



**Leaders in Developing Allogeneic  $\gamma\delta$ 1 CAR T Cell Therapies to Fight Autoimmune Diseases and Cancer**



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# Adicet Bio: Leaders in Developing Allogeneic $\gamma\delta$ CAR T Cell Therapies

## Adicet's $\gamma\delta$ 1 CAR T Pipeline is Uniquely Positioned to Deliver Best-in-Class Cell Therapies

Demonstrated  
Clinical POC

Off-the-shelf

Robust  
exposure

Favorable  
safety profile

Traffic to  
tissues

## Differentiated pipeline offers significant commercial opportunities, with potential for short- and long-term value creation

### Autoimmune Disease / ADI-001

- Complete CD19+ B cell depletion in blood and secondary lymphoid tissue
- No significant risk of CRS, ICANS or T cell malignancies
- 6 autoimmune indications in clinical development
- **Initial ADI-001 Clinical Data in LN 1H/2025**

### Oncology/ ADI-270

- Innate anti-tumor activity
- Retained potent activity in CD70-low tumors
- Engineered resilience to TGF $\beta$  in tumor
- Engineered to increase persistence
- **Initial Clinical Data in RCC in 1H/2025**

# Developing Broad Pipeline of Allogeneic $\gamma\delta 1$ T Cell Therapies for Autoimmune Diseases and Cancer

Program	Target	Indication	Research	IND-Enabling	Clinical	Status
<b>AUTOIMMUNE DISEASES</b>						
<b>ADI-001</b>	CD20	LN & SLE				Enrolling LN patients • Fast Track Designation • Clinical update 1H/2025 SLE enroll Phase 1 1Q/2025
		SSc				Enroll Phase 1 1Q/2025 Clinical update 2H/2025
		IIM/ SPS				Enroll Phase 1 1Q/2025 Clinical update 2H/2025
		AAV				Enroll Phase 1 2H/2025 Clinical update 2H/2025
<b>ONCOLOGY</b>						
<b>ADI-270</b>	CD70 (TGF $\beta$ -DNR)	RCC & Other ST / Heme				Enrolling RCC patients • Fast Track Designation • Clinical update 1H/2025
<b>ADI-xxx</b>	PSMA (w/ Armor)	mCRPC				Preclinical activities

AAV= anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis; ccRCC= Clear cell renal cell carcinoma; IIM= idiopathic inflammatory myopathy; IND= Investigational new drug; LN= lupus nephritis; mCRPC= Metastatic castration-resistant prostate cancer; PSMA= Prostate specific membrane antigen; SLE= systemic lupus erythematosus; SPS= stiff person syndrome; SSc= systemic sclerosis; ST= Solid tumor

Timing subject to site activation, patient enrollment, data readouts and regulatory feedback

# Adicet Bio Leadership Team



Chen Schor  
President and CEO



Nick Harvey  
Chief Financial Officer



Blake Aftab, Ph.D.  
Chief Scientific Officer



Don Healey, Ph.D.  
Chief Technology Officer



Nancy Boman, M.D., Ph.D.  
Chief Regulatory Officer



Amy Locke  
Head of Human Resources



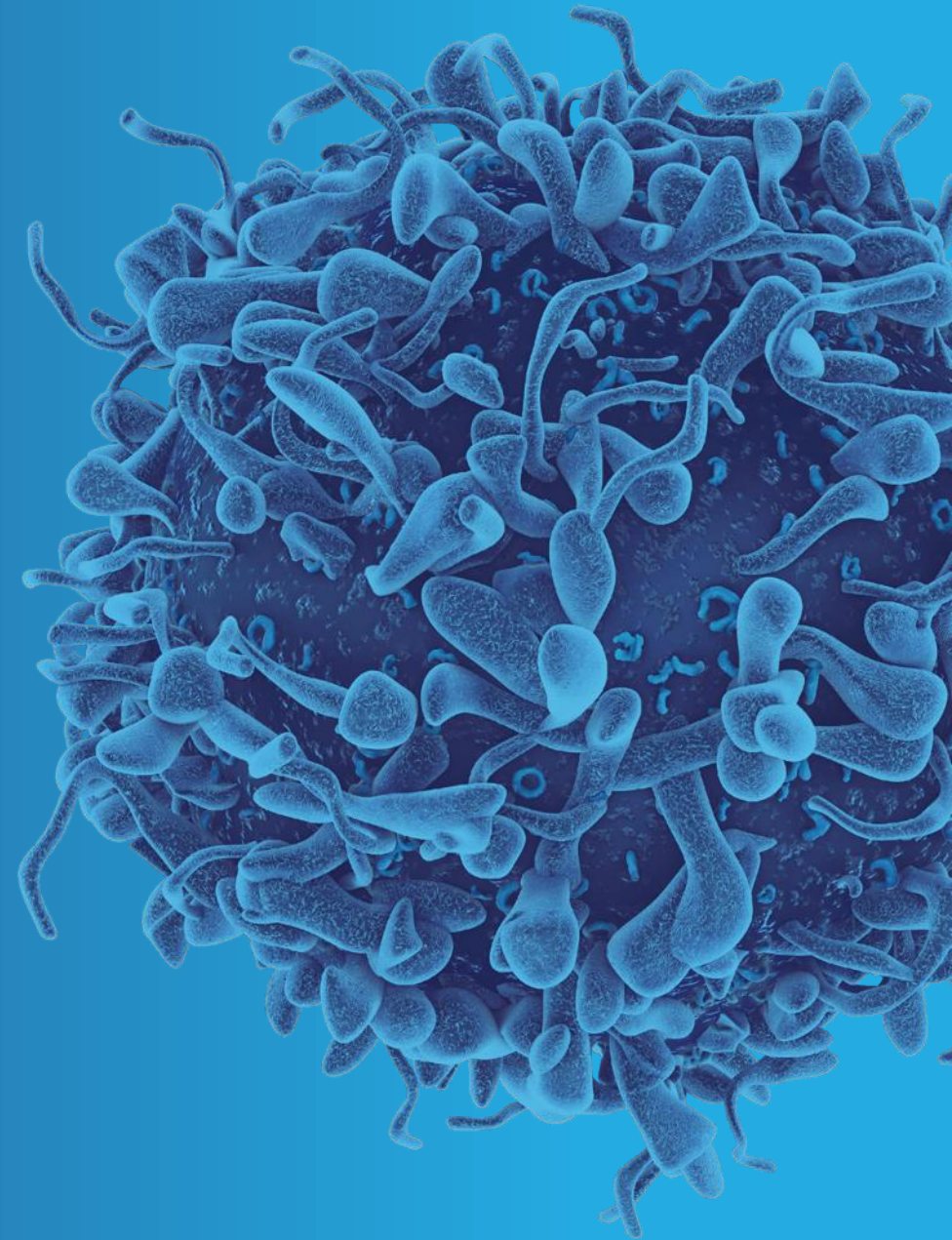
Julie Maltzman, M.D.  
Chief Medical Officer





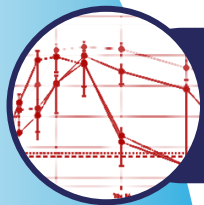
# ADI-001

## Autoimmune Diseases

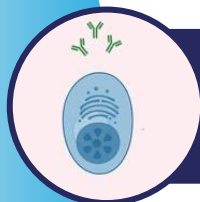


# ADI-001: Multiple Levels of Evidence Support Potential in Autoimmune Disease

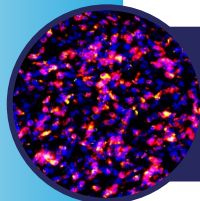
## Multiple Levels of Evidence Supporting ADI-001



**Robust PK exposure**, consistent with autologous alpha-beta CAR T in autoimmune, resulting in complete CD19+ B cell depletion in blood



Targeting CD20 has been shown to **fully deplete the B cell lineage in the peripheral blood, including plasmablasts<sup>1</sup>**



**Significant tissue exposure and CAR-T activation** resulting in complete CD19+ B cell depletion in secondary lymphoid tissue



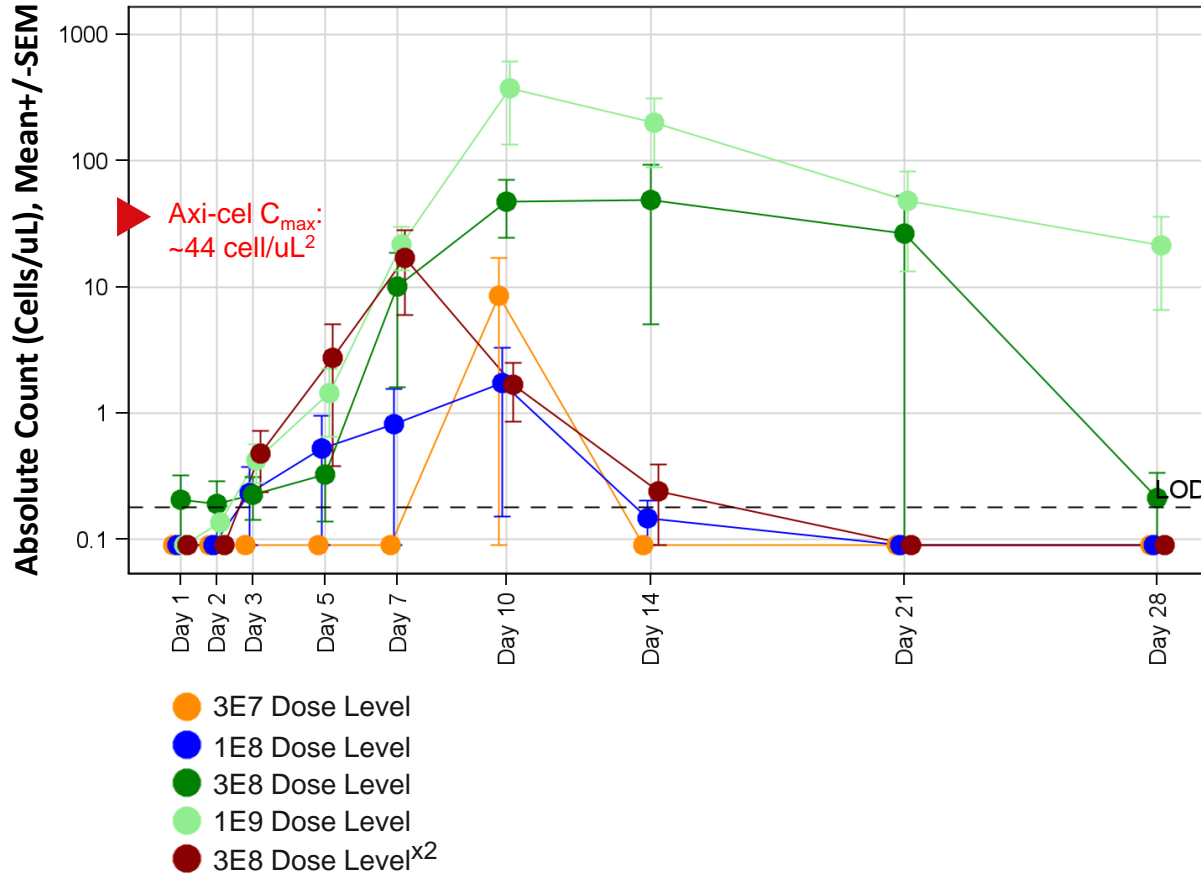
**Off-the-shelf; No significant risk of CRS, ICANS or T cell Malignancies; Potential to Dose in Community Setting**

