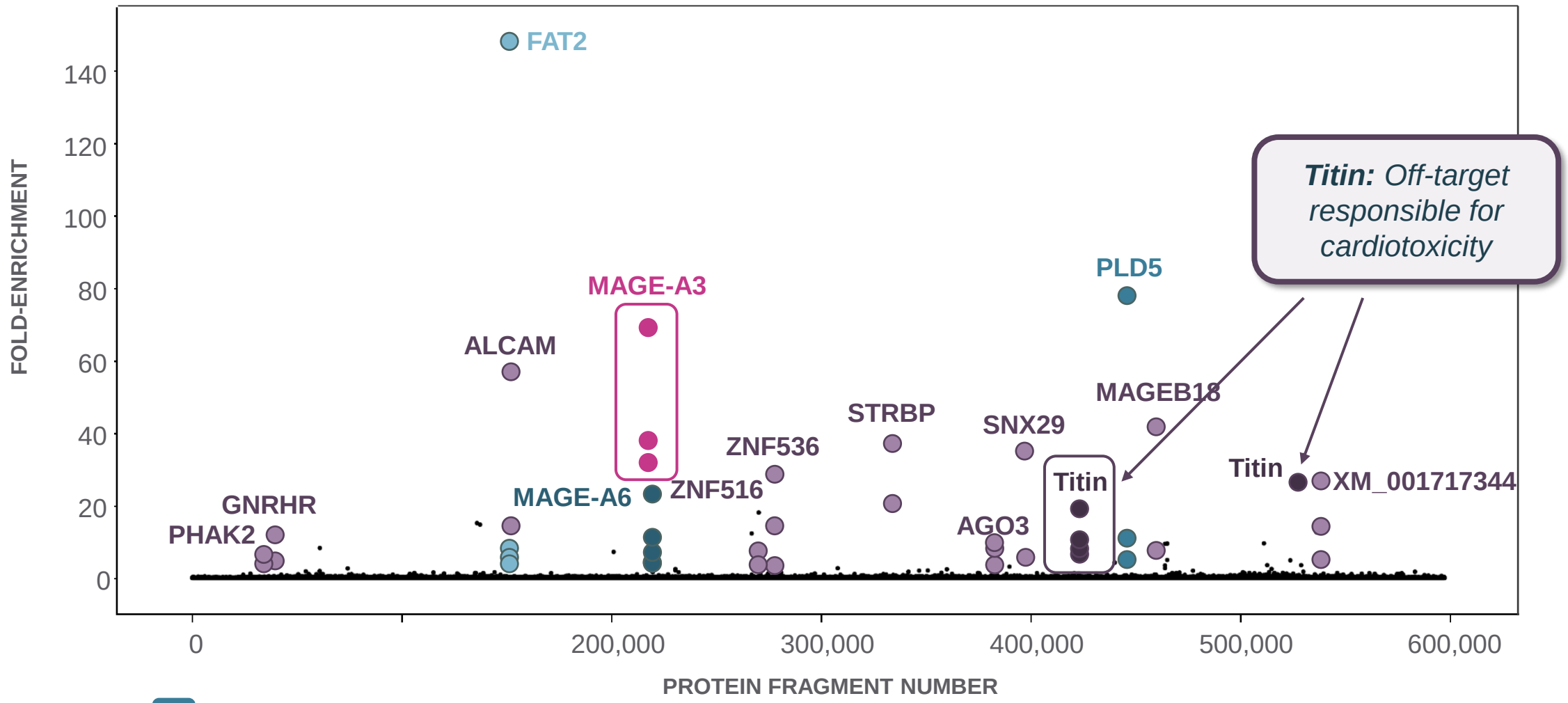
TargetScan identifies the targets of Class I TCRs

