



# First-in-class Allogeneic gamma delta CAR T Cells to Fight Cancer



# Forward-Looking Statements

This presentation contains "forward-looking statements" of Adicet Bio, Inc. (Adicet) within the meaning of the Private Securities Litigation Reform Act of 1995 relating to business and operations of Adicet. These forward-looking statements include, but are not limited to, express or implied statements regarding the potential safety, durability, tolerability and therapeutic effects of ADI-001, including the expected design, implementation, timing and success of ADI-001; plans and timing for the release of additional clinical data from Adicet's Phase 1 trial of ADI-001 in relapsed/refractory NHL patients; future progress of the GLEAN study, including ongoing patient enrollment; expectations regarding future regulatory filings for product candidates in the Company's pipeline; and timing of a dose selection for the Phase 2 trial in the second half of 2022 and initiation of a potentially pivotal program in the first half of 2023. 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 COVID-19 on Adicet's business and financial results, including with respect to disruptions to its clinical trials, business operations, 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 clinical study may not necessarily be predictive of the results of future or ongoing clinical 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. 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 subsequent filings with the SEC. All information in this presentation is as of the date its 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.

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

## ▶ Clinically Validated First-in-Class $\gamma\delta$ CAR-T Cell Platform

- Off-the-shelf  $\gamma\delta$  CAR T cell platform demonstrating preliminary efficacy and safety
- Positive readout with ADI-001 in heavily pre-treated NHL patients with wide therapeutic window
- At least one additional Phase 1 NHL clinical update H2 '22

## ▶ Robust pipeline

- ADI-001 potentially advancing to pivotal program in H1'23
- ADI-001 expansion studies in NHL subtypes / lines of therapies (DLBCL, MCL, FL)
- ADI-002\* for GPC3 solid tumors; six additional internal pre-clinical and discovery programs

## ▶ Proprietary Scalable Allogeneic Platform

- Cost-effective cGMP compliant manufacturing process
- Strong IP protection

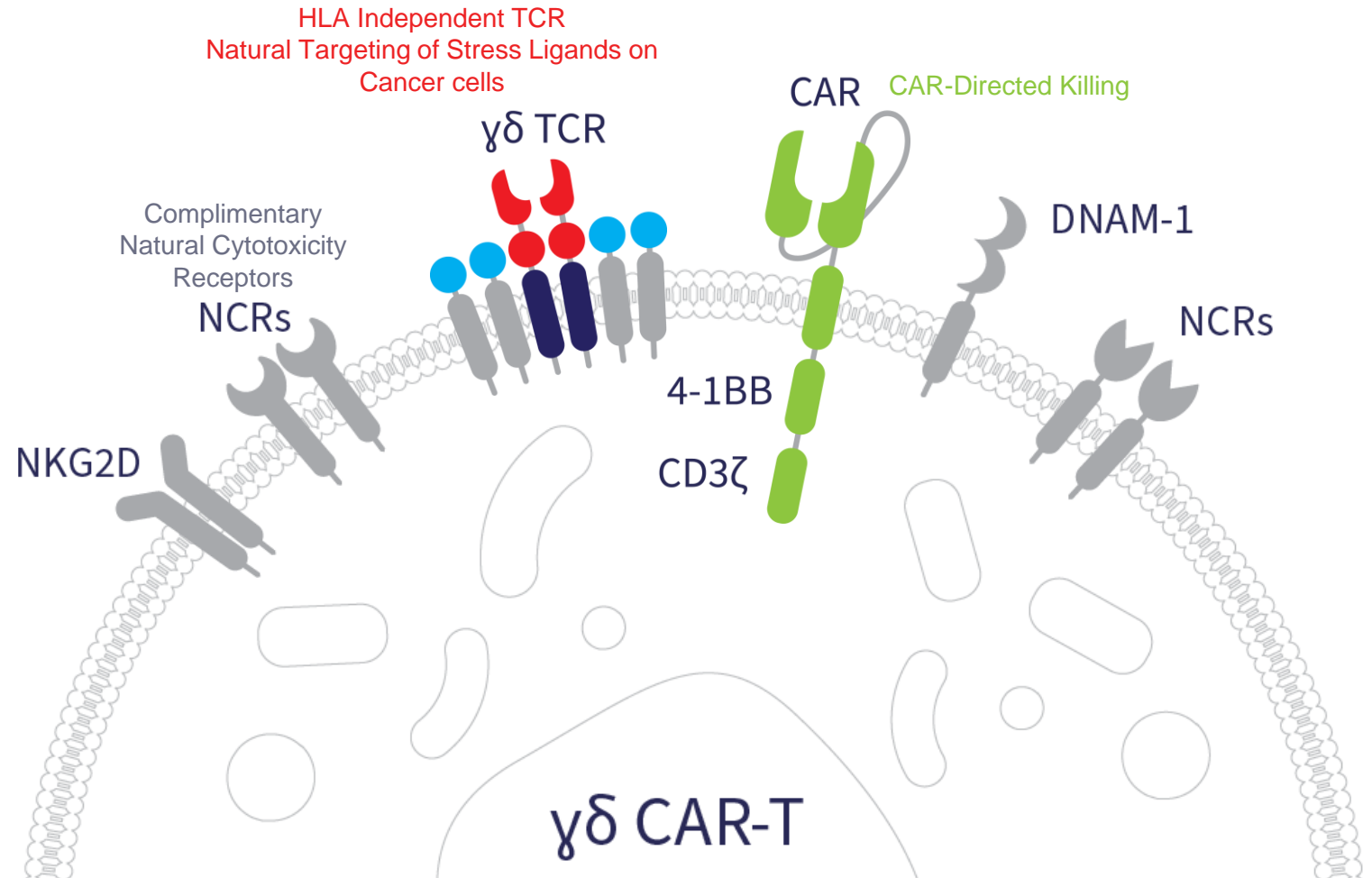
## ▶ \$277.9M cash and cash equivalents (as of 3/31/22)

# Adicet's $\gamma\delta$ 1 CAR T Cells: 3 Mechanisms for Anti-tumor Activity

$\gamma\delta$  CAR T cells designed to provide three mechanisms for anti-tumor activity; More limited ability for tumor escape

1. Innate anti-tumor activity targeting multiple surface proteins selected by evolution to mark tumors for cell killing
2. Adaptive anti-tumor activity via  $\gamma\delta$  TCR
3. CAR mediated anti-tumor activity

- No requirement for gene editing to remove TCR
- Potential for outpatient administration
- Intrinsically home to and function in tissues and solid malignancies










# ADI-001: Encouraging Early Efficacy Data in Heavily Pretreated Aggressive NHL Patients (Indolent Lymphoma Such as FL Not Enrolled)

- 75% ORR and CR rate with favorable safety and tolerability profile observed in the study to date\*
- 80% ORR and CR rate at dose level 2 and 3 combined
- 100% ORR and CR rate in three patients that relapsed after prior autologous anti-CD19 CAR T therapy
- 50% of evaluable patients with at least 6 months follow up remain cancer free
- Dose-related increase of ADI-001 exposure observed in blood
- Potential for best-in-class ORR, CR and durability given the anti-tumor activity offered by  $\gamma\delta 1$  CAR T cells
- Preliminary safety and efficacy data to date offer potential for a broad pivotal program across NHL types and lines of therapies



# Building a Broad Pipeline of First-in-Class $\gamma\delta$ CAR T Cell Therapy

Program	Target	Potential Indication	Discovery	Preclinical	IND	Ph 1	Ph 2/3	Commercial Rights
ADI-001	CD20	NHL						 Adicet Bio
ADI-002*	GPC3	HCC						<b>REGENERON</b>
ADI-003	Undisclosed	Solid / Heme						 Adicet Bio
ADI-004	Undisclosed	Solid / Heme						 Adicet Bio
ADI-005	Undisclosed	Solid / Heme						 Adicet Bio
ADI-006	Undisclosed	Solid / Heme						 Adicet Bio
ADI-007	Undisclosed	Solid / Heme						 Adicet Bio
ADI-008	Undisclosed	Solid / Heme						 Adicet Bio

## Milestones

- 2H/2022: Preclinical pipeline update
- One new IND planned every 12-18 months, including one new IND for internal program in 2023

\*Regeneron exercised its option to license the exclusive worldwide rights to ADI-002 in January 2022

# Anticipated Near-Term Milestones

- Complete dose escalation through DL4 to establish recommended Phase 2 dose in 2H/2022
- Backfill enrollment to DL3 with additional potential patients in 2H/2022
- Discuss with the FDA and EMA the design of two pivotal studies and a potential path to support a BLA and MAA for ADI-001
- Anticipate at least one additional clinical update for ADI-001 in 2H/2022
- Initiate at least one potentially pivotal study with ADI-001 in 1H/2023
- Preclinical pipeline update 2H/2022
- One new IND planned every 12-18 months, including one new IND for internal program in 2023

# Adicet Bio Leadership Team



Chen Schor  
President and CEO



Don Healey, Ph.D.  
Chief Technology Officer



Blake Aftab, Ph.D.  
Chief Scientific Officer



Nick Harvey  
Chief Financial Officer



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





# Adicet $\gamma\delta$ CAR T Cell Platform Potential Advantages: Designed to Address Activity, Tumor Homing, Safety, and COGs Limitations

