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HARNESSING THE POWER OF ENGINEERED MACROPHAGES

Carisma Therapeutics

April 2023

Cautionary Note Regarding Forward-Looking Statements Regarding Carisma

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.

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) risks associated with the possible failure to realize certain anticipated benefits of the merger, including with respect to future financial and operating results; (ii) the effect of the completion of the merger on Carisma's business relationships, operating results and business generally; (iii) the outcome of any legal proceedings related to the merger agreement or the transactions contemplated thereby; (iv) Carisma's ability to obtain, maintain and protect its intellectual property rights related to its product candidates; (v) Carisma's ability to advance the development of its product candidates under the timelines it anticipates in planned and future clinical trials; (vi) Carisma's ability to replicate in later clinical trials positive results found in preclinical studies and early-stage clinical trials of its product candidates; (vii) 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; (viii) 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; (ix) changes to clinical trial designs and regulatory pathways; (x) risks associated with Carisma's ability to manage expenses; (xii) changes in capital resource requirements; (xii) risks related to the inability of Carisma to obtain sufficient additional capital to continue to advance its product candidates and its preclinical programs; and (xiii) legislative, regulatory, political and economic developments. For a discussion of other risks and uncertainties, and other important factors, any of which could cause the Company's actual results to differ from those contained in the forward-looking statements, see the "Risk Factors" set forth in Exhibit 99.3 to Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on March 8, 2023, as well as discussions of potential risks, uncertainties, and other important factors in the Company's most recent filings with the Securities and Exchange Commission. Any forward-looking statements that are made in this press release speak on as of the date of this press release. 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 press release, whether as a result of new information, future developments or otherwise, except as required by the federal securities laws.

Carisma is Positioned for Success

Rapid progress with significant opportunity to become a breakthrough therapeutics company

COMPANY HIGHLIGHTS:

- Cutting edge research and bioengineering:
  - Proprietary platform for macrophage targeted therapies
  - Autologous/ allogeneic/ in-vivo modalities
  - Broad potential therapeutic applications, in oncology & beyond
- Strong patent position covering all CAR-M therapies
- Early clinical data for lead program demonstrating feasibility, tolerability, and MoA in HER2+ solid tumors
- Validating partnership with Moderna to develop up to 12 in-vivo cancer therapies with $80M upfront ($45M cash plus $35M equity in a convertible note), full R&D funding, and potential significant milestones and royalties
- Received $105M from reverse merger with Sesen Bio and concurrent financing, providing anticipated operating runway through 2024, with multiple potential value inflection points over the next 18 month

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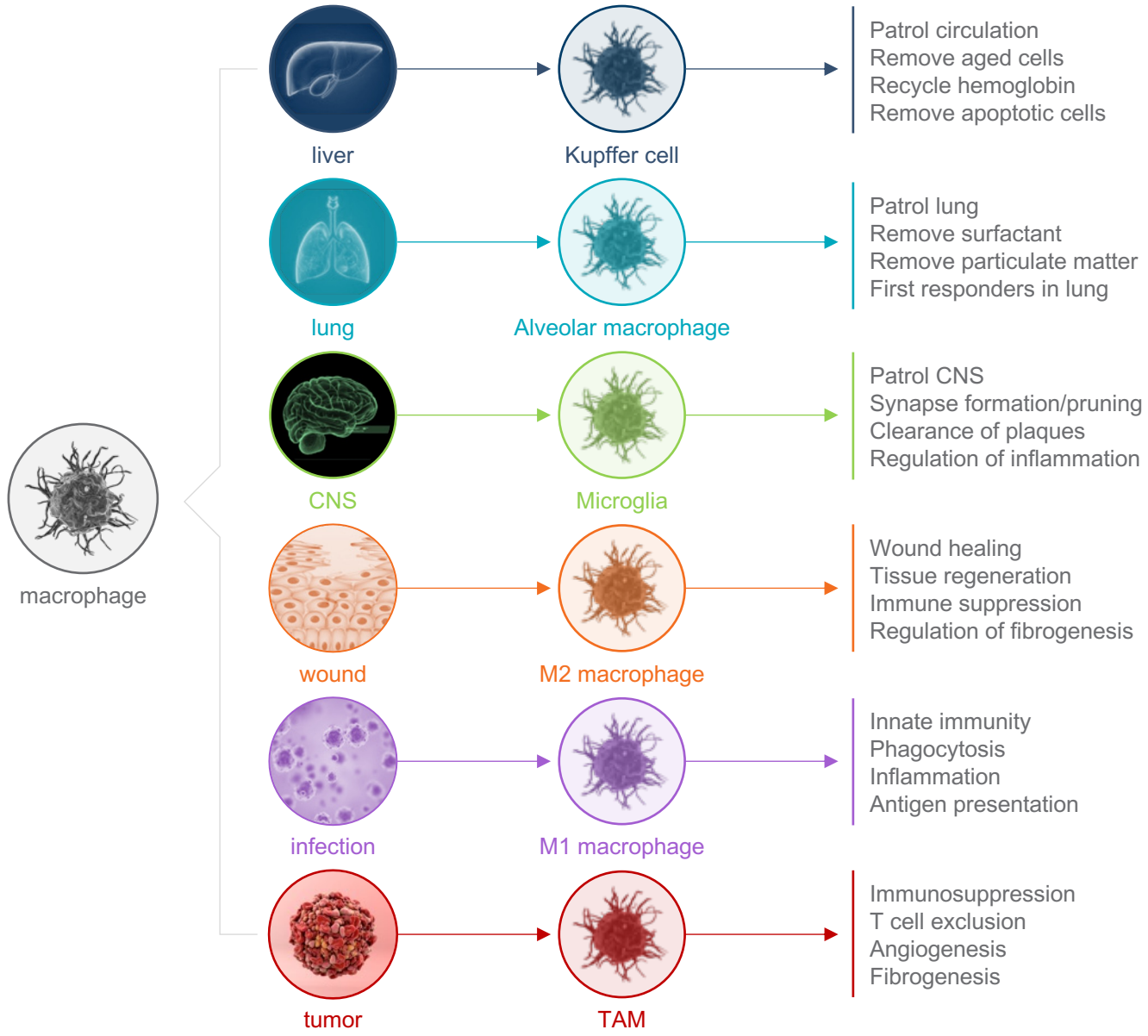
CAR-M = Chimeric Antigen Receptor Macrophage
MoA = Mechanism of action

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



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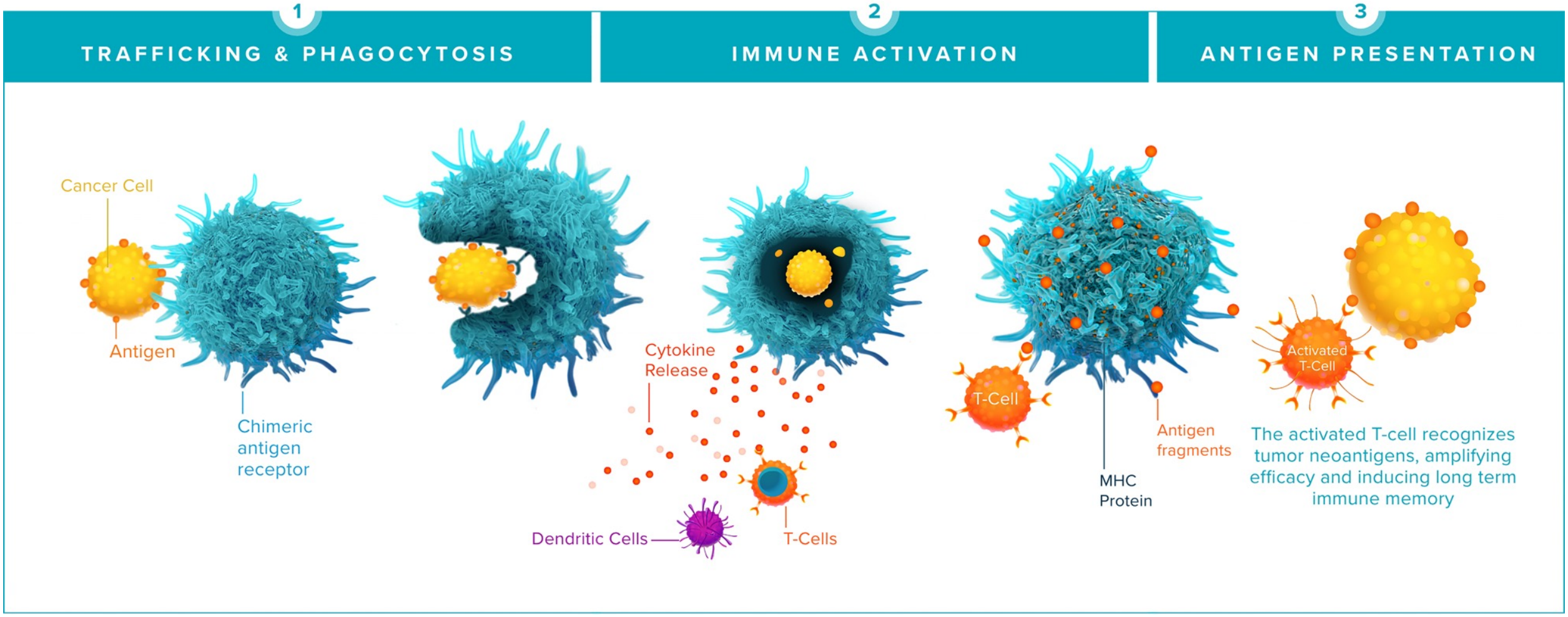
CAR-M Mechanism of Action: Multi-Pronged Attack on Cancer

