



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



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This presentation contains "forward-looking statements" of Adicet Bio, Inc. (Adicet or the Company) within the meaning of the Private Securities Litigation Reform Act of 1995 relating to the business and operations of Adicet. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, but are not limited to, express or implied statements regarding: preclinical and clinical development of Adicet's product candidates, including future plans or expectations for ADI-001 and ADI-270, including the potential submission or timing of clearance of INDs in autoimmune diseases, and the potential safety, durability, tolerability and efficacy of these product candidates; the progress, timing and success of the Company's ongoing and planned Phase 1 clinical trials of ADI-001 in autoimmune diseases and cancer, including expectations for site activation, enrollment and data readouts; the Company's plan to expand into other autoimmune indications in the future; the Company's expectations regarding regulatory filings and clearances, including the submission of an IND for ADI-270 in renal cell carcinoma in the second quarter of 2024; and expectations regarding the Company's uses of capital, expenses and financial results, including the expected cash runway. Any forward-looking statements in this presentation are based on management's current expectations and beliefs of future events, and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements, including without limitation, the effect of global economic conditions and public health emergencies on Adicet's business and financial results, including with respect to disruptions to our preclinical and clinical studies, business operations, employee hiring and retention, and ability to raise additional capital; Adicet's ability to execute on its strategy including obtaining the requisite regulatory approvals on the expected timeline, if at all; that positive results, including interim results, from a preclinical or clinical study may not necessarily be predictive of the results of future or ongoing studies; clinical studies may fail to demonstrate adequate safety and efficacy of Adicet's product candidates, which would prevent, delay, or limit the scope of regulatory approval and commercialization; and regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time-consuming, and inherently unpredictable; and Adicet's ability to meet production and product release expectations. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause Adicet's actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in Adicet's most recent annual report on Form 10-K and our periodic reports on Form 10-Q and Form 8-K filed with the U.S. Securities and Exchange Commission (SEC), as well as discussions of potential risks, uncertainties, and other important factors in Adicet's other filings with the SEC. All information in this press release is as of the date of the release, and Adicet undertakes no duty to update this information unless required by law.

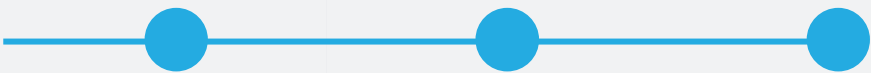
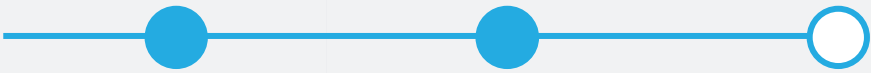
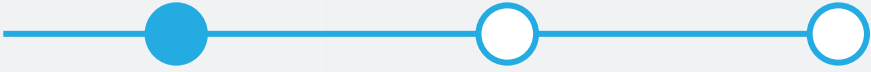
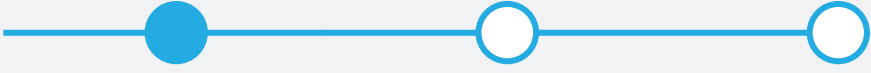
## Industry and Market Information

Information regarding market share, market position and industry data pertaining to Adicet's business contained in this presentation consists of estimates based on data and reports compiled by industry professional organizations and analysts and Adicet's knowledge of their industry. Although Adicet believes the industry and market data to be reliable, this information could prove to be inaccurate. You should carefully consider the inherent risks and uncertainties associated with the market and other industry data contained in this presentation. Forward-looking information obtained from third-party sources is subject to the same qualifications and the additional uncertainties as the other forward-looking statements in this presentation.

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

| Program | Target | Potential Diseases | Research | IND-Enabling | Clinical | Status |
|---------|--------|--------------------|----------|--------------|----------|--------|
|---------|--------|--------------------|----------|--------------|----------|--------|

## ADICET WHOLLY OWNED PROGRAMS

|                |                            |                          |  |  |  |   |
|----------------|----------------------------|--------------------------|--|--|--|---|
| <b>ADI-001</b> | CD20                       | Autoimmune               |   |  |  | IND in LN cleared Dec 2023<br>Initiate LN Phase 1 2Q 2024<br>Update planned 2H 2024<br>AI expansion opportunities |
| <b>ADI-001</b> | CD20                       | NHL                      |   |  |  | MCL Phase 1 ongoing*<br>Update planned 2H 2024  |
| <b>ADI-270</b> | CD70<br>(TGF $\beta$ -DNR) | RCC & Other<br>ST / Heme |   |  |  | IND submission in RCC<br>expected 2Q 2024   |
| <b>ADI-xxx</b> | PSMA (w/ Armor)            | mCRPC                    |   |  |  | Preclinical activities  |
| <b>ADI-925</b> | Tumor stress<br>ligands    | Multiple Solid /<br>Heme |  |  |  | Preclinical activities  |

## PARTNERED PROGRAMS

|                |      |     |   |  |  |                  |
|----------------|------|-----|---|--|--|------------------|
| <b>ADI-002</b> | GPC3 | HCC |  |  |  | <b>REGENERON</b> |
|----------------|------|-----|---|--|--|------------------|

\*Adicet is focused on advancing MCL enrollment in the GLEAN trial and has deprioritized enrolling large B-cell lymphoma patients.

AI=Autoimmune; GPC3= Glypican-3; HCC= Hepatocellular carcinoma; IND= Investigational new drug; LN= Lupus nephritis; mCRPC= Metastatic castration-resistant prostate cancer; MCL= Mantle cell lymphoma;

NHL= Non-Hodgkin's lymphoma; PSMA= Prostate specific membrane antigen; RCC= Renal cell carcinoma; ST= Solid tumor

# Adicet Bio Leadership Team



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Officer



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Chief Scientific Officer



Nick Harvey  
Chief Financial Officer



Francesco Galimi, M.D., Ph.D.  
Chief Medical Officer



Amy Locke  
Head of Human Resources



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

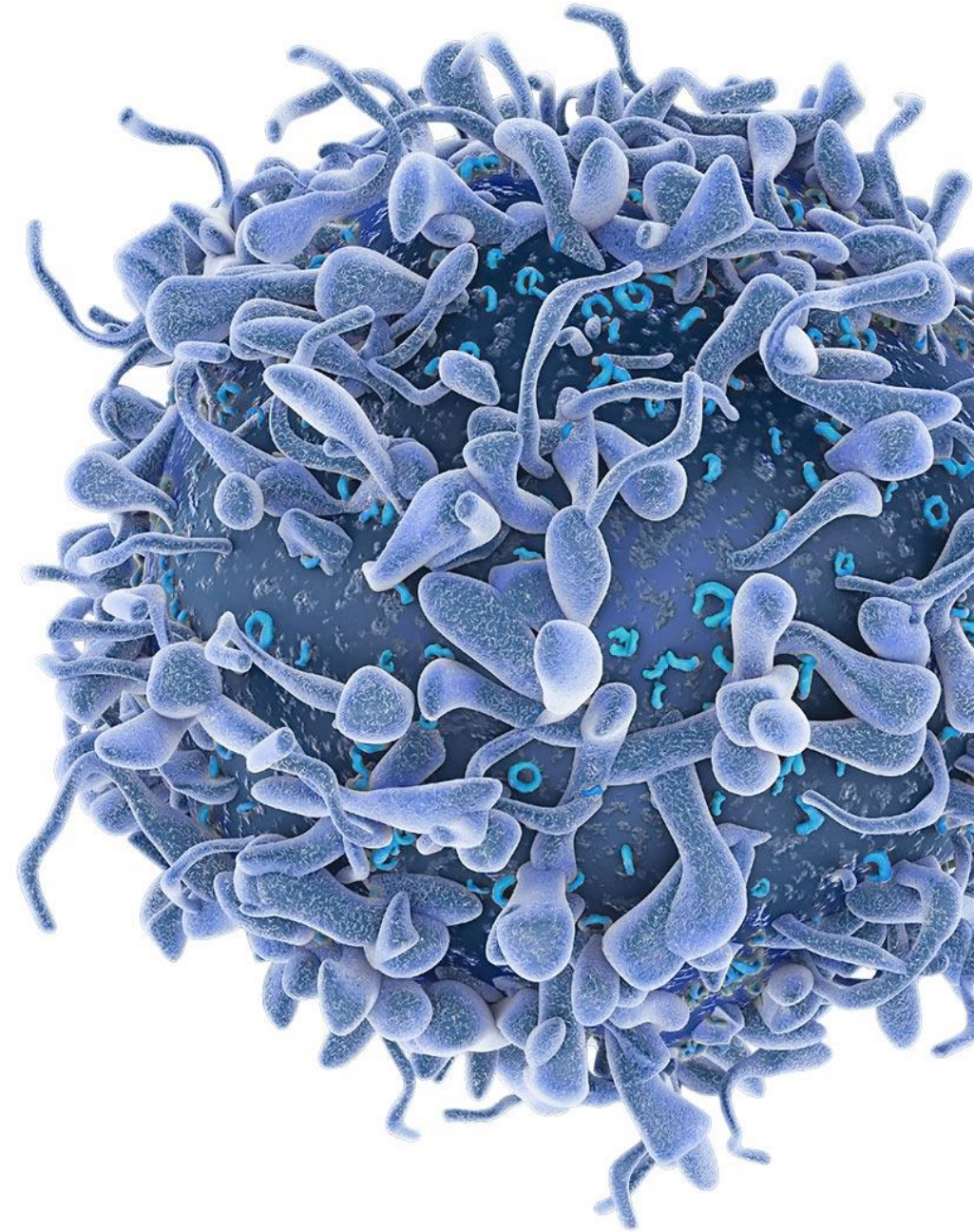






# ADI-001

## 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



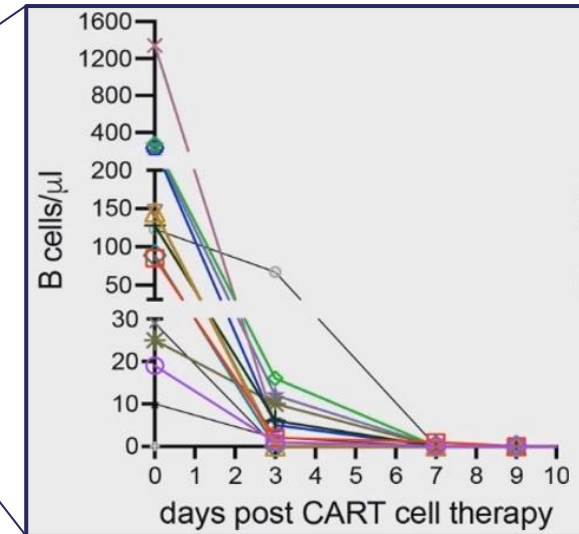
AUC= Area Under the Curve; Cmax= Peak plasma concentration; CRS= Cytokine release syndrome; ICANS= Immune effector cell-associated neurotoxicity syndrome; IIM= idiopathic inflammatory myopathy; SLE= systemic lupus erythematosus; SSC= systemic sclerosis

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

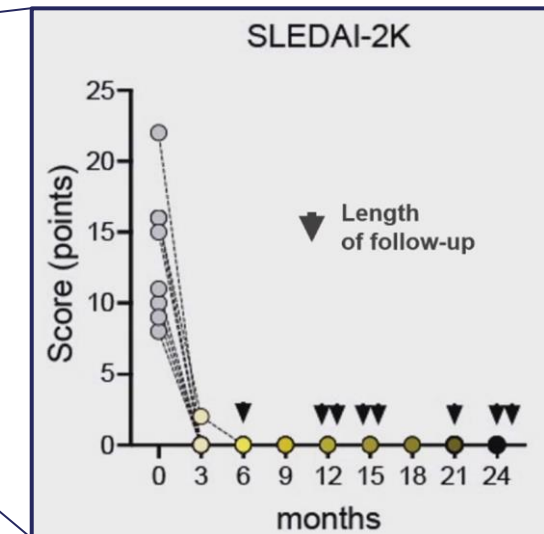


# CAR-T Therapy Depleted B-cells, Drove an Immune Reset, and Achieved Treatment-Free Remissions in Patients with Autoimmune Diseases<sup>1</sup>

- Schett et al. treated 15 patients with autoimmune diseases (SLE, IIM, & SSc) with autologous CD19 CAR T
- Deep B-cell depletion & immune reset observed in all patients



- Lasting treatment-free remissions observed in all SLE patients
- Symptom control with no additional disease-specific treatment achieved in all patients
- Robust efficacy demonstrated in IIM and SSc patients



<sup>1</sup> CD19.CAR-T Cell in Refractory Systemic Autoimmune Diseases: A Monocentric Experience from the First 15 Patients. ASH 2023  
Note: Third-party data summarized on this slide does not employ ADI-001.

