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Leaders in Developing Allogeneic γδ1 CAR T Cell Therapies to Fight Autoimmune Diseases and Cancer

γδ= Gamma delta; CAR= Chimeric antigen receptor

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Developing Broad Pipeline of Allogeneic γδ1 T Cell Therapies for Autoimmune Diseases and Cancer

Program	Target	Indication	Research	IND-Enabling	Clinical	Status
AUTOIMMMUNE DISEASES						
ADI-001	CD20	LN & SLE	●	●	●	IND Cleared Initiate LN Phase 1 Q3/2024 LN Fast Track Designation Initiate SLE Phase 1 H2/2024 Clinical update planned: H1/2025
		SSc	●	●	●	IND Cleared Initiate Phase 1 H2/2024 Clinical update planned: H1/2025
		AAV	●	●	●	IND Cleared Initiate Phase 1 H2/2024 Clinical update planned: H1/2025
ONCOLOGY						
ADI-270	CD70 (TGFβ-DNR)	RCC & Other ST / Heme	●	●	●	IND cleared RCC ccRCC Fast Track Designation Initiate RCC Phase 1 Q4/2024 Clinical update planned: H1/2025
ADI-xxx	PSMA (w/ Armor)	mCRPC	●	○	○	Preclinical activities

ccRCC= Clear cell renal cell carcinoma; IND= Investigational new drug; mCRPC= Metastatic castration-resistant prostate cancer; PSMA= Prostate specific membrane antigen; ST= Solid tumor

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Adicet Bio Leadership Team

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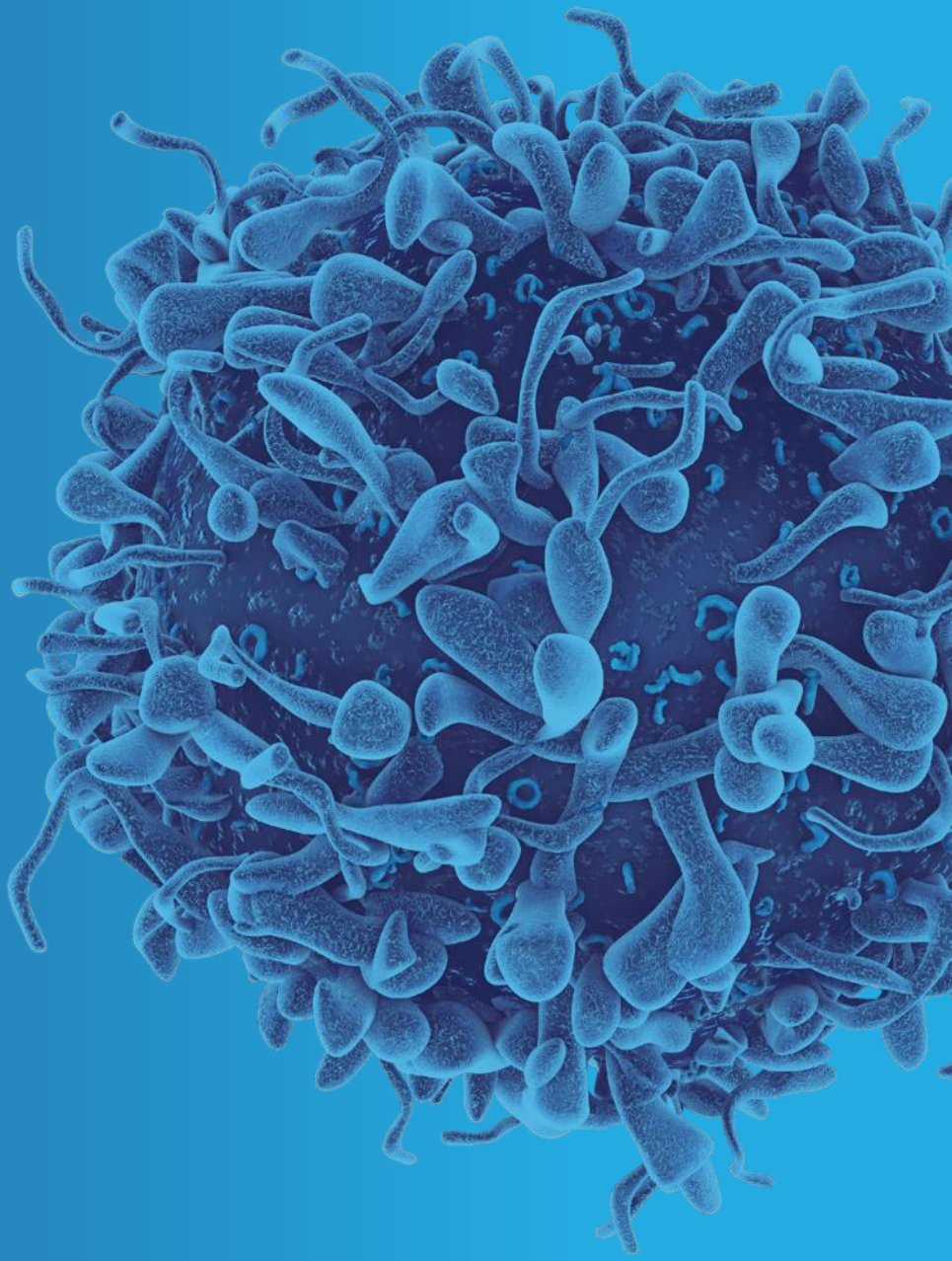
ADI-001
Autoimmune Diseases



Adicet γδ1 CAR T Cell Therapy For Autoimmune Indications

ADI-001 Data in NHL Provides Strong Foundation for Future Development in Autoimmune Diseases

Exposure Consistent with Approved Autologous CAR T (Cmax, Day 28 Persistence and AUC)

No Significant Risk of CRS, ICANS, or T cell Malignancies Compared to Autologous CAR T*

B-Cell Depletion Consistent with Autologous CD19 CAR T in SLE, SSc and IIM

Readily Available, "Off-the-Shelf"

Preferentially Trafficking to Organs/ Tissues

Potential to Dose in Community Setting

AUC= Area Under the Curve; Cmax= Peak plasma concentration; CRS= Cytokine release syndrome; ICANS= Immune effector cell-associated neurotoxicity syndrome; IIM= idiopathic inflammatory myopathy; SLE= systemic lupus erythematosus; SSC= systemic sclerosis

* ADI-001 May 4, 2023 Data-cut date, n=24 evaluable patients

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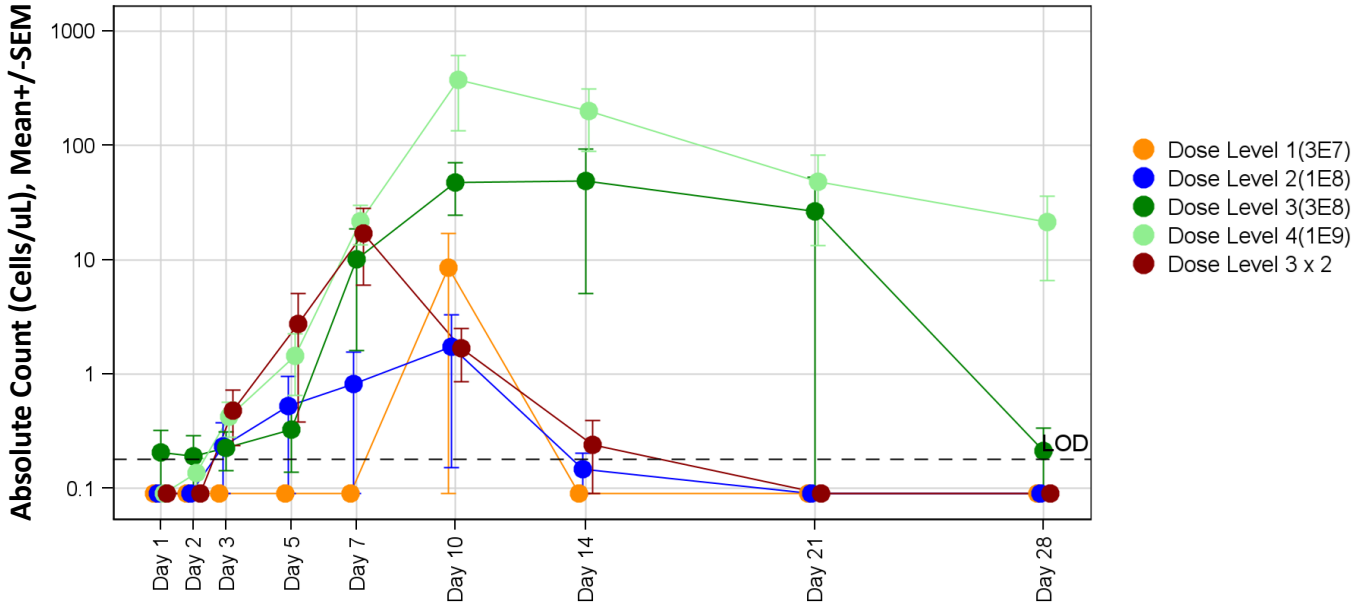
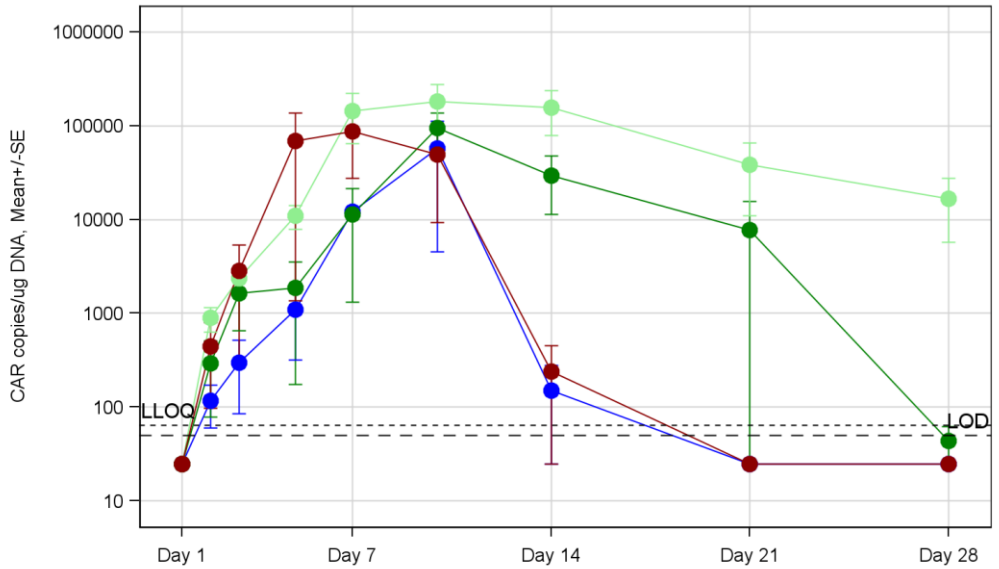
ADI-001's Cmax, D28 Persistence and AUC Are Consistent with Values Reported for Approved Autologous CD19 CAR T[1]

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
DL4	363.80	201,666	26.51	16,553
DL3	56.34	98,177	0.04	44

[1]Badbaran, A. Cancers 2020;12, 1970; Locke et al. N Engl J Med 2022; 386:640-654; Neelapu et al. N EnglJ Med. 2017;377:2531-2544; Ogasawara et al. Clin Pharmacokinet 60, 1621–1633 (2021)
D28= Day 28