**6 Autoimmune Indications in Clinical Development  
Preliminary LN Clinical Data H1/2025**

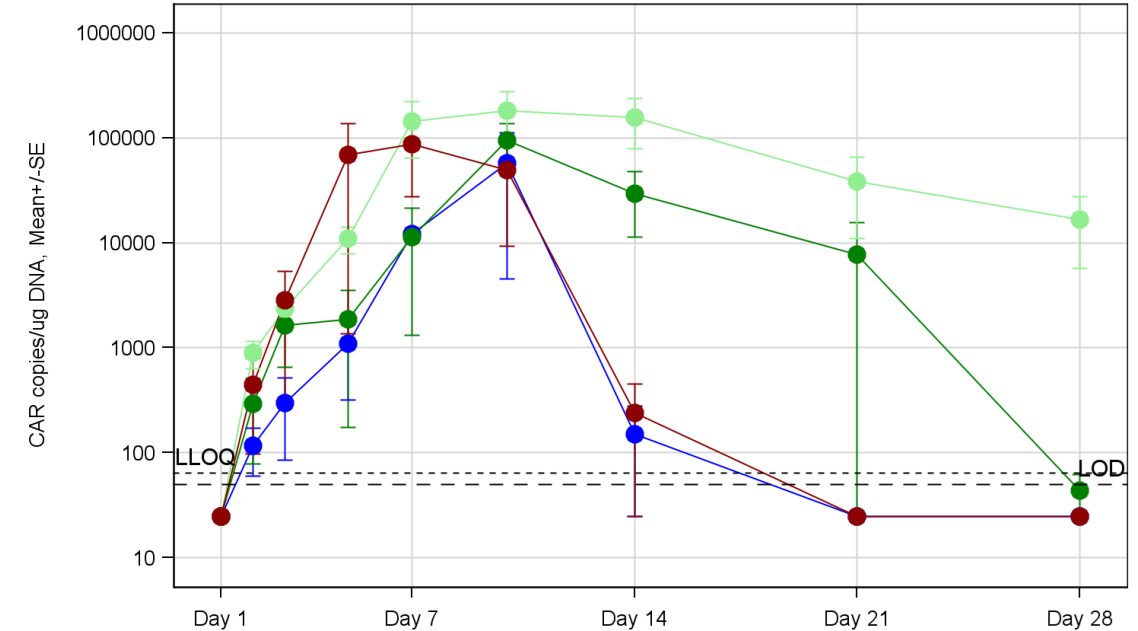
<sup>1</sup>Furie RA et al. Ann Rheum Dis (2022); Tur C, et al. Ann Rhum Dis (2024); CRS= Cytokine release syndrome; ICANS= Immune effector cell-associated neurotoxicity syndrome

# ADI-001's Cmax, D28 Persistence and AUC Are Consistent with Values Reported for Approved Autologous CD19 CAR T<sup>1</sup>

## ADI-001 CAR by Flow Cytometry



## ADI-001 CAR by ddPCR



Dose Level	Mean Cmax		Mean D28	
	CAR+ Vd1 cells/ul	Copies/ug	CAR+ Vd1 cells/ul	Copies/ug
1E9	363.80	201,666	26.51	16,553
3E8	56.34	98,177	0.04	44

<sup>1</sup>Badbaran, A. Cancers 2020;12, 1970; Locke et al. N Engl J Med 2022; 386:640-654; Neelapu et al. N Engl J Med. 2017;377:2531-2544; Ogasawara et al. Clin Pharmacokinet 60, 1621-1633 (2021)

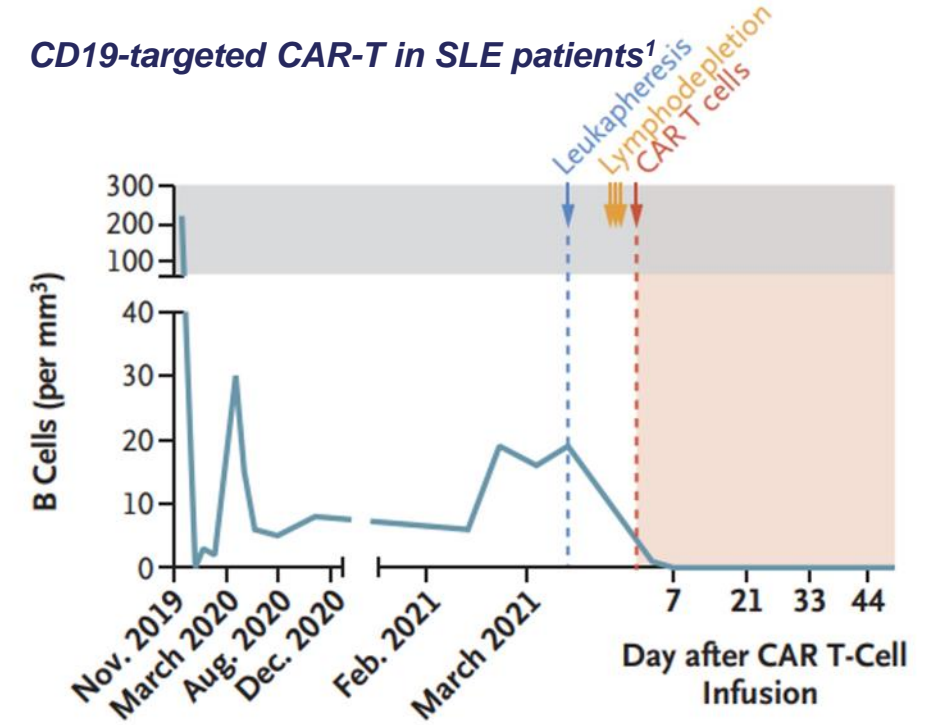
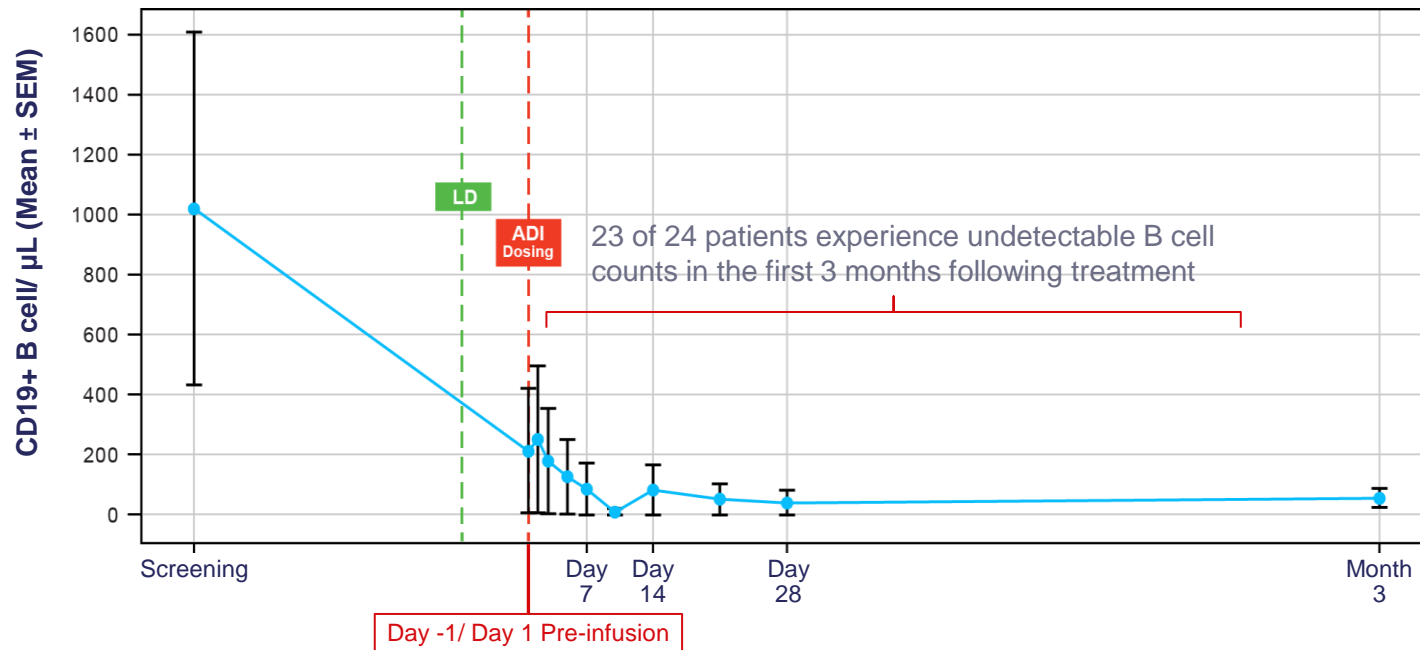
<sup>2</sup>YESCARTA® (axicabtagene ciloleucel) prescribing information rev. June 2024

Cmax= Mean maximum concentration of ADI-001; D28= Day 28, AUC= Area under the curve d0-28



# ADI-001 in Autoimmune Diseases: B-Cell Depletion Consistent with Autologous CD19 CAR T in SLE Academic Studies<sup>1,2</sup>

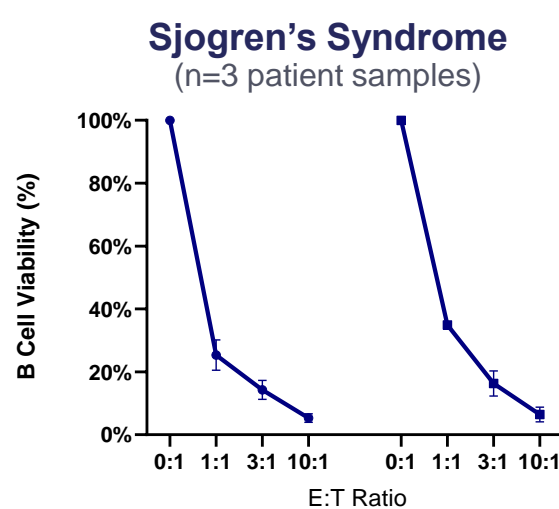
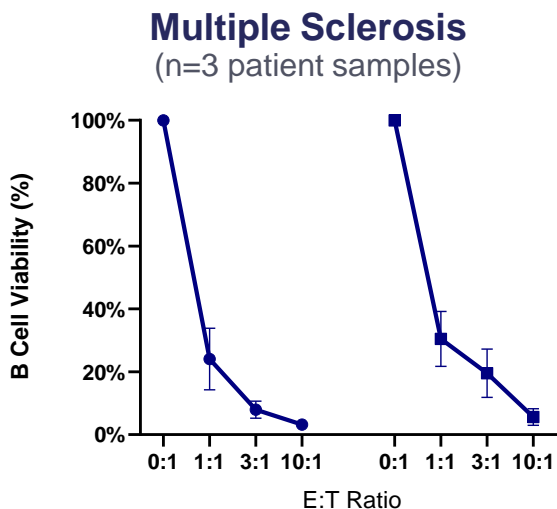
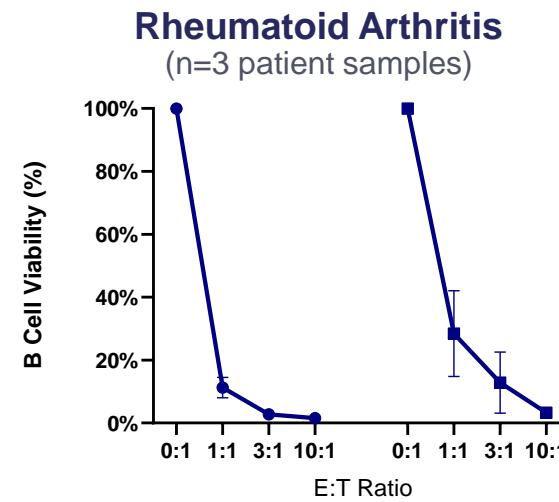
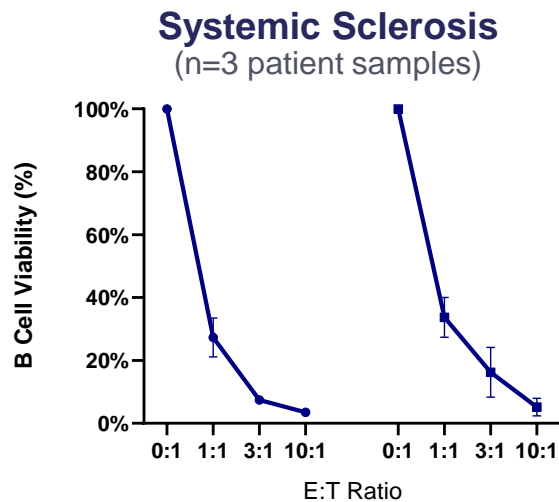
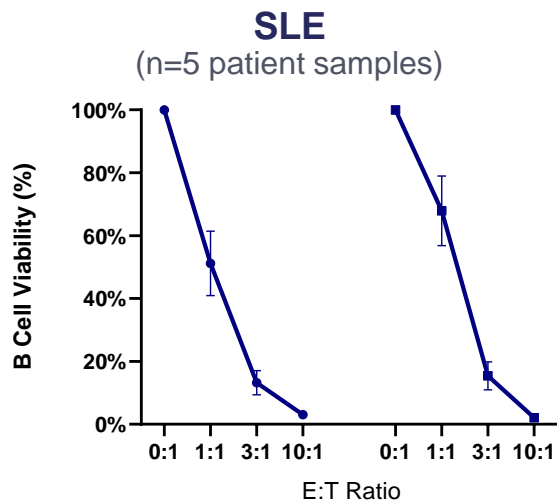
## Adicet Bio CD20-targeted, ADI-001, in B-NHL patients<sup>3</sup>



1. Mougiakakos MD et al. NEJM 2021  
 2. Mackensen A et al. Nature Medicine 2022  
 3. Adicet internal data

SOC= Standard of care

# ADI-001 Exhibited Potent Killing of Patient-Derived CD19+ B Cells in Multiple Autoimmune Diseases



● ADI-001 Lot 1  
■ ADI-001 Lot 2

B cells from 5 SLE patients and 3 patients each for SSc, RA, Multiple sclerosis, and Sjogren's syndrome were co-cultured with ADI-001 manufactured from two independent donors at varying effector-to-target (E:T) ratios for 24 hours and then analyzed by flow cytometry to quantify live B cells relative to negative controls.

