Charting a new course for CAR-NK cell therapies

Off-the-shelf immunotherapies for solid tumors

BIO Partnering Conference

Nonconfidential Overview

June 2022

Catamaran is purpose-built to address the challenges of developing safe and effective cell therapies in solid tumors by first intent

Two pipeline programs progressing toward the clinic

CAT-179 (HER2 CAR): *in vivo* efficacy established; FDA aligned on path to IND in Y23

CAT-248 (CD70 CAR): high-potential for both solid and heme malignancies

Platform can be efficiently deployed against additional targets

TAILWIND™ platform: end-to-end CAR-NK design and manufacturing

Scalable manufacturing process with cryopreserved, off-the-shelf product

Non-viral engineering method for large payloads and efficient manufacturing

Proprietary synthetic biology solutions overcome tumor microenvironment

Building an exceptional cell therapy team

45 FTEs in Boston's Seaport District with highly experienced R&D and CMC groups

$42M raised to date ($55M post-money)

Initiating Series B to fund programs at least through first IND and support CMC

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Catamaran is pursuing a differentiated strategy to address the challenges of solid tumor treatment

PROBLEM: multiple challenges in solid tumors

1. Overcoming tumor microenvironment (TME) immunosuppression
2. Tumor targeting
3. Functional persistence

Current cell therapies do not address all of these

SOLUTION: Catamaran TAILWIND Platform

1. Synthetic biology solutions to overcome TME immunosuppression
2. Optimized CAR architecture
3. Built-in cytokine support to improve functional persistence

* **Transposon-based manufacturing**
- Larger payloads vs. viral methods
- Simple, efficient and scalable

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Catamaran has made significant advancements highlighted by in vivo efficacy data in tumor xenograft models

KEY MILESTONES

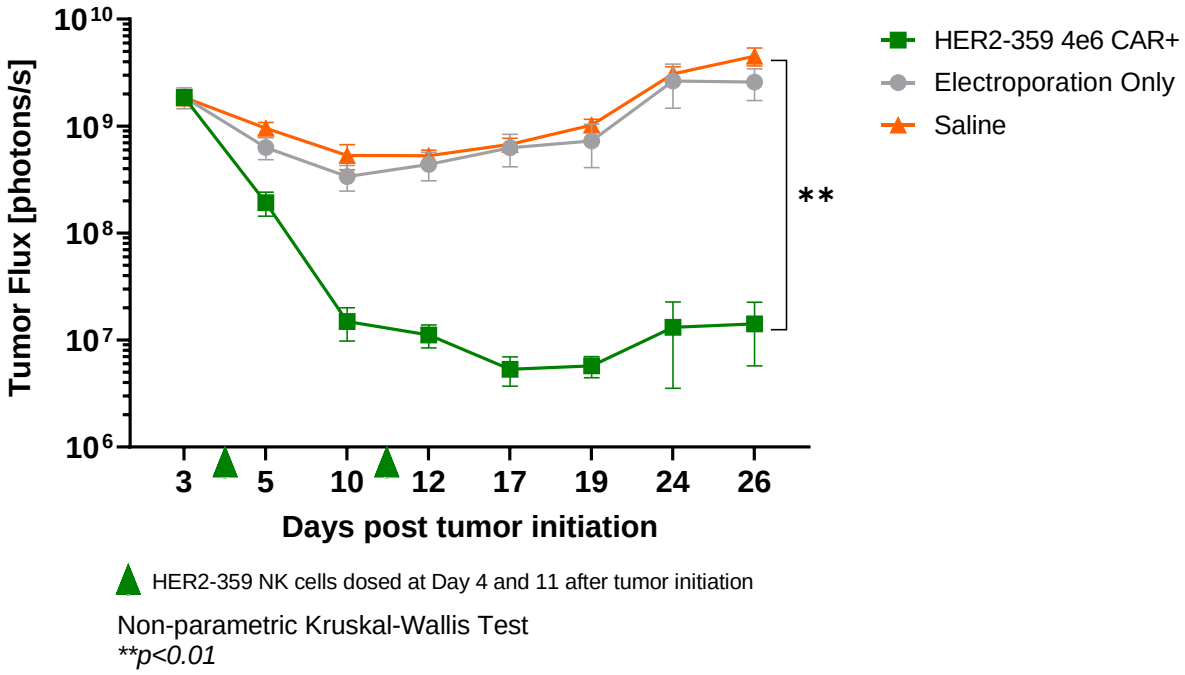
Pipeline

- ☑ In vivo efficacy and positive FDA feedback on HER2 CAR-NK program, setting path to IND
- ☑ Early In vivo efficacy with CD70 CAR-NK

Platform

- ☑ Scalable GMP manufacturing process capable of producing ~500 doses from a single leukopak
- ☑ Versatile transposon-based CAR-NK manufacturing platform; proprietary know-how
- ☑ Modular synthetic biology solutions for tumor microenvironment and persistence; enables broad tumor applications

CAT-179 IS EFFICACIOUS IN PRECLINICAL MODELS



Non-parametric Kruskal-Wallis Test
***p<0.01*

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Catamaran has clear avenues of differentiation in the NK Cell Therapy landscape

	catamaranBIO	nkarta	SENTI BIO	Takeda	artiva	Fate THERAPEUTICS	CENTURY THERAPEUTICS	SHORELINE biosciences
Lead CAR Programs	• ***HER2*** • ***CD70***	• NKG2D • CD19	• CD33 & FLT3 • GPC3	• CD19	• HER2 • CD19	• CD19 • BCMA	• CD19 • CD133 & EGFR	Undisclosed
Manufacturing	***Transposon***	Gamma-retrovirus	Viral	Gamma-retrovirus	Lentivirus	Gamma-retrovirus	Homology Directed Repair	Undisclosed
Tumor Micro-Environment Solution	✓	✗	✗	✗	✗	✗	✗	✗
Cell Source	***PBMC***	PBMC	PBMC	Cord Blood	Cord Blood	IPSC	IPSC	IPSC

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Experienced leadership team with deep cell therapy expertise

Management Team

Alvin Shih, MD, MBA
Chief Executive Officer

Pfizer · Retrophin · disarm therapeutics · LEK · Enzyvant · McKinsey & Company

Cherry Thomas, MD
Chief Medical Officer

ARRAY BIOPHARMA · Bristol Myers Squibb · CARIBOU BIOSCIENCES · NOVARTIS

Scott Holmes, MS, MBA
Chief Financial Officer

disarm therapeutics · Kiadis pharma · KERYX BIOPHARMACEUTICALS, INC · amag pharmaceuticals

Vipin Suri, PhD, MBA
Chief Scientific Officer

gsk · Pfizer · OBSIDIAN THERAPEUTICS · RazeTherapeutics

Mark Boshar, JD
Chief Operating Officer

Takeda MILLENNIUM THE TAKEDA ONCOLOGY COMPANY · RubiusTherapeutics · synlogic · WILMERHALE

Michael DeRidder, PhD
SVP, Corporate Strategy & New Product Planning

gsk · LEK

Lilian Yengi, PhD
VP, Preclinical Development & Biomarkers

Dyne therapeutics · bluebirdbio · AstraZeneca · Wyeth

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VP, Human Resources

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Enara Bio

Alvin Shih
Catamaran Bio

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Our scientific co-founders and SAB bring strong background in NK cells, TME clinical expertise, and cellular engineering

Scientific Co-Founders

Branden Moriarity, PhD
University of Minnesota

- Pioneer in non-viral engineering and editing of immune cells for cell therapy
- Led teams optimizing TcBuster for high efficiency engineering of NK cells
- Helped deliver first TcBuster engineered immune cell IND
- Focus on translational research in cell therapy to the clinic