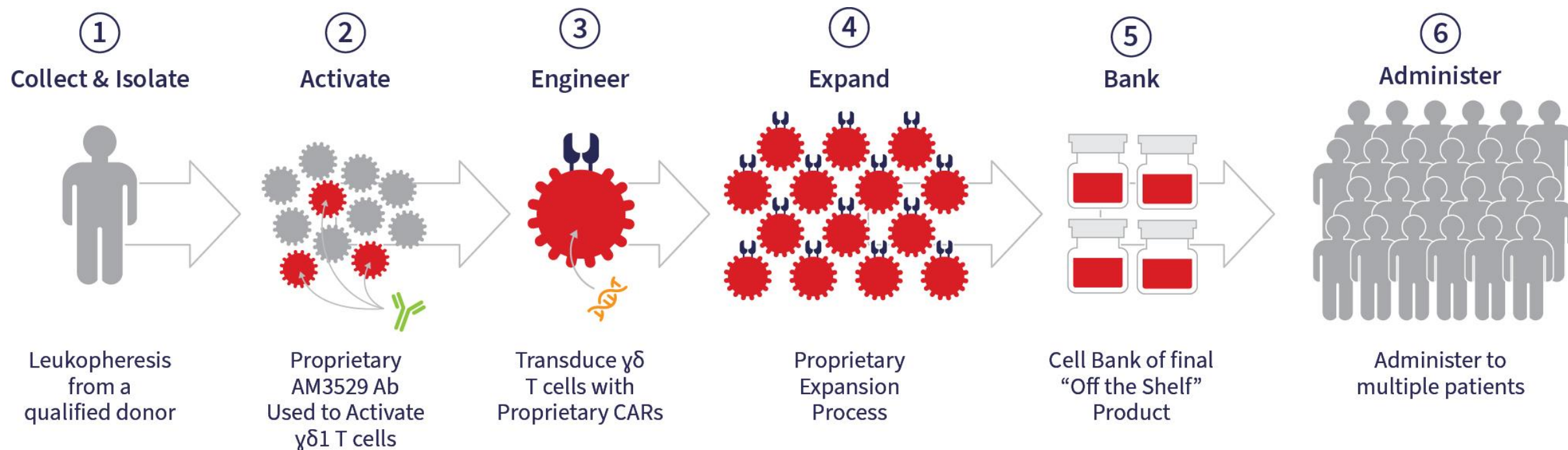
		Allogeneic CAR $\alpha\beta$ T Cells	Allogeneic CAR NK Cells	Allogeneic CAR $\gamma\delta$ T Cells
Activity*	Innate anti-tumor response		✓	✓
	Adaptive anti-tumor response	✓		✓
	Active tumor homing			✓
	Predominantly activating receptor expression	(Limited number) ✓	(Balance with inactivating) ✓	✓
	Preclinical persistence by repeat tumor challenge			✓
	Prognostic value of tumor infiltration		✓	✓ ✓
Safety*	Low GvHD risk	(Requires $\alpha\beta$ TCR deletion) ✓	✓	✓
	Low risk of cytokine release syndrome $\geq$ grade 3 risk		✓	✓
COGS	No gene editing required (May affect efficacy)		✓	✓
	Scalable manufacturing	Limited without exhaustion ✓	✓	✓ ✓

# Advantages of $\gamma\delta$ 1 T Cells

	Feature	V $\delta$ 1+ T cells	V $\delta$ 2+ T cells	Comment
Activity	Diverse VDJ rearranged TCR			V $\delta$ 2+ T cells generally express invariant TCR
	Programmed adaptations for tissue survival			V $\delta$ 1+ T cells tolerate hypoxic and low nutrient conditions
	Expression of tumor homing receptors			V $\delta$ 1+ T cells express CCR5 and tumor homing receptors
	Long lifespan & adaptive immune response			V $\delta$ 1+ T cells oligoclonally expand to pathogenic antigens
	MHC unrestricted TCR			V $\delta$ 1+ T cells recognized antigen independent of MHC
	NKG2D & broad NCR expression			Prevents immune escape of tumor cells
	High granzyme & perforin expression			V $\delta$ 1+ T cells are highly cytolytic (similar to CD8 $\alpha\beta$ T cells)
	Broad anti-tumor toxicity			V $\delta$ 1+ T cells recognize numerous malignant cell types
	Low / no KIR Expression			Adicet's V $\delta$ 1+ T cells display low inhibitory KIR
Potential safety	GvHD incompatible TCR			V $\delta$ 1+ T cells cannot be activated by unmatched MHC
	No IL-17 / ROR $\gamma$ t expression (Th17)			Adicet's V $\delta$ 1+ T cells never express "protumorigenic" IL-17 or ROR $\gamma$ t
	Moderate IL-2 expression			Adicet's V $\delta$ 1+ T cells don't hyperproliferate
	High expansion without exhaustion			Adicet's V $\delta$ 1+ T have potential for 2E11 fold expansion

IL: Interleukin; KIR: killer cell immunoglobulin like receptor; MHC: major histocompatibility complex;  
NCR: natural cytotoxicity receptor; NK: natural killer; TCR: T cell receptor; Th: T helper

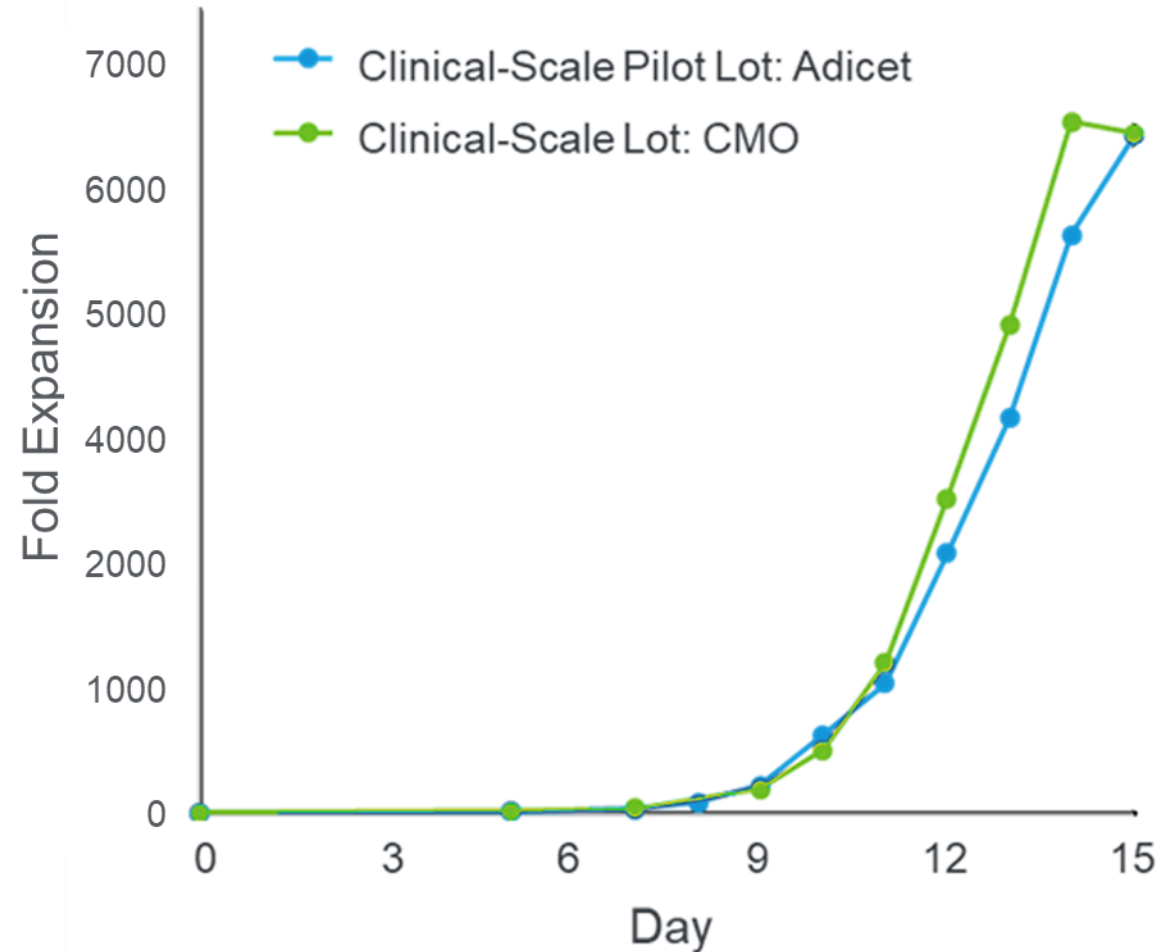
# Large-Scale Manufacture of Off-The-Shelf $\gamma\delta$ T Cell Candidates



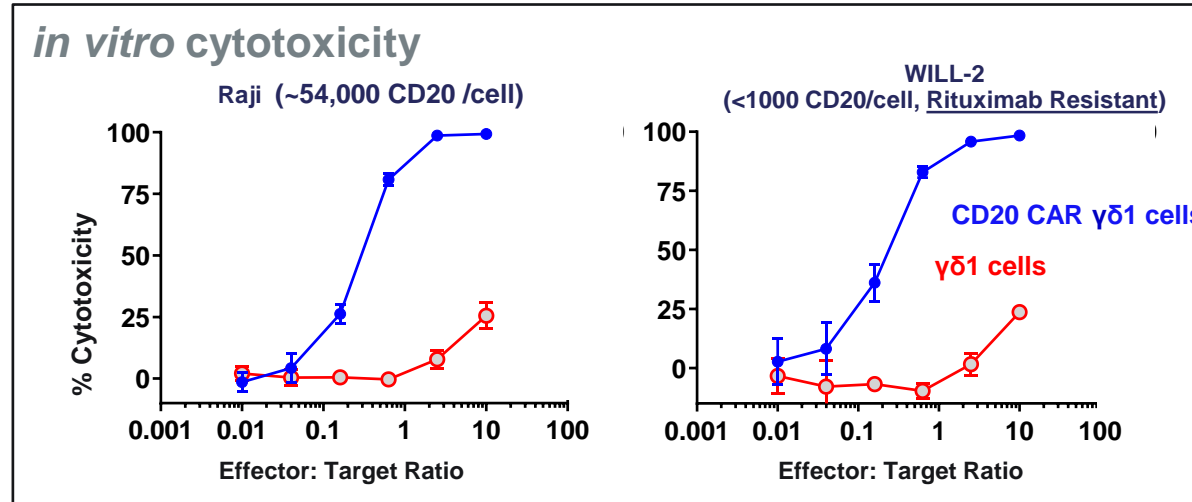
Proprietary AM3529 activating antibody designed to expand  $\gamma\delta 1$  T cells; Proprietary Vectors; Proprietary Scalable Process

# Potential for Consistent Proprietary Large-Scale Expansion

- Manufacturing process designed to be fully cGMP-compliant
- Available on demand for single or repeated dosing
- Designed to enable consistent clinical-scale manufacture
- >6,000 fold expansion of  $\gamma\delta 1$  T cells at clinical scale
- Highly cost efficient: Up to 1,000 doses / batch