Carisma's technology has the potential to address the key challenges involved in treating solid tumors



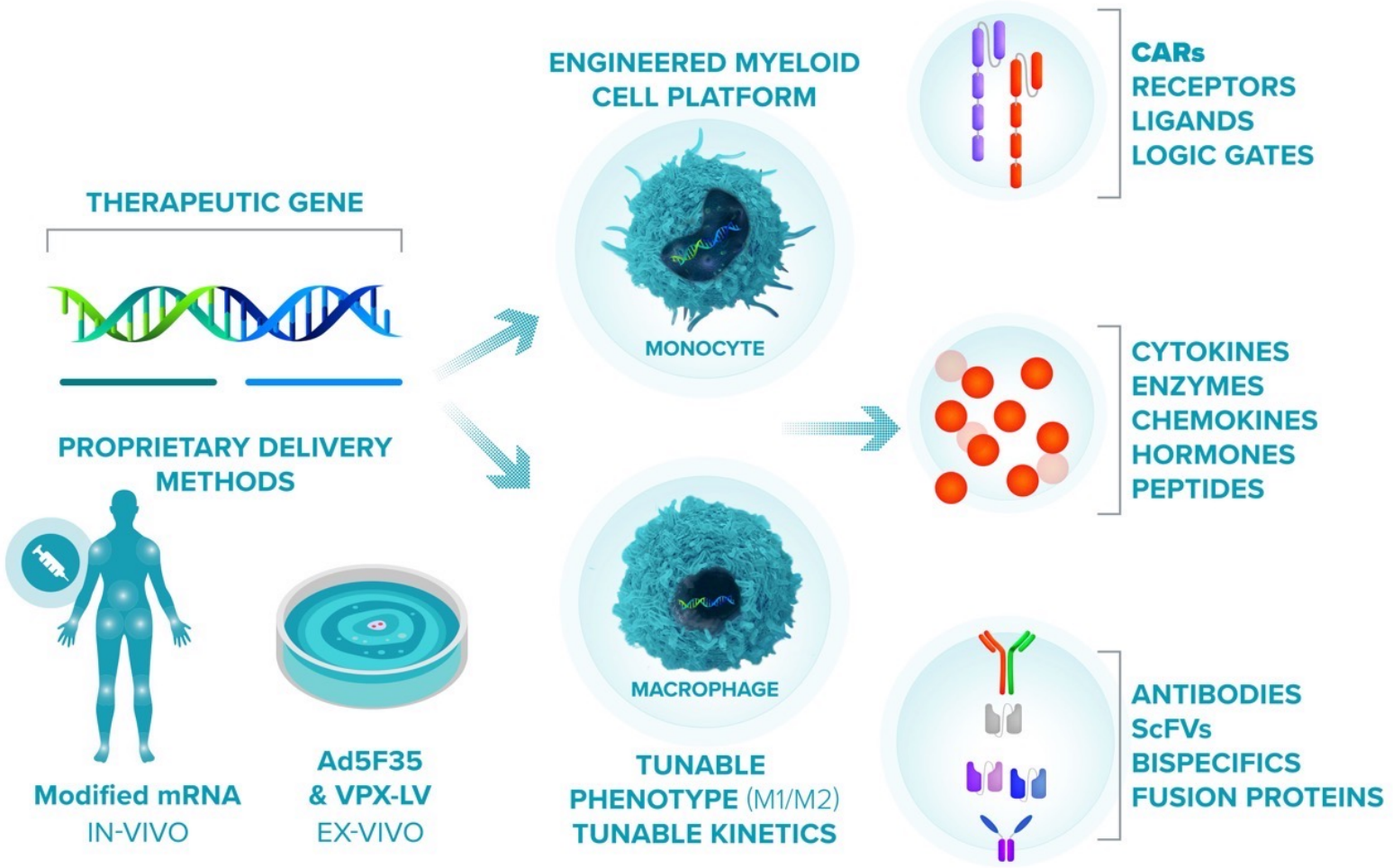
MHC = Major Histocompatibility Protein

Carisma's Broad Myeloid Cell Engineering Platform

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

Monocyte & Macrophage Engineering Capabilities:

- Proprietary platforms for durable macrophage engineering with Ad5f35 or Vpx-LV viral vectors
- Proprietary platform for transient macrophage engineering: Modified mRNA
- Methods to control macrophage phenotype toward M1 & M2
- Ability to deliver large/ multiplexed payloads
- Efficient gene editing methods using CRISPR/ Cas9



ScFV = Single-chain variable fragment

Strong Patent Position

Broad Coverage for Monocyte and Macrophage Targeted Therapies

16

PATENTS GRANTED WORLDWIDE*

40+

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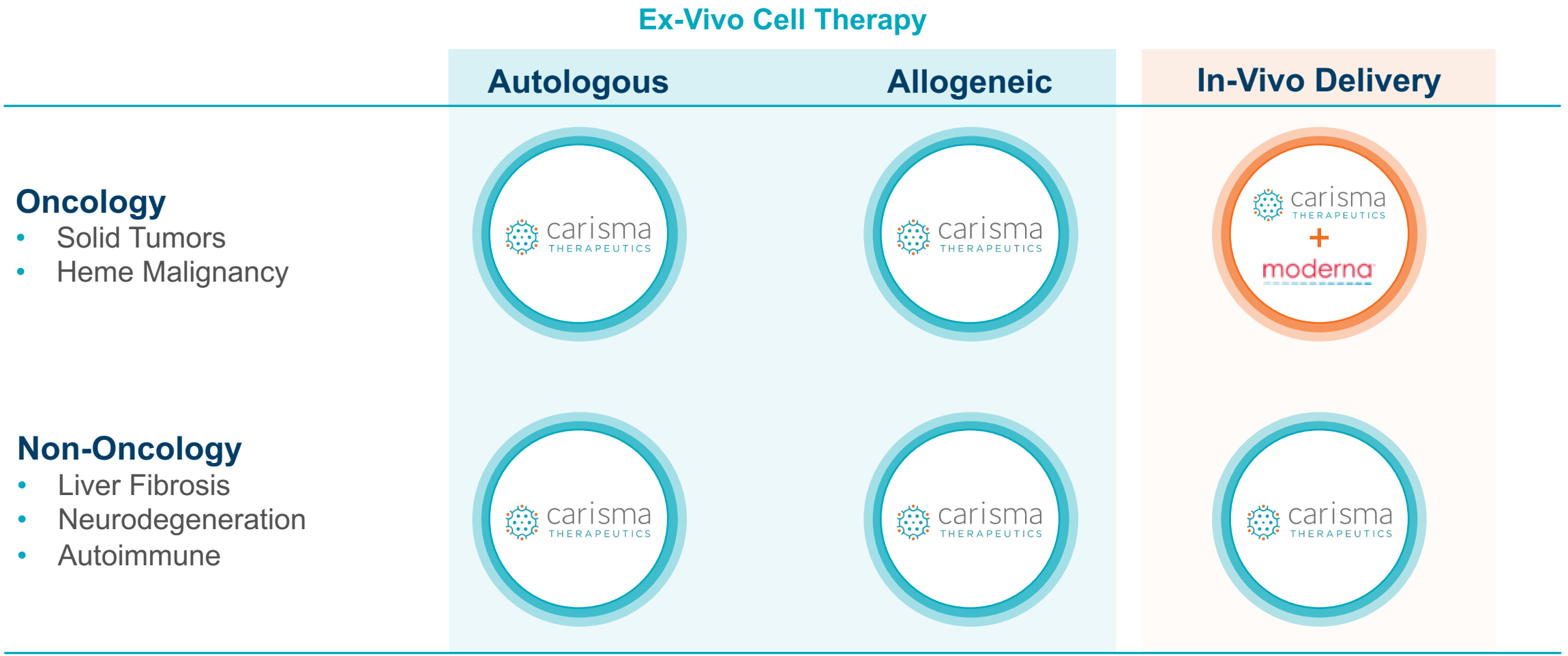
* Total includes Carisma-owned patents and patents exclusively licensed from The University of Pennsylvania and New York University

