# Unlocking Next Generation Therapies

Washington DC
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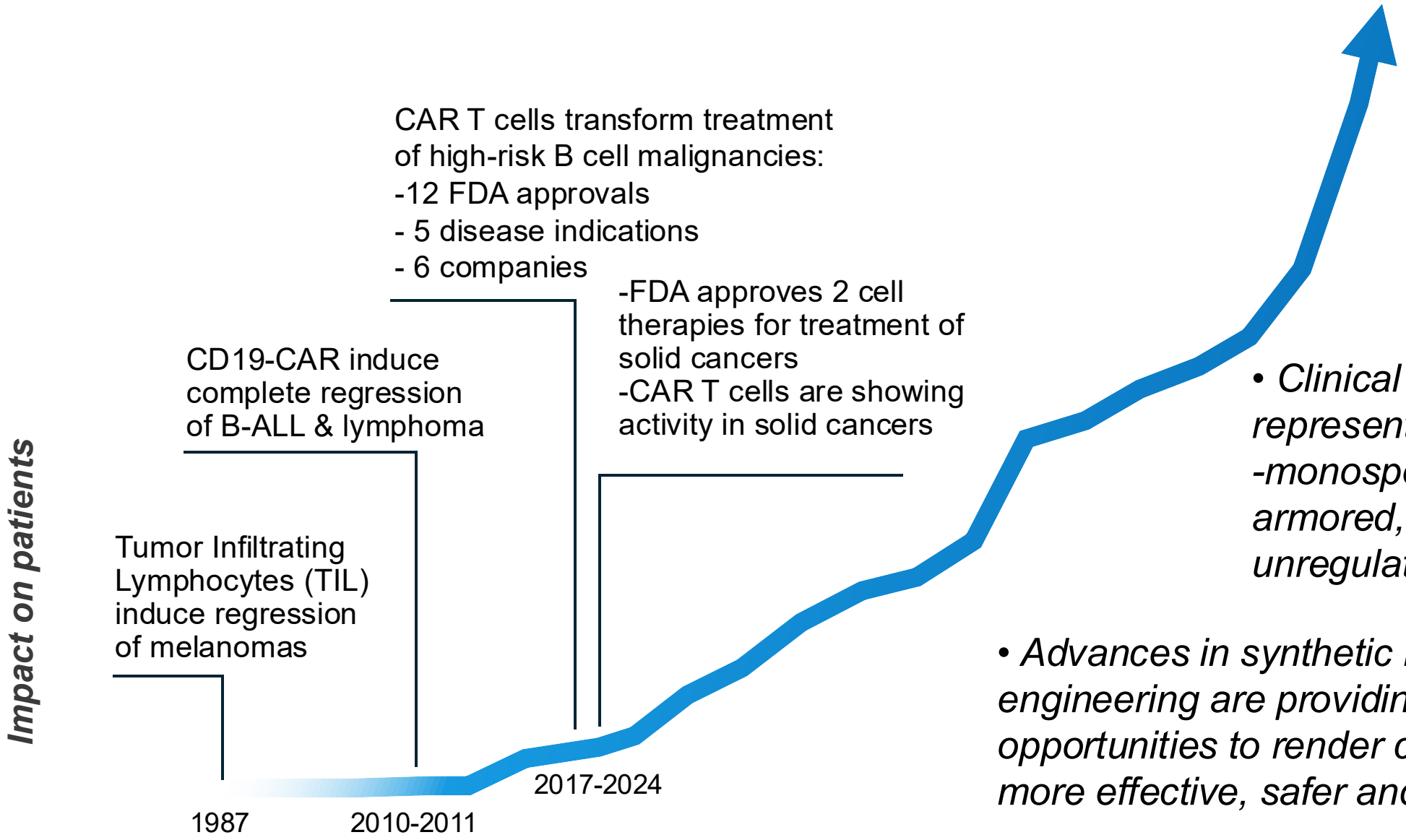
FRIENDS of CANCER RESEARCH