Catherine Bollard, MD
Childrens National Medical Center

- 20+ years of treating patients with cell therapies
- Leading cell therapy/IO clinician and scientist/investigator – serves/has served as the Sponsor on over 15 IO INDs
- Engineered immune cells, including NK cells, with syn bio switches (published) to overcome TME immunosuppression
- Translated novel cell therapies to over 20 clinical trials

Scientific Advisory Board

Lewis Lanier, PhD
UCSF

Catherine Blish, MD, PhD
Stanford

Yvonne Chen, PhD
UCLA

Gianpietro Dotti, MD
University of North Carolina, Chapel Hill

Timothy Harris, PhD
Repertoire Immune Medicines

Chris Klebanoff, MD
Memorial Sloan Kettering Cancer Center

Eric Yvon, PhD
George Washington School of Medicine

TAILWIND™ platform

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Clinical trials with allogeneic engineered NK products provides strong evidence for safety and efficacy

Takeda

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

B-cell malignancies
73% OR
0 CRS 0 ICANS/GvHD

Fate THERAPEUTICS

B-cell malignancies
58% - 73% OR
1 CRS (Gr 1) 0 ICANS/GvHD

nkarta THERAPEUTICS

B-cell malignancies and AML
60% - 83% OR
0 CRS 0 ICANS/GvHD

EFFICACY
ORRs from 50%-80% and CRs up to 60% in heme malignancies

SAFETY
No CRS/ICANS/GVHD, outpatient administration likely

CELL SOURCE
Responses from Cord blood, PBMC, and iPSC cell lines

PERSISTENCE
Engineered IL15 enhances persistence and expansion

DOSING
Durable efficacy will likely require multiple doses

[1]Liu et al (2020), N Engl J Med;382:545-53, [2]https://ir.fatetherapeutics.com/news-releases/news-release-details/fate-therapeutics-announces-positive-interim-clinical-data-its, [3]https://ir.nkartatx.com/static-files/6d097f5f-2f67-4e80-8903-2c96b455b244

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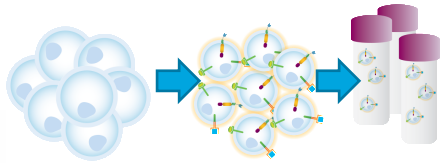
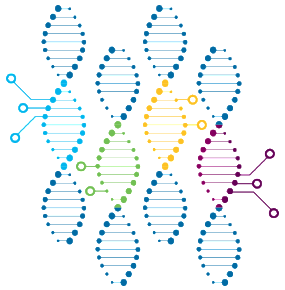
TAILWIND Platform is differentiated on key dimensions



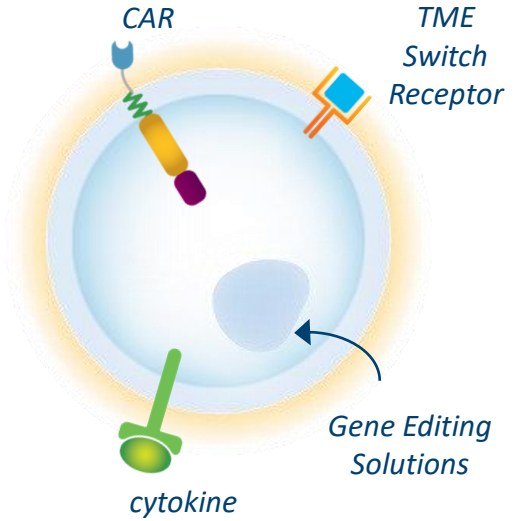
1 SCALABLE & VERSATILE NON-VIRAL MANUFACTURING PROCESS

- Optimized cell process that requires <20d and produces **hundreds of doses** from a single run
- Improved **efficiency** of editing (>60-75%) vs other engineering methods
- **Larger payload capacity** and multi-plex engineering



2 SYNTHETIC BIOLOGY-ENABLED TUMOR MICROENVIRONMENT (TME) and PERSISTENCE SOLUTIONS

- TGFβ Trap effectively **negates TME** immunosuppression
- Switch receptors turn TGFβ and other factors into **stimulatory signals** for immune cells
- IL15 construct enhances persistence >165d in mice
- Source of **novel IP and partnership** substrate



TAILWIND™ Platform

Scalable, versatile process enables rapid, cost-effective manufacturing

19-day manufacturing process yields ~500 doses of CAR-NK product

	ISOLATION & ACTIVATION	ELECTROPORATION	EXPANSION	CRYOPRESERAVATION
PARAMETERS	~5E8 NK Cells / Leukopak	50-80% Efficiency	~2000 fold	>90% viability post-thaw ~1E12 CAR+ NK Cells
INNOVATIONS	Feeder free activation	Non-viral TcBuster transposon system for large cargoes and multiplexing	Single K562 feeder addition	High recovery of functional cells
BENEFITS	Improved safety	Non-viral, versatile, efficient, reduced cost	Improved safety and activity	Frozen, off-the-shelf product

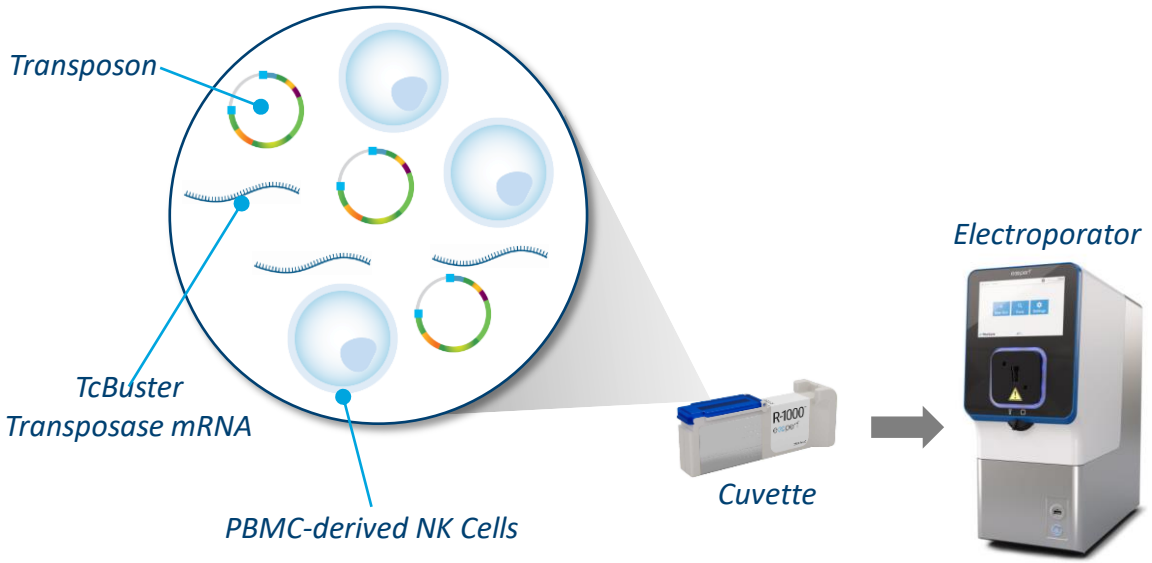
Transposon-based NK cell modification enables design optionality and more efficient manufacturing

TcBuster Transposon System

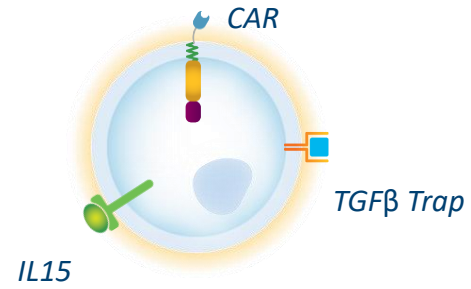
Simple, Cost-effective Manufacturing
Fewer GMP components than viral systems

