Precision Immunotherapy for Oncogenic Driver Mutations

Non-Confidential Corporate Presentation

June 2023

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RIGHT TARGETS. RIGHT CELLS. RIGHT PLACE.

Our goal is to orchestrate the immune system to target oncogenic driver mutations and deliver transformative therapies for patients with solid tumors

Experienced Management Team Supported by Blue-Chip Investor Syndicate

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Exceptional Scientific Co-Founders and SAB Specialized in T Cell Biology and Immunology

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Targeting Oncogenic Driver Mutations like KRAS Strikes at the Core of Tumor Biology

Cancer cells are dependent on oncogenic drivers

Oncogenic driver mutations initiate and maintain cancer growth, and are present in each tumor cell

Minimizes tumor heterogeneity and escape mechanisms

KRAS mutations are present in 30% of all solid tumors

KRAS represents the most frequently mutated oncogene in difficult-to-treat solid tumors

Provides impact for a high unmet medical need

Targeting KRAS has been clinically de-risked by approved G12C therapies

Recent drug approvals demonstrate single agent activity but need improved duration of response

Robust Pharma interest for drugs targeting KRAS

Affini-T TCRs have high specificity for KRAS and other oncogenic drivers

Affini-T leverages TCRs to attack only cancer cells, utilizing synthetic biology to enhance persistence

Therapeutic modality with clinical PoC

Tran et al. NEJM (2016), Leidner et al. NEJM (2022), From Joglekar AV and Li G, Nat Methods (2021), From Junttila MR and Sauvage FJ, Nature (2013)

Leveraging Oncogenic Driver Targets, Cell Selection and Synthetic Biology to Treat Solid Tumors

RIGHT TARGETS

Targeting oncogenic drivers optimizes solid tumor target specificity and leverages cancer dependency

RIGHT CELLS

Building a path to persistence using T cells enriched for stemness and coordinating a CD4/CD8 T cell response

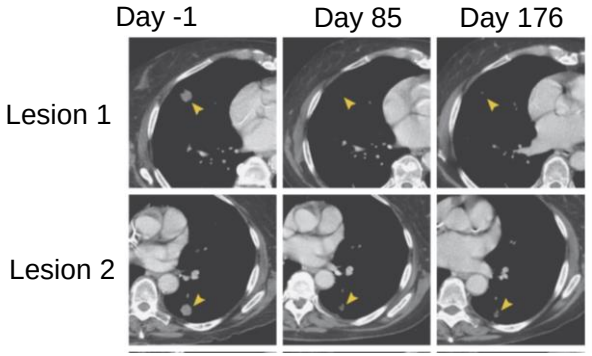
RIGHT PLACE

Synthetic biology empowers T cells to convert signals in the hostile TME into T cell survival and proliferation drives

The NEW ENGLAND JOURNAL of MEDICINE

Neoantigen T-Cell Receptor Gene Therapy in Pancreatic Cancer

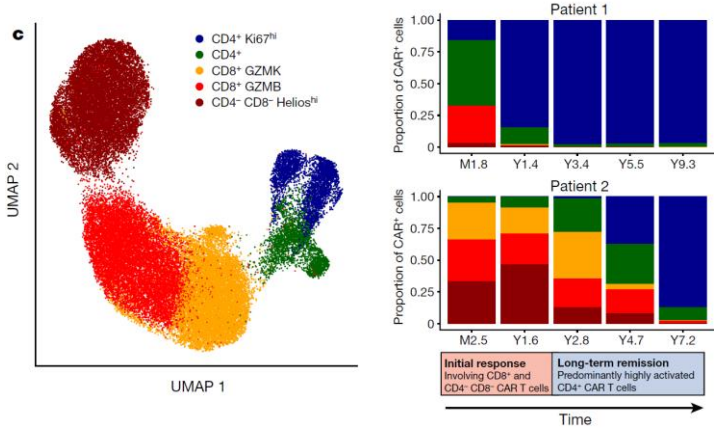
– Leidner and Tran et al.



nature

Decade-long leukaemia remissions with persistence of CD4⁺ CAR T cells

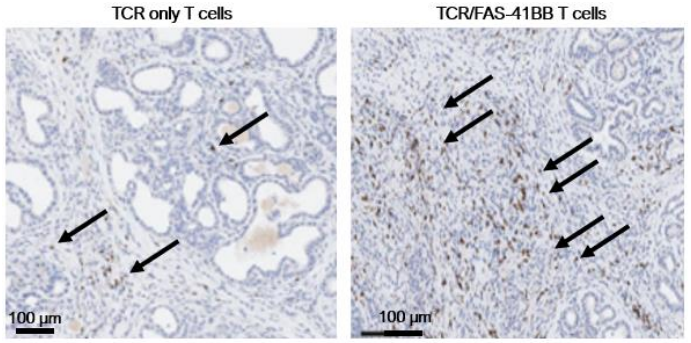
– Melenhorst and June et al.



JEM Journal of Experimental Medicine

A Fas-4-1BB fusion protein converts a death to a pro-survival signal and enhances T cell therapy

– Oda and Greenberg et al.



No / limited T cell invasion in tumor bed (blue)

Tumor bed (blue) are invaded by T cells (brown)

TME = Tumor Microenvironment

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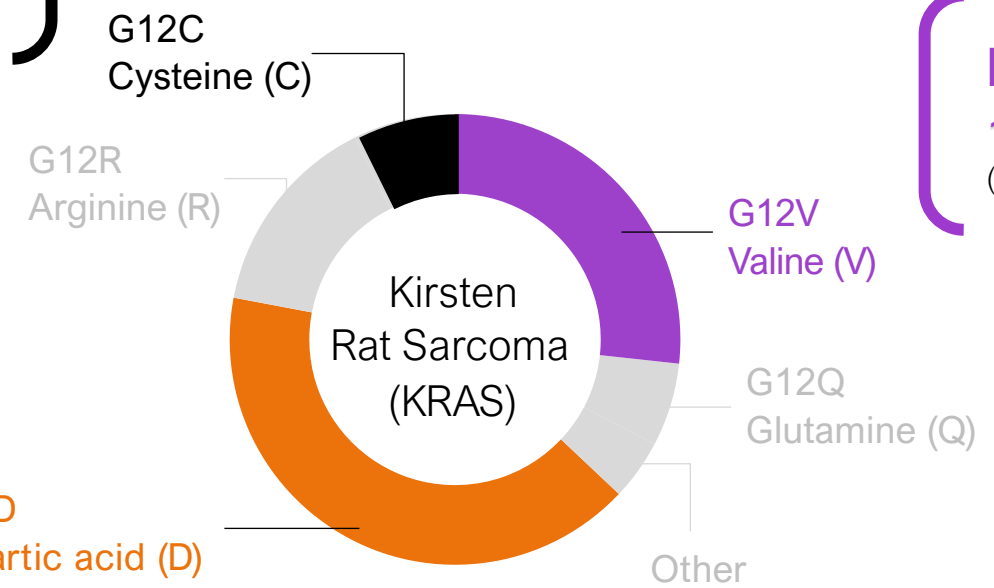
Targeting KRAS: Large Unaddressed Patient Populations with G12 Mutations

Addressable KRAS G12 mutations across multiple solid tumor populations: **~ 380K annually**

LUMAKRAS (sotorasib) 120 mg tablets
KRAZATI (adagrasib) 200 mg TABLETS

56K G12C Patients
(HLA-A3, -A11)



NO THERAPIES

185K G12V Patients
(HLA-A2, -A3, -A11)

NO THERAPIES

139K G12D Patients
(HLA-A3, -A11)

Affini-T estimates based on 2020 American Cancer Society (USA) and WHO IARC (EU, UK, CN, and JP) incidence (newly diagnosed patients/yr), frequencies of mutations from Hofmann et al. Cancer Discovery (2022), and HLA frequencies from National Marrow Donor Program (USA, census adjusted) and Immune Epitope Database (Europe, CN, JP). Indications include lung, CRC, PDAC, and endometrial. Total number of lung cancer patients was adjusted by 40% for lung adenocarcinoma. "Market Report: Lumakras Drug Clinical Insight & Sales Forecast 2026. ID 5368077.