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ADI-001 in Autoimmune Diseases: B-Cell Depletion Consistent with Autologous CD19 CAR T in SLE Academic Studies

B-cell Depletion

- B-cell depletion data from ADI-001 trial in NHL mirrored experience of autologous CD19 CAR T in SLE[1,2]
- B-cell depletion via CD20 targeting validated by CD20-targeted antibody (obinutuzumab) which demonstrated efficacy on top of SOC in lupus nephritis in a Phase II clinical study[3]

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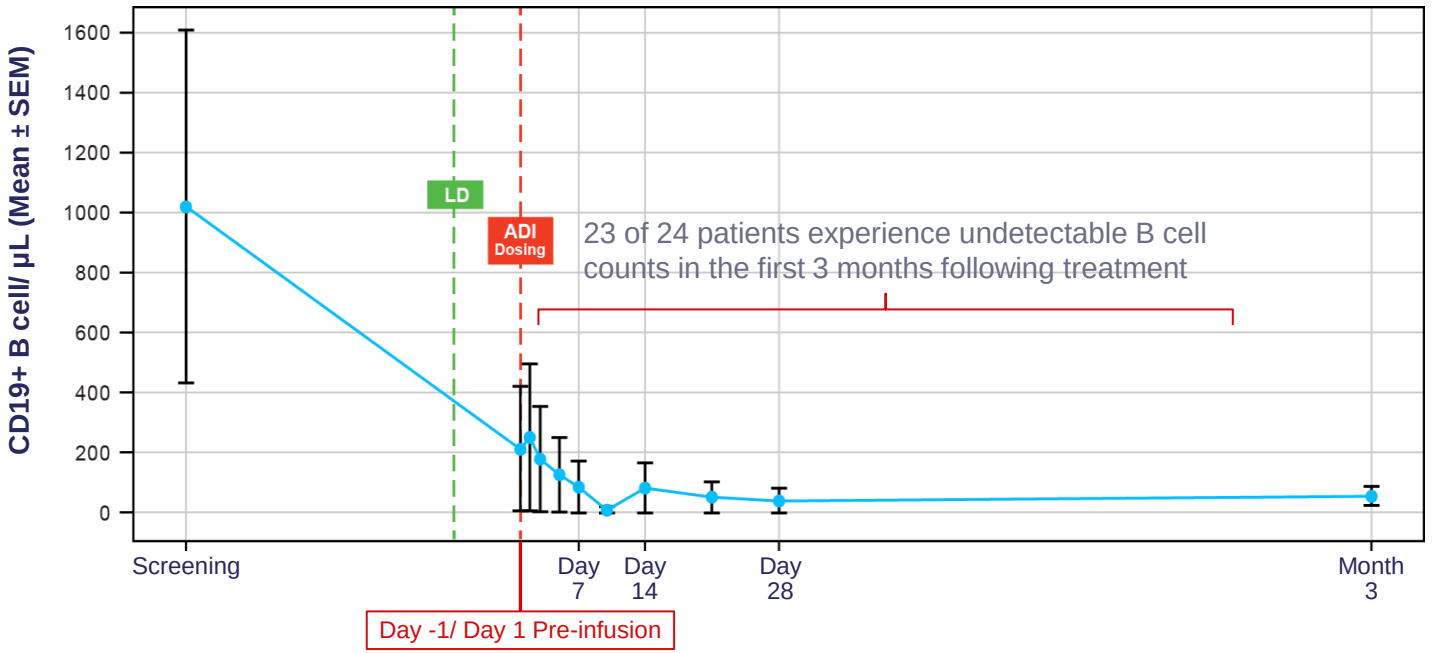
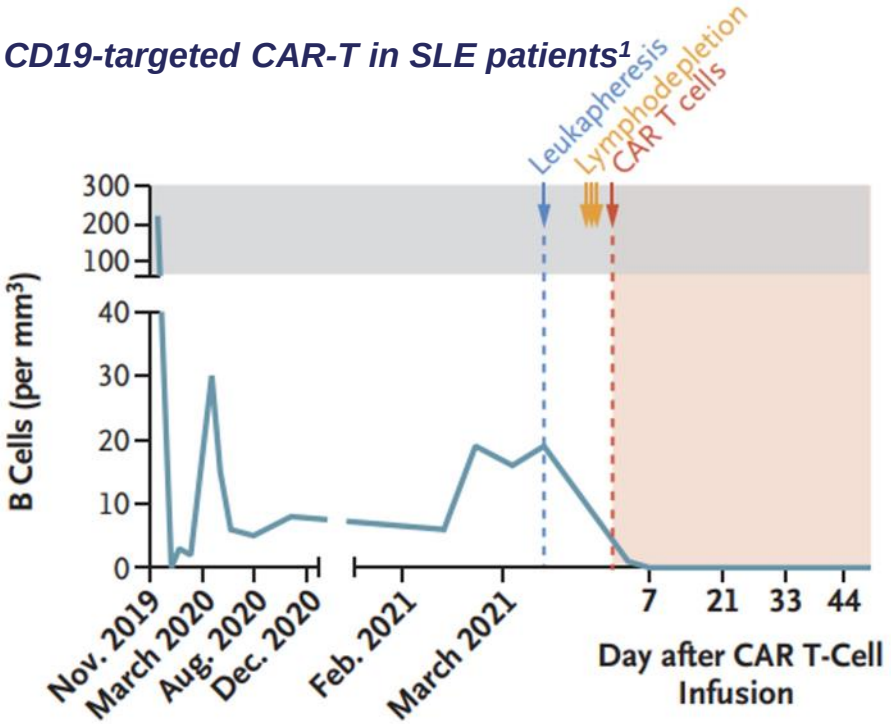
CD20-targeted, ADI-001, in B-NHL patients[4]



CD19-targeted CAR-T in SLE patients[1]



1. Mougiakakos MD et al. NEJM 2021
2. Mackensen A et al. Nature Medicine 2022
3. Furie RA et al. Ann Rheum Dis. 2022
4. Adicet internal data

SOC= Standard of care

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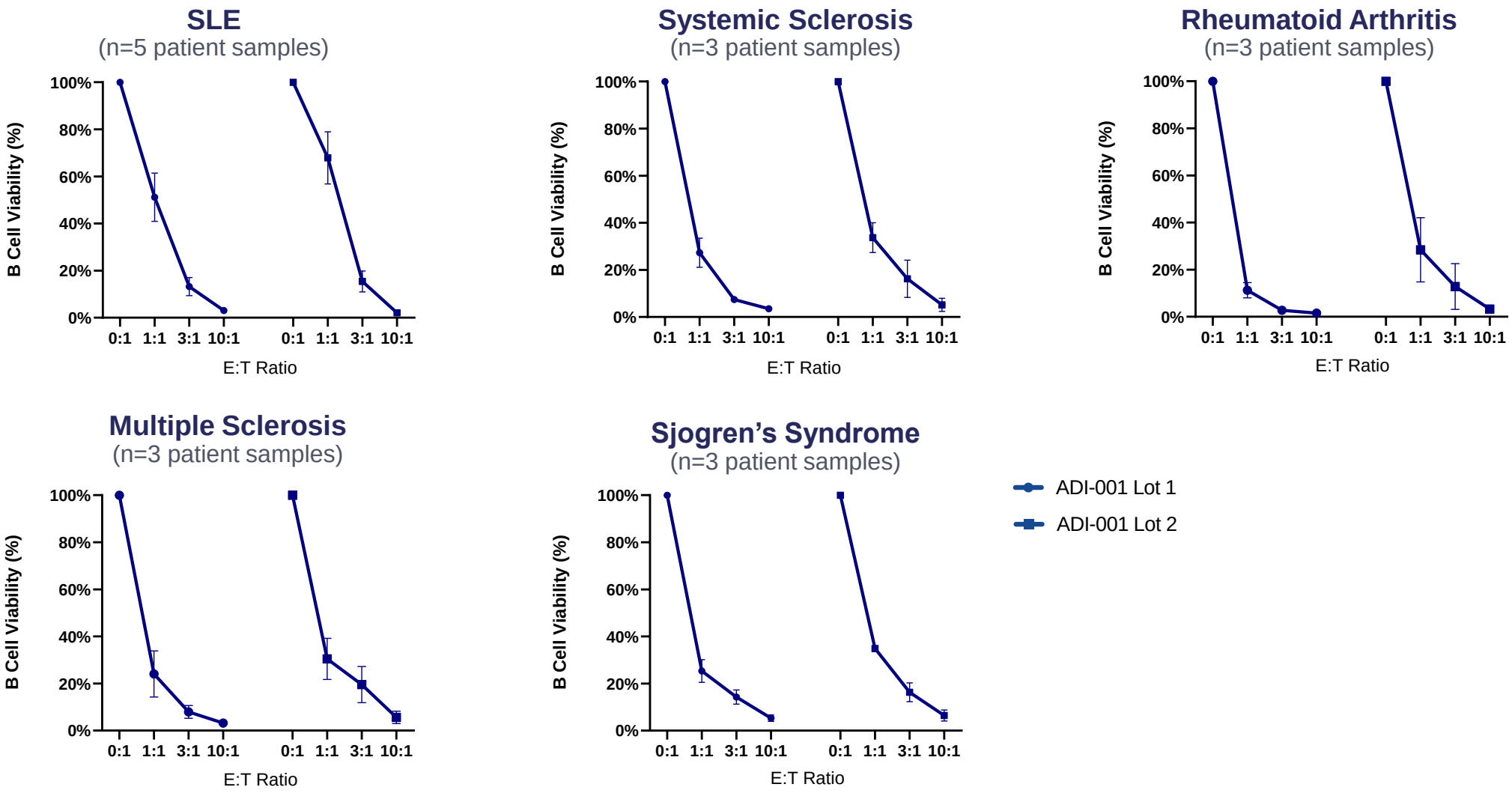
ADI-001 Exhibited Potent Killing of Patient-Derived CD19+ B Cells in Multiple Autoimmune Diseases



B cells from 5 SLE patients and 3 patients each for SSc, RA, Multiple sclerosis, and Sjosgren'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.

