carisma THERAPEUTICS

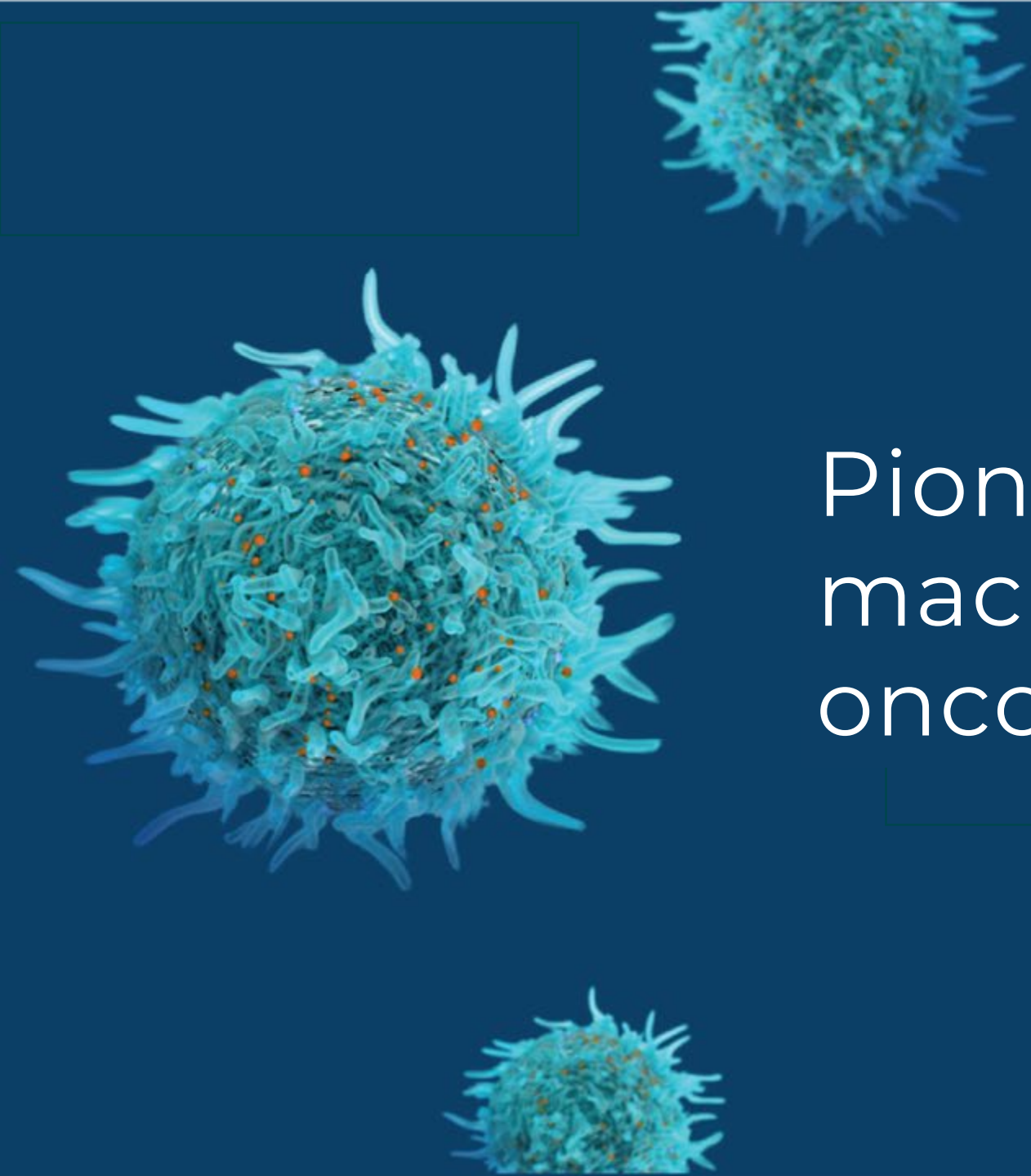
HARNESSING THE POWER OF MACROPHAGES

April 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.

Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. These risks and uncertainties include, but are not limited to, (i) Carisma's ability to obtain, maintain and protect its intellectual property rights related to its product candidates; (ii) Carisma's ability to advance the development of its product candidates under the timelines it anticipates in planned and future clinical trials and with its current financial and human resources; (iii) Carisma's ability to replicate in later clinical trials positive results found in preclinical studies and early-stage clinical trials of its product candidates; (iv) Carisma's ability to realize the anticipated benefits of its research and development programs, strategic partnerships, research and licensing programs and academic and other collaborations; (v) regulatory requirements or developments and Carisma's ability to obtain and maintain necessary approvals from the U.S. Food and Drug Administration and other regulatory authorities; (vi) changes to clinical trial designs and regulatory pathways; (vii) risks associated with Carisma's ability to manage expenses; (viii) changes in capital resource requirements; (ix) risks related to the inability of Carisma to obtain sufficient additional capital to continue to advance its product candidates and its preclinical programs; and (x) legislative, regulatory, political and economic developments. . For a discussion of these risks and uncertainties, and other important factors, any of which could cause Carisma's actual results to differ from those contained in the forward-looking statements, see the "Risk Factors" set forth in the Company's Annual Report on Form 10-K for the year ended December 31, 2023, as well as discussions of potential risks, uncertainties, and other important factors in Carisma's other recent filings with the Securities and Exchange Commission. Any forward-looking statements that are made in this presentation speak as of the date of this presentation. Carisma undertakes no obligation to revise the forward-looking statements or to update them to reflect events or circumstances occurring after the date of this presentation, whether as a result of new information, future developments or otherwise, except as required by the federal securities laws.



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-0508 trial to conclude post Regimen 2 of sub-study in combination with pembrolizumab
- CT-0525 data is expected end of 2024

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 preclinical proof of concept data expected in 2Q 2024

Corporate

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

carisma THERAPEUTICS

* In late March 2024, Carisma made the decision to pause further development of CT-1119, pending additional financing
MoA: Mechanism of Action

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)*	4Q 2024: Initial data[1]	
	CT-0508*	CAR-Macrophage *(1st Gen CAR)*	2Q 2024: Combination data[1]	
Mesothelin+ solid tumors	CT-1119**	CAR-Monocyte *(Next-Gen CAR[2])*		
***In Vivo* Oncology**				
Oncology	Solid Tumor Antigen[3]	CAR-Macrophage + mRNA/LNP		moderna
	4 Additional Targets[4]	CAR-Macrophage + mRNA/LNP		
Fibrosis and Immunology				
Liver Fibrosis	TBD	Engineered macrophage	2Q 2024: Preclinical proof of concept data[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

carisma THERAPEUTICS

Drive to 2025

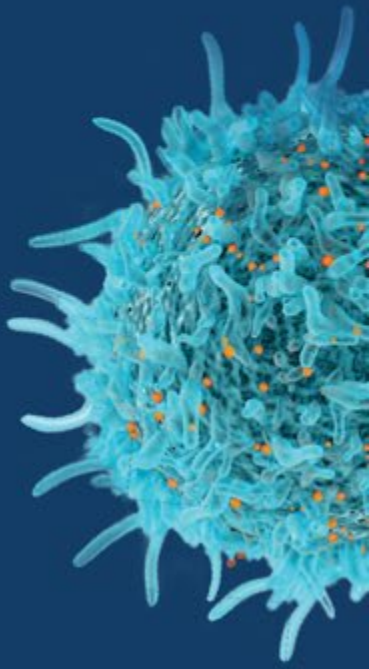
Leverage world-leading macrophage engineering platform to deliver three product opportunities

Program	2024 Tactical Plan	2025 Objectives
HER2 CAR-M	♦ CT-0525[1] Safety Study Cohort 1: 3 Billion Cells ♦ CT-0525[1] Safety Study Cohort 2: 10 Billion Cells	**Phase II/III Regimen Identified[2]**
***In vivo* CAR-M** *(Collaboration with Moderna)*	♦ IND-enabling activities for lead candidate ♦ Pre-clinical studies for additional identified targets	**Undisclosed Development & Regulatory Milestones**
Liver Fibrosis	♦ Pre-clinical proof-of-concept studies ♦ Development candidate identified	**IND-enabling Activities**

carisma THERAPEUTICS

1. CAR-Monocyte; 2. In late March 2024, the Company selected CAR-Monocyte approach for the Phase II/III Regimen Identified

Targeting HER2:
CT-0525 and CT-0508



carisma THERAPEUTICS

HER2 Development Strategy

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

Demonstrate Safety, Tolerability, Feasibility & MOA:
CAR-Macrophage (CT-0508*)

Phase 1: No Further Data Expected

Increase Dose:
CAR-Monocyte (CT-0525)

Phase 1: Initial Data Expected 4Q'24

Overcome T Cell Exhaustion:
CAR-Macrophage (CT-0508) + Pembrolizumab

Phase 1: Data Expected 2Q'24

Potential Registrational Profile

Cell Type	Dose	Monotherapy vs. Combo Therapy	Line of Therapy	Tumor Type

carisma THERAPEUTICS

MOA: Mechanism of Action

* In late March 2024, Carisma made the decision to cease further development of CT-0508, including monotherapy and in combination with pembrolizumab