# ADI-001 Demonstrated CD20-Targeted Activity Against Tumors

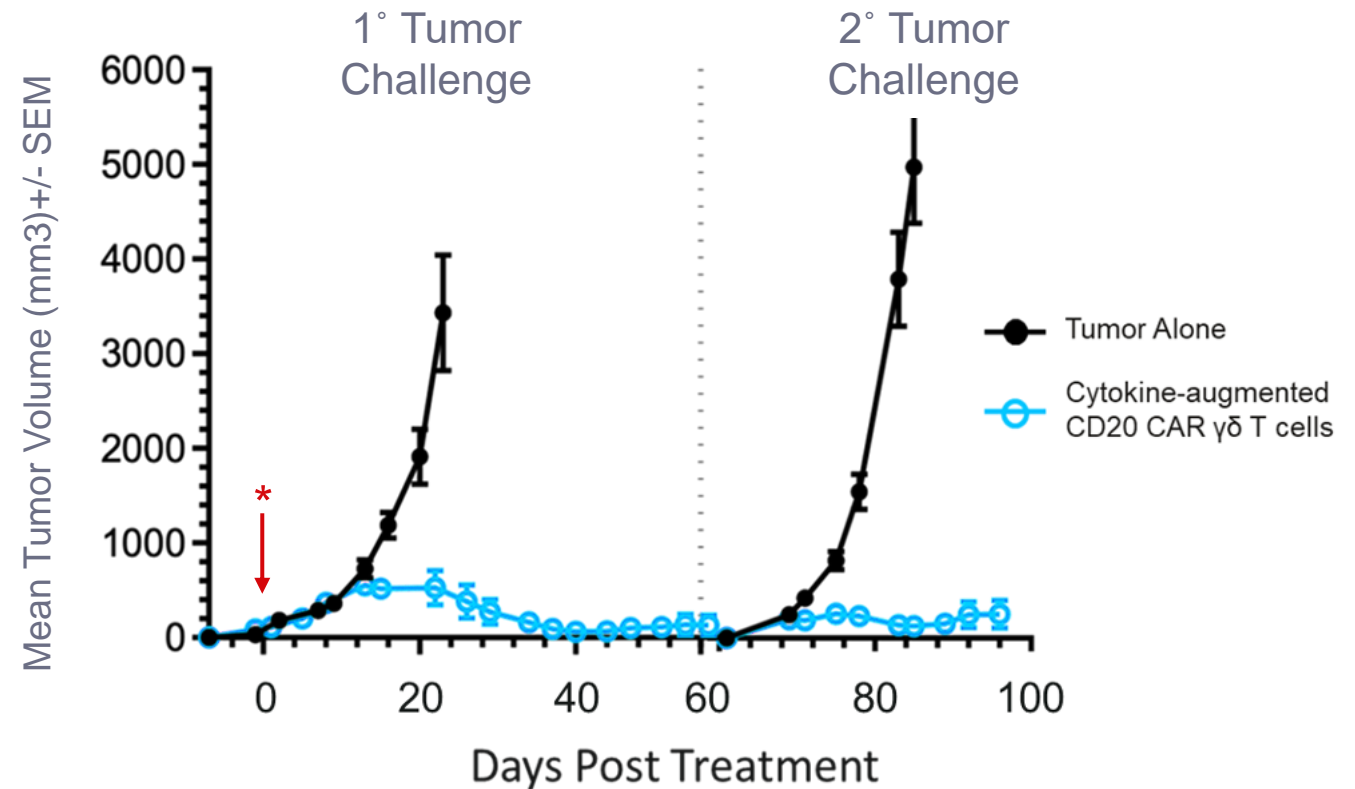


- In pre-clinical studies, ADI-001 effectively targeted CD20+ cancer cells with high potency
- CD20 targeting moiety is engineered to retain potency in rituximab-resistant cancers where CD20 is downregulated
- Potency of the CD20 CAR is complemented by killing through innate cytotoxicity receptors, including NKG2D

# CD20 $\gamma\delta$ CAR-T Cells Controlled Repeat Lymphoma Challenges and Demonstrated Functional Persistence for 100 Days

- Repeat tumor challenge is one of the most stringent preclinical tests of anti-tumor activity
- CD20 CAR  $\gamma\delta$  T cell treatment initiated\* when tumor volume  $\geq 200$  mm<sup>3</sup>
- Excellent tumor control observed in all animals at day 55
- Secondary tumor challenge at day 60
- CD20 CAR  $\gamma\delta$  T demonstrated functional persistence and control of tumor growth to 100 days

## *In Vivo* Subcutaneous Raji Tumor Killing †





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

### Key eligibility criteria:

- R/R high grade B-cell lymphomas (indolent lymphomas, such as FL, were not enrolled)
- At least 2 prior regimens, including anti-CD20 Ab and anthracycline based chemotherapies for DLBCL
- Measurable disease by Lugano 2014
- >18 years; ECOG 0 or 1
- Prior CAR T therapies allowed

# Patient Characteristics

Patient Characteristics	N (%) (Total N = 8)
Age – median (range)	62 (45 - 75)
Sex – number of male	5 (63)
<b>B cell malignancy (WHO 2017 classification)</b>	
Large B cell lymphoma (LBCL)	7 (87.5)
• R/R diffuse large B cell lymphoma	4 (50)
• R/R high grade B cell lymphoma, double/triple hit	2 (25)
• R/R high grade B cell lymphoma, NOS	1 (12.5)
R/R mantle cell lymphoma (MCL)	1 (12.5)
<b>IPI score - median (range)</b>	4 (2-5)
<b>Stage III &amp; IV disease</b>	8 (100)
<b>Sum of the product of the diameters at screening - median (range)</b>	3,739 (1,307- 6,922) mm <sup>2</sup>
<b>Prior lines of therapies - median (range)</b>	4 (2-5)
<b>Prior anti-CD19 CAR T therapies</b>	3 (38)
<b>Prior Autologous Stem Cell Transplant</b>	2 (25)
<b>Prior systemic anti-cancer therapy</b>	
CD20 mAB + anthracycline-based chemo	7 (88)
CD20 mAB + non-anthracycline-based chemo	7 (88)
POLA or POLA-BR	3 (38)
BTK inhibitors	2 (25)
Lenalidomide + Tafasitamab	1 (13)
<b>Refractory status at study entry</b>	
Refractory to first-line therapies	4 (50)
Refractory to second-line	4 (50)
Refractory to the last course of anti-cancer systemic therapy	5 (63)

- 10 patients enrolled; 8 efficacy evaluable
- All patients had aggressive B-cell lymphoma – 7 LBCL and 1 MCL; indolent lymphomas were not enrolled
- Most patients were heavily pre-treated with poor prognostic factors and relatively high tumor burden
- >60% of patients were refractory to the last course of systemic therapy, and the remaining had relapsed
- 3 DLBCL patients (38%) with prior anti-CD19 CAR T cell therapy progressed following Yescarta (Axi-cel) and JCAR17 (Liso-cel)
- All patients were CD20 positive in prior treatment biopsies

# Efficacy-Evaluable Patient Characteristics\*

Median number of prior therapies: 4; >60% of patients were refractory to last systemic therapy, the remainder had relapsed

Cancer Type	Age/Sex	# Prior Lines of Therapy	Prior Lines of Therapies	sLD or eLD	ADI-001 Dose Level	Prior CAR T?	Stage	Status
Transformed DLBCL (from CLL)	62/F	5 prior lines	<ul style="list-style-type: none"> <li>R-CHOP</li> <li>Rituximab-abbs, gemcitabine, and CDDP</li> <li>Rituximab-abbs, gemcitabine, carboplatin</li> <li>Polatuzumab + Bendamustine/rituximab</li> <li>Obinutuzumab - hyper cyclophosphamide and dexamethasone</li> </ul>	sLD	DL1	No	IV	Off study
Transformed HGBCL (from FL)	66/F	4 prior lines	<ul style="list-style-type: none"> <li>R-CHOP</li> <li>Ibrutinib</li> <li>Bendamustine/rituximab</li> <li>Rituximab</li> </ul>	sLD	DL1	No	III	Off study
Triple-hit HGBCL	75/M	5 prior lines	<ul style="list-style-type: none"> <li>R-CHOP + intrathecal methotrexate</li> <li>Liso-cel</li> <li>Liso-cel (reinfusion)</li> </ul> <ul style="list-style-type: none"> <li>Revlimid</li> <li>Tafasitamab-cxix</li> </ul>	eLD	DL1	Yes	IV	Off study
MCL	62/M	5 prior lines	<ul style="list-style-type: none"> <li>Bendamustine/rituximab</li> <li>Zanubrutinib</li> <li>Bendamustine/obinutuzumab</li> </ul> <ul style="list-style-type: none"> <li>Bendamustine/rituximab</li> <li>Rituximab/gemcitabine/dexamethasone/carboplatin</li> </ul>	eLD	DL2	No	III	Active
DLBCL	45/M	3 prior lines	<ul style="list-style-type: none"> <li>R-CHOP</li> <li>R-ICE</li> <li>Polatuzumab</li> </ul>	eLD	DL2	No	IV	Off study
DLBCL	61/M	2 prior lines	<ul style="list-style-type: none"> <li>R-CHOP</li> <li>R-ICE</li> </ul>	eLD	DL2	No	III	Active
Double-hit HGBCL	62/M	4 prior lines	<ul style="list-style-type: none"> <li>Da-R-EPOCH + intrathecal methotrexate</li> <li>R-Gemcitabine/oxaliplatin</li> </ul> <ul style="list-style-type: none"> <li>Axi-cel</li> <li>Polatuzumab + bendamustine/rituximab</li> </ul>	eLD	DL3	Yes	IV	Active
DLBCL	64/F	4 prior lines	<ul style="list-style-type: none"> <li>R-CHOP</li> <li>R-Gemcitabine/oxaliplatin</li> </ul> <ul style="list-style-type: none"> <li>Axi-cel</li> <li>Polatuzumab + rituximab</li> </ul>	eLD	DL3	Yes	IV	Active

\*The first 2 patients in DL1 progressed and left the study before completing the DLT window and were replaced per protocol. One was a Burkitt lymphoma, a histology no longer included in the study.

