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# The In Vivo Immune Cell Programming Company

Program any immune cell. Scale globally.

# CREATE Medicines: A New Paradigm for Improving Patient Outcomes

## Transforming immunotherapy through in vivo programming

**Direct in Vivo Programming** of immune cells inside the patient eliminates complex ex vivo manufacturing and reduced time to treatment.

**Multi-Cell Immune Engagement** activates and coordinates T cells, NK cells, and myeloid cells to generate a robust and durable anti-tumor response.

**Improved Patient Outcomes** result from a scalable, repeatable, and accessible approach, expanding treatment availability, lowering costs, and delivering meaningful clinical benefit.

**Broad Therapeutic Potential** derived from a versatile platform that can be applied across multiple tumor types and therapeutic areas, enhancing long-term growth and impact.

# Proven Platform. Focused Pipeline. Clear Path to Value

## Clinical Validation

- First therapy to reprogram immune cells inside the body using mRNA-LNPs
- **Tolerable repeat dosing** with proof of mechanism in multiple tumor types

## Versatile Platform

- Can program T cells, NK cells, and myeloid cells with **one flexible system**
- **Selective receptors and targeted LNPs** tailored for in vivo therapies

## Efficiency, Scale, Access

- Capital efficient product development: concept to clinic in **<12 months**
- Established GMP manufacturing (>3 yr stability) and regulatory precedent

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# Validated Mechanism, Safety, and Potency Driving Clinical Success

**Lessons from the first in vivo CAR programming of myeloid cells**

**40+ patients treated across two trials**

**Proven mechanism and safe dosing links to a high probability of success**

**Proven Delivery, Biology, and Safety**

| Attribute | Proven in Patients |
|---|---|
| Tolerable safety and repeat IV dosing | ✓ |
| Uptake by multiple immune cells | ✓ |
| CAR expression | ✓ |
| Immune cell tumor infiltration | ✓ |
| Antigen presentation | ✓ |
| Cytokine and chemokine release | ✓ |
| Switch toward proinflammatory TME | ✓ |
| Evidence of clinical activity | ✓ |

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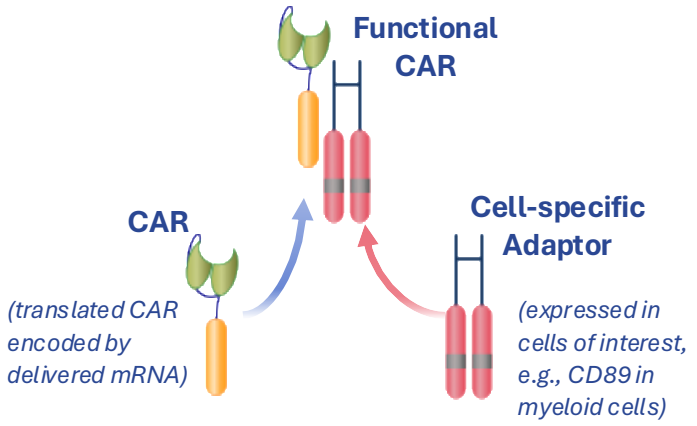
# Proprietary RNA and LNP Toolbox for Precise, Cell-Selective In Vivo Programming

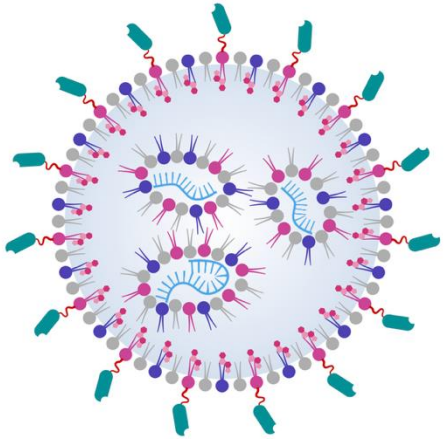
## Each RNA cargo is designed to express only in its target immune cell, ensuring precision and safety.

### Modular CARs Designed for Selective Immune Programming



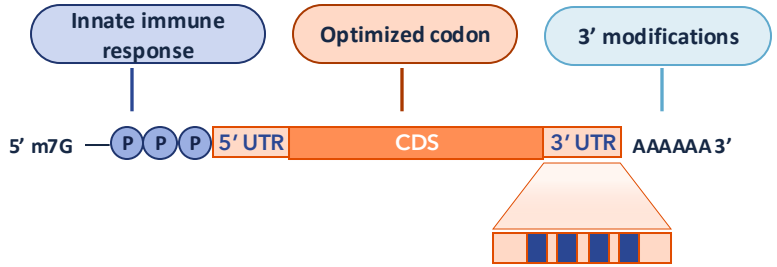

- Clinically validated CARs with precise, cell-selective expression
- Modular design programs only cells of interest
- Multiple CARs encoded in one product

### Targeted LNPs for Immune Cell Uptake



- Proprietary LNPs with targeted and pan-targeted delivery
- Immune cell uptake confirmed in patients
- Low systemic and liver toxicity

### RNA Optimized for Durable, Safe Expression




- Industry leading transient expression (>8 days)
- Minimal reactogenicity in patients
- Supports repeat dosing and durable immune activation
- Stably integrating retrotransposon

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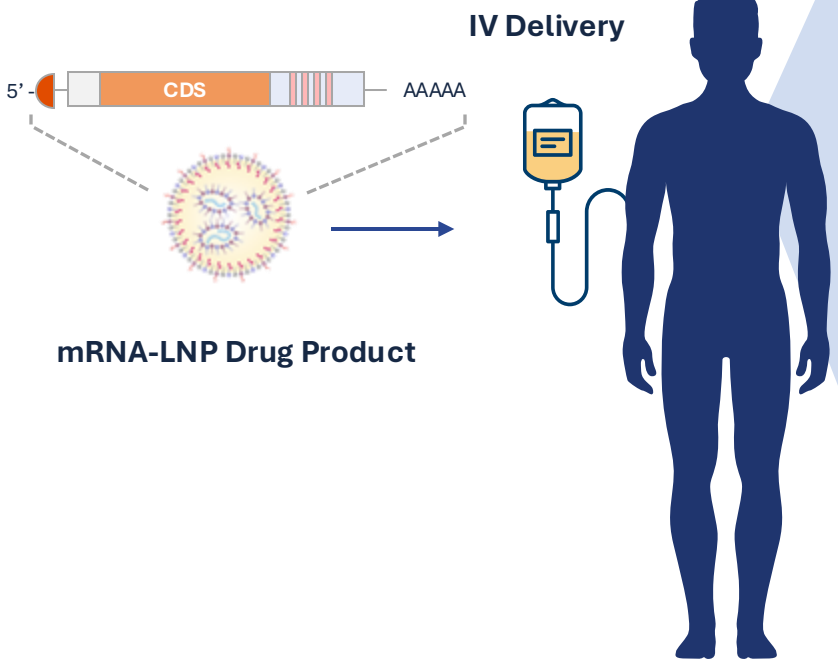
# Transforming Immunotherapy Through In Vivo CAR Programming

