



HARNESSING THE POWER OF ENGINEERED MACROPHAGES

CARISMA Therapeutics
September 2021





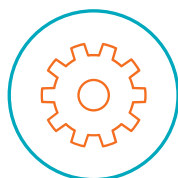
Harnessing the Power of Engineered Macrophages

CARISMA is a private, clinical stage, vertically integrated biotech company developing our first-in-class CAR-M technology for advanced cancers

Proprietary Platform and Capabilities



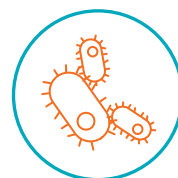
**Myeloid specific
cell engineering**



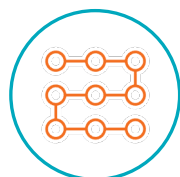
**Proprietary
Vectors**



**Gene Editing
Capabilities**



**Allo
Platform**



**Cell & Vector
Manufacturing**



**World Class
Leadership**



Significant IP

First-in-Class CAR-M Pipeline

- Solid tumor targets (HER2, Meso, PSMA) in development
- CT-0508 (HER2) in Phase I Safety (NCT04660929)
- Rationally selected heme malignancy targets (CD7)
- Broad R&D efforts to establish next-gen CAR-M
- Non-oncology applications (liver fibrosis, neurodegeneration, and auto-immunity)

Established Leadership and Strategy

- Deep research, clinical and operational expertise in cell therapy and oncology
- Leading IP position with broad claims encompassing CAR's and myeloid cells
- Capital efficient manufacturing structure with short vein-to-vein time and scalable platform

~\$120M raised to date

Strong Leadership Team and Advisors

Management



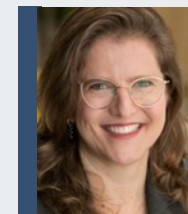
Steven Kelly
President & CEO



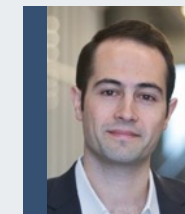
Dan Cushing, PhD
CDTO



Rich Morris
CFO



Debora Barton, MD
CMO



**Michael Klichinsky,
PharmD PhD**
Co-Founder & SVP, Research



Tom Wilton
CBO

Advisors



Saar Gill, MD PhD
Co-Founder
U Penn



Carl June, MD
University of
Pennsylvania



Hy Levitsky, MD
Former CSO of Juno
Therapeutics



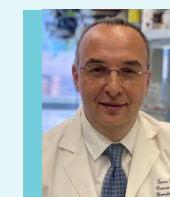
Lisa Coussens, PhD
Oregon Health &
Science University



**Prasad
Adusumilli, MD**
MSKCC



**Nina Bhardwaj,
MD, PhD**
Mt. Sinai

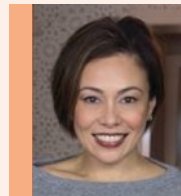


Nabil Ahmed, MD
Baylor College
of Medicine

Board of Directors



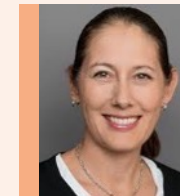
Briggs Morrison
Independent



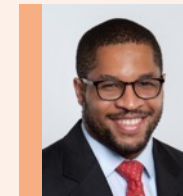
Margarita Chavez
AbbVie Ventures



**Jacob
Gunterberg**
HealthCap



Regina Hodits
Wellington



**Chidozie
Ugwumba**
Symbiosis

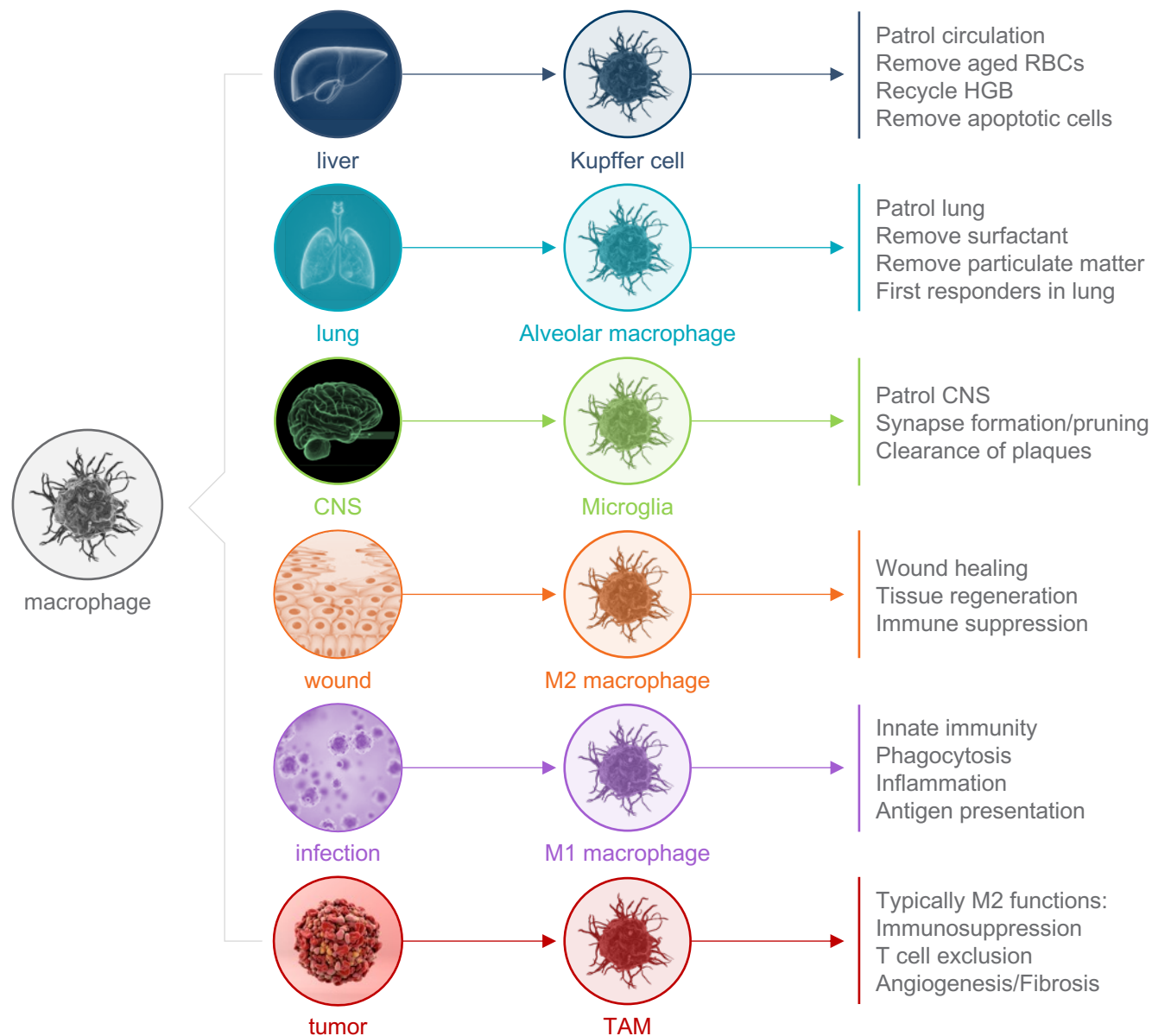


Macrophages: The Ultimate Multitasker

Macrophages are powerful immune cells that drive both innate and adaptive immunity

