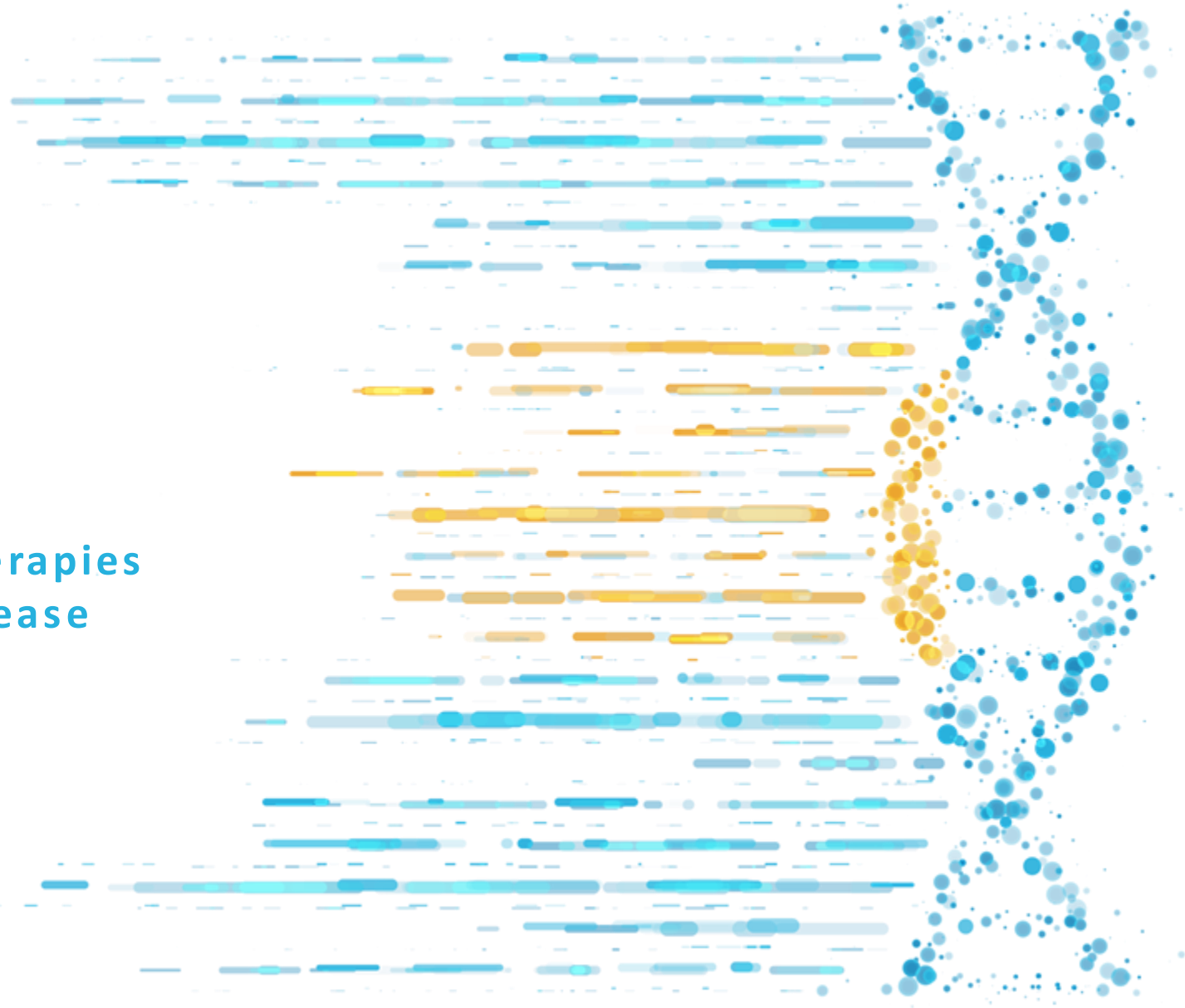
POSEIDA THERAPEUTICS

# Cell Therapy R&D Day

## Differentiated Allogeneic Cell Therapies in Oncology and Autoimmune Disease



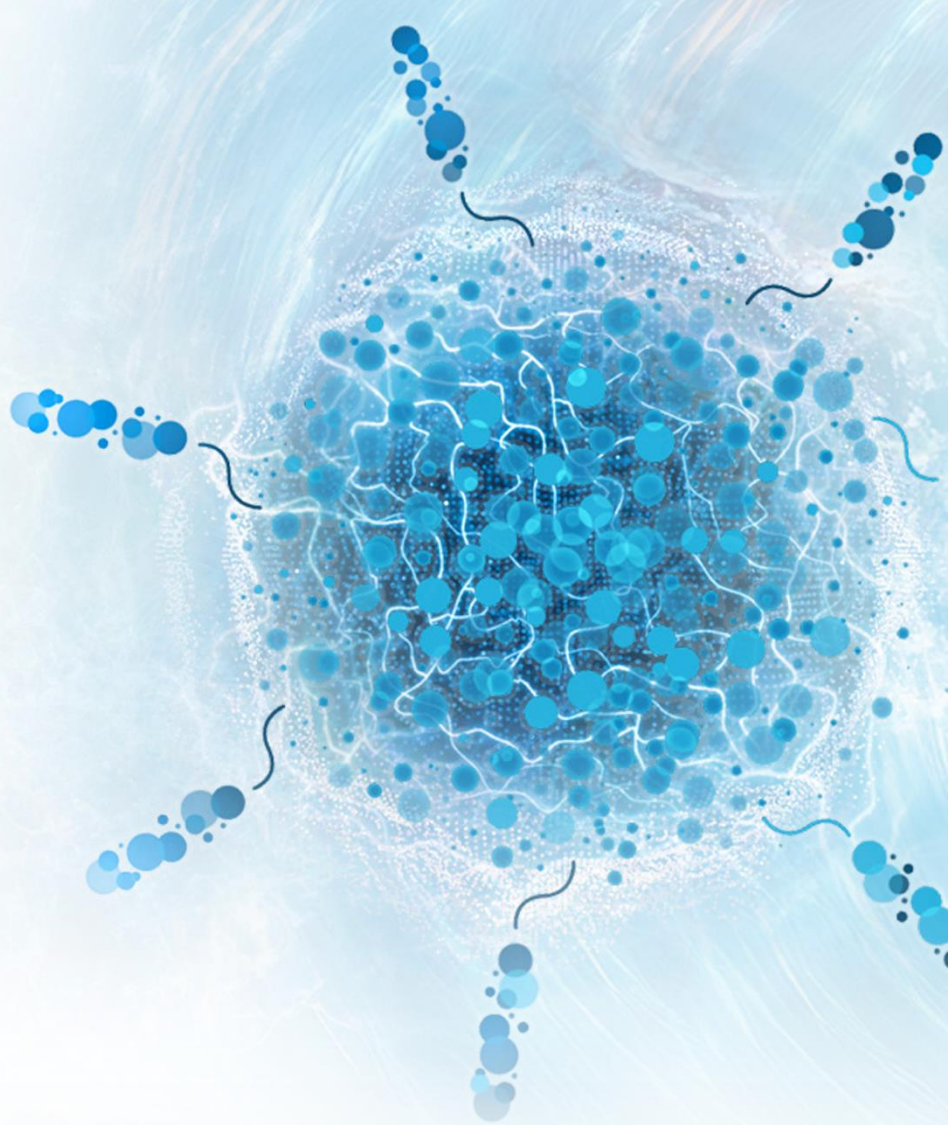
**NOVEMBER 14, 2024**

# Disclaimer

This presentation and any accompanying oral commentary contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts and include, without limitation, statements related to future events; our future financial performance or condition; business strategy; expected timing and plans with respect to development milestones, clinical trials, and regulatory and manufacturing activities; estimated market opportunities for product candidates; potential capabilities and benefits of our technology platforms and product candidates, including the efficacy, tolerability and safety profile of such product candidates; the quotes from Drs. Dholaria and Martin; our plans and strategy with respect to developing our technologies and product candidates; our ability to exploit and consummate additional business development opportunities; statements regarding the upfront payment and other potential fees, milestone and royalty payments we may receive pursuant to our collaboration agreements and research and development activities under our collaboration agreements; and future results of anticipated development efforts. Words such as "expect(s)," "feel(s)," "believe(s)," "will," "may," "anticipate(s)", "potentially" or negative of these terms or similar expressions are intended to identify forward-looking statements. These forward-looking statements are based on management's current expectations of future events only as of the date of this presentation and are subject to a number of important 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. These risks and uncertainties include, but are not limited to: the fact that interim data from the Company's clinical trials may change as more patient data become available and remain subject to audit and verification procedures that could result in material differences from the final data; our ongoing and planned clinical trials; the fact that our collaboration agreements may be terminated early such that we may not fully realize the benefits of such collaborations; the fact that we will have limited control over the efforts and resources our collaborators devote to advancing development programs under our collaboration agreements and we may not receive the potential fees, reimbursements and payments under our collaboration agreements; risks and uncertainties associated with conducting clinical trials; whether any of our product candidates will be shown to be safe and effective; our ability to finance continued operations; our reliance on third parties for various aspects of our business; competition in our target markets; our ability to protect our intellectual property; our ability to retain key scientific or management personnel; risks and uncertainties associated with development and regulatory approval of novel product candidates in the biopharmaceutical industry; and other risks and uncertainties described in our filings with the Securities and Exchange Commission, including under the heading "Risk Factors". Except as required by law, we assume no obligation to update these forward-looking statements, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

POSEIDA THERAPEUTICS

# Introduction: Poseida poised to lead in allogeneic cell therapy



**Kristin Yarema, PhD**

*President & CEO*

**Introduction: Poseida poised to lead in allogeneic cell therapy**
*Kristin Yarema, PhD*

**Heme malignancies: P-BCMA-ALLO1 leads a portfolio of allogeneic $T_{SCM}$-rich CAR-T programs**
*Syed Rizvi, MD*

**From hematology to autoimmune disease: Poseida's BCMA-CD19 dual CAR-T**
*Kurinji Pandiyan, PhD*

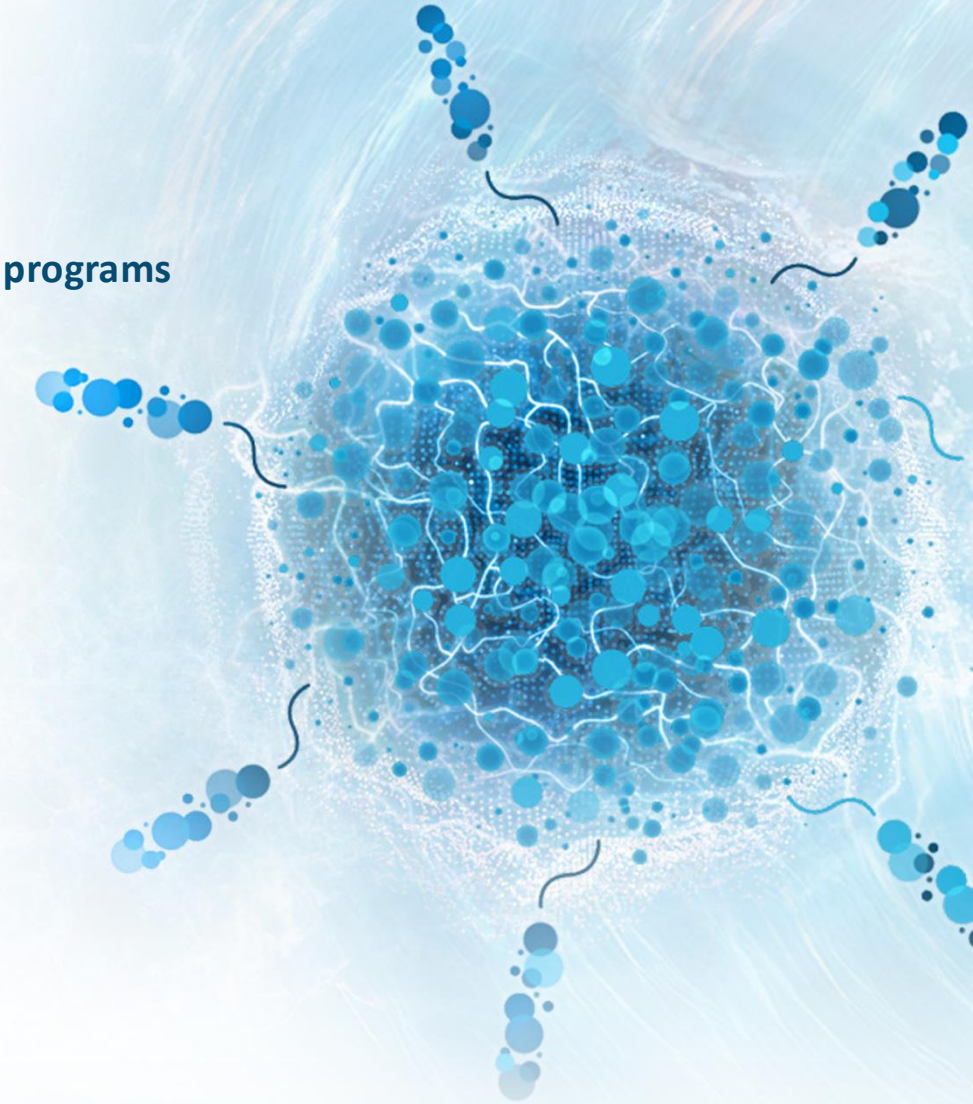
**Waves of innovation in solid tumor cell therapy**
*Devon J. Shedlock, PhD*

**The power of partnerships fireside chat**
*Peter Sandor, MD (Astellas) & Karen Basbaum*

**In-house GMP manufacturing capabilities**
*Loren Wagner*

**Concluding remarks**
*Kristin Yarema, PhD*

**Q&A**
*Executive and Scientific Leadership*



# On a mission to advance a new class of cell therapies & genetic medicines

## ALLOGENEIC CAR-T

Enabling broad and rapid patient access to transformational CAR-T

Roche

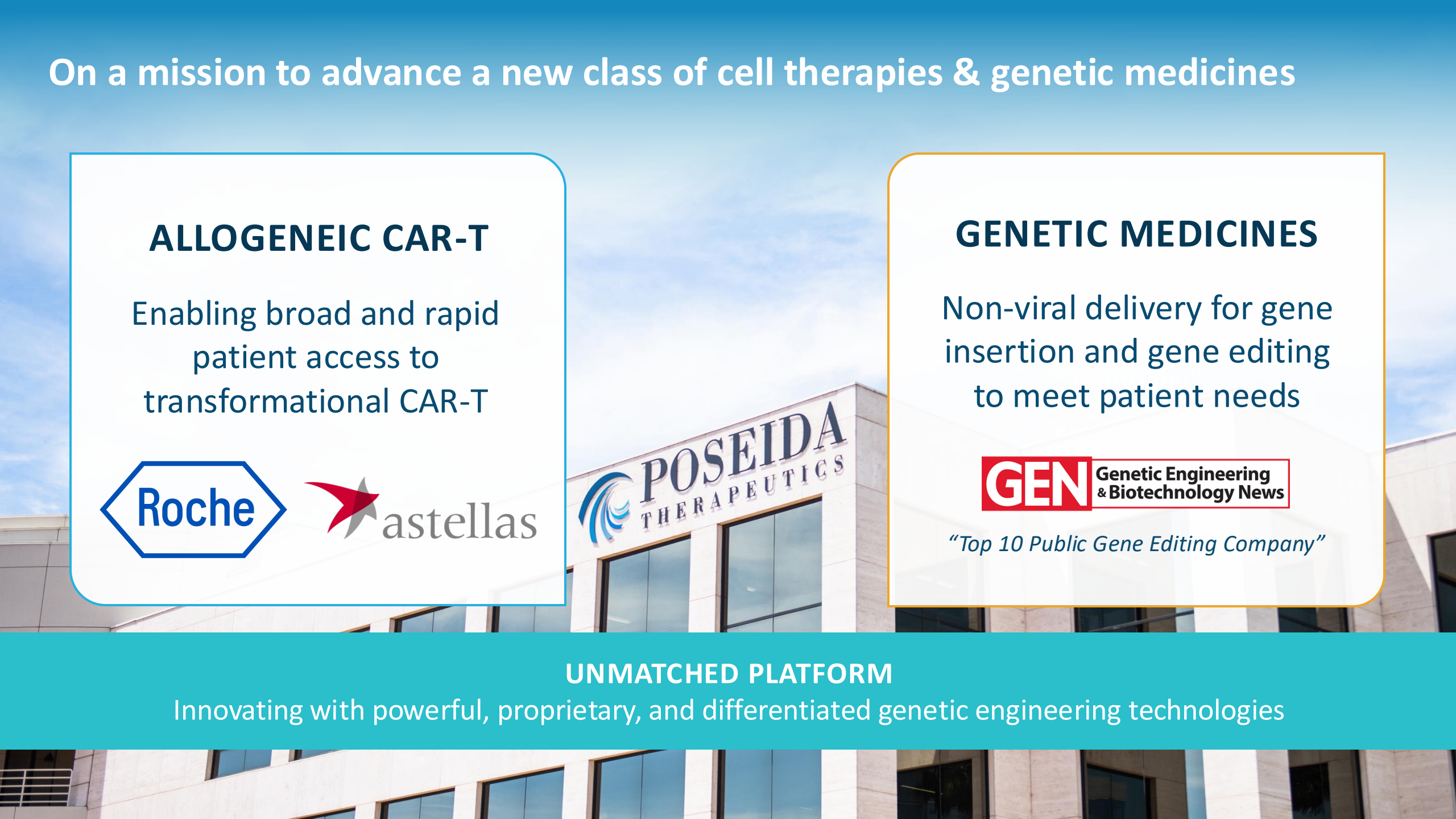
astellas

## GENETIC MEDICINES

Non-viral delivery for gene insertion and gene editing to meet patient needs

GEN Genetic Engineering & Biotechnology News

*"Top 10 Public Gene Editing Company"*

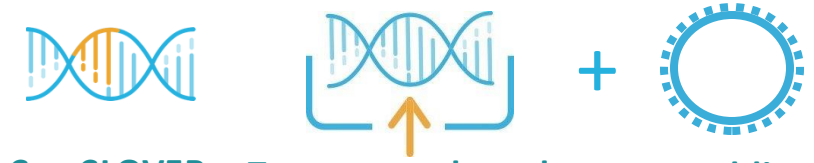



**UNMATCHED PLATFORM**

Innovating with powerful, proprietary, and differentiated genetic engineering technologies