## T cells, NK cells, myeloid cells: programmed directly inside the body

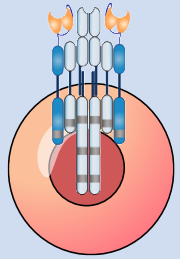
### Multi-Immune Programming in Action

### Clinically Proven mRNA-LNP Delivery

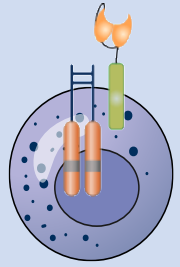
**Repeat dosing & off-the-shelf, no lymphodepletion**



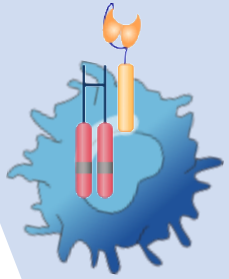

### In Vivo CARs



**T Cells**



**NK Cells**



**Myeloid Cells**

### Transforming outcomes across diseases

- Oncology
- Autoimmunity
- Fibrosis

# Robust Clinical Pipeline Across Multiple Indications

| PRODUCT | CELL TYPE(S) | INDICATION | PRECLINICAL | PHASE 1 | PHASE 2 | PHASE 3 |
|---|---|---|---|---|---|---|
| **Myeloid Cell Programming** | | | | | | |
| **MT-303 (GPC3)** | Myeloid Cells | HCC | | | | |
| **MT-302 (TROP2)** | Myeloid Cells | Frontline GEJ (IST) | | | | |
| **Multi-immune Cell Programming** | | | | | | |
| **MT-304 (HER2)** | NK and Myeloid Cells | Breast Cancer | | | | |
| **CRT-401 (HER2+TROP2)** | T, NK, and Myeloid Cells | Epithelial Tumors | | | | |
| **CRT-402 (CD19)** | T Cells | B Cell Depletion | | | | |

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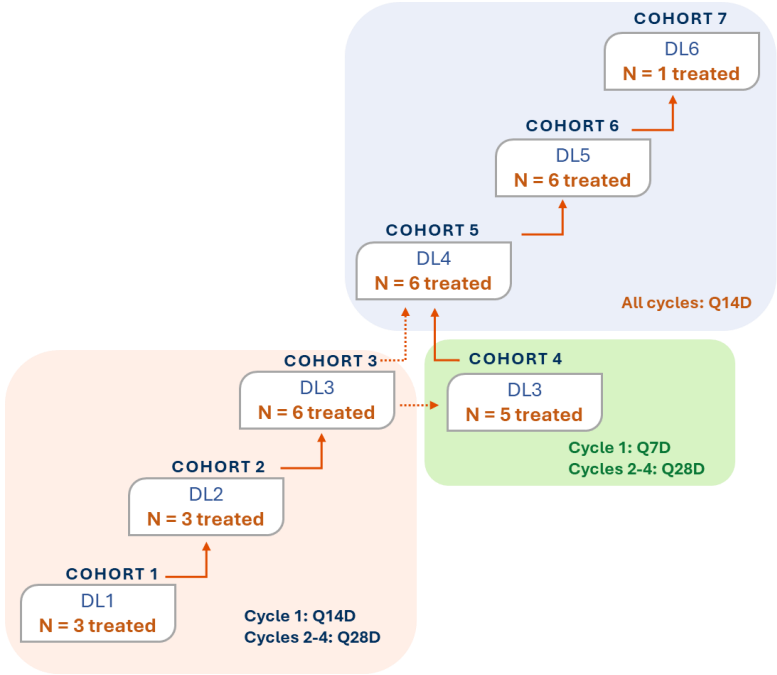
# MT-302: TROP2 Myeloid CAR, Phase 1/2 Clinical Trial

## Phase 1/2 Program

- 30 patients treated, 7 dose cohorts, 12 heterogenous solid tumor sub-types
- High baseline tumor burden, numerous prior metastatic therapies
- Clinical and biological activity observed across dose levels

## Dose Escalation Design




**Clinical data readout at SITC**

**BOIN dose escalation to evaluate safety, pharmacodynamics, and early biologic activity**

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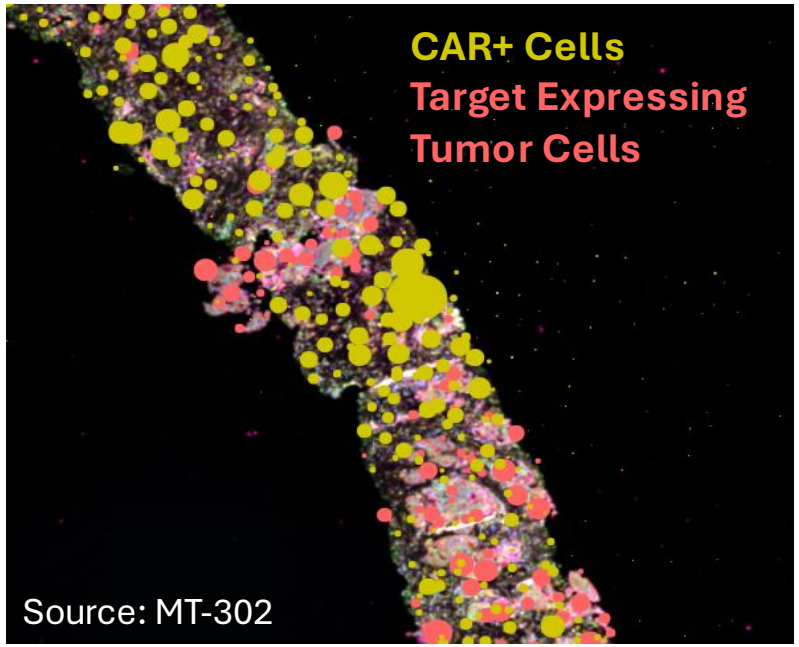
# Demonstrated Proof of Mechanism in Humans

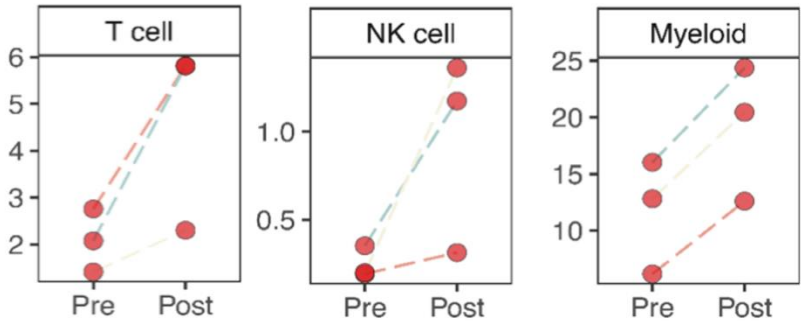
## In Vivo CAR expression and immune activation in cold tumors

### CAR Expression in Targeted Cells




- CAR+ myeloid cells infiltrate tumors and attack tumors.