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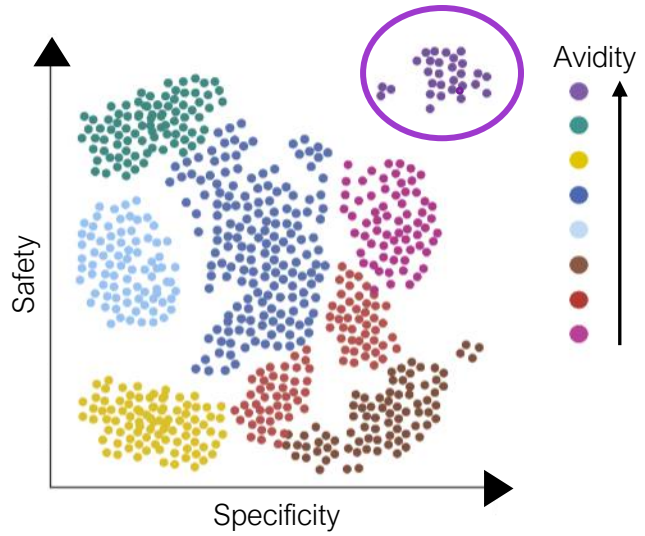
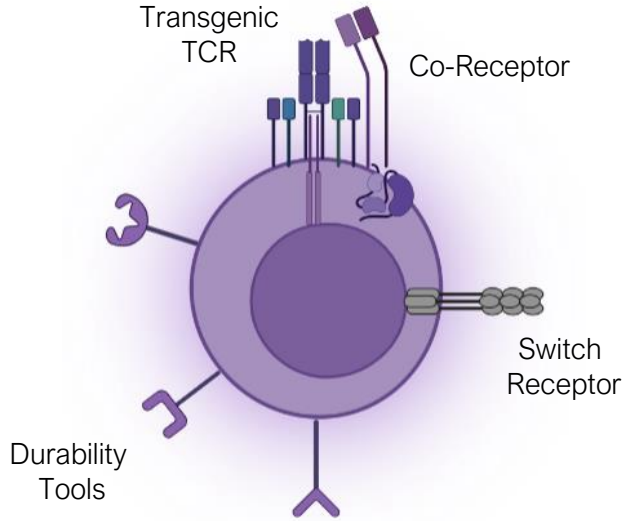
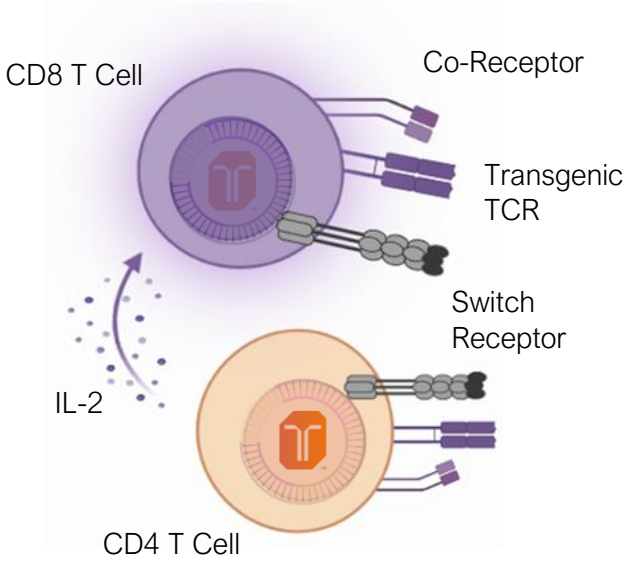
Extensive Portfolio of Proprietary Technologies

	TAILOR™ TCR Discovery	TUNE™ Synthetic Biology	THRIVE™ Engineering and Manufacturing
Tools Build a state-of-the-art platform	• Predictive algorithms and machine learning • High throughput screening	• Switch receptors • Co-receptors • Others (e.g., armoring, persistence)	• Single LVV transduction of CD4/CD8 T Cells • Gene editing with Type II and Type V systems • Cryopreserved cell product
Rationale Equip cells to sustain anti-tumor response	• Leverage tumor dependency • Expand patient access globally	• Improve T cell persistence in TME to enhance therapeutic durability • Reduce/prevent T cell exhaustion	• Gene knock-out and non-viral knock-in • High yield TCR+ T cells per run of naïve and memory T cells
Approach Streamline processes and materials			

First-In-Class Potential for Multiple Products Targeting Oncogenic Drivers in Solid Tumors

Program	Target	Syn Bio	Discovery	Preclinical	Clinical
Oncogenic Driver Programs					
AFNT-111	KRAS G12V	CD8 Co-Receptor	HLA-A11		*IND Submission 2H '23
AFNT-211	KRAS G12V	CD8 CoR + FAS-41BB	HLA-A11		*IND Submission 2H '23
	KRAS G12V	TUNE™	HLA-A2		
	KRAS G12V	TUNE™	HLA-A3		
AFNT-212	KRAS G12D	CD8 CoR + TUNE™	HLA-A11		*IND Submission 2024
	KRAS G12D	TUNE™	HLA-A3		
	KRAS G12C	TUNE™	Multiple		
	P53 R175H	TUNE™	HLA-A2		
	PIK3CA	TUNE™	Multiple		
	Undisclosed	TUNE™	Multiple		
Viral Antigen Driver Programs					
	Undisclosed	TUNE™	Multiple		

**Planned submission dates*

CD8 CoR = CD8 Co-Receptor

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AFNT-211: Early-Phase Clinical Development Plan

FSD → OBD / POCC → ORR / DoR

Phase 1a Basket Trial Dose Finding

KRAS G12V-mutated tumors & HLA-A*11:01 allele

Sample size N=15-20

Non-small-cell lung (NSCLC) | Colorectal (CRC) | Pancreatic (PDAC) | Tissue Agnostic*

Seamless Transition to Phase 1b/2

Phase 1b/2 Expansion Cohorts

Sample size up to N=20 per indication

- NSCLC → 2nd/3rd line (IA)
- CRC → 2nd/3rd line (IA)
- PDAC → 2nd/3rd line (IA)
- Tissue-agnostic* → 2nd/3rd line (IA)

Transition to registration study in target indication

- Approximately 10 US clinical trial sites planned for Phase 1a dose finding

- Expand clinical trial sites to 35-40 in US, EU5, and CAN
- Accelerated approval based on ORR & DoR data
- Total sample size N=~80 per indication

Excluding primary brain tumors

FSD – First Subject Dosed
OBD – Optimal Biological Dose
POCC – Proof of Clinical Concept

ORR – Overall Response Rate
DoR – Duration of Response
IA – Interim Analysis

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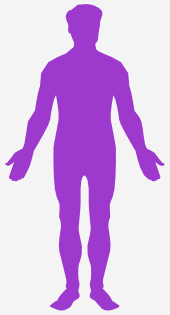
THRIVE™ Biomanufacturing for Optimal Cell Fitness and Yield