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

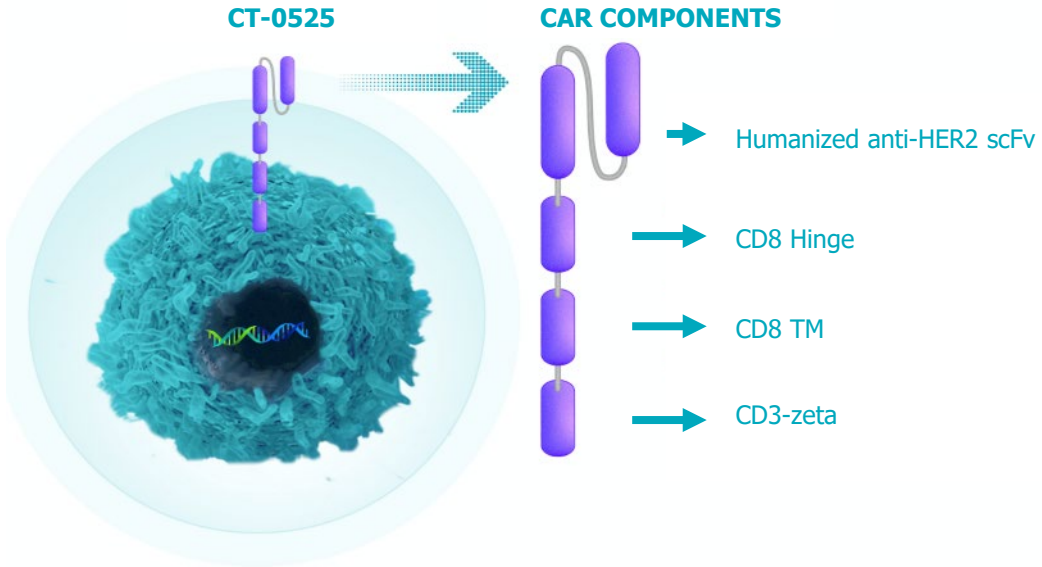
- Higher cell numbers
- Faster manufacturing (1 day)
- Reduced COGS

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 expected to be treated in 2Q 2024
- Initial data expected in 4Q 2024



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

carisma THERAPEUTICS

* Compared to CAR-Macrophage

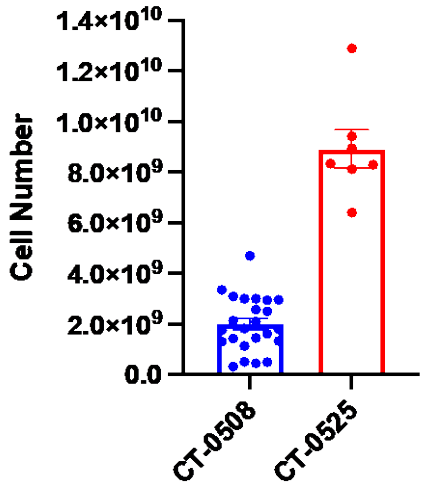
CT-0525: Multiple Potential Improvements Over CT-0508

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

5X

Cell Number

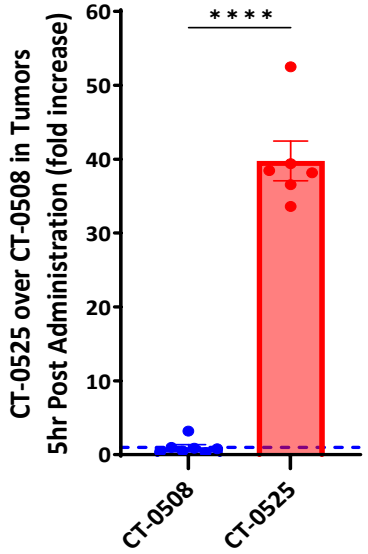
Cells Produced from Single Apheresis:



40X

Tumor Infiltration

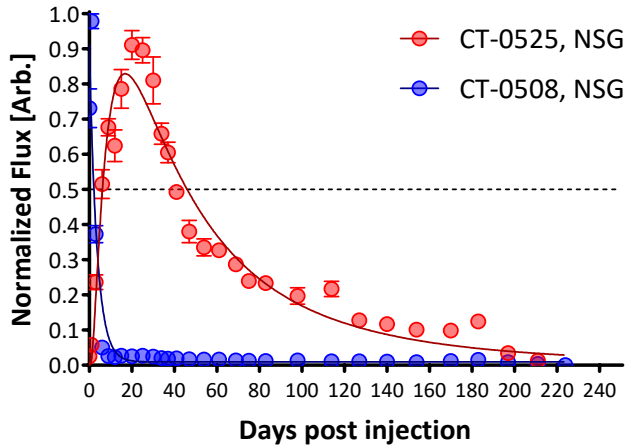
Trafficking in solid tumor model:



10X

Persistence

CT-0525 half-life is ~45 days:



carisma THERAPEUTICS

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

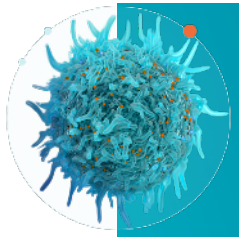
Cohort 1: Up to 3 billion cells of CT-0525 in bolus dose D1 (n≥3)

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

Manufacturing and clinical site activation being mobilized

Expect to treat first patient in 2Q 2024 and to report initial data in 4Q 2024

Potential subsequent development plans could include combination with a T cell checkpoint inhibitor, and additional dose-ranging and dose schedule (among others)



PRIMARY OUTCOMES

- Safety and tolerability
- Manufacturing feasibility

SECONDARY OUTCOMES[1]

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

carisma THERAPEUTICS

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-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

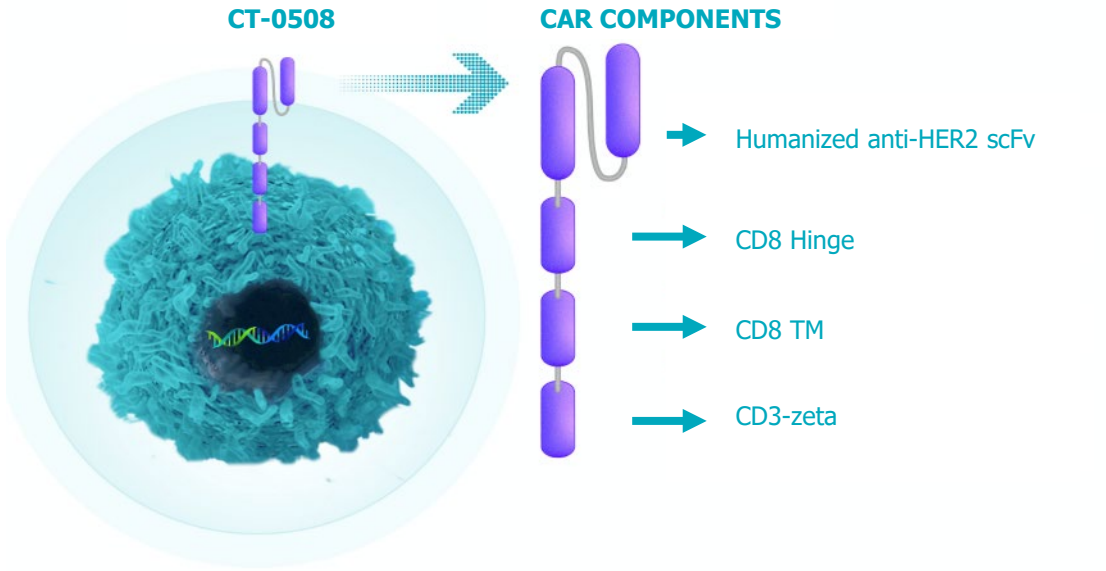
- Study 101 Group 1 (fractionated dosing): 9 patients
- Study 101 Group 2 (bolus dosing): 5 patients
- Study 101 sub-study (pembrolizumab combination): 6 patients
- Determined to ceased further development in late March 2024

Key Study Takeaways To Date - Monotherapy

- Generally 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	1st Generation

carisma THERAPEUTICS

MOA: Mechanism of Action

* Regimen 1 data from Study 101 pembrolizumab sub-study was presented at AACR in April 2024. Regimen 2 data is expected 2Q 2024

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 (n≈27)

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

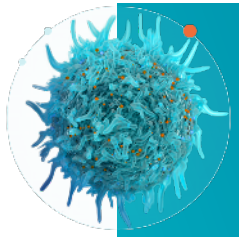
Group 1: CT-0508 fractionated dose D1,3,5 (n=9) — **Complete**

Group 2: CT-0508 bolus dose D1 (n≤9) — **No Further Enrollment**

Pembro Sub-study: CT-0508 + pembrolizumab (n≥9) — **No Further Enrollment**

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

Anticipate presenting data from Pembro Sub-study in 2Q 2024



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

carisma THERAPEUTICS

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 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