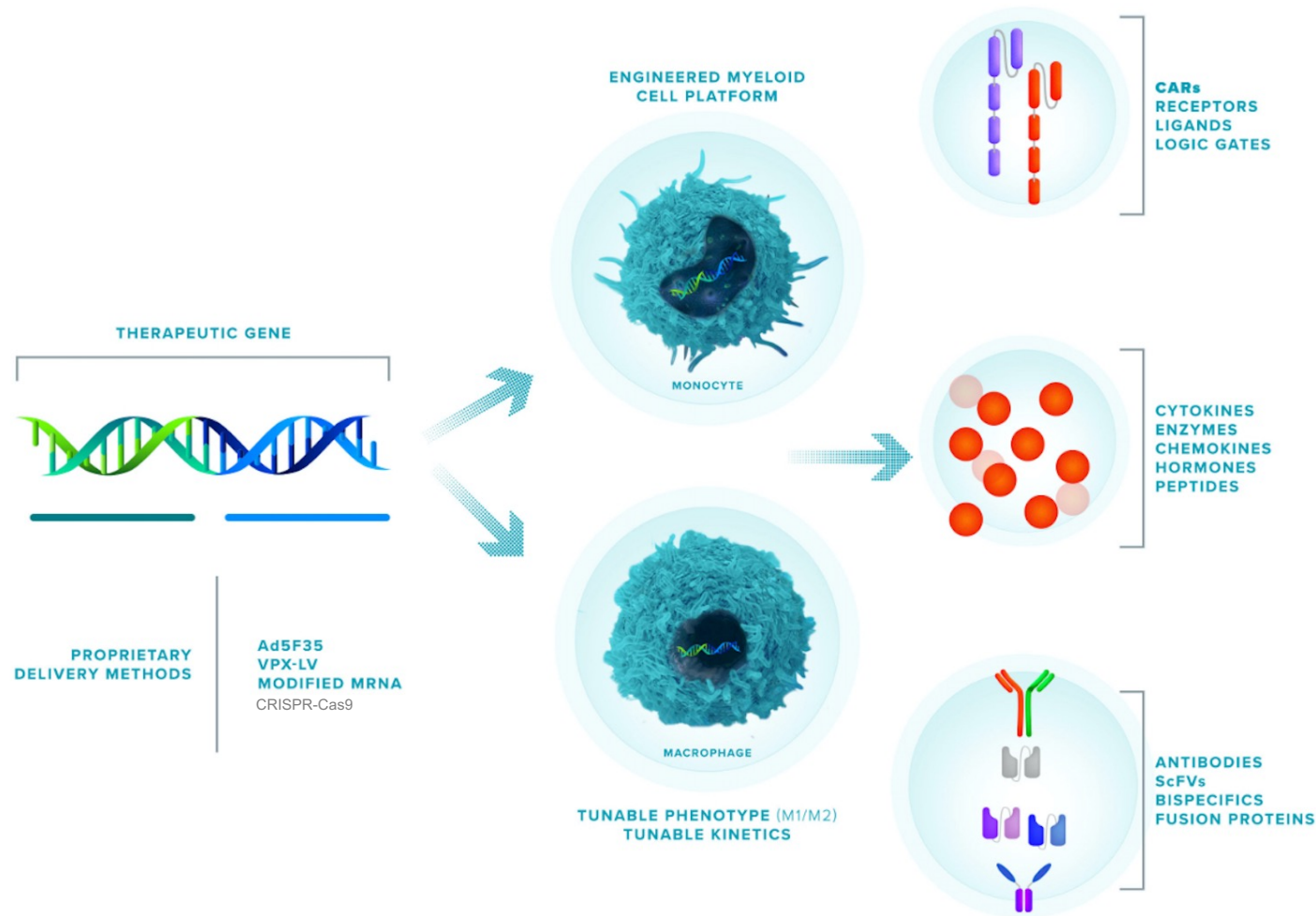
Macrophages can:

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



CARISMA's Broad Myeloid Cell Engineering Platform

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



Monocyte & Macrophage Engineering Capabilities:

- Proprietary platforms for durable macrophage engineering with Ad5f35¹ and Vpx-LV²
- Proprietary platform for transient macrophage engineering: Modified mRNA³
- Methods to control macrophage phenotype toward M1 & M2³
- Ability to deliver large/multiplexed payloads
- Efficient gene editing methods using CRISPR/Cas9³

Key Challenges for Cell Therapy Treatment of Solid Tumors

Incredible Progress in Cell Therapy...

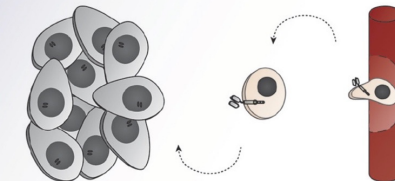
- CAR-T is revolutionizing treatment of hematological malignancies
- Three products now approved – Kymriah, Yescarta and Abecma

... But Challenges Remain in Solid Tumors

1

Lack of Trafficking to Tumors

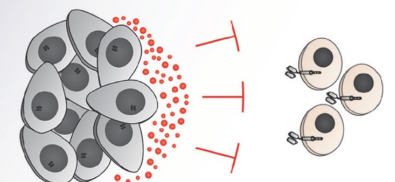
Need natural recruitment to tumors and metastatic sites



2

Suppressive TME

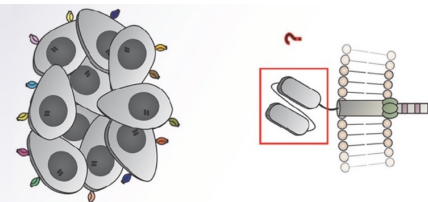
Need ability to induce a pro-inflammatory TME