### Immune Activation




Source: MT-302

- Immune activation observed across T cells, NK cells, and myeloid compartments
- Repeat dosing tolerated with sustained CAR expression
- Established foundation for next-line and combinational studies

**Tumor penetration and immune activation validate the CREATE platform mechanism in patients**

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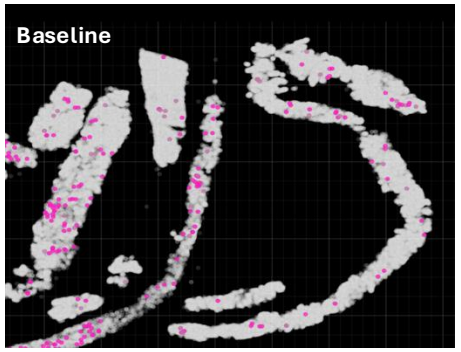
# Translating Early Insights to Durable Reponses

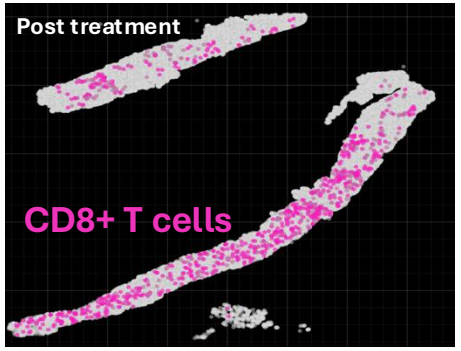
## Immune infiltration and checkpoint expression reveal opportunity to enhance responses

### T Cell Infiltration

Before: few T cells in tumor

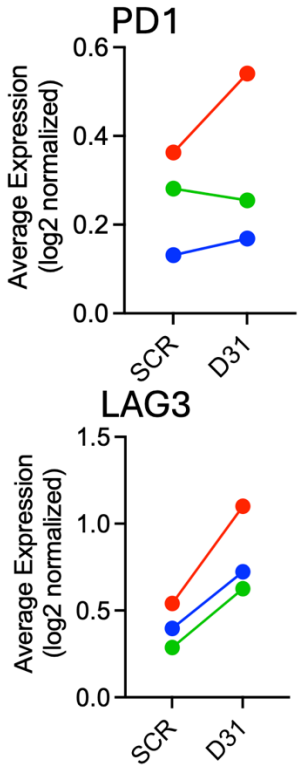



After: CD8+ T cells move into tumor




### Checkpoint Expression

Rising Checkpoint Expression Shows Active Tumor-Immune Engagement:




- **T cell infiltration** and **checkpoint upregulation** confirm tumor engagement
- **Checkpoint induction** may have limited activity in refractory patients
- **Combination with checkpoint inhibitors** expected to restore T cell function and amplify response

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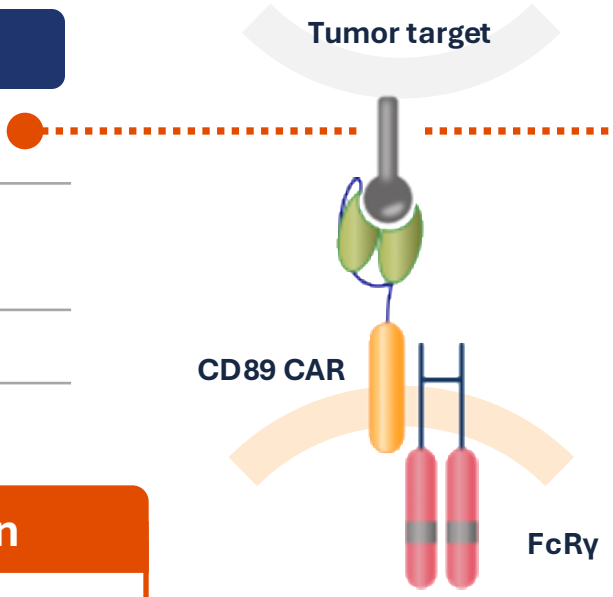
# Advancing 302 and 303 into Frontline Settings

## Ph1 results establish mechanism and safety; translational findings define next-phase combinations

### MT-302: GEJ IST

| | |
|---|---|
| **M8 Incidence:** | ~40,000/yr |
| **Advanced 5 Yr Survival:** | 16% |
| **Current Response Rate:** | **1L: 58%**<br>2L: 28% |




### MT-303: HCC

| | |
|---|---|
| **M8 Incidence:** | ~290,000/yr |
| **Advanced 5 Yr Survival:** | 3% |
| **Current Response Rate:** | **1L: 30%**<br>2L: 18% |

### Phase 2 IST Frontline Regimen


**$2.5B+ Market Opportunity**

### Phase 1/2 Frontline Regimen


**$3.2B+ Market Opportunity**

**Earlier-line patients and checkpoint combinations build on immune activation demonstrated in phase 1**

M8: US, France, Germany, Italy, Spain, UK, Japan, China

# Proven myeloid programming provides a pathway to better survival and outcomes in large, underserved patient groups

# Proven Myeloid Programming Sets the Foundation for Multi-Immune Approach

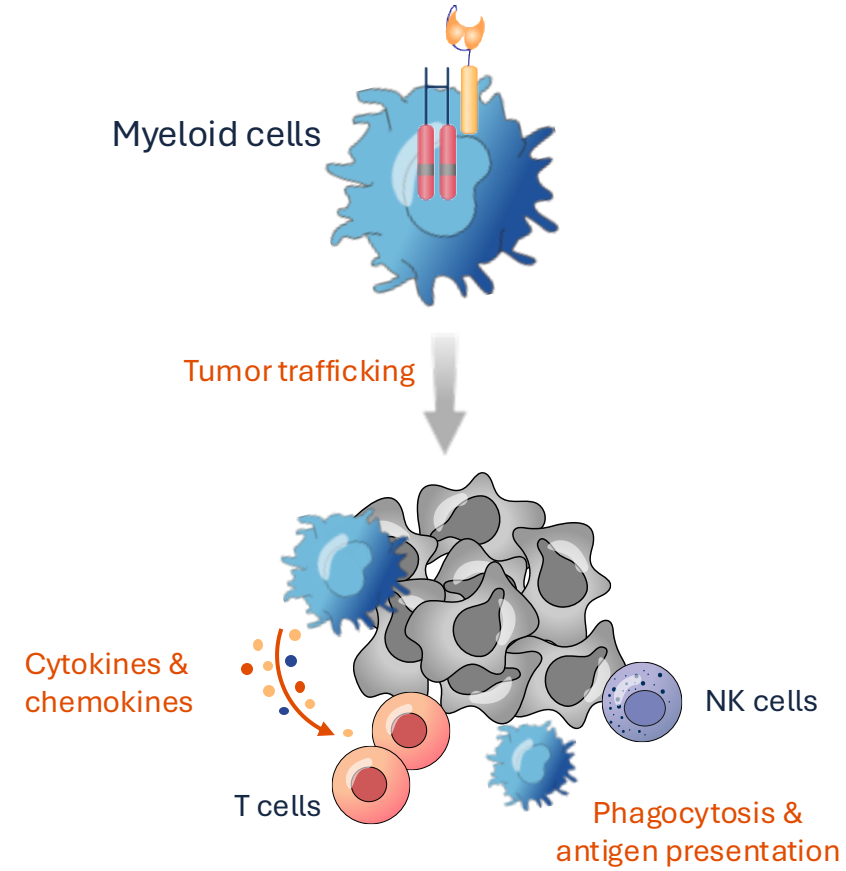
**MT-302 and MT-303 showed that myeloid cells:**

- ✓ **Mechanistic proof in patients**
- ✓ **Present a tolerable safety profile with repeat dosing**
- ✓ **Show durable CAR expression in patient immune cells**
- ✓ **Induce proinflammatory tumor immune activation**
- ✓ **Enable direct mRNA CAR delivery to primary immune cells**

**Our myeloid approach laid the foundation**

Now we are advancing **multi-immune cell programming** for deeper, more durable responses