# 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<sup>1,2,3</sup>
  - Systemic sclerosis<sup>2</sup>
  - Idiopathic inflammatory myopathies<sup>2</sup>
  - Myasthenia gravis<sup>4,5</sup>
- 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

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. Haghighi A et al. Lancet Neurology 2023

5. Granit V et al. Lancet Neurology (2023)

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

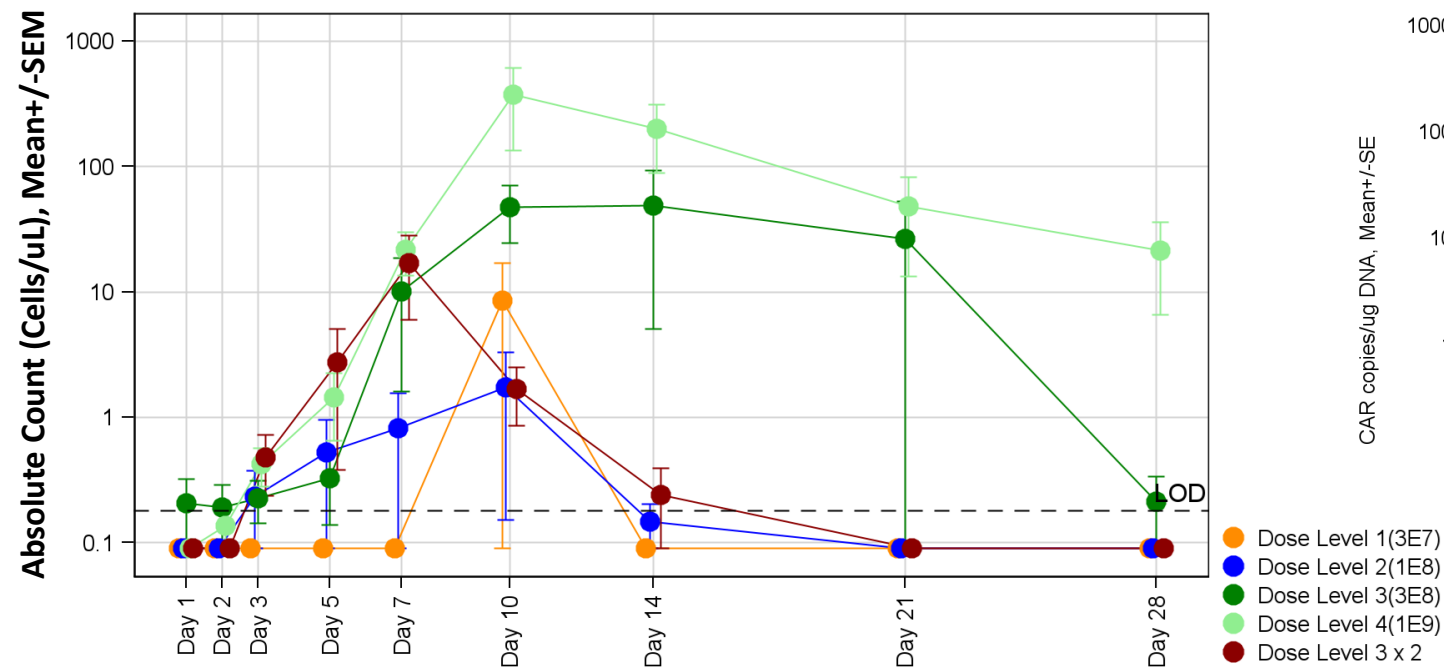
|                   |                    |                    |                        |
|-------------------|--------------------|--------------------|------------------------|
| Lupus nephritis   | SLE                | MS                 | Moderate to severe RA  |
| ~150K             | ~160-410K  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

\*Not an exhaustive list

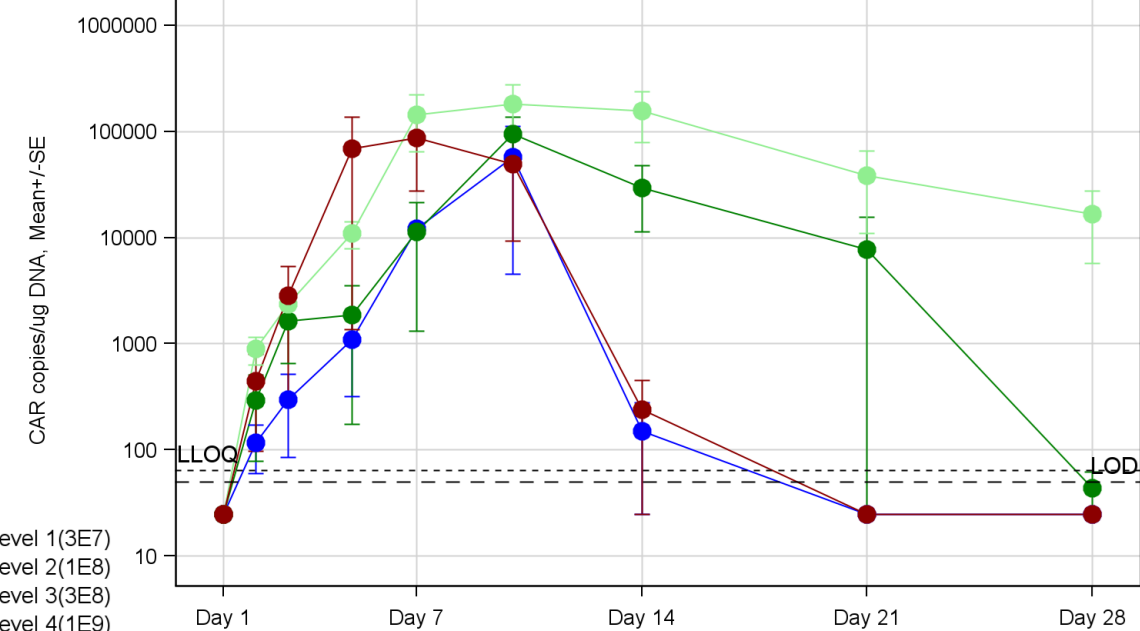


# Cmax, D28 Persistence and AUC Consistent Values Reported for Approved Autologous CD19 CAR T<sup>1</sup>

ADI-001 CAR by Flow Cytometry



ADI-001 CAR by ddPCR

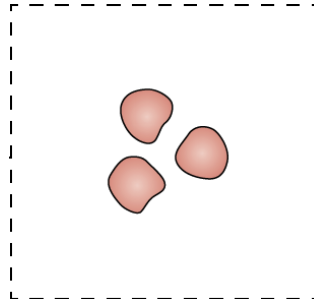
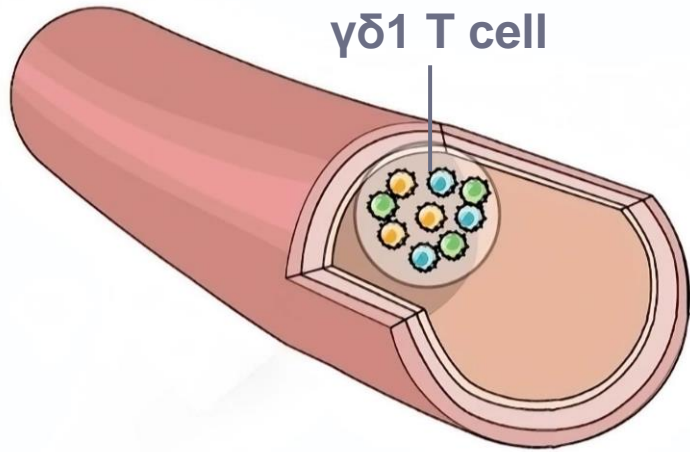


| Dose Level | Mean Cmax         |           | Mean D28          |           |
|------------|-------------------|-----------|-------------------|-----------|
|            | CAR+ Vd1 cells/ul | Copies/ug | CAR+ Vd1 cells/ul | Copies/ug |
| DL4        | 363.80            | 201,666   | 26.51             | 16,553    |
| DL3        | 56.34             | 98,177    | 0.04              | 44        |

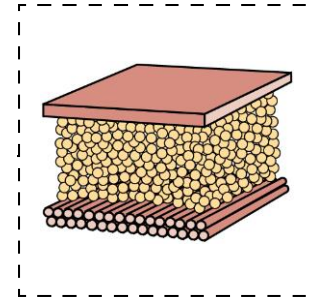
<sup>1</sup>Badbaran, A. Cancers 2020;12, 1970; Locke et al. N Engl J Med 2022; 386:640-654; Neelapu et al. N Engl J Med. 2017;377:2531-2544; Ogasawara et al. Clin Pharmacokinet 60, 1621–1633 (2021)  
D28= Day 28

# $\gamma\delta$ 1 T Cells Preferentially Home to Tissues

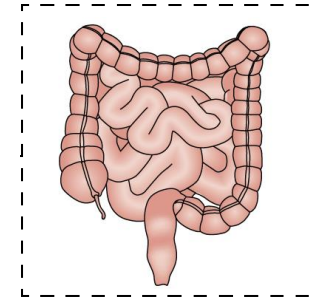
**peripheral blood<sup>10, 11</sup>**  
% of CD3+: ~1-3%



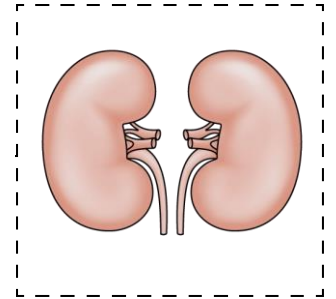
**lymph node<sup>3,4</sup>**  
CD27+  
CD62L+  
V $\delta$ 1+  $\uparrow\uparrow$   
V $\delta$ 2+  $\downarrow\downarrow$



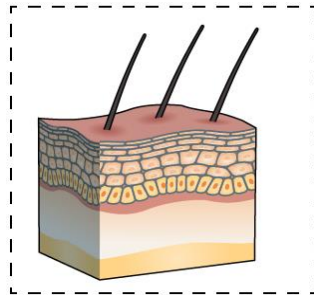
**breast<sup>5</sup>**  
tissue/blood: ~15X  
**adipose**  
tissue/blood: 9X



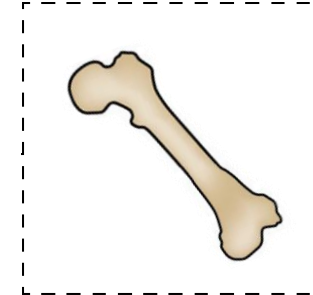
**GI<sup>6</sup>**  
tissue/blood: 11X



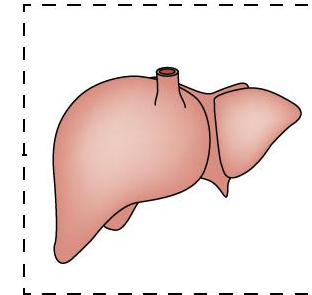
**kidney<sup>1</sup>**  
tissue: >3X  $\gamma\delta$  vs  $\alpha\beta$   
~3X more V $\delta$ 1 vs V $\delta$ 2+



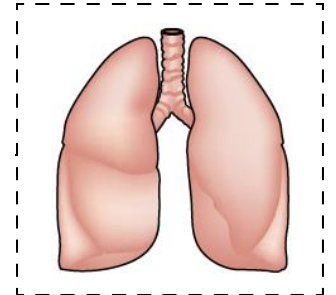
**skin<sup>8</sup>**  
tissue/blood: 8X



**bone marrow<sup>2</sup>**  
tissue/blood: 4X



**liver<sup>7</sup>**  
tissue/blood: 3X



**lung<sup>9</sup>**  
tissue/blood: 9X

Ratios empirically calculated or approximated from proportion of %CD3 from literature reports in relative compartment

Images adapted from Hunter *et al J Hepatol.* 2018 and Ribot *et al Nat Rev Immunol.* 2021

