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HARNESSING THE POWER OF MACROPHAGES

November 2024

Cautionary Note Regarding Forward-Looking Statements

Statements in this slide deck about future expectations, plans and prospects, as well as any other statements regarding matters that are not historical facts, may constitute “forward-looking statements” within the meaning of The Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements relating to Carisma’s business, strategy, future operations, cash runway, the advancement of Carisma’s product candidates and product pipeline, and clinical development of Carisma’s product candidates, including expectations regarding timing of initiation and results of clinical trials. The words “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “goals,” “intend,” “may,” “might,” “outlook,” “plan,” “project,” “potential,” “predict,” “target,” “possible,” “will,” “would,” “could,” “should,” and similar expressions are intended to identify forward-looking statements, although not all forward- looking statements contain these identifying words.

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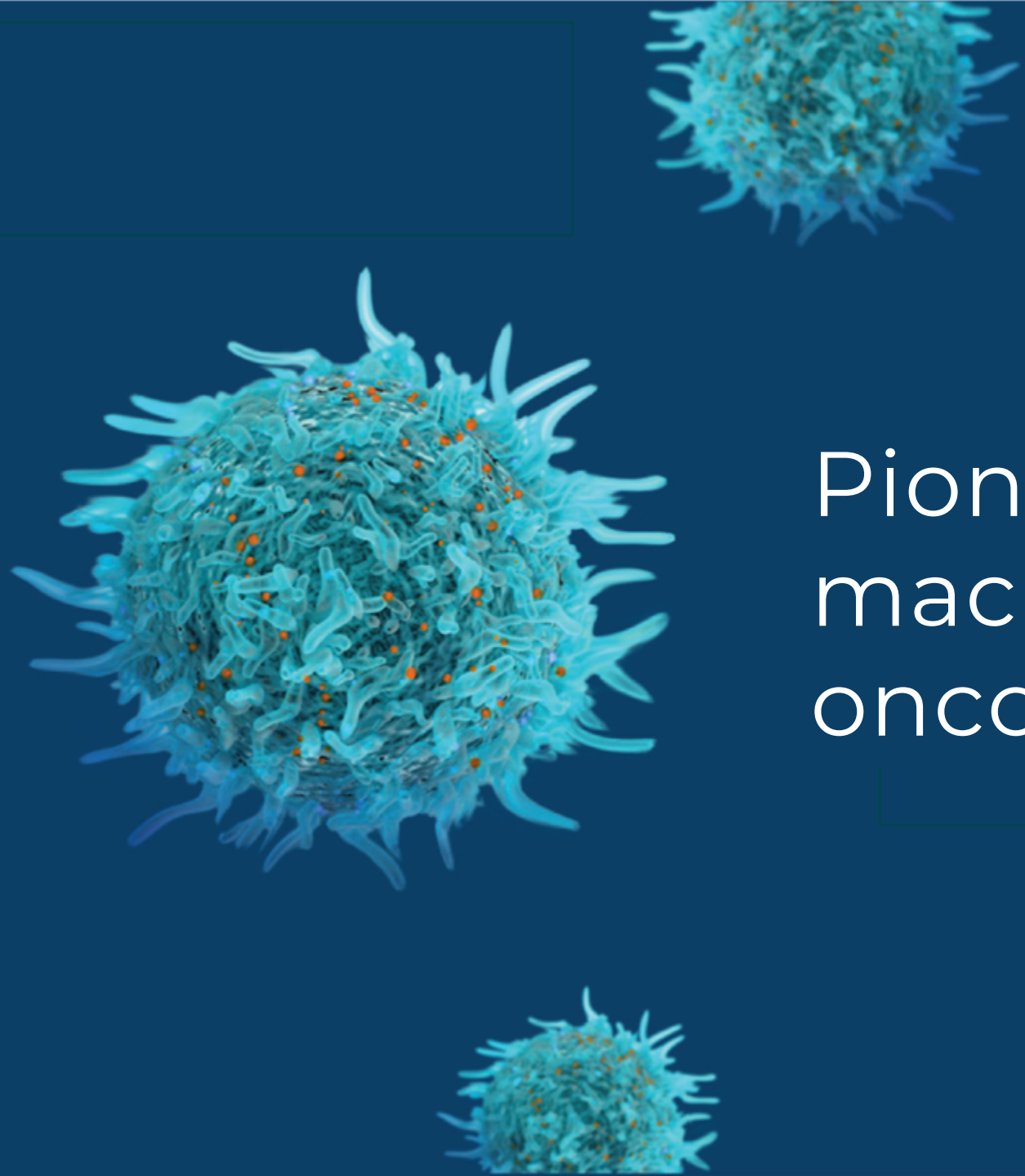
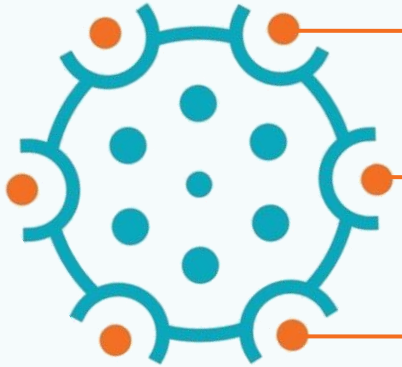


Pioneering engineered macrophages in oncology and beyond

Engineering Myeloid Cells: CAR-M and Beyond



Technology	Current Status
***Ex Vivo* CAR-M**	Phase 1 clinical program for HER2+ solid tumors
In Vivo* CAR-M Collaboration with moderna	*Oncology:* First Development Candidate targets GPC3 for the treatment of solid tumors, including HCC
	Autoimmune disease: Expanded Collaboration and nominated two targets**
Anti-fibrotic macrophages	Discovery programs in liver and lung fibrosis; Preclinical PoC achieved in liver fibrosis[1]

Corporate

- **Cash:** Runway into 3Q 2025, funding multiple clinical and preclinical catalysts
- **Intellectual Property:** Strong IP leadership position in the CAR-M/engineered myeloid cell fields (37 granted patents, 100+ pending)
- **Partnership:** All programs wholly owned beyond *in vivo* oncology partnership with Moderna

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CAR-M: chimeric antigen receptor monocytes and macrophages; GPC3: Glypican-3; HCC: Hepatocellular carcinoma; PoC: proof of concept; *IND-enabling studies for 1st of up to 12 programs; **Carisma retains all rights in autoimmune disease beyond the two nominated targets, which will be exclusively partnered with Moderna; [1]Sloas C, et al. ASGCT 2024

First-in-Class Pipeline

Multiple value inflection points across therapeutic areas and modalities

PRODUCT CANDIDATE	INDICATION	PLATFORM	DISCOVERY	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	COLLABORATOR
Oncology								
CT-0525	HER2+ solid tumors	CAR-Monocyte (Autologous)			Next milestone: Initial Phase 1 data[1] (1Q 2025)			
Undisclosed	GPC3+ solid tumors[2]	CAR-M/mRNA/LNP (*In Vivo*)			Next milestone: IND filing (Undisclosed)			moderna
CT-1119*	Mesothelin+ solid tumors	CAR-Monocyte[3] (Autologous)						
4 Nominated Targets	Undisclosed	CAR-M/mRNA/LNP (*In Vivo*)			Next milestone: Lead nomination (Undisclosed)			moderna
Fibrosis and Autoimmune								
TBD	Liver Fibrosis	Engineered macrophage			Next milestone: Development candidate nomination[1] (1Q 2025)			
2 Nominated[4] Targets	Autoimmune Disease	CAR-M/mRNA/LNP (*In Vivo*)			Next milestone: Lead nomination (Undisclosed)			moderna

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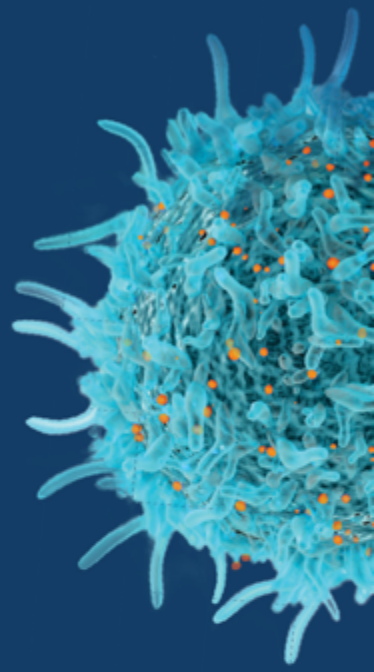
*CT-1119 development was paused pending further fundraising; 1. Anticipated milestones; 2.Moderna collaboration has nominated 5 total oncology targets, with the option to nominate an additional 5 oncology targets; First Development Candidate was nominated in 2Q 2024; GPC3:Glypican-3; 3. Includes SIRPα knockdown technology; 4: Carisma retains all rights in autoimmune disease beyond the two nominated targets, which will be exclusively partnered with Moderna.



Targeting HER2:
From CAR-Macrophages (CT-0508)
to CAR-Monocytes (CT-0525)

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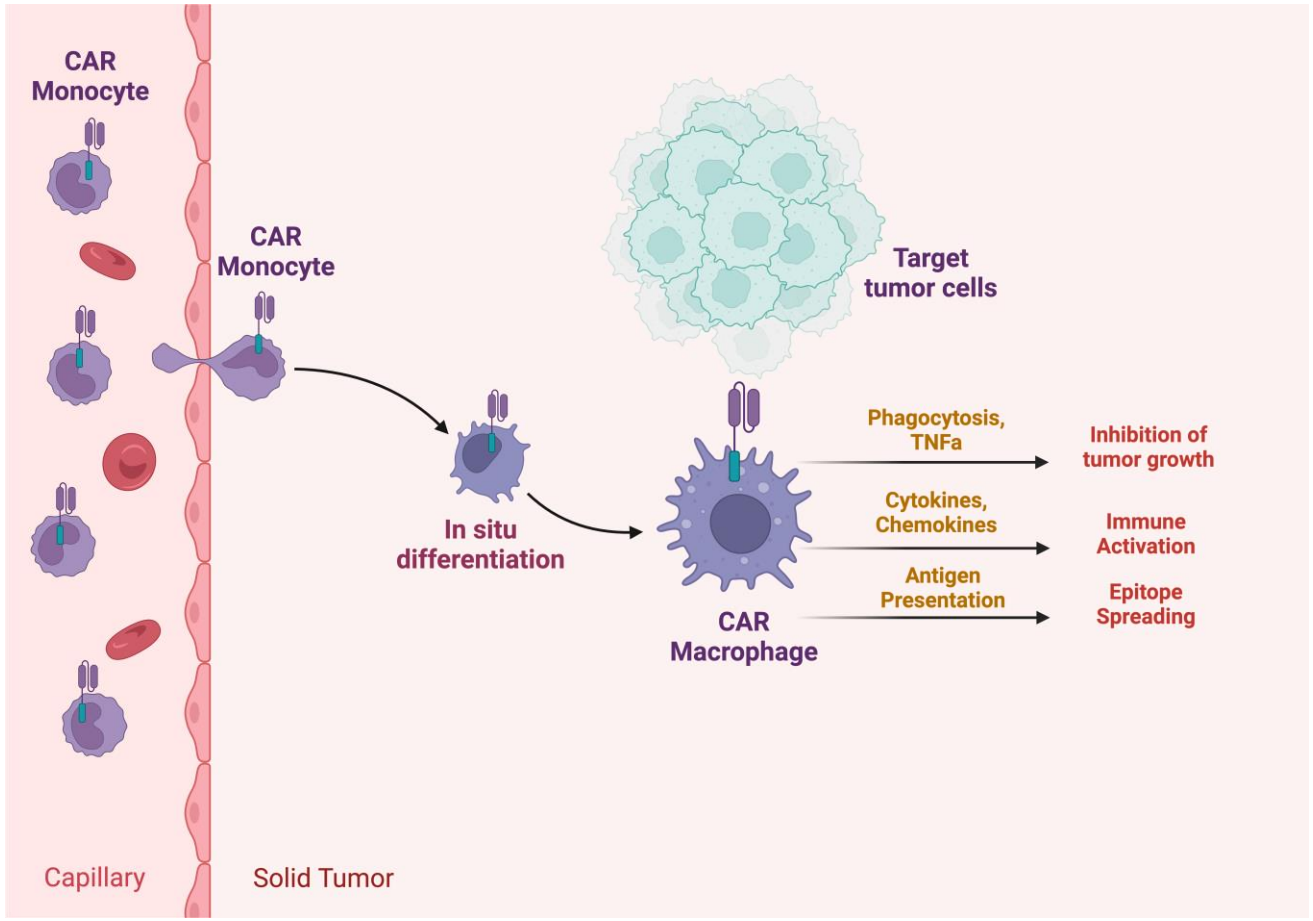
Macrophages are Ideally Suited for Solid Tumor Cell Therapy

CAR-M: Carisma's proprietary technology converts myeloid cells into targeted therapies with CARs

CAR-Monocytes differentiate into CAR-Macrophages *in vivo*

- Myeloid cells are abundantly recruited to tumors
- Carisma's proprietary platforms enable robust *ex vivo* and *in vivo* myeloid cell engineering with CARs
- The CAR-M mechanism of action includes:
  - Eradication of cancer cells via phagocytosis
  - Immune activation via cytokine release
  - Recruitment of immune cells via chemokine release
  - Antigen presentation to T cells leading to adaptive anti-tumor immunity
- Monocytes differentiate into macrophages in tissues
- Initial clinical development focused on monocyte-derived-macrophages to evaluate the safety of the final effector cell
- Ongoing development is focused on precursor monocytes which have biological, pharmacokinetic, and manufacturing advantages



Strong Rationale for Advancing anti-HER2 CAR-M Development

CT-0508 Phase 1 study

- ✓ **Primary Endpoints Achieved**: The study met potential goals for safety, tolerability, and manufacturing feasibility.
- ✓ **Monotherapy Study**: CT-0508 demonstrated tolerability and clear evidence of activity in advanced HER2 3+ solid tumor patients.
  - ✓ **Anti-Tumor Activity**: 75% of HER2 3+ patients showed a decrease in ctDNA, indicating anti-tumor activity.
- ✓ **Combination with Pembrolizumab**: The combination was well-tolerated and contributed to enhanced TME activation.

Informed Development of the Next-Generation CAR-Monocyte Platform

- ➢ Tumor biopsies illustrated the need for improved pharmacokinetics (persistence and trafficking) intended to be addressed by CT-0525
- ➢ Translational findings support future combination study with checkpoint inhibitors
- ➢ Safety data helped abbreviate dose escalation stage of CT-0525 Phase 1 study
- ➢ Study 102 enrollment is limited to HER2 3+ patients

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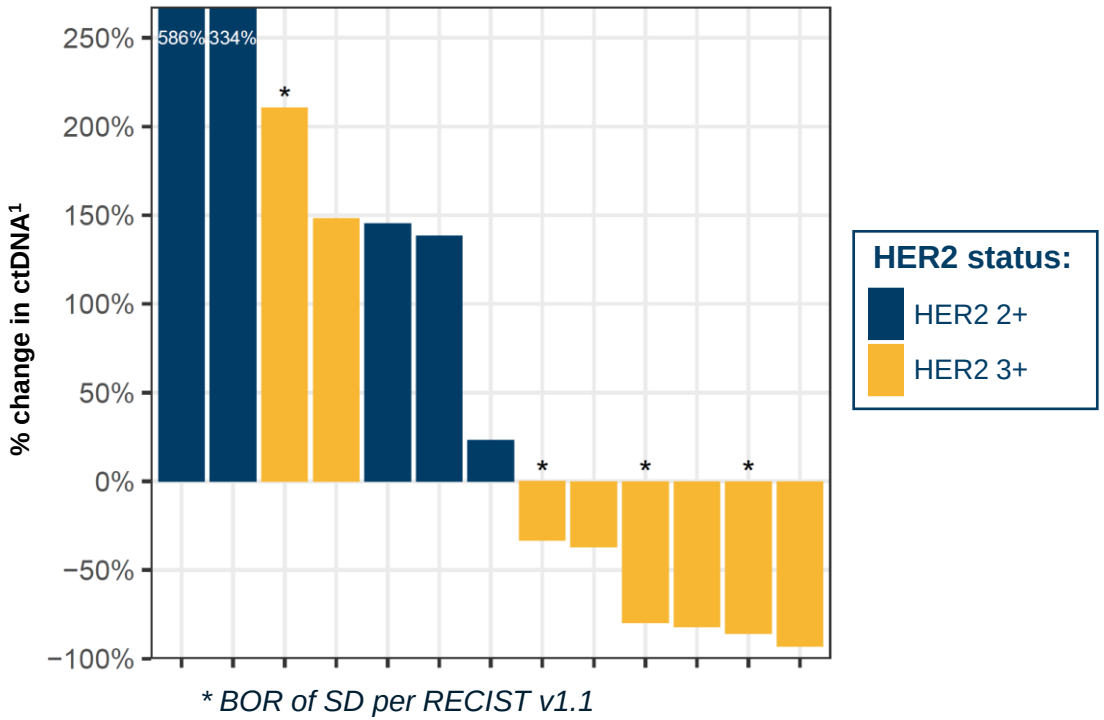
ctDNA: Circulating Tumor DNA; ctDNA is a biomarker of tumor burden; TME: Tumor Microenvironment

ctDNA Reduction Observed in 75% of HER2 3+ Patients

ctDNA reductions are clear evidence of clinical activity

Change in tumor ctDNA at week 4 based on HER2 status:



** BOR of SD per RECIST v1.1*

KEY TAKEAWAYS

- **Best Overall Response of Stable Disease** was seen in HER2 3+ (n=4/9, 44% SD)
- **75% (6/8) of HER2 3+ patients** exhibited a decrease in ctDNA, indicating anti-tumor activity
- **Up to 93% decrease in ctDNA levels**
- **Decreases were observed in multiple tumor** types
- **Peak response occurred ~4 weeks** post CT-0508 infusion, suggesting potential timing for redosing
- **Consistent with clinical assessments,** no decreases in ctDNA were observed in HER2 2+ patients

ctDNA: Circulating Tumor DNA; PFS: Progression-Free Survival; Signatera assay used for ctDNA; 1. From day 8 to week 4; PD: Progressive disease