**Myeloid Cell Programming**

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# Next Step: Multi-Immune Cell Activation

**Expanding to engage T cells and NK cells for deeper, more durable responses in oncology and autoimmunity**

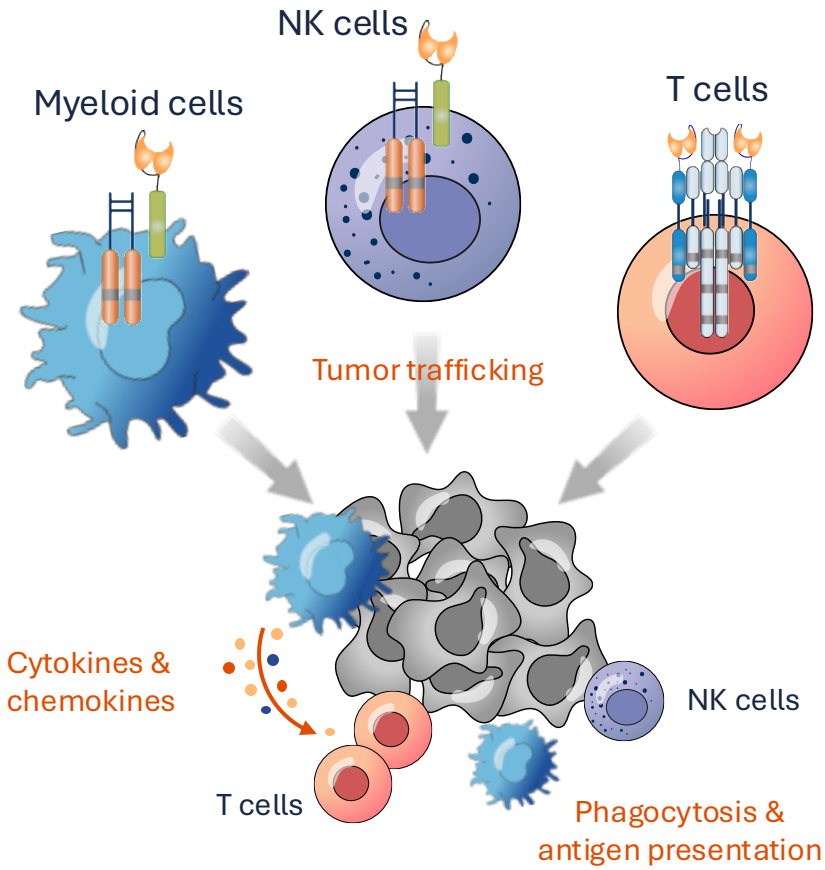
## Adding T and NK cells to our proven platform will:

- ✓ **Synergize with programmed myeloid cells**
- ✓ **Enhance direct anti-tumor activity**
- ✓ **Overcome resistance mechanisms for durable responses**
- ✓ **Leverage science to expand into heme and autoimmunity**

## New pipeline candidates advancing this vision

- MT-304 first new class of multi-immune CAR therapy
- CRT-401 and CRT-402 integrate CAR-T into the pipeline in solid tumors, hematological malignancies, and autoimmune

## Multi-Immune Cell Programming

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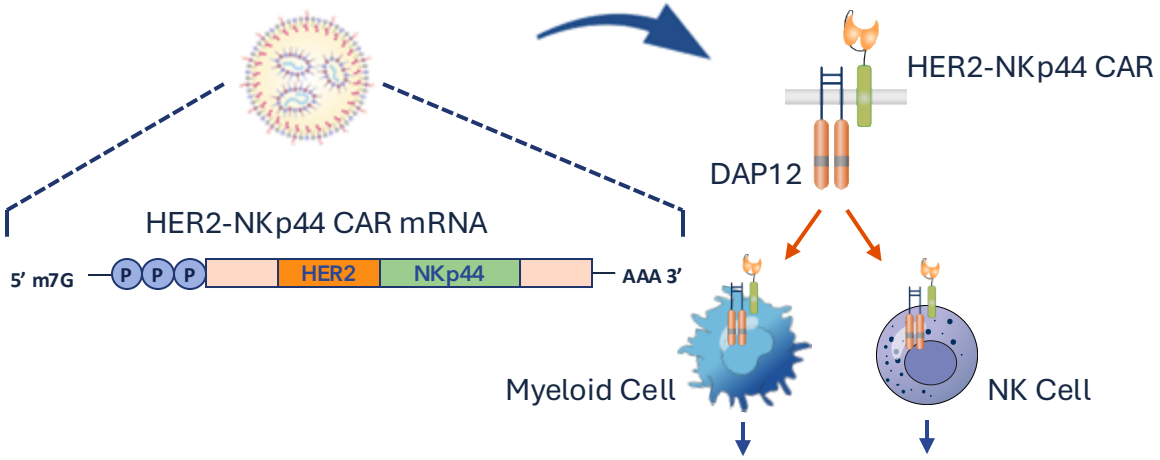
# MT-304: First Clinical Candidate From CREATE'S Multi-Immune Platform

## HER2-NKp44 CAR extends validated myeloid programming to NK cell engagement for enhanced cytotoxicity

### NKp44 CAR Design

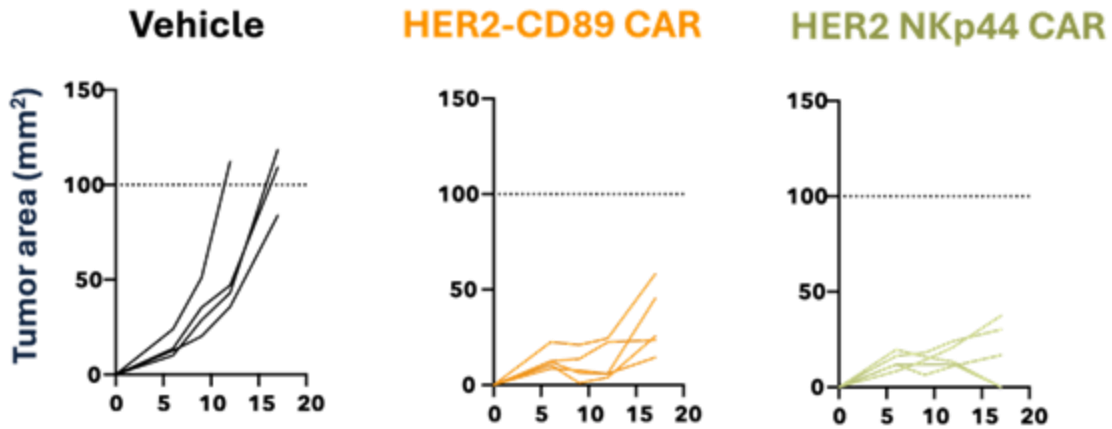
- DAP12 ensures **cell-specific activity**
- **Stronger immune cytotoxicity**
- Myeloid programming to co-ordinates innate and adaptive immune killing




**Stronger anti-tumor activity**

### Preclinical Data Demonstrate Superior Efficacy

- **Greater activity** than CD89-based CAR in HER2 tumor models
- **Tumor regressions** observed in models refractory to CAR-T and checkpoint inhibitors
- Establishes **MT-304 as first-in-class dual-cell therapeutic** with enhanced cytotoxic potency