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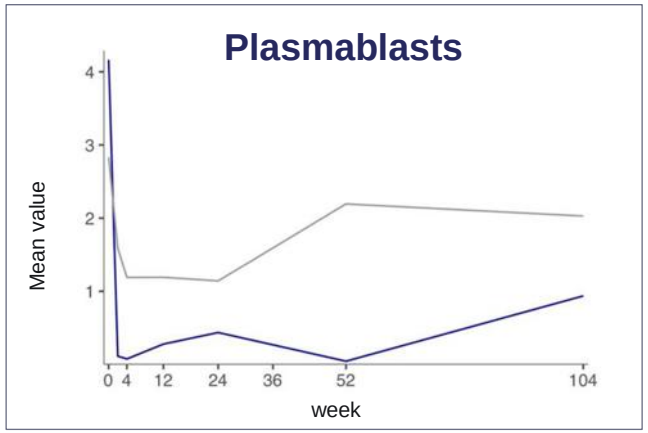
CD20 Targeting With Obinutuzumab Depleted B Cells in Blood Including Plasmablasts, Memory B Cells, and Naïve B-Cells in LN Patients

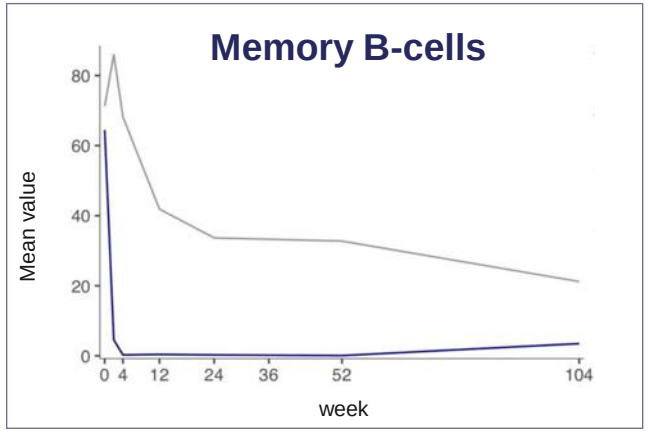
CLINICAL SCIENCE

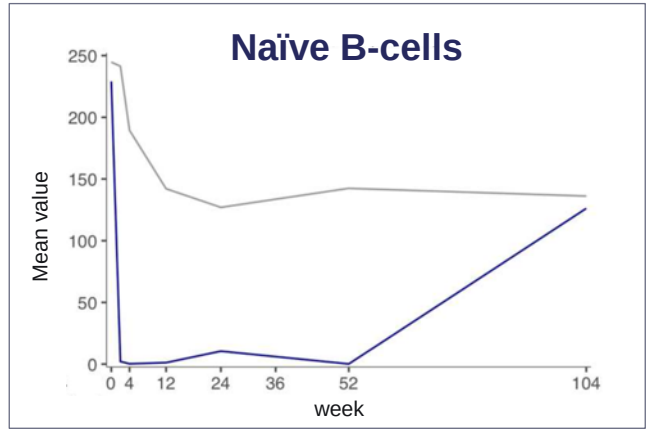
B-cell depletion with obinutuzumab for the treatment of proliferative lupus nephritis: a randomised, double-blind, placebo-controlled trial

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

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







— 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

1. Furie RA et al. Ann Rheum Dis (2022)
2. Reddy VR et al. Rheumatology (2022)
3. Kamburova EG et al. American Journal of Transplantation (2013)

Memory B-cells: $CD45^+$, $CD19^+$, $CD27^+$
Naïve B-cells: $CD45^+$, $CD19^+$, IgD^+, $CD27^-$, $CD38^{dim/-}$
Plasmablasts: $CD45^+$, $CD19^+$, $CD27^+$, $CD38^{bright}$

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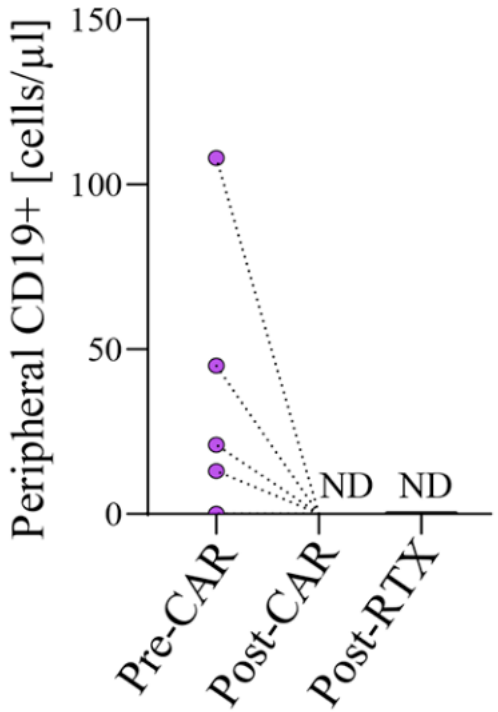
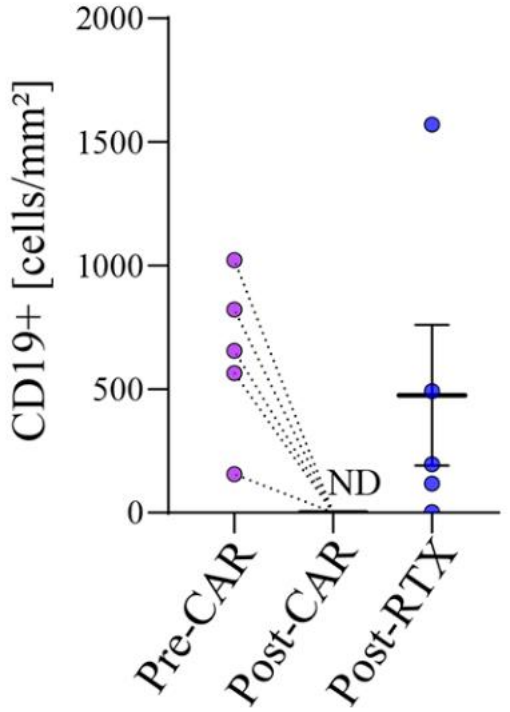
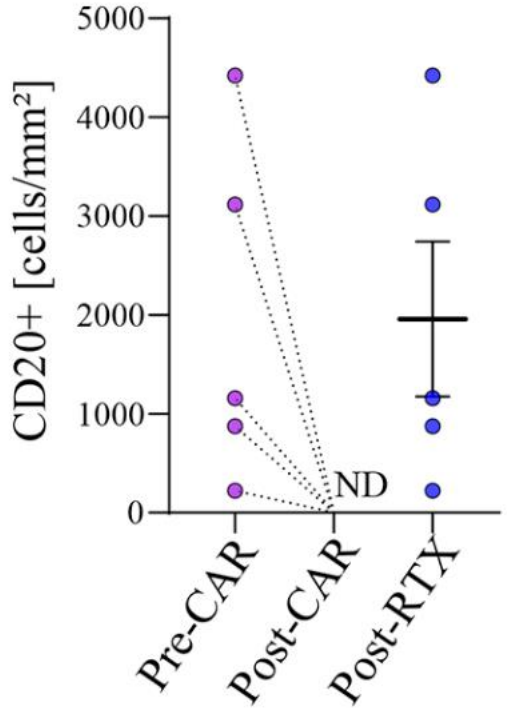
CAR T Cell Therapy But Not Antibody-Based Therapies Led to Complete Depletion of B Cells from Lymph Nodes in Autoimmune Patients



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





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

Tur C, et al. Ann Rhum Dis 2024
ND= Non detectable; RTX= Rituximab

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Update: ADI-001 Phase 1 Study in Mantle Cell Lymphoma

- Closed MCL clinical study to prioritize autoimmune disease indications; reported topline results:

ADI-001 Efficacy Summary across all doses in Evaluable Patients as of 8/22/24

Median Prior Lines of Therapy (% post CAR T)	ORR (%)	CR Rate (%)	Median Durability of Complete Response
3 (30%)	**8/10 (80%)**	**6/10 (60%)**	**17.5 months**

- Demonstrated favorable safety and tolerability profile
- Heavily pre-treated patients: median 3 prior lines of therapy; 30% prior CAR T
- No occurrences of GvHD; low incidence of Grade ≥3 CRS, neurotoxicity - compared favorably to autologous CD19 CAR T in MCL

August 22, 2024, n=10 evaluable patients.
CR= Complete response; GvHD= Graft-versus-host disease; MCL= Mantle cell lymphoma; ORR= Overall response rate

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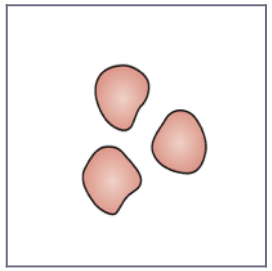
γδ1 T Cells Preferentially Traffic to Solid Tissues: Addressing a Source of Resistance to Antibody Therapies



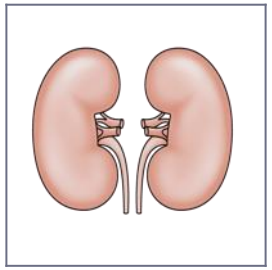
lymph node[1,2]

CD27+

CD62L+

Vδ1+ ↑↑

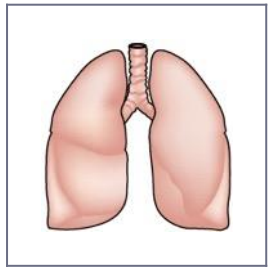
Vδ2+ ↓↓



kidney[3]

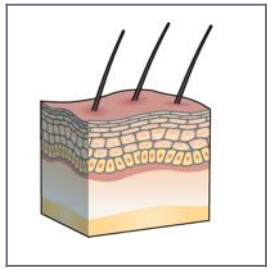
tissue: **>3X** γδ vs αβ

~3X more **Vδ1 vs Vδ2+**



lung[4]

issue/blood: **9X**

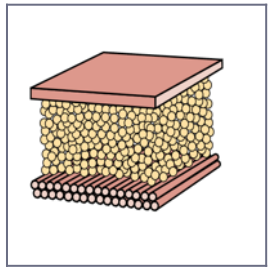


skin[5]

tissue/blood: **8X**

bone marrow[6]

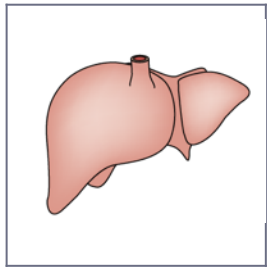
tissue/blood: **4X**



breast[7]

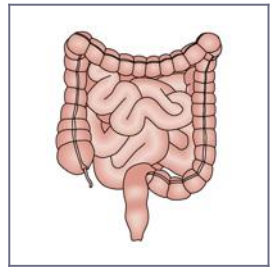
tissue/blood: **~15X**

adipose tissue/blood: **9X**



liver[8]

tissue/blood: **3X**



GI[9]

tissue/blood: **11X**

Ratios empirically calculated or approximated from proportion of %CD3 from literature reports in relative compartment[3,6]

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

[1]Davey et al Trends Immunol (2018)
[2]Uger et al Sci Rep (2018)
[3]Rancan et al Nat Immunol (2023)
[4]Wisnewski et al Am J Respir Cell Mol Biol (2000)
[5]Toulon et al J Exp Med (2009)
[6]Brauneck et al Front Med (2021)
[7]Wu et al Sci Transl Med (2019)
[8]Melo et al Clin Immunol (2021)
[9]Deutsch et al Eur J Immunol (1991)

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ADI-001 in Autoimmune Diseases: B-Cell Depletion Consistent with Autologous CD19 CAR T

"Off-the-Shelf" with Advantageous Tissue Tropism and Safety Profile

B-cell depletion

- B-cell depletion data from ADI-001 trial in NHL mirrors experience of autologous CD19 CAR T in SLE, systemic sclerosis and idiopathic inflammatory myopathy (IIM)[1,2]
- B-cell depletion in peripheral blood via CD20 targeting validated by CD20-targeted antibody (obinutuzumab) which demonstrated efficacy on top of SOC in lupus nephritis in Phase II clinical study[3] and Rituximab[8]

γδ1 T cell homing to tissues of interest

- Inability to deplete tissue-resident B cells in secondary lymphoid organs or other tissues is a contributing reason for failure of targeted agents in lupus[4,5,6,8]
- γδ1 T cells preferentially traffic to organs/tissues[7] and may be ideally suited to deplete B cells in secondary lymphoid organs, kidneys and other organs

Favorable safety profile

"Off-the-shelf"

- No significant risk of CRS, ICANS or T cell malignancies compared to autologous CAR T*
- ADI-001 is an "off-the-shelf" investigational therapy potentially well suited for autoimmune diseases
  - Ability to dose in community setting, lower COGs, faster turnaround time

