



Attacking Solid Tumors with Novel TCR-T Cell Therapies

| September 2022

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Shareholder Value Creation:

A Clinical Stage TCR-T Company Targeting Solid Tumors



Weaponizing the immune system with powerful TCRs to treat solid tumors

Targeting driver mutations using T cells genetically modified with proprietary non-viral *Sleeping Beauty* platform

Vision 2022 – Execution Mindset, Delivering Results

- 1 Phase 1/2 TCR-T Library Trial Enrolling; Confirmed Partial Response in First Patient (NSCLC); Now Treating at Dose Level 2
- 2 Clinical Library of 10 TCRs (*KRAS*, *TP53*, *EGFR*) Targeting Six Solid Tumor Indications
- 3 Utilizing Internal cGMP Manufacturing Facility For TCR-T Library Trial
- 4 Proprietary TCR Discovery Platform, hunTR™, Expanding and Advancing the Pipeline

TCR-T Platform with Multiple Solid Tumor Programs in Pipeline

PROGRAM	TARGETS	INDICATION	DISCOVERY	PRECLINICAL	IND-ENABLING	PHASE 1
Library TCR-T cell Therapy (Company Sponsored at MDACC - NCT05194735)	KRAS, TP53 & EGFR Hotspot Mutations	Lung	█	█	█	█
		Colon/rectum	█	█	█	█
		Endometrium	█	█	█	█
		Pancreas	█	█	█	█
		Ovary	█	█	█	█
		Bile Duct	█	█	█	█
mbIL-15 TCR-T cell Therapy	KRAS & TP53 Hotspot Mutations	Solid Tumors	█	█	█	█
Undisclosed Targets & Modalities (hunTR™)	Cancer-specific Somatic Mutations	Cancers with Hotspot Mutations	█			

TCR-T is Superior to Other Cell Therapy Approaches for Solid Tumors

	TCR-T	CAR-T	TIL
Target Intracellular & Extracellular Antigens	✓		✓
Proven Efficacy in Solid Tumors	✓		✓
Defined Target Specificity	✓	✓	
Targets Somatic Neoantigens	✓		✓
Established Transposon-based Gene Transfer	✓	✓	

Table above not based on head-to-head trials

A Differentiated TCR-T Program Targeting Solid Tumors



Targeting Hotspot Mutations

Hotspot mutations are ideal targets for defeating cancer



Sleeping Beauty Technology

Non-viral transposition technology has favorable safety profile

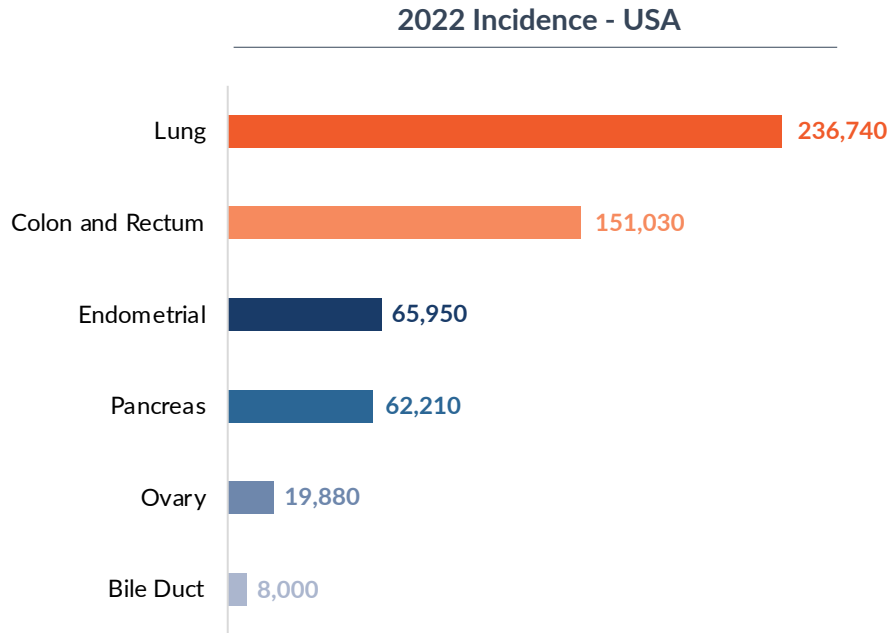
Rapid, flexible & cost-effective manufacturing



hunTR™ Platform (human neoantigen T cell Receptor)