# MT-304 Phase 1/2 Clinical Trial: Translating Multi-Immune Programming into Patients

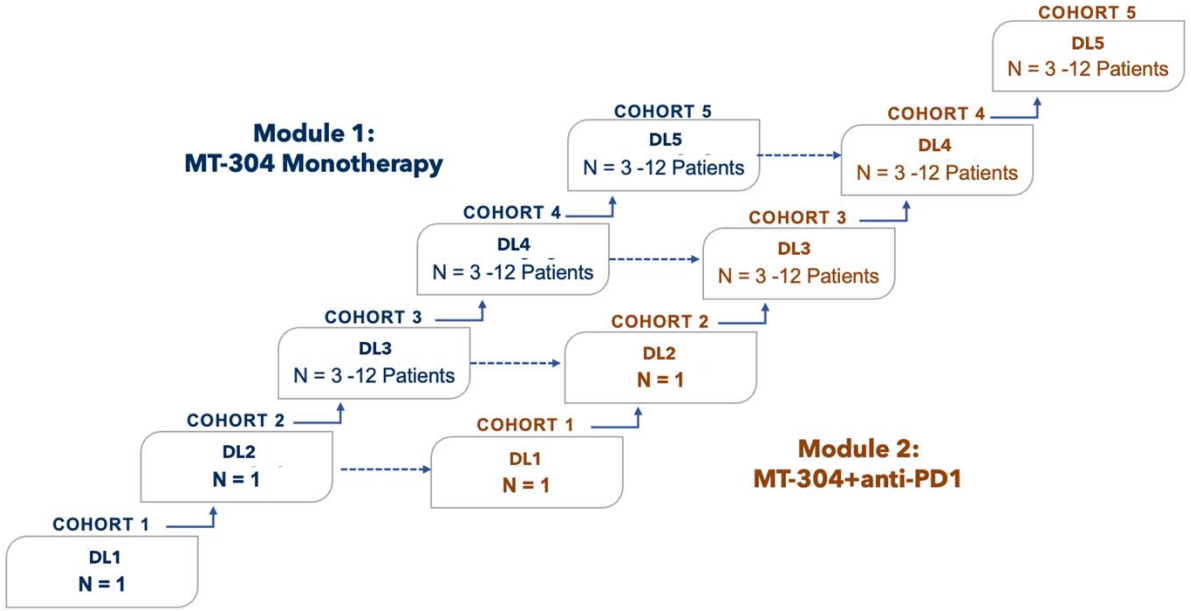
**First-in-human study evaluating safety, repeat dosing, and activity: monotherapy and checkpoint combination**

## Phase 1/2 Program

### Overview

- Basket study of pretreated solid tumors expressing HER2
- Standard safety, efficacy endpoints
- Evaluating activity as a monotherapy and in combination with anti-PD1

## Dose Escalation Design




**First Patient Expected Q4 2025**

**Goal for MT-304 to Increase Response Rates without Sacrificing Tolerability**

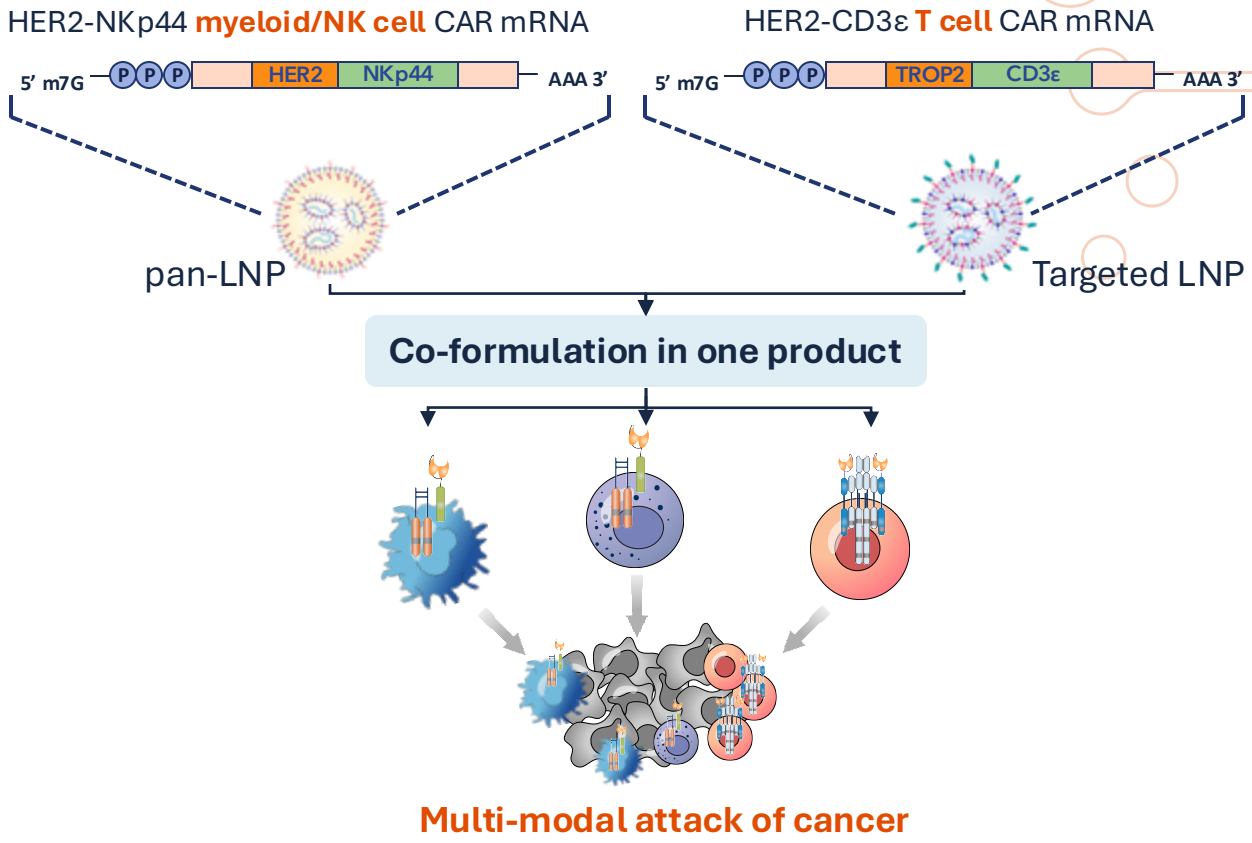
**Our next step is to incorporate T-cell engagement, completing the multi-immune circuit for deeper, more durable responses.**

# CRT-401: Completing the Multi-Immune Network with T cell Programming

## Combining the innate power of myeloid and NK cells with the precision and persistence of T cells

**Superior in vivo product, tailored for solid tumors**

- Builds on MT-304's validated HER2 immune framework
- Adds **targeted T cell programming** for direct cytotoxicity and durable immune memory
- **Targeted LNP enhances RNA uptake** in T cells while preserving myeloid and NK delivery
- Delivers **multi-modal attack** on tumors by coordinating innate and adaptive immune responses




**CRT-401 is the first product to integrate myeloid, NK, and T-cell programming, enabling a unified immune assault on solid tumors.**

