



ADI-001 Phase 1 Interim Data

First-in-class allogeneic, off-the-shelf
gamma delta ($\gamma\delta$) CAR T cells



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Agenda



Welcome and Introductory
Remarks

Chen Schor

President and Chief Executive Officer



ADI-001 Clinical Update

Francesco Galimi, M.D., Ph.D.

SVP and Chief Medical Officer



Commentary:
ADI-001 Interim Data

Sattva Neelapu, M.D.

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Closing Remarks/Q&A

Chen Schor/All

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

- ADI-001 is a first-in-class, allogeneic, investigational $\gamma\delta$ CAR T cell therapy to reach clinical trials and report clinical data
- $\gamma\delta$ T cells may provide significant advantages both in terms of anti-tumor activity and safety compared to other cell therapy platforms or bispecifics
- $\gamma\delta 1$ T cells may provide benefits as compared to $\gamma\delta 2$ T cells
- Robust, scalable, “off the shelf” cGMP-compliant manufacturing process; broad patent portfolio
- Six additional internal $\gamma\delta 1$ T cell therapy programs in preclinical development
- One new IND planned every 12-18 months

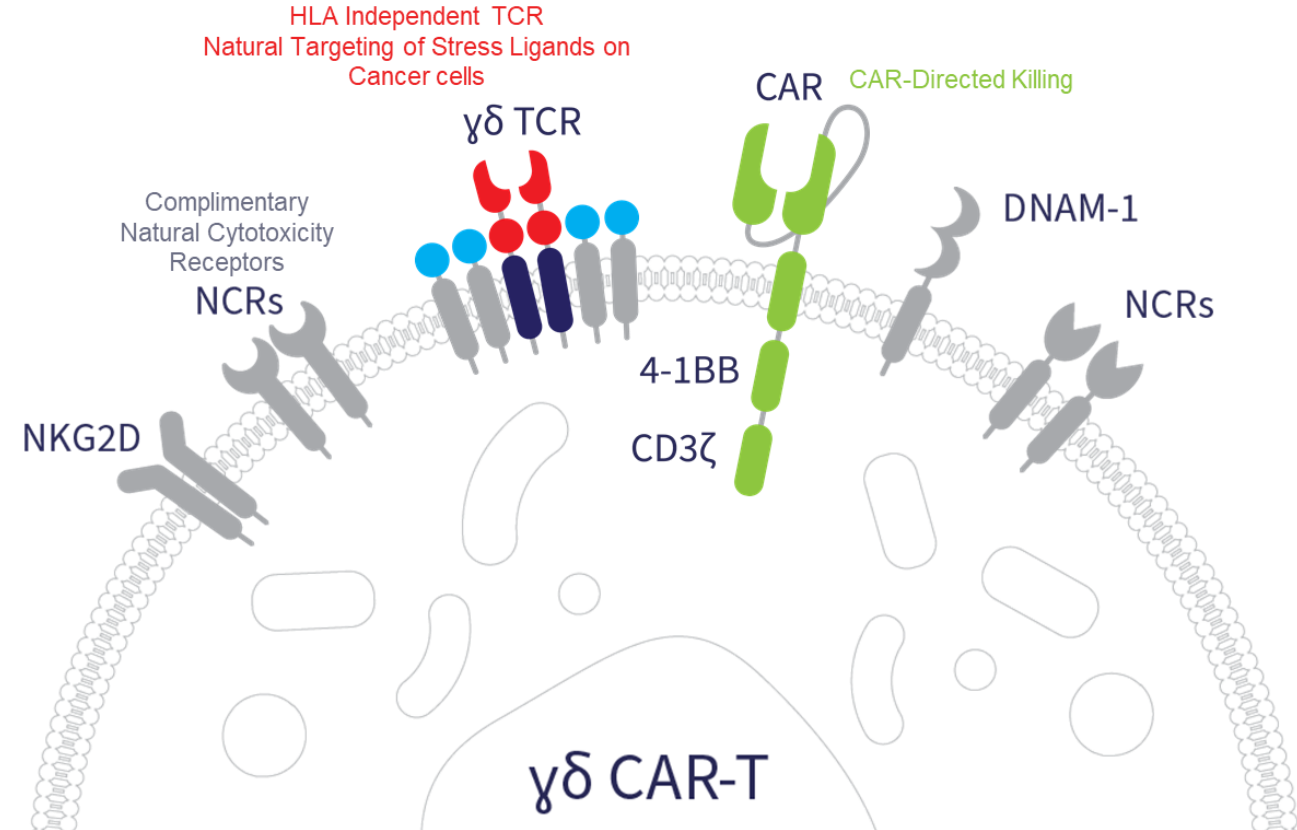
ADI-001: Encouraging Early Efficacy Data in Heavily Pretreated Aggressive NHL Patients (Indolent Lymphoma Such as FL Not Enrolled)

- 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

* May 31, 2022 Data-cut date, n=8 evaluable patients
CR= Complete response rate; FL= Follicular lymphoma; NHL= Non-Hodgkin's lymphoma; ORR= Overall response rate;

ADI-001: First-in-class, Allogeneic Gamma Delta CAR T Cell Therapy for R/R NHL Targeting B-Cell Antigen CD20