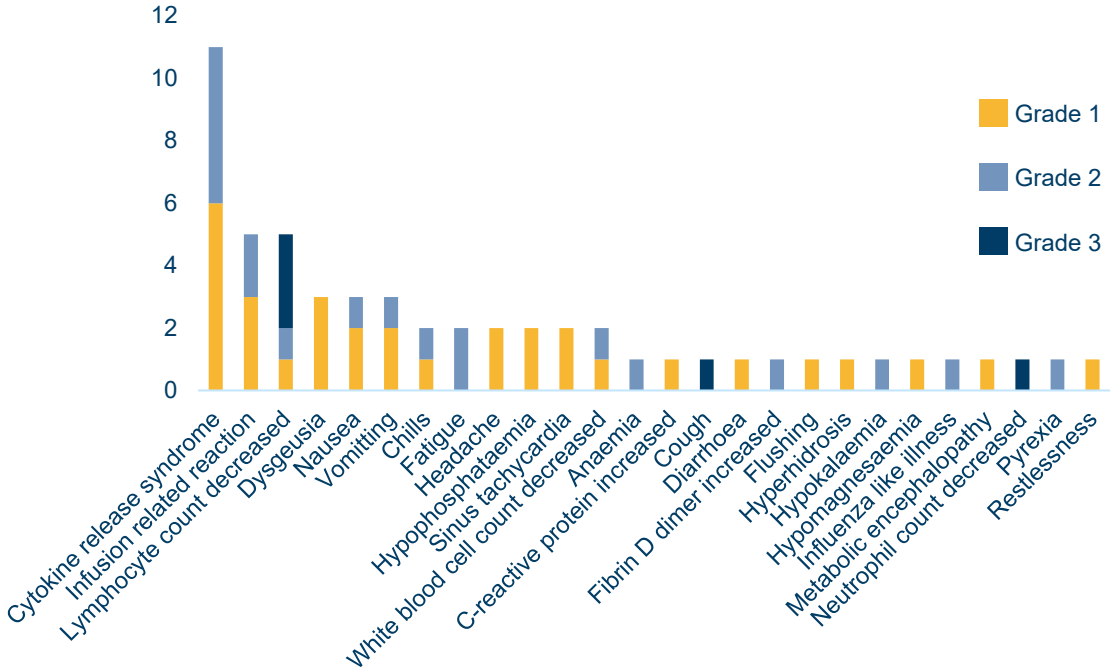
carisma THERAPEUTICS

CAR-M: CAR-Macrophage and CAR-Monocyte;
CRS: Cytokine release syndrome; ICANS: immune effector cell-associated neurotoxicity syndrome; SD: stable disease; TME: tumor microenvironment; MoA: mechanism of action

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

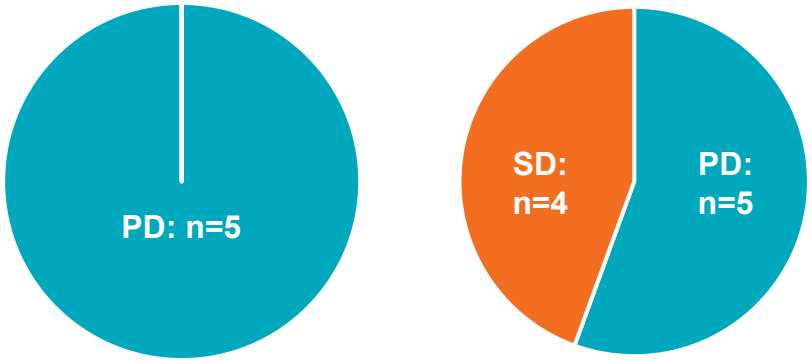
carisma THERAPEUTICS

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.

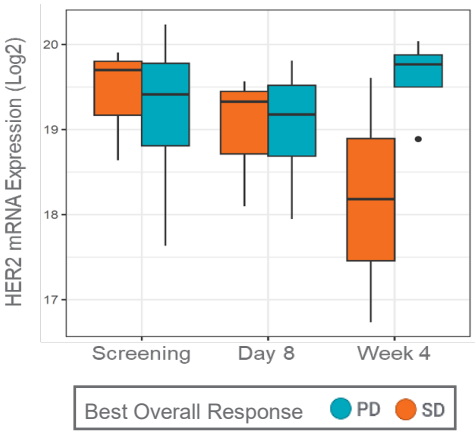
Biologically Active with Antigen Dependent MOA

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

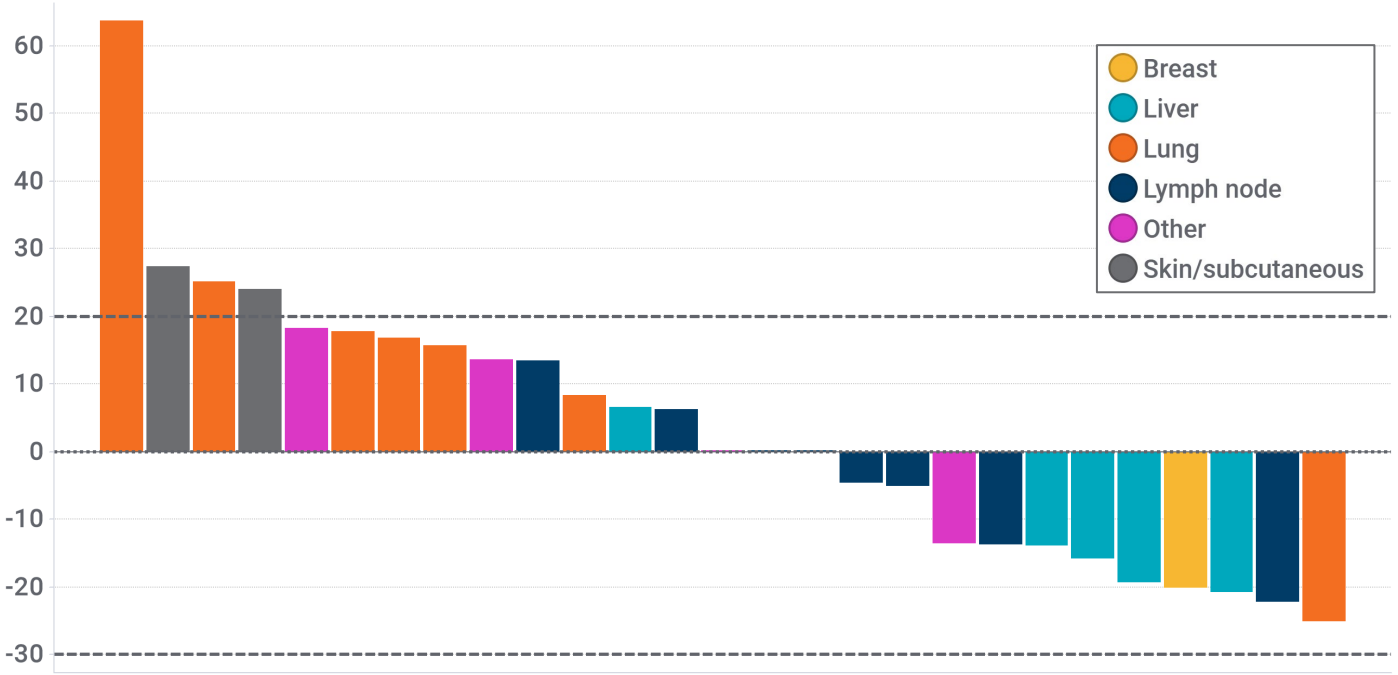
- Best Overall Response of Stable Disease in 4 of the 14 evaluated participants (28.6%)*+
- Largest reduction in target lesion include 20% reduction in breast cancer patient and 14% reduction in salivary gland cancer patient
- Stable Disease was enriched in HER2 3+ subpopulation (n=4/9, 44.4% SD)
- Stable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

carisma THERAPEUTICS

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
*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 got a scan post infusion for re-staging, hence data is unavailable for this patient.

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

Best changes in individual target lesions by anatomic site:



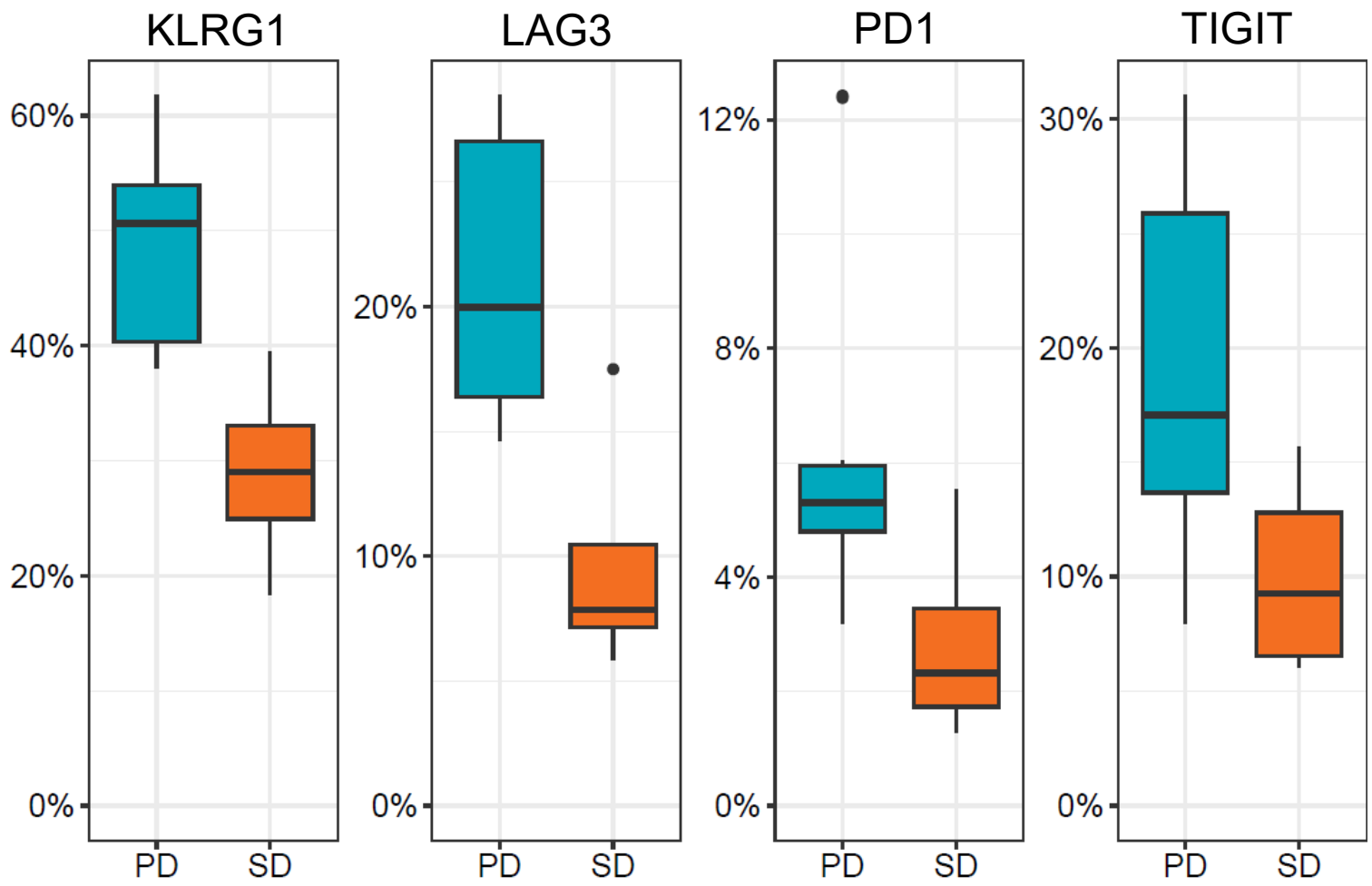
Each column represents a single target tumor lesion, not a patient.