3

Antigen Heterogeneity

Need ability to activate the immune system via antigen presentation



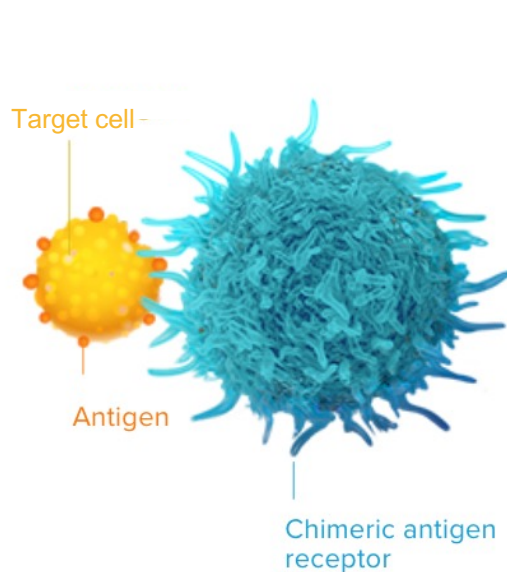


CAR-M's Multi-Factorial Attack on Cancer

Carisma's technology addresses the key challenges involved in treating solid tumors

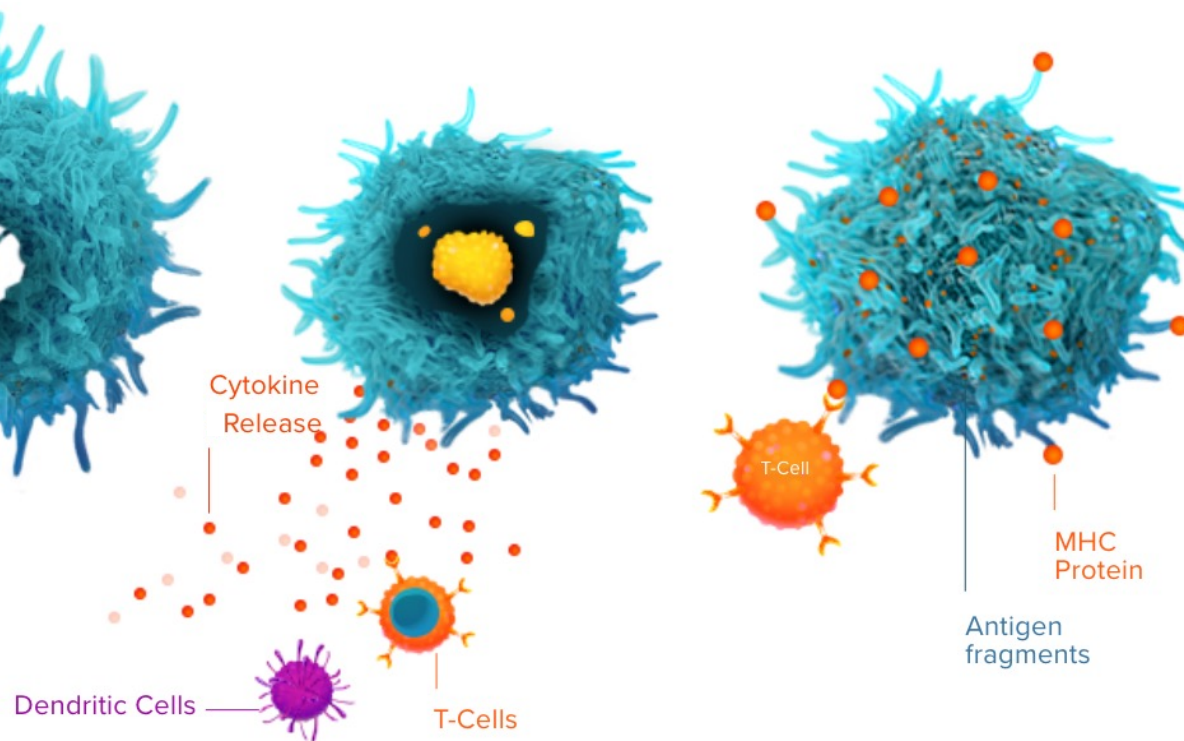
1

TRAFFICKING AND PHAGOCYTOSIS



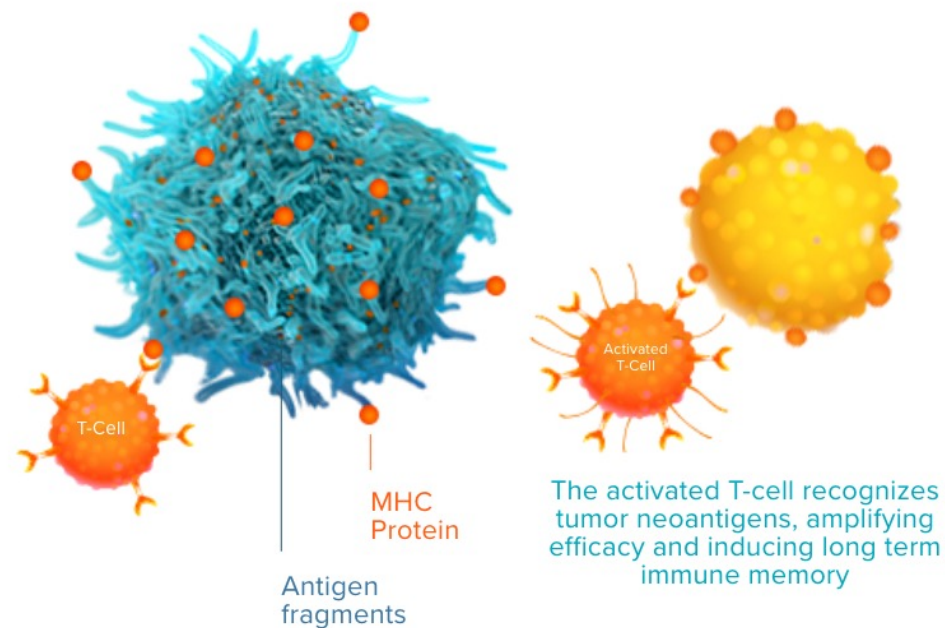
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IMMUNE ACTIVATION