# Our unique system of non-viral tools can be used individually or together – with the capacity to treat cancer, autoimmune and rare diseases

## POSEIDA SYSTEM OF NON-VIRAL TOOLS



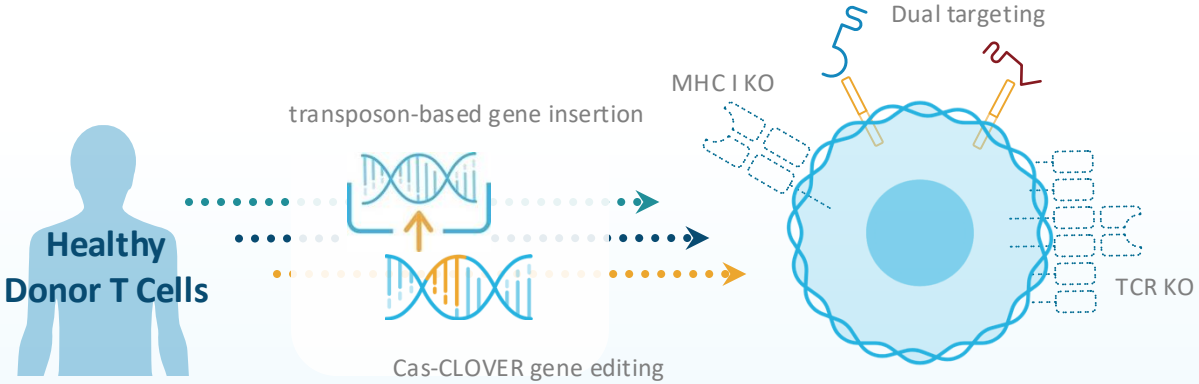
Cas-CLOVER Gene Editing

Transposon-based DNA insertion

\+

Enabling technologies

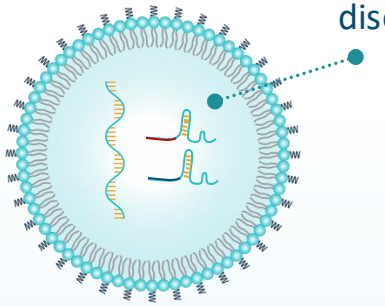
## ALLOGENEIC CAR-T



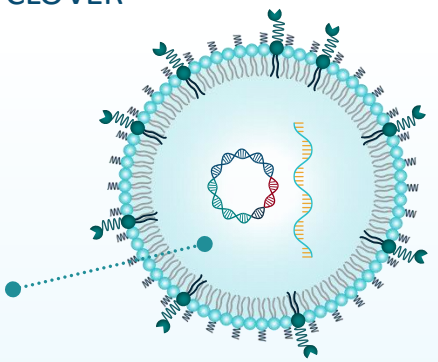

**$T_{SCM}$-rich CAR-T cells**

## NON-VIRAL GENETIC MEDICINES

Non-viral, in vivo editing of disease-relevant gene using Cas-CLOVER



Whole gene insertion via non-viral transposon for functional correction



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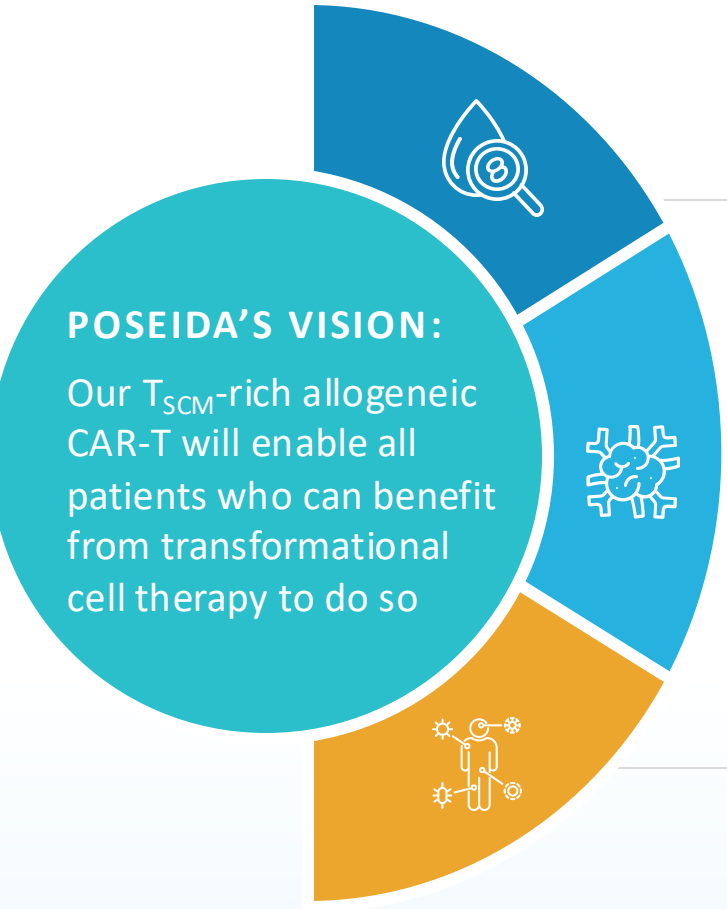
# Poseida's robust platform underpins and enables work in three cell therapy areas

*Areas of unmet need poised for disruption with the right allogeneic CAR-T platform*




| | Opportunity |
|---|---|
| **Hematology**<br>Despite auto CAR-T approvals, access heavily restricted with safety issues further compounding need for novel safe & efficacious options | **200K**<br>New U.S. patients per year, representing ~10% of all new cancer incidences[1,2] |
| **Solid Tumor**<br>Significant unmet need, historically elusive to CAR-T, requiring novel, innovative approaches for success | **2M+**<br>New U.S. patients per year[1,2] |
| **Autoimmune Disease**<br>Exciting potential for CAR-Ts to deliver "immune reset" across a broad range of diseases, with the right allo platform crucial to unlock opportunity | **5M+**<br>U.S. patients living with **MS, RA, and Lupus**, which are increasing in prevalence[3,4] |

Note: size of circles not to scale

1. Cancer Facts & Figures 2024, American Cancer Society. 2. Cancer Statistics 2024, National Cancer Institute. 3. National MS Society, Arthritis.org, CDC.
4. Miller FW. Curr Opin Immunol. 2023 Feb;80:102266.

# Poseida has built a full set of capabilities needed for success in allogeneic cell therapy

| | OTHERS | POSEIDA SYSTEM | POSEIDA ADVANTAGE |
|---|---|---|---|
| **CELL TYPE** | • Differentiated T cells<br>• Variety of other immune cell types | • T stem cell memory cells ($T_{SCM}$) | • **Product profile unique in 'stemness'**<br>• **Expected better safety**<br>• **Persistent, self-renewing cells** |
| **GENE INSERTION (add CAR)** | • Viruses (single-gene capacity) | • Nonviral transposon (multigene capacity) | • **Safety**<br>• **Product purity**<br>• **Multi-CAR products**<br>• **Maintains $T_{SCM}$ type** |
| **GENE EDITING (for alloreactivity)** | • Older technologies with lower fidelity* | • Cas-CLOVER, high-fidelity | • **Safety, quality**<br>• **Maintains $T_{SCM}$ type** |
| **SCALABLE MANUFACTURING** | • Often outsourced<br>• Challenging to reach high yields | • Wholly-owned onsite GMP facility<br>• Booster molecule-enabled yield | • **Proven CMC capability (up to over 100 doses/batch yields)**<br>• **Scalable, lower cost** |




*E.g., TALEN, Cas9
CMC, Chemistry, manufacturing and controls; GMP, good manufacturing practice.

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# Our unique and proprietary toolkit has the capabilities required to produce $T_{SCM}$-rich allogeneic CAR-T, with potential to drive depth and durability of response

## Fully Non-Viral Approach

Transposon

**Non-viral gene insertion system** 1

- ✓ **Preferentially insert into $T_{SCM}$**
- High cargo capacity enhances functionality
- Allows inclusion of multiple safety features + functionality

Cas-CLOVER

**Gene editing system** 2

- ✓ **Preserve $T_{SCM}$ cell type**
- Designed to address GVH & HVG alloreactivity
- ~25x greater fidelity vs. CRISPR-Cas9

Enabling Tech

**Quality manufacturing at scale** 3

- ✓ **Preserve $T_{SCM}$ cell type**
- High yield at low cost
- Pure CAR-T cell product
- Stored in inventory and ready for use

**Poseida IP-protected tools designed to work together as a system**

**$T_{SCM}$ correlates with depth and durability of response**




GVH, graft-versus-host; HVG, host-versus-graft

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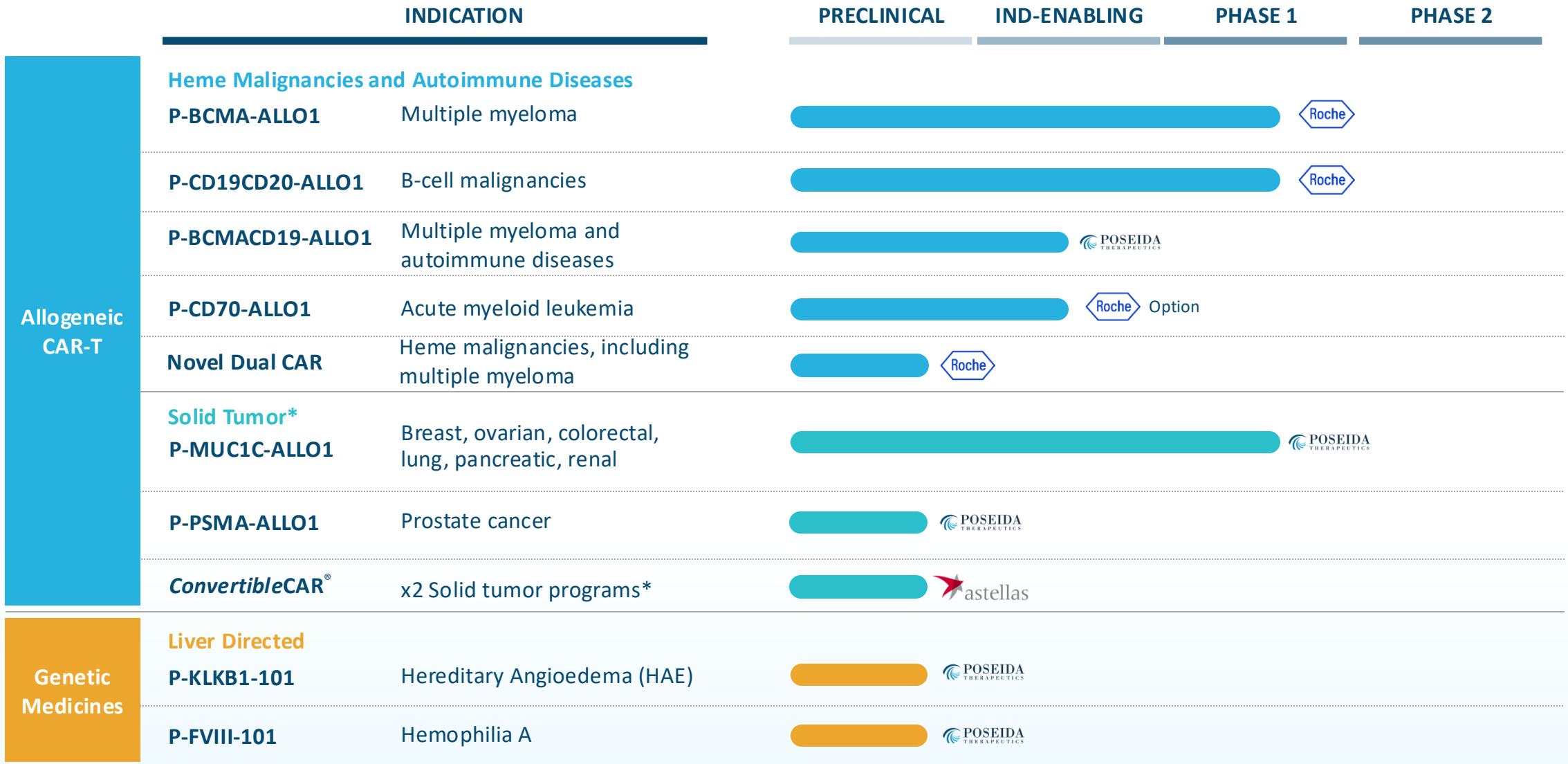
# Our rich pipeline includes partnered and wholly-owned allogeneic CAR-T as well as non-viral genetic medicines






*Solid tumor targets identified in conjunction with the research collaboration and license agreement with Astellas are yet to be disclosed

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# Poseida's path to value creation in allogeneic cell therapy

*Presently heading into our second growth horizon*

*Build Foundation*

## VALIDATE PLATFORM

- Advance non-viral allogenic CAR-$T_{SCM}$ assets in the clinic
  - P-BCMA-ALLO1 in Phase 1b; RMAT designation
  - 3 clinical stage programs across liquid & solid tumors
- Establish partnerships with Roche and Astellas
- Manufacture GMP product in-house

*Extend Approach*

## DRIVE VALUE

- Enter autoimmune disease space
- Deepen and extend pharma partnerships
- Grow wholly-owned asset pipeline
- Refine next-generation tools & technologies
- Further strengthen manufacturing, healthy donor competencies

*Disrupt Cell Therapy*

## DELIVER FOR PATIENTS

- Stream assets from allogeneic CAR-$T_{SCM}$ product engine
- Launch new cell therapy platforms for greater reach (CAR-TCR and beyond)
- Manufacture high volume, low COGS products at scale
- Commercialize partnered and own assets that have strong value propositions

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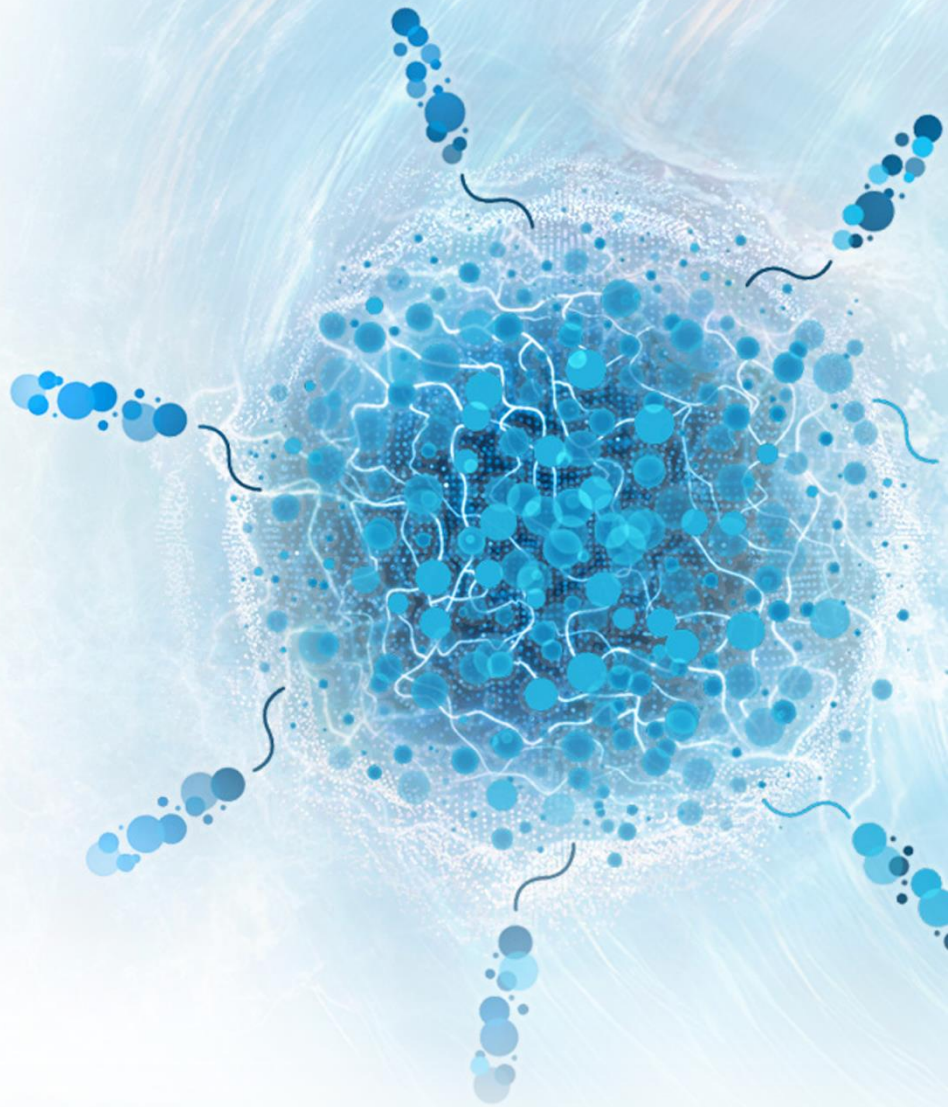
# Heme malignancies: P-BCMA-ALLO1 leads a portfolio of allogeneic $T_{SCM}$-rich CAR-T programs



**Syed Rizvi, MD**

*Chief Medical Officer*

**Bhagirathbhai Dholaria, M.D.**

Associate Professor of Medicine (Hematology/Oncology) at the Vanderbilt-Ingram Cancer Center

"Right off the bat, I was very impressed with the rapid responses we saw in a couple of initial patients we treated, including several patients of my colleagues who had failed other standard therapies, including a significant amount of extramedullary disease. And within 4 to 6 weeks, the disease melted away with the clearance of bone marrow. The other thing I was very happy to see was the safety of this therapy compared to other CAR-T cell therapy, [where] we are seeing severe CRS and ICANS including prolonged cytopenia. The overall incidence of CRS was quite manageable, and severity was so low that now we are treating most of our patients on this trial on a complete outpatient basis."

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"I was very impressed with the overall response rate. The overall response rate in the patients who were BCMA naive was 100%, and the overall response rate in patients who were BCMA exposed was 86%.

And even in the seven patients who had exposure to BCMA and talquetamab or GPRC5D, the overall response rate was 86%. That's quite impressive in this, in fact, quite refractory patient population. And the duration of response was also quite impressive. So, between 5 and 10 months."

