



HARNESSING THE POWER OF MACROPHAGES

May 2024

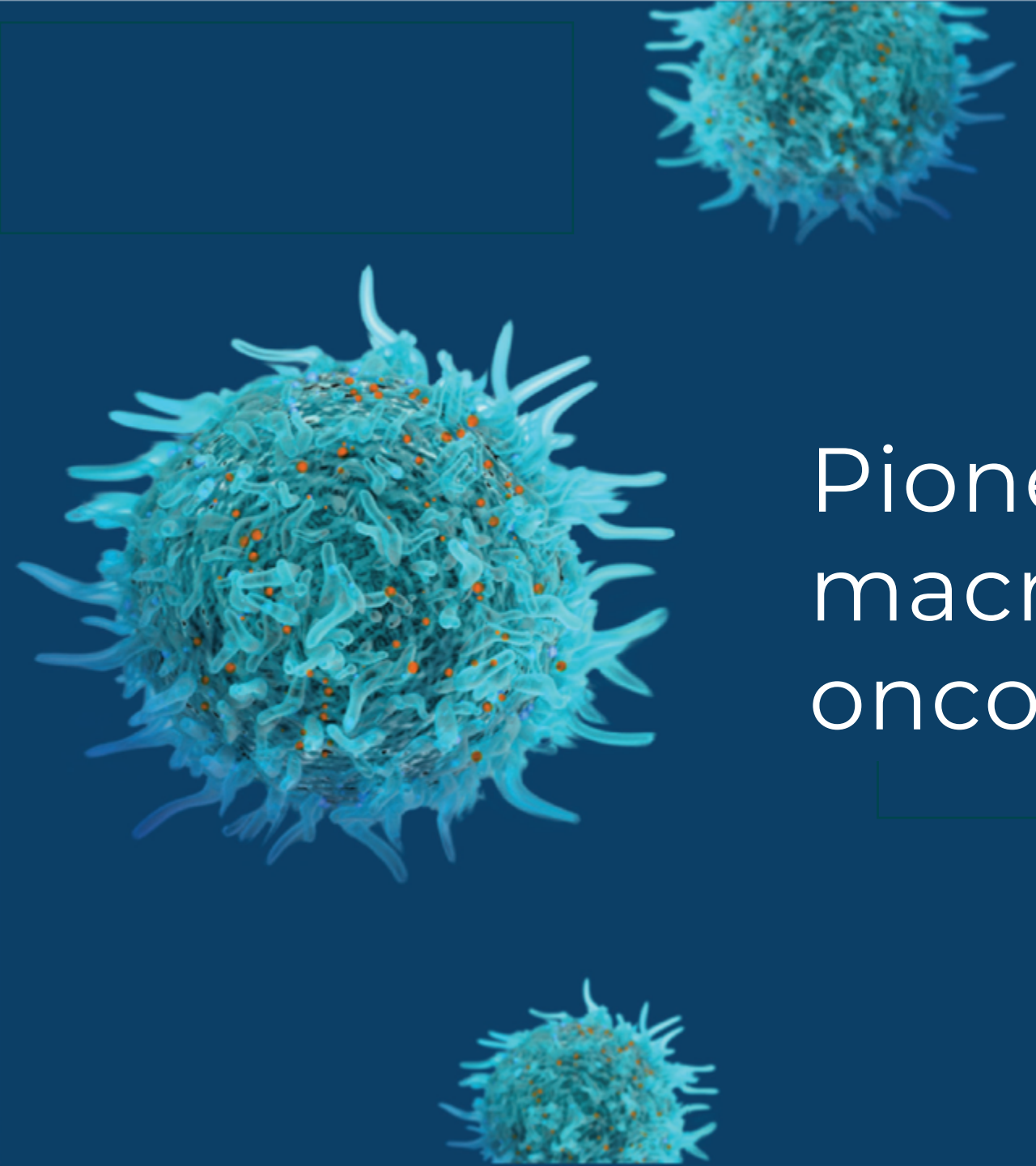




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Statements in this press release about future expectations, plans and prospects, as well as any other statements regarding matters that are not historical facts, may constitute “forward-looking statements” within the meaning of The Private Securities 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



Harnessing the Power of Macrophages

Developing unique and transformative cell therapies for patients with devastating diseases



HER2 Program

- Focused development of CT-0525 (CAR-Monocyte), which we believe is best suited to deliver benefit to patients with HER2 over-expressing solid tumors refractory to available treatments
- CT-0525 initial data is expected end of 2024
- CT-0508 trial to conclude post Regimen Level 2 of sub-study in combination with pembrolizumab



Beyond HER2*

- *In Vivo* Oncology: Advancing multiple targets in our *in vivo* CAR-M program in collaboration with Moderna
- Fibrosis: Advancing an engineered macrophage in liver fibrosis, with development candidate nomination expected in the first quarter of 2025



Corporate

- Cash runway into 3Q 2025, funding multiple clinical and preclinical catalysts
- Strong IP position
- Potential for collaborations (except *in vivo* oncology)



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

CAR-M has the potential for key solid tumor advantages over both

	CAR-T	CAR-NK	CAR-M
Mechanism of Action			
Effector Cell	CD4/CD8 T cells	Natural Killer Cells	Macrophages or Monocytes
Persistence	High	Low	Intermediate
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	Monocyte: 1 day



First-in-Class Pipeline

Multiple value inflection points across therapeutic areas and modalities

THERAPEUTIC AREA	PRODUCT CANDIDATE	PLATFORM	DISCOVERY	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	COLLABORATOR
Ex Vivo Oncology								
HER2+ solid tumors	CT-0525	CAR-Monocyte (1st Gen CAR)	<div></div>			4Q 2024: Initial data ¹		
	CT-0508*	CAR-Macrophage (1st Gen CAR)	<div></div>			2Q 2024: Combination data ¹		
Mesothelin+ solid tumors	CT-1119**	CAR-Monocyte (Next-Gen CAR ²)	<div></div>					
In Vivo Oncology								
Oncology	Solid Tumor Antigen ³	CAR-Macrophage + mRNA/LNP	<div></div>					
	4 Additional Targets ⁴	CAR-Macrophage + mRNA/LNP	<div></div>					
Fibrosis and Immunology								
Liver Fibrosis	TBD	Engineered macrophage	<div></div>			1Q 2025: Development candidate nomination ¹		

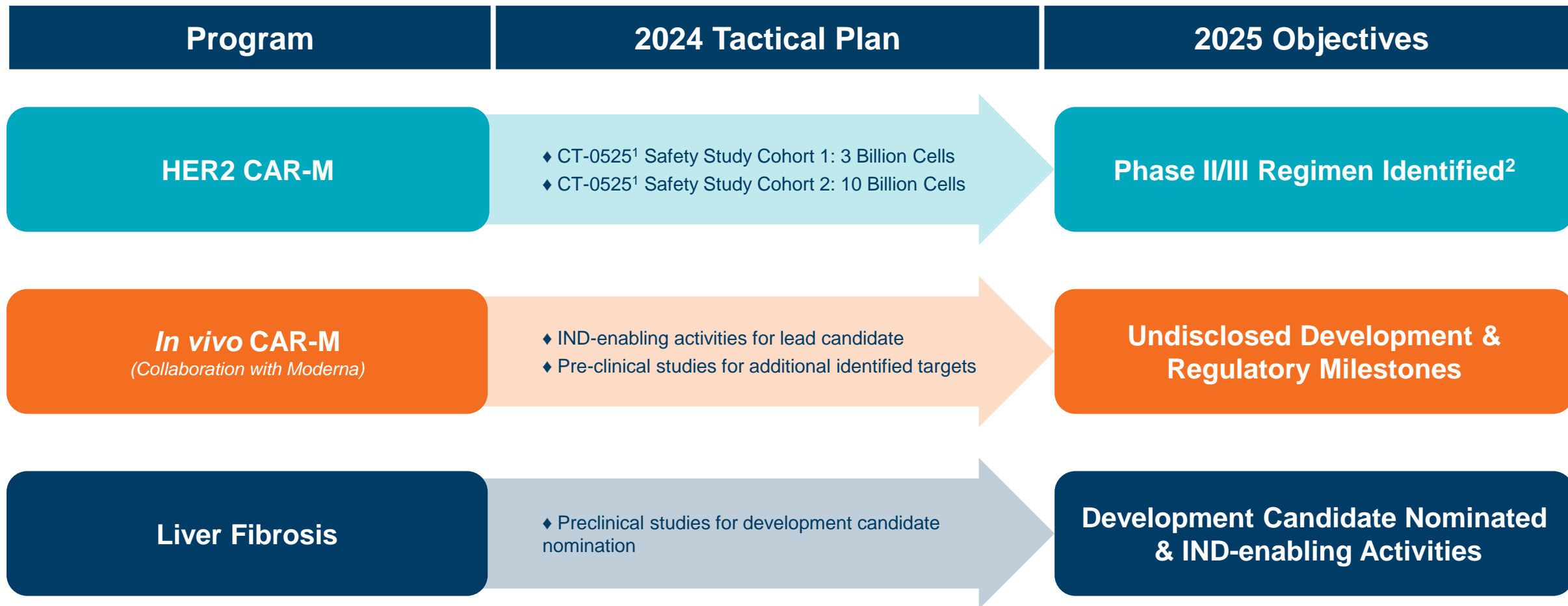


* In late March 2024, Carisma made the decision to cease further development of CT-0508, including monotherapy and in combination with pembrolizumab
** In late March 2024, Carisma made the decision to pause further development of CT-1119, pending additional financing
1. Anticipated milestones; 2. Includes SIRPα knockdown technology; 3. Target undisclosed
4. Moderna collaboration has identified 5 total oncology targets, with the option to identify an additional 7 oncology targets; First lead candidate was nominated in 4Q 2023

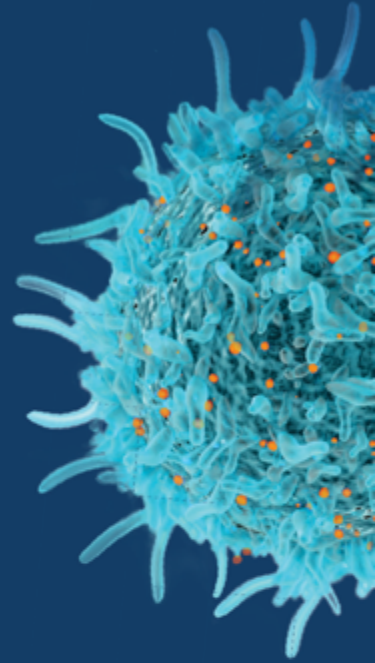


Drive to 2025

Leverage world-leading macrophage engineering platform to deliver three product opportunities

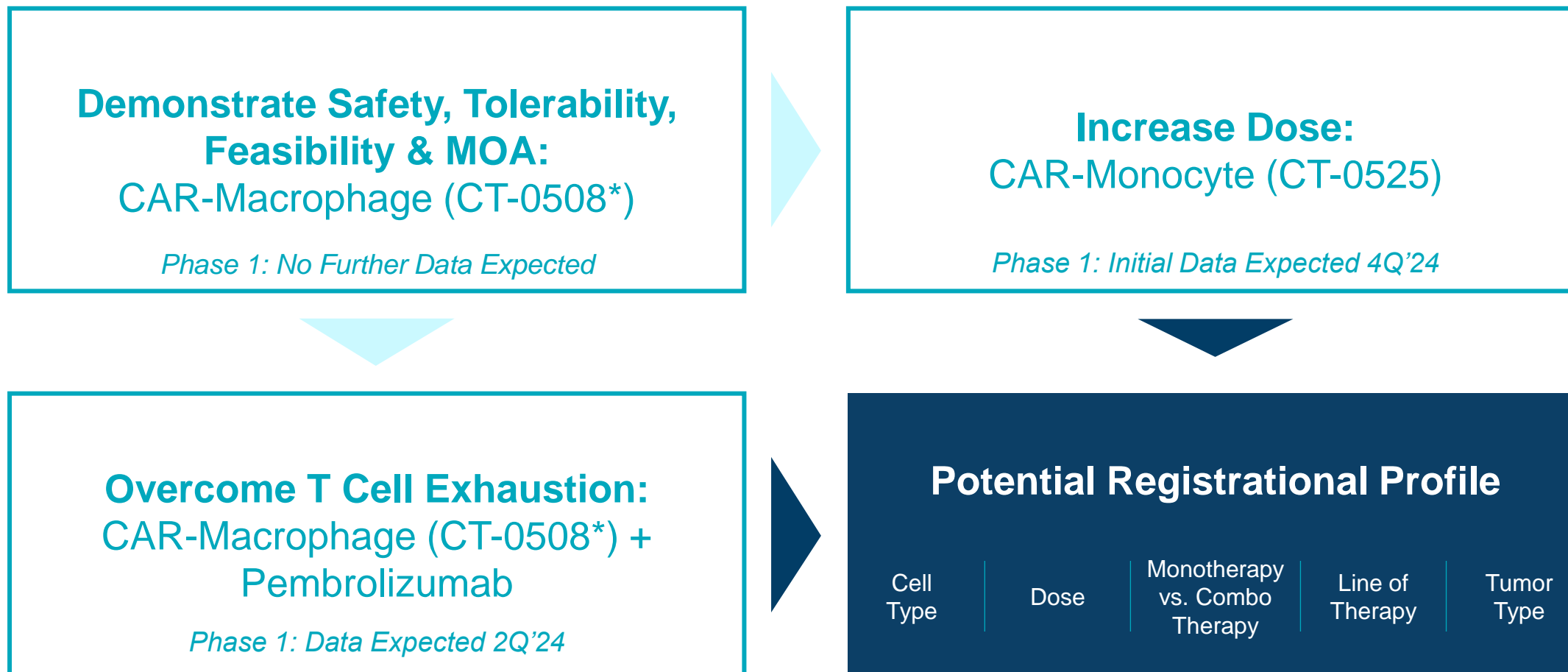


Targeting HER2: CT-0525 and CT-0508



HER2 Development Strategy

CT-0525 selected as HER2 product candidate, with additional considerations to be informed by ongoing studies



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



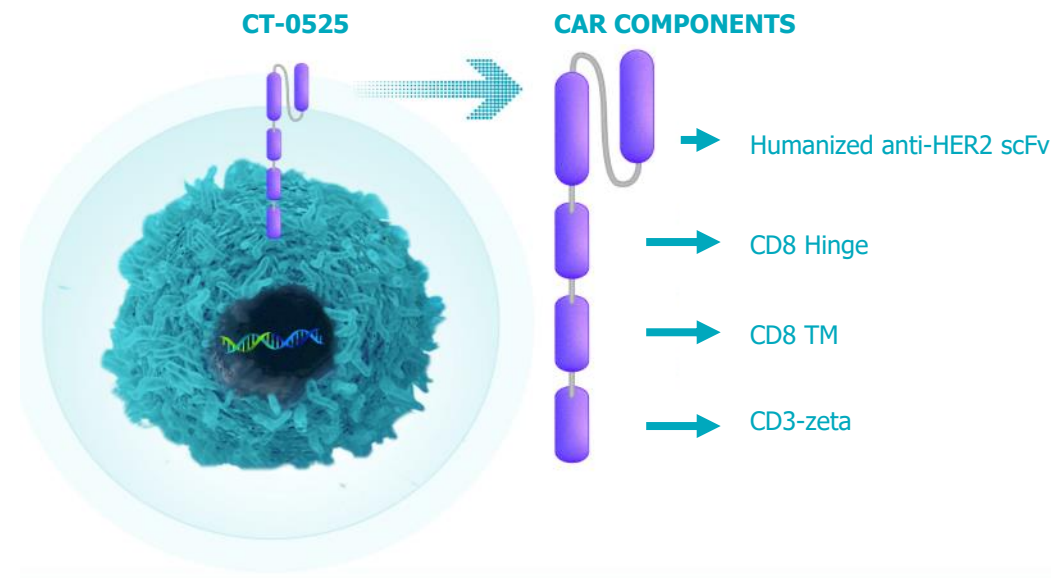
Potential Biological Advantages Over CAR-Macrophage

- 2,000-fold increased exposure
 - Cell count, trafficking, and persistence
- Increased potency
 - Killing, cytokine release, and antigen presentation
- Dosing flexibility



Development Plan & Timeline

- ✓ IND cleared
- ✓ First patient treated in 2Q 2024
- Initial data expected in 4Q 2024



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

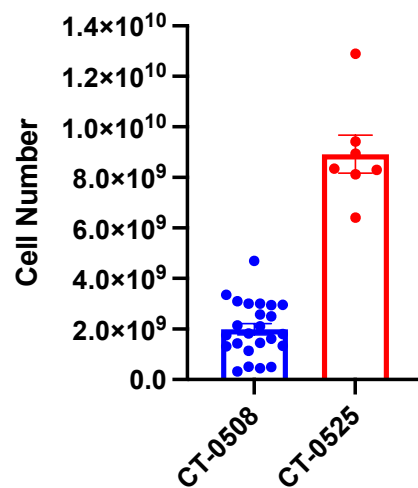
CT-0525: Multiple Potential Improvements Over CT-0508

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

5X

Cell Number

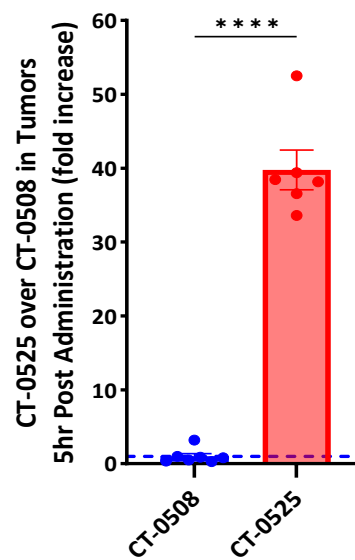
Cells Produced from Single Apheresis:



40X

Tumor Infiltration

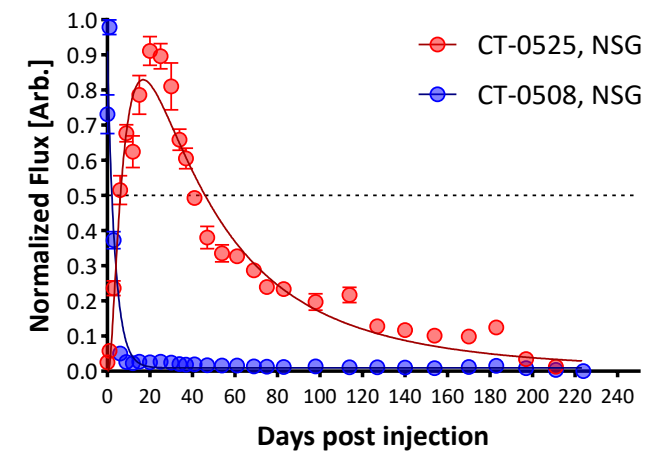
Trafficking in solid tumor model:



10X

Persistence

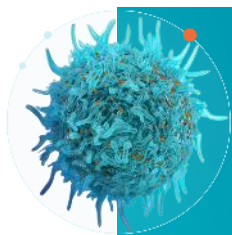
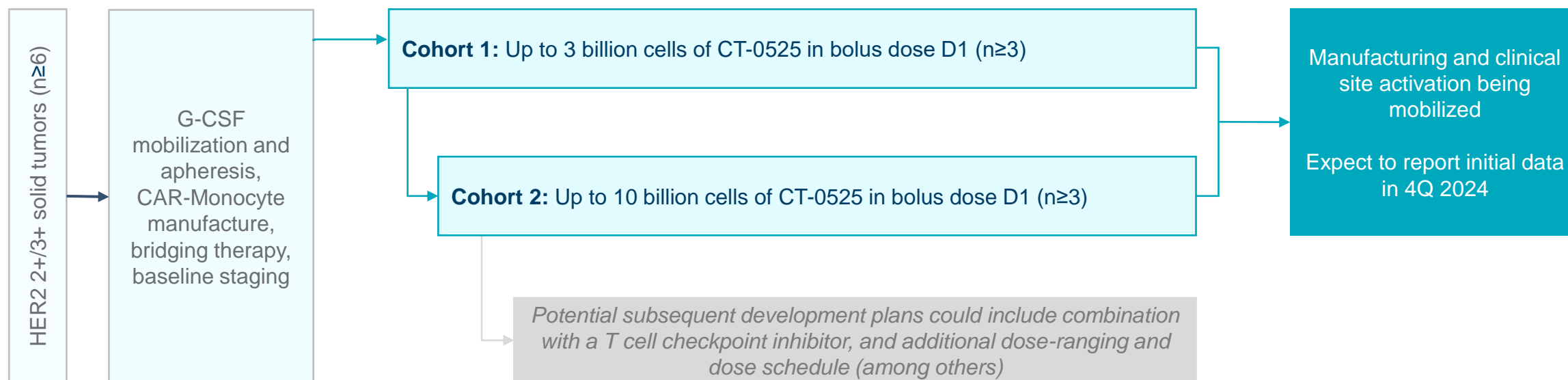
CT-0525 half-life is ~45 days:





CT-0525 Study 102: Phase 1 Clinical Trial Design

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



PRIMARY OUTCOMES

- Safety and tolerability
- Manufacturing feasibility

SECONDARY OUTCOMES¹

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

CT-0508: HER2 Targeted CAR-Macrophage

Well-tolerated and active therapy in safety study sets the stage for further development of anti-HER2 CAR-M

Highlights



Study Status

- Study 101 Group 1 (fractionated dosing): 9 patients
- Study 101 Group 2 (bolus dosing): 5 patients
- Study 101 sub-study (pembrolizumab combination): 6 patients
- Determined to cease further development in late March 2024



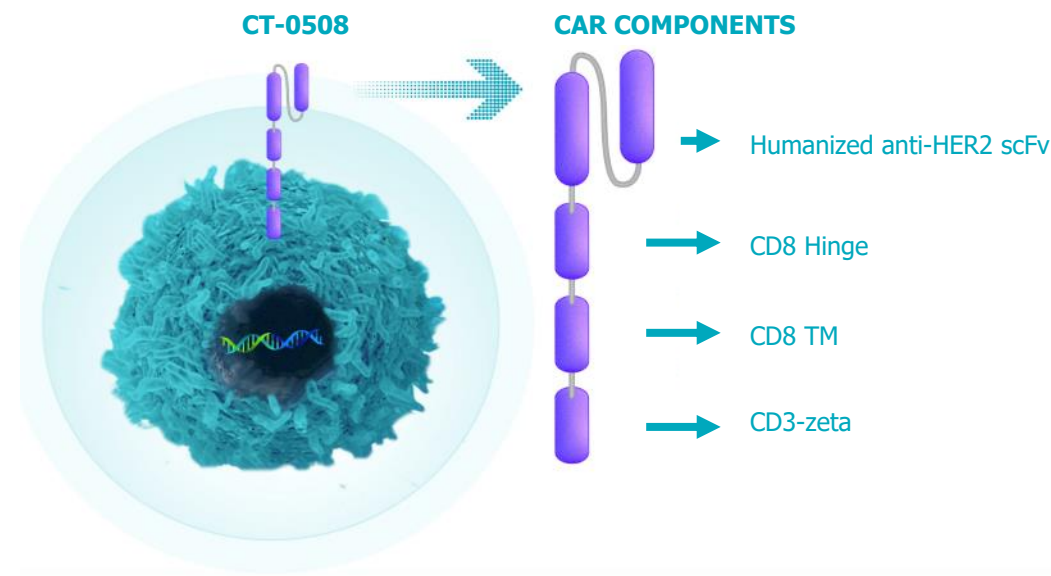
Key Study Takeaways To Date

- Monotherapy and combination with pembrolizumab was well-tolerated
- No tolerability differences between fractionated and bolus dosing
- Demonstrated manufacturing feasibility
- Clear MOA and anti-tumor activity observed in HER2 3+ patients
- Low trafficking, low persistence
- Patient population with exhausted T cells



Upcoming Activities

- Complete Study 101 pembrolizumab sub-study Regimen 2
- Study 101 pembrolizumab sub-study data expected 2Q 2024*

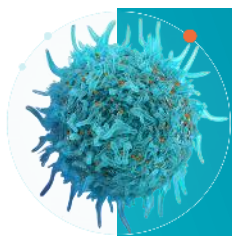
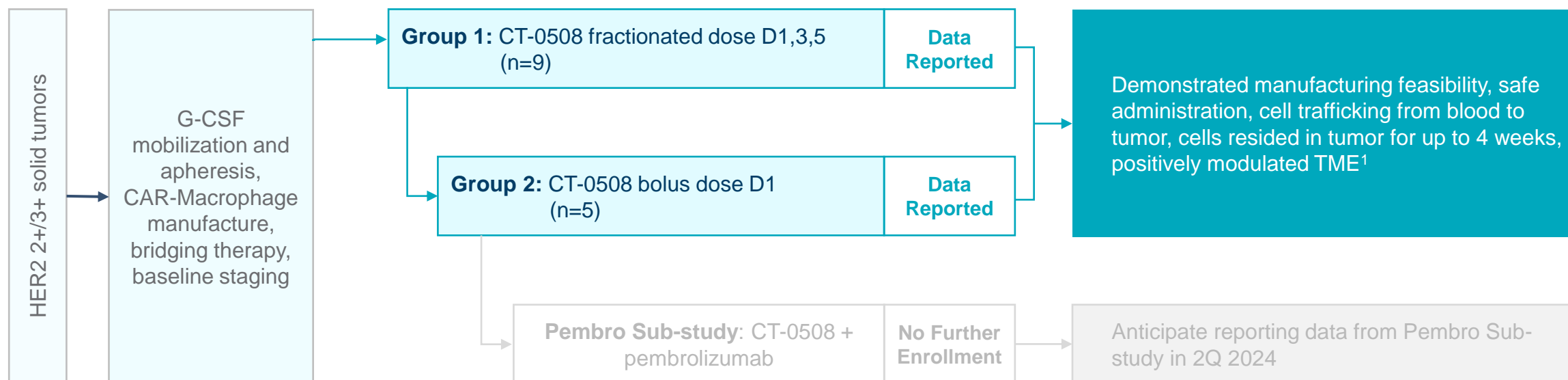


	CT-0508 Product Description
Cells	Autologous monocyte derived macrophages
Vector	Ad5f35
Phenotype	M1
CAR	1 st Generation



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

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



PRIMARY OUTCOMES²

- Safety and tolerability
- Manufacturing feasibility

SECONDARY OUTCOMES & ADDITIONAL ANALYSES²

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



Key Takeaways from CT-0508 Study 101 (Monotherapy)

Well-tolerated and active therapy in safety study sets the stage for further development of anti-HER2 CAR-M



Safety, Tolerability and Feasibility

- Well-tolerated with no severe CRS, no ICANs, and no on-target off-tumor toxicity
- Successfully manufactured autologous, functional, M1 polarized anti-HER2 CAR-Macrophages
- Median dose of 1.66B cells across 14 patients (9 fractionated dosing, 5 bolus dosing)



Secondary and Exploratory Analyses

- SD in 28.6% of patients (n=4/14), per RECIST 1.1
- Any individual target lesion reduction in 40.7% of target lesions (n=11/27)
- HER2 3+ patients demonstrated enhanced clinical outcomes, with 44.4% (n=4/9) achieving SD
- Patients with lower CD8 T cell exhaustion / higher T cell fitness achieved SD
- CT-0508 detected in TME of 11/12 patients, but at low numbers (~1-2 per biopsy slide)

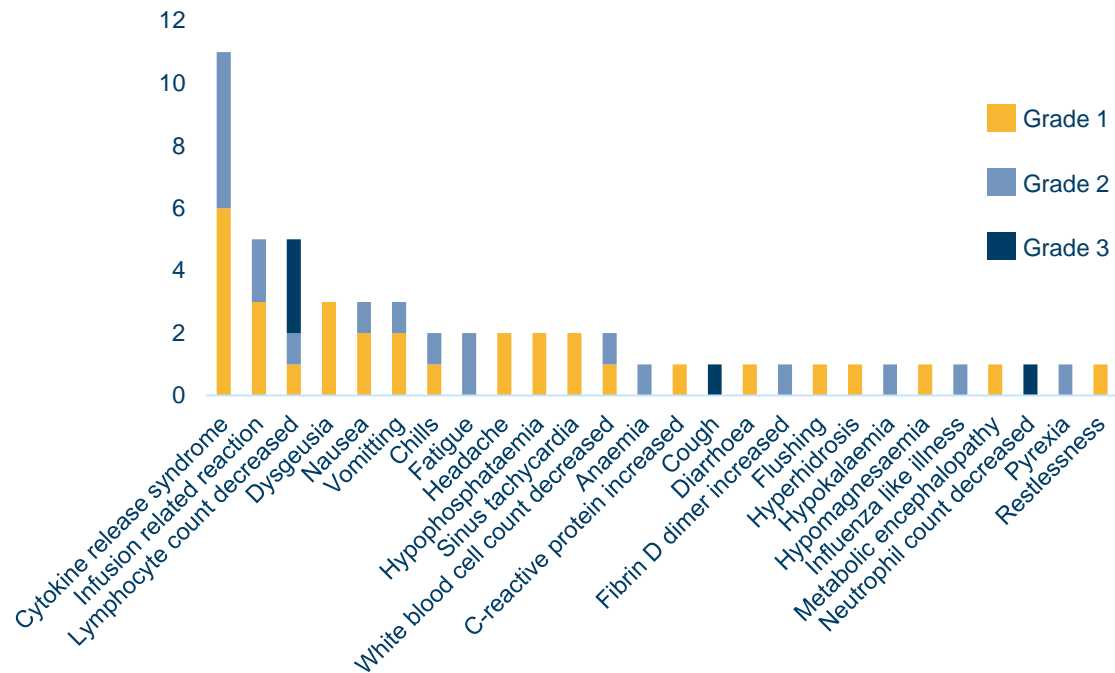
CT-0508 is a well-tolerated therapy, which has shown clear MOA and biological activity in HER2 3+ patients, despite low trafficking, low persistence and a patient population with exhausted T cells



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

Preliminary data supports a safe and tolerable 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

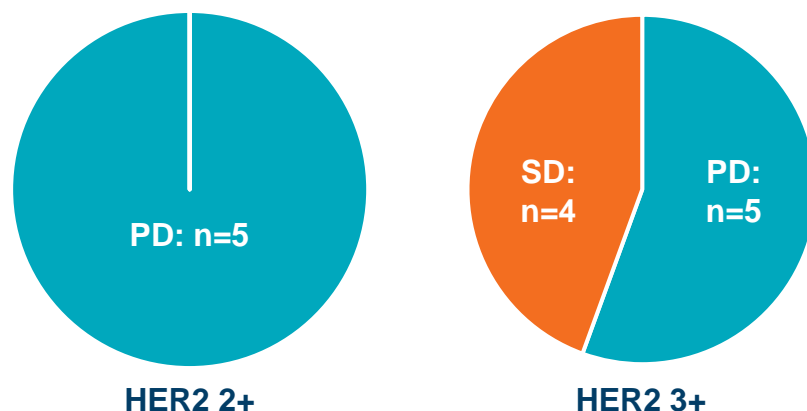
No severe CRS or ICANS

Majority of adverse events were Grade 1-2

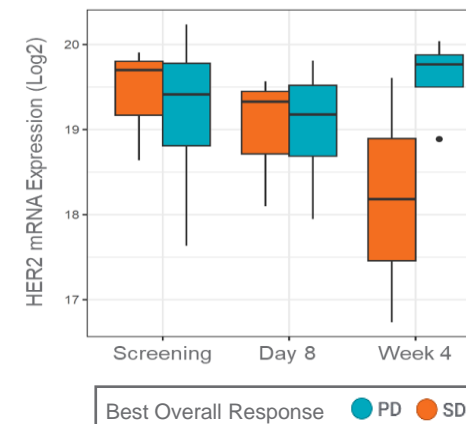
Biologically Active with Antigen Dependent MOA

Single agent CAR-M demonstrated target lesion shrinkage

Correlation between HER2 status and Best Overall Response



Trend Toward Decrease in HER2+ Tumor Cells in Patients with Stable Disease (SD)

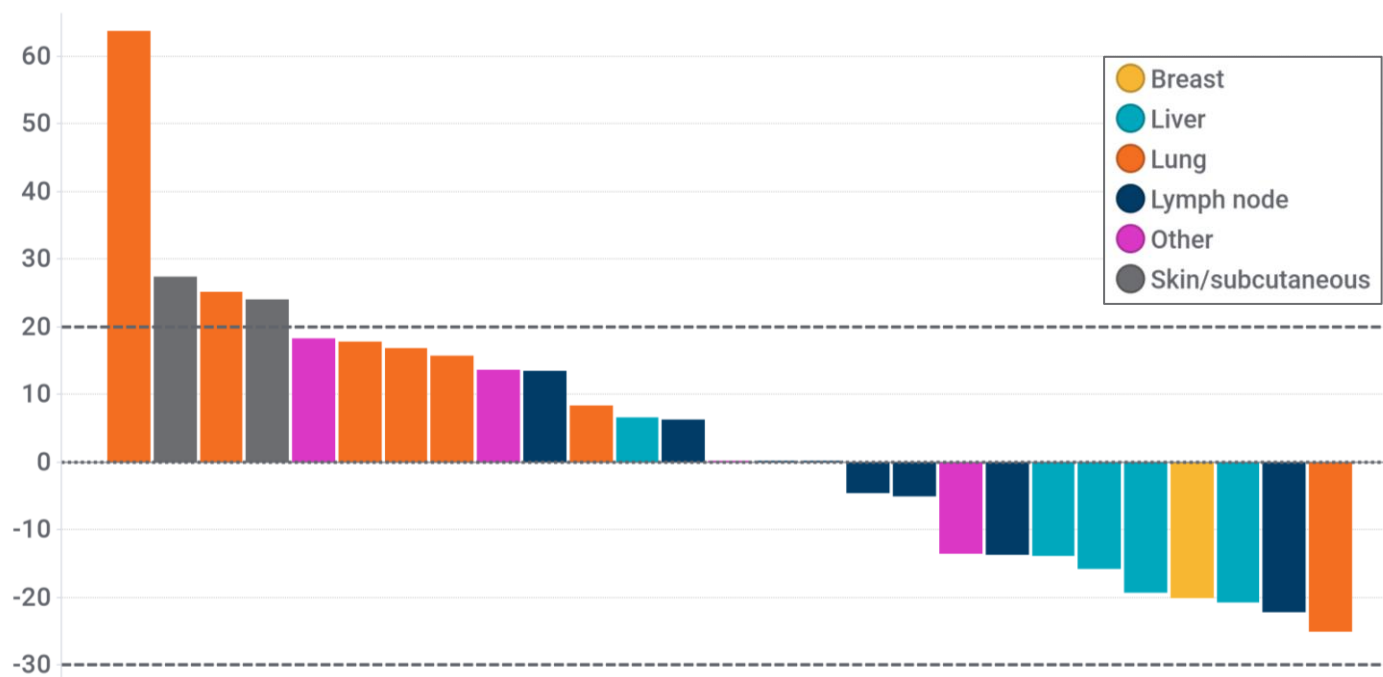


KEY TAKEAWAYS

- Best Overall Response of Stable Disease in 4 of the 14 evaluated participants (28.6%)*+
- Largest reduction in target lesion include 20% reduction in breast cancer patient and 14% reduction in 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