Carisma's Strategic Approach to Platform Expansion

Initial focus on ex-vivo autologous approach expected to drive expansion into higher risk/reward modalities



Platform Enhancements Drive First-in-Class Pipeline

Multiple value inflection points with significant partner support/funding

IND = Investigational new drug application

* Phase 1 study is currently active and ongoing

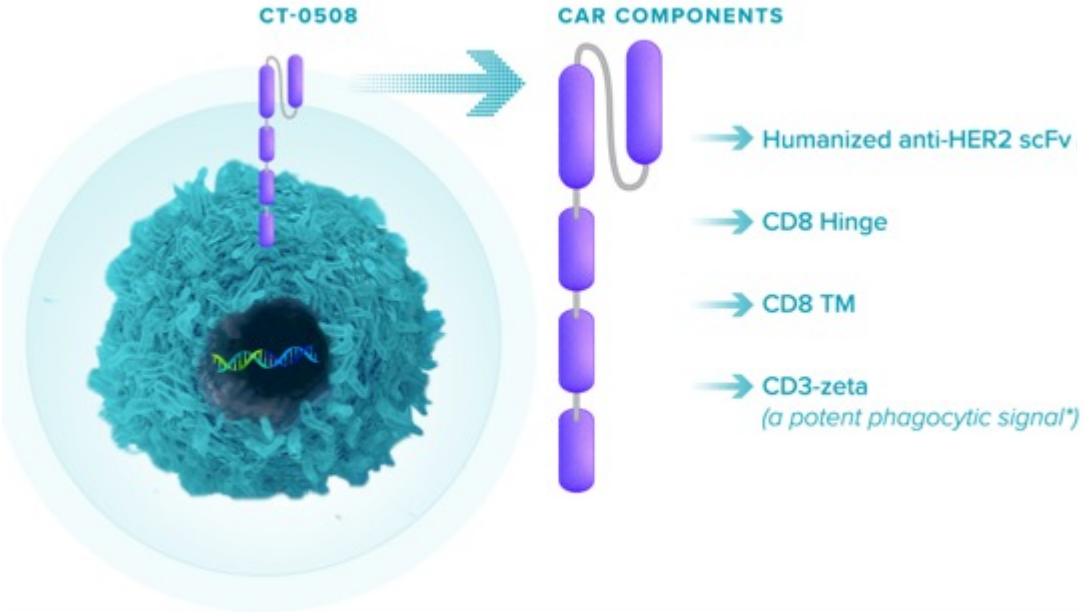
Lead Program CT-0508: HER2 Targeted CAR-Macrophage

Program Status

- Phase I study ongoing at seven clinical sites
- Early data presented at the SITC supports platform's safety and MoA
- Expanded clinical program including regional administration and T cell checkpoint combination initiated

Future Milestones

- Continue to enroll in all sub-studies through 2023
- Data update planned for 2H 2023
- File IND for HER2 targeted CAR-Monocyte in 2H 2023



Cells: Autologous monocyte derived macrophages
Vector: Ad5f35
Phenotype: M1
Target: HER2

FDA Fast Track Designation Granted Sept 2021

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SITC = Society for Immunotherapy of Cancer (SITC) 37th Annual Meeting
MoA = Mechanism of action
IND = Investigation new drug application

CT-0508 Study 101 Interim Data Supports CAR-M Hypothesis

FEASIBILITY

- CT-0508 was successfully manufactured from autologous mobilized monocytes
- Patient product demonstrated high CAR expression, purity, viability, M1 polarization and confirmed functionality
- No lymphodepletion

PRELIMINARY CLINICAL PROFILE

- No dose limiting toxicities
- No AEs leading to dose modification or discontinuation
- No severe CRS, no ICANS, and no major organ system toxicity observed
- Best overall response of SD in 4/9 patients with single dose, monotherapy

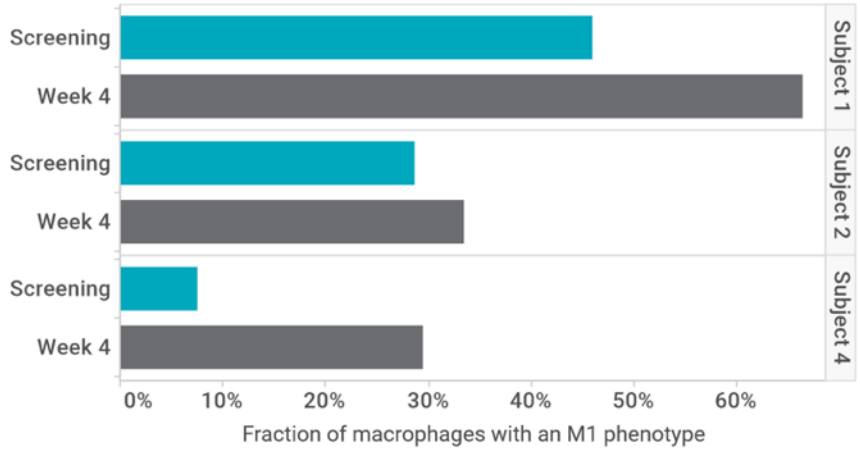
MECHANISM OF ACTION

- CT-0508 tumor infiltration detected in 8/9 patients
- Increased infiltration of effector T cells and M1 macrophages in TME post CT-0508
- Significant expansion of novel T cell clones in the TME with concomitant CD8 T cell activation, suggesting induction of anti-tumor immunity

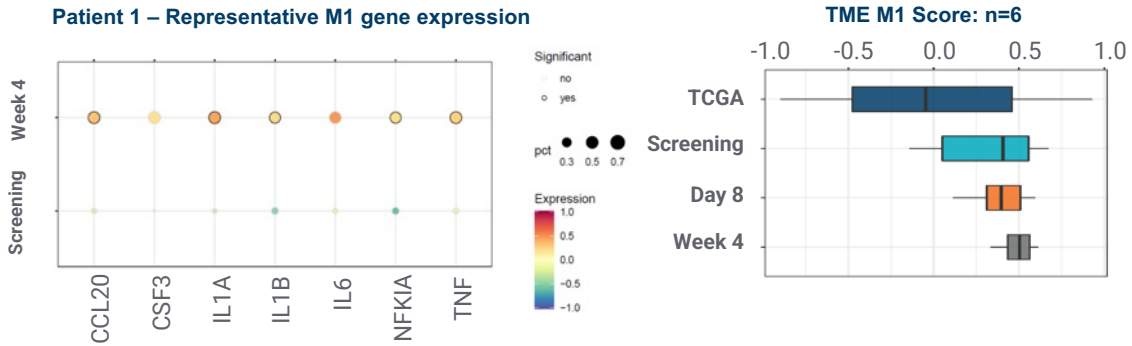
AE = Adverse event
CRS = Cytokine release syndrome
ICANS = Immune effector cell-associated neurotoxicity syndrome
SD = Stable disease