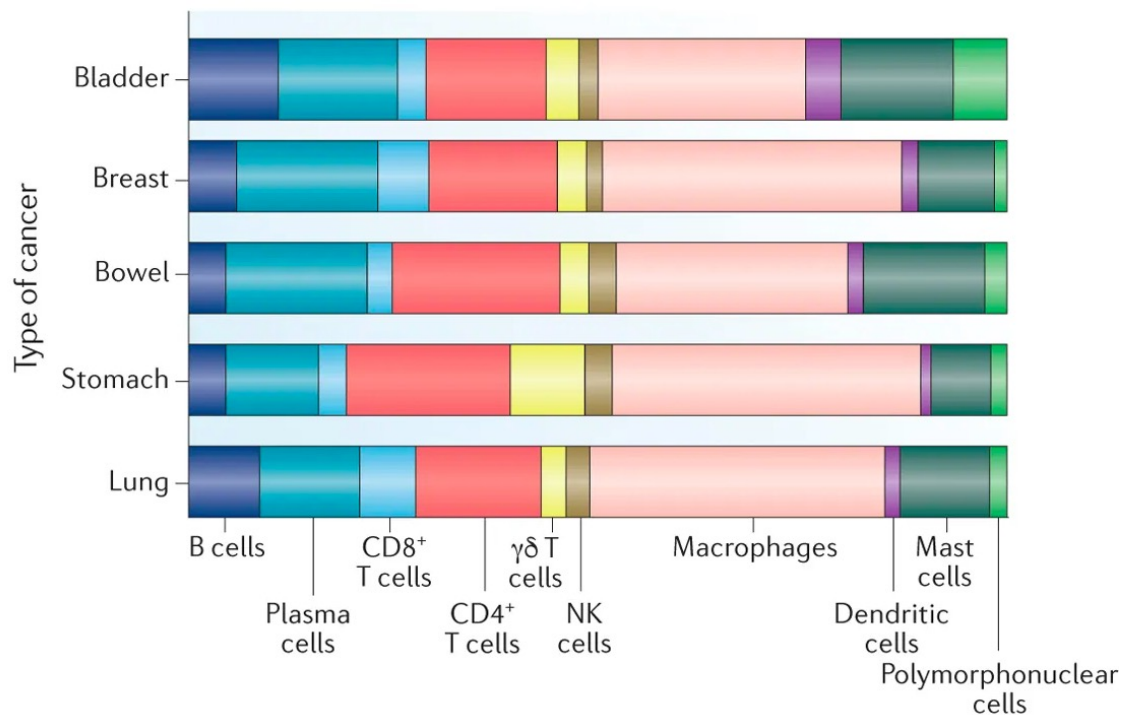
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ANTIGEN PRESENTATION



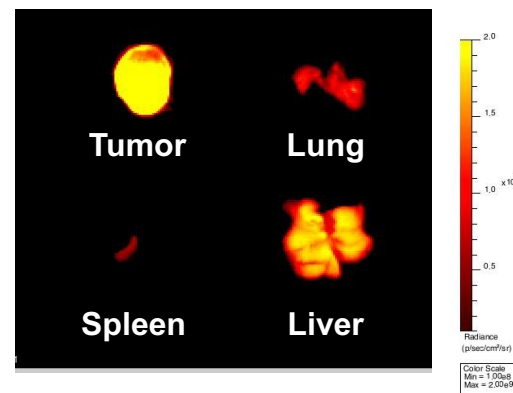
Monocytes & macrophages home to tumors

Myeloid cells are abundant in solid tumors



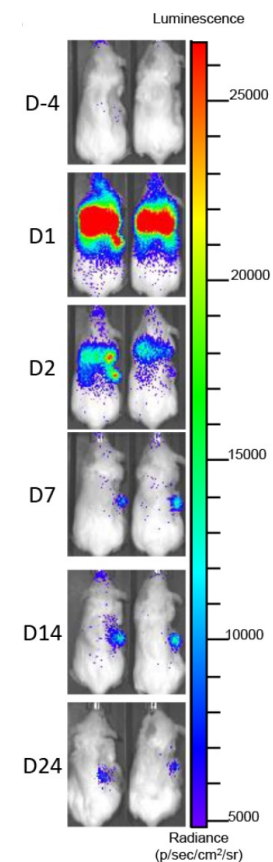
Pollard JW, et al. Nat Rev Drug Discov. 2019.

Adoptively transferred macrophages home to tumors



Biodistribution of IR-labeled human CAR-M (Gastric carcinoma xenograft model)

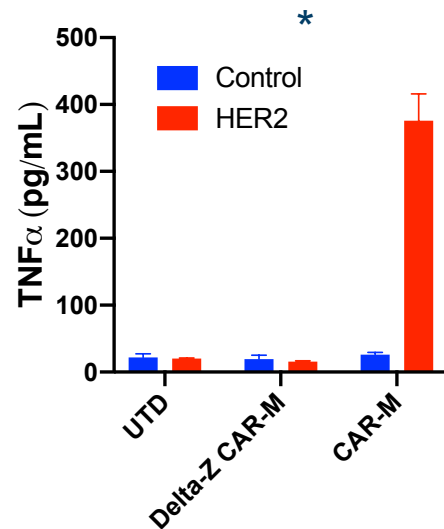
Klichinsky M, et al. 2020.



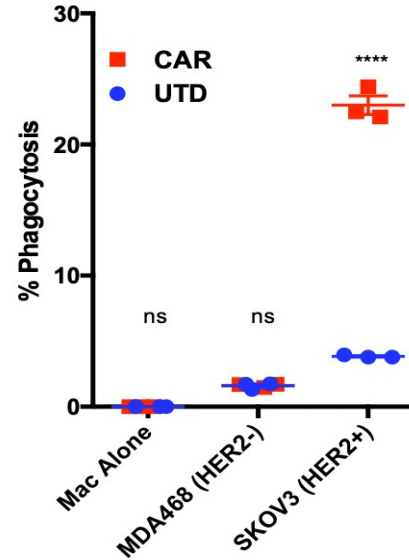
Brempeles K, et al. 2020.