## References:

<sup>1</sup>Rancan *et al Nat Immunol* 2023

<sup>2</sup>Brauneck *et al Front Med* 2021

<sup>3</sup>Davey *et al Trends Immunol* 2018

<sup>4</sup>Uger *et al Sci Rep* 2018

<sup>10</sup>Wang Q. *et al Exp Ther Med* 2020

<sup>11</sup>Déchanet *et al J Infect Dis* 1999

<sup>5</sup>Wu *et al Sci Transl Med* 2019

<sup>6</sup>Deusch *et al Eur J Immunol* 1991

<sup>7</sup>Melo *et al Clin Immunol* 2021

<sup>8</sup>Toulon *et al J Exp Med* 2009

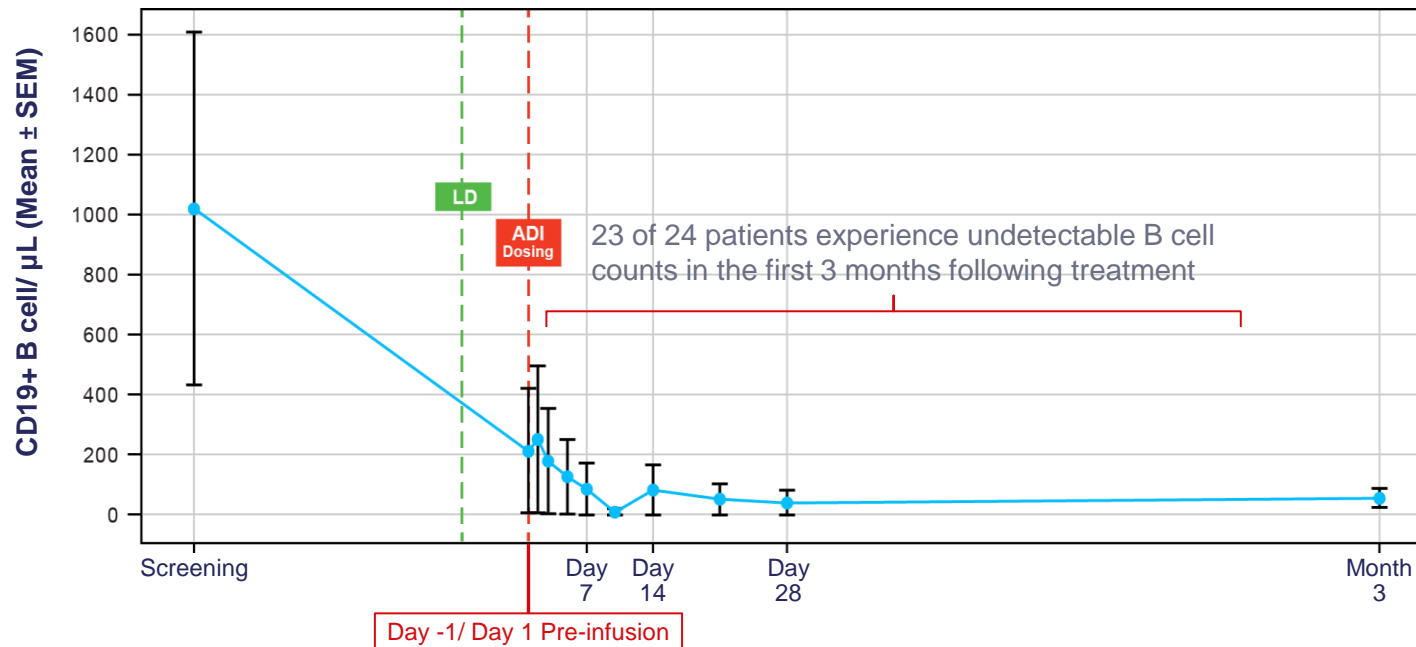
<sup>9</sup>Wisniewski *et al Am J Respir Cell Mol Biol* 2000

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

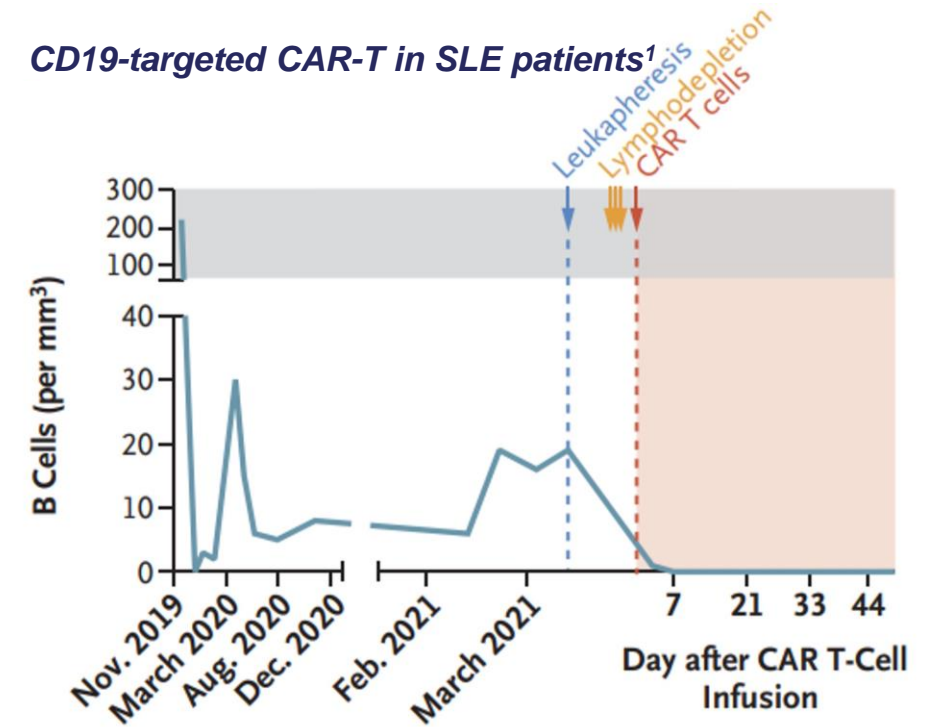
## B-cell Depletion

- B-cell depletion data from ADI-001 trial in NHL mirrored experience of autologous CD19 CAR T in SLE<sup>1,2</sup>
- 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<sup>3</sup>

### Adicet Bio CD20-targeted, ADI-001, in B-NHL patients<sup>4</sup>



### CD19-targeted CAR-T in SLE patients<sup>1</sup>



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



# 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)<sup>1,2</sup>
- B-cell depletion via CD20 targeting validated by CD20-targeted antibody (obinutuzumab) which demonstrated efficacy on top of SOC in lupus nephritis in Phase II clinical study<sup>3</sup>

### $\gamma\delta$ 1 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<sup>4,5,6</sup>
- $\gamma\delta$ 1 T cells preferentially traffic to organs/tissues<sup>7</sup> 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<sup>\*</sup>
- 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

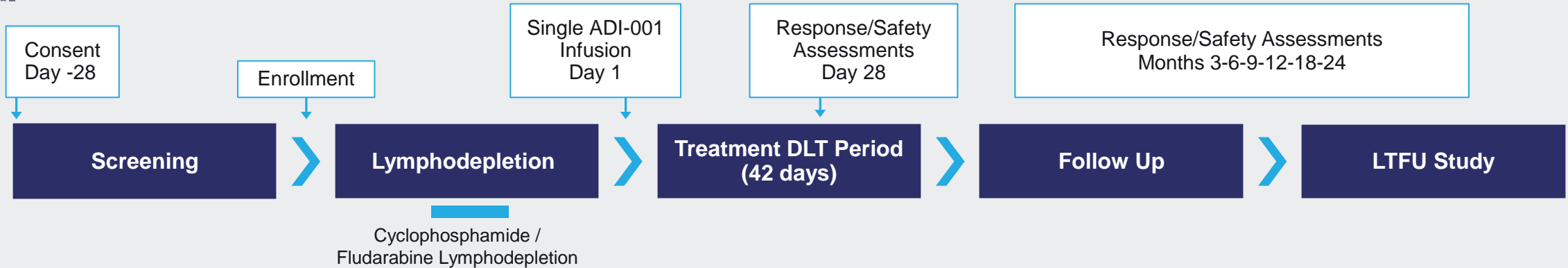
5. Reddy VK et al. Rheumatology 2022  
6. Sadun RE and Foster MH AJKD 2019  
7. Zhang, PJ Hematol Oncol 2023

COGs= Cost of goods

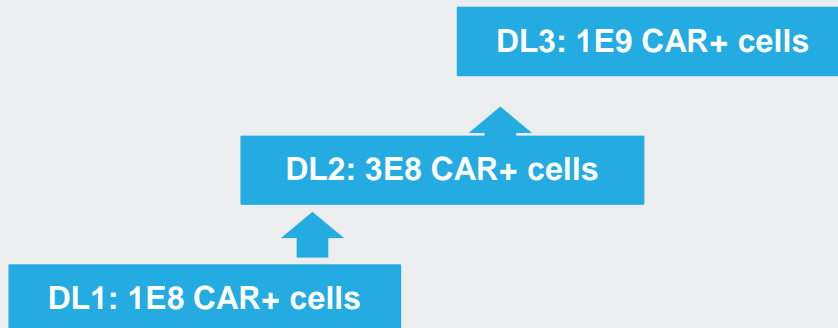
<sup>\*</sup> ADI-001 May 4, 2023 Data-cut date, n=24 evaluable patients

# ADI-001 Phase 1 Study Design: Lupus Nephritis

A.



B.



3+3 design

C.

Lupus Nephritis  
Dose Expansion  
(approx. 20 patients)

# ADI-001 in Lupus Nephritis: Key Endpoints

## Primary endpoints

### Part 1

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

### Part 2

- Safety profile at the MTD/MAD/RP2D of ADI-001 in patients with LN

## Secondary endpoints

- Levels of ADI-001 cells in peripheral blood
- Response to treatment:
  - CR or PR on day 28 and month 3, 6, 9, 12, 18, 24 after infusion of ADI-001
- Biomarkers associated with response to treatment:
  - Antibody to dsDNA, antinuclear antibody (ANA) and complement levels

## Exploratory endpoints

- Response per SLEDAI-2K/DORIS criteria



# ADI-001: Lupus Nephritis

## Opportunity

- Type of kidney disease caused by SLE, an autoimmune disease which affects an estimated 325,000 people in the U.S.<sup>1</sup>
- LN is a serious complication of SLE which affects approximately 40% of patients with SLE<sup>2</sup> and occurs when the immune system attacks the kidneys<sup>3</sup>
- Current treatment aims to reduce symptoms, keep the disease from getting worse, and keep the kidneys working well enough not to need dialysis or a kidney transplant

## Next Steps

- IND cleared for ADI-001 in lupus nephritis in December 2023
- Expect to initiate Phase 1 study 2Q 2024
- Expand to additional AI indications

1. Arthritis Rheum 2008 Jan;58(1):15-25. doi: 10.1002/art.23177.- Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part 1.