PARKER INSTITUTE FOR CANCER IMMUNOTHERAPY

# Cell Therapies for Cancer Have Made Steady Gains but Have the Potential for Much Greater Impact




- *Clinical successes thus far represent v1.0 engineering: -monospecific, non-armored, unenhanced, unregulated*

- *Advances in synthetic biology and cellular engineering are providing countless opportunities to render cancer cell therapies more effective, safer and less costly*

# CAR T Cell Therapies Have Demonstrated the Ability to Cure "Incurable" Pediatric Cancers

*The Remarkable Story of Emily Whitehead*


April 17, 2012

- Emily had B-ALL that was refractory to all standard therapies.
- She was the first child to receive CD19-CAR T cell therapy.
- She remains free of disease to this day.

# 16 FDA Approvals for Cell Therapies for Cancer

*Only one cell therapy is approved for the treatment of children with cancer*

| YEAR | AGENT | INDICATION | TYPE | TARGET | Signaling Domain | AGE |
|---|---|---|---|---|---|---|
| 2017 | Tis-cel | R/R B-ALL | CAR | CD19 | BB.z | ≤ 26 years |
| 2017 | Axi-cel | 3rd line LBCL | CAR | CD19 | 28.z | ≥ 18 yrs |
| 2019 | Tis-cel | 3rd line LBCL | CAR | CD19 | BB.z | ≥ 18 yrs |
| 2020 | Brex-cel | R/R Mantle Cell Lymphoma | CAR | CD19 | 28.z | ≥ 18 yrs |
| 2021 | Axi-cel | R/R Follicular lymphoma | CAR | CD19 | 28.z | ≥ 18 yrs |
| 2021 | Liso-cel | 3rd line LBCL | CAR | CD19 | BB.z | ≥ 18 yrs |
| 2021 | Ide-cel | 5th line Multiple Myeloma | CAR | BCMA | BB.z | ≥ 18 yrs |
| 2021 | Brex-cel | R/R B-ALL | CAR | CD19 | 28.z | ≥ 18 yrs |
| 2022 | Cilta-cel | 5th line Multiple Myeloma | CAR | BCMA | BB.z | ≥ 18 yrs |
| 2022 | Axi-cel | 2nd line LBCL | CAR | CD19 | 28.z | ≥ 18 yrs |
| 2022 | Liso-cel | 2nd line LBCL | CAR | CD19 | BB.z | ≥ 18 yrs |
| 2022 | Tis-cel | R/R Follicular lymphoma | CAR | CD19 | BB.z | ≥ 18 yrs |
| 2024 | Liso-cel | CLL/SLL | CAR | CD19 | BB.z | ≥ 18 yrs |
| 2024 | Lifi-cel | Metastatic melanoma | Non-engineered | unknown | none | ≥ 18 yrs |
| 2024 | Afami-cel | Metastatic synovial cell sarcoma | TCR | MAGE-A4 | none | ≥ 18 yrs |
| 2024 | Obecel | R/R B-ALL | CAR | CD19 | BB.z | ≥ 18 yrs |

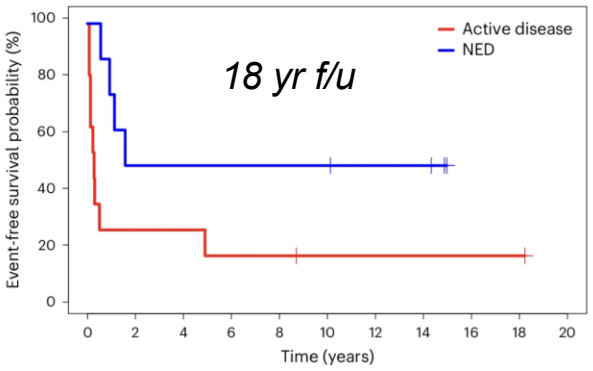
# Several CAR T Cells have Demonstrated Clinical Activity in Pediatric Cancers But Are Not Being Developed by Biopharma