10-Day Autologous Manufacturing Process

Patient



Apheresis

Shipment

Receive

Selection & Activation

Cell Engineering

Cell Expansion

Cryo storage

Shipment

QA/QC Release

Lymphodepletion

Patient

Bed Side Thawing and Infusion

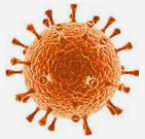
Days	-1	0	1	3-8	10	16	21

Cryopreserve / Thaw

Sequential Immunomagnetic Selection

Cytokines and Activation

LVV Transduction

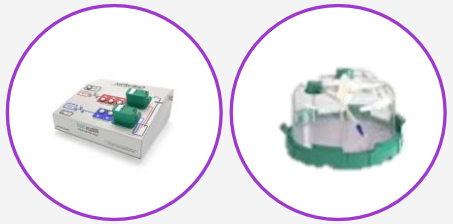


TCR αβ

CD8 αβ Receptor

FAS-41BB Switch

Media Feeds



Harvest & Formulation

Fill & Finish

Cryopreservation

QC Testing

Flu/Cy

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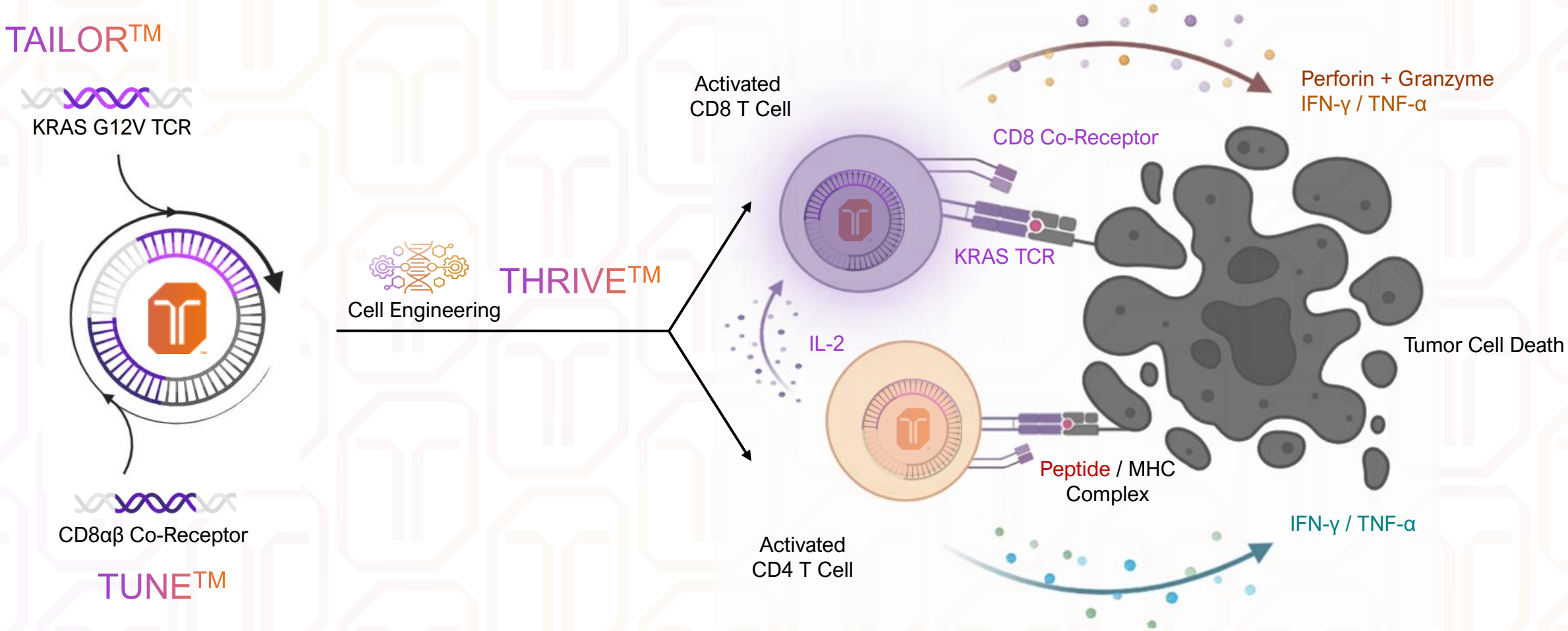
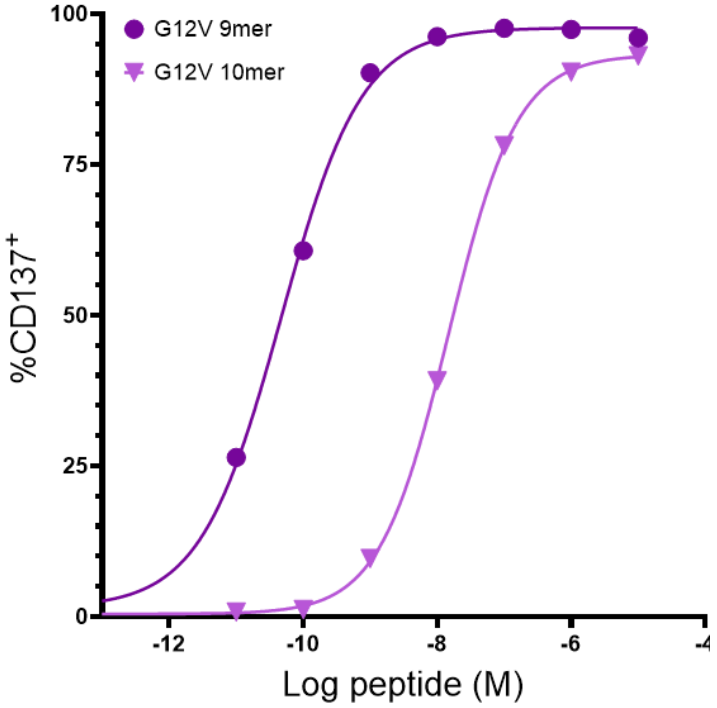
AFNT-111: KRAS A11 G12V TCR Engineered T Cells + CD8 Co-Receptor

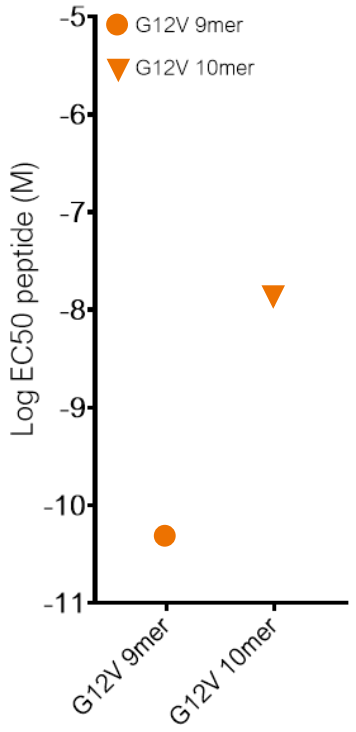


Robust Preclinical Avidity of KRAS A11 G12V TCR Candidate

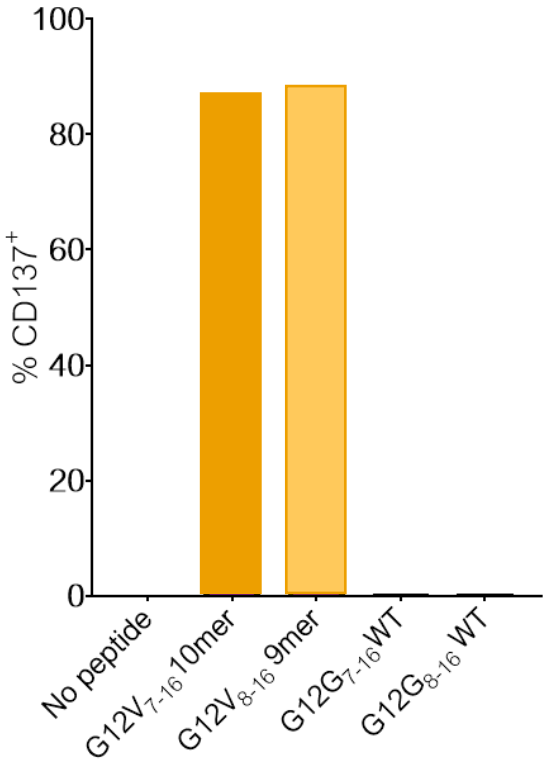
Peptide Stimulated T Cell Proliferation



High Affinity and Functional Avidity



Dual Epitope Recognition: 9mer & 10mer

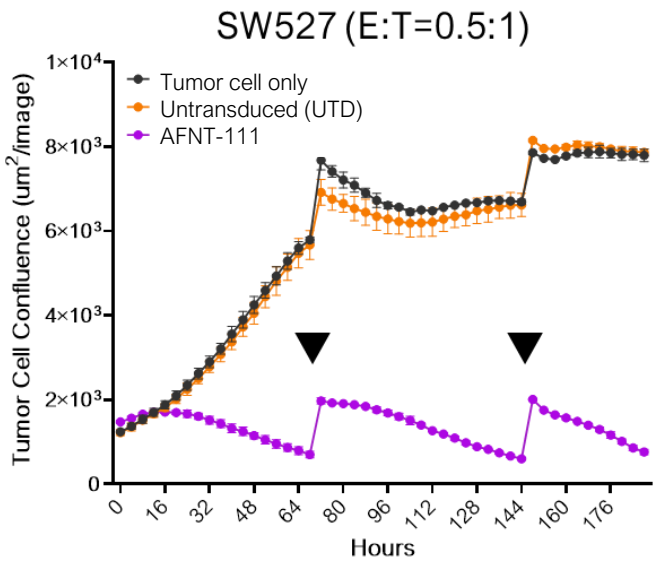


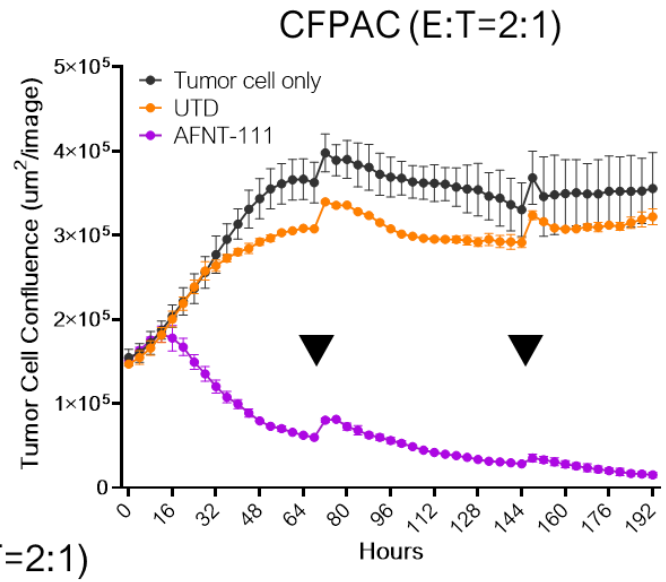
- Lead AFNT-111 TCR exhibits high functional avidity: EC50 in low pM
- Recognition of both 9mer and 10mer KRAS G12V epitopes with no reactivity to WT KRAS

**Peptide dose response CD137 T cell activation assay*

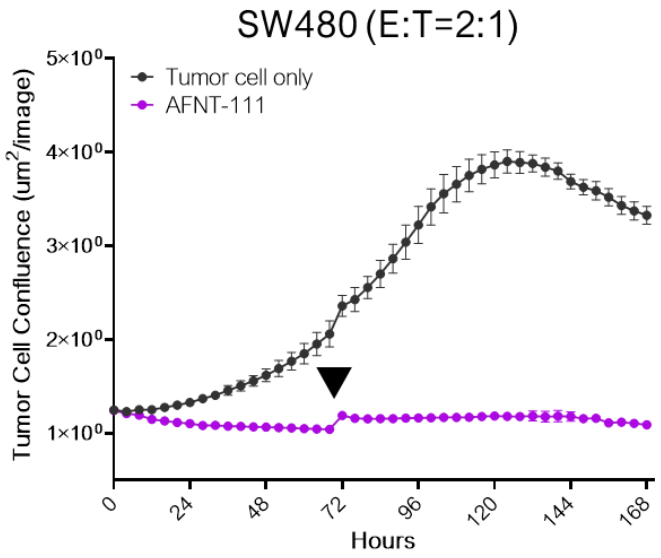
Adapted from Lam, et. al…Vincent. *SITC* (2022)

