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**ADI-001 Phase 1 Interim
First in Human Clinical Data**

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

December 6, 2021

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Agenda

▶	**Welcome and Introductory Remarks**	**Chen Schor** President and CEO
▶	**Review of ADI-001 Interim Phase 1 Data**	**Francesco Galimi, M.D., Ph.D.** Chief Medical Officer
▶	**Opportunities Offered by γδ T Cell Therapy**	**Sattva Neelapu, M.D.** MD Anderson Cancer Center
▶	**Closing Remarks/Q&A**	**Chen Schor/All**

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Adicet Bio: Leaders in γδ CAR T Cell Therapy
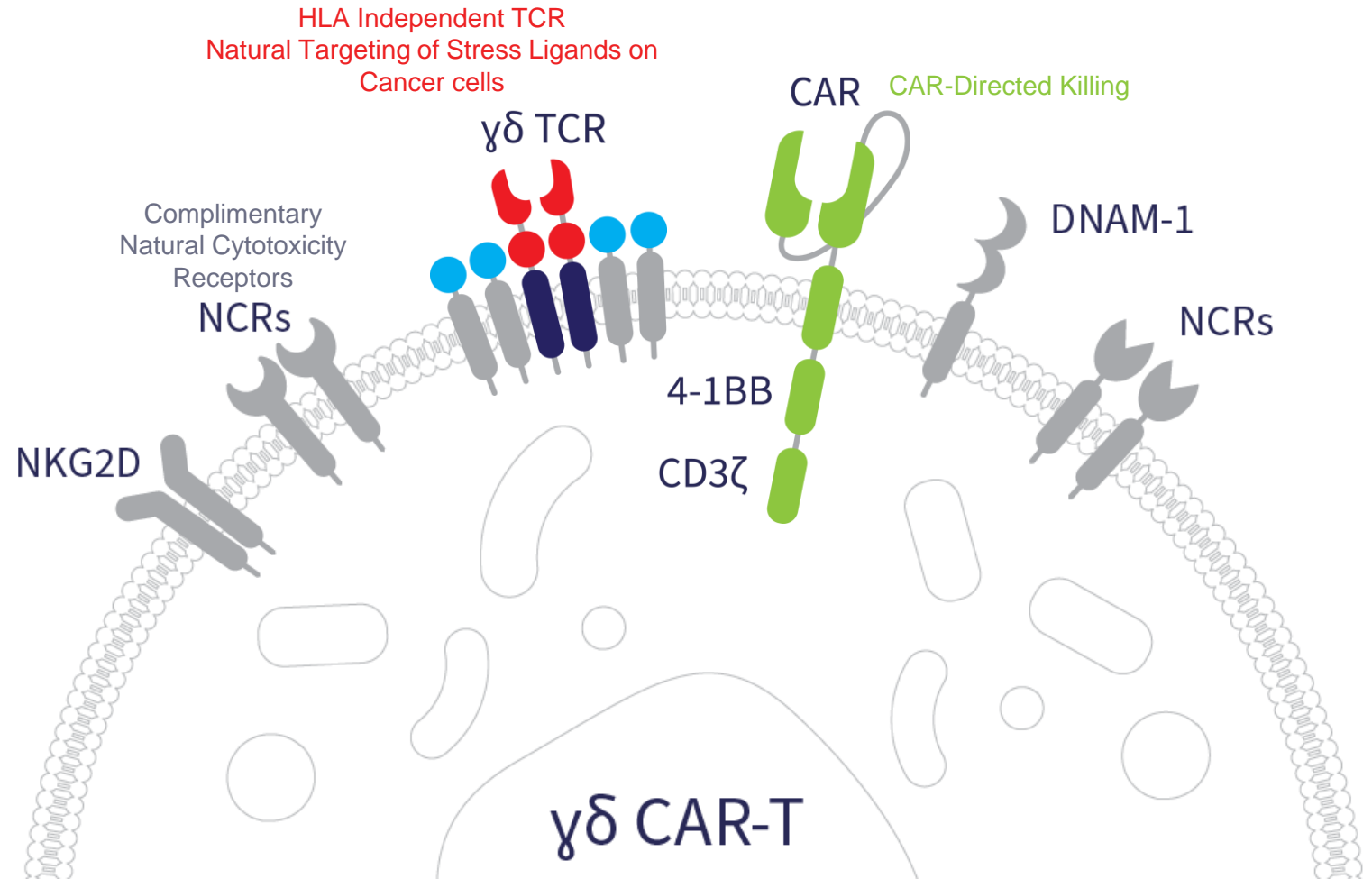
- ADI-001 is the first-ever off-the-shelf, γδ CAR T cell investigational therapy to reach clinical trials and report clinical data

- Interim clinical data indicate that ADI-001 is highly clinically active with a favorable safety profile in patients treated to date

- γδ T cells may provide significant clinical advantages both in terms of anti-tumor activity and safety compared to other allogeneic cell platforms or bispecifics

- γδ1 T cells may provide benefits as compared to γδ2 T cells

Adicet's γδ1 CAR T Cells: 3 Mechanisms for Anti-tumor Activity

γδ 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 γδ 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

HLA Independent TCR
Natural Targeting of Stress Ligands on Cancer cells

γδ TCR

CAR

CAR-Directed Killing

Complimentary Natural Cytotoxicity Receptors

NCRs

DNAM-1

NCRs

NKG2D

4-1BB

CD3ζ

γδ CAR-T

CAR: Chimeric Antigen Receptors; DNAM-1: DNAX accessory molecule-1; GvHD: Graft Versus Host Disease; HLA: Human Leukocyte Antigen; MHC: Major Histocompatibility Complex; NCR: Natural Cytotoxicity Receptors; NK: Natural Killer; TCR: T Cell Receptor; NKG2D: NK Group 2D