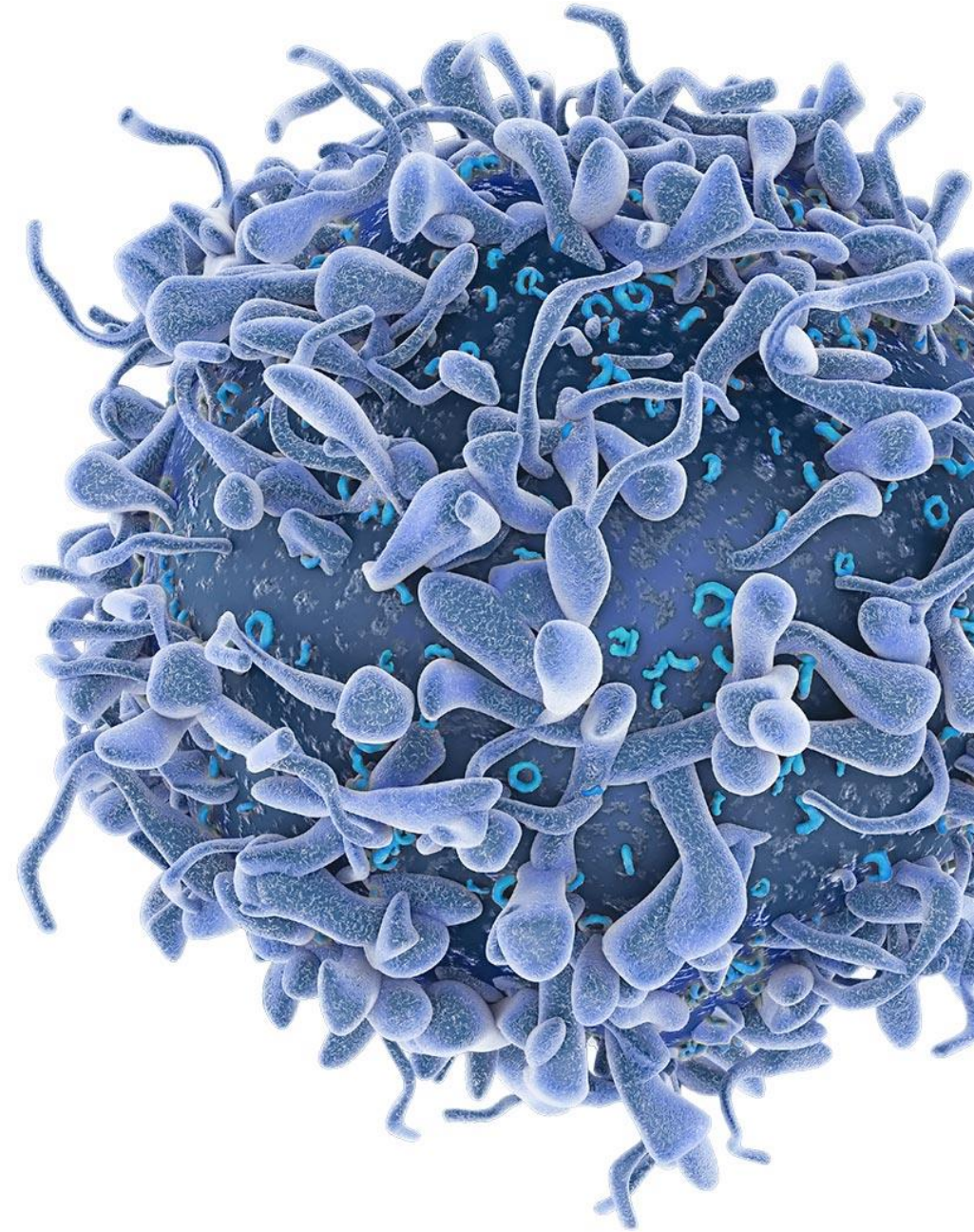
2. Hoover PJ et al.; Kidney Int 2016

3. Crampton, Steve P. et al. "Skin Malar rash Discoid rash CNS Spleen Splenomegaly Kidney Serum Glomerulonephritis Anti-nuclear antibodies Blood IFN signature Plasma blasts Anemia Thrombocytopenia Neurological damage Affective disorder Lung Inflammation Joints Arthritis." (2014).



# ADI-001

## Mantle Cell Lymphoma

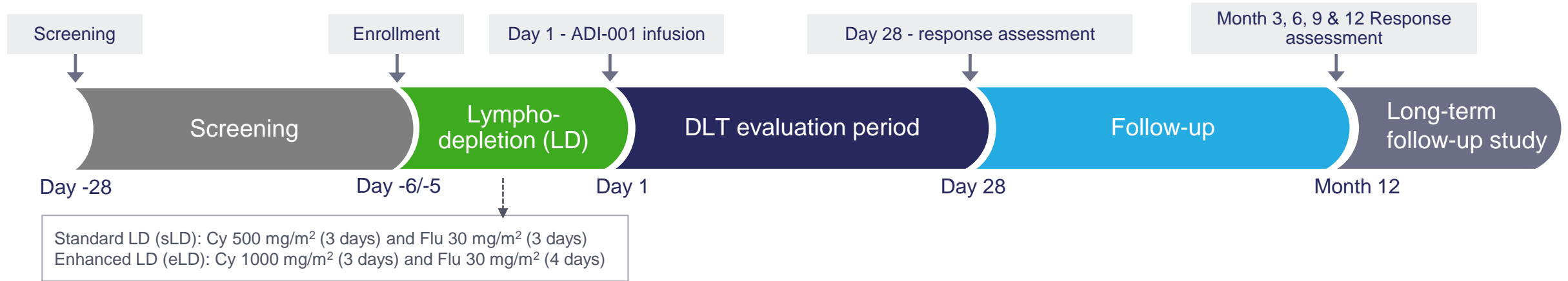


# ADI-001: Encouraging Early Efficacy Data in Heavily Pretreated NHL Patients

- Demonstrated efficacy and favorable safety in 24 patients with aggressive r/r B-cell NHL
  - Heavily pre-treated patients: median 4 prior lines of therapy with 50% prior CAR T
  - Across All Doses: 71% ORR and 63% CR (LBCL & MCL)
  - RP2D: 75% ORR, 63% CR, 25% 6-months CR rate (LBCL & MCL)
  - MCL (all doses): 80% CR rate, 60% 6-months CR rate
  - No significant incidence of CRS or ICANS or T cell malignancy risk; “off-the-shelf”
  - DL4 (RP2D) Cmax, D28 persistence, AUC consistent with approved CD19 autologous CAR T
- Potential for highly differentiated profile for MCL: High CR Rate, favorable durability, safety, “off-the-shelf” dosing, and ability to dose in community setting
- Evaluating option of advancing to a potentially pivotal study in MCL under an accelerated approval pathway
- Strong foundation for growing pipeline of next-generation engineered  $\gamma\delta 1$  T cell therapies



# GLEAN: ADI-001 First-in-Human Study (CD20 CAR+ $\gamma\delta$ 1 T cells)



## ADI-001 Dose (CAR+ Cells) (3 + 3 escalation design)\*

| DL1 | DL2 | DL3 | DL4 |
|-----|-----|-----|-----|
| 3E7 | 1E8 | 3E8 | 1E9 |

### Primary endpoint:

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

### Secondary endpoint:

- ORR, DOR, PFS, TTP, and OS
- PK, immunogenicity

### MCL:

- Enrolling MCL patients 3L+, DL4
- Prior CAR-T allowed

\*Protocol part 1b includes patients receiving single lymphodepletion and two infusions at DL3 (two doses 300 million CAR+ cells, one on day 1 and the second dose on day 7)

# ADI-001: Patient Characteristics

| Patient Characteristics  | N (%) (Total N = 24)              |
|--|-----------------------------------|
| <b>Age – median (range)</b>  | 66.5 (44 - 75)                    |
| Sex – number of male   | 17 (70.8)                         |
| <b>B cell malignancy (WHO 2017 classification)</b>                       |                                   |
| Large B cell lymphoma (LBCL)   | 18 (75.0)                         |
| · <i>R/R diffuse large B cell lymphoma</i>                               | 13 (54.2)                         |
| · <i>R/R high grade B cell lymphoma, double/triple hit</i>               | 4 (16.7)                          |
| · <i>R/R high grade B cell lymphoma, NOS</i>                             | 1 (4.2)                           |
| R/R mantle cell lymphoma (MCL)   | 5 (20.8)                          |
| Follicular   | 1 (4.2)                           |
| <b>IPI score (LBCL) - median (range)</b>                                 | 2.5 (1 - 4)                       |
| Simplified MIPI score-median (range)                                     | 5 (4 - 8)                         |
| Follicular IPI score-median(range)                                       | 2 (2 - 2)                         |
| Stage III & IV disease   | 17 (70.8)                         |
| <b>Sum of the product of the diameters at screening - median (range)</b> | 3001 (150 - 7919) mm <sup>2</sup> |
| Prior lines of therapies - median (range)                                | 4 (2 - 9)                         |
| <b>Prior anti-CD19 CAR T therapies</b>                                   | 12 (50.0)                         |
| <b>Prior systemic anti-cancer therapy</b>                                |                                   |
| CD20 mAB + anthracycline-based chemo                                     | 23 (95.8)                         |
| CD20 mAB + non-anthracycline-based chemo                                 | 15 (62.5)                         |
| Only chemotherapy  | 1 (4.2)                           |
| POLA or POLA-R or POLA-BR  | 7 (29.2)                          |
| BTK inhibitors +/- other drugs (except CD20 combination)                 | 5 (20.8)                          |
| CD20 mAB   | 7 (29.2)                          |
| CD19 biologics or combinations   | 5 (20.8)                          |
| Anti-CD19 CAR T  | 12 (50.0)                         |
| Other experimental therapies   | 2 (8.3)                           |
| CD20 +/- Lenalidomide/Bortezomib/Venatoclax/Ibrutinib                    | 2 (8.3)                           |
| <b>Refractory status at study entry</b>                                  |                                   |
| Refractory to first-line therapies                                       | 10 (41.7)                         |
| Refractory to second-line therapies                                      | 12 (50.0)                         |
| Refractory to the last course of anti-cancer systemic therapy            | 13 (54.2)                         |

- 23 patients had aggressive B-cell lymphoma: 18 LBCL and 5 MCL; 1 patient enrolled with follicular lymphoma
- Most patients were heavily pre-treated with **median four prior lines of therapy**, relatively high tumor burden and poor prognostic outlook
- **Twelve patients (50%) progressed following approved autologous anti-CD19 CAR T cell therapy** - Yescarta (axi-cel), Breyanzi (liso-cel) or Tecartus (brexu-cel)
  - 8/12 of patients progressed within less than 6 months from date of autologous CAR T administration
- **~70% of patients were refractory** to the last course of systemic therapy, and the remaining had relapsed

# ADI-001: Efficacy Summary by Dose Level

|                        | Median No.<br>of Prior Lines | ORR (%)             | CR Rate (%)       | 6-month<br>CR Rate (%) |
|------------------------|------------------------------|---------------------|-------------------|------------------------|
| DL4 (RP2D; LBCL & MCL) | 4                            | 6/8 (75.0%)         | 5/8 (62.5%)       | 2/8 (25.0%)            |
| <b>DL 4 MCL</b>        | <b>4</b>                     | <b>2/2 (100.0%)</b> | <b>2/2 (100%)</b> | <b>2/2 (100%)</b>      |
| All Doses (LBCL & MCL) | 4                            | 17/24 (70.8%)       | 15/24 (62.5%)     | 4/24 (16.7%)           |
| <b>All Doses MCL</b>   | <b>4</b>                     | <b>4/5 (80%)</b>    | <b>4/5 (80%)</b>  | <b>3/5 (60%)</b>       |

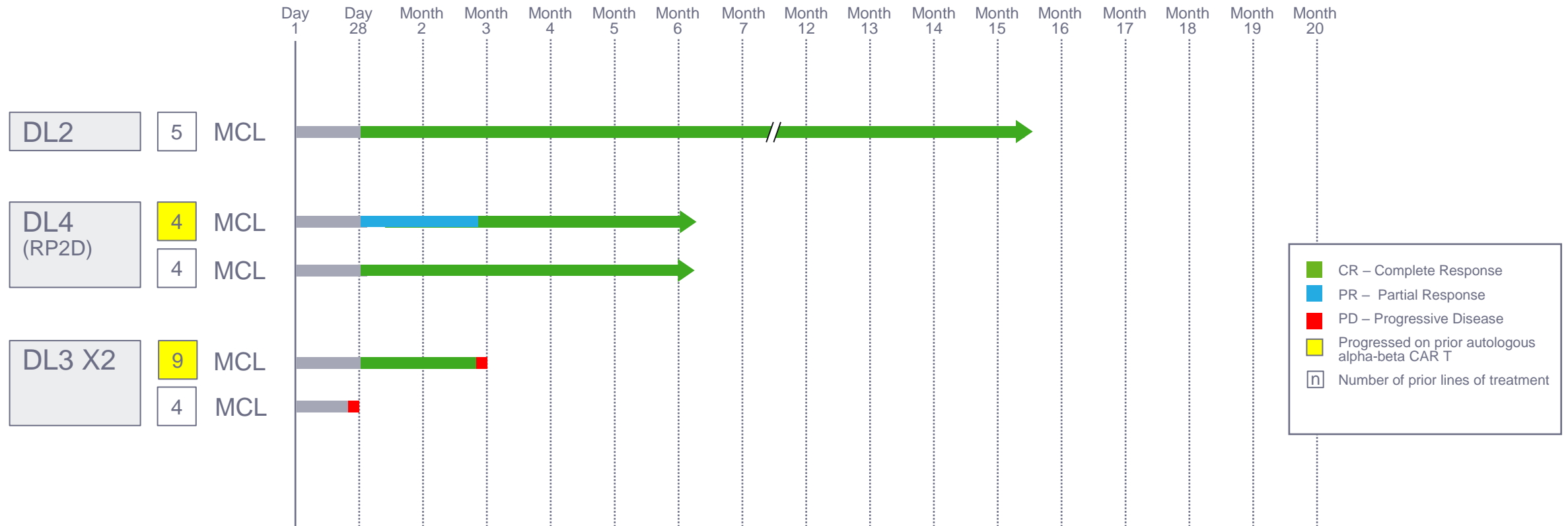
High CR rate and favorable durability in MCL



