

Attacking Solid Tumors with Novel TCR-T Cell Therapies

| July 2023

Forward Looking Statements

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Delivering the Promise:

Revolutionizing Solid Cancer Treatment with TCR-T

2022

Significant Accomplishments

First TCR-T objective clinical response in solid tumors

Doubled addressable market

Doubled manufacturing capacity

Validated hunTR®

2023

Anticipated Milestones

Phase 2 readiness

Expand TCR library to 15

File IND for mbIL-15 TCR-T

2024+

Building for the Future

Pivotal clinical trials

Combination therapies

Treat patients with multiple TCRs

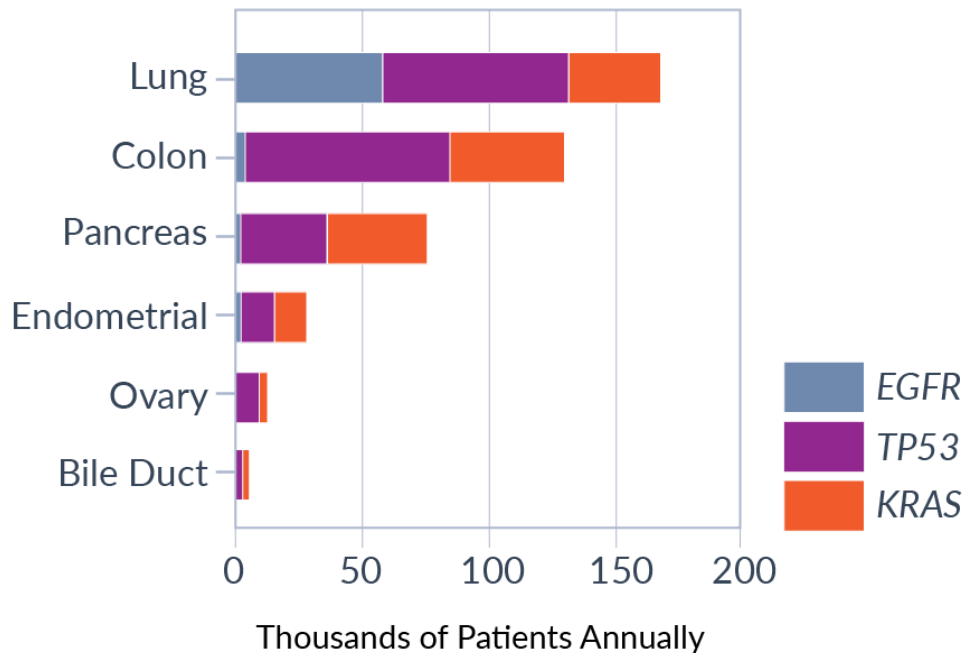
Robust Solid Tumor Program Pipeline with Multiple Near-Term Inflection Points

PROGRAM	TARGETS	INDICATION	PRECLINICAL	IND-ENABLING	PHASE 1	PHASE 2
Library TCR-T Cell Therapy	KRAS <i>G12D & G12V</i> TP53 <i>R175H, R248W, R273C & Y220C</i> EGFR <i>E746-A750del</i>	Lung				
		Colon/Rectum				
		Endometrium				
		Pancreas				
		Ovary				
		Bile Duct				
mbIL-15 TCR-T Cell Therapy	KRAS & TP53 Mutations	Solid Tumors				
Multiplex TCR-T Cell Therapy	Multiple targets per patient	Solid Tumors				

Driver Mutations are Ideal Targets for TCR-T Cells to Treat Solid Tumors

Target	Examples	Key Advantages	Key Disadvantages
Driver Mutations	Mutated <i>EGFR</i>, <i>KRAS</i> or <i>TP53</i>	<ul style="list-style-type: none">• Drives cancer• Highly expressed targets• Not on normal tissue• Large addressable market	<ul style="list-style-type: none">• Single targets
Tumor Associated Antigens	NY-ESO-1, MAGE, PRAME, MART-1, gp100	<ul style="list-style-type: none">• Overexpressed on multiple cancer types	<ul style="list-style-type: none">• Small addressable market• Potential cross reactivity with normal tissues
Viral Antigens	HPV, EBV, HBV	<ul style="list-style-type: none">• Not on normal tissues• Highly expressed target	<ul style="list-style-type: none">• Limited to few cancers• Immune editing from chronic viral infection
Individualized Mutations	Mutations expressed by patient's cancer	<ul style="list-style-type: none">• Treatment of multiple targets• Large addressable market	<ul style="list-style-type: none">• Long time to treatment• Labor intensive• Inherent difference between patients