CT-0508 Treatment Led to Increased Myeloid Activation in TME

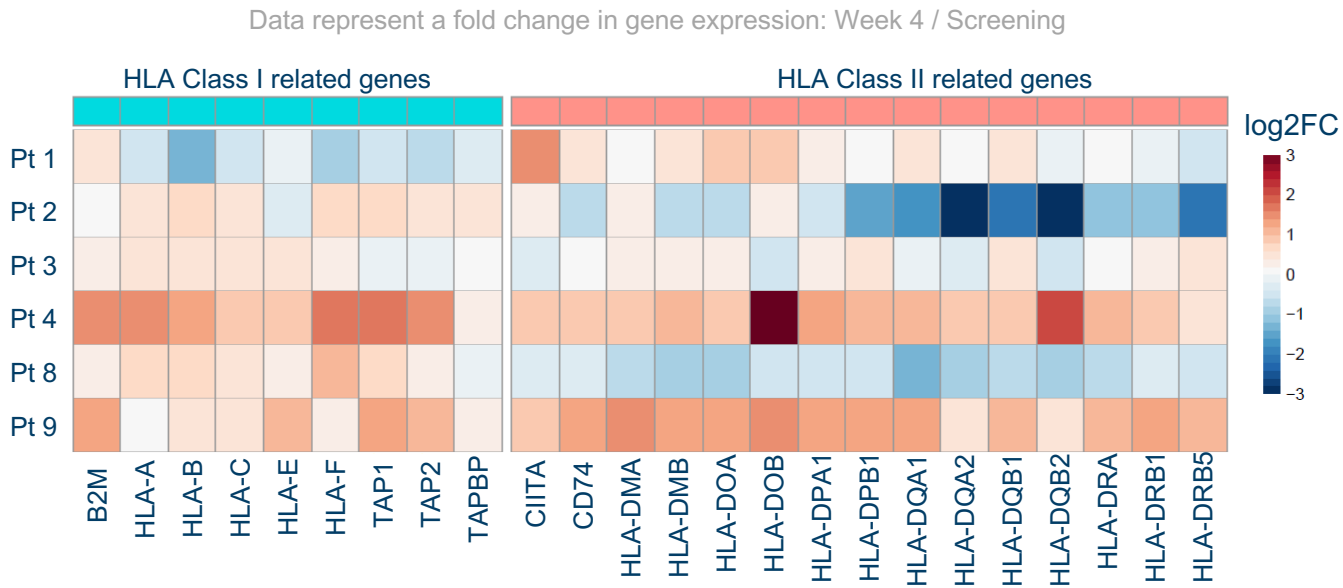
A. Increased fraction of M1 macrophages in TME



B. Upregulation of M1 associated gene expression in TME



C. Increased Antigen Presentation Machinery in TME



Summary: CT-0508 treatment led to increased effector M1 macrophage frequency within the TME (Figure A). Representative data from Patient 1's TME scRNA Seq analysis demonstrate induction of pro-inflammatory genes in the tumor infiltrating myeloid compartment (Figure B, left). The overall M1 signature in the TME increased on treatment (Figure B, right) and antigen presentation machinery was upregulated within the tumor (Figure C).

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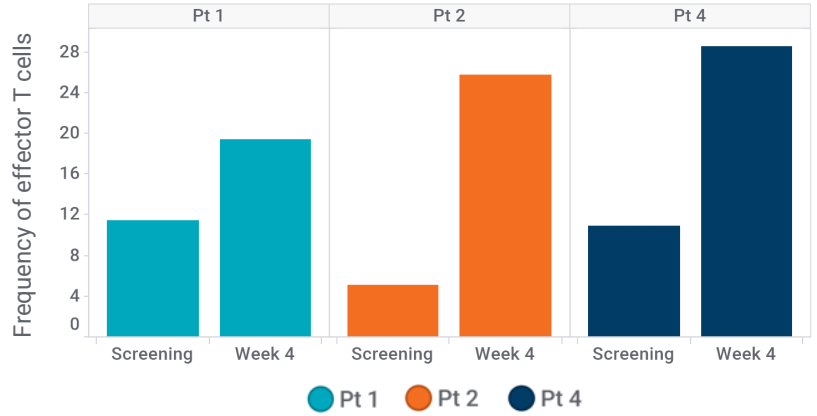
Figure A. N = 3/3 pts with paired biopsy scRNA SEQ data.
Figure B, right. N =6/6 pts with paired biopsy bulk RNA SEQ data.
Figure C. N = 6/6 pts with paired biopsy bulk RNA SEQ data.

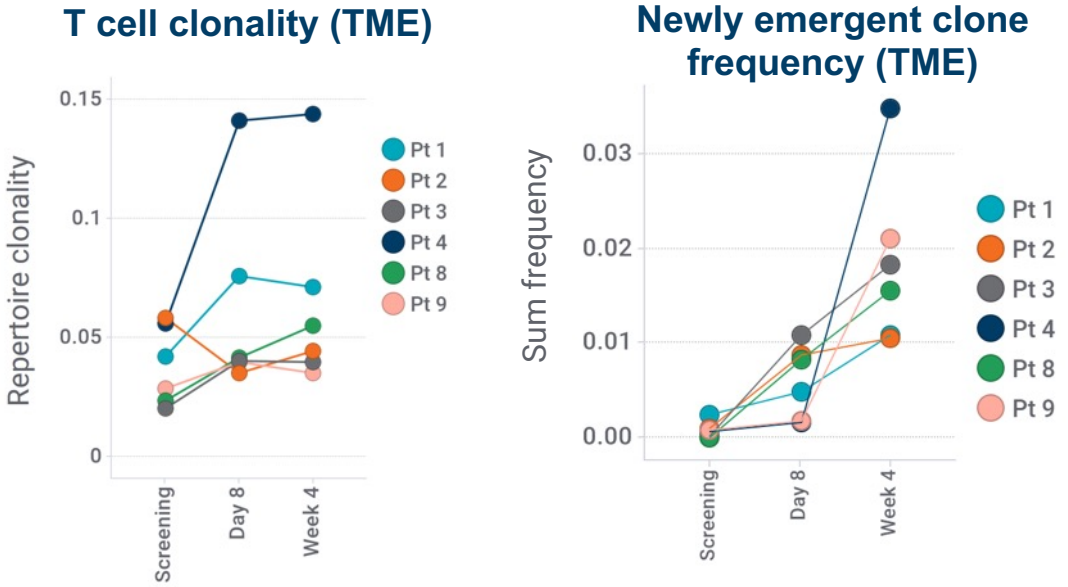
CT-0508 Shown to Induce Adaptive Anti-Tumor Immunity

A. Increased Effector T Cell Infiltration in TME

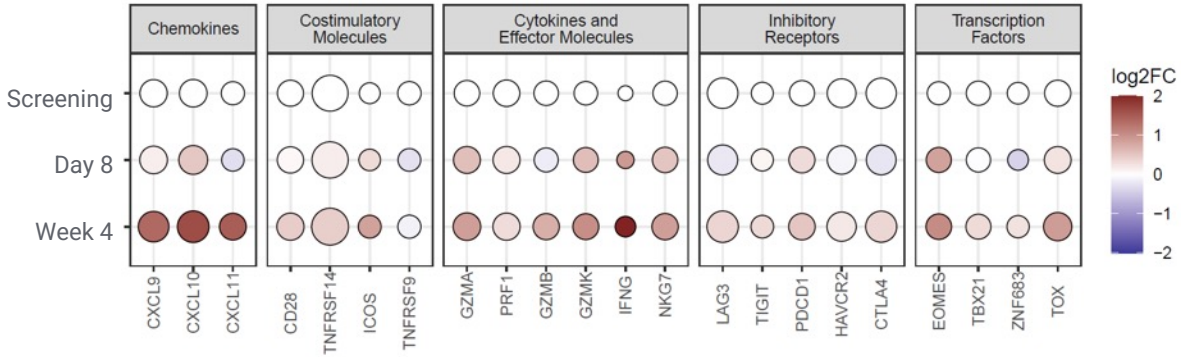


N = 3 pts with paired biopsy scRNA SEQ data.

B. Accumulation of peripherally expanded clones in the TME



C. Increased T Cell Activation in TME



N = 6 pts with paired biopsy bulk RNA SEQ data.

Summary: CT-0508 treatment led to increased effector T cell infiltration of the TME (Figure A). T cell clonality increased within the TME (Figure B, left). Newly emergent, previously undetectable T cell clones accumulated within the TME over time (Figure B, right). T cell activation markers were upregulated within the TME following CT-0508 treatment (Figure C). Together, these data suggest induction of anti-tumor immunity.

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Figure A. N = 3/3 pts with paired biopsy scRNA SEQ data.
Figure B. N = 6/6 pts with paired biopsy TCR SEQ data.
Figure C. N = 6/6 pts with paired biopsy bulk RNA SEQ data.