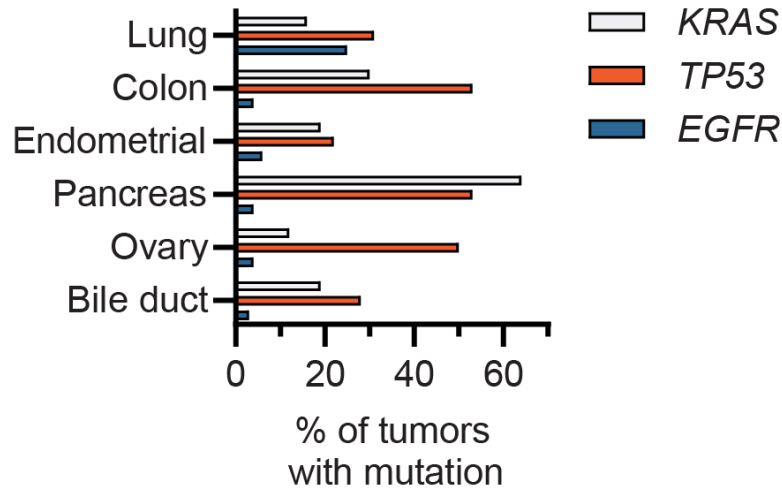
Robust discovery engine enables expansion of TCR Library

Our TCR-T Cell Platform Targets Solid Tumors in Large Patient Populations with Unmet Clinical Need



- In the US, 92% of new cancer cases are solid tumors
- 4,804 patients are diagnosed every day with cancerous solid tumor
- 1,548 patients die every day from a solid tumor cancer

KRAS, TP53, EGFR Mutations are Commonly Expressed in Targeted Indications



High frequency tumor targets, not expressed in normal tissues

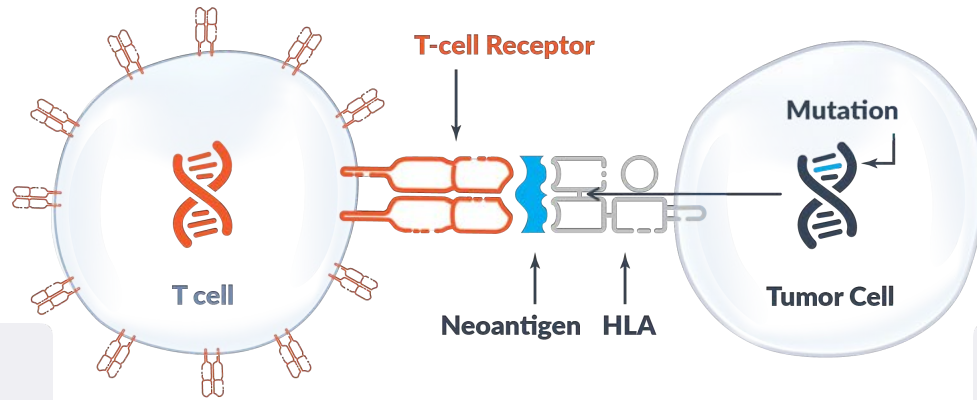


Killer TCR-T cells specific for the mutation without off-tumor toxicity



Unmet clinical need for patients with solid tumors

TCRs Can Give Patients' T Cells a New Ability to Recognize and Kill Tumor Cells with Common Mutations



T-cell Receptors

- Naturally occurring
- Highly specific
- Intracellular and extracellular targets