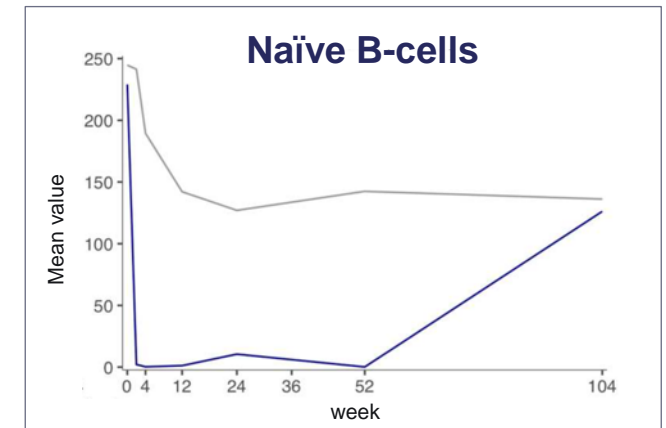
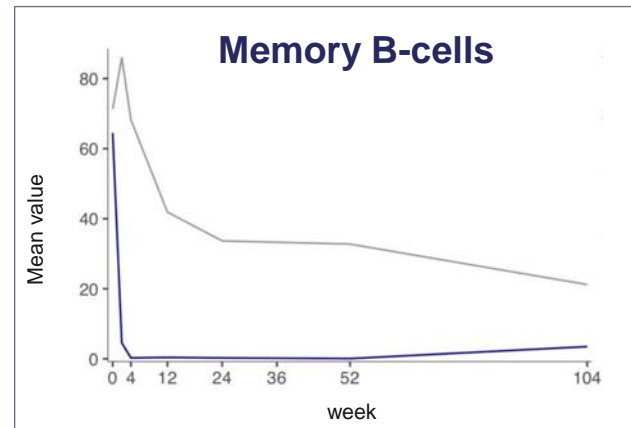
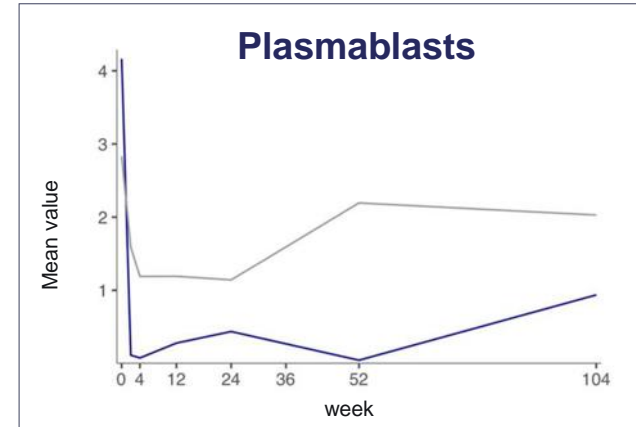
# CD20 Targeting With Obinutuzumab Depleted B Cells in Blood Including Plasmablasts, Memory B Cells, and Naïve B-Cells in LN Patients

## CLINICAL SCIENCE

B-cell depletion with obinutuzumab for the treatment of proliferative lupus nephritis: a randomised, double-blind, placebo-controlled trial

Richard A Furie,<sup>1</sup> Gustavo Aroca,<sup>2</sup> Matthew D Cascino,<sup>3</sup> Jay P Garg,<sup>3</sup> Brad H Rovin,<sup>4</sup> Analia Alvarez,<sup>5</sup> Hilda Fragoso-Loyo,<sup>6</sup> Elizabeth Zuta-Santillan,<sup>7</sup> Thomas Schindler,<sup>8</sup> Paul Brunetta,<sup>3</sup> Cary M Looney,<sup>3</sup> Imran Hassan,<sup>9</sup> Ana Malvar<sup>10</sup>

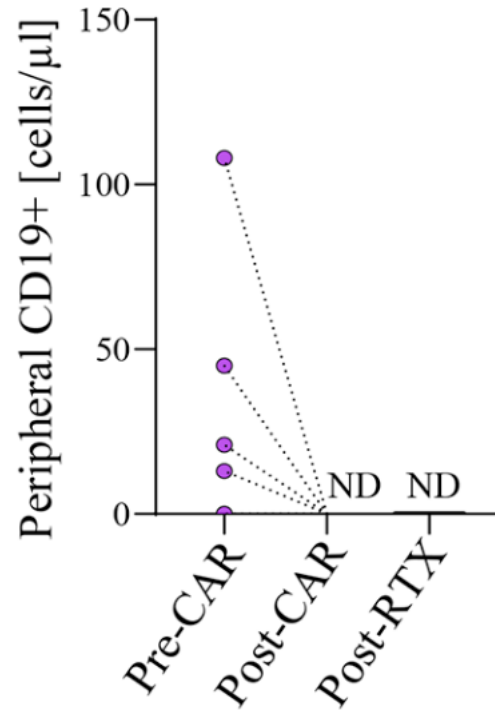
- In a third-party Phase 2 study in LN, obinutuzumab drove depletion of the B-cell compartment in the blood, including plasmablasts<sup>1</sup>
- Poor B-cell depletion in tissues is a noted challenge to efficacy of antibody-based approaches in autoimmune disorders<sup>2,3</sup>



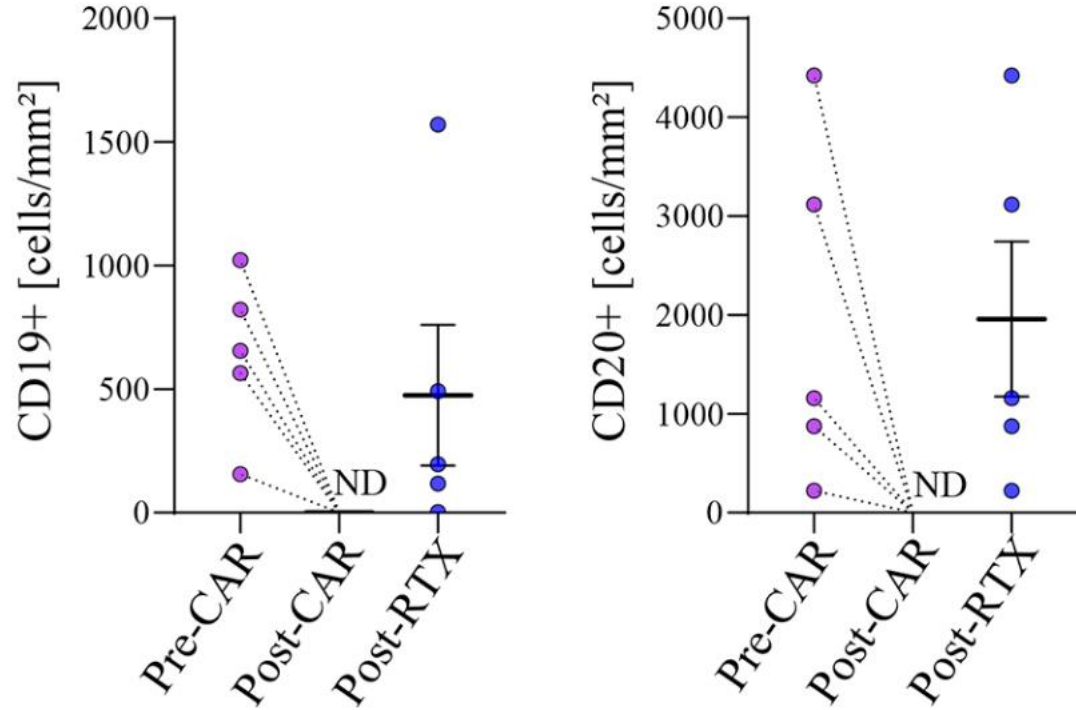
— Obinutuzumab + MMF (n=63) — Placebo + MMF (n=62)

Obinutuzumab or placebo dosed on day 1 and weeks 2, 24 and 26 in 125 LN patients

# CAR T Cell Therapy But Not Antibody-Based Therapies Led to Complete Depletion of B Cells from Lymph Nodes in Autoimmune Patients



Both CD19 CAR T and CD20 Ab (Rituximab) led to complete CD19+ B cell depletion in peripheral blood



CD19 CAR T but not CD20 Ab (Rituximab) led to complete CD19+ B cell depletion in lymph nodes

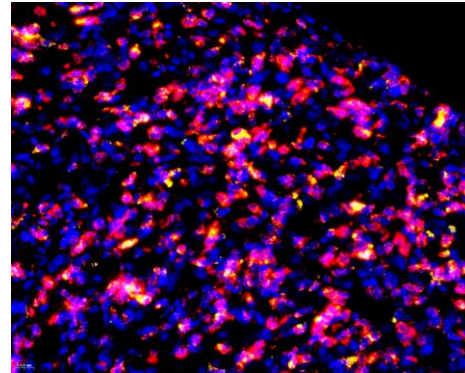
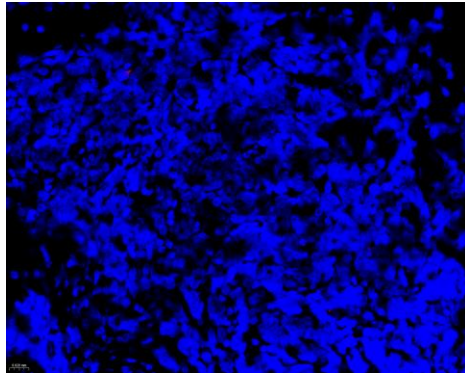
# ADI-001 Clinical Data Demonstrated Tissue Trafficking and CAR Activation, Exceeding that Reported for Axi-cel

## ADI-001 Clinical Tissue Analyses

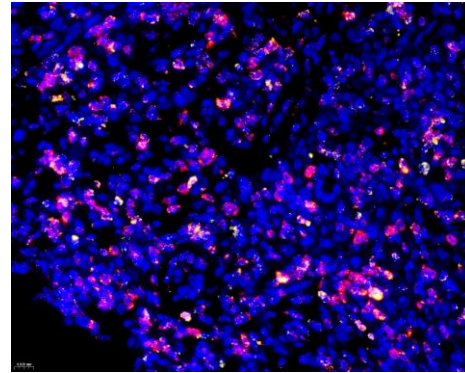
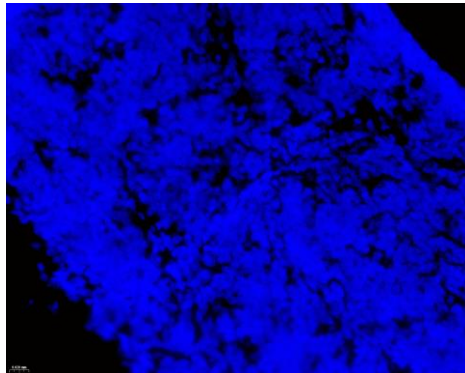
Screening Biopsy

Day 10 Post-Dose ADI-001

DLBCL  
Lymph Node  
Biopsy



MCL  
Lymph Node  
Biopsy



Blue : Nuclei    Yellow: ADI-001 CAR    Red: Granzyme (T Cell Activation)

## ADI-001 Tissue Trafficking Exceeds Data Reported for Axi-cel<sup>1</sup>

Lymph Node Exposure	ADI-001 Average CAR T per Million Cells
1E8-1E9 Dose Levels	236,701
1E9 Dose Level	461,867 (276,588 – 647,163)

Lymph Node Exposure <sup>1</sup>	Axi-cel <sup>2</sup>
Axi-cel Patient #011	62,948
Axi-cel Patient #014	19,647

Robust tissue tropism for ADI-001 observed in lymph node biopsies across dose levels