*Genome-wide screen of a Class I **TCR known to recognize MAGE-A3***

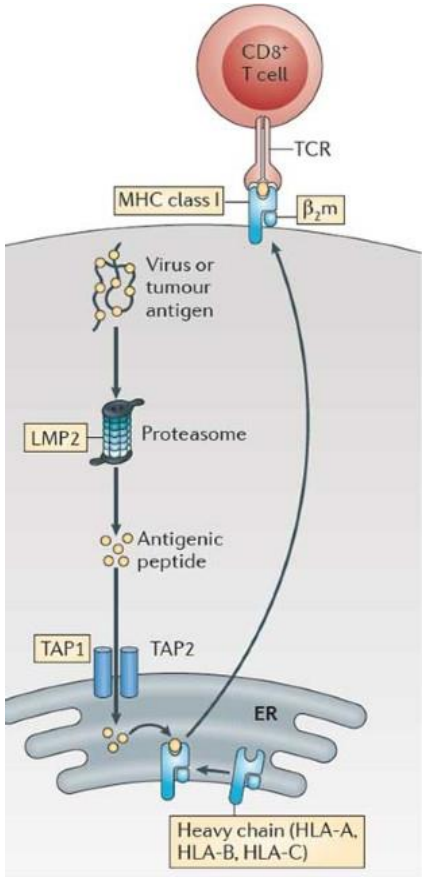


SafetyScan identifies clinically relevant off-targets

*Genome-wide screen of **affinity-enhanced MAGE-A3 TCR***

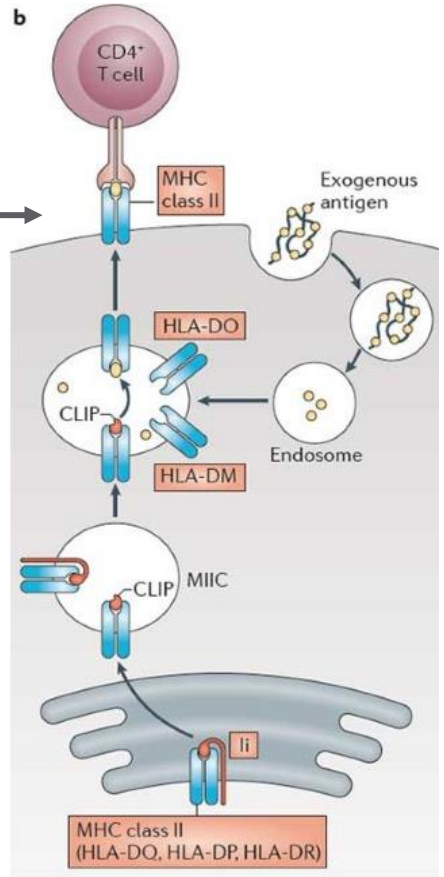


TargetScan screening extended to class II HLAs to identify targets of CD4+ T cells mediating many autoimmune diseases



Class I HLAs present antigens to CD8+ T-cells relevant for TScan oncology program and select autoimmune diseases

Class II HLAs present antigens to CD4+ effector and regulatory T cells mediating many additional autoimmune diseases



Kobayashi *et al*, *Nat Rev Immunol*, 2012

TScan has initiated tissue collection and novel target discovery for other T cell-mediated autoimmune diseases such as:

Ankylosing spondylitis, celiac disease, multiple sclerosis (MS), psoriasis, scleroderma, vitiligo and others

ReceptorScan identifies ultrahigh affinity, naturally occurring TCRs with low risk of off-target effects

Key Problem

CHALLENGE

Most naturally-occurring TCRs to self antigens have low affinity and/or low activity

CURRENT SOLUTIONS

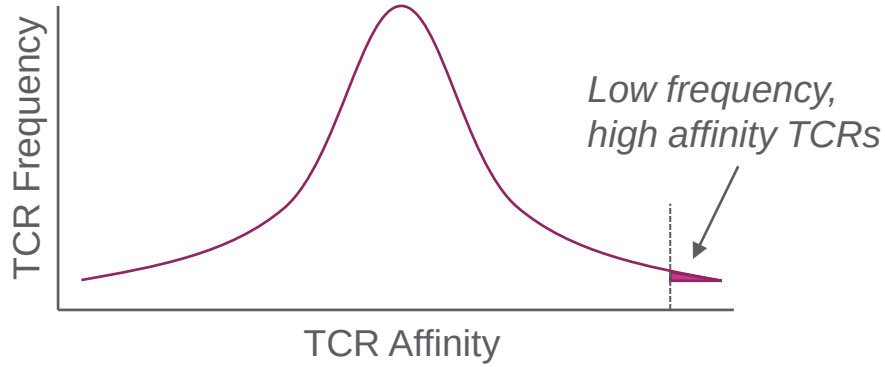
- Mutate TCRs to enhance affinity
- Raise TCRs in transgenic mice