# ADI-001: Preliminary Safety Data in Efficacy-Evaluable Patients

Adverse Events Types	DL1 (3E7) N=3		DL2 (1E8) N=3		DL3 (3E8) N=2		Total N=8	
	All Grade N (%)	Gr ≥3 N (%)	All Grade N (%)	Gr ≥3 N (%)	All Grade N (%)	Gr ≥3 N (%)	All Grade N (%)	Gr ≥3 N (%)
CRS	2 (67%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (25)	0 (0)
ICANS	0 (0%)	0 (0%)	1 (33%)	0 (0%)	0 (0%)	0 (0%)	1 (13)	0 (0)
GvHD	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0)	0 (0)
DLTs	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0)	0 (0)
Infection*	1 (33%)	1 (33%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (13)	1 (13)
SAE - TEAE	1 (33%)	1 (33%)	1 (33%)	0 (0%)	0 (0%)	0 (0%)	2 (25)	1 (13)

- Safety assessment was performed using CTCAE (v5) and ASTCT
- No Grade ≥ 3 CRS or ICANS
- The only ADI-001 related AESI was a Grade 1 ICANS at DL2, which resolved within 24 hours without medical intervention
- No DLTs or GvHD
- No treatment discontinuations due to AEs
- 2 patients administered sLD; 6 patients eLD
- No eLD-associated clinical infection

Data-cut date: May 31, 2022

\*One patient in DL1 who received sLD developed COVID-19 related pneumonia approximately two and a half months after ADI-001 administration and later died of complications from it, unrelated to ADI-001. This patient was previously reported as a partial response (PR) by local radiological assessment and has been assessed as a CR by independent central reading.

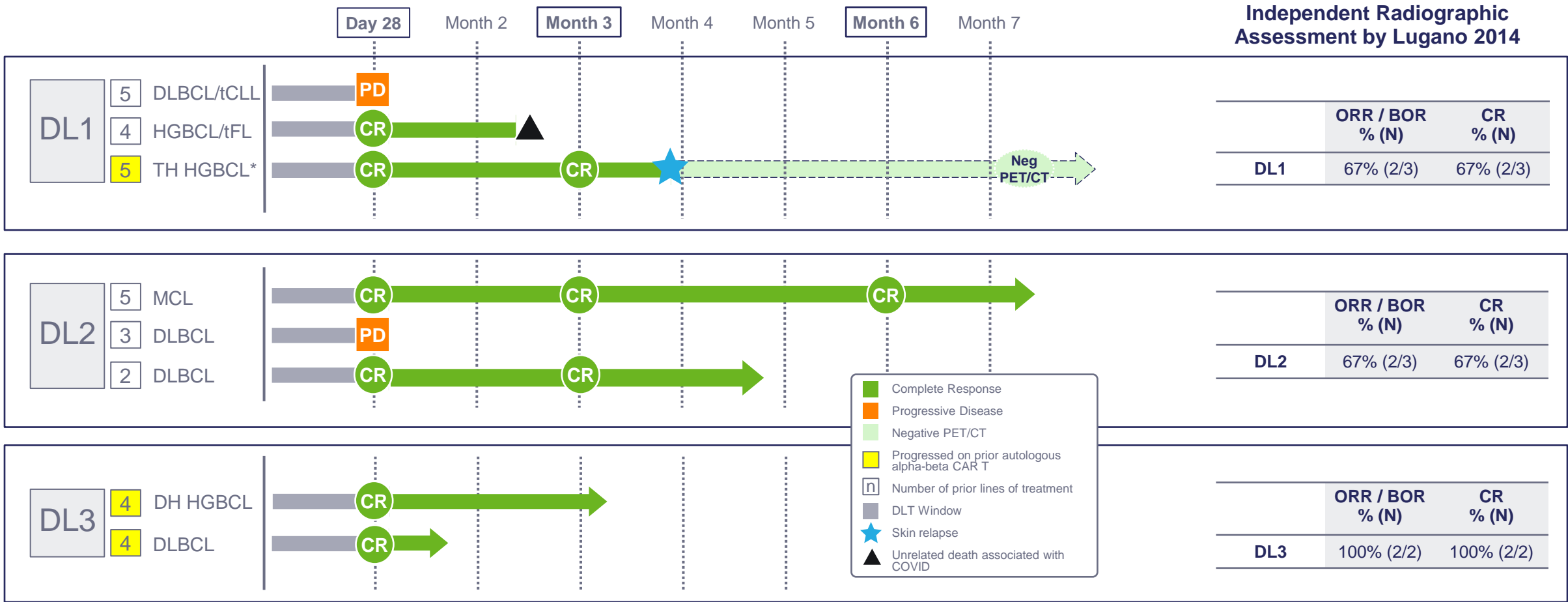
# ADI-001: Preliminary Efficacy Data

*Per protocol analysis, independent radiographic assessment using Lugano 2014*

	DL1 (3E7) (N=3)	DL2 (1E8) (N=3)	DL3 (3E8) (N=2)	Total (N=8)	Prior CD19 CAR-T (N=3)
ORR / BOR	67% (2/3)	67% (2/3)	100% (2/2)	75% (6/8)	<b>100% (3/3)</b>
CR, % (N)	67% (2/3)	67% (2/3)	100% (2/2)	75% (6/8)	<b>100% (3/3)</b>

- **Overall in study: ORR = 75%, CR = 75%**
- **DL2 + DL3: ORR = 80%, CR = 80%**
- **100% ORR and CR in patients previously treated with autologous CAR-T**
  - 2 patients who had previously achieved **PRs to Axi-cel** and progressed, have **achieved CRs to ADI-001**

# ADI-001: Preliminary Efficacy and Durability Data



Data-cut date: May 31, 2022

Preliminary data may suggest potential dose-related increase in durability

TH=triple hit; DH=double hit; DLBCL=diffuse large B-cell lymphoma; tCLL=transformed chronic lymphocytic leukemia; HGBCL=high grade B-cell lymphoma; MCL=mantle cell lymphoma

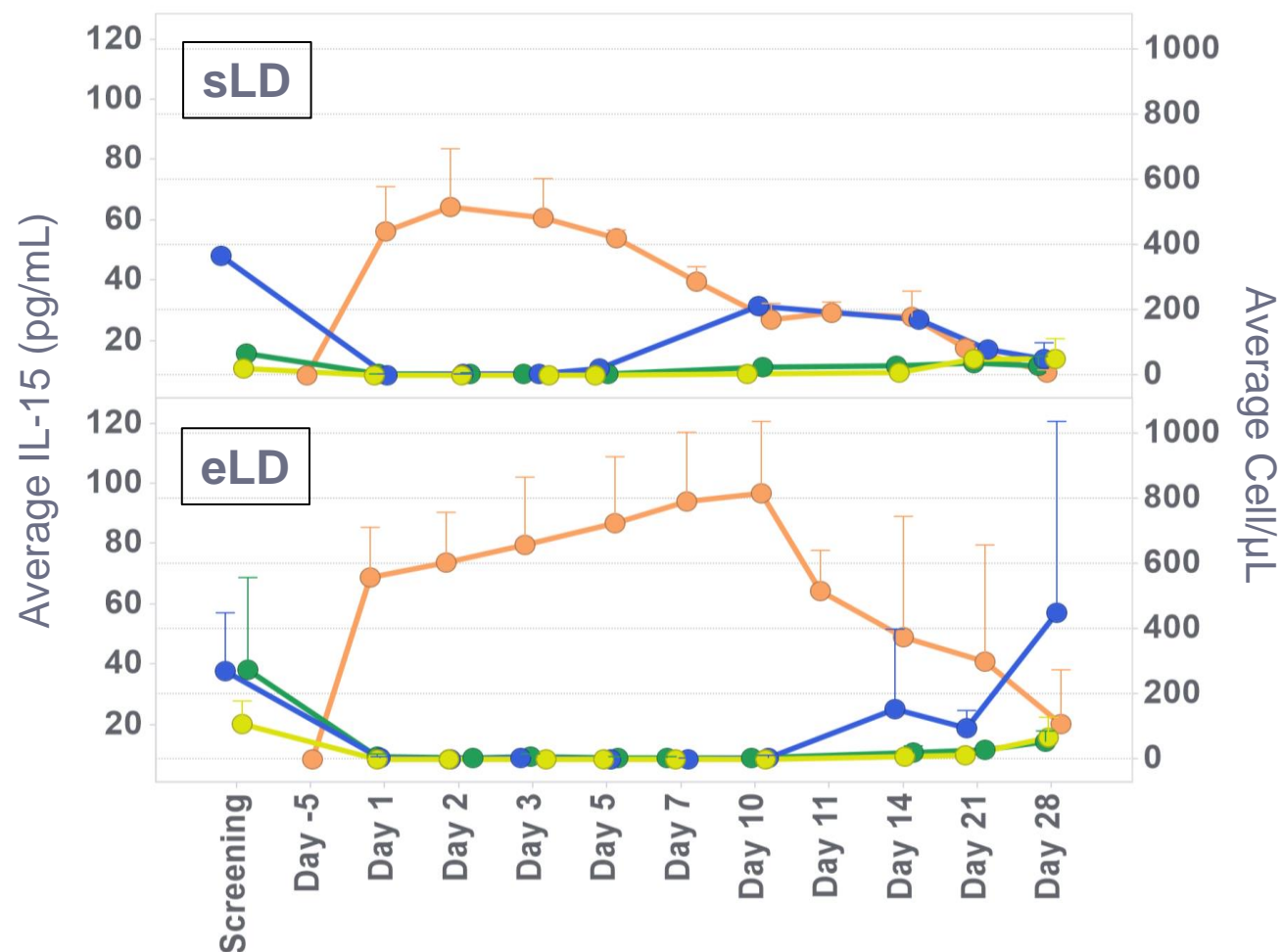
\*One prior CD19 CAR T-relapsed patient developed a new local skin relapse at 4 months while PET/CT still showed CR. Local radiotherapy was administered.