CAR-M Platform Development Strategy

Four parallel approaches to unlock the therapeutic potential of CAR-M cell therapy

Phase I FIH Study Data Supports CAR-M Hypothesis & Is Meeting Study Objectives

- Generally well tolerated
- Feasible manufacturing
- Demonstrated CAR-M mechanism of action

1

CAR-M + PD1 Blockade

Overcome late-stage patients' T cell exhaustion

- Phase I/II CT-0508 + Pembrolizumab study currently recruiting

2

CAR-Monocyte (Macrophage Precursor)

Increase dose & improve trafficking/persistence

- CAR-Monocyte IND expected to be filed 2H 2023

3

Next Gen Constructs

Enhance CAR-M killing, cytokine release, & T cell priming

- CAR modification (hinge & co-stimulation) + additional payloads

4

Novel Modalities

Alternatives to autologous cell therapy

- Allogeneic iPSC myeloid cells; Direct in vivo reprogramming

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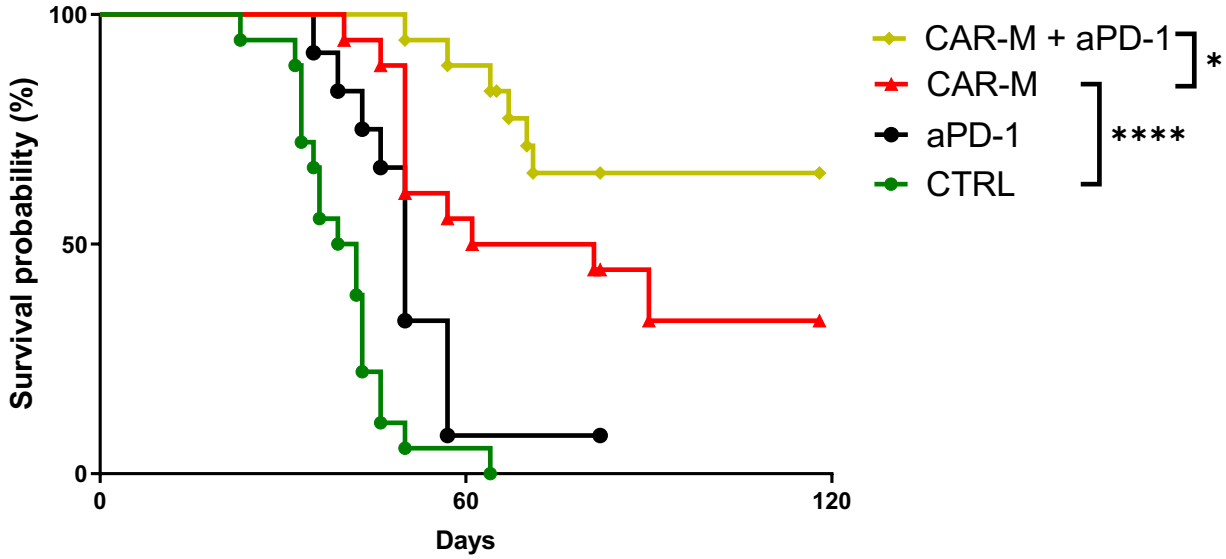
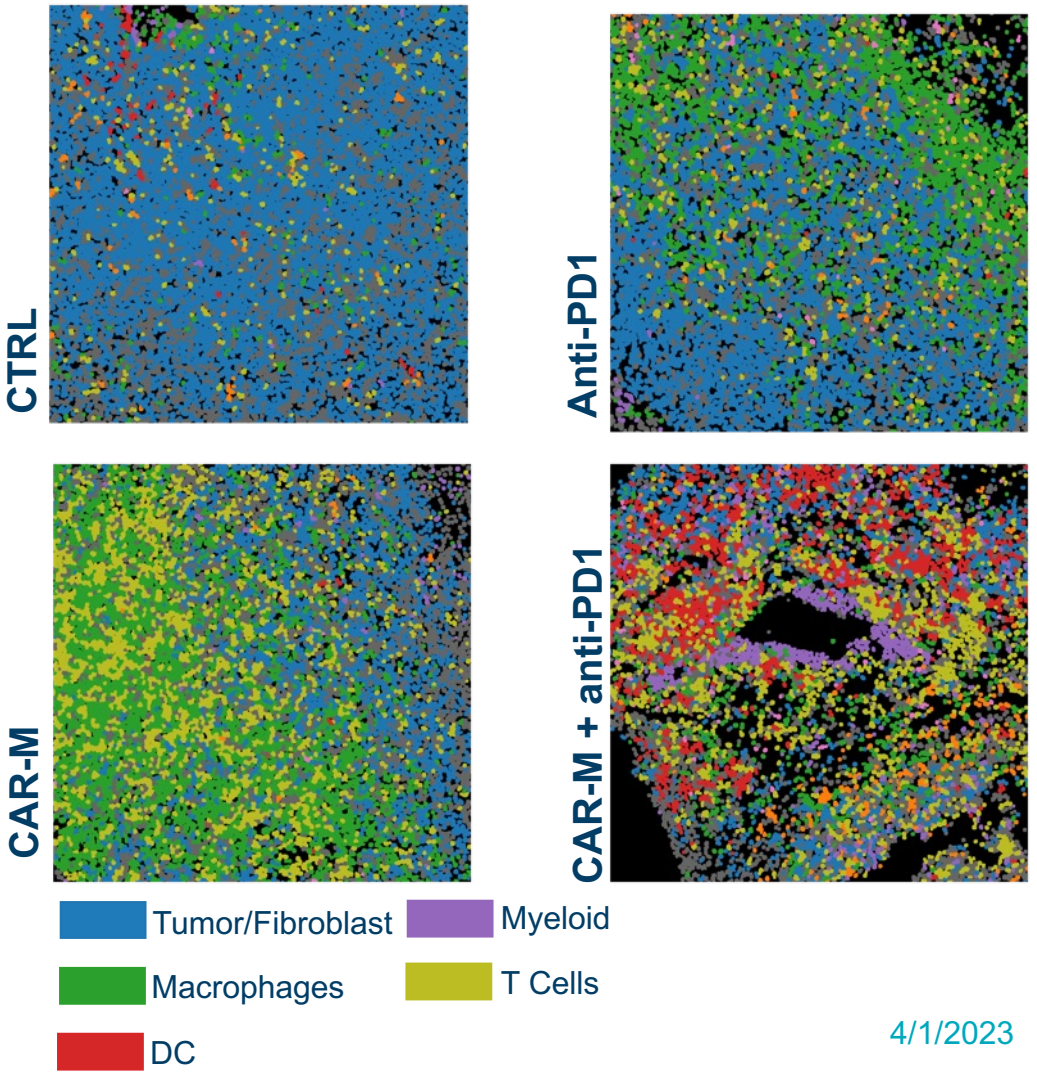
iPSC = Induced pluripotent stem cell

CT-0508 Has Potential to Reverse Immune Checkpoint Blockade Resistance and Demonstrates Robust Synergy*

Synergistic anti-tumor activity



Profound TME modulation with combination



DC = Dendritic cell
Ctrl = Control

* Data from pre-clinical models

1 CAR-M + Pembrolizumab Phase I Clinical Design

Study Design and Planning: A multi center, single arm Phase I study to establish safety and feasibility of intravenously administered adenoviral transduced HER-2 specific CAR modified autologous macrophage cells in combination with Pembrolizumab in patients with recurrent/metastatic solid tumors

N=9 HER-2 overexpressing solid tumors

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

Group 1, N=3
CT-0508 C1D1-3-5
Pembro 200mg C1D8

→ **Group 2**, N=3
CT-0508 C1D1-3-5
Pembro 200mg C1D1

→ **Group 3**, N=3
CT-0508 C1D1
Pembro 200mg C1D1

→ Pembro 200mg
Q21 days until tx completion

Day 1	Day 8-12	Week 4	Week 8	Week 52
Tumor biopsy before infusion	Tumor biopsy	Efficacy assessments Tumor biopsy	First RECIST 1.1 assessment	→

Study Objectives

Primary
- Safety
- Manufacture feasibility

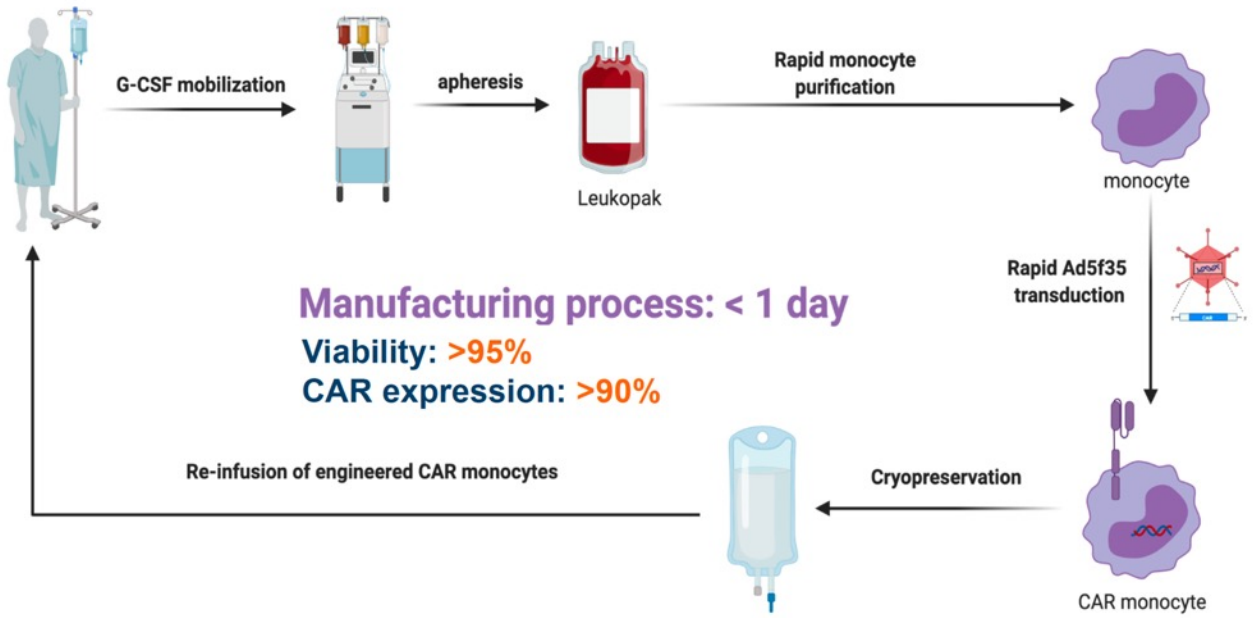
Secondary
- Trafficking
- OR (RECIST 1.1)
- OS and PFS
- Persistence