Primary human CAR-M demonstrate broad anti-tumor activity

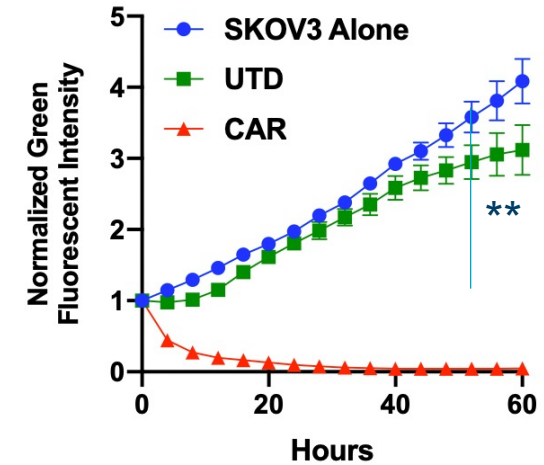
CAR-M Cytokine Production



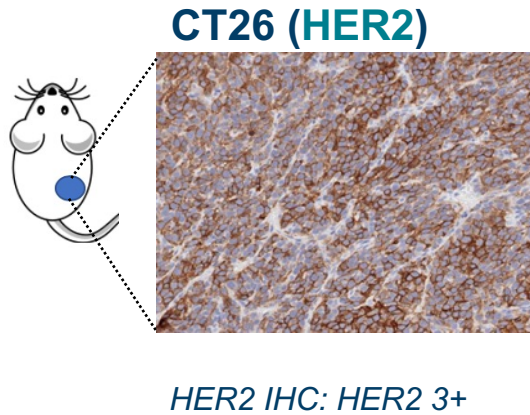
CAR-M Phagocytosis



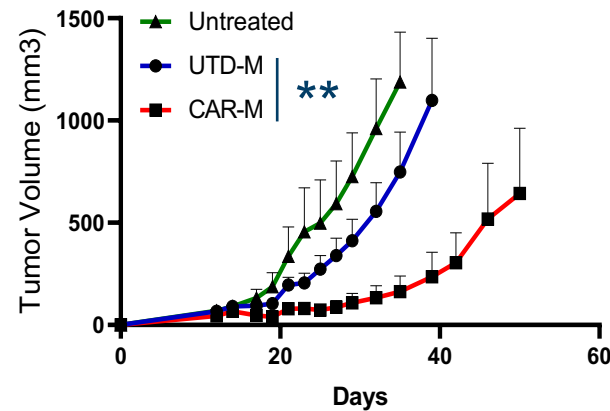
CAR-M Killing



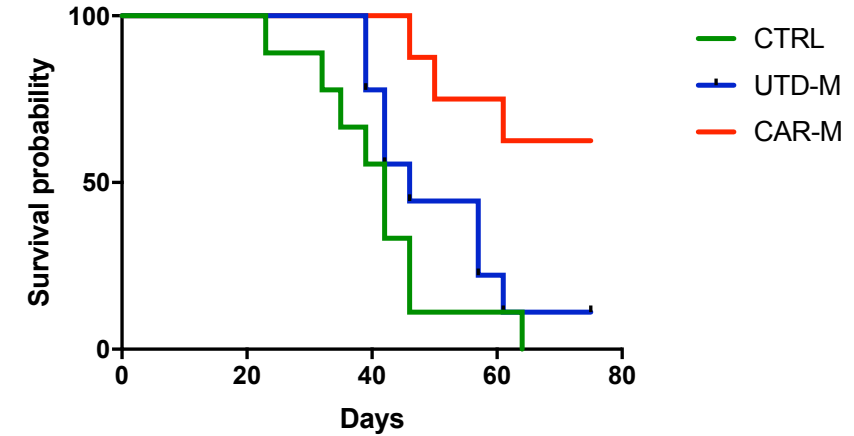
CAR-M shrink tumors, modulate the TME, and induce systemic T cell responses in immunocompetent models



Average tumor growth curves:

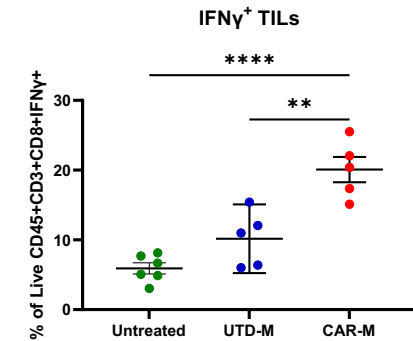
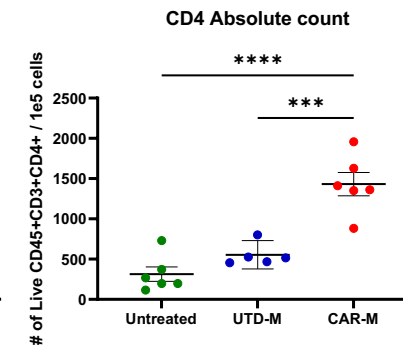
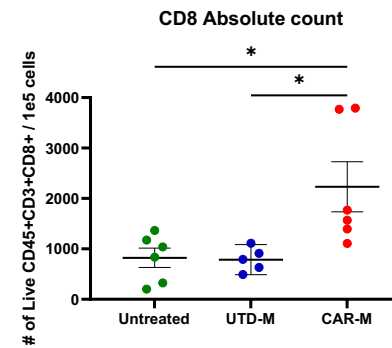
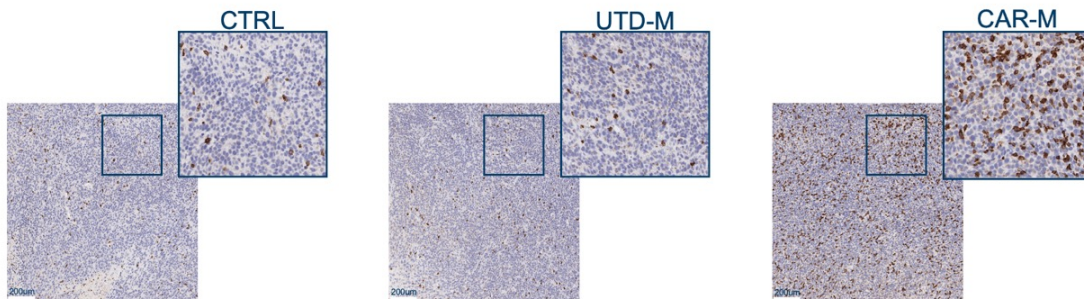


Kaplan Meier Survival Curve:



CAR-M modulate the TME – CD8+ T cell infiltration

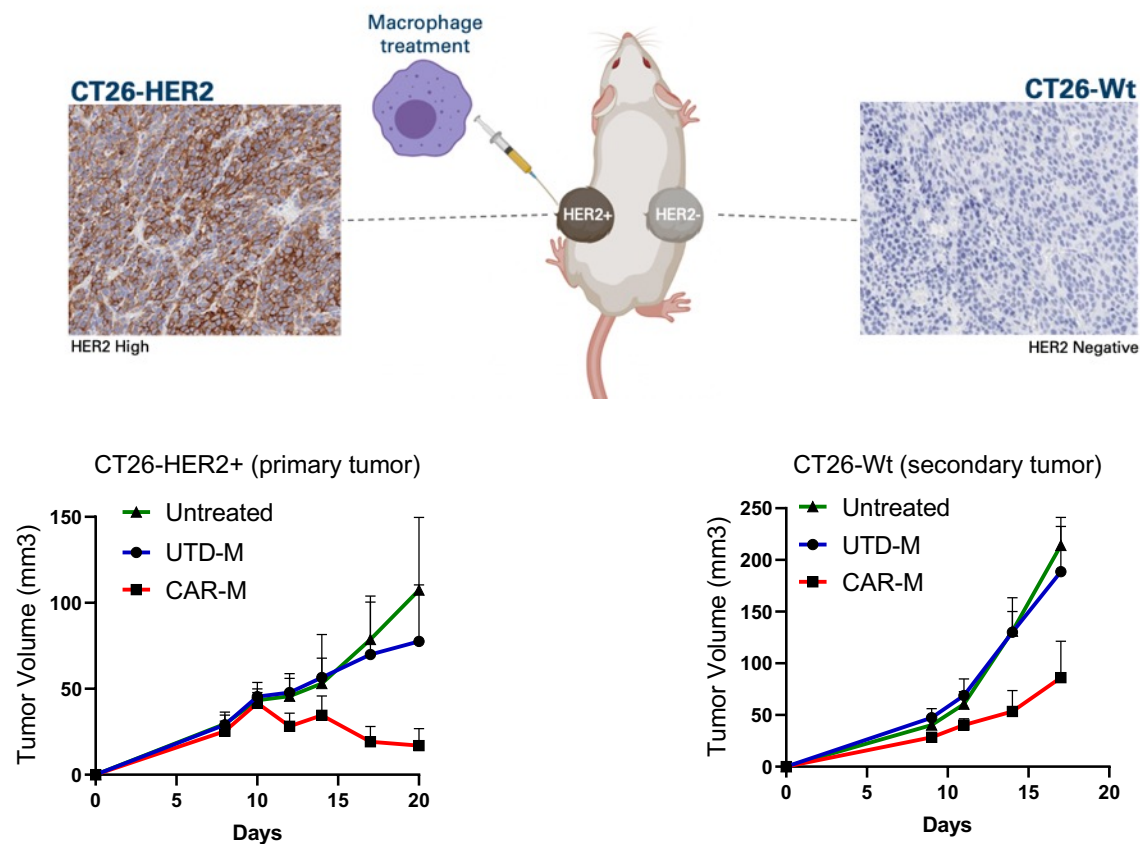
Representative CD8 IHC on CT26-HER2 tumor samples