**ADI-001 cells represent 27%-64% of total cellular material** detected by ddPCR in lymph nodes at 1E9 dose level

Axi-cel= Axicabtagene ciloleucel

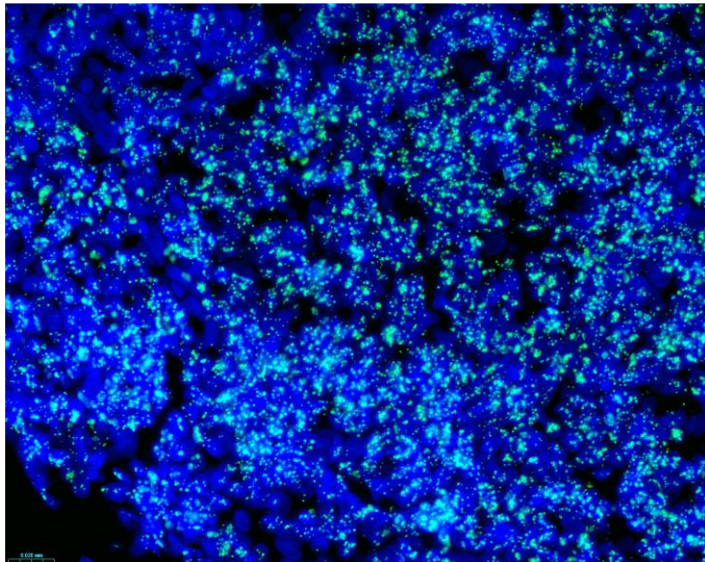
<sup>1</sup>Head-to-head studies have not been conducted

<sup>2</sup>Table 3. Excerpt for Axi-cel assay. Badbaran, A et al., Cancers (2020)

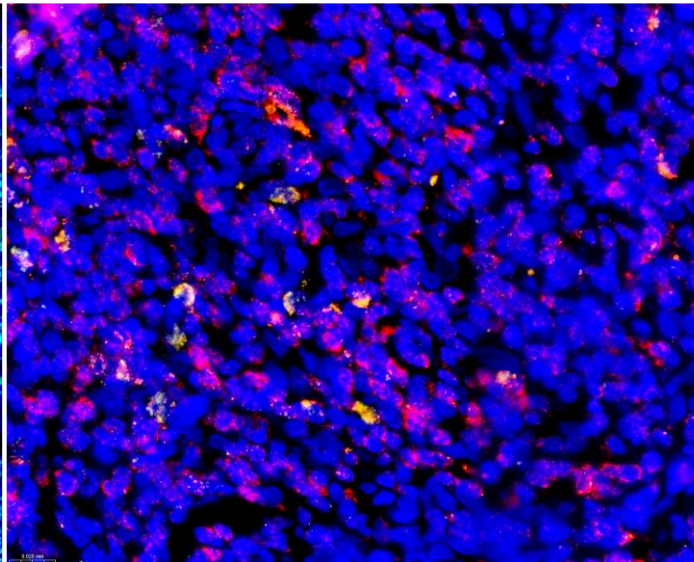
# Confirmation of CD19+ B-Cell Depletion Within Tissues

MCL Patient Lymph Node Biopsies

Screening Biopsy



Day 10 Post ADI-001 Dose



Blue : Nuclei    Green: CD19+ cells    Yellow: ADI-001 CAR    Red: Granzyme B (T Cell Activation)

73y M, 4 prior lines (including rituximab and SCT), 1E9 Dose Level CR

**Complete depletion of CD19+ B cells observed at day 10 within secondary lymphoid tissue**

Intramuscular DLBCL

Baseline



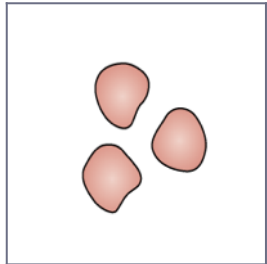
Day 28 Post ADI-001



75y M, 5 prior lines (incl. CD19 CAR-T); Sagittal view of the right leg

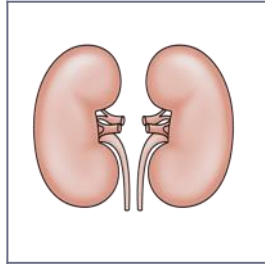
**Clinical responses observed in extra-nodal tissue**

# $\gamma\delta$ T Cells Preferentially Traffic to Solid Tissues: Addressing a Source of Resistance to Antibody Therapies



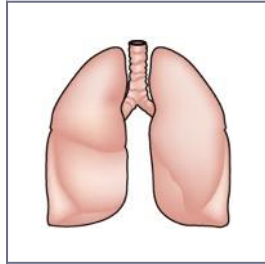
**lymph node**<sup>1,2</sup>

CD27+  
CD62L+  
V $\delta$ 1+  $\uparrow\uparrow$   
V $\delta$ 2+  $\downarrow\downarrow$



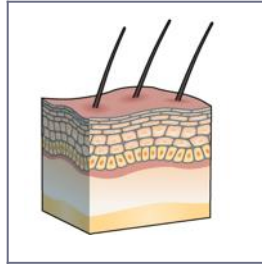
**kidney**<sup>3</sup>

tissue: **>3X**  
 $\gamma\delta$  vs  $\alpha\beta$   
~**3X** more  
V $\delta$ 1 vs  
V $\delta$ 2+



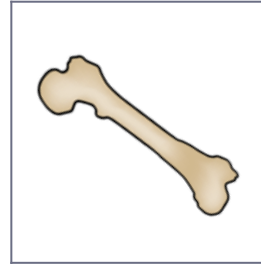
**lung**<sup>4</sup>

issue/blood:  
**9X**



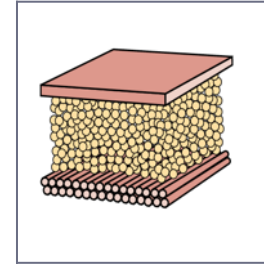
**skin**<sup>5</sup>

tissue/blood:  
**8X**



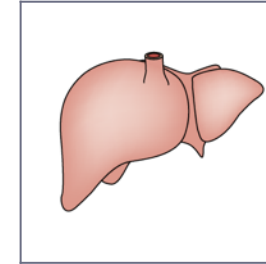
**bone marrow**<sup>6</sup>

tissue/blood:  
**4X**



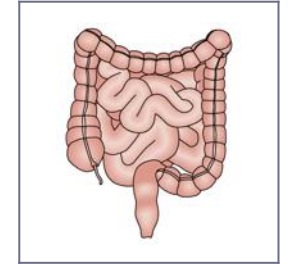
**breast**<sup>7</sup>

tissue/blood:  
**~15X**  
**adipose**  
tissue/blood:  
**9X**



**liver**<sup>8</sup>

tissue/blood:  
**3X**



**GI**<sup>9</sup>

tissue/blood:  
**11X**

Ratios empirically calculated or approximated from proportion of %CD3 from literature reports in relative compartment<sup>3,6</sup>

Images adapted from Hunter et al J Hepatol (2018) and Ribot et al Nat Rev Immunol (2021)

<sup>1</sup>Davey et al Trends Immunol (2018)

<sup>3</sup>Rancan et al Nat Immunol (2023)

<sup>5</sup>Toulon et al J Exp Med (2009)

<sup>7</sup>Wu et al Sci Transl Med (2019)

<sup>2</sup>Uger et al Sci Rep (2018)

<sup>4</sup>Wisniewski et al Am J Respir Cell Mol Biol (2000)

<sup>6</sup>Brauneck et al Front Med (2021)

<sup>8</sup>Melo et al Clin Immunol (2021)

<sup>9</sup>Deutsch et al Eur J Immunol (1991)

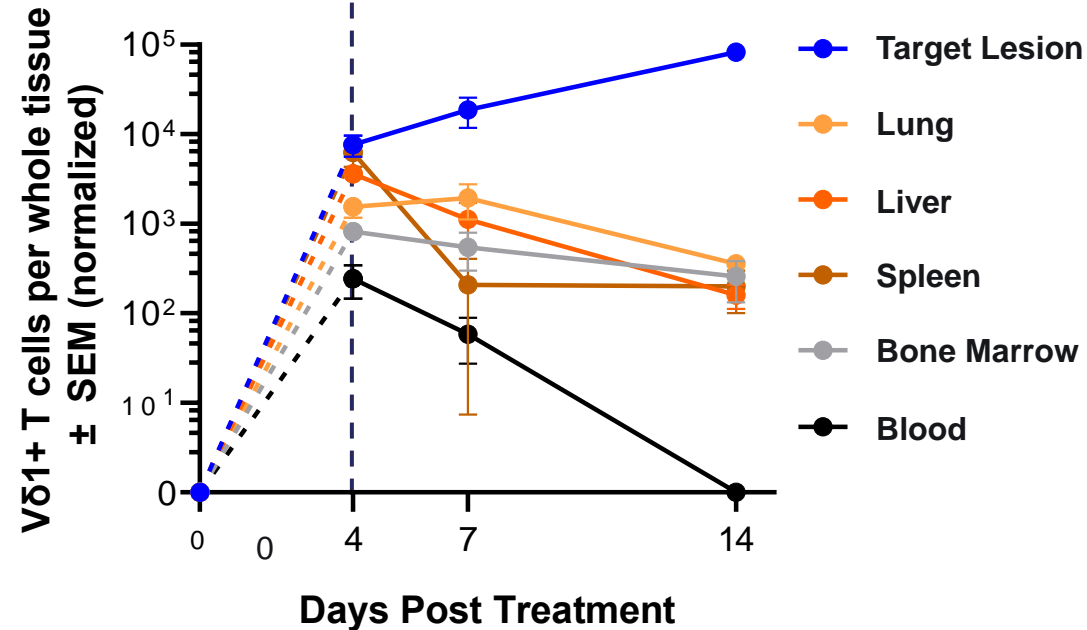
# Preclinical Data Highlights $\gamma\delta 1$ T Cells Tissue Residence

$\gamma\delta 1$  actively homed and biodistributed to relevant tissues

## Homing

## Expansion

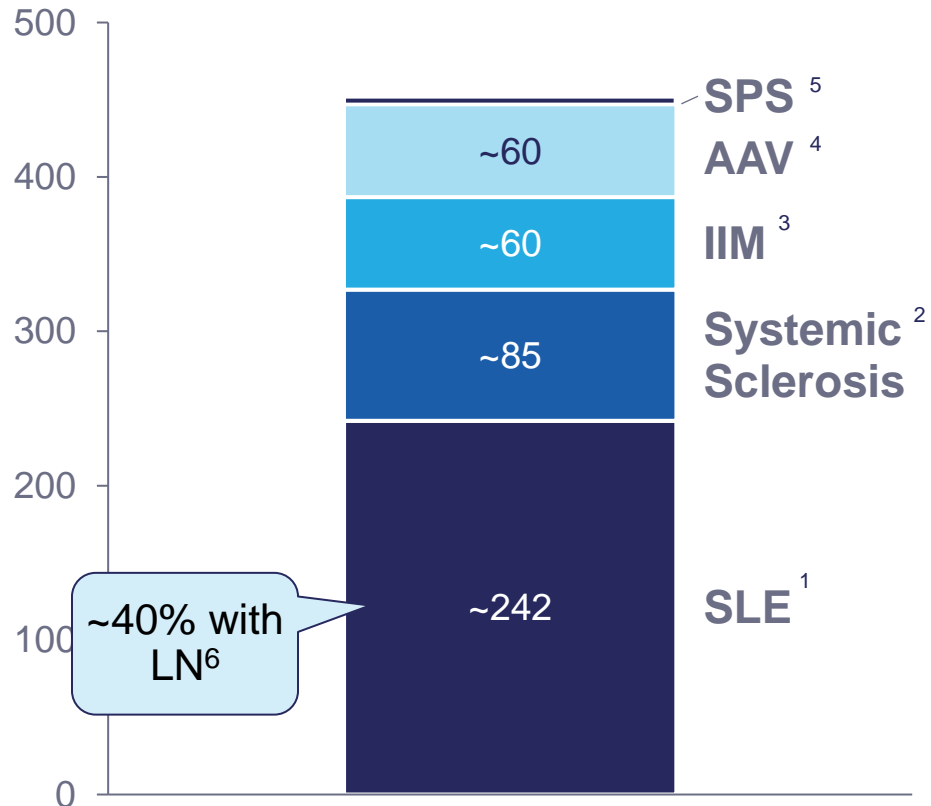
Tissue residence of  $\gamma\delta 1$  and selective expansion within target lesions