1. Mougiakakos MD et al. NEJM 2021
2. Mackensen A et al. Nature Medicine 2022
3. Furie RA et al. Ann Rheum Dis. 2022
4. Kamburova EG et al. American Journal of Transplantation 2013
5. Reddy VK et al. Rheumatology 2022
6. Sadun RE and Foster MH AJKD 2019
7. Zhang, PJ Hematol Oncol 2023
8. Tur C, et al. Ann Rhum Dis 2024

COGs= Cost of goods

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Opportunity to Address Unmet Needs in a Large Number of B-Cell Mediated Autoimmune Diseases

- POC for CAR-T mediated B-cell depletion demonstrated in multiple autoimmune diseases
  - Lupus and lupus nephritis[1,2,3]
  - Systemic sclerosis[2]
  - Idiopathic inflammatory myopathies[2]
  - Myasthenia gravis[4,5]
- B-cell depletion via CD20 antibodies (i.e., rituximab, obinutuzumab) further validate the therapeutic approach in several of these diseases
- Deep B-cell depletion in the tissues and secondary lymphoid organs highly desirable for therapeutic success

Potential autoimmune diseases for development* & U.S. prevalence

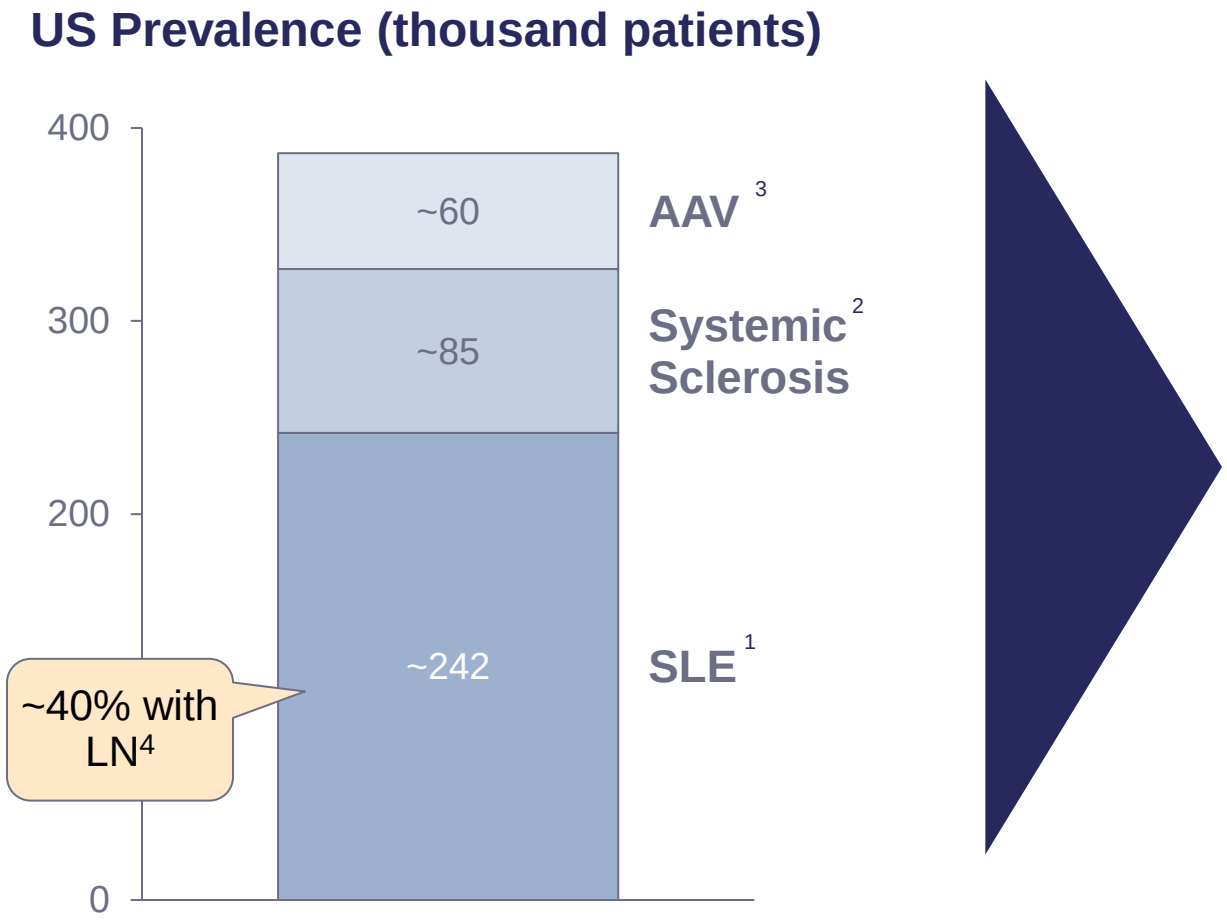
Lupus nephritis **~150K**	SLE **~160-410K**	MS **>900K**	Moderate to severe RA **>1M**
Myasthenia gravis **~36-60K**	ANCA+ vasculitis **~40-75K**	Sjogren's **~260K**	Membranous nephropathy **~70-90K**
NMOSD **~20K**	Pemphigus vulgaris **~19K**	Systemic sclerosis **~68K**	IIM **~60-70K**

**Not an exhaustive list*

1. Mackensen A et al. Nature Medicine 2022
2. CD19.CAR-T Cell in Refractory Systemic Autoimmune Diseases: A Monocentric Experience from the First Fifteen Patients. ASH 2023
3. YTB323 Poster @ American College of Rheumatology Convergence November 2023
4. Haghikia A et al. Lancet Neurology 2023
5. Granit V et al. Lancet Neurology (2023)

ANCA = Antineutrophilic cytoplasmic antibody; NMOSD= Neuromyelitis optica spectrum disorder; MS= Multiple sclerosis; POC= Proof of concept; RA= Rheumatoid arthritis

Expanding ADI-001 Autoimmune Development: SLE, SSc and AAV



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. Berti A et al. Arthritis & Rheumatology (2017)
4. Morales E et al. Nephron (2021)

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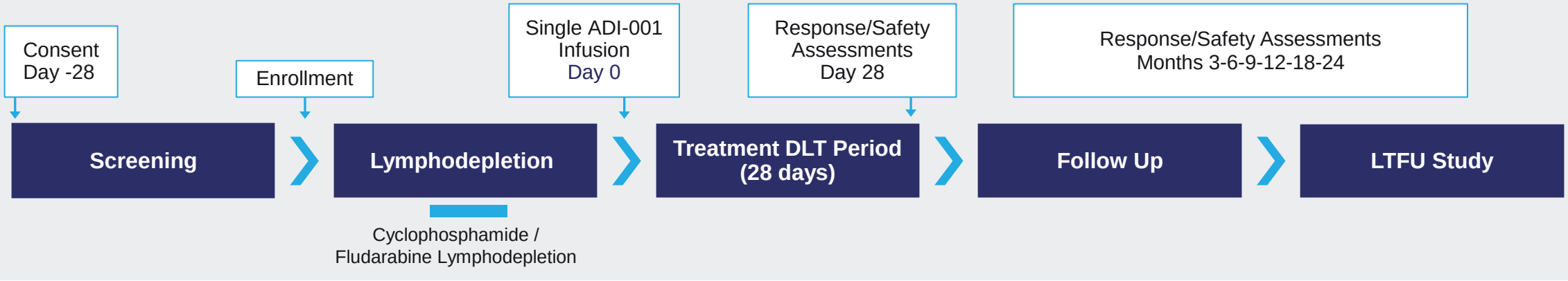
ADI-001: Phase 1 Autoimmune Study Design



Part 1

- LN / SLE Arm
- SSc Arm
- AAV Arm

3+3 design
3E8 starting dose

Part 2

Dose Expansion Cohorts

Some patients may be initially dosed with 1E8 until amendment for starting dose of 3E8 becomes effective; For each indication starting dose is 3E8 with potential to escalate up to 1E9 (based on 3+3 design) or de-escalate down to DL1 of 1E8 (in all cases CAR+ cells); LTFU= Long term follow up

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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
- Disease activity score: SLE (SLEDAI-2K/DORIS remission), LN (CR/PR based on kidney function), SSc (CRISS score, mRSS in diffuse cutaneous, FVC% predicted in ILD), AAV (CR per BVAS)

DORIS = definition of remission in systemic lupus erythematosus; SLEDAI-2K = systemic lupus erythematosus disease activity index 2000; CR/PR = complete/partial response; CRISS = American College of Rheumatology Composite Response Index in Systemic Sclerosis; mRSS = modified Rodnan Skin Score; FVC% predicted = percent predicted forced vital capacity; BVAS = Birmingham Vasculitis Activity Score