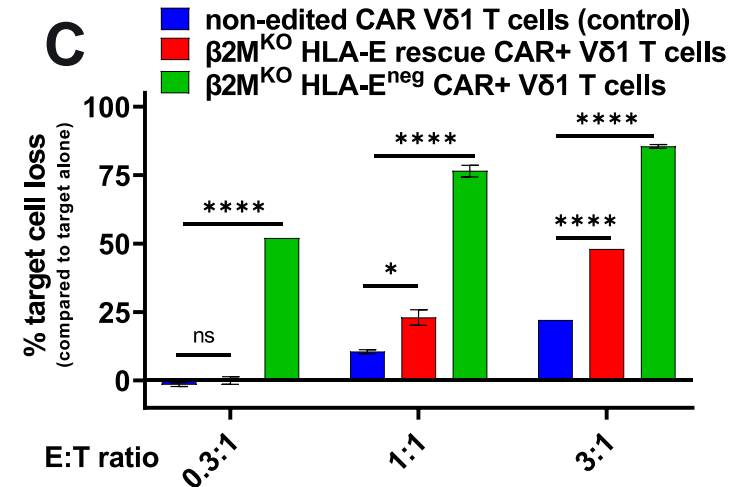
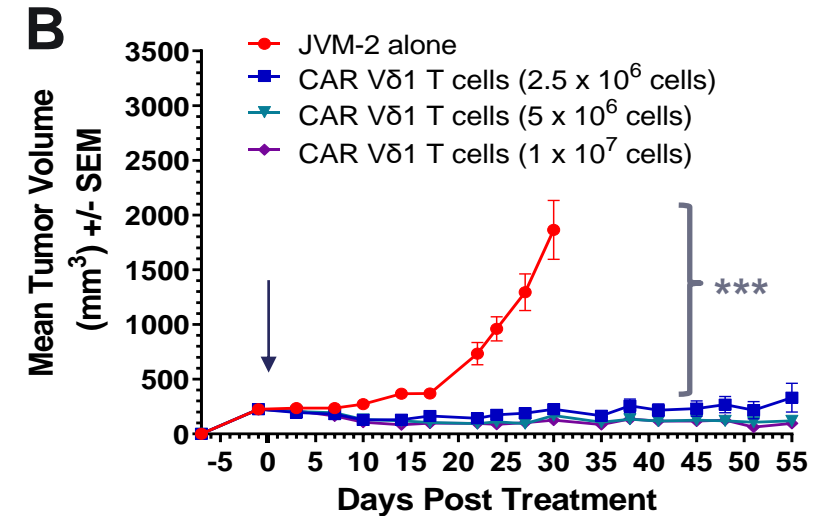
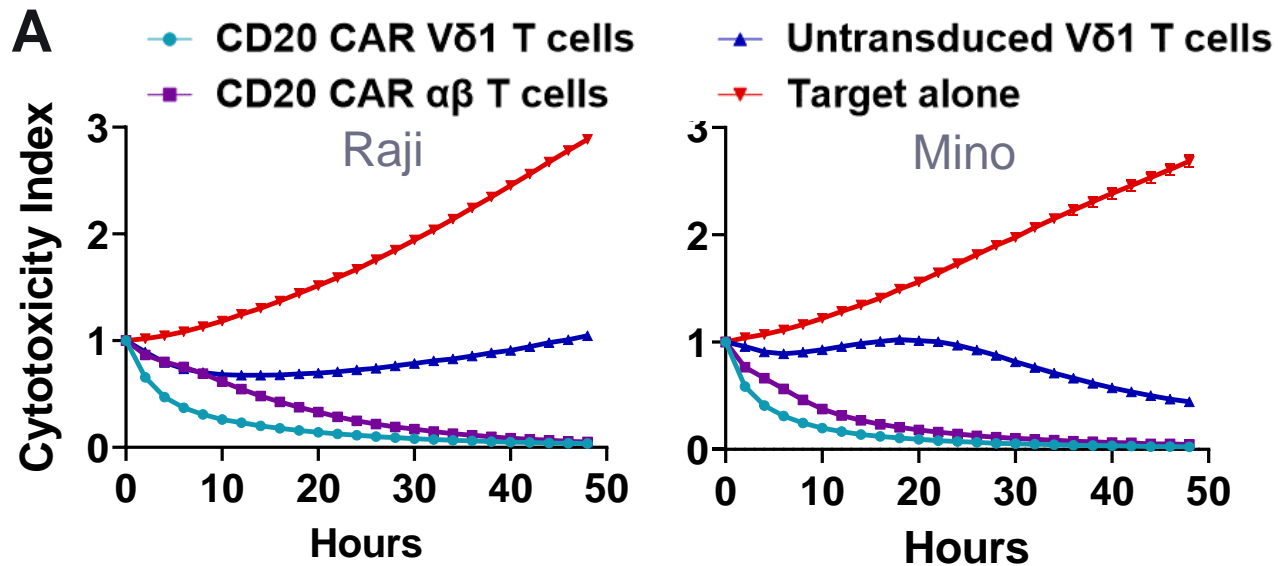
- Gamma delta ($\gamma\delta$) CAR T cells may provide three mechanisms of anti-tumor activity, limiting ability for tumor escape
 - Innate anti-tumor activity targeting multiple surface proteins selected by evolution to mark tumors for cell killing
 - **Adaptive anti-tumor activity via $\gamma\delta$ TCR**
 - **CAR mediated anti-tumor activity**
- Express MHC independent $\gamma\delta$ TCR; lower GvHD risk without the need for gene editing
- Readily available, “off-the-shelf” product candidate with scalable cGMP manufacturing process
- Advantage of CD20 as a CAR target:
 - CD20 is expressed in over 98% of advanced B-cell malignancies at diagnosis¹
 - CD20 cell surface expression is stable over time despite prior treatment with CD20 antibodies²
 - 95% of tumors relapsing after CD19 CAR T therapies remain CD20 positive²



¹Castillo JJ et al. Expert Rev Hematol 2015. ²Plaks V et al. Blood 2021. 138(12):1081-85

Preclinical Functional Characteristics of ADI-001

- A. Rapid killing kinetics compared to $\alpha\beta$ CAR T
- B. Potent and functionally persistent *in vivo* activity in lymphoma models
- C. Superior resilience to Host vs Graft compared to common gene-editing approaches



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



Dose Escalation of ADI-001 (3 + 3 design)