CAR-M Lead to Epitope Spreading In Vivo

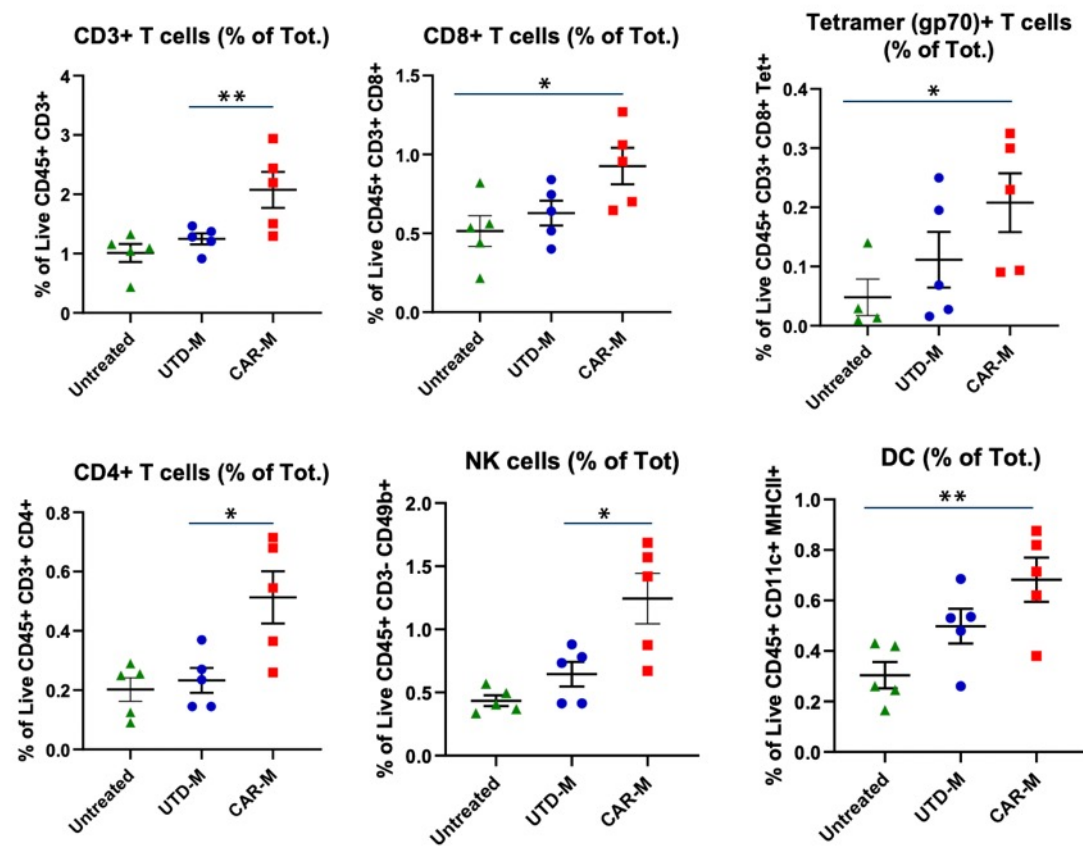
Anti-HER2 CAR-M shrink HER2+ tumors and reduce growth of HER2- tumors