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

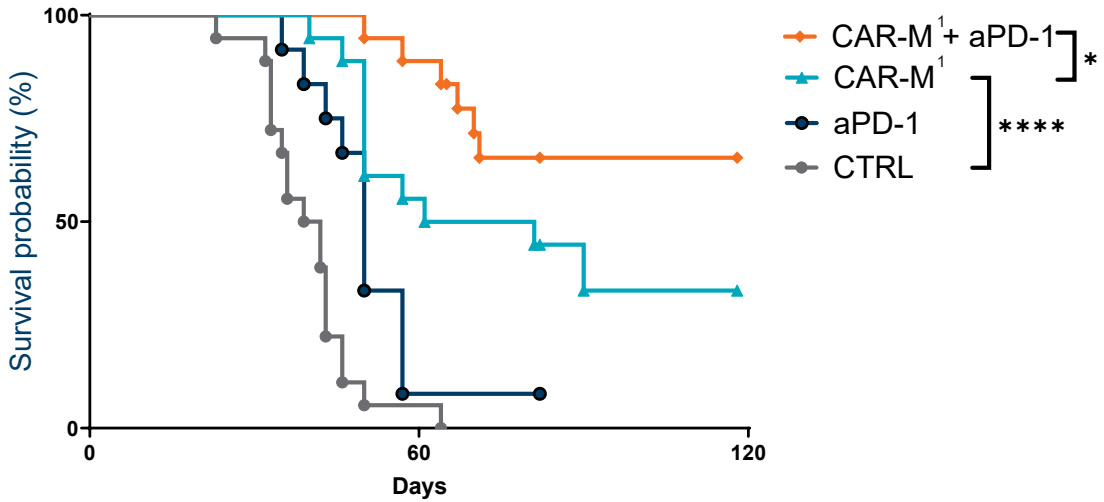


Based on single-cell RNAseq analysis of CD8 T cells within apheresis material.
SD: Stable Disease; PD: Progressive Disease

CT-0508 + Anti-PD1: Robust Synergy

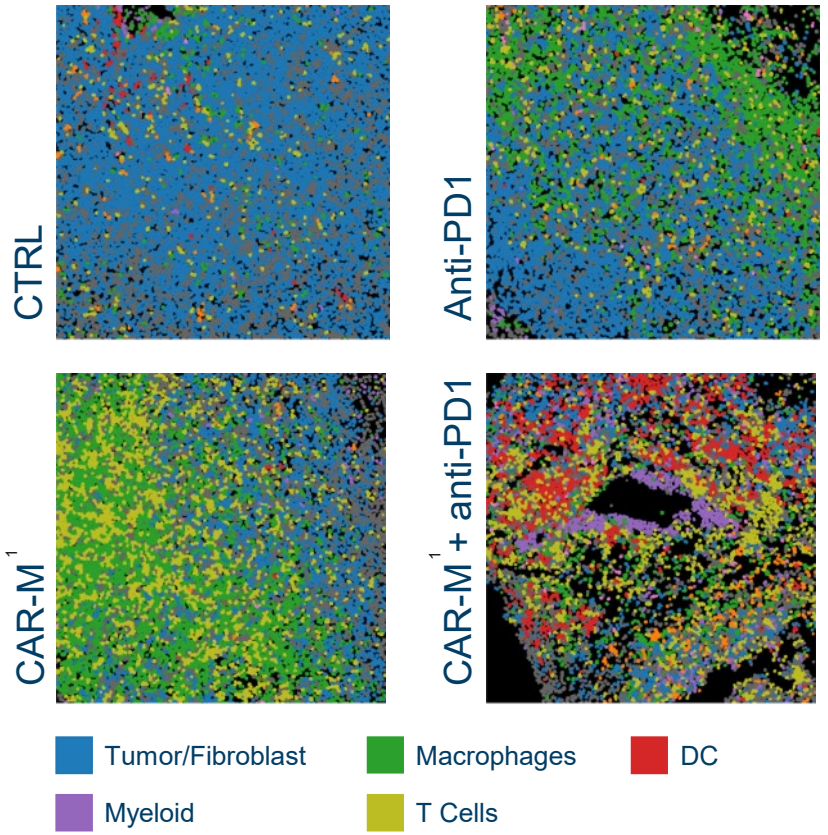
Synergy in a solid tumor model that is resistant to anti-PD1 monotherapy

Synergistic anti-tumor activity



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

Synergistic TME modulation with combination



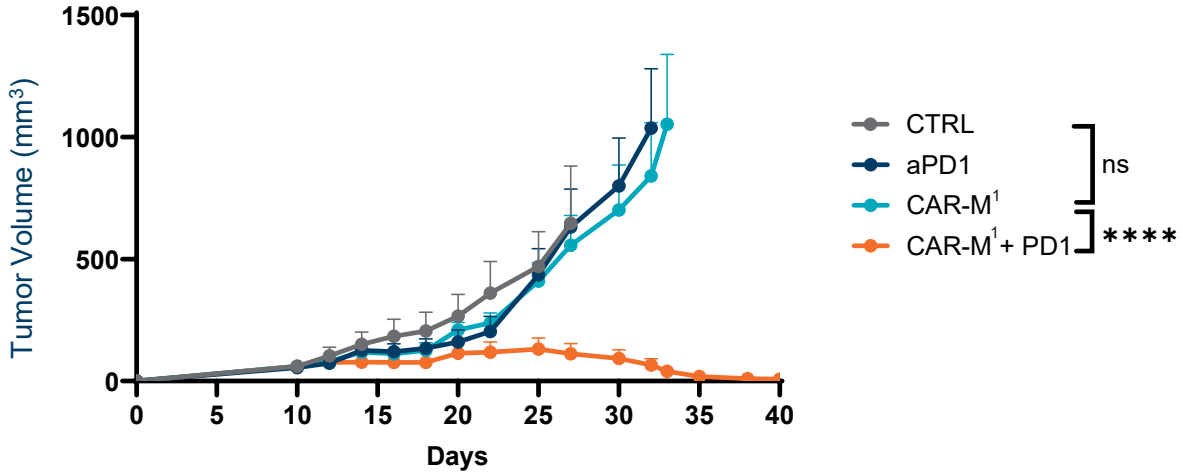
carisma THERAPEUTICS

Data from preclinical models.
1: CAR-M: CAR-Macrophage
DC: Dendritic Cell; CTRL: Control

CT-0508 + Anti-PD1: Robust Synergy

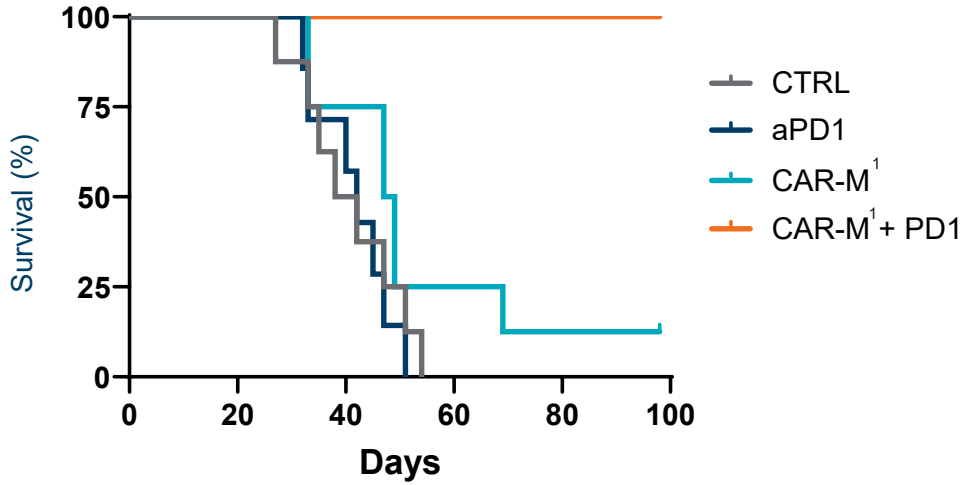
Synergy in a solid tumor model that is resistant to both CAR-Macrophage *and* anti-PD1 monotherapy