Alaunos Evaluating TCR-T Against the Most Frequently Mutated Genes in Solid Tumors: *KRAS*, *TP53*, *EGFR*



Nearly 2 million solid tumors cases diagnosed in United States annually



Limited approved drugs for these high value targets



These six indications represent ~600,000 new cases per year

Confirmed Responses from Leading Academic Institutions Corroborate Targeting Driver Mutations with TCR-T Cells

THE NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Neoantigen T-Cell Receptor Gene Therapy in Pancreatic Cancer

Rom Leidner, M.D., Nelson Sanjuan Silva, B.S., Huayu Huang, M.S., David Sprott, B.S., Chunhong Zheng, Ph.D., Yi-Ping Shih, Ph.D., Amy Leung, B.S., Roxanne Payne, M.N., Kim Sutcliffe, B.S.N., Julie Cramer, M.A., Steven A. Rosenberg, M.D., Ph.D., Bernard A. Fox, Ph.D., Walter J. Urba, M.D., Ph.D., and Eric Tran, Ph.D.

Greater than 70% tumor reduction of metastatic pancreatic cancer six months after infusion of KRAS-G12D and HLA-C*08:02 reactive TCR-T cells

CANCER IMMUNOLOGY RESEARCH | RESEARCH ARTICLE

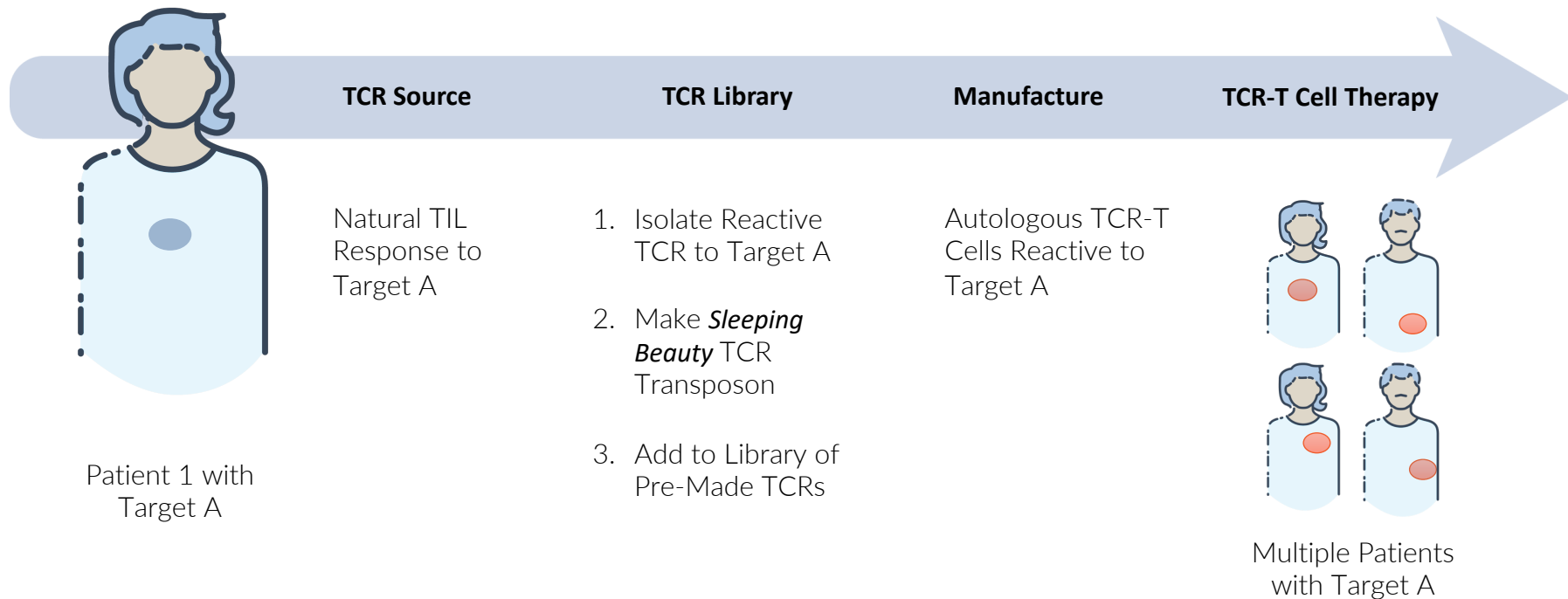
Adoptive Cellular Therapy with Autologous Tumor-Infiltrating Lymphocytes and T-cell Receptor-Engineered T Cells Targeting Common p53 Neoantigens in Human Solid Tumors