40.7% of all target lesions had reduced in size on at least 1 scan

Best changes in individual target lesions by anatomic site



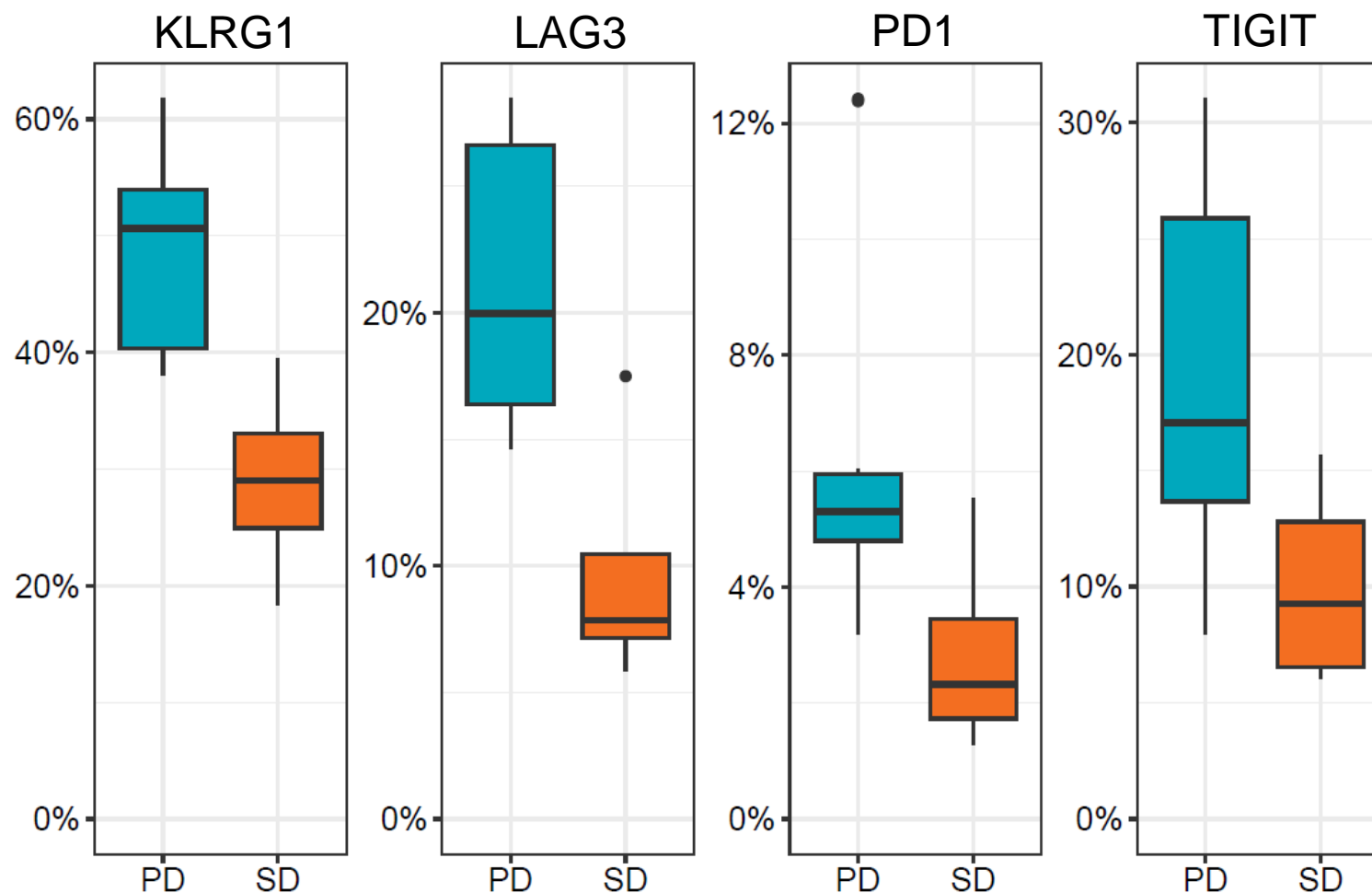
Note: Each column represents a single target tumor lesion, not a patient.

Target lesion reduction by anatomic site

Anatomic Location	Frequency of tumor lesions that reduced on treatment on at least 1 scan
Breast	1/1 (100%)
Liver	4/5 (80%)
Lung	1/7 (14.3%)
Lymph Node	4/8 (50%)
Other	1/4 (25%)
Skin/Subcutaneous	0/2 (0%)
All Lesions	11/27 (40.7%)

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

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

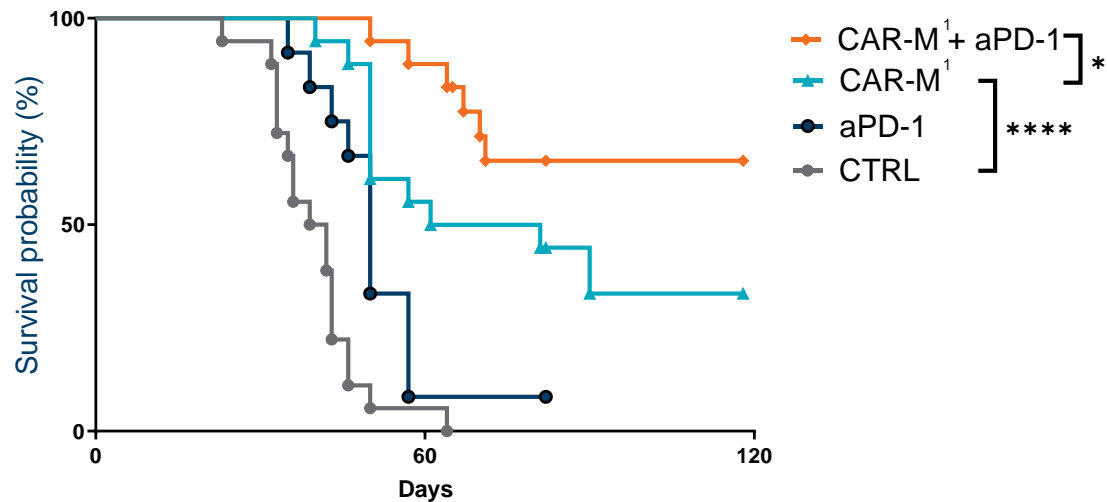




CT-0508 + Anti-PD1: Robust Synergy

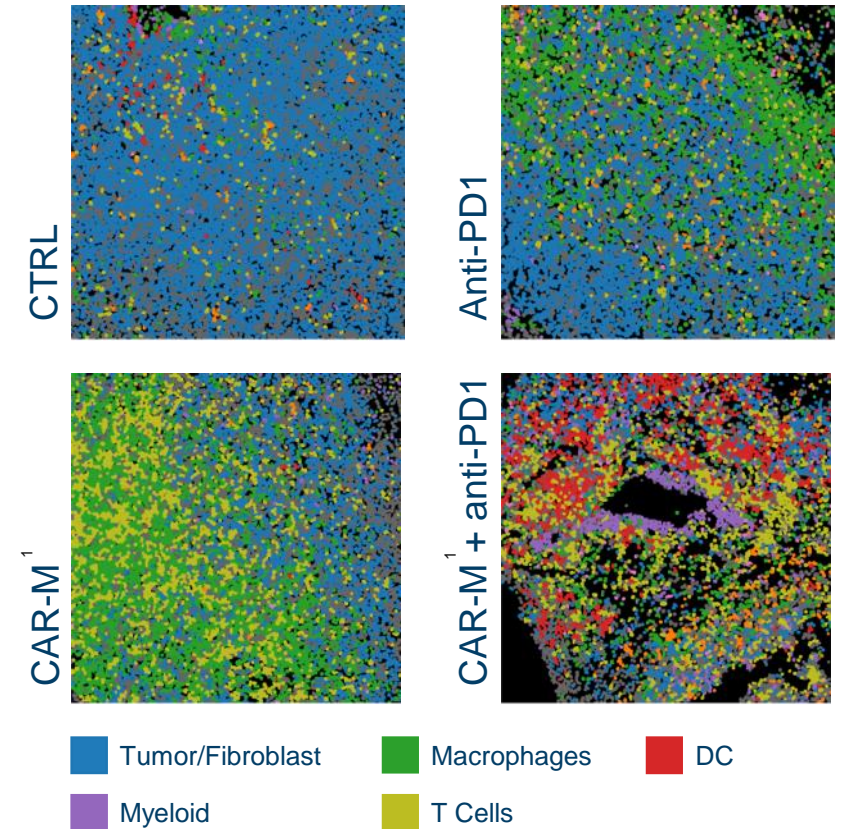
Synergy in a solid tumor model that is resistant to anti-PD1 monotherapy

Synergistic anti-tumor activity



Syngeneic CT26-HER2 solid tumor model.
Resistant to anti-PD1 monotherapy.

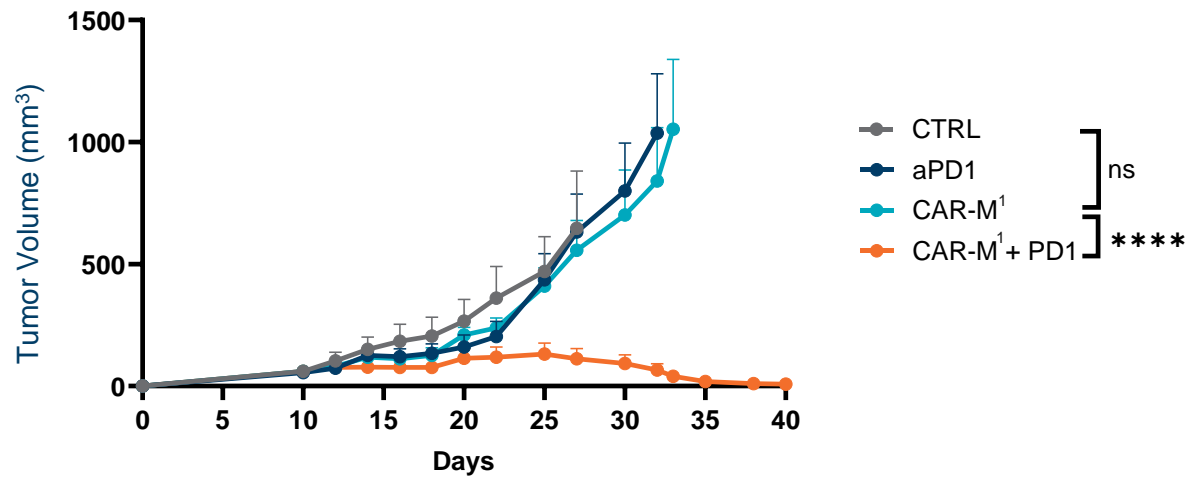
Synergistic TME modulation with combination



CT-0508 + Anti-PD1: Robust Synergy

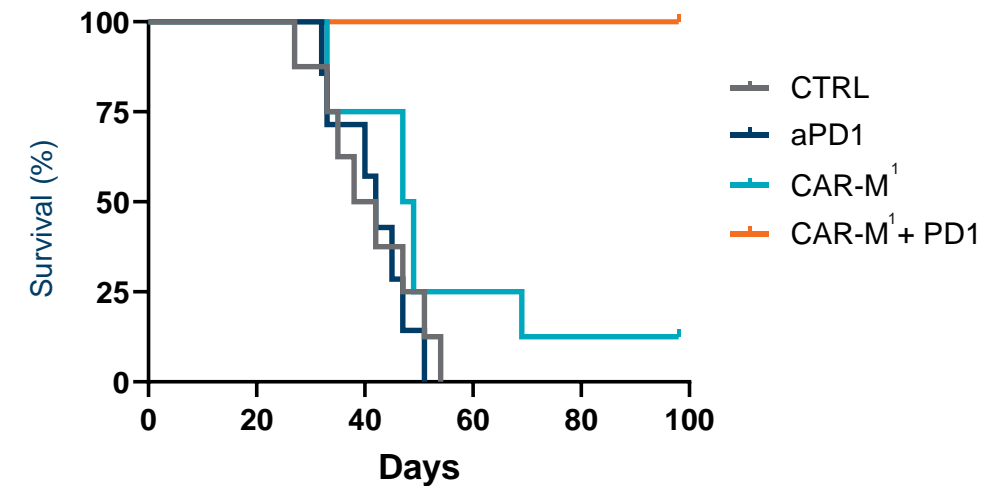
Synergy in a solid tumor model that is resistant to both CAR-Macrophage *and* anti-PD1 monotherapy

I.V. CAR-M¹ + anti-PD1 leads to synergistic tumor control



Syngeneic CT26-HER2 solid tumor model.
Resistant to anti-PD1 monotherapy.

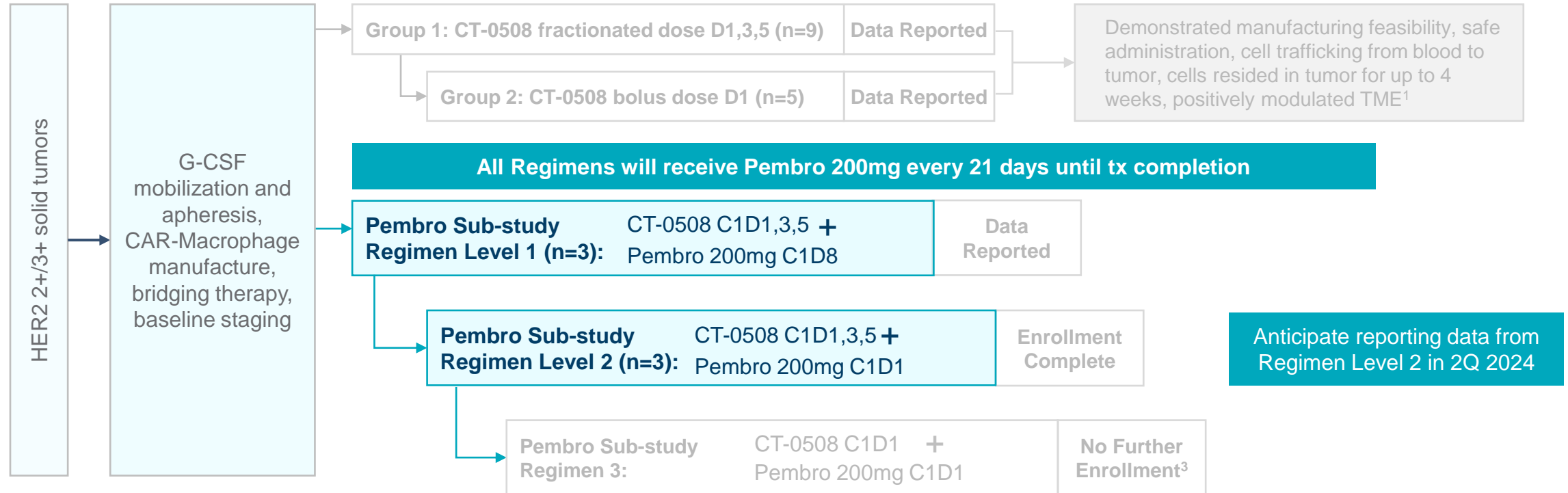
I.V. CAR-M¹ + anti-PD1 leads to 100% survival





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

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

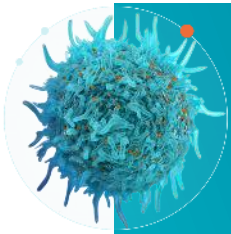


PRIMARY OUTCOMES²

- Safety and tolerability

SECONDARY OUTCOMES & ADDITIONAL ANALYSES²

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



Key Takeaways from CT-0508 + Pembrolizumab Regimen Level 1

First regimen promising, meeting safety and feasibility endpoints and demonstrating biologic activity

+ Safety, Tolerability and Feasibility

- Well-tolerated with no severe CRS, no ICANs, and no on-target off-tumor toxicity
- Patients 1 and 2 treated with corticosteroids which limits CT-0508 activity
- Successfully manufactured autologous, functional, M1 polarized anti-HER2 CAR-Macrophages
- Median dose of 2.95B cells

+ Secondary and Exploratory Analyses

- Patient 3 had greatest increase in peripheral blood T cell clonality (~3x) seen to date
- Patient 3 had greatest individual lesion reduction (46%) seen to date
- Patient 3 achieved a BOR of SD* despite having high baseline T-cell exhaustion
- SD in 50% of patients in sub-study with HER2 3+ disease (n=1/2)

Regimen Level 1 was well-tolerated.

Administration of corticosteroids in 2 of 3 patients limits the interpretation of these results.

Patient without corticosteroid administration demonstrated potentially meaningful biologic activity.

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

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

No severe CRS or ICANS

CT-0508+Pembro Sub-study: 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 Capecitabine, 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

CT-0508+Pembro Sub-study: Individual Case Study

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

Dosing

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

Tumor assessments

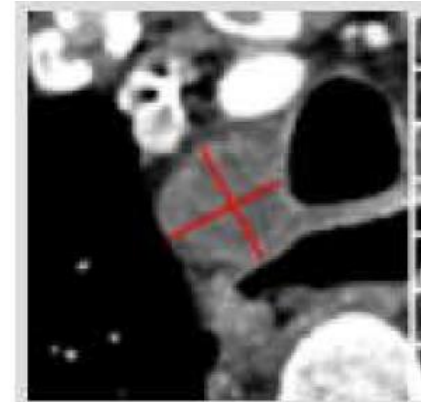
- Paratracheal target lesion reduction of 46% by week 13; 21.9mm to 11.8mm
- Mediastinal mass target lesion grew 31% by week 13; 26.9 to 35.3mm

Clinical assessments

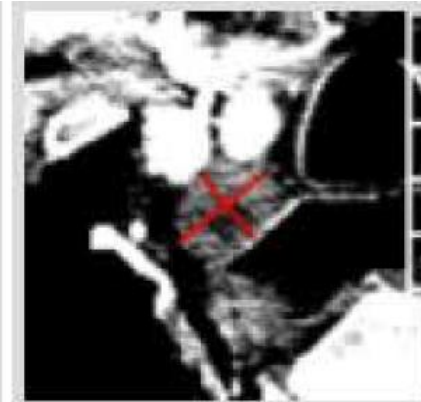
- Achieved a BOR of SD per RECIST 1.1
- PD per RECIST at week 13 due to new CNS metastasis
- PFS of 3.25 months (13.3 weeks)

