



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



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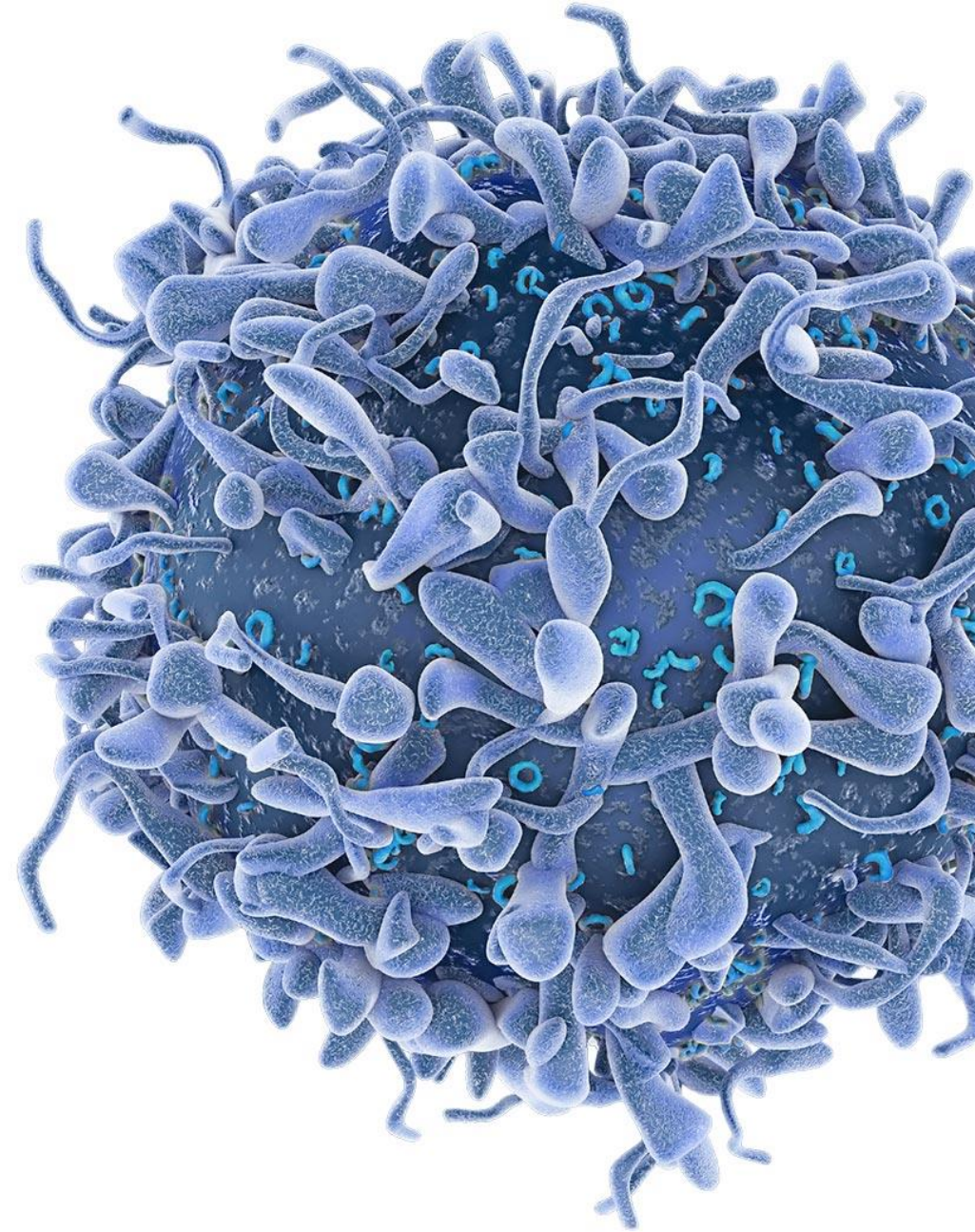
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ADI-001