DL1	DL2	DL3
3E7 CAR+ Cells	1E8 CAR+ Cells	3E8 CAR+ Cells

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 cell malignancy (WHO 2017 classification)	
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)
IPI score - median (range)	4 (2-5)
Stage III & IV disease	8 (100)
Sum of the product of the diameters at screening - median (range)	3,739 (1,307- 6,922) mm ²
Prior lines of therapies - median (range)	4 (2-5)
Prior anti-CD19 CAR T therapies	3 (38)
Prior Autologous Stem Cell Transplant	2 (25)
Prior systemic anti-cancer therapy	
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)
Refractory status at study entry	
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"> R-CHOP Rituximab-abbs, gemcitabine, and CDDP Rituximab-abbs, gemcitabine, carboplatin Polatuzumab + Bendamustine/rituximab Obinutuzumab - hyper cyclophosphamide and dexamethasone 	sLD	DL1	No	IV	Off study
Transformed HGBCL (from FL)	66/F	4 prior lines	<ul style="list-style-type: none"> R-CHOP Ibrutinib Bendamustine/rituximab Rituximab 	sLD	DL1	No	III	Off study
Triple-hit HGBCL	75/M	5 prior lines	<ul style="list-style-type: none"> R-CHOP + intrathecal methotrexate Liso-cel Liso-cel (reinfusion) 	eLD	DL1	Yes	IV	Off study
MCL	62/M	5 prior lines	<ul style="list-style-type: none"> Bendamustine/rituximab Zanubrutinib Bendamustine/obinutuzumab 	eLD	DL2	No	III	Active
DLBCL	45/M	3 prior lines	<ul style="list-style-type: none"> R-CHOP R-ICE Polatuzumab 	eLD	DL2	No	IV	Off study
DLBCL	61/M	2 prior lines	<ul style="list-style-type: none"> R-CHOP R-ICE 	eLD	DL2	No	III	Active
Double-hit HGBCL	62/M	4 prior lines	<ul style="list-style-type: none"> Da-R-EPOCH + intrathecal methotrexate R-Gemcitabine/oxaliplatin 	eLD	DL3	Yes	IV	Active
DLBCL	64/F	4 prior lines	<ul style="list-style-type: none"> R-CHOP R-Gemcitabine/oxaliplatin 	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.

ADI-001: Preliminary Efficacy Data

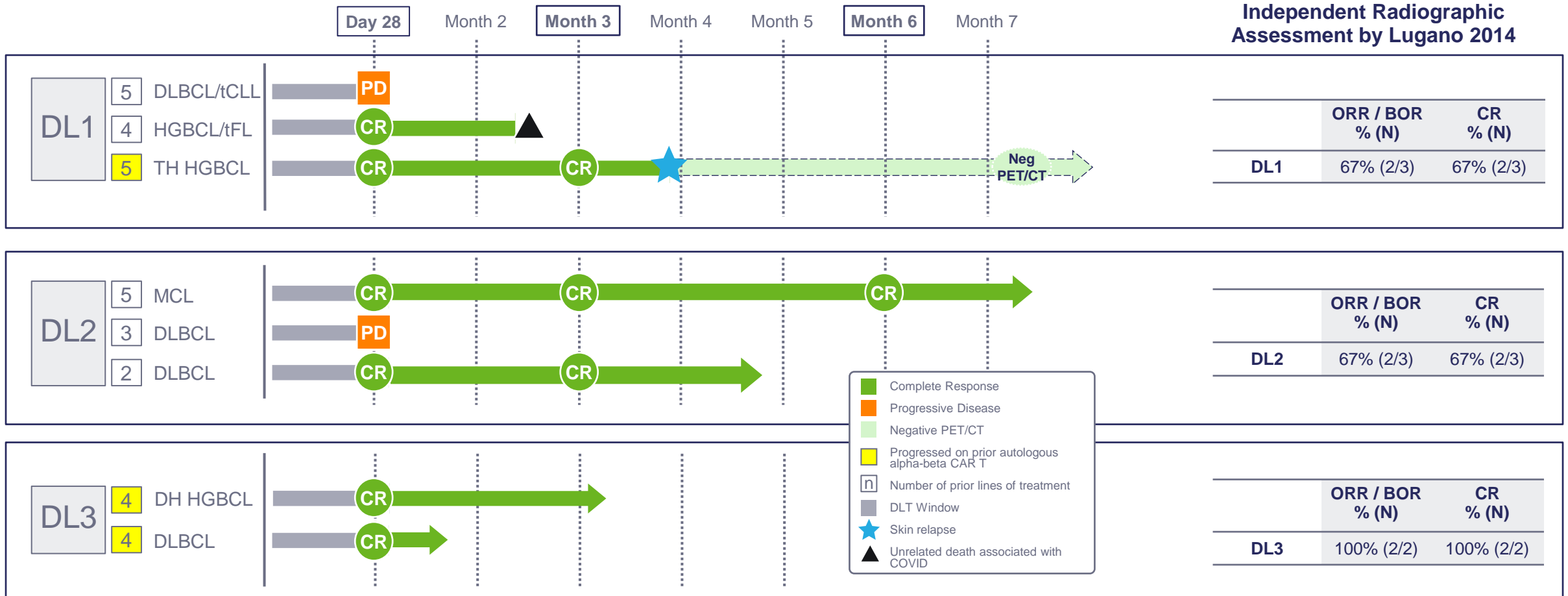
Per protocol analysis, independent radiographic assessment using Lugano 2014

	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)	100% (3/3)
CR, % (N)	67% (2/3)	67% (2/3)	100% (2/2)	75% (6/8)	100% (3/3)

- **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**

Data-cut date: May 31, 2022

ADI-001: Preliminary Efficacy and Durability Data



Data-cut date: May 31, 2022

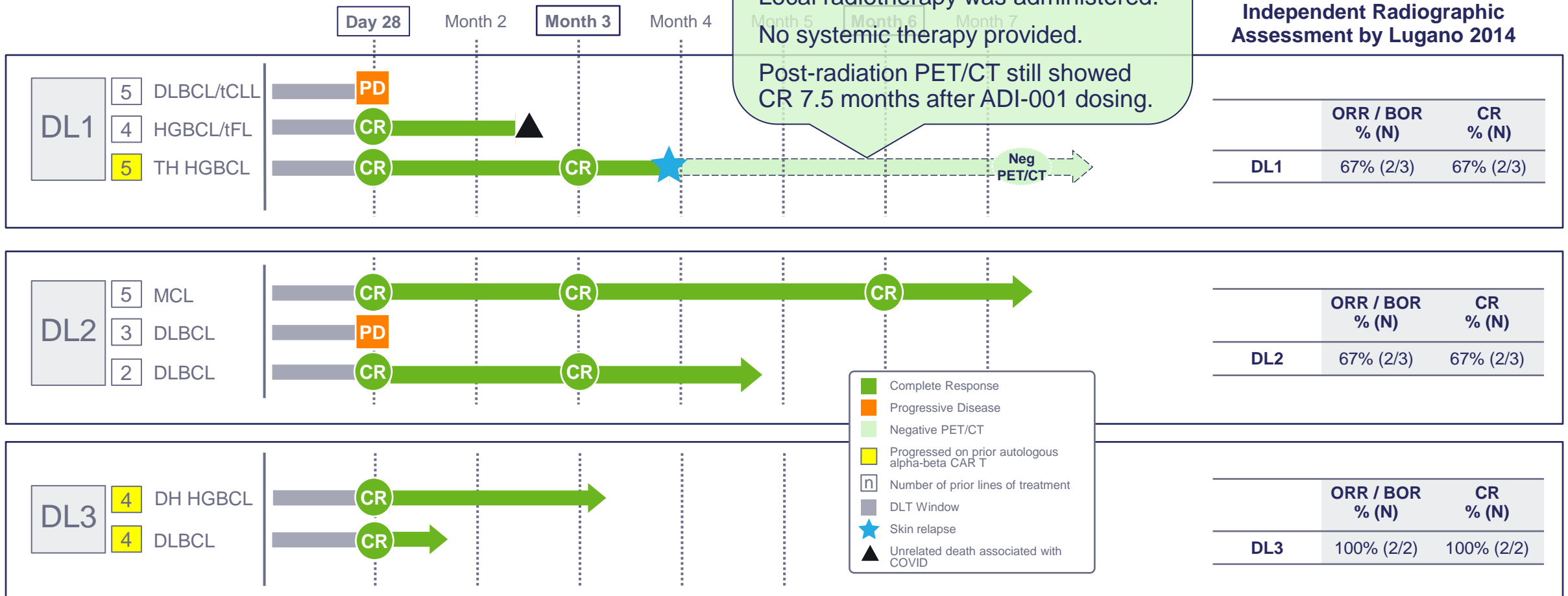
Preliminary data may suggest potential dose-related increase in durability