Paratracheal LN Target Lesion: 46% reduction by week 13

Baseline



Week 8



Week 13

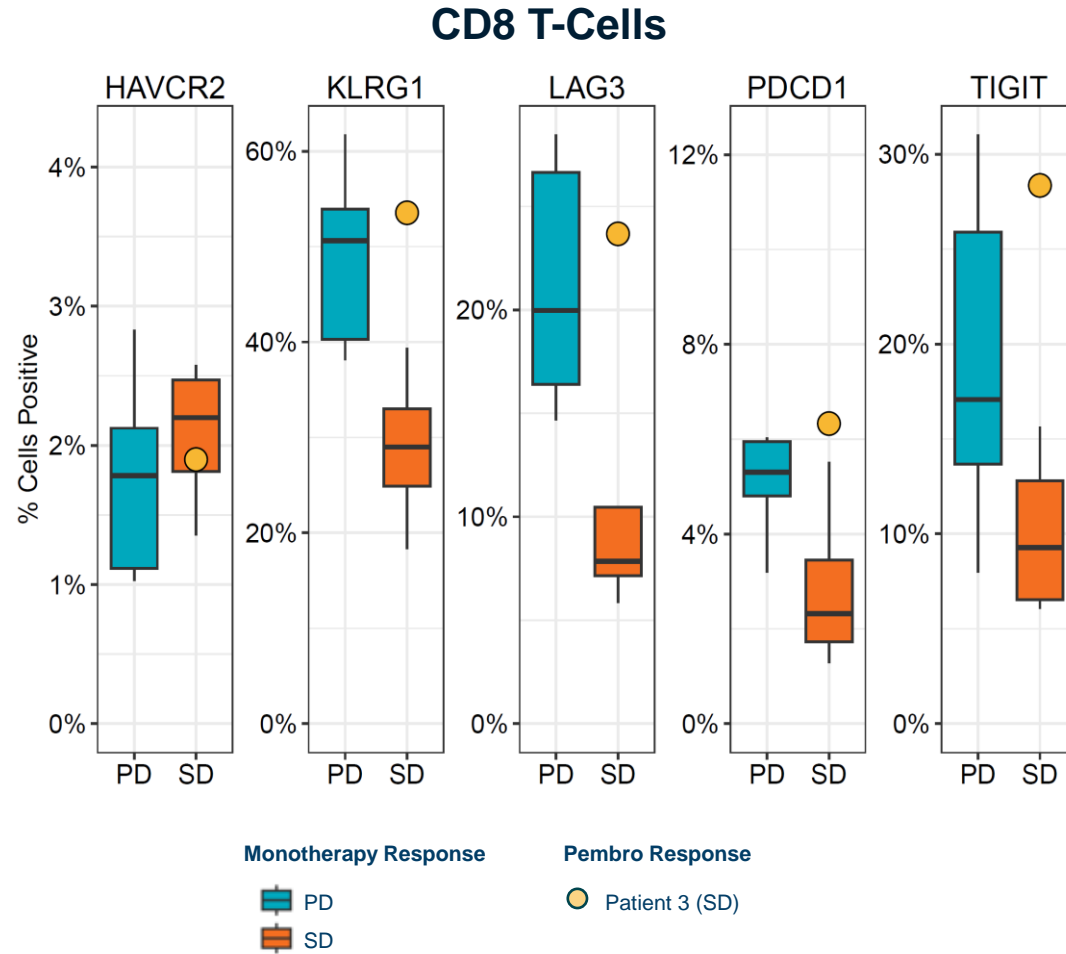


Outcome Comparators	PFS
Patient 3 – Regimen 1 CT-0508 / Pembro	3.25 months
Patient 3 – 6 th Line of Therapy on Enhertu	2.0 months
Pembrolizumab monotherapy in KEYNOTE 180*	1.5 months

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

CT-0508+Pembro Sub-study: Individual Case Study

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

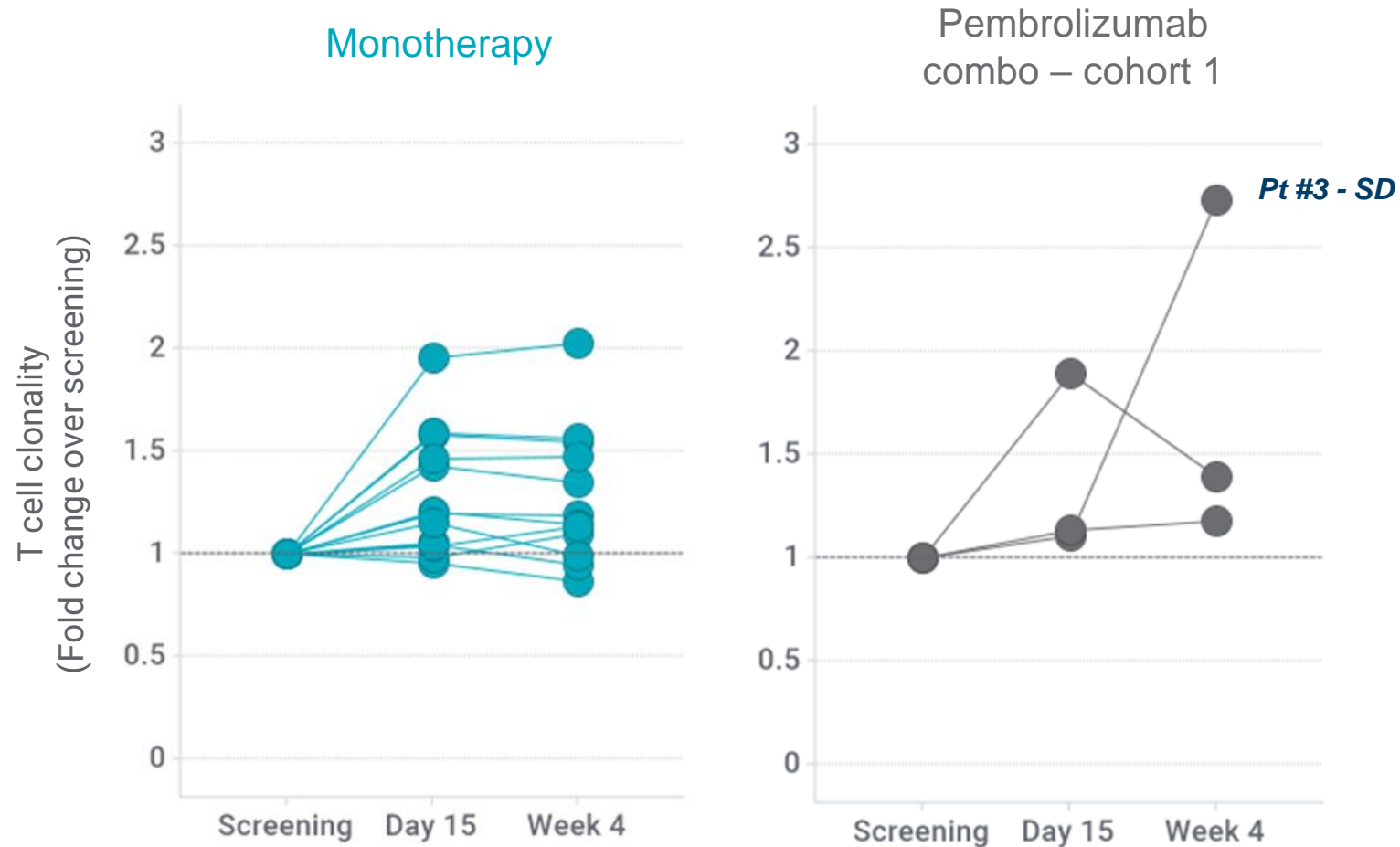


Patient 3 achieved BOR of SD despite high baseline peripheral CD8 T cell exhaustion

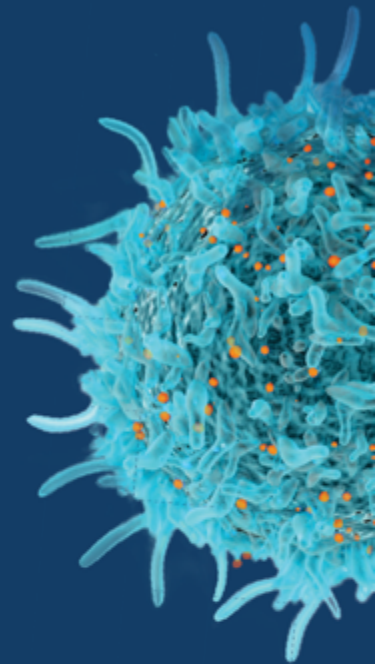
CT-0508+Pembro Sub-study: Individual Case Study

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



In Vivo Oncology



In Vivo CAR-M

Collaboration with Moderna to discover, develop and commercialize *in vivo* CAR-M in oncology

Highlights



Collaboration Overview

- Combines Carisma's engineered macrophage technology with Moderna's mRNA and LNP technologies
- First *in vivo* CAR-M lead candidate nominated



Key Advantages of *in vivo* CAR-M

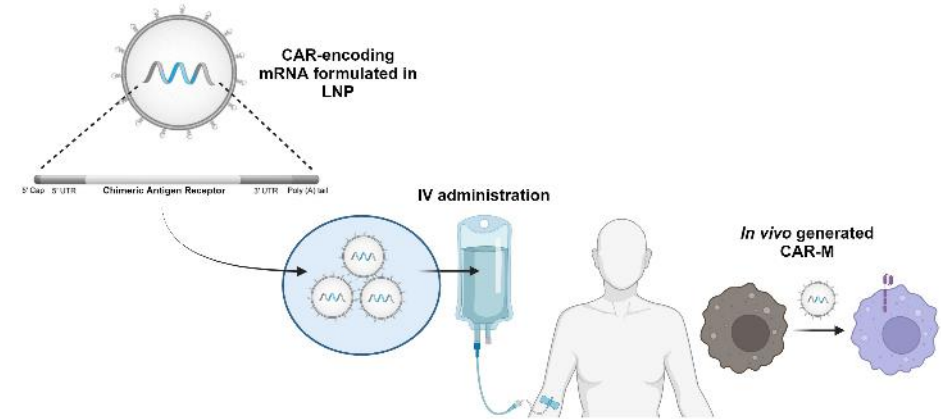
- Robust platform with applications in diverse indications
- Off-the-shelf product with ability to re-dose
- Maintains functionality of *ex vivo* CAR-M



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

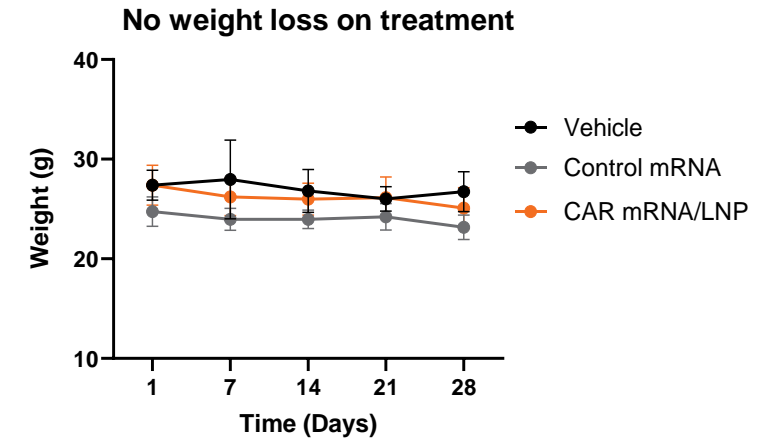
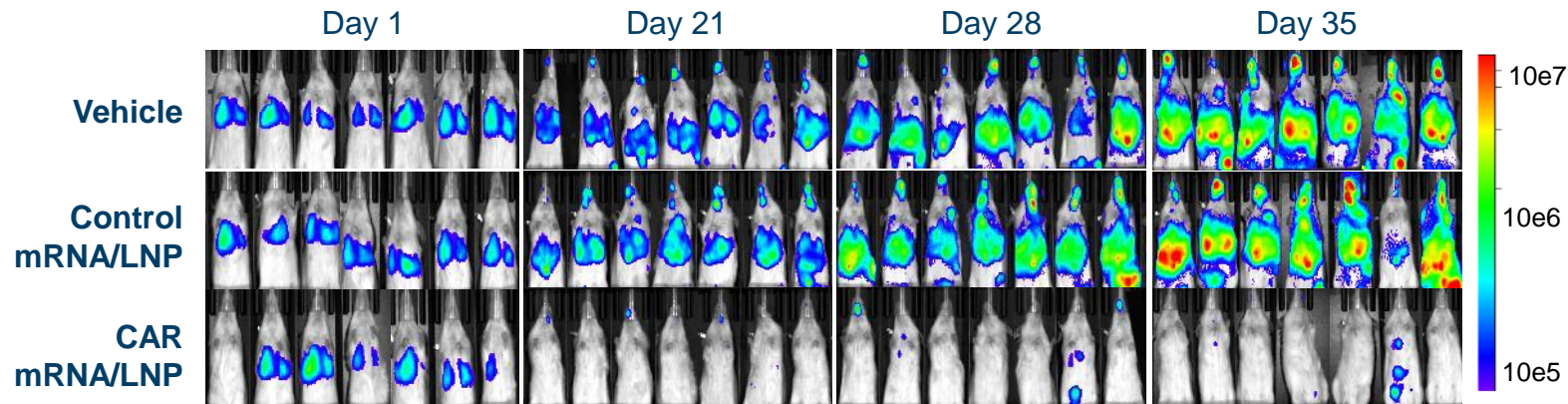
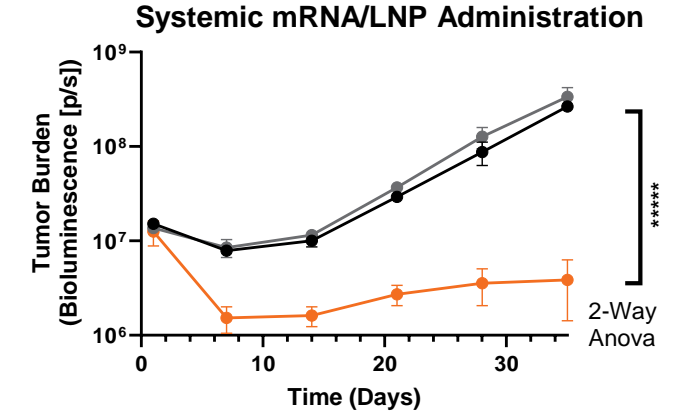
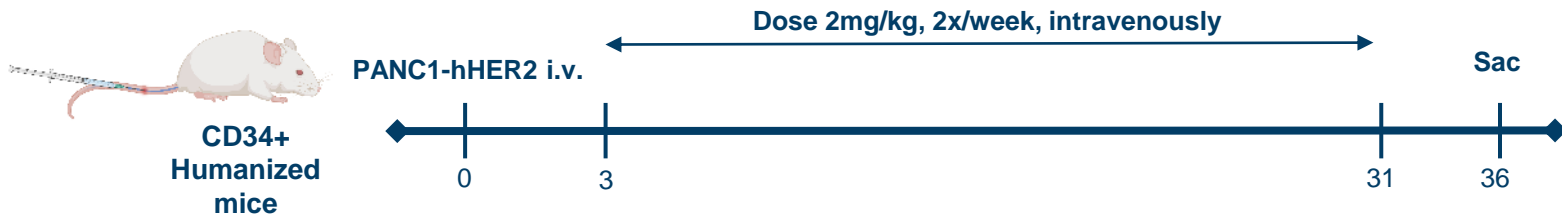
Redirecting endogenous myeloid cells with mRNA for cancer immunotherapy



 Collaboration Terms 	
Number of Targets	Up to 12 (5 Identified)
Upfront Payment	\$80M
Total Potential Milestones and Royalties	\$3B+
R&D Funding	Fully funded by Moderna

In Vivo CAR-M Controls Metastatic Pancreatic Cancer

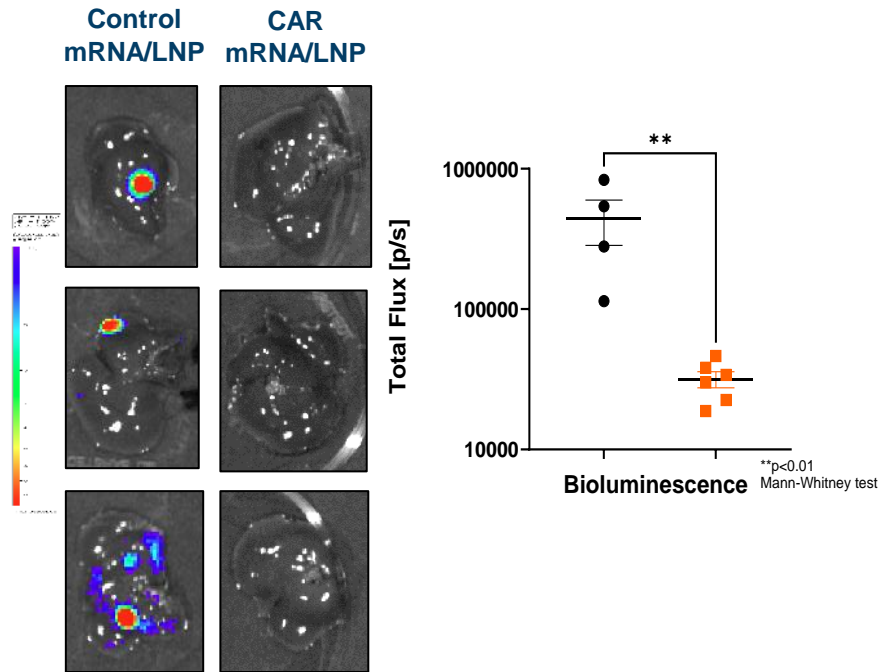
Systemic LNP administration in humanized mouse model of pancreatic cancer



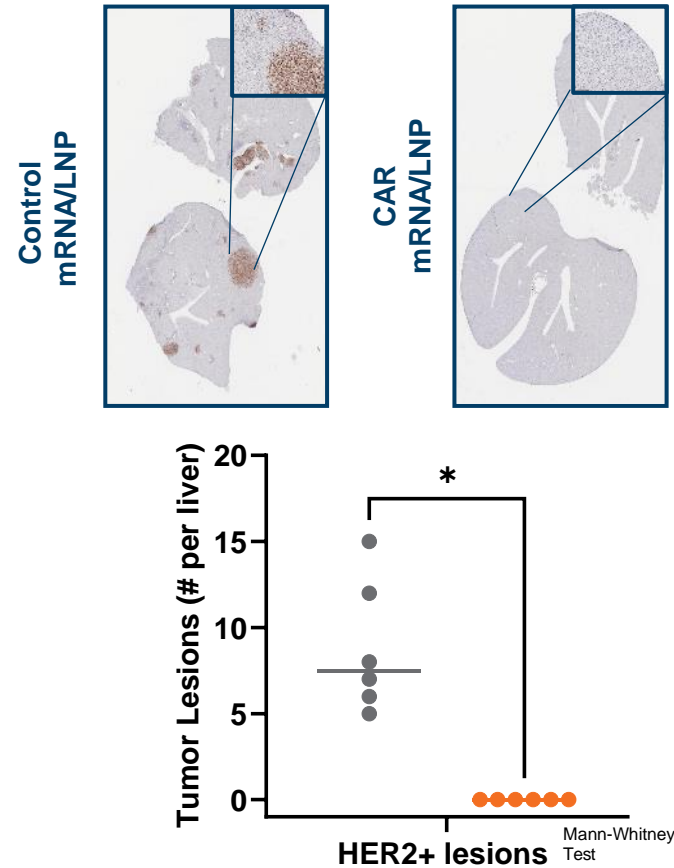
In Vivo CAR-M Suppresses Liver and Lung Metastasis