Large Genetic Payloads
Capacity for significantly larger genetic payloads than viral systems

Single-step Multiplex Engineering
Can simultaneously insert and knock-out genes in one step



CAR-NK cell with multiple components ready for expansion



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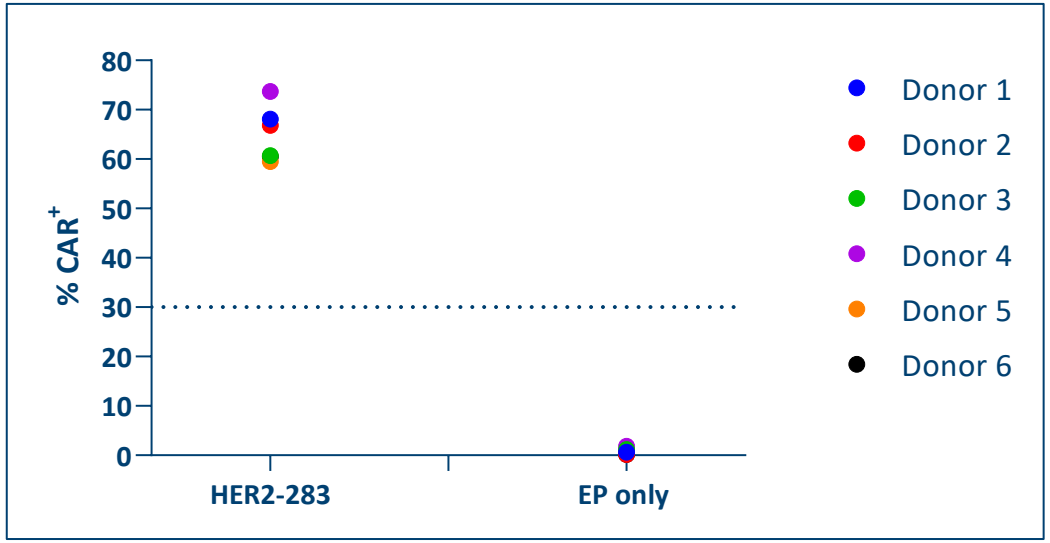
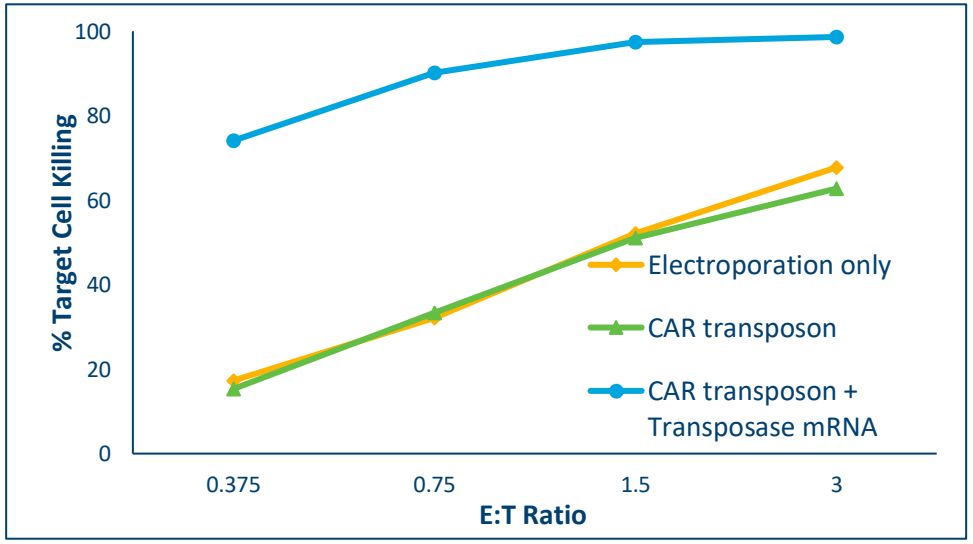
Transposon-based modification is highly efficient and yields active CAR-NK cells

Transposon engineering efficiencies are consistent across multiple donors (Day 8 post electroporation)



- 50% - 80% efficiency in multiple donors
- Vector copy number show <5 copies/genome

Transposon-modified NKs are highly active



- CAR-NK cells demonstrate CAR-dependent in vitro cytotoxicity

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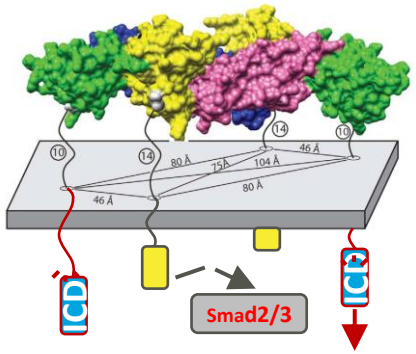
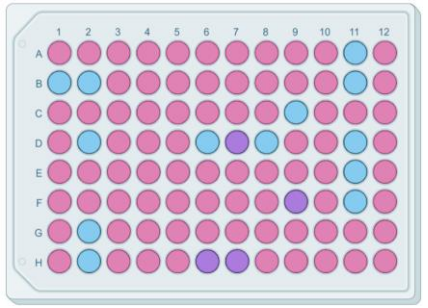
Integrated synthetic biology platform for identifying, designing, and testing solutions for solid tumor microenvironment hurdles

IDENTIFY

DESIGN & ENGINEER

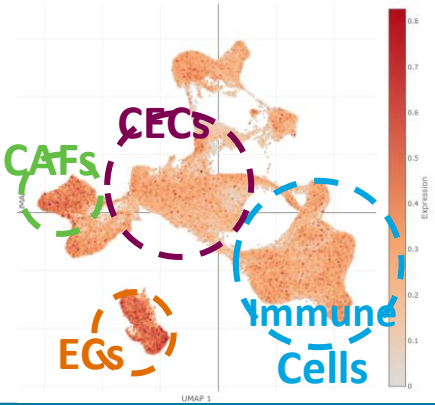


TEST



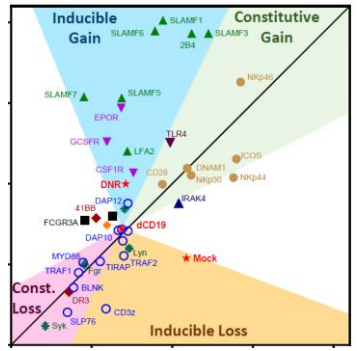
Example: TGFβ

Bioinformatics approach identifies high TGFβ activity signature in tumors



Structure and signaling guided design of TGFβ switch receptors

TGFβ induced cell proliferation in NK cells engineered with switch receptors



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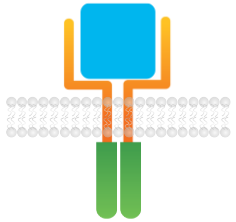
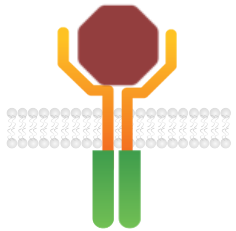
Switch receptor (SR) platform: Tailored modules for durable solid tumor efficacy

		TGFβ-Trap 	TGFβ-Switch Receptor 	TME-Switch Receptor 
BENEFITS		**PRESERVE** CAR-NK activity and function in high TGFβ tumors.	**ENHANCE** CAR-NK proliferation and function in high TGFβ tumors	**EXTEND** to other TME factors to broadly enable solid tumor efficacy
STRUCTURE	Extracellular domain	TGFβRII	TGFβRII	Various TME factors
	Intracellular domain	None	Signaling optimized for function	Signaling optimized for function
FUNCTION	Protect engineered and surrounding cells	+++	+++	+++
	Enhance function	-	+++	+++
	Modularity	CAR + TGFβ Trap CAT-179, CAT-248	CAR + TGFβSR	Multifunctional NK cells