CAR-M lead to an abscopal effect against HER2- tumors



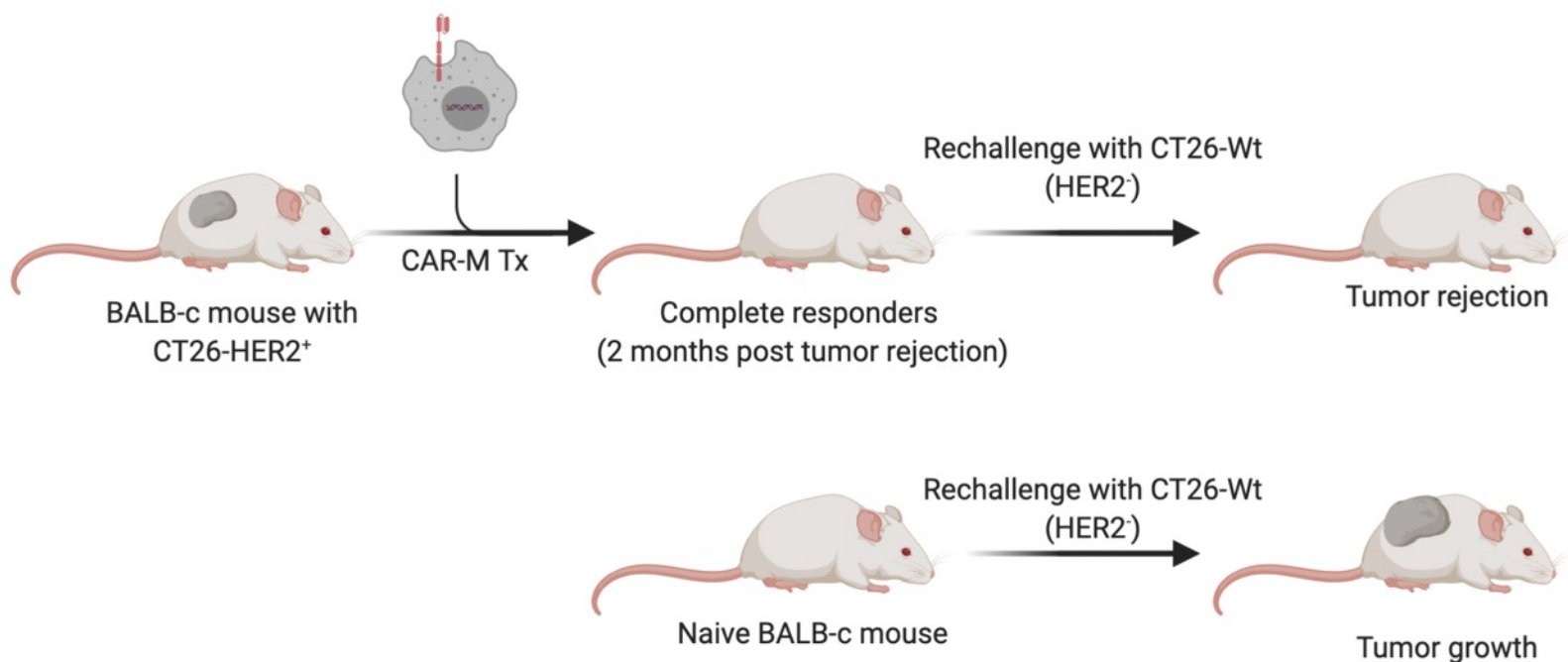
n=7-8 mice per group

Evaluation of the HER2- tumor TME (2 weeks post Tx)

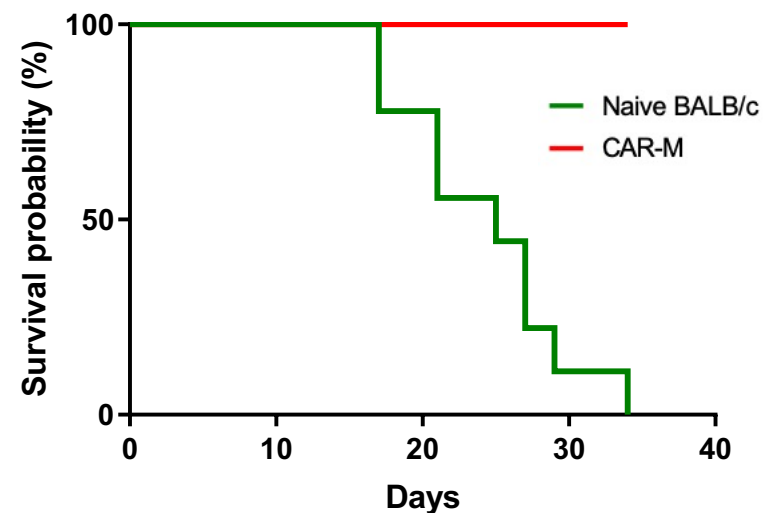


CAR-M Therapy Vaccinates Mice Against Tumor Recurrence and Prevents Antigen Negative Relapse

Mice that achieved CRs post anti-HER2 CAR-M therapy rejected HER2- tumors upon rechallenge 2 months later, demonstrating long term immune memory