Autoimmune Diseases



Adicet $\gamma\delta 1$ 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

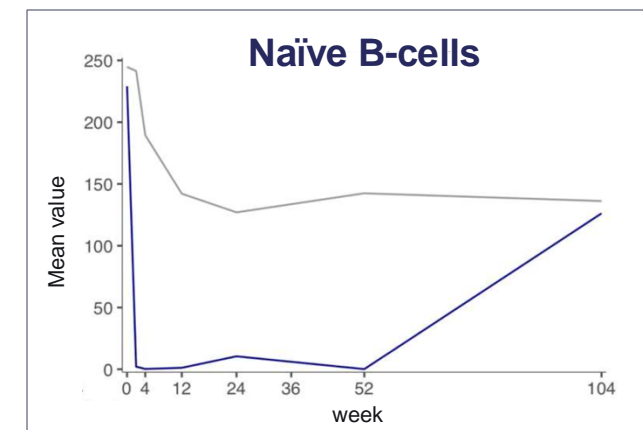
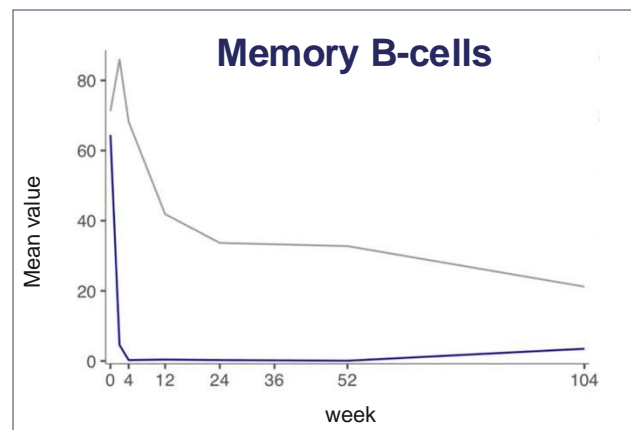
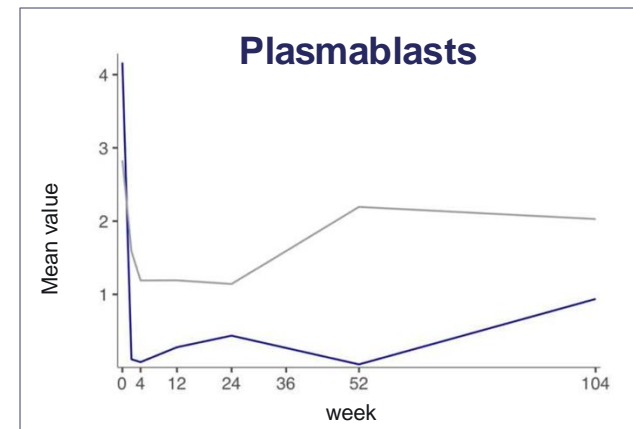
CD20 Targeting With Obinutuzumab Depleted B Cells in Blood Including Plasmablasts, Memory B Cells, and Naïve B-Cells in LN Patients

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 Malvar¹⁰

- In a third-party Phase 2 study in LN, obinutuzumab drove depletion of the B-cell compartment in the blood, including plasmablasts¹
- Poor B-cell depletion in tissues is a noted challenge to efficacy of antibody-based approaches in autoimmune disorders^{2,3}



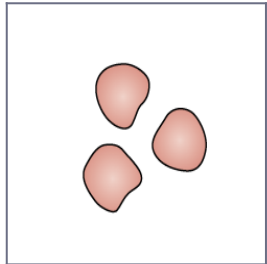
— Obinutuzumab + MMF (n=63) — Placebo + MMF (n=62)

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)

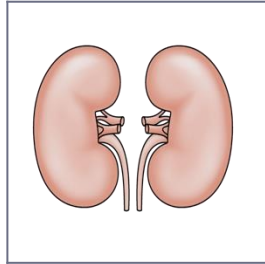
Memory B-cells: CD45⁺, CD19⁺, CD27⁺
 Naïve B-cells: CD45⁺, CD19⁺, IgD⁺, CD27⁻, CD38^{dim/-}
 Plasmablasts: CD45⁺, CD19⁺, CD27⁺, CD38^{bright}

$\gamma\delta$ 1 T Cells Preferentially Traffic to Solid Tissues: Addressing a Source of Resistance to Antibody Therapies