Correlates
- Phenotype
- Bioactivity
- Immune cell interaction

Carisma's CAR Monocyte Platform

Rapid manufacture & durable persistence

Rapid Manufacturing Process



Key Characteristics*

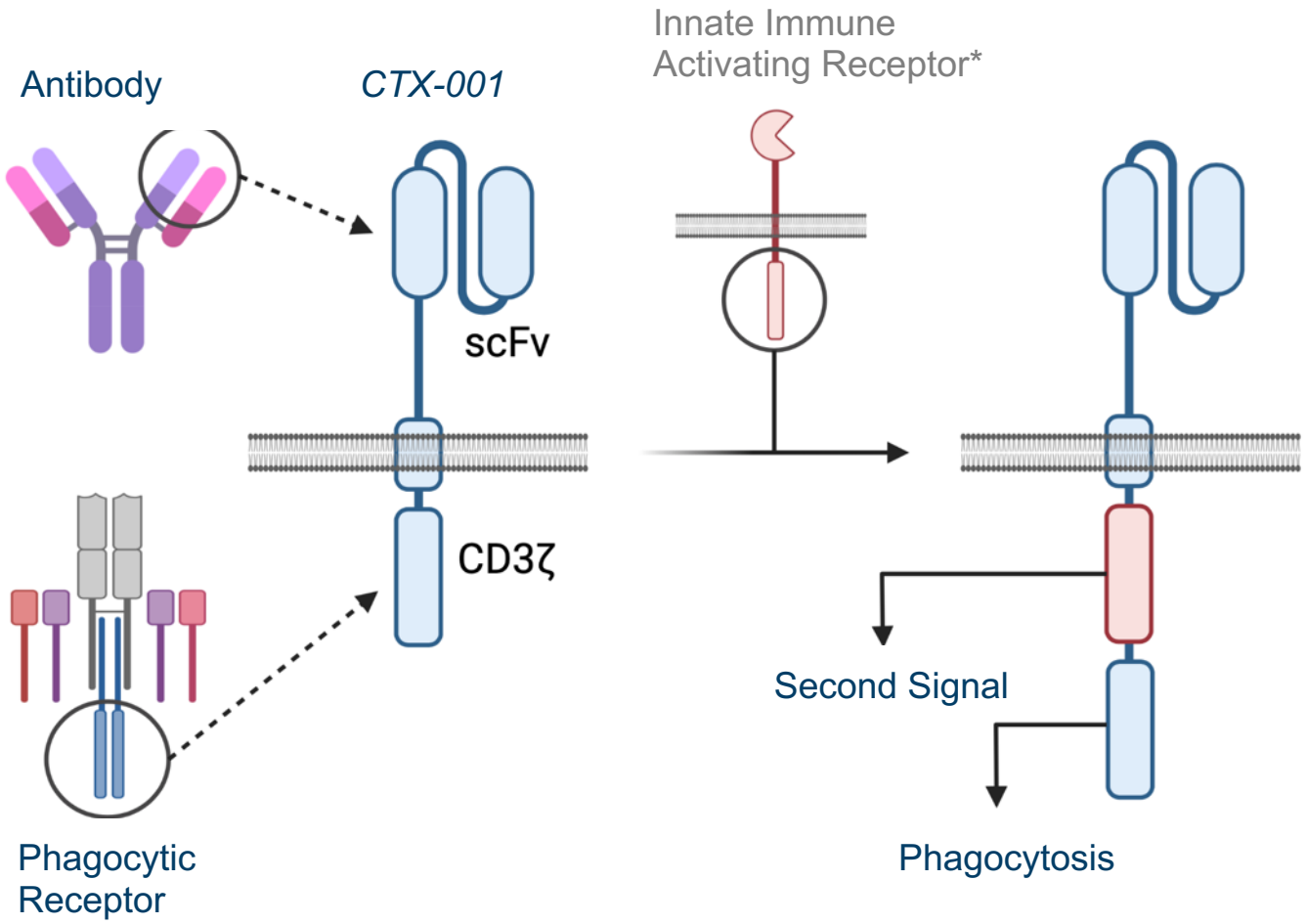
- Improved cell dose and dosing flexibility
- Improved trafficking
- Improved persistence
- Improved killing
- Improved cytokine release
- Improved potential for antigen presentation
- Reduced COG's

With the proprietary Ad5f35 vector and optimized CAR-Mono process, cells can be manufactured in 1 day and persisted for months after a single dose in pre-clinical studies.

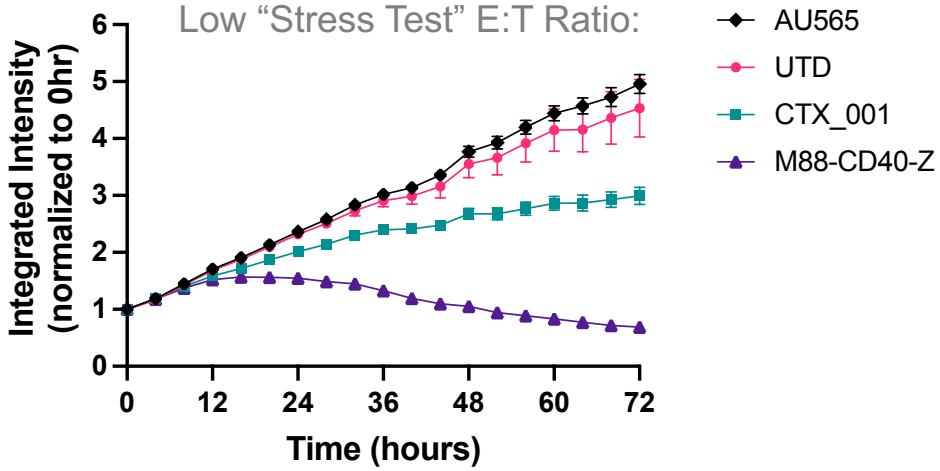
* Compared to macrophage cells

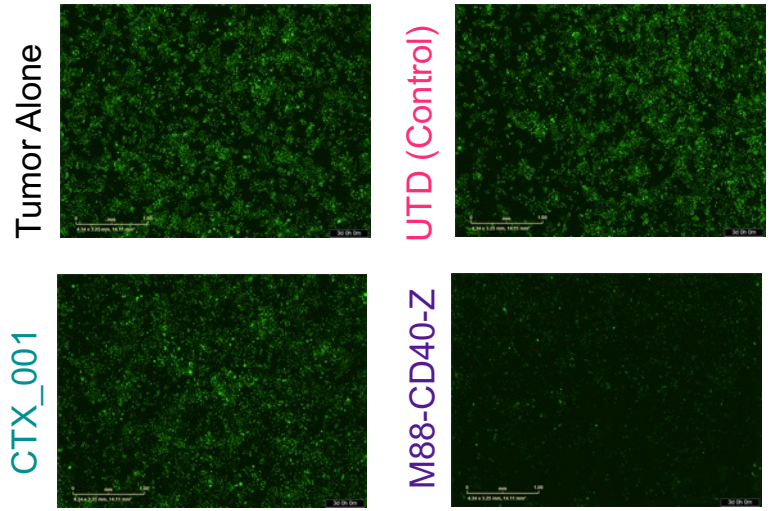
Next Gen CAR-M Discovery

Potential to increase potency & functionality



Adding MYD88/CD40 significantly increases anti-tumor potency in pre-clinical studies:





GFP labeled HER2+ AU565 breast cancer cells co-cultured with CAR-M at low E:T ratio for 72 hours.