**Tom Martin, M.D.**

Clinical Professor of Medicine, Adult Leukemia and Bone Marrow Transplantation Program and Director of Hematology, Blood and Marrow Transplantation and Cellular Therapy at UCSF

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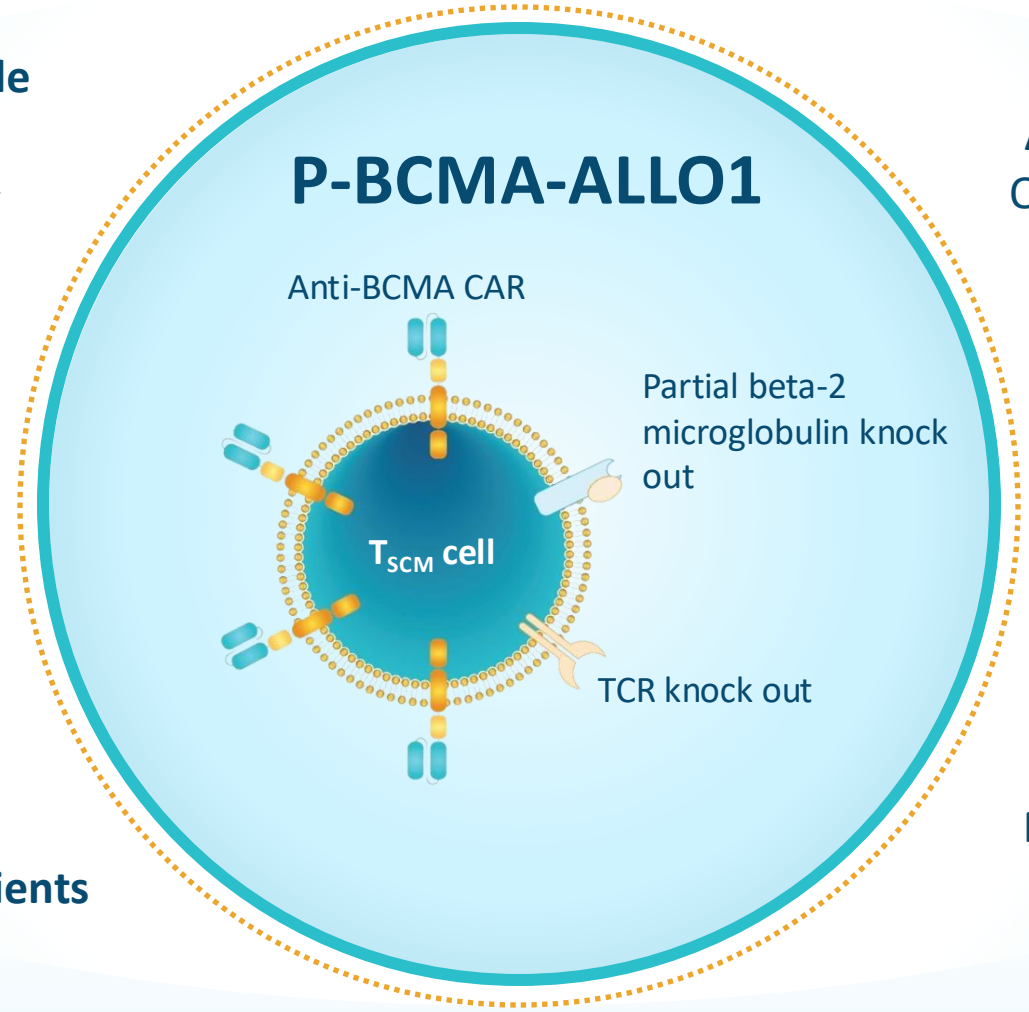
# P-BCMA-ALLO1 is a first-in-kind allogeneic CAR-T for multiple myeloma

**MM** is a **common and incurable** blood cancer, with ~12,500 estimated U.S. deaths in 2024[1]

**~179,000** people living with myeloma in the U.S., treated across multiple lines of therapy[1]

Large market, ~**$23B global, U.S. ~$14B**, projected to grow at 9-10% annually[2]

**Auto CAR-T** deliver meaningful outcomes but **only ~10% of patients can benefit today**[2]




**FDA Regenerative Medicine Advanced Therapy (RMAT)** and Orphan Drug Designation (ODD)

**Healthy donor-derived, non-viral,** $T_{SCM}$-rich CAR-T with **novel VH binder**

Developed in collaboration with **Roche; Phase 1b** clinical trial underway

**Manufactured by Poseida** in La Jolla, CA

1. SEER, American Cancer Society. 2. EvaluatePharma – 2024 projections for Global / US sales. CAGR calculated based on 2024-2036 sales projections. Patients receiving treatment calculated based on sales projections and estimated average sale price for marketed autologous CAR T. ClearView Healthcare Partners Analysis.
MM = multiple myeloma

# An allogeneic approach can greatly simplify and enable patient access to transformational CAR-T

**AUTOLOGOUS PATIENT JOURNEY**

- TREATMENT DECISION
- SCHEDULE PATIENT FOR APHERESIS (4-8 HRS)
- POTENTIAL NEED FOR RE-APHERESIS
- BRIDGING THERAPY
- PATIENT CELL PROCESSING
- SHIPMENT
- TREATMENT INITIATION
- PATIENT RESPONSE: 30 DAYS AFTER INFUSION[1]

WEEKS to MONTHS

**MONTHS**
**TIME TO CLINICAL BENEFIT**

**ALLOGENEIC PATIENT JOURNEY**

***Based on Poseida Clinical Trial Experience***

- TREATMENT DECISION
- HEALTHY DONOR PRODUCT SHIPPED — TREATMENT INITIATION 1 DAY
- PATIENT RESPONSE — 16 DAYS* AFTER INFUSION

**~3.5* WEEKS**
**TIME TO CLINICAL BENEFIT**




Source: Adapted from Elverum K, Whitman et al. Gene Therapy. April 2019. 1. Carvykti [package insert] - median time to first response was 1 month. *Based on interim data from Phase 1 P-BCMA-ALLO1 clinical trial announced at IMS in September 2024, Arms A and B.

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# P-BCMA-ALLO1 Phase 1: Background and methods

## Phase 1, open-label, dose escalation study in patients with relapsed/refractory multiple myeloma

- Must have had ≥ 3 prior lines of therapy including a PI, IMiD & CD38 mAb or be triple refractory
- **Prior BCMA targeting therapy allowed**
- ECOG 0 or 1

- **Primary Objectives:** Safety and MTD/RDE
- **Secondary Objectives:** Anti-myeloma effect; cell dose & lymphodepletion regimen selection

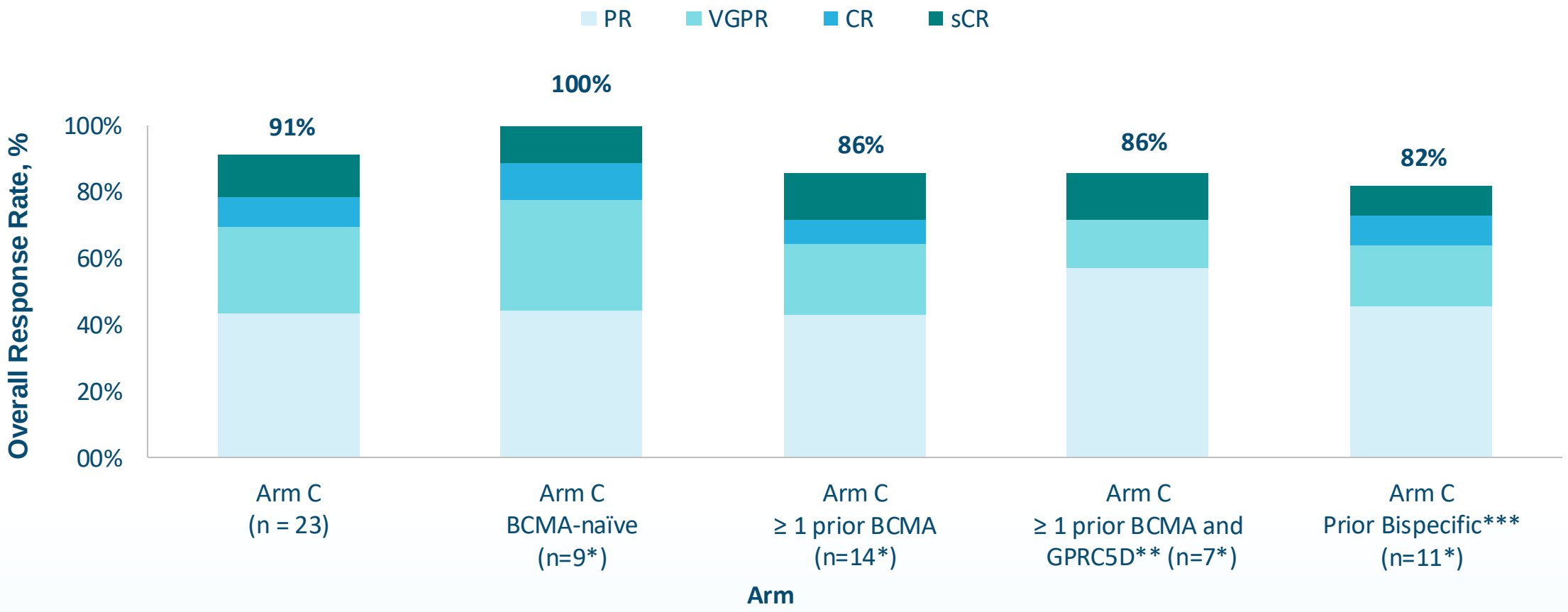
## Dosing Information

| Arm/LD dose (mg/m²)* | P-BCMA-ALLO1 Dose (cells/kg) | Total Patients† |
|---|---|---|
| Arm S (Cy 300/ Flu 30) | Range of 0.25-6 X $10^6$ | N=25 |
| Arm A (Cy 500/ Flu 30) | 2 x $10^6$ | N=19 |
| Arm B (Cy 1000/ Flu 30) | 2 x $10^6$ | N=10 |
| Arm C (Cy 750/ Flu 30) | 2 x $10^6$ | N=23 |

† Arm S includes 3 retreated subjects (received second lymphodepletion regimen followed by second P-BCMA-ALLO1 cell dose) and 1 subject treated with two P-BCMA-ALLO1 cell doses following one LD; Arm C includes 2 retreated subjects; BCMA, B cell maturation antigen; CAR-T, chimeric antigen receptor T-cell; CD38, cluster of differentiation 38; Cy, cyclophosphamide; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; Flu, fludarabine; IMiD, immunomodulatory imide drug; LD, lymphodepletion; mAb, monoclonal antibody; MTD, maximum tolerated dose; PI, protease inhibitor; RRMM, relapsed/refractory multiple myeloma.
* Flu/Cy given × 3 days. All patients in arms A, B and C dosed at P-BCMA-ALLO1 cell dose with range of 1.822 to 5.589 × 106 cells/kg

Data cutoff for safety analysis was July 31st, 2024, and September 6th, 2024, for efficacy analysis.

# P-BCMA-ALLO1 is highly clinically active in BCMA-naïve and BCMA-experienced patients




ORR= sCR, CR, VGPR or PR, including confirmed and unconfirmed responses. Evaluable patients: Obtained first response assessment by IMWG m-protein criteria or PD/death and completed Week 4 visit. Arm: C = LD – cy 750 mg/m$^2$, flu 30mg/m$^2$. All dosed Cohort 2 = Range 2.0 to < 6.0 × 10$^6$ cells/kg. Note: 2 Re-Treatment subjects included in arm C. *Includes 1 retreatment subject
**talquetamab, a GPRC5D bispecific T cell engager *** Patients may have received another BCMA targeting agent in addition to bispecific
PR, partial response; VGPR, very good partial response; CR, complete response; sCR, stringent complete response.

# P-BCMA-ALLO1 Phase 1: A higher risk, difficult to treat and more refractory patient population*

| | KarMMa[2] Idecel | Cartitude-1[3] Ciltacel | MajesTEC-1[4] Teclistamab | MonumenTAL-1[5] Talquetamab | MagnetisMM-3[6] Elranatamab | P-BCMA-ALLO1 all patients[1] | P-BCMA-ALLO1 arm C[1] |
|---|---|---|---|---|---|---|---|
| | N=128 | N=97 | N=165 | N=130 (subcut cohorts) | N=123 | **N=72** | **N=21** |
| **Age group ≥ 65, # (%)** | 45 (35%) | 35 (36%) | 24 (15%) (age≥ 75) | 37 (29%) (age >=70) | 80 (65%) | **43 (60%)** | **10 (48%)** |
| **Minority patient representation** | NA | 20 (21%) | 31 (19%) | 23 (18%) | 26 (21%) | **24 (33%)** | **8 (38%)** |
| **ECOG 0** | 57 (45%) | 39 (40%) | 55 (33%) | -- | 45 (37%) | **12 (29%)** | **8 (38%)** |
| **High risk cytogenetics, # (%)*** | 45 (35%) | 23 (24%) | 38** (26%) | 18 ***(16%) | 31 (25%) | **50 (69%)** | **13 (62%)** |
| **EMD, # (%)** | 50 (39%) {incl. bone-based lesions} | 13 (13%) | 8 (20%) | -- | 39 (32%) | **19 (26%)** | **8 (38%)** |
| **Previous ASCT** | 120 (94%) | 87 (90%) | 135 (81%) | 111 (85%) | -- | **42 (58%)** | **14 (67%)** |
| **1 prior anti-BCMA/GPRC5D** | 0 | 0 | 0 | 42 (34%) (# of prior BCMA not specified) | 0 | **31 (43%)** | **13 (62%)** |
| **Multiple prior BCMA/GPRC5D** | 0 | 0 | 0 | -- | 0 | **15 (21%)** | **8 (38%)** |
| **Bridging Therapy, # (%)** | 112 (88%) | 73 (75%) | NA | NA | NA | **0 (0%)** | **0 (0%)** |

*Defined as the presence of Del 17p, t(14;16), t(4;14) for comparators; defined as t(4:14), t(14:16); p53 deletion; del17p; t(14:20); gain 1q for P-BCMA-ALLO1; No head-to-head trial has been conducted evaluating P-BCMA-ALLO1 against other products included herein. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, study design, and other factors; **Reported as 38/148 patients ***reported as 18/112 patients.

[1] interim data as of Jul 31st, 2024.[2]Munshi et al.; [3]Berdeja et al.; [4]Martin et al. (2023). [5] Chari et al, 2022 [6]Lesokhin, et al. 2023

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# P-BCMA-ALLO1 early safety and efficacy results appear encouraging in comparison with marketed **autologous CAR-T therapies***

## Safety

| Late-line MM Patients | ABECMA[1] | CARVYKTI[2] | P-BCMA-ALLO1 (Arm C) |
|---|---|---|---|
| **Safety Pop** | N=349 | N=285 | N=23*** |
| **CRS, All Grade** | 89% | 84% | **39%** |
| **ICANS, All Grade** | 40% (all CAR-T Neurotox) | 13% | **13%** |
| **All infections** | 61% | 57% | **47%** |
| **Parkinsonism** | Yes | Yes | **No** |
| **Bridging Tx** | Yes | Yes | **No** |
| **SPM signal** | Yes | Yes | **No** |

## Efficacy

| Late-line MM Patients | ABECMA (ITT)[1] | CARVYKTI (ITT)[2] | P-BCMA-ALLO1 (ARM C) |
|---|---|---|---|
| **Efficacy Pop** | N=135 | N=113 | N=23*** |
| **ORR** | **53%** | **84%** | **91%** |
| **sCR + CR** | 21% | 69% | 22%** |
| **VGPR+** | **39%** | **81%** | **48%**** |

**P-BCMA-ALLO1 had consistent and favorable safety profile in both BCMA-naïve & BCMA-experienced patients**

*No DLTs, no grade ≥3 CRS or ICANS, no GvHD, no parkinsonism*

*Quick cytopenia resolution and low serious infection rates*

***ABECMA, CARVYKTI and TECVAYLI enrolled BCMA-naïve patients only***

1. . Abecma [package insert]. Summit, NJ: Celgene Corporation; 2024; 2. Carvykti [package insert]. Horsham, PA: Janssen Biotech; 2024

*No head-to-head trial has been conducted evaluating P-BCMA-ALLO1 against other products included herein. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, study design, and other factors. **Data Maturing *** Includes unconfirmed responses and 2 retreated subjects. Full safety database includes N=72 and results are consistent with Arm C.

SPM, secondary primary malignancy; DLT, dose limiting toxicities; CRS, cytokine release syndrome; ICANS, immune effector cell associated neurotoxicity syndrome; GvHD, graft versus host disease; ORR, overall response rate




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# P-BCMA-ALLO1 early safety and efficacy results appear encouraging in comparison with marketed **bispecific therapies***

## Safety

| Late-line MM Patients | TALVEY[1] | TECVAYLI[2] | ELFREXIO[3] | P-BCMA-ALLO1 (Arm C) |
|---|---|---|---|---|
| **Safety Pop** | N=339 | N=165 | N=183 | N=23*** |
| **CRS, All Grade** | 76% | 72% | 58% | **39%** |
| **ICANS, All Grade** | 9% (N=265) | 6% | 3% | **13%** |
| **All infections** | 53% | 61% | 42% | **47%** |
| **SPM signal** | - | - | - | **No** |

## Efficacy

| Late-line MM Patients | TALVEY (ITT)[1] | TECVAYLI (ITT)[2] | ELREXFIO (ITT)[3] | P-BCMA-ALLO1 (ARM C) |
|---|---|---|---|---|
| **Efficacy Pop** | N=87 | N=110 | N=97 | N=23*** |
| **ORR** | **74%** | **62%** | **58%** | **91%** |
| **sCR + CR** | 33% | 28% | 26% | 22%** |
| **VGPR+** | **58%** | **57%** | **52%** | **48%**** |

Bispecifics are dosed weekly and in cycles after cycles, tethering the patient to the medical center affecting the quality of life of the patient; meanwhile CAR-T has “one and done” dosing approach.

1. Talvey [package insert]. Horsham, PA: Janssen Biotech, 2023; 2.Tecvayli [package insert]. Horsham, PA: Janssen Biotech; 2022. 3. Elrexfio [package insert]. New York, NY Pfizer Inc: 2023.