Neoantigens

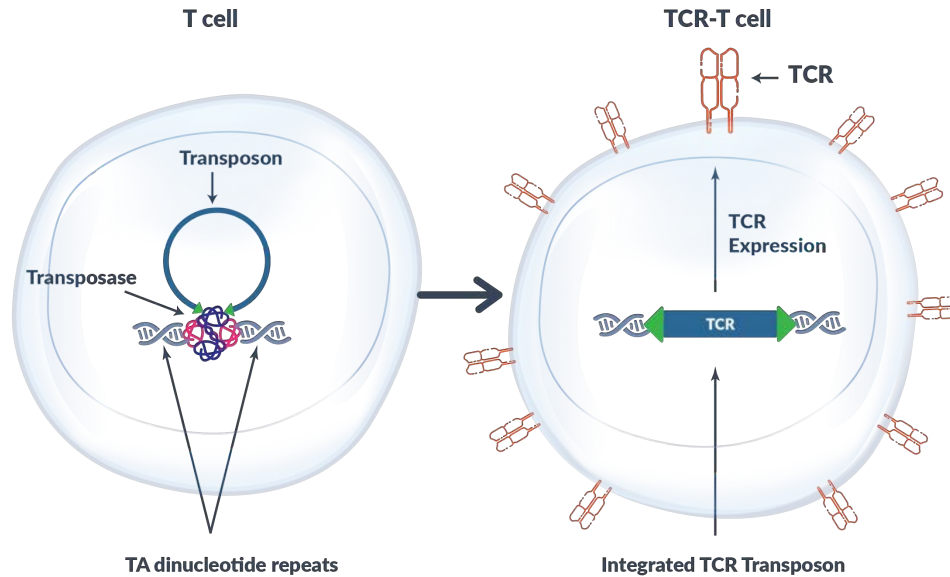
- Derived from mutations
- Expressed by tumor, not in normal tissues
- Presented on the tumor surface by HLA

TCR Library Captures High Frequency Mutations and HLA Types



- Common HLAs are represented in our TCR library
- Certain mutations have more than one HLA restriction
- As more TCRs are added to our library, the addressable patient market size will further increase

Non-viral *Sleeping Beauty* Platform for Manufacturing TCR-T Cells without the Complexity of Gene Editing



- Efficient integration without the complexity of gene editing or viral approaches
- Rapid, cost-effective manufacturing
- Flexible approach to add TCRs; attractive choice for library
- Platform can accommodate large transgene size
- Process scalable for clinical production

TCR-T Cells Recognize *KRAS*, *TP53*, *EGFR* Mutations and Kill Solid Tumor Cells



Powerful TCRs:

Naturally-occurring, high avidity TCRs recognize low levels of neoantigens



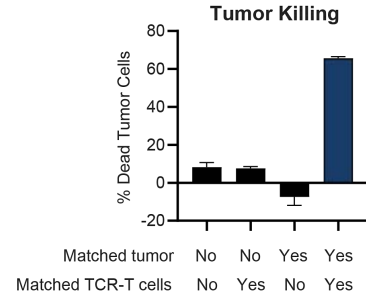
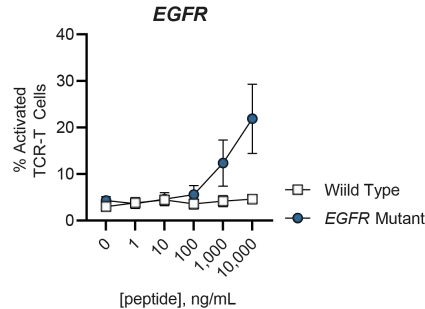
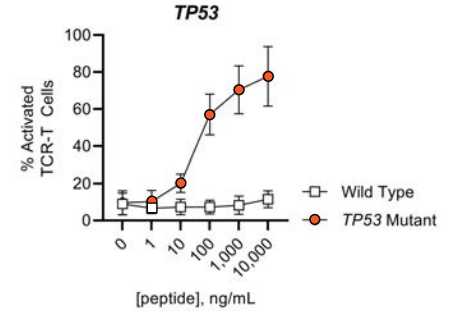
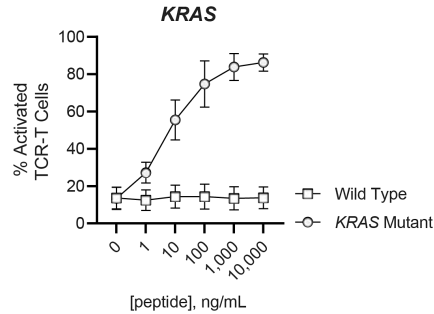
No off-target toxicity observed:

Specificity for the mutation with negligible recognition of the wild type sequences