No systemic therapy provided. Post-radiation PET/CT still showed CR 7.5 months after ADI-001 dosing

TH= Triple hit; DH= Double hit; DLBCL=diffuse large B-cell lymphoma; tCLL=transformed chronic lymphocytic leukemia; HGBCL=high grade B-cell lymphoma; MCL= Mantle cell lymphoma



# eLD Increased Circulating IL-15 Levels by Approximately 2-fold



- Comparable lymphodepletion with sLD and eLD regimens (\*)
- No infections reported in patients receiving eLD

- IL-15 (pg/mL)
- CD4 T cells (cell/ $\mu$ L)
- CD8 T cells (cell/ $\mu$ L)
- NK cells (cell/ $\mu$ L)

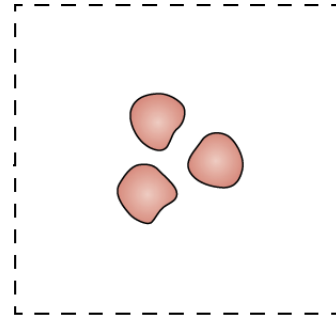
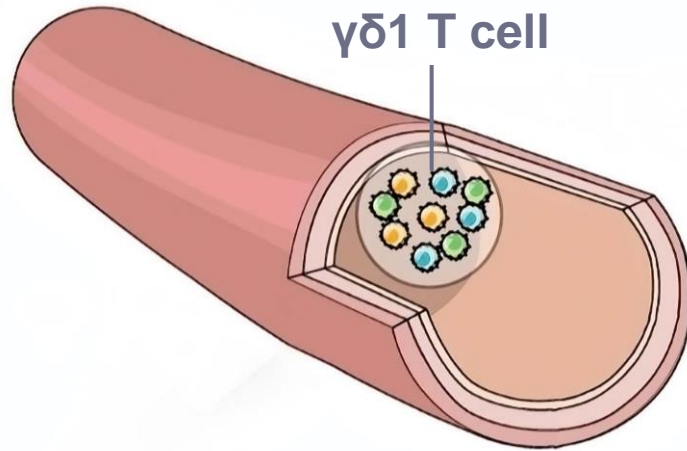
**Number of subjects:**  
Standard LD = 2  
Enhanced LD = 5

(\*) Standard LD (sLD): Cy 500 mg/m<sup>2</sup> (3 days) and Flu 30 mg/m<sup>2</sup> (3 days)  
Enhanced LD (eLD): Cy 1000 mg/m<sup>2</sup> (3 days) and Flu 30 mg/m<sup>2</sup> (4 days)

# Gamma Delta1 T Cells Preferentially Home to Tissues

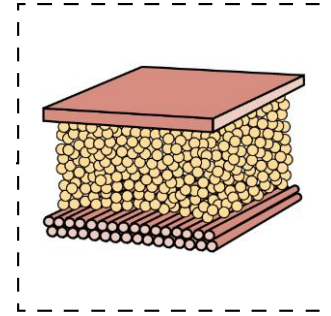
## peripheral blood

% of CD3+: ~1-3%



## lymph node

CD27+  
CD62L+  
Vδ1+ ↑↑  
Vδ2+ ↓↓

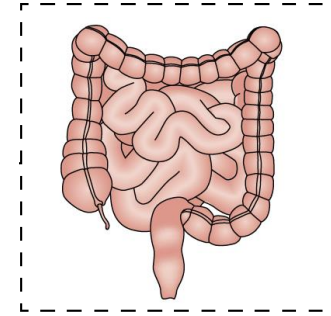


## breast

tissue/blood: ~15X

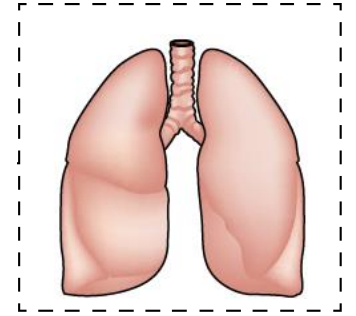
## adipose

tissue/blood: 9X



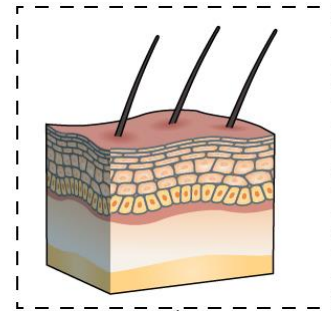
## GI

tissue/blood: 11X



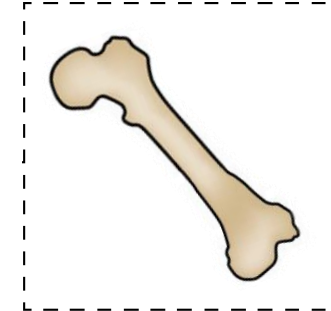
## lung

tissue/blood: 9X



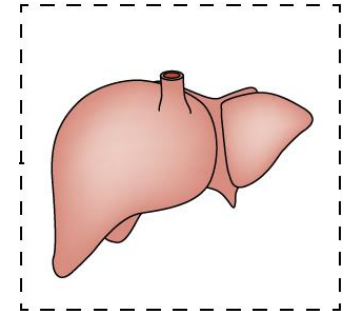
## skin

tissue/blood: 8X



## bone marrow

tissue/blood: 4X



## liver

tissue/blood: 3X

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

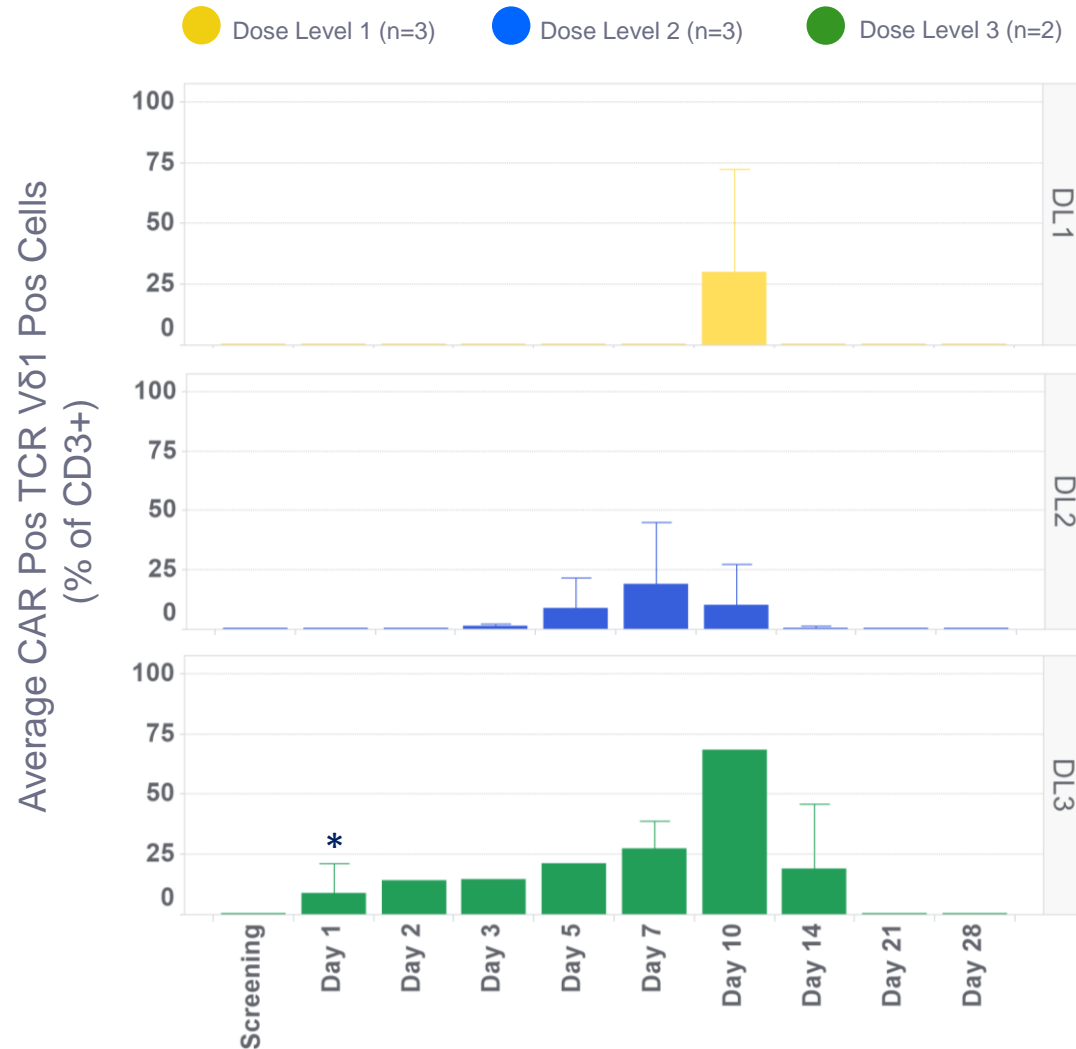
Images adapted from Hunter *et al J Hepatol.* 2018 and Ribot *et al Nat Rev Immunol.* 2021

## References:

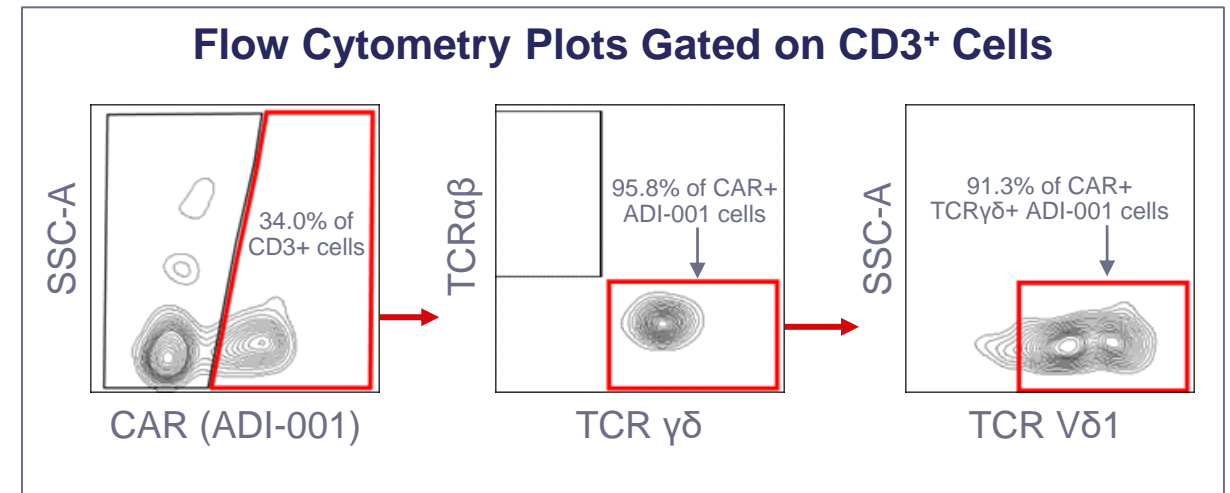
Brauneck *et al Front Med* 2021  
Davey *et al Trends Immunol* 2018  
Uger *et al Sci Rep* 2018  
Wang *et al Exp Ther Med* 2020  
Wu *et al Sci Transl Med* 2019

Deusch *et al Eur J Immunol* 1991  
Melo *et al Clin Immunol* 2021  
Toulon *et al J Exp Med* 2009  
Wisniewski *et al Am J Respir Cell Mol Biol* 2000