ADI-001: Preliminary Efficacy and Durability Data

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.

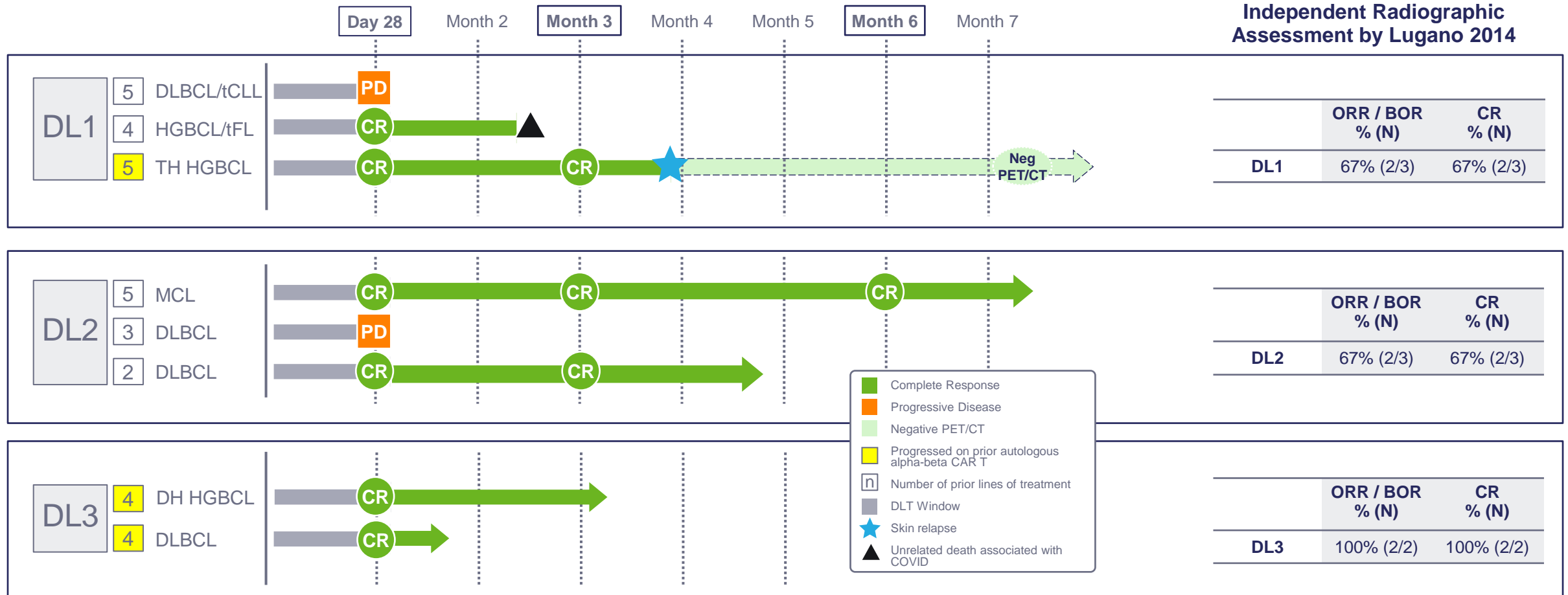


Preliminary data may suggest potential dose-related increase in durability

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

Data-cut date: May 31, 2022

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

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/μL)
- CD8 T cells (cell/μL)
- NK cells (cell/μL)

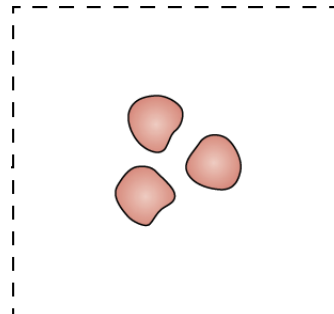
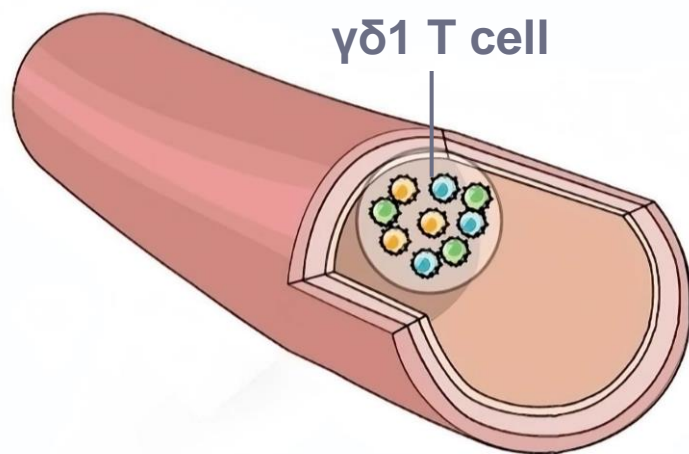
Number of subjects:
 Standard LD = 2
 Enhanced LD = 5

(*) Standard LD (sLD): Cy 500 mg/m² (3 days) and Flu 30 mg/m² (3 days)
 Enhanced LD (eLD): Cy 1000 mg/m² (3 days) and Flu 30 mg/m² (4 days)