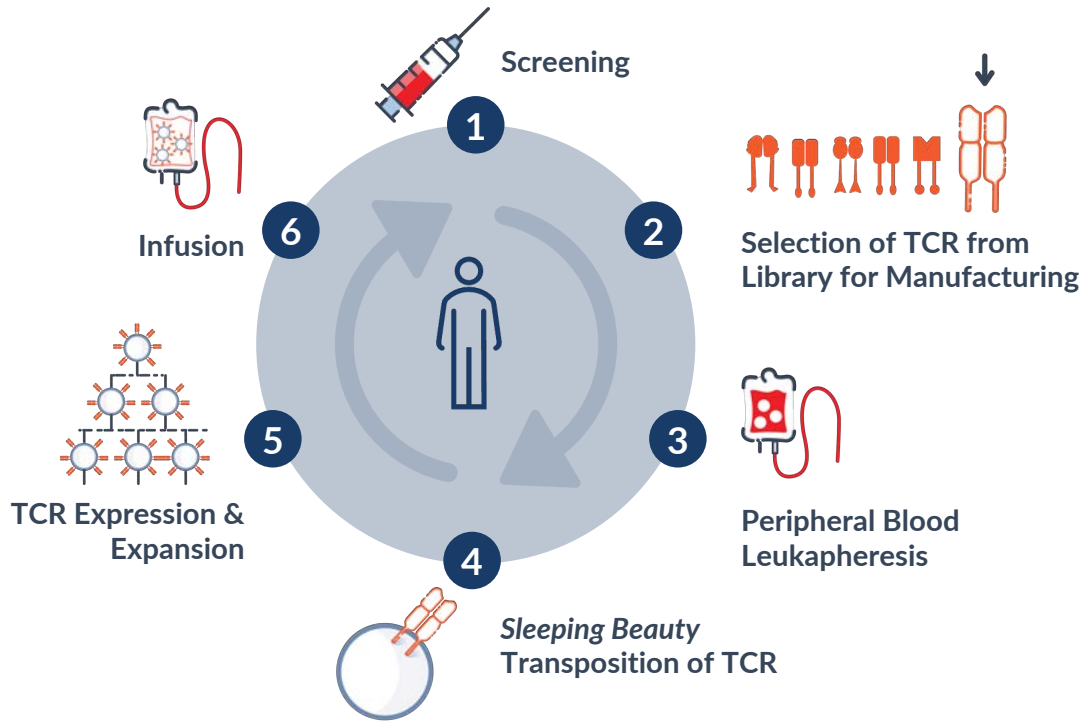
Tumor killing:

Recognition of tumor cells that express mutation and HLA



Note: Refers to *TP53* mutant reactive TCRs

Each Autologous TCR-T Cell Product is Manufactured with a TCR Matched for the Patient's Mutation and HLA Type



Actively Enrolling First-in-Human TCR-T Clinical Trial with Innovative Library Approach



- ✓ Trial enrolling patients where a TCR matching a neoantigen / HLA pairing is available in our TCR-T library
- ✓ Phase I is a prospective, open-label, dose-escalation study of TCR-T cells in patients with progressive or recurrent solid tumors where standard therapy has failed to control disease
- ✓ Bayesian optimal interval design (BOIN) with accelerated dose escalation
- ✓ Enrolling in one of three dose cohorts: 5×10^9 , 4×10^{10} , 1×10^{11}

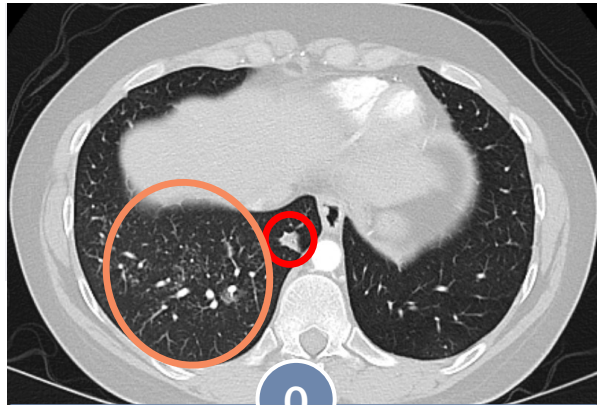
Phase I Objectives:

- ✓ Define dose limiting toxicity (DLT) and the maximum tolerated dose (MTD) or recommended phase II dose (RP2D)
- ✓ Evaluate the feasibility of TCR-T cell drug product manufacturing

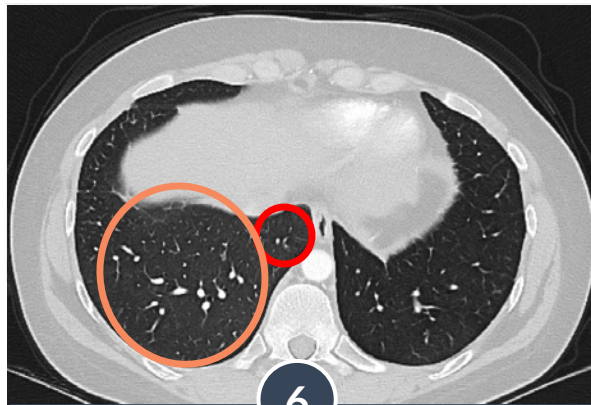
Confirmed Partial Response in Patient #1 Following Treatment with *Sleeping Beauty* TCR-T Cells