*No head-to-head trial has been conducted evaluating P-BCMA-ALLO1 against other products included herein. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, study design, and other factors.
**Data Maturing
*** Includes unconfirmed responses and 2 retreated subjects.
Full safety database includes N=72 and results are consistent with Arm C.




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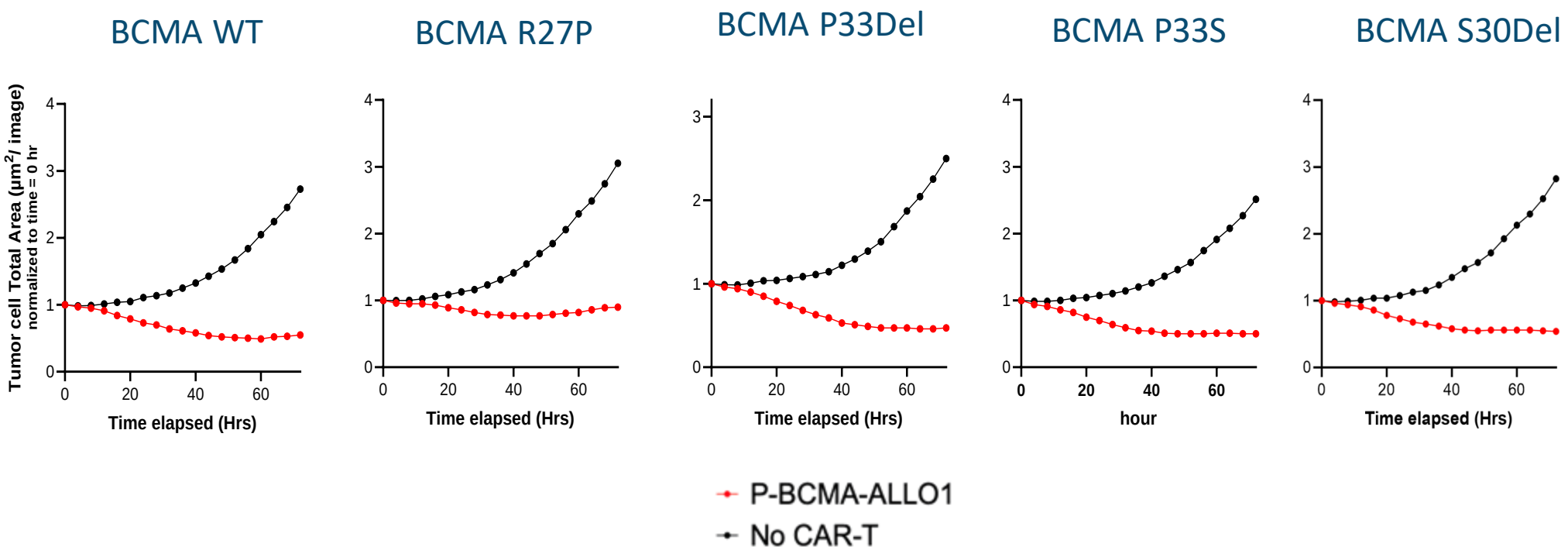
# P-BCMA-ALLO1 effectively targets mutations that are known to arise in patients with relapse after prior anti-BCMA therapies

NEW DATA

## P-BCMA-ALLO1 kills tumor cells expressing wild type BCMA or clinically identified BCMA escape mutants




Poseida data on file

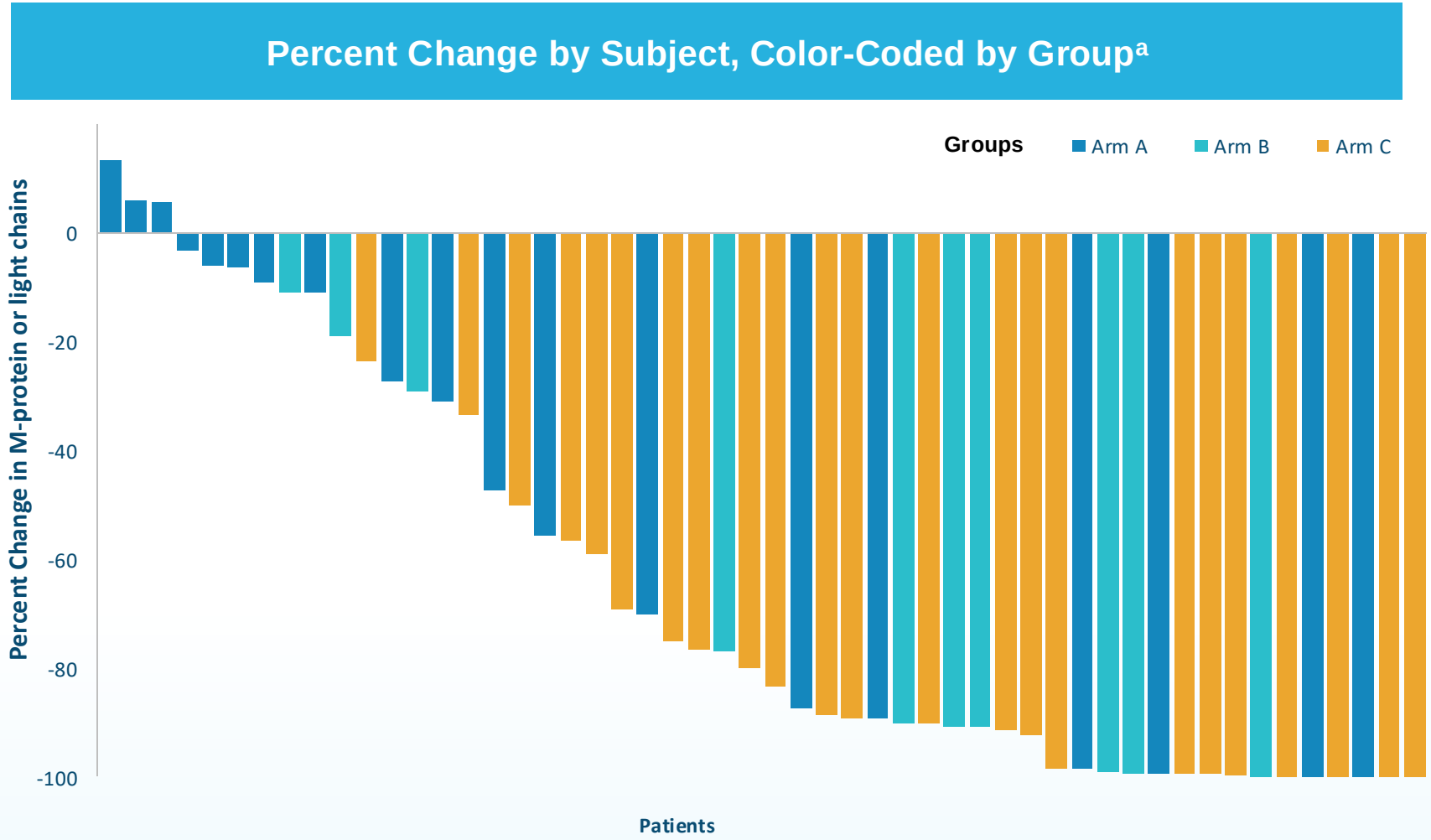



POSEIDA THERAPEUTICS

# Patients across Arms A, B, and C show response in disease markers, with encouraging early mTTR and mDOR

| Median Time to Response<br><br>(Pooled Arms A + B) | Median Duration of Response for Patients with ≥ 6 Months of Follow Up<br><br>(Pooled Arms A + B) |
|---|---|
| **16 Days**<br>(95% CI 15 - 22) | **232 Days**<br>(95% CI 158 - 308) |

**Note**: Arm C is the least mature cohort (most recently enrolled). Current median follow up of Arm C is less than 3.5 months, therefore DOR could not be estimated at this time




[a] The % change on Y axis is based on the myeloma parameter that was measurable at baseline and is used to determine response on each subject over time, such as SPEP, UPEP or FLC.
MTTR: median time to response; mDOR: median duration of response; SPEP, serum protein electrophoresis; UPEP, urine protein electrophoresis; FLC, free light chain.




POSEIDA THERAPEUTICS

# Summary: P-BCMA-ALLO1 demonstrates compelling early efficacy and safety results in heavily pretreated patients while delivering on the patient experience promise

## High efficacy (ORR) in BCMA-naive and BCMA-experienced patients[1]

- **ORR in Arm C is 91%**
- **100% ORR in BCMA naïve patients**
- **Impressive efficacy seen in BCMA experienced patients,** including **86% ORR** in pts with ≥ 1 prior BCMA/ ≥ 1 prior BCMA + GPRC5D
- **P-BCMA-ALLO1 is effective following prior bispecific therapy** with an 82% ORR

## Compelling Emerging Safety Results[2]

- **Differentiated safety** vs. auto CAR-T and bispecific/T-cell engagers
- **No** GvHD, DLTs, Parkinson's-like symptoms observed
- **Low CRS, neurotoxicity** all Gr ≤2
- Majority of **AEs were Grade 1/2**
- **Fully non-viral approach** and available safety switch vs. autologous/virus SPM concerns

## Superior Patient Experience

- **100% of enrolled patients treated** with in-spec product
- **Outpatient** optionality for ease and reimbursement
- **No** waiting…available on-demand from inventory
  - **No** invasive patient apheresis
  - **No** anti-myeloma bridging therapy
- **~3.5 weeks from patient enrollment to clinical response**




[1] Interim data as of September 6, 2024. [2]Interim data as of July 31, 2024

POSEIDA THERAPEUTICS

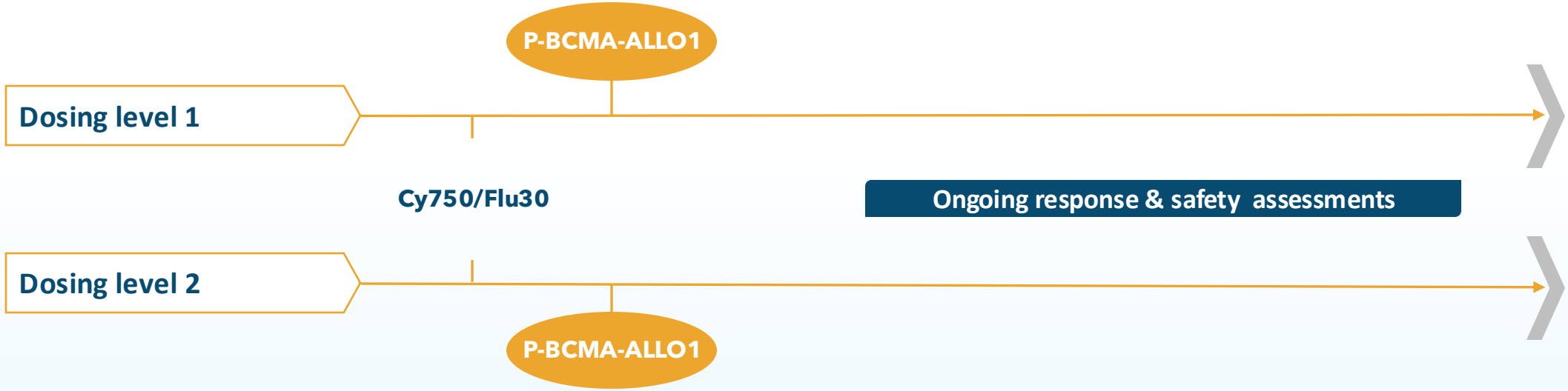
# Phase 1b study schema, dose expansion is actively enrolling two dosing cohorts

**Phase 1/1b, open-label, dose expansion study in patients with relapsed/refractory multiple myeloma**

**Key Inclusion**:

- Must have had ≥ 3 prior lines of therapy including a PI, IMiD & CD38 mAb or be triple refractory
- Documented measurable disease
- ECOG 0 or 1
- n=40

- **Primary Endpoints:** ORR based on IMWG criteria
- **Secondary Endpoints:** Safety, tolerability and efficacy of P-BCMA-ALLO1 (ORR, CR/sCR, TTR, DOR, PFS, OS)
- **Exploratory Endpoints**: MRD, cellular kinetics, BCMA expression in the bone marrow, soluble BCMA in the blood





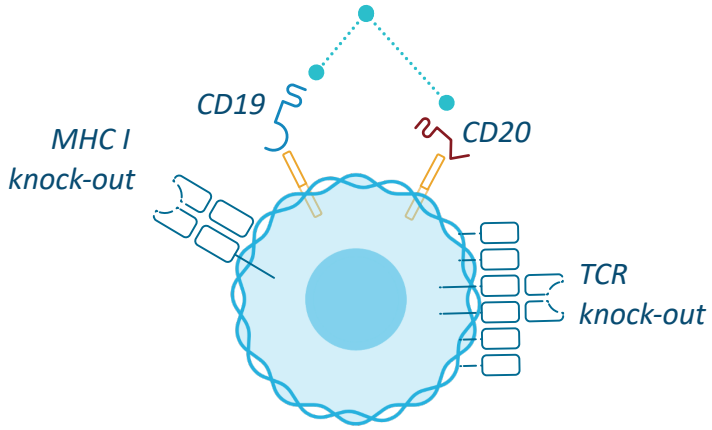


IMWG, International Myeloma Working Group; MRD, minimal residual disease; DOR, duration of response; PFS, progression-free survival; OS, overall survival; TTR, time to response

POSEIDA THERAPEUTICS

# P-CD19CD20-ALLO1 – Poseida's first dual CAR-T is being developed in partnership with Roche

**Differentiated, carrying 2 full length CARs and other Poseida platform elements[1]**




- **Relapse due to target escape remains a common problem in B-cell malignancies**
- **Early autologous CD19/CD20 CAR-T data suggests dual targeting can be more effective**

***Preclinical data planned for ASH 2024; Clinical data planned for 2025****

## Clinical Trial

- Phase 1 study enrolling selected B-cell malignancies, prior Auto CAR-T and TCE is allowed (NCT04960579)
- 3x3 design, with flexibility for expansion, exploring multiple LD regimens

## Status

- Multiple learnings from other Poseida programs have been incorporated
- Dose escalation is ongoing




*Subject to coordination with Roche
1. Safety switch, selectable marker, TCR KO, β2M KO

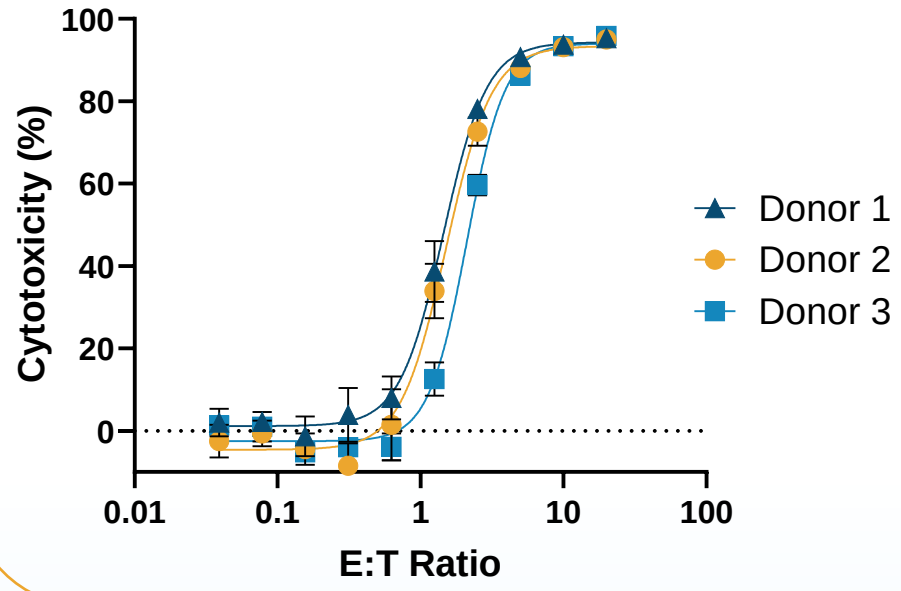
POSEIDA THERAPEUTICS

# P-CD19CD20-ALLO1 is a potent CAR-T product against CD19- and CD20-dual positive B-Cell malignancies

NEW DATA

- **High in vitro potency** against CD19- and CD20-positive Raji model
- **High in vivo antitumor efficacy** across CAR-T lots produced from multiple healthy donors and dose levels

## In vitro potency




## In vivo antitumor efficacy

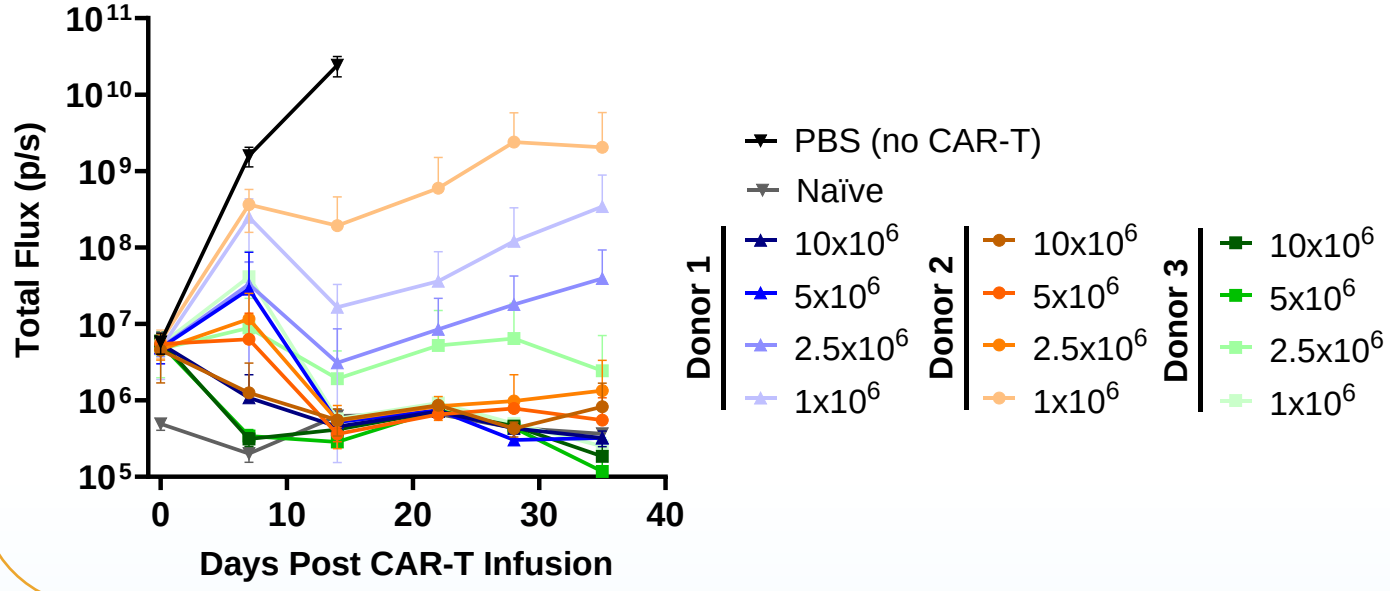



**Figure 2. P-CD19CD20-ALLO1 CAR-T cells produced from three healthy donors exhibit robust antitumor efficacy against CD19- and CD20-dual positive Raji Burkitt's lymphoma cell line in vitro and in vivo.** Left Panel. Luciferase-expressing WT Raji cells (CD19+CD20+) were co-cultured for 48 hours with P-CD19CD20-ALLO1 CAR-T cells at the indicated Effector:Target (E:T) ratios and viable cells were quantified using a luminescence-based assay. Cytotoxicity was calculated by normalization to Raji cells alone samples. Right Panel. NSG mice were intravenously implanted with WT Raji (CD19+CD20+) cells and received 4 days later the indicated doses of P-CD19CD20-ALLO1 CAR-T cells. Tumor burden was monitored by bioluminescence imaging. Data is presented as mean ± SEM (n=5 mice/group).