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Adicet CAR γδ T Cell Platform Potential Advantages: Designed to Address Activity, Tumor Homing, Safety, and COGs Limitations
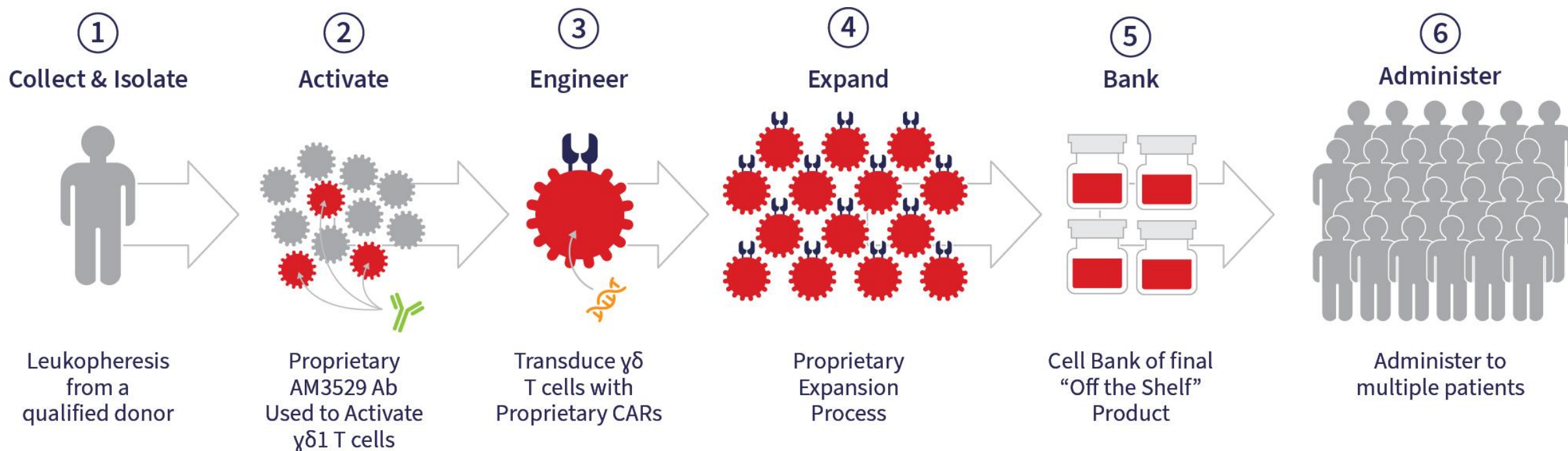
		Allogeneic CAR αβ T Cells	Allogeneic CAR NK Cells	Allogeneic CAR γδ T Cells
Activity*	Innate anti-tumor response		✔	✔
	Adaptive anti-tumor response	✔		✔
	Active tumor homing			✔
	Predominantly activating receptor expression	✔ (Limited number)	✔ (Balance with inactivating)	✔
	Preclinical persistence by repeat tumor challenge			✔
	Prognostic value of tumor infiltration		✔	✔✔
Safety*	Low GvHD risk	✔ (Requires αβ TCR deletion)	✔	✔
	Low risk of cytokine release syndrome ≥ grade 3 risk		✔	✔
COGS	No gene editing required (May affect efficacy)		✔	✔
	Scalable manufacturing	✔ Limited without exhaustion	✔	✔✔

*For illustrative purposes only; no clinical head to head studies have been conducted to date

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Advantages of γδ1 T Cells

	Feature	Vδ1+ T cells	Vδ2+ T cells	Comment
Activity	Diverse VDJ rearranged TCR	🟩	🟥	Vδ2+ T cells generally express invariant TCR
	Programmed adaptations for tissue survival	🟩	🟧	Vδ1+ T cells tolerate hypoxic and low nutrient conditions
	Expression of tumor homing receptors	🟩	🟧	Vδ1+ T cells express CCR5 and tumor homing receptors
	Long lifespan & adaptive immune response	🟩	🟥	Vδ1+ T cells oligoclonally expand to pathogenic antigens
	MHC unrestricted TCR	🟩	🟩	Vδ1+ T cells recognized antigen independent of MHC
	NKG2D & broad NCR expression	🟩	🟧	Prevents immune escape of tumor cells
	High granzyme & perforin expression	🟩	🟧	Vδ1+ T cells are highly cytolytic (similar to CD8 αβ T cells
	Broad anti-tumor toxicity	🟩	🟧	Vδ1+ T cells recognize numerous malignant cell types
	Low / no KIR Expression	🟩	🟩	Adicet' s Vδ1+ T cells display low inhibitory KIR
Potential safety	GvHD incompatible TCR	🟩	🟩	Vδ1+ T cells cannot be activated by unmatched MHC
	No IL-17 / RORγt expression (Th17)	🟩	🟩	Adicet' s Vδ1+ T cells never express "protumorigenic" IL-17 or RORγt
	Moderate IL-2 expression	🟩	🟧	Adicet's Vδ1+ T cells don't hyperproliferate
	High expansion without exhaustion	🟩	🟥	Adicet' s Vδ1+ 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

Gentles, A. et al. Nat. Med. 21, 938–945 (2015); Girardi, M. et al. J. Exp. Med. 198, 747–755 (2003); Girardi, M. et al. Science 294, 605–609 (2001); Godder, K. T. et al. Bone Marrow Transplant. 39, 751–757 (2007); Minculescu, L. et al. Front. Immunol. https://doi.org/10.3389/fimmu.2019.01997 (2019); Nussbaumer, O. & Koslowski, M. Immuno-Oncology Technol. 1, 3–10 (2019).

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Large-Scale Manufacture of Off-The-Shelf γδ T Cell Candidates

① Collect & Isolate
Leukopheresis from a qualified donor

② Activate
Proprietary AM3529 Ab Used to Activate γδ1 T cells

③ Engineer
Transduce γδ T cells with Proprietary CARs

④ Expand
Proprietary Expansion Process

⑤ Bank
Cell Bank of final "Off the Shelf" Product

⑥ Administer
Administer to multiple patients

Proprietary AM3529 activating antibody designed to expand γδ1 T cells, Proprietary Vectors, Proprietary Scalable Process

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ADI-001 FIH: Key Topics Adicet Set Out to Answer

Safety — Will we see GvHD, neurotoxicity or high-grade CRS commonly associated with other cell therapies?

Expansion/ Proliferation — Will ADI-001 proliferate and be detected in the blood?

PD Biomarkers — Will we see any pharmacodynamic biomarkers consistent with ADI-001 activation?

Anti-Tumor Activity — Will we see any signs of anti-tumor activity?

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ADI-001 FIH: Key Findings to Date

Safety
Favorable safety profile in patients treated to date; No GvHD, neurotoxicity, or high-grade CRS reported

Expansion/ Proliferation
Evidence of *in vivo* expansion

PD Biomarkers
Evidence of circulating pharmacodynamic biomarkers consistent with ADI-001 activation

Anti-Tumor Activity
Complete and near-complete responses observed starting at ADI-001's lowest dose level, including a CR in a CAR T relapsed patient (ORR=75%, CR=50%)

Data supports potential of Adicet's first-in-class allogeneic γδ CAR T cell platform

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GLEAN1 – Interim Data
Gamma deLta adoptive thErApy for B cell NHL

First in Human Study for ADI-001
(CD20 γδ CAR T cells)

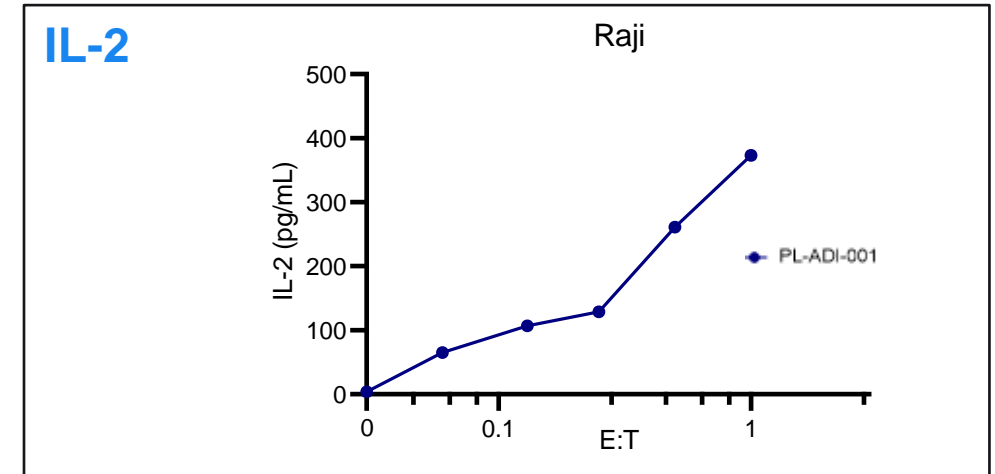Francesco Galimi, M.D., Ph.D.
Chief Medical Officer

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 does not compete with rituximab and 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

- Together, ADI-001 has demonstrated significant and durable *in vivo* anti-tumor activity

in vitro cytotoxicity

Raji (~54,000 CD20 /cell)

WILL-2
(<1000 CD20/cell, Rituximab Resistant)

CD20 CAR Vδ1 cells
Vδ1 cells

in vivo activity

Intravenous Raji Tumor Growth

Tumor Alone
CD20 CAR Vδ1 cells

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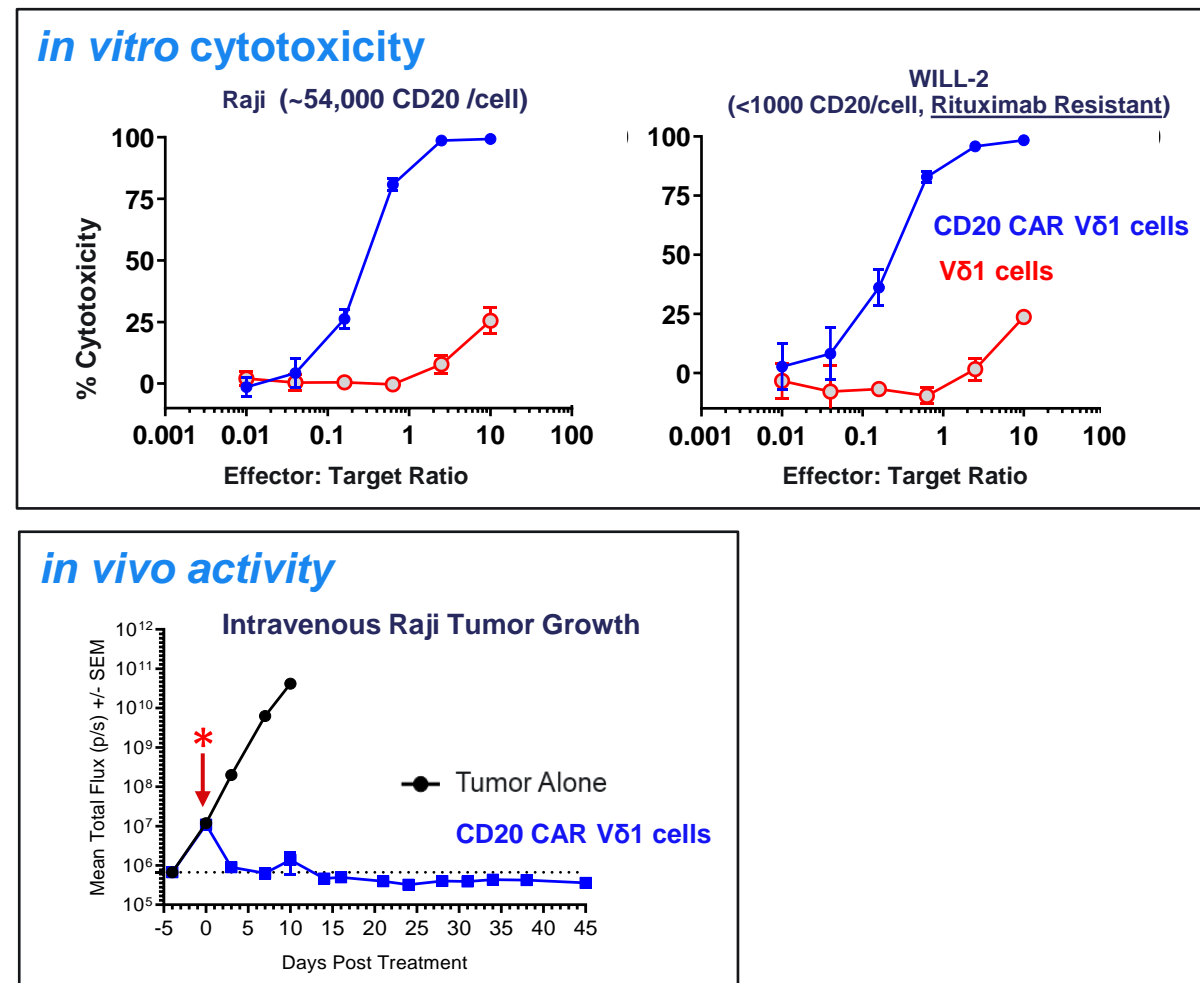
Cytokine Profile for ADI-001 Cancer Cell Engagement and Activation

- ADI-001 activation and cytotoxicity against CD20+ lymphoma cells is accompanied by secretion of polyfunctional cytokines

- These include secretion of IL-2 & IL-8

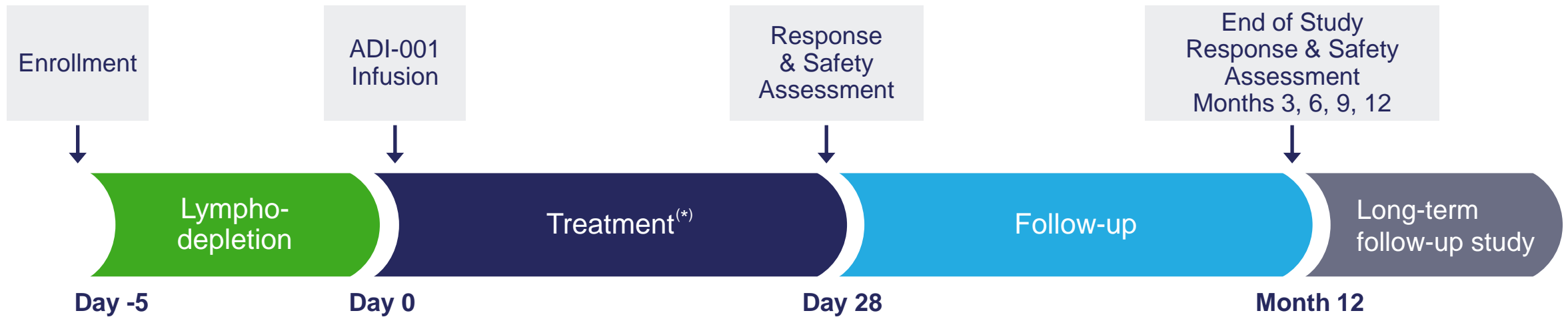- Notably, IL-6 is not commonly a component of the cytokine profile for ADI-001 activation

IL-2

Raji

IL-2 (pg/mL) vs E:T; PL-ADI-001

IL-8

Raji

IL-8 (pg/mL) vs E:T; PL-ADI-001, Untransduced γδ

E:T = Effector: Target Ratio

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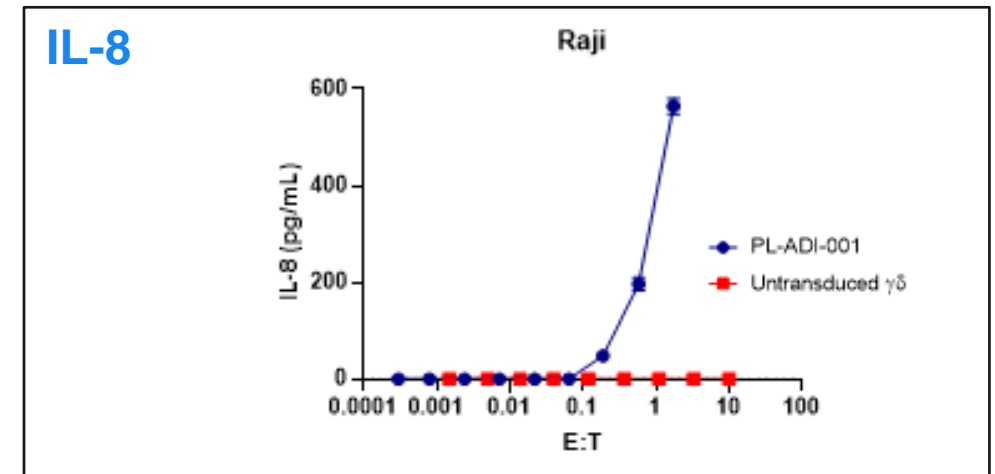
First Clinical Experience: Allogeneic γδ CAR T Investigational Therapy

Today we will discuss ADI-001's:

- Initial safety profile for 1st allogeneic γδ CAR T cell investigational therapy

- Initial evidence of cell expansion in patients

- Initial evidence of pharmacodynamic engagement

- Complete and near-complete responses observed starting at ADI-001's lowest dose level (30M CAR+ cells)

  - Yescarta - 30M CAR+ cells is approximately 5X lower than the approved dose for Yescarta (an autologous CD19 $\alpha\beta$ T cell therapy)

  - CAR NK Cell therapy - 30M CAR+ cells is the first dose level in a CD19 CAR NK cell therapy study where one PR was observed out of three evaluable patients

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GLEAN-1: ADI-001 FIH Study (CD20 γδ CAR T cells)

Enrollment

ADI-001 Infusion

Response & Safety Assessment

End of Study Response & Safety Assessment Months 3, 6, 9, 12

Lympho-depletion → **Treatment**(*) → **Follow-up** → **Long-term follow-up study**

Day -5 **Day 0** **Day 28** **Month 12**

Optional ADI-001 retreatment

Potential DLBCL dose expansion / Pivotal study

Potential MCL dose expansion / Pivotal study

Phase 1 study design

- NHL patients relapsing from 2 or more prior lines of treatment

- 3 cohorts expected for dose escalation/safety: 3E7, 1E8 and 3E8 CAR+ cells

- Up to 50 patients at the selected dose
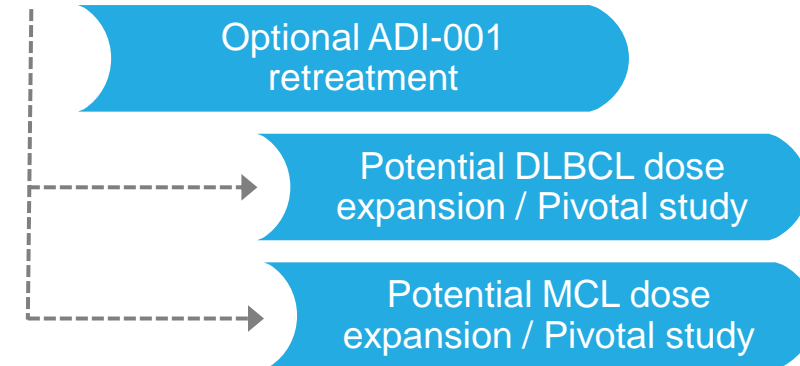
Lymphodepletion Regimen: Flu/Cy
Fludarabine: 30 mg/m^2/d x 3 days, Cyclophosphamide 500 mg/m^2/d x 3 days
Protocol allows for enhanced lymphodepletion regimen

First Patient First Dose: May 2021

(*) Dose escalation study

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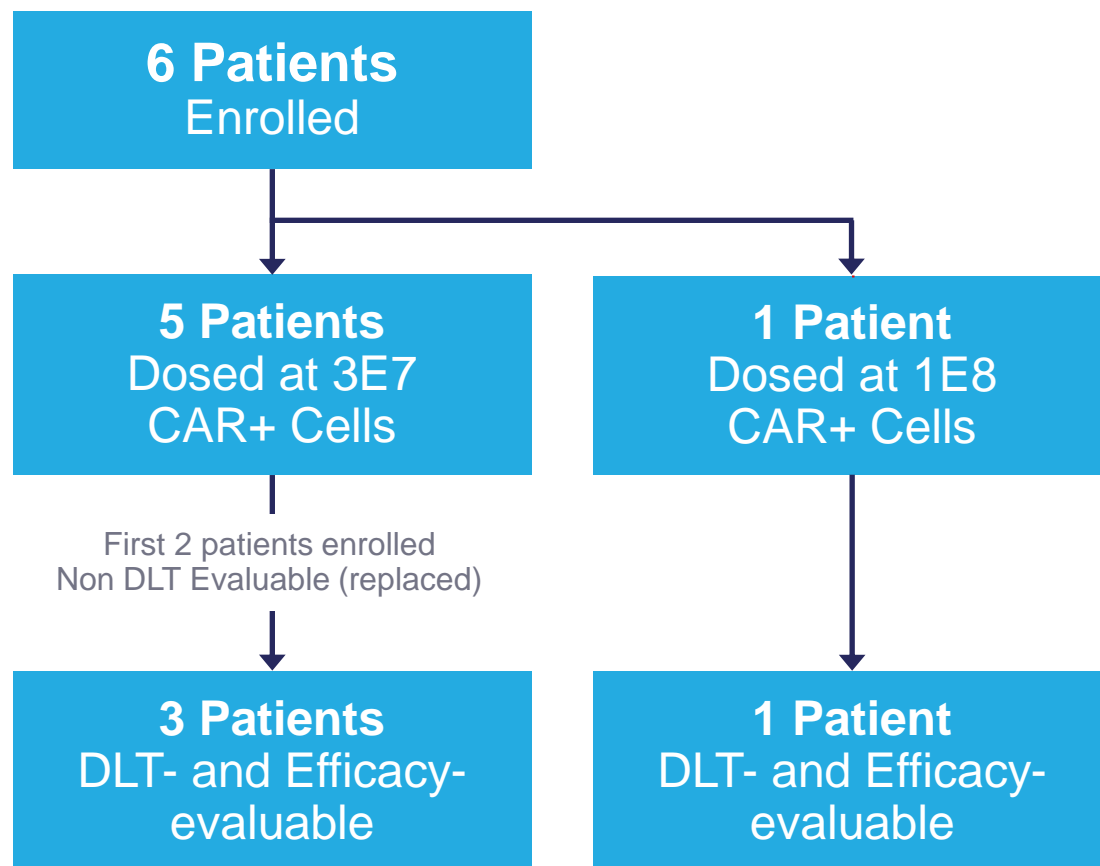
- Safety Subset: 6 patients
- Efficacy Subsets: 4 patients
  - 3 patients at 3E7 CAR+ cells (starting dose level) *(2 patients received standard lymphodepletion and 1 received enhanced lymphodepletion)*
  - 1 patient at 1E8 CAR+ cells *(1 received enhanced lymphodepletion)*

Note:

The **safety subset** includes all patients who received ADI-001

The **efficacy subset** includes all patients who completed at least one response assessment

Cut-off date: November 22, 2021

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Cancer Type	Age/ Sex	Prior Therapies		sLD or eLD	ADI-001 CAR + Cells	Prior CAR T?	DLT eval?	DLT	Stage
Transformed DLBCL (from CLL)	62/F	5 prior lines with PD as best response, including:	• R-CHOP • rituximab-abbs, gemcitabine, and CDDP • rituximab-abbs, gemcitabine, carboplatin • polatuzumab + BR x 2 • obinutuzumab - hyper cyclophosphamide and dexamethasone	sLD	3E7 cells	No	Yes	No	IV
Transformed high grade B cell tumor (from FL)	66/F	4 prior lines:	• R-CHOP • ibrutinib • bendamustine/rituximab • rituximab	sLD	3E7 cells	No	Yes	No	IV
DLBCL	75/M	5 prior lines:	• R-CHOP; IT MTX • liso-cel • liso-cel (reinfusion) • revlimid • tafasitamab-cxix	eLD	3E7 cells	Yes	Yes	No	IV
MCL	62/M	5 prior lines:	• bendamustine/rituximab • zanubrutinib • bendamustine/obinutuzumab • bendamustine/rituximab • rituximab/gemcitabine/dex/carboplatin	eLD	1E8 cells	No	Yes	No	IV
First 2 patients enrolled did not complete DLT period and were replaced per protocol:									
Primary Refractory Burkitt	29/M	3 prior lines with PD as best response:	• R-CODOX-M/R-IVAC • cy/flu/rituximab + FT516 Trial • R-EPOCH	sLD	3E7 cells	No	No	N/A	IV
Double hit DLBCL	52/M	5 prior lines, including:	• DA-EPOCH R with IT MTX/ARA-C • R-ICE • polatuzumab/rituximab • tisagenlecleucel • gemcitabine/oxliplatin	sLD	3E7 cells	Yes	No	N/A	IV

- All patients heavily pre-treated, with at least 3 prior lines of systemic therapy
- Disease measured by Lugano 2014
- Enrolled multiple subtypes of NHL
- 2 patients had received prior autologous CD19 CAR T

Lymphodepletion:

Standard (sLD): fludarabine (30 mg/m^2/day for 3 days) plus cyclophosphamide (500 mg/m^2/day for 3 days)

Enhanced (eLD): fludarabine (30 mg/m^2/day for 4 days) plus cyclophosphamide (1000 mg/m^2/day for 3 days)

Cut-off date: November 22, 2021

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ADI-001 FIH Study: Safety Profile

TEAE	All Grades (%)	Grade 3+ (%)
IRR	- (0%)	- (0%)
CRS	3 (50%)	- (0%)
ICANS	- (0%)	- (0%)
GvHD	- (0%)	- (0%)
Infection*	2 (33%)	1 (17%)

- N = 6
- No DLTs
- No ICANS
- No GvHD
- No Grade 3+ CRS

One patient with COVID-19 infection Grade 2 and pneumonia Grade 3; one patient with candida Grade 1

TEAE = Treatment-emergent adverse events; CRS= cytokine release syndrome; GvHD= graft vs host disease ;
ICANS= immune effector cell associated neurotoxicity; IRR= infusion-related reaction

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ADI-001 FIH Study: Responses in Efficacy-Evaluable Patients

Status	Cancer Type	Age/Sex	Prior Therapies		sLD or eLD	ADI-001 CAR+ Cells	Prior CAR T?	DLT eval?	DLT	Stage	Best Response
Off Study	Transformed DLBCL (from CLL)	62/F	5 prior lines with PD as best response, including:	• R-CHOP • rituximab-abbs, gemcitabine, and CDDP • rituximab-abbs, gemcitabine, carboplatin • polatuzumab + BR x 2 • obinutuzumab - hyper cyclophosphamide and dexamethasone	sLD	3E7 cells	No	Yes	No	IV	PD
Off study	Transformed high grade B cell tumor (from FL)	66/F	4 prior lines:	• R-CHOP • ibrutinib • bendamustine/rituximab • rituximab	sLD	3E7 cells	No	Yes	No	IV	PR (near CR)
Active	DLBCL	75/M	5 prior lines:	• R-CHOP; IT MTX • liso-cel • liso-cel (reinfusion) • revlimid • tafasitamab-cxix	eLD	3E7 cells	Yes	Yes	No	IV	CR
Active	MCL	62/M	5 prior lines:	• bendamustine/rituximab • zanubrutinib • bendamustine/obinutuzumab • bendamustine/rituximab • rituximab/gemcitabine/dex/carboplatin	eLD	1E8 cells	No	Yes	No	IV	CR

ORR = 3/4 patients (75%)   CR = 2/4 patients (50%)

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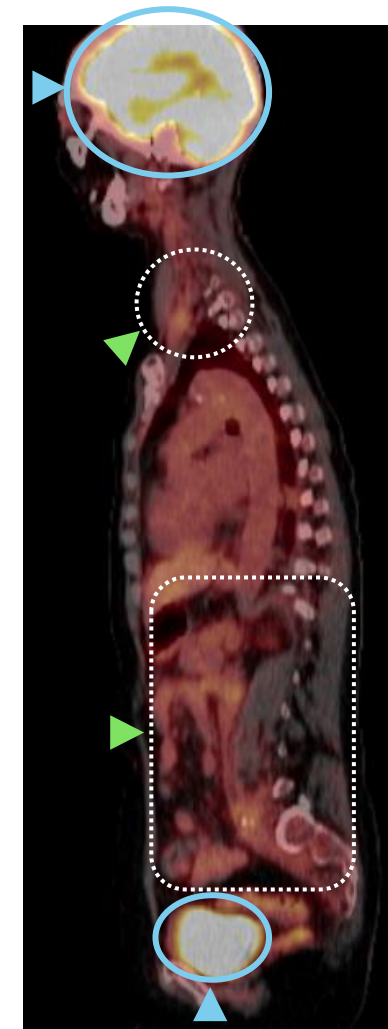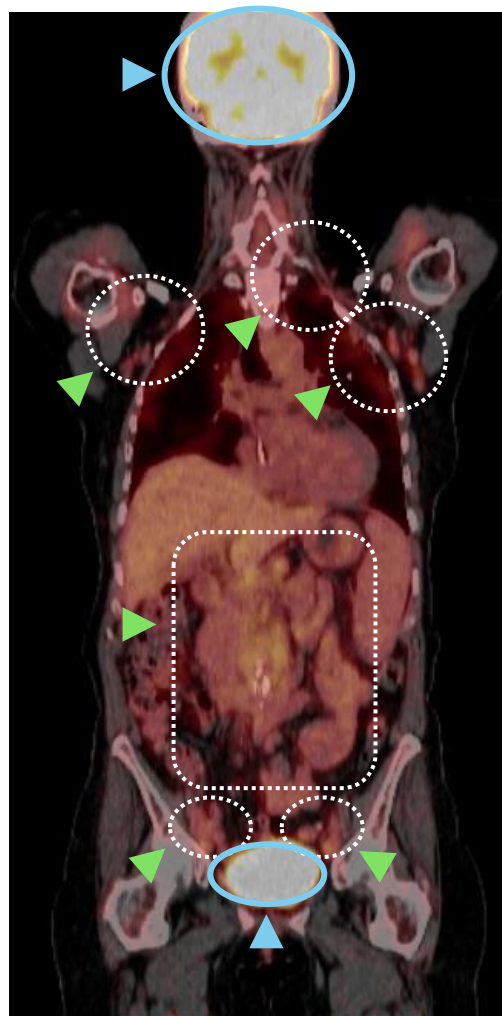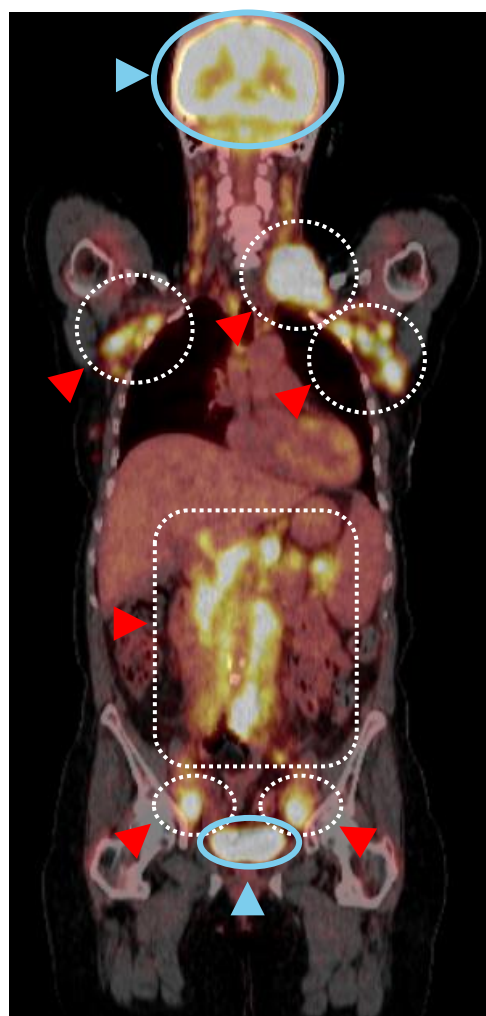
ADI-001 FIH Study: Dose Level 1 (30M Cells) Near Complete Response

- 66 yo female
- Transformed high grade B cell tumor (from FL)
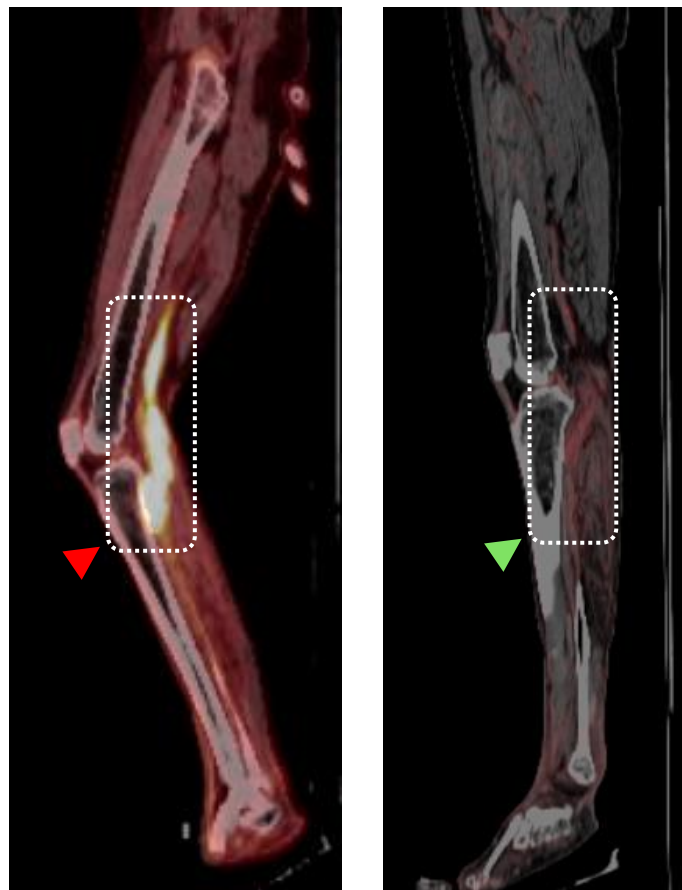- 4 prior lines
- ADI-001 dose: 3E7 CAR+ cells

Baseline: 12-Aug-2021
D28: 29-Sep-2021

▶ *FDG uptake by normal tissues

▶ Baseline FDG uptake by tumor lesions

▶ Sites of tumor response

Baseline

D28

Baseline

D28

*FDG = fluorodeoxyglucose   Note: Response was assessed as PR per Lugano 2014

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- 75 yo male
- Diffuse Large B-Cell Lymphoma
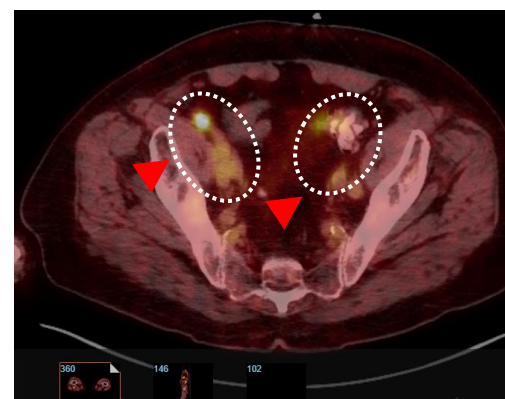- 5 prior lines, including anti-CD19 CAR T
- ADI-001 dose: 3E7 CAR+ cells
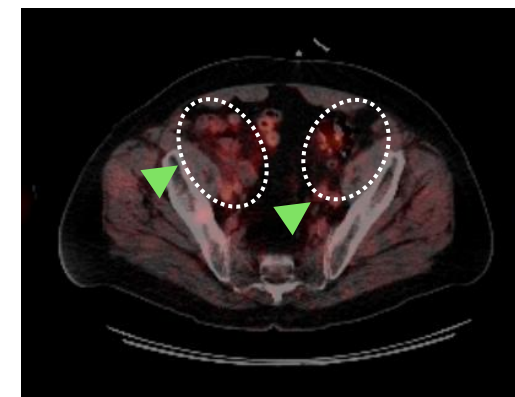
Baseline: 8-Sep-2021
D28: 29-Sep-2021

▶ Baseline FDG uptake by tumor lesions

▶ Sites of tumor response

Sagittal view of the right leg

Baseline

D28
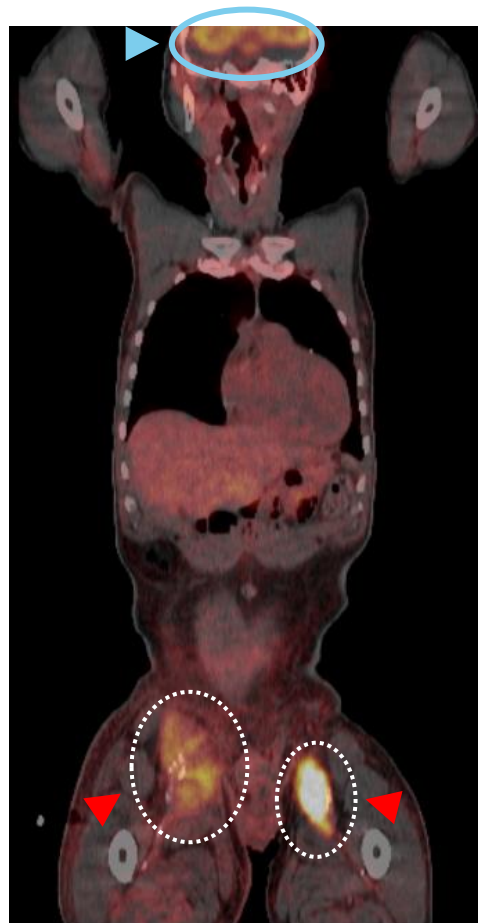
Transverse view of the pelvis

Baseline

D28

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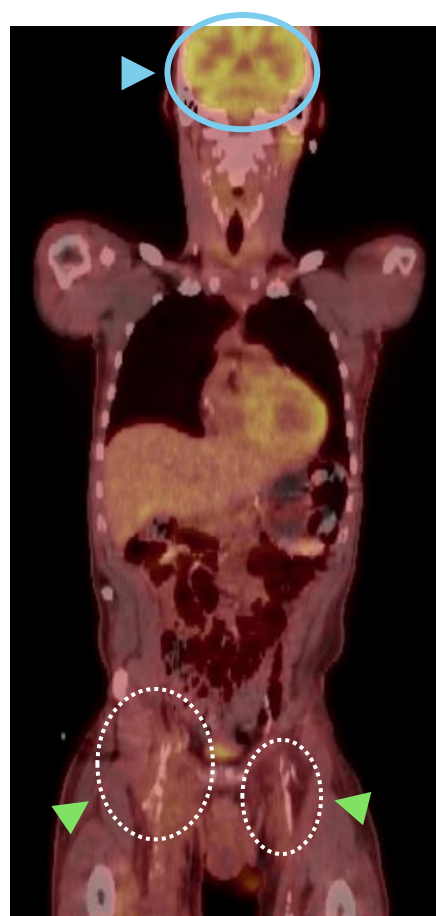# ADI-001 FIH Study: Dose Level 2 (100M Cells) Complete Response

- 62 yo male
- Mantle Cell Lymphoma
- 5 prior lines
- ADI-001 dose: 1E8 CAR+ cells

Baseline: 8-Oct-2021
D28: 19-Nov-2021

▶ FDG uptake by normal tissues

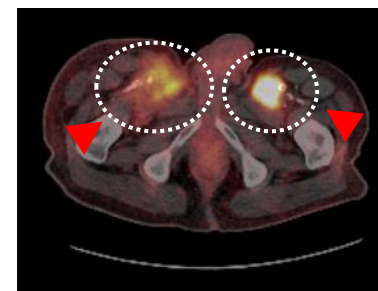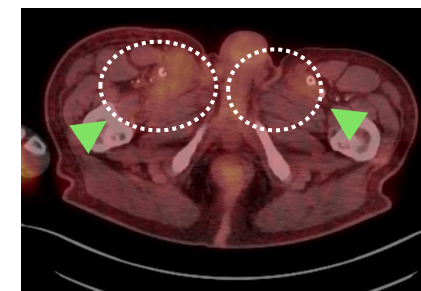▶ Baseline FDG uptake by tumor lesions

▶ Sites of tumor response

Baseline

D28

Transverse view

Baseline

D28

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ADI-001 FIH Study: *In Vivo* Expansion and Pharmacodynamic Biomarkers Consistent with ADI-001 Activation Was Observed

- Consistent increase in IL-15 during 28-day window following lymphodepletion, potentially providing additional cytokine support for the proliferation of ADI-001

- Detection of circulating ADI-001 in the blood by flow cytometry and qPCR indicates expansion of ADI-001 in patients

- Cytokine production, primarily IL-2 and IL-8, observed during the first 14 days from ADI-001 dosing, consistent with observed time-to-peak for similar cytokines for autologous alpha-beta T cells and consistent with activation profile for ADI-001

- No meaningful increase in IL-6, except for one patient during COVID-19 infection, suggesting potentially reduced likelihood for high grade CRS and ICANS

> Preliminary data provide evidence of ADI-001 cell proliferation, *in vivo* expansion, target engagement, and anti-tumor activity

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ADI-001 FIH Study: Summary

- ADI-001 administration was generally well tolerated in the initial part of the dose escalation; in patients treated to date there were no GvHD, neurotoxicity, or high-grade CRS reported

- Of the four efficacy-evaluable patients, one achieved a near complete response and two achieved a complete response (ORR = 75%, CR = 50%)

- Complete and near-complete responses observed starting at ADI-001's lowest dose level (30M CAR+ cells), including a CR in a CAR T relapsed patient

- Preliminary data provide evidence of ADI-001 cell proliferation, *in vivo* expansion, target engagement, and anti-tumor activity

- Next data update expected in H1 2022

- Potential expansion cohorts in patients relapsing after autologous CD19 CAR T and in NHL subtypes (DLBCL, MCL, FL)

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Opportunities Offered by Gamma Delta T Cell therapy
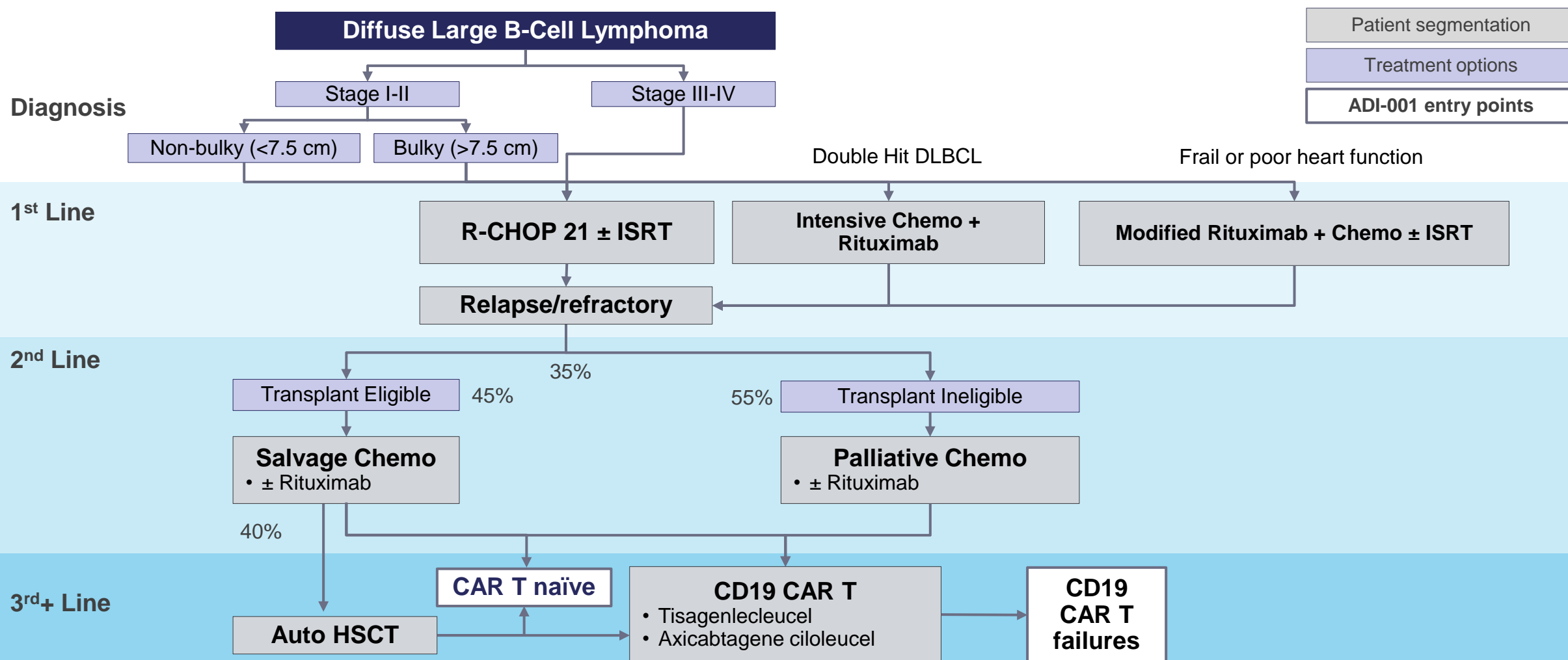
Sattva Neelapu, M.D.,
MD Anderson Cancer Center

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Rationale for Allogeneic γδ CAR T-Cell Therapy

- Potential to benefit from CAR, adaptive and innate anti-tumor immune response

- Potential for reasonable safety profile

  - Long-term risk of mutagenesis unlikely given no requirement for gene editing

  - Potentially lower risk for CRS and ICANS

  - Long-term B-cell aplasia and hypogammaglobulinemia unlikely

- Potential to improve efficacy as T-cell fitness is expected to be better than autologous products

- Consistent product quality while eliminating wait period for patients (off-the-shelf alternative)

- Potential to lower the cost of CAR T cell therapy

- Possibly wider access at non-transplant centers

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ADI-001: Preliminary Clinical Experience

- High response rate at low dose was measured in patients with bulky disease, including one with prior CAR-T therapy

- Early data seems promising with 75% ORR and 50% CR rate for the first four evaluable patients

- Safety profile seems favorable, no GvHD, no ICANS, and no high-grade CRS reported to date

- Biology of γδ CAR T cells and initial data from first four evaluable patients may support favorable durability:

  – Complementary innate, adaptive, and CAR-T mediated antitumor effects

  – Combination of multiple mechanisms may improve durability and minimize emergence of tumor resistance

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DLBCL Detailed Treatment Algorithm

CHBC Primary Research, NCCN, UpToDate, Medscape, SEER, HRSA Transplant Data, CA Cancer J Clin. 2016 Sep 12, Blood. 1997 Jun 1;89(11):3909-18.

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MCL Treatment Algorithm

Diagnosis

Newly Diagnosed Mantle Cell Lymphoma

Stage I or non-bulky Stage II

Stage II bulky or Stage III-IV

| Patient segmentation |
| Treatment options |
| ADI-001 entry points |

1st Line

Induction Chemoimmunotherapy

Transplant Ineligible

Transplant Eligible

80% **Maintenance Rituximab**

Auto HSCT 20%

2nd + Line

Chemotherapy ± Rituximab

CD19 CAR T

CD19 CAR T failures

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Wrap Up

Chen Schor, President and CEO

Adicet Bio: Leaders in Engineered γδ CAR T Cell Therapy

- First and only off-the-shelf γδ CAR T cell investigational therapy to report clinical data

- Complete and near-complete responses observed starting at ADI-001's lowest dose level, including a CR in a CAR T relapsed patient

- Favorable safety profile to-date with ADI-001

- Evidence of *in vivo* expansion and circulating pharmacodynamic biomarkers consistent with ADI-001 activation

- Adicet allogeneic γδ CAR T cell investigational therapy may offer:

  – CAR, innate and adaptive mediated anti-tumor activity; More limited ability for tumor escape

  – No requirement for gene-editing

- $192.2M cash, cash equivalents & marketable securities (09/30/21)

- Multiple near-term milestones, including ADI-001 clinical update in H1 2022

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Building a Broad Pipeline of First in Class γδ CAR T Cell Therapy

Program	Target	Potential Indication	Discovery	Preclinical	IND	Ph 1	Ph 2	Ph 3 / Commercial	Anticipated Milestone
ADI-001	CD20	NH Lymphoma							Additional Clinical Data: **H1'22**
ADI-002	GPC3	HCC							File IND: **Q2'22**
ADI-003	Undisclosed	Solid and Heme							File IND: **2023**
ADI-00x	Undisclosed	Solid / Heme							File IND: **2024**
ADI-00x	Undisclosed	Solid / Heme							File IND: **2025**

HCC: Hepatocellular Carcinoma; NH: Non-Hodgkin's

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Potential Upcoming Milestones

ADI-001

- Phase 1 NHL clinical update H1'22
- Identify RP2D (recommended Ph2 dose)
- Initiation of expansion study in patients relapsing after autologous CD19 CAR T*
- Initiation of expansion studies in NHL subtypes (DLBCL, MCL, FL)*

ADI-002

- File IND for GPC3+ tumors
- Initiation of Phase 1 in HCC, squamous cell carcinoma of the lung, other GPC3+ tumors

Expand γδ CAR T pipeline

- New clinical program every 12-18 months

*Potential pivotal

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Leaders in γδ CAR T Cell Therapy

CAR: Chimeric Antigen Receptors; DNAM-1: DNAX accessory molecule-1; GvHD: Graft Versus Host Disease; HLA: Human Leukocyte Antigen; MHC: Major Histocompatibility Complex; NCR: Natural Cytotoxicity Receptors; NK: Natural Killer; TCR: T Cell Receptor; NKG2D: NK Group 2D