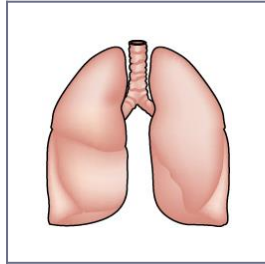
lymph node^{1,2}

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



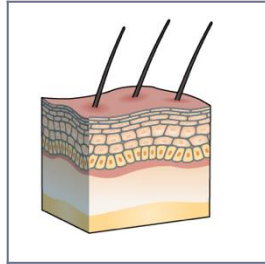
kidney³

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



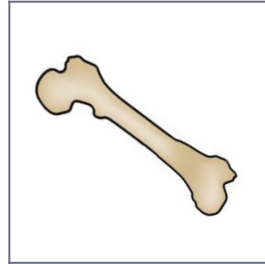
lung⁴

issue/blood:
9X



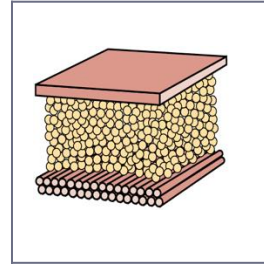
skin⁵

tissue/blood:
8X



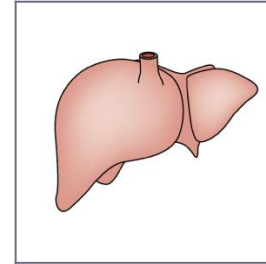
bone marrow⁶

tissue/blood:
4X



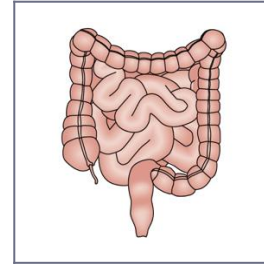
breast⁷

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



liver⁸

tissue/blood:
3X



GI⁹

tissue/blood:
11X

Ratios empirically calculated or approximated from proportion of %CD3 from literature reports in relative compartment^{6,6}

¹Davey et al Trends Immunol (2018)

³Rancan et al Nat Immunol (2023)

⁵Toulon et al J Exp Med (2009)

⁷Wu et al Sci Transl Med (2019)

²Uger et al Sci Rep (2018)

⁴Wisnewski et al Am J Respir Cell Mol Biol (2000)

⁶Braunack et al Front Med (2021)

⁸Melo et al Clin Immunol (2021)

⁹Deutsch et al Eur J Immunol (1991)

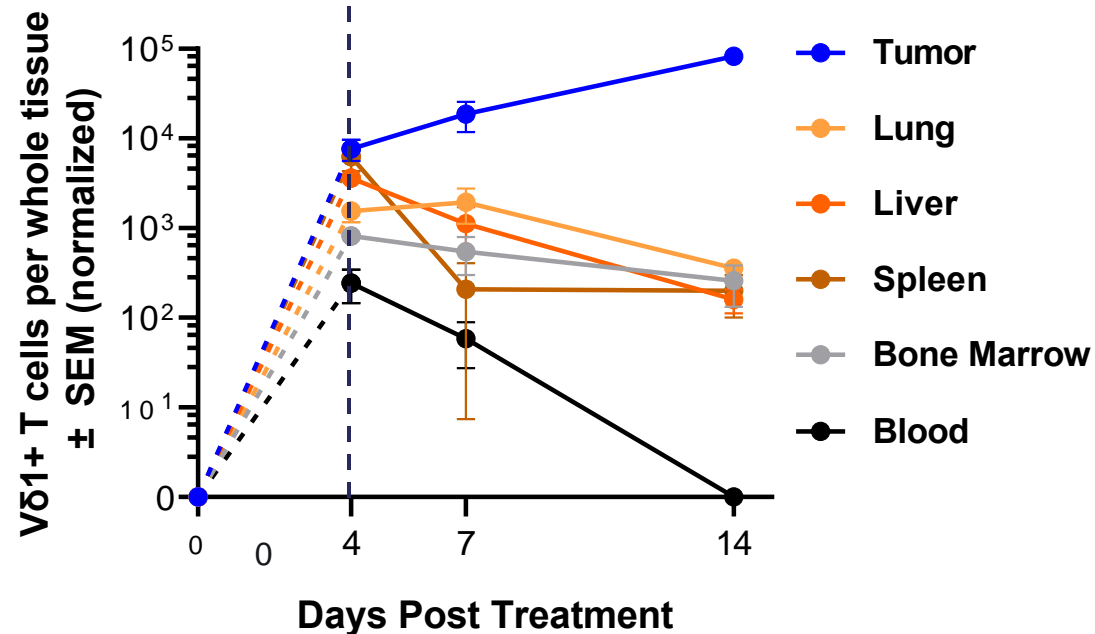
Preclinical Data Highlights $\gamma\delta 1$ T Cells Tissue Residence