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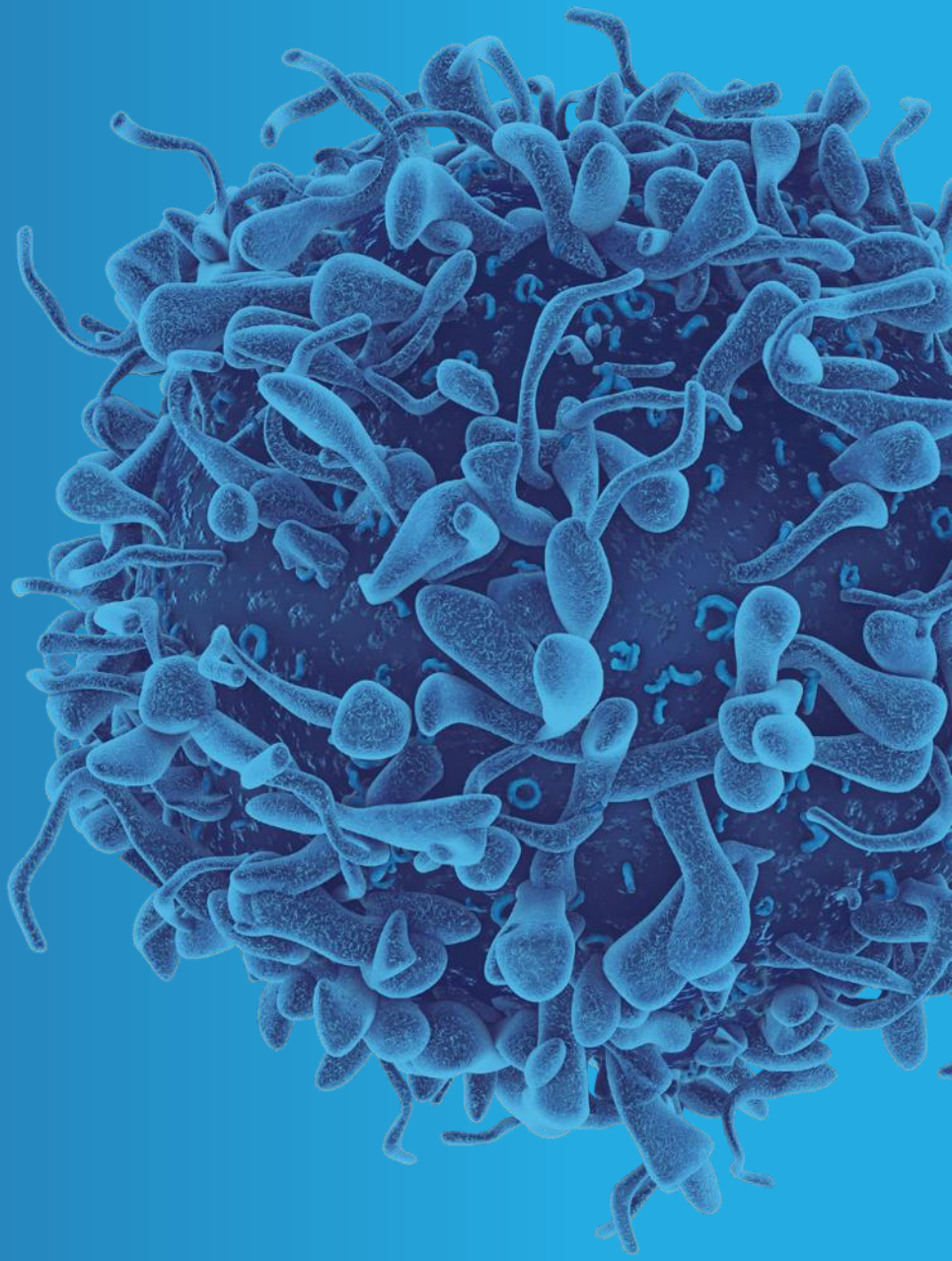
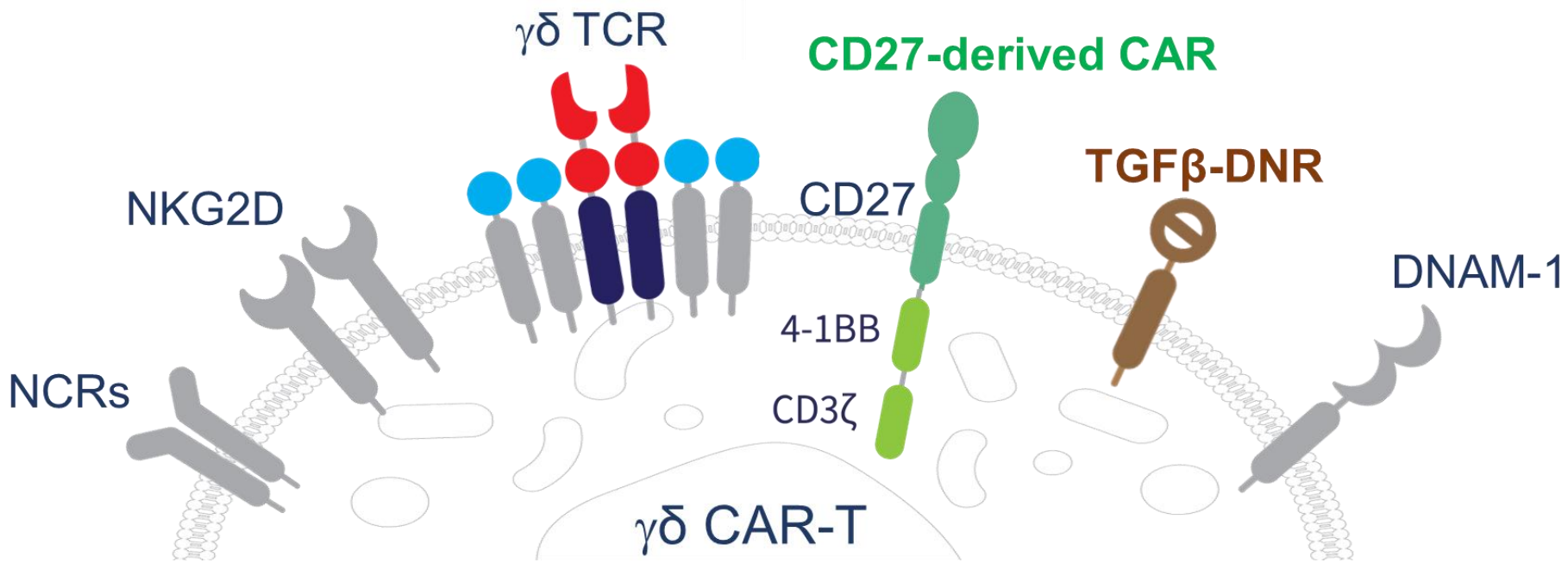
ADI-270
Renal Cell Carcinoma & Other CD70+ Diseases



ADI-270: Designed to Address Multiple Refractory Cancers



- CAR utilizes CD27 as binding domain; contains CD27 and 4-1BB costimulatory domains plus CD3ζ (3rd gen)
- Inactive form of TGFβ receptor II to mitigate the immunosuppressive effects of TGFβ within the tumor microenvironment
- Host vs graft armoring against alloreactive activated CD70+ T cells to increase persistence
- Combines endogenous γδ innate and adaptive mechanisms to recognize and kill malignant cells

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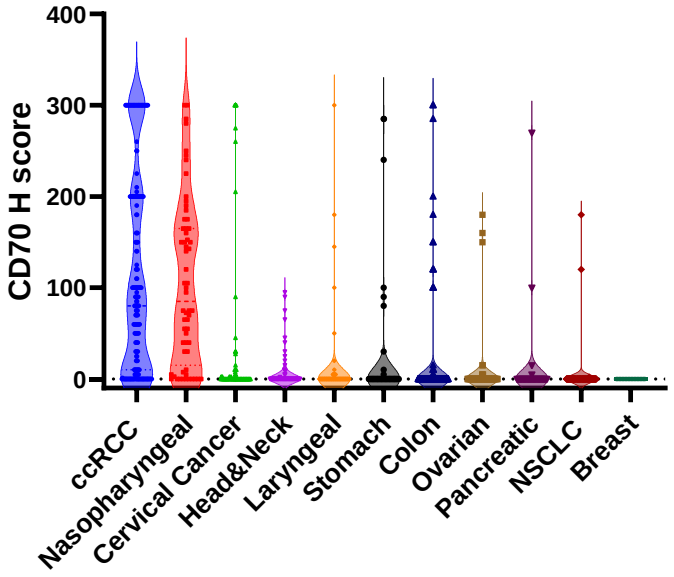
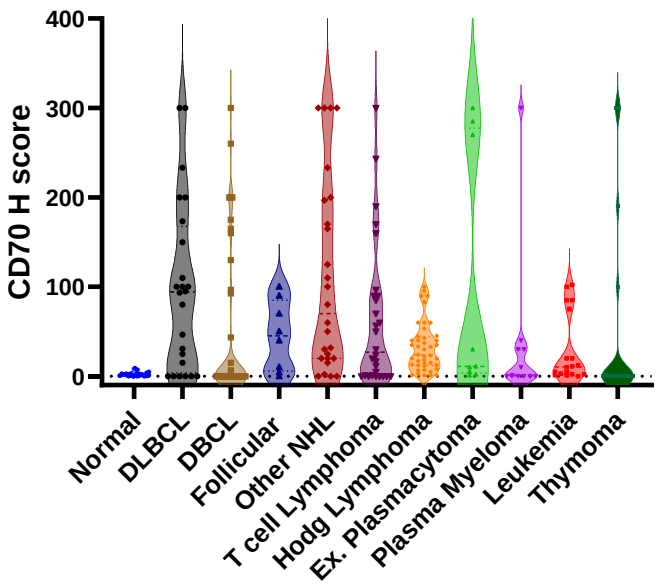
CD70 is Expressed on Multiple Solid and Hematological Cancers with Limited Expression in Normal Tissues

- 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

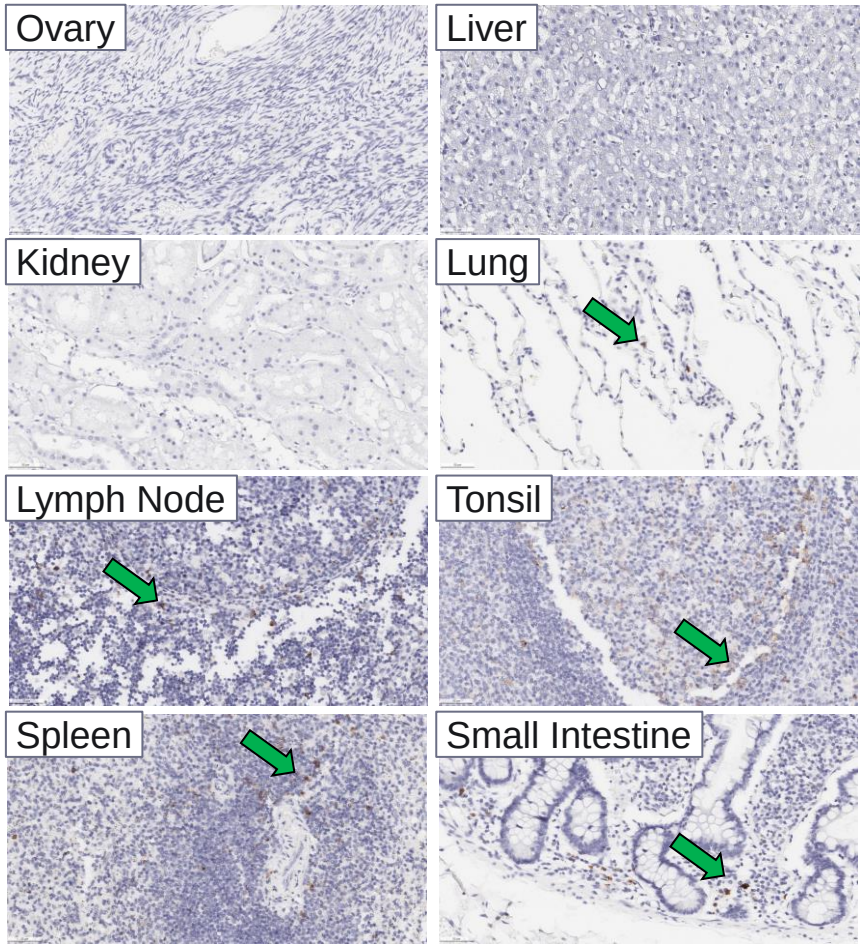
Solid tumors



Hematological malignancies



Representative images from a normal tissue array stained for CD70

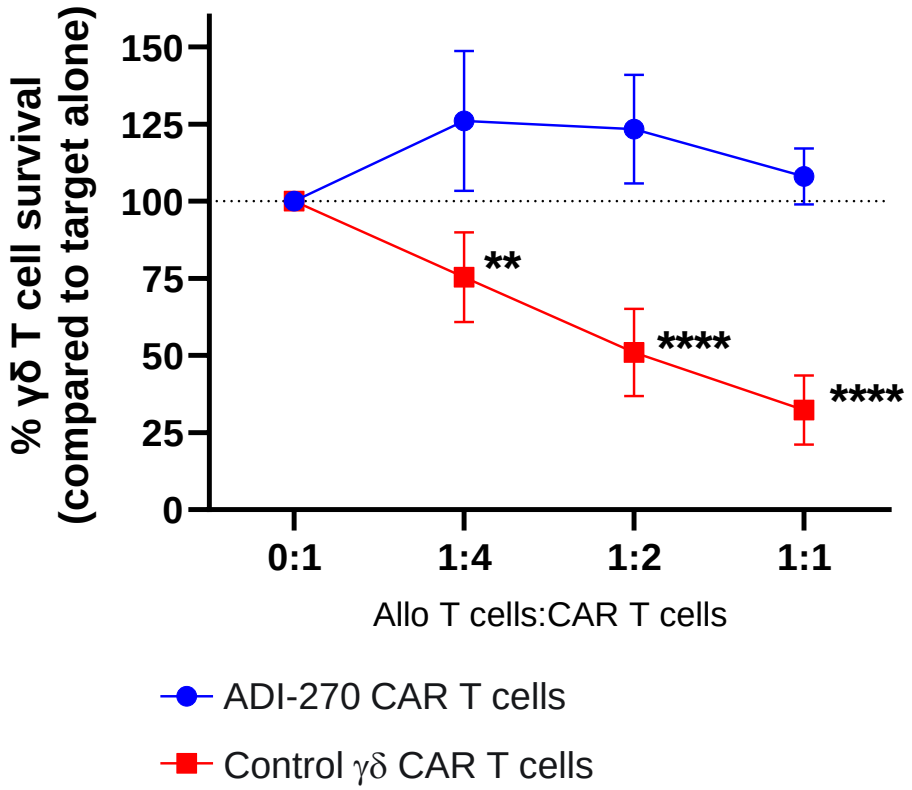


Adicet Bio internal data
ccRCC= Clear cell renal cell carcinoma; NPC= Nasopharyngeal carcinoma