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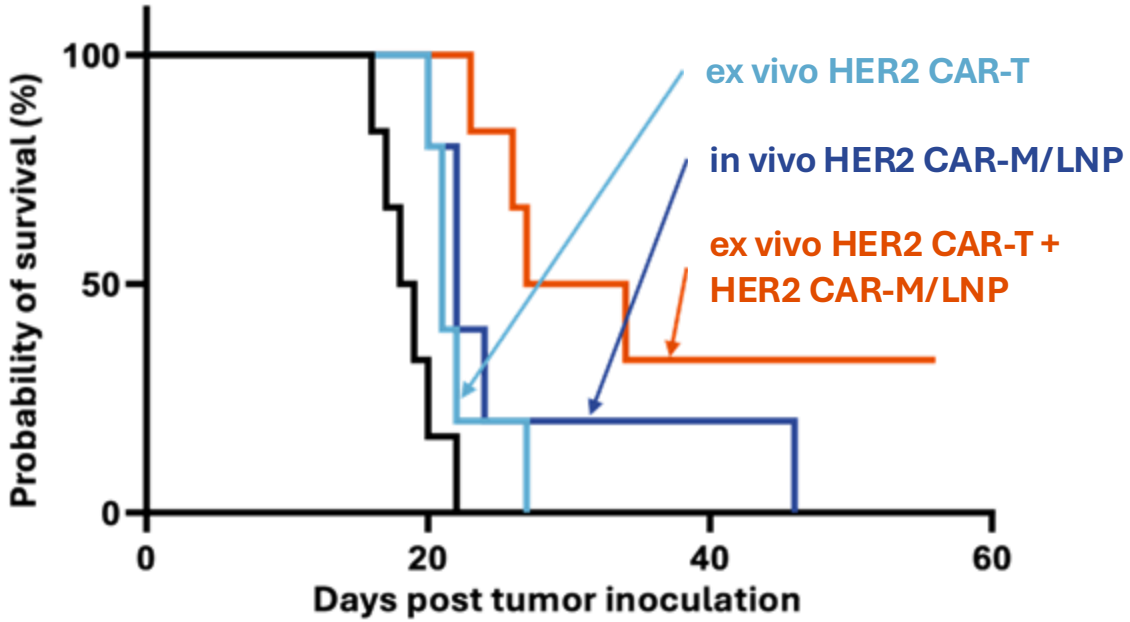
# CAR-Engineered Myeloid Cells Solve Limitations of CAR-T Cells

**Multi-immune programming overcomes the limitations of ex vivo CAR-T and delivers curative potential.**

## In vivo engineered myeloid cells provide survival benefit in combination with ex vivo CAR-T

- Ex vivo HER2 CAR-T monotherapy yields limited benefit
- In vivo myeloid CAR-LNP drives strong innate immune activation
- Combining in vivo CAR-M with CAR-T produces **complete, durable tumor regression**
- Provides mechanistic foundation for next-generation **multi-immune therapeutics (MT-304 → CRT-401)**

**hHER2 tg mouse solid tumor model**




**Preclinical synergy validates CREATE's multi-immune programming approach for durable tumor clearance.**

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# Extending CREATE's RNA Platform Beyond Solid Tumors

## One RNA Platform — Dual Capability

Transient CAR expression for B cell depletion in autoimmunity

Stable CAR integration for durable B cell malignancy depletion

# CREATE's mRNA-LNP Innovation Improves In Vivo B cell Depletion, Validated in Humans

## Human data confirm clinical potential of in vivo CAR-T therapies

### Validation in Oncology

- Lentivirus- EsoBiotech
- Shenzen, China September 18th 2025

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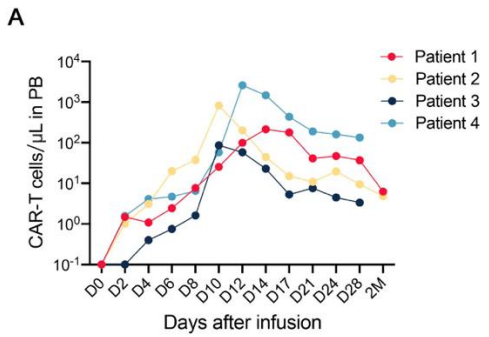
In-vivo B-cell maturation antigen CAR T-cell therapy for relapsed or refractory multiple myeloma

Jia Xu [a] · Lin Liu [a] · Philippe Parone [b] · Wei Xie [a] · Chunyan Sun [a] · Zhaozhao Chen [a] · et al. Show more

Affiliations & Notes Article Info




### CD19 CAR-T in Autoimmunity

- mRNA- CD8 targeted tLNP
- Wuhan, China September 18th 2025

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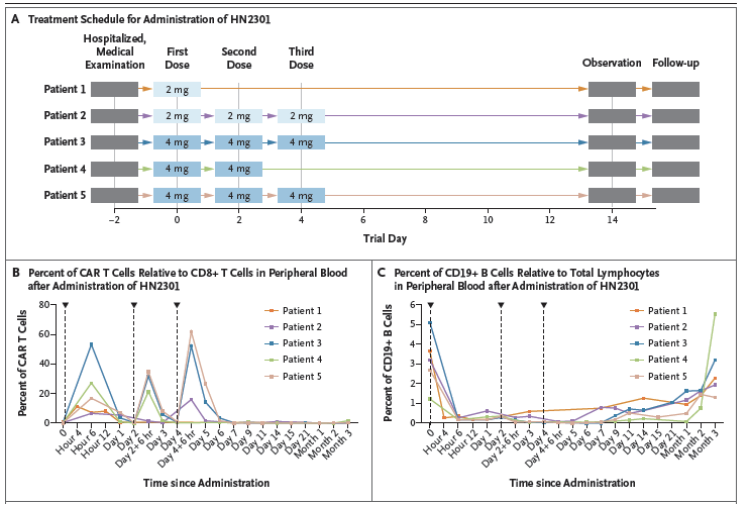
In Vivo CD19 CAR T-Cell Therapy for Refractory Systemic Lupus Erythematosus




**CREATE is advancing a clinically validated concept with a safer, more scalable RNA–LNP platform that enables transient or stable B-cell depletion as needed.**

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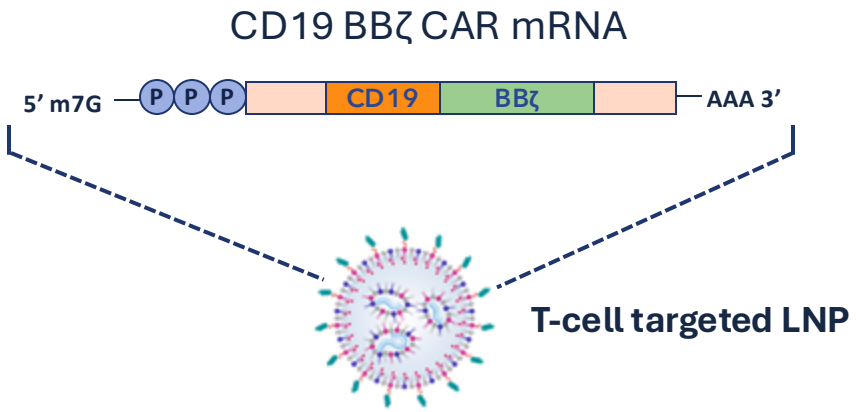
# CRT-402: Dual RNA System for Precise In Vivo CAR-T Control