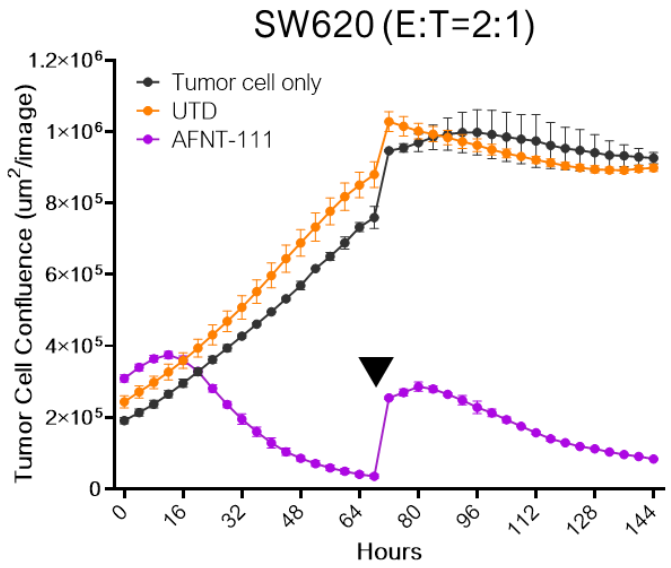
Sustained Cancer Cell Killing with AFNT-111 TCR for *In Vitro* Repeat Tumor Challenge Assay





Indicates fresh tumor rechallenge



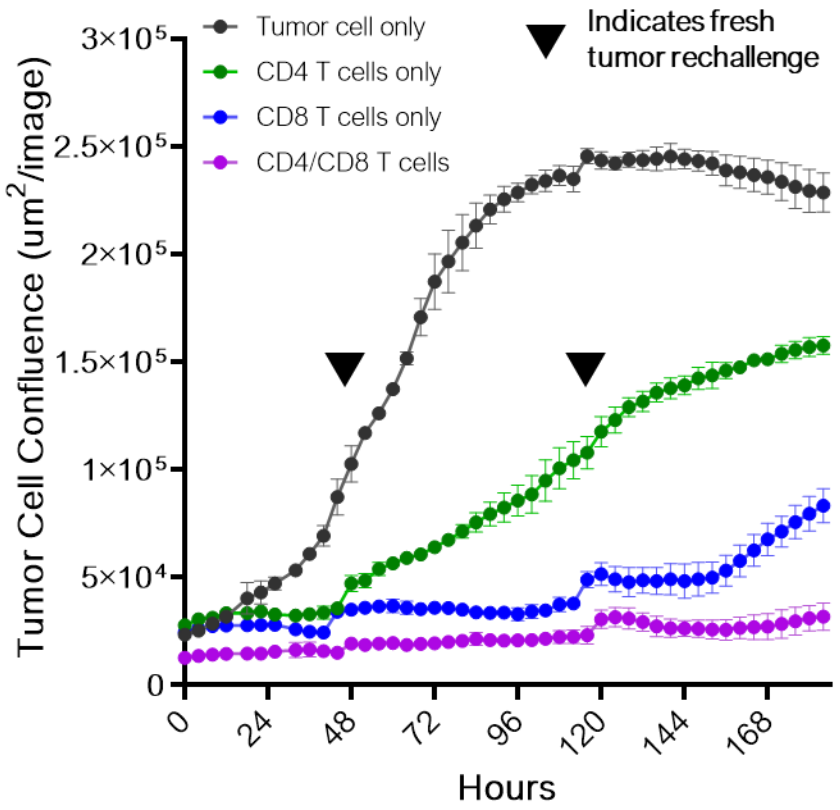


**Incucyte live tumor cell visualization assay*

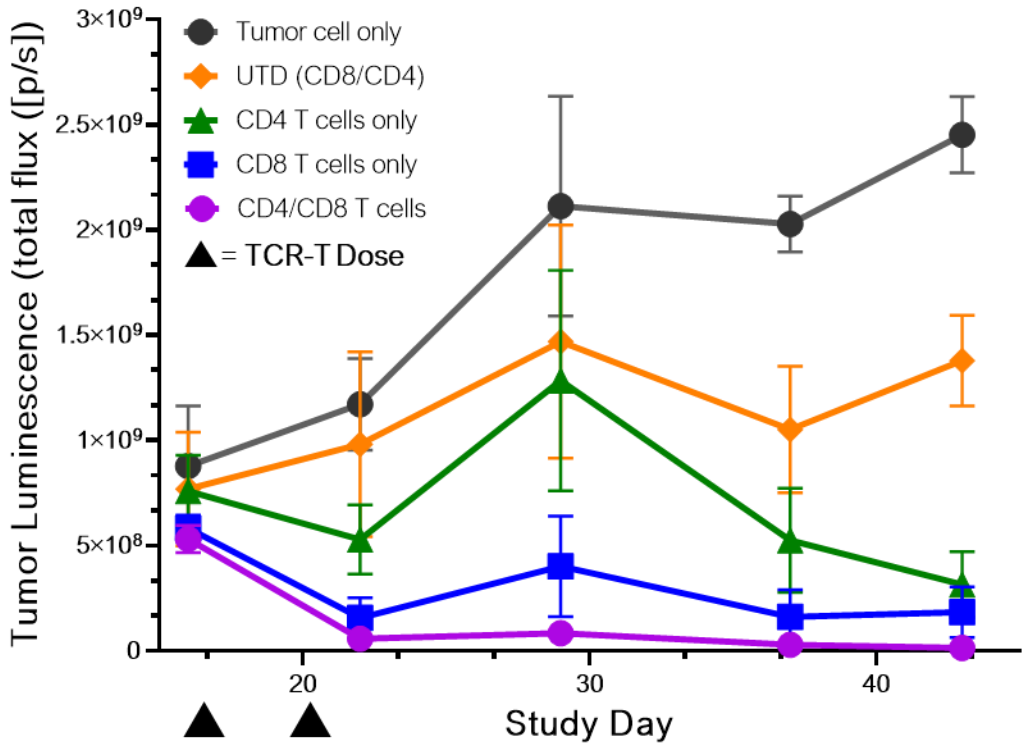
Adapted from Lam, et. al...Vincent. *SITC* (2022)

AFNT-111: CD8α/β Co-Receptor Enhances Tumor Control by Driving Coordinated CD4⁺/CD8⁺ Response

CFPAC (*In vitro* tumor challenge)



CFPAC-Luc (*In vivo* tumor challenge)



CD8⁺ T cell killing is enhanced by the presence of CD4⁺ T cells both *in vitro* and *in vivo*

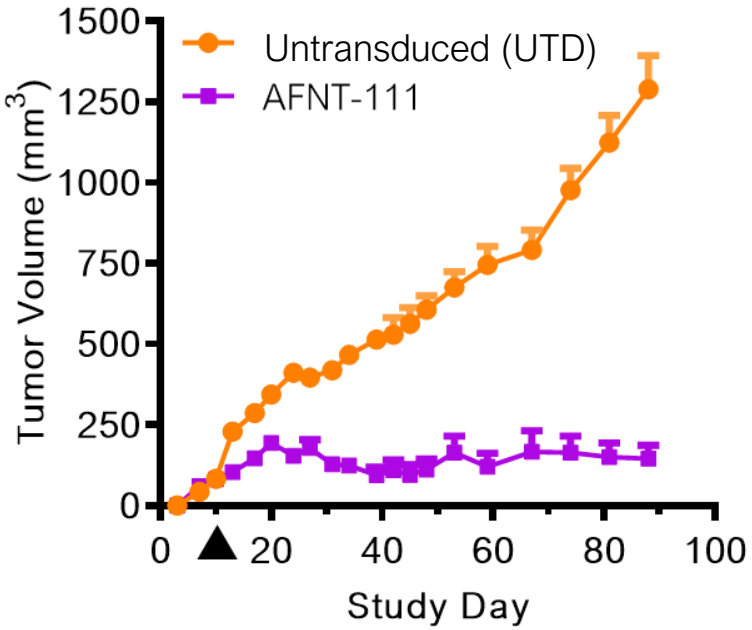
**Incucyte live tumor cell visualization assay; Total T cells kept constant in CD4 only, CD8 only and CD4/CD8 groups*

NSG mice randomized after IP tumor implantation (5 mouse/group)
Dose: two administrations of 7x10⁶ (D8) and 8x10⁶ (D21) AFNT-111 TCR-T cells

Adapted from Lam, et. al…Vincent. *SITC* (2022)

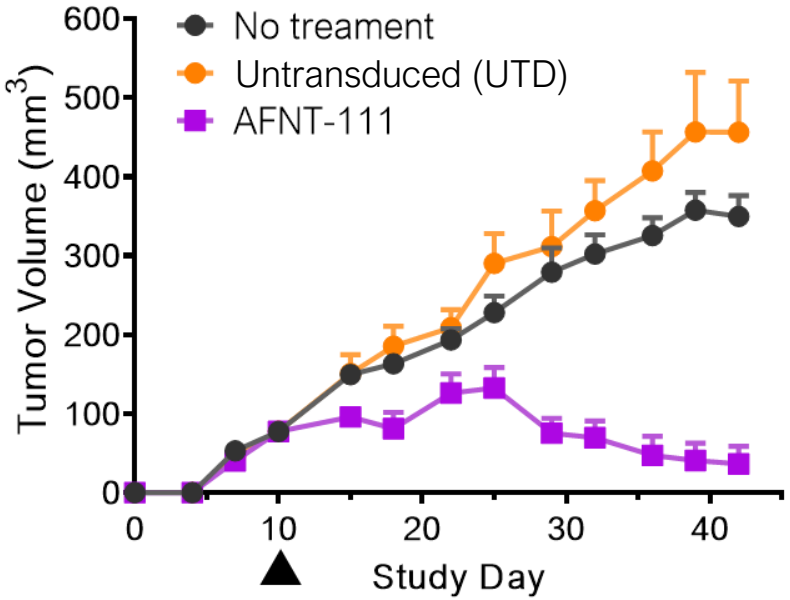
AFNT-111: T Cells Targeting KRAS G12V Reduce Tumor Volume Across Several *In Vivo* Tumor Models