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

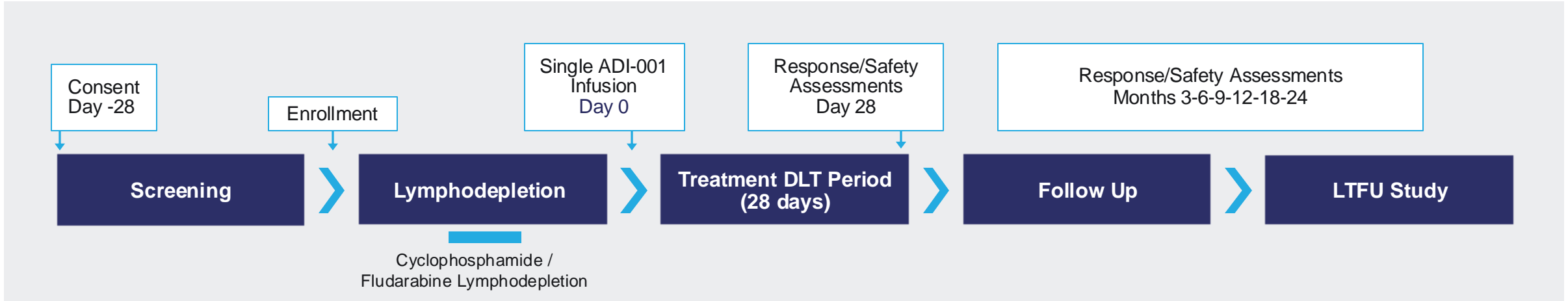
Homing

Expansion

Tissue residence of $\gamma\delta 1$ and selective expansion within tumor tissues



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

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)

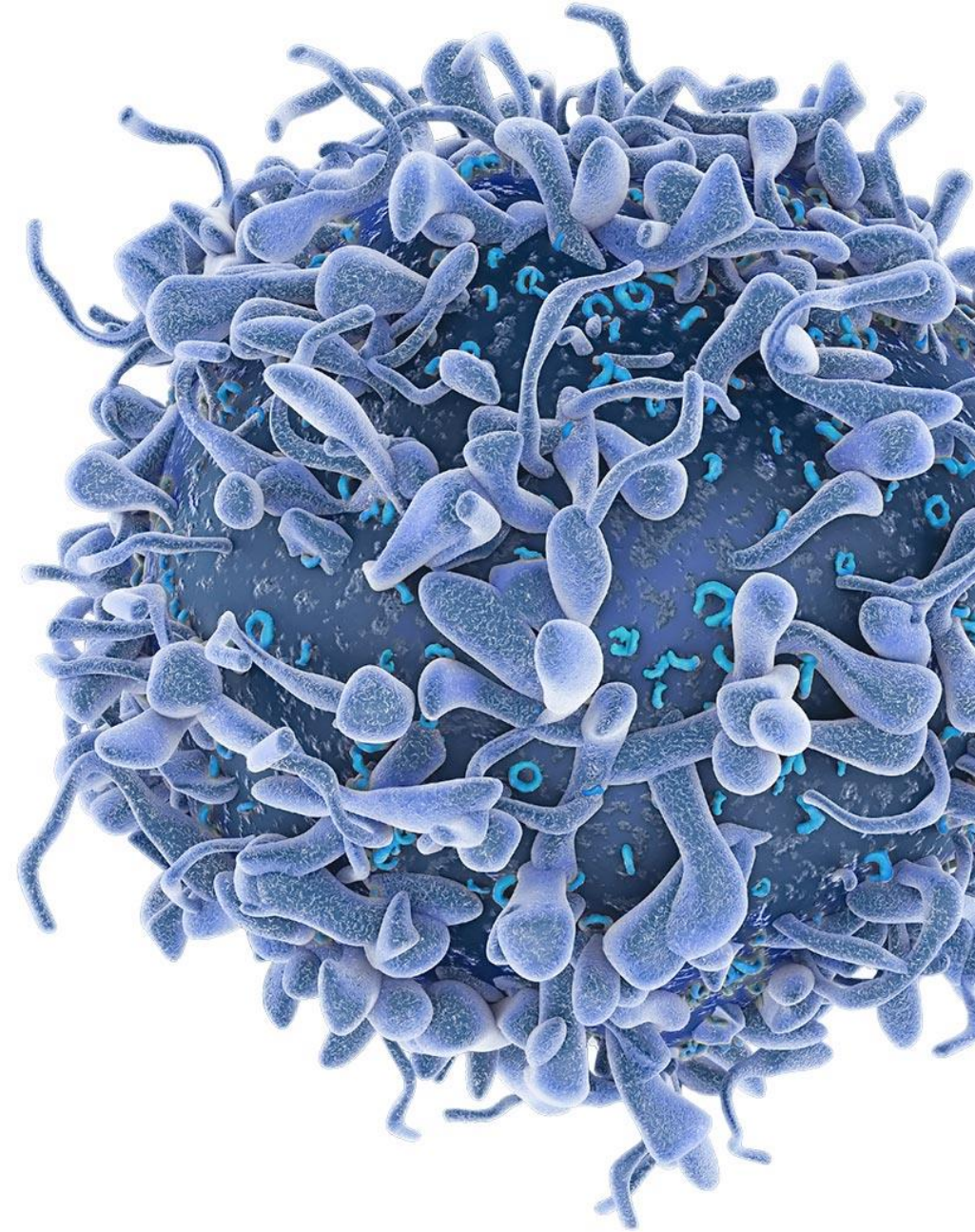
Secondary & Exploratory Endpoints

- 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)