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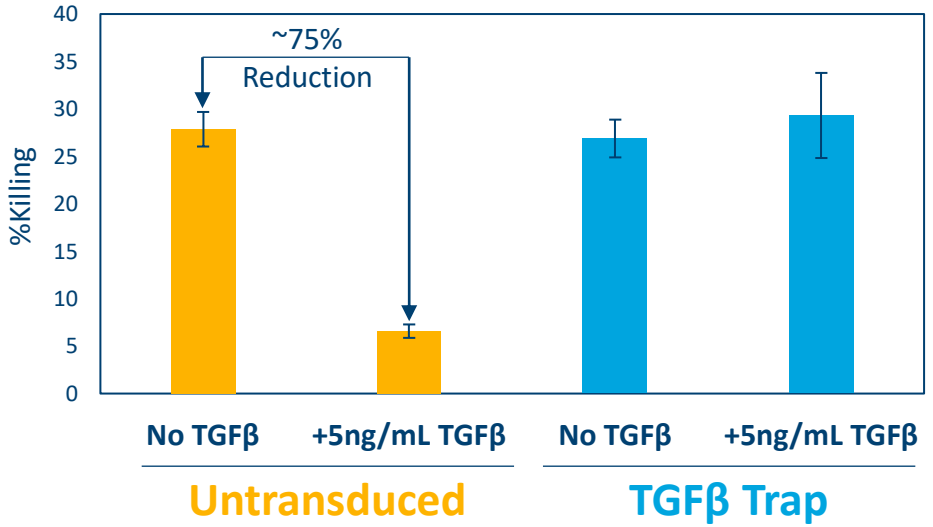
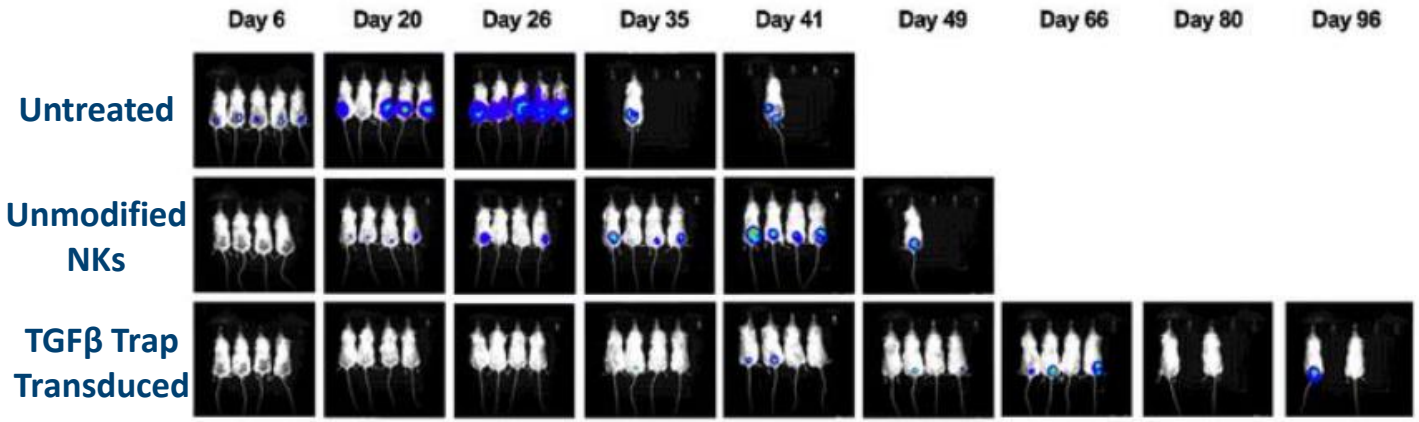
TGFβ Trap protects NK cells from TGFβ-mediated immuno-suppression in vitro and in vivo

NK cell cytotoxicity fully retained in vitro



- NK cells engineered to express TGFβ Trap are incubated with K562 tumor cells (1:3 E:T) in the presence or absence of TGFβ for 3 hours
- NK cell expressing TGFβ DNR maintain high levels of tumor cell killing in the presence of immunosuppressive TGFβ

NK cell efficacy enhanced in vivo



Burga et al. 2019

- Mice implanted with neuroblastoma model (SHSY5Y) are infused with unmodified NK cells or NK cells engineered to express the TGFβ Trap
- NK cells expressing the TGFβ Trap have superior tumor clearance relative to unmodified NK cells

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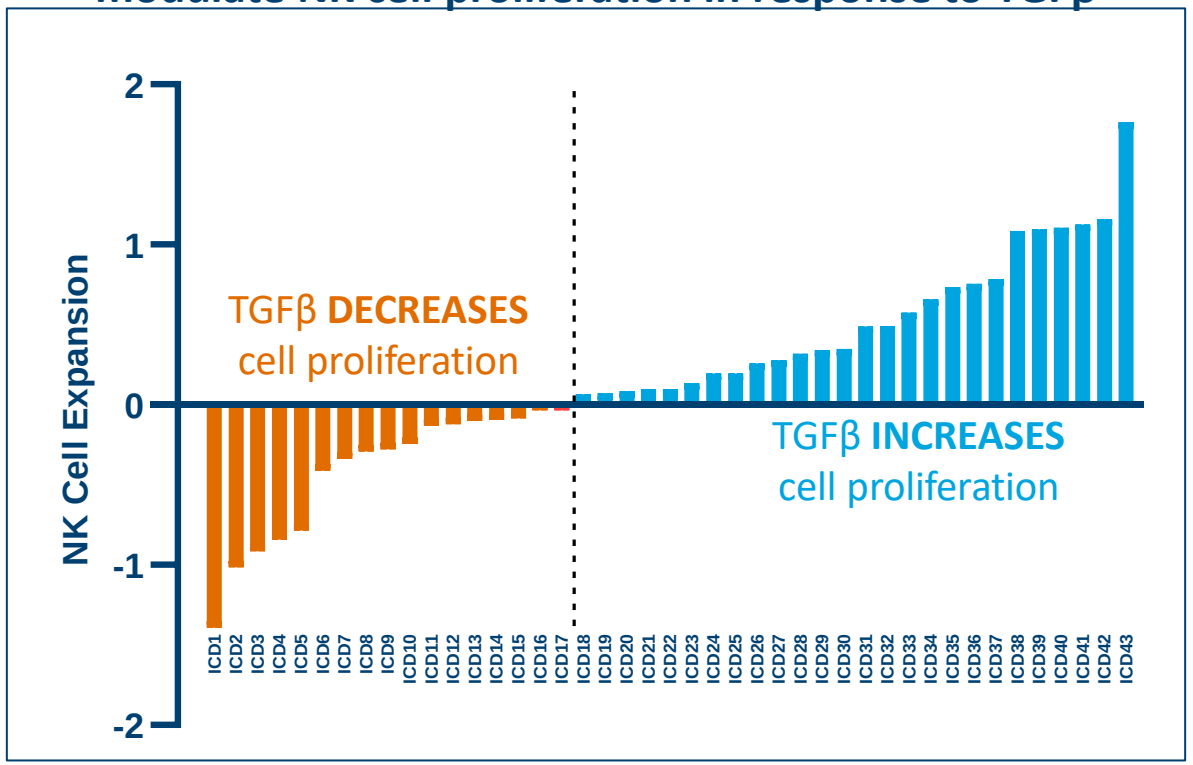
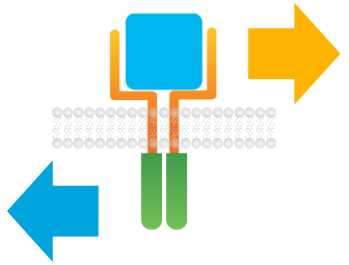
Next generation solutions can enable tunable responses to any of a variety of tumor microenvironment (TME) factors

