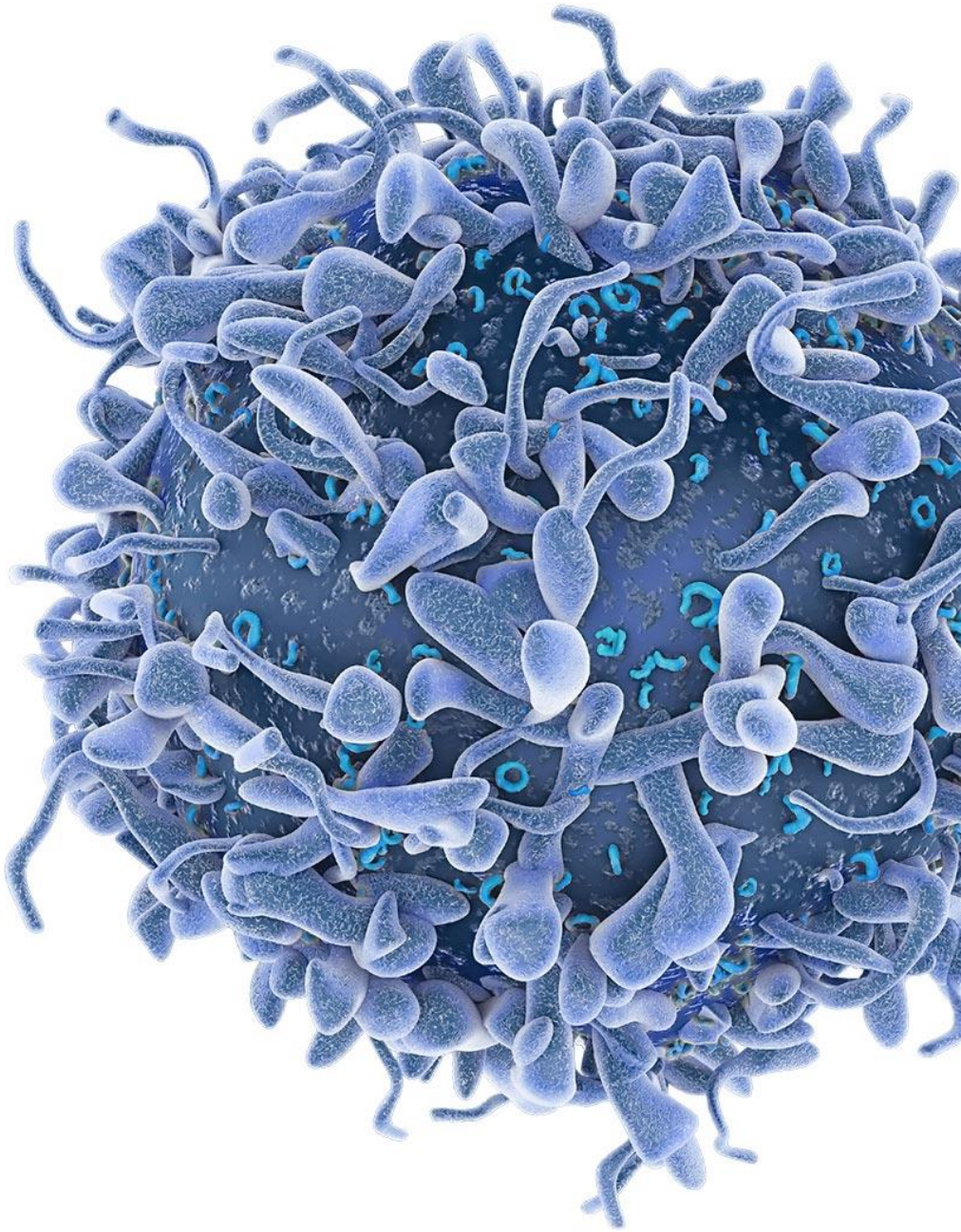
Adicet Bio

# Virtual R&D Event

November 10, 2022



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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 and preclinical programs, including the implementation, timing and success of ADI-001, ADI-925 and the additional preclinical programs in Adicet's pipeline; 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 Phase 1 trial of ADI-001, including ongoing patient enrollment; expectations regarding future regulatory filings for product candidates in the Company's pipeline, including the planned IND submission for ADI-925 in the second half of 2023; timing of a dose selection for the Phase 2 trial by the end of 2022 and initiation of a potentially pivotal program in the first half of 2023, expectations for the in-house manufacturing capabilities in Adicet's Redwood City facility; and Adicet's growth as a company and expectations regarding the advancement of its product candidates and 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 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.

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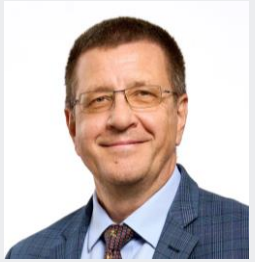
# Agenda

| | |
|---|---|
| **Introduction** | Chen Schor |
| **Preclinical Program Overview** | Blake Aftab, Ph.D. |
| **Perspectives** | Marco Davila, M.D., Ph.D. |
| **Closing Remarks** | Chen Schor |
| **Q&A** | Chen Schor<br>Blake Aftab, Ph.D.<br>Marco Davila, M.D., Ph.D.<br>Francesco Galimi, M.D., Ph.D.<br>Nick Harvey |

Chen Schor
President and CEO

Blake Aftab, Ph.D.
Chief Scientific Officer

Marco Davila, M.D., Ph.D.
Roswell Park Comprehensive Cancer Center



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

Nick Harvey
Chief Financial Officer

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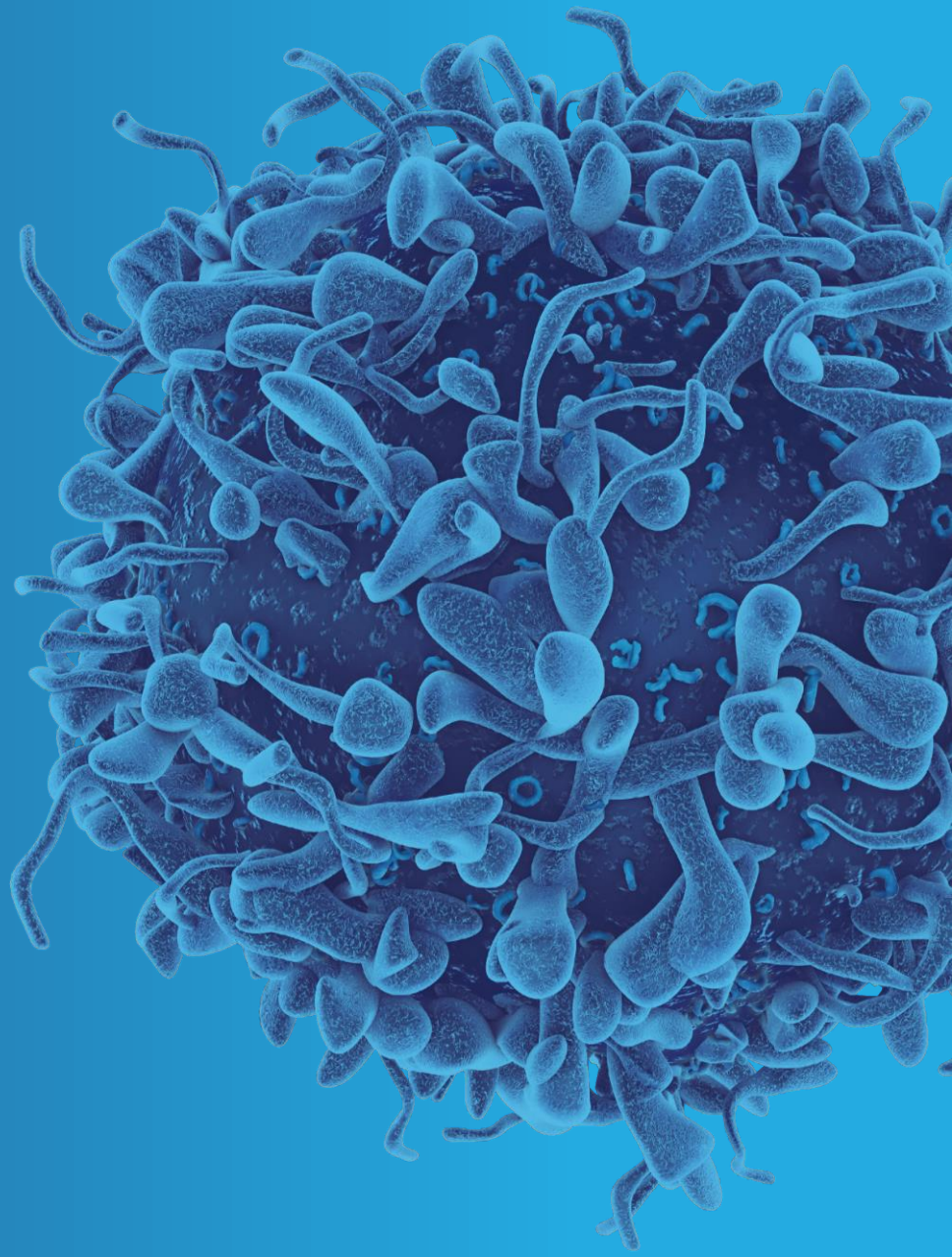
# Leaders in Developing Allogeneic CAR and CAd γδ T Cell Therapies to Fight Cancer



Chen Schor, President and CEO

# Adicet Highlights: Leading The Way With γδ T Cell Therapies To Fight Cancer

## 2015

- Adicet Bio Founded

## 2015 – 2021

- Developed fundamental understanding of γδ T cell biology
- Optimized robust manufacturing process for allogeneic off-the-shelf γδ1 T cell therapy
- Built foundational IP portfolio

## Dec 2021

- 50% CR rate with ADI-001 in aggressive NHL

## June 2022

- 75% CR rate, encouraging preliminary durability, no significant CRS, ICANS or Gr3+ infection rate in aggressive NHL
- Potential for outpatient dosing

## November 2022

- Four new highly differentiated γδ T cell therapy pipeline programs
- Building on years of expertise, IP and know-how in γδ T cell biology

## Now & Future

- ASH clinical update
- Initiate at least one potentially pivotal program in H1/2023
- IND submission for ADI-925 expected in H2/2023

CR: Complete response; CRS: Cytokine release syndrome; γδ: Gamma delta; Gr3: Grade three; ICANS: Immune effector cell-associated neurotoxicity syndrome; IP: Intellectual property; NHL: Non-Hodgkin's lymphoma

# Adicet CAR γδ T Cell Platform Potential Advantages: Engineered to Address Activity, Tumor Homing, Safety, and COGs Limitations

| | | CAR γδ T Cells | Key Supporting Data |
|---|---|---|---|
| Activity* | Innate anti-tumor response | ✓ | **PRE-CLINICAL:**<br>1) Nishimoto et. al. Clinical & Translational Immunology 2022; Makkouk et. al. JITC 2021; Azameera et. al. ISCT 2022<br>2) Single dose protects from repeat tumor challenge (Romero et al. ASGCT 2019)<br>3) Gamma delta 1 CAR T cells expansion capacity is better than CAR NK cells and comparable or better then alpha-beta CAR T cells (Nishimoto et al)<br>4) Predominantly activating receptors (Nishimoto, Makkouk, and Azameera et. al. publications)<br>**CLINICAL:**<br>1) CRs demonstrated with ADI001 starting at 30M CAR+ cells (flat dose) in bulky tumors > 6,000 mm (ASCO 2022 presentation)<br>2) Active dose of ADI-001 ~ 1% of NK total dose per lympho-depletion cycle (ASCO 2022 presentation)<br>3) Gentles et. Al. Nat Med. 2015 |
| | Adaptive anti-tumor response | ✓ | |
| | Active tumor homing | ✓ | |
| | Predominantly activating receptor expression | ✓ | |
| | Preclinical persistence by repeat tumor challenge | ✓ | |
| | Prognostic value of tumor infiltration | ✓ | |
| Safety* | Low GvHD risk | ✓ | **CLINICAL:**<br>No GvHD and no ≥ grade 3 GvHD cases with ADI-001 (ASCO 2022) |
| | Low risk of cytokine release syndrome ≥ grade 3 risk | ✓ | |
| COGS | No gene editing required (may affect efficacy) | ✓ | **PRE-CLINICAL:**<br>(1) No gene editing with ADI-001<br>(2) Manufacturing for pivotal and commercial with CRO |
| | Scalable manufacturing | ✓ | |



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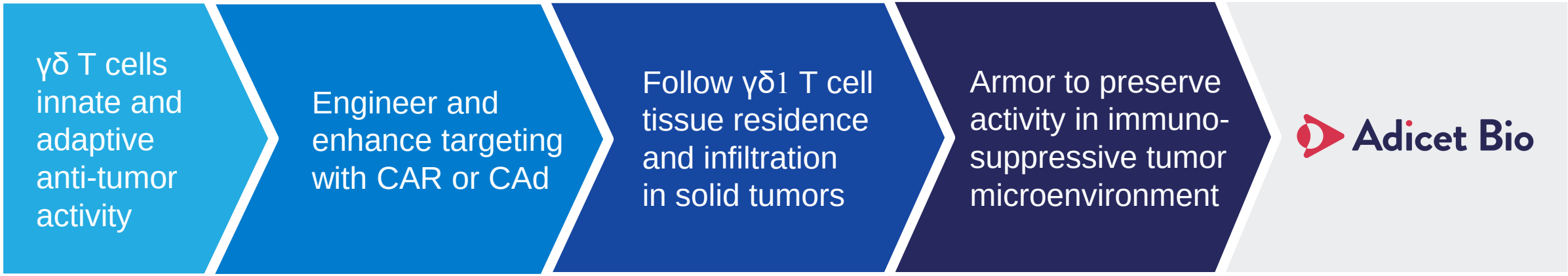
# Adicet's Pipeline Strategy

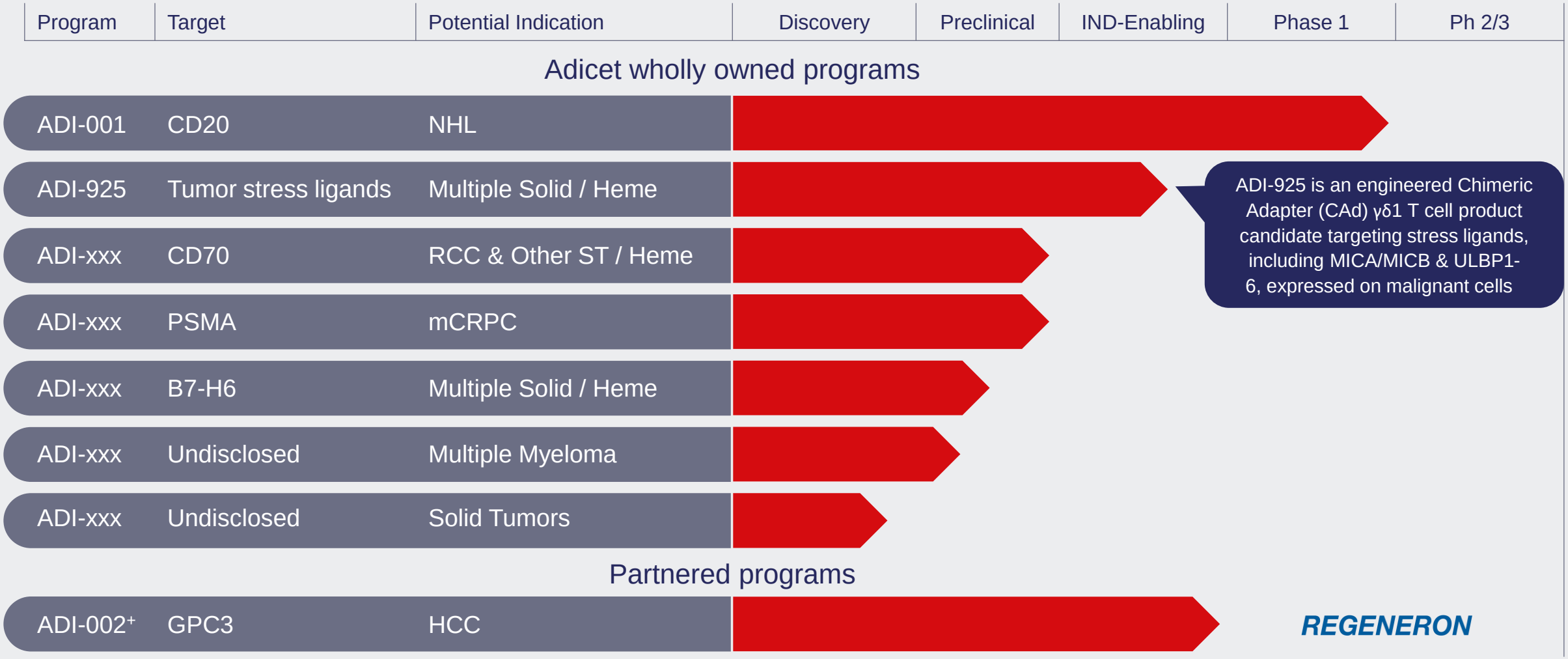
- Unmet medical need
- Current standard of care
- Competitive landscape




1) Hematologic malignancies where Adicet established clinical POC, or
2) Indications where infiltrating γδ T cells correlated with OS, or
3) Indications where donor lymphocyte infusions, enriched with γδ T cells, have shown clinical benefit

- Opportunity for highly differentiated clinical benefits

# Building a Broad Pipeline of First-in-Class CAR and CAd γδ T Cell Product Candidates




+ Regeneron exercised its option to license the exclusive worldwide rights to ADI-002
HCC: Hepatocellular carcinoma; mCRPC: Metastatic castration-resistant prostate cancer; MICA/MICB: Major histocompatibility complex (MHC) Class I chain-related protein A/B; NHL: Non-Hodgkin's lymphoma; PSMA: Prostate-specific membrane antigen; RCC: Renal cell carcinoma; ST: Solid tumor; ULBP: UL16 binding protein



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# ADI-925: First-in-Class Enhanced γδ 1 T Cell Product Candidate for Multiple Heme and Solid Tumors

**We engineered our γδ 1 T cells to significantly enhance their intrinsic innate and adaptive anti-tumor activity by rewiring signaling pathways in the cell**

**This means that one cell therapy product may demonstrate anti-tumor activity in multiple hematologic malignancies and solid tumors without a CAR.**

ADI-925 may provide these benefits to cancer patients

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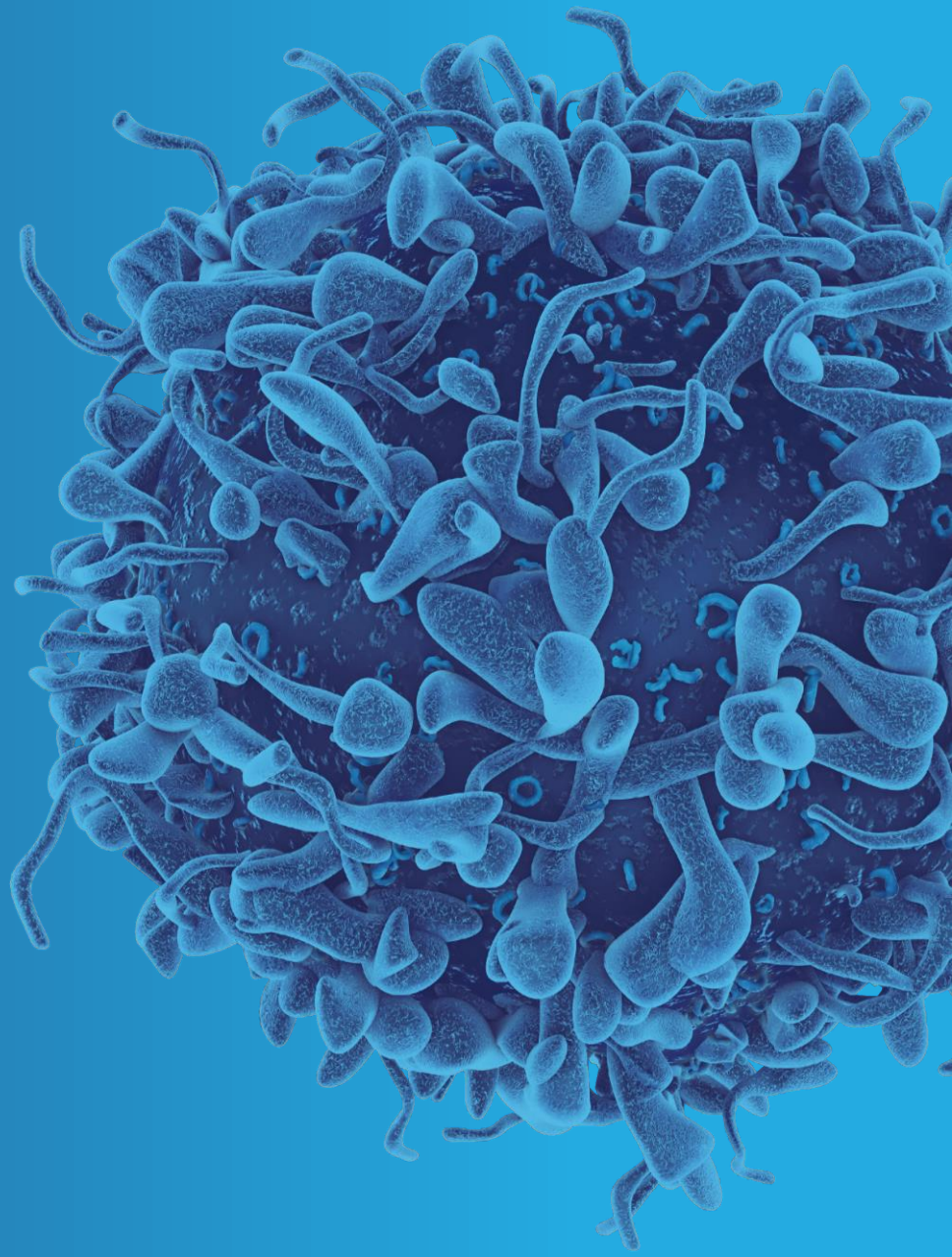
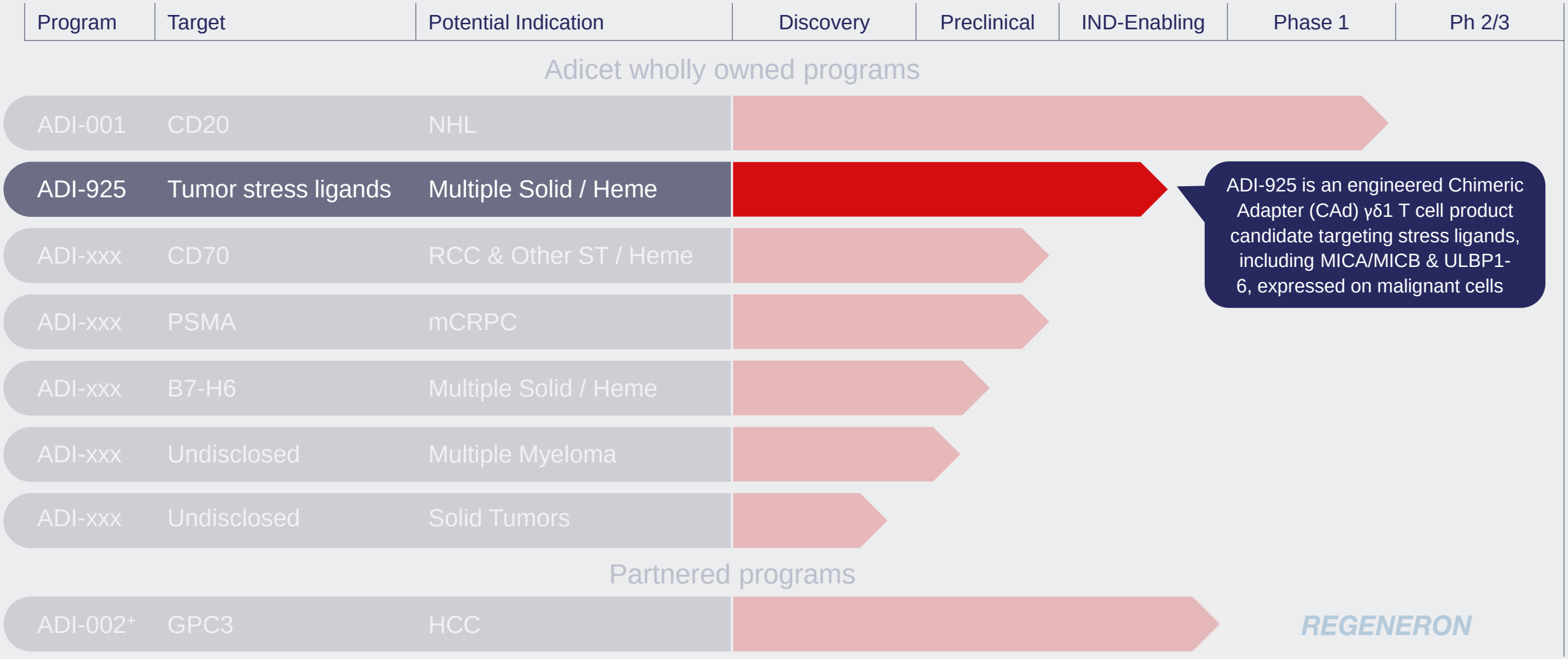
# Preclinical Pipeline Overview

Blake Aftab, Ph.D.
Chief Scientific Officer



# Building a Broad Pipeline of First-in-Class CAR and CAd γδ T Cell Product Candidates



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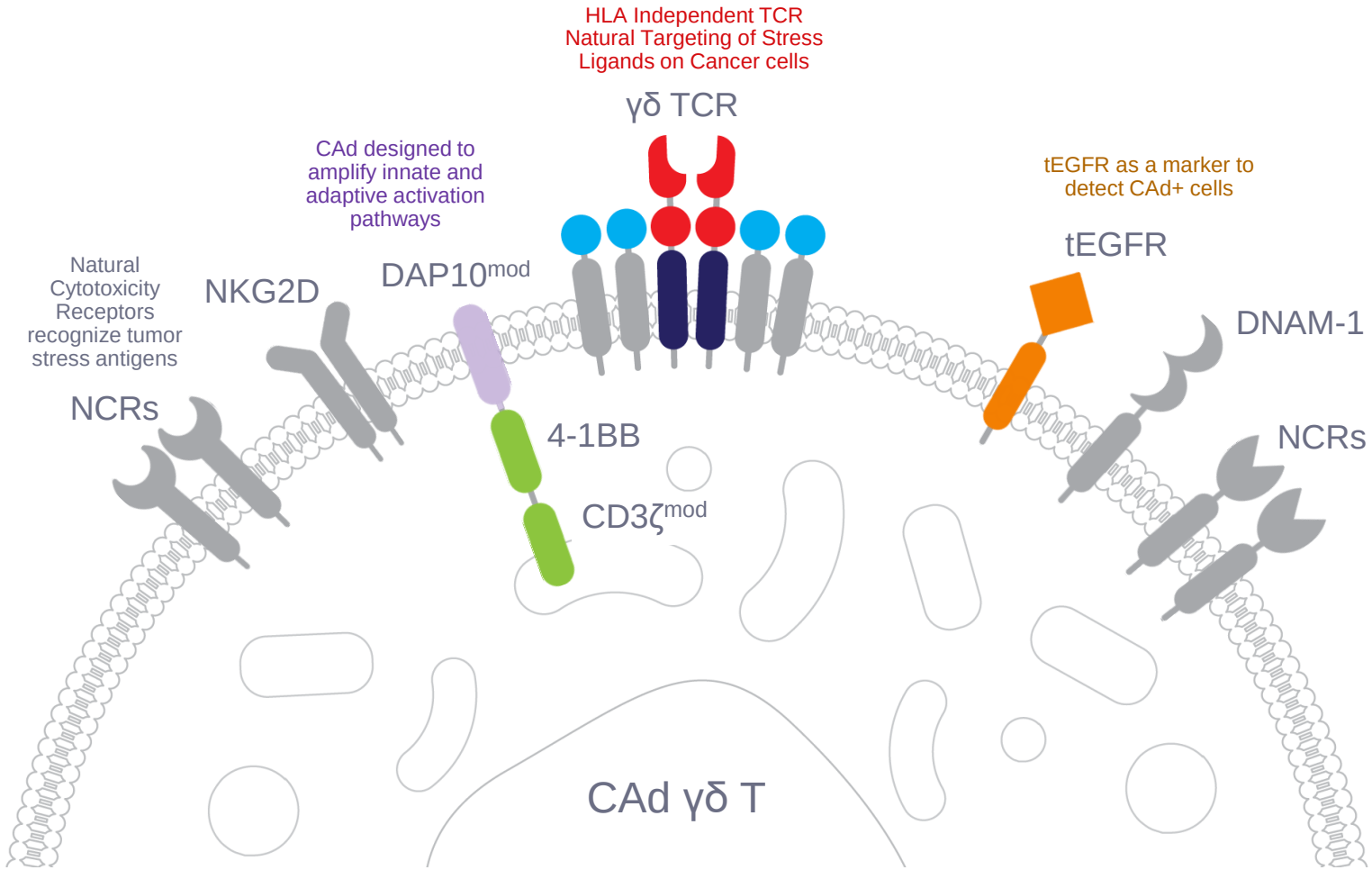
# ADI-925: Engineered γδ1 Chimeric Adaptor T Cell Product Candidate

- ADI-925 is designed to enhance the innate and adaptive anti-tumor activity of Vδ1 T cell
- ADI-925 is an engineered Chimeric Adapter (CAd) Vδ1 T cell therapy candidate targeting stress ligands, including MICA/MICB & ULBP1-6 expressed on malignant cells
- ADI-925 has demonstrated increased anti-tumor activity at lower concentrations of Vδ1 T cells
- Developed in-house with broad IP on file




DAP10: Hematopoietic cell signal transducer; DNAM: DNAX accessory molecule; MIC: Major histocompatibility complex class I chain-related protein; mod: Modified domain(s); NCR: natural cytotoxicity receptor; NKG2D: Killer cell lectin like Receptor K1; TCR: T cell receptor; tEGFR: Truncated epidermal growth factor receptor



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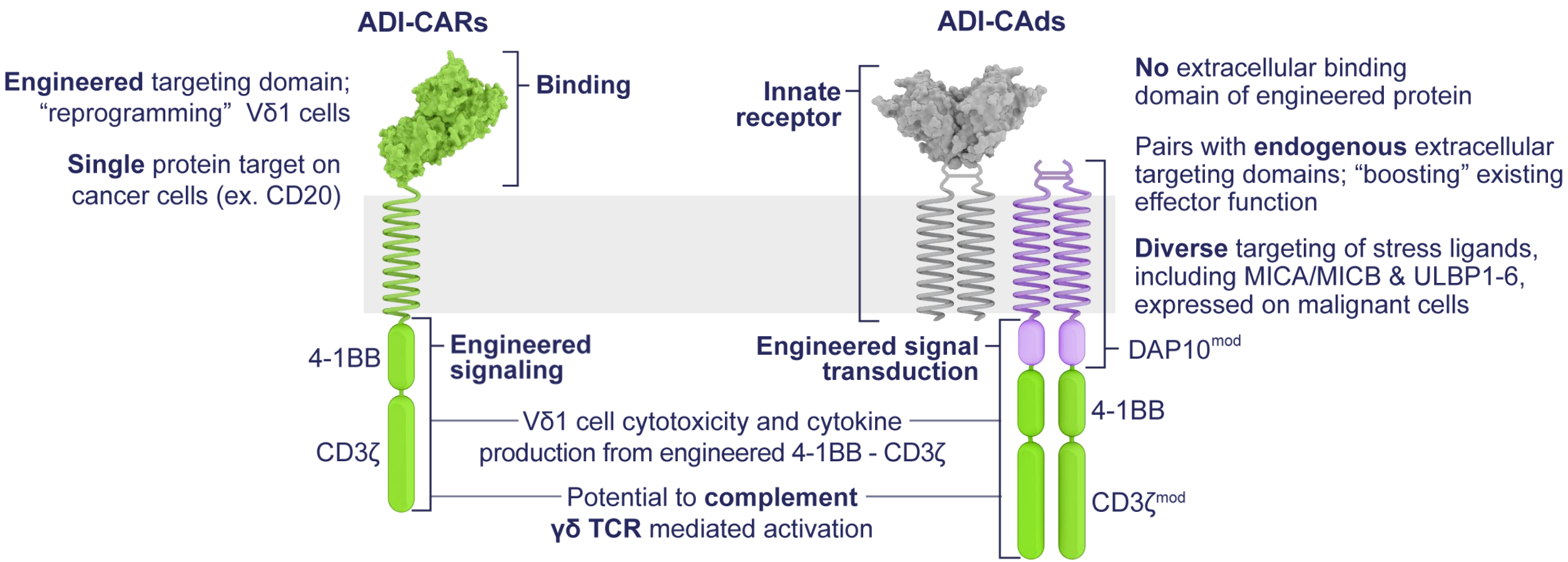
# First-in-class CAd Enhancement of Intrinsic γδ T Cell Activity




ADI: Adicet Bio, ULBP: UL16-binding protein



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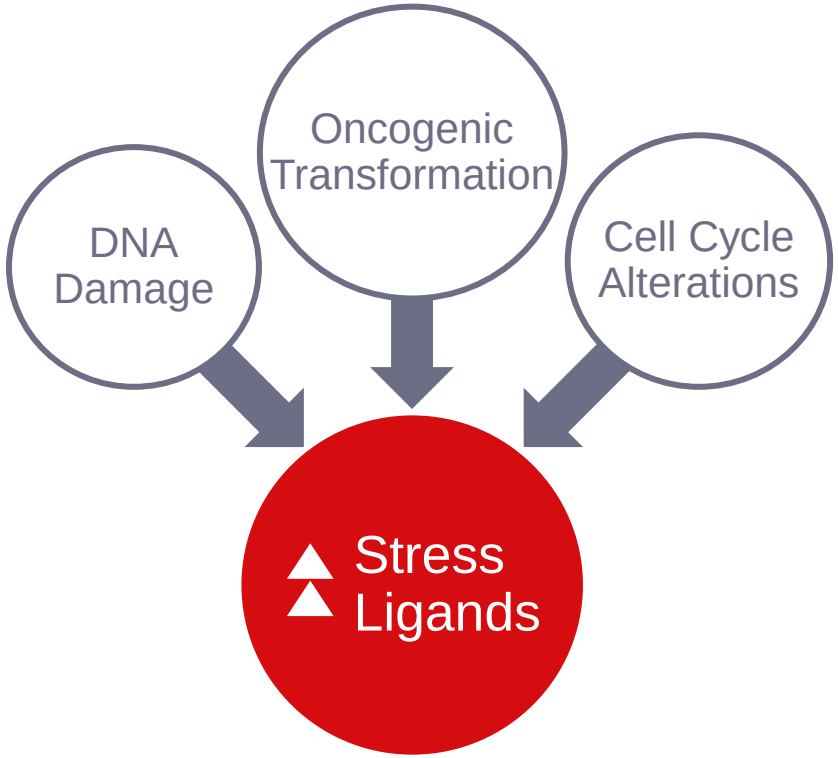
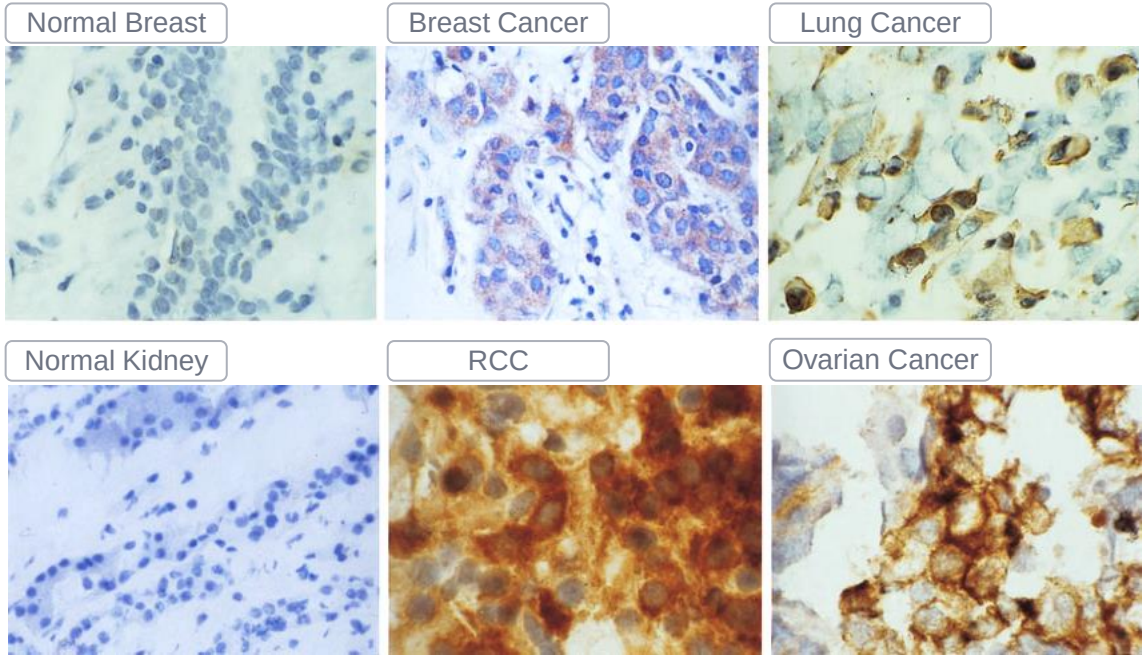
# Tumor Stress Ligands Targeted by ADI-925 Are Ubiquitously Expressed Across a Broad Range of Indications

## Expression of stress ligands across indications is coupled to drivers of tumor formation[1]




## Expression of stress ligands present in broad range of primary tumor specimens

AML, MM, melanoma, MCC, TNBC, HCC, Cervical, NSCLC, RCC, prostate, colorectal, CLL, bladder cancers and others[2,3]




MICA/MICB staining by immunohistochemistry
Expression of ULBP 1, 2, 3, 4, 5, 6 not shown

Groh et al. *PNAS* (1999)



1. Jones et al. *Cancers* (2022)
2. Zhao et al. *Oncotarget* (2017)
3. Groh et al. *PNAS* (1999)

CLL: Chronic lymphocytic leukemia; MM: Multiple myeloma; MCC: Merkel cell carcinoma, TNBC: Triple negative breast cancer, NSCLC: Non-small cell lung cancer, RCC: Renal cell carcinoma

# ADI-925 Targets a Broad Panel of Malignancies

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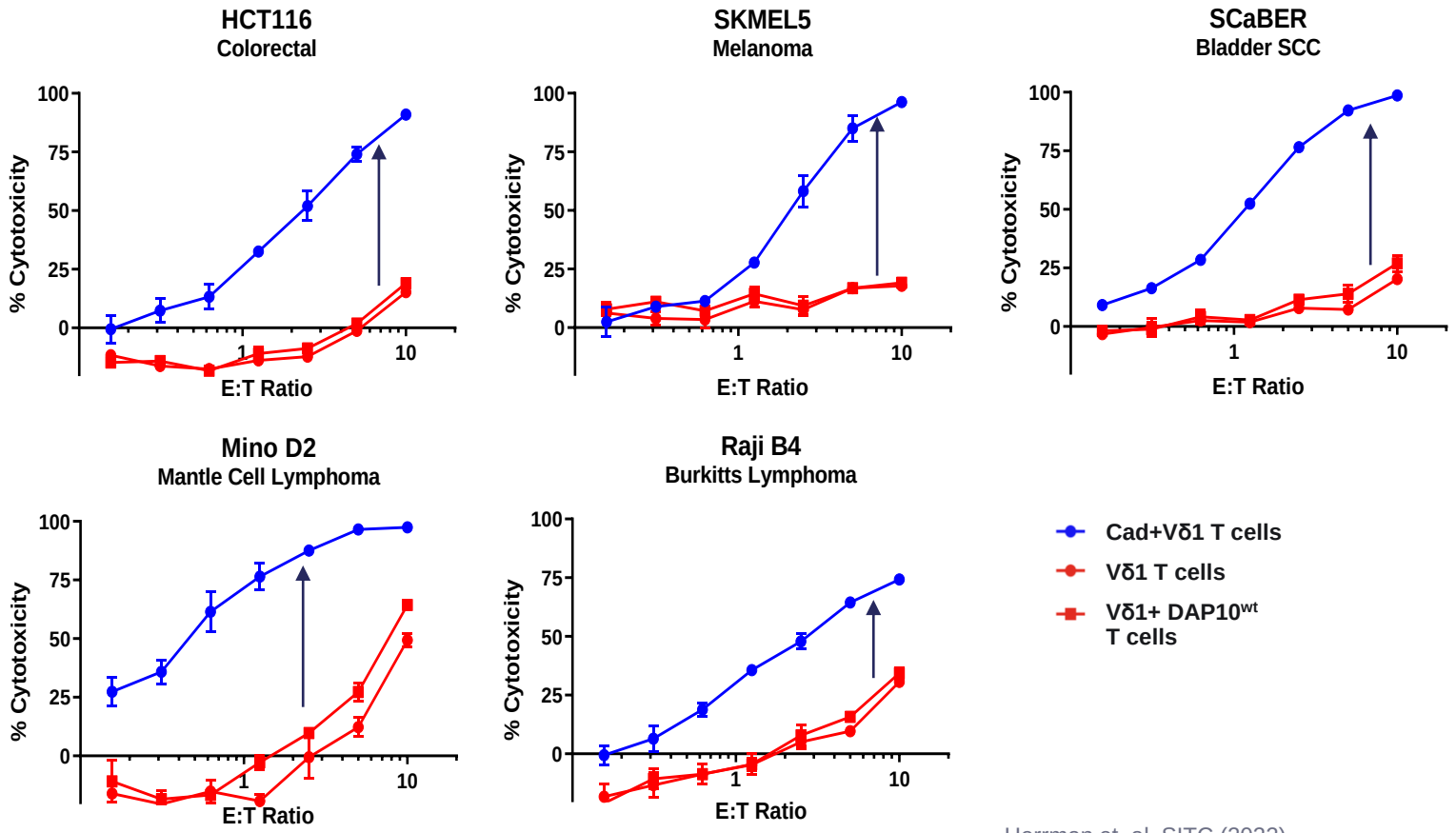
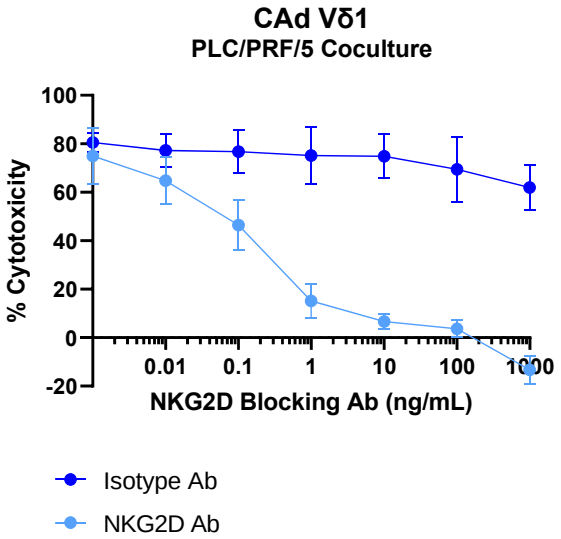
## ADI-925 effectively enhanced cytotoxic potency of γδ T cells in broad panel of cancer cell lines




## Enhancement was primarily driven via endogenous NKG2D




Herrman et. al. SITC (2022)



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# ADI-925 Demonstrated Enhanced Potency of γδ T Cells

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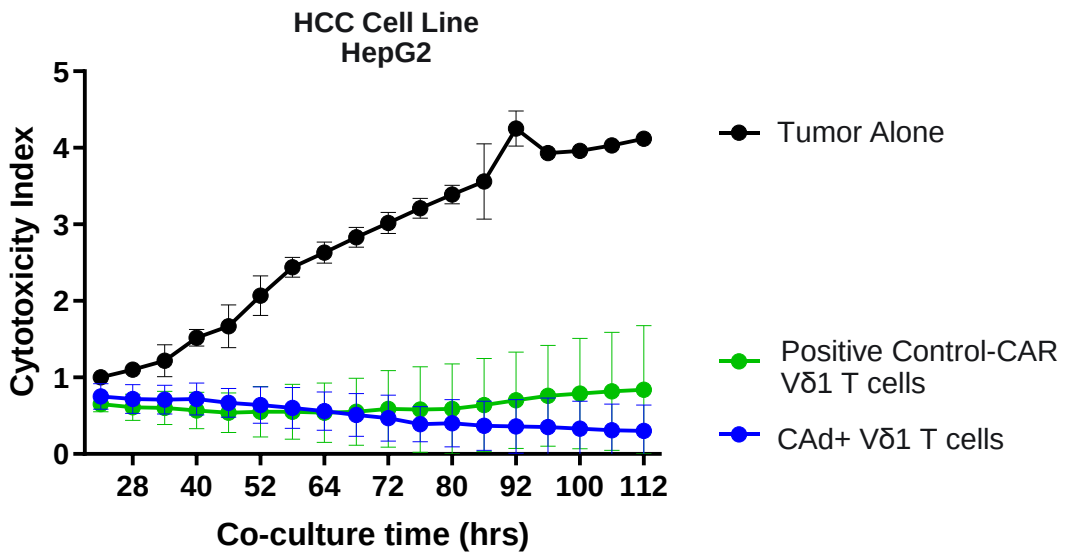
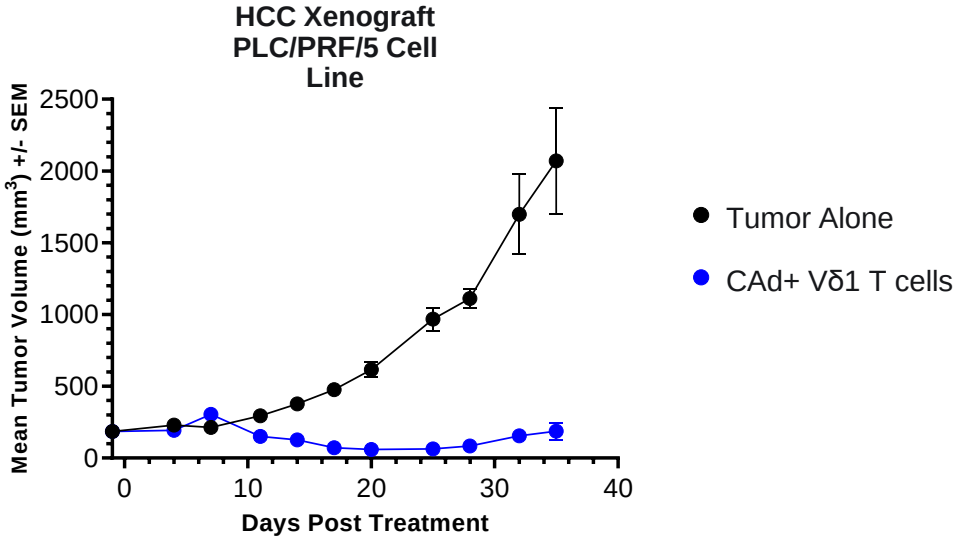
## Potent Killing with CAd Engineered γδ T Cells




## Potent Activity in Solid Tumor Models




Herrman et. al. SITC (2022)



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# ADI-925 Illustrated Preferential Homing and Expansion Within Tumors

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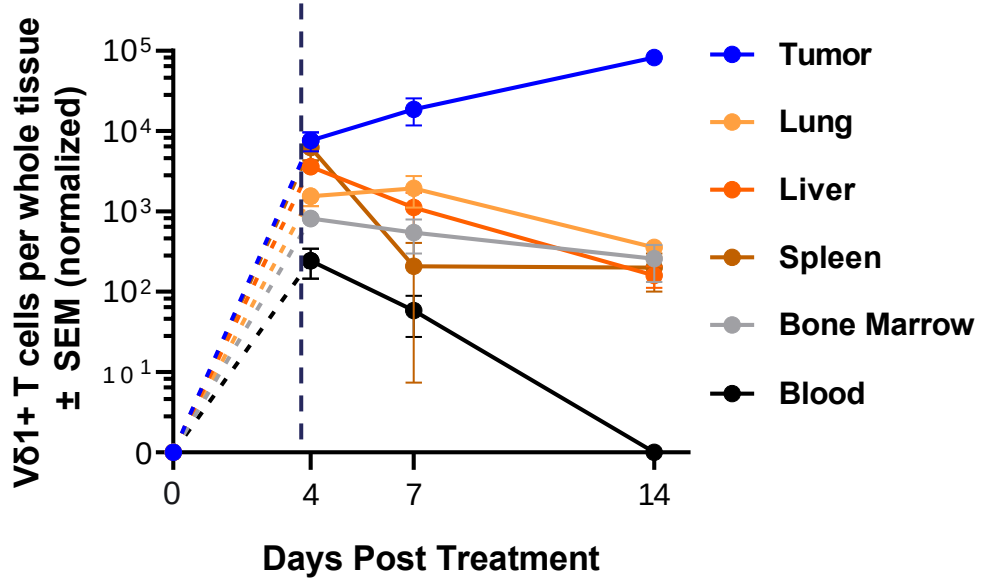
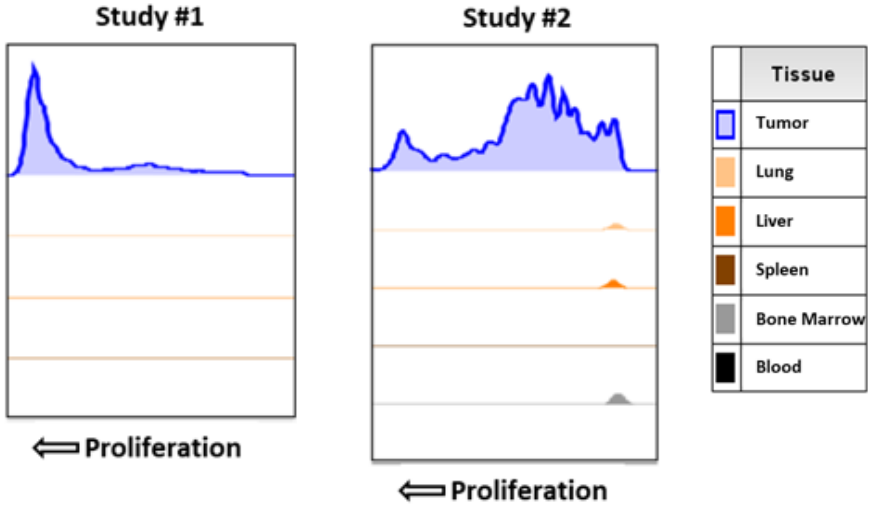
## Hepatocellular Carcinoma Tumor Model

**Homing**
ADI-925 actively homed and biodistributed to relevant tissues

**Expansion**
Tissue residence of ADI-925 and selective expansion within tumor tissues

**Proliferation**
ADI-925 expansion coupled to selective γδ T cell proliferation within tumor tissues




Herrman et. al. SITC (2022)



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# ADI-925: Opportunity For Differentiation

## Target validation

- Presence of γδ **T cells** in tumors **correlates with OS**[3,4,5,6]
- **Many stress antigens** selected by **evolution** to mark malignant cells
- Unmodified allogeneic γδ T cell therapy shows **encouraging clinical signal in AML**[1,2]
- Orthogonal NKG2D CARs have **demonstrated clinical POC**[7]

## Key challenges

- **Potency** of non-engineered cell monotherapy may be limited
- **Lack of approaches** to **enhance intrinsic γδ T cell activity** beyond that of correlation
- Solid tumors may require **engineered effector targeting** coupled to **tumor and tissue specific homing**

## Opportunity for ADI-925 to address broad landscape

- **Enhanced natural cytotoxic effector function**
- Targeting **multiple stress antigens addressing** tumor **heterogeneity**
- Broad, clinically relevant **homing in solid tumors**
- **Prominent cell expansion** capacity within tumor

**IND filing expected H2/2023**



1. NCT03533816; Ph1 update
2. NCT03790072; Ph1 update
3. Gentles et al. *Nat Med* (2015)
4. Arruda et al. *Blood Adv* (2019)
5. Godder et al. *Bone Marrow Trans* (2007)
6. Meraviglia et al. *Oncoimmunology* (2017)
7. NCT04623944; Ph1 update

OS: Overall survival

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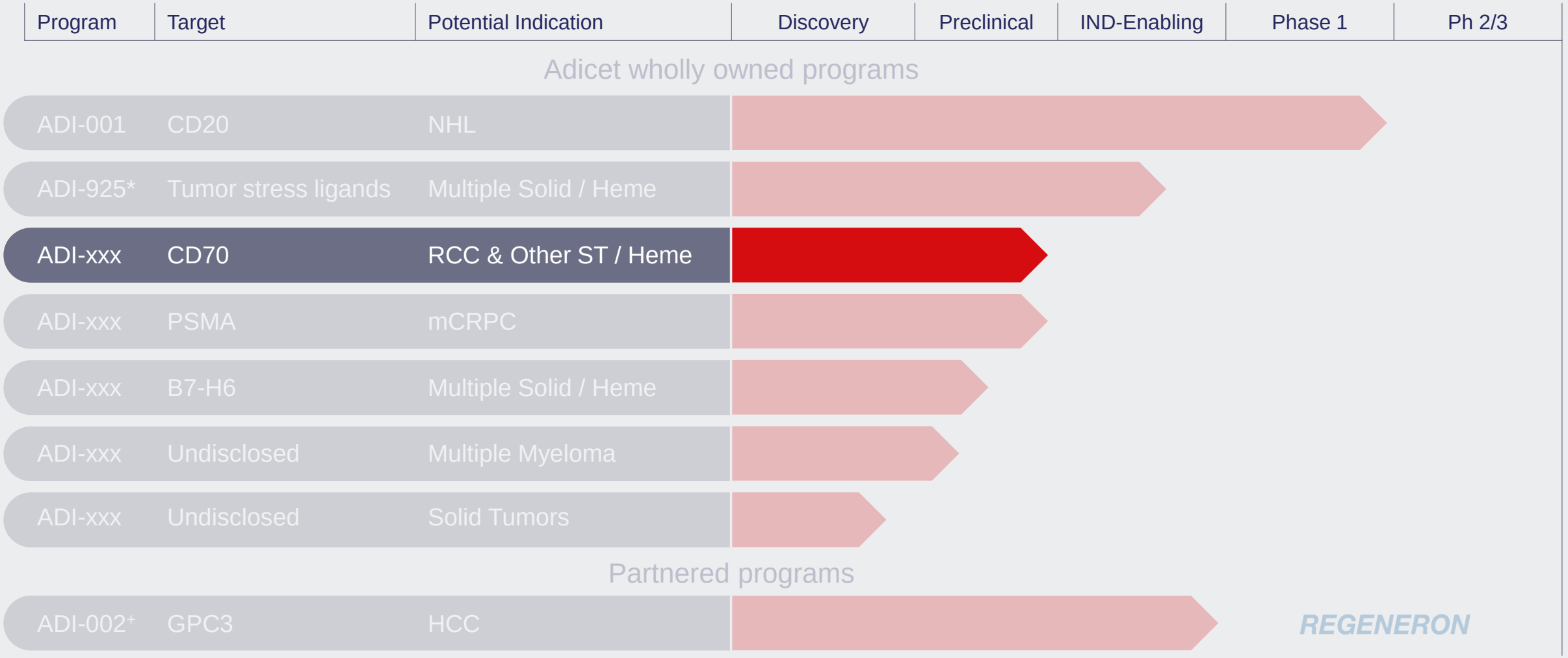
# Building a Broad Pipeline of First-in-Class CAR and CAd γδ T Cell Product Candidates




*ADI-925 is an engineered Chimeric Adapter (CAd) γδ1 T cell product candidate targeting stress ligands, including MICA/MICB & ULBP1-6, expressed on malignant cells



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# Armored CD70 CAR γδ T Cell Opportunity For Differentiation

## Target validation

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

## 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, αβ T-cell therapy)
- **Payload-driven toxicities** with ADCs
- **Immunosuppressive environment of RCC and other solid tumors**

## Opportunity for Adicet and γδ T cells

- **Response to low antigen density** by design with **CD27-based CAR** (compared to scFv-based CAR)[3]
- **Three mechanisms of action** designed to address tumor heterogeneity
- **Homing** of γδ T cells reported in RCC
- **Inclusion of armoring** to address suppressive TME

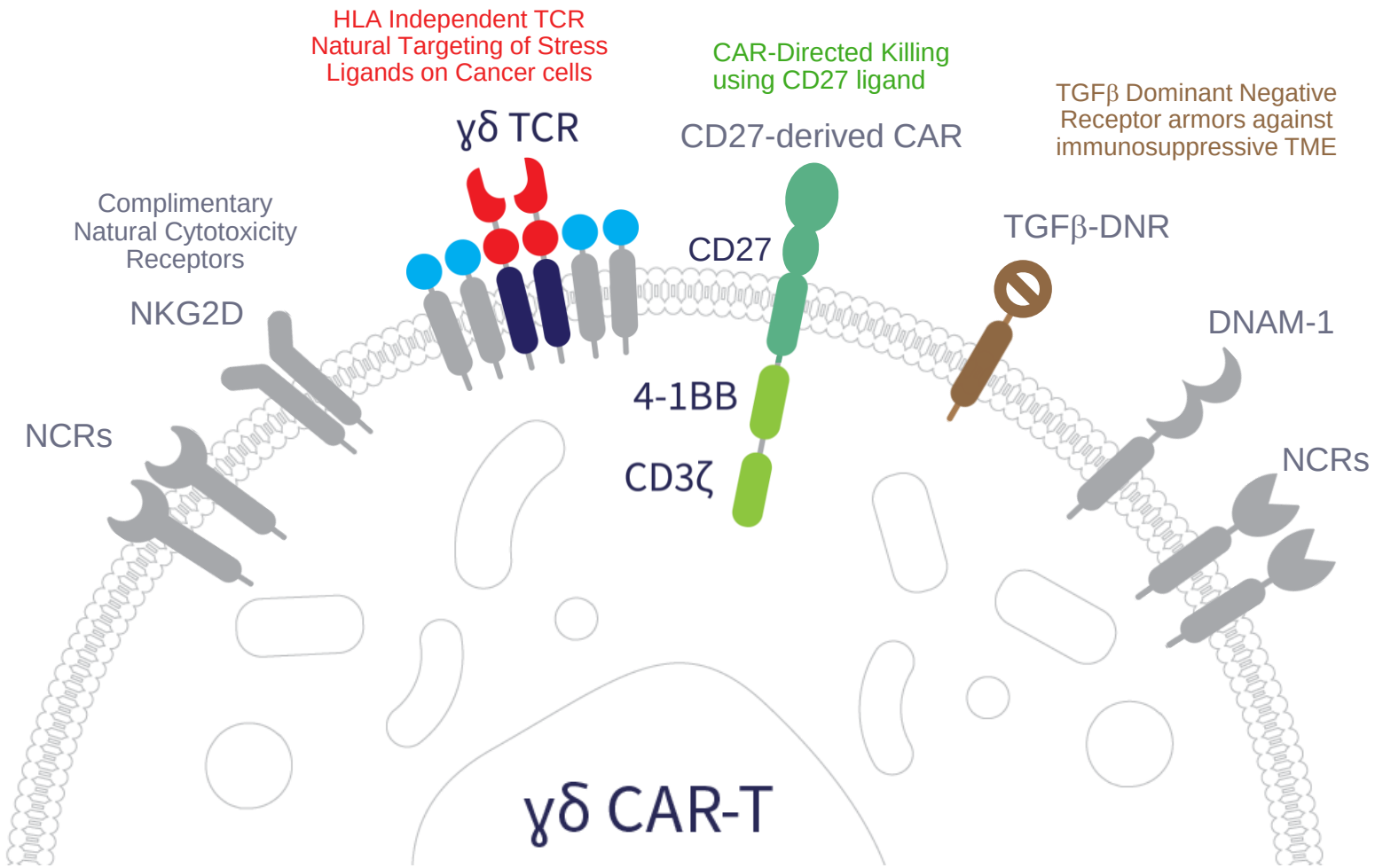


1. Adam et al. *BJC* (2006)
2. Riether et al. *JEM* (2016)
3. Sauer et a. *Blood* (2021)
4. Aftimos et al. *Clin Cancer Res* (2017)
5. Roboz et al. *ASH* (2021)
6. Tanner et al. *Invest New Drugs* (2014)
7. Massard et al. *Cancer Chemother Pharmacol* (2019)
8. CRISPR Therapeutics Presentation (2022)

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

# Adicet's Armored CD70 CAR γδ T Cell

- Targeting CD70 via CD27-ligand has shown superiority to scFv CARs[1]
- Innate and adaptive targeting mechanisms associated with activity in AML and RCC indications
- Armoring via dominant negative receptor; addresses TGFβ in TME[2]
- Lead CAR demonstrated potency and improved serial killing, and resilience against suppressive factors
- Supports functional enhancement illustrated in preclinical models




1. Sauer et al. Blood (2021)
2. Junker et al. *Cytokine* (2000)



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# Armored CD70 CAR γδ T Cells Generated with High Efficiency

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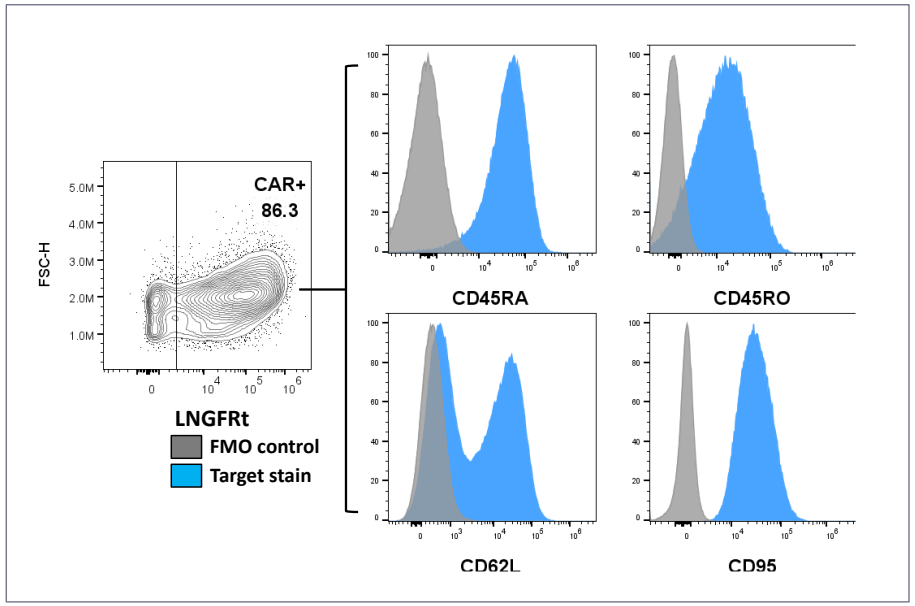
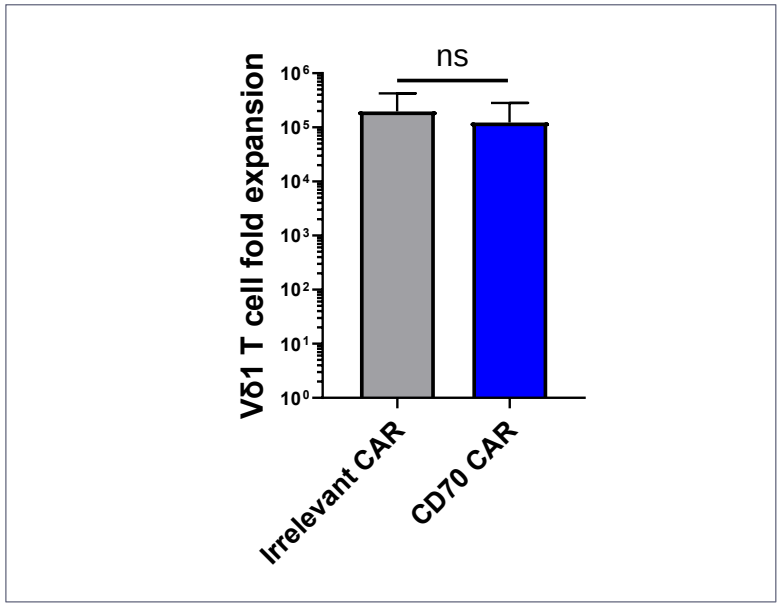
- CD70 CAR γδ T cells produced with high transduction efficiency
- Phenotype similar to that of Adicet's established ADI-001 process[1]
- Production of CD70 CAR γδ T cells does not indicate fratricide

**High Efficiency Production of CD70 CAR with Resulting Phenotype Consistent to ADI-001**




**No Evidence of Fratricide Impeding Manufacture**




Lamture et. al. SITC (2022)



1. Nishimoto et. al. *Clin Trans Immunol* (2022)

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# CD70 CAR γδ T Cells Retained Cytotoxicity Across Range of Target Expression

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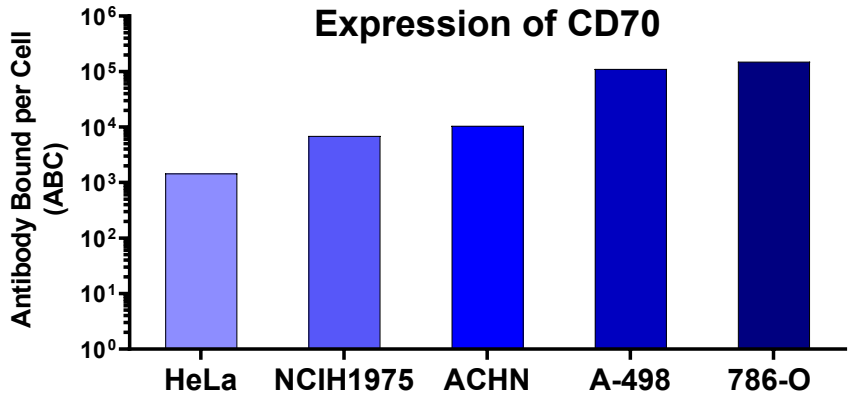
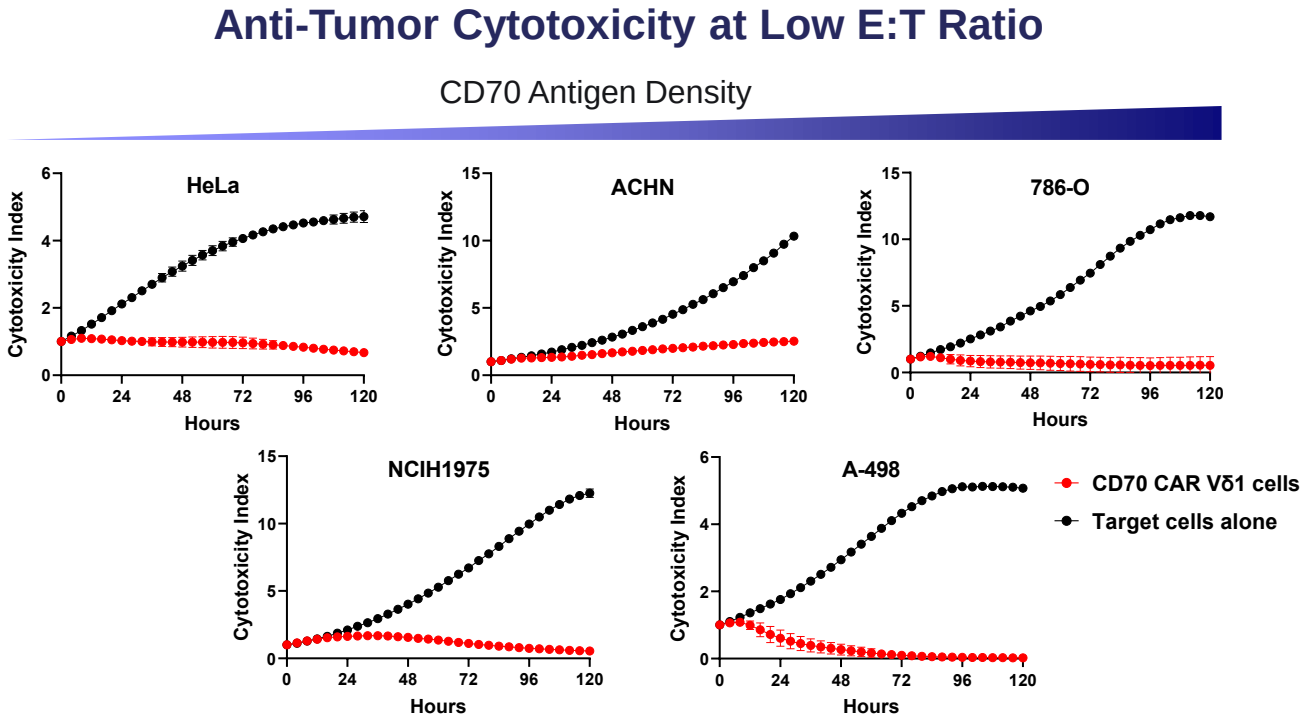
- CD27-derived targeting of CD70 resulted in activation and anti-tumor activity across range of target antigen densities
- Target recognition applicable across range of indications and cell lines
  - Lung Adenocarcinoma, Renal Cell Carcinoma (x3), and Cervical Carcinoma shown




Lamture et. al. SITC (2022)



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# TGFβ Plays a Key Immunosuppressive Factor in TME

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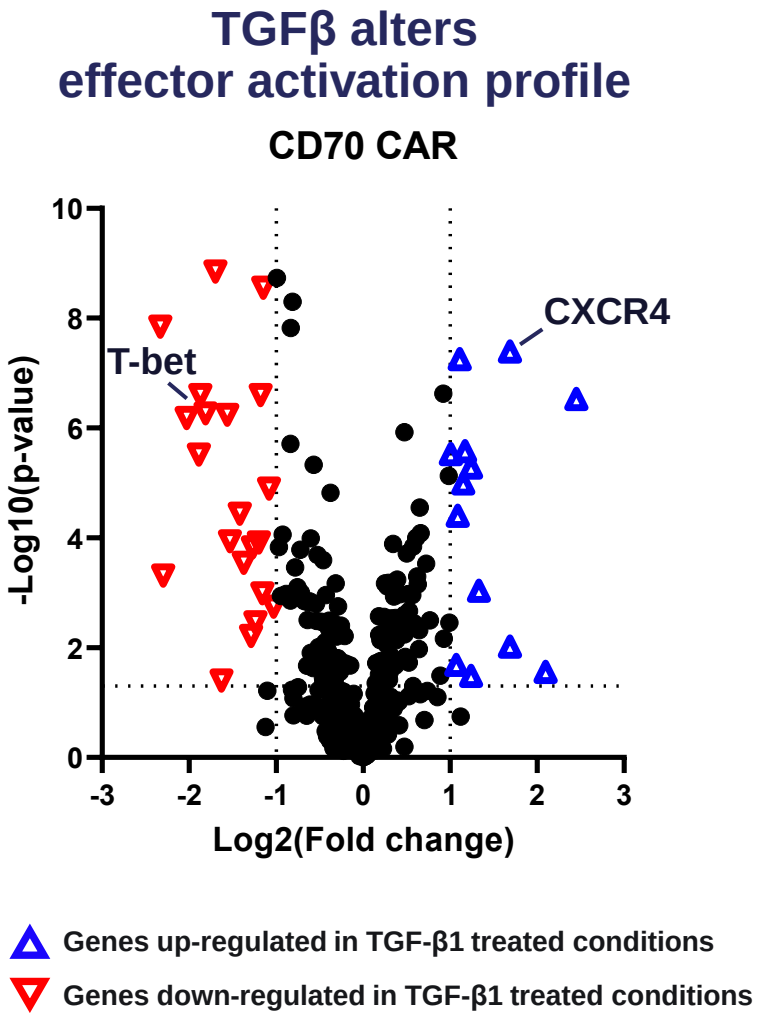


## What is the purpose for armoring cells?

- High levels of TGFβ in tumor microenvironment resulted in differentially downregulated (red) or upregulated (blue) genes
- Alterations propagate immunosuppressive effects[1] and may blunt efficacy of immunotherapies[2] and CAR T[3]
- **Armoring aims to preserve T cell function in the presence of immunosuppressive factors like TGFβ**

Lamture et. al. SITC (2022)



1. Batlle & Massagué. *Immunity* (2019)
2. Silk et al. *Immunology* (2022)
3. Zhang et al. *Front Cell Dev Biol* (2021)

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# Armoring CD70 CAR γδ T Cell Improved Resilience

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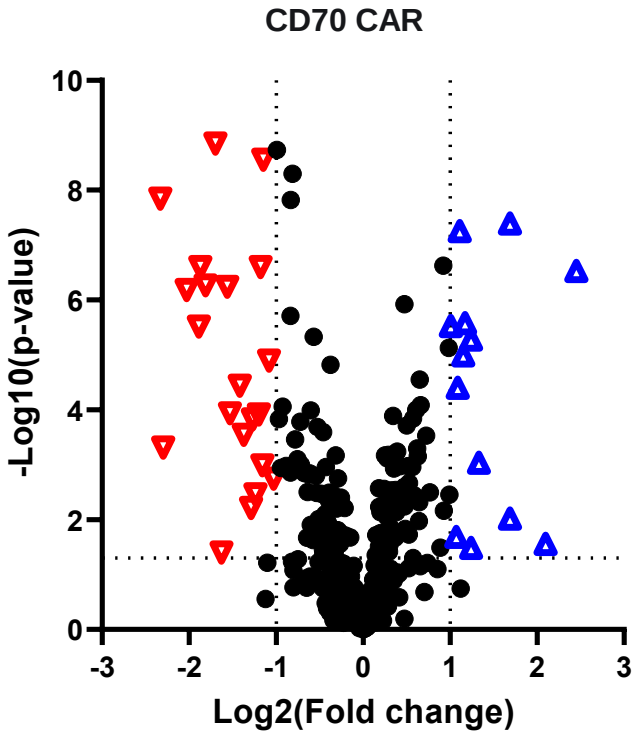
## TGFβ alters effector activation profile




**Add TGFβ-DNR Armor**

Lamture et. al. SITC (2022)



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# Armoring CD70 CAR γδ T Cell Improved Resilience

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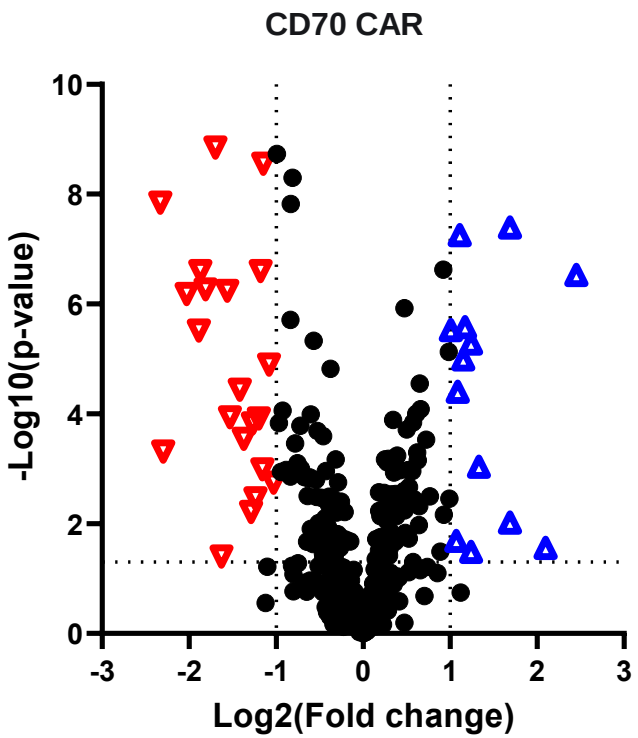
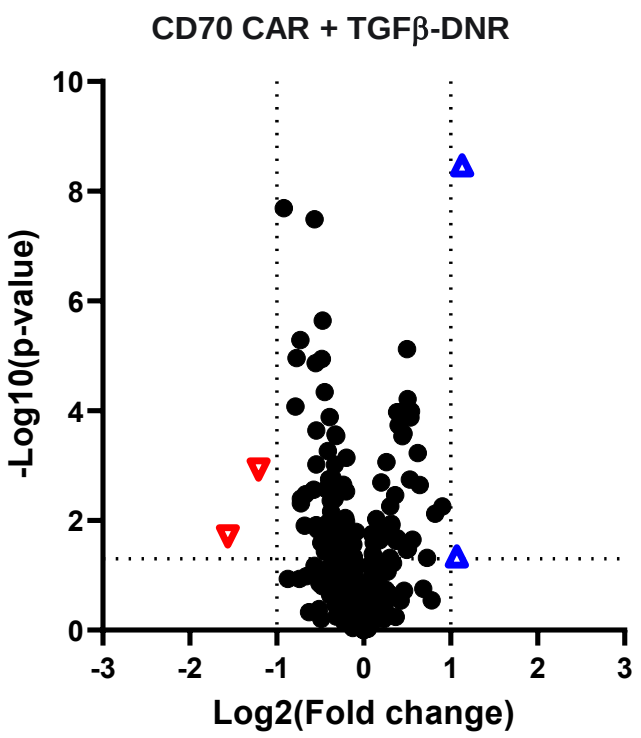
## TGFβ alters effector activation profile




Add TGFβ-DNR Armor

## Resilient activation profile in presence of TGFβ




Lamture et. al. SITC (2022)



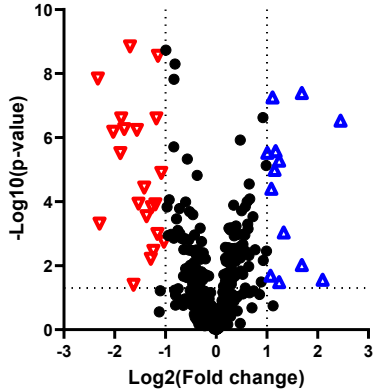
Adicet Bio

# Armoring CD70 CAR γδ T Cell Improved Resilience

PRESENTED AT SITC 2022

**TGFβ alters effector activation profile**

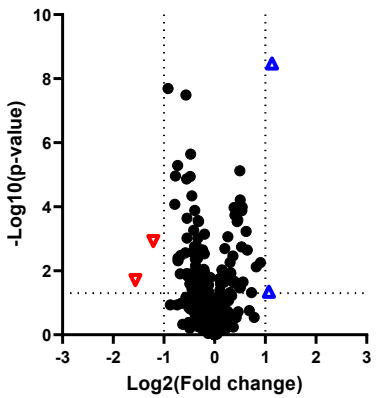
CD70 CAR



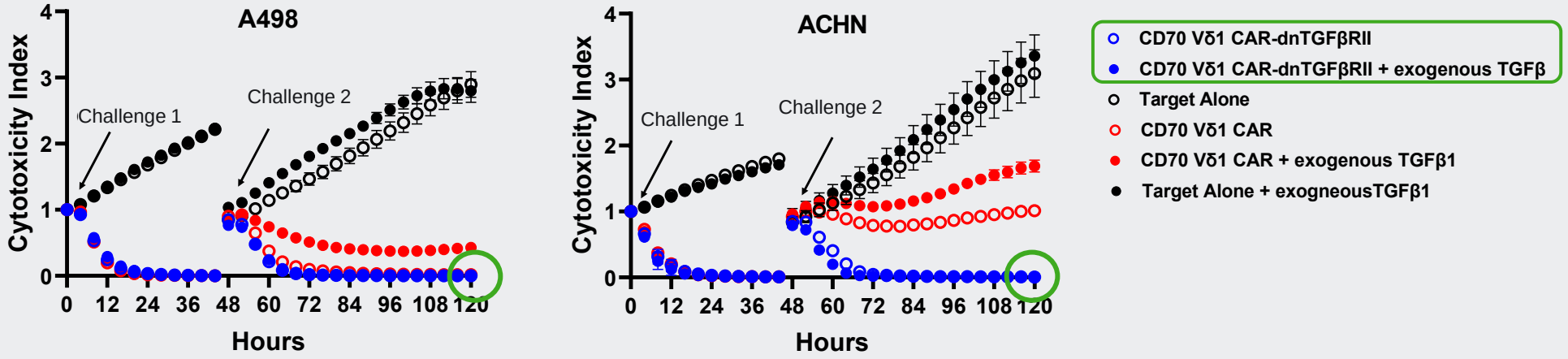

Add TGFβ-DNR Armor

**Resilient activation profile in presence of TGFβ**

CD70 CAR + TGFβ-DNR




Armor Associated with Resilient Serial Killing and Functional Persistence in Rechallenge Model




Lamture et. al. SITC (2022)



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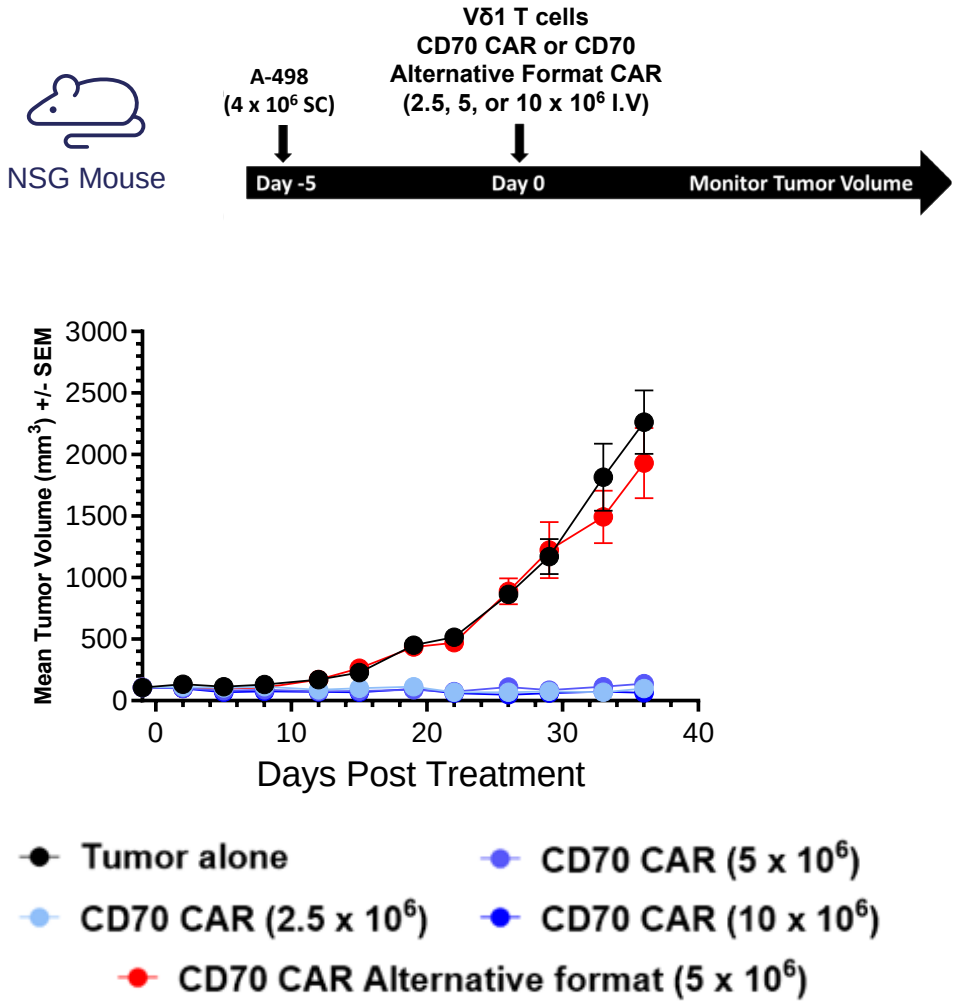
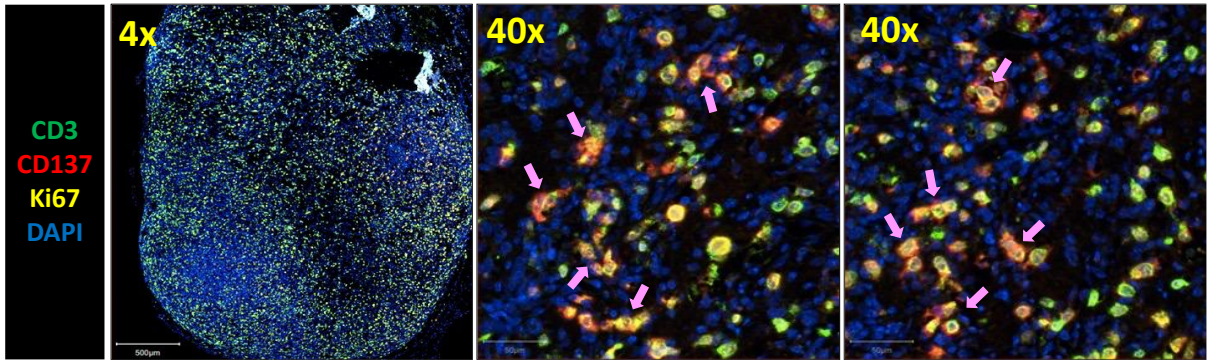
# CD70 CAR γδ T Cells Demonstrated Activity In Vivo and Proliferated Within Tumors

PRESENTED AT SITC 2022




## Tumor Infiltration and Proliferation of γδ CAR T cells




- CD70 CAR γδ T cells demonstrated robust tumor growth inhibition
- Anti-tumor activity associated with CAR γδ T cell tumor infiltration and proliferation within the tumor bulk

Lamture et. al. SITC (2022)



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# Armored CD70 CAR γδ T Cells: Summary and Next Steps

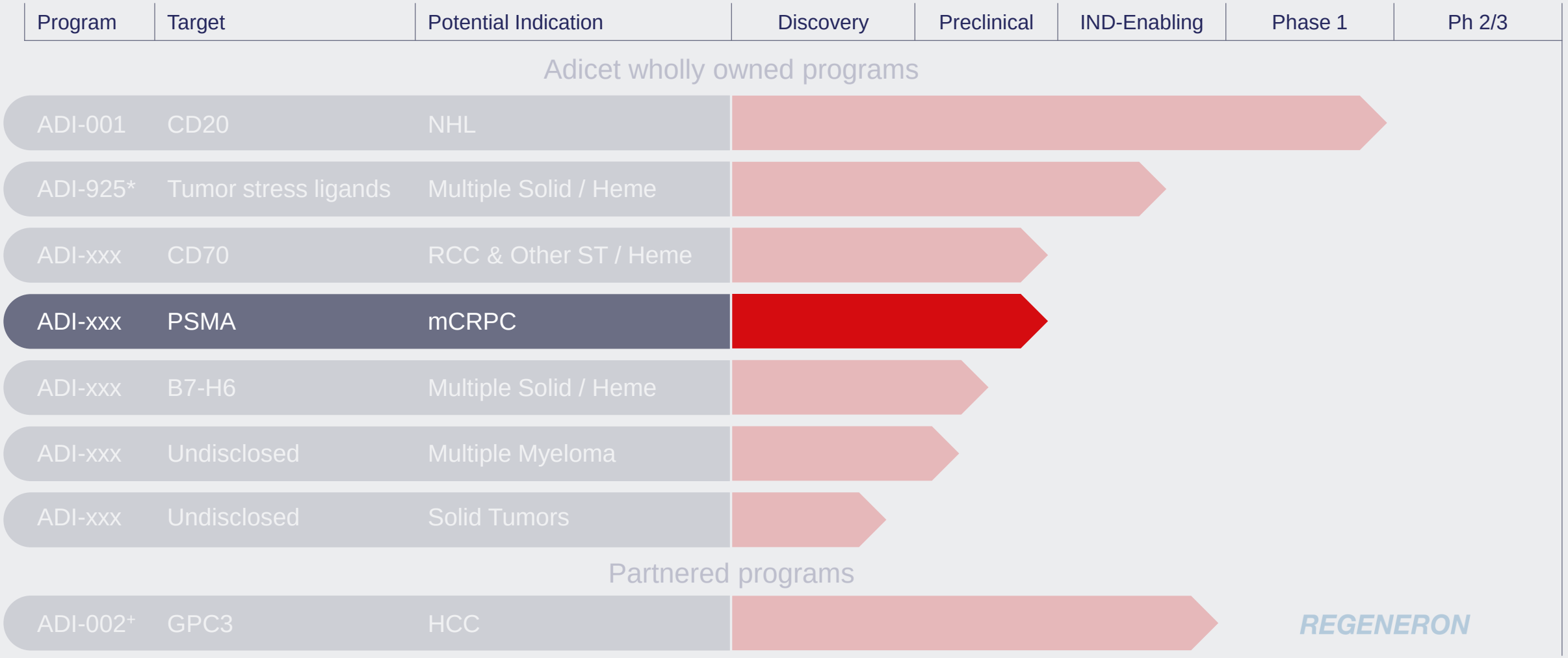
- Armored CD70 CAR γδ T cell program produced a compelling lead that warrants further development
- Program on-track for achieving differentiated target profile and proceeding to IND-candidate nomination
- Additional data expected to be presented in 2023

## Opportunity for Adicet and γδ T cells

- **Response to low antigen density** by design with **CD27-based CAR** (compared to scFv-based CAR)[3]
- **Three mechanisms of action** designed to address tumor heterogeneity
- **Homing** of γδ T cells documented in RCC and improved AML OS
- **Inclusion of armoring** to address suppressive TME

1. Sauer et al. *Blood* (2021)

# Building a Broad Pipeline of First-in-Class CAR and CAd γδ T Cell Product Candidates




*ADI-925 is an engineered Chimeric Adapter (CAd) γδ1 T cell product candidate targeting stress ligands, including MICA/MICB & ULBP1-6, expressed on malignant cells



Adicet Bio

# Armored PSMA CAR γδ T Cell Opportunity For Differentiation

## Target validation

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

## 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[4,6]
- **Single mechanism of targeting** limits activity in heterogeneous tumors
- **Immunosuppressive environment** of mCRPC associated with TGFβ[7]

## Opportunity for Adicet and γδ T cells

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



1. Adam et al. *BJC* (2006)
2. Sartor et al. *N Eng J Med* (2021)
3. De Bono et al. *JCO supp* (2021)
4. Tran et al. *Ann Onc.* (2020)
5. Slovin et al. *JCO supp* (2022)
6. Narayan et al. *Nat Med* (2022)
7. Mirazaei et al. *Int J Biol Macromol* (2022)

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

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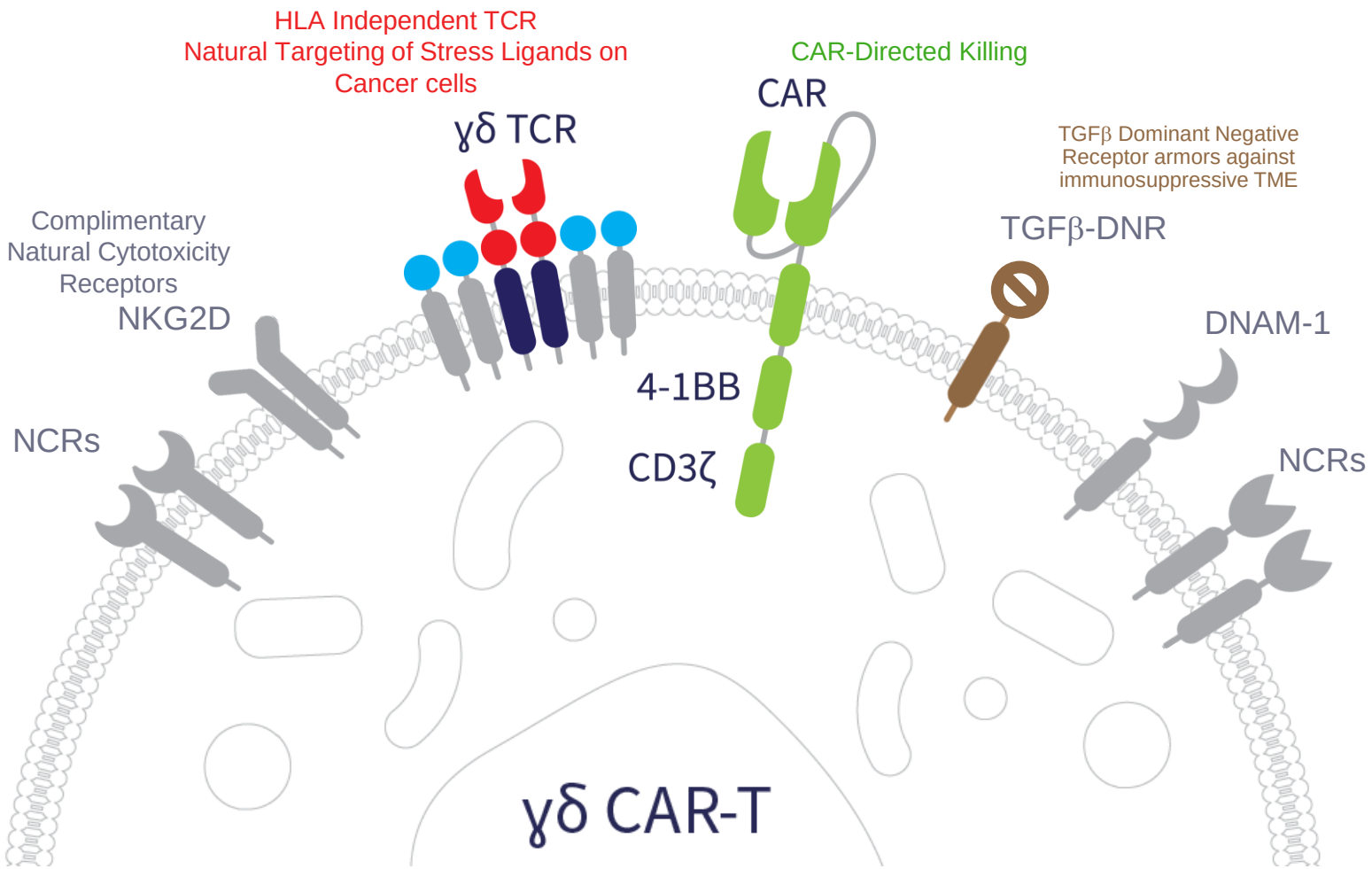
# Armored PSMA CAR γδ T Cell Program

- Lead candidate targeting PSMA demonstrated improved characteristics versus benchmark[1]
- Heterogeneous PSMA
- Armoring technology via TGFβ-DNR improved activity, serial killing, and functional resilience




1. Liu et al. *Cancer Res.* (1997)



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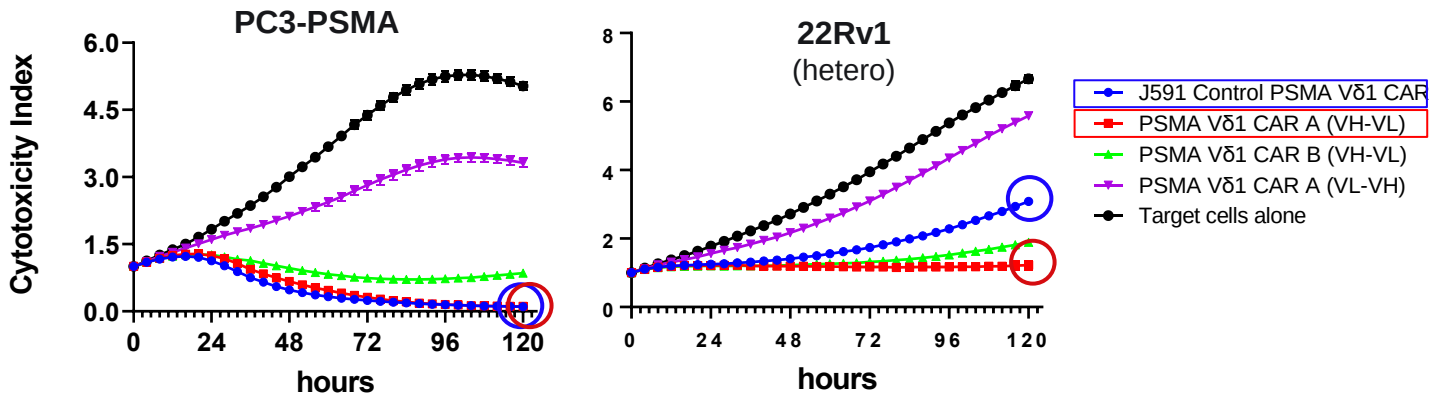
# Adicet's Lead PSMA CAR Construct Demonstrated Improved Cytotoxicity and Targeting Over Benchmark

PRESENTED AT SITC 2022

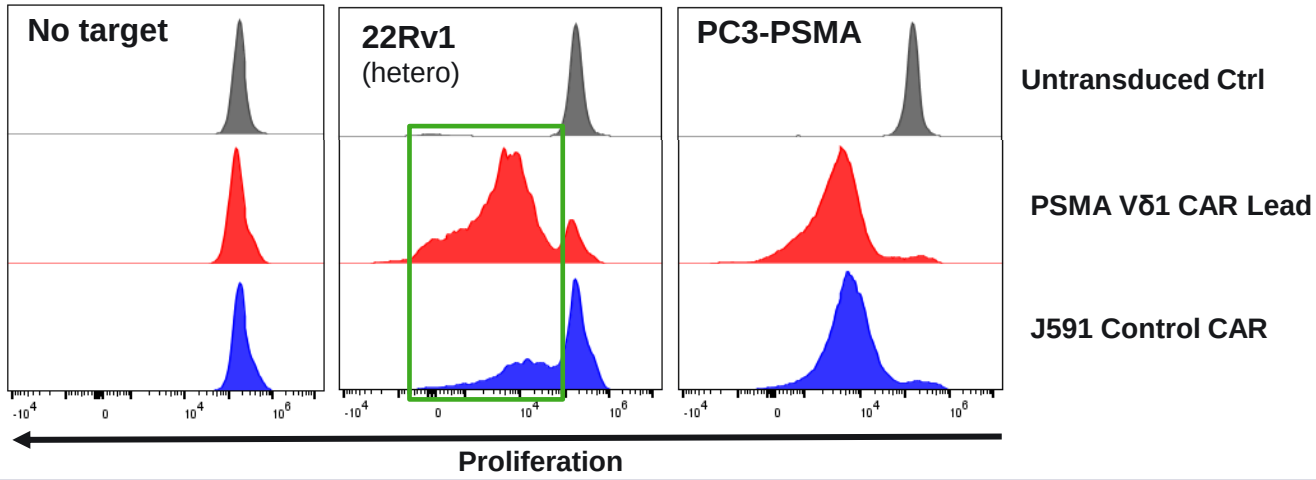
## Lead CAR Construct demonstrated:

- Efficient activation of NFAT signaling
- Recognition of intermediate/ heterogeneous PSMA expression
- Broad target-associated proliferation
- Improved cytotoxicity over benchmark[1]
- Improved in vivo activity over benchmark[1]

### Cytotoxicity at Low E:T Ratio




### Target-Associated Proliferation




Ramadoss et. al. SITC 2022

1. Liu et al. *Cancer Res.* (1997)

NFAT: Nuclear factor of activated T-cells



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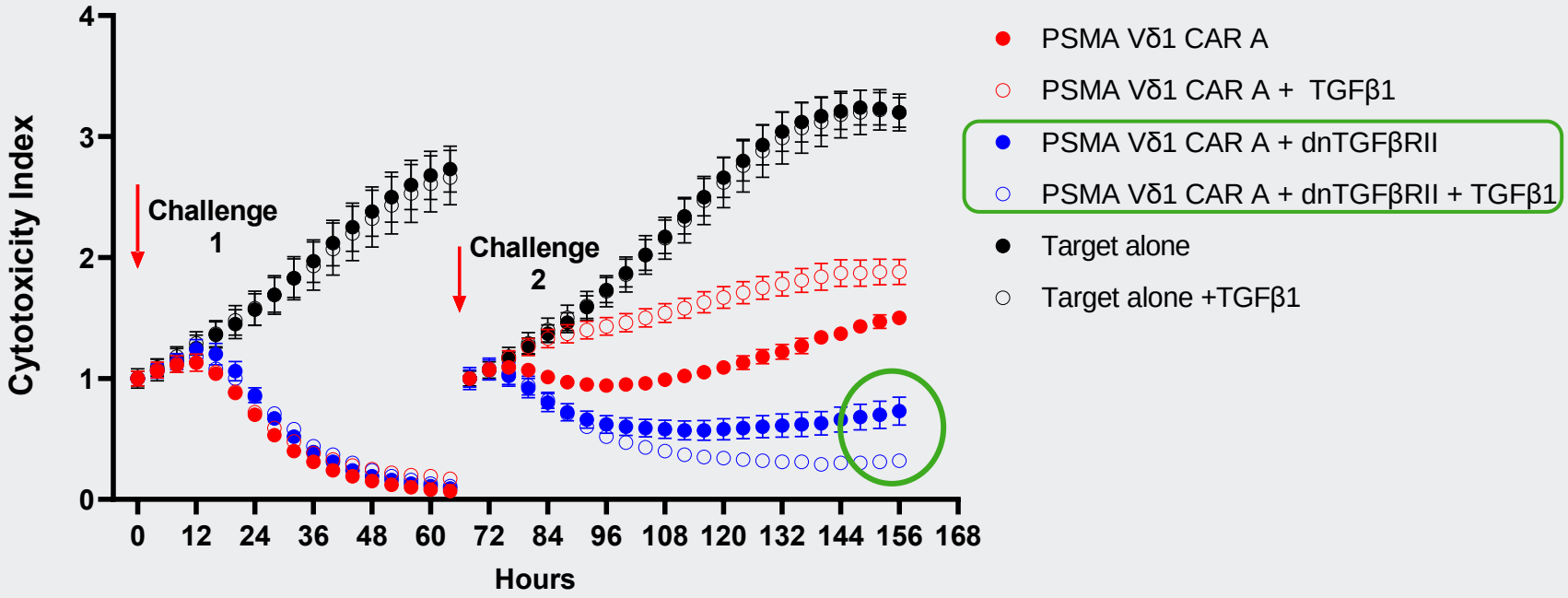
# Armored PSMA CAR γδ T Cell Program Improved Resilience with TGFβ-DNR

PRESENTED AT SITC 2022

## Armor Associated with Resilient Serial Killing and Functional Persistence




Ramadoss et. al. SITC (2022)



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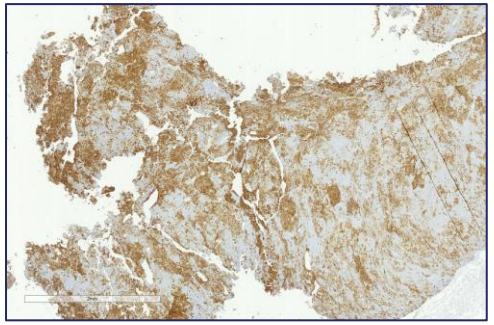
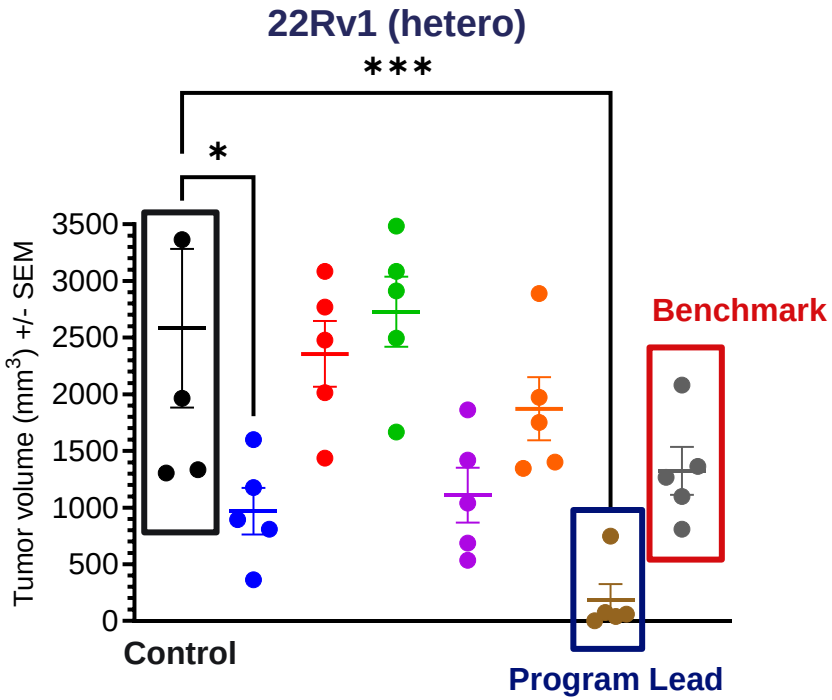
# Armored PSMA CAR γδ T Cell Program In Vivo Activity and Next Steps

PRESENTED AT SITC 2022

## 22Rv1 Tumors Express Intermediate and Heterogeneous PSMA



PSMA 2X




- Armored PSMA CAR γδ T cell program demonstrated significant antitumor activity across mCRPC models
- Program lead is progressing through efficacy and manufacturing assessment for IND-candidate confirmation

Ramadoss et. al. SITC (2022)



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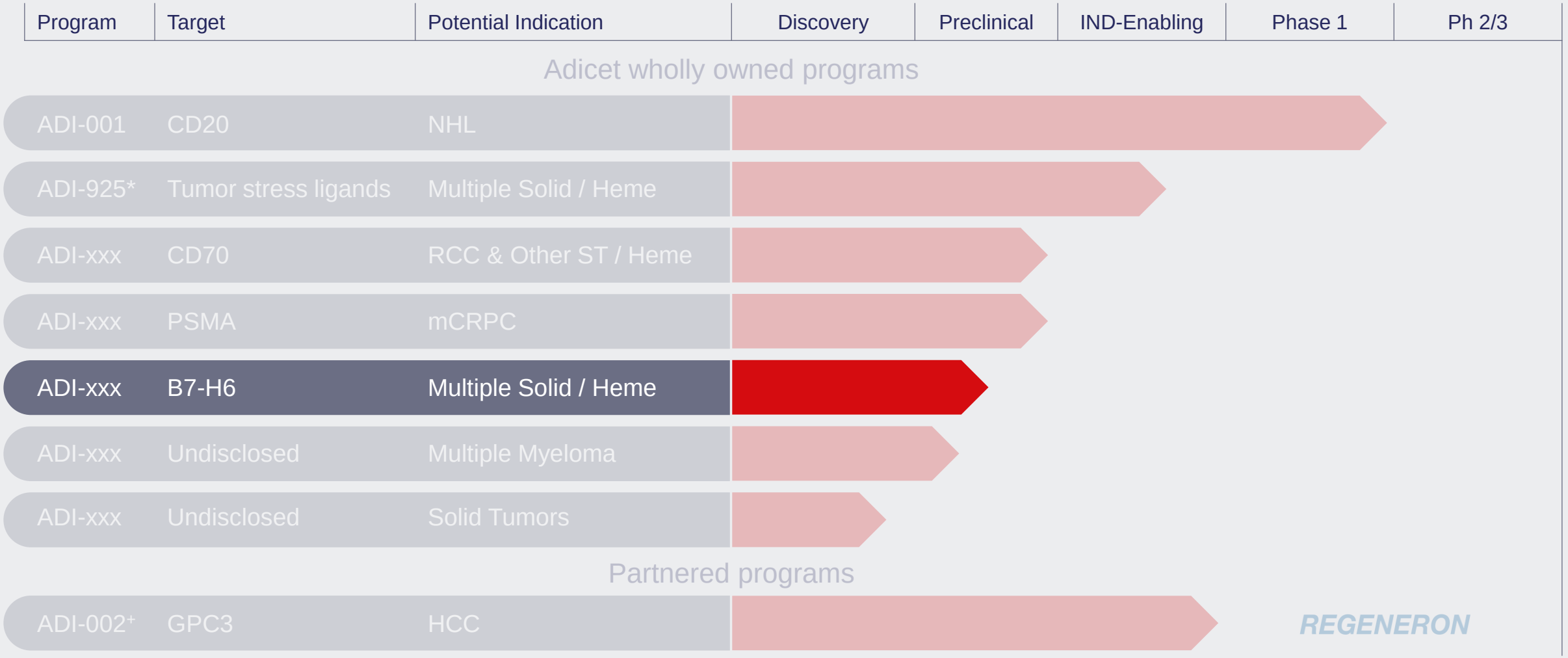
# Building a Broad Pipeline of First-in-Class CAR and CAd γδ T Cell Product Candidates




*ADI-925 is an engineered Chimeric Adapter (CAd) γδ1 T cell product candidate targeting stress ligands, including MICA/MICB & ULBP1-6, expressed on malignant cells



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# Armored B7-H6 CAR γδ T Cell Opportunity For Differentiation

## Target validation

- **B7-H6 is expressed in >95% of CRC** cases, and other **gastrointestinal cancers**, with limited expression in normal tissues[1]
- Well **established biological role** in natural tumor surveillance and **active clinical development**[1]
- **Preclinical activity** with bispecific T-cell engaging antibodies[2] and NKp30 related CAR T[3]
- **In vivo activity** with B7-H6 targeted therapies against both **hematological and solid tumor** indications[2,3,4]

## Key challenges

- Susceptibility to inhibition by **shed antigen**
- **Selective and specific** antigen targeting
- Single MOA overcome by **heterogeneous antigen expression** in solid tumors
- Limited intratumoral **homing and proliferation**
- **Immunosuppressive TME**

## Opportunity for Adicet and γδ T cells

- **Potential to be first-in-class** B7-H6 targeted cell therapy product into clinic
- Designed to retain **activity in presence of shed antigen** and **armored against TME**
- **High level of homing** for Vδ1 T cells in **GI and colorectal** tissues
- **Three mechanisms** for anti-tumor activity (CAR, innate, and adaptive immunity) **designed to address tumor heterogeneity**



1. NCT04752215
2. Zhang et al. *Clin Can Res* (2022)
3. Zhang et al *J Immunol* (2012)
4. Brandt et al *J exp Med* (2009)

CRC: Colorectal cancer; GI: Gastrointestinal; MOA: Mechanism of action

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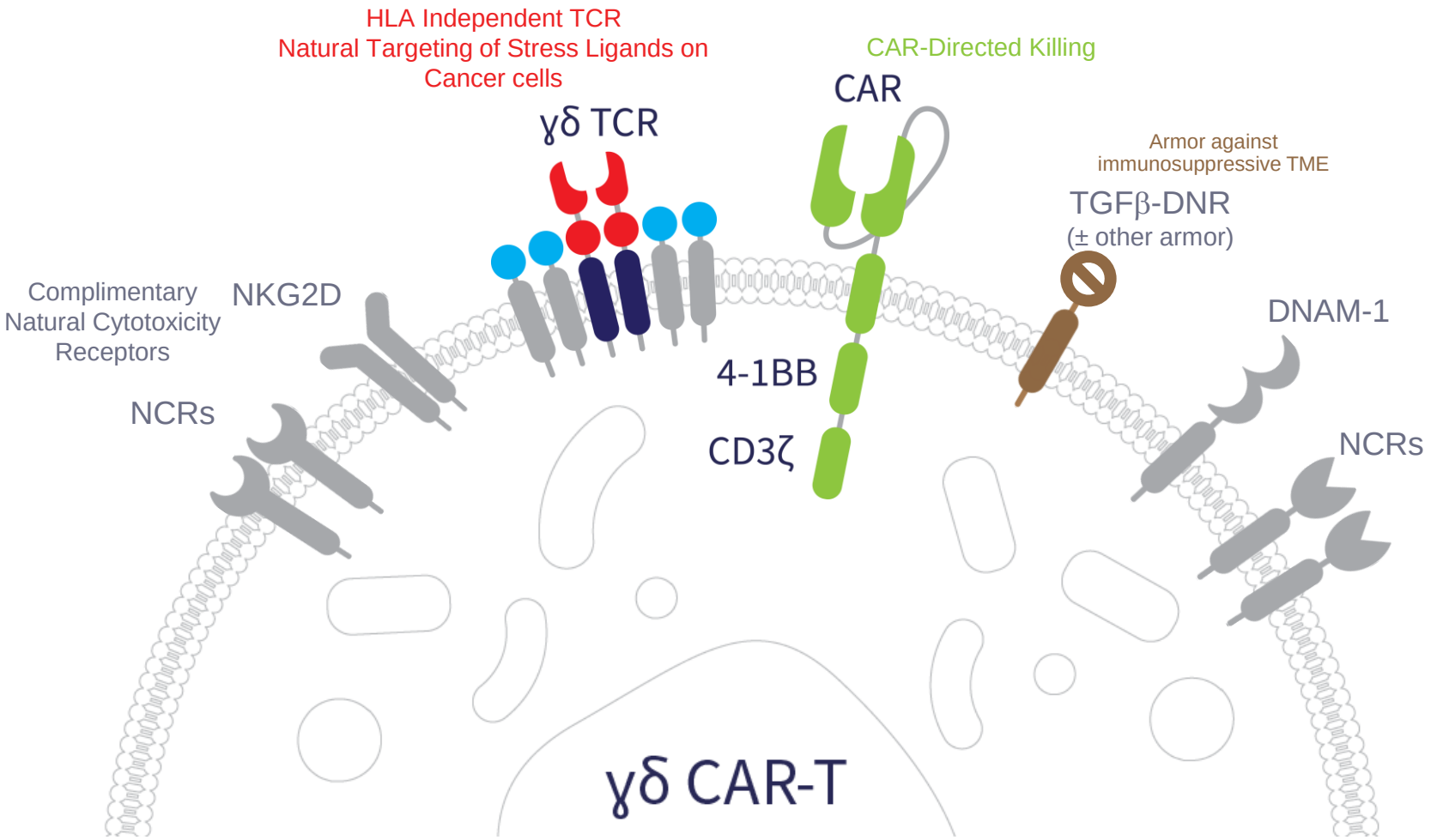
# Armored B7-H6 CAR γδ T Cell Program

- Library of de novo CAR constructs screened for binding characteristics and improved performance versus benchmark[1]
- CAR optimization underway to define lead construct in 2023
- Iterative and novel armoring enhancements being explored




1. Hua et al. *Protein Eng Des Sel.* (2017)



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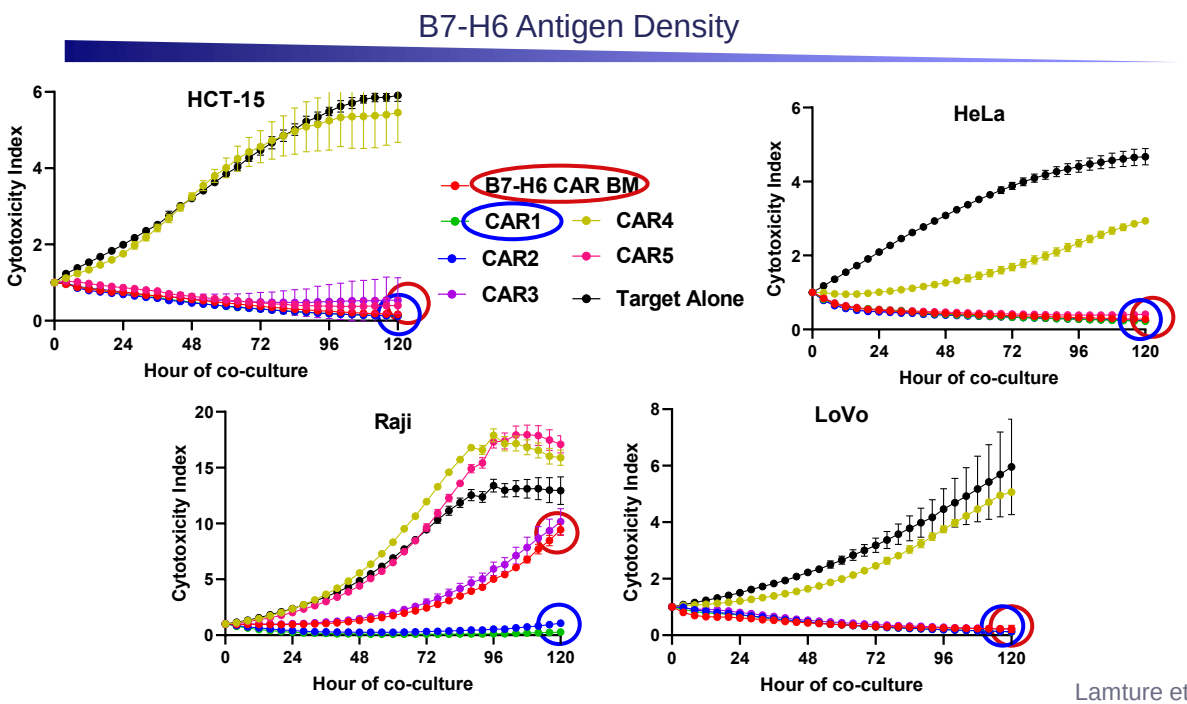
# B7-H6 CAR γδ T Cells Applicable Across Range of Indications

PRESENTED AT SITC 2022

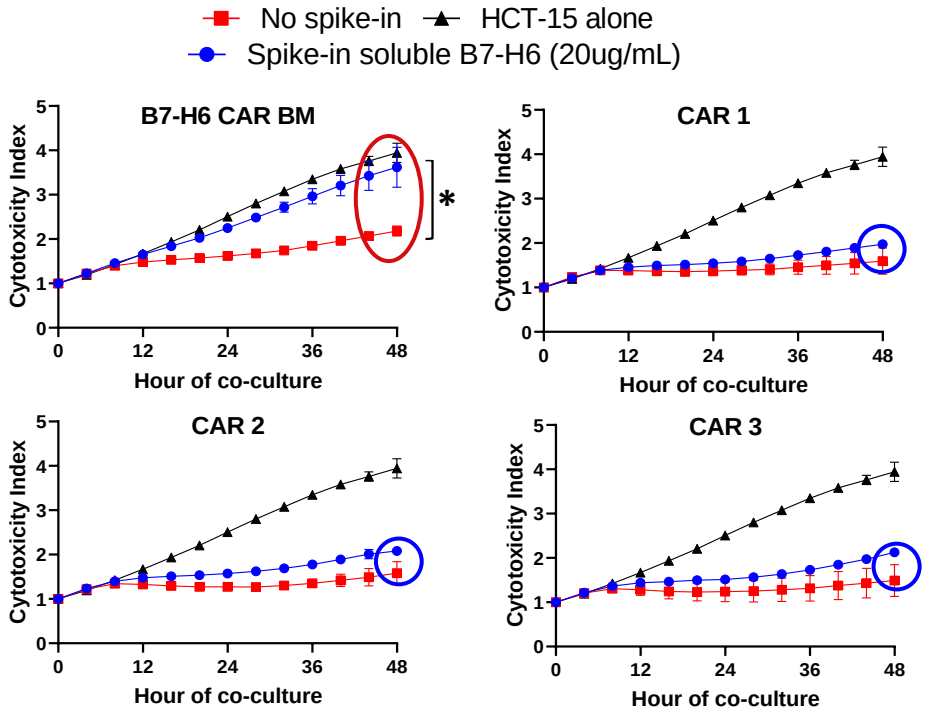
- B7-H6 CAR γδ T cells demonstrated anti-tumor activity across range of target antigen densities and indications
- Adicet's tailored scFv screening strategy has yielded CAR leads resilient to inhibition by shed antigen compared to benchmark[1]

## Anti-Tumor Cytotoxicity




Lamture et. al. SITC (2022)

## Resilience to Inhibition by Shed B7-H6 Antigen




BM: Benchmark



1. Hua et al. *Protein Eng Des Sel.* (2017)

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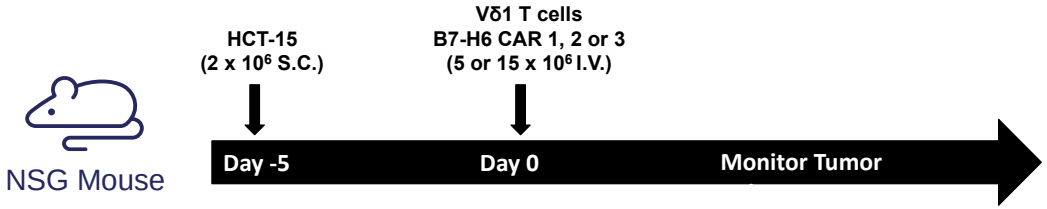
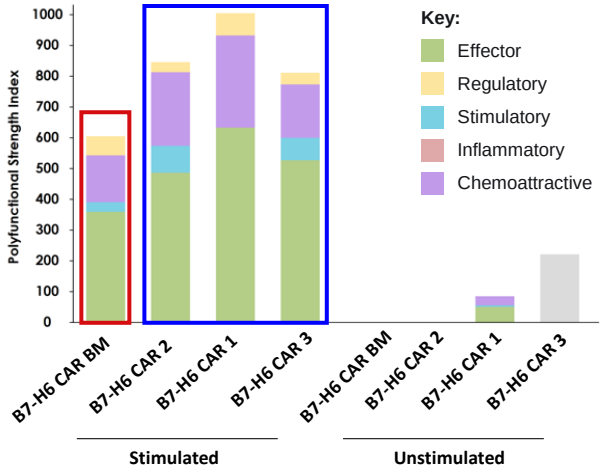
# B7-H6 CAR γδ T Cells Demonstrated Anti-Tumor Activity and Improved Polyfunctional Strength

PRESENTED AT SITC 2022

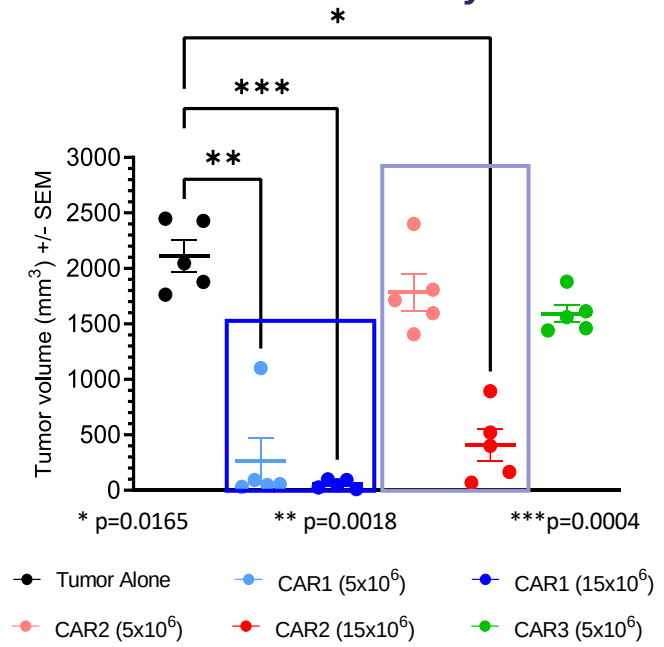



- B7-H6 CAR γδ T cells demonstrated improved polyfunctional strength compared to benchmark CAR[1]
- Efficacy studies support potent anti tumor activity
- Lead discovery proceeding with additional armoring technologies

## Polyfunctional Strength Index (PSI)




## Tumor Volume on Day 29




Lamture et. al. SITC (2022)



1. Hua et al. *Protein Eng Des Sel.* (2017)

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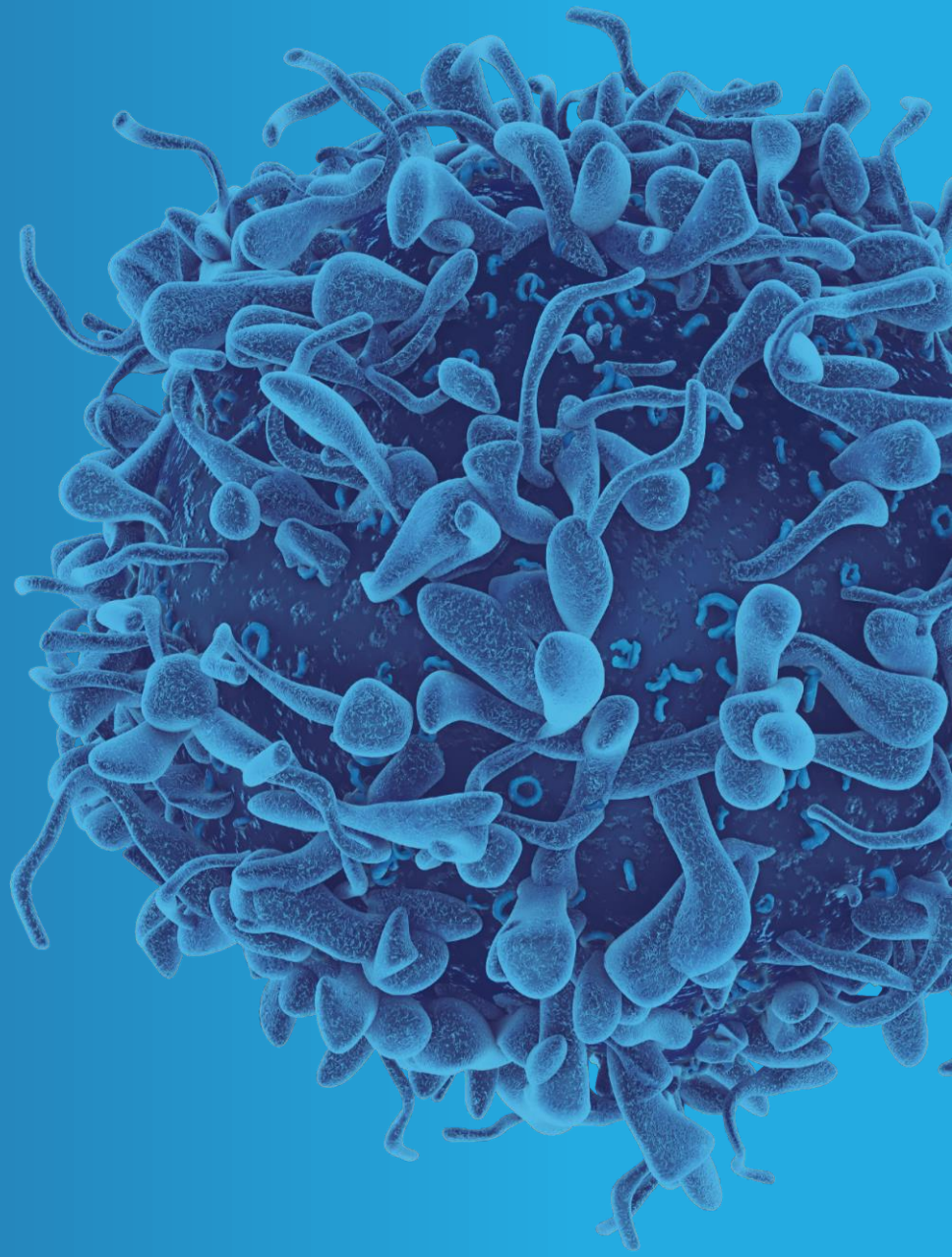
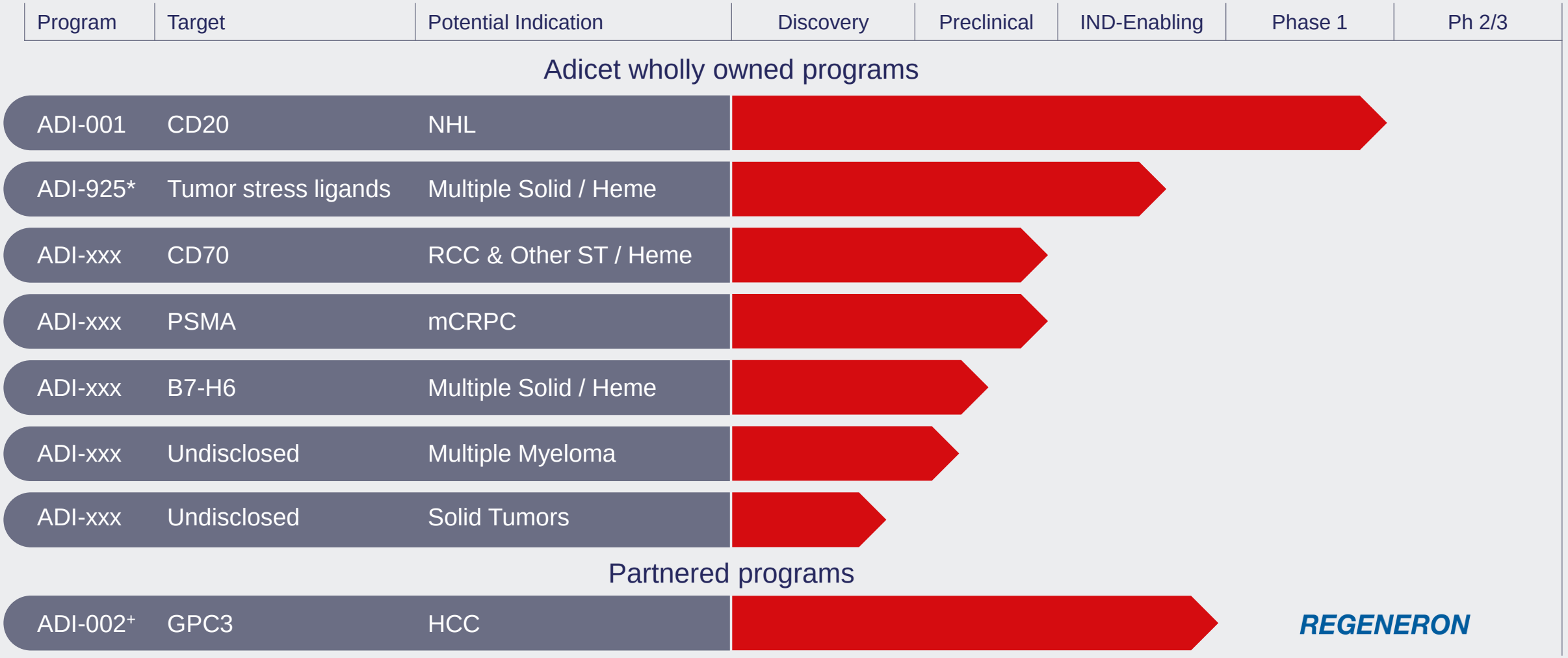
# Summary of Pipeline and 2022 SITC Data

Blake Aftab, Ph.D.
Chief Scientific Officer



# Building a Broad Pipeline of First-in-Class CAR and CAd γδ T Cell Product Candidates




*ADI-925 is an engineered Chimeric Adapter (CAd) γδ1 T cell product candidate targeting stress ligands, including MICA/MICB & ULBP1-6, expressed on malignant cells



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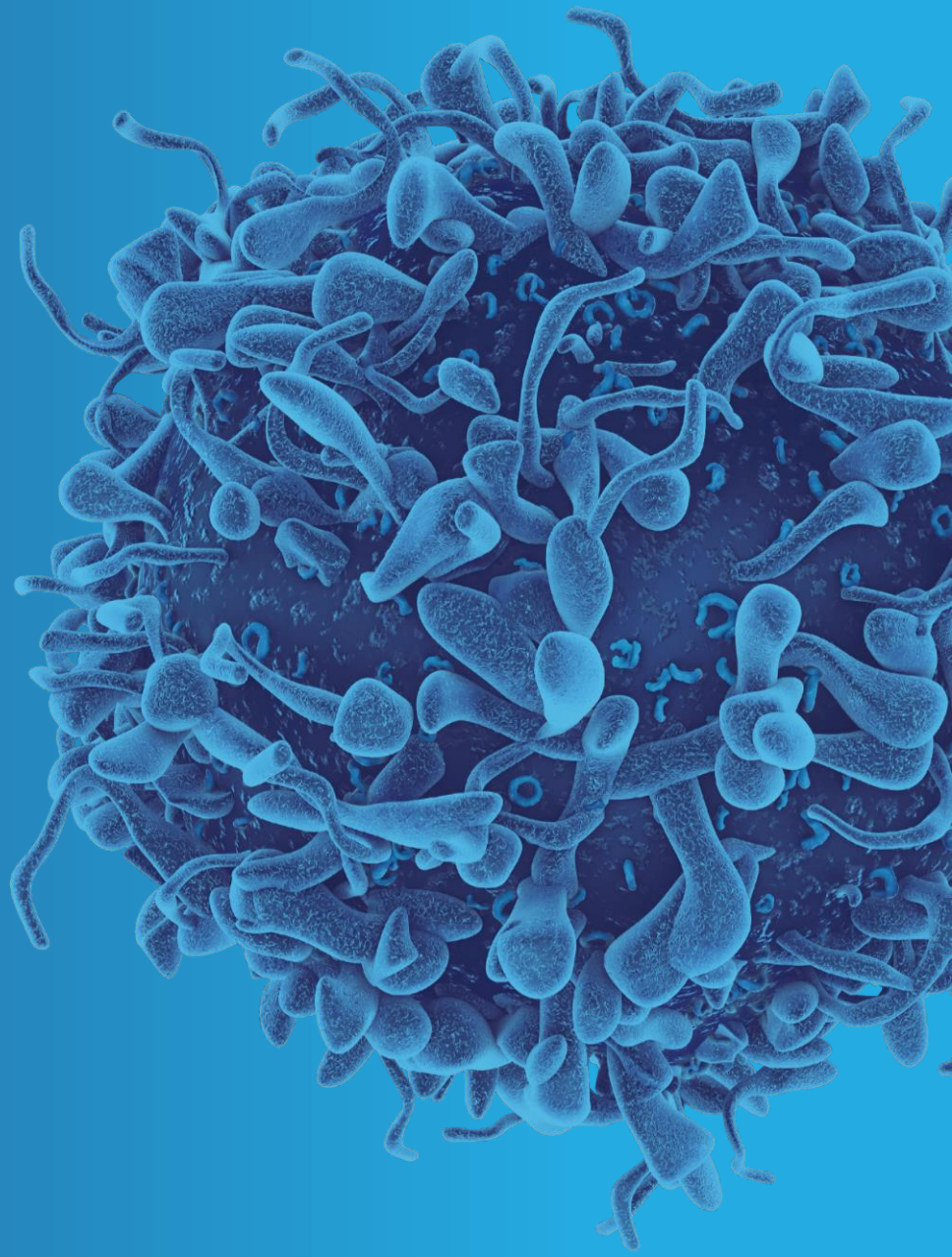
# Perspectives: Adicet γδ T Cell Pipeline

Marco Davila, M.D., Ph.D.
Roswell Park Comprehensive Cancer Center



# Perspectives

Marco Davila M.D., Ph.D.