I.V. CAR-M^1 + anti-PD1 leads to synergistic tumor control



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

I.V. CAR-M^1 + anti-PD1 leads to 100% survival



carisma THERAPEUTICS

Data from preclinical models.
1: CAR-M: CAR-Macrophage
CTRL: Control

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 (n≈27)

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

Group 1: CT-0508 fractionated dose D1,3,5 (n=9)	Complete
Group 2: CT-0508 bolus dose D1*	No Further Enrollment

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

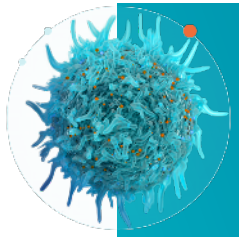
Pembro Sub-study Regimen 1 (n=3): CT-0508 C1D1,3,5 + Pembro 200mg C1D8

Pembro Sub-study Regimen 2 (n=3): CT-0508 C1D1,3,5 + Pembro 200mg C1D1

Pembro Sub-study Regimen 3 (n≥3): CT-0508 C1D1 + Pembro 200mg C1D1

No Longer Enrolling

Anticipate reporting data from Pembro sub-study in 2Q 2024



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

carisma THERAPEUTICS

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.

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.

carisma THERAPEUTICS

BOR: Best Overall Response; SD: Stable Disease
*per RECIST 1.1

Pembro Substudy: 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

carisma THERAPEUTICS

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.

Pembro Substudy: Patient 3 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

carisma THERAPEUTICS

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

Pembro Substudy: 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

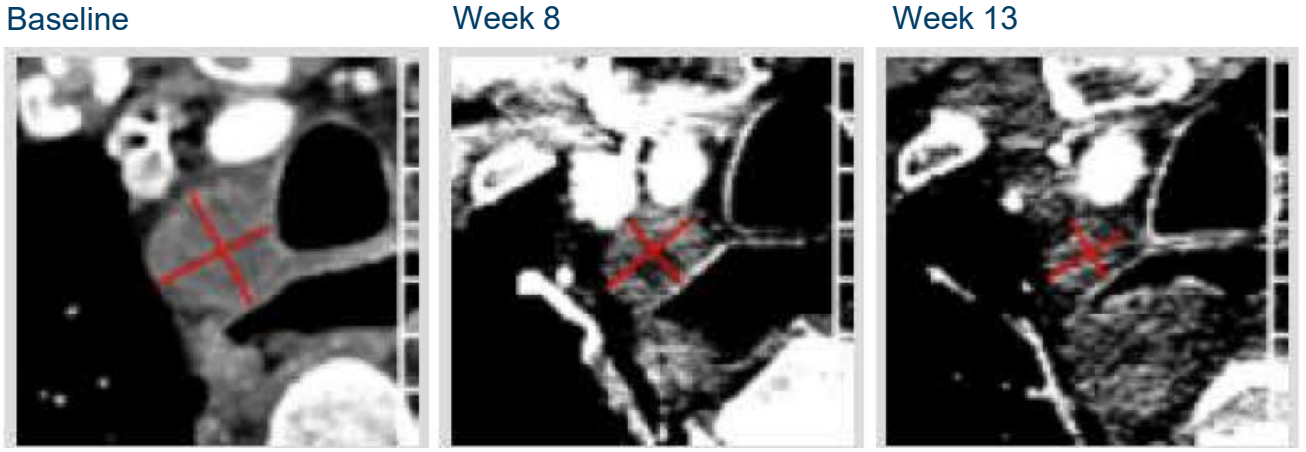
Tumor assessments

- 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



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

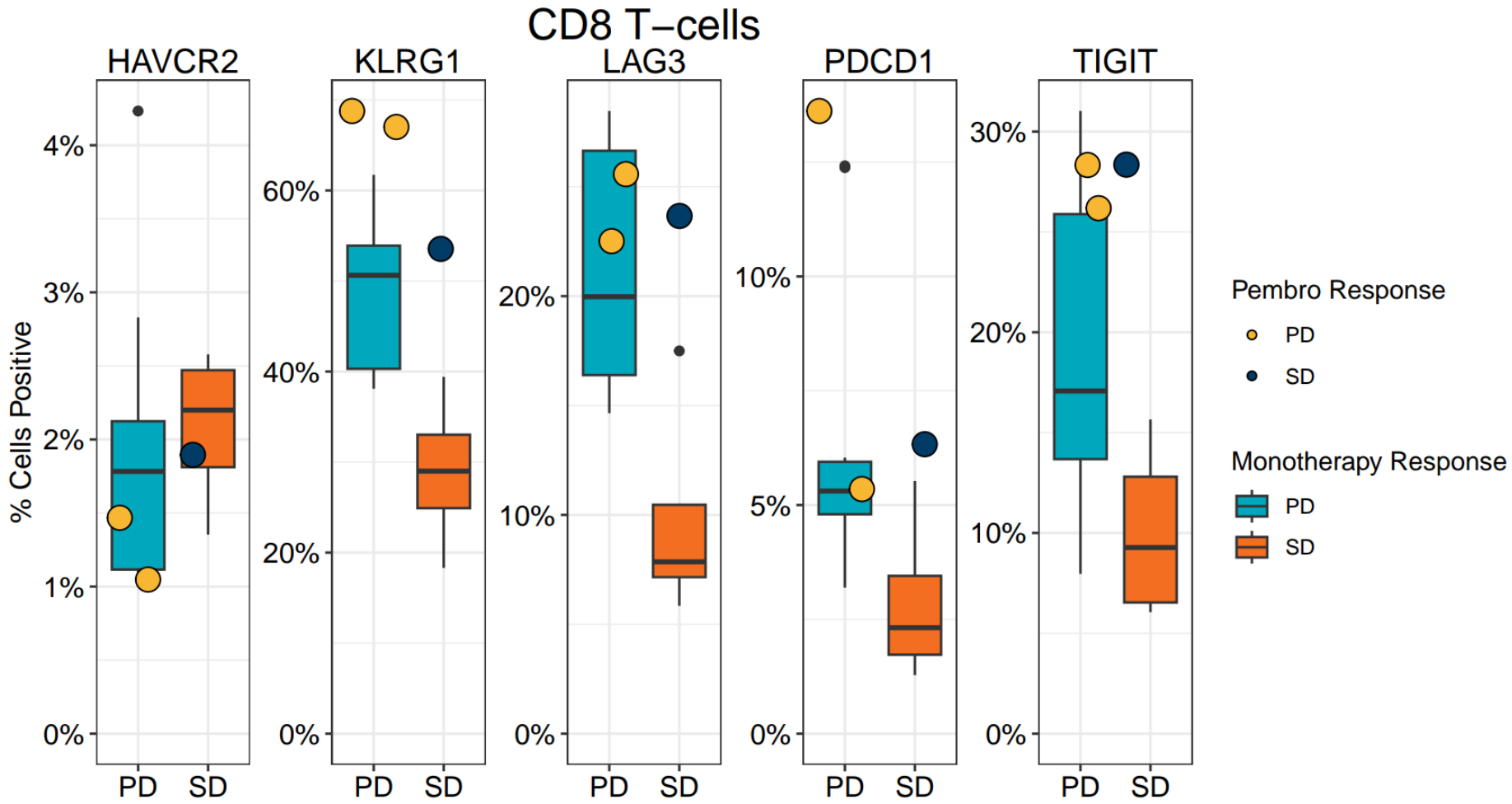
Patient 3's paratracheal target lesion reduction of 46% was the largest reduction of tumor in any patient treated with CT-0508

carisma THERAPEUTICS

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/Pembro Sub-study: Individual Case Study