Sanghyun P. Kim¹, Nolan R. Vale¹, Nikolaos Zacharakis¹, Sri Krishna¹, Zhiya Yu¹, Billel Gasmis², Jared J. Gartner¹, Sivasish Sindiri¹, Parisa Malekzadeh¹, Drew C. Deniger¹, Frank J. Lowery¹, Maria R. Parkhurst¹, Lien T. Ngo¹, Satyajit Ray¹, Yong F. Li¹, Victoria Hill¹, Maria Florentin¹, Robert V. Masi¹, Biman C. Paria¹, Noam Levin¹, Alakesh Bera¹, Elizabeth A. Hedges¹, Agnes Choi¹, Praveen D. Chatani¹, Anup Y. Parikh¹, Shoshana Levi¹, Samantha Seitter¹, Yong-Chen Lu¹, Zhili Zheng¹, Todd D. Prickett¹, Li Jia³, Jonathan M. Hernandez⁴, Chuong D. Hoang⁵, Paul F. Robbins¹, Stephanie L. Goff¹, Richard M. Sherry¹, James C. Yang¹, and Steven A. Rosenberg¹

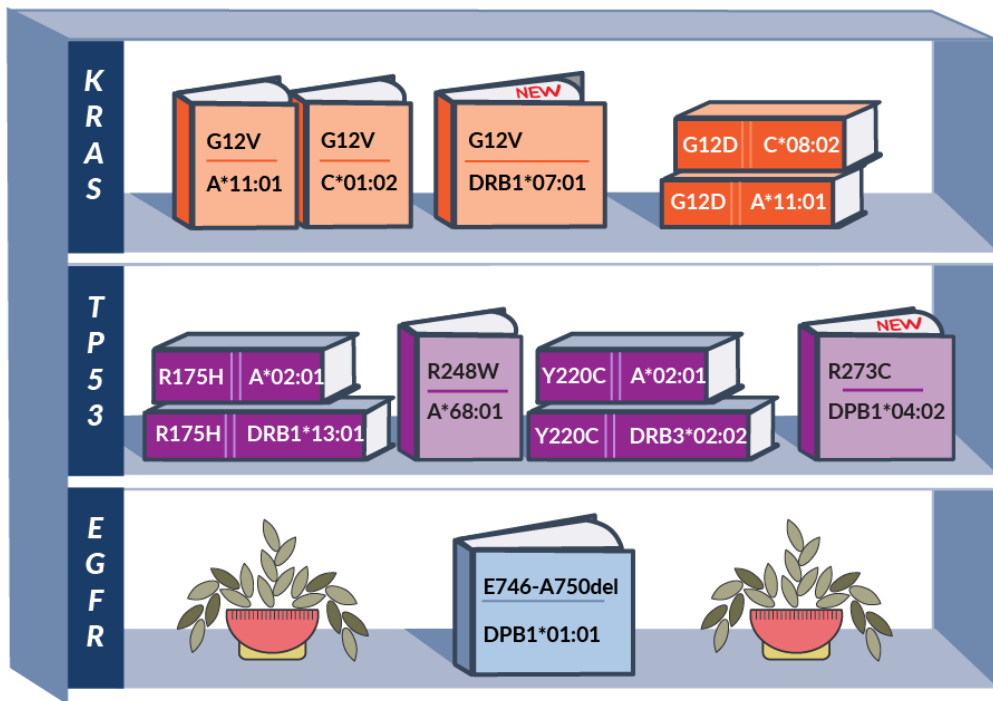
55% tumor reduction of metastatic breast cancer six months after infusion of TP53-R175H and HLA-A*02:01 reactive TCR-T cells