By modifying intracellular domains, switch receptors can modulate NK cell proliferation in response to TGFβ

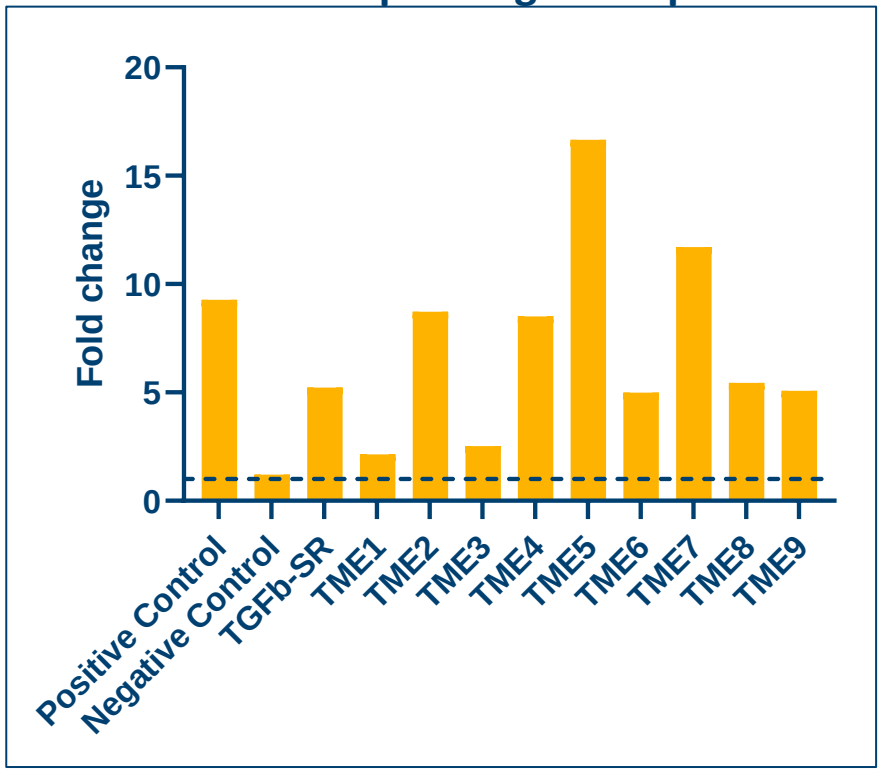


- 43 different intracellular domains (ICD 1 – 43) were coupled to the TGFβ receptor to create a tunable response to this immunosuppressive signal
- NK cell numbers were counted after 5 days expansion with or without 10 ng/ml TGFb

Signal Inverter



Switch receptors against various TME factors induce reporter gene expression



- The extracellular domains of 9 different TME factors (TME 1 – 9) were coupled to a reporter to create switches to various immunosuppressive elements relevant across multiple solid tumor indications
- Readout is reporter gene in Jurkat cells after 24hrs incubation with the inducers

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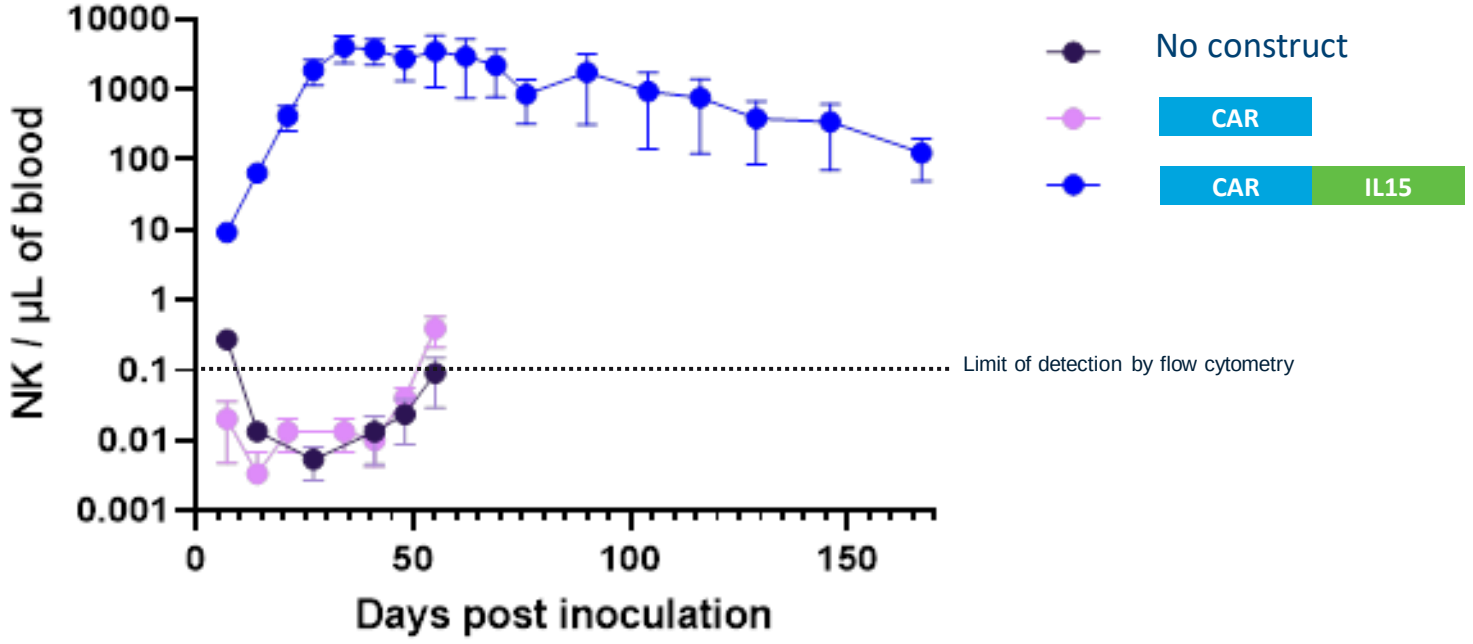
IL15 construct imparts expansion and prolonged persistence to CAR-NK cells without exogenous cytokine support

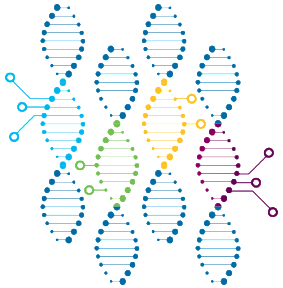
- IL15 enhances persistence of engineered NK cells in clinical studies
- CAR-IL15-NK cells continue to be functional and effectively **lyse tumor cells at 150d**

Persistence of human NK cells *in vivo*
(5M NK cells / NSG mice / IV)

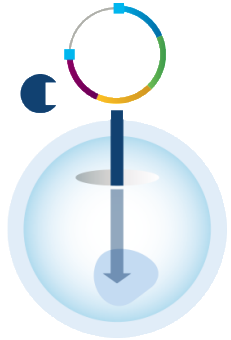


Catamaran's TAILWIND™ platform provides end-to-end CAR-NK cell engineering and cell processing

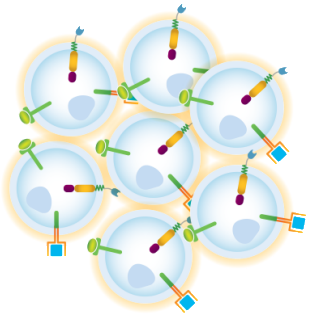
NK Cell Source



Synthetic Biology

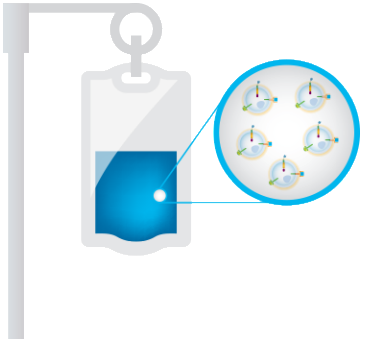


Transposon Engineering



Cell Expansion

Cryopreservation



Allogeneic Product

- We have developed and end-to-end process to predicably and efficiently manufacture CAR-NK
  - Current estimate is that >100 doses can be made from a single leukopak
  - Transposon approach offers superior payload capacity and flexibility
- TAILWIND enables a scalable manufacturing process without the need for selection and minimal use of feeder cell line

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Pipeline

Initial programs will target HER2 and CD70

PROGRAM	TARGET	INDICATIONS	IND	DISCOVERY	LEAD OPTIMIZATION	IND ENABLING
CAT-179	HER2	Breast & Gastric Cancer	2023			
CAT-248	CD70	Renal Cell Carcinoma & AML	2024			
Undisclosed	Undisclosed	Solid Tumors				

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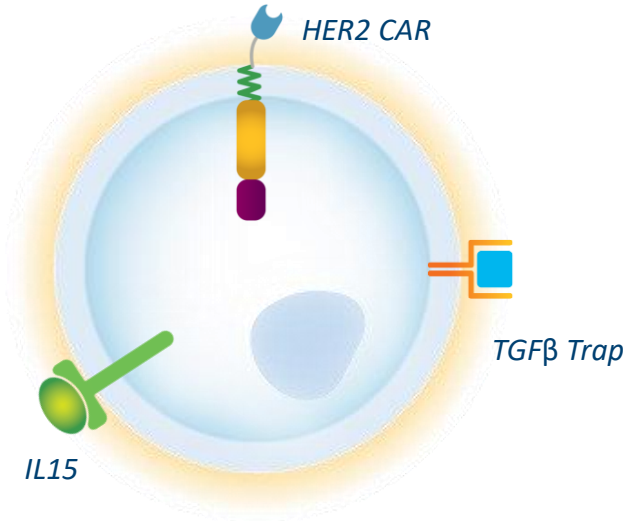
Catamaran HER2 CAR-NK program will target solid tumors

CAT-179 overview



Binder	Humanized anti-HER2 scFv
CAR Architecture	CAR optimized for NK cells
TME Solution	TGFβ Trap
NK Persistence	Native IL15

	CAT-179: **HER2 CAR-NK**
Target Rationale	• Broad tumor expression, driver oncogene • Low expression in normal tissue • Extensive clinical validation with antibodies/ADCs
Indications	• $HER2^{+}$ breast and gastric cancer • Other HER2-overexpressing tumors (ovarian, salivary)
Unmet Need	• Frequent antigen positive relapse after antibodies/ADCs • CAR-T minimally efficacious to date
Competitive Landscape	• Multiple mAbs/ADCs approved • Multiple CellTx approaches in clinical or preclinical development
Key Differentiators	• **CAT-179 is the only HER2-directed cell therapy that addresses tumor microenvironment**

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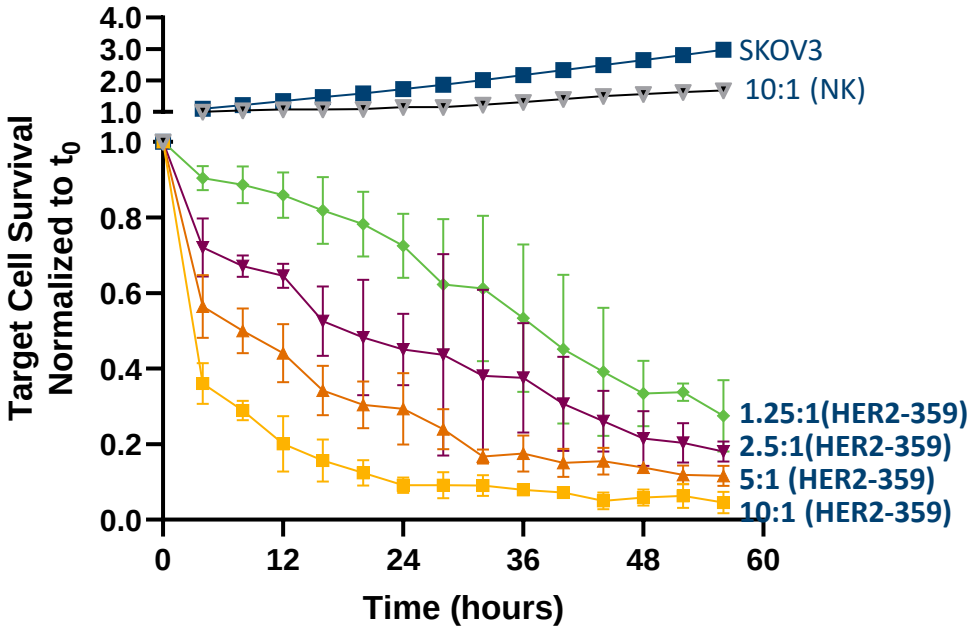
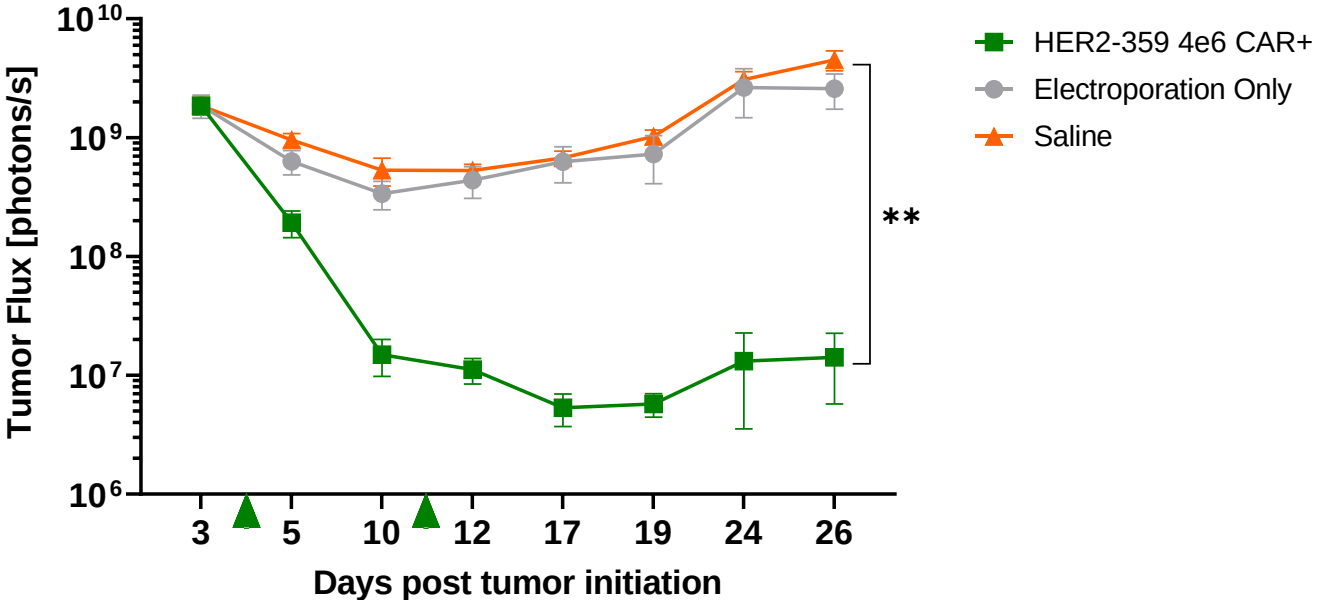
HER2 CAR-NK lead demonstrates anti-tumor activity *in vitro* and *in vivo*

HER2-359 shows cytotoxicity against SKOV3 cells



Therapeutic efficacy of HER2-359 in SKOV3 xenograft model



Therapeutic dosing: D4, D11

Non-parametric Kruskal-Wallis Test
***p<0.01*

- In vitro, HER2-359 demonstrates CAR dependent cytotoxicity against multiple HER2 expressing cell lines
- In vivo, therapeutic HER2-359 dosing results in significant reduction in tumor signal compared to control groups

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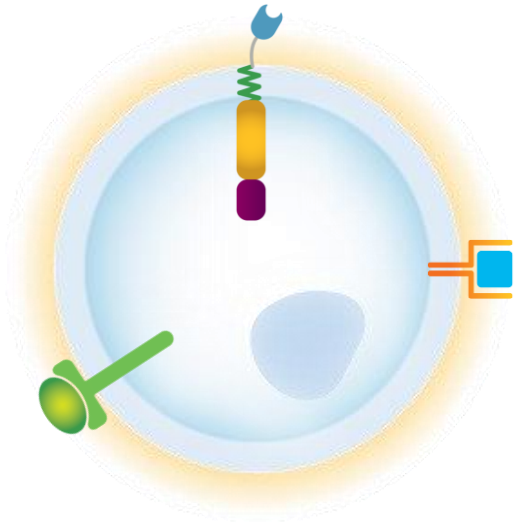
CD70 is an attractive CAR-NK cell target for a broad spectrum of malignancies

CAT-248



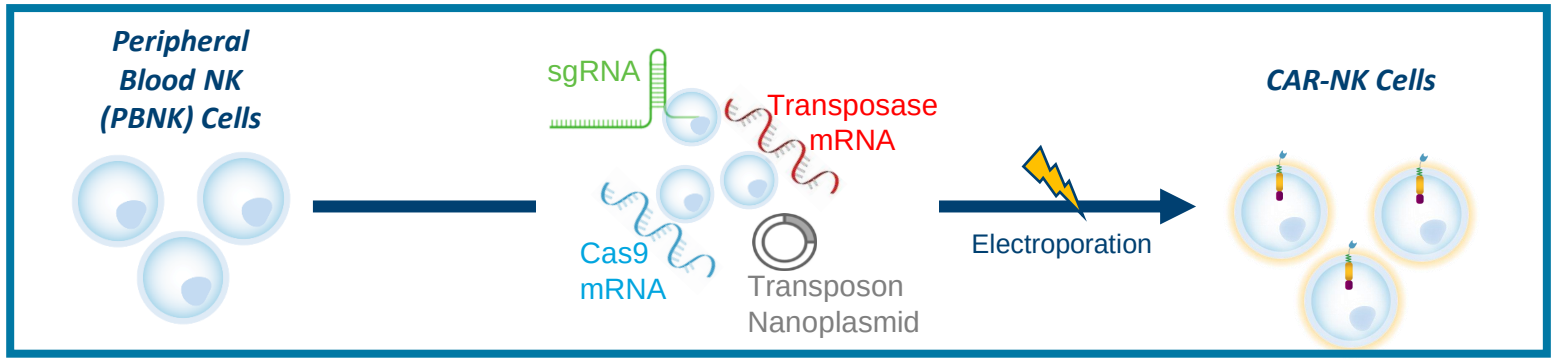
Binder	anti-CD70 scFv
CAR Architecture	CAR optimized for NK cells
TME Solution	TGFβ Trap
NK Persistence	Native IL15
CD70 Expression on NKs	CD70 Fratricide solution

	CAT-248: **CD70 CAR-NK**
Target Rationale	• CD70 present in solid and heme malignancies • Low expression in normal tissue • Initial clinical efficacy with antibodies and ADCs
Indications	• Renal cell carcinoma • Hematologic malignancies (AML)
Unmet Need	• Poor prognosis solid tumors and heme malignancies
Competitive Landscape	• Cusatuzamab/Azacytidine in PhIIa (AML) • Allogeneic CD70 CAR (CRSP, ALLO, Nkarta) for solid tumors and heme
Key Differentiators	• **CAT-248 will address TME challenges in RCC** • **CD70 knockout (required for manufacture) can be multiplexed with other edits via transposon**

Source: Perna et al (2017); Flieswasser et al. (2019); Ryan et al. (2010); Riether et al. (2016); Inaguma et al. (2020); Riether et al. (2020); Pal et al. (2019); SEER

CAT-248 produced via single-step multiplex engineering

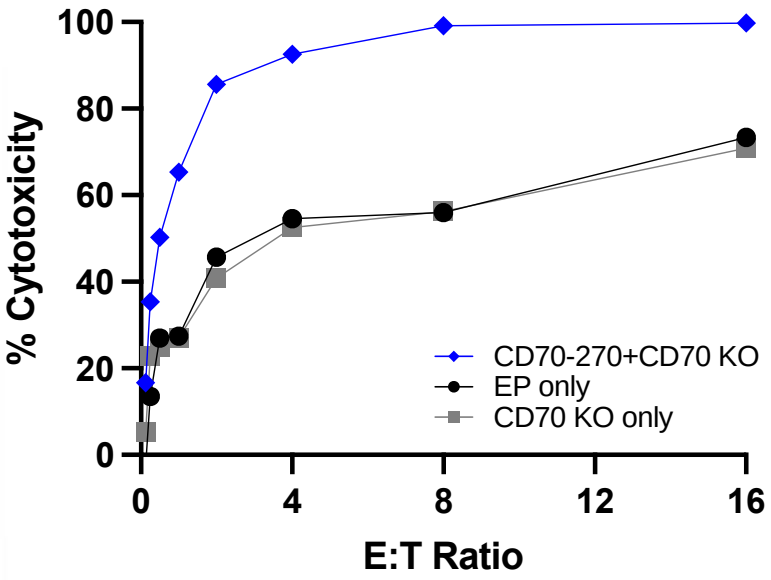
Single-step delivery of CAR and CRISPR/Cas9 editing in NK cells using the TAILWIND™ platform