# Expanding ADI-001 Autoimmune Development Across Six Indications

## US Prevalence (thousand patients)



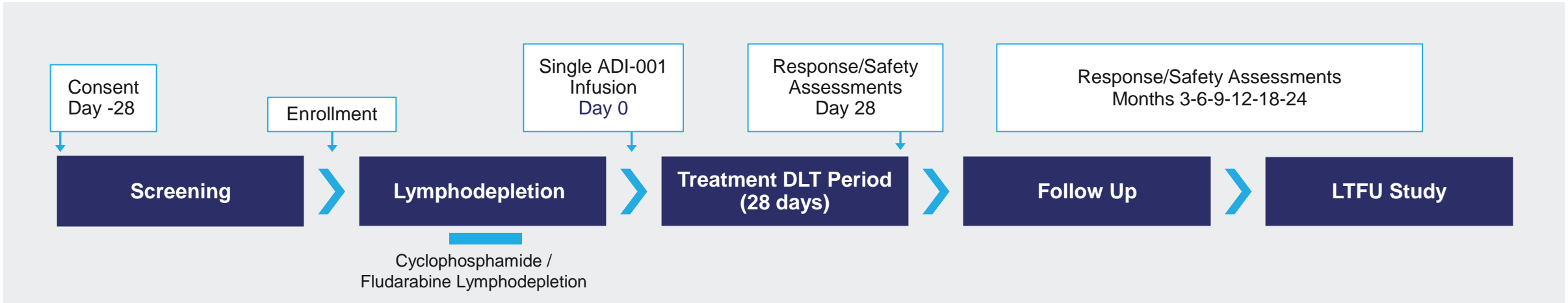
## Prioritized indications where:

- ADI-001 has the potential to materially impact patient outcomes
- Probability of success viewed favorably given validated role of B-cell depletion
- Opportunity to leverage expanding clinical footprint in rheumatology

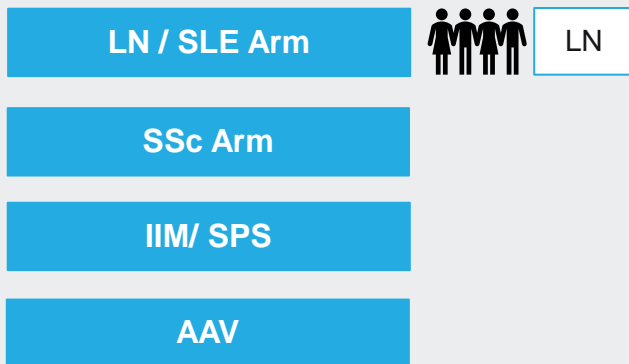
1. Helmick CG et al. Arthritis & Rheumatism (2008)  
2. Bairkdar M et al. Rheumatology (2021)  
3. Lundberg IE et al. Nature Reviews (2021)

4. Berti A et al. Arthritis & Rheumatology (2017)  
5. Ortiz JF et al. Cureus (2020); U.S. prevalence <1K  
6. Morales E et al. Nephron (2021)

# ADI-001: Phase 1 Autoimmune Study Design



## Part 1



3+3 design  
3E8 starting dose

## Part 2

Dose Expansion  
Cohorts

# ADI-001 Phase 1 Autoimmune Study Endpoints

## Primary Endpoints

Incidence of treatment-emergent adverse events (TEAEs), including severity, seriousness, and relatedness

Incidence of DLTs at each dose (in Part 1 only)

## Secondary & Exploratory Endpoints

Cellular Kinetics: Levels of ADI-001 cells in peripheral blood

Pharmacodynamics after treatment with ADI-001:

- Dynamics of B cell depletion and reconstitution
- Dynamics of host immune cell recovery in peripheral blood
- Autoantibody titers

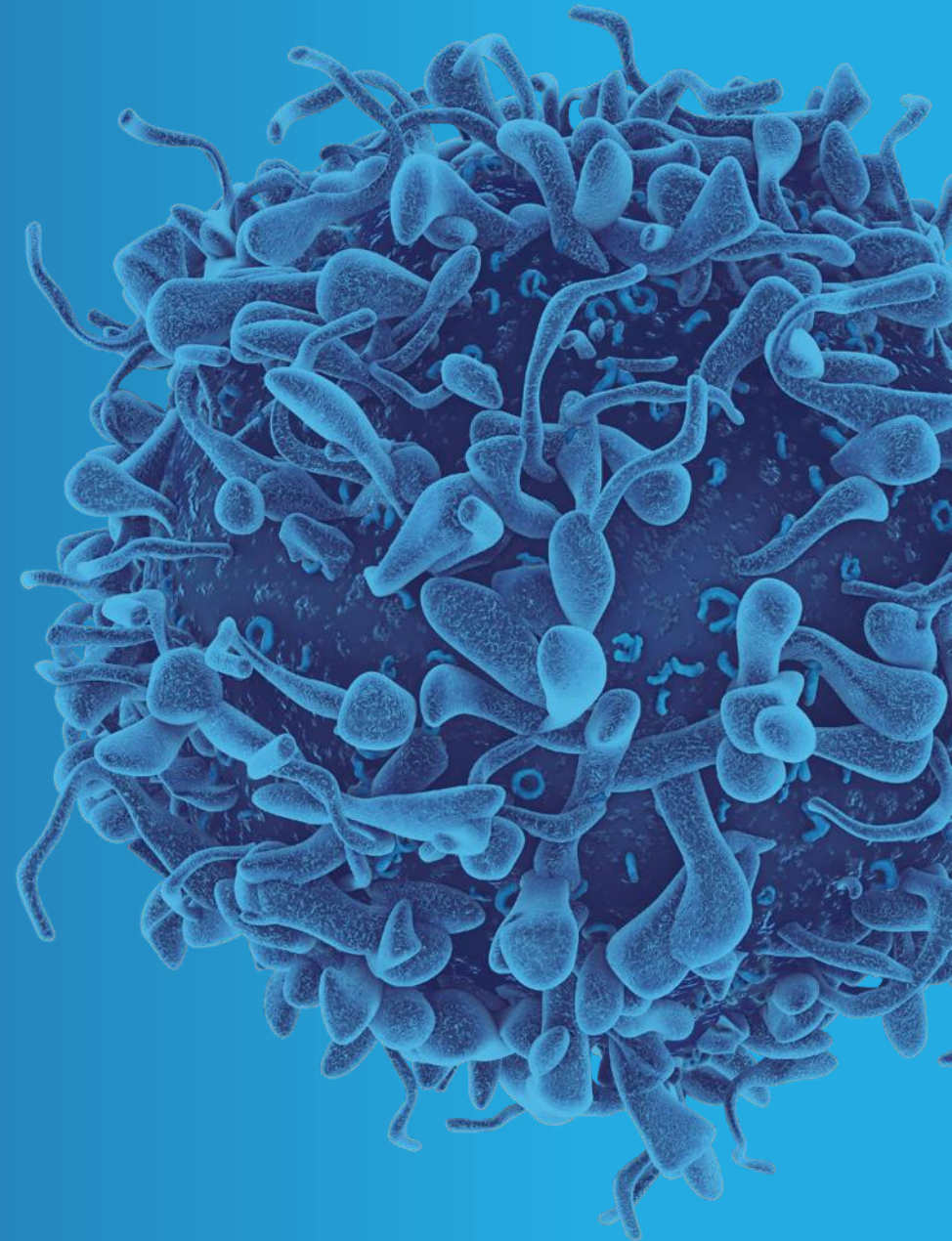
Efficacy endpoints:

- LN: CR/PR based on kidney function
- SLE: SLEDAI-2K/DORIS remission
- SSc: CRISS score, mRSS in diffuse cutaneous, FVC% predicted in ILD
- IIM: changes in MMT-8 and muscle enzymes, Total Improvement Score
- DM: CDASI
- SPS: Distribution of Stiffness Index, Timed 25 foot walk, Rankin scale
- AAV: CR per BVAS

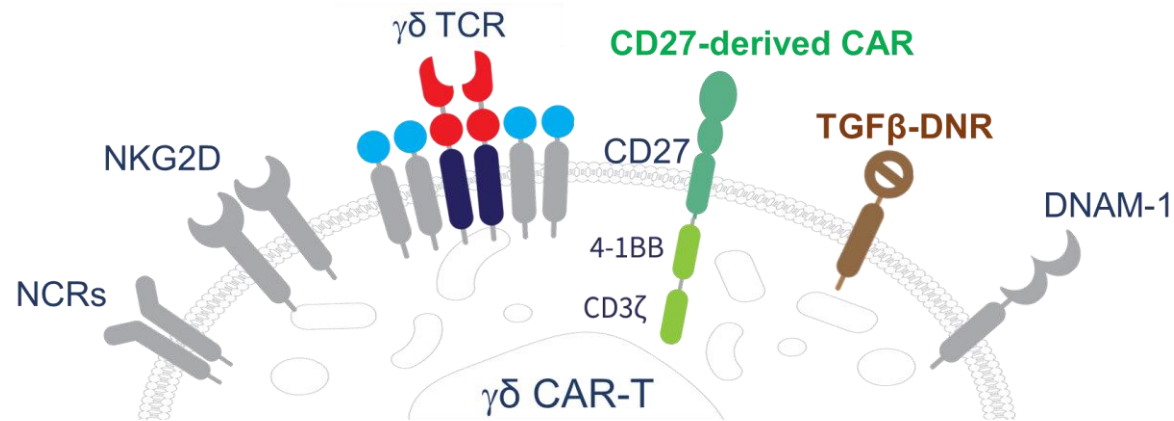


# ADI-270

## Renal Cell Carcinoma & Other CD70+ Diseases



# ADI-270: Designed to Address Multiple Refractory Cancers



## Enrolling RCC patients in Phase 1 study

- Fast Track Designation
- Clinical update 1H/2025

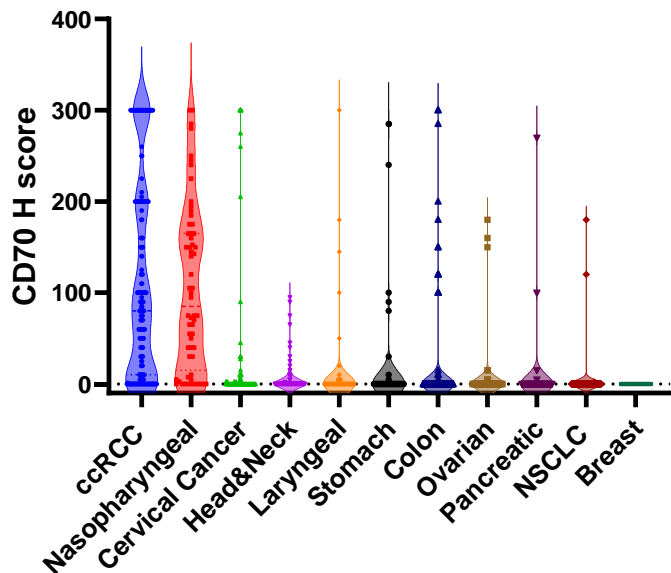
- CAR utilizes CD27 as binding domain; contains CD27 and 4-1BB costimulatory domains plus CD3 $\zeta$  (3<sup>rd</sup> gen)
- Inactive form of TGF $\beta$  receptor II to mitigate the immunosuppressive effects of TGF $\beta$  within the tumor microenvironment
- Host vs graft armoring against alloreactive activated CD70+ T cells to increase persistence
- Combines endogenous  $\gamma\delta$  innate and adaptive mechanisms to recognize and kill malignant cells