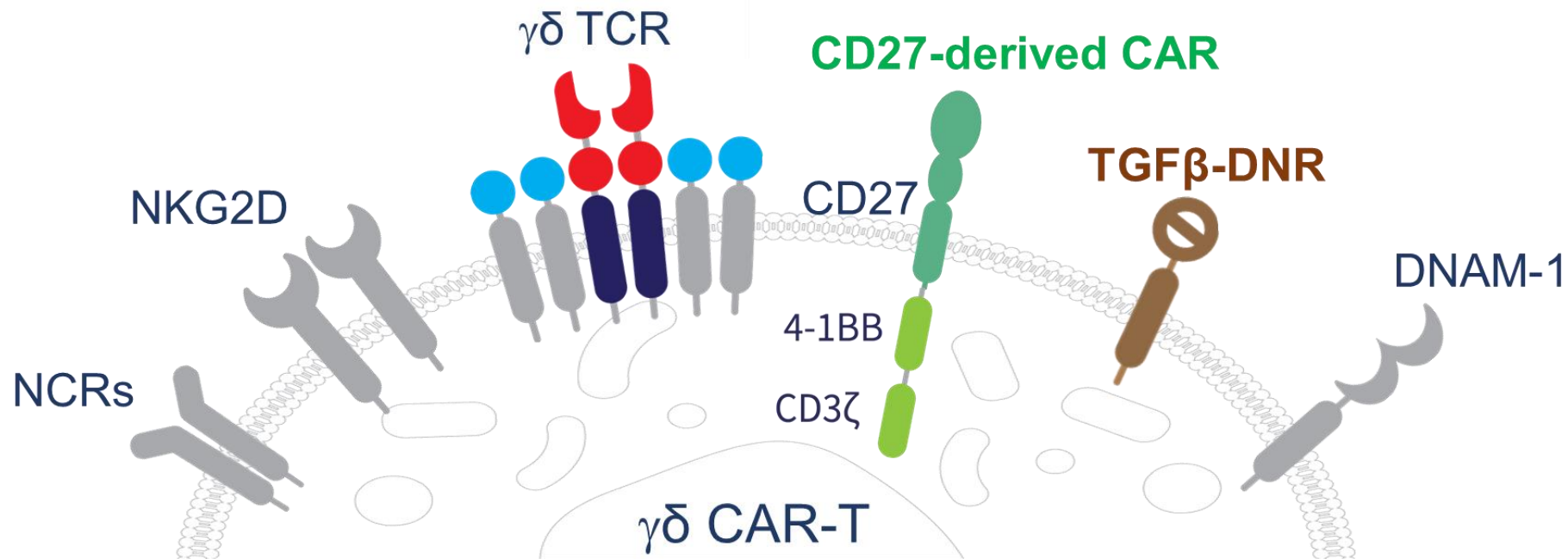


ADI-270

Renal Cell Carcinoma & Other CD70+ Diseases

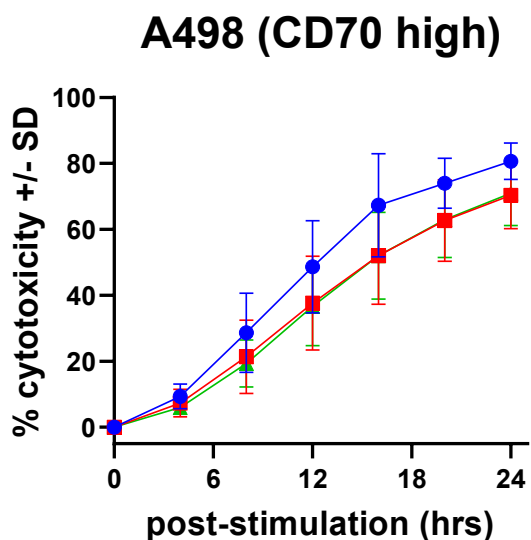
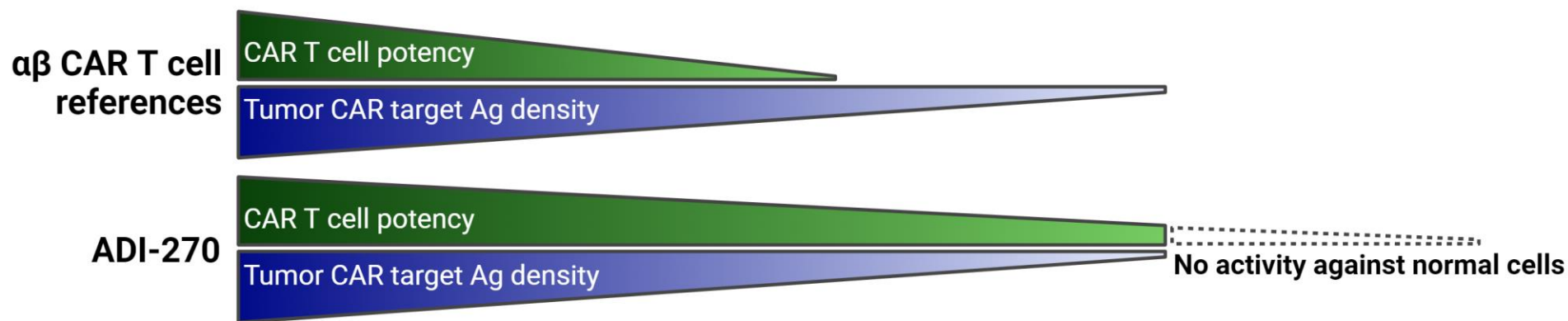