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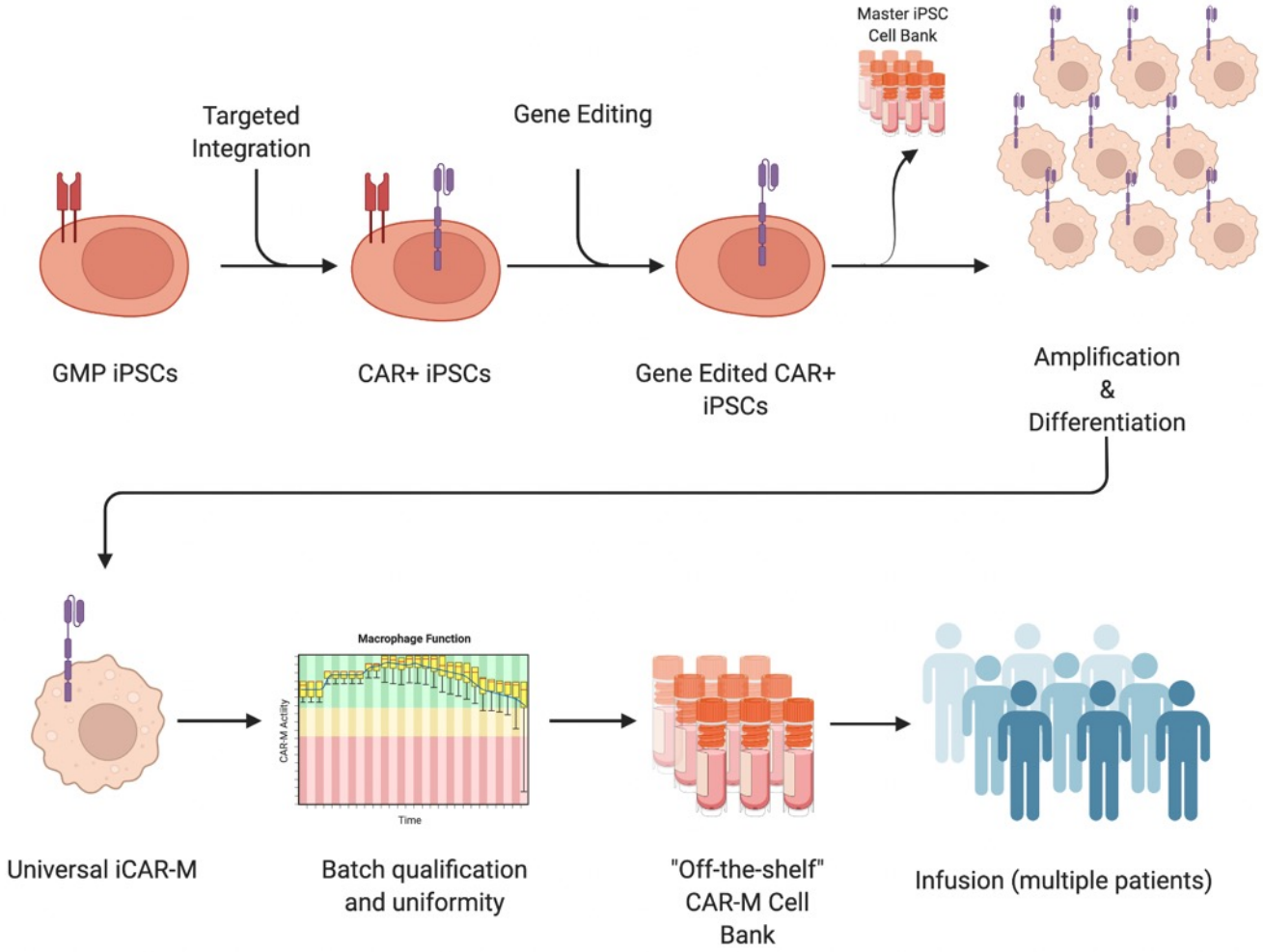
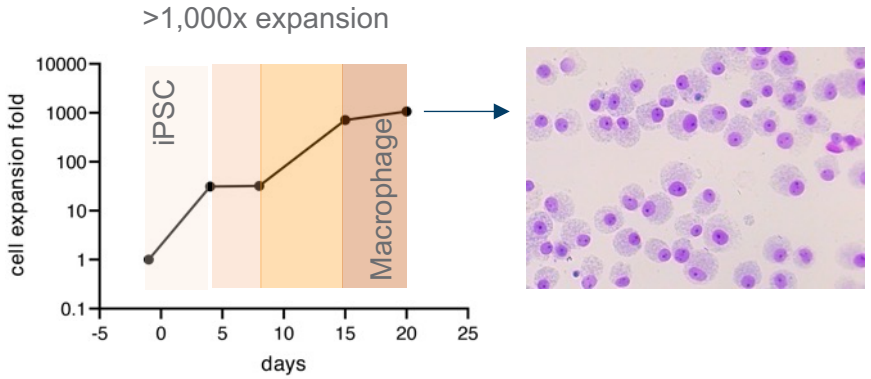
* Example: CD40, TLR2, TLR4, MyD88, Dectin-1, etc.

Off-the-Shelf iPSC Derived Myeloid Cells

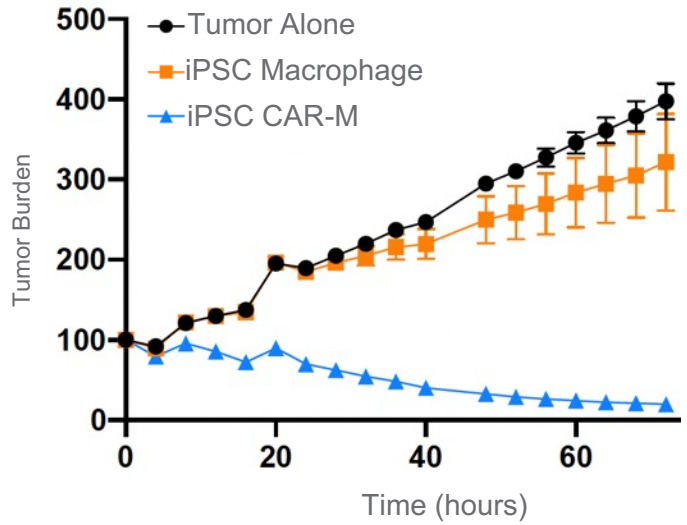
Expandable, allogeneic, and potentially broadly applicable