# Preliminary Pharmacokinetics of ADI-001 by Flow Cytometry



- Dose-related increase of ADI-001 exposure
- Durability >6 months already associated with ADI-001 exposure in the blood



Non-QC'ed data for representative measure on Day 10

\*One of the blood samples on Day 1 was collected post-infusion of ADI-001 instead of pre-infusion

# Summary: ADI-001 Is a Potential Best-in-Class Cell Therapy for NHL

- ADI-001, a CD20-targeting first-in-class investigational  $\gamma\delta$ 1 CAR T product was **well tolerated**, with an excellent safety profile in this first-in-human study; no GvHD or DLT, no Grade  $\geq$ 3 CRS or ICANS
- Encouraging early efficacy data with ADI-001 in heavily pre-treated aggressive NHL patients (Indolent lymphoma, such as FL, was not enrolled in trial), including those who had prior CD19 CAR T therapies
  - **75% ORR and CR rate observed in the study to date**
  - **100% ORR and CR rate** in three patients relapsed after prior autologous anti-CD19 CAR T therapy
- **Early data suggest encouraging durability of responses**
  - Preliminary data may suggest potential dose related increase in durability
- **Potential for best-in-class ORR, CR rate and durability** given ADI-001 mechanism of action
- Detection of circulating ADI-001 in the blood by flow cytometry indicates expansion and dose-related increase of ADI-001 exposure in patients
- Dose escalation is ongoing: Given safety profile to date, protocol amended to include a new DL4 (1E9 CAR+ cells) and potential ADI-001 consolidation dosing at DL3 to finalize recommended Phase 2 dose

# Development Plan May Include a Pivotal Intent Study to Provide Potential Path for Accelerated Approval

- Autologous alpha-beta CD19-targeted CAR T therapy has been approved for second and third line DLBCL
- There is no effective therapeutic option for patients progressing following autologous CD19-targeted CAR T therapy
- ADI-001 demonstrated 100% ORR and CR in three patients that relapsed after prior autologous alpha-beta CD19-targeted CAR T therapy, including two CRs in a patients that had a PR to prior autologous CAR T therapy
- Pending discussions with FDA, ADI-001 may be tested in a pivotal-intent single, arm clinical trial in CD19 CAR T-relapsed aggressive NHL

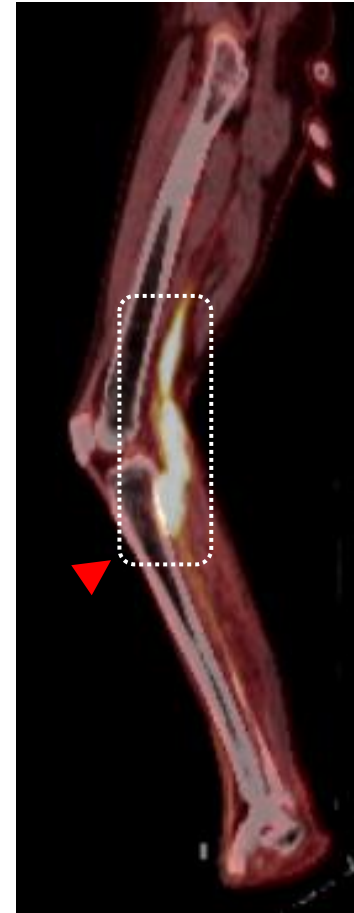
# ADI-001 Case Study 1: Dose Level 1 (3E7 cells)

- 75-year-old male
- HGBCL, non-GCB, **triple hit** (c-MYC+, BCL2+, BCL6+)
- IPI score 3, Stage 4, extra nodal involvement
- SPD 1,307 mm<sup>2</sup>
- 5 prior lines of therapy
  - R-CHOP+IT-Methotrexate
  - Liso-cel (best response: CR)
  - Liso-cel reinfusion (best response: CR)
  - Revlimid
  - Tafasitamab-cxix

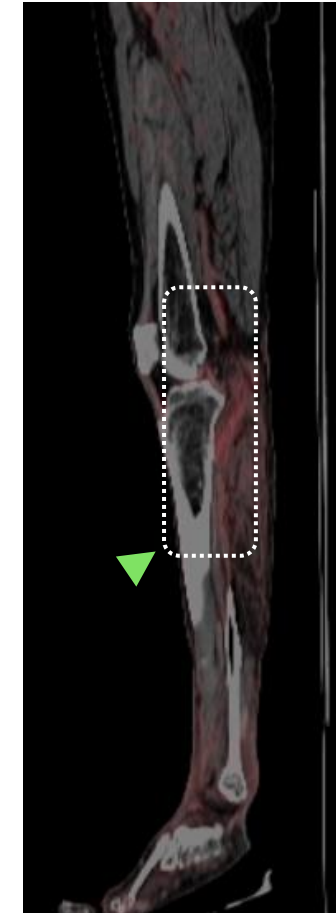
- Efficacy Data:
  - CR on PET/CT @ Day-28 and Month-3.
  - Skin (right leg) relapse at 3.9 months while repeat PET/CT remained in CR.
  - Only received focal radiation to the skin. Lesion resolved. No systemic therapy administered.
  - **Post-radiation PET/CT continues to be negative more than 7.5 months after ADI-001 dosing.**
- Safety Data:
  - No ADI-001 related AEs
  - No ICANS or CRS
  - No SAE-TEAE, DLT, GvHD

Sagittal view of the right leg  
SPD = sum of products of diameters  
GCB = germinal center B-cell like sub-type

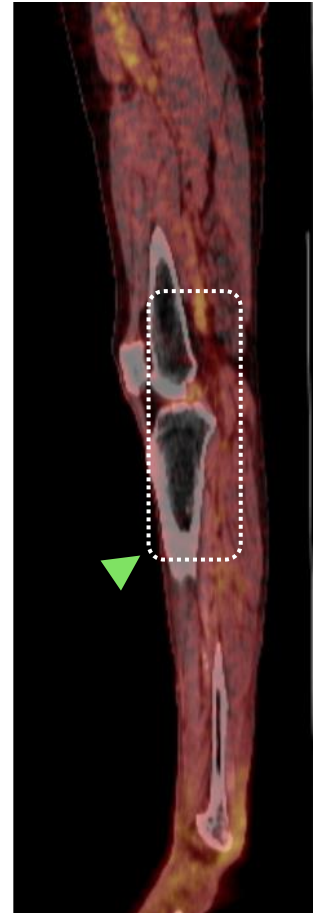
- ▶ Baseline FDG uptake by tumor lesions    ▶ Sites of tumor response



Baseline



Day 28



Month 3



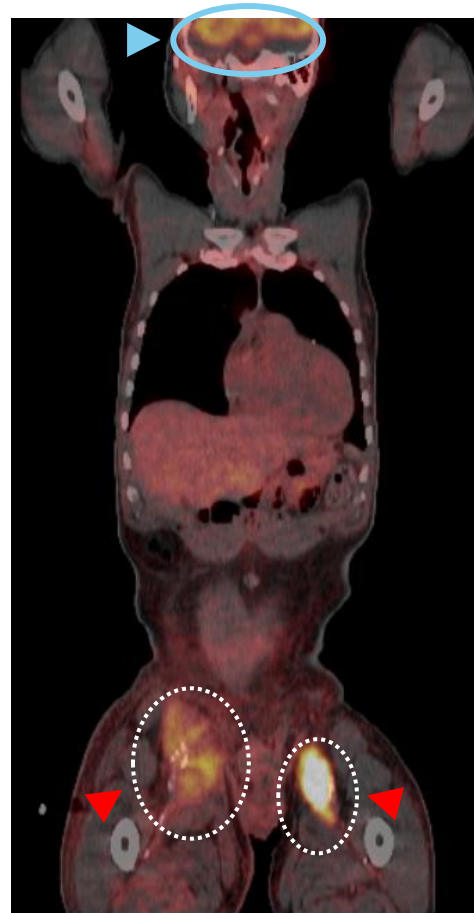
# ADI-001 Case Study 2: Dose Level 2 (1E8 cells)

- 62-year-old male
- Mantle Cell Lymphoma
- MIPI score 4, Stage III
- SPD 6,472mm<sup>2</sup> at baseline
- 5 prior lines of therapy
  - Bendamustine + Rituximab
  - Zanubrutinib
  - Bendamustine + Obinutuzumab
  - Bendamustine + Rituximab
  - R-GDC

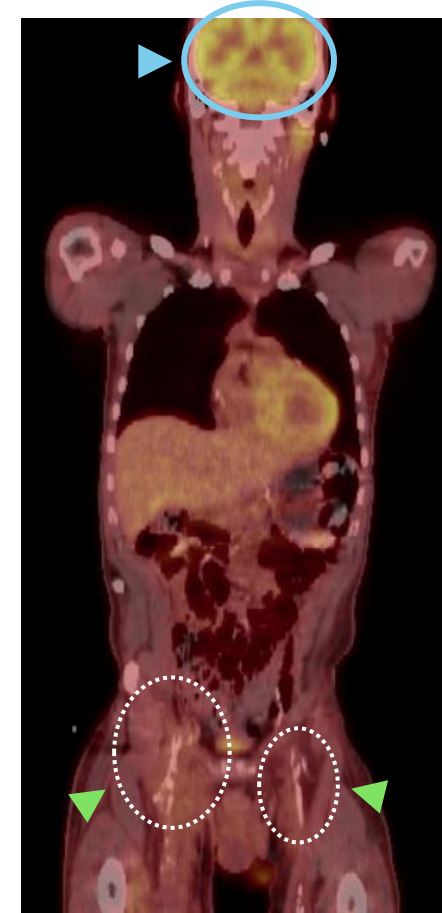
- Efficacy Data:
  - **Ongoing CR > 7 months**

- Safety Data:
  - No ADI-001 related AEs
  - No ICANS or CRS
  - No SAE-TEAE, DLT, GvHD