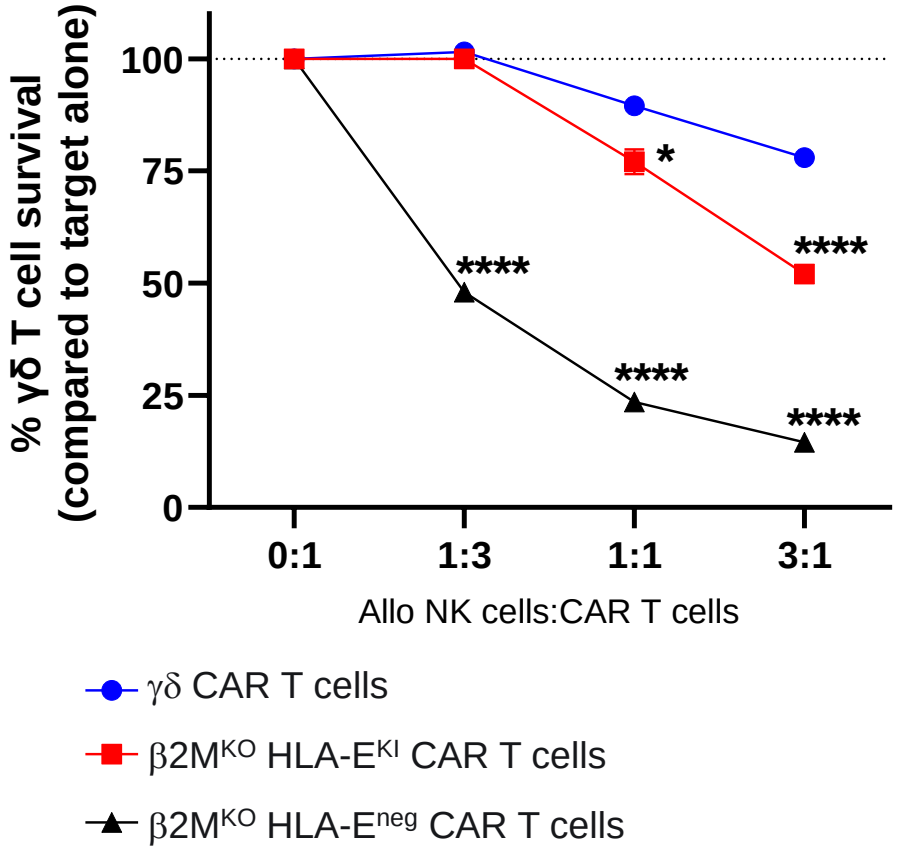
Adicet Bio

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

CD70 targeting less susceptible to T cell rejection



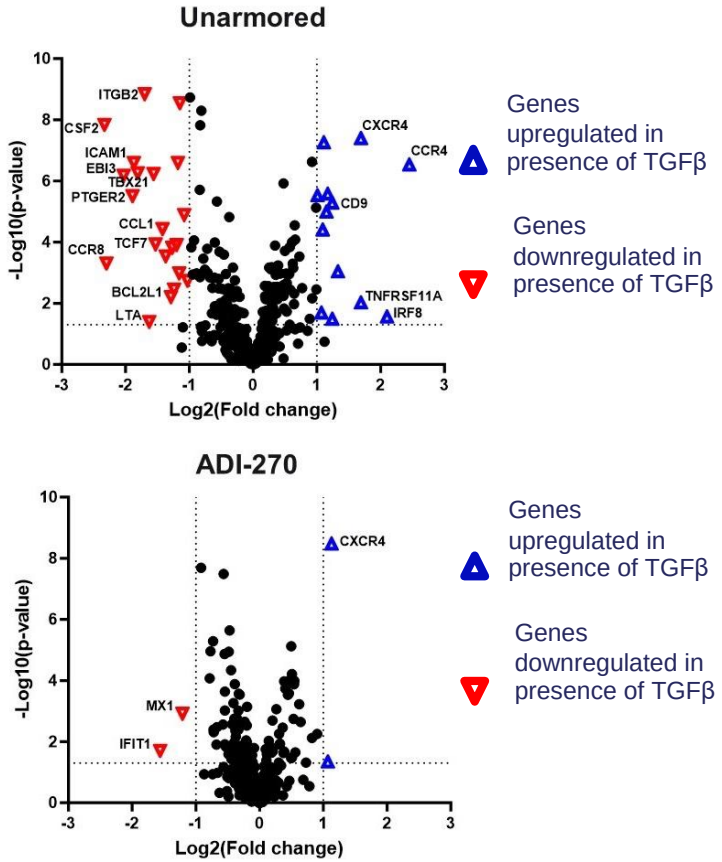
γδ1 CAR T cells less susceptible to NK rejection

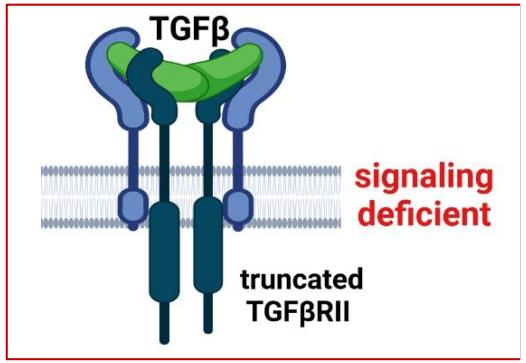


Adicet Bio

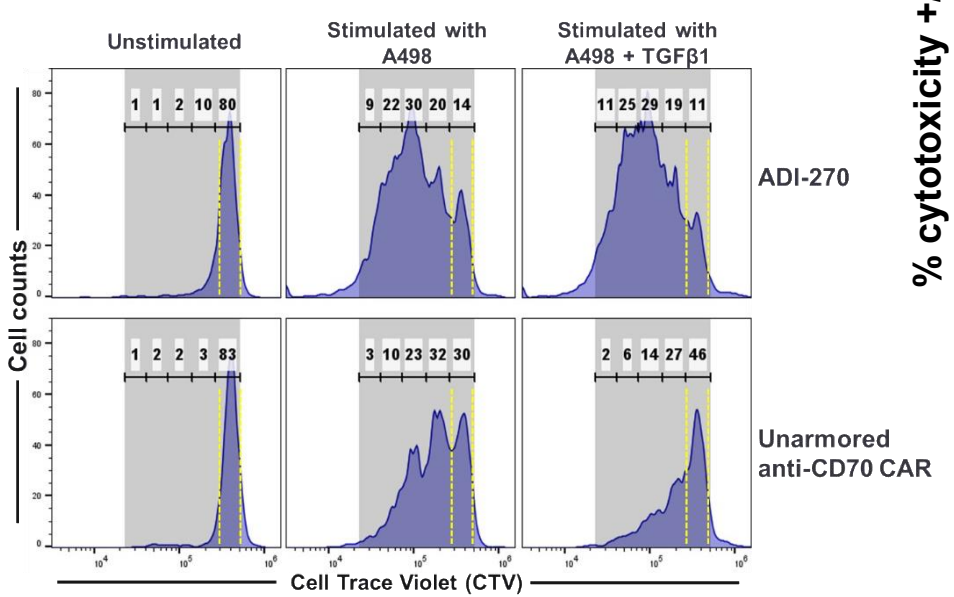
ADI-270 is Resilient to the Inhibitory Effects of TGFβ