POSEIDA THERAPEUTICS

# P-CD19CD20-ALLO1 may prevent relapse due to antigen escape by targeting single-positive tumor cells

NEW DATA

- P-CD19CD20-ALLO1 shows **dose-dependent and high tumor control** in two in vivo models of antigen escape

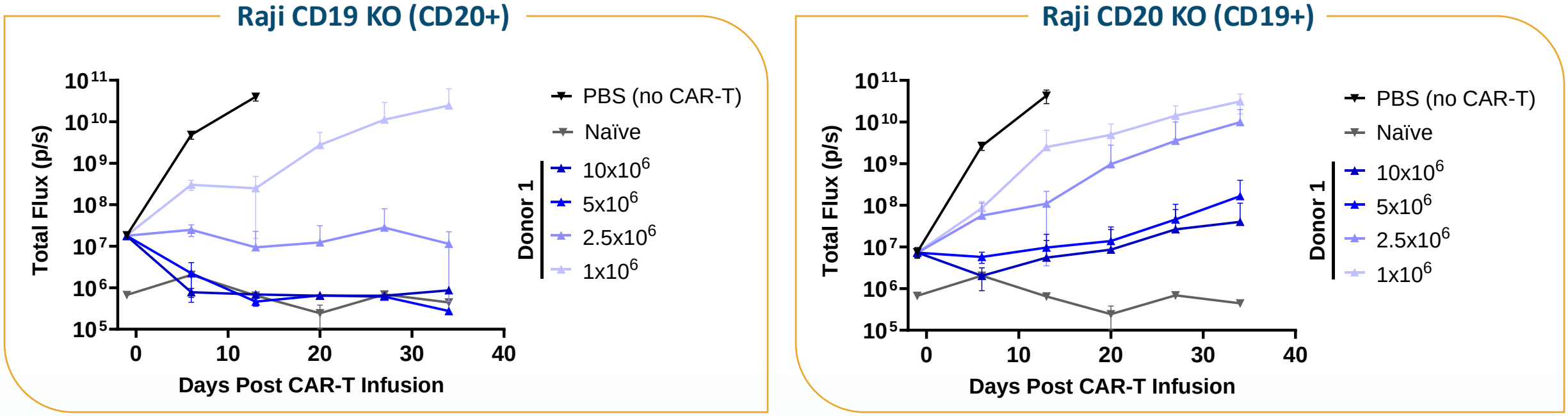


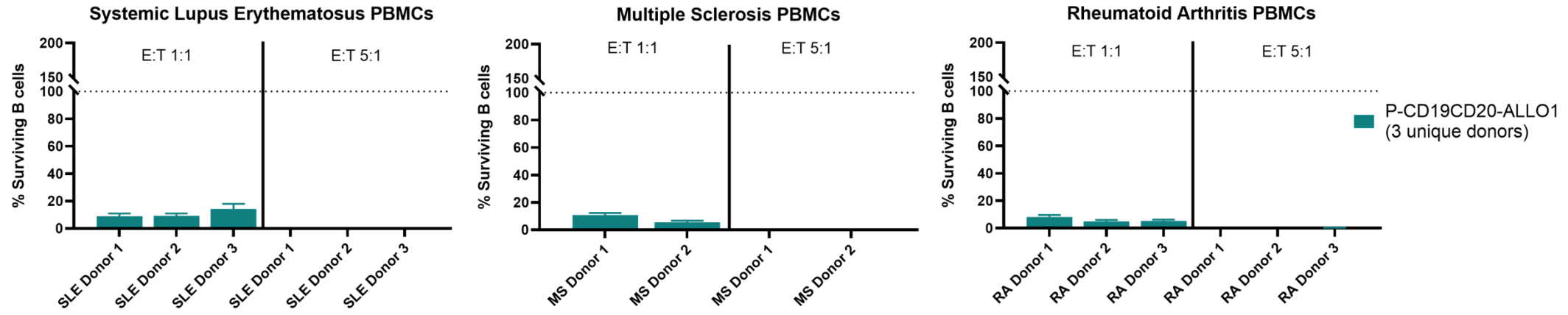

**Figure 3. Dual-targeting P-CD19CD20-ALLO1 CAR-T cells can prevent relapse due to antigen loss.** P-CD19CD20-ALLO1 show strong in vivo antitumor efficacy against Raji cells genetically engineered to express only CD20 (CD19 KO – left panel) or CD19 (CD20 KO – right panel) in a dose-dependent manner. NSG mice were intravenously implanted with CD19 or CD20-single positive Raji cells and 4 days later received the indicated doses of P-CD19CD20-ALLO1 CAR-T cells. Tumor burden was monitored by bioluminescence imaging. Data is presented as mean ± SEM (n=5 mice/group).




POSEIDA THERAPEUTICS

# P-CD19CD20-ALLO1: Robust killing of B cells from primary human autoimmune PBMCs

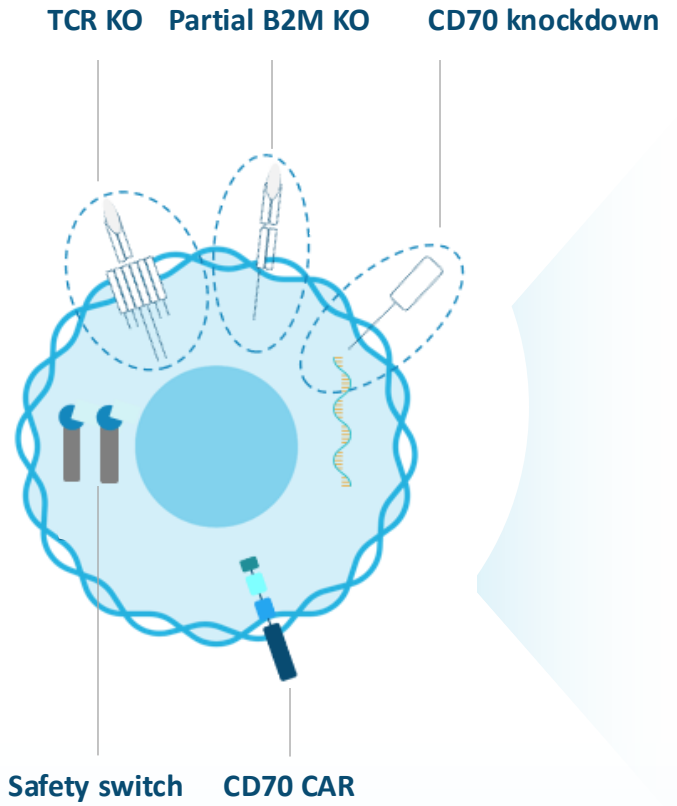
NEW DATA




- P-CD19CD20-ALLO1 assayed for cytotoxicity against B cells in primary human PBMCs from autoimmune patients (RA, SLE, MS)
  - Average of 3 lots of P-CD19CD20-ALLO1 (3 unique donors)
- Robust depletion of B cells in most samples at 5:1 E:T
  - No cytotoxicity observed against NK cells or macrophages above no CAR-T controls
  - CD20+ T cell depletion was expected and observed
    - ~5-8% of T cells in MS are CD20+; <2% in healthy donors
- Data are similar to P-BCMA-ALLO1 cytotoxicity against cancerous B cell lines

E:T, Effector:Target ratio

# P-CD70-ALLO1: Introducing an IND-enabling stage asset with multi-indication potential, including in heme malignancies and solid tumors




## Key features

**Novel allogeneic, $T_{SCM}$-rich CD70-targeting CAR-T engineered for potency, safety, and manufacturability**

- Unique shRNA knockdown of CD70 from a multi-cistronic transgene to avoid fratricide and increase potency, with no genotoxicity risk
- Potent cytotoxicity against CD70+ AML cell lines in vitro and in vivo, without impacting normal hematopoietic stem and progenitor cells
- Ablates CD70+ activated alloreactive lymphocytes, which may prolong persistence by inhibition of immune rejection (T cell shield)

**Proof-of-concept exists for use of CD70 approaches in solid (RCC) and liquid tumor (AML), including from early CAR-T studies and monoclonal antibodies**

- Roche has an exercisable option on this program

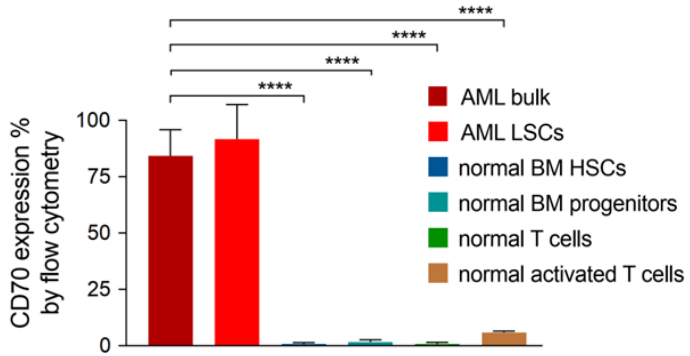
**P-CD70-ALLO1 has great potential in high unmet medical need diseases**

# CD70 is an attractive antigen target for CAR-T, given expression levels as well as early clinical evidence in solid and liquid tumors

*CD70 expression seen across tumor types*

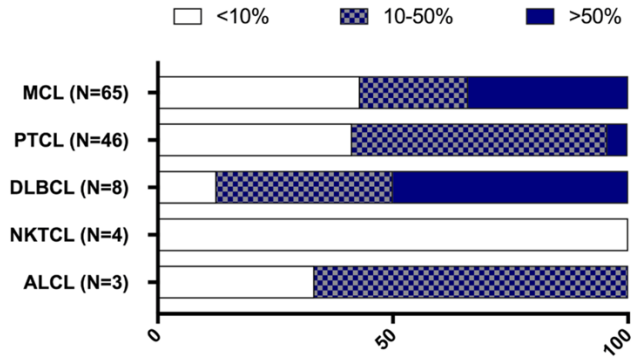
## Liquid tumors

### AML



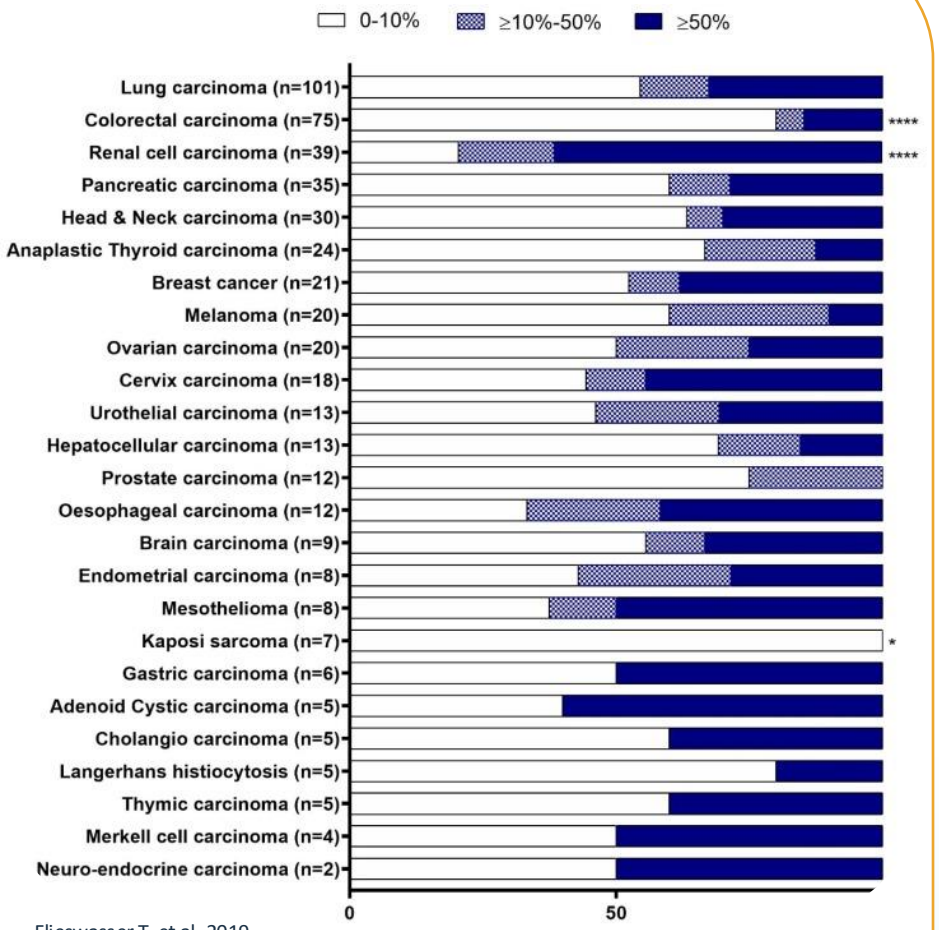

Perna F et al. 2017

### Lymphomas




Flieswasser T et al, 2019

## Solid tumors




Flieswasser T, et al, 2019

**Early clinical validation of CD70 exists across modalities** (CAR-T, ADCs) and therapeutic areas (AML, RCC) [1,2], with a **solid emerging safety record** attributed to no expression on normal hemopoietic stem cells[3]




[1]Pabst et al. 2023. [2]Pal SK et al. 2024. [3]Perna et al, 2017; Riether et al, 2017; Sauer et al 2021.

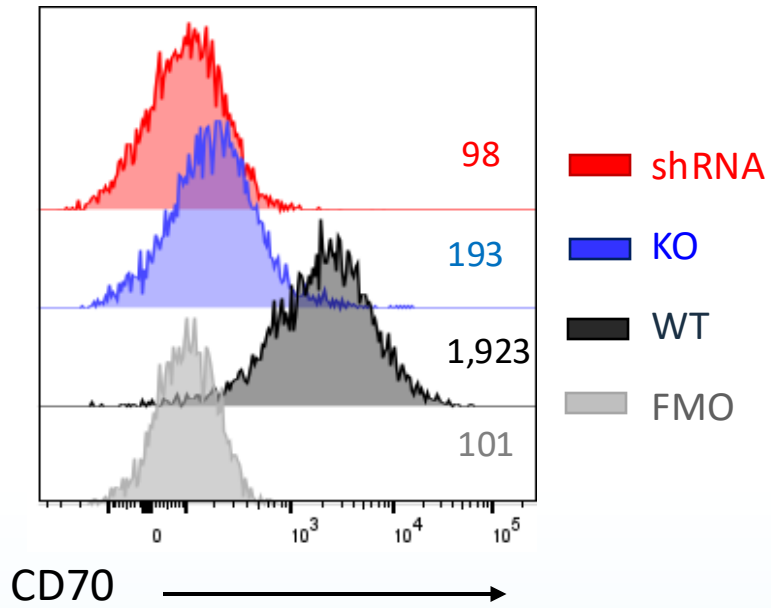
POSEIDA THERAPEUTICS

# Poseida approach using robust shRNA-mediated depletion (knockdown) of CD70 yields CAR-T with optimal in vivo potency

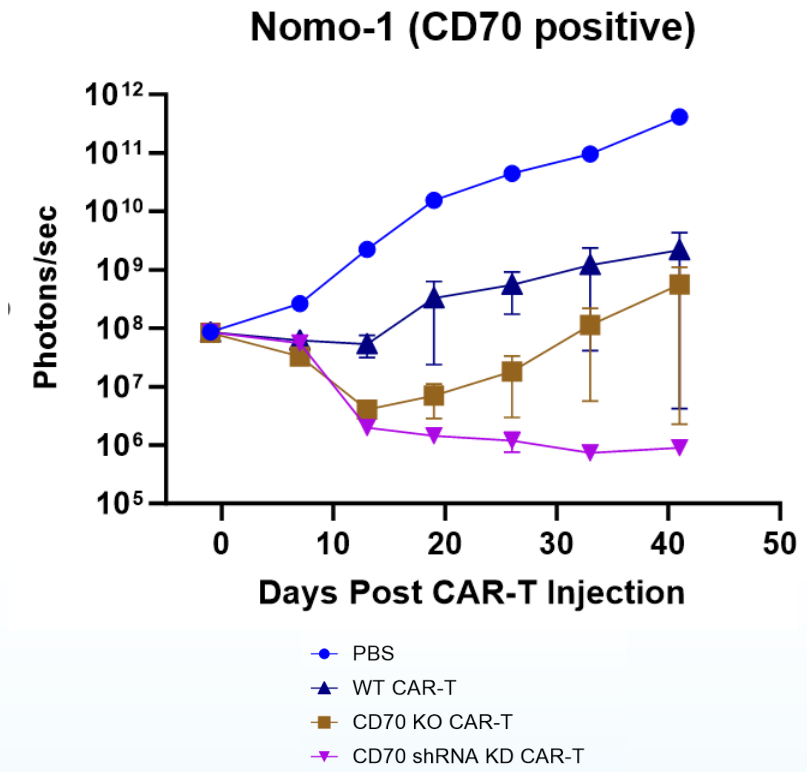
*Superior to CD70 knockout through gene editing*