Gamma Delta1 T Cells Preferentially Home to Tissues

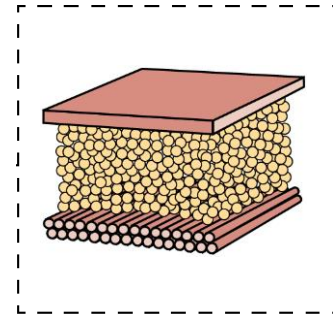
peripheral blood

% of CD3+: ~1-3%



lymph node

CD27+
CD62L+
Vδ1+ ↑↑
Vδ2+ ↓↓

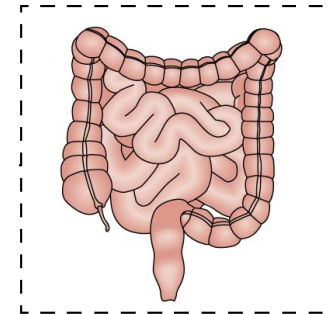


breast

tissue/blood: ~15X

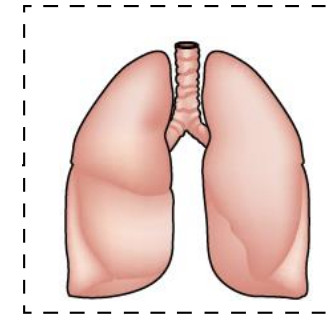
adipose

tissue/blood: 9X



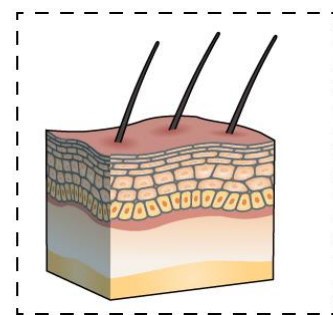
GI

tissue/blood: 11X



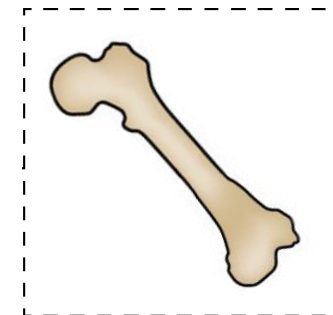
lung

tissue/blood: 9X



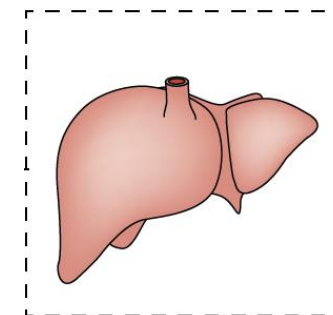
skin

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

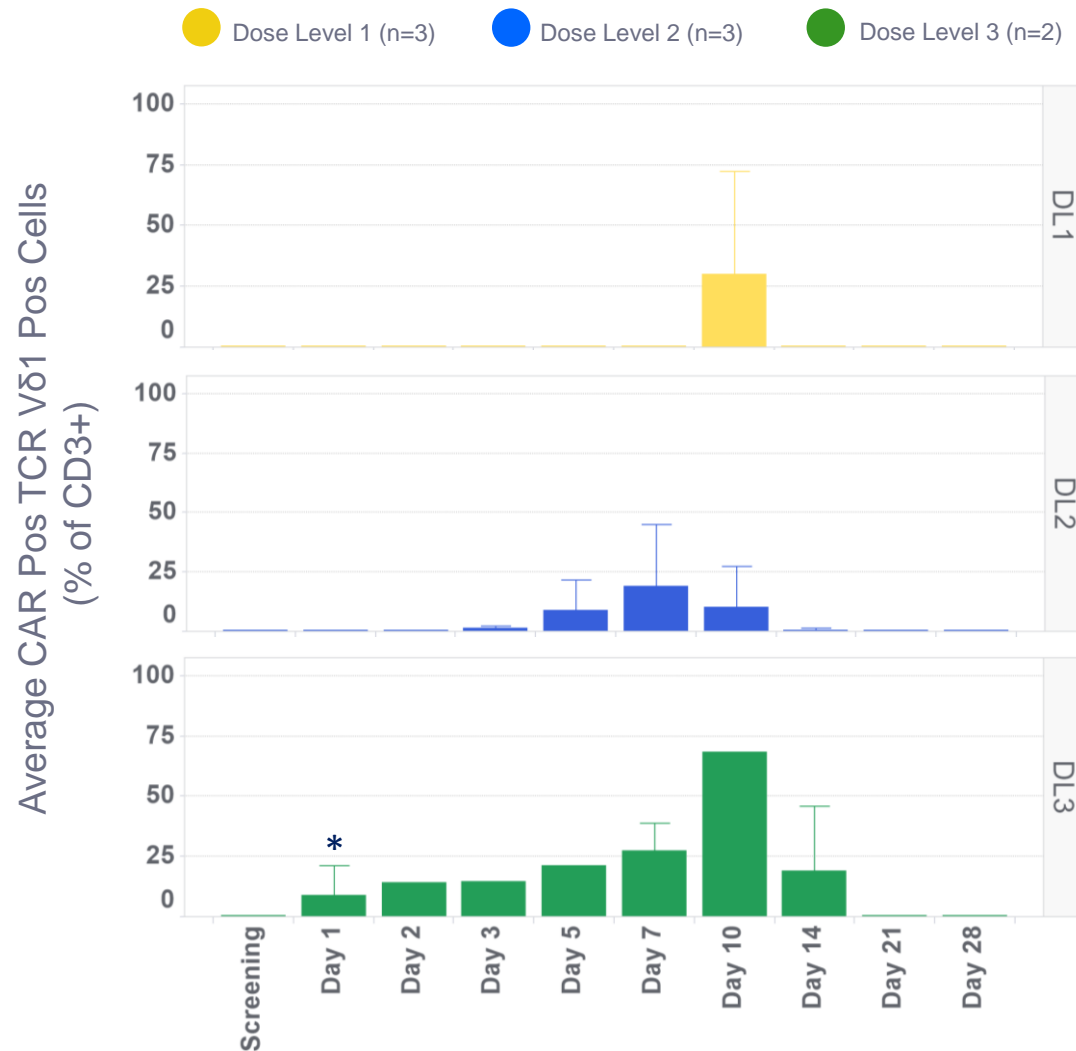
Images adapted from Hunter *et al J Hepatol.* 2018 and Ribot *et al Nat Rev Immunol.* 2021