# ADI-001: Safety Data in Efficacy Evaluable Patients

|                         | DL1 (N=3)    |              | DL2 (N=3)    |              | DL3 (N=6)    |              | DL3 X2 (N=4)  |              | DL4 (N=8)    |              | Total (N=24)  |               |
|-------------------------|--------------|--------------|--------------|--------------|--------------|--------------|---------------|--------------|--------------|--------------|---------------|---------------|
|                         | Any Grade    | Gr>=3        | Any Grade    | Gr>=3        | Any Grade    | Gr>=3        | Any Grade     | Gr>=3        | Any Grade    | Gr>=3        | Any Grade     | Gr>=3         |
| <b>CRS</b>              | 2<br>(66.7%) | 0            | 0            | 0            | 1<br>(16.7%) | 1<br>(16.7%) | 4<br>(100.0%) | 0            | 4<br>(50.0%) | 0            | 11<br>(45.8%) | 1<br>(4.2%)   |
| <b>ICANS</b>            | 0            | 0            | 1<br>(33.3%) | 0            | 0            | 0            | 1<br>(25.0%)  | 1<br>(25.0%) | 1<br>(12.5%) | 0            | 3<br>(12.5%)  | 1<br>(4.2%)   |
| <b>GvHD</b>             | 0            | 0            | 0            | 0            | 0            | 0            | 0             | 0            | 0            | 0            | 0             | 0             |
| <b>DLT</b>              | 0            | 0            | 0            | 0            | 0            | 0            | 0             | 0            | 0            | 0            | 0             | 0             |
| <b>Infection</b>        | 1<br>(33.3%) | 1<br>(33.3%) | 2<br>(66.7%) | 0            | 3<br>(50.0%) | 2<br>(33.3%) | 2<br>(50.0%)  | 1<br>(25.0%) | 3<br>(37.5%) | 2<br>(25.0%) | 11<br>(45.8%) | 6<br>(25.0%)  |
| <b>SAE-TEAE</b>         | 1<br>(33.3%) | 1<br>(33.3%) | 2<br>(66.7%) | 2<br>(66.7%) | 4<br>(66.7%) | 3<br>(50.0%) | 2<br>(50.0%)  | 2<br>(50.0%) | 3<br>(37.5%) | 2<br>(25.0%) | 12<br>(50.0%) | 10<br>(41.7%) |
| <b>Related SAE-TEAE</b> | 1<br>(33.3%) | 0            | 1<br>(33.3%) | 1<br>(33.3%) | 3<br>(50.0%) | 2<br>(33.3%) | 2<br>(50.0%)  | 2<br>(50.0%) | 3<br>(37.5%) | 2<br>(25.0%) | 10<br>(41.7%) | 7<br>(29.2%)  |

# Strong CR Rate and Durability in 4L+ MCL Patients



**ORR: 80%, CR rate: 80%, 6-month CR rate: 60%**

**No significant CRS or ICANS**

# Data Provides Strong Foundation for Future Development in MCL

- ✓ High CR rate
- ✓ Favorable durability in late-line patients
- ✓ Superior cell killing potency compared to autologous CAR T<sup>1</sup>
- ✓ Cmax, Day 28 persistence and AUC consistent with approved CD19 autologous CAR T
- ✓ Favorable safety profile with no significant risk of CRS, ICANS, or T-cell malignancy
- ✓ Potential to dose in community setting

# Focused Investments in Differentiated Early-Stage Pipeline

## ADI-270: Renal cell carcinoma and other solid tumors

- IND submission in RCC expected 2Q 2024
- Targeting CD70 via CD27-ligand has shown superiority to scFv CARs in preclinical studies
- Innate and adaptive targeting mechanisms associated w/ activity in RCC, AML, and other malignancies
- Armoring via TGF $\beta$  dominant-negative receptor addresses suppressive TME and HvG resilience
- Lead CAR demonstrated potency and improved serial killing & resilience against suppressive factors in preclinical models

## Metastatic castration-resistant prostate cancer program

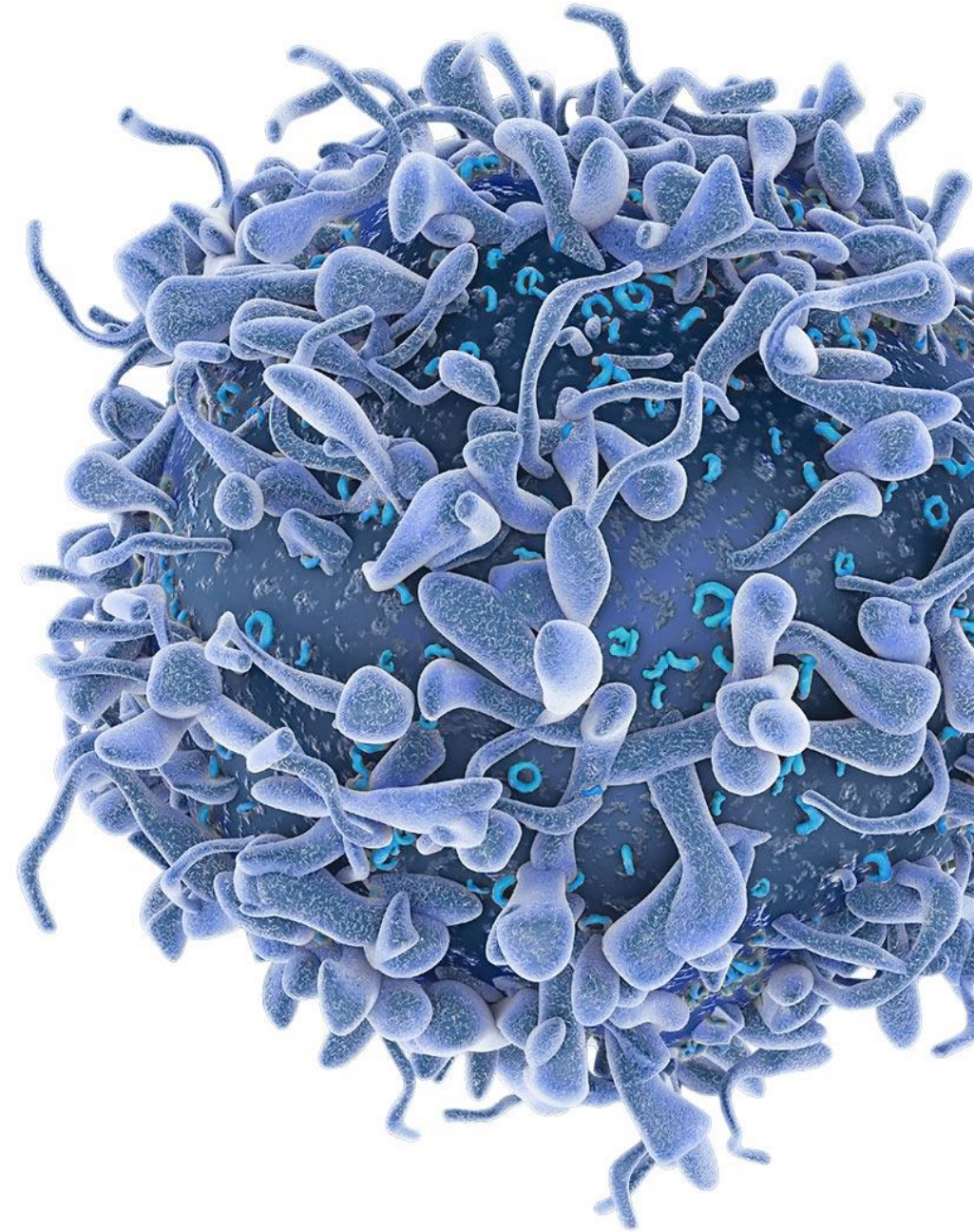
- Adicet lead scFv antibody designed to have similar binding determinants as approved radioligand therapy
- Highly potent cell therapy with armoring intended to address immunosuppressive solid tumor environment & heterogeneous PSMA expression
- Leveraging  $\gamma\delta 1$  T cell tropism to solid tissues
- Multiple modes of cell killing: CAR mediated, innate and adaptive immunity