SW527 (Breast)



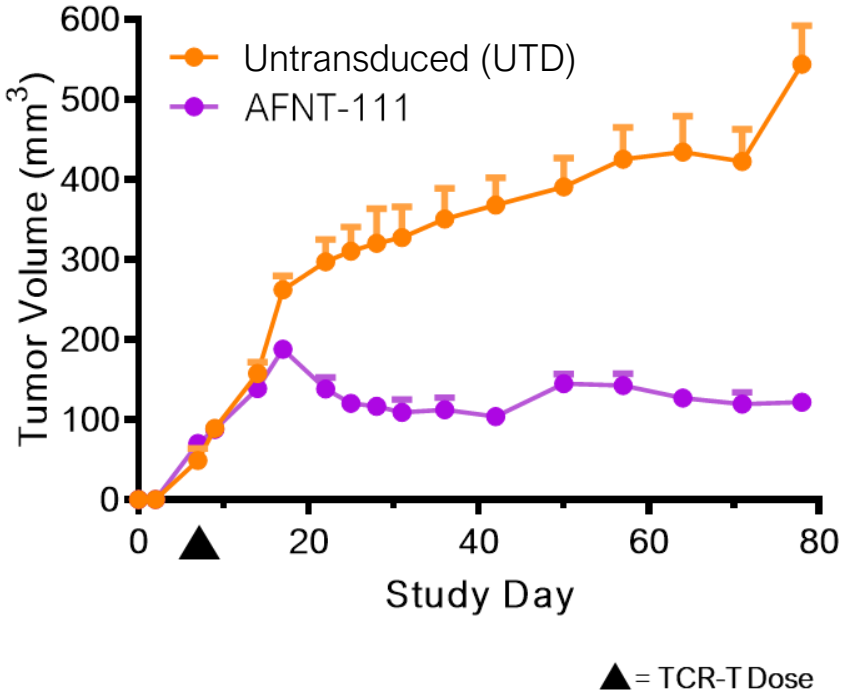
- NSG mice randomized after SC tumor implantation (5 mouse/group)
- Dose: single IV administration of $3x10^6$ AFNT-111 TCR-T cells on D7

CFPAC (Pancreatic)



- NSG mice randomized after SC tumor implantation (5 mouse/group)
- Dose: single IV administration of $1x10^7$ AFNT-111 TCR-T cells on D10

SW620 (Colon)



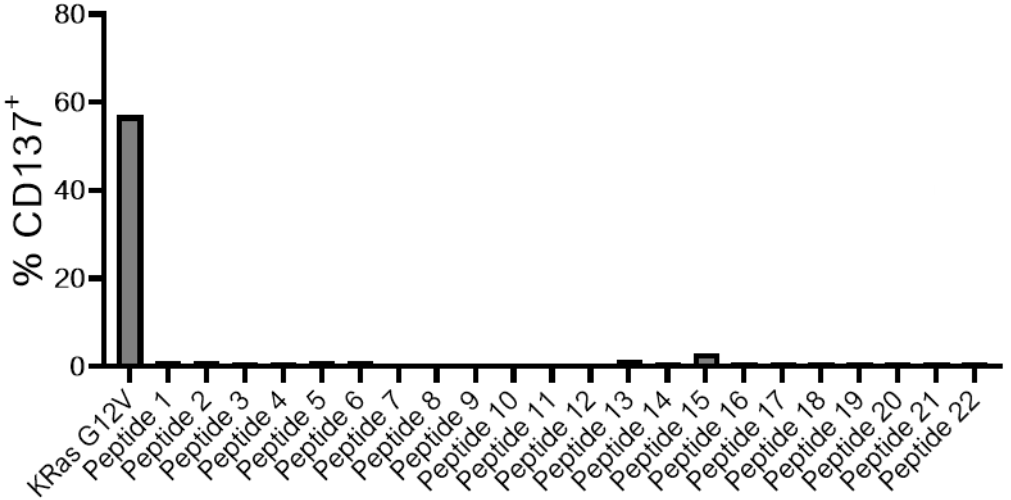
- NSG mice randomized after SC tumor implantation (5 mouse/group)
- Dose: single IV administration of $3x10^6$ AFNT-111 TCR-T cells on D9

Adapted from Lam, et. al…Vincent. *SITC* (2022)

AFNT-111 TCR-T Cells Exhibit Low Off-Target Potential and Strong Preclinical Tolerability

Cross-Reactivity

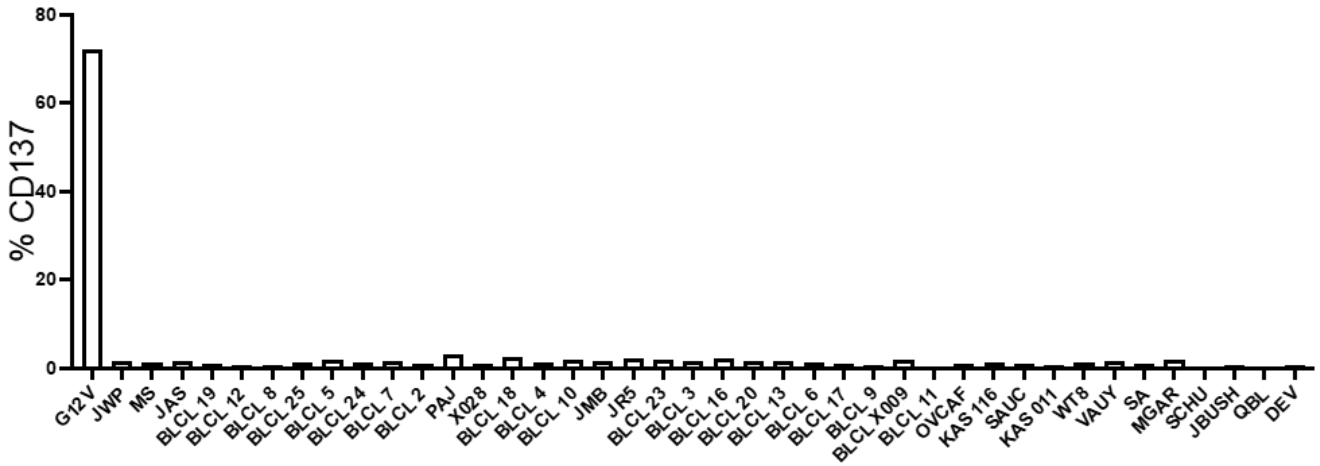
XScan cross-reactivity assay used to define the peptide recognition motif of AFNT-111 yielded a tolerable preclinical safety profile



- No cross-reactive self-peptides of concern identified out of 22 identified via XScan and *in silico* analysis

Allo-Reactivity

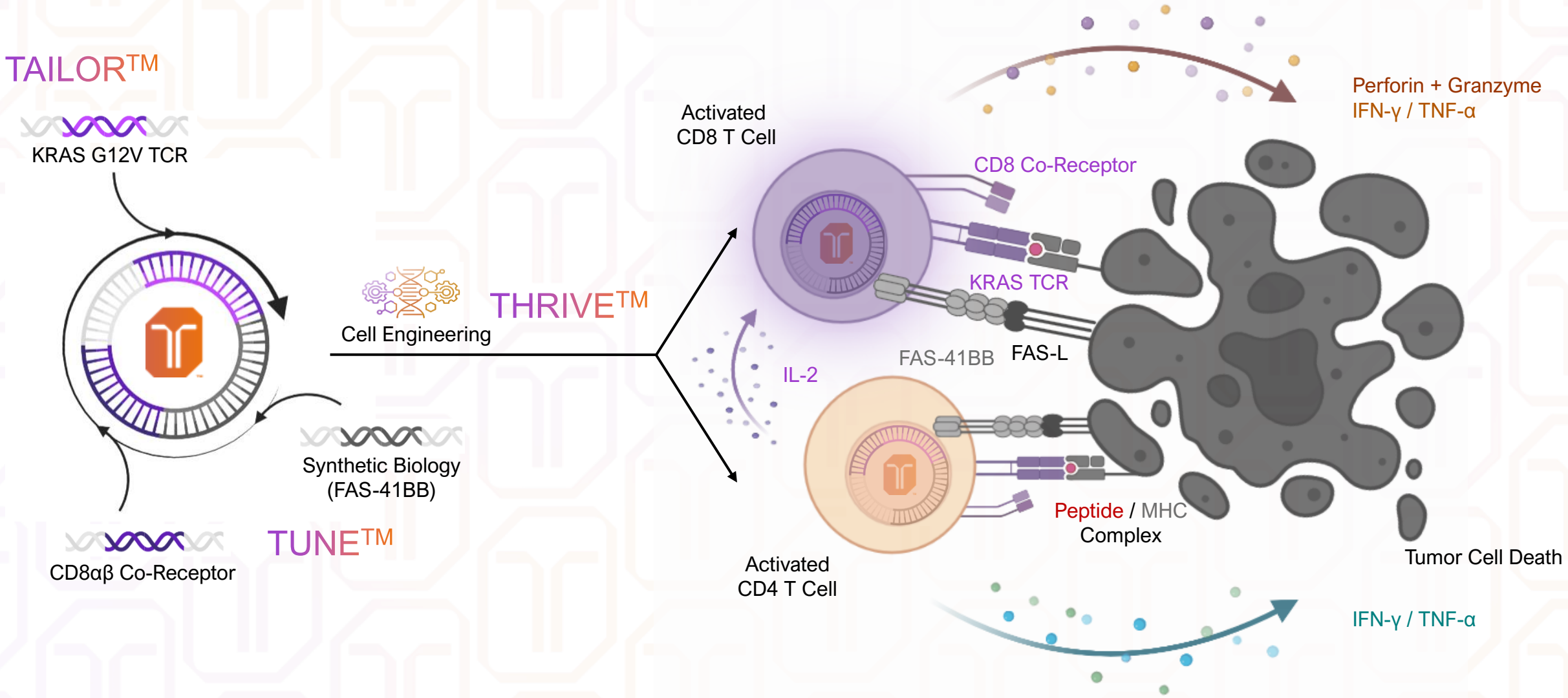
Allo-reactivity screen conducted with 40 B-Lymphoblastoid Cell Lines (B-LCL) had no responses detected