ADI-270: Designed to Address Multiple Refractory Cancers



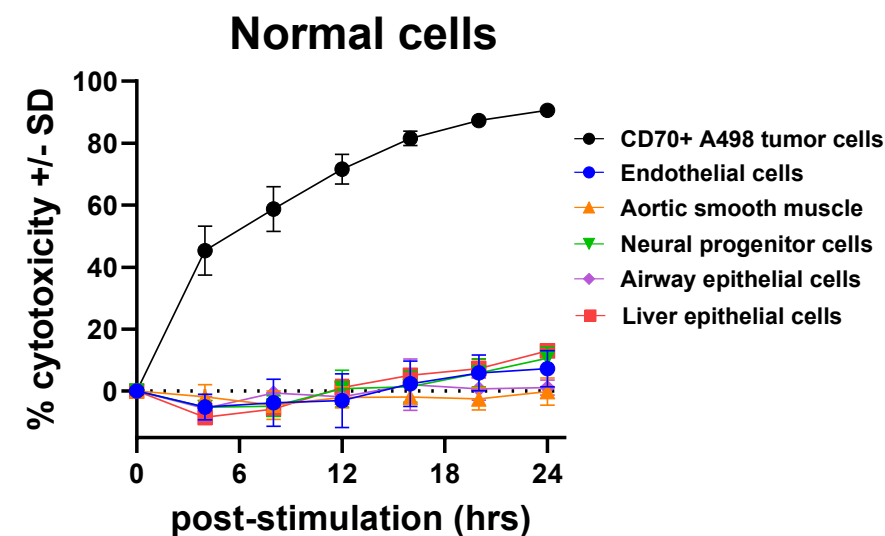
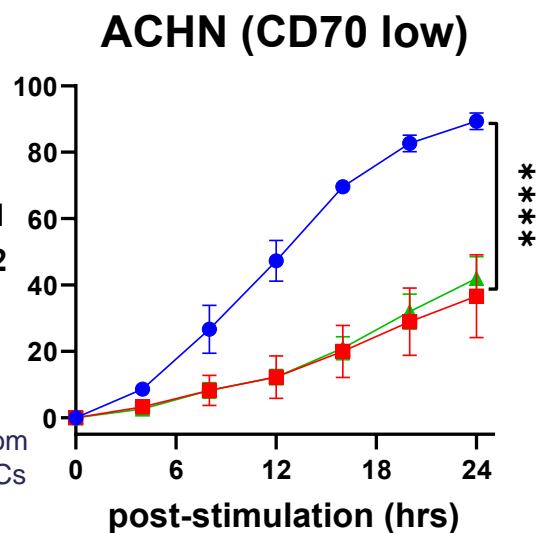
- CAR utilizes CD27 as binding domain; contains CD27 and 4-1BB costimulatory domains plus CD3 ζ (3rd gen)
- Inactive form of TGF β receptor II to mitigate the immunosuppressive effects of TGF β within the tumor microenvironment
- Host vs graft armoring against alloreactive activated CD70+ T cells to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