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

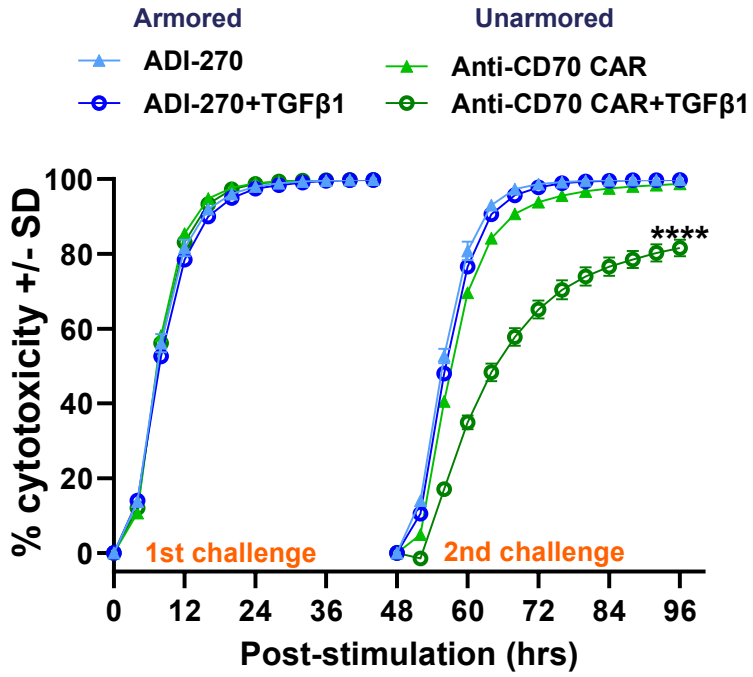




ADI-270 maintained proliferation in the presence of TGFβ

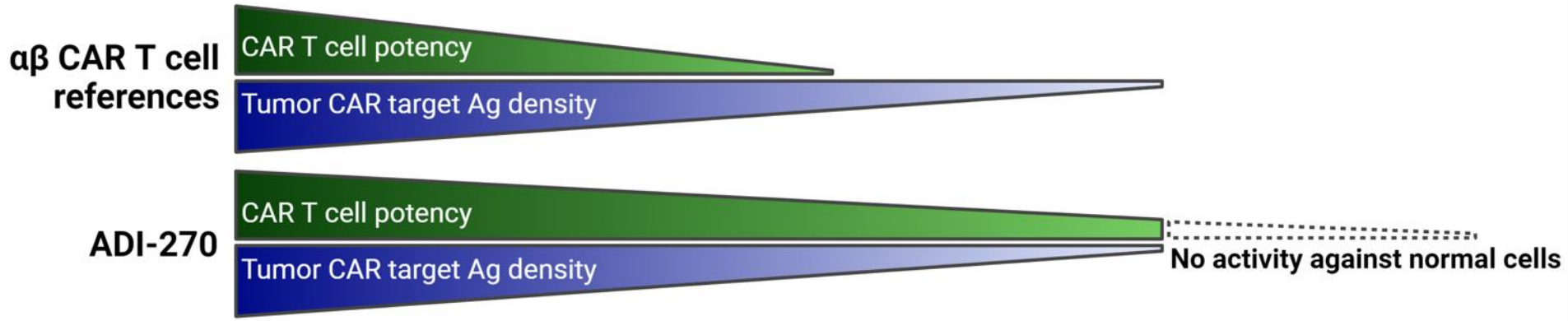


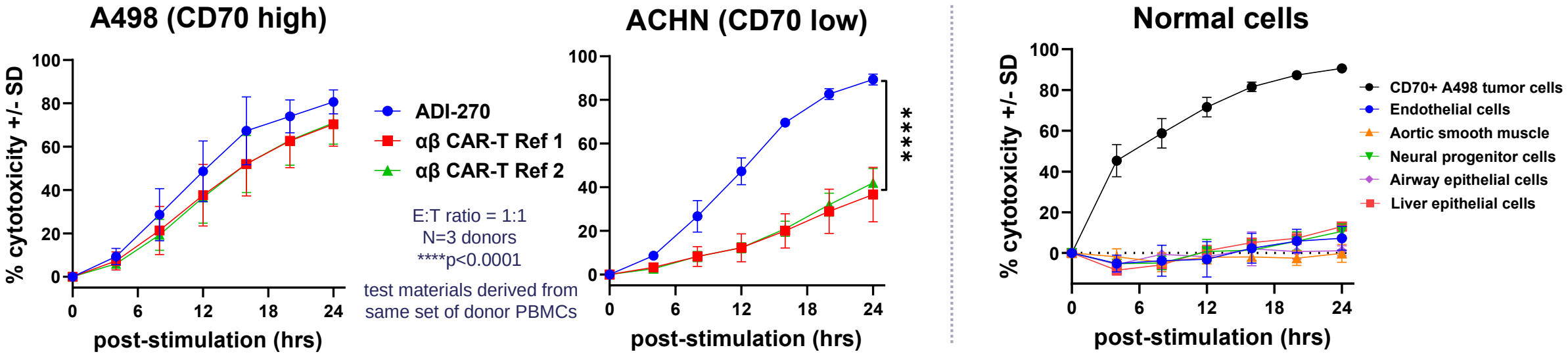
ADI-270 maintained cytotoxicity in the presence of TGFβ



Adicet Bio

ADI-270 Retained Potent Activity in the Context of CD70-Low Tumors Compared to Clinically Relevant CD70-Targeting αβ CAR T Cell Benchmarks

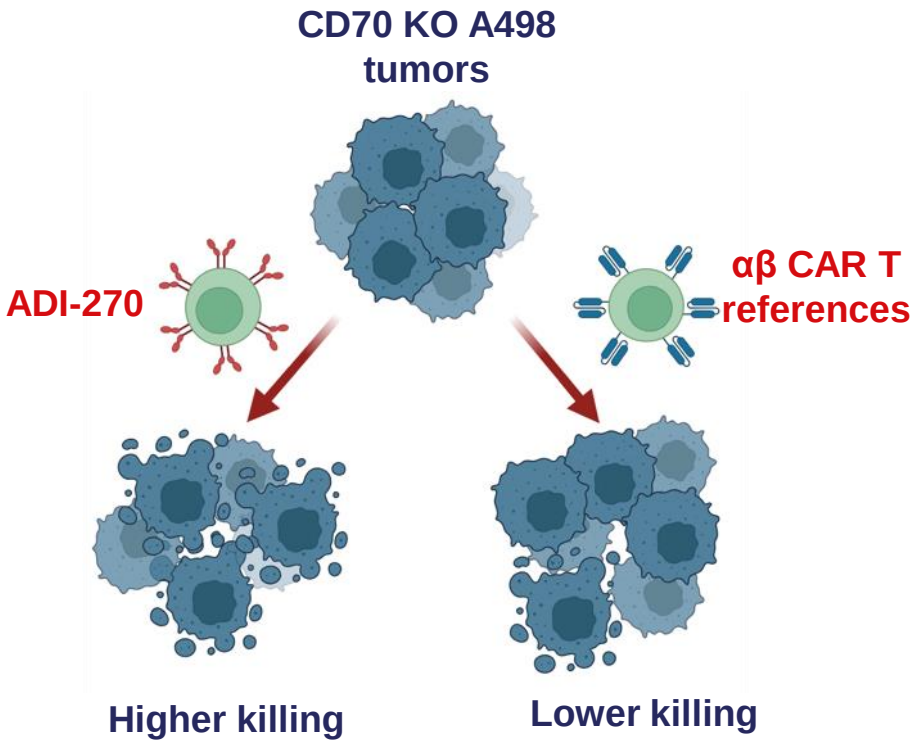


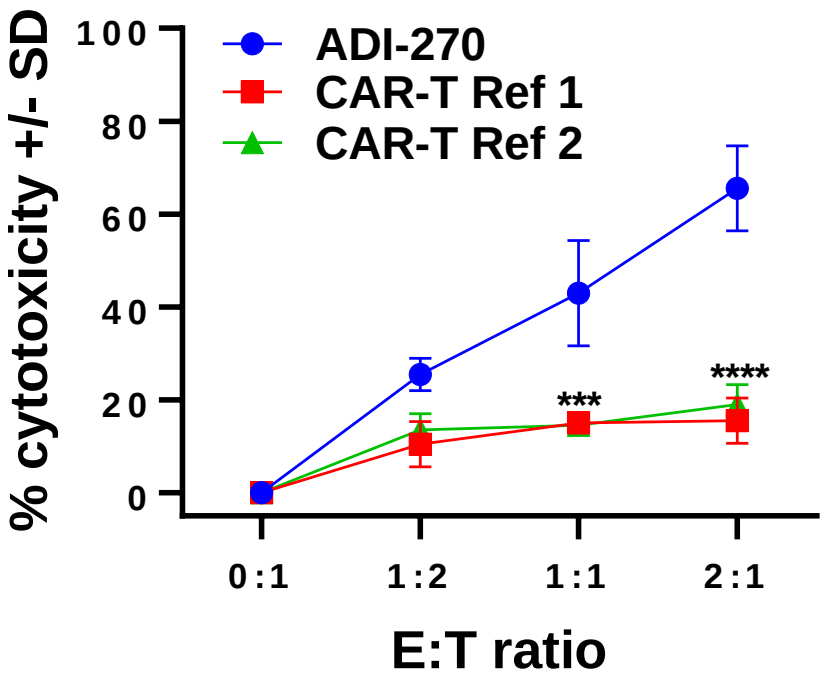


Adicet Bio internal data

Adicet Bio

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





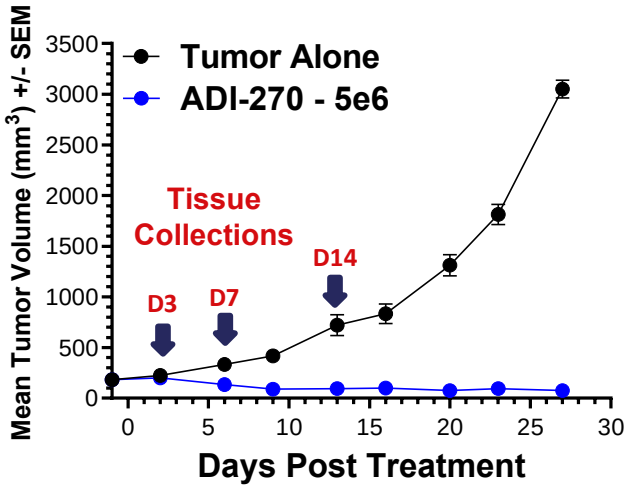
***p<0.001, ****p<0.0001

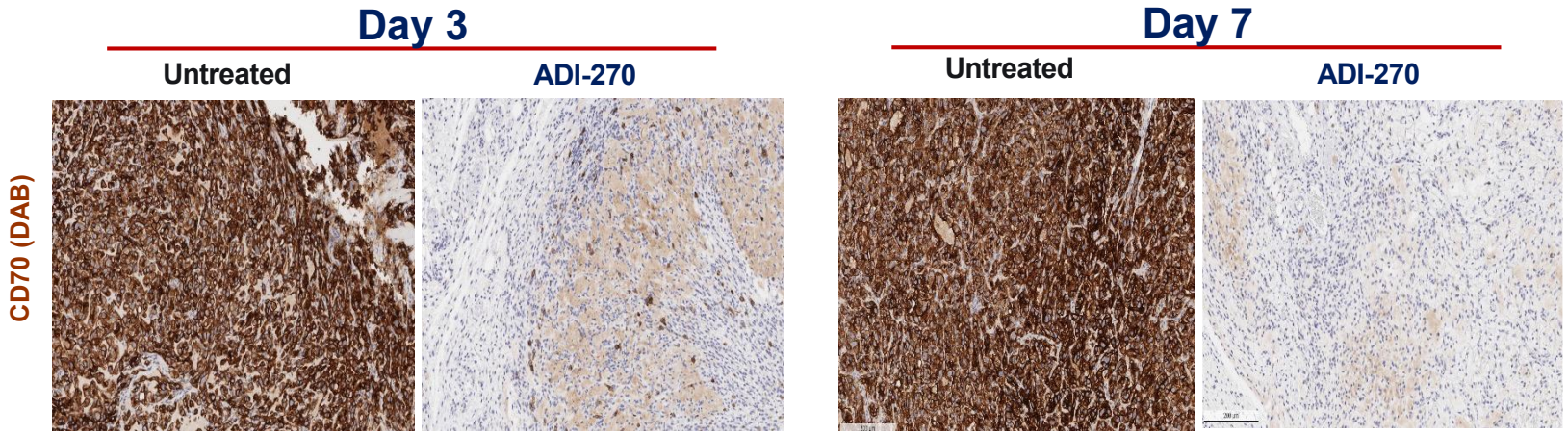
test materials derived from same donor PBMCs

Adicet Bio

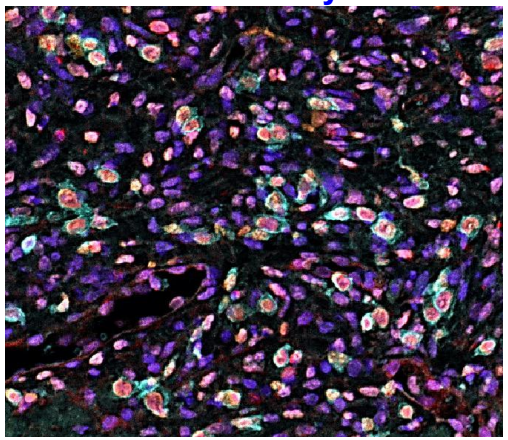
ADI-270 Demonstrated Rapid Homing, Activation and Killing Kinetics in ccRCC Xenografts Resulting in Tumor and Target Eradication

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



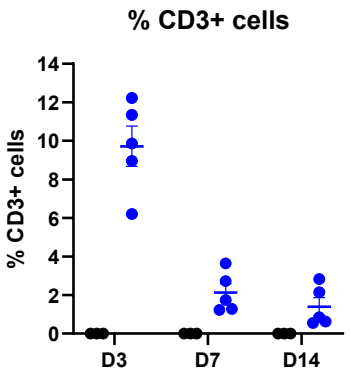


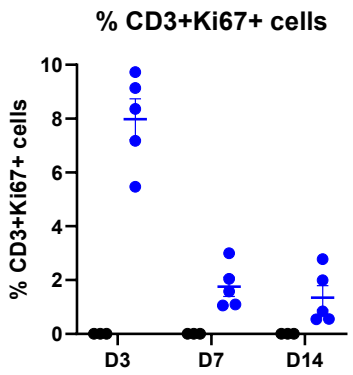
ADI-270 Day 3

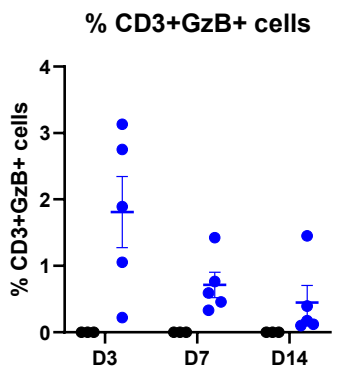


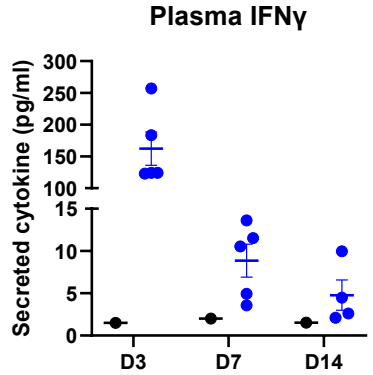
DAPI +CD3 (cyan)+ Ki67 (orange) + Granzyme B (red)