Alaunos is the only company in the clinic with these TCRs in its library

Differentiated Approach to Convert Natural T-Cell Responses into TCR-T Cell Therapy for a Broad Patient Population

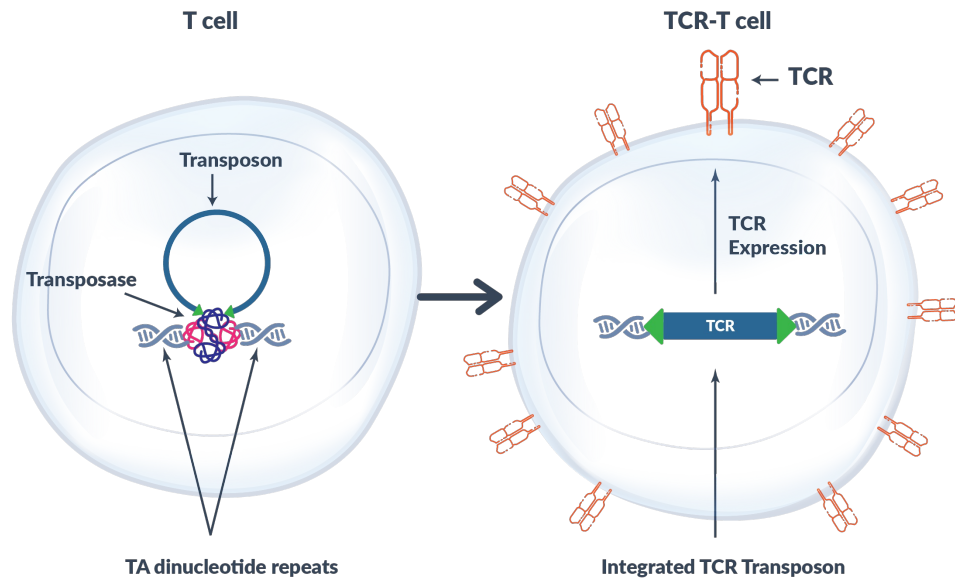


Industry Leading TCR Library Captures Both High Frequency Mutations and HLA Types



- ◀ In over 700 patients screened, 15% match rate to a TCR in our library
- ◀ Two-pronged library expansion strategy:
 1. Add more HLAs to existing mutations
 2. Add more mutations to KRAS, TP53, EGFR
- ◀ Our TCR library contains mutations from genes that are known to drive cancer and are highly expressed by tumors
- ◀ Mutations in our library are among the most frequent and most mutated genes in solid tumors
- ◀ HLAs that present our mutations are prevalent in the United States

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



- Efficient, essentially random integration without 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
- Expected to be scalable for commercialization

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



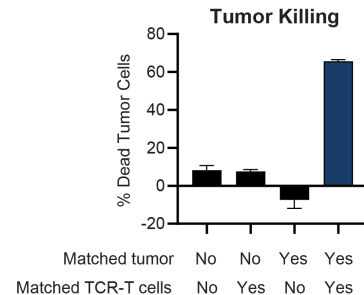
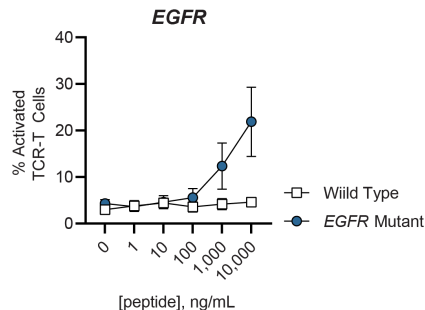
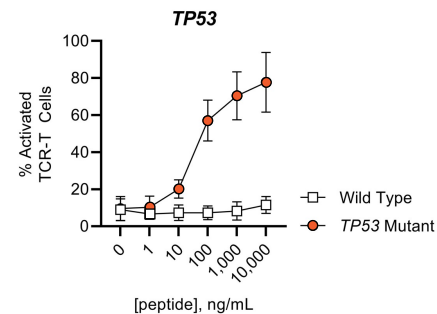
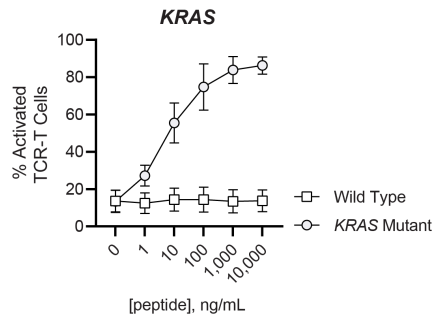
No off-target toxicity observed:

Specificity for the mutation with negligible recognition of wild type sequences



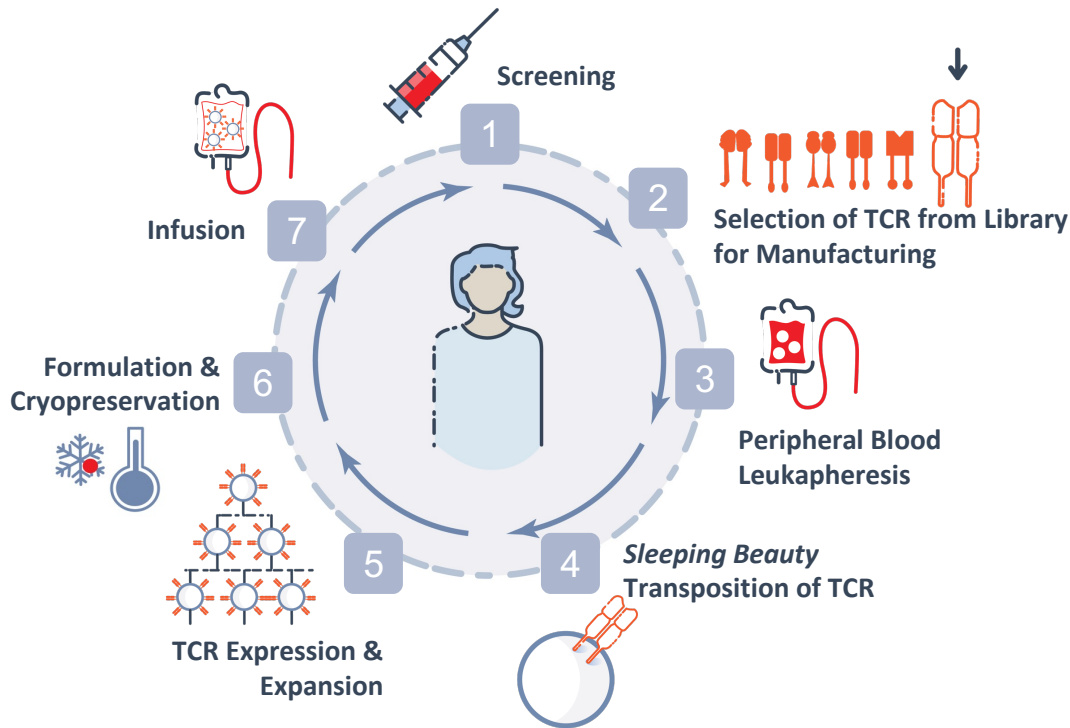
Tumor killing:

Recognition of tumor cells that express mutation and HLA



Note: Refers to TP53 mutant reactive TCRs

TCR-T Cell Products are Manufactured with a TCR Matched to Each Patient's Tumor Mutation and HLA Type



Universal, In-House Manufacturing Platform Delivers High Quality TCR-T Cell Products

	Patient 1	Patient 2	Patient 3
Mutation	KRAS-G12D	TP53-R175H	KRAS-G12V
Indication	Lung	Colorectal	Pancreatic
Dose Level	One	Two	Two
Viability	97%	93%	93%
Total TCR-T Cells	9 Billion	64 Billion	58 Billion
CD3+ Purity	99.7%	99.7%	99.1%
TCR+	95%	92%	91%