NEW DATA

## Highly efficient knockdown of CD70 in CAR-T cells using shRNA




## Robust in vivo activity against AML models







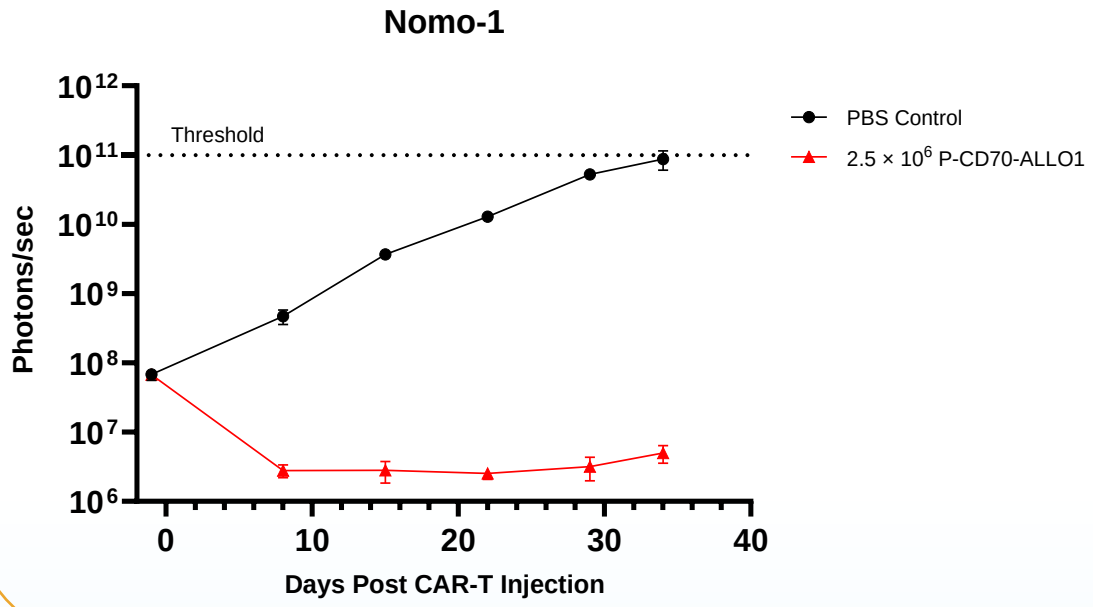
AML, acute myeloid leukemia; FMO, fluorescence-minus-one control; KO, knockout; PBS, phosphate buffered saline; shRNA, short hairpin ribonucleic acid; WT, wildtype

POSEIDA THERAPEUTICS

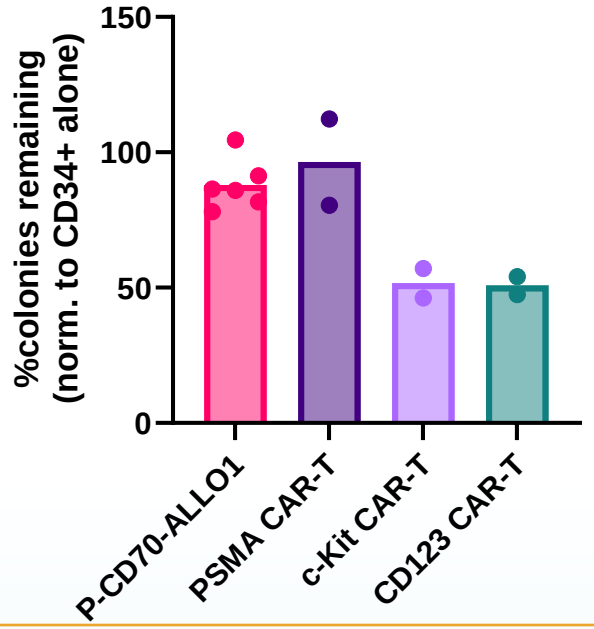
# P-CD70-ALLO1 exhibits robust anti-AML effect in vivo with no HSC toxicity

NEW DATA

## P-CD70-ALLO1 has robust in vivo potency against CD70+ AML Nomo-1 xenograft




## Healthy donor HSC are killed by c-Kit & CD123 CAR-T, but not by P-CD70-ALLO1 or control PSMA CAR-T







Note: P-CD70-ALLO1 cells were produced from 3 individual healthy donors, and co-cultured with healthy donor HSC

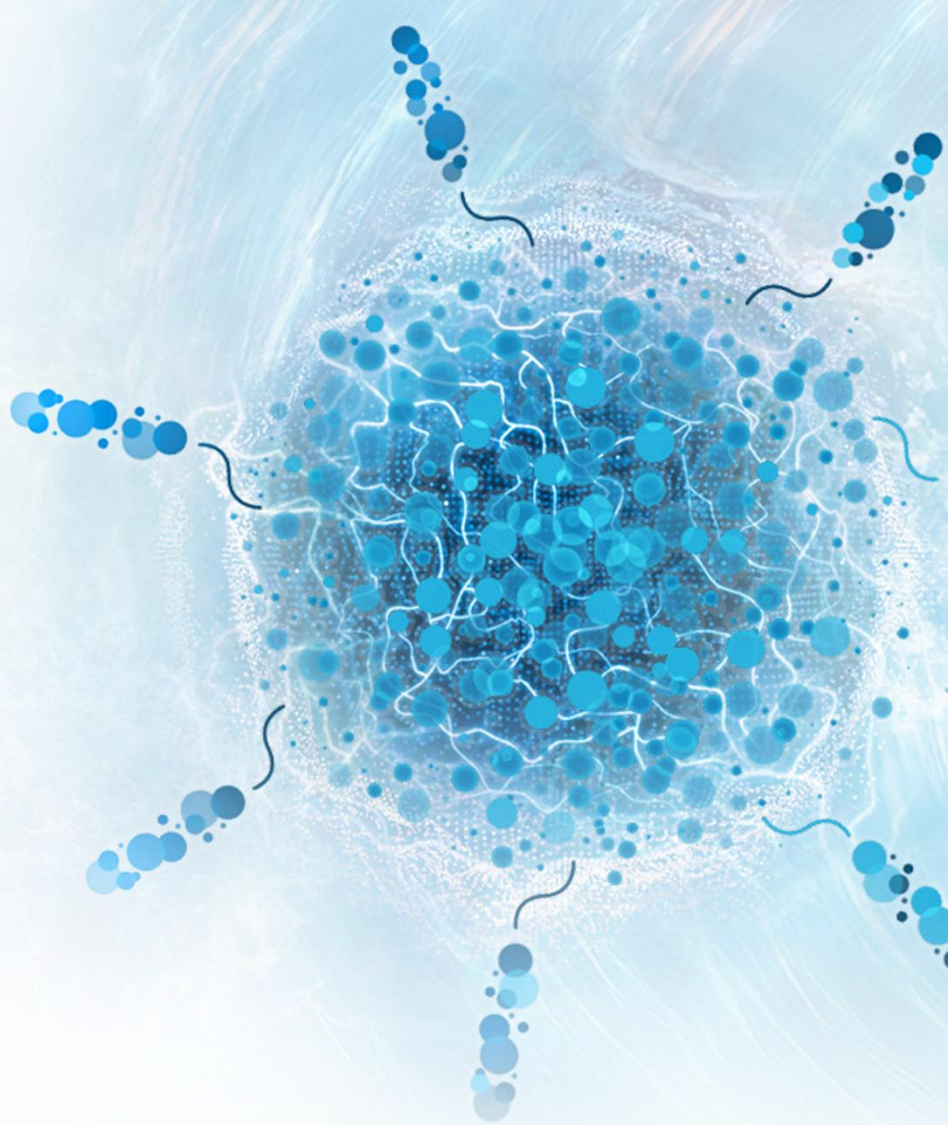
POSEIDA THERAPEUTICS

POSEIDA THERAPEUTICS

# From hematology to autoimmune disease: Poseida's BCMA-CD19 dual CAR-T

**Kurinji Pandiyan, PhD**

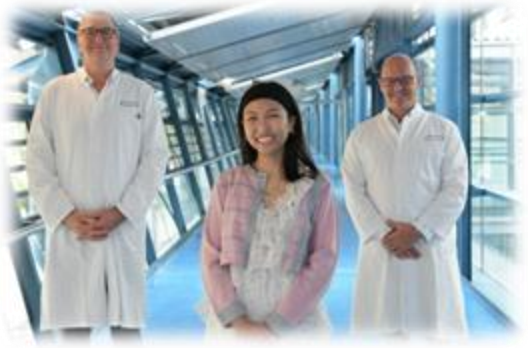
*Vice President, Portfolio & Strategy*



# CAR-T and related immunotherapies show great promise and present new questions in autoimmune disease

## 2021

- Seminal results from Georg Schett group sparked explosive interest



- **Unmet need and market potential appear vast**

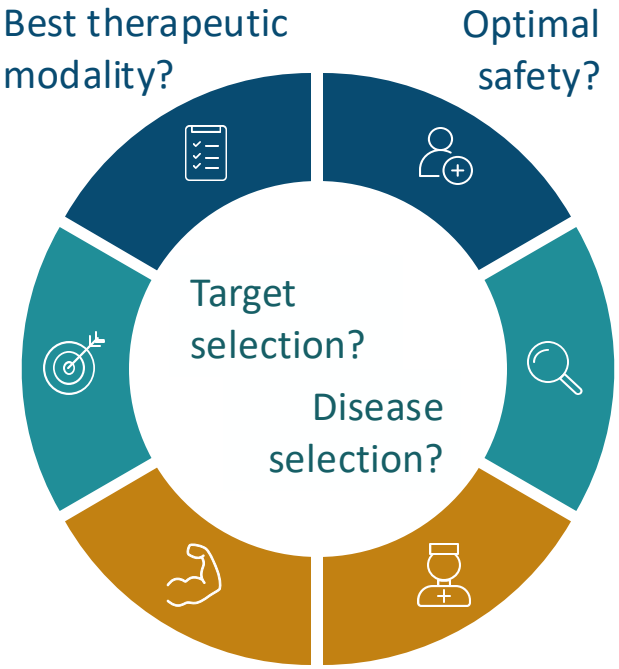
## 2022 – 2024

- Rapid pivot of oncology / cell therapy companies, especially allogeneic players
- Many trials underway in multiple diseases

**Mixed Results:**

- Encouraging early efficacy, including allogeneic
- Questions emerging on safety, durability of remissions

## Today's questions







POSEIDA THERAPEUTICS

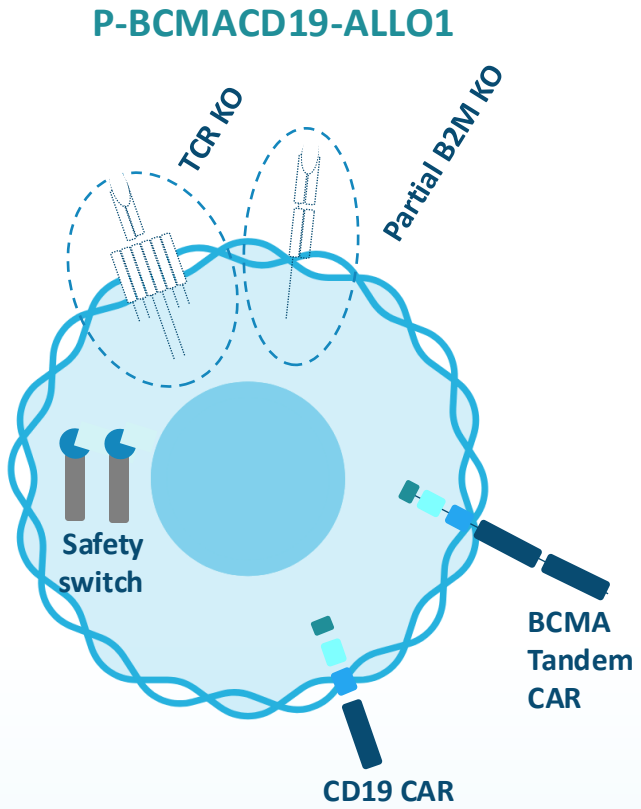
# Poseida's clinically validated $T_{SCM}$-based platform is well-suited to autoimmune disease applications

| DESIRED PROFILE OF IMMUNOTHERAPY FOR AUTOIMMUNE DISEASE | | POSEIDA PLATFORM FEATURES |
|---|---|---|
| **Efficacy** | • Deep depletion of B cells, then rapid recovery<br>• Ability to target cell populations of interest | ✓ **Clinical validation** of CAR-$T_{SCM}$ through oncology work<br>✓ Pipeline programs include **targets of interest** (BCMA, CD19, CD20, CD70)<br>✓ **Transposon technology** enables multi-target dual CARs, CAR-TCRs |
| **Safety** | • Near term tolerability (CRS, neurotox, infections)<br>• Long term safety (secondary malignancies) | ✓ Distinctively **low rates & mild** in oncology, despite higher cell burden<br>✓ Fully **non-viral** technology, rapid-acting **embedded safety switch**<br>✓ **High fidelity** gene editor |
| **Patient reach & experience** | • Immediate and reliable treatment<br>• Outpatient and community care settings | ✓ Some Poseida oncology patients receiving all **treatment outpatient**<br>✓ Multiple **lymphodepletion strategies**<br>✓ **Off-the-shelf,** to simplify logistics and treat patients with no waiting |
| **Manufacturing scalability for volume & COGS** | • Ability to meet patient demand in higher – prevalent diseases<br>• COGS able to support AID volume proposition | ✓ Proven ability to **manufacture at scale** from **healthy donors**<br>✓ Targeting **biologics-like COGM** |




AID, autoimmune disease; CRS, cytokine release syndrome; COGS, cost of goods sold; COGM, cost of goods manufactured

# P-BCMACD19-ALLO1 (IND-enabling stage): Poseida's wholly owned investigational therapy for autoimmune disease and hematological malignancies

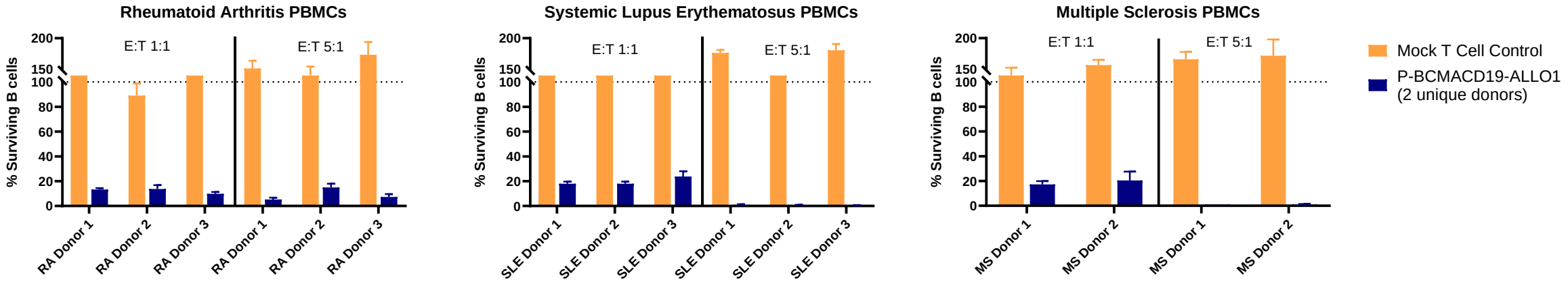



- **Potent cytotoxicity against BCMA and CD19, a key feature for both autoimmune disease and in oncology given cells that need to be targeted**
- **Key construct attributes:**
  - Dual CAR configuration, with tandem BCMA CAR, for optimal potency
  - Intracellular domain (ICD) combination gives superior potency
  - Incorporation of Poseida allo platform & process improvements
- **Preclinical proof-of-concept established for use of BCMA-CD19 in autoimmune and oncology models**
- **Clinical validation of dual BCMA-CD19 targeting with autologous CAR-T**