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

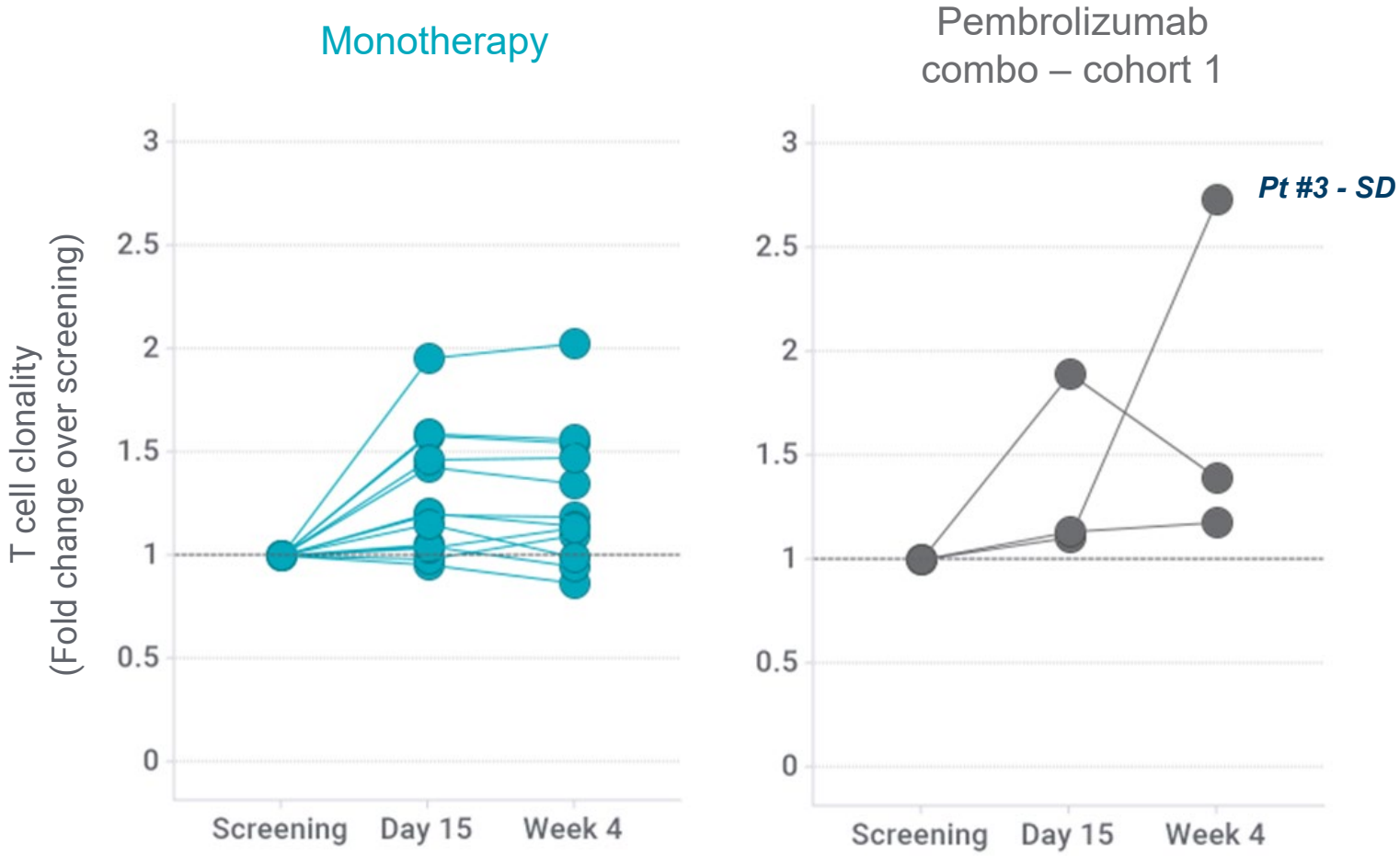


BOR: Best Overall Response; SD: Stable Disease

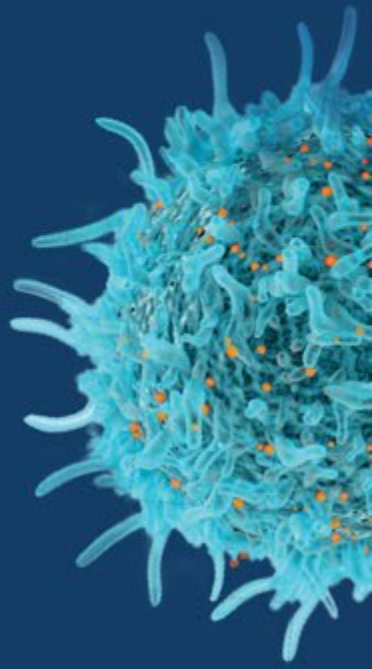
CT-0508/Pembro Sub-study: Individual Case Study

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



carisma THERAPEUTICS

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

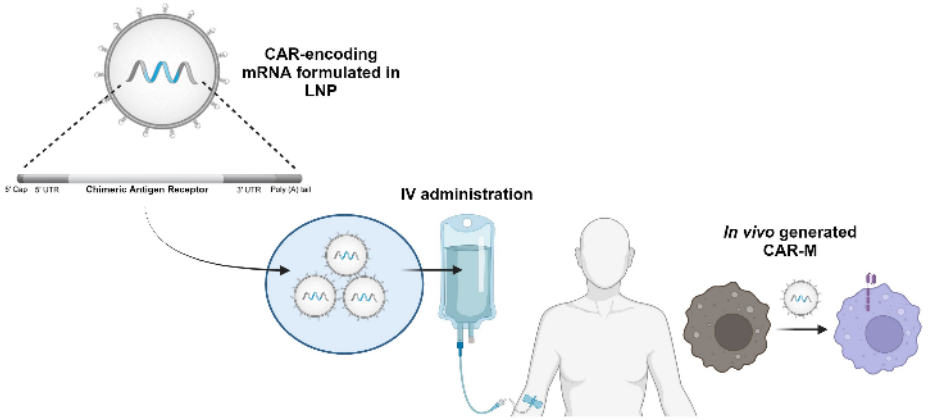
Key Advantages of *in vivo* CAR-M

- 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

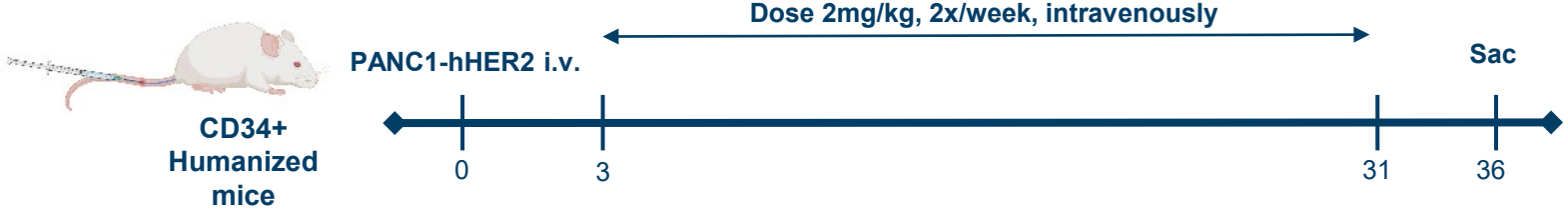


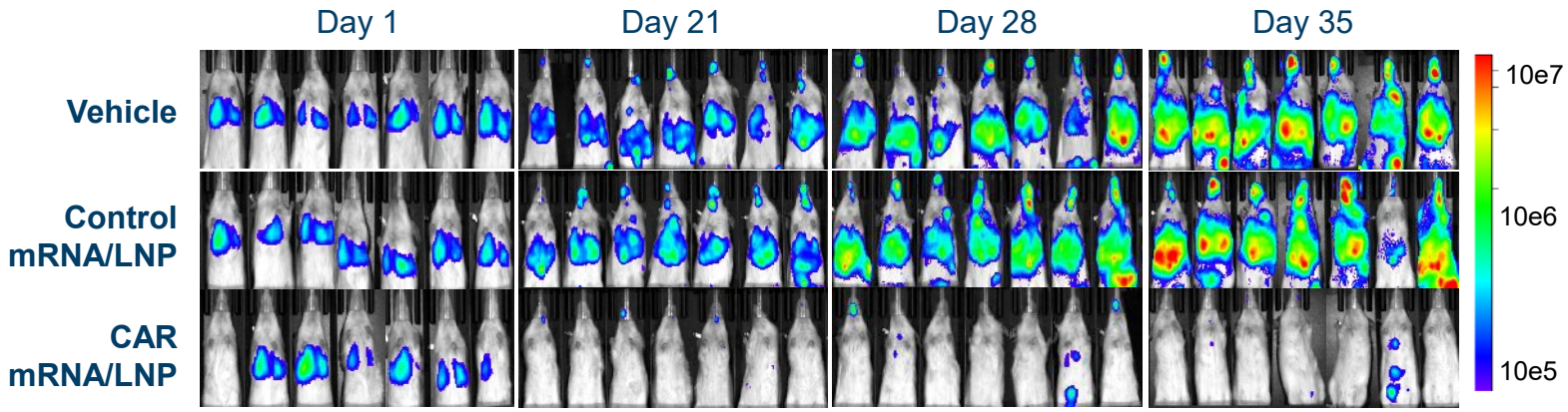
carisma THERAPEUTICS	Collaboration Terms	moderna
Number of Targets	Up to 12 (5 Identified)	
Upfront Payment	$80M	
Total Potential Milestones and Royalties	$3B+	
R&D Funding	Fully funded by Moderna	

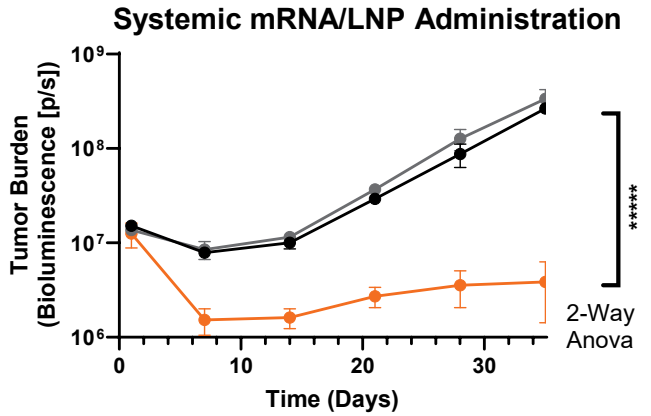
mRNA: Messenger RNA; LNP: Lipid Nanoparticle