## CD30-CAR for Hodgkin Disease

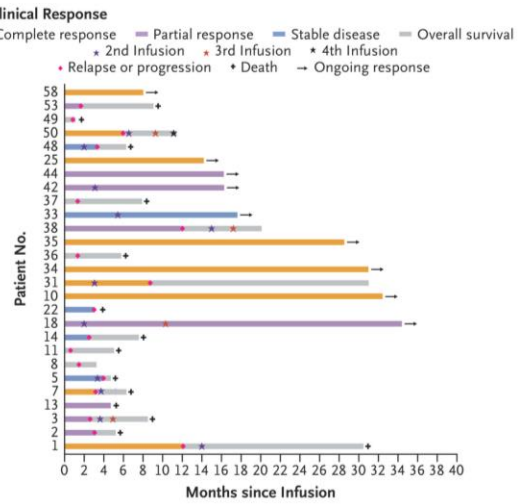
| Response | All Patients (N = 37) | Benda (n = 5) | Benda-Flu (n = 15) | Cy-Flu (n = 17) |
|---|---|---|---|---|
| ORR | | | | |
| CR + PR | 23 (62) | 0 (0) | 12 (80) | 11 (65) |
| Response rate | | | | |
| CR | 19 (51) | 0 (0) | 11 (73) | 8 (47) |
| PR | 4 (11) | 0 (0) | 1 (7) | 3 (18) |
| SD | 4 (11) | 1 (20) | 1 (7) | 2 (11) |
| PD | 10 (27) | 4 (80) | 2 (13) | 4 (24) |