References:

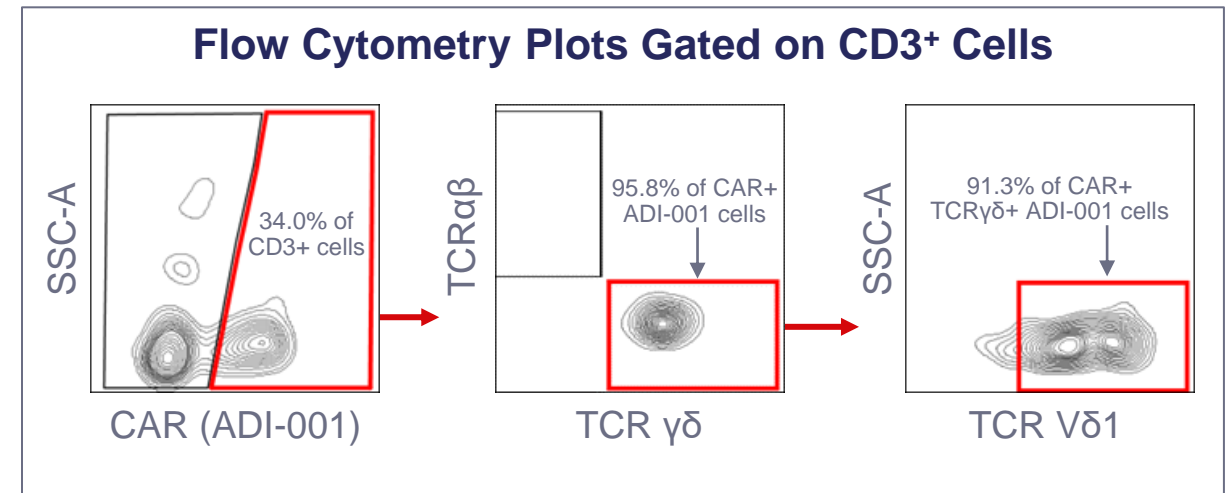
Brauneck *et al Front Med* 2021
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Uger *et al Sci Rep* 2018
Wang *et al Exp Ther Med* 2020
Wu *et al Sci Transl Med* 2019

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

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 mm²
- 5 prior lines of therapy
 - R-CHOP+IT-Methotrexate
 - Liso-cel (best response: CR)
 - Liso-cel reinfusion (best response: CR)
 - Revlimid
 - Tafasitamab-cxix

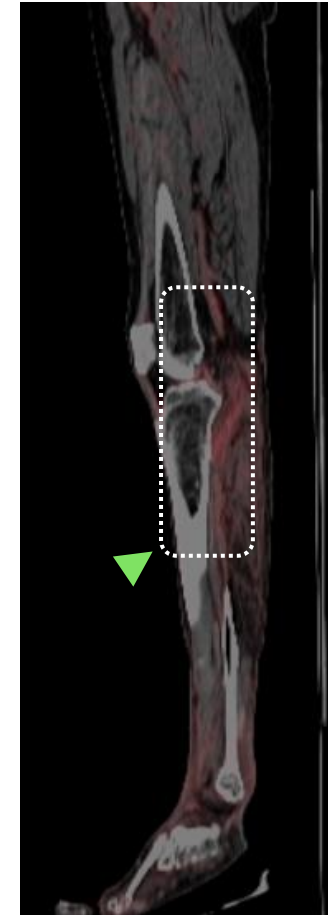
- Efficacy Data:
 - CR on PET/CT @ Day-28 and Month-3.
 - Skin (right leg) relapse at 3.9 months while repeat PET/CT remained in CR.
 - Only received focal radiation to the skin. Lesion resolved. No systemic therapy administered.
 - **Post-radiation PET/CT continues to be negative more than 7.5 months 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

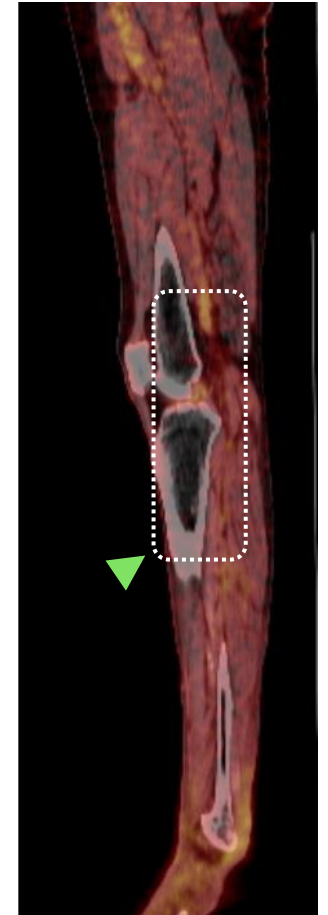
- ▶ Baseline FDG uptake by tumor lesions ▶ Sites of tumor response



Baseline



Day 28



Month 3

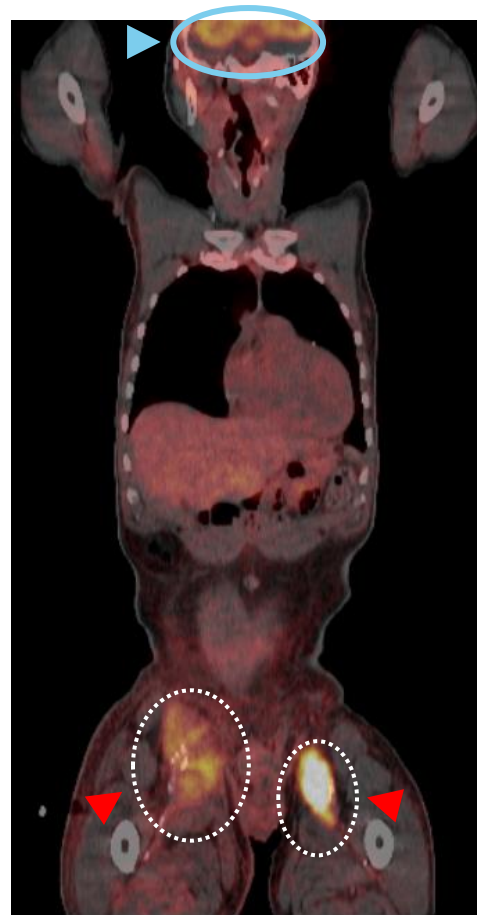
ADI-001 Case Study 2: Dose Level 2 (1E8 cells)