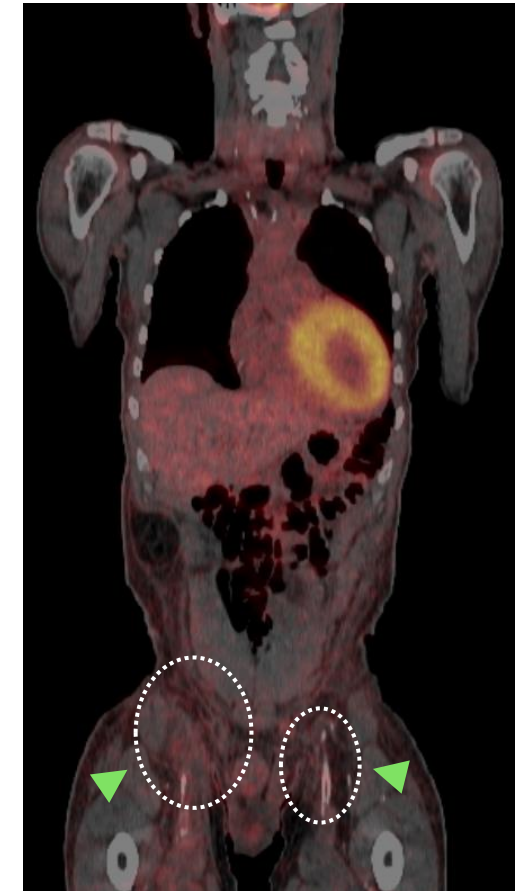
- ▶ FDG uptake by normal tissues
- ▶ Baseline FDG uptake by tumor lesions
- ▶ Sites of tumor response



Baseline



D28



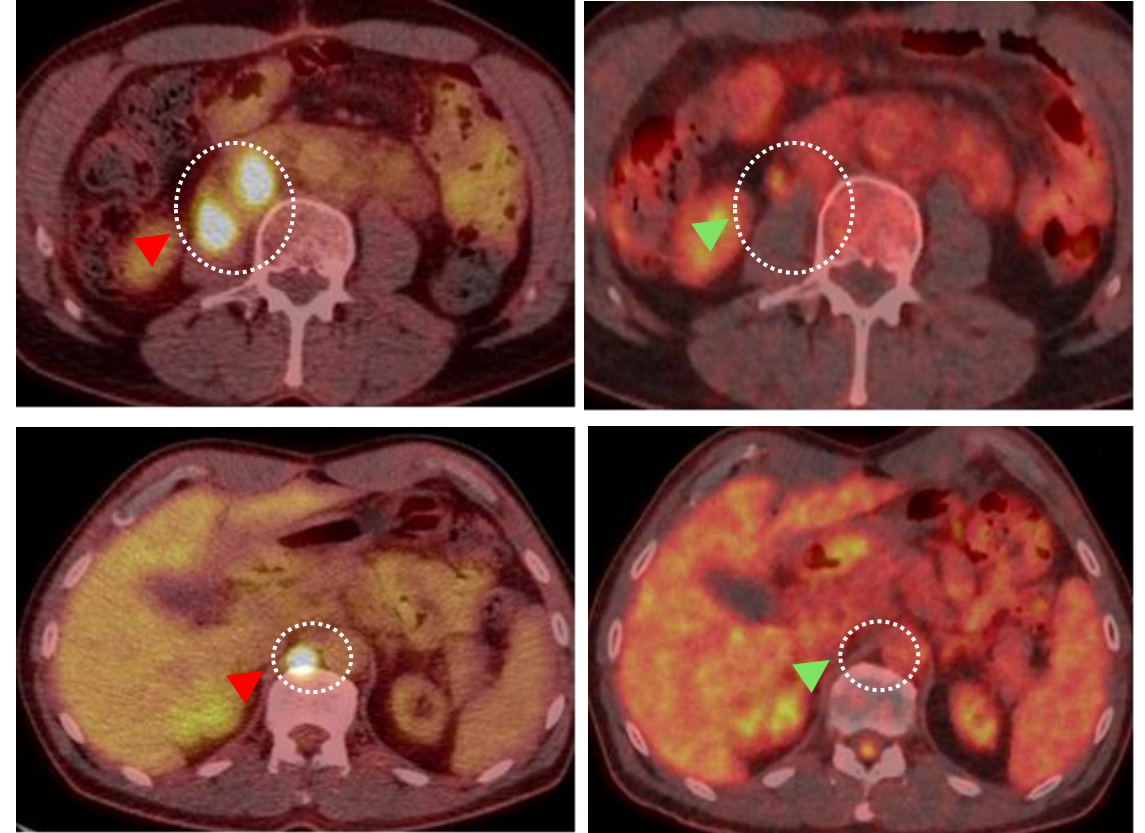
Month 6

# ADI-001 Case Study 3: Dose Level 3 (3E8 cells)

- 62-year-old male
- HGBCL, **double hit**
- IPI score 4, Stage IV
- SPD 1,677 mm<sup>2</sup> at baseline
- 4 prior lines of therapy
  - DA-EPOCH-R / IT-MTX
  - R-GemOx
  - **Axi-cel (best response: PR)**
  - Pola-BR

- Efficacy Data:
  - **CR at Day-28**
- Safety Data:
  - No ADI-001 related AEs
  - No ICANS or CRS
  - No SAE-TEAE, DLT, GvHD

- ▶ Baseline FDG uptake by tumor lesions
- ▶ Sites of tumor response



Baseline

D28

**CR in a patient previously treated with Axi-cel (best response to Axi-cel was PR)**

# ADI-002: Allogeneic GPC3- $\gamma\delta$ -CAR T Cell Candidate for Solid Tumors





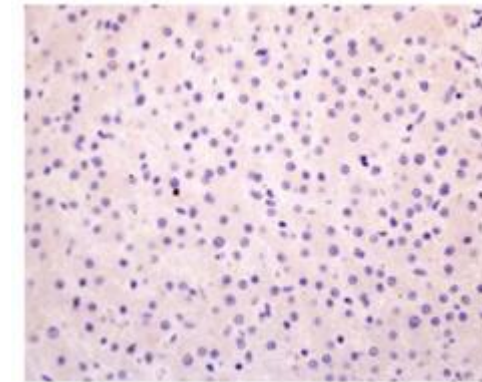
# ADI-002: GPC3 is highly expressed on a broad range of solid tumors, with limited expression levels on normal tissues

**Table 1**  
**Glypican 3 Expression in Tumors\***

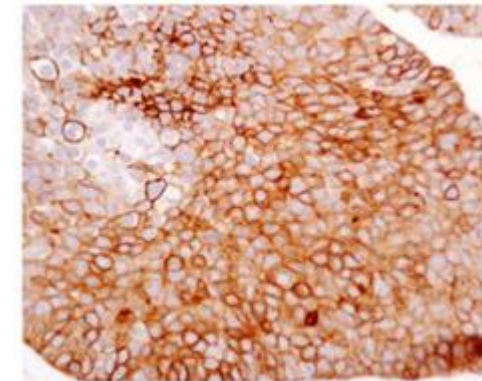
Tumor Entity	No. of Cases	No. (%) Staining	
		Negative	Positive
Hepatocellular carcinoma	44	15 (34)	29 (66)
Squamous cell carcinoma of the lung	50	23 (46)	27 (54)
Liposarcoma	29	14 (48)	15 (52)
Testicular nonseminomatous germ cell tumor	62	30 (48)	32 (52)
Cervical intraepithelial neoplasia (grade 3)	29	17 (59)	12 (41)
Malignant melanoma	48	34 (71)	14 (29)
Adenoma of the adrenal gland	15	11 (73)	4 (27)
Schwannoma	46	34 (74)	12 (26)
Malignant fibrous histiocytoma	29	22 (76)	7 (24)
Adenocarcinoma of the stomach (intestinal subtype)	45	36 (80)	9 (20)
Chromophobe renal cell carcinoma	15	12 (80)	3 (20)
Invasive lobular carcinoma of the breast	46	37 (80)	9 (20)
Medullary carcinoma of the breast	30	25 (83)	5 (17)
Squamous cell carcinoma of the larynx	49	41 (84)	8 (16)
Small cell carcinoma of the lung	49	41 (84)	8 (16)
Invasive transitional cell carcinoma of the urinary bladder	43	36 (84)	7 (16)
Mucinous carcinoma of the breast	26	22 (85)	4 (15)
Squamous cell carcinoma of the cervix	41	35 (85)	6 (15)

\* Includes all cases with ≥15% positive cases with ≥15 cases tested by multitumor array.