*Ramos, J Clin Oncol, 2020*

## GD2-CAR for Neuroblastoma

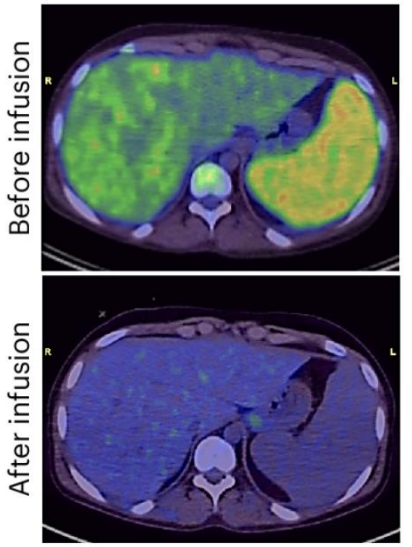



*Li et al, Nat Med 2025*



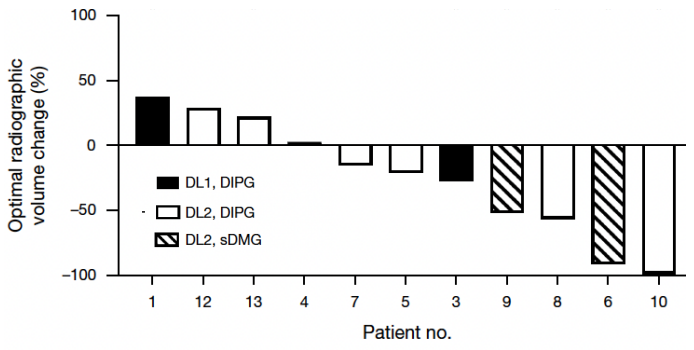

*Del Bufalo, NEJM, 2023*

## CD7-CAR T for T-ALL



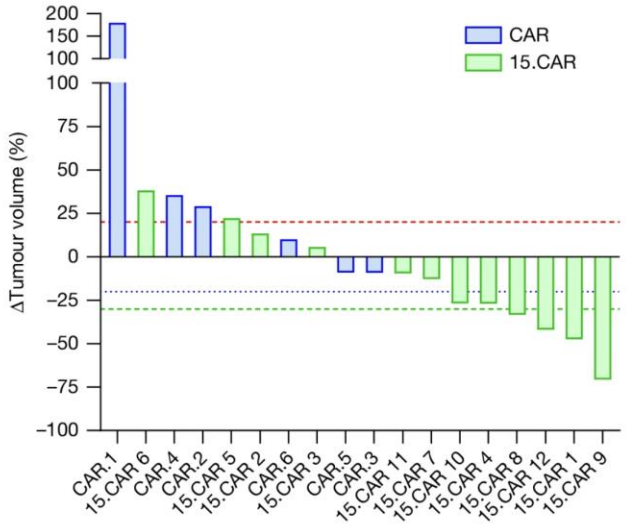

*Oh, Nat Med, 2024*

## GD2-CAR for Diffuse Midline Gliomas



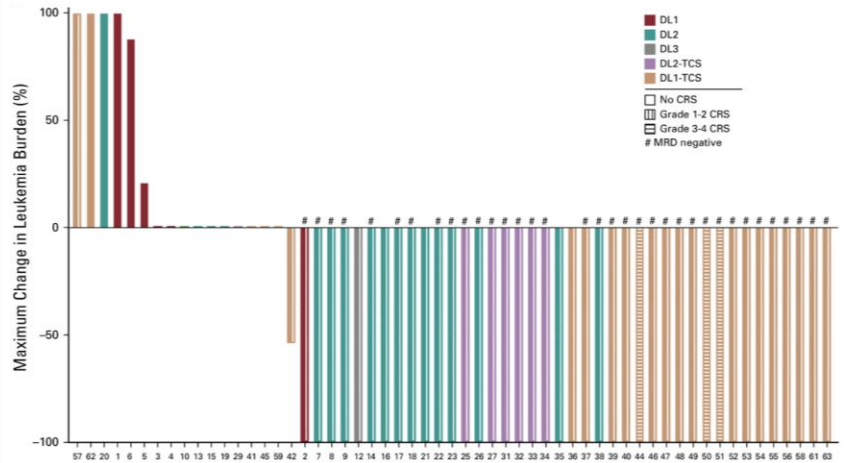

*Monje et al, Nature 2022, 2024*

## GPC3.15-CAR for Solid Cancers




*Steffin, Nature, 2025*

## CD22-CAR for CAR19 Refractory B-ALL




*Fry Nat Med 2018, Shah J Clin Onc 2020*

# High Costs of Developing and Delivering Cell Therapies Is Adversely Impacting the Entire Sector, Even for Common Diseases

AI Overview

The total cost of developing an oncology cell therapy, from target identification to filing a marketing application, is estimated to be **between $500 million and $600 million**. This includes costs like clinical trials, manufacturing, and regulatory approval.

DEVELOPMENTAL THERAPEUTICS—IMMUNOTHERAPY

**ASCO Educational Book 2023**

## High Cost of Chimeric Antigen Receptor T-Cells: Challenges and Solutions

Edward R. Scheffer Cliff, MBBS, MPH[1,2]; Amar H. Kelkar, MD[2,3]; David A. Russler-Germain, MD, PhD[4]; Frazer A. Tessema, BA[1,2]; Adam J.N. Raymakers, PhD[1,2]; William B. Feldman, MD, DPhil, MPH[1,2,5]; and Aaron S. Kesselheim, MD, JD, MPH[1,2]

March 11, 2025 *Updated 06:40 AM* | Deals, Pharma, Cell/Gene Tx

## Bristol Myers buys out cell therapy partner 2seventy bio

## Cell and gene therapy investment, once booming, is now in a slump

Much less money is flowing into the sector as venture investors focus on technologies with less risk and easier paths to market.

August 29, 2024

Reuters World Business Markets Sustainability Legal Breakingviews Technology Investigations