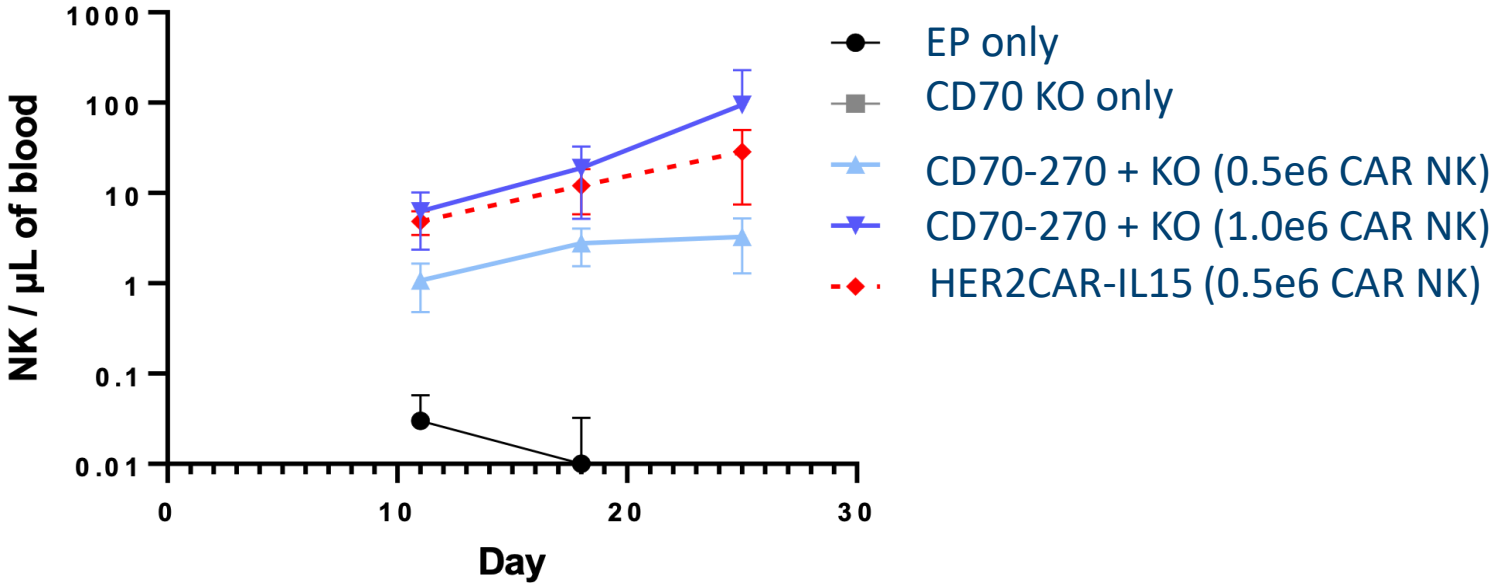
- Multiple RNA / DNAs / RNPs can be delivered in a single electroporation step
  - Simplified manufacturing and versatile engineering of multiply edited NK cells
  - Compatible with Transposases, CRISPR, TALEN/ZFNs, Base editors and other genome modifying technologies
- CAT-248 product is manufactured in a single step (60% CAR+,85% CD70 KO)
  - Efficiently lyse CD70 expressing target cell lines in vitro
  - Efficacious in AML and RCC CD70 expressing cell line xenografts

CAT-248 demonstrates CAR activity & IL15 dependent persistence

CAR function in vitro
CD70⁺ 786-0 cell killing



IL15 dependent in vivo persistence
NSG IV 1x IV dosing



CD70-270 CAR

- KO of CD70 in NK cells does not impede engineering, expansion, CAR-independent cytotoxicity or IL15 dependent persistence
- CD70 CAR significantly enhances NK cell cytotoxicity towards CD70 expressing cell lines

CD70 CAR enhances survival in vivo models for RCC and AML

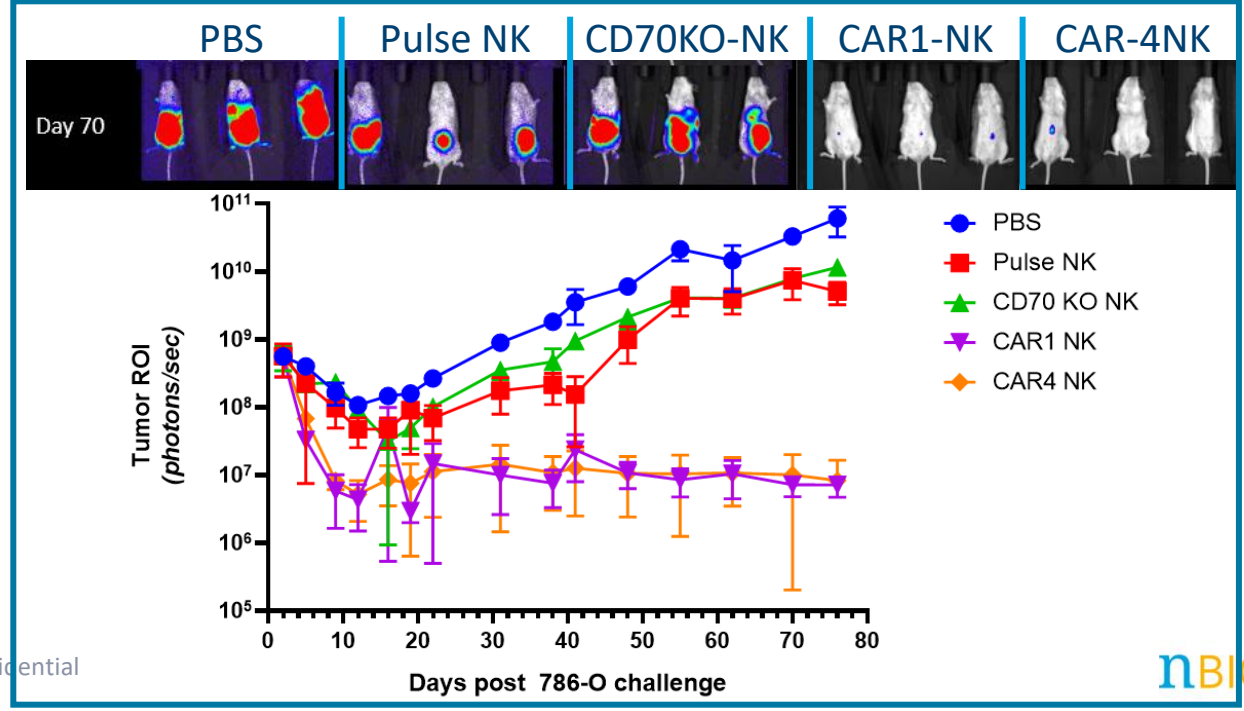
Collaboration with B Moriarity - Univ of Minnesota

Exploratory pharmacology studies with CD70 CAR-NK cells

Study	Construct	CAR-NK cell dose (+ IL15 3X/wk)	Route
786-O-luc (Renal Cell Carcinoma) IP xenograft	CAR1-NK CAR4-NK	5E6 CAR-NK cells at days 3, 6, 10, 13 after 1E6 tumor cells	IP
MOLM-13-luc (Acute Myeloid leukemia) IV xenograft	CAR1-NK CAR4-NK	5E6 CAR-NK cells at days 3, 6, 10, 13 after 0.25E6 tumor cells	IV

- CAR1 (CD27) and CAR4 (ScFv) are:
  - Delivered via transposon engineering and simultaneous CD70 KO into NK cells
  - CAR only constructs (do not express IL15 or TGFβ Trap)
- CAR4 enhances survival in MOLM13 AML model to 27d (control = 17-20d)
  - NK cells detected in bone marrow and periphery

CD70 CAR is efficacious in 786-O xenograft model



nBIO

Catamaran is purpose-built to address the challenges of developing safe and effective cell therapies in solid tumors by first intent

Two pipeline programs progressing toward the clinic

CAT-179 (HER2 CAR): *in vivo* efficacy established; FDA aligned on path to IND in Y23

CAT-248 (CD70 CAR): high-potential for both solid and heme malignancies

Platform can be efficiently deployed against additional targets

TAILWIND™ platform: end-to-end CAR-NK design and manufacturing

Scalable manufacturing process with cryopreserved, off-the-shelf product

Non-viral engineering method for large payloads and efficient manufacturing

Proprietary synthetic biology solutions overcome tumor microenvironment

Building an exceptional cell therapy team

45 FTEs in Boston's Seaport District with highly experienced R&D and CMC groups

$42M raised to date ($55M post-money)

Initiating Series B to fund programs at least through first IND and support CMC

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