Ongoing Process Optimization



Automation and closed process steps to increase throughput



Reduction in overall manufacturing days and cost



Improving the long-term viability of the commercial process

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

Phase 1

- Defines safety and dose with any TCR and any indication
- Enrolling in one of three dose cohorts: 5, 40 and 100 billion TCR-T cells

Phase 2

- Defines efficacy at recommended dose with any TCR in library
- Each cancer type will be a distinct cohort

Pivotal

- Selected indications and selected TCRs with efficacy in Phase 2
- IND can start while Phase 2 continues for other indications/TCRs

Vision for Commercial Product

- Multiple TCRs for use in multiple cancer types
- Early guidance from FDA supports our approach

First-in-Human Confirmed Response in Solid Tumors by *Sleeping Beauty* TCR-T Cell Therapy

SAFETY

Manageable safety profiles
in first two dose levels

No DLTs

No ICANs

PERSISTENCE

Persisting TCR-T cells
(20%-30%) in blood

TCR-T cells trafficking to
tumor

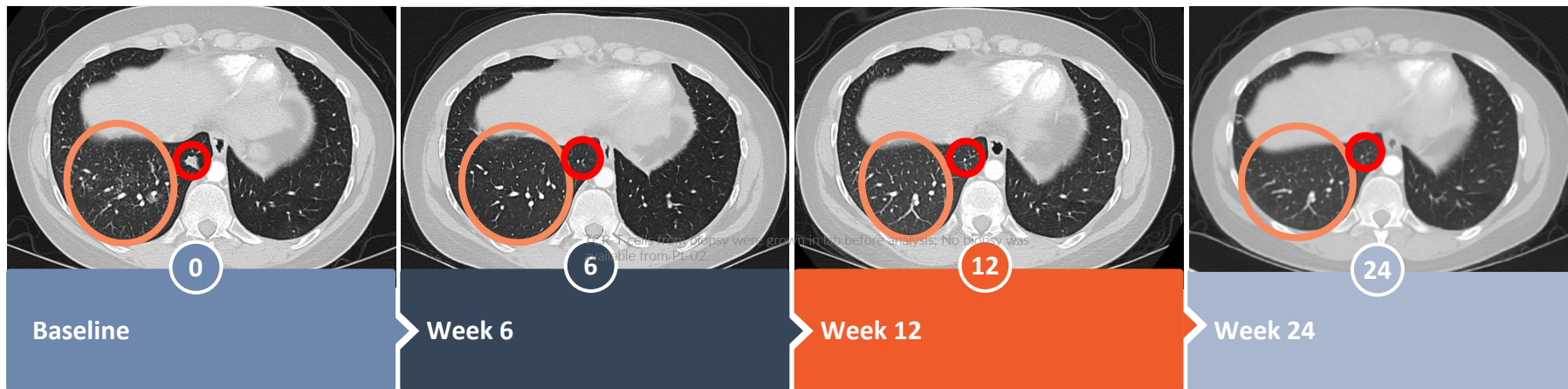
Maintenance of mutation
and HLA post-treatment

EFFICACY

First TCR-T cell response in
checkpoint inhibitor
refractory NSCLC
(>50% reduction)

Six-month progression-free
survival comparable to
approved KRAS drug

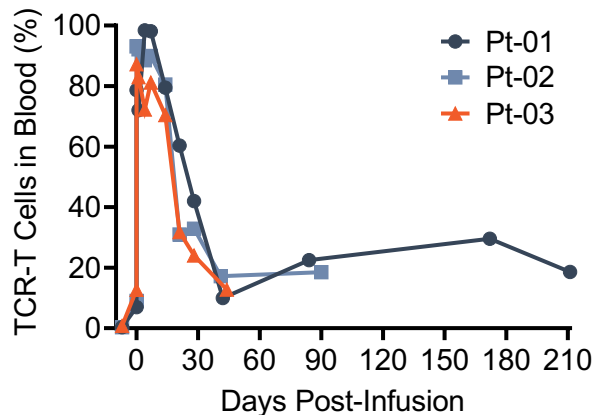
Patient 1 Showed Durable, Complete Resolution of NSCLC Lesion Through Six Months