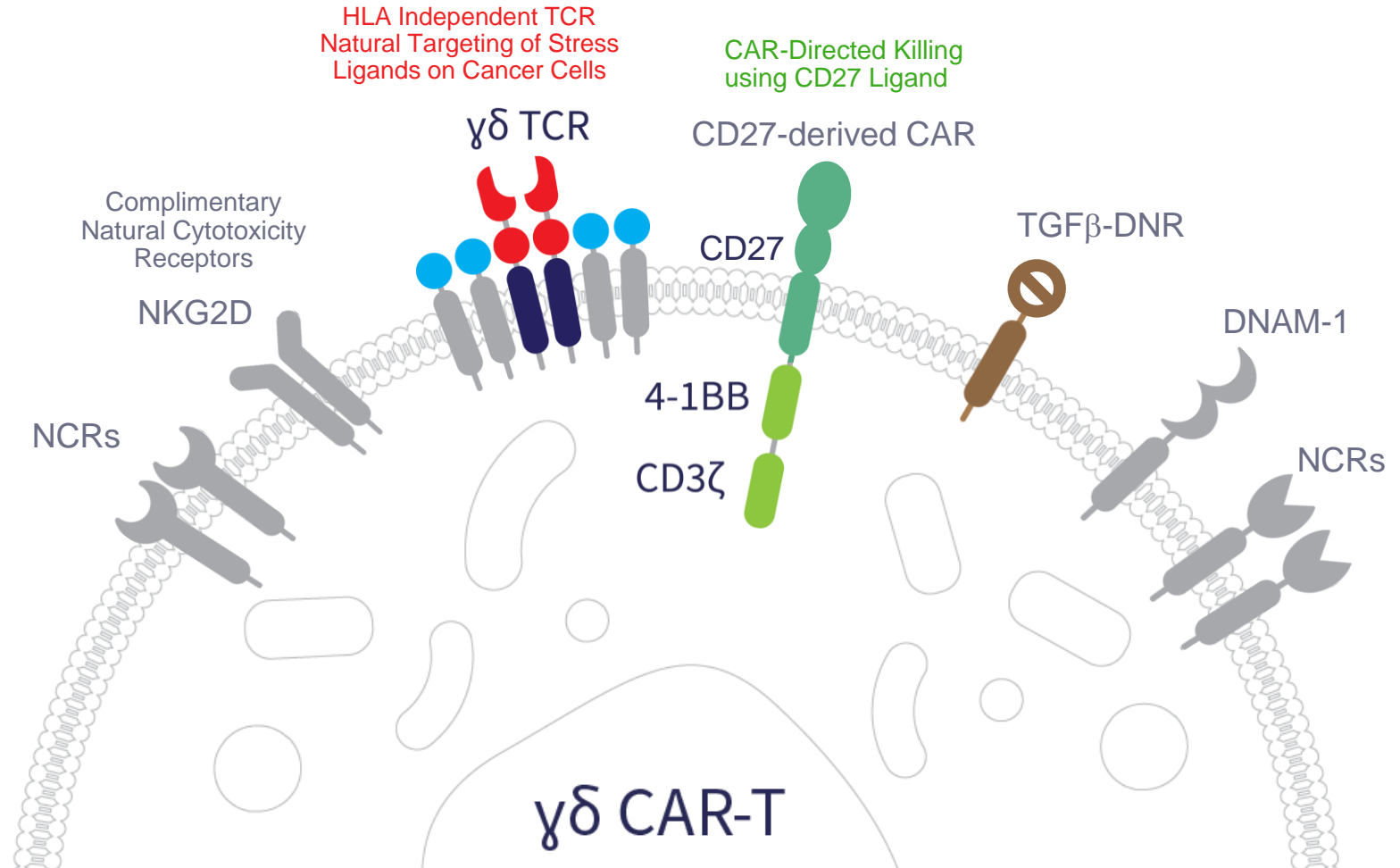
# ADI-270

## Renal Cell Carcinoma & Other CD70+ Diseases



# ADI-270: Adicet's Armored CD70 CAR $\gamma\delta$ T Cell

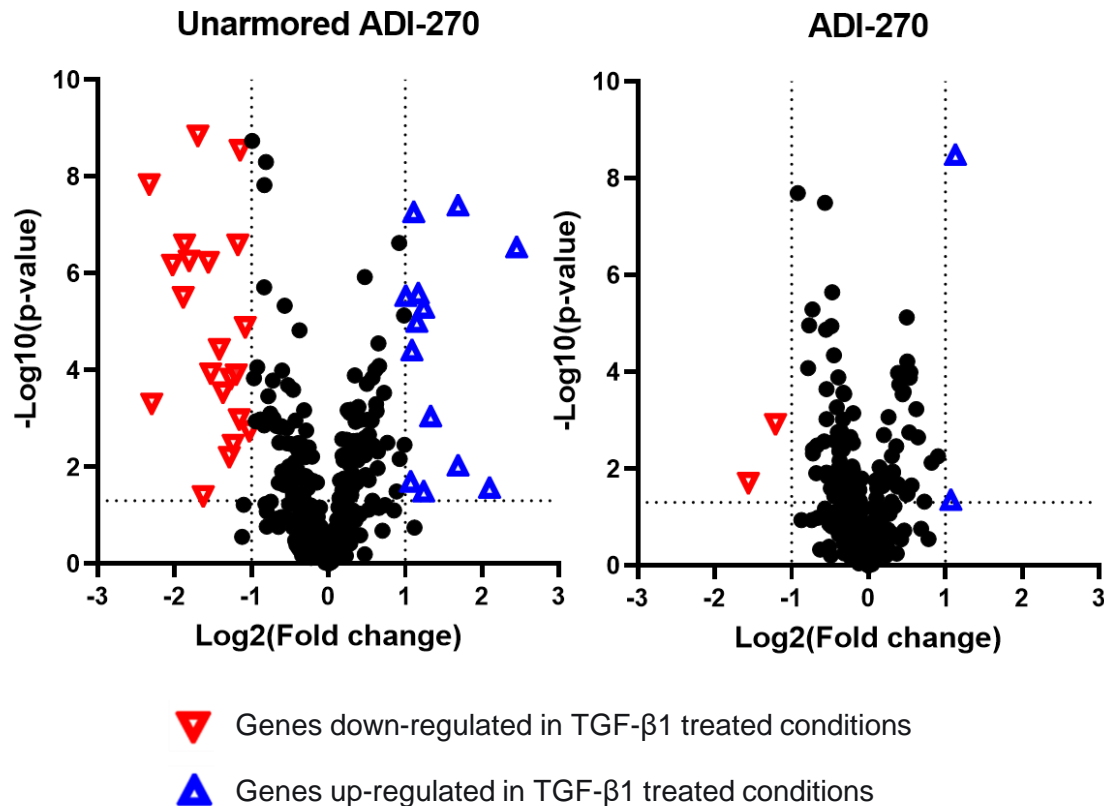
- Targeting CD70 via CD27-ligand has shown superiority to scFv CARs<sup>1</sup>
- Innate and adaptive targeting mechanisms associated with activity in RCC and other indications<sup>2</sup>
- Armoring via dominant negative receptor; addresses TGF $\beta$  in TME<sup>3</sup>
- Next-generation CAR format demonstrated potency and improved serial killing, and resilience against suppressive factors and HvG
- Homing and activity of  $\gamma\delta$  T cells demonstrated in RCC<sup>2</sup>



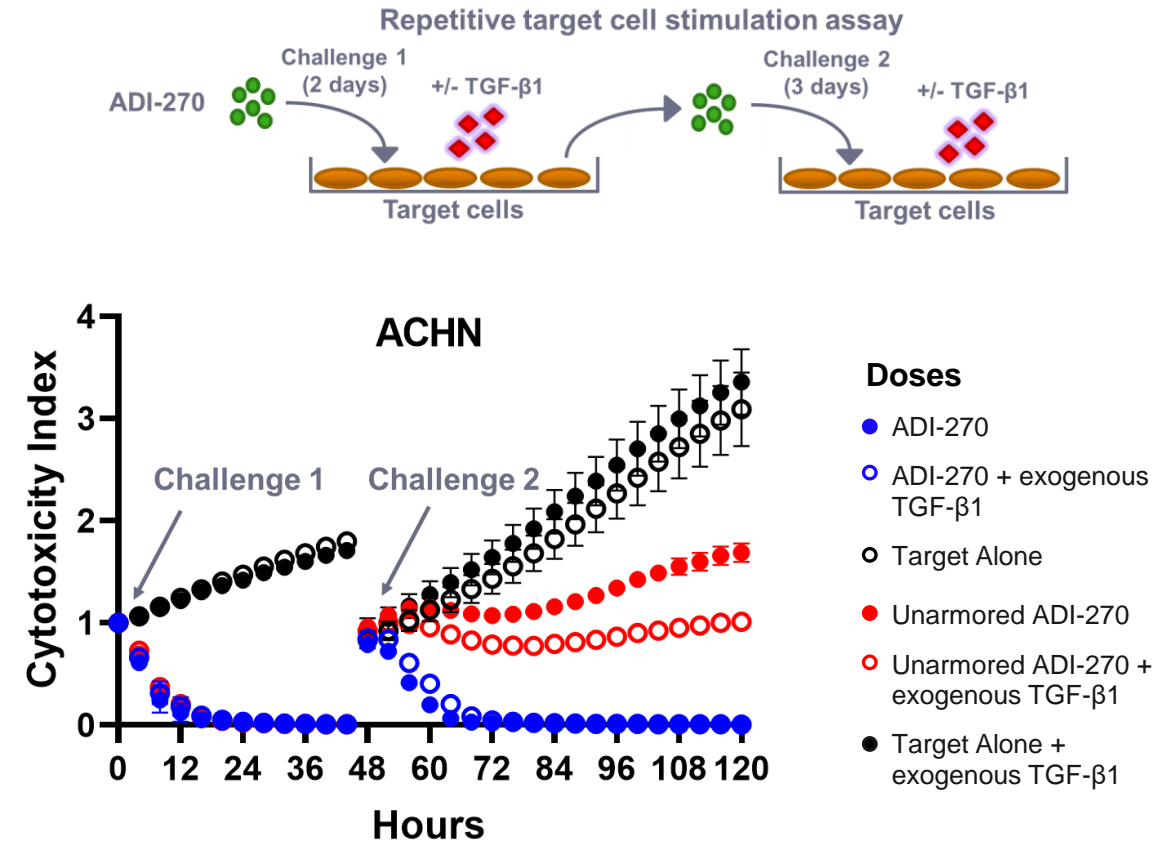
<sup>1</sup> Sauer et al. Blood (2021); <sup>2</sup> Rancan et al. Nat Immunol 2023; <sup>3</sup> Junker et al. Cytokine (2000); HvG=Host vs. Graft

# Armored CAR Demonstrated Resilience Against TGF $\beta$ and Maintained Potent Cytotoxic Function in Preclinical Models

Armored ADI-270 cells are protected against TGF $\beta$ -mediated alterations to activation expression profile

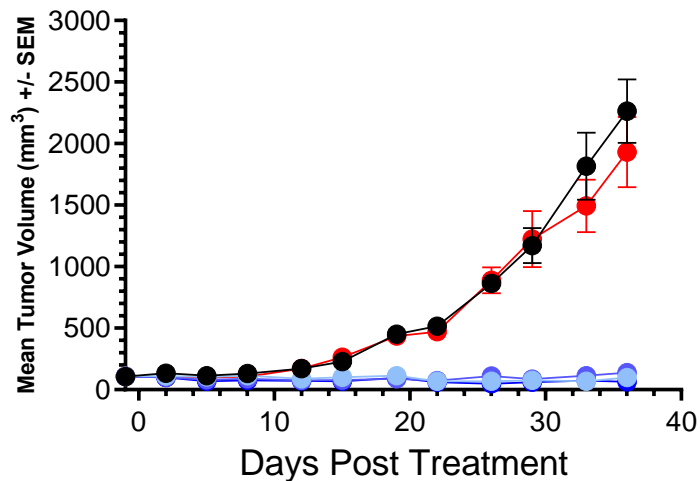
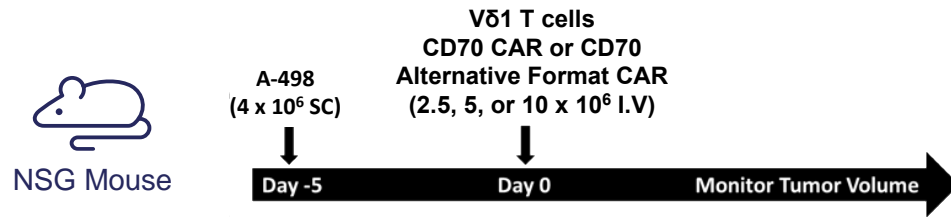


Armored CAR demonstrated improved serial killing



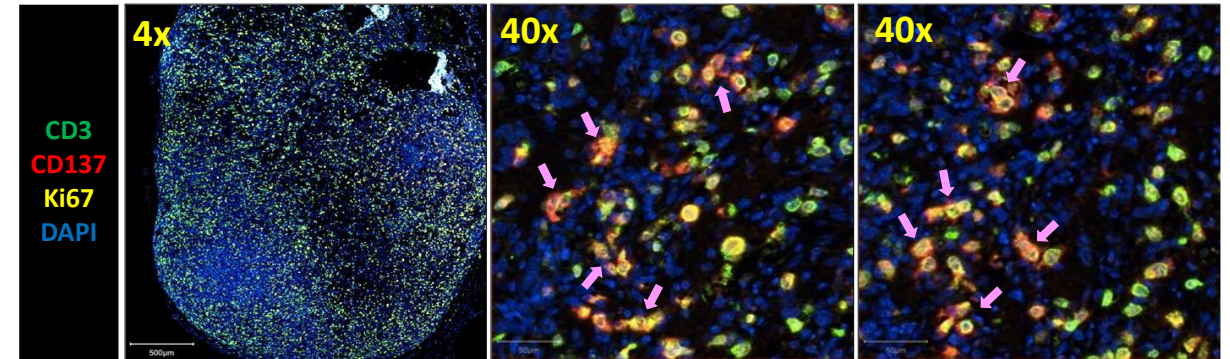


# CD70 CAR $\gamma\delta$ 1 T Cells Demonstrated Activity In Vivo and Proliferated Within Tumors



- Tumor alone
- CD70 CAR ( $2.5 \times 10^6$ )
- CD70 CAR ( $5 \times 10^6$ )
- CD70 CAR ( $10 \times 10^6$ )
- CD70 CAR Alternative format ( $5 \times 10^6$ )\*

## Tumor Infiltration and Proliferation of $\gamma\delta$ 1 CAR T cells



- Anti-tumor activity associated with CAR  $\gamma\delta$ 1 T cell tumor infiltration and proliferation within the tumor bulk as evidenced by areas of marker colocalization noted with pink arrows



# Armored CD70 CAR $\gamma\delta$ 1 T Cell Opportunity For Differentiation

## Target validation

- **CD70 expression is present in majority of patients with RCC (80%)<sup>1</sup> & AML (>96%)<sup>2</sup>**
  - Including, **expression on both leukemic blasts and leukemic stem cells**<sup>3</sup>
- **Preliminary clinical validation of target in both AML and RCC:**
  - Clinical activity observed in AML with CD70-targeted mAb<sup>4,5</sup>
  - Single-digit ORR and double-digit SD rates with ADCs in RCC (& AML), limited by payload-driven toxicities<sup>6,7,8</sup>
  - Disease control seen with unarmored allogeneic  $\alpha\beta$  T-cell therapy (incl. one CR in advanced RCC patient)<sup>8</sup>