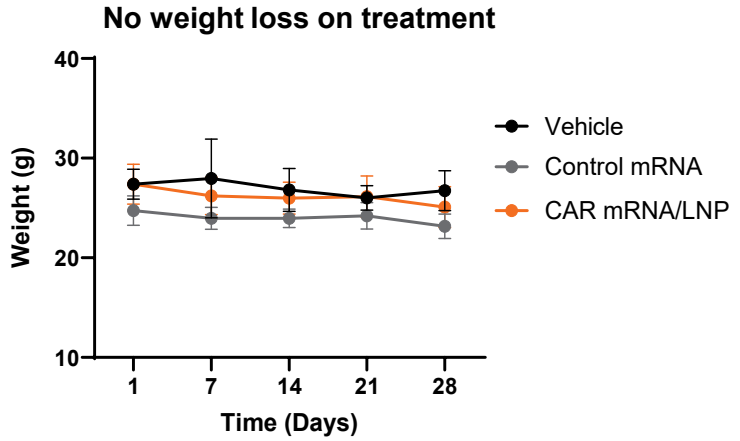
In Vivo CAR-M Controls Metastatic Pancreatic Cancer

Systemic LNP administration in humanized mouse model of pancreatic cancer







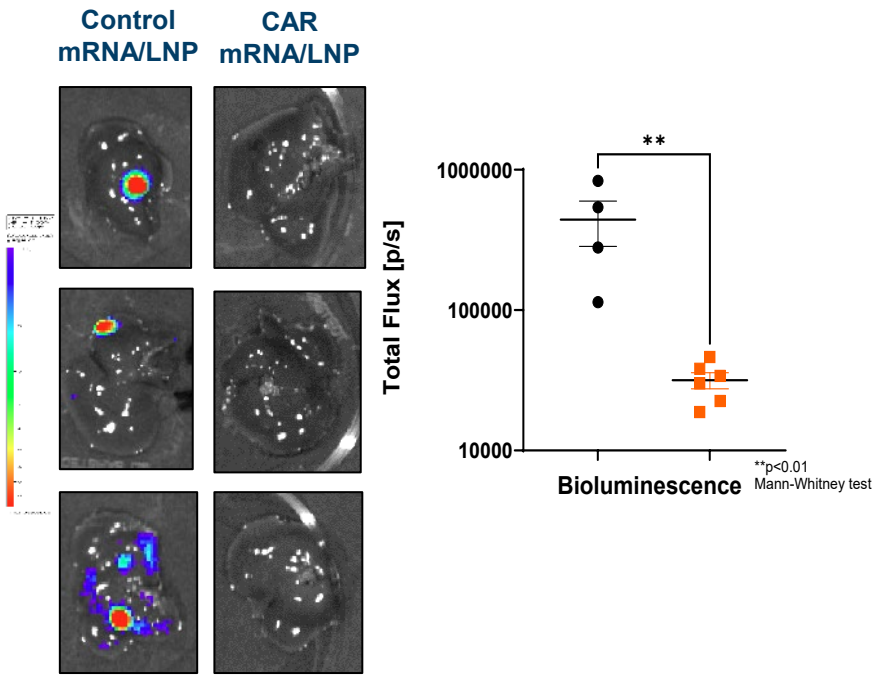


mRNA: Messenger RNA; LNP: Lipid Nanoparticle

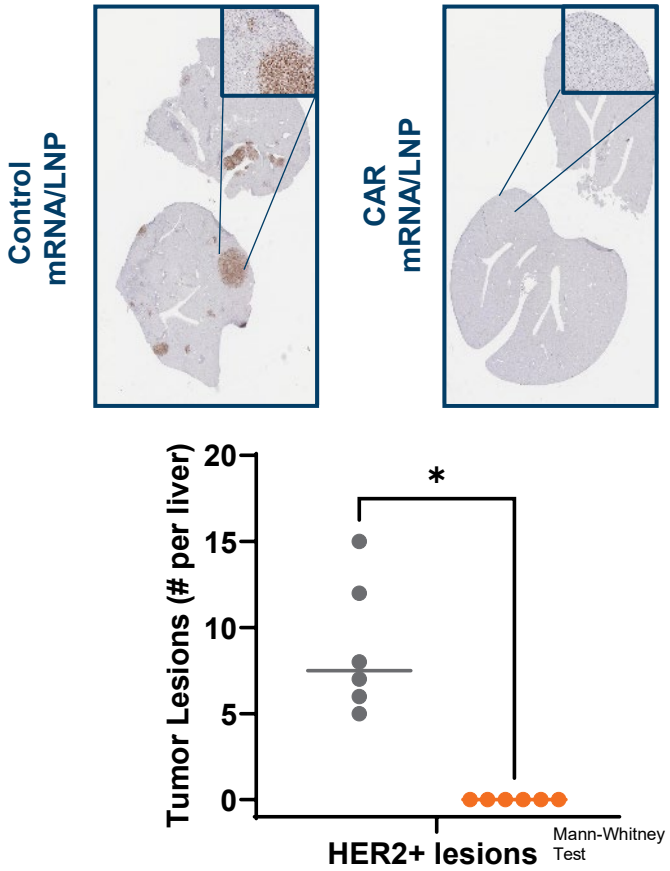
In Vivo CAR-M Suppresses Liver and Lung Metastasis

Systemic LNP administration in humanized model leads to robust disease control

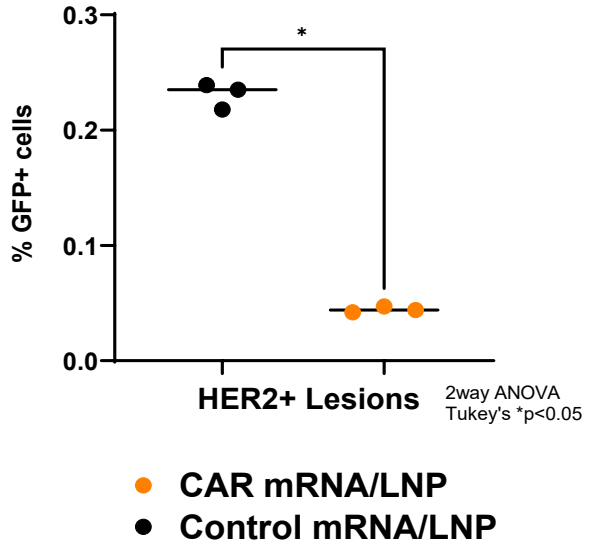
Tumor Lesions in Liver (BLI)



Tumor Lesions/Liver (IHC)

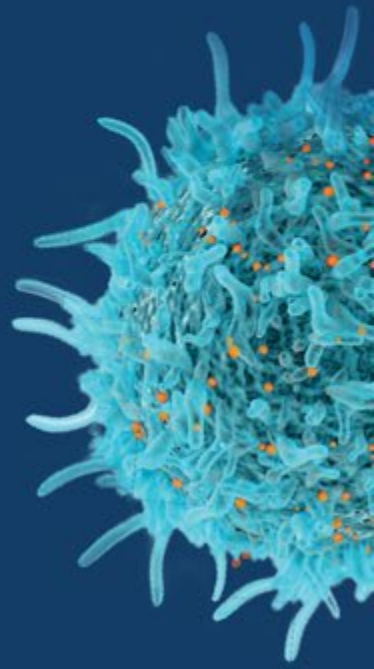


Tumor Lesions in Lung (IHC)



mRNA: Messenger RNA; LNP: Lipid Nanoparticle

Developing macrophage cell therapies beyond oncology: Fibrosis

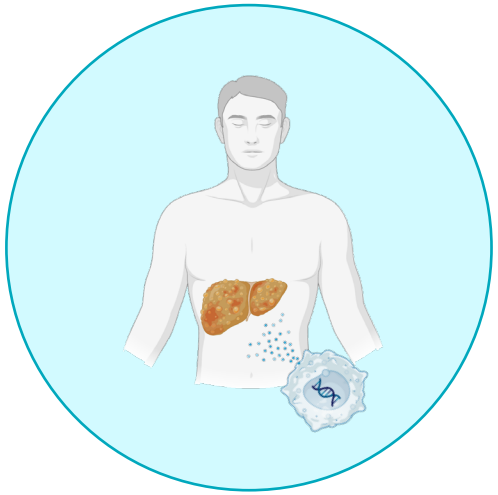


carisma THERAPEUTICS

Engineered Macrophages For Liver Fibrosis

Significant Unmet Need

- Chronic liver disease and cirrhosis account for over 1M deaths per year globally[1]
- Risk of liver-related mortality substantially increases in Stage 3/4 MASH with significant fibrosis
- No approved curative or fibrosis modifying therapies
- GLP-1 agonist 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 trials[3]
- Genetically engineered macrophages have the potential to engraft in the liver and provide a source for disease modifying therapeutic factors

Preclinical POC data on engineered macrophages in liver fibrosis expected in 2Q 2024

carisma THERAPEUTICS

MOA: mechanism of action; POC: proof of concept

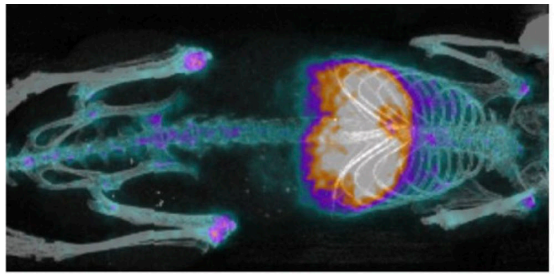
1. Gidener T, et al. Hepatology. 2022.2: Mamilos A, et al. Cells. 2023 Jan; 12(2): 276. 3. Younossi Z, et al. Clinical and Experimental Hepatology.
4. Moroni F, et al. Nature Medicine. 2019. 5. Brennan PN, et al. Hepatology. AASLD Abstract #160. 2023.