Baumhoer et al., Am J Clin Pathol 2008;129:899-906



Non-tumor

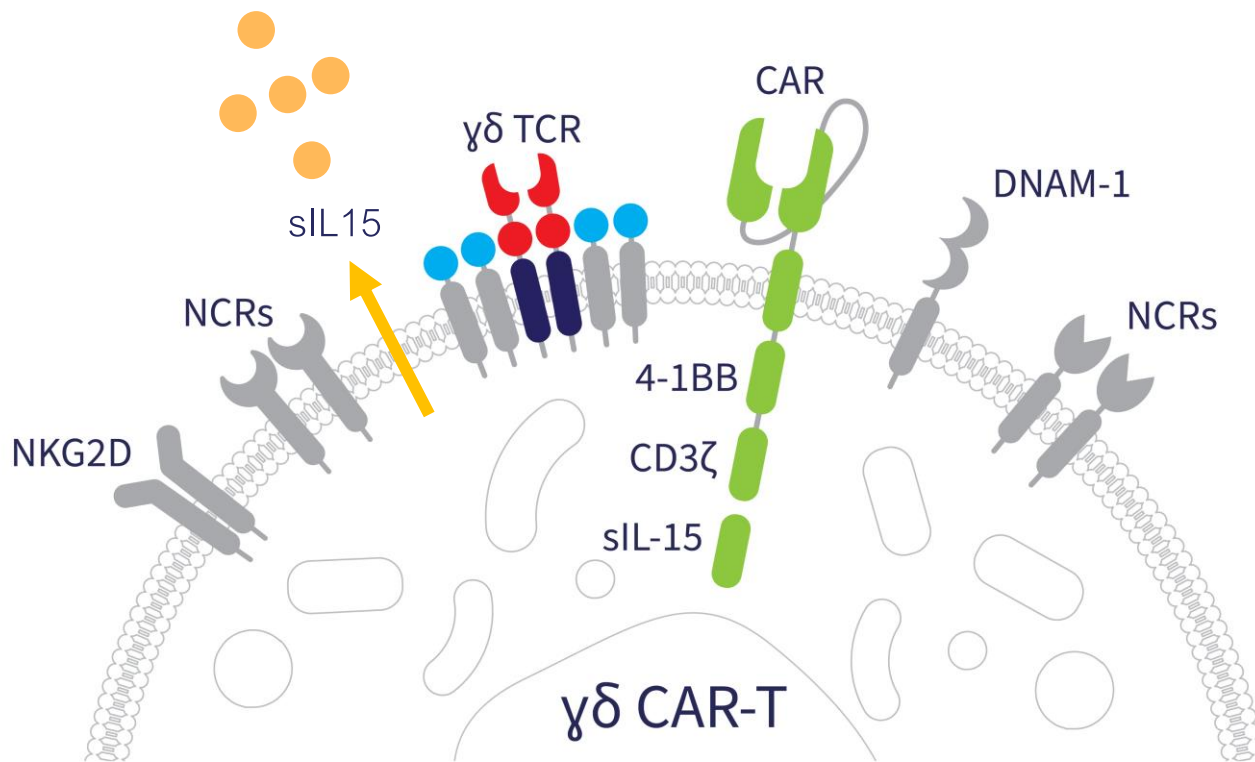


Tumor

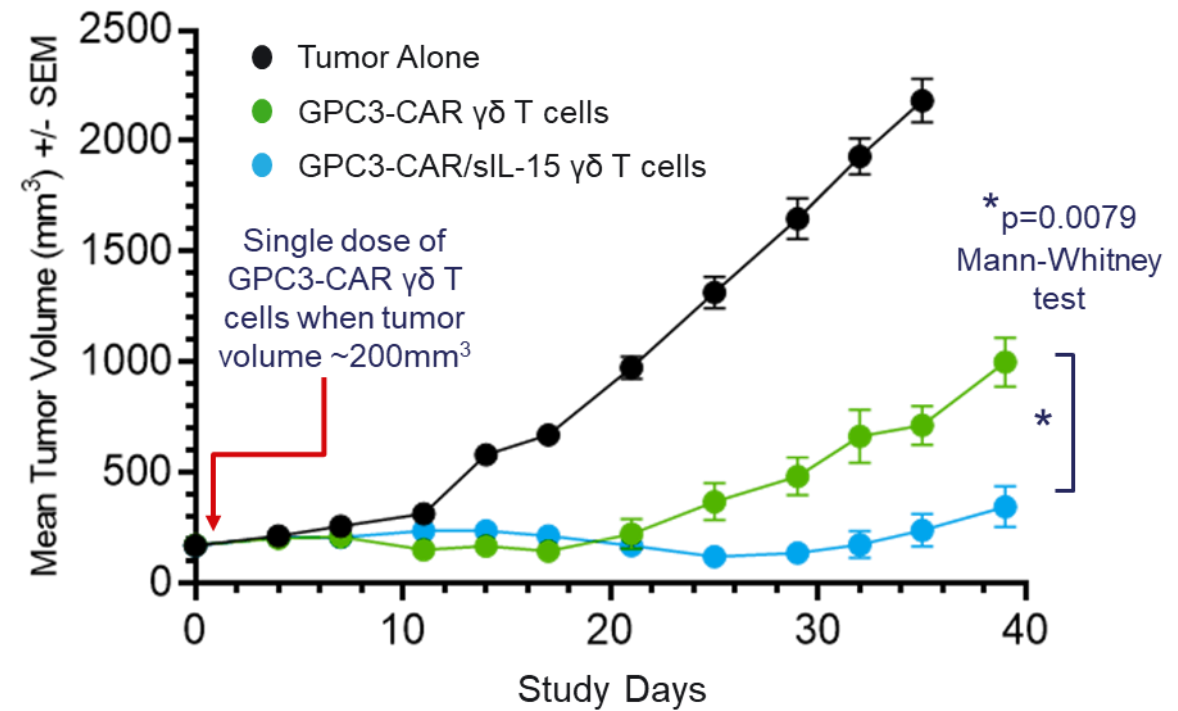
IHC Detection of GPC3 in human HCC vs normal liver

Ho et al., PLoS ONE 2012; 7: e37159

# Secretion of IL-15 Enhanced Potency of ADI-002 Cells in Solid Tumors in Preclinical Studies

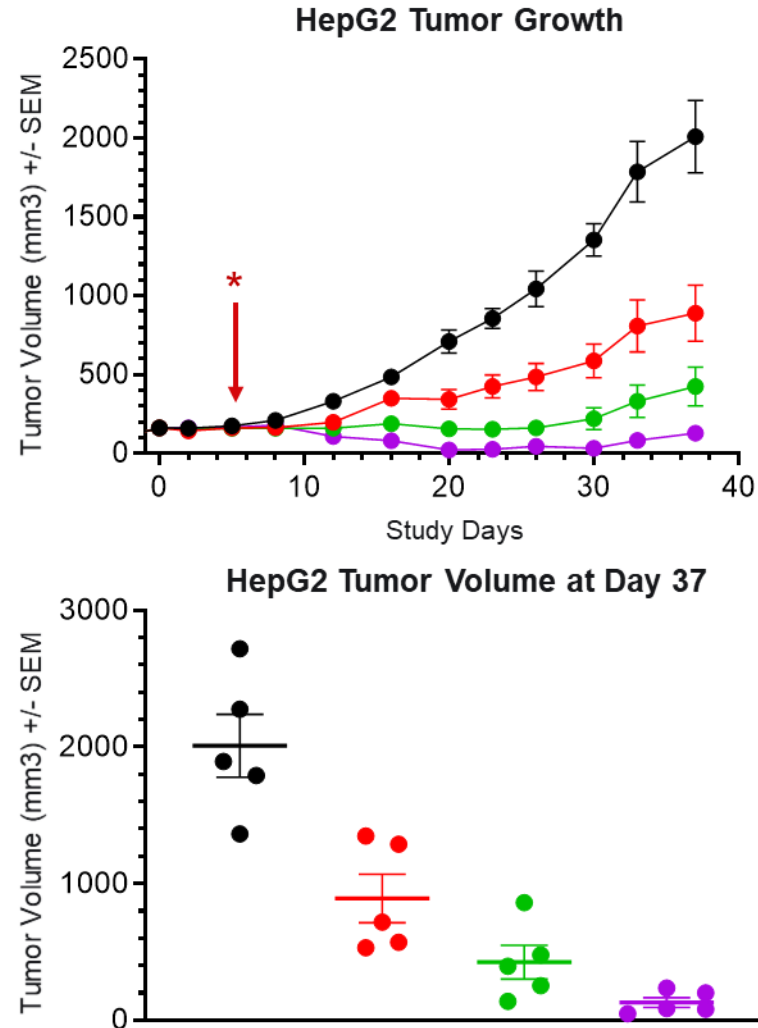


GPC3 CAR / sIL-15  $\gamma\delta$  T cells controlled subcutaneous hepatocellular carcinoma growth in NSG mice<sup>1</sup>



# Dose Dependent Anti-Tumor Activity of $\gamma\delta 1$ CAR T Cells with GPC3-Targeting sIL15 CAR $\gamma\delta 1$ T Cells Observed in Liver Cancer Model <sup>†</sup>

- GPC3-targeting chimeric antigen receptor construct also encodes secretion of IL15
- Single dose  $\gamma\delta$  CAR T cell treatment was initiated\* when tumor volumes reached  $\sim 200\text{mm}^3$
- Excellent  $\gamma\delta$  CAR T dose-dependent control of tumor growth observed



<sup>†</sup>internal Adicet study



# TCR-L Platform: Intracellular Solid Tumor Targets



# TCR-L Platform: CAR-T Using Intracellular Solid Tumor Targets

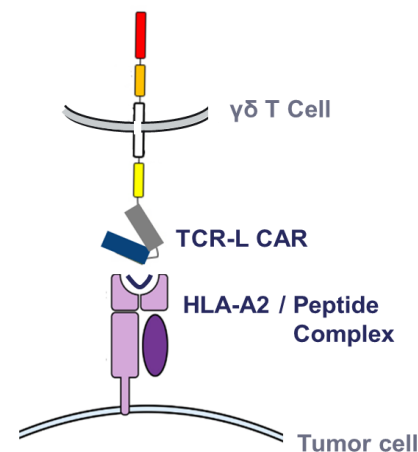
## Challenge

- Lack of disease-specific cell surface targets in solid tumors

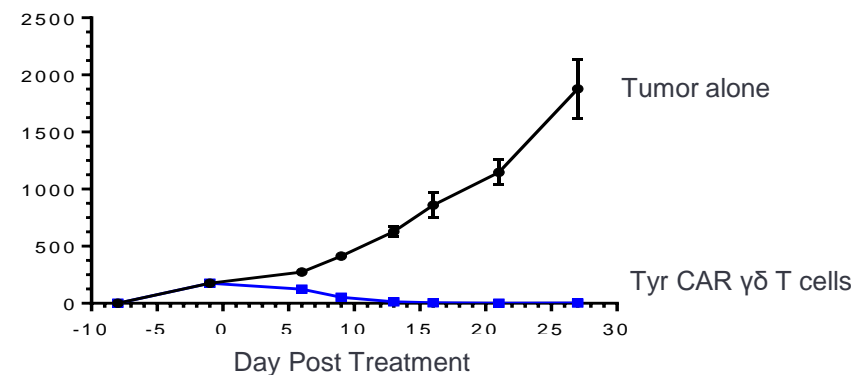
## TCR-L Proposed Solution

- Ability to target disease-specific intracellular proteins via peptide MHC complexes highly expands the target pool
- Unlikely to express on normal cells
- Adicet has generated multiple TCR-Like (TCR-L) antibodies to various intracellular targets in key solid tumor indications
  - These antibodies have mimicked TCR specificity with higher affinity of mAbs
  - scFv observed for chimeric antigen receptors for cellular therapy

TCR-like antibodies engineered as CARs into  $\gamma\delta$  T cells



WM266.4 Tumor Growth in NSG Mice†



# Anticipated Near-Term Milestones

- Complete dose escalation through DL4 to establish recommended Phase 2 dose in 2H/2022
- Backfill enrollment to DL3 with additional potential patients in 2H/2022
- Discuss with the FDA and EMA the design of two pivotal studies and a potential path to support a BLA and MAA for ADI-001
- Anticipate at least one additional clinical update for ADI-001 in 2H/2022
- Initiate at least one potentially pivotal study with ADI-001 in 1H/2023
- Preclinical pipeline update 2H/2022
- One new IND planned every 12-18 months, including one new IND for internal program in 2023



# Leaders in $\gamma\delta$ CAR T Cell Therapy