- 62-year-old male
- Mantle Cell Lymphoma
- MIPI score 4, Stage III
- SPD 6,472mm² at baseline
- 5 prior lines of therapy
 - Bendamustine + Rituximab
 - Zanubrutinib
 - Bendamustine + Obinutuzumab
 - Bendamustine + Rituximab
 - R-GDC

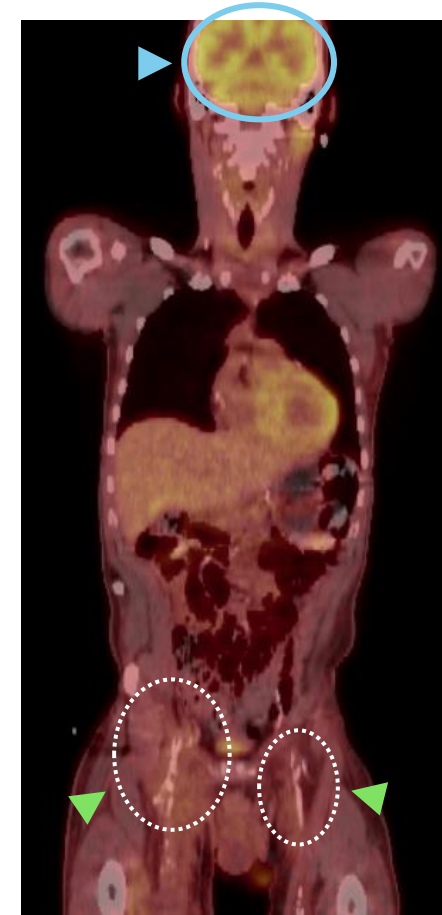
- Efficacy Data:
 - **Ongoing CR > 7 months**

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

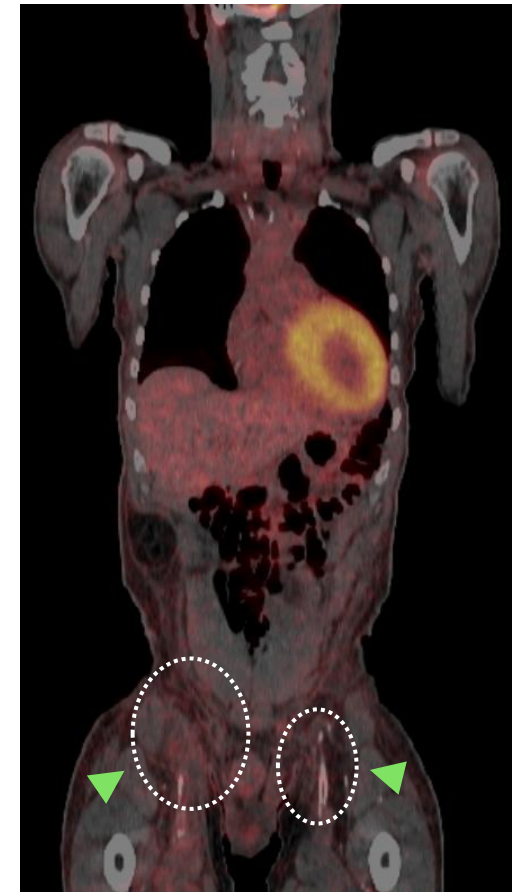
- ▶ FDG uptake by normal tissues
- ▶ Baseline FDG uptake by tumor lesions
- ▶ Sites of tumor response



Baseline



D28



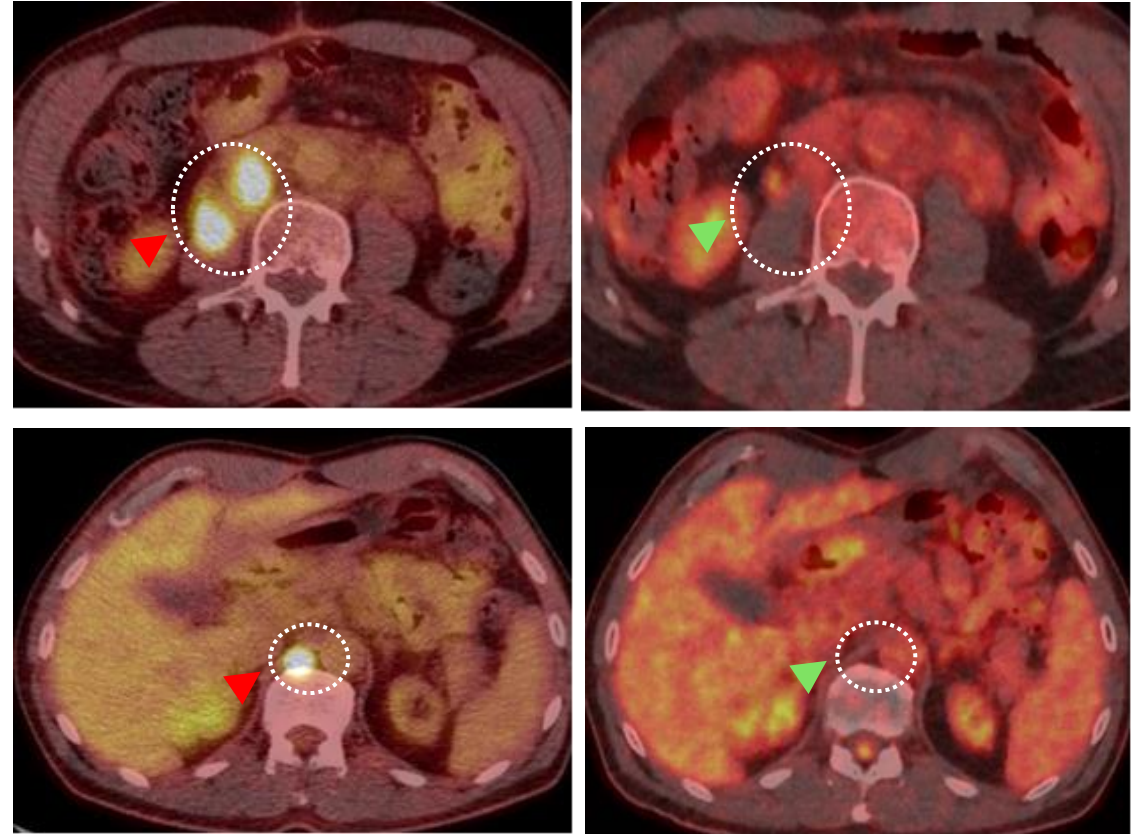
Month 6

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 mm² 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)

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

Commentary: ADI-001 Phase 1 Interim Data



Sattva Neelapu, M.D.