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



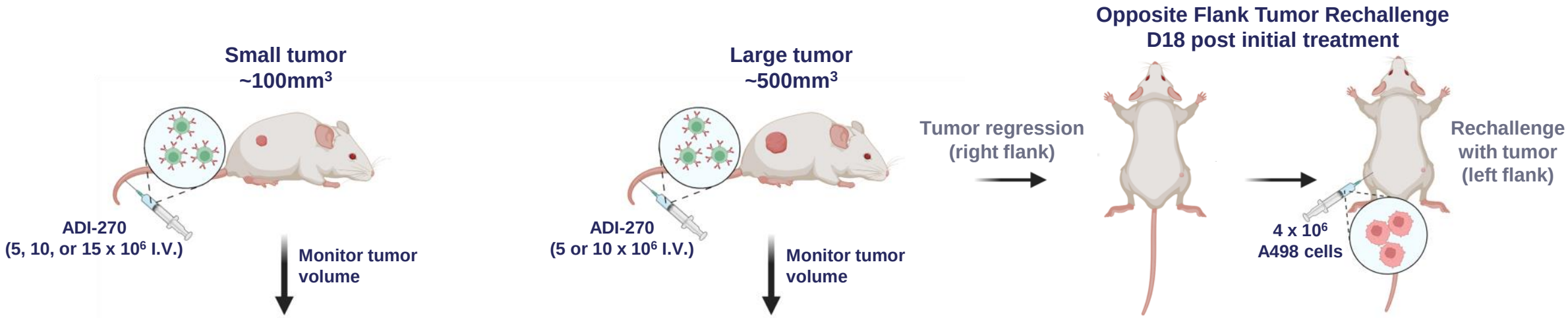


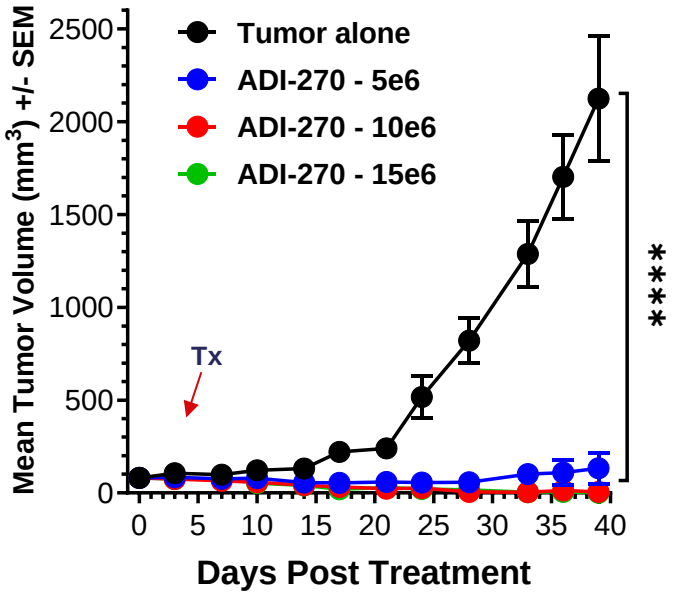


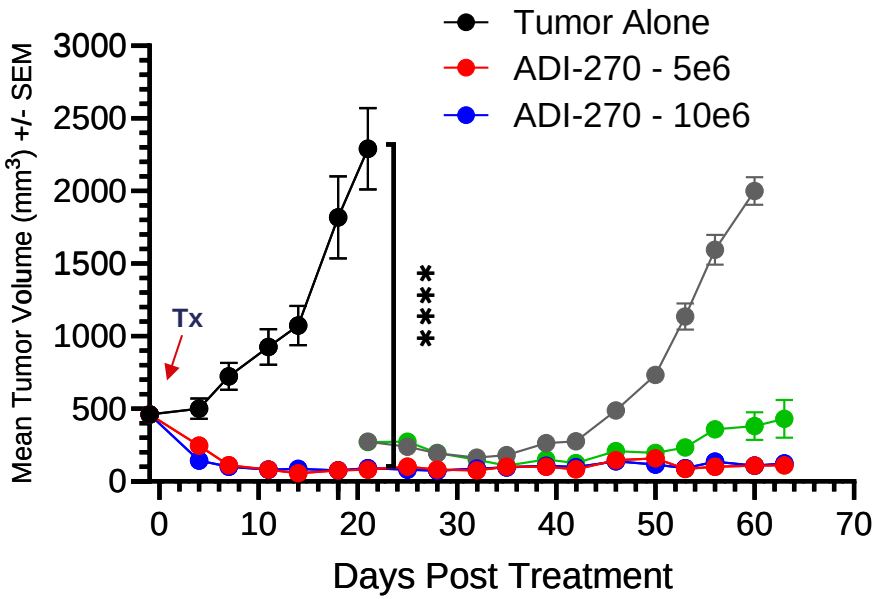


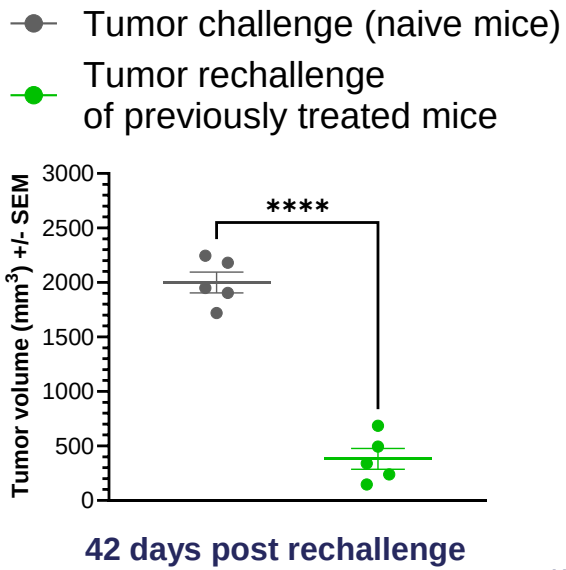
Adicet Bio

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





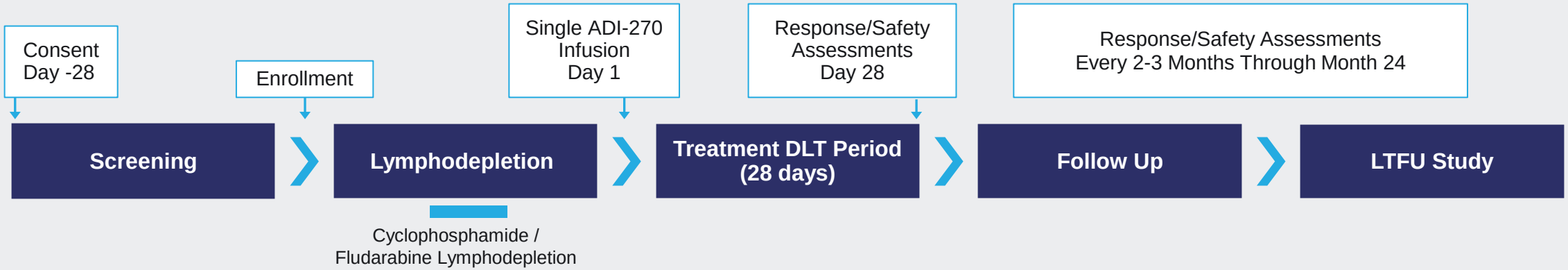




****p<0.0001

Adicet Bio

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



Dosing Arms:

DL2: 1E9 CAR+ cells

DL1: 3E8 CAR+ cells

3+3 design

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

Clinical protocol enables to de-escalate down to DL-1 of 1E8 CAR+ Cells; Patients meeting CR, PR or SD per RECIST v1.1may be eligible to a second dose of ADI-270 following within the first 6 month from initial dose
DCR= Disease control rate; DOR= Duration of response; PFS= Progression free survival; TTP= Time to progression

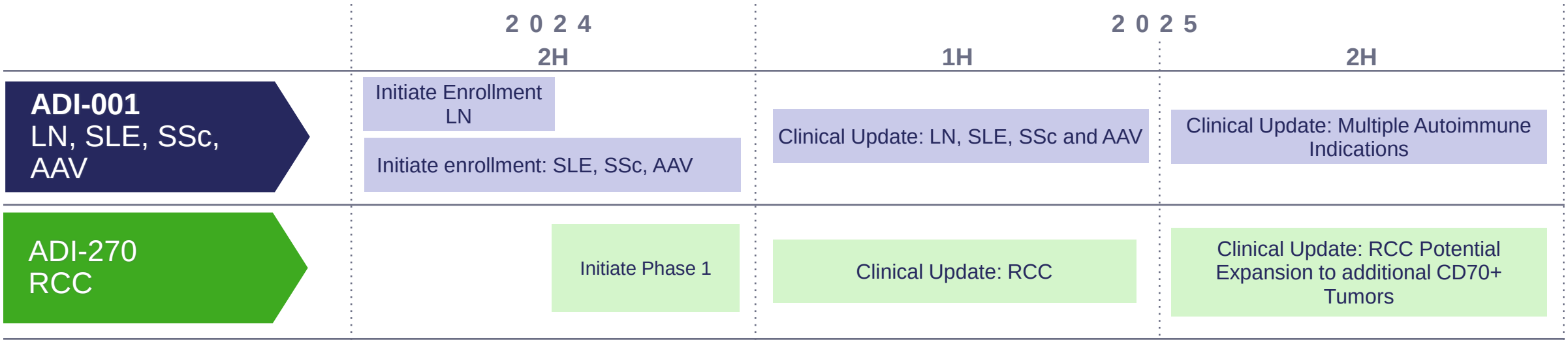
Adicet Bio

ADI-270 Summary

- ADI-270 represents potential evolution of γδ CAR T cell-based therapeutics
- CD27-based 3rd gen CAR demonstrated significant potency advantages[1,2,3,4]
- Armoring against TGFβ 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
- Initiating Phase 1 study in 4Q/2024; Preliminary clinical data expected 1H/2025

[1]Shaffer et al., Blood 2011
[2]Acharya et al., Blood 2023
[3]Leick et al., Cancer Cell 2022
[4]Kasap et al., BioRxiv 2024

Potential Near-Term Milestones



Cash and cash equivalents: ~$224.1M (6/30/24)
Projected cash runway into H2 2026

Subject to site activation, patient enrollment, data readouts and regulatory feedback

Adicet Bio

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Leaders in Developing Allogeneic γδ1 CAR T Cell Therapies to Fight Autoimmune Diseases and Cancer

γδ= Gamma delta; CAR= Chimeric antigen receptor