## Key challenges

- **Modest responses rates** with CD70-targeted agents to-date
- Agents with **limited mechanisms of action** do not address tumor heterogeneity
- **No tissue-specific mechanisms** for tropism with any agents (ADCs, mAbs,  $\alpha\beta$  T-cell therapy)
- **Payload-driven toxicities** with ADCs
- **Immunosuppressive environment of RCC and other solid tumors**

## Opportunity for Adicet and $\gamma\delta$ 1 T cells

- **Response to low antigen density** by design with **CD27-based CAR** (compared to scFv-based CAR)<sup>3</sup>
- **Three mechanisms of action** designed to address tumor heterogeneity
- **Homing** of  $\gamma\delta$ 1 T cells reported in RCC
- Next-generation CAR format enhanced durability and **improved HvG resilience**
- **Inclusion of armoring to address suppressive TME**

**IND filing expected 2Q 2024**

1. Adam et al. *BJC* (2006)  
2. Riether et al. *JEM* (2016)  
3. Sauer et al. *Blood* (2021)

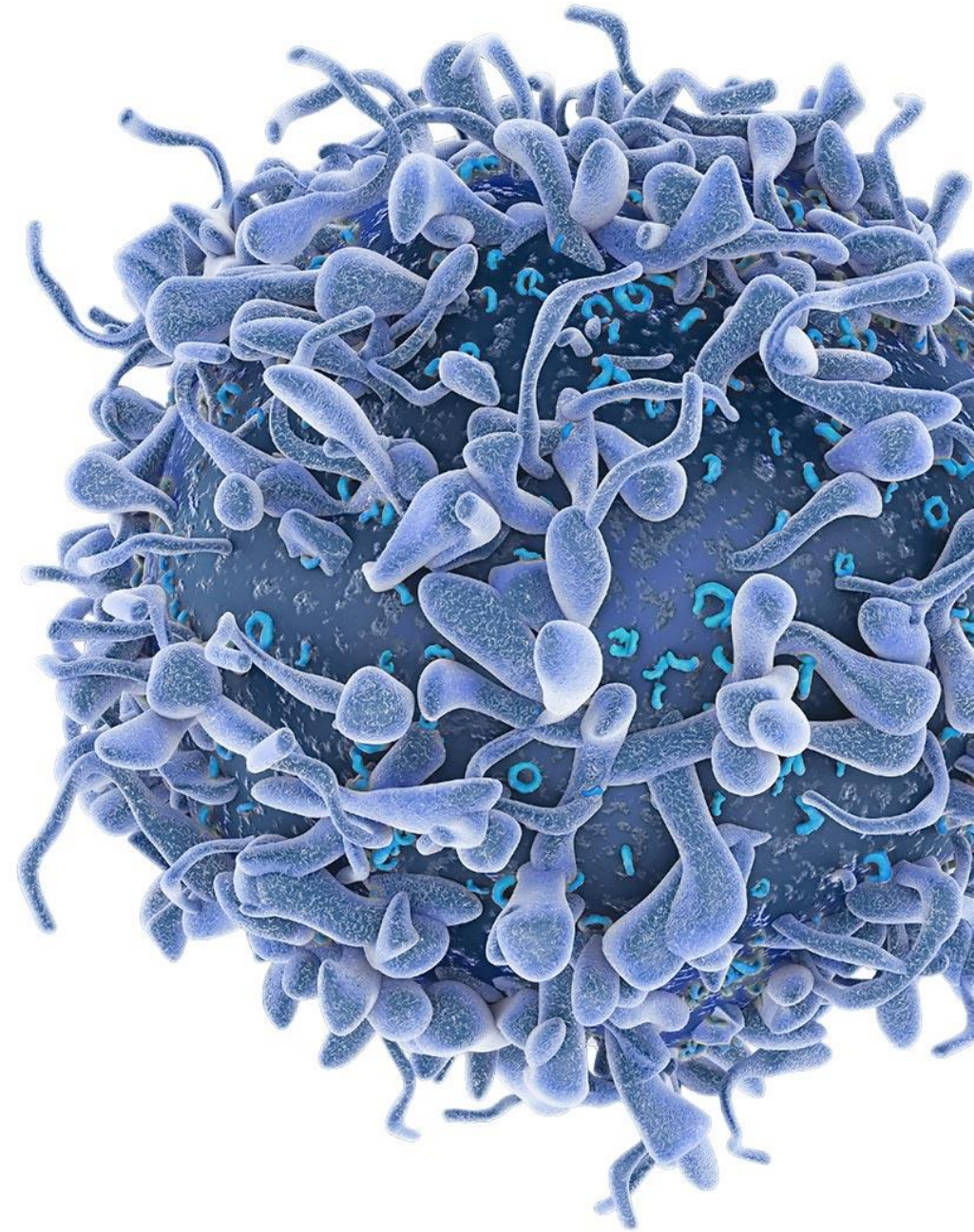
4. Aftimos et al. *Clin Cancer Res* (2017)  
5. Roboz et al. *ASH* (2021)  
6. Tanner et al. *Invest New Drugs* (2014)

7. Massard et al. *Cancer Chemother Pharmacol* (2019)  
8. CRISPR Therapeutics Presentation (2022)

ADC= Antibody-drug conjugate; AML= Acute myeloid leukemia; mAb= Monoclonal antibody; RCC= Renal cell carcinoma; SD= Stable disease; TME= Tumor microenvironment



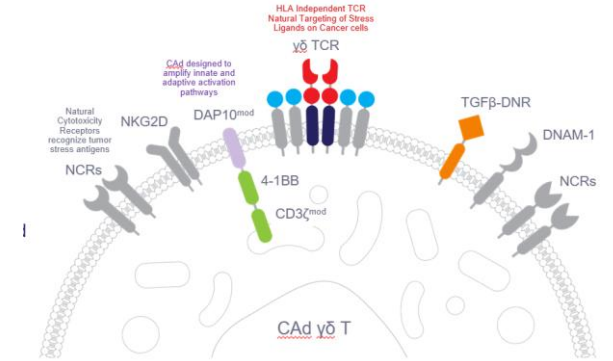
# PSMA Program



# Armored PSMA CAR $\gamma\delta$ 1 T Cell Program

## Program:

- Allogeneic PSMA CAR  $\gamma\delta$ 1 T cell therapy candidate for prostate cancer (PCa)
- Armoring demonstrated with TGF $\beta$ -DNR provides functional advantage for treating solid tumors
- Demonstrated penetration & killing in mCRPC primary tumor organoids



## Historical challenge:

- Safety issues with PSMA-targeted immunotherapies
- Modest efficacy with PSMA-targeted immunotherapies
- Immunosuppressive TME & poor T cell infiltration in PCa

## Adicet approach:

- Radioligand therapies are **the only approved PSMA-targeted agents** and bind functional PSMA homodimer, **associated with a favorable and differentiated off-tissue AE profile**<sup>1</sup>
- **Adicet's CAR is designed to have similar binding determinants as radioligand therapies**, recognizing a conformational epitope present on the homodimer ( $\uparrow$  selectivity)<sup>1,2</sup>
- **Promising safety profile for  $\gamma\delta$ 1 T cells observed in ADI-001 clinical trial**
- **Highly potent cell therapy compatible with armoring** to address immunosuppressive solid tumor environment & heterogeneous PSMA expression
- **Multiple modes of cell killing** – CAR mediated, innate and adaptive immunity
- Natural tropism of  $\gamma\delta$ 1 T cells to solid tissues
- **Infiltration of  $\gamma\delta$ 1 T cells reported and demonstrated in prostate cancer**

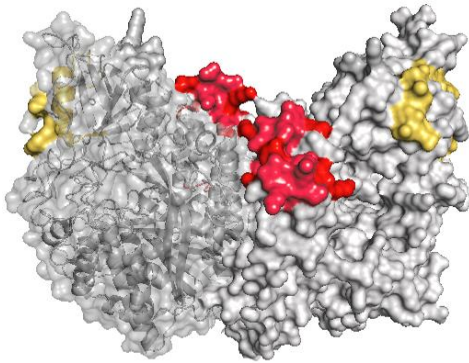
1. Deshayes E et al. Cancer (2023)

2. Schülke N et al. PNAS (2003)



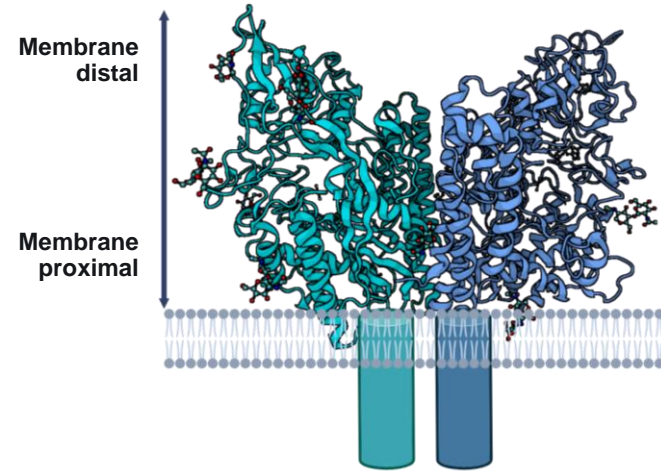
# Lead PSMA CAR Binding Determinants Designed to be Consistent With Pluvicto, The Only PSMA-Targeted Therapy With Validated Efficacy & Safety Profile

## Binding interface of mAbs on PSMA

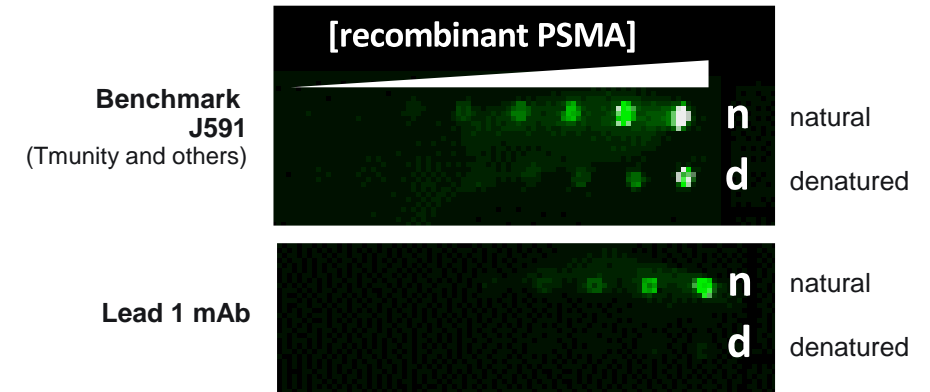


*Binding interface of Adicet lead binder (red) & benchmark binder J591 (yellow; Tmunity)*