Department of Lymphoma-Myeloma
Division of Cancer Medicine

The University of Texas, MD Anderson Cancer Center

1. Based on your clinical experience, can you comment on ADI-001 durability data to-date?
2. Can you comment on ADI-001 persistence data to-date?
3. What are your thoughts regarding other cell therapy approaches for NHL such as alpha-beta CAR T, CAR NK and bi-specifics compared to ADI-001?
4. Where do you see next steps for this program?

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4. Where do you see next steps for this program?

Commentary: ADI-001 Phase 1 Interim Data



Sattva Neelapu, M.D.

Department of Lymphoma-Myeloma
Division of Cancer Medicine

The University of Texas, MD Anderson Cancer Center

1. Based on your clinical experience, can you comment on ADI-001 durability data to-date?
2. Can you comment on ADI-001 persistence data to-date?
3. What are your thoughts regarding other cell therapy approaches for NHL such as alpha-beta CAR T, CAR NK and bi-specifics compared to ADI-001?
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ADI-001: 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

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	[Red arrow spanning Discovery, Preclinical, IND, Ph 1, and Ph 2/3]					Adicet Bio
ADI-002*	GPC3	HCC	[Red arrow spanning Discovery, Preclinical, and IND]					REGENERON
ADI-003	Undisclosed	Solid / Heme	[Red arrow spanning Discovery, Preclinical, and IND]					Adicet Bio
ADI-004	Undisclosed	Solid / Heme	[Red arrow spanning Discovery, Preclinical, and IND]					Adicet Bio
ADI-005	Undisclosed	Solid / Heme	[Red arrow spanning Discovery and Preclinical]					Adicet Bio
ADI-006	Undisclosed	Solid / Heme	[Red arrow spanning Discovery and Preclinical]					Adicet Bio
ADI-007	Undisclosed	Solid / Heme	[Red arrow spanning Discovery and Preclinical]					Adicet Bio
ADI-008	Undisclosed	Solid / Heme	[Red arrow spanning Discovery and Preclinical]					Adicet Bio

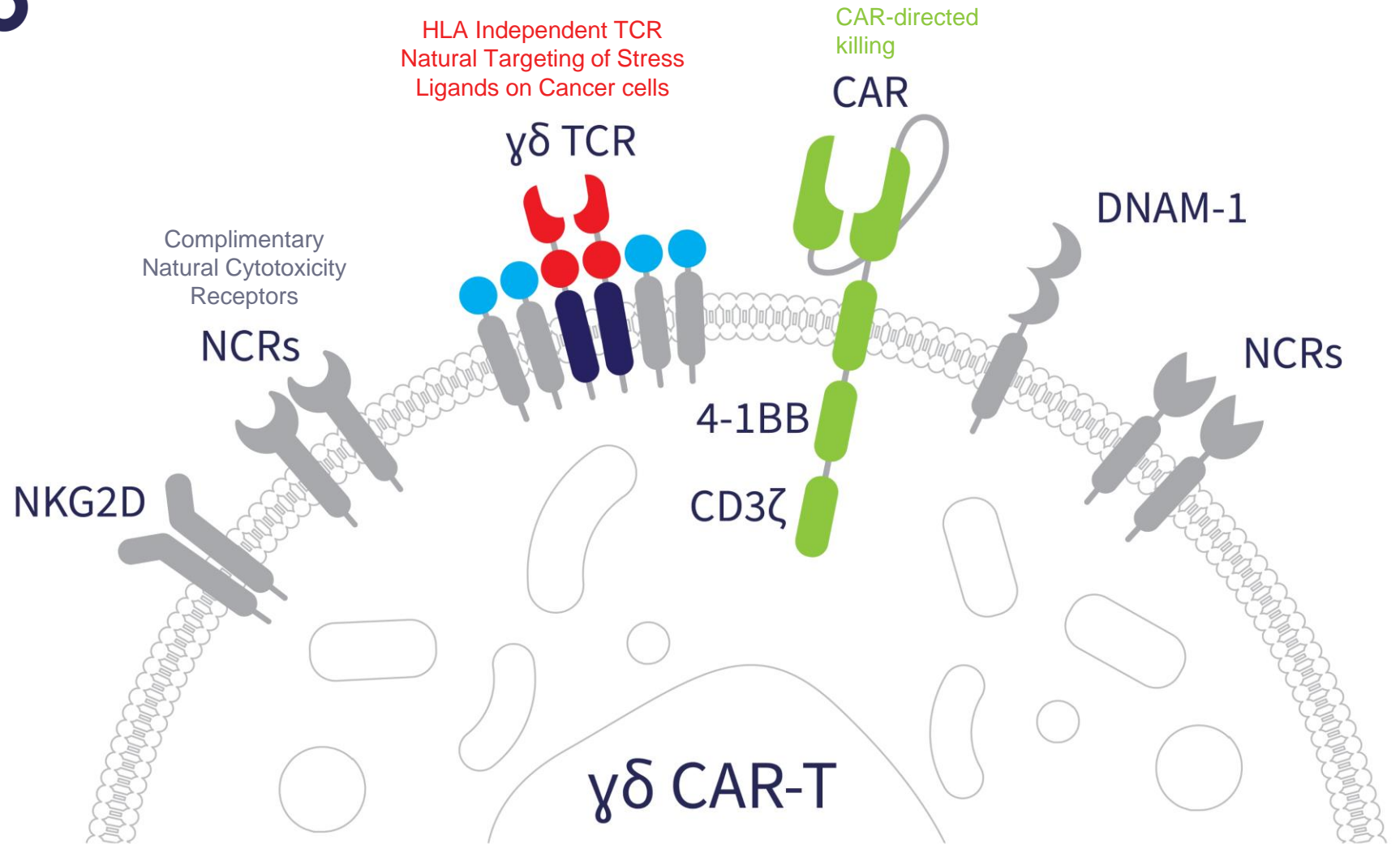
Milestones

- 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



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





ADI-001 Phase 1 Interim Data

First-in-class allogeneic, off-the-shelf
gamma delta ($\gamma\delta$) CAR T cells