Systemic LNP administration in humanized model leads to robust disease control

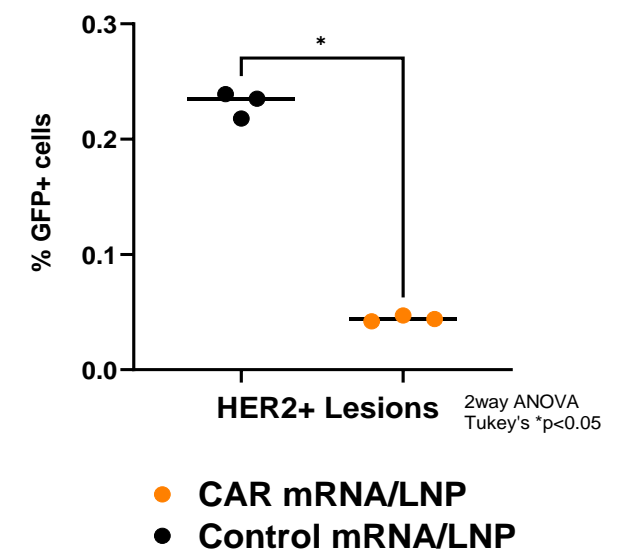
Tumor Lesions in Liver (BLI)



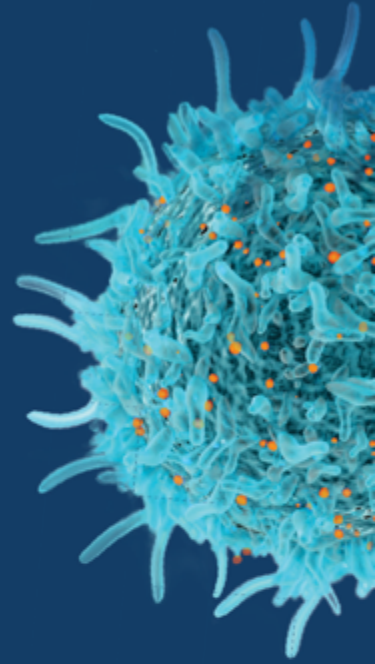
Tumor Lesions/Liver (IHC)



Tumor Lesions in Lung (IHC)



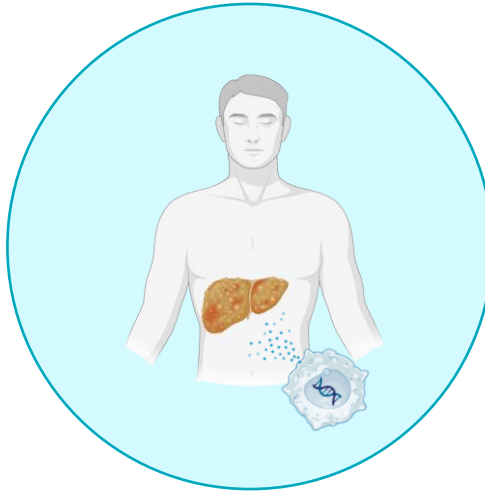
Developing macrophage cell therapies beyond oncology: Fibrosis



Engineered Macrophages For Liver Fibrosis

Significant Unmet Need

- Chronic liver disease and cirrhosis account for over 1M deaths per year globally¹
- Risk of liver-related mortality substantially increases in Stage 3/4 MASH with significant fibrosis
- High unmet need for safe and effective MASH treatments that correct both steatosis and fibrosis
- GLP-1 agonists have had no impact on fibrosis



Potential of Macrophages In the Liver

- Macrophages are critical regulators of **inflammation, fibrosis deposition, and fibrosis resolution**²
- Non-engineered macrophage cell therapy has **demonstrated** efficacy in mouse models and **safety**⁴/**activity**⁵ in clinical trials³
- Genetically engineered macrophages have the potential to engraft in the liver and provide a source for disease modifying therapeutic factors

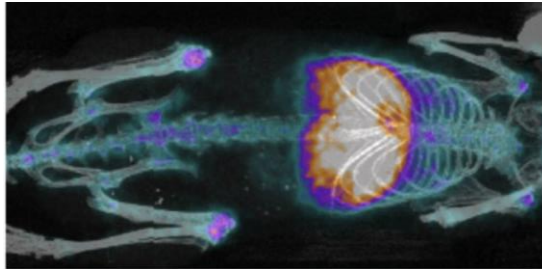
**Achieved preclinical proof of concept in liver fibrosis program⁶;
Development candidate nomination expected in the first quarter of 2025**

Engineered Macrophages For Liver Fibrosis

A Novel Strategy For A Significant Unmet Medical Need

Macrophages engraft in the liver

Robust engraftment of engineered macrophages intravenously injected in the liver



PET imaging of mice intravenously injected with Zn⁸⁹ labeled human macrophages¹

Engineered macrophages can persist for months in the liver, serving as durable “hepatic micropharmacies” secreting therapeutic payloads²

Engineered macrophages expressing disease modifying factors may reverse liver fibrosis¹



Reduce inflammation



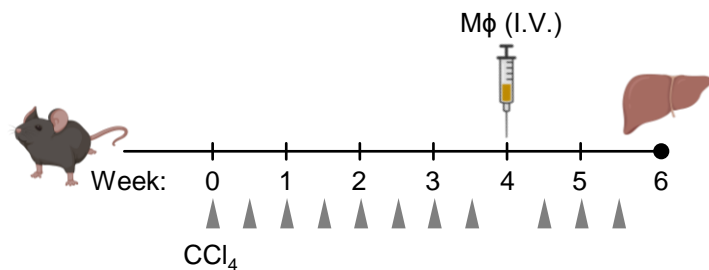
Reverse established fibrosis



Promote tissue regeneration

• A Single Dose of Engineered Macrophages Significantly Reduced Liver Fibrosis¹

CCl₄ model of established fibrosis



Engineered Mφ significantly reduced hepatic collagen

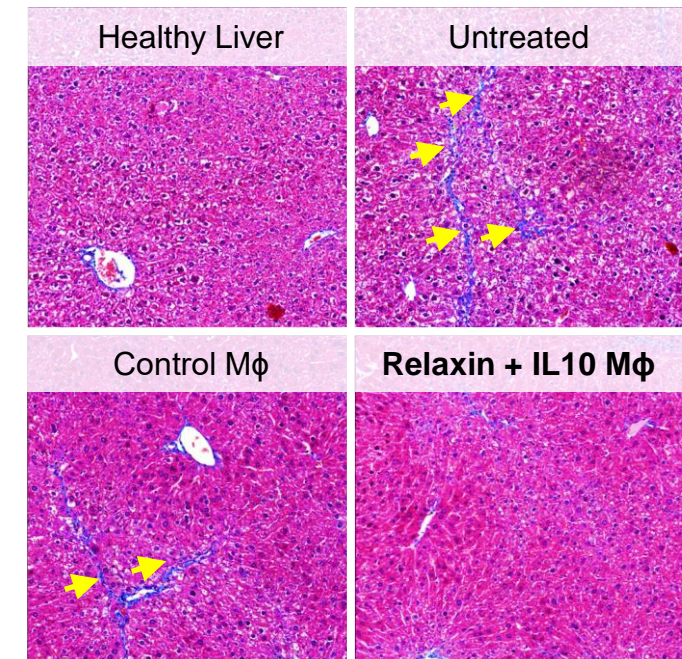
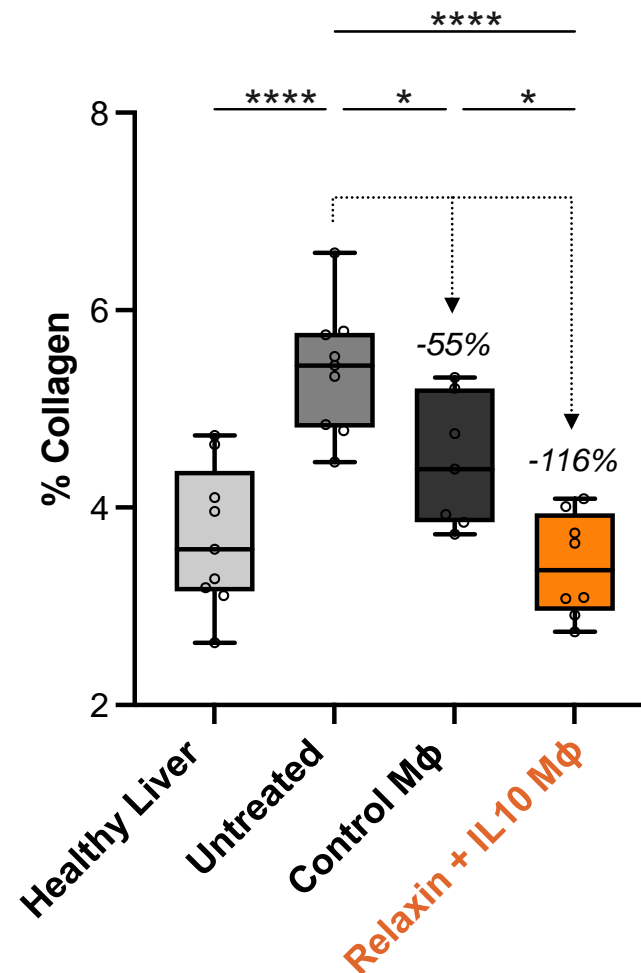
Control Mφ:

- 55% reduction in collagen

Relaxin-IL10 Mφ:

- >100% reduction in collagen²
- 8/8 mice return to healthy range

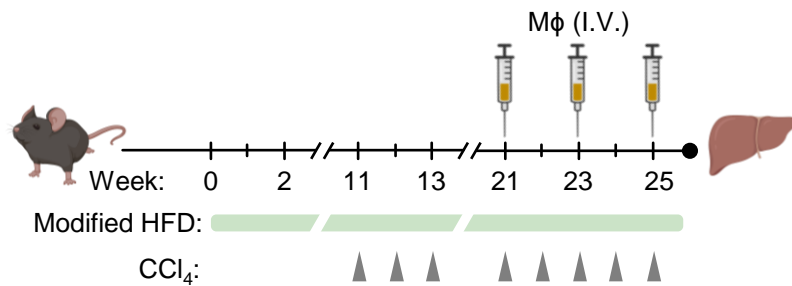
Relaxin-IL10 macrophages significantly reduced established fibrosis



Masson's Trichrome Staining
Fibrosis shown in blue

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

High fat diet MASH model



Engineered Mφ significantly reduced fibrotic collagen

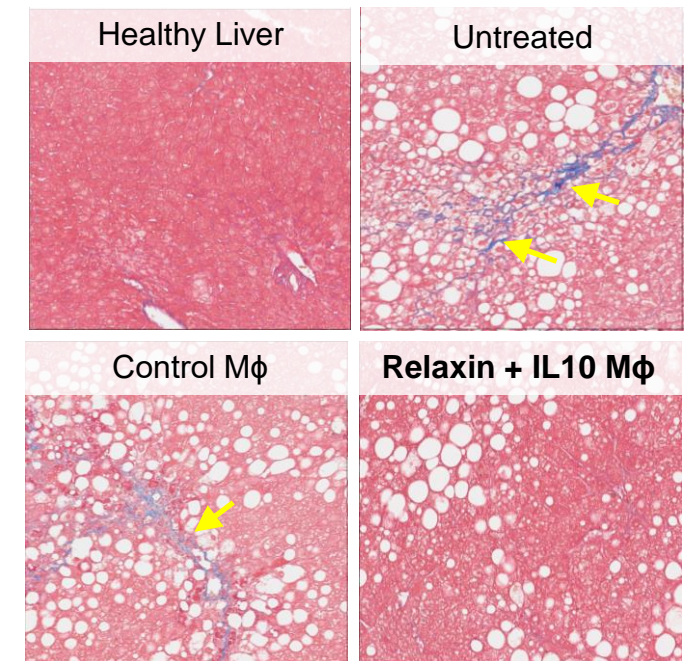
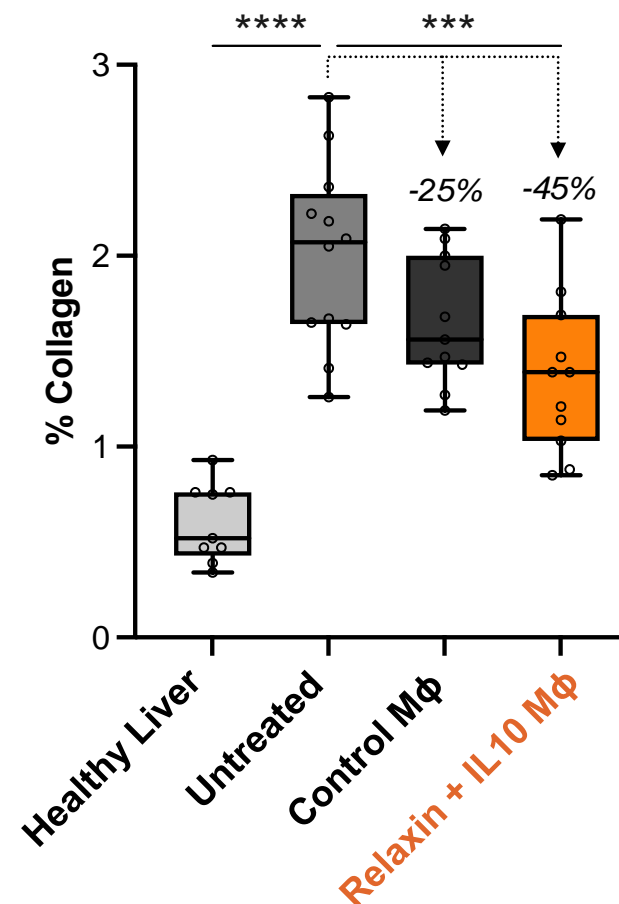
Control Mφ:

- 25% reduction in collagen

Relaxin-IL10 Mφ:

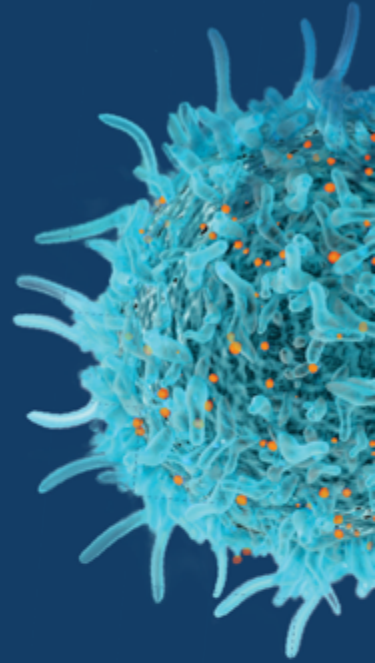
- 45% reduction²

Relaxin-IL10 macrophages significantly reduced fibrosis



Masson's Trichrome Staining
Fibrosis shown in blue

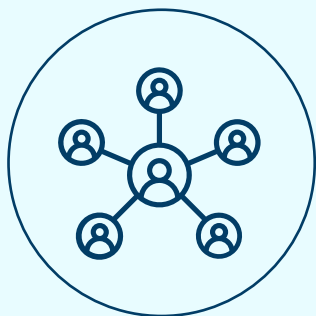
Corporate & Financial





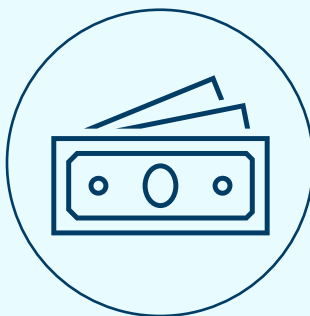
Financial Snapshot

As of March 31, 2024



41.5M

Shares outstanding



\$56.5M

Cash and cash equivalents



Into 3Q 2025

Expected cash runway*



Operating Plan and Corporate Milestones

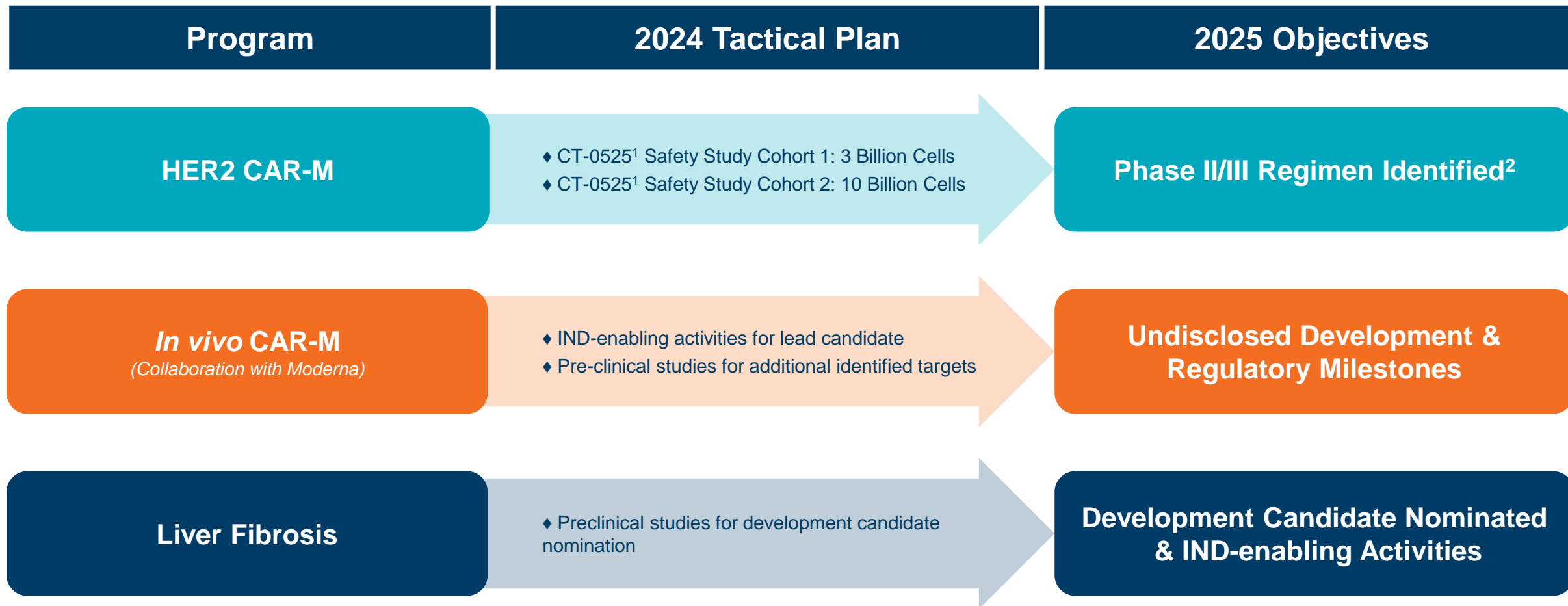
Capital efficient R&D program designed to reach significant value inflection points