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 Zn^{89} labeled human macrophages[1]

Engineered macrophages can persist for months in the liver, serving as durable “hepatic micropharmacies” secreting therapeutic payloads[2]

Engineered macrophages expressing disease modifying factors may reverse liver fibrosis[1]

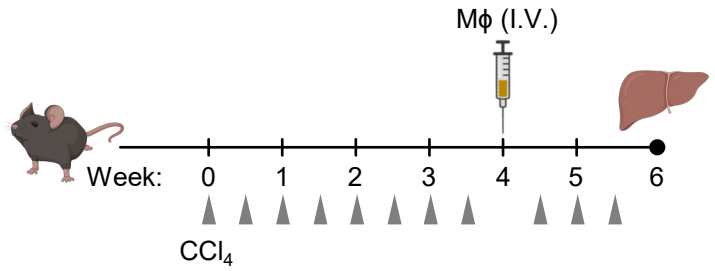
- **Reduce inflammation**
- **Reverse established fibrosis**
- **Promote tissue regeneration**

carisma THERAPEUTICS

1. Carisma preclinical studies. 2.Klichinsky M, et al. Nat Biotechnol. 2020 Aug;38(8):947-95)

A Single Dose of Engineered Macrophages Fully Reversed Liver Fibrosis[1]

CCl4 model of established fibrosis

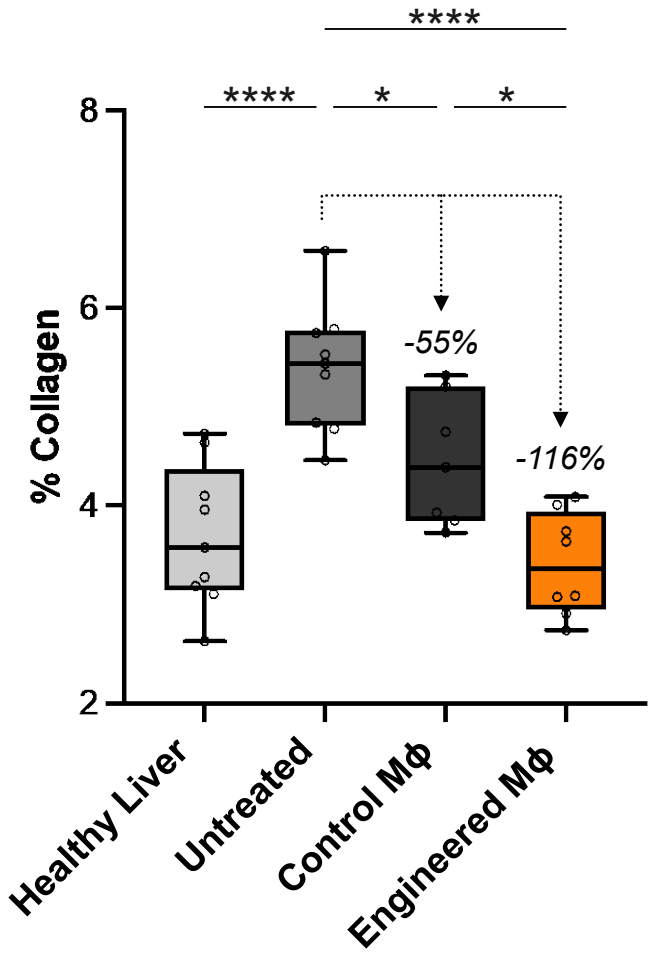


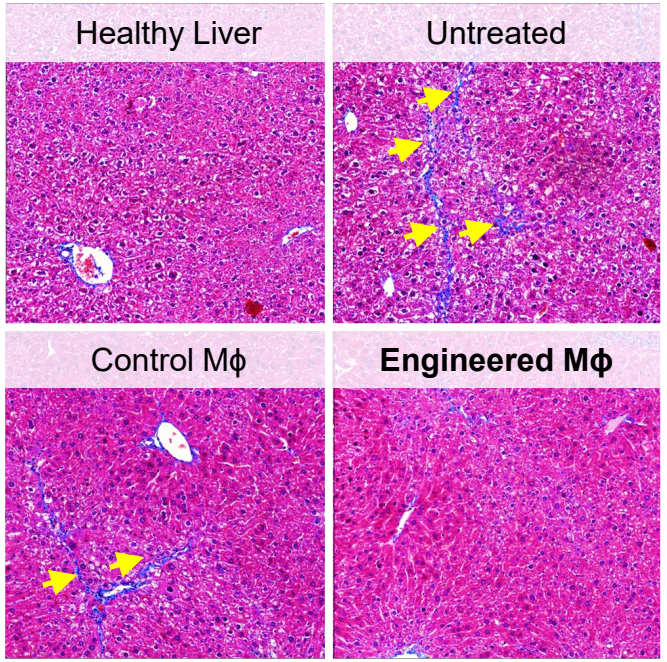
Engineered Mϕ significantly reduced hepatic collagen

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

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

Engineered macrophages fully reverse fibrosis

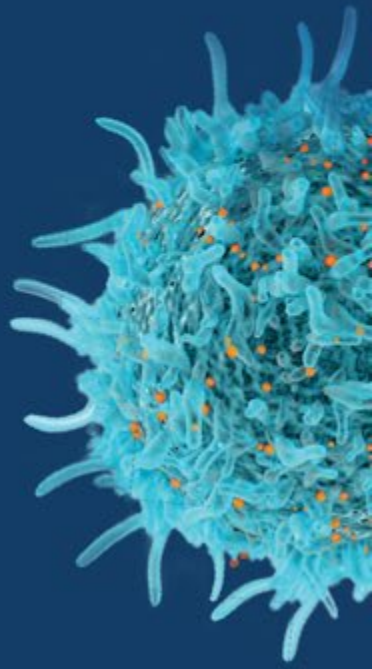




Masson's Trichrome Staining
Fibrosis shown in blue

Mϕ: Macrophage;
1: Carisma preclinical data; 2: Compared to Untreated

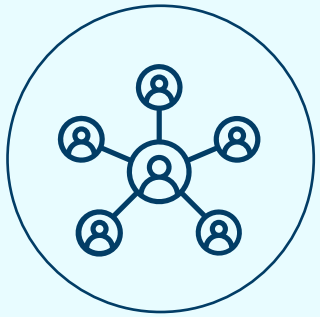
Corporate & Financial



carisma THERAPEUTICS

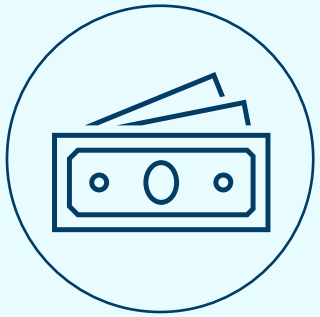
Financial Snapshot

As of December 31, 2023



40.6M

Shares outstanding



$77.6M

Cash and cash equivalents

Into 3Q 2025

Expected cash runway*

carisma THERAPEUTICS

* Implementation of March 2024 revised operating plan, including pausing development of CT-1119, reducing workforce, and decreasing non-essential activities is expected to reduce expenses in 2024.

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 *(1st Gen CAR)*	**4Q'23**	IND cleared	✓
			2Q'24	Treat first patient	☐
			4Q'24	Report data from Phase 1 study	☐
	CT-0508*	CAR-Macrophage *(1st 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 *in vivo* CAR-M lead candidate	✓
			TBD	Development candidate selection	☐
	4 Additional Targets[2]	CAR-Macrophage + mRNA/LNP	**4Q'23**	Report proof of concept data for *in vivo* CAR-M (SITC 2023)	✓
Fibrosis and Immunology					
Liver Fibrosis	TBD	Engineered macrophage	**2Q'24**	Report pre-clinical POC data	☐

carisma THERAPEUTICS

* In late March 2024, Carisma made the decision to cease further development of CT-0508, including monotherapy and in combination with pembrolizumab
1. Target undisclosed; 2. Moderna collaboration has identified 5 total oncology targets, with the option to identify an additional 7 oncology targets

Drive to 2025

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

Program	2024 Tactical Plan	2025 Objectives
HER2 CAR-M	♦ CT-0525[1] Safety Study Cohort 1: 3 Billion Cells ♦ CT-0525[1] Safety Study Cohort 2: 10 Billion Cells	**Phase II/III Regimen Identified[2]**
***In vivo* CAR-M** *(Collaboration with Moderna)*	♦ IND-enabling activities for lead candidate ♦ Pre-clinical studies for additional identified targets	**Undisclosed Development & Regulatory Milestones**
Liver Fibrosis	♦ Pre-clinical proof-of-concept studies ♦ Development candidate identified	**IND-enabling Activities**

1. CAR-Monocyte; 2. In late March 2024, the Company selected CAR-Monocyte approach for the Phase II/III Regimen Identified

THANK YOU

carisma THERAPEUTICS

carismatx.com