## Targeting CD19 for hematologic malignancies and autoimmunity with transient or stable in vivo CAR-T

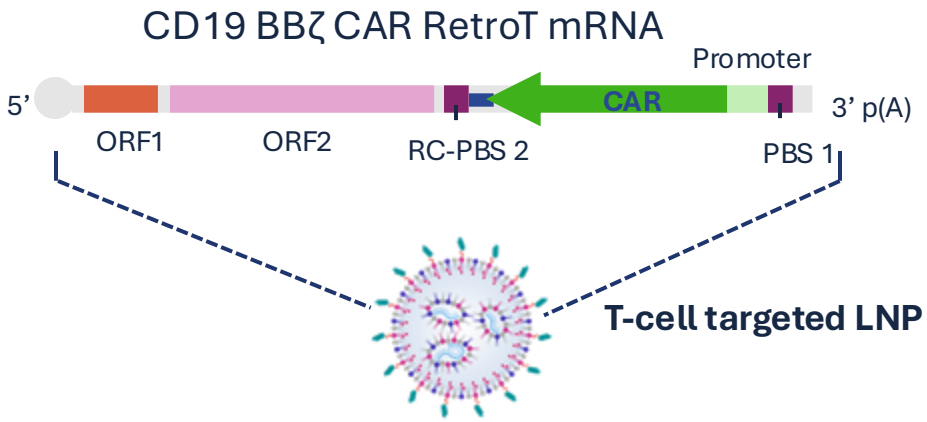
### Transient In Vivo T Cell Programming




- Delivers **episomal CD19 CAR mRNA** directly to T cells via targeted LNPs
- Enables **repeat dosing** for controlled and reversible CAR expression
- Designed for **temporary B-cell depletion** in autoimmune disease

**Transient mRNA: reversible, tunable, redosable**

### Stable Integration via All-RNA RetroT System




- Utilizes CREATE's **fully human RetroT** mechanism for CAR gene integration
- Achieves **permanent CAR expression** directly within T cell genome
- Enables **durable B-cell clearance** in hematologic malignancies

**Genomic integration of CD19 CAR: stable, precise, and long-lasting**

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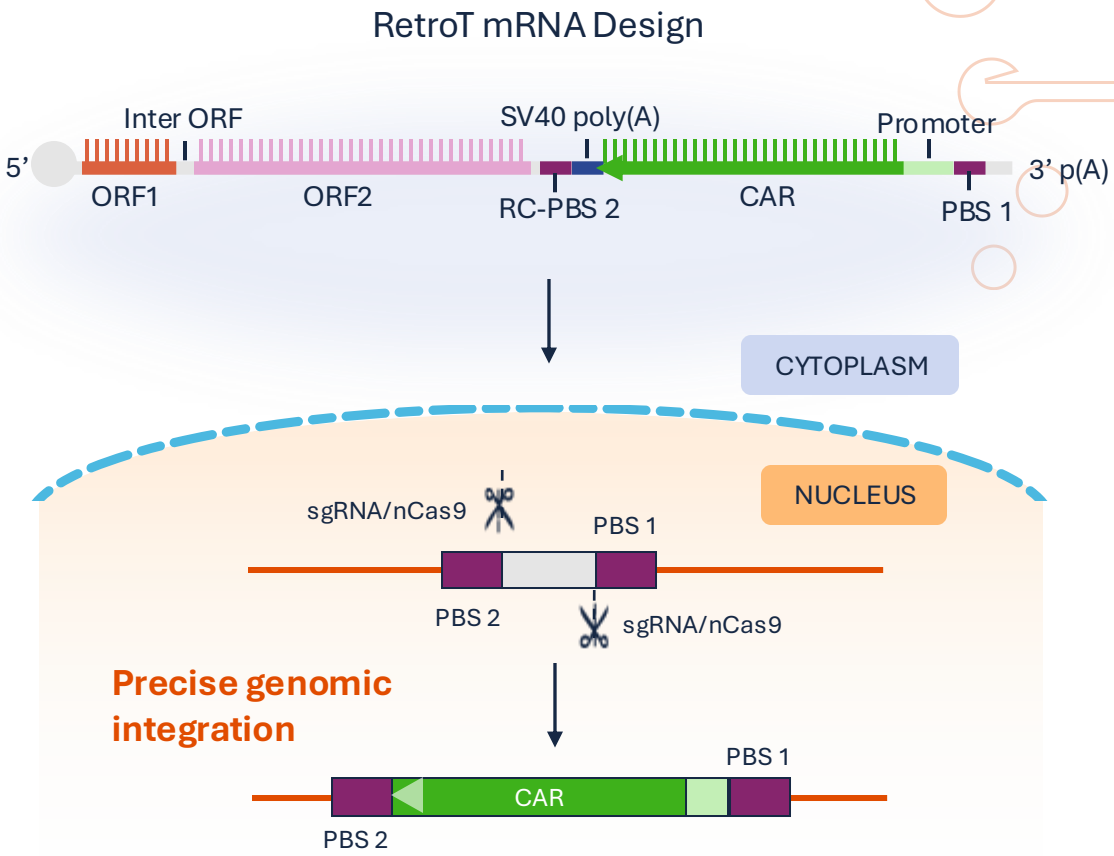
# CREATE RetroT: Precise RNA Integration Enabling Stable In Vivo CAR-T Programming

- **All RNA integration system**
  - **Fully RNA based:** No DNA templates or viral vectors
  - Leverages CREATE's RetroT mechanism for **direct CAR integration** into the T cell genome
- **Integration efficiency**
- **Precision safety**
  - **Controlled, biallelic integration observed** – no evidence of partial or off-target insertions
  - Maintains normal T cell viability and proliferation
- **Functional Validation**
  - RetroT-integrated CART cells show **robust, specific CD19+ tumor killing**
  - Engineered CART secrete effector cytokines (GM-CSG, IFN-γ) upon tumor engagement




**RetroT delivers safe, efficient, and precise RNA integration, unlocking stable in vivo CAR-T therapy for the first time.**

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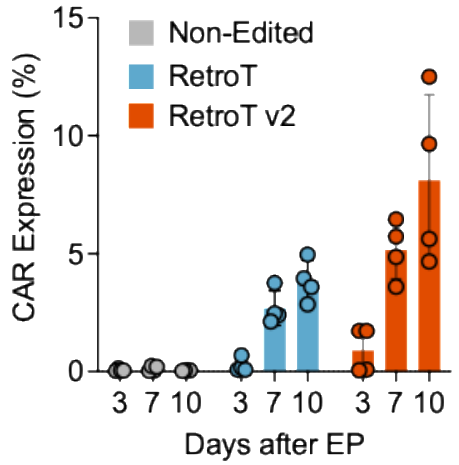
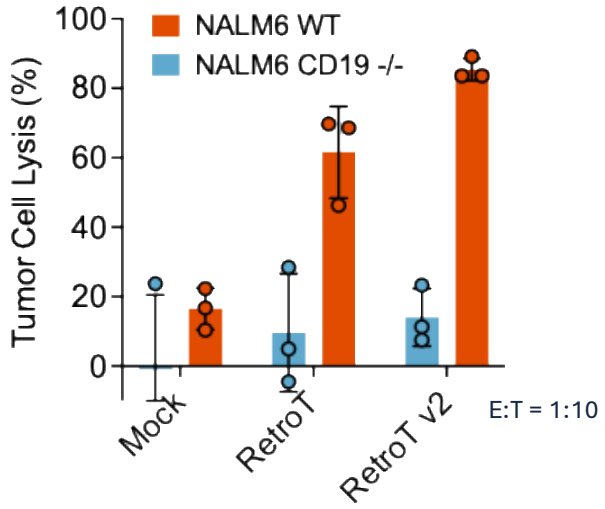
# RetroT-integrated CD19 CAR-T Cells Demonstrate Potent, Precise and Durable Function