Therapeutic Area	Product Candidate	Platform	Recent and Anticipated Milestones		
Ex Vivo Oncology					
HER2+ solid tumors	CT-0525	CAR-Monocyte (1 st Gen CAR)	4Q'23	IND cleared	✓
			2Q'24	Treat first patient	✓
			4Q'24	Report initial data from Phase 1 study	□
	CT-0508*	CAR-Macrophage (1 st Gen CAR)	2Q'24	Report data from Phase 1 combination sub-study	□
In Vivo Oncology					
Oncology	Solid Tumor Antigen ¹	CAR-Macrophage + mRNA/LNP	4Q'23	Nominate first <i>in vivo</i> CAR-M lead candidate	✓
			TBD	Development candidate selection	□
	4 Additional Targets ²	CAR-Macrophage + mRNA/LNP	4Q'23	Report proof of concept data for <i>in vivo</i> CAR-M (SITC 2023)	✓
Fibrosis and Immunology					
Liver Fibrosis	TBD	Engineered macrophage	2Q'24	Report preclinical proof of concept data (ASGCT 2024)	✓
			1Q'25	Nominate development candidate	□



Drive to 2025

Leverage world-leading macrophage engineering platform to deliver three product opportunities

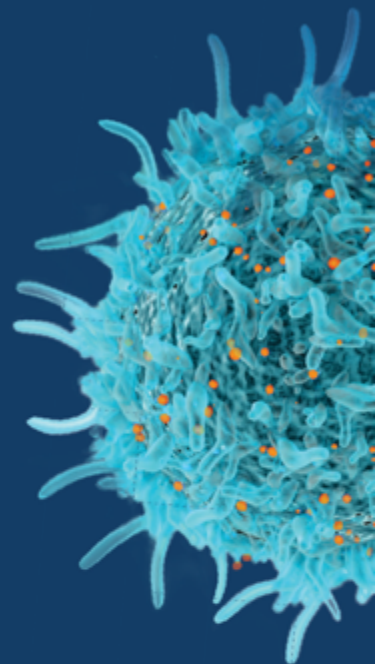


APPENDIX



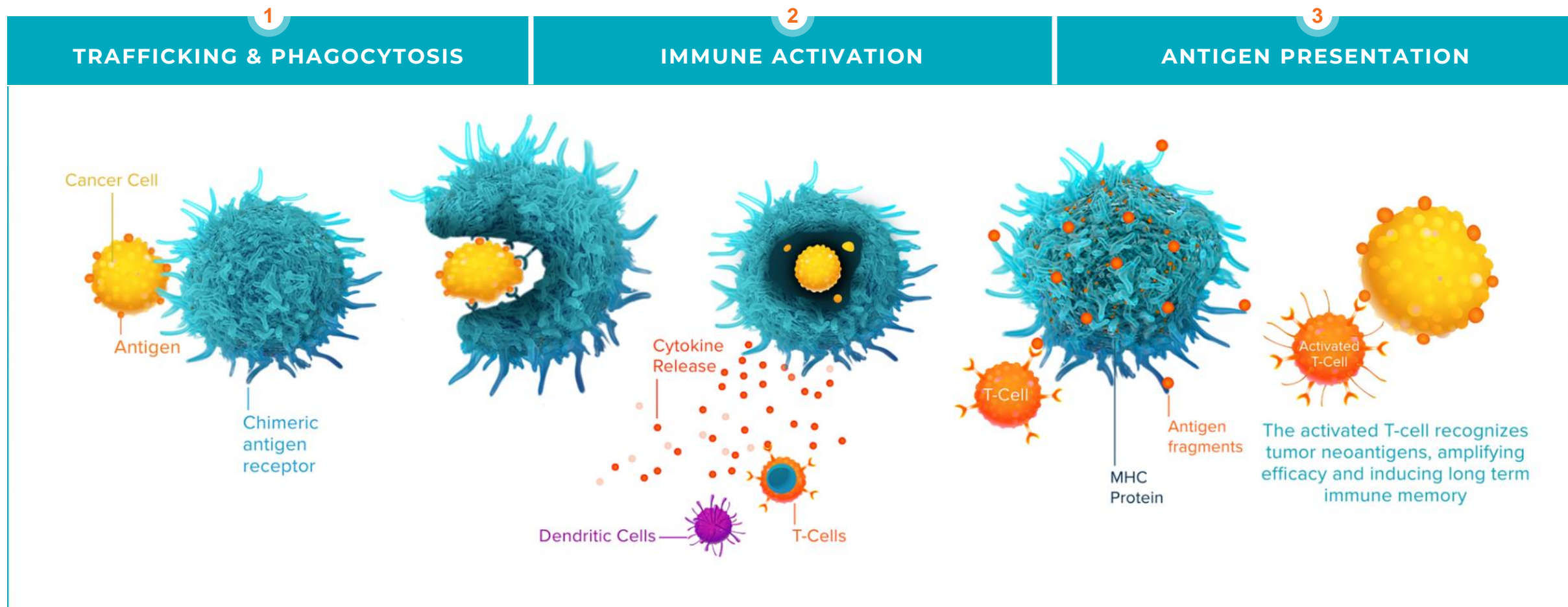
carisma
THERAPEUTICS

Carisma Platform



CAR-M Mechanism of Action in Oncology

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



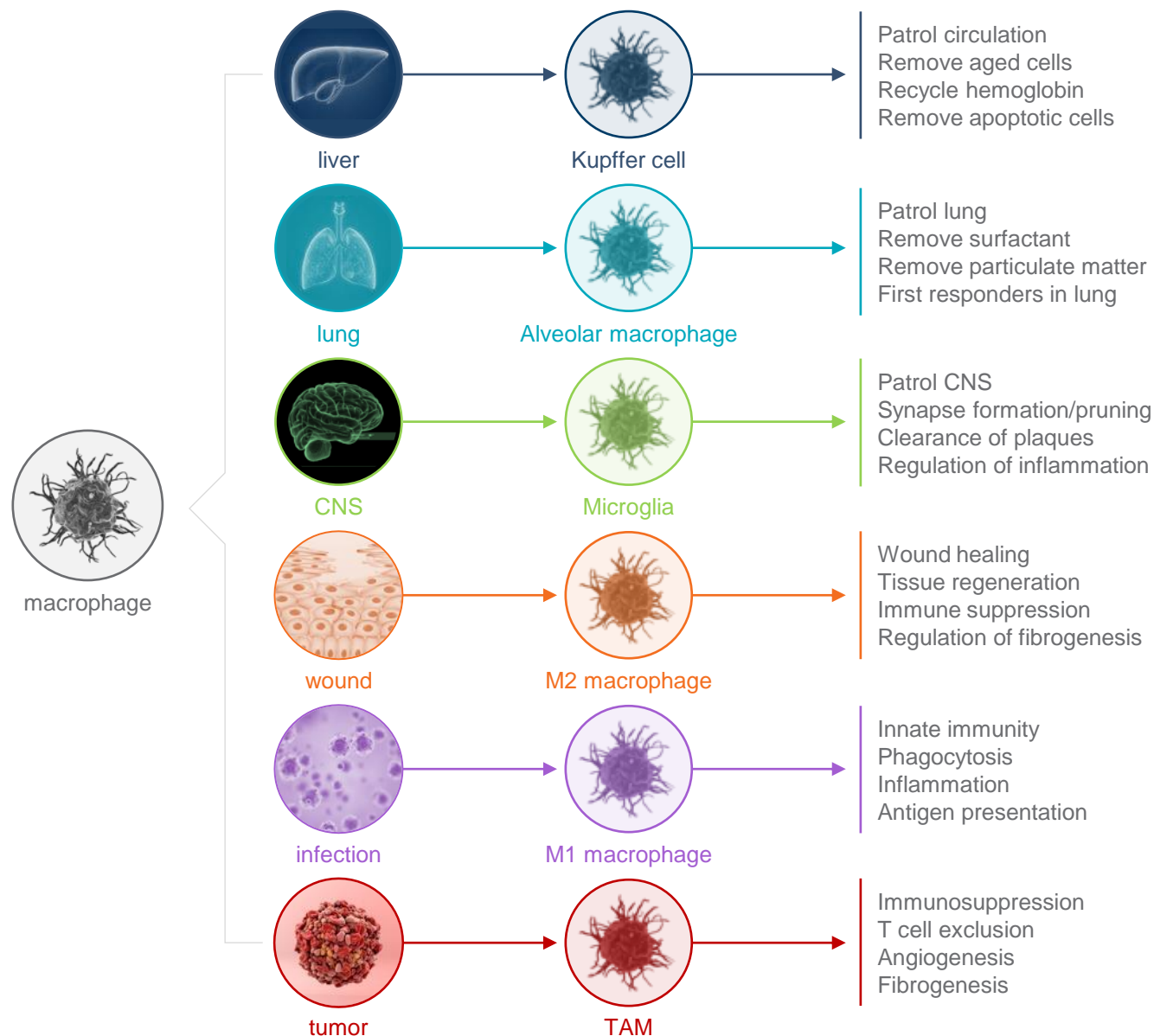


Macrophages:

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

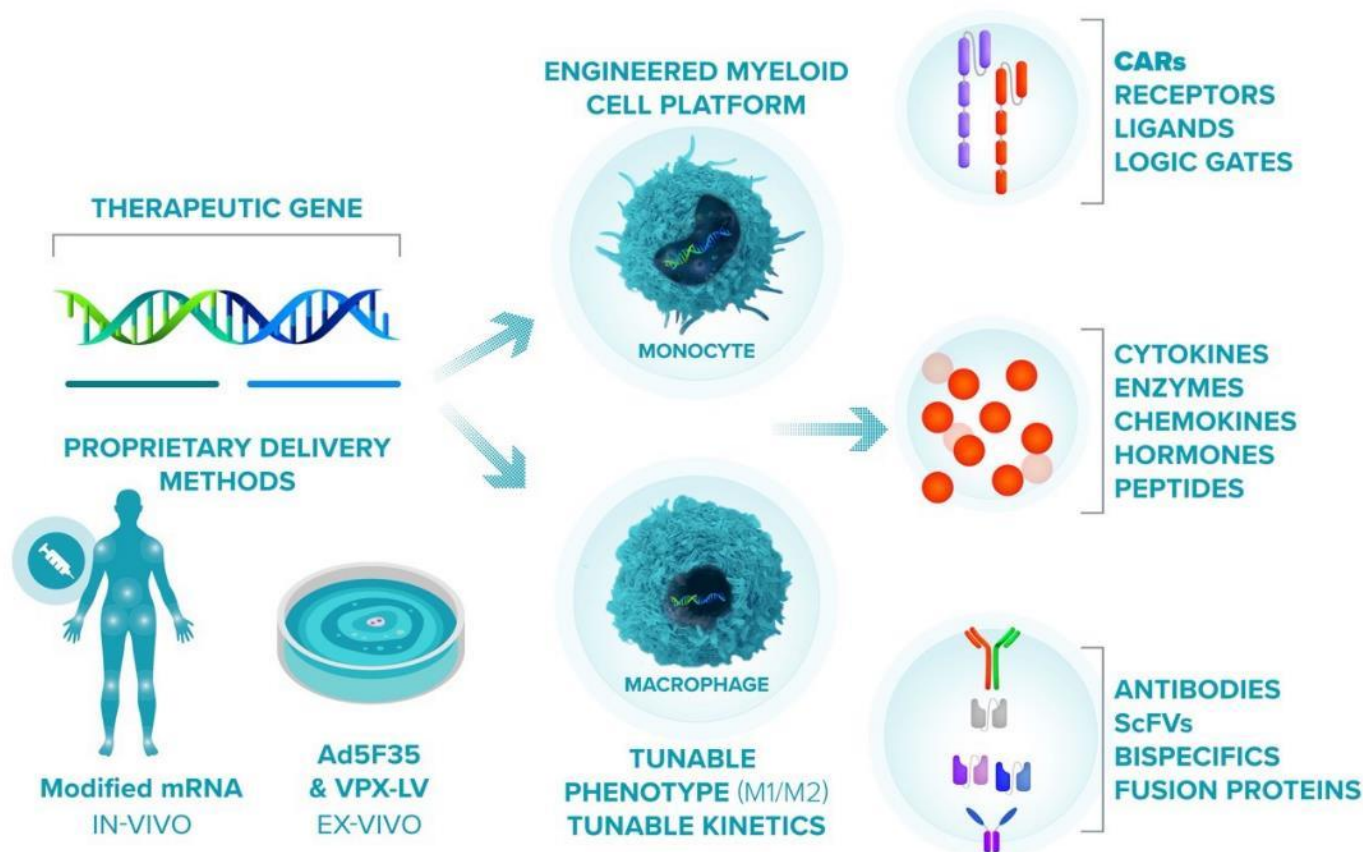


CARISMA's Broad Myeloid Cell Engineering Platform

- 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

26

PATENTS GRANTED
WORLDWIDE*

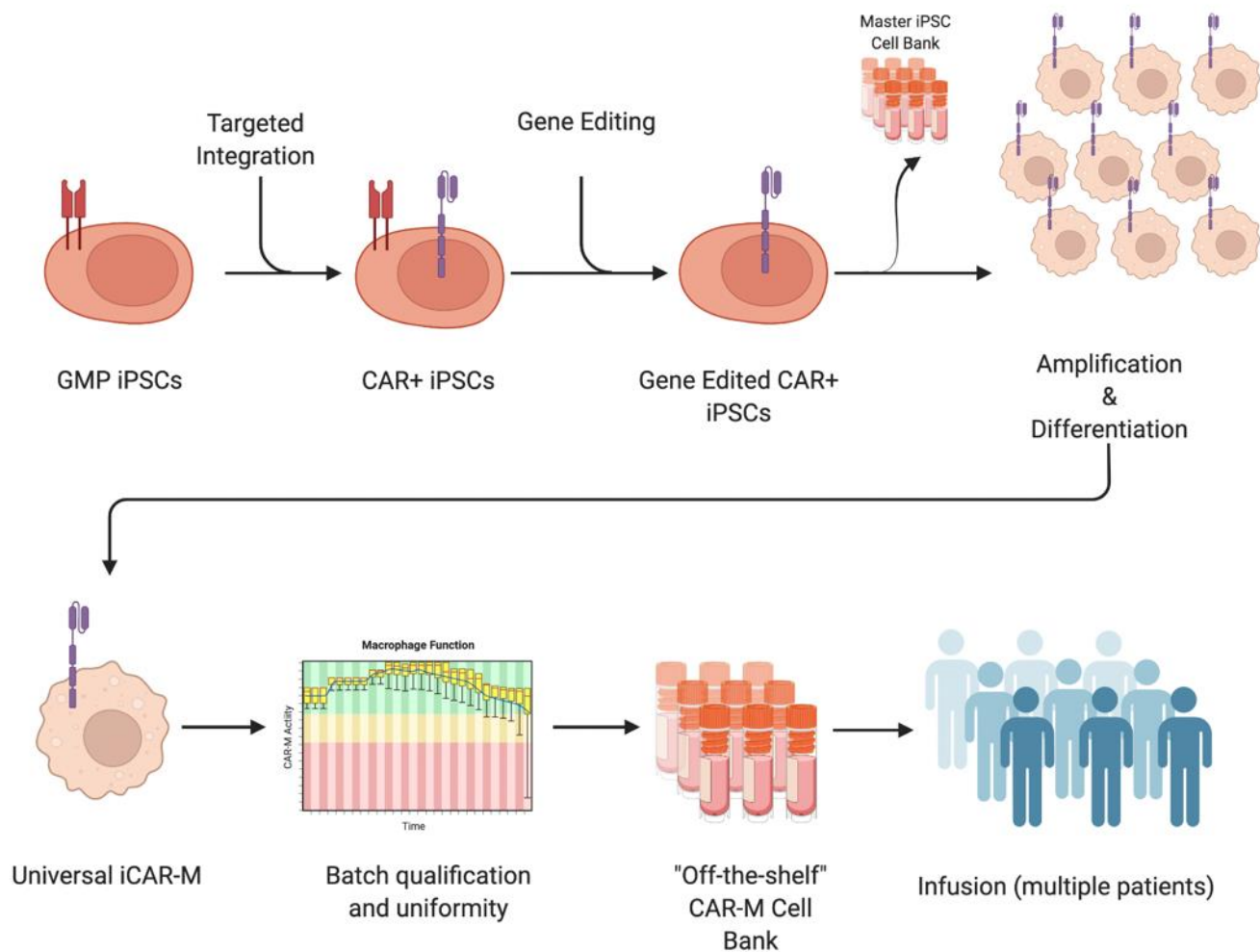
100+

PATENT APPLICATIONS
PENDING WORLDWIDE*

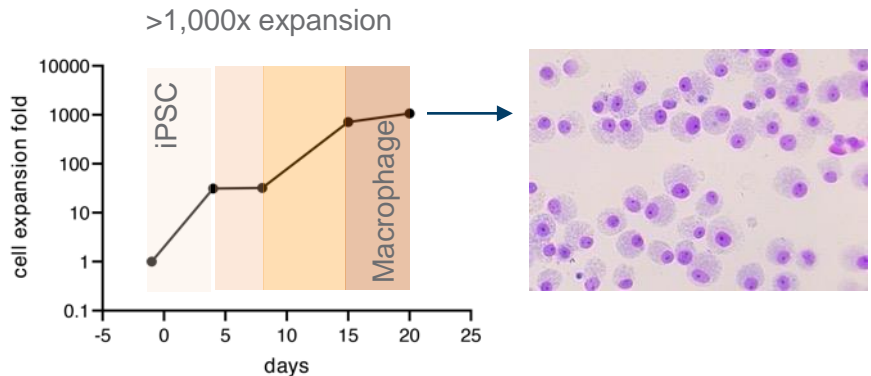
- Worldwide patent coverage with issued and pending applications in major markets
- Multiple issued US patents covering CAR-M composition of matter
- Broad patent portfolio covering:
 - Viral and non-viral methods for engineering monocytes and macrophages
 - Methods for treatment of protein aggregate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