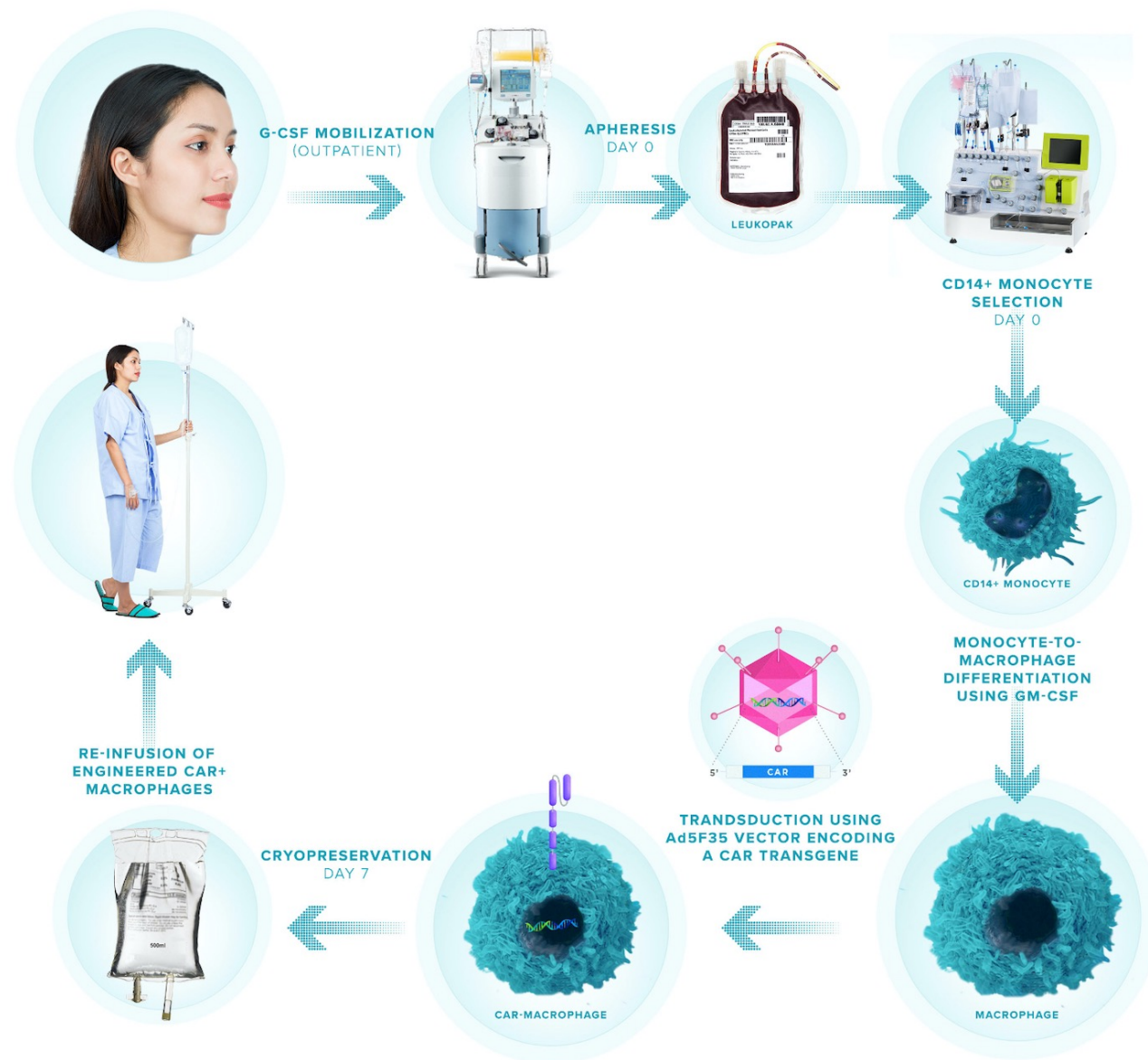


CT26 Wt (HER2-) rechallenge:
Kaplan Meier Survival Curve



CAR-M Manufacturing Process and Partners

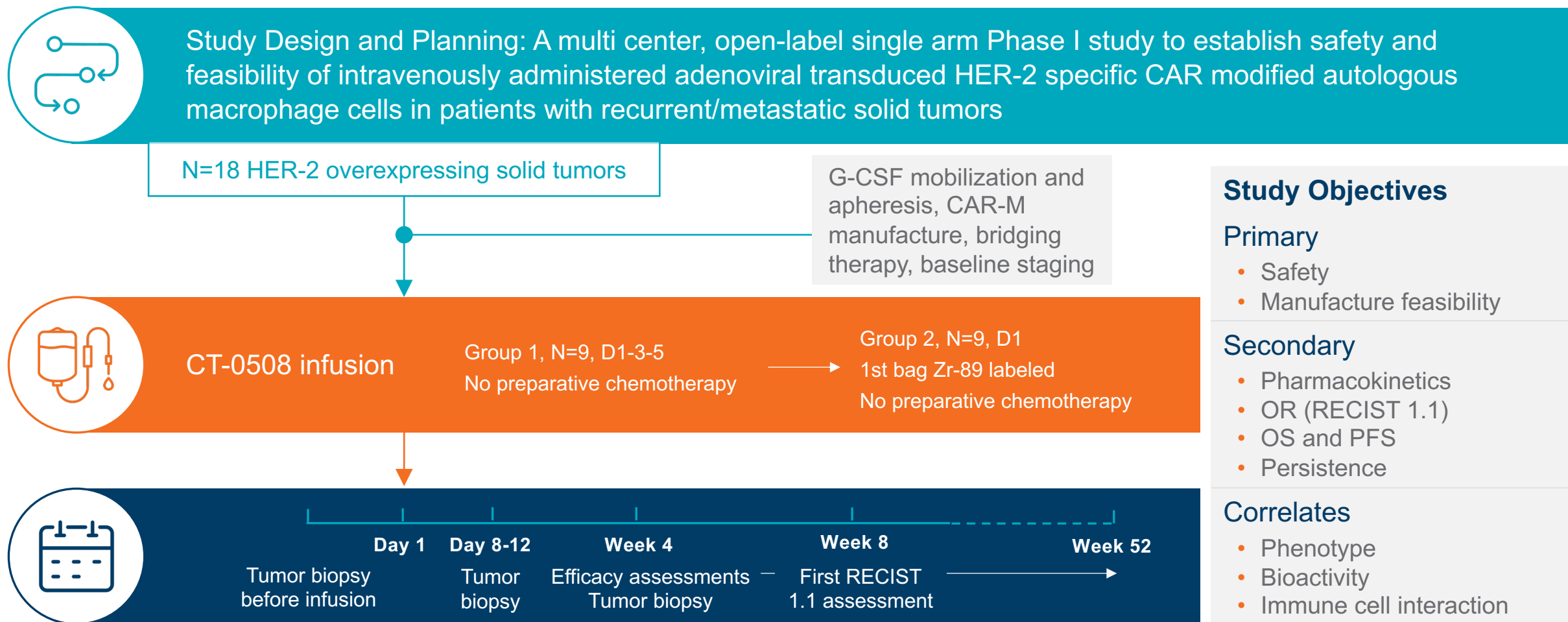
- **Source:** Autologous mobilized peripheral blood
- **Manufacturing time:** 7-days
- **Vein to vein:** 3 weeks
- **Vector:** Ad5f35
- **Process:** Partially automated
- **Fill format:** Cryopreserved 20mL bags



Powering the Engine of Next-Generation Cell Therapies

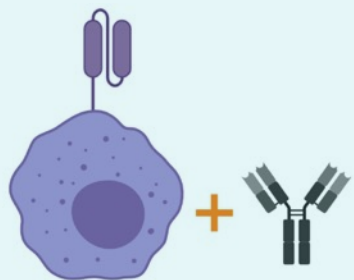
| Current Pipeline | Target | Indication | Route | Discovery | Preclinical | Phase I |
|---------------------|-------------|--------------------------------|----------|-----------|-------------|---------|
| CT-0508 | HER2 | Solid tumors | IV | | | |
| CT-0508 | HER2 | Intraperitoneal ovarian cancer | IP | | | |
| CT-0508 | HER2 | BC brain mets/primary gliomas | ICV | | | |
| CT-0508 + anti-PD1 | HER2 | Solid tumors | multiple | | | |
| CT-0508 + anti-CD47 | HER2 | Solid tumors | multiple | | | |
| CT – 1119 | Mesothelin | Solid tumors | multiple | | | |
| CT – 0729 | PSMA | mCRPC | IV | | | |
| R&D ENGINE | | | | | | |
| Heme malignancy | Undisclosed | | | | | |
| Liver Fibrosis | Undisclosed | | | | | |
| Neurodegeneration | Undisclosed | | | | | |

CT-0508 Phase I Clinical Design

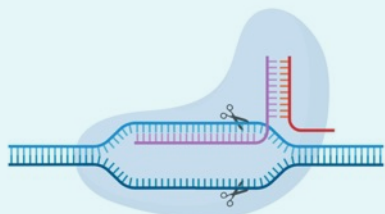


Robust Internal & External R&D Program Driving Platform Enhancements

Platform Enhancements



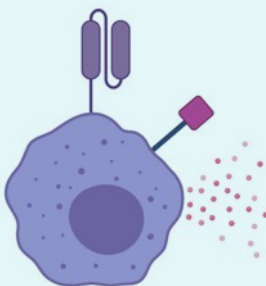
Combination
therapies



Gene edited
CAR-M



Novel CAR
designs

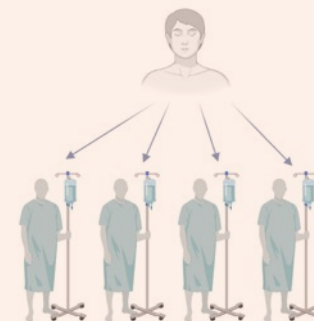


Multiplexed
engineering

Product Enhancements



CAR
Monocytes



Allogeneic
CAR-M



Corporate Summary

CARISMA is The Leader in Engineered Macrophage Technology with Broad Therapeutic Applications Including the Treatment of Solid Tumors



Proprietary Engineered Macrophage Platform



Emerging Pipeline of Oncology CAR-Ms



Established GMP Vein-to-vein Supply Chain



Experienced Leadership Team and Advisors



Multiple Value Catalysts over Next 12 Months

THANK YOU



carisma
THERAPEUTICS

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