CAR-Macrophage Monotherapy: Case Study

Clear but transient activity in patient with HER2 3+ inflammatory breast cancer with skin involvement

Cancer Type & Prior History

- Stage IV Inflammatory Breast Cancer (IBC)
- HER2 3+
- Patient progressed on 8 prior lines of therapy

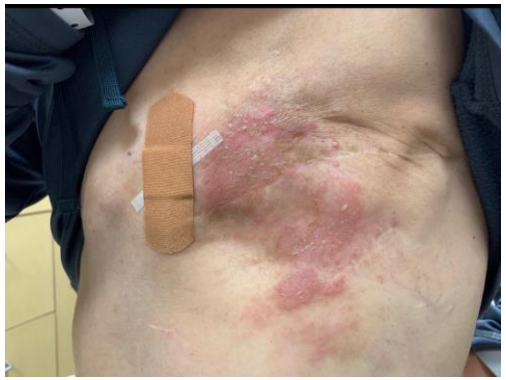
Dosing

- Patient received 1.3E+09 cells as bolus administration

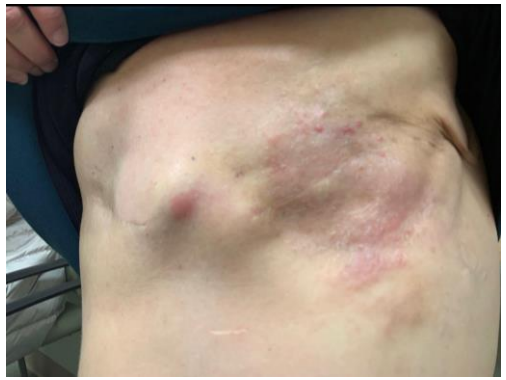
Clinical assessments

- 93% reduction in ctDNA at week 4, consistent with skin lesion improvement post infusion
- Overall response was mixed with transient activity
- Patient progressed at first on treatment scan per RECIST v1.1 (increase in target lesion and new lesion)

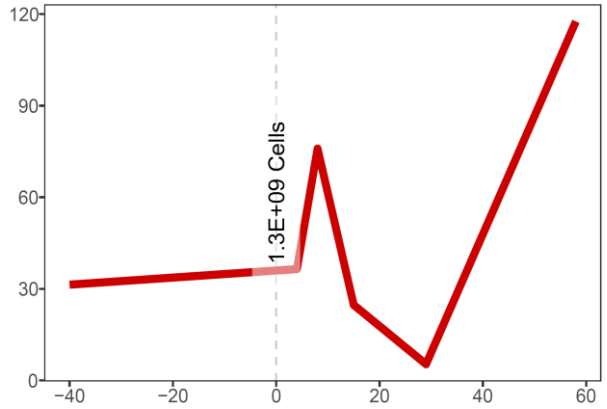
Prior to treatment



X weeks following treatment



Circulating Tumor DNA: 93% reduction

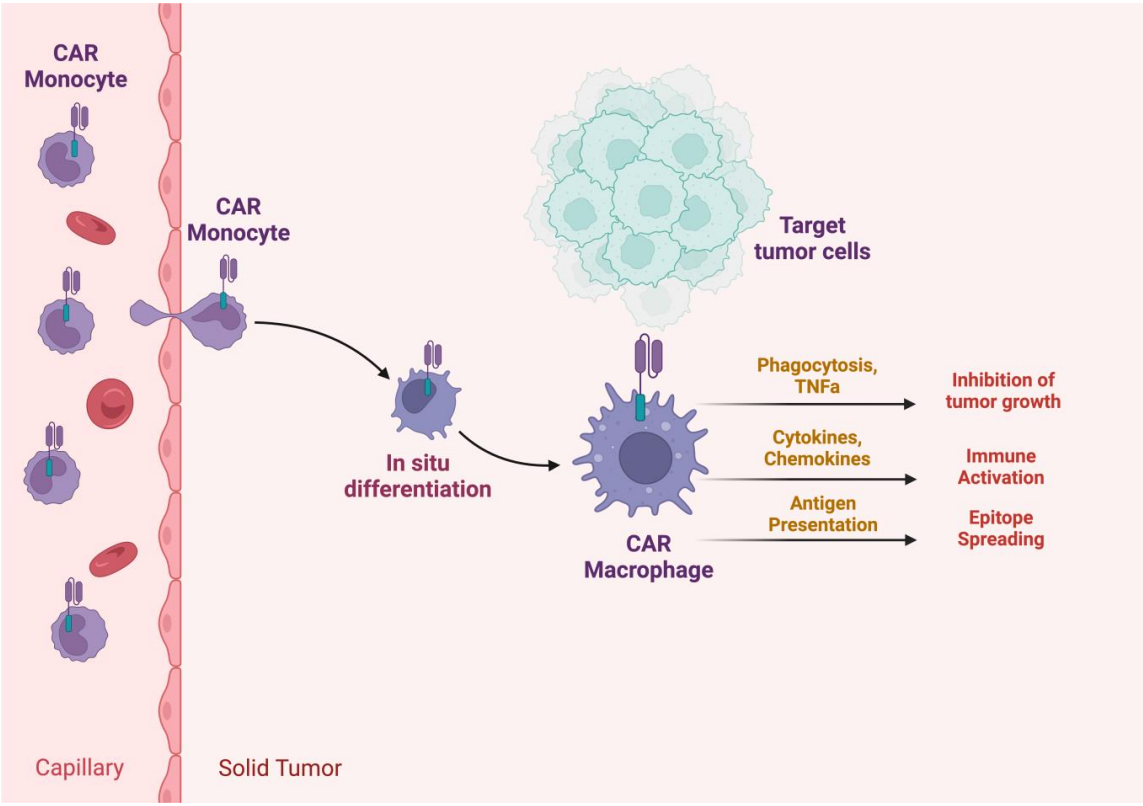


9th line HER2 3+ inflammatory breast cancer demonstrated transient improvement in cancerous skin involvement and concomitant deep reduction (93%) in ctDNA

From CAR-Macrophage to CAR-Monocyte:

CAR-Monocytes differentiate into CAR-macrophages *in vivo,* improving persistence, trafficking, and cell yield[1]

CAR-Monocyte Mechanism of Action:



Benefits to the CAR-Monocyte platform:

- Increased persistence[1]
- Increased tumor infiltration[1]
- Increased anti-tumor activity[1]
- *In vivo* differentiation into CAR-macrophages[1]
- Rapid manufacturing time (1 day)
- Increased cell yield enabling higher dose and dosing flexibility

Carisma's CAR-Monocyte Process:

- Proprietary, fully automated, autologous process with 1-day manufacturing
- Phenotype locked into M1 (inflammatory)
- High yield, CAR expression, viability and purity

CAR-Monocyte enables higher dose, improved persistence, enhanced trafficking, one day manufacturing, and potential for redosing[2]

1. Based on pre-clinical data, compared to macrophages; 2. Based on pre-clinical data

CT-0525: HER2 Targeted CAR-Monocyte (Macrophage Precursor)

Potential to significantly improve upon the observed biological activity of CT-0508

Highlights

Key Manufacturing Advantages Over CAR-Macrophage

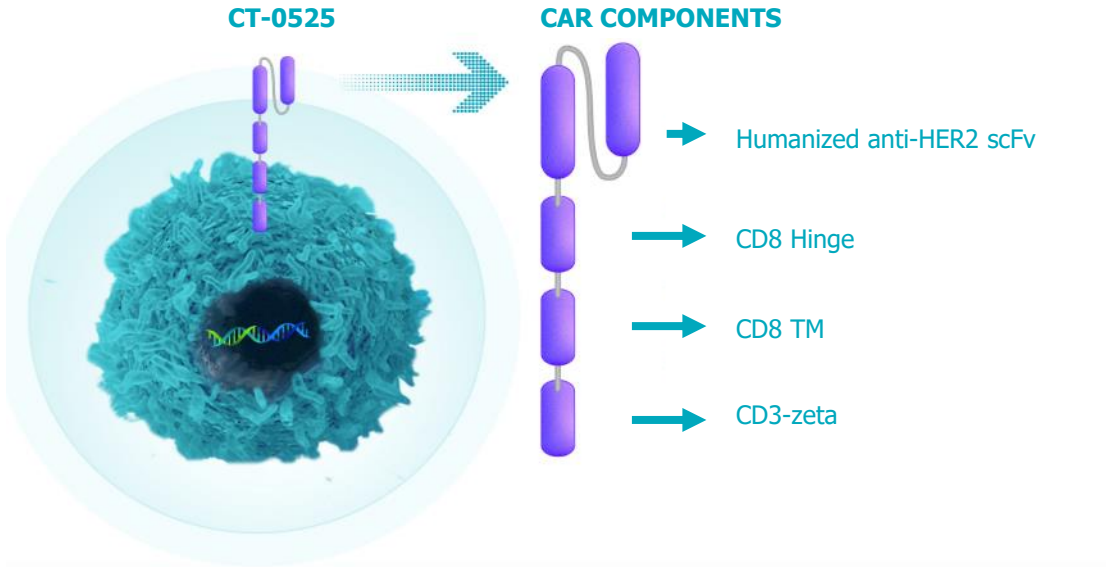
- Higher cell numbers
- Faster manufacturing (1 day)
- Reduced COGS

Potential Biological Advantages Over CAR-Macrophage

- 2,000-fold increased exposure
  - Manufacturing yield, trafficking, and persistence
- Increased potency
  - Killing, cytokine release, and antigen presentation
- Dosing flexibility (high yield enables redosing)

Development Plan & Timeline

- ✓ IND cleared
- ✓ First patient treated in 2Q 2024
- Initial data expected in 1Q 2025



	CT-0525 Product Description
Cells	Autologous monocytes
Vector	Ad5f35
Phenotype	M1
CAR	1st Generation

CT-0525 Directly Addresses the Key Limitations of CT-0508

Pre-clinical models demonstrate increased potency with ~2,000-fold increased exposure over CT-0508

Dose

5X↑

Cell Number

Trafficking

40X↑

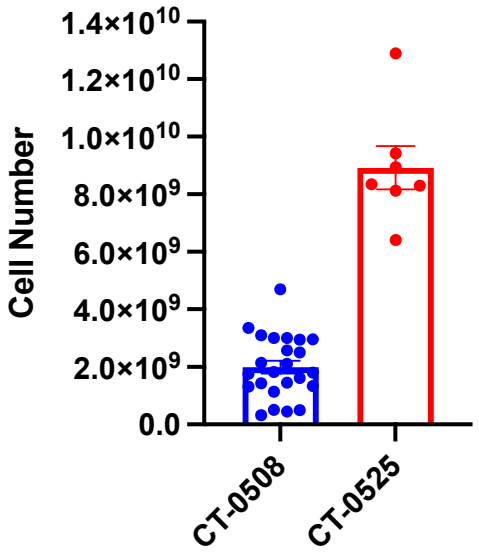
Tumor Infiltration

Persistence

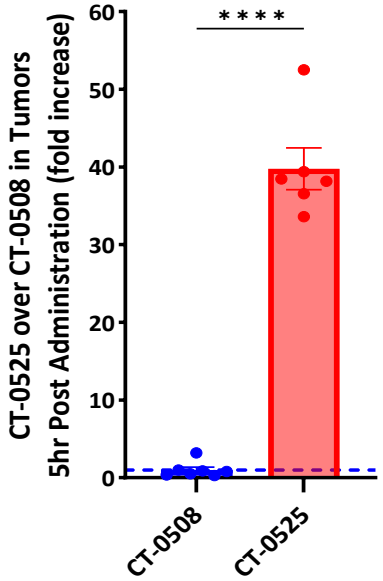
10X↑

in vivo half-life

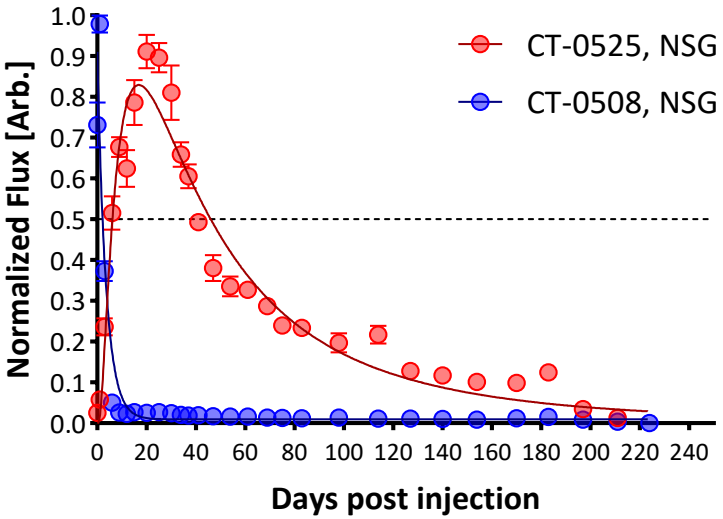
Cells Produced from Single Apheresis:



Trafficking in solid tumor model:



CT-0525 half-life is ~45 days*:



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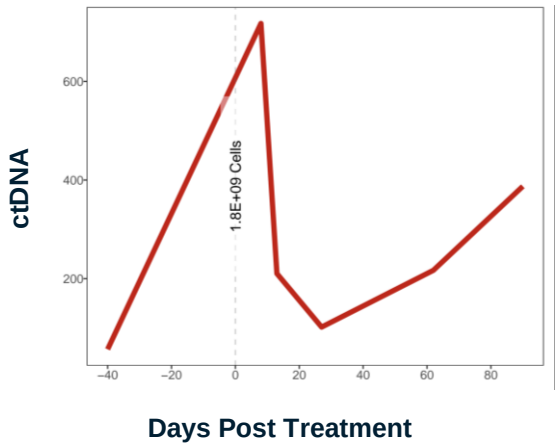
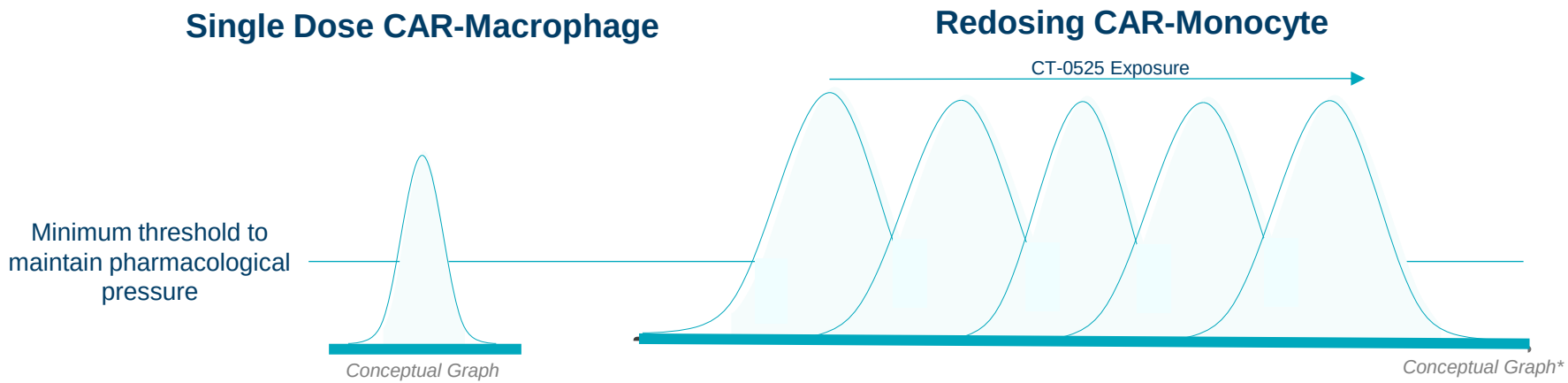
Human CAR-Mono persistence in NSG mice; CT-0508 - CAR-Macrophage

Potential to Enhance Response with Repeat Dosing of CT-0525

ctDNA: single dose CT-0508



Improved persistence plus redosing to increase potential response



Potential Development Strategies for CT-0525

- **Repeat dosing:** Maintain pharmacologic pressure on tumor to potentially deepen and prolong response
- **Combination therapy with pembrolizumab:** Potentially increases long-term anti-tumor immunity and may lead to durable clinical benefit

*Actual number of repeat doses will be determined clinically

CT-0525 Study 102: Phase 1 Clinical Trial Design

Assessing safety, tolerability, and manufacturing feasibility of CT-0525; additional analyses on TME impact

HER2 2+/3+ solid tumors (n≥6)

G-CSF mobilization and apheresis, CAR-Monocyte manufacture, bridging therapy, baseline staging

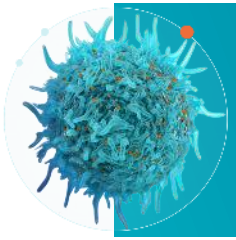
Cohort 1: Up to 3 billion cells of CT-0525 in bolus dose D1 (n≥3)

Cohort 2: Up to 10 billion cells of CT-0525 in bolus dose D1 (n≥3)

Cohort 3:
- **Repeat dosing of CT-0525 in combination with pembrolizumab**
- Bolus dosing of CT-0525 in combination with pembrolizumab
- Repeat dosing of CT-0525 monotherapy
- Bolus dosing of CT-0525 monotherapy

Enrolling

Expect to report initial data in 1Q 2025



PRIMARY OUTCOMES

- Safety and tolerability
- Manufacturing feasibility

SECONDARY OUTCOMES[1]

- In vivo cellular kinetics profile (levels, persistence, trafficking)
- ORR (RECIST 1.1)
- DOR

Biopsy performed at screening, Day 8, and Week 6; ORR: Objective Response Rate; DOR: Duration of Response; 1.Other tertiary/exploratory outcomes are being explored

CT-0525: Advancing the Next Stage of CAR-M Development

CT-0508 Phase 1 Study

- ✓ **Manufacturing:** Successfully Achieved
- ✓ **Safety:** Well-tolerated (both Monotherapy & Combination)
- ✓ **Clinical Activity**: Evidence of clinical activity observed

CT-0525 Phase 1 Study (Cohorts 1 and 2)