## Full-length PSMA



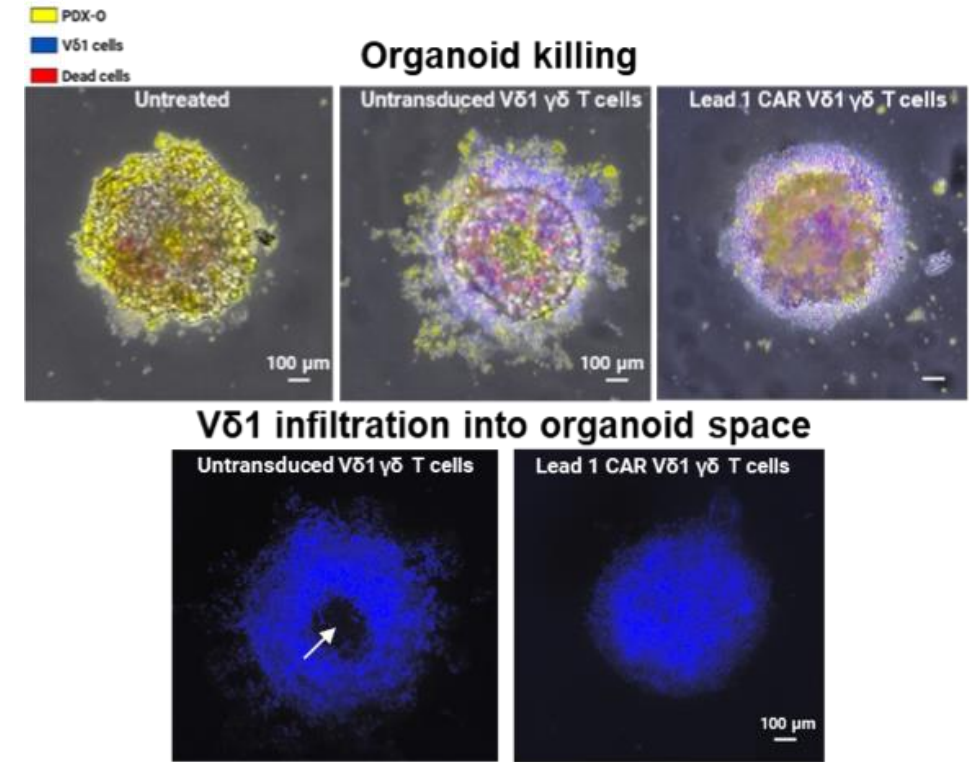
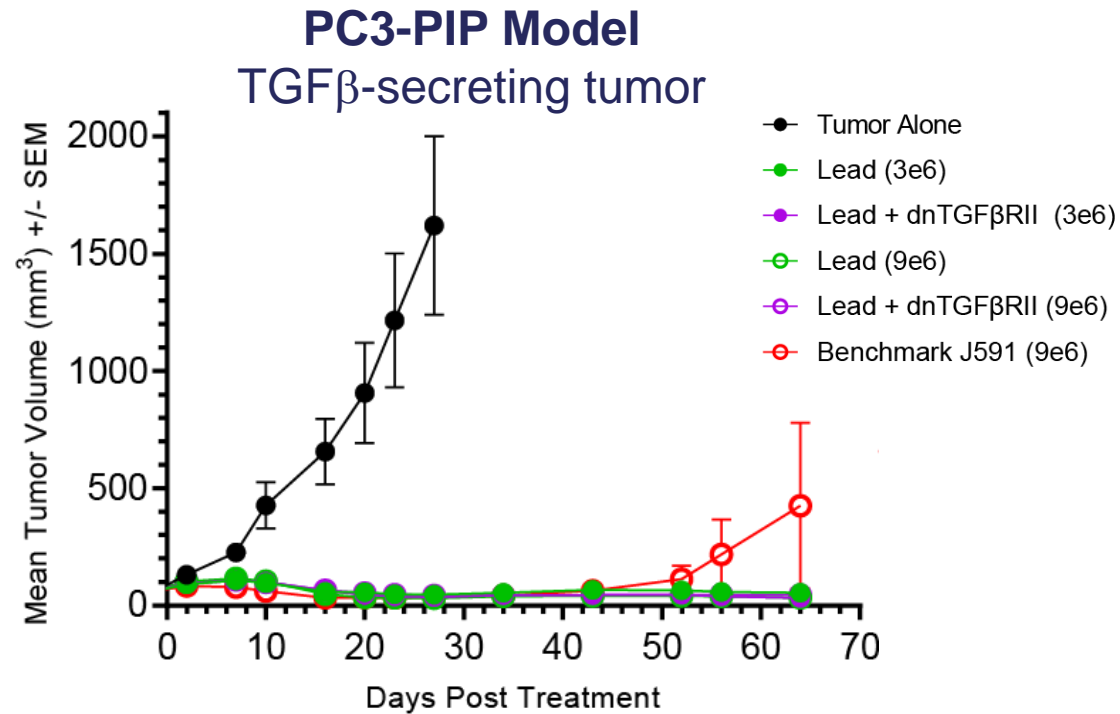
## PSMA Antigen Capture Assay



*Molecular determinants for J591 vs Adicet Lead are demonstrated to be conformationally distinct*

- Radioligand therapies bind the functional PSMA homodimer and are **associated with a favorable efficacy and off-tissue AE profile, and is the only approved PSMA-targeted therapy**
- **Adicet's lead scFv antibody is designed to have similar binding determinants as radioligand therapies**, recognizing a conformational binding epitope and enzymatically active homodimeric form (↑ selectively)
- This profile is distinct and differentiated from other approaches for CAR, ADC, and bispecifics that recognize non-conformational, linear, or monomeric epitopes

# PSMA CAR $\gamma\delta$ 1 T-Cell Activity Observed in Primary Patient mCRPC Organoids



- Adicet PSMA CAR and armored versions retained tumor control in TGF $\beta$ -secreting prostate cancer model

- Adicet's unarmored lead CAR retained maximal control beyond 65 days at 3e6 CAR cell dose

- Benchmark CAR (J591) lost control of tumor despite a significant 9e6 CAR T cell dose

- Demonstrated infiltration and killing of primary patient derived tumor organoids

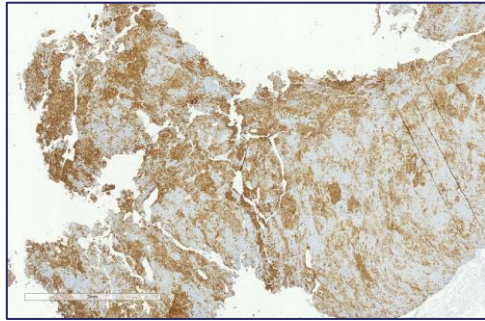
- V $\delta$ 1 T cells alone demonstrated intrinsic infiltration and killing, consistent with reported anti-tumor activity in mCRPC

- Infiltration and killing further enhanced with PSMA CAR



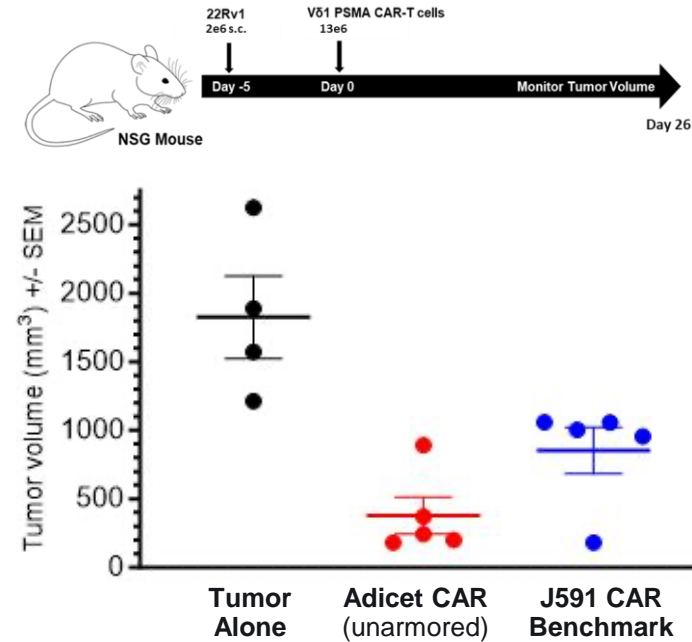
# CAR $\gamma\delta 1$ T Cells Highly Active Against 22Rv1 Xenograft Model, A Challenging Model With Intermediate & Heterogenous PSMA Expression

## 22Rv1 Tumors Express Intermediate and Heterogeneous PSMA

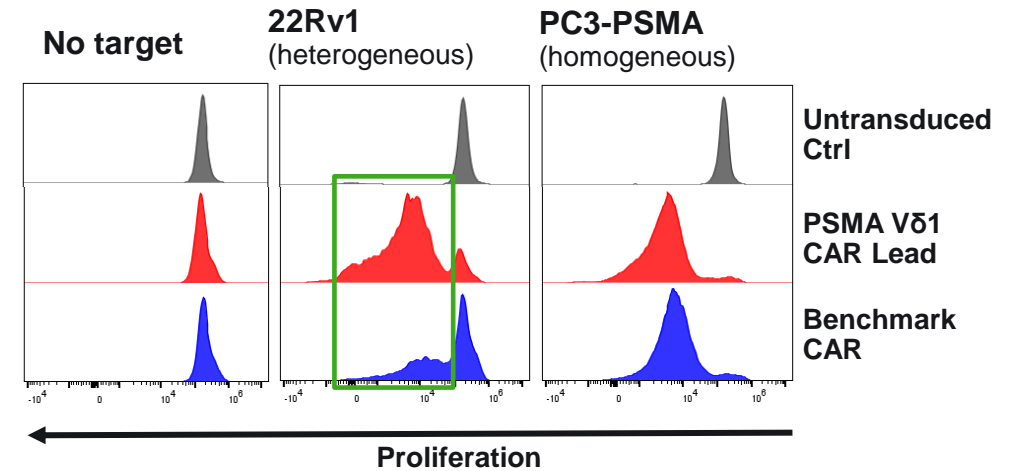


PSMA 2X

## Day 30 Tumor Volumes



## Target-Associated Proliferation



- Lead PSMA CAR retained robust target-associated proliferation in heterogenous PSMA expressing models
  - Benchmark CAR (J591) did not retain robust proliferation in the context of heterogenous mCRPC
  - Adicet's lead CAR retained superior tumor control versus benchmark CAR

# Armored PSMA CAR $\gamma\delta$ 1 T Cell Opportunity For Differentiation

## Target validation

- **PSMA expression** is present in **>85% of patients with mCRPC** with limited expression in normal tissues (100-1,000 times overexpressed)<sup>1</sup>
- **Clinically validated** via multiple modalities:
  - **PSMA targeted radiotherapy** approved for mCRPC<sup>2</sup>
  - **Immunotherapies** (T-cell engaging antibodies and cell therapies) demonstrated **PSA, PSMA-radiographic, and RECIST responses** in early clinical studies<sup>3,4,5</sup>

## Key challenges

- **Limited therapeutic index** due to CRS, ICANS, and macrophage activation syndrome with PSMA targeted **T cell engagers** and **alpha-beta CAR T cell** approaches<sup>3,6</sup>
- **Single mechanism of targeting** limits activity in heterogeneous tumors
- **Immunosuppressive environment** of mCRPC associated with TGF $\beta$ <sup>7</sup>

## Opportunity for Adicet and $\gamma\delta$ 1 T cells

- **Potent CAR construct** active against **heterogeneous PSMA**
- **Three mechanisms of action** designed to address tumor heterogeneity
- **Homing** of  $\gamma\delta$ 1 T cells documented in mCRPC
- **Inclusion of armoring** to address suppressive TME
- **No significant CRS and ICANS** demonstrated with Adicet CAR  $\gamma\delta$ 1 T cells in clinical trials reported to-date; **potential to address therapeutic index**

1. Friedlaender A et al. *healthbook TIMES Onco Hema* (2023)

2. Sartor et al. *N Eng J Med* (2021)

3. Tran et al. *Ann Onc.* (2020)

4. Bendell et al. *JCO* (2020)

5. Slovin et al. *JCO* (2022)

6. Narayan et al. *Nat Med* (2022)

7. Mirzaei et al. *Int J Biol Macromol*

mCRPC= metastatic castrate-resistant prostate cancer; PSMA= Prostate-specific membrane antigen; RECIST= Response Evaluation Criteria in Solid Tumors

# Potential Near-Term Milestones

|                             | 2024   |   | 2025   |   |
|-----------------------------|--|---|--|---|
|                             | 1H   | 2H  | 1H   | 2H  |
| ADI-001 Autoimmune Diseases | Initiate LN Phase 1<br>Expand to 1-2 Additional Autoimmune Indications | Preliminary Clinical Data in LN<br>Preliminary Clinical Data in 1-2 Additional Autoimmune Indications |  | Clinical Data in 3 Autoimmune Indications |
| ADI-001 MCL                 | Study Enrollment Ongoing   | Clinical Update   | Define Regulatory Path for Potentially Pivotal Phase 2 Study         | Clinical Update                           |
| ADI-270 RCC                 | ADI-270 IND Submission   |   | Clinical Data RCC and Potential Expansion to additional CD70+ Tumors | Clinical Update                           |

Proforma adjusted cash and cash equivalents : ~\$270.8M (12/31/23)<sup>1</sup>

Projected cash runway into 2H 2026

Subject to data readouts and regulatory feedback

<sup>1</sup>As of December 31, 2023, we had \$159.7M of cash and cash equivalents. The Proforma adjusted figure includes \$91.8M in net proceeds from a public follow-on offering and \$19.3M in net proceeds received under our at-the-market program in January 2024, after deducting estimated underwriting discounts, sales commissions and estimated offering expenses.



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