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

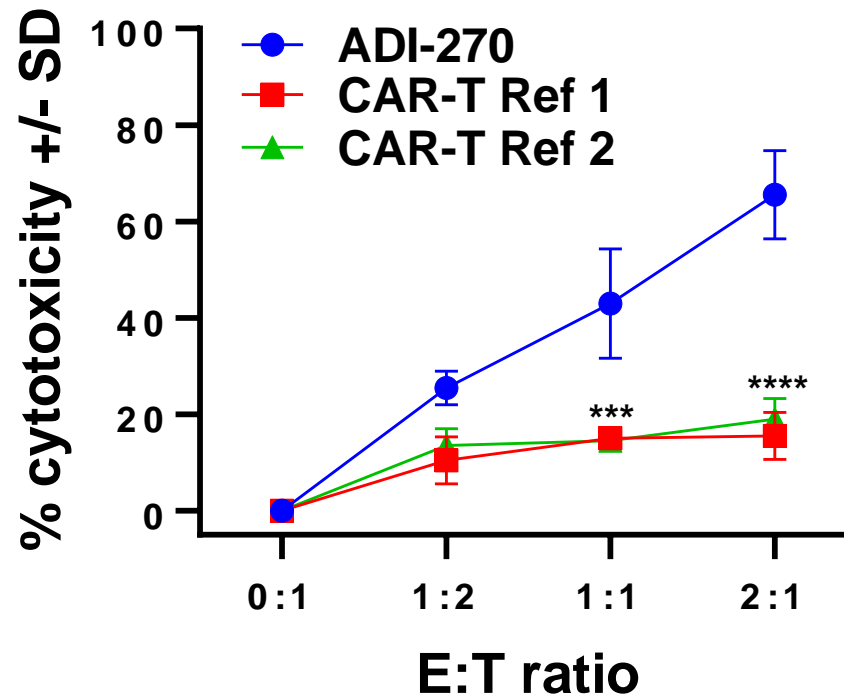
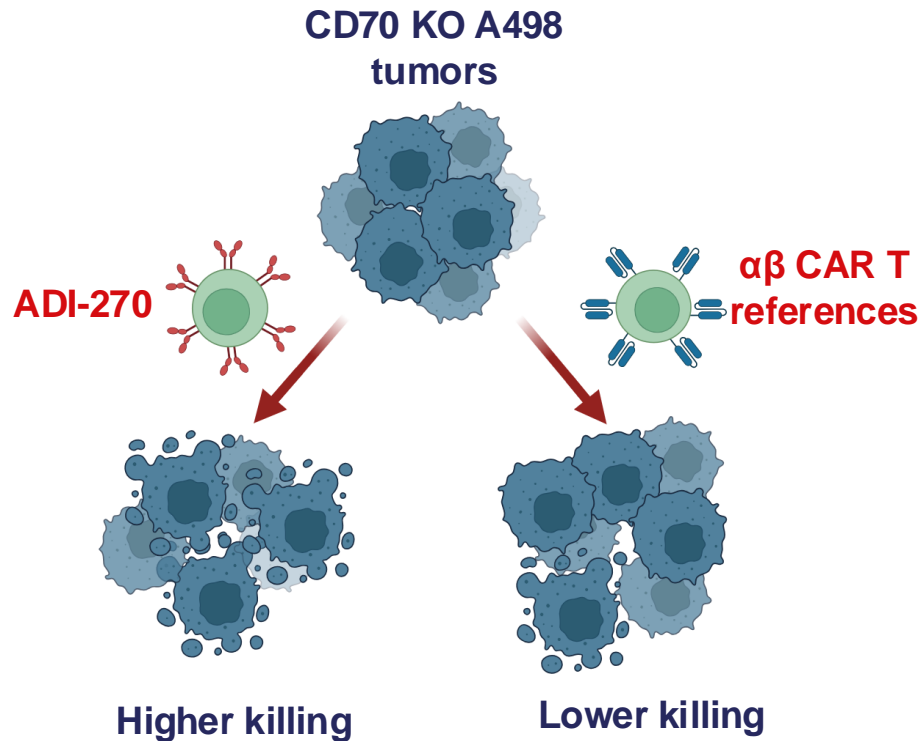


● ADI-270
 ■ $\alpha\beta$ CAR-T Ref 1
 ▲ $\alpha\beta$ CAR-T Ref 2
 E:T ratio = 1:1
 N=3 donors
 **** $p < 0.0001$

test materials derived from same set of donor PBMCs



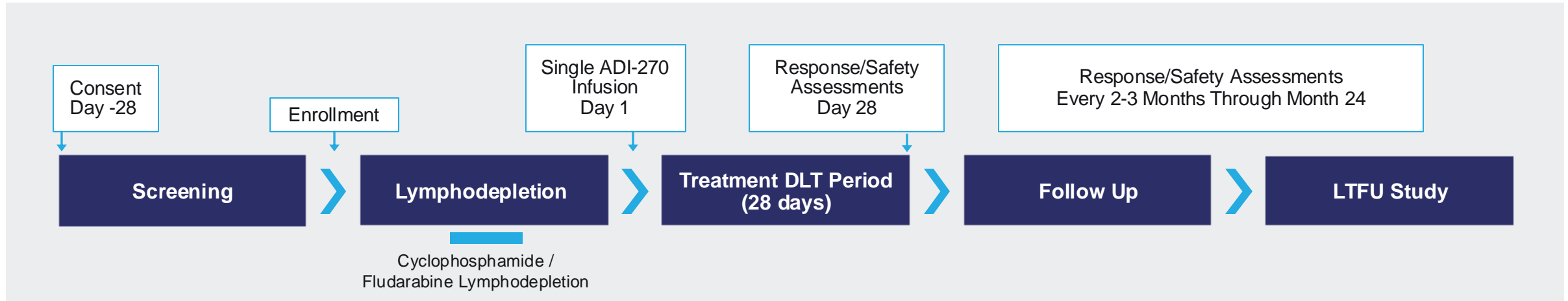
ADI-270 Demonstrated Higher Innate Cytolytic Activity Against CD70 Negative Tumor Cells Compared to CAR-T Cell References