- No allo-reactive responses detected
- B-LCL library covers >95% of the most common HLA alleles

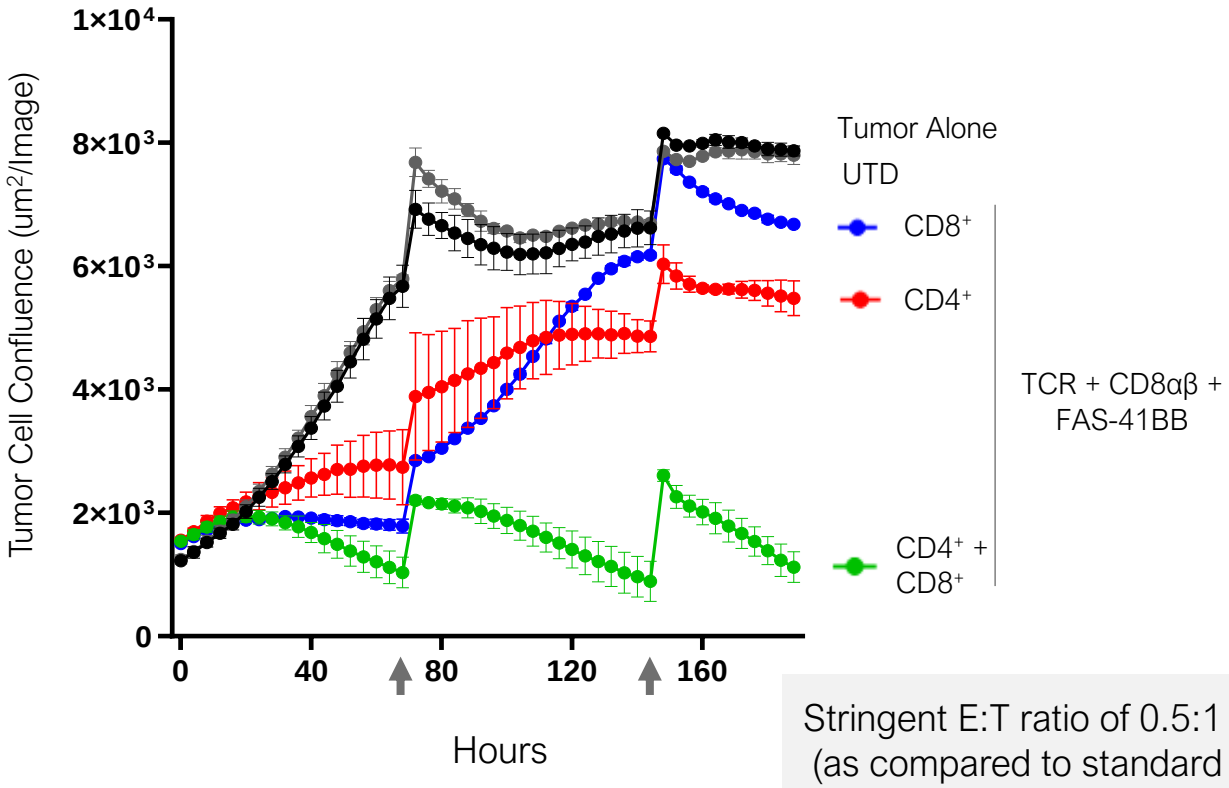
Adapted from Lam, et. al...Vincent. *SITC* (2022)

AFNT-211: KRAS A11 G12V TCR Engineered T Cells + FAS-41BB Durability Switch Receptor



FAS-41BB Switch Triggers *In Vitro* Expansion and Tumor Killing via Coordinated CD4 / CD8 Response

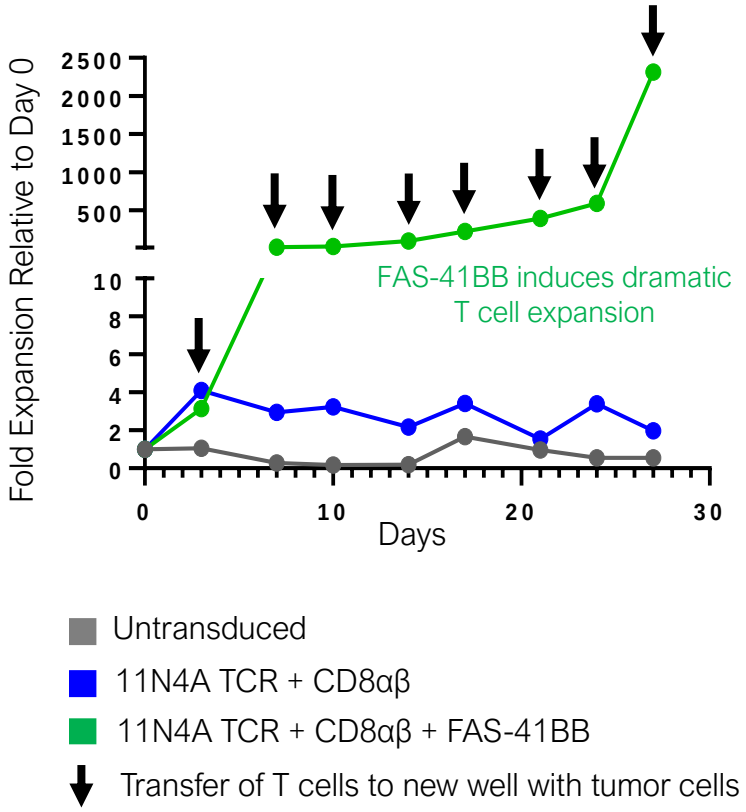
Co-Culture of SW527 and Exhausted T Cells



Stringent E:T ratio of 0.5:1 (as compared to standard 10:1 and 5:1 E:T ratios)

↑ Indicates fresh SW527 tumor cells added to same plate

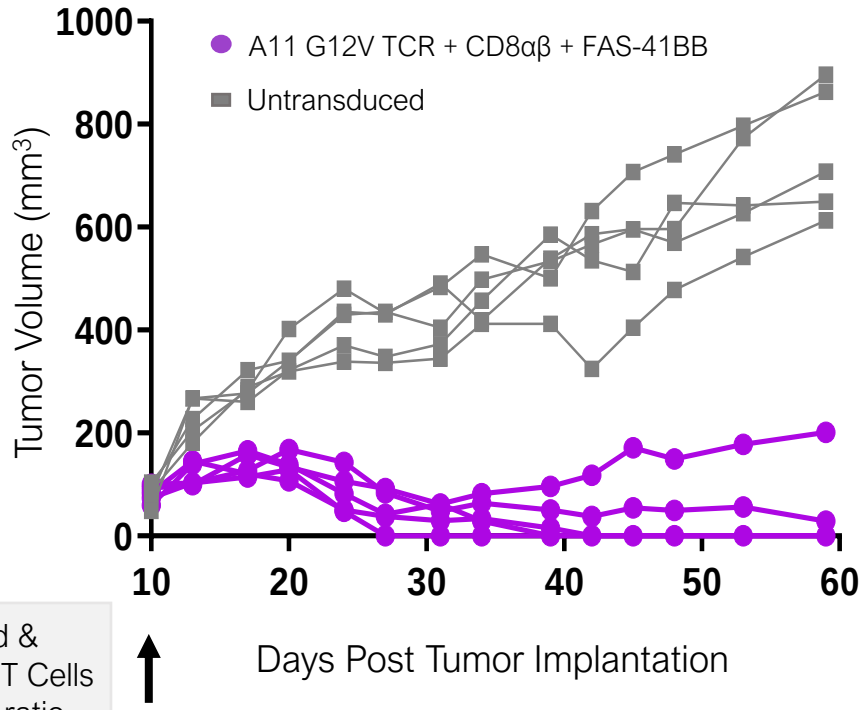
FAS-41BB Increases Cell Proliferation in SW527 Model