# CD70 is Expressed on Multiple Solid and Hematological Cancers with Limited Expression in Normal Tissues

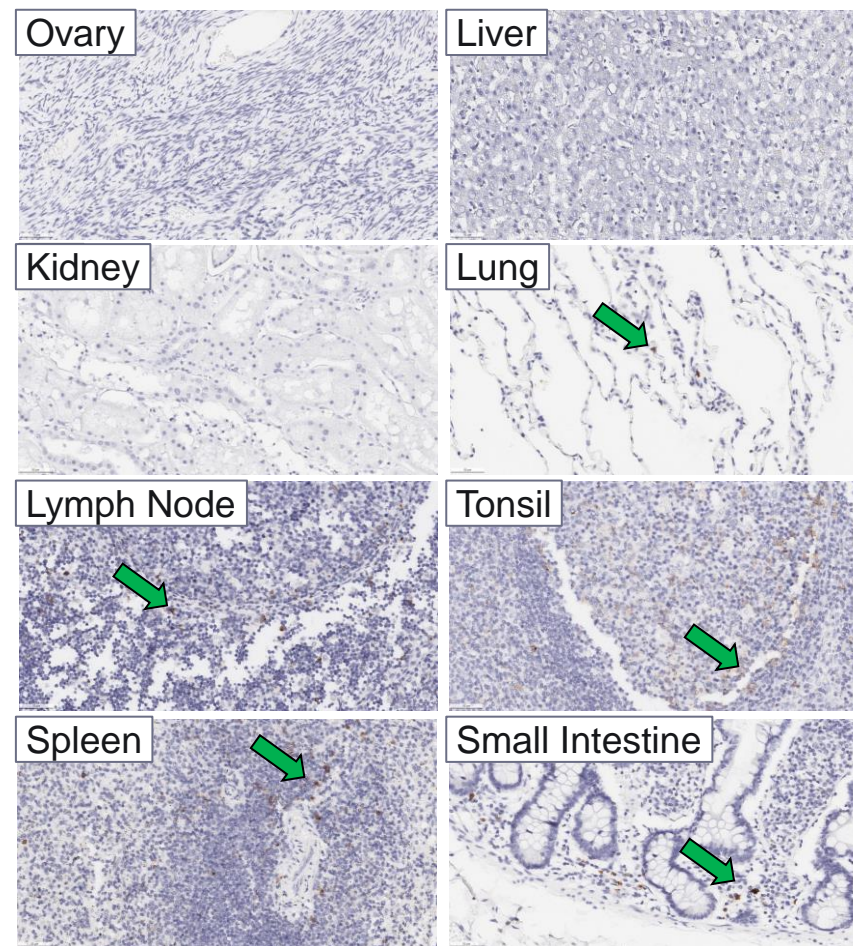
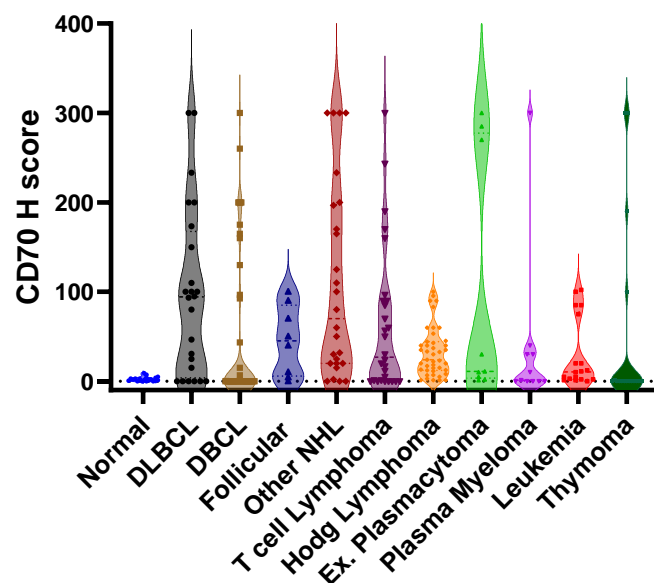
- High expression in multiple solid and heme malignancies
  - Beyond ccRCC and NPC, multiple solid tumors are of interest when paired with CD70 screening
- Minimal expression on normal tissues (activated lymphocytes)
- Target has clinical safety experience

Representative images from a normal tissue array stained for CD70

## Solid tumors

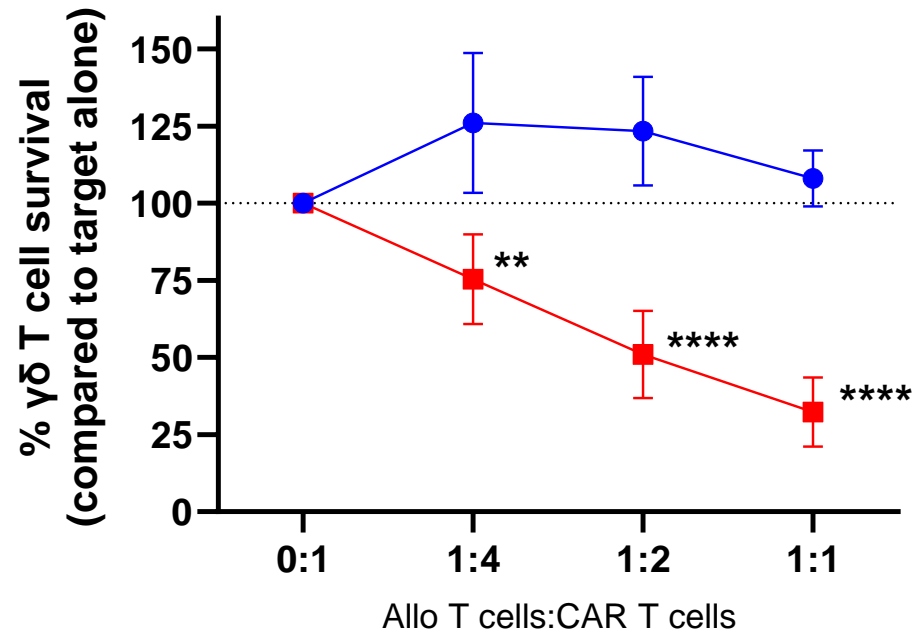


## Hematological malignancies



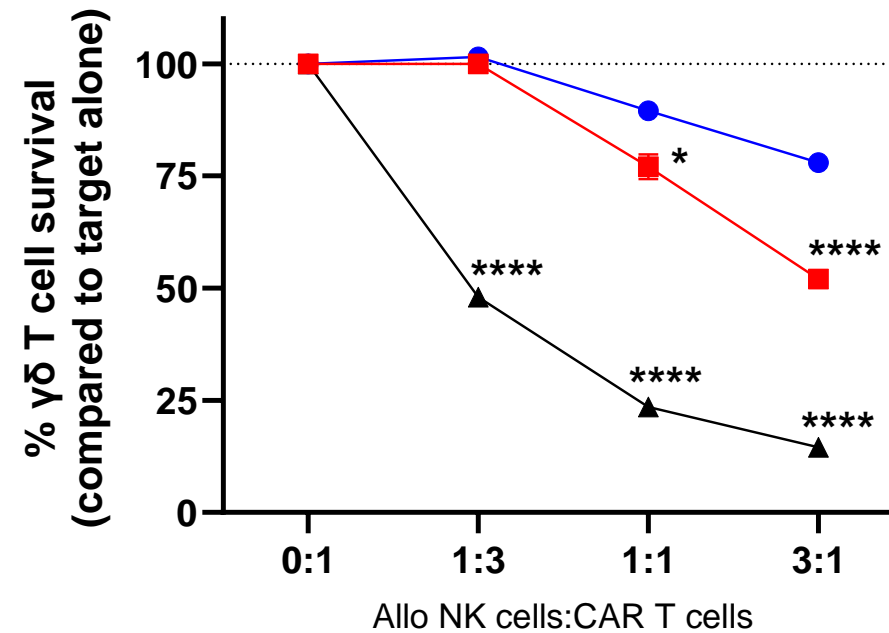
# ADI-270 May Be Less Susceptible to T and NK Rejection by Host

## CD70 targeting less susceptible to T cell rejection



- ADI-270 CAR T cells
- Control  $\gamma\delta$  CAR T cells

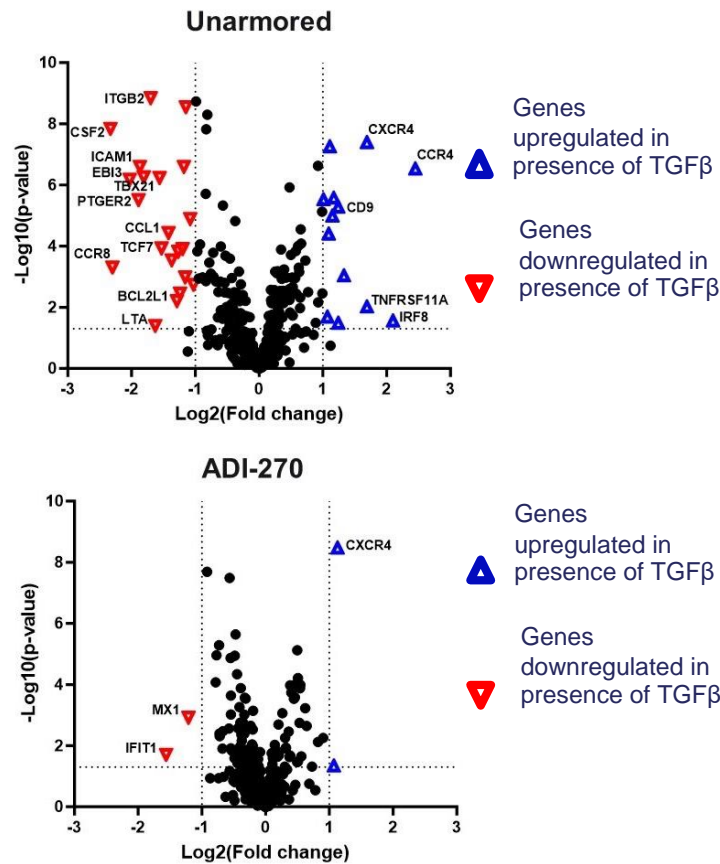
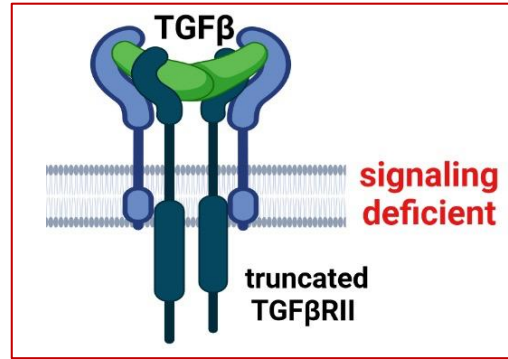
## $\gamma\delta$ CAR T cells less susceptible to NK rejection



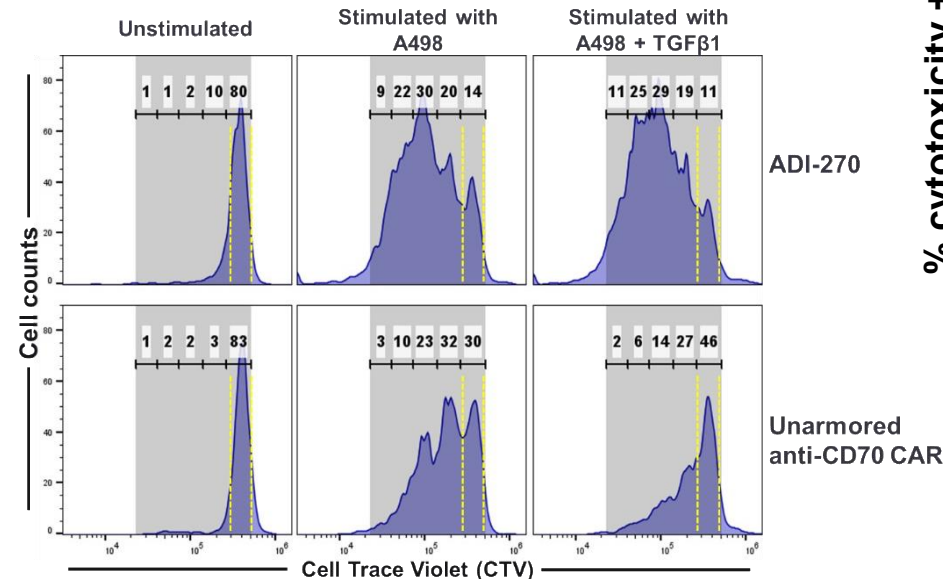
- $\gamma\delta$  CAR T cells
- $\beta 2M^{KO}$  HLA-E<sup>KI</sup> CAR T cells
- ▲  $\beta 2M^{KO}$  HLA-E<sup>neg</sup> CAR T cells

# ADI-270 is Resilient to the Inhibitory Effects of TGFβ

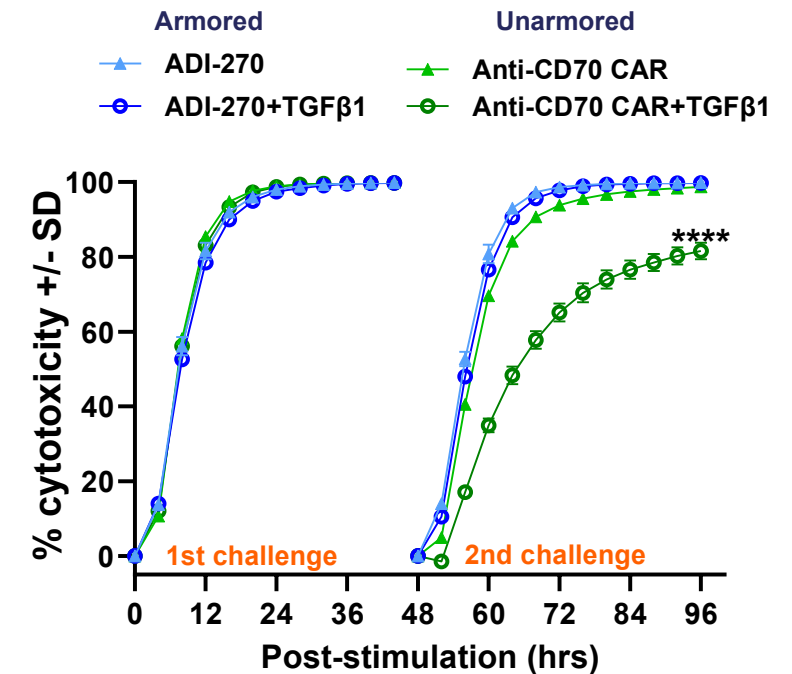
ADI-270 showed **resilience** to transcriptional changes driven by TGFβ signaling