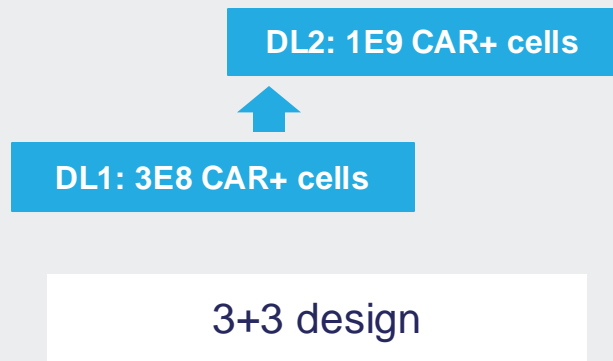
*** $p < 0.001$, **** $p < 0.0001$

test materials derived from same donor PBMCs

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



Dosing Arms:



Primary endpoints:

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

Secondary endpoints:

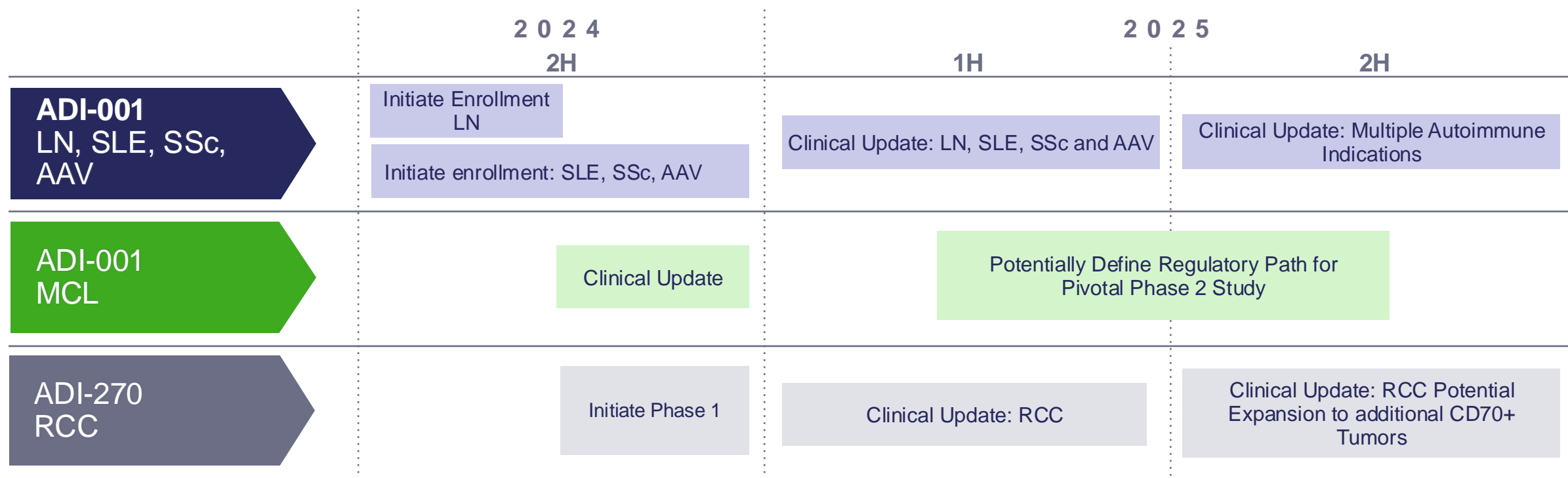
- ORR, DOR, PFS, TTP, and OS
- PK, host immune cell recovery

Dose Expansion:

- RCC
- Other CD70+ tumors

Clinical protocol enables to de-escalate down to DL-1 of 1 E8 CAR+ Cells; Patients meeting CR, PR or SD per RECIST v1.1 may be eligible to a second dose of ADI-270 following within the first 6 month from initial dose

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



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