Off-the-Shelf iPSC Derived Myeloid Cells

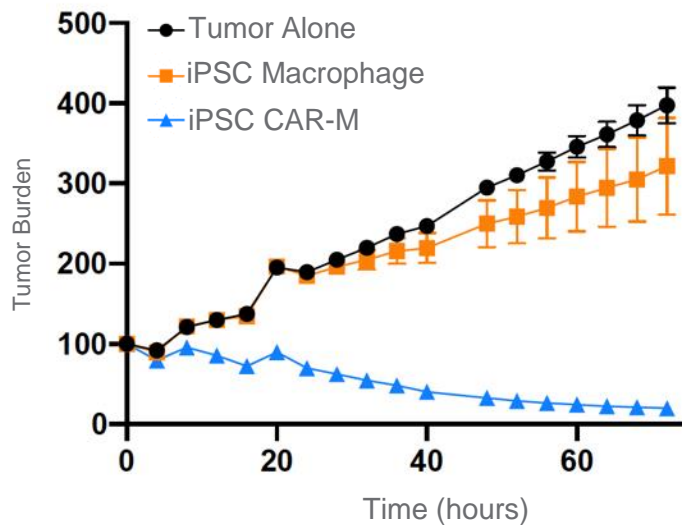
Expandable, allogeneic, and potentially broadly applicable



Production of iCAR-M



iCAR-M anti-tumor function in-vitro



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, PHARM D 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

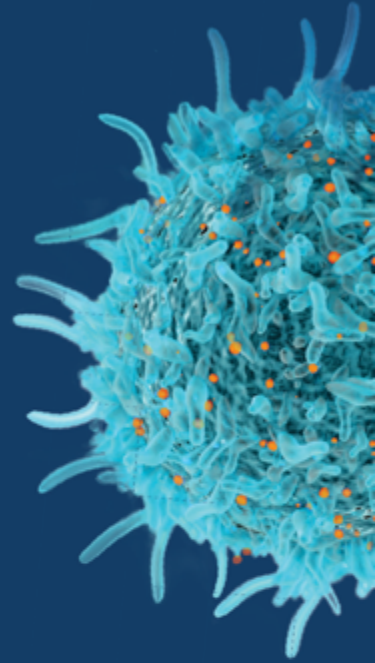
Board of Directors

- Sanford Zweifach – Chairperson
- Steven Kelly – President and CEO
- Briggs Morrison, MD – Independent Director
- Björn Odlander, PhD – HealthCap
- Regina Hodits, PhD – Wellington Partners
- Michael Torok – Independent Director
- John Hohneker, MD – 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
- Prasad S. Adusamilli, MD FACS – MSKCC
- Nina Bhardwaj, MD, PhD – Mt Sinai
- Lisa Coussens, PhD – OHSU
- Lin Guey, PhD – Moderna Tx
- Padmanee Sharma, MD, PhD - MDACC

Targeting HER2: CT-0508 Monotherapy



CT-0508 Study 101: Phase 1 Study Patient Demographics

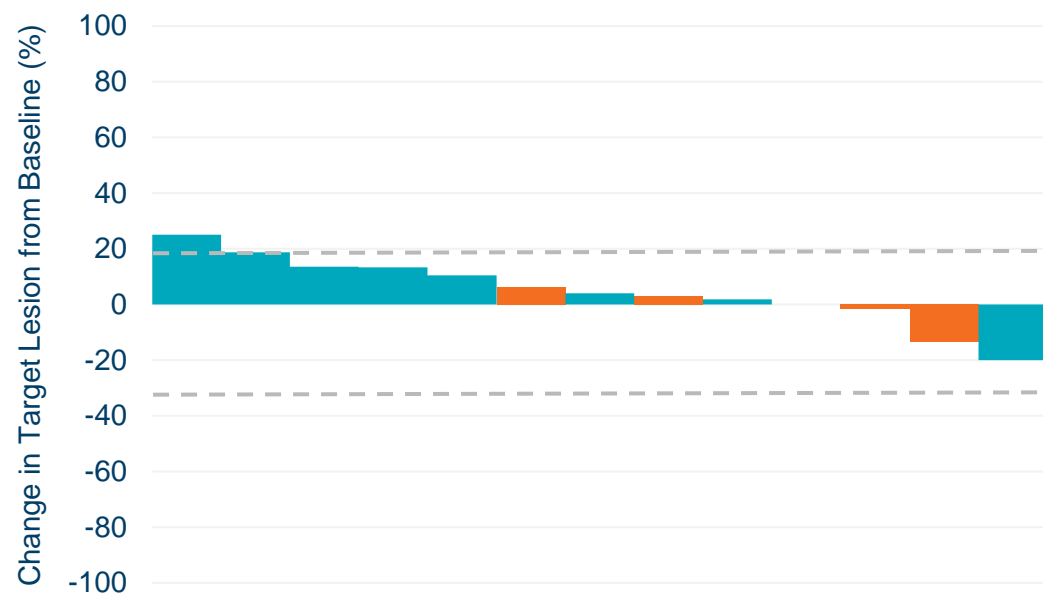
Heavily pre-treated patients with Stage IV HER2 2+/3+ solid tumors

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)

Early Efficacy Evaluation

Best Overall Response of Stable Disease

Best Overall Change in Tumor Burden

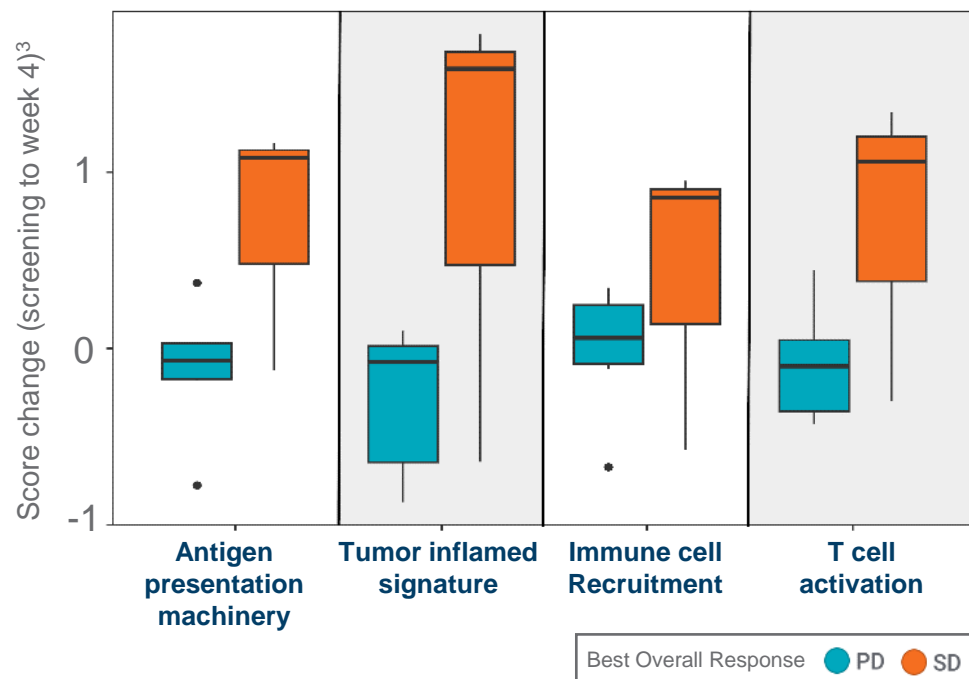


RESULTS

- 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

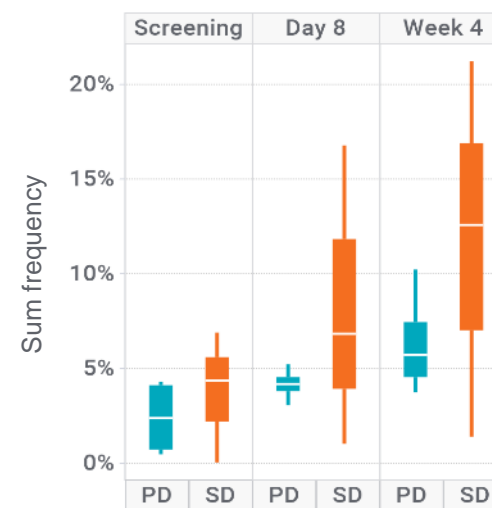
CT-0508 remodeled the TME and induced anti-tumor T cell immunity

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

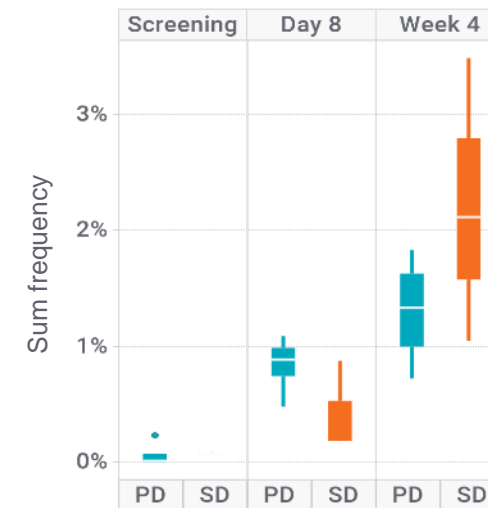


TME activation, based on multiple gene sets, was enriched in patients that had Stable Disease

Expanding T Cell Clones



Emergent T Cell Clones

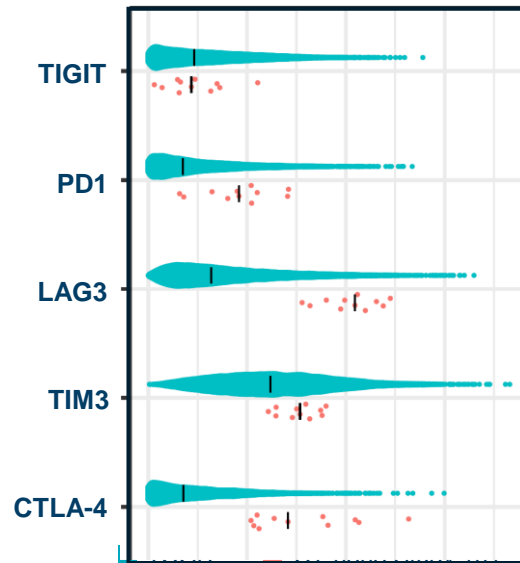


Accumulation of peripherally expanded and emergent T cell clones was increased in patients that had Stable Disease

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

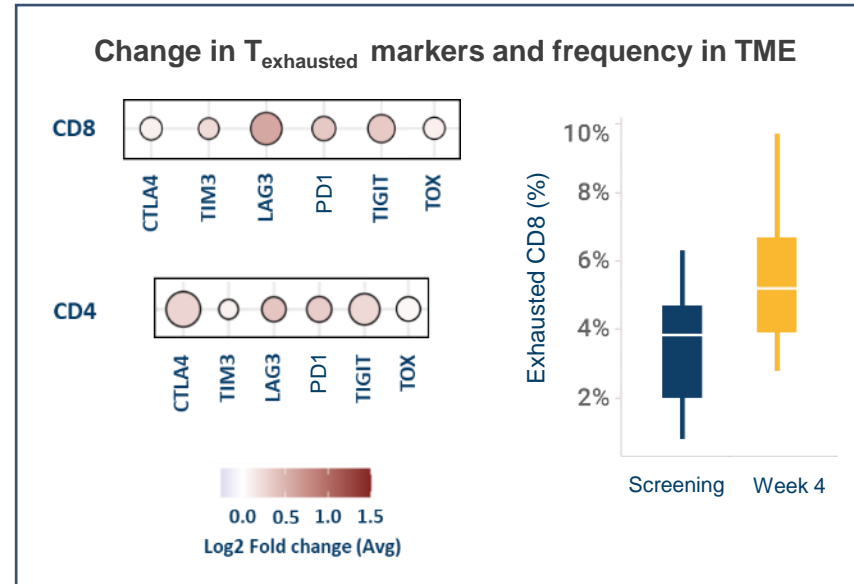
Study 101 patients show high baseline T cell exhaustion, and inhibitory pathways are further upregulated

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



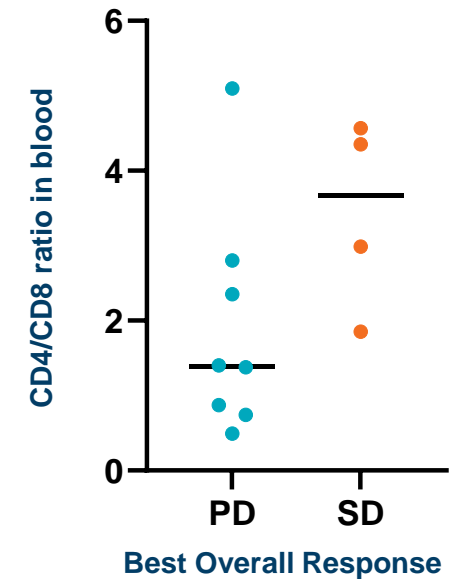
High T cell exhaustion in the TME of Study 101 pts

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



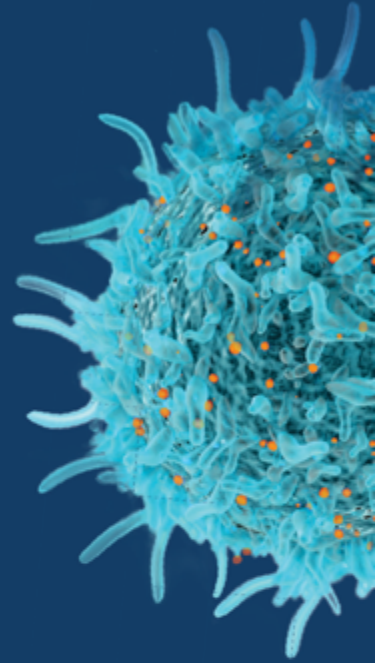
The pro-inflammatory effects of CT-0508 further upregulate inhibitory pathways

Correlation of outcomes with baseline peripheral blood T cell fitness



T cell fitness¹ correlates with clinical outcome

Targeting HER2: CT-0508 + anti-PD1





Pembro Sub-study: Regimen Level 1 Demographics

Patient Demographics were consistent with Group 1 and Group 2

Summary of Participant and Tumor Characteristics			
Characteristic	N = 3	Characteristic	N = 3
Median age (range), years	62 (50, 73)	Tumor Type, n (%)	
Gender, n (%)		Breast Cancer	1 (33.3)
Male	1 (33.3)	Esophageal Cancer	1 (33.3)
Female	2 (66.7)	Ovarian Cancer	1 (33.3)
Race, n (%)		Median Number of Prior Cancer Therapies, n (range)	6 (5, 7)
White	3 (100.0)	Median Number of Prior Anti-HER2 Therapies, n (range)	4 (0, 5)
ECOG PS, n (%)		Subjects with Prior Anti-HER2 Therapy	2 (66.7)
0	0 (0.0)	Prior Radiotherapy, n (%)	
1	3 (100.0)	Yes	2 (66.7)
HER2 Overexpression, n (%)		Tumor Mutational Burden (TMB)*	
IHC 3+	2 (66.7)	Low (<10 mut/Mb)	2 (66.7)
IHC 2+/FISH+	1 (33.3)	High (≥10 mut/Mb)	1 (33.3) [†]
Microsatellite Instability (MSI)*			
MSS/MSI-Low	3 (100.0)		
MSI-High	0 (0)		

Pembro Sub-study: Regimen Level 1 (n=3) Summary

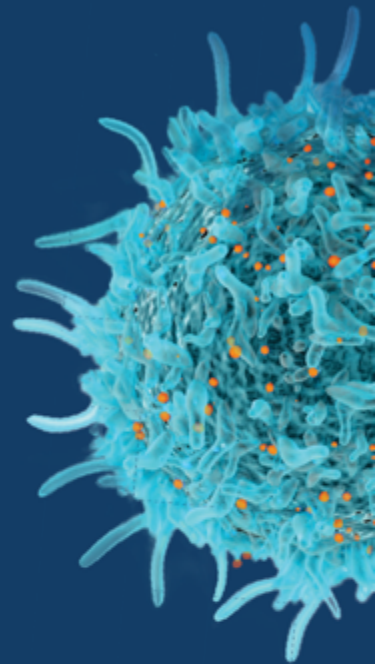
First two patients received corticosteroids prior to pembrolizumab

Patient	Steroids Given Prior to Pembro	Best Overall Response	Disease	HER2 Status	Additional Treatment Details
Patient 1	Yes	PD	Stage IV Breast Cancer	HER2 2+	<ul style="list-style-type: none"> Treated with dexamethasone due to G2 CRS post CT-0508 infusion, prior to pembrolizumab administration
Patient 2	Yes	PD	Stage IV Ovarian Cancer	HER2 3+	<ul style="list-style-type: none"> Treated with methylprednisolone 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	No	SD (One out of two target lesions reduced by ~46%)	Stage IV Esophageal Cancer	HER2 3+	<ul style="list-style-type: none"> 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

Additional Information on Corticosteroids and CT-0508

- Systemic corticosteroids have the potential to reverse the activity of CT-0508.
- Based on *in vitro* studies, corticosteroids lead to CT-0508 cell death.
- Steroids were given post CT-0508, pre-pembrolizumab.