ADI-270 maintained **proliferation** in the presence of TGFβ

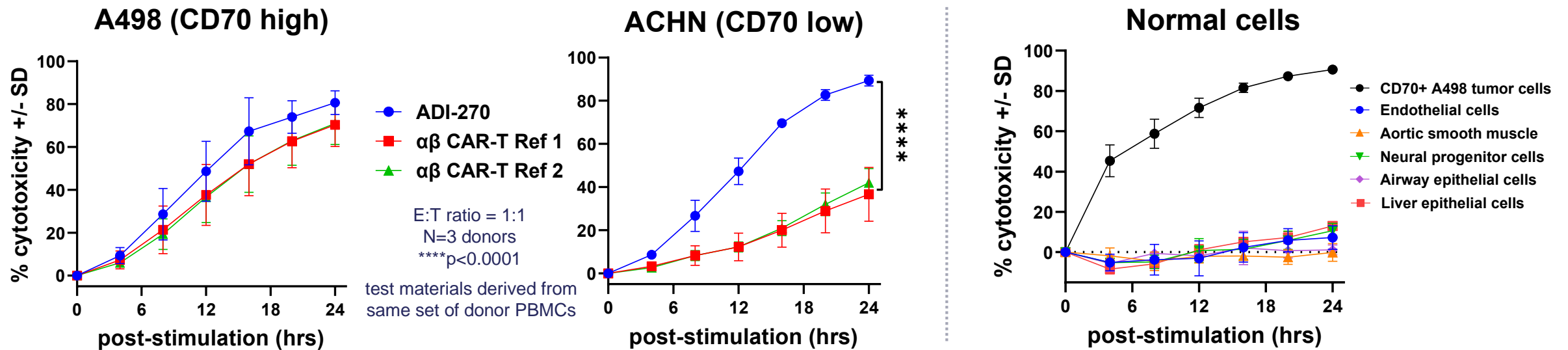
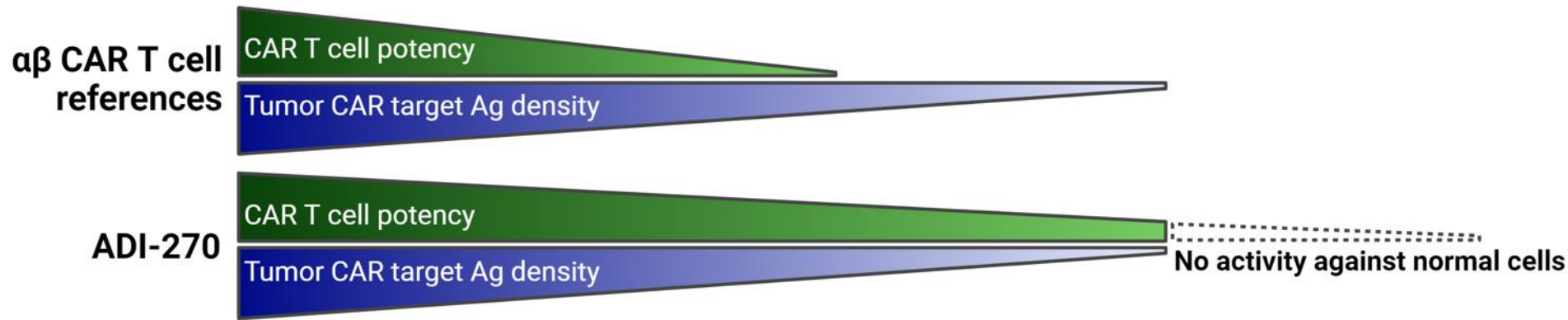


ADI-270 maintained **cytotoxicity** in the presence of TGFβ

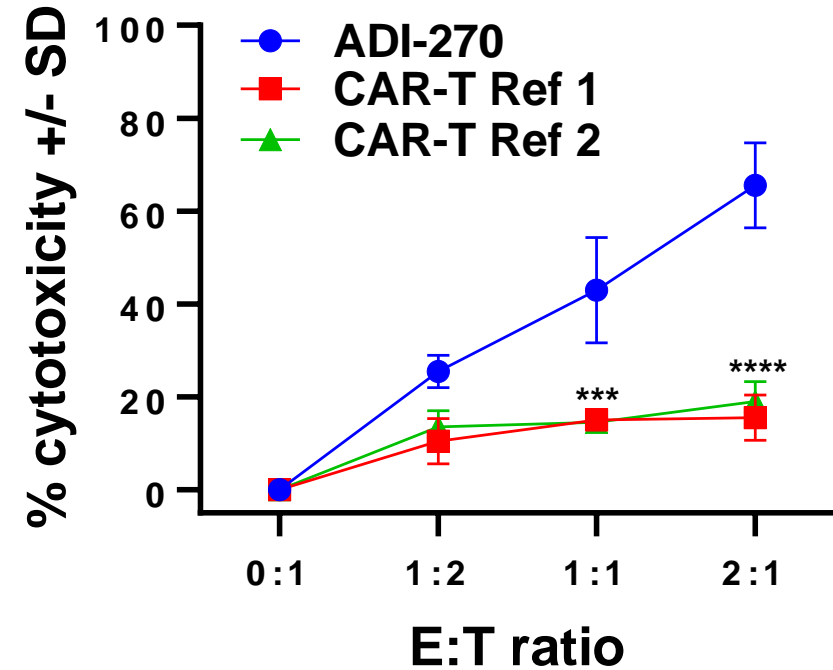
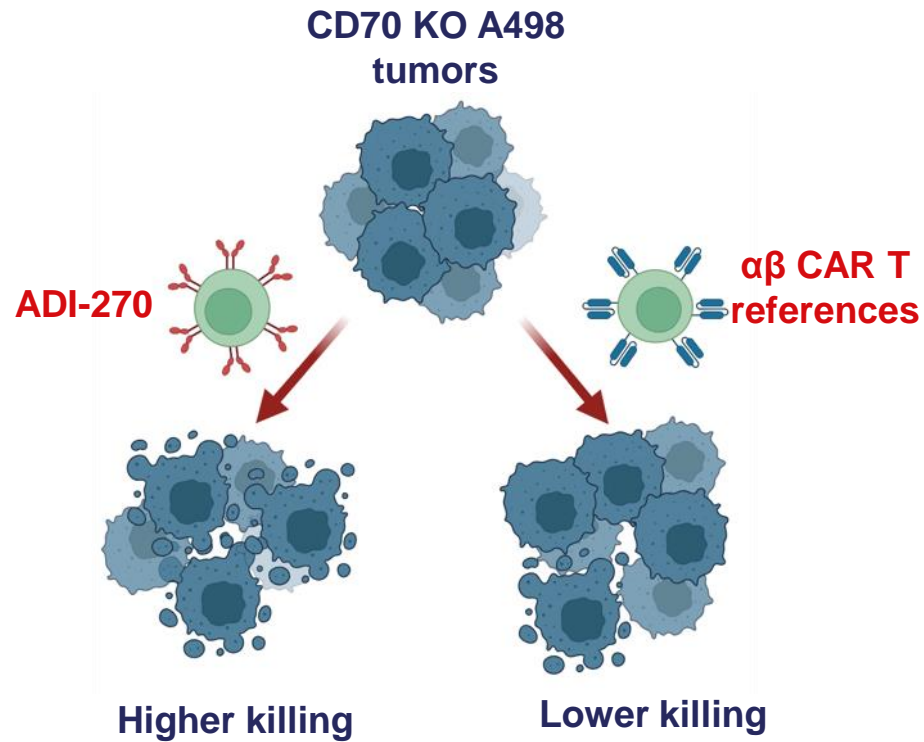




# ADI-270 Retained Potent Activity in the Context of CD70-Low Tumors Compared to Clinically Relevant CD70-Targeting $\alpha\beta$ CAR T Cell Benchmarks



# ADI-270 Demonstrated Higher Innate Cytolytic Activity Against CD70 Negative Tumor Cells Compared to CAR-T Cell References

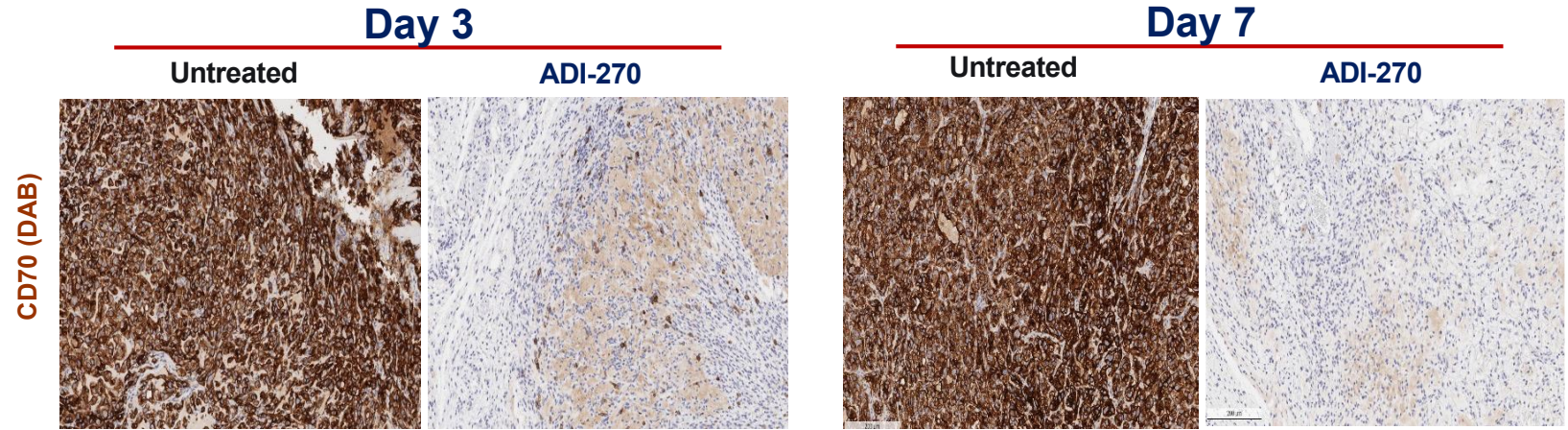
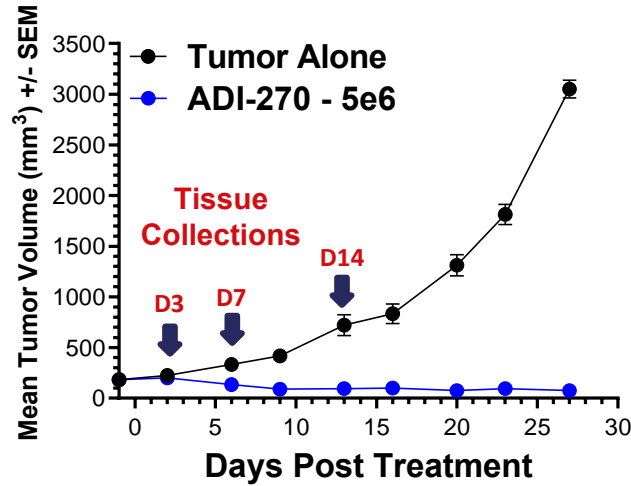


\*\*\*p<0.001, \*\*\*\*p<0.0001

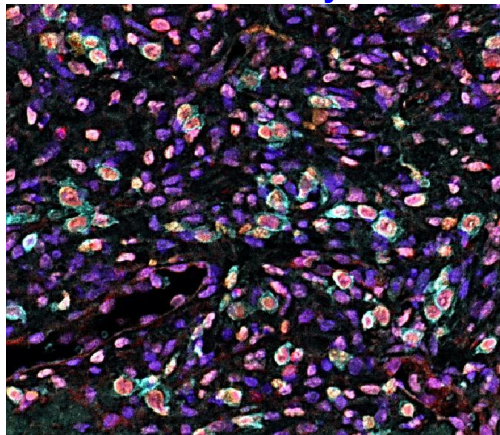
test materials derived from same donor PBMCs

# ADI-270 Demonstrated Rapid Homing, Activation and Killing Kinetics in ccRCC Xenografts Resulting in Tumor and Target Eradication