Production of iCAR-M

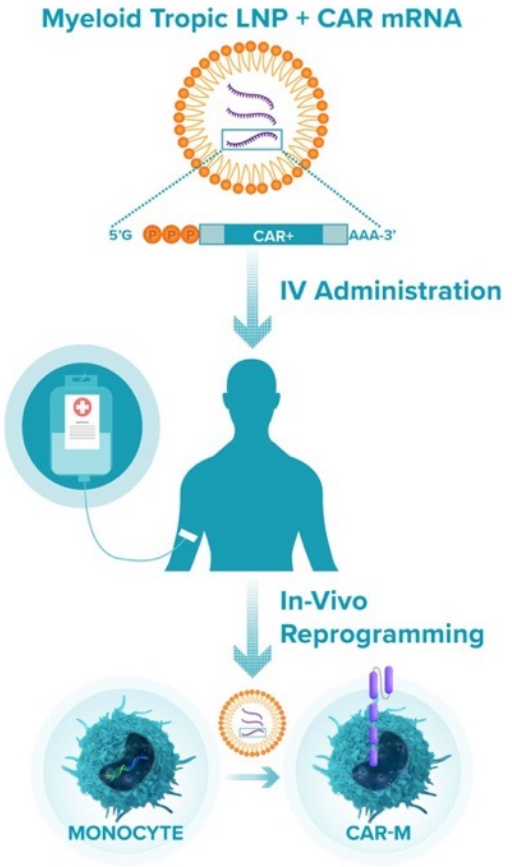


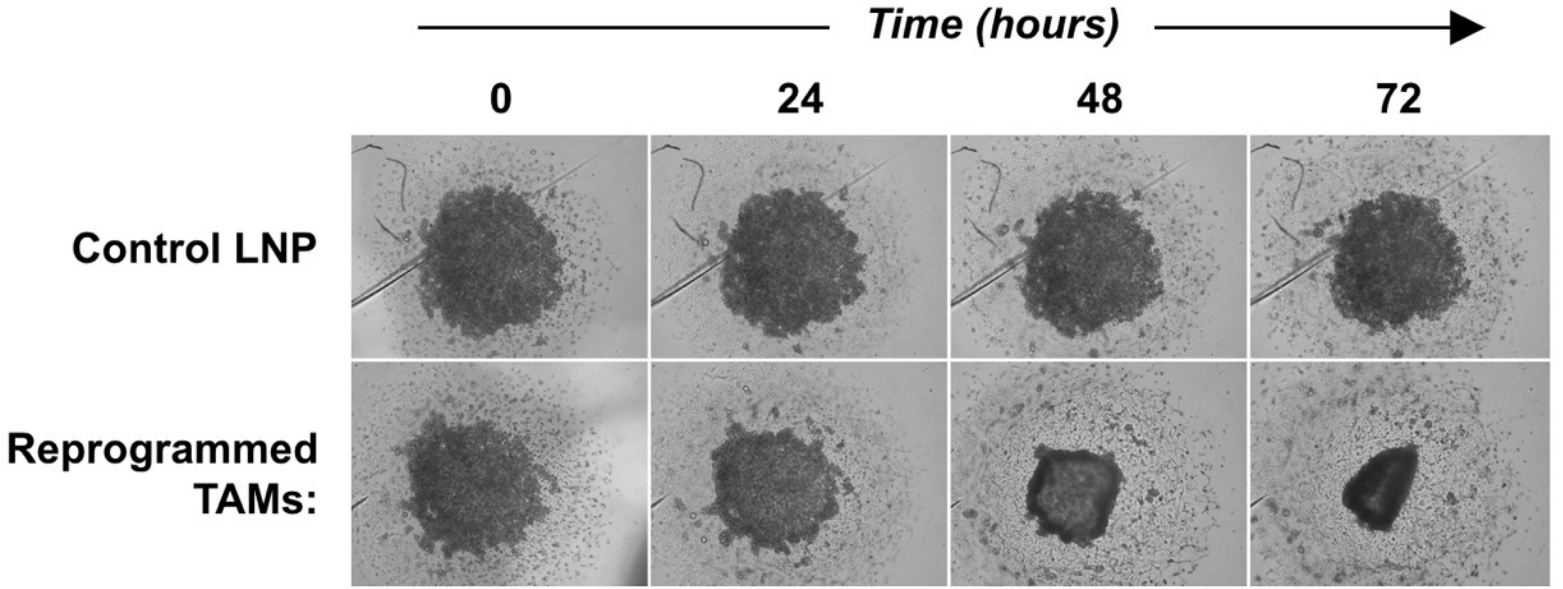
iCAR-M anti-tumor function in-vitro



GMP = Good manufacturing practice

4 Directly Reprogramming Myeloid Cells In Vivo with mRNA/LNP



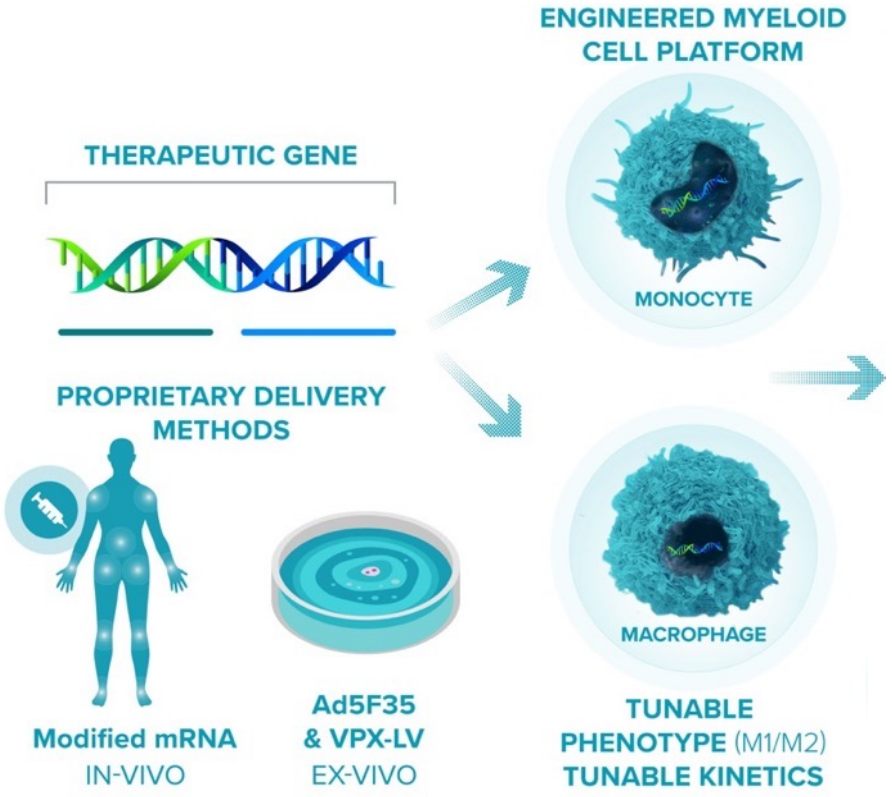


Tumor spheroids containing HER2+ breast cancer cells and TAMs.
LNPs are added to spheroids, and TAMs are directly reprogrammed to CAR-M to kill tumors cells.

- Myeloid tropic LNP have demonstrated specificity and efficient transfection in vivo
- LNP have proven safety profile in previous clinical studies; repeat dosing well tolerated
- High CAR expression and function in vitro
- In vivo studies ongoing
- Lead identified for first target, early in-vitro POC demonstrated

Platform Enables Potential Non-Oncology Applications

Significant opportunity for strategic partnerships



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Anti-inflammatory, anti-fibrotic macrophages:

- **Modality**: Auto/Allo Cell Therapy
- **Potential indication**: Liver Fibrosis
- **Payload**: Immunosuppressive cytokine + anti-fibrotic enzyme

2

In vivo reprogrammed microglia:

- **Modality**: In vivo reprogramming (LNP)
- **Potential indication**: Alzheimer's, Parkinson's
- **Payload**: Anti-Aβ CAR, Anti-αSyn CAR, Anti-Tau CAR

3

Switch receptors for inflammatory disease:

- **Modality**: Auto/Allo Cell Therapy
- **Potential field**: Immunologic/Transplant
- **Payload**: Proprietary M1 → M2 switch receptors

Strong Leadership Team and Advisors

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

Management

STEVEN KELLY
President & CEO

MICHAEL KLICHINSKY, PHD
Co-Founder & CSO

DANIEL CUSHING, PHD
Chief Technology & Development Officer

RICHARD MORRIS
Chief Financial Officer

TOM WILTON
Chief Business Officer

Board of Directors

- Sanford Zweifach – Chairperson
- Steve Kelly – President and CEO
- Briggs Morrison – Independent Director
- Björn Odlander – HealthCap
- Regina Hodits – Wellington Partners
- Chidozie Ugwumba – SymBiosis
- Michael Torok – Independent Director

Key Advisors

- 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

Operating Plan and Corporate Milestones

Capital efficient R&D program designed to reach significant value inflection points over next 18 months

Complete expanded CT-0508 Phase I study

- Cohort 2: Bolus dosing
- IP Administration
- Anti-PD1 combination

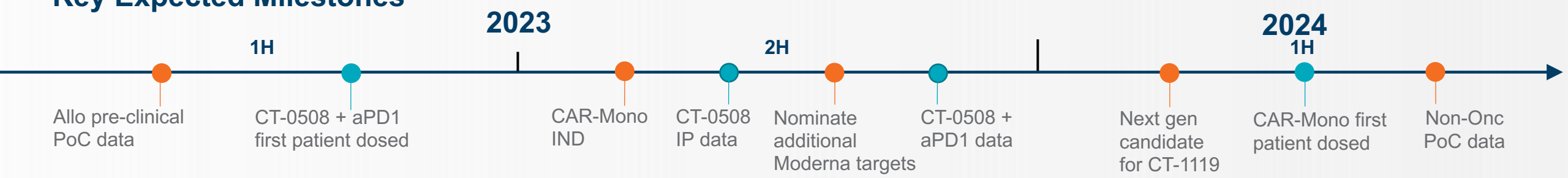
Advance our engineered macrophage platform

- Progress next gen CAR-M design to candidate selection
- Develop CAR-Mono and Allo to expand the performance and utility of the platform
- Expand internal in-vivo capability

Advance CAR-M pipeline

- Deliver in-vivo animal data with Moderna and nominate additional targets
- Initiate a Phase 1 clinical study for the CAR-Monocyte program
- Progress neurodegeneration and liver fibrosis programs to PoC

Key Expected Milestones



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Clinical milestone

Pre-clinical milestone

Corporate Summary

Significant opportunity to become a breakthrough therapeutics company

- Proprietary engineered macrophage platform
- Emerging pipeline of oncology CAR-Ms
- Validating partnership and clinical data
- Experienced leadership team and advisors
- Multiple potential value catalysts over next 18 months