## Gene therapy loses luster as investors eye quicker returns from weight-loss drugs

By Deena Beasley

March 11, 2025 Updated 2 months ago

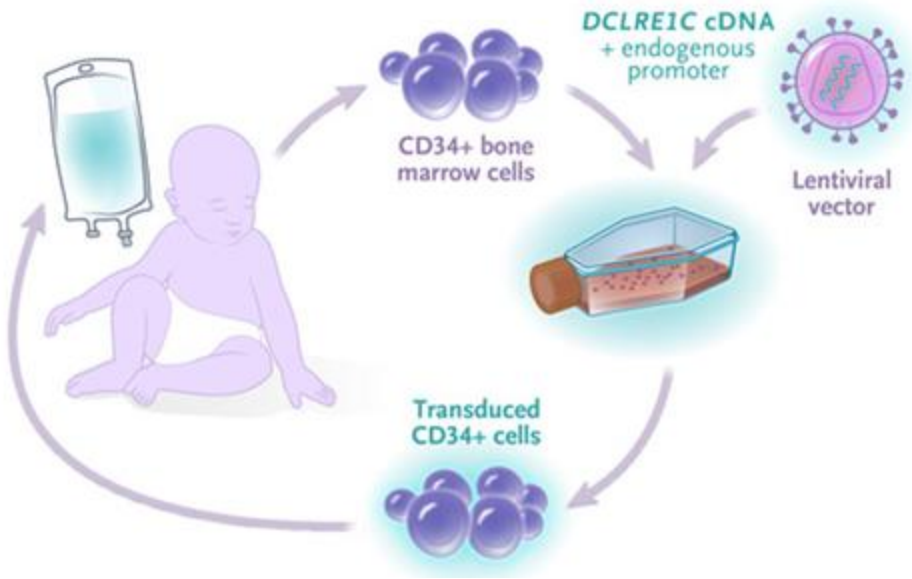
April 24, 2025 DT *Updated 04:26 PM* | People, R&D, Cell/Gene Tx

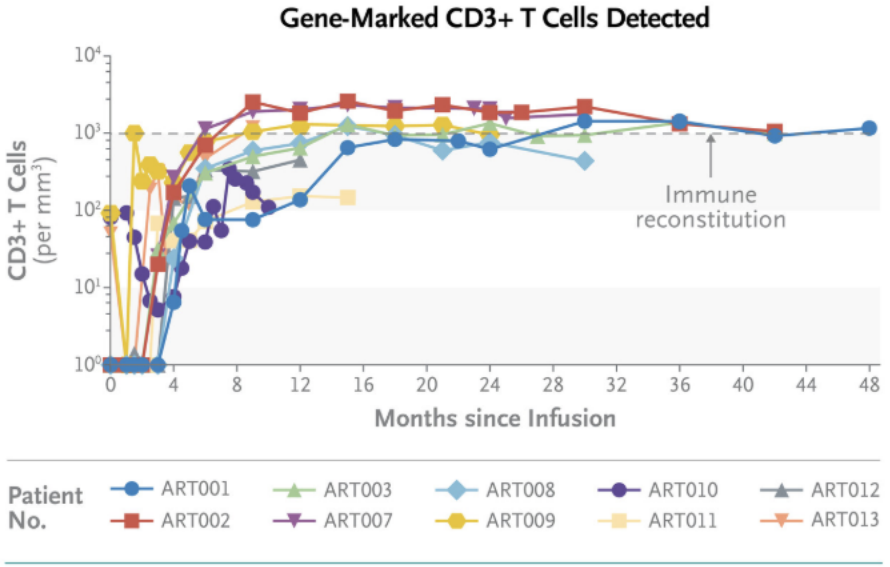
## Caribou lays off 32% of staff, cuts lupus cell therapy program before first patient

# Case Study - ARTEMIS-SCID

*Courtesy: Mort Cowan MD, Jennifer Puck MD, Brian Shy MD, PhD, UCSF*

- **Disease:** Severe combined immunodeficiency (SCID) results from mutations in the Artemis gene (*DCLRE1C);* 2-3% of all SCID with high incidence among persons of Navajo or Apache descent. There are 3-4 patients per year in the U.S. and Canada.
- **Standard-of-care**: HCT is carries a high risk of graft rejection and graft-versus-host disease (GVHD), and late adverse effects (short stature, dental maldevelopment, endocrinopathies, and premature death).
- **Treatment:** Lentiviral transduction of DCLRE1C cDNA restores physiologic expression of the Artemis protein in autologous CD34+ bone marrow cells from infants with newly diagnosed ART-SCID following low-exposure busulfan conditioning.
- As of 2025, **17 patients treated and all demonstrate essentially complete correction of their immunodeficiency**. Toxicity include transient cytopenias and autoimmune hemolytic anemia. No mortality related to the treatment.
- This therapy is curative therapy for this life-threatening immune disorder.
- Long-term sustainable patient access requires direct reimbursement. There is no commercial interest under current framework. With critical support from CIRM, UCSF, and philanthropy, UCSF is pursuing a BLA to provide continued access to this life saving treatment.