Adapted from He, et. al…Vincent. *SITC* (2022)

FAS-41BB-Engineered T Cells Reduce Tumor Volume in Mouse Model

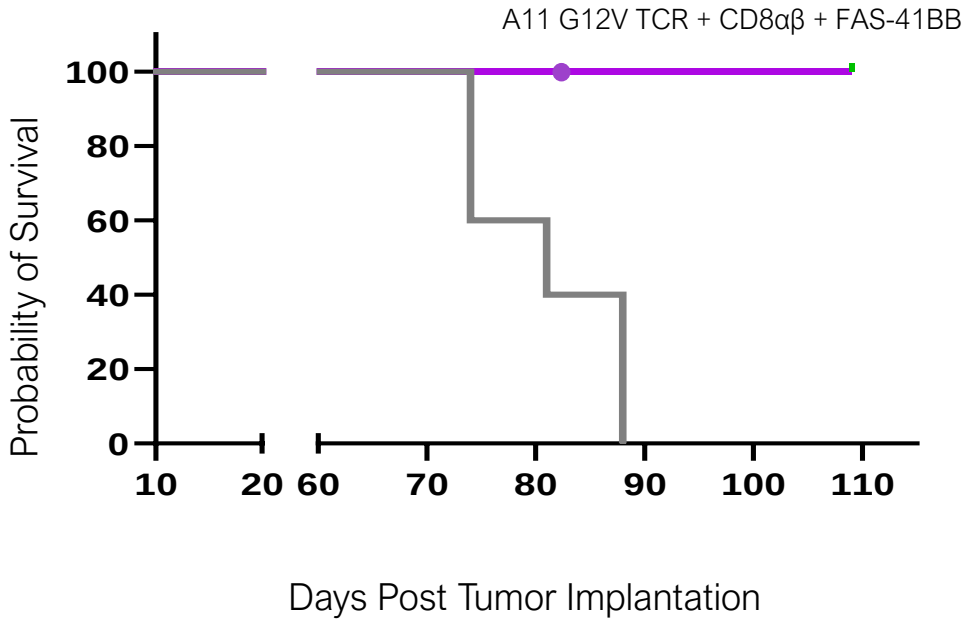
Average Data Across Study Groups (N=5)



Mice Randomized &
10M CD4+/CD8+ T Cells
Injected IV at 1:1 ratio

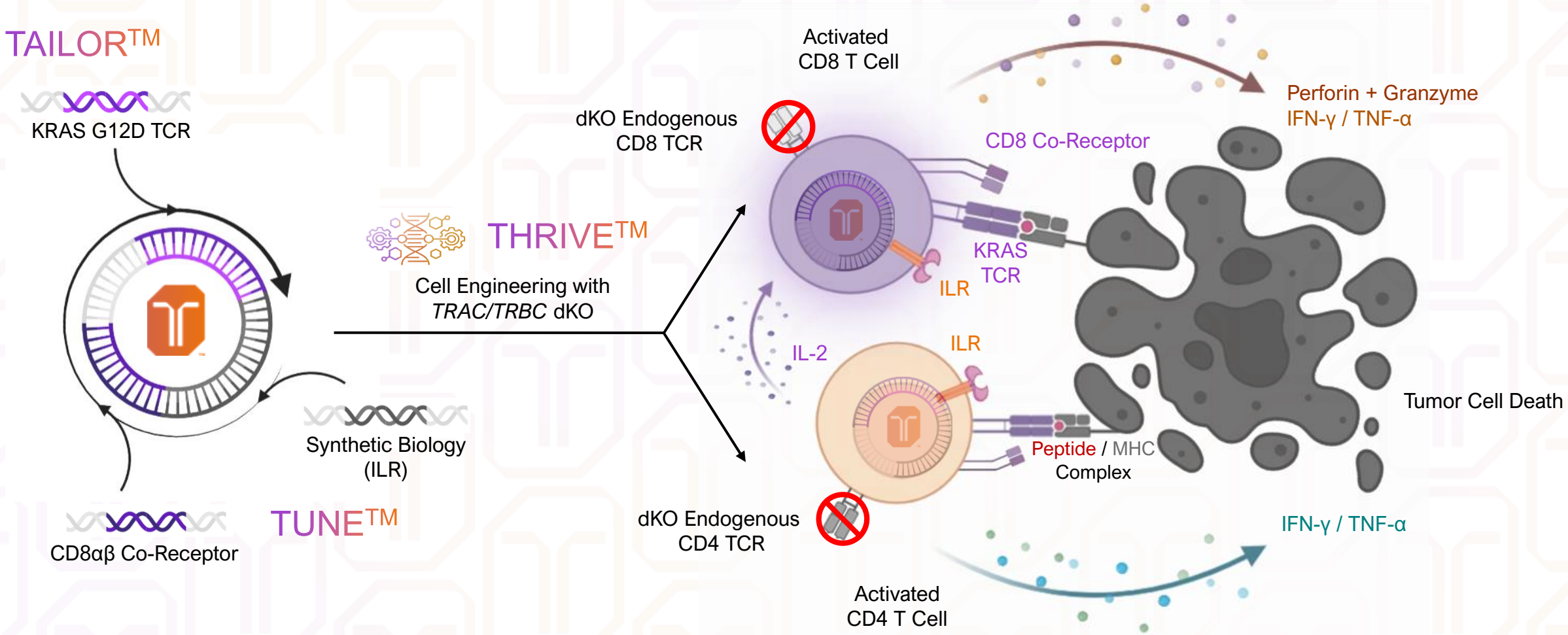
- SW527 inoculated SC to NSG mice
- Single IV administration of 10x10^6 engineered T cells

Kaplan-Meier Survival Curve



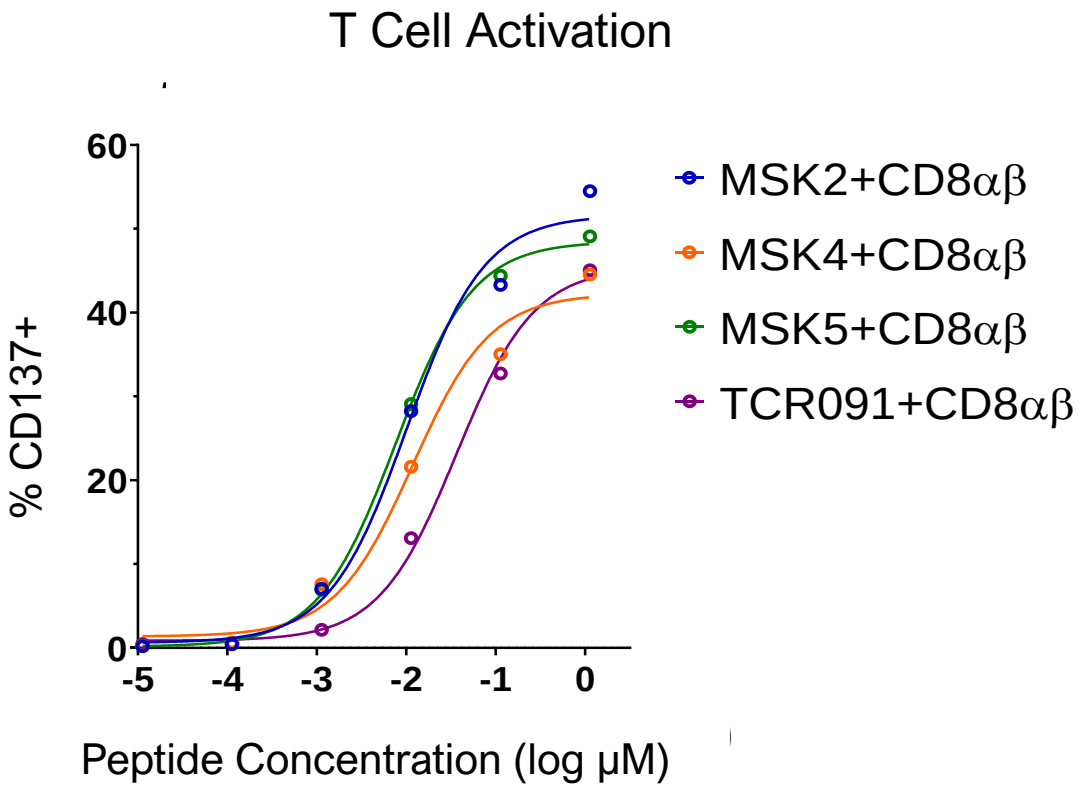
Adapted from He, et. al…Vincent. *SITC* (2022)

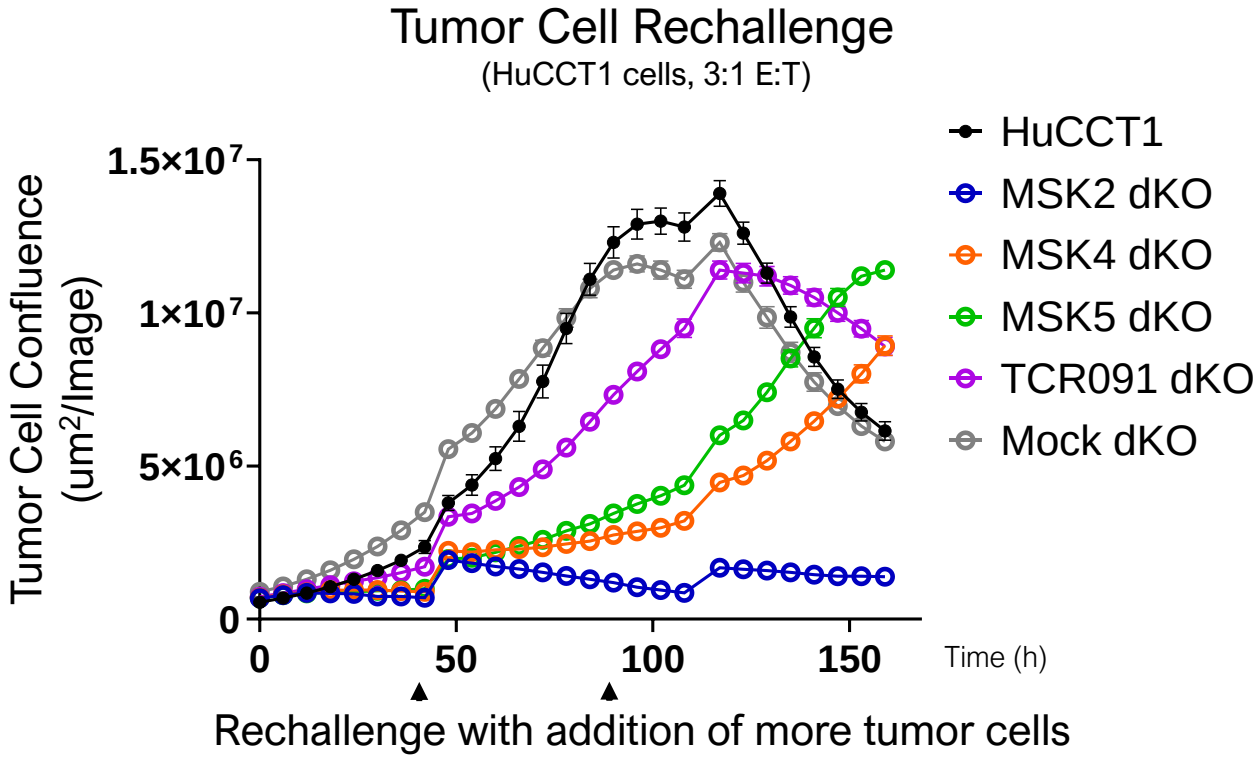
AFNT-212: KRAS A11 G12D TCR Engineered T Cells + Durability Switch Receptor + Gene Editing



dKO = Double knockout of *TRAC/TRBC* genes

Endogenous *TRAC/TRBC* dKO Improves Activity and Cytotoxicity of KRAS G12D TCR-T Cells *In Vitro*

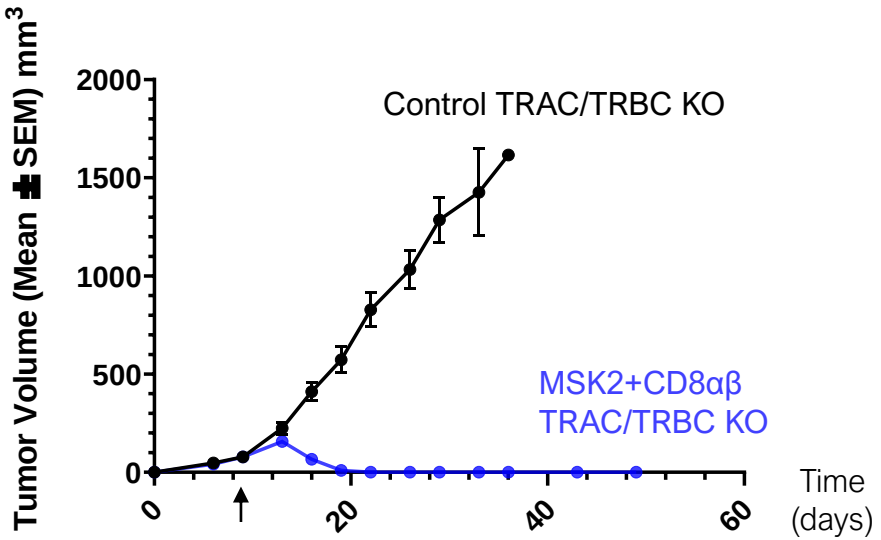




Adapted from Gupta, et. al...Vincent. *AACR* (2023)

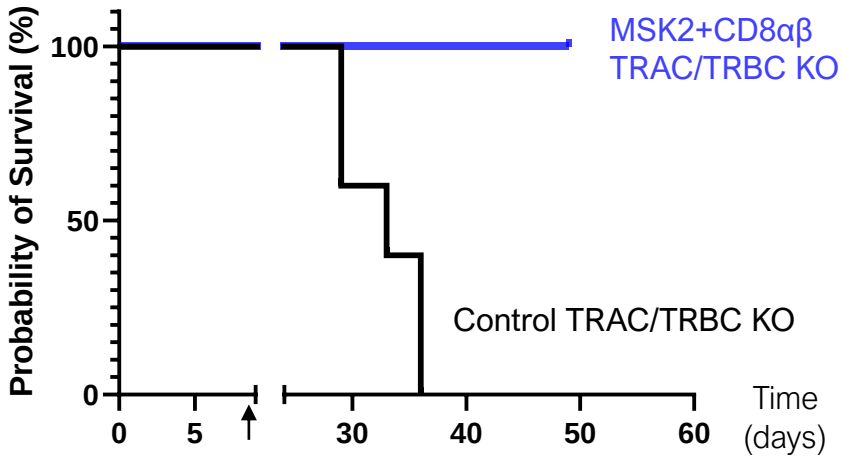
KRAS G12D TCR-T Cells with Endogenous *TRAC/TRBC* dKO Show Robust Preclinical Activity *In Vivo*

Average Data Across Study Groups



↑ IV administration of 10x10^6 KRAS G12D TCR-engineered CD4+ and CD8+ T cells (1:1 ratio)

Kaplan-Meier Survival Curve



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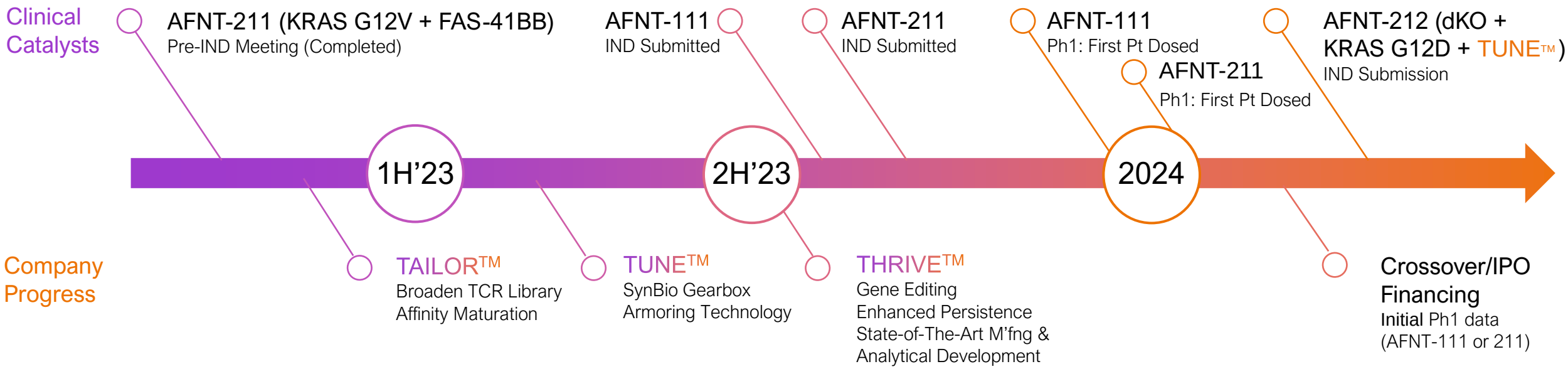
Adapted from Gupta, et. al...Vincent. *AACR* (2023)

The Affini-T Opportunity

Affini-T: Current Status and Key Clinical Catalysts



Affini-T is the premier Precision Immunotherapy company targeting oncogenic driver mutations to develop curative therapies for patients with solid tumors

Funding, Team and Culture

- $194M raised to date
- Skilled team of >90
- Headquartered in Watertown, MA

Strategic Partnerships

- *The Fred Hutch and Memorial Sloan Kettering* – TCR discovery and synthetic biology
- *ElevateBio* – phase-appropriate M'fng capabilities with path to commercialization
- *Metagenomi* – world class gene editing capabilities to power next-gen products
- *Adimab* – affinity maturation and T cell engager constructs

Programs Tracked against Key Clinical Catalysts

- AFNT-211 and AFNT-111: lead assets targeting KRAS G12V completed positive pre-INDs and tracking for 2H23 INDs
- AFNT-212: first gene edited asset targeting KRAS G12D transitioning to IND enabling studies
- Robust discovery pipeline resourced to target additional oncogenic drivers including P53 and PIK3CA
- Establishing non-viral knock-in gene transfer product platform

* All catalysts and milestones planned but not guaranteed

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