Patient #1	
Indication	Checkpoint inhibitor and chemotherapy refractory NSCLC
TCR Library Match	KRAS G12D mutation and HLA-A*11:01
Dose Level	Treated at dose level 1 with 9 billion TCR-T cells
Safety	Manageable safety profile with no dose limiting toxicities observed
Persistence	TCR-T cell persistence greater than 22% of total T cells and ongoing at three months post infusion

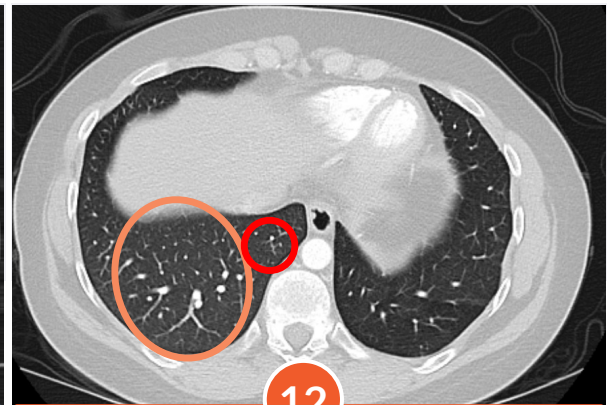
Patient #1: Complete Resolution of Right Lower Lobe Target Lesion



Baseline
1.3 cm



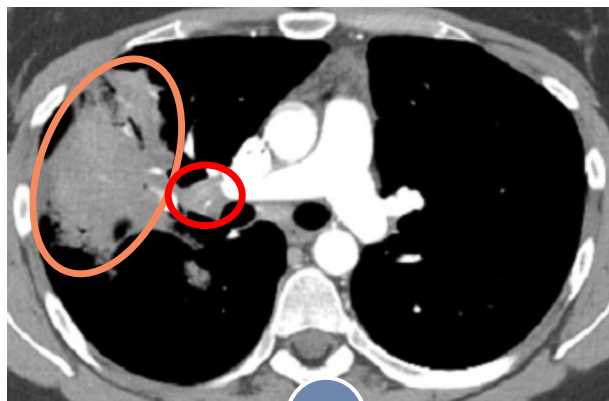
Week 6
0.0 cm



Week 12
0.0 cm

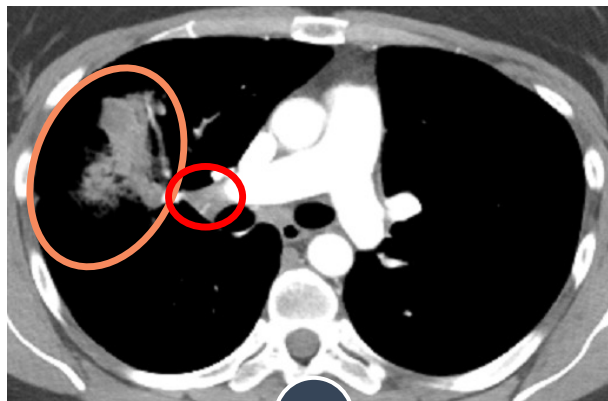
Note: Red circle represents target lesion