## Editing Efficiency



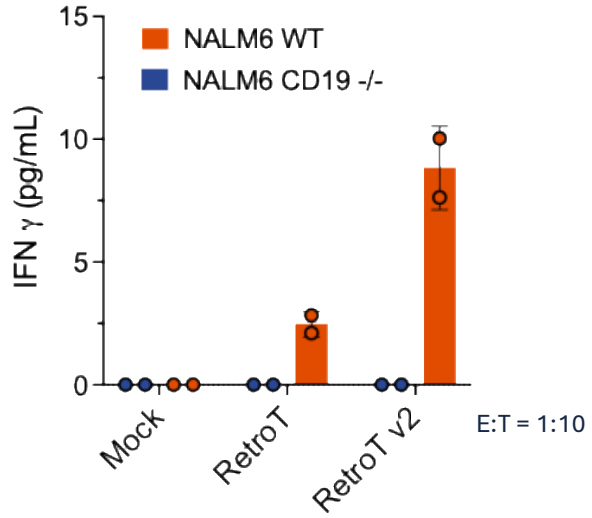

- Consistent CD19 CAR integration in up to 12% of T cells
- Achieved without DNA templates or viral vectors

## Tumor Cell Lysis




- Specific and robust kill of CD19+ NALM6 tumor cells
- No activity against CD19⁻ cells confirms target specificity

## Cytokine Production




- Activation-dependent cytokine production consistent with CAR activation
- Demonstrates proper immune signaling upon target engagement

**CREATE RetroT achieves precise RNA integration and potent CAR-T function — validating the first fully RNA-based platform for stable in vivo cell programming.**

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# Integration of Technology and Manufacturing Enable Rapid, Scalable, and Cost-effective Product Development

## Integrated technology platform

- Proprietary RNA: 8+ days of expression; transient and permanent CAR integration
- Targeted CAR constructs: cell-specific activation
- LNP delivery: targeted and pan-immune LNPs
- Strong IP estate: 115+ patents/applications filed

## Proven Manufacturing

- End-to-end GMP capability: PD, pDNA, mRNA, LNP, Fill-Finish
- Proven scale: >4 GMP batches
- Stability and quality: >3 years stability
- Flexible platform: speed and lower COGS

## Product-focused Approach

- Global reach: open sites in Australia, Korea, Taiwan, USA and the EU
- Rapid path to clinical data: in less than 12 months concept to clinic
- Cost efficient path: via platform-based regulatory strategy
- Aligned with agencies: strategy built with regulatory insights

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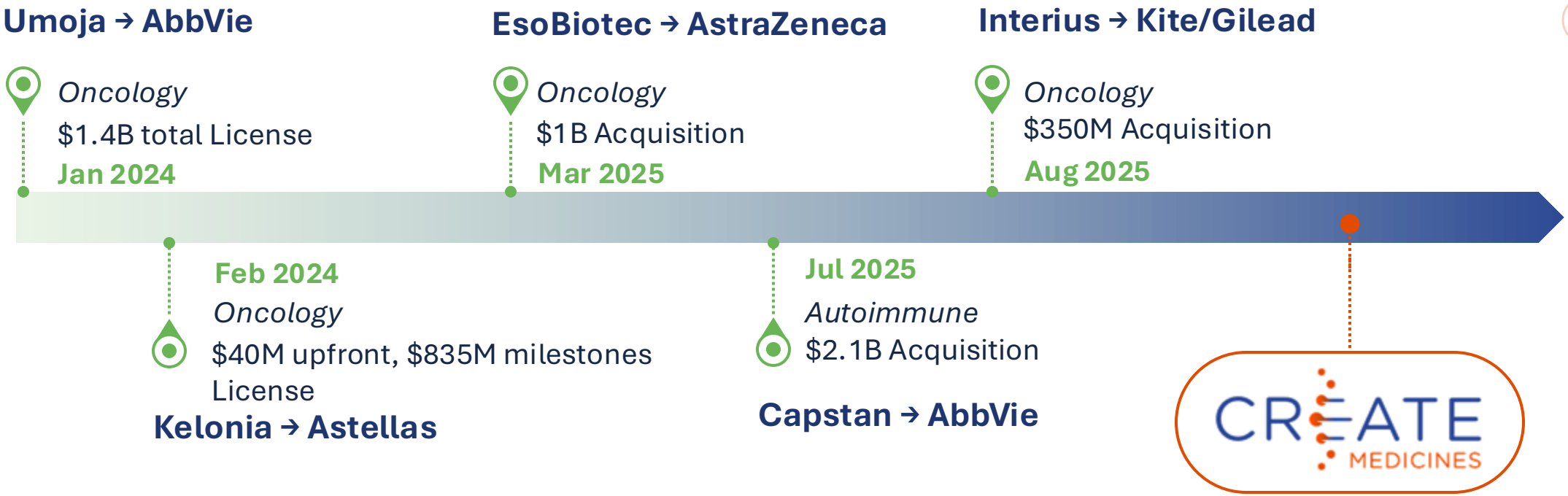
# The Market Wants In Vivo CAR Therapies

## Strategic interest shows it to be an area of rapid growth and focus




**CREATE is positioned to be the engine for biopharmas looking to accelerate in vivo CAR capabilities across oncology and autoimmunity**

# Blockbuster Product Potential Across Oncology and Autoimmunity

## From frontline programs to next-generation multi-immune therapies

| Focus Area | Assets | Summary Observations |
|---|---|---|
| **Oncology** | Myeloid<br>**MT-302-TROP2**<br>**MT-303-GPC3** | **Human validation of in vivo CARs**<br>• Tolerable safety, repeat dosing (>20 doses)<br>• Early efficacy signals as monotherapy and tolerable safety profile (Data SITC 2025)<br>• Advancing to frontline settings (Data Q2 2026) |
| | Multi-Lineage<br>**MT-304-HER2**<br>**CRT-401-HER2+TROP2** | **Multi-immune cell programming to conquer solid tumors leveraging T, NK and myeloid cells**<br>• Encouraging preclinical data for MT-304 and CRT-401 programming to date<br>• Q4 2025 FPI for MT-304 (Data Q4 2026) |
| **Autoimmune** | CART<br>**CRT-402-CD19/BCMA** | **B cell depletion (CD19/BCMA)**<br>• Uniquely toggle between transient and stable CAR expression, tailoring immune rest (temporary deletion) vs durable B cell removal<br>• Positioned to compete directly in the CD19 autoimmune reset race, but with broader flexibility (multi-lineage, transient/stable) |
| **Platform** | | • **Industry leading RNA engineering and LNP delivery technology**<br>• Demonstrated mRNA delivery to **T, NK, and myeloid cells**<br>• Manufacturing moat: GMP-ready, scalable, low COGS, <12 months concept-to-clinic, > 3 years stability<br>• **Ideation to clinical trial in < 12 months** |

# Supported by Strong Investor Syndicate and Management Team

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