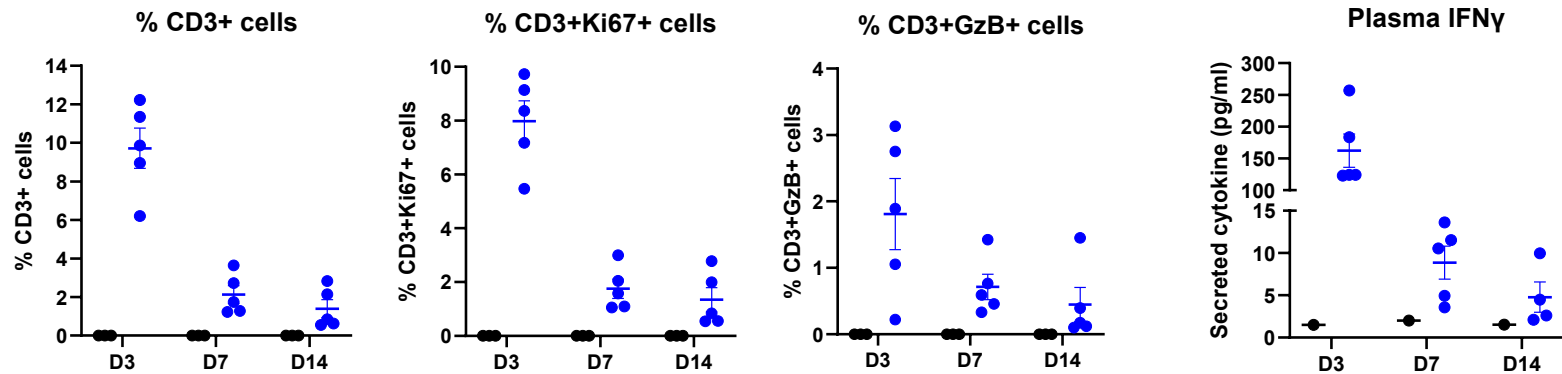
A single dose of ADI-270 showed potent efficacy in A498 tumors, rapidly eradicating CD70+ cells



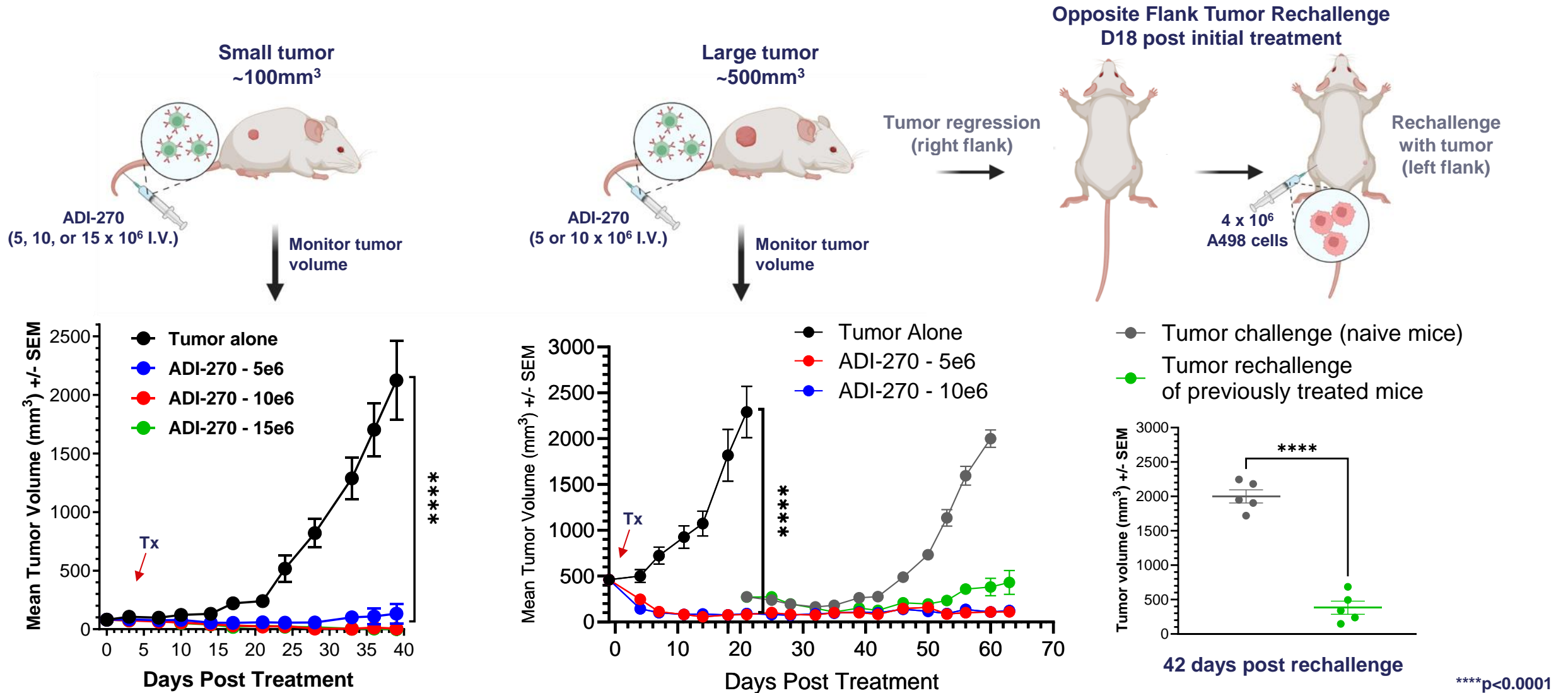
ADI-270 Day 3



ADI-270 infiltrates, proliferates, and has effector function as early as Day 3



# A Single Dose of ADI-270 Showed Potent Regression and Sustained Systemic Anti-Tumor Activity in ccRCC Xenograft Models



# Renal Cell Carcinoma: A Critical Unmet Need

## Substantial Addressable Patient Population

- **Kidney cancer incidence of ~80K in the US<sup>1</sup> and ~71K in the EU<sup>2</sup>, clear cell RCC (ccRCC) makes up approximately 80% of cases<sup>3</sup>**
- **High expression of CD70 in ccRCC (80%)** and expression is maintained in primary and metastatic disease<sup>4,5</sup>
- Approximately 25% of patients receive first-line systemic treatment for metastatic disease and of those approximately 50% will receive second-line therapy<sup>6,7</sup>

## Critical Unmet Need

- In the US approximately 14K deaths due to renal cancer in 2024<sup>1</sup>
- **5-year survival for stage IV kidney cancer ~ 15%<sup>8</sup>**

## Poor Treatment Options in Advanced Setting

- Therapies post early-line treatment options of VEGF TKI inhibitors and checkpoint inhibitors (CPI) offer limited benefit to patients
- Significant share of patients receive TKI combined with PD-1 in 1L setting
- **Post VEGF TKI and CPI therapies offer response rates of ~20% with mPFS of <6 months<sup>9,10,11</sup>**

1. SEER

2. Globocan

29 3. <https://www.cancer.gov/pediatric-adult-rare-tumor/rare-tumors/rare-kidney-tumors/clear-cell-renal-cell-carcinoma#:~:text=How%20common%20is%20ccRCC?,young%20adult%20kidney%20cancer%20cases>.

4. Adam PJ et al. Br J Cancer (2006)

5. Huang RR et al. Clin Genitourin Cancer (2024)

6. Mori K et al. Cancer Immunol Immunother (2020)

7. Stukalin I et al. Kidney Cancer (2018)

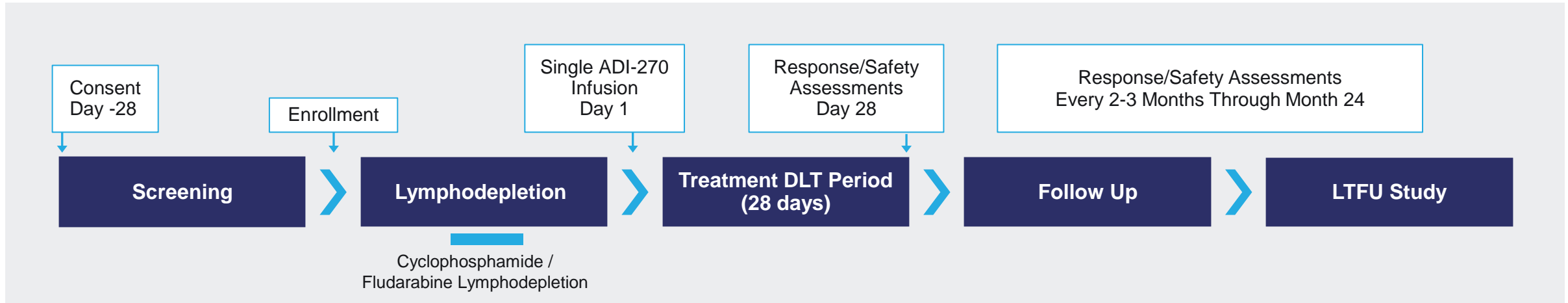
8. Cancer Research UK

9. Rini BI et al. Lancet oncology (2020)

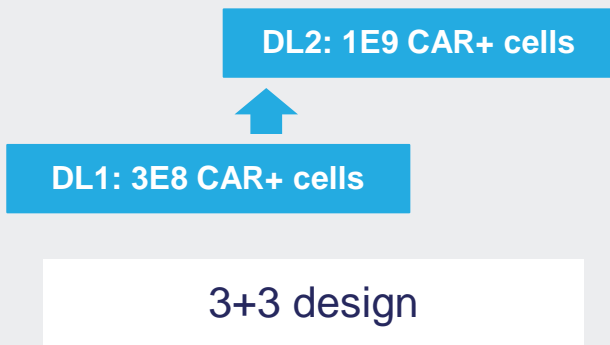
10. Albiges et al. ESMO 2023

11. FDA labels for tivozanib and belzutifan

# ADI-270 Phase I Study (CD70-dnTGFβ CAR+ γδ1 T cells)



## Dosing Arms:



## Primary endpoints:

- Number of DLTs
- Treatment emergent and treatment-related AEs

## Secondary endpoints:

- ORR, DCR, DOR, PFS, TTP, and OS
- PK, host immune cell recovery

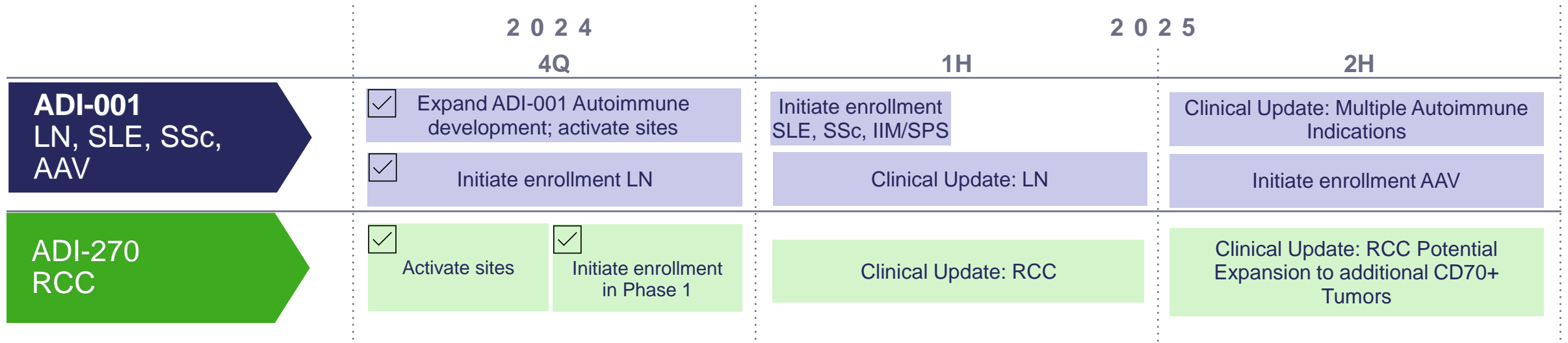
## Dose Expansion:

- RCC
- Other CD70+ tumors

# ADI-270 Summary

- ADI-270 represents potential evolution of  $\gamma\delta$  CAR T cell-based therapeutics
- CD27-based 3<sup>rd</sup> gen CAR demonstrated significant potency advantages<sup>1,2,3,4</sup>
- Armoring against TGF $\beta$  and alloreactive T cells confirmed and characterized preclinically
- Robust efficacy maintained across multiple relevant tumor models of varying stringency
- Desirable preclinical safety profile with lower potential for CRS and macrophage activation syndrome
- IND cleared and Fast Track Designation received for metastatic/advanced ccRCC
- Enrollment open in Phase 1 study; Preliminary clinical data expected 1H/2025

# Potential Near-Term Milestones



Cash and cash equivalents: ~\$202.1M (9/30/24)

Projected cash runway into 2H/2026





**Leaders in Developing Allogeneic  $\gamma\delta$ 1 CAR T Cell Therapies to Fight Autoimmune Diseases and Cancer**