NEW DATA

# P-BCMACD19-ALLO1: Robust killing of B cells across multiple autoimmune diseases

## In vitro proof-of-concept in autoimmune disease




**Robust in vitro elimination of primary autoimmune patient derived B cells across different effector to target ratios**

PBMC, peripheral blood mononuclear cells

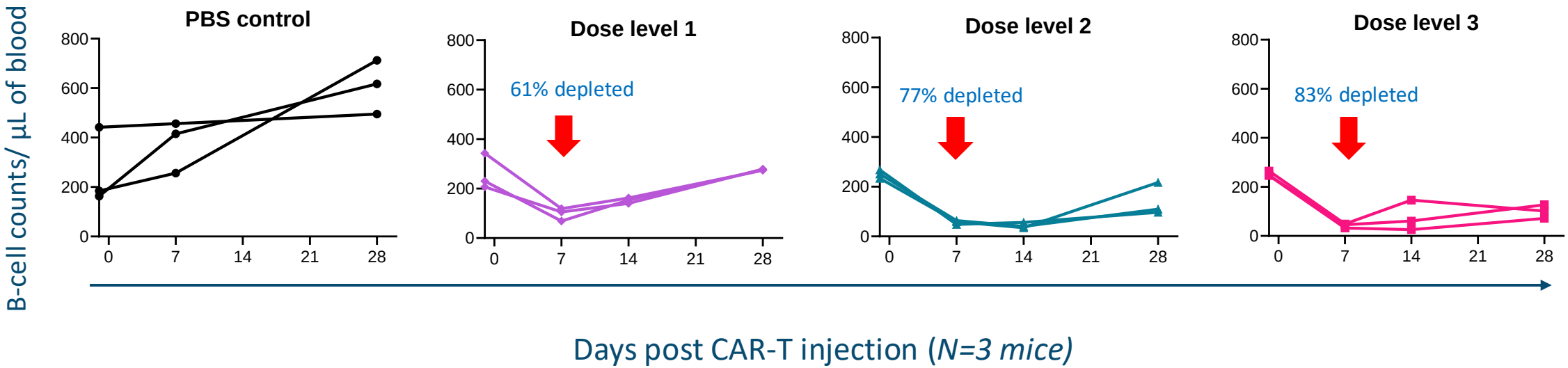



POSEIDA THERAPEUTICS

NEW DATA

# P-BCMACD19-ALLO1 depletes primary human B cells in humanized mouse model

## In vivo proof-of-concept of robust B cell depletion




**Dose-dependent depletion of primary B cells in a humanized NOG-EXL mouse model generated with human CD34+ cells**




NOG-EXL, highly immunocompromised mouse model

POSEIDA THERAPEUTICS

# Immense potential of P-BCMACD19-ALLO1 to address growing needs across autoimmune diseases

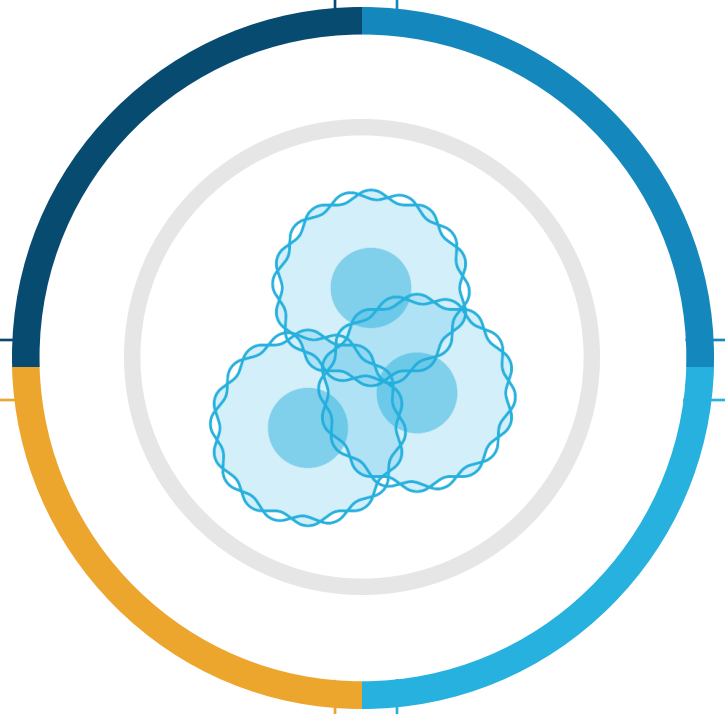
*Illustrative examples, not exhaustive*

## Plasma cell and B cell targeting have strong mechanistic relevance

- Myasthenia Gravis: 70K
- IgA Nephropathy: 140K
- ANCA Vasculitis: 100K

## Deeper, more durable response, potential in diseases with emerging CAR-T efficacy

- Lupus (SLE & LN): 370K
- Immune Mediated Myopathies: 46K-70K
- Systemic Sclerosis: 100K



## Large product scale and off-the-shelf availability is important to meet patient needs

- Rheumatoid Arthritis: 1.3M
- Sjögren's syndrome: 340K
- Multiple Sclerosis: 950K – 1M

## Significant unmet need across autoimmune diseases, yet to be explored for CAR-T treatment

- Membranous Nephropathy: 70K
- Autoimmune Encephalitis: 22K
- IgG4 Related Disease: 18K

Estimated U.S. prevalence, not to scale
Sources: Global Data, Evaluate

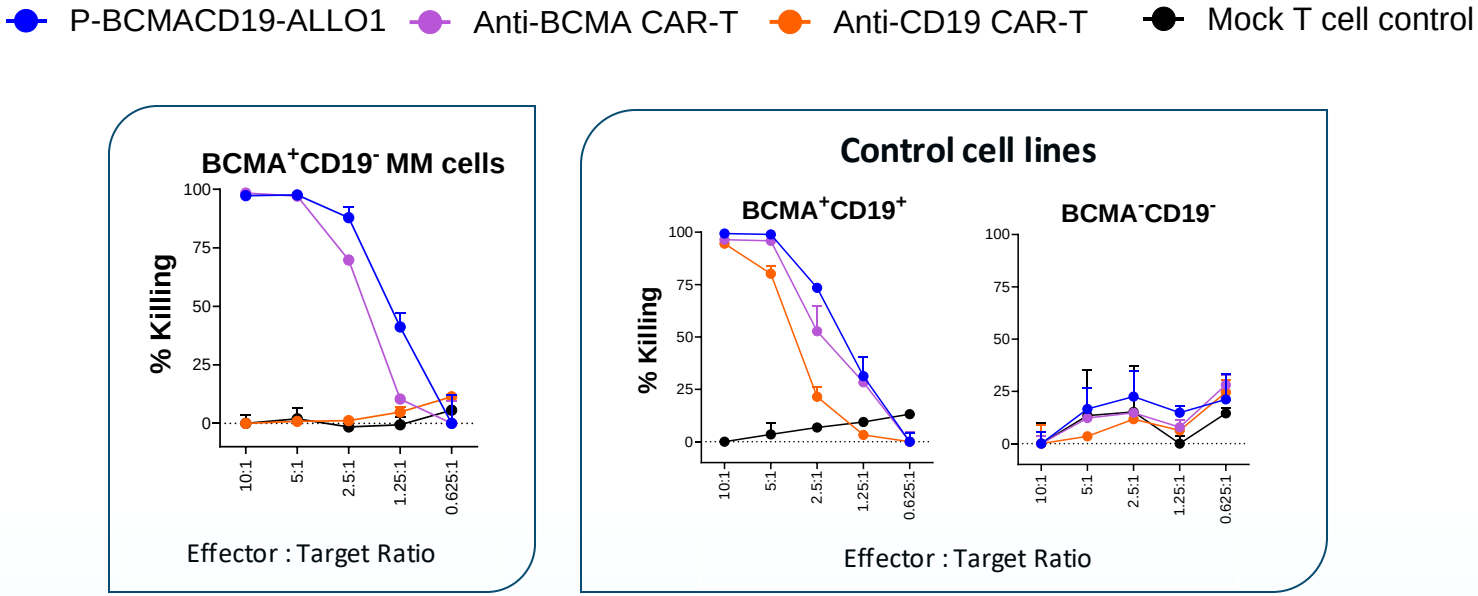



POSEIDA THERAPEUTICS

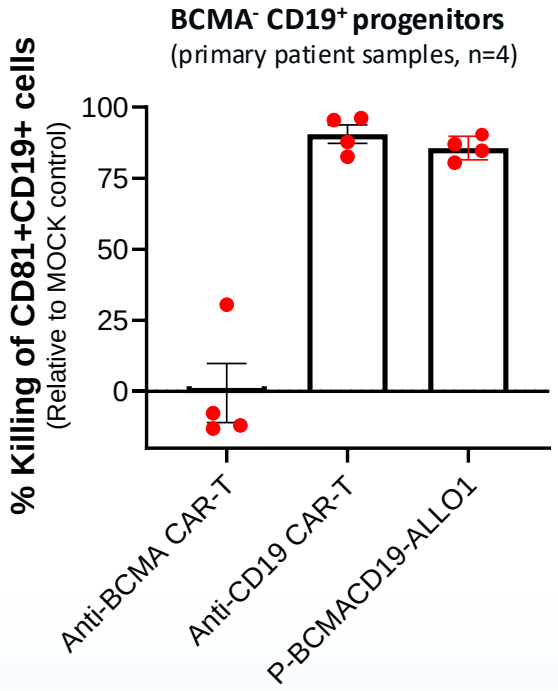
NEW DATA

# P-BCMACD19-ALLO1 effectively eliminates BCMA+ multiple myeloma bulk tumor cells and CD19+ bone marrow progenitor cells

## Potent killing of MM cell lines with BCMA+ targeting




## Progenitor killing with CD19+ targeting





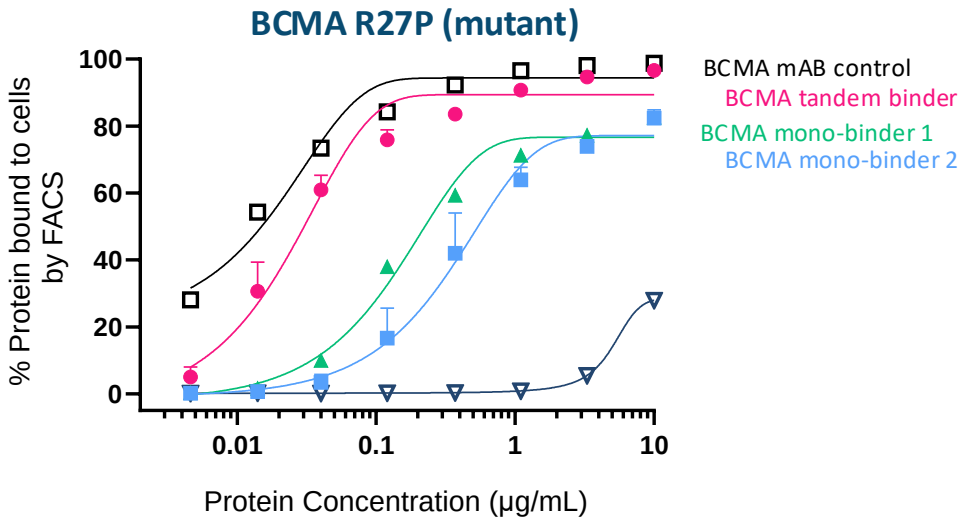


POSEIDA THERAPEUTICS

NEW DATA

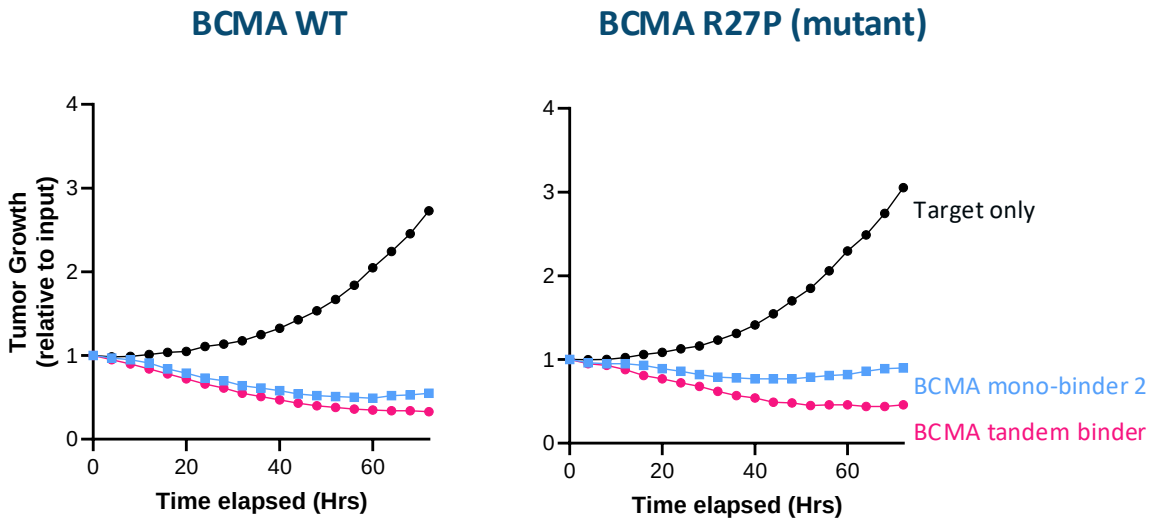
# Tandem BCMA binder has equal activity against wild-type (WT) BCMA & identified clinical escape mutants, including teclistamab-associated mutation R27P

## BCMA tandem binder effectively binds BCMA mutant




In vitro binding assay of BCMA R27P protein expressed by K562 cells via mRNA

## Potent cytotoxicity against WT & BCMA mutant cells




In vitro cytotoxicity against K562 expressing BCMA WT or R27P mutant

Note: Binding to other BCMA isoforms (WT, P33Del, P33S and S30Del) also confirmed (data not shown)

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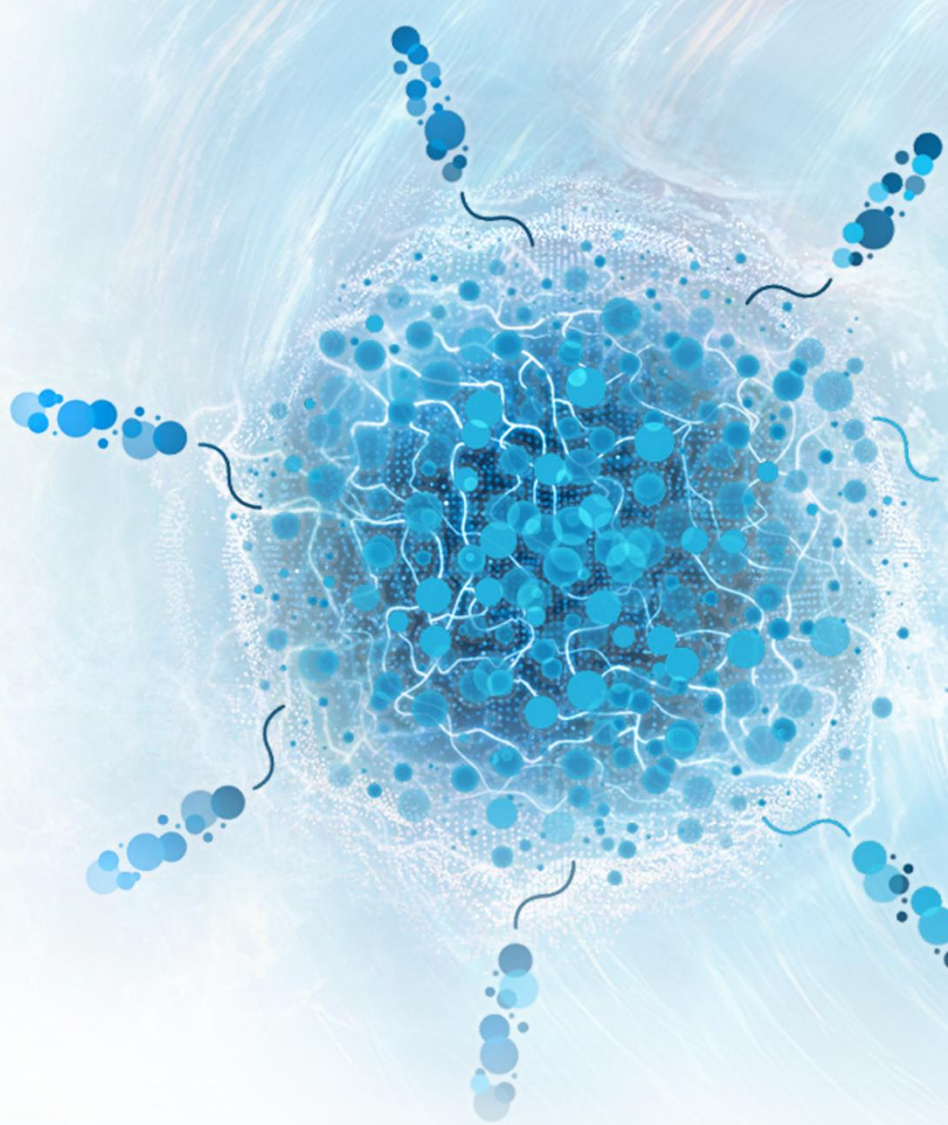
# Waves of innovation in solid tumor cell therapy



**Devon J. Shedlock, PhD**

*CSO, Cell Therapy*

# Solid tumors pose unique challenges for development, requiring bold innovations to overcome and address significant unmet need

## No CAR-Ts approved for solid tumors*

*Key roadblocks*

- **Antigen Heterogeneity**
- **CAR-T Cell Tracking & Infiltration**
- **On Target Off Tumor Tox**
- **Hostile Tumor Microenvironment**

**90%**
*of cancers are solid tumors[1]*

**1.8M**
*Estimated incidence (U.S.)[1]*

**550K**
*Patients dying annually (U.S.)[1]*

**$190B**
*Market size[2]*

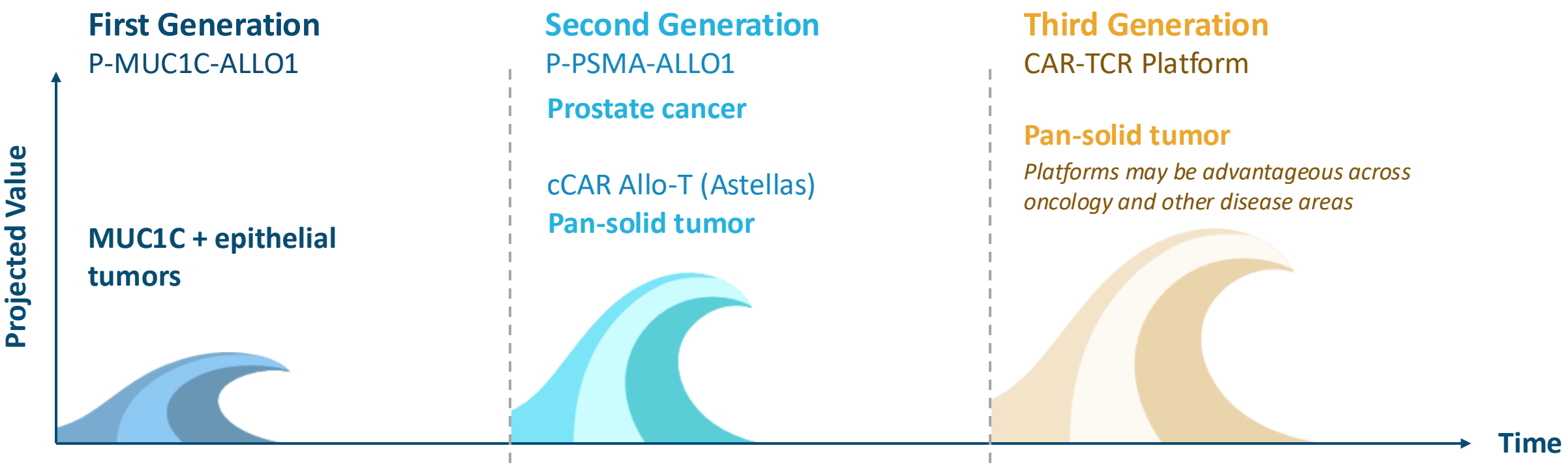
**BOLD INNOVATIONS AN IMPERATIVE**




* Does not include approvals for engineered T cell receptor (TCR) and tumor-infiltrating lymphocyte (TIL) therapy
1. SEER, American Cancer Society (2024) – solid tumor estimates
2. Global Market Size in 2023. Source: Global Oncology Trends, 2024 (IQVIA)