PROBLEM WITH THESE SOLUTIONS

TCRs that have not undergone negative selection in the thymus may exhibit off-target effects

TScan Solution

ReceptorScan is a high-throughput platform that identifies the best TCR for a desired target from >1 billion T cells



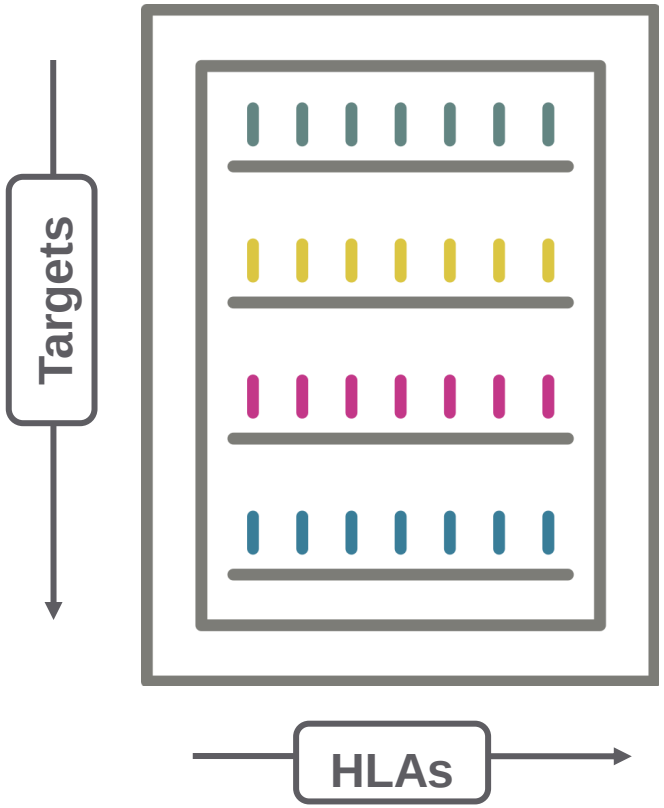
All TCRs are fully human and naturally occurring, yet exhibit affinities equal to or better than clinical-stage TCRs

TargetScan, ReceptorScan & SafetyScan used to generate ImmunoBank of de-risked antigens/TCRs

Suite of TScan Discovery Technologies

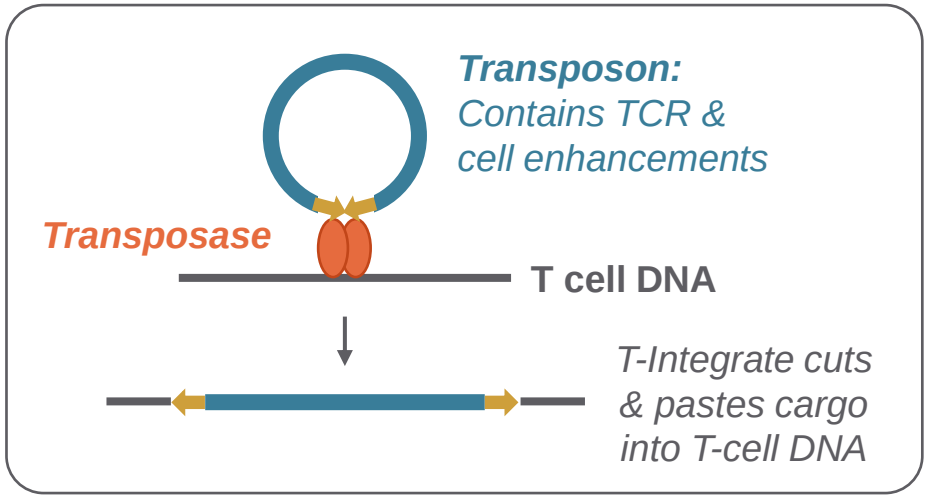
- TargetScan
- ReceptorScan
- SafetyScan