- Patient 1 had multiple lines of prior therapy and was refractory to checkpoint inhibitors
- Treated with 9 billion TCR-T cells (dose level 1) targeting KRAS-G12D and HLA-A*11:01 with manageable safety profile
- Confirmed partial response; patient is now off-study after six-month progression-free survival

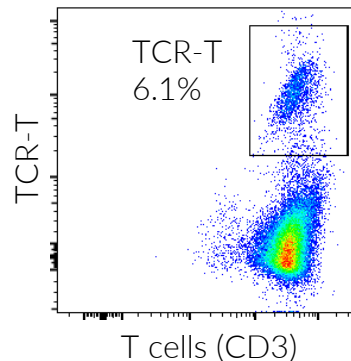
TCR-T Cells Persist in Blood and Traffic to Tumor Microenvironment

TCR-T Cell Expansion and Persistence in Blood

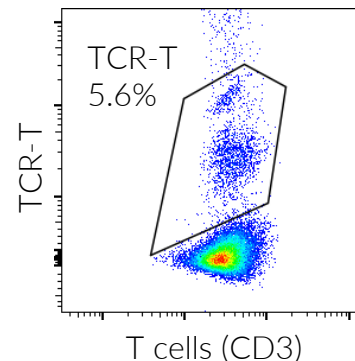


TCR-T cells were detected in peripheral blood at last follow-up

Patient 1:
Seven-Month Tumor Biopsy



Patient 3:
Six-Week Tumor Biopsy

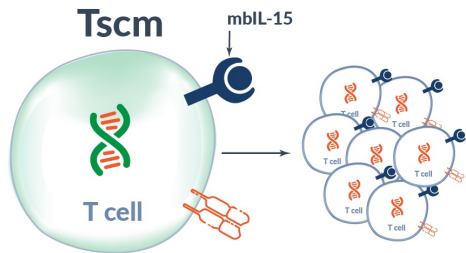


Tumor trafficking up to seven months after infusion observed

TCR-T cells from biopsy were grown in lab before analysis. No biopsy was available from Pt-02.

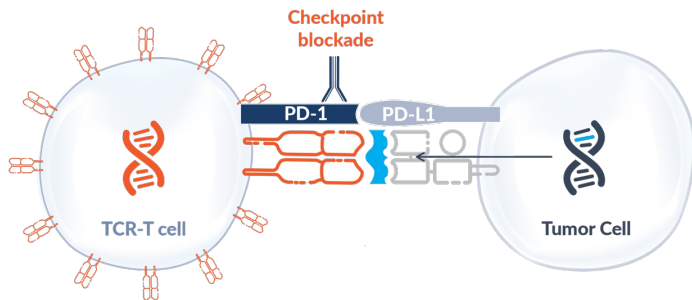
Next-Generation TCR-T Efforts Aim to Deepen Clinical Responses

Augmenting TCR-T Survival via Co-Expression of mBIL-15



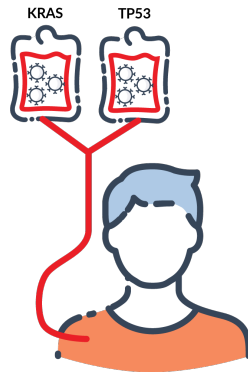
Regeneration of effector TCR-T cells in the tumor