Patient #1: Reduction of Right Hilar Lymph Node



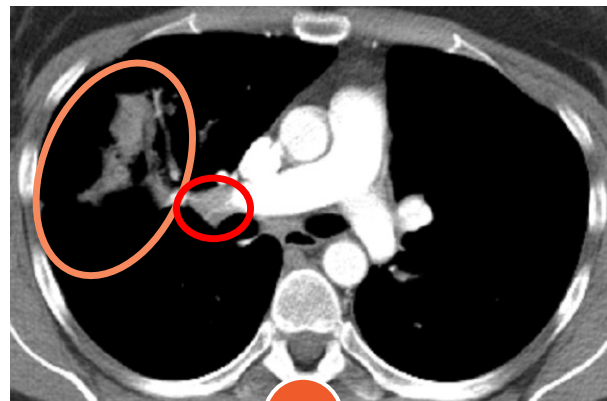
0

Baseline
1.5 cm



6

Week 6
1.1 cm



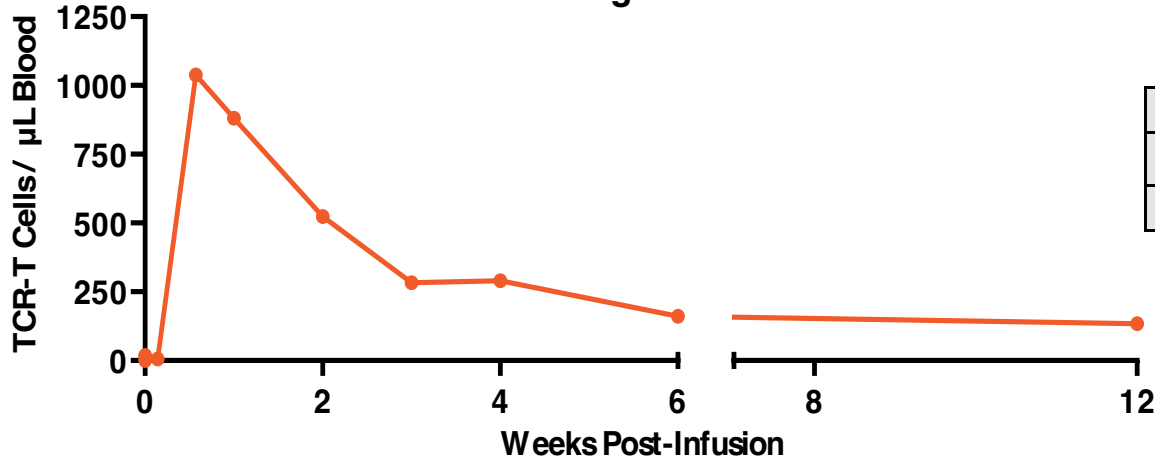
12

Week 12
1.0 cm

Note: Red circle represents target lesion

Patient #1: TCR-T Cells Exhibited Rapid Expansion and Ongoing Persistence at Week 12

Circulating TCR-T Cells



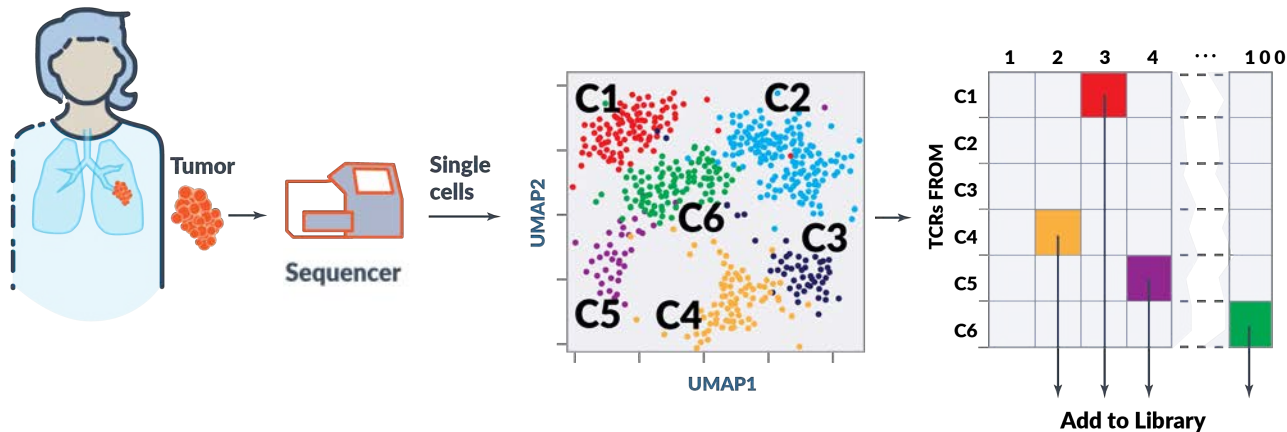
	Day 4	Week 12
TCR-T Cells/μL	1,038	134
TCR-T Copies/μg	5×10^5	2.5×10^4
% TCR-T+ of CD3+	98.4%	22.5%

Promising Data Demonstrates Potential of TCR-T Cell Therapy in Solid Tumors

Patient	Dose (TCR-T Cells)	Best Response	Time on Trial
1	9 Billion	Partial Response	5 months and ongoing
2	64 Billion	Stable Disease	3 months