POSEIDA THERAPEUTICS

# Poseida's flexible platform sets up waves of innovation in allogeneic cell therapy for solid tumors, including entirely new platforms




- Initial foray into solid tumors with Allo-$T_{SCM}$ platform
- Significant learnings on lymphodepletion needs
- Initial exploration of LD + low-dose MTX

- Leveraging clinical experience from P-PSMA-101
- New technologies and process science, LD strategies
  - Modifications for viability, potency persistence
- Robust Allo-$T_{SCM}$ platform + flexible targeting with Astellas cCAR

- New technology leveraging clinical learnings and our Allo platform / process advances
- CAR-TCR targets both extra- and intracellular tumor-associated antigens
  - CAR-TCR / TCE synergy




MUC1C, C-terminal domain of Mucin 1; $T_{SCM}$, stem memory T cell; LD, lymphodepletion; MTX, methotrexate; PSMA, prostate-specific membrane antigen; Allo, allogeneic; cCAR, convertible CAR; TCR, T cell receptor; TCE, T cell engager

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# P-MUC1C-ALLO1 is Poseida's lead solid tumor allogeneic CAR-T program

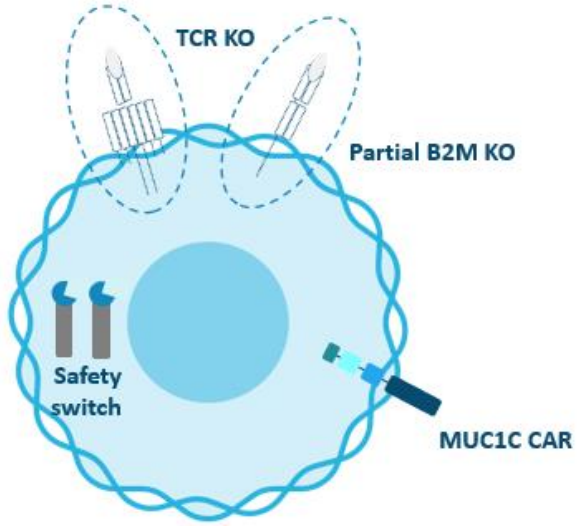
## Motivation

- High unmet medical need in many epithelial cell-derived tumors
- Poseida's earlier autologous PSMA program showed clinical potential of $T_{SCM}$-rich CAR-T in a solid tumor

## Clinical Trial

- Phase 1 basket study enrolling treatment resistant breast, ovarian, colorectal and other tumors (NCT05239143)
- 3x3 dose escalation; Poseida-produced GMP product
- Ongoing exploration of dosing regimen and lymphodepletion

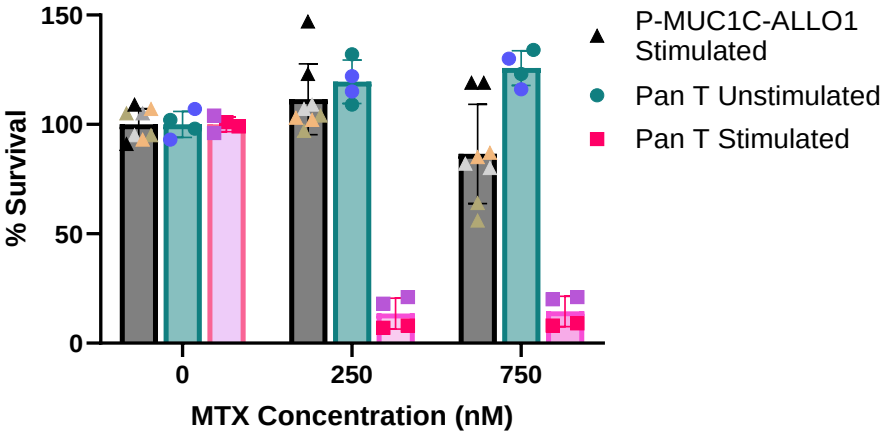
## P-MUC1C-ALLO1




**Unique approach to targeting MUC1C protein at tumor specific moiety**

**Also carries Poseida's platform[1] elements**

## Exploit (MTX) resistance of Poseida's CAR-T for unique, additive LD strategy




- At low MTX doses, equivalent to those used for autoimmune disease therapy, activated T cells are killed, while P-MUC1C-ALLO1 cells are not
- LD/MTX approach may enhance CAR-T expansion/persistence and is in study design

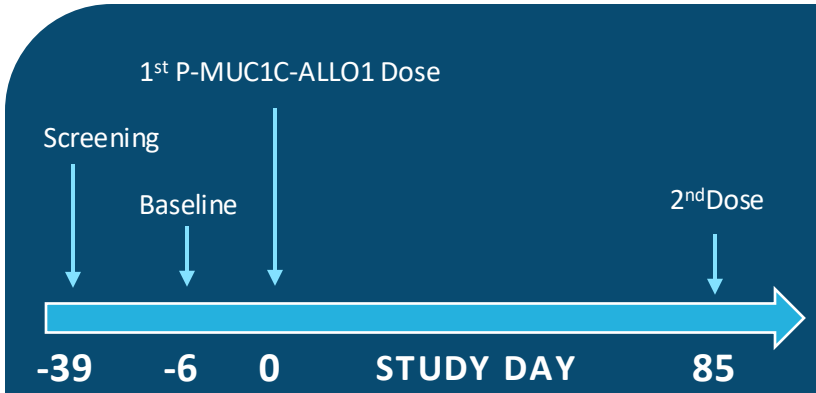
**Data update planned for ESMO-IO 2024**

1. Safety switch, selectable marker, TCR KO, β2M KO

PSMA, prostate-specific membrane antigen; $T_{SCM}$, stem memory T cell; GMP, good manufacturing practice; TCR, T cell receptor; B2M, beta-2 microglobulin; MUC1C, C-terminal domain of Mucin 1; LD, lymphodepletion; SLE, systemic lupus erythematosus; RA, rheumatoid arthritis; nM, nanomolar;MTX, methotrexate

NEW DATA

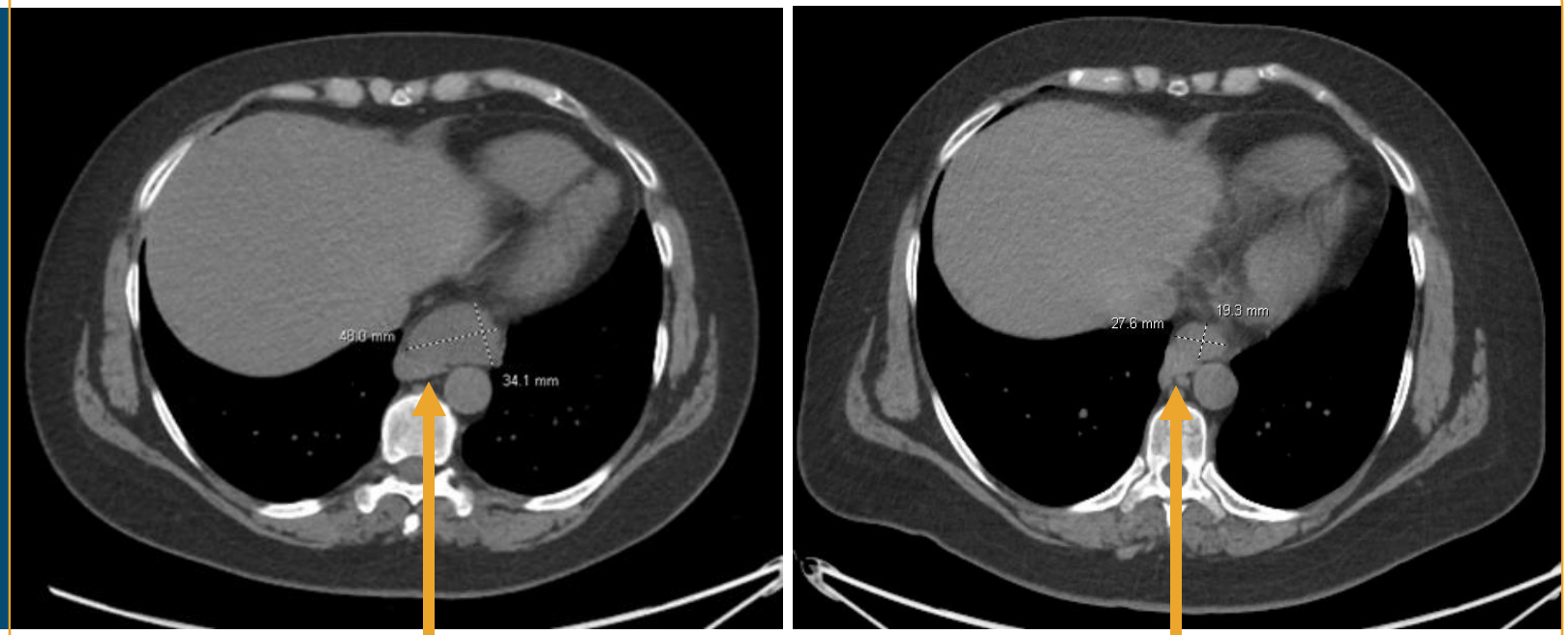
# Substantial tumor size decrease and prolonged stable disease (~1 year) in patient with heavily pretreated appendiceal carcinoma




**LD – 1st Dose**
Cy 500 mg/m²
Flu 30 mg/m² × 3d

**LD – 2nd Dose**
Cy 500 mg/m²
Flu 30 mg/m² × 3d

**Baseline** → **Day 344**




Enlarged paraesophageal lymph node: 42 mm

Paraesophageal lymph node decreased in size to 28 mm (42% decrease)




MUC1C, C-terminal domain of Mucin 1; LD, lymphodepletion; Cy, cyclophosphamide; Flu, Fludarabine; mm, millimeter

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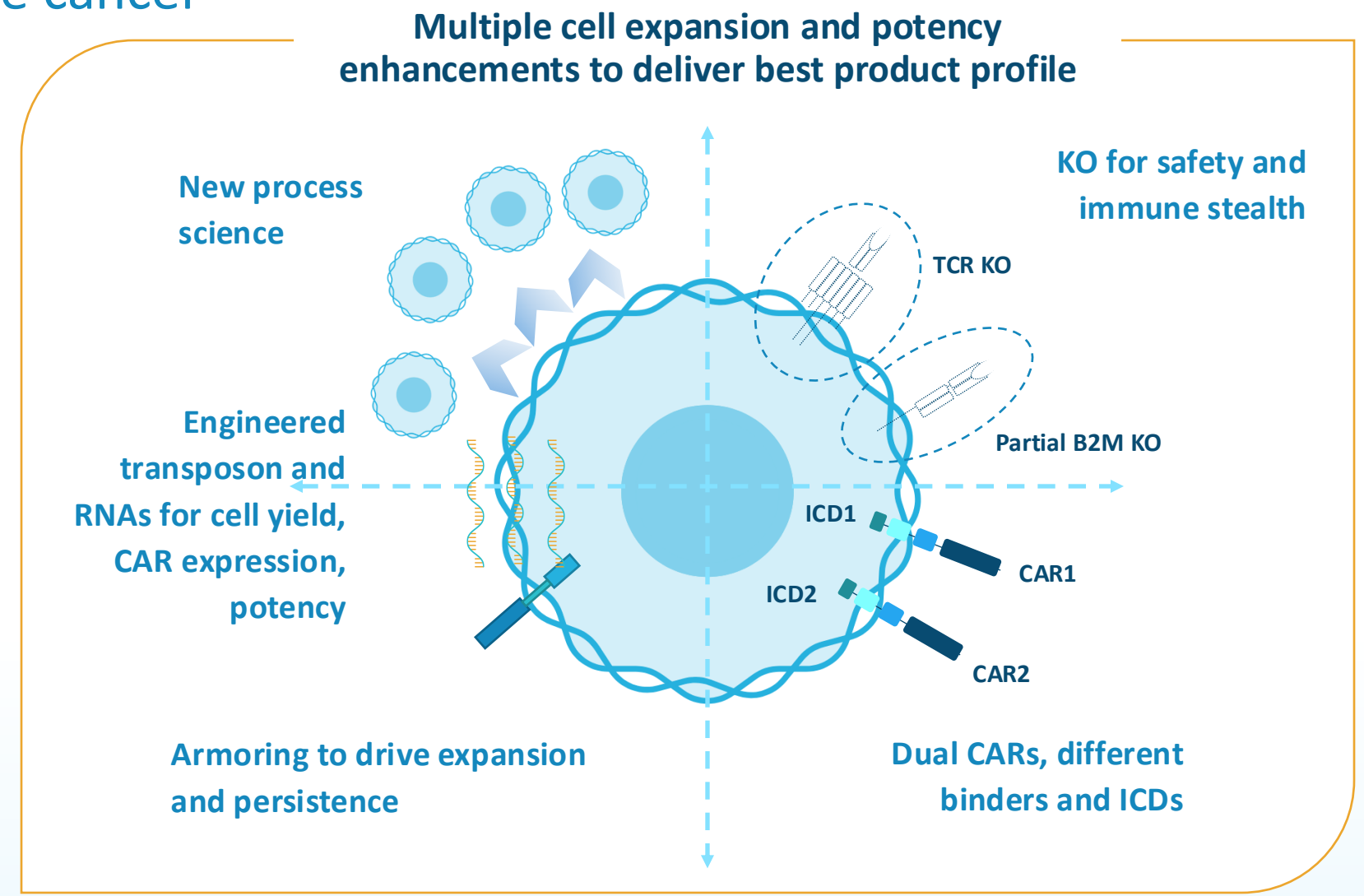
NEW DATA

# P-PSMA-ALLO1 builds upon Poseida's earlier PSMA autologous CAR-T program to tackle prostate cancer

- Dual CAR format has shown improved efficacy compared to the autologous program Centyrin™ binder in xenograft tumor models
- P-PSMA-ALLO1 includes latest process development and allogeneic CAR-T platform improvements for improved cell health, viability, potency, and persistence







PSMA, prostate-specific membrane antigen; KO, knock out; TCR, T cell receptor; B2M, beta-2 microglobulin; ICD, intracellular domain

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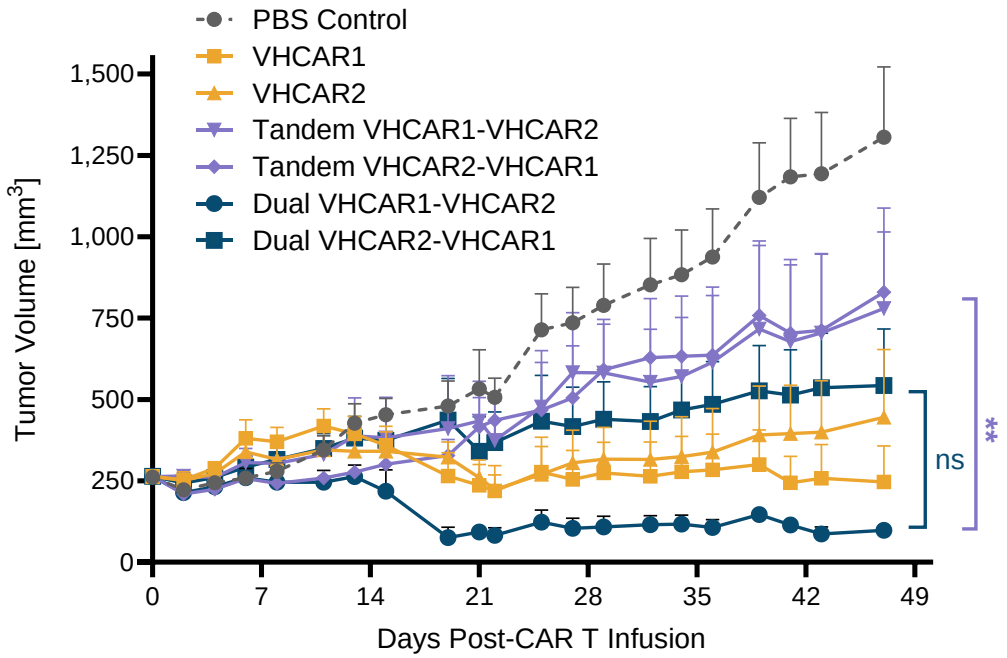
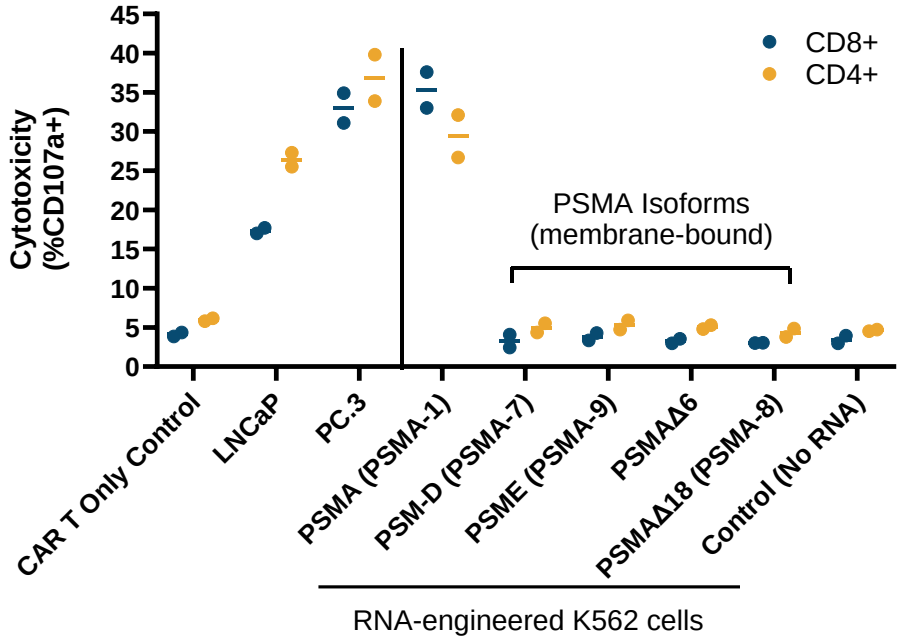
# Fully dual CAR P-PSMA-ALLO1 outperformed single and tandem binder CAR-Ts

NEW DATA

## In vