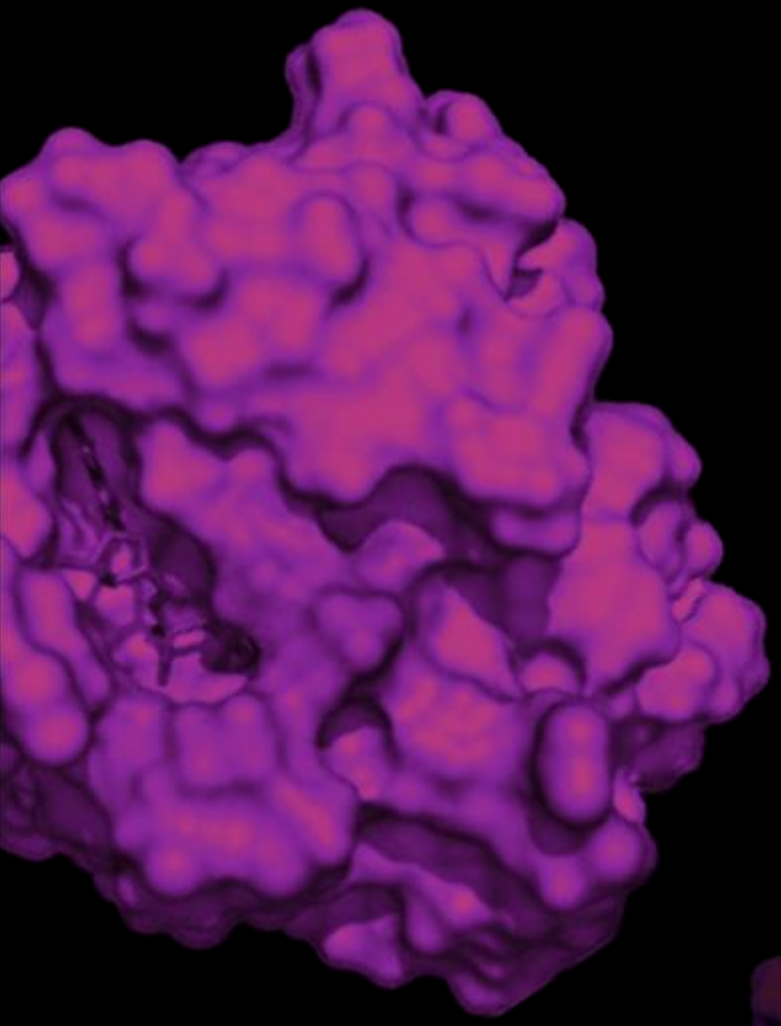

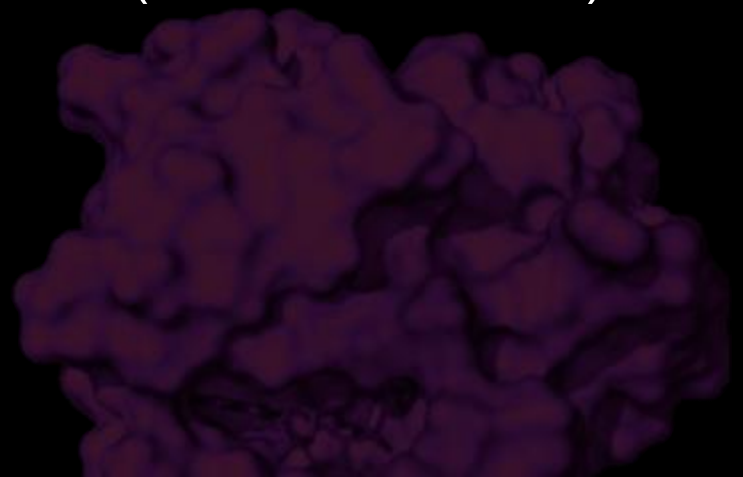

AFNT-111, a preclinically safe and effective TCR-engineered T cell therapy targeting the oncogenic driver KRAS G12V mutation (Poster #244)

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11 November 2022

Investigational agents and forward-looking statements

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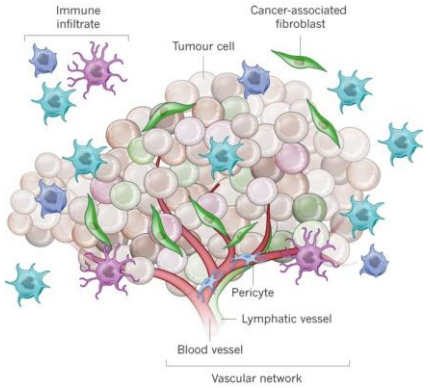
This presentation also includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties as well as our own estimates of potential market opportunities. All of the market data used in this presentation involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

Strike at the core of tumor biology by targeting oncogenic driver mutations

- Oncogenic driver mutations responsible for the initiation and maintenance of cancer are ideal targets
  - Addresses tumor heterogeneity (cancer dependency on oncodrivers)
  - Neoantigens are unique to cancer and limit on-target/off-tumor tox

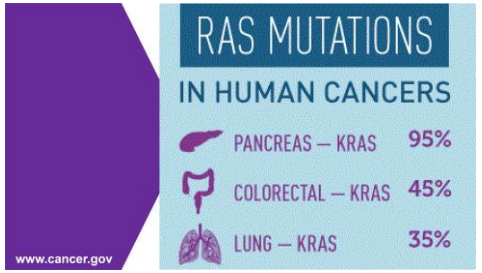


From Joglekar AV and Li G, Nat Methods (2021)

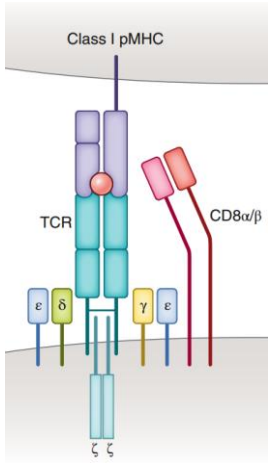
Address tumor heterogeneity and escape mechanisms

- KRAS is the most frequently mutated oncogene in solid tumors
  - KRAS mutations (mKRAS) promote cell growth and suppress apoptosis
  - RAS family of genes are responsible for up to 30% of all human cancers

Tackle a high unmet medical need



- TCR-T cell therapies are an optimal modality to attack mKRAS
  - Able to target intracellular KRAS presented on the cancer cell surface
  - Clinical proof of concept for targeting KRAS demonstrated in multiple T cell therapy clinical studies[1,2]

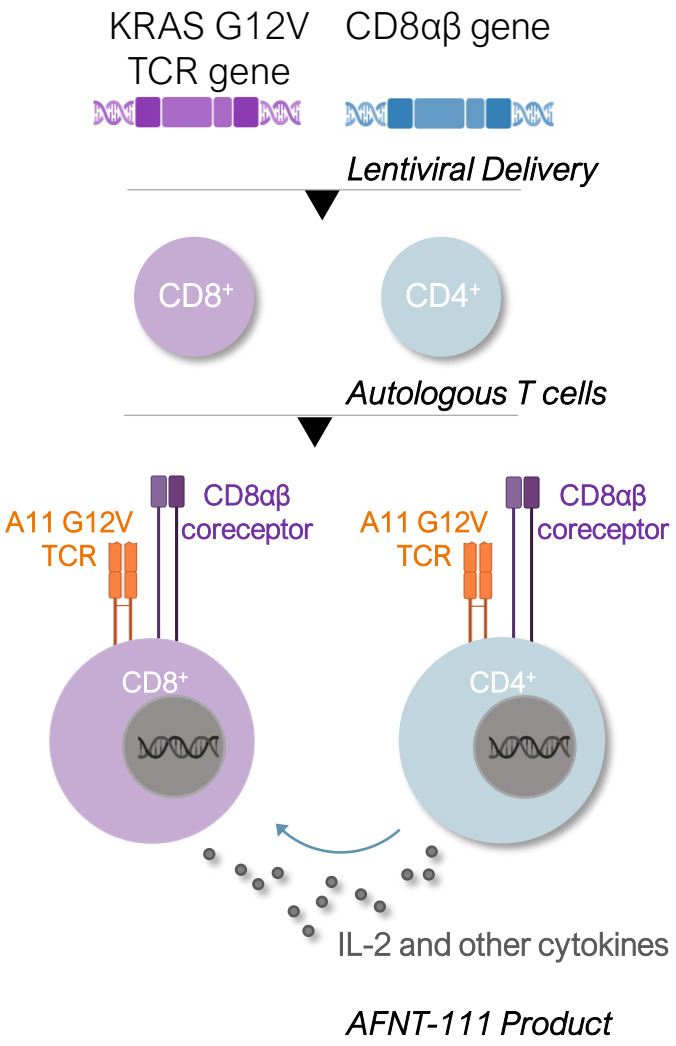


From Junttila MR and Sauvage FJ, Nature (2013)

Utilize a therapeutic modality with clinical PoC

[1]Tran et al. NEJM (2016), [2]Leidner et al. NEJM (2022)

AFNT-111: TCR engineered T cells targeting solid tumors with a KRAS G12V mutation



AFNT-111 Product

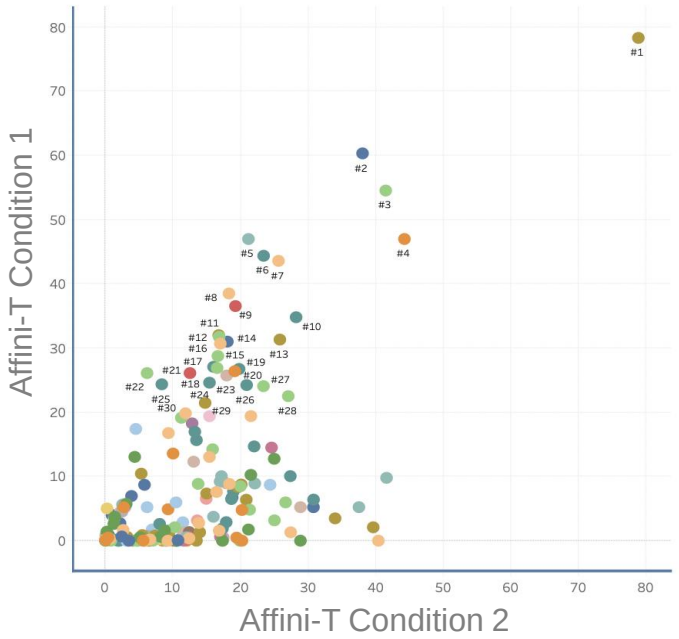
I. TCR Therapy

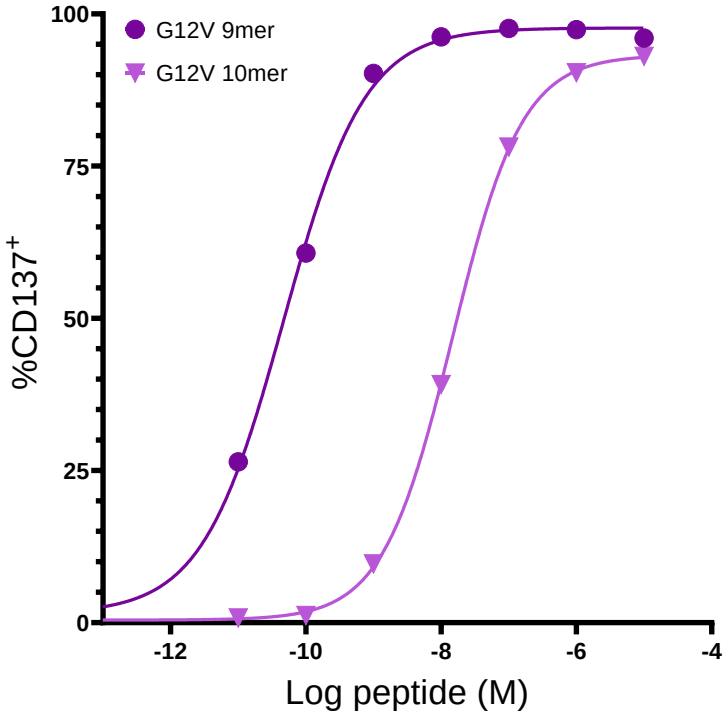
- Robust TCR Discovery platform identifies high affinity, high functional avidity TCRs from the natural TCR repertoire of healthy donors (no affinity maturation)
- AFNT-111: Autologous $CD4^+$ and $CD8^+$ T cells lentivirally-transduced with CD8αβ co-receptor and high affinity TCR to KRAS G12V presented by HLA-A*11:01

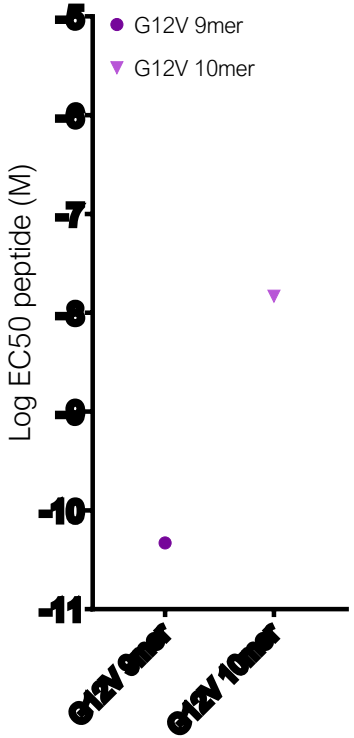
II. Coordinated $CD8^+$ and $CD4^+$ T Cell Response

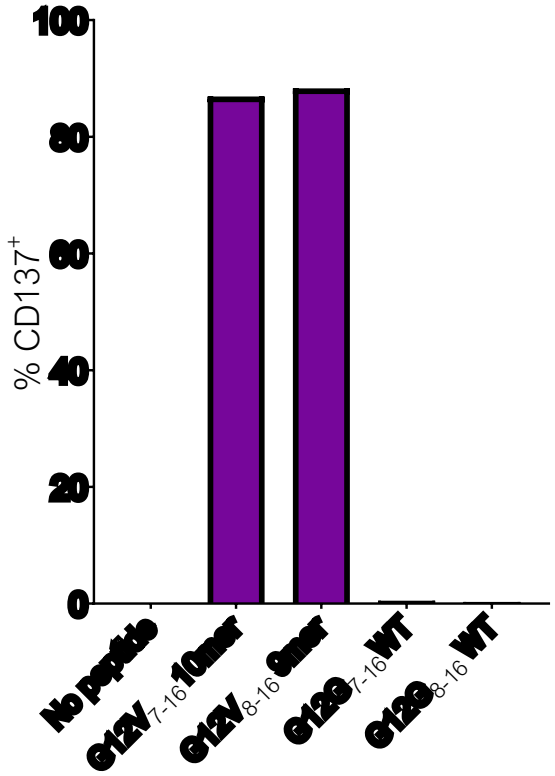
- CD8α/β co-receptor expression in $CD4^+$ T cells enables MHC I target recognition and a coordinated $CD8^+$/$CD4^+$ T cell response
- $CD4^+$ T cells retain a helper phenotype, engage $CD8^+$ T cells in the TME, promote effector activation, and prevent T cell exhaustion leading to enhanced $CD8^+$ T cell persistence

Identification of an HLA-A11 KRAS G12V TCR with potent functional avidity









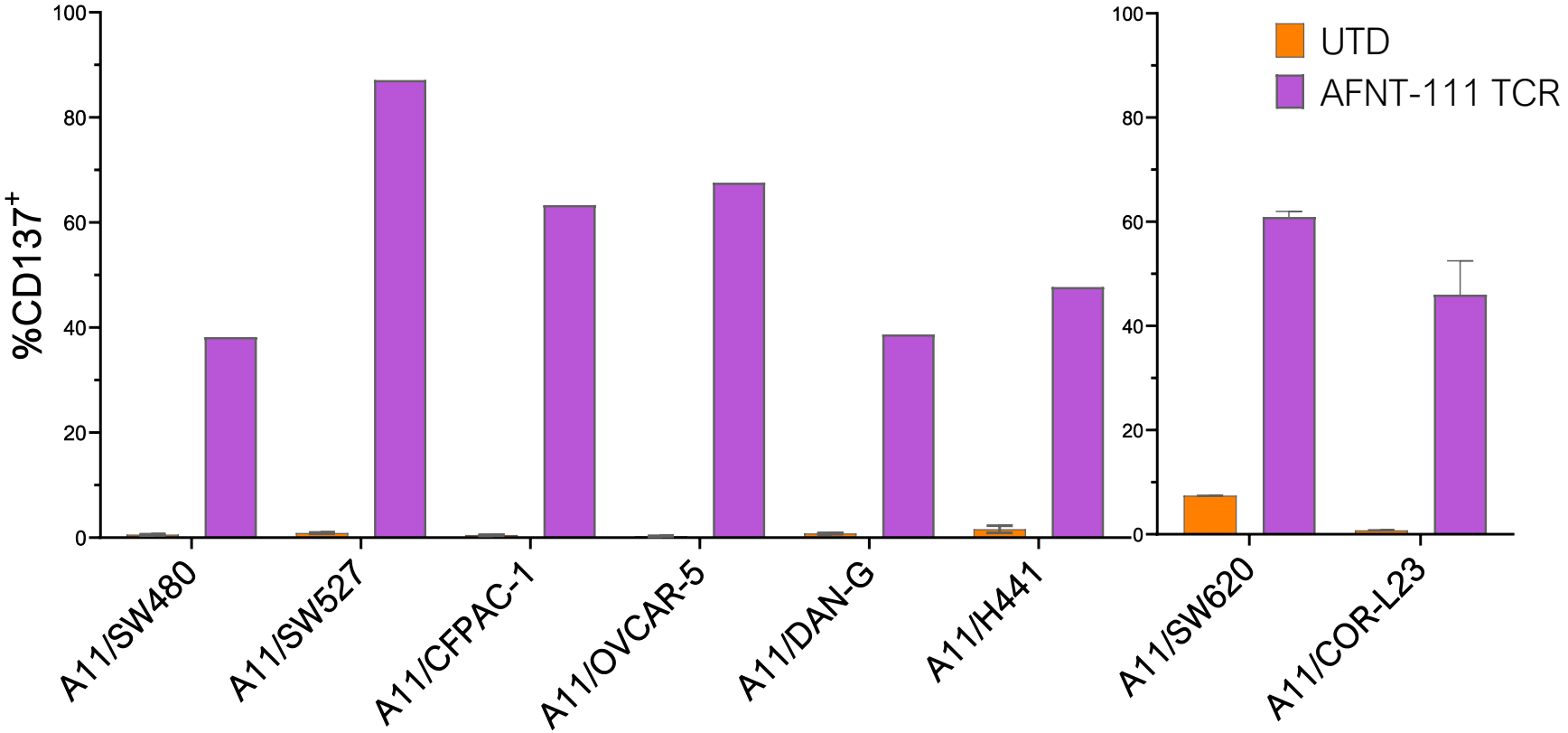
- High affinity KRAS G12V TCR candidates identified from healthy donors that have cleared thymic selection

- 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*

AFNT-111 TCR is activated by endogenously presented KRAS G12V across diverse tumor cell lines

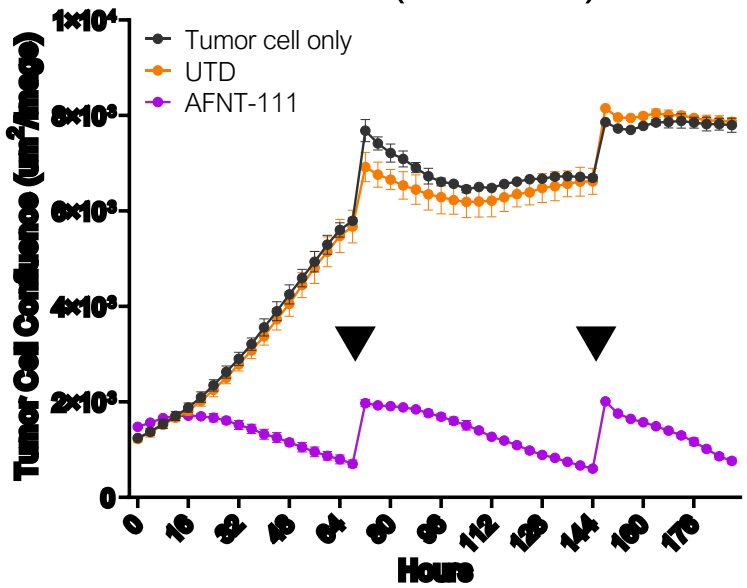
Cell lines used	Cancer derivation
CFPAC-1	Pancreatic
DAN-G	Pancreatic
SW620	Colon
SW480	Colon
COR-L23	Lung
NCI H441	Lung
SW527	Breast
OVCAR-5	Ovarian



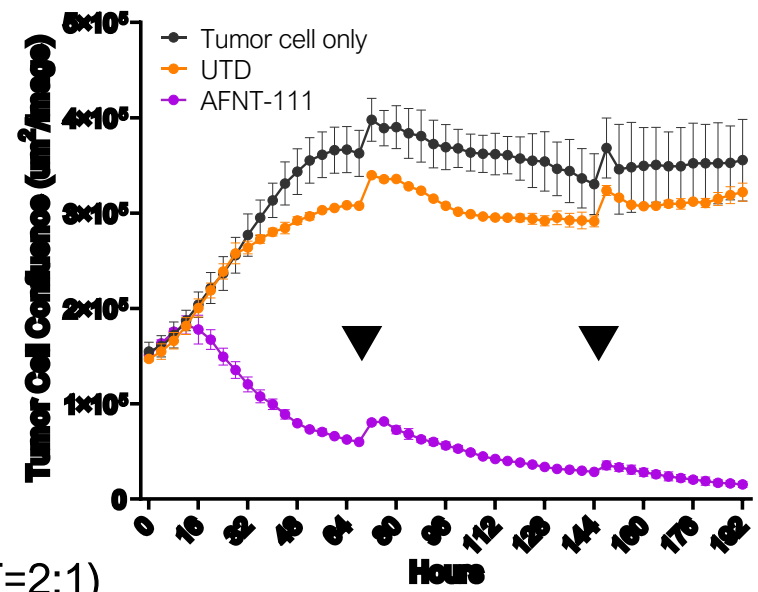
**CD137 T cell activation assay after co-culture with tumor cell lines*

AFNT-111 T cells exhibit robust *in vitro* cancer killing in repeat tumor challenge assay

SW527 (E:T=0.5:1)

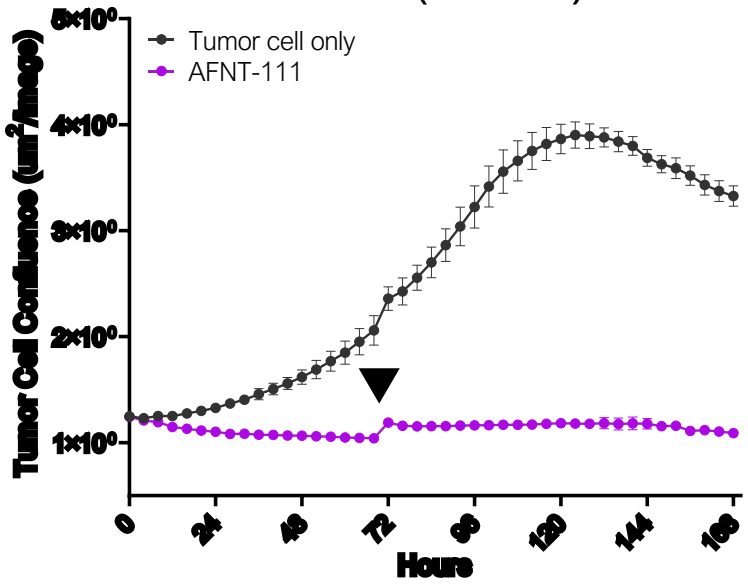


CFPAC (E:T=2:1)

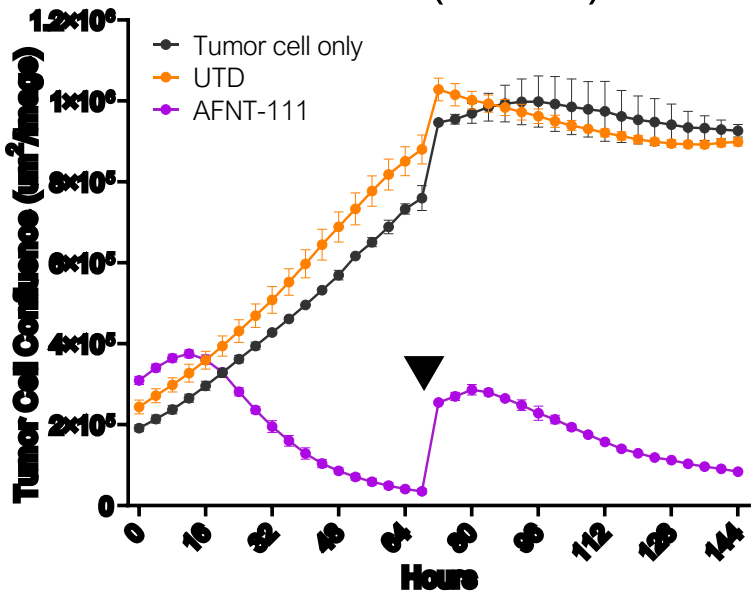


▼ Indicates fresh tumor rechallenge

SW480 (E:T=2:1)



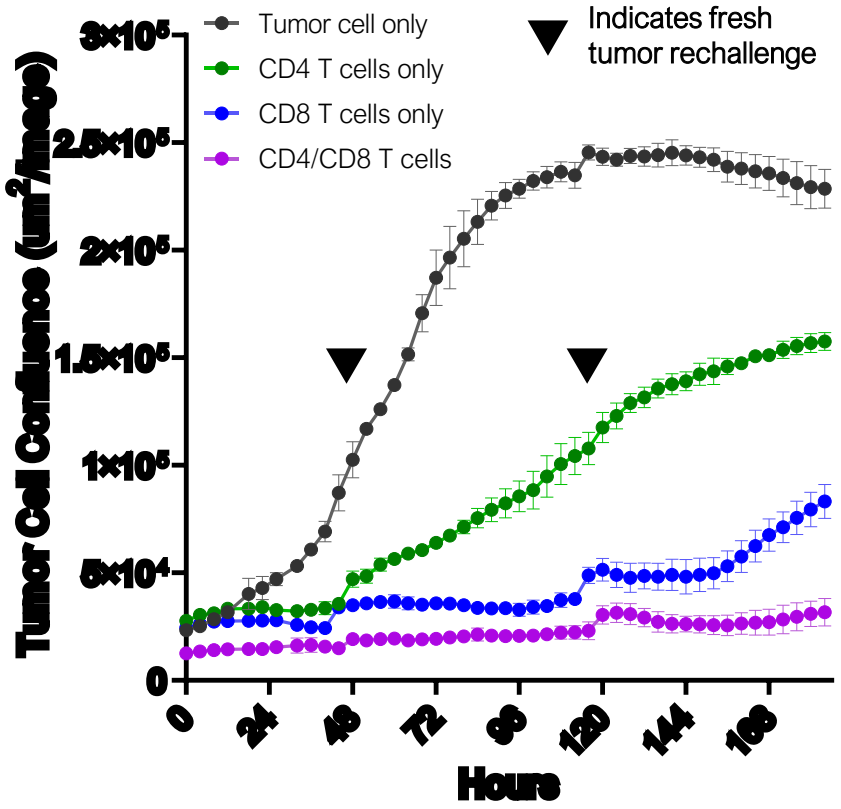
SW620 (E:T=2:1)



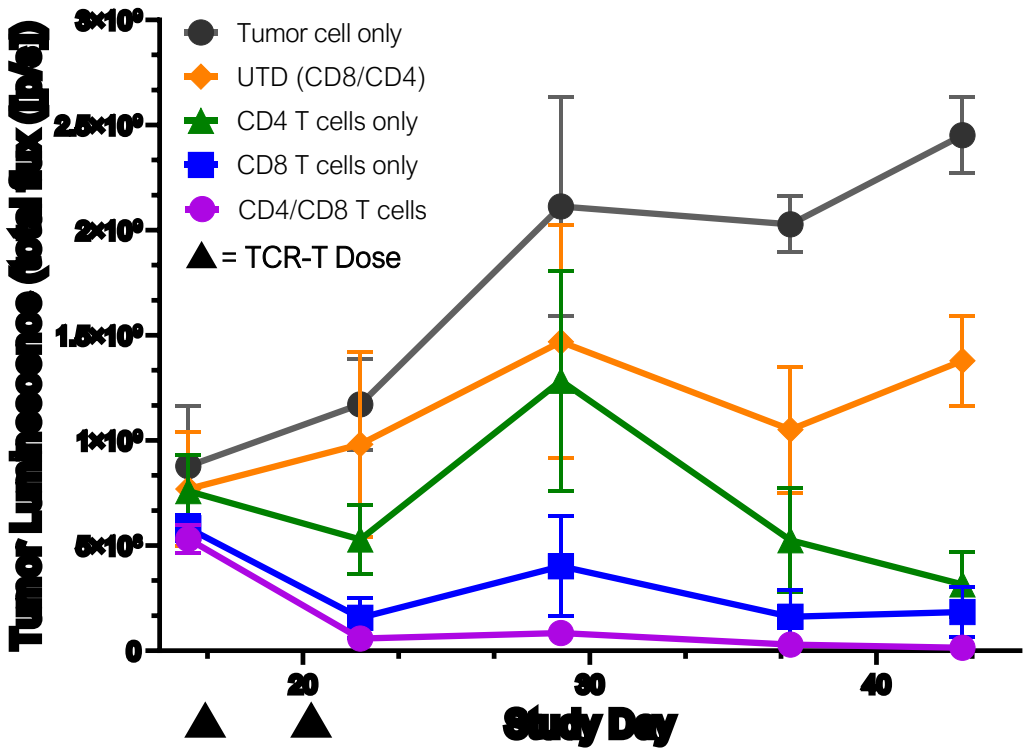
**Incucyte live tumor cell visualization assay*

CD8α/β enhances AFNT-111 tumor control by driving a coordinated CD4⁺/CD8⁺ T cell response

CFPAC (*In vitro* tumor challenge)



CFPAC-Luc (*In vivo* tumor challenge)



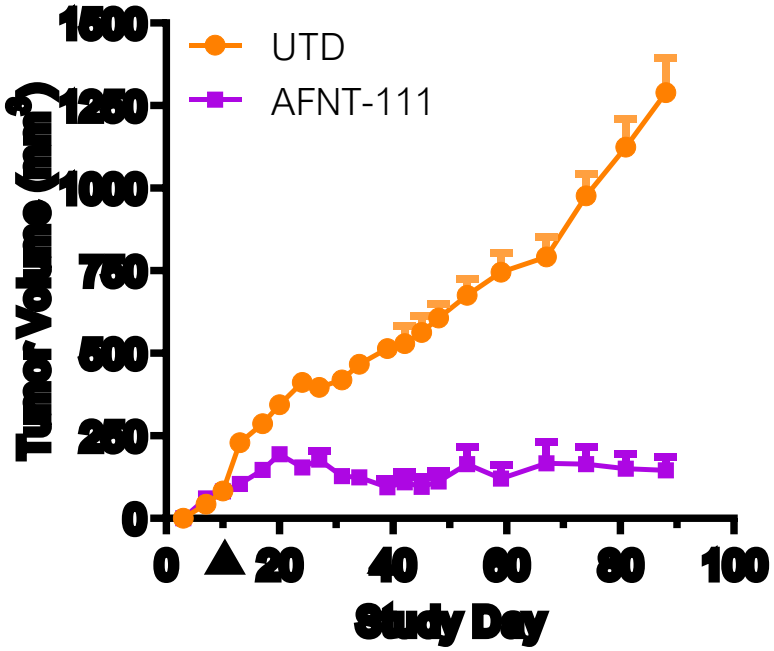
CD8⁺ T cell killing is enhanced by the presence of CD4⁺ T cells both *in vitro* and *in vivo*

**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 T cells

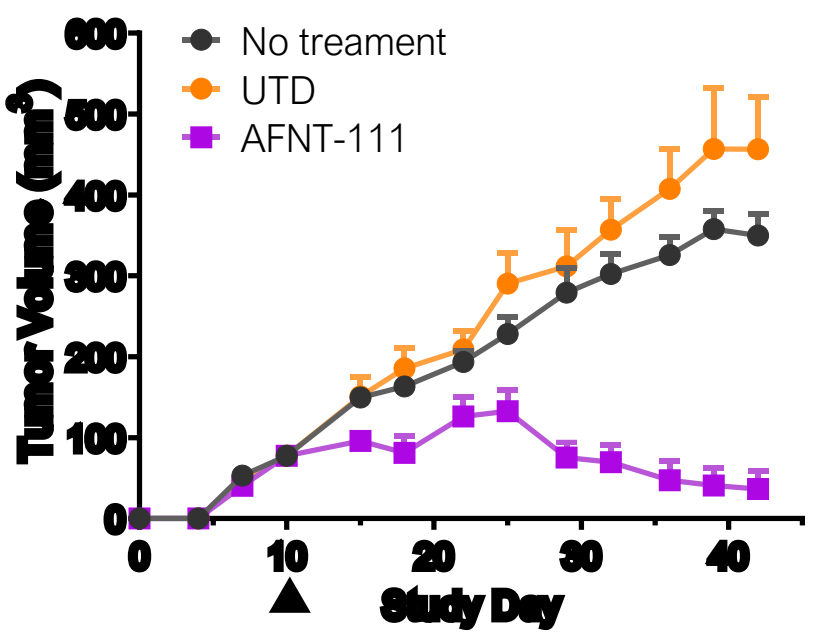
AFNT-111 T cell therapy induces robust preclinical efficacy across several *in vivo* tumor models

SW527 (Breast)



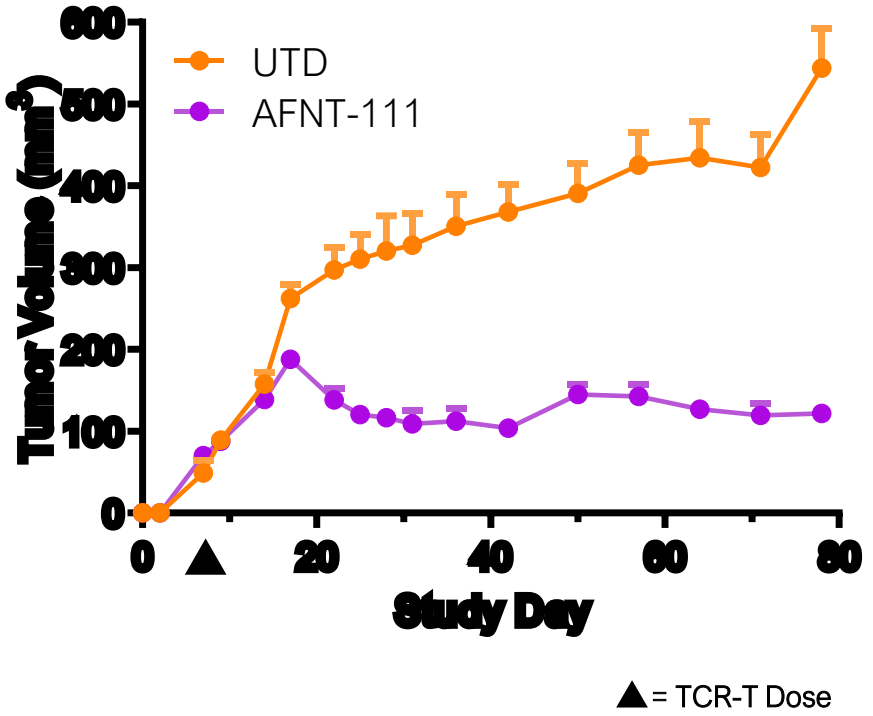
- *NSG mice randomized after SC tumor implantation (5 mouse/group)*
- *Dose: single IV administration of 3x10⁶ AFNT-111 T cells on D07*

CFPAC (Pancreatic)



- *NSG mice randomized after SC tumor implantation (5 mouse/group)*
- *Dose: single IV administration of 1x10⁷ AFNT-111 T cells on D10*

SW620 (Colon)



- *NSG mice randomized after SC tumor implantation (5 mouse/group)*
- *Dose: single IV administration of 3x10⁶ AFNT-111 T cells on D09*

The AFNT-111 TCR is a highly selective T cell therapy with low potential for cross-reactivity

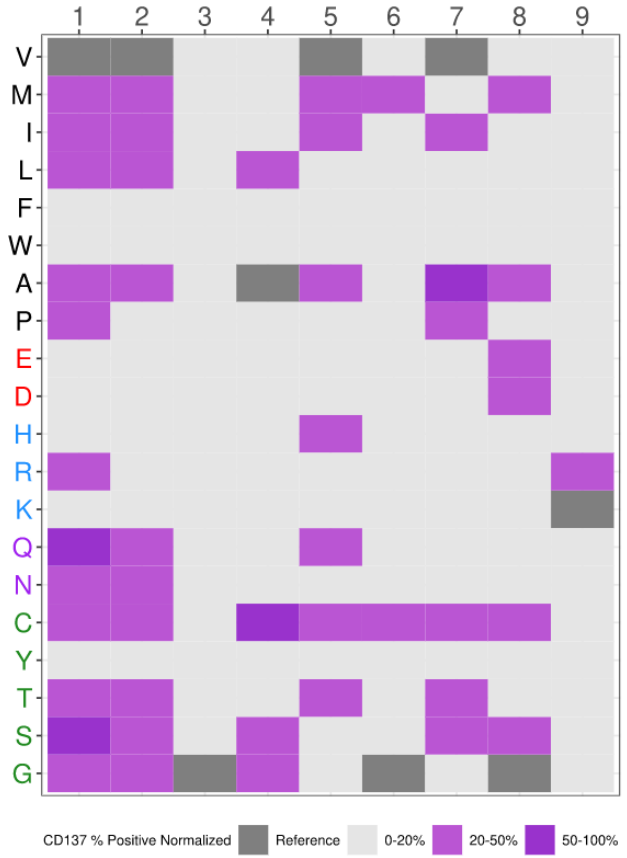
XScan mutagenesis assay

p1 p2 p3 p4 p5 p6 p7 p8 p9

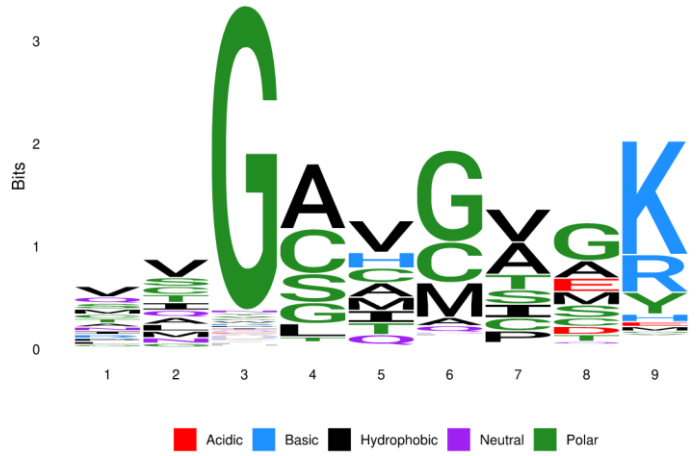
X V G A V G V G K
V X G A V G V G K
V V X A V G V G K
V V G X V G V G K
V V G A X G V G K
V V G A V X V G K
V V G A V G X G K
V V G A V G V X K
V V G A V G V G X

X= All other 19 amino acids

Data summary



Recognition motif of AFNT-111 TCR

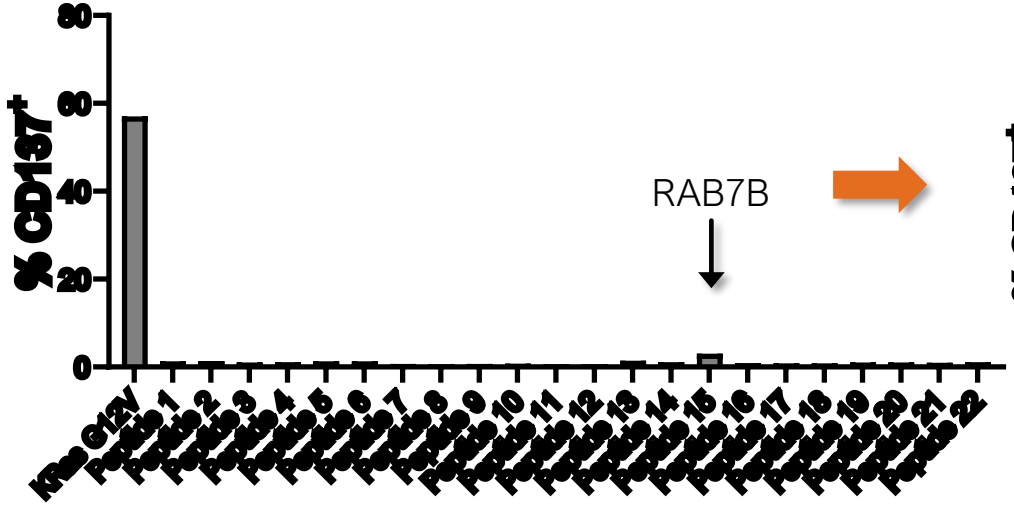


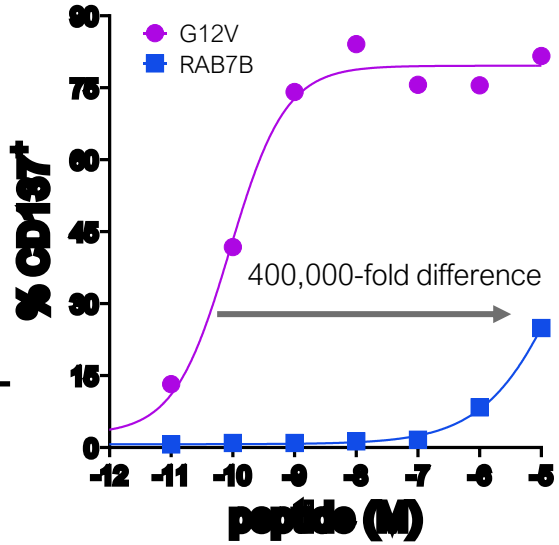
- XScan assay used to define the peptide recognition motif of AFNT-111
- *In silico* assessment across human proteome reveals only 22 peptides of potential concern (next slide)

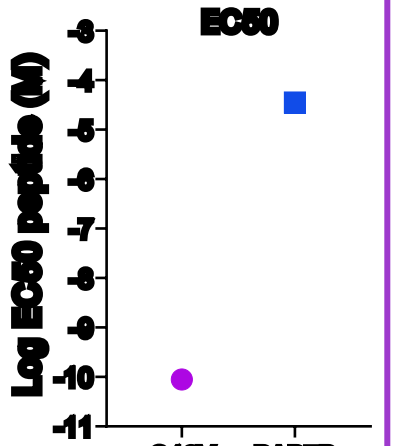
**AFNT-111 T cells incubated with XScan peptides and assessed for CD137⁺ T cell activation*

AFNT-111 TCR exhibits a strong preclinical safety profile

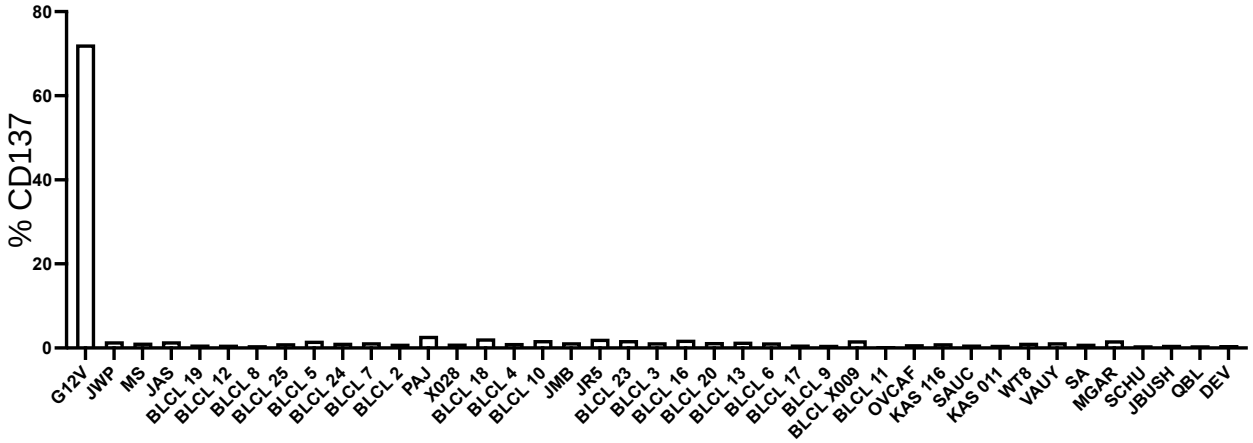
- No cross-reactive self-peptides of concern identified
- Peptide dose response studies confirm that TCR does not respond to physiological concentrations of RAB7B



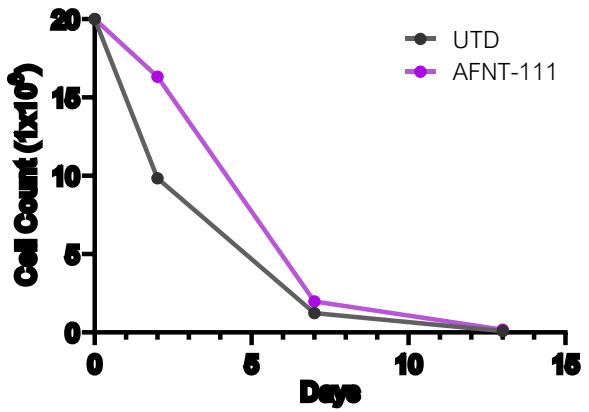




- No allo-reactive responses detected
- B-LCL library covers >95% of the most common HLA alleles



- No cytokine-independent growth



Summary and next steps

AFNT-111, a preclinically safe and effective TCR-engineered T cell therapy targeting the oncogenic driver KRAS G12V mutation (Poster #244)

- AFNT-111 is a potent and specific preclinical TCR-engineered T cell therapy that is cytotoxic to KRAS G12V-expressing tumor cells both *in vitro* and *in vivo*
- Crossreactivity and alloreactivity assessments established a strong AFNT-111 preclinical safety profile
- AFNT-111 IND anticipated in 1H'23
- First-in-human clinical studies in collaboration with Fred Hutch Cancer Research Center
  - Phase I Objectives: Safety, tolerability, maximum tolerated dose (MTD), and preliminary efficacy
  - Clinical Indications: Advanced or metastatic Pancreatic ductal adenocarcinoma (PDAC), Colorectal adenocarcinoma (CRC), Non-small cell lung cancer (NSCLC)
  - Target population: HLA-A*11:01^{+}; KRAS G12V^{+} patients

KRAS G12V T cell receptor-engineered T cells expressing the durability FAS-41BB switch receptor exhibit a potent, persistent, coordinated CD4/CD8 anti-tumor response in vitro and in vivo (Poster #342)

- Affini-T therapeutics is also developing a next generation TCR-T cell therapy with novel FAS-41BB switch receptor armoring to increase fitness, persistence, and anti-tumor activity

Acknowledgements

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