- First report of successful TCR-T cell therapy using non-viral *Sleeping Beauty* system for solid tumors
- Proof of concept of manufacturing TCR-T targeting *KRAS* and *TP53*
- Phase I enrollment ongoing at dose level 2 for patients with advanced solid tumors

hunTR™ Program Rapidly Expands TCR Library Targeting Hotspot Mutations



Focus on neoantigens, particularly those arising from hotspot mutations

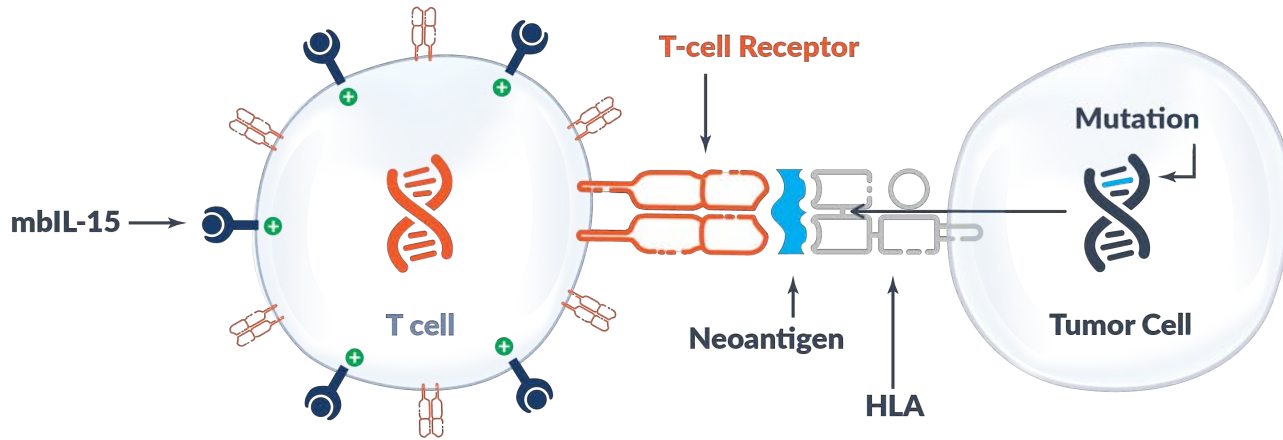


Empirical screening of TCRs from CD4+ and CD8+ T cells directly from tumor



High-throughput TCR screening

mbIL-15 Improves the Persistence and Anti-tumor Activity of TCR-T cells in the Tumor Microenvironment (TME)



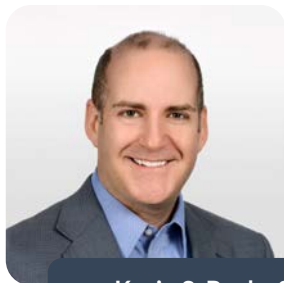
✓ Pro-survival signaling limits negative signals from the TME

✓ Stem-cell memory mbIL-15 TCR-T cells regenerate TCR-T cells

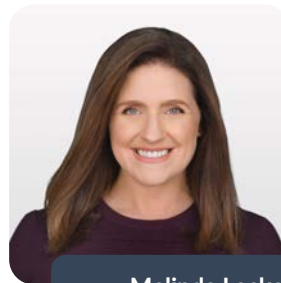
✓ Limit effects of HLA loss by supporting TILs and NK cells

✓ Potential for TCR-T cell therapy without lymphodepletion

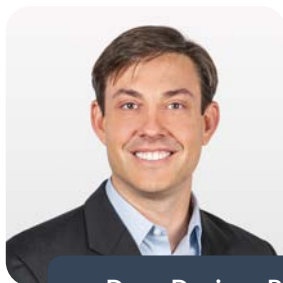
Experienced Management Team



Kevin S. Boyle, Sr.
Chief Executive Officer



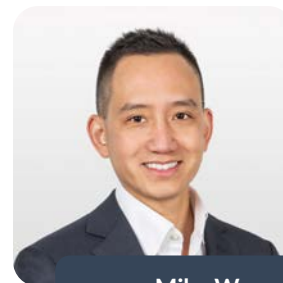
Melinda Lackey
SVP Legal



Drew Deniger, PhD
VP Research & Development



Abhishek Srivastava, PhD
VP Research & Development



Mike Wong
VP Finance

Shareholder Value Creation:

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