Combine TCR-T and Immune Checkpoint Inhibitors



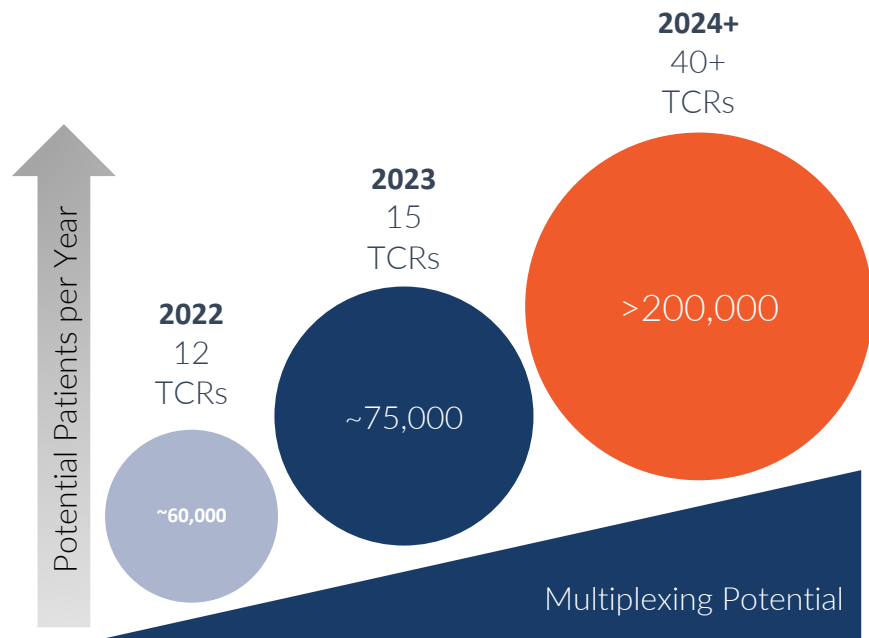
Reinvigorate TCR-T cells in the tumor microenvironment

Multiple TCRs Infused into the Same Patient



Attack multiple targets on the tumor to potentially synergize TCR-T

hunTR[®] Expands TCR Library, Increases Addressable Market and Enables Multiplexed TCR-T Cell Therapy



Add new HLAs to existing mutations and add more key mutations within *EGFR*, *KRAS*, *TP53*



Matching data from clinical efforts inform which HLA/mutation combinations to prioritize

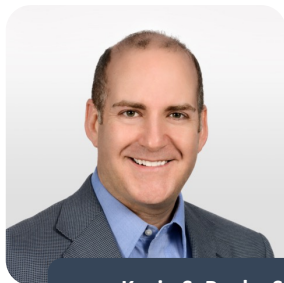


Sleeping Beauty expected to allow for cost-effective and efficient expansion of TCR library for clinic



Expect out-licensing opportunities of selected proprietary TCRs

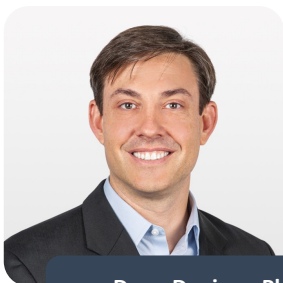
Experienced Management Team



Kevin S. Boyle, Sr.
Chief Executive Officer



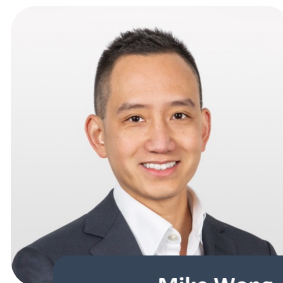
Melinda Lackey
SVP Legal



Drew Deniger, PhD
VP Research & Development

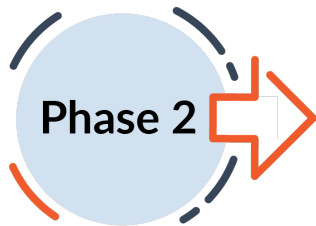


Abhishek Srivastava, PhD
VP Technical Operations

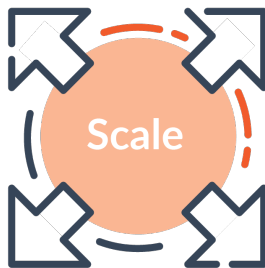


Mike Wong
VP Finance

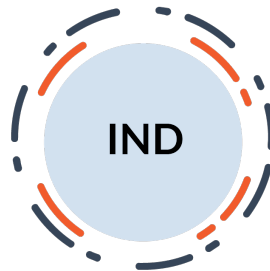
2023 Milestones Designed to Cement Our Leadership Position in TCR-T Cell Therapy for the Treatment of Solid Tumors



**Advance TCR-T
Library trial to
Phase 2**



**Optimize
manufacturing
process towards
commercial
scalability**



**New IND for
mbIL-15 TCR-T**



Expand TCR Library to 15 TCRs
**Translational assessment-
driven next-gen TCR-T**