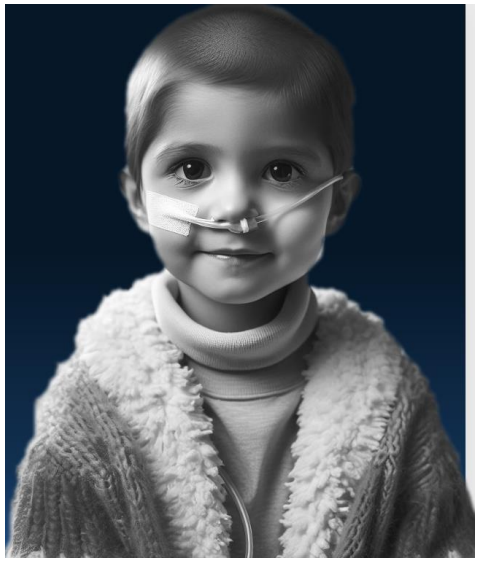

*Cowan MJ et al, NEJM, 2022.*

*Courtesy: Mort Cowan MD, Jennifer Puck MD, Brian Shy MD, PhD, UCSF*

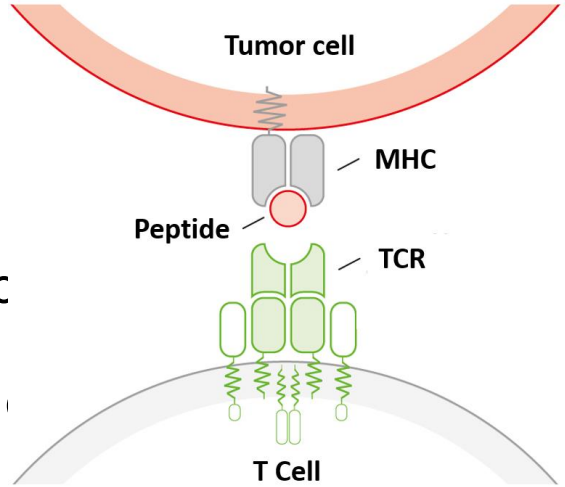
# High Costs to Qualify Critical Starting Material for Pivotal Studies and Commercial Manufacturing Pose Barrier to Development of Curative Therapy for ARMTEMIS-SCID

- Current lot of **ARTEMIS GMP vector** produced by academic vendor (Indiana University) has demonstrated safety and efficacy across 17 patients, stability out to ~6 years, and is of sufficient quantity to treat 50 patients.

# Increasing Focus on Enhancing Therapeutic Development for Rare Disease



Cancers and other rare diseases are among the top 10 causes of death for children in the US, with an estimated 7,000 children lost every year




Advances in molecular immunotargeting of canc is driving opportunities to deliver ultra-targeted cellular therapeutics for hundreds or thousands unique cancer populations and potentially even n=1.


**Goal 1: Further Advance Regulatory Science of Rare Disease Therapies (fda.gov)**

**BioCentury – Makary: New ultrarare path will provide approval based on 'plausible mechanism'**

April 21, 2025

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FDA Commissioner Marty Makary's proposal to roll out a new drug approval pathway is heightening hope for the rare disease industry,

# Workshop Focus and Goals

- We will discuss regulatory, manufacturing, and cost recovery strategies to address the barriers that prevent promising cell therapies from reaching patients with a focus on cancer.
- Our goal is to inform future policy discussions, highlight areas for regulatory clarity, and identify operational solutions to support sustained therapy development
- Key Focus Areas
  - ✓Regulatory Engagement and Flexibility
  - ✓Manufacturing Adaptability
  - ✓Sustainable Pre-Market Access
- **Panel 1: Advancing Regulatory Frameworks for Cell-Based Therapies**
  - Michael Kalos, Lee Fleisher, Holly Fernandez-Lynch, Kristen Hege, Nicole Verdun