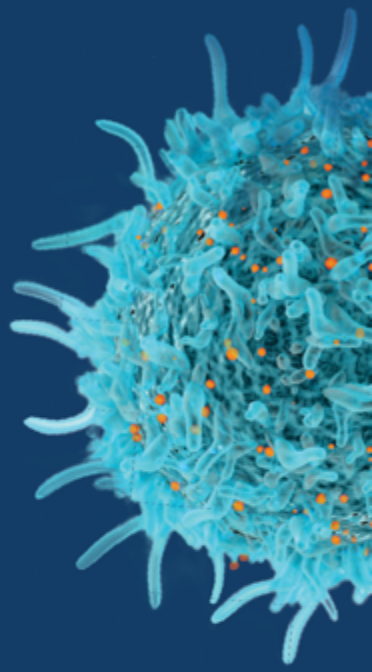
- **FDA Fast Track Designation:** Granted
- **Objectives**: Initial assessment of safety, tolerability, feasibility, and MOA
- **Study Status:** Enrolling
- **Upcoming Milestone:** Initial data anticipated in 1Q 2025

CT-0525 Phase 1 Study (Cohort 3)

- **Protocol:** Study 102 IND amended
- **Next Steps**: Cohort 3 to commence following Cohort 2 completion
- **Priority:** Repeat dosing in combination with Pembrolizumab

Advancing CT-0525: Carisma anticipates reporting initial Phase 1 data in 1Q 2025

In Vivo CAR-M: Oncology & Autoimmune disease



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In Vivo CAR-M

Collaboration with Moderna to discover, develop & commercialize *in vivo* CAR-M in oncology & autoimmune disease

Highlights

Collaboration Overview

- Combines Carisma's CAR macrophage technology with Moderna's mRNA/LNP platform
- *In vivo* CAR-M for oncology: First Development Candidate nominated, targets GPC3 for the treatment of HCC
  - Nomination triggered $2 million milestone payment to Carisma
- *In vivo* CAR-M for autoimmune disease: Nominated two targets[1]

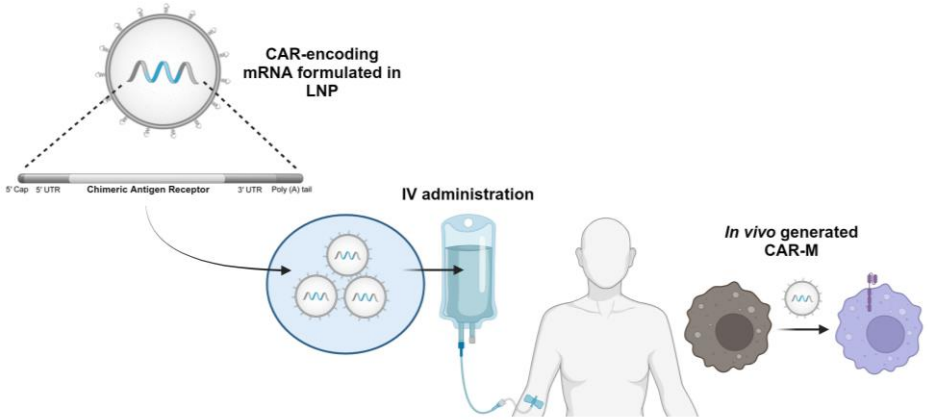
Key Advantages of *in vivo* CAR-M

- Robust platform with applications in diverse indications
- Off-the-shelf product with ability to re-dose
- Maintains functionality of *ex vivo* CAR-M

Key Takeaways from Pre-clinical Data

- mRNA/LNP CAR-M are highly functional
- *In vivo* CAR-M controls tumors upon regional or systemic administration and clears metastasis
- *In vivo* CAR-M well-tolerated in pre-clinical models

Redirecting endogenous myeloid cells with mRNA for cancer immunotherapy



carisma THERAPEUTICS	Collaboration Terms	moderna
Number of Targets	Up to 12 (7 nominated)	
Upfront Payment	$80M	
Total Potential Milestones and Royalties	$3B+	
R&D Funding	Fully funded by Moderna	

mRNA: Messenger RNA; LNP: Lipid Nanoparticle; GPC-3: Glypican-3; HCC: Hepatocellular carcinoma; 1:Carisma retains all rights in autoimmune disease beyond the two nominated targets, which will be exclusively partnered with Moderna.

Glypican-3 (GPC3): A validated target in HCC

HCC remains an area of significant unmet medical need

HCC overview:

- **>40,000 new cases** in the US in 2024**, and the 2nd leading** cause of cancer-deaths worldwide[1,2]
- **22% 5-year** survival for all HCC cases; **3.5% 5-year** survival for advanced HCC[1]

GPC3

- GPC3 is a cell surface tumor-associated antigen
- Overexpressed in 70-80% of HCC cases, linked to poor prognosis[2]
- Silenced postnatally, minimally expressed in healthy tissues[2]
- Safety demonstrated with antibodies, ADCs, and CAR-T cells[2]
- No approved GPC3-targeted therapies

Development Candidate

- Direct *in vivo* CAR-M utilizing mRNA/LNP encoding a novel, next-gen CAR targeting GPC3
- Preclinical data demonstrates that anti-GPC3 CAR mRNA/LNP induces robust anti-tumor activity in humanized metastatic solid tumor model[3]

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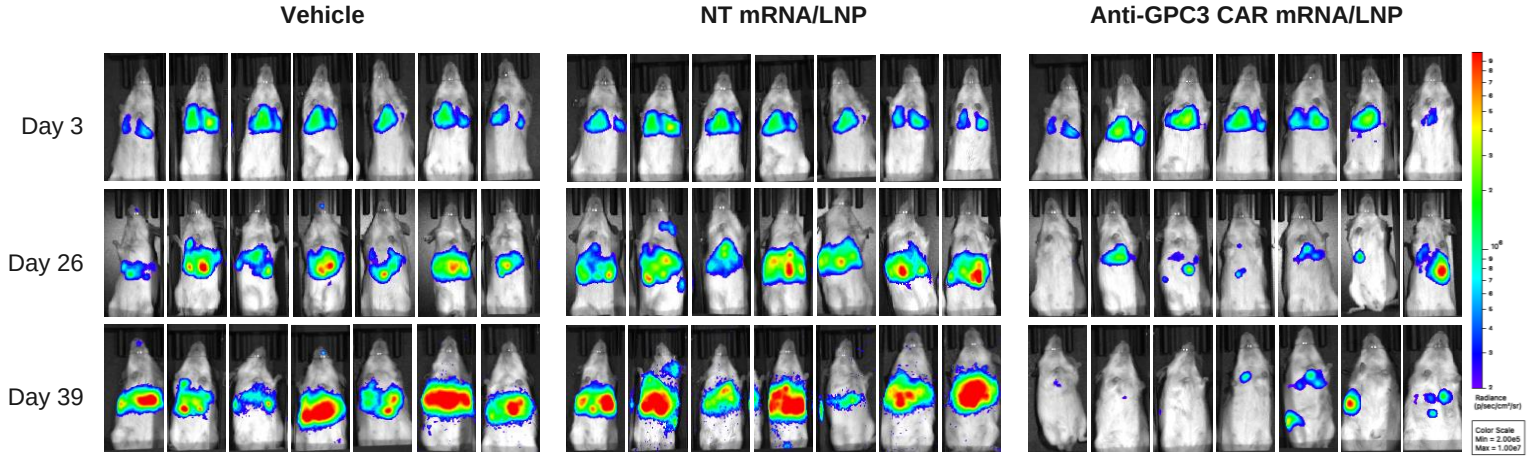
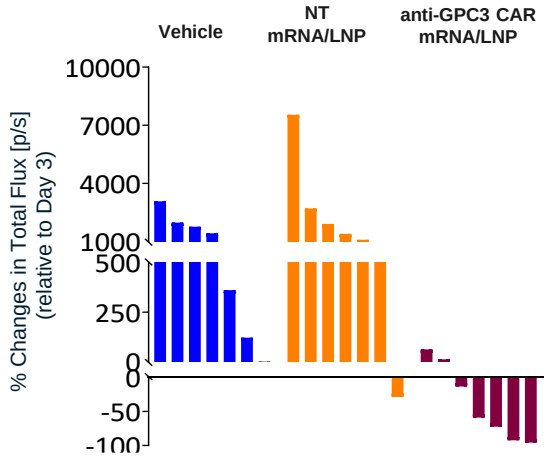
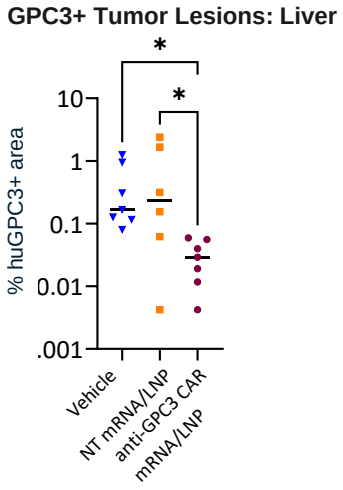
HCC: Hepatocellular carcinoma; SITC: Society for Immunotherapy of Cancer; 1. SEER Cancer Stat Facts: Liver and Intrahepatic Bile Duct Cancer. National Cancer Institute; 2. Guo M, Zhang H, Zheng J, Liu Y. Glypican-3: a new target for diagnosis and treatment of hepatocellular carcinoma. J Cancer. 2020;11(8):2008-2021; 3: Bagashev A, et al. SITC 2024.

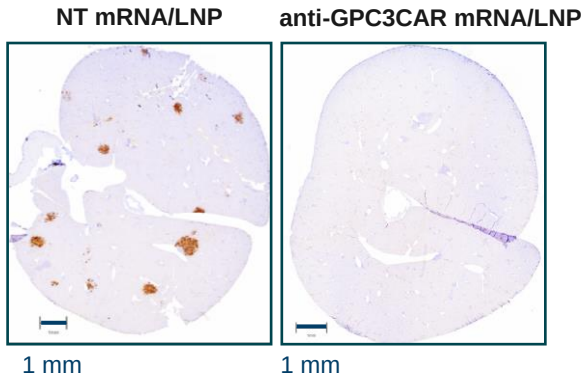
Anti-GPC3 *In Vivo* CAR-M Induces Robust Anti-Tumor Activity*

Advanced/metastatic HCC remains an area of significant unmet medical need









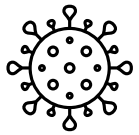
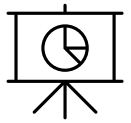
- GPC3 is highly overexpressed on HCC with minimal normal tissue expression
- Systemic administration of anti-GPC3 CAR mRNA/LNP **induces robust anti-tumor** activity in humanized metastatic solid tumor model

In vivo reprogramming of myeloid cells with CARs using mRNA/LNP offers a **promising off-the-shelf** therapy for advanced solid tumors, including HCC.

1: Bagashev A, et al. SITC 2024.; HCC: Hepatocellular carcinoma;; NT: Non-translating control; CAR: Chimeric antigen receptor; GPC3: glypican-3; *Pre-clinical data

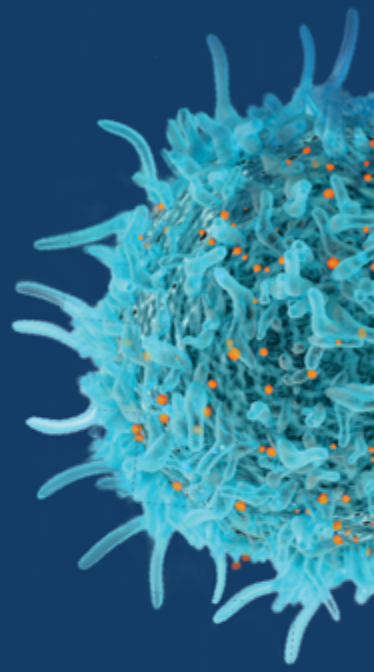
In Vivo CAR-M: Next Steps

Strategic alliance, fully funded by Moderna

Rationale	PoC achieved	Next Steps
		
• **Off-the-shelf:** *In vivo* CAR-M are LNP/mRNA based and engineer patient myeloid cells directly within their body	✓ **Robust data:** • **Platform:** Pre-clinical data demonstrate robust production of CAR-M *in vivo* leading to anti-tumor activity in multiple models • **GPC3 target** validated preclinically	• **Lead Program:** Advance lead program, a GPC3 targeted *in vivo* CAR-M, into clinic for HCC • **Advance four additional** oncology[1] targets • **Advance two autoimmune** disease targets • **Expand** the universe of selected targets

mRNA: Messenger RNA; LNP: Lipid Nanoparticle; PoC: Proof of concept; 1: Five additional oncology targets that can be nominated under Moderna Collaboration.

Developing macrophage cell therapies beyond oncology: Fibrosis



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Macrophages have Robust Anti-fibrotic and Anti-inflammatory Potential

Substantial Unmet Need In Liver Fibrosis

Large (and growing) patient population

Limited success in improving fibrosis in late-stage MASH patients

Clinical Evidence of Macrophage Cell Therapy

Non-engineered macrophage cell therapy has demonstrated therapeutic potential in the clinic[1,2]

Promising Preclinical Results from Engineered Macrophages

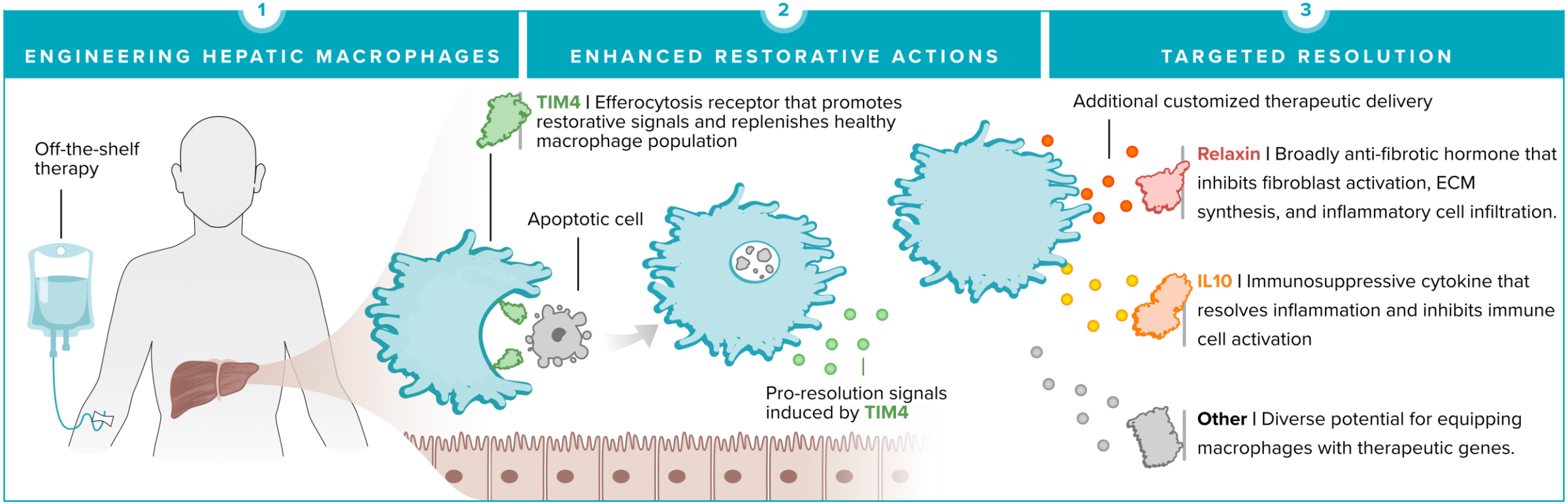
Carisma's engineered macrophages have shown significant reduction of established liver fibrosis in multiple preclinical studies[3]

Carisma's pre-clinical proof-of-concept data demonstrate that engineered macrophages can improve liver fibrosis and outperform non-engineered macrophages[3]

1: Moroni F, et al. Nature Medicine, 25, 1560–1565 (2019); 2. Brennan P, et al. AASLD 2023; Abstract 160; 3: Sloas C, et al. ASGCT 2024; Sloas C, et al. AASLD 2024.

Carisma's Platform: Engineered Anti-fibrotic Macrophages

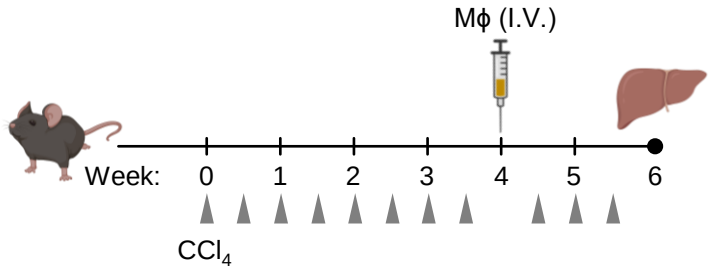
Engineering hepatic macrophages to address the underlying pathology in liver fibrosis



ECM: Extracellular matrix

A Single Dose of Engineered Macrophages Significantly Reduced Liver Fibrosis[1]

CCl4 model of established fibrosis

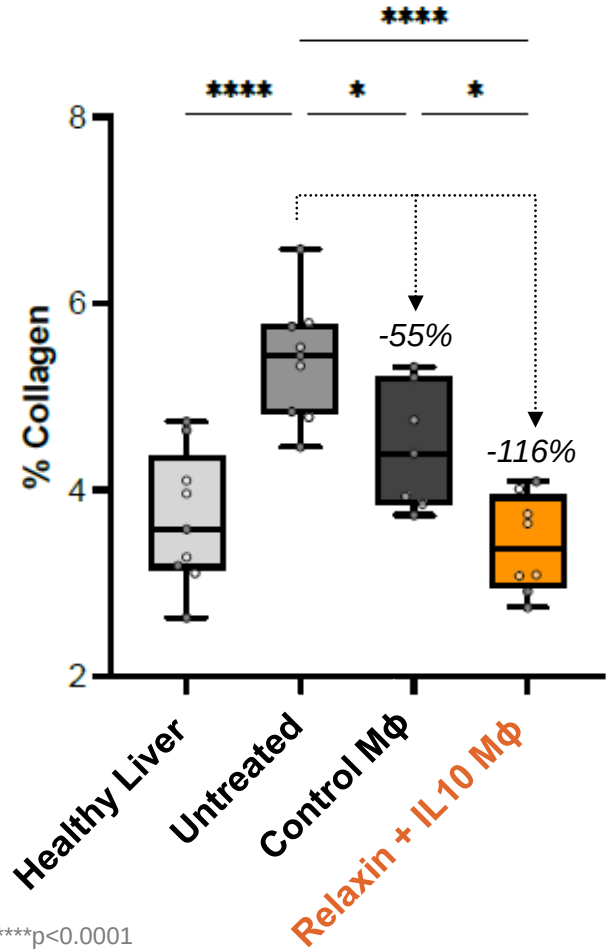


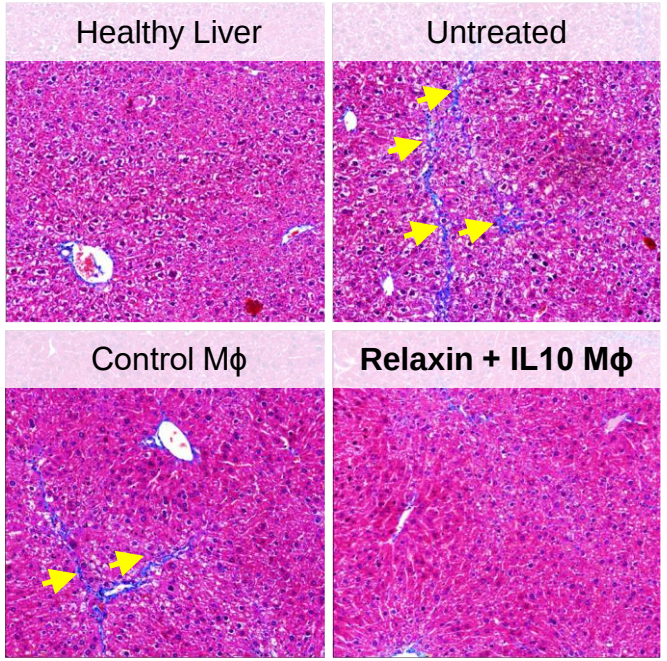
Engineered Mϕ significantly reduced hepatic collagen

Control Mϕ:
- **55%** reduction in collagen

Relaxin-IL10 Mϕ:
- **>100%** reduction in collagen[2]
- 8/8 mice return to healthy range

Relaxin-IL10 macrophages significantly reduced established fibrosis



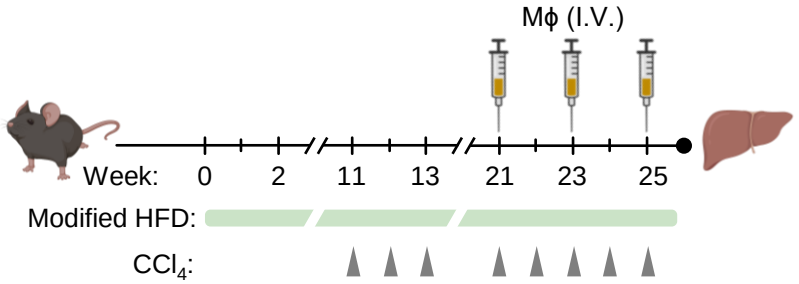


Masson's Trichrome Staining
Fibrosis shown in blue

Mϕ: Macrophage; CCl4: Carbon tetrachloride;
1: Sloas C, et al. ASGCT 2024.; 2: Compared to Untreated; *p<0.05; ****p<0.0001

Engineered Macrophages Reduced Liver Fibrosis in a High Fat Diet-Induced Model[1]

High fat diet MASH model

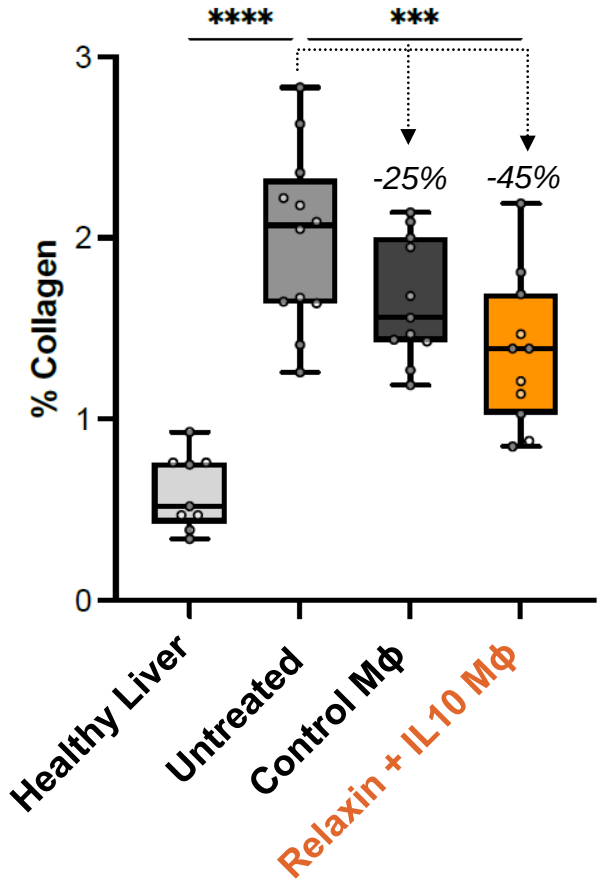


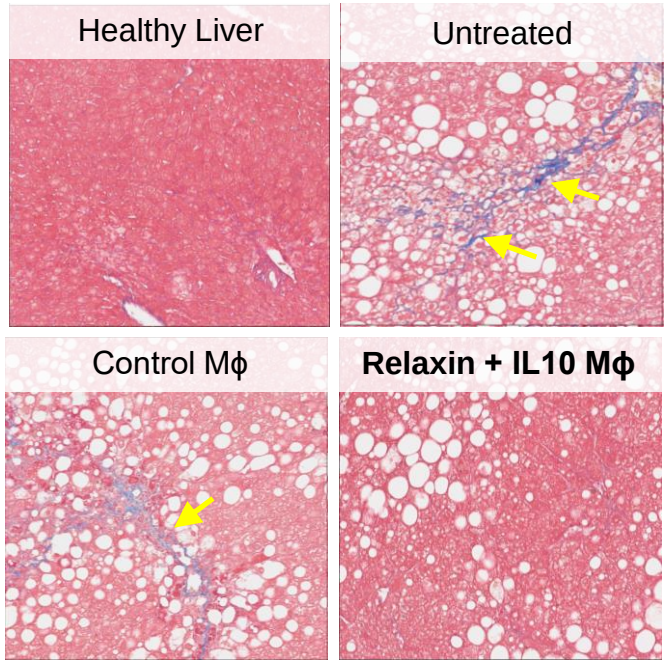
Engineered Mϕ significantly reduced fibrotic collagen

Control Mϕ:
- **25%** reduction in collagen

Relaxin-IL10 Mϕ:
- **45%** reduction[2]

Relaxin-IL10 macrophages significantly reduced fibrosis

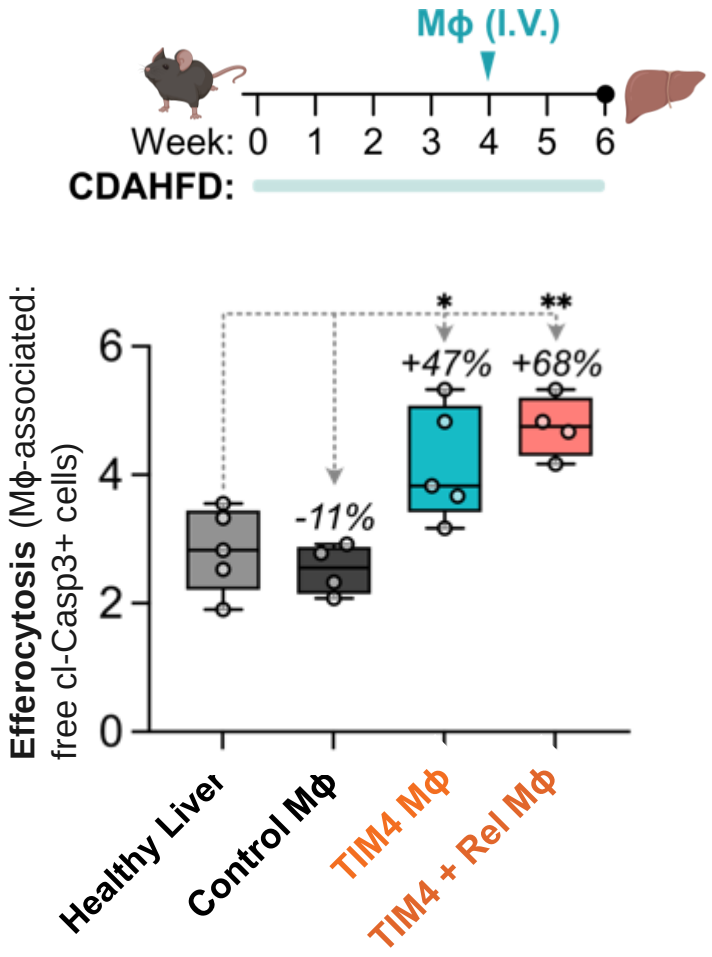


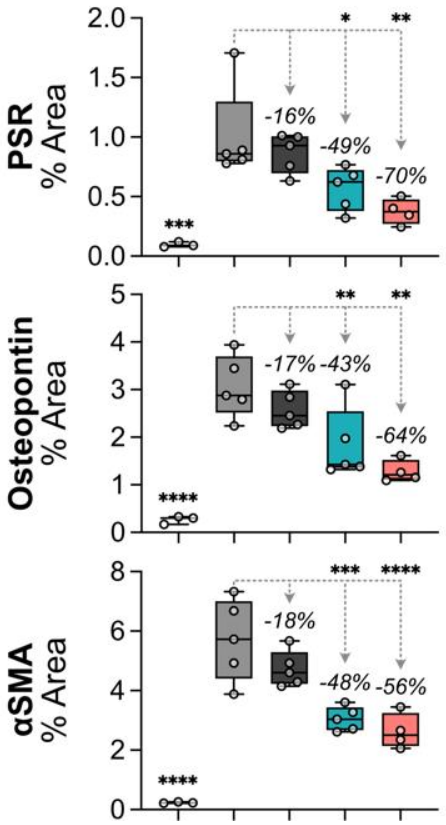


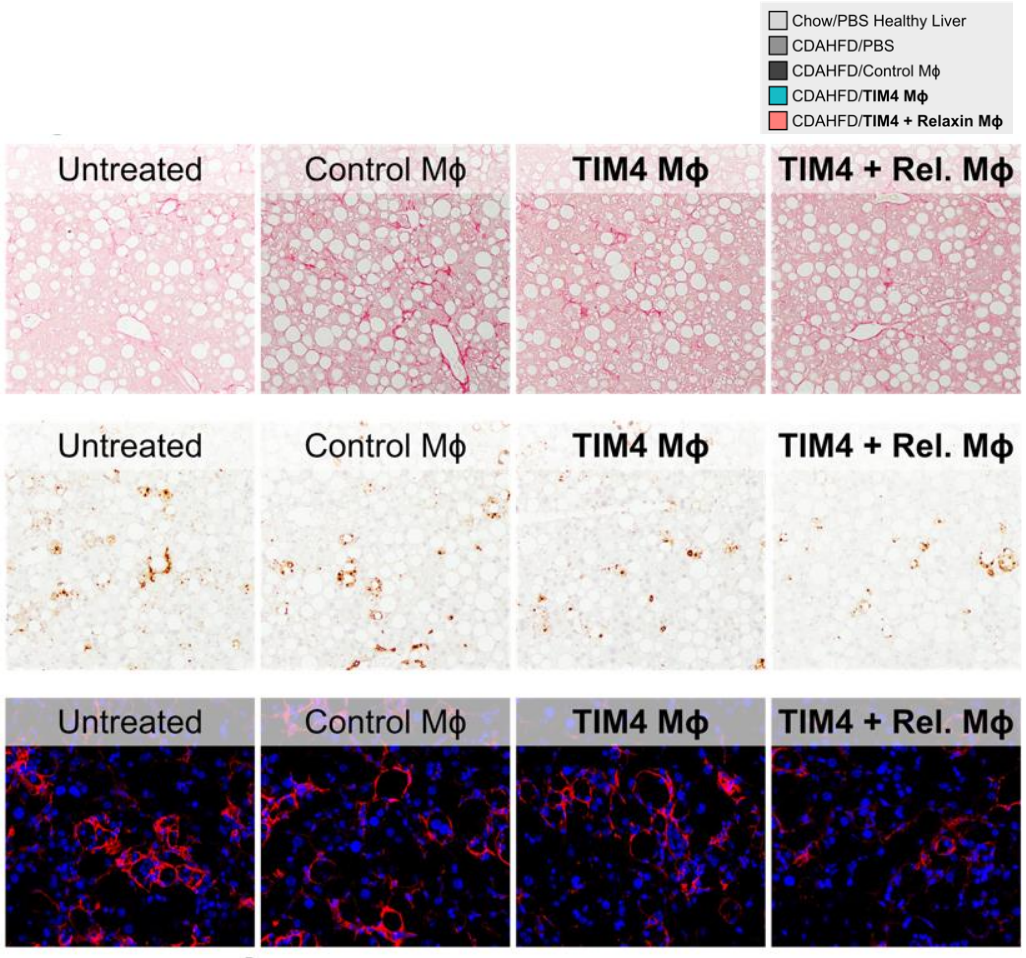
Masson's Trichrome Staining
Fibrosis shown in blue

Mϕ: Macrophage; CCl4: Carbon tetrachloride; MASH: metabolic dysfunction-associated steatohepatitis; 1: Sloas C, et al. ASGCT 2024.; 2: Compared to Untreated; ***p<0.001; ****p<0.0001

Engineered efferocytic macrophages expressing TIM4 improve fibrosis in a CDAHFD model[1]





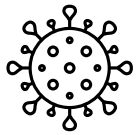
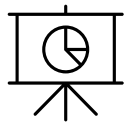


PSR and Immunohistochemistry

Mϕ: Macrophage; CCl4: Carbon tetrachloride; CDAHFD: Choline-deficient, L-amino acid-defined, high-fat diet; **Rel.:** Relaxin; **αSMA:** Alpha smooth muscle actin; **PSR:** Picrosirius red;
1: Sloas C, et al. AALSD 2024.

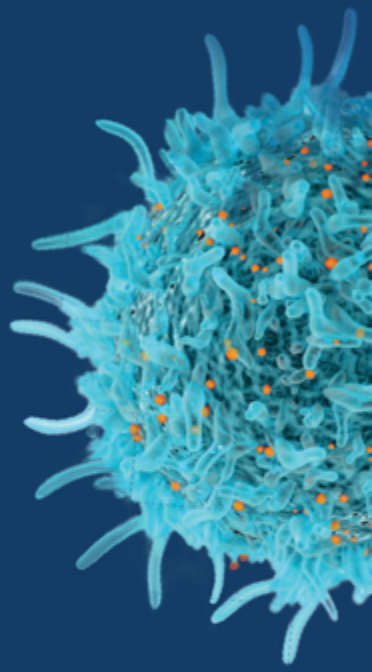
Liver Fibrosis: Next steps

Wholly-owned program

Rationale	PoC achieved	Next Steps
		
• **Resolution of liver fibrosis**: Engineered macrophages enhance innate activity of macrophages in liver • **Off-the-shelf:** Development of an off-the-shelf **approach** ongoing	✓ **Preclinical** results demonstrate that macrophages can be genetically engineered to target specific key pathways underlying liver disease with factors including **TIM4, Relaxin and IL10**[1] ✓ **Clinical data** with non-engineered macrophages have shown clinical benefit in patients	• **Optimize** anti-fibrotic constructs • **Nomination** of development candidate expected in 1Q 2025 • **Expand** fibrosis program beyond liver

PoC: Proof of concept; AASLD: American Association for the Study of Liver Diseases; 1: Sloas C, et al. ASGCT 2024; Sloas C, et al. AASLD 2024.

Corporate & Financial



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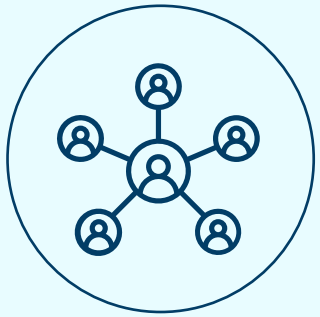
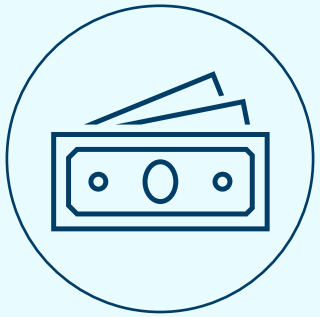
Financial Snapshot

As of September 30, 2024



41.5M

Shares outstanding



$26.9M

Cash and cash equivalents

Into 3Q 2025

Expected cash runway

Operating Plan and Corporate Milestones

Capital efficient R&D program designed to reach significant value inflection points

INDICATION	PRODUCT CANDIDATE	PLATFORM	RECENT AND ANTICIPATED MILESTONES	
Oncology				
HER2+ solid tumors	CT-0525	CAR-Monocyte (Autologous)	**4Q'23** IND cleared	✓
			2Q'24 Treat first patient	✓
			1Q'25 Report initial data from Phase 1 study	□
GPC3+ solid tumors	Undisclosed	CAR-M/mRNA/LNP (*In Vivo*)	**4Q'23** Nominate first *in vivo* CAR-M lead candidate	✓
			2Q'24 Development Candidate nominated	✓
			TBD IND submission	□
Undisclosed	4 Nominated Targets[1]	CAR-M/mRNA/LNP (*In Vivo*)	**TBD** Nominate next lead candidate	□
Fibrosis and Immunology				
Liver Fibrosis	TBD	Engineered macrophage	**2Q'24** Report preclinical proof of concept data (ASGCT 2024)	✓
			1Q'25 Nominate Development Candidate	□
Autoimmune disease	2 Nominated Targets	CAR-M/mRNA/LNP (*In Vivo*)	**TBD** Nominate lead candidate	□

1. Moderna collaboration has identified 5 total oncology targets, with the option to identify an additional 5 oncology targets

THANK YOU

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APPENDIX

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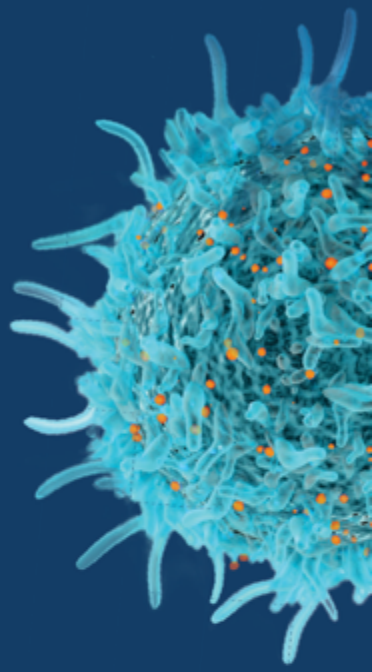
Carisma Platform



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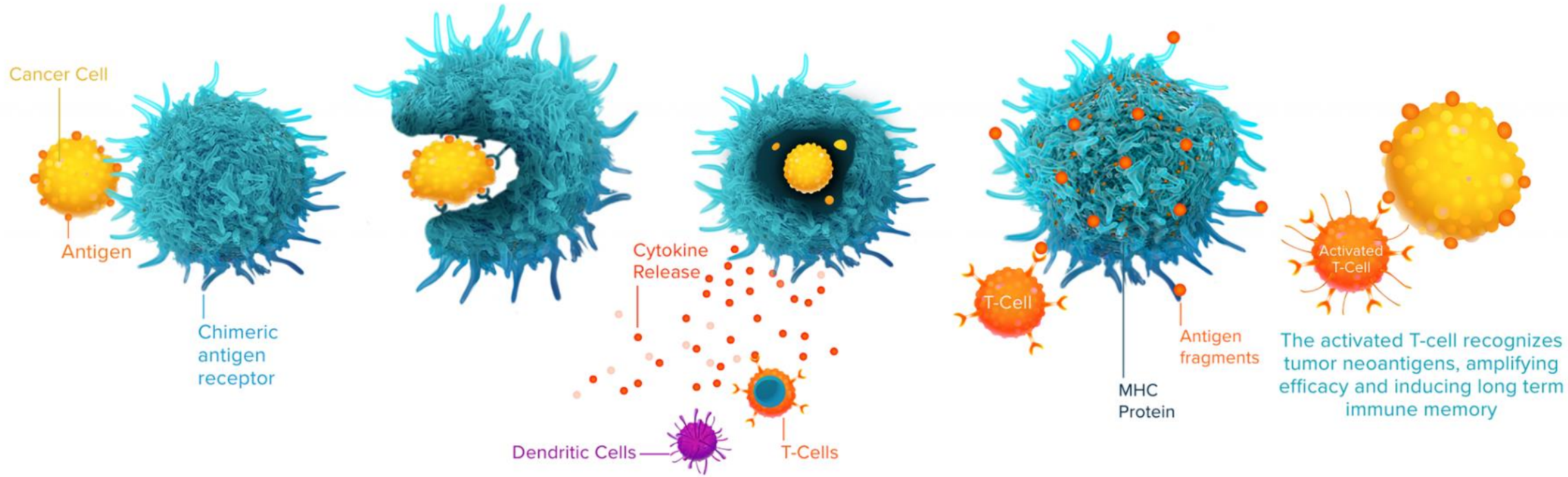
CAR-M Mechanism of Action in Oncology

Potential to address the challenges of treating solid tumors with cell therapies

1 TRAFFICKING & PHAGOCYTOSIS	2 IMMUNE ACTIVATION	3 ANTIGEN PRESENTATION

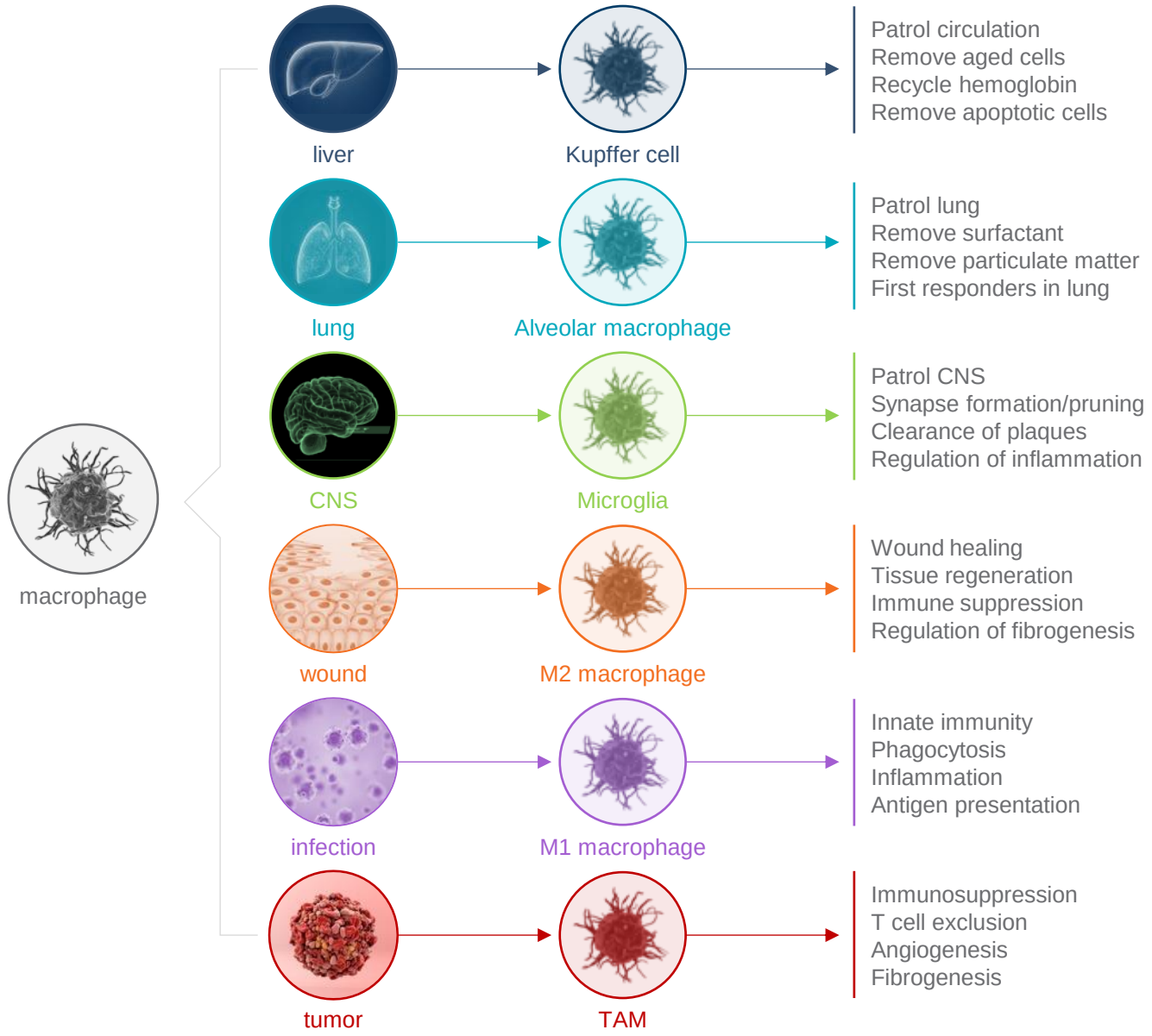


MHC: Major Histocompatibility Complex

Macrophages:
The Ultimate Multitasker

Macrophages can:

- Traffic to tumors/inflammation
- Phagocytose
- Initiate immune response
- Present antigen to T-cells
- Resolve fibrosis
- Induce tissue regeneration
- Resolve immune response

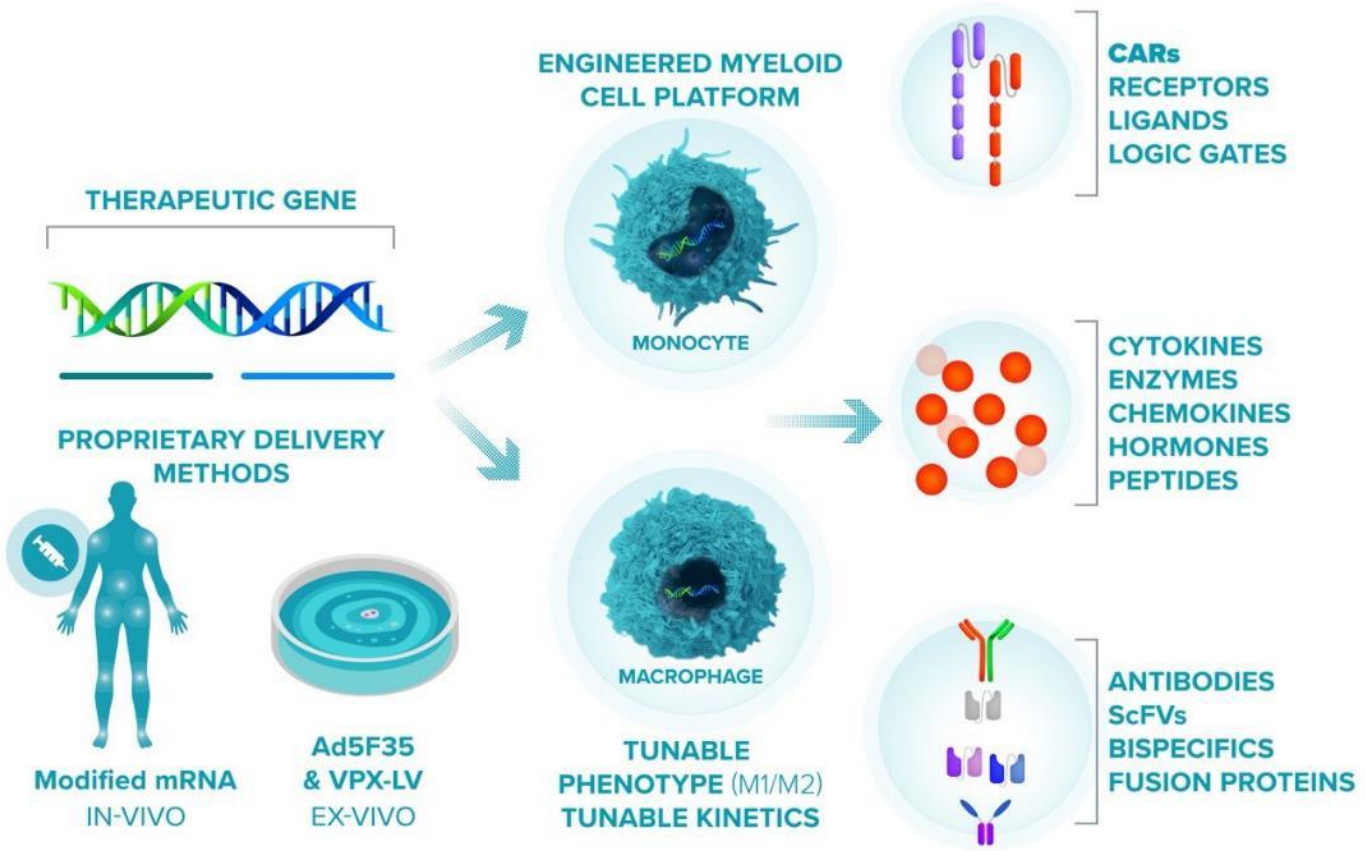


CARISMA's Broad Myeloid Cell Engineering Platform

Proprietary technology, world-leading macrophage engineering know-how, and strong IP position ensure leadership position

Monocyte & Macrophage Engineering Capabilities:

- **Proprietary platforms** for robust/durable monocyte & macrophage engineering
- **Established rapid GMP manufacturing** processes for monocytes and macrophages
- **In vivo myeloid cell reprogramming** using LNP/mRNA technology
- **Novel next-gen CAR constructs**
- **Cytokine targeting** with switch receptor platform
- Applications **beyond oncology**



Strong Patent Position

Broad Coverage for Monocyte and Macrophage Targeted Therapies

37

PATENTS GRANTED WORLDWIDE*

100+

PATENT APPLICATIONS PENDING WORLDWIDE*

- Worldwide patent coverage with issued and pending applications in major markets
- Multiple issued US patents covering CAR-M composition of matter
- Broad patent portfolio covering:
  - Viral and non-viral methods for engineering monocytes and macrophages
  - Methods for treatment of protein aggregate disorders
  - Methods for in vivo targeting of monocytes and macrophages

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* Total includes Carisma-owned patents and patents exclusively licensed from The University of Pennsylvania and New York University

Strong Leadership Team and Advisors

Deep research, clinical and operational expertise in cell and gene therapy and oncology

Management

STEVEN KELLY
President &
Chief Executive Officer

MICHAEL KLICHINSKY, PHARMD PHD
Co-Founder &
Chief Scientific Officer

EUGENE KENNEDY, MD
Chief Medical Officer

KENNETH LOCKE
SVP, Technical Operations

RICHARD MORRIS
Chief Financial Officer

TERRY SHIELDS
SVP, Human Resources

ERIC SIEGEL
General Counsel &
Corporate Secretary

TOM WILTON
Chief Business Officer

Board of Directors

- Sanford Zweifach – Chairperson
- Steven Kelly – President and CEO
- Briggs Morrison, MD – Independent Director
- John Hohneker, MD – Independent Director
- David Scadden, MD – Independent Director
- Marella Thorell – Independent Director
- Sohanya Cheng– Independent Director

Scientific Advisory Board

- Saar Gill, MD, PhD – Penn (Co-Founder, Co-Inventor)
- Carl June, MD – Penn (Co-Inventor)
- Hy Levitsky, MD – Century Tx (Advisor)
- Prasad S. Adusamilli, MD FACS – MSKCC
- Nina Bhardwaj, MD, PhD – Mt Sinai
- Lisa Coussens, PhD – OHSU
- Lin Guey, PhD – Moderna Tx
- Scott Friedman, MD – Mt Sinai
- Ira Tabas, MD, PhD – Columbia University

CAR-Monocytes: Differentiated from CAR-T and CAR-NK

CAR-M has advantages that are potentially key for solid tumor oncology

	CAR-T	CAR-NK	CAR-Mono
Mechanism of Action			
Effector Cell	CD4/CD8 T cells	Natural Killer Cells	Monocytes
Persistence	Months/Years	Days/Weeks	45-day half-life*
Trafficking Potential	Low	Low	High
TME Activation	Low	Low	High
Antigen Presentation	None	None	High
Epitope Spreading	Low	Low	High
Safety			
Chemotherapy Conditioning	Yes	Yes	No
CRS / ICANS	High / High	Low / Low	Low / Low
Manufacturing			
Manufacturing Time	Days to weeks	Days to weeks	1 day

CAR-M has direct anti-tumor effects as well as immune activation

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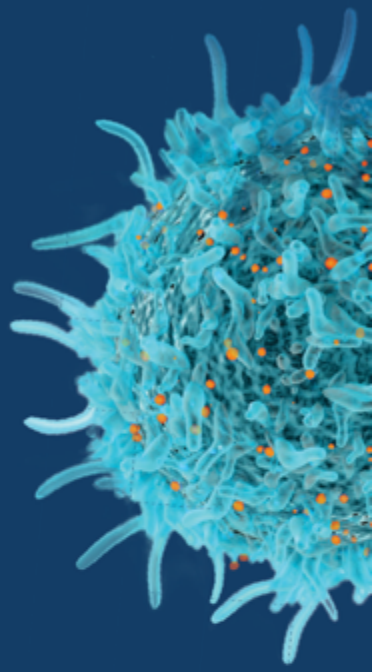
* Human CAR-Mono persistence in NSG mice

CAR Monocytes: Numerous Advantages Over CAR Macrophages

	CAR Macrophage	CAR Monocyte
Cell Characteristics		
Origin	Monocyte-derived macrophage (ex vivo differentiated for 7 days)	CD14+ monocyte from peripheral blood
Natural location	Macrophages: Various tissues	Monocytes: Blood
Cell size	16-20µm	10µm
Differentiation Potential	M1/M2 polarization in response to cytokines	Macrophages or dendritic cells
Trafficking Potential	Low (tissue resident cells)	High (blood to tissue via chemotaxis)
Persistence	Limited (5-day half-life)	High (45-day half-life)
Mechanism of Action		
Direct Killing/Phagocytosis	Yes	Yes; increases w/ differentiation
Cytokine/Chemokine Release	Yes	Yes
Antigen Presentation	Yes	Yes
Manufacturing/Dosing		
Manufacturing Time	8 days	1 day
Cell Yield Per Apheresis	~$2x10^9$	Up to $1x10^{10}$
Chemotherapy Conditioning	No	No
Ability to Re-dose	Limited	Up to 5 doses per apheresis

Targeting HER2:
CT-0525



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CT-0525 Manufacturing Process

One day, automated process yielding up to 5x more cells per apheresis than CT-0508

Highlights

CAR Expression: >90%*

Viability: >90%*

Purity: >95%*

Ad5f35 (adenovirus) based process

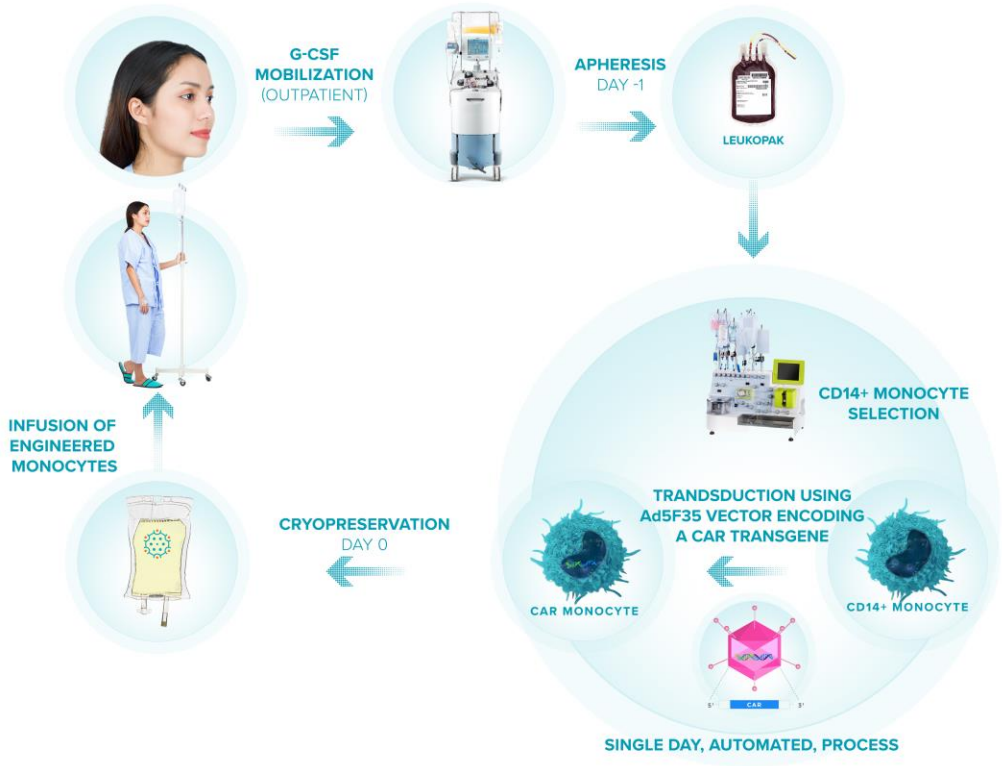
Monocytes are primed to support *in situ* differentiation into M1 macrophages

---

First patient successfully manufactured/treated in 2Q 2024

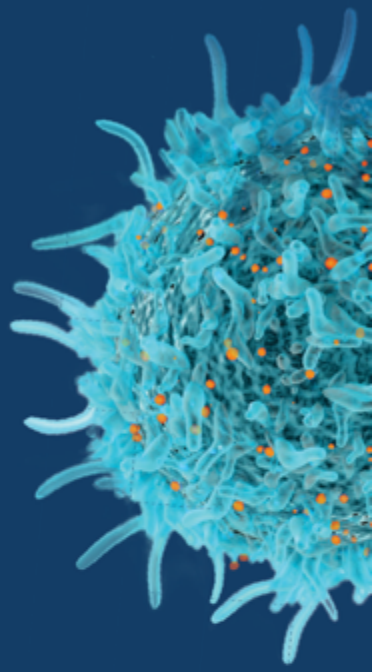
Can produce up to 10B cells

CAR-Monocyte Rapid Manufacturing Process



* Average from healthy donor development batches

Targeting HER2:
CT-0508 Monotherapy



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CT-0508 Study 101: First in Human Phase 1 Clinical Design

Assessing safety, tolerability, feasibility and TME impact of CT-0508 monotherapy

HER2 2+/3+ solid tumors

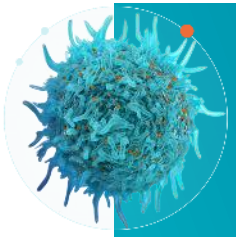
G-CSF mobilization and apheresis, CAR-Macrophage manufacture, bridging therapy, baseline staging

Group 1: CT-0508 fractionated dose D1,3,5 (n=9) — **Data Reported**

Group 2: CT-0508 bolus dose D1 (n=5) — **Data Reported**

Pembro Sub-study: CT-0508 + pembrolizumab — **Data Reported**

Demonstrated manufacturing feasibility, safe administration, cell trafficking from blood to tumor, cells resided in tumor for up to 4 weeks, positively modulated TME[1]



PRIMARY OUTCOMES[2]

- Safety and tolerability
- Manufacturing feasibility

SECONDARY OUTCOMES & ADDITIONAL ANALYSES[2]

- ORR (RECIST 1.1)
- PFS
- Trafficking
- TME activation
- T cell recruitment/activation
- T cell expansion/clonality

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Biopsy performed at screening, Day 8, Week 4 and Week 6 or 7 RECIST v1.1
ORR: Objective Response Rate; PFS: Progression-Free Survival
1. Data from Reiss, et al. SITC 2022; and Klichinsky, et al. CAR-TCR 2023. 2. Outcomes are specific to Group 1 and Group 2 study.

Key Learnings from CT-0508 Monotherapy Study*

CT-0508 was a well-tolerated and active therapy; strong rationale for further development of anti-HER2 CAR-M

Safety and Tolerability	• Well-tolerated with no severe CRS, no ICANS, and no dose-limiting toxicities
Manufacturing	• Successful autologous manufacturing with high CAR expression, viability, purity, M1 phenotype • Median dose 1.66x10^9 cells
Anti-tumor activity	• SD in 29% of patients (n=4/14), per RECIST 1.1 • Clear evidence of activity as measured by ctDNA
Mechanism of action	• Remodeling of the TME observed • Evidence of immune system activation correlating with Best Overall Response
Pharmacokinetics	• CT-0508 detected in tumor samples of 75% of patients at Day 8, 27% at Week 4 • CT-0508 detected at low numbers (~1-2 per biopsy slide)
Observations	• Activity of CT-0508 superior in patients with higher HER2 expression • HER2 3+ pts experienced greater anti-tumor effects with SD in 44% vs 0% in HER2 2+ • Lower baseline CD8 T cell exhaustion correlated with improved Best Overall Response

CT-0508 is well-tolerated and shows clear evidence of activity in advanced HER2 3+ patients
Persistence, trafficking, dose, and exhaustion of patient T cells limit clinical potential

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CRS: Cytokine release syndrome; ICANS: immune effector cell-associated neurotoxicity syndrome; SD: stable disease; ctDNA: Circulating Tumor DNA; TME: tumor microenvironment; MOA: mechanism of action (increased antigen presentation, tumor inflammation, immune cell recruitment, and T cell activation; *CT-0508 Study 101; CT-0508 - CAR-Macrophage

CT-0508 Study 101: Phase 1 Study Patient Demographics

Heavily pre-treated patients with Stage IV HER2 2+/3+ solid tumors

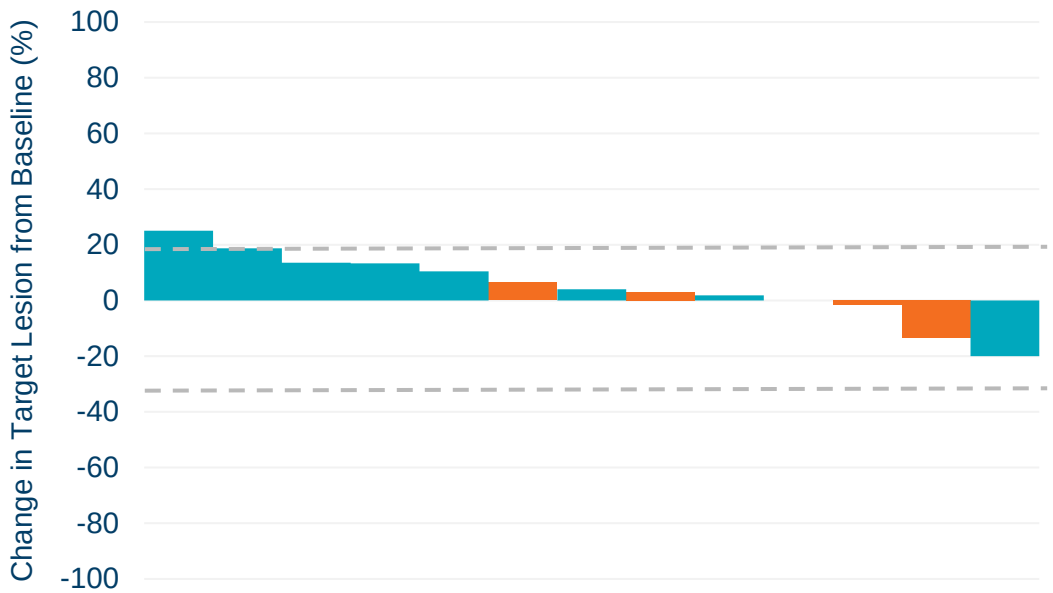
Characteristics	N=14
Tumor Type, n (%)	
Breast Cancer	8 (57.1)
Esophageal Cancer	2 (14.3)
Salivary Carcinoma	2 (14.3)
Cholangiocarcinoma	1 (7.1)
Ovarian Cancer	1 (7.1)
HER2 Overexpression, n (%)	
IHC 3+	9 (64.3)
IHC 2+/FISH+	5 (35.7)
Pre-Treatment History	
Median Number of Prior Cancer Therapies, n (range)	5 (2, 12)
Median Number of Prior Anti-HER2 Therapies, n (range)	2 (0, 9)
Subjects with Prior Anti-HER2 Therapy	13 (92.9)
Tumor Mutational Burden (TMB)	
Low (<10 mut/Mb)	11 (78.6)
High (≥10 mut/Mb)	2 (14.3)†
Unknown	1 (7.1)
Microsatellite Instability (MSI)	
MSS/MSI-Low	13 (92.9)
MSI-High	0 (0)
Unknown	1 (7.1)

† 1 patient had received 12 lines of prior therapy, and 1 patient has demonstrated HLA-A and HLA-C loss of heterozygosity

Early Efficacy Evaluation

Best Overall Response of Stable Disease

Best Overall Change in Tumor Burden



RESULTS

- Best Overall Response of Stable Disease in 4 of the 14 evaluated participants (28.6%)*+
- Largest reduction in target lesion
  - 20% in a breast cancer patient
  - 14% in a salivary gland cancer patient
- Stable Disease was enriched in HER2 3+ subpopulation (n=4/9, 44.4% SD)
- Stable Disease correlated with CT-0508 induced TME remodeling and T cell activation

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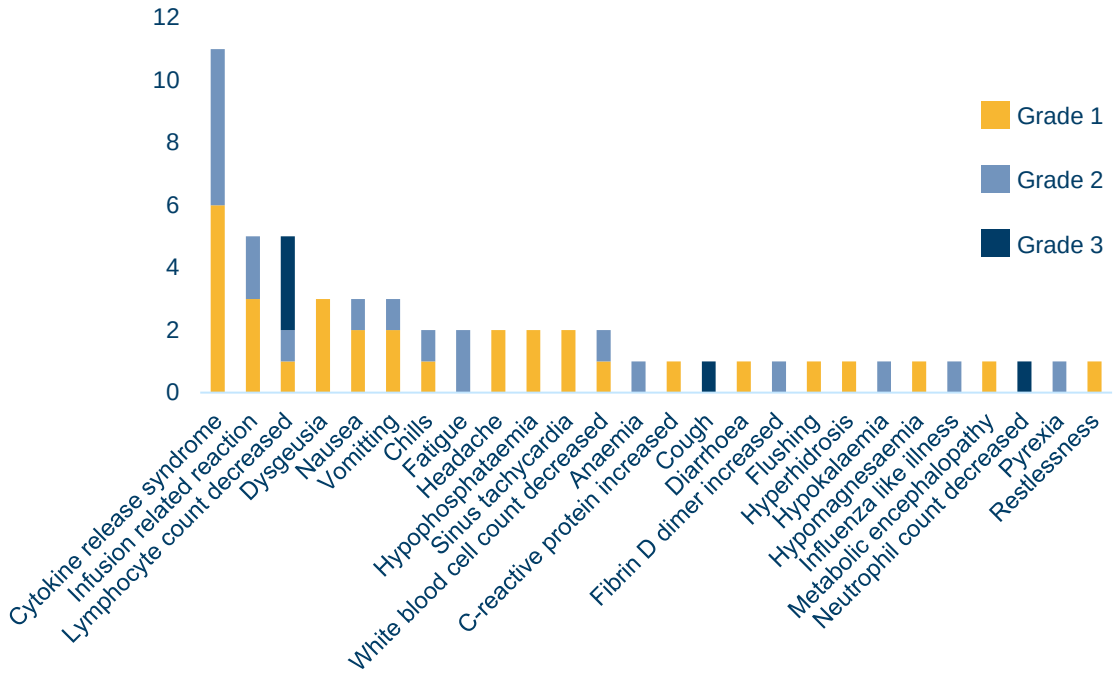
Data from Reiss, et al. SITC 2022; and Klichinsky, et al. CAR-TCR 2023. Includes data from combined Group 1 and Group 2.
*Best Overall Response (RECIST 1.1); As of 08/02/2023, all patients discontinued to disease progression.
+1 patient in group 1 discontinued the study 2 weeks post infusion and never received a scan post infusion for re-staging, hence data is unavailable for this patient.

CT-0508 is Well-Tolerated with No Dose Limiting Toxicities

Preliminary data supports a safe and well-tolerated product profile

Number of Adverse Events



Adverse Event Data by Patient

	G1: Fractionated	G2: Bolus	Combined
Patients Treated	**N=9 (%)**	**N=5 (%)**	**N=14 (%)**
Cytokine release syndrome (CRS)	**6** (67)	**3** (60)	**9** (64)
Grade 1-2	**6** (67)	**3** (60)	**9** (64)
Grade 3-4	**0** (0)	**0** (0)	**0** (0)
Infusion Reaction	**2** (22)	**1** (20)	**3** (21)
Grade 1-2	**2** (22)	**1** (20)	**3** (21)
Grade 3-4	**0** (0)	**0** (0)	**0** (0)
ICANS	**0** (0)	**0** (0)	**0** (0)
SAEs Related To Treatment[1]	**2** (22)	**3** (60)	**5** (36)

Similar safety profile between Group 1 and Group 2

No severe CRS or ICANS

Majority of adverse events were Grade 1-2

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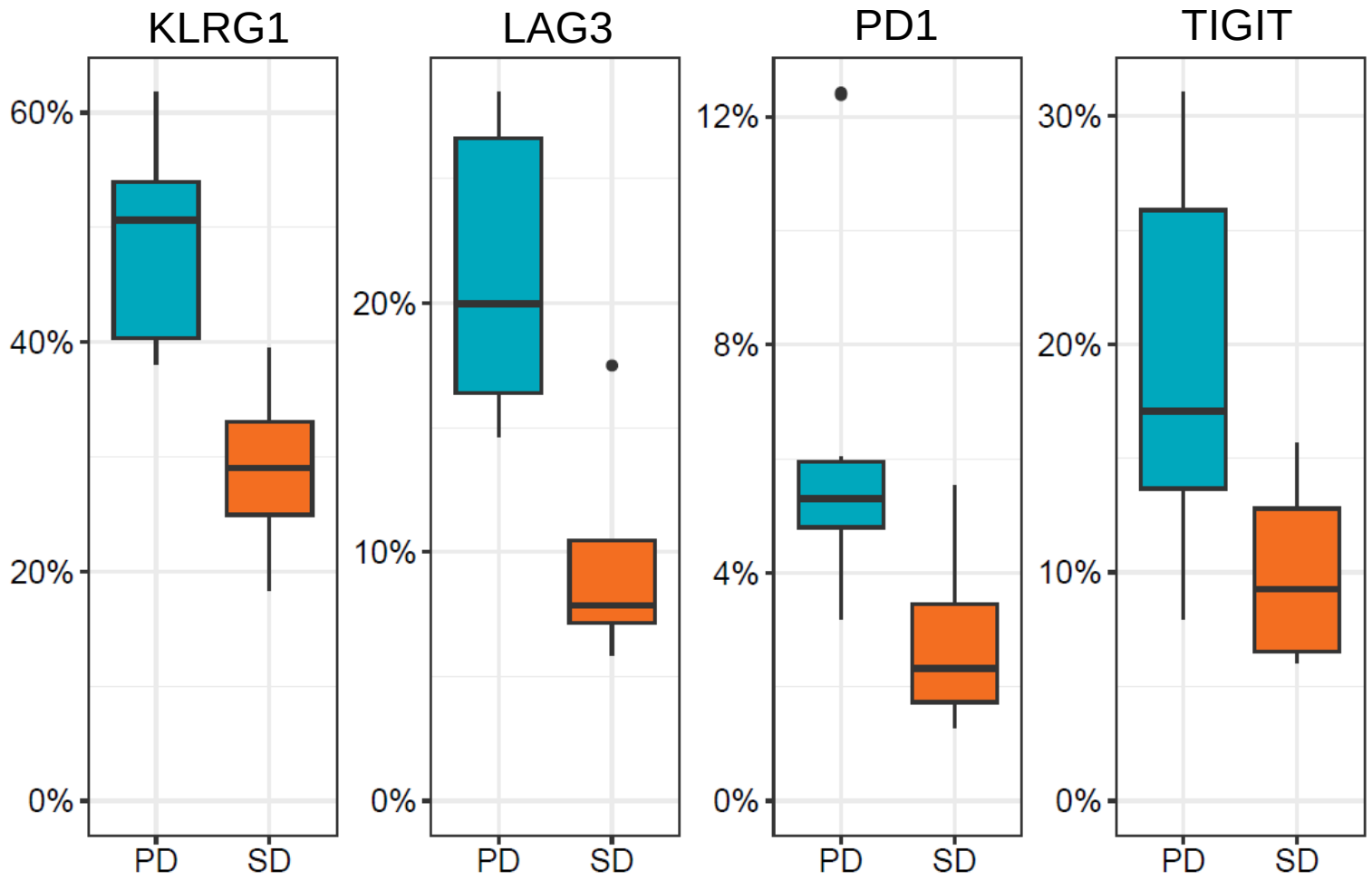
Data from Reiss, et al. SITC 2022; and Klichinsky, et al. CAR-TCR 2023. Includes data from combined Group 1 and Group 2.

1. All SAEs related to treatment were due to hospitalization for monitoring of either Grade 2 CRS or Grade 2 infusion reaction; CT-0508 - CAR-Macrophage.

T cell Exhaustion Was a Limiting Factor to CAR-Macrophage Efficacy

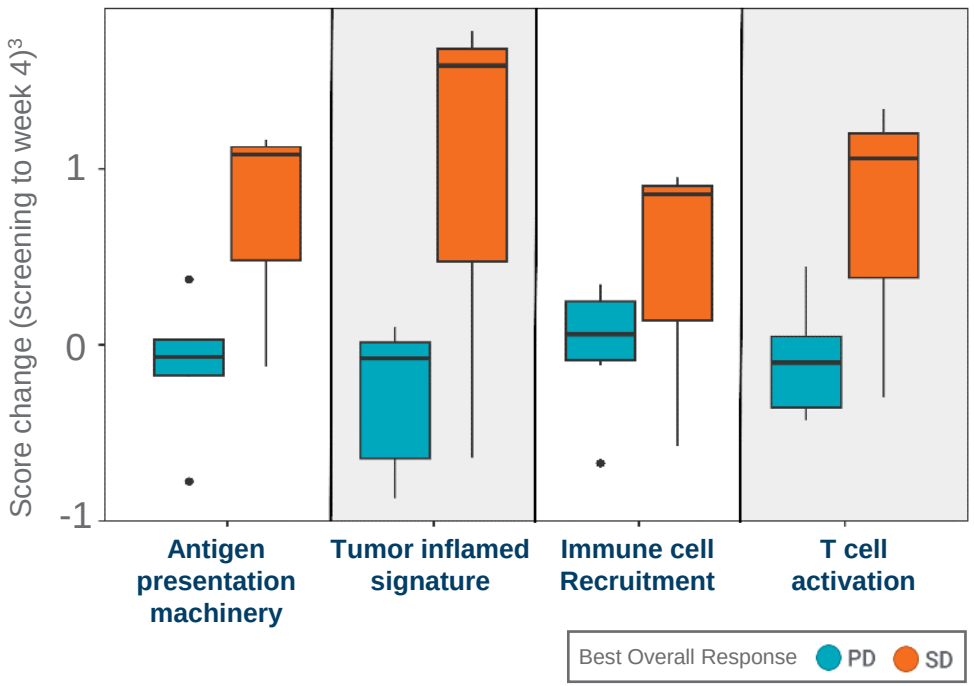
Study 101 patients with lower baseline CD8 T cell exhaustion (in blood) trended toward Stable Disease



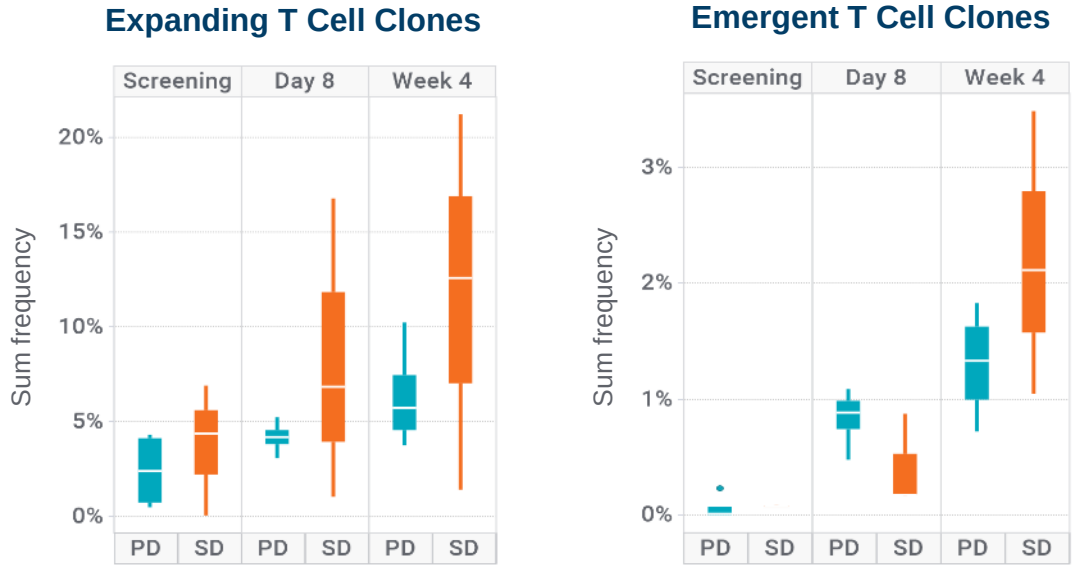
Based on single-cell RNAseq analysis of CD8 T cells within apheresis material.;SD: Stable Disease; PD: Progressive Disease

CT-0508 remodeled the TME and induced anti-tumor T cell immunity

Improved TME remodeling and T cell dynamics seen in patients that achieved Stable Disease



TME activation, based on multiple gene sets, was enriched in patients that had Stable Disease



Accumulation of peripherally expanded and emergent T cell clones was increased in patients that had Stable Disease

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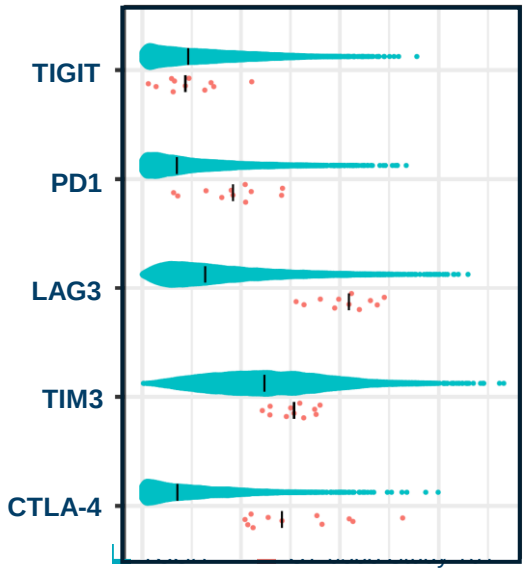
Data from Reiss, et al. SITC 2022; and Klichinsky, et al. CAR-TCR 2023. Includes data from combined Group 1 and Group 2.
SD: Stable Disease; PD: Progressive Disease, TME: Tumor Microenvironment

T cell Exhaustion is a Limiting Factor to CAR-Macrophage Efficacy

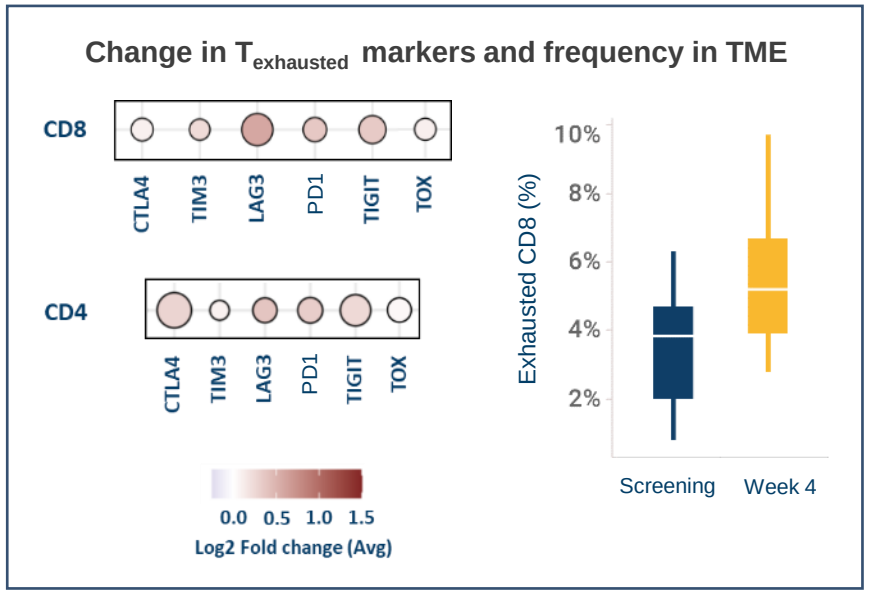
Study 101 patients show high baseline T cell exhaustion, and inhibitory pathways are further upregulated

T cell exhaustion markers in CT-0508 Study 101 pts compared to ~10,000 cancer patients in the TCGA database



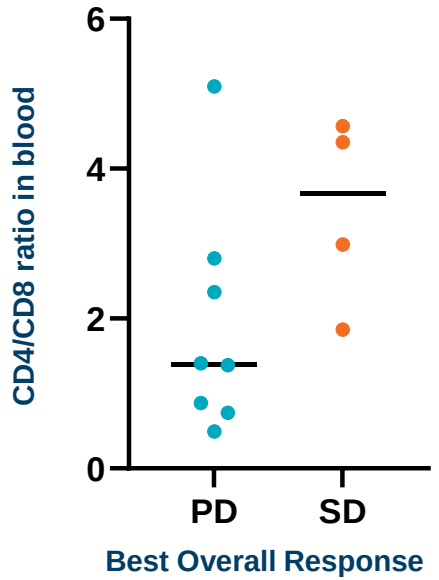
High T cell exhaustion in the TME of Study 101 pts

Changes in exhaustion markers (left) and exhausted CD8 T cell frequency (right) in the TME (Week 4 vs. Screening)



The pro-inflammatory effects of CT-0508 further upregulate inhibitory pathways

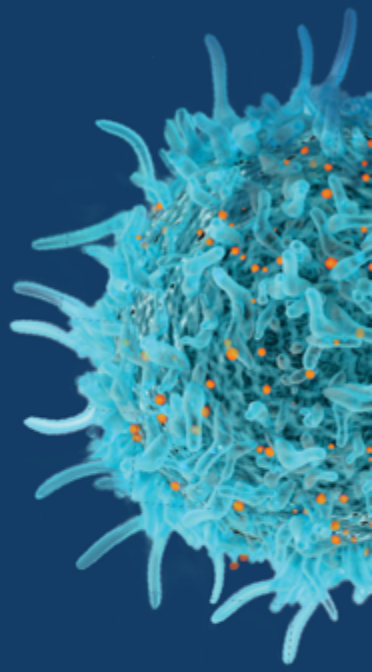
Correlation of outcomes with baseline peripheral blood T cell fitness



T cell fitness[1] correlates with clinical outcome

Data from Reiss, et al. SITC 2022; and Klichinsky, et al. CAR-TCR 2023. Includes data from combined Group 1 and Group 2.
1. CD4/CD8 ratio and frequency of CD8+ T stem central memory in apheresis material were used as measures of T cell fitness.
SD: Stable Disease; PD: Progressive Disease

Targeting HER2:
CT-0508 + anti-PD1



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CT-0508 Study 101: CT-0508 + Pembrolizumab Sub-study

Assessing safety, tolerability and TME impact of CT-0508 in combination with anti-PD1 pembrolizumab

HER2 2+/3+ solid tumors

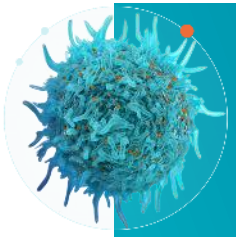
G-CSF mobilization and apheresis, CAR-Macrophage manufacture, bridging therapy, baseline staging

Group 1: CT-0508 fractionated dose D1,3,5 (n=9)	Data Reported
Group 2: CT-0508 bolus dose D1 (n=5)	Data Reported

Demonstrated manufacturing feasibility, safe administration, cell trafficking from blood to tumor, cells resided in tumor for up to 4 weeks, positively modulated TME[1]

All Regimens will receive Pembro 200mg every 21 days until tx completion

Pembro Sub-study Regimen Level 1 (n=3):	CT-0508 C1D1,3,5 + Pembro 200mg C1D8	Data Reported
Pembro Sub-study Regimen Level 2 (n=3):	CT-0508 C1D1,3,5 + Pembro 200mg C1D1	Data Reported
Pembro Sub-study Regimen 3:	CT-0508 C1D1 + Pembro 200mg C1D1	**No Further Enrollment[3]**



PRIMARY OUTCOMES[2]

- Safety and tolerability

SECONDARY OUTCOMES & ADDITIONAL ANALYSES[2]

- ORR (RECIST 1.1)
- PFS
- Trafficking
- TME activation
- T cell recruitment/activation
- T cell expansion/clonality

Biopsy performed at screening, Day 8, Week 4 and Week 6 or 7 RECIST v1.1; *Enrolled 5 patients; ORR: Objective Response Rate; PFS: Progression-Free Survival; 1. Data from Reiss, et al. SITC 2022; and Klichinsky, et al. CAR-TCR 2023. 2. Outcomes are specific to pembro sub-study. 3. In March 2024, Carisma has ceased recruitment of new patients into Study 101 and its sub-studies.

Key Learnings from CT-0508+Pembrolizumab Combination*

Study successfully met its primary endpoint of safety, tolerability and manufacturing feasibility

Safety and Tolerability	• Well-tolerated with no severe CRS, no ICANs, and no on-target off-tumor toxicity
Feasibility	• Successful manufacturing of CT-0508 for 6/6 pts; Median dose of $2.7x10^9$ cells administered
Anti-tumor activity	• SD seen in 1/6 patients; heavily pretreated HER2 3+ esophageal adenocarcinoma • Mixed response with 46% reduction in one of two target lesions in this patient • 3/6 patients either treated with corticosteroids or presented with baseline HLA-I loss of heterozygosity, both potentially limiting the CAR-M mechanism of action
Synergistic immune activation	• Increase in peripheral blood T cell clonality compared to CT-0508 alone • Increase in the frequency of activated and effector memory CD8+ T cell in the peripheral blood compared to CT-0508 alone • Activation of the TME, leading to an increase in the PD-L1 CPS – a biomarker associated with improved response to immunotherapy

Combination of CT-0508 and pembrolizumab was well tolerated and the checkpoint inhibitor combination strategy will be further explored with our CT-0525 lead program

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SD: stable disease per RECIST 1.1; CRS: Cytokine release syndrome; ICANS: immune effector cell-associated neurotoxicity syndrome; CPS: Combined positive score; *Study 101 RL1/2: Regimen level 1 and 2 in combination with pembrolizumab).

CT-0508+Pembrolizumab Combination: Demographics[1]

Patient Demographics were consistent with patients enrolled in the monotherapy groups

Summary of Participant and Tumor Characteristics			
Characteristic	**N = 6**	**Characteristic**	**N = 6**
Median age (range), years	58 (45, 73)	Tumor Type, n (%)	
Gender, n (%)		Breast Cancer	3 (50.0)
Male	2 (33.3)	Esophageal Cancer	1 (16.7)
Female	4 (66.7)	Ovarian Cancer	1 (16.7)
		Colorectal Cancer	1 (16.7)
Race, n (%)		Median Number of Prior Cancer Therapies, n (range)	6 (3, 10)
White	6 (100.0)		
ECOG PS, n (%)		Median Number of Prior Anti-HER2 Therapies, n (range)	5 (0, 7)
0	1 (16.7)	Subjects with Prior Anti-HER2 Therapy	4 (66.7)
1	5 (83.3)		
HER2 Overexpression, n (%)		Prior Radiotherapy, n (%)	
IHC 3+	5 (83.3)	Yes	5 (83.3)
IHC 2+/FISH+	1 (16.7)		
Microsatellite Instability (MSI)*		Tumor Mutational Burden (TMB)*	
MSS/MSI-Low	6 (100.0)	Low (<10 mut/Mb)	5 (83.3)
MSI-High	0 (0)	High (≥10 mut/Mb)	1 (16.7)†

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* MSI-high and TMB high are known biomarkers associated with improved response to immune checkpoint
† patient has demonstrated HLA-A, HLA-B and HLA-C loss of Heterozygosity; 1: CT-0508+Pembrolizumab Regimen Level 1 and 2

CT-0508+Pembrolizumab Combination: Well-Tolerated, No Dose Limiting Toxicities

Similar safety profile to CT-0508 monotherapy

	CT-0508 Monotherapy Group 1: Fractionated Dosing	CT-0508 Monotherapy Group 2: Bolus Dosing	CT-0508 + Pembrolizumab Regimen 1	CT-0508 + Pembrolizumab Regimen 2
Patients Treated	**N=9 (%)**	**N=5 (%)**	**N=3 (%)**[1]	**N=3 (%)**
Any treatment-emergent AEs (TEAE)	**9** (100)	**5** (100)	**3** (100)	**3** (100)
Grade 1-2	**4** (44)	**2** (40)	**1** (33)	**2** (66)
Grade 3-4	**5** (56)	**3** (60)	**2** (66)	**1** (33)
Any TEAEs related to CT-0508	**8** (89)	**4** (80)	**3** (100)	**3** (100)
Any TEAEs related to pembrolizumab	N/A	N/A	**1** (33)	**2** (66)
Any treatment-emergent SAEs (TESAE)	**4** (44)	**3** (60)	**3** (100)	**1** (33)
Any TESAEs related to CT-0508[2]	**2** (22)	**2** (40)	**3** (100)	**1** (33)
Any TESAEs related to pembrolizumab	N/A	N/A	**0** (0)	**0** (0)
Cytokine release syndrome (CRS)	**6** (67)	**3** (60)	**2** (67)	**3** (100)
Grade 1-2	**6** (67)	**3** (60)	**2** (67)	**3** (100)
Grade 3-4	**0** (0)	**0** (0)	**0** (0)	**0** (0)
ICANS	**0** (0)	**0** (0)	**0** (0)	**0** (0)

Similar safety profile between CT-0508 as monotherapy & in combination with pembrolizumab

No severe CRS or ICANS

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1. 2 of the 3 patients in the combination study were treated with corticosteroids post CT-0508, prior to pembrolizumab
2. All TESAEs related to CT-0508 were due to hospitalization for monitoring of either Grade 2 CRS or Grade 2 infusion reaction.

CT-0508+Pembro Combination: Regimen Level 1 and 2 Summary

Patient	Regimen Level	Best Overall Response	Disease	HER2 Status	Additional Treatment Details
Patient 1	RL1	PD	Stage IV Breast Cancer	HER2 2+	• Treated with dexamethasone due to G2 CRS post CT-0508 infusion, prior to pembrolizumab administration
Patient 2	RL1	PD	Stage IV Ovarian Cancer	HER2 3+	• Treated with methylpredinosolone due to G3 Infusion reaction post CT-0508 infusion, prior to pembrolizumab administration • Triple HLA Class I loss of heterozygosity (HLA-A, B and C deletion in tumor genome).
Patient 3	RL1	SD (One out of two target lesions reduced by ~46%)	Stage IV Esophageal Cancer	HER2 3+	• Missed an early cycle (2nd infusion) of pembrolizumab due to medical issues unrelated to therapy • Patient had brain metastasis and progressed per RECIST 1.1 week 14 due to new brain met
Patient 4	RL2	PD	Stage IV Breast Cancer	HER2 3+	• Total 2 Pembro doses administered
Patient 5	RL2	PD	Stage IV Breast Cancer	HER2 3+	• Total 2 Pembro doses administered
Patient 6	RL2	PD	Stage IV Colorectal Cancer	HER2 3+	• Missed 2nd cycle of pembrolizumab - Total 1 Pembro doses administered • Triple HLA Class I loss of heterozygosity (HLA-A, B and C deletion in tumor genome).

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SD: Stable Disease; PD: Progressive disease; HLA: human leukocyte antigen

CT-0508+Pembrolizumab Combination: Individual Case Study

Patient 3: EAC patient with 6 prior lines of therapy and refractory to Enhertu

Cancer type: Stage IV Esophageal adenocarcinoma (EAC), HER2 3+

Prior history: 6 Prior lines of therapy; Most recent prior line: achieved BOR* of PD and discontinued in 2 months on Enhertu

Pembrolizumab clinical studies in EAC:

- EAC is often refractory to pembrolizumab monotherapy
- Pembrolizumab monotherapy in EAC: ORR 5%, PFS 1.5 months (KEYNOTE 180)
- Pembrolizumab did not show a survival benefit over SOC chemotherapy in PDL1+ EAC (KEYNOTE 181)

Patient 3 - Prior Line	Prior Therapy	Start Time	End Time	Best Overall Response
1	Neoadjuvant carboplatin/paclitaxel	Feb 2019	April 2019	CR
2	Adjuvant Capacitabine, oxaliplatin, trastuzumab	Nov 2020	Nov 2020	Unknown
3	Fluorouracil, folinic acid, oxaliplatin, trastuzumab	Dec 2020	April 2021	PR
4	Fluorouracil, trastuzumab	May 2021	March 2022	SD
5	Paclitaxel, ramucirumab, trastuzumab, tucatinib	May 2022	Jan 2023	SD
6	Enhertu	Feb 2023	April 2023	PD

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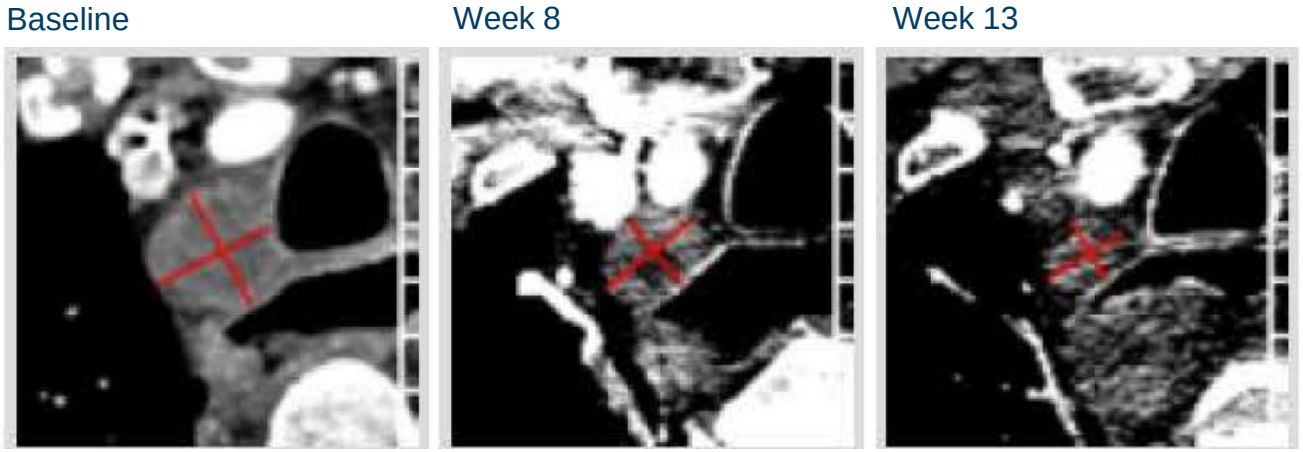
* BOR: Best Overall Response
CR: Complete Response; PR: Partial Response; SD: Stable Disease; PD: Progressive disease

CT-0508+Pembrolizumab Combination : Individual Case Study

Patient 3: 46% reduction in 1 of 2 target lesions

Paratracheal LN Target Lesion: 46% reduction by week 13



Dosing

- Patient received 3.10E+09 cells
- Patient missed the 2nd cycle of pembrolizumab

Tumor assessments

- Paratracheal target lesion reduction of 46% by week 13; 21.9mm to 11.8mm
- Mediastinal mass target lesion grew 31% by week 13; 26.9 to 35.3mm

Clinical assessments

- Achieved a BOR of SD per RECIST 1.1
- PD per RECIST at week 13 due to new CNS metastasis
- PFS of 3.25 months (13.3 weeks)

Outcome Comparators	PFS
Patient 3 – Regimen 1 CT-0508 / Pembro	3.25 months
Patient 3 – 6th Line of Therapy on Enhertu	2.0 months
Pembrolizumab monotherapy in KEYNOTE 180*	1.5 months

Patient 3's paratracheal target lesion reduction of 46% was the largest reduction of tumor in any patient treated with CT-0508

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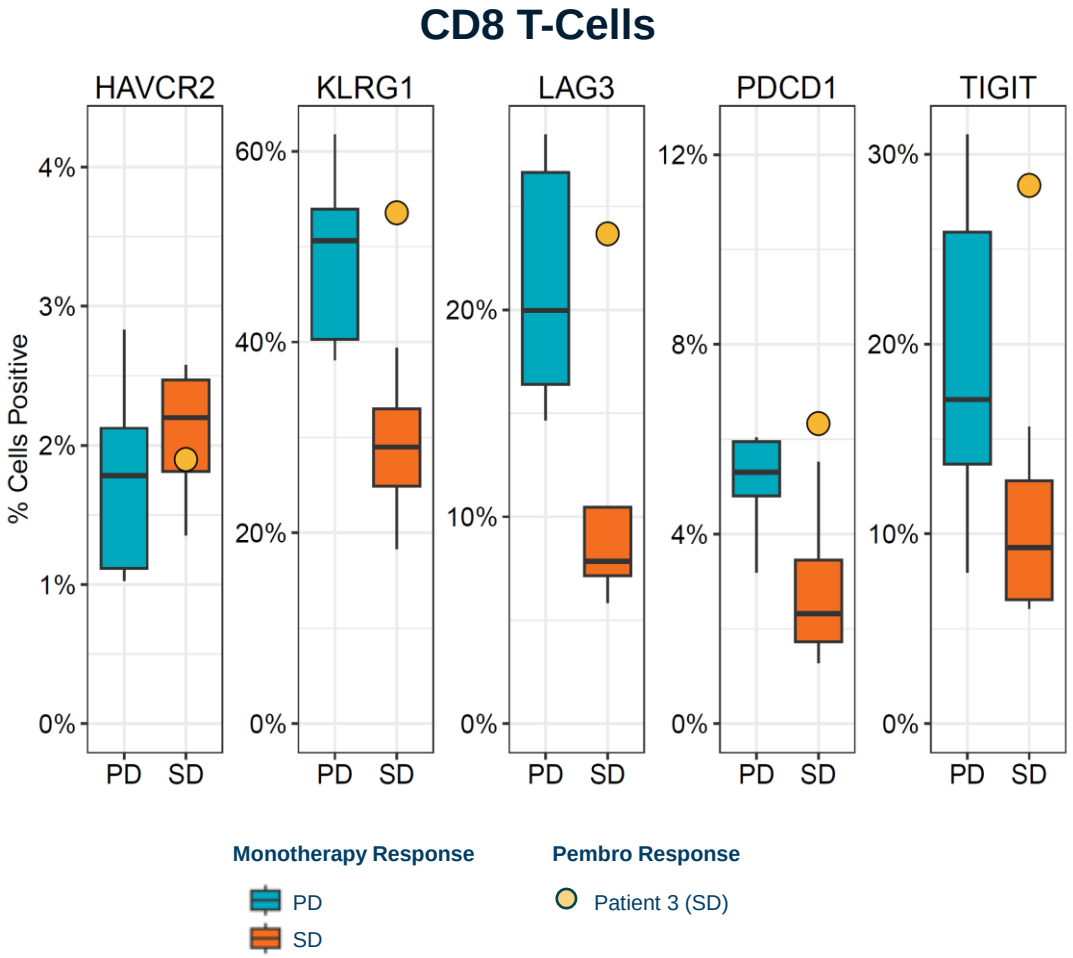
KEYNOTE 180: Efficacy and Safety of Pembrolizumab for Heavily Pretreated Patients With Advanced, Metastatic Adenocarcinoma or Squamous Cell Carcinoma of the Esophagus. JAMA Oncology. 2019.

CT-0508+Pembrolizumab Combination : Individual Case Study

Patient 3: High baseline peripheral CD8 T cell exhaustion and achieved BOR of SD



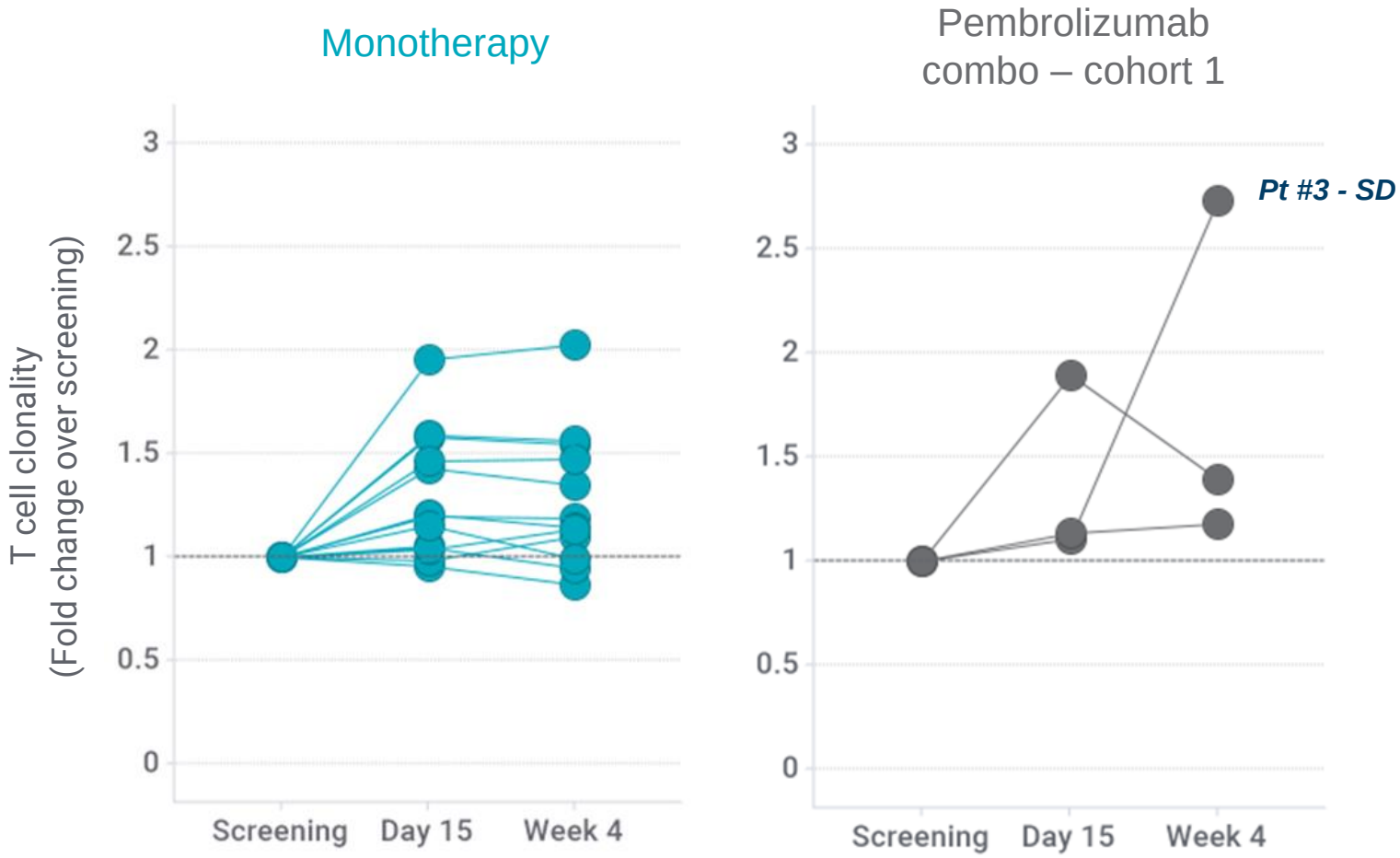
Patient 3 achieved BOR of SD despite high baseline peripheral CD8 T cell exhaustion

BOR: Best Overall Response; SD: Stable Disease

CT-0508+Pembrolizumab Combination : Individual Case Study

Patient 3: Greatest increase in peripheral blood T cell clonality seen to-date across all 17 patients treated with CT-0508

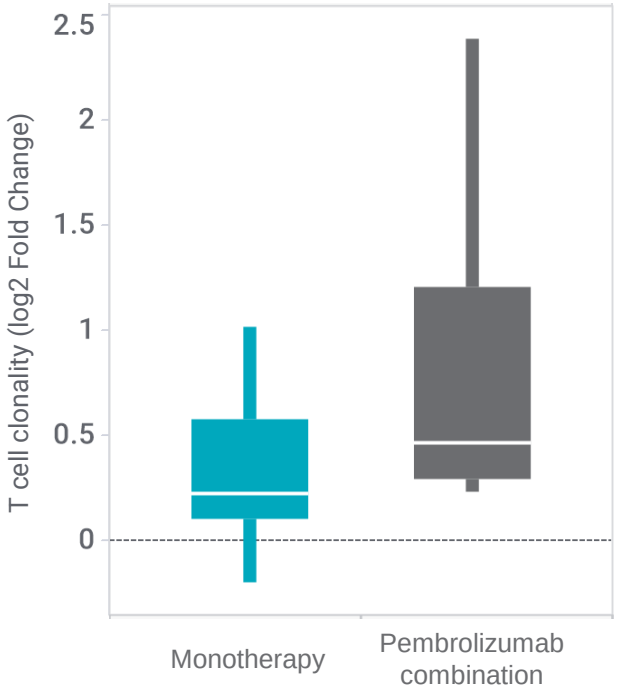
Increased T cell clonality in the peripheral blood



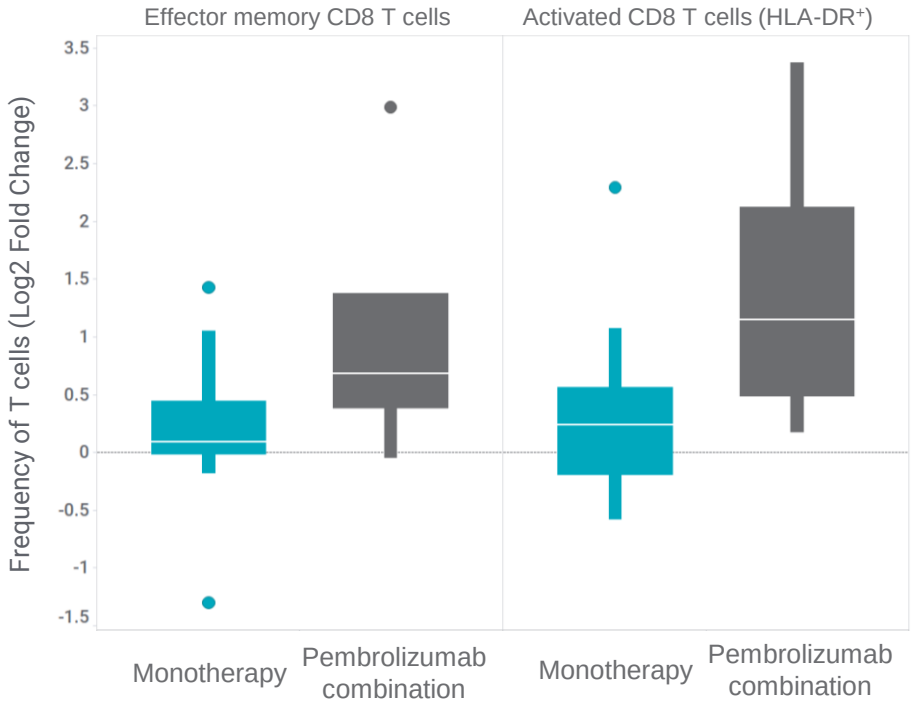
Synergistic Immune Activation

Pembrolizumab Potentiates the Ability of CT-0508 to Stimulate the Adaptive Immune System

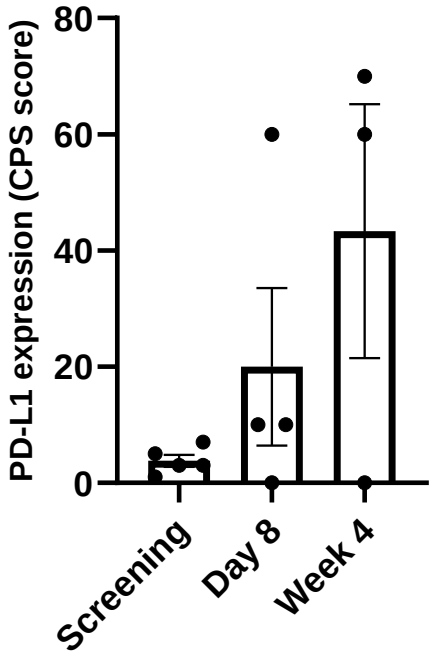
Increased T cell clonality (blood)[1]



Increased effector memory and activated CD8 T cells (blood)[2]



Increased PDL1 CPS in TME, a biomarker of CPI response[3]



1: Peripheral blood T cell clonality comparing week 4 to screening; 2: Frequency of T cell subsets in PBMC comparing week 4 to screening; 3: PD-L1 expression in the TME assessed by IHC (PD-L1 22C3 pharmDx); CPS: Combined positive score, TME: Tumor microenvironment, CPI: Checkpoint inhibitor