Targeting Mesothelin: CT-1119



CT-1119: Anti-Mesothelin Autologous CAR-Monocyte

Highlights



Significant Unmet Need

- Mesothelin is overexpressed in many solid tumors¹
- No approved anti-mesothelin therapy



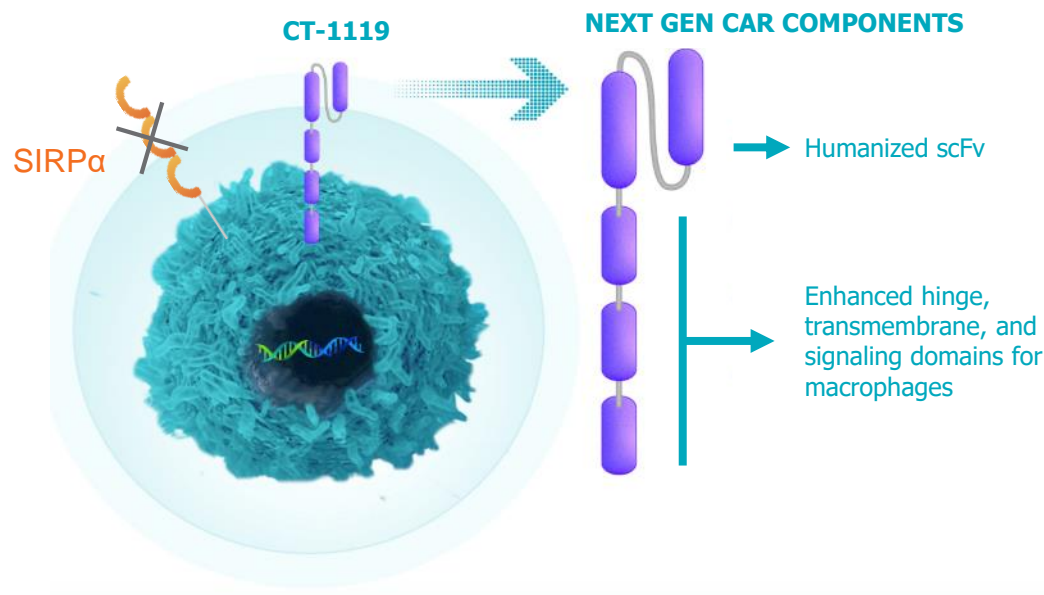
Program Summary

- Incorporating next-gen CAR and SIRPα knockdown
- Utilizing engineered monocyte manufacturing
- Preclinical stage: In vitro and *in vivo* PoC established



Development Plan & Timeline

- Multiple solid tumors
- Opportunity to evaluate systemic and regional treatment
- Development currently paused, pending additional financing

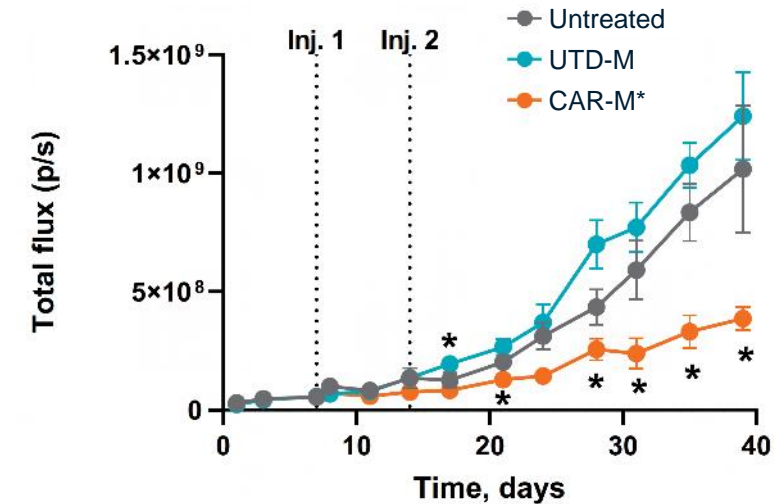
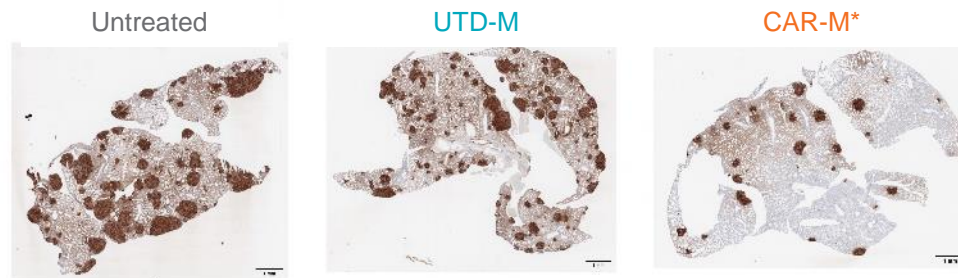


Product Description	
Cells	Autologous monocytes
Vector	Ad5f35
Phenotype	M1
CAR	Next Generation
Other Enhancements	SIRPα knockdown

Development of CT-1119: Anti-Mesothelin CAR-Monocyte

In vivo, CT-1119 significantly reduced tumor burden in a murine xenograft model of lung cancer

Mesothelin(+) NSCLC Xenograft Model:



Key Takeaways



CAR-M* significantly reduced tumor burden in a mesothelin overexpressing metastatic lung cancer xenograft model



Lead candidate will incorporate multiple additional platform enhancements:

- Next-gen CAR
- SIRPα knockdown

Next-Gen CAR Design Has Superior Profile

Enhanced CAR hinge, transmembrane, and signaling components incorporated into CT-1119

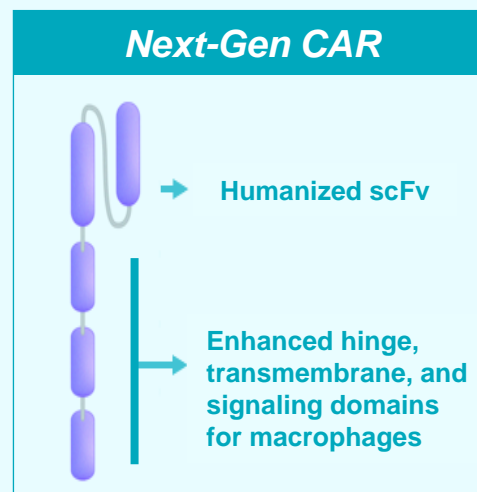
Key Takeaways*

↑ Increased cytokine release

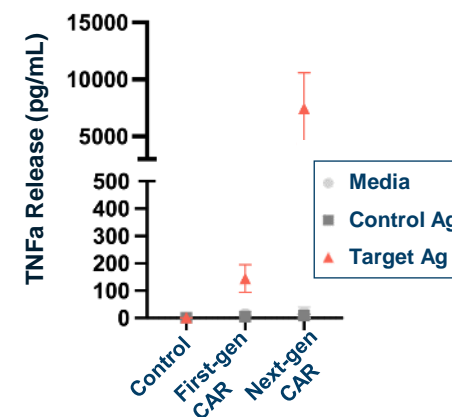
↑ Increased killing of target tumor cells

↑ Increased macrophage activation

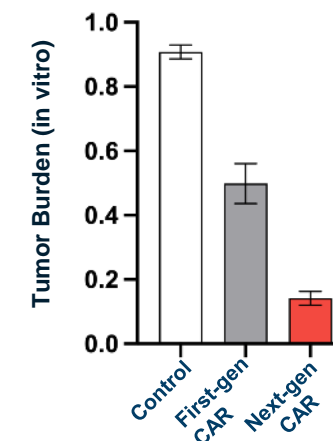
↑ Improved tumor control *in vivo*



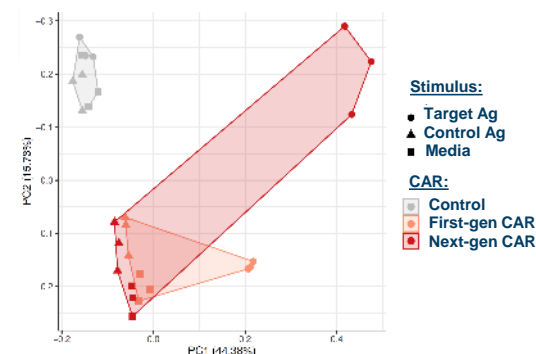
Increased Cytokine Release



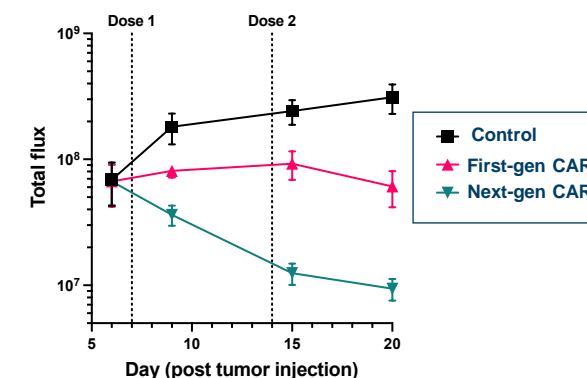
Improved Killing



Increased Macrophage Activation



Improved Tumor Control in a Xenograft Model



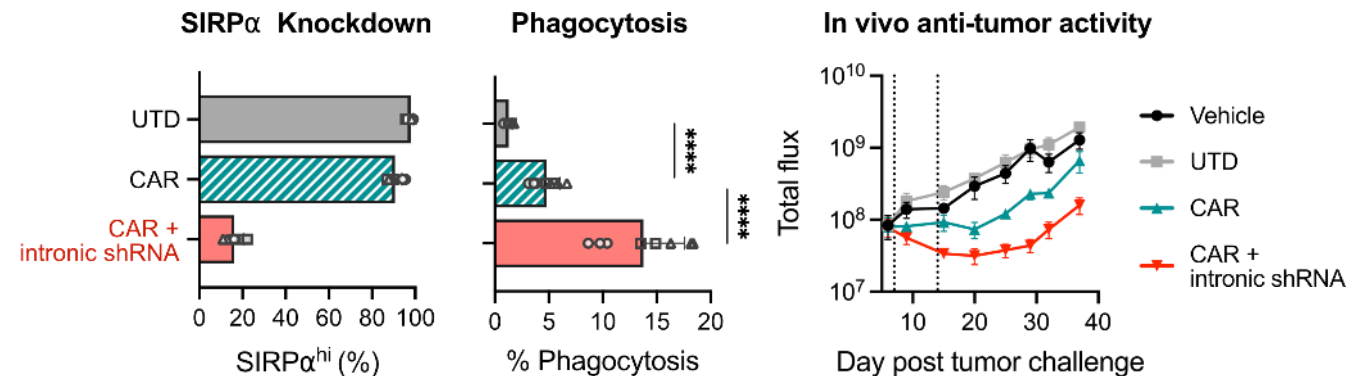
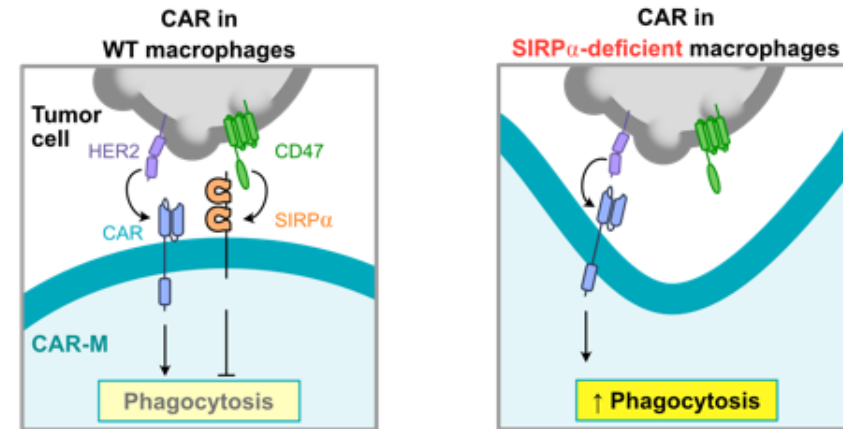
SIRP α Knockdown Enhances Anti-Tumor Activity of CAR-M

Overcoming the CD47 checkpoint enhances CAR-M potency

Key Takeaways

- ✓ Overcomes the CD47 “do-not-eat-me” signal expressed by tumor cells
- ✓ Increased killing, activation, and cytokine release
- ✓ Improved tumor control *in vivo*
- ✓ No phagocytosis of normal tissue
- ✓ Proprietary intronic shRNA platform

Overcoming CD47 Inhibition

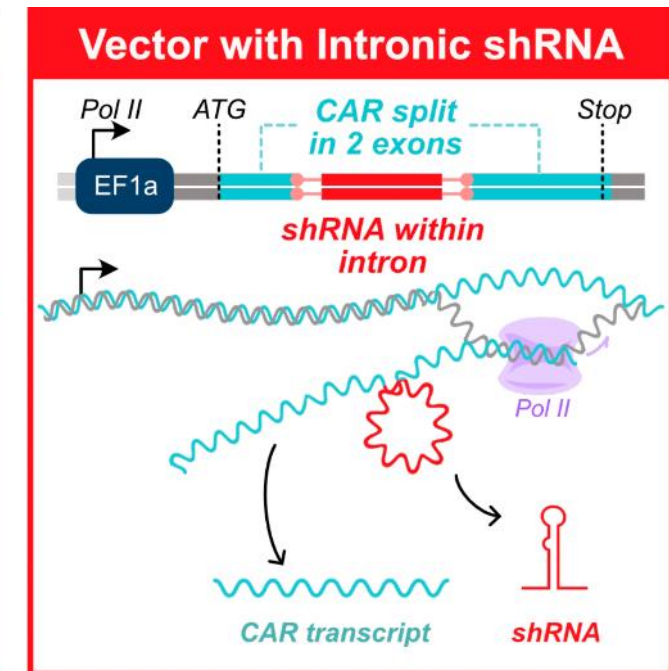
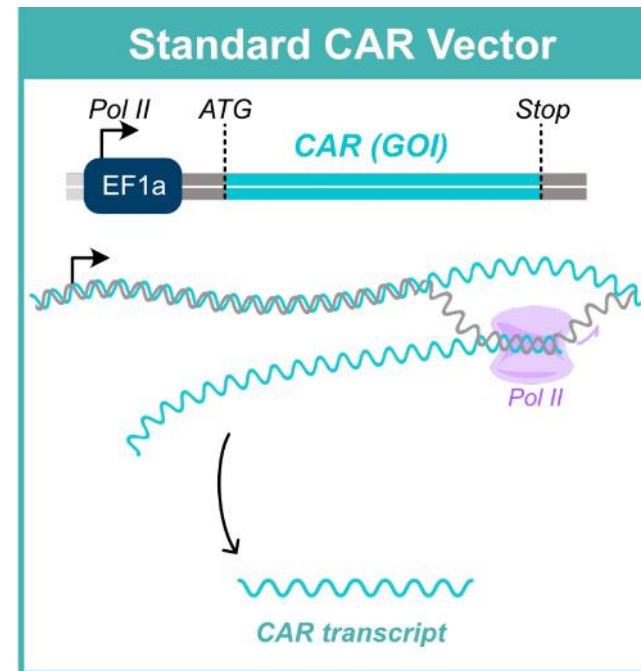


Intronic shRNA Enables CAR Delivery and Gene Silencing

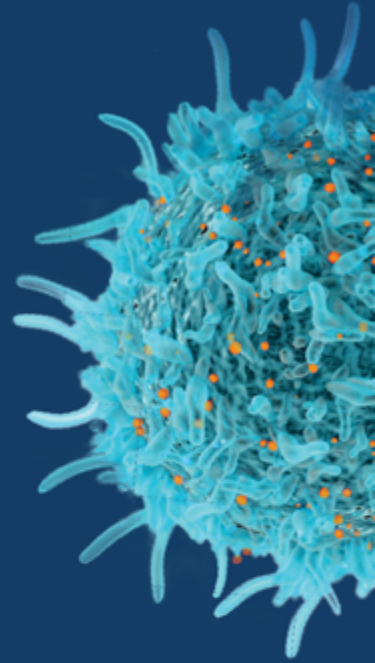
Proprietary technology utilized for the first time in CT-1119

Key Takeaways

- ✓ Simultaneous CAR delivery and SIRPα silencing with a single vector
- ✓ Single Ad5f35 vector, 1-day CAR-Monocyte process
- ✓ More efficient than CRISPR/Cas9 editing*

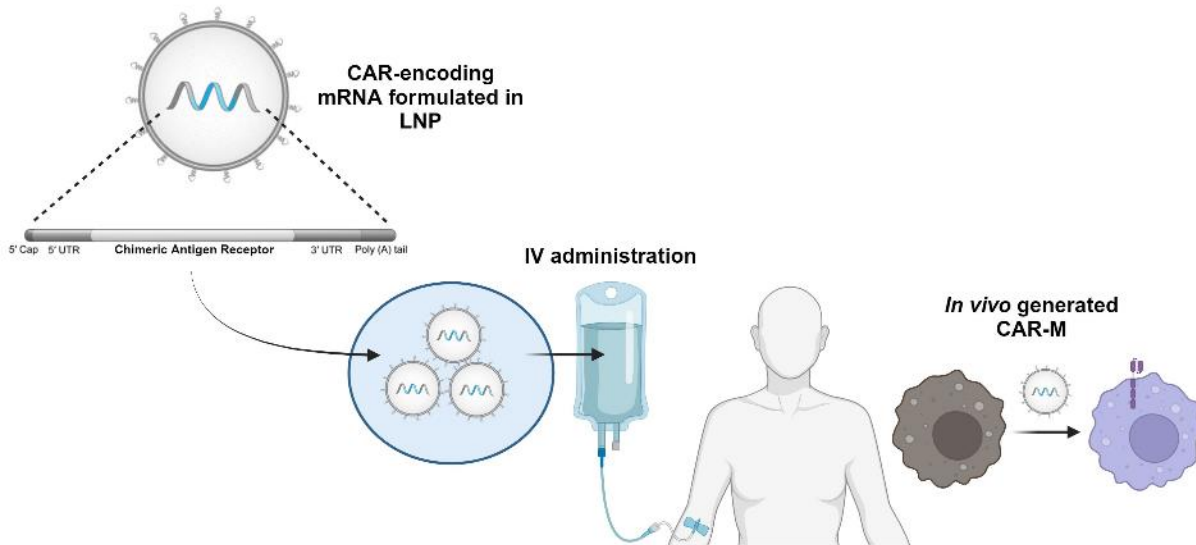


In Vivo Oncology

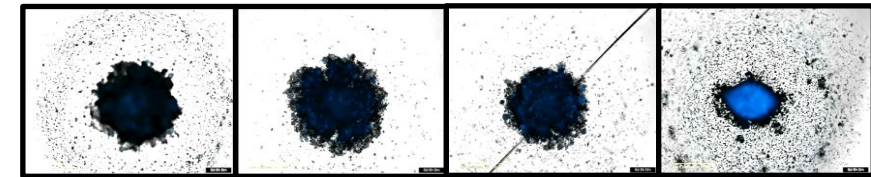


Directly Reprogramming Myeloid Cells *In Vivo* with mRNA/LNP

Redirecting endogenous myeloid cells with mRNA for cancer immunotherapy



Direct TAM reprogramming shrinks tumors*



Control mRNA/LNP

Anti-HER2 CAR mRNA/LNP

CAR Distribution *in vivo* (Mouse Blood)