Associate Director and SVP Translational Research

Roswell Park Comprehensive Cancer Center

Adicet Bio Scientific Advisory Board Member

**Question 1**: Can you share your preliminary thoughts on the pipeline we presented today? What do these engineered γδ1 T cell programs offer?



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# Perspectives

Marco Davila M.D., Ph.D.

Associate Director and SVP Translational Research

Roswell Park Comprehensive Cancer Center

Adicet Bio Scientific Advisory Board Member

**Question 1:** Can you share your preliminary thoughts on the pipeline we have compiled here? What do these engineered γδ1 T cell programs offer?

**Question 2:** Can you share your thoughts on ADI-925 and the chimeric adaptor technology?



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# Perspectives

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Associate Director and SVP Translational Research

Roswell Park Comprehensive Cancer Center

Adicet Bio Scientific Advisory Board Member

**Question 1:** Can you share your preliminary thoughts on the pipeline we have compiled here? What do these engineered γδ1 T cell programs offer?

**Question 2:** Can you share your thoughts on ADI-925 and the chimeric adaptor technology?

**Question 3:** With CD70 and PSMA, can you provide your perspectives in the context of previous approaches to these targets?

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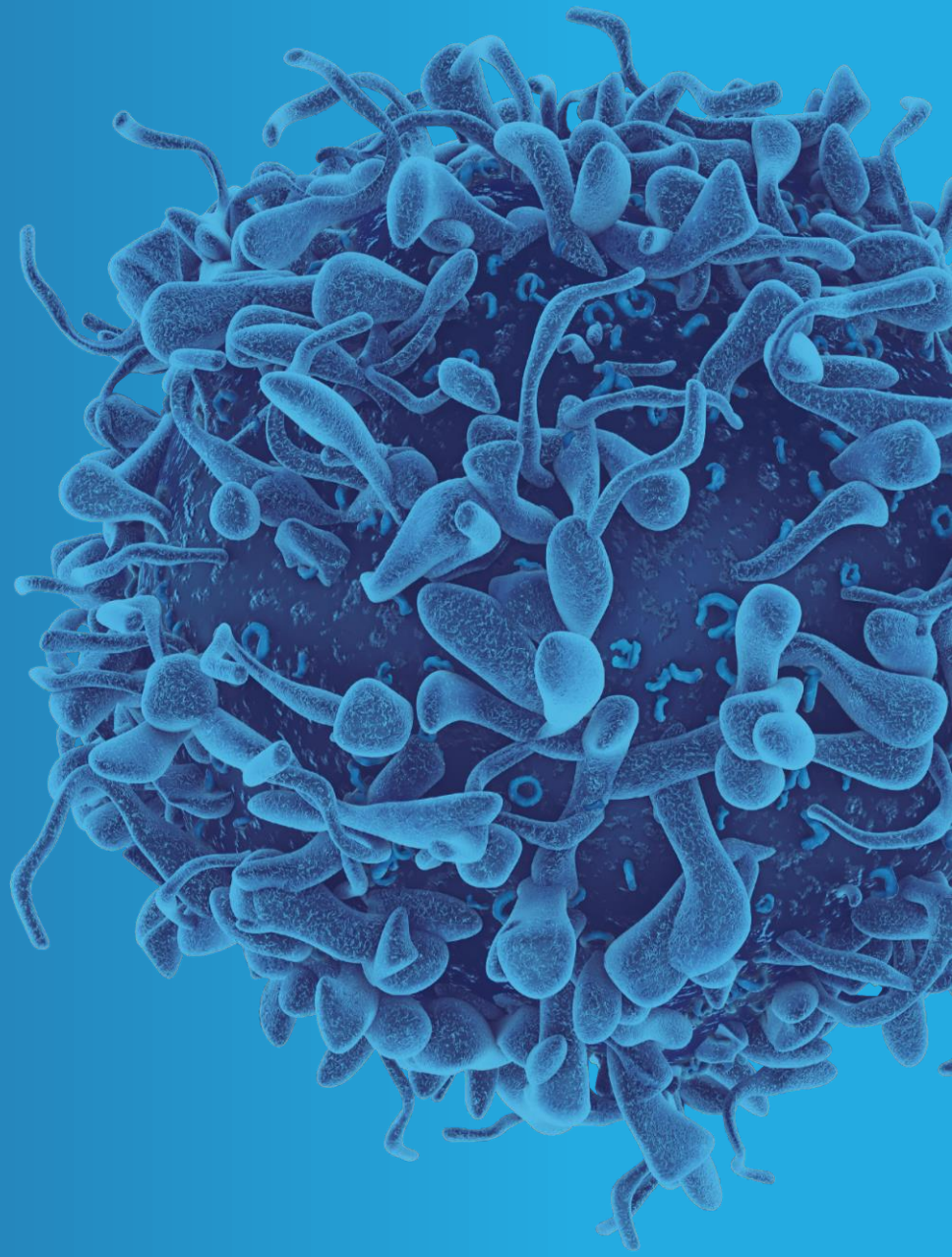
# Closing Remarks



Chen Schor, President and CEO

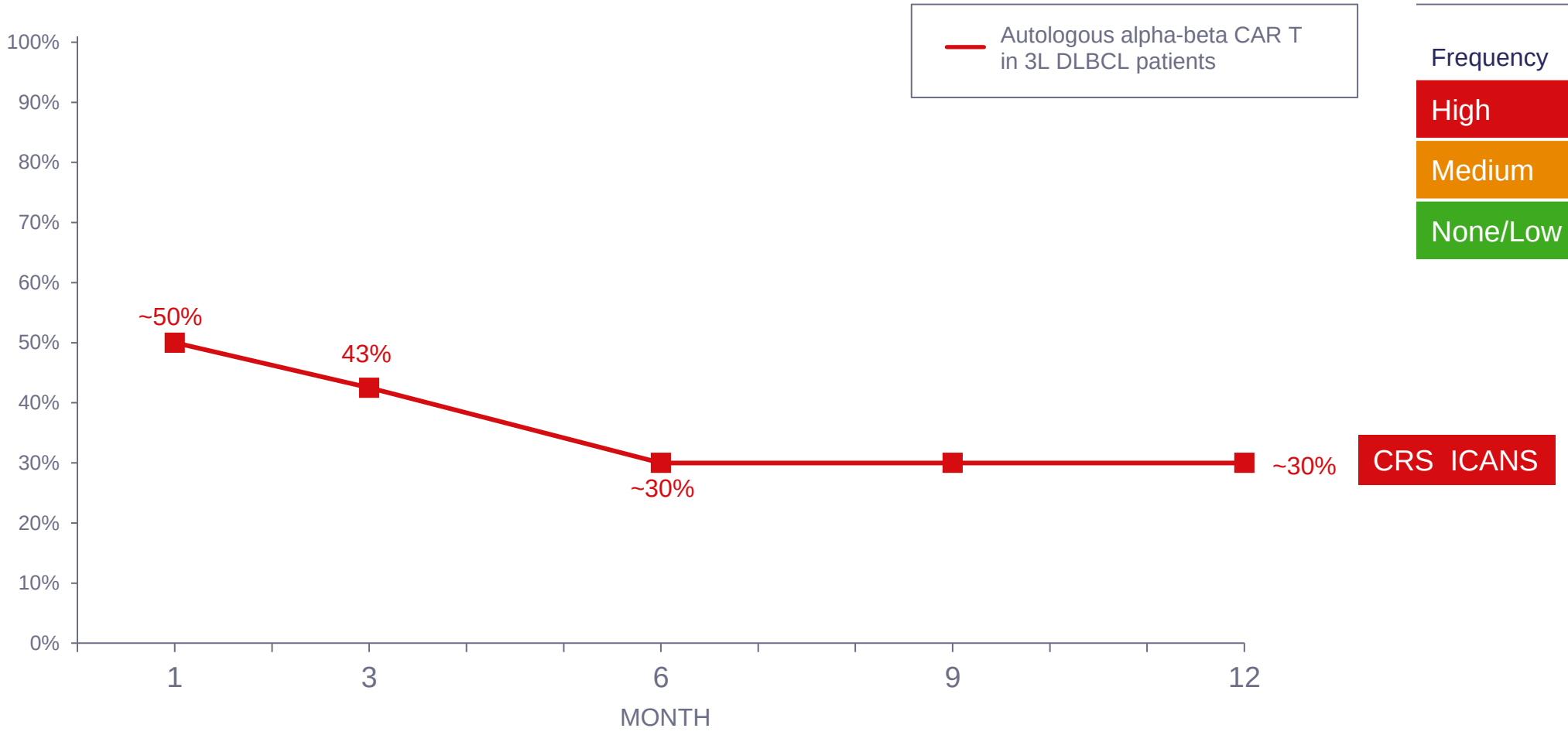
**Sattva Neelapu, M.D.**
Department of Lymphoma-Myeloma
Division of Cancer Medicine
The University of Texas, MD Anderson Cancer Center

# Adicet Bio to discuss recent data from ongoing Phase 1 clinical study in R/R aggressive B-cell NHL

When: Sunday, December 11 at 8:00 a.m. CT/ 9:00 a.m. ET

Adicet Bio

# Advanced Therapies CR Rate Over Time in 3L and 4L Aggressive NHL




| Frequency | Grade3+ CRS | Grade 3 ICANS |
|---|---|---|
| High | CRS | ICANS |
| Medium | CRS | ICANS |
| None/Low | CRS | ICANS |



**Autologous alpha-beta CAR T in 3L DLBCL patients**
*N Engl J Med.* (2017) December 28; 377(26): 2531–2544.
*J Clin Oncol* 38:3095-3106.
Yescarta EPAR Public Assessment Report

**CD20 bispecifics in 4L DLBCL patients post autologous CAR T**
Glofitamab ASCO (2022), Epcoritamab EHA (2022), GMAB PR June 11 (2022)
* CR rate durability for post-CAR T bispecifics modeled as durability of 3L+ autologous CAR-T (for modeling purpose only)
3L= Third line; 4L= Fourth line

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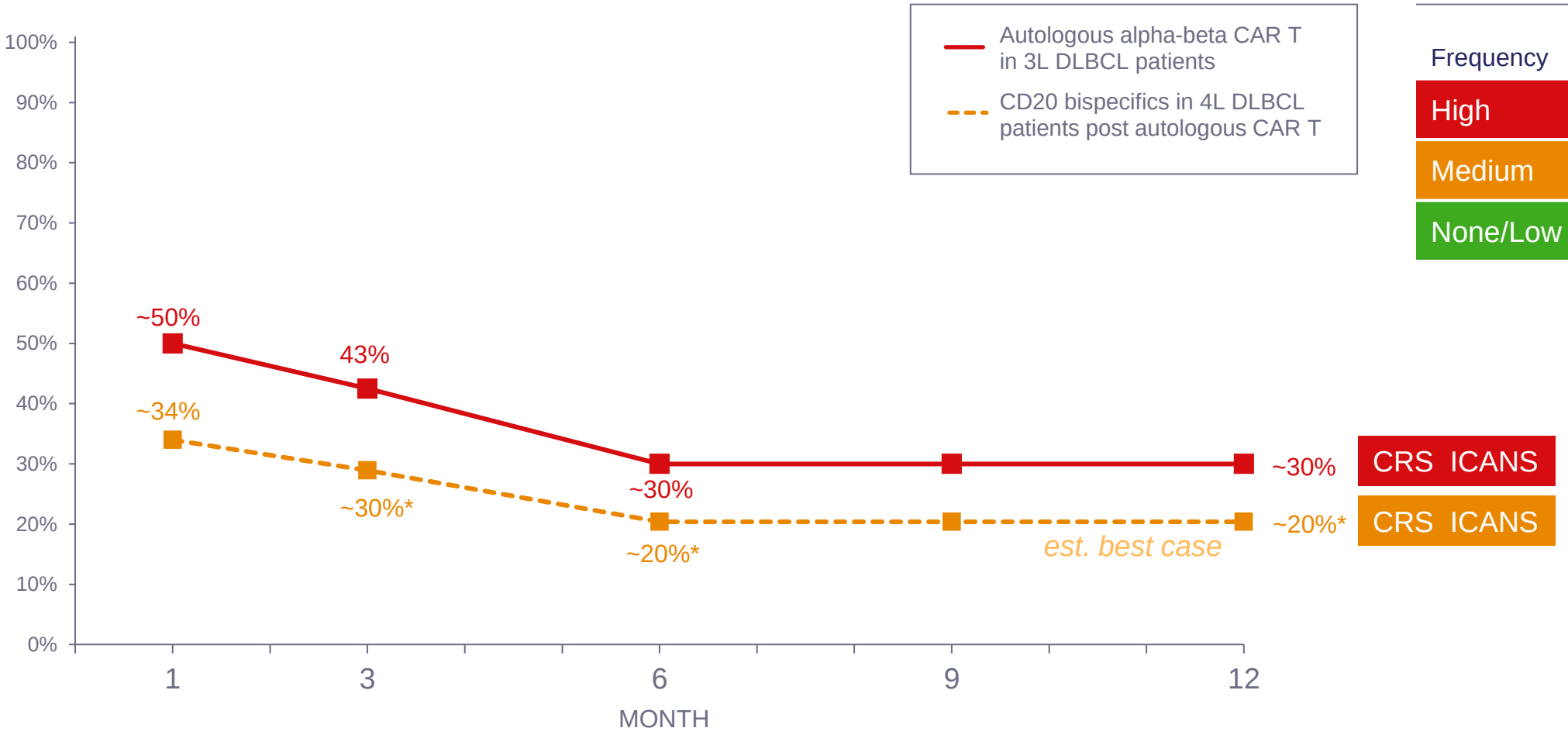
# Advanced Therapies CR Rate Over Time in 3L and 4L Aggressive NHL




| Frequency | Grade3+ CRS | Grade 3 ICANS |
|---|---|---|
| High | CRS | ICANS |
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| None/Low | CRS | ICANS |

CRS ICANS

CRS ICANS

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# Anticipated Near-Term Milestones

## ADI-001 Phase 1 Study in R/R NHL

- Complete dose escalation through DL4; backfill enrollment to DL3
- ASH clinical update Dec. 11 at 8:00 a.m. CT
- Establish recommended Phase 2 dose by end of 2022

## Pipeline and Manufacturing

- ADI-925: IND submission expected H2/2023
- One new IND planned every 12-18 months
- Leverage in-house GMP manufacturing to support expanding clinical pipeline

## ADI-001 – Expansion

- Discuss with the FDA and EMA the design of two potentially pivotal studies and a path to support BLA and MAA submissions
- Initiate a potentially pivotal program in H1/2023
- Initiate additional expansion cohorts in 2023

## Corporate

- Well financed into H1/2025 with $282M cash and cash equivalents (as of 9/30/22)



BLA: Biologics License Application; DL: Dose level; EMA: European Medicines Agency; FDA: U.S. Food and Drug Administration; MAA: Marketing Authorization Application; R/R= Relapsed/refractory

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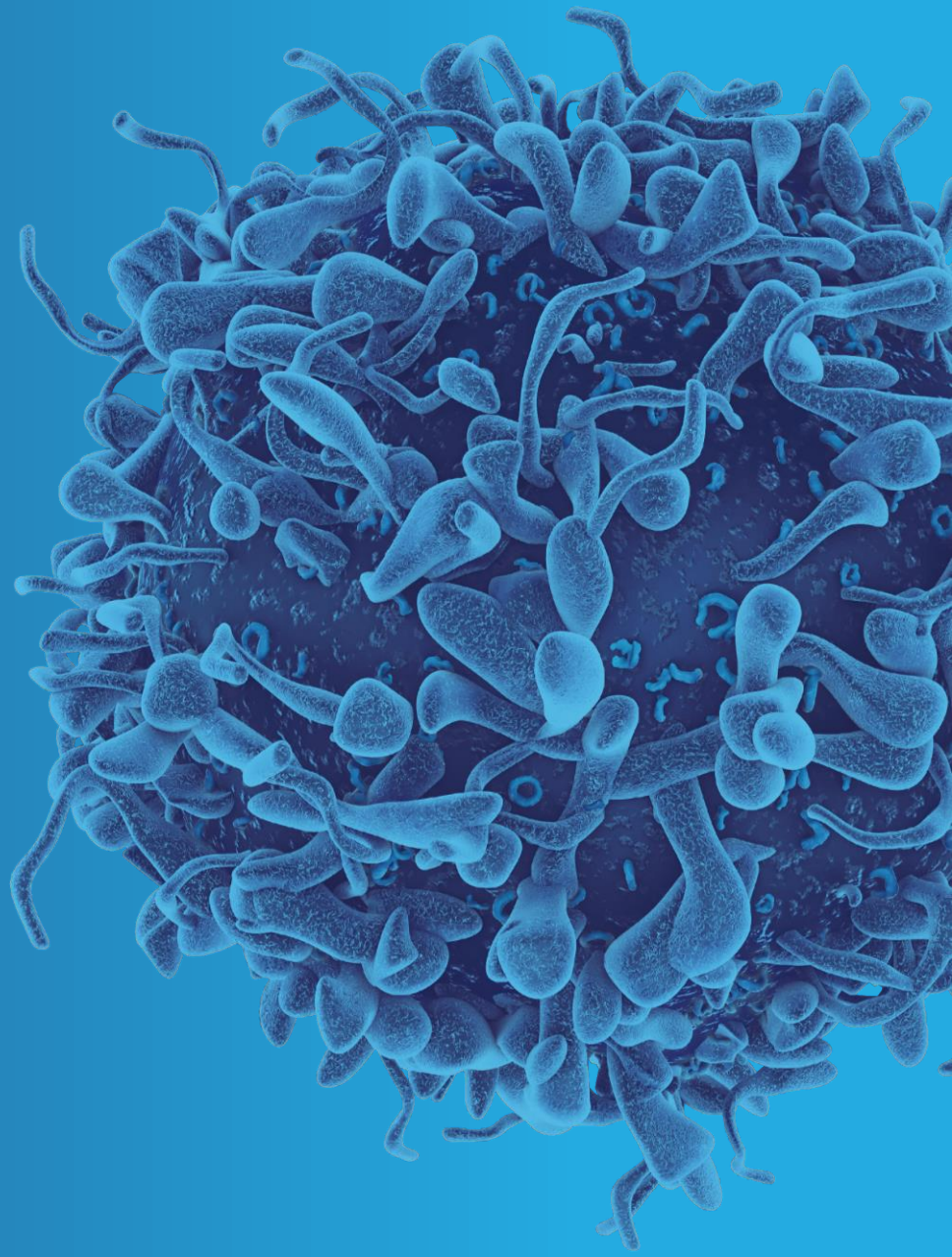
# Q&A



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# Leaders in Developing Allogeneic CAR and CAd γδ T Cell Therapies to Fight Cancer