ImmunoBank of Therapeutic TCRs



T-Integrate manufacturing platform overcomes lentiviral size constraints - enables production of enhanced TCR-T cells

T-Integrate:
Genetic Cargo Delivery System



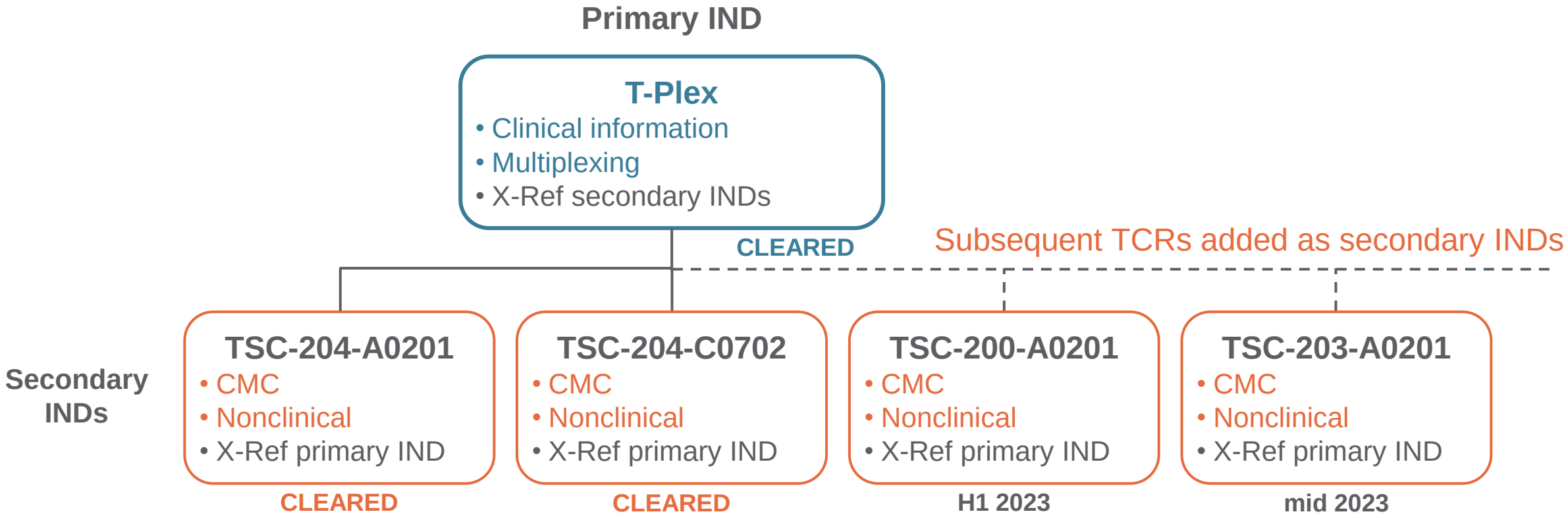
*Transposon/transposase technology enables delivery of the **TCR** as well as many **cell enhancements** (e.g., CD8α/β, DN-TGFβRII, purification tags)*

Advantages of T-Integrate non-viral delivery over lentivirus:

- Greater cargo size enables delivery of T cell functional enhancements
- Rapid process development
- Cost-effective manufacturing

All cell manufacturing is performed in-house at TScan
GMP facility supports manufacturing >250 TCR-Ts / year

FDA feedback provides clear path to building ImmunoBank and developing multiplexed TCR-T



- Master clinical protocol resides in one Primary IND
- IND filing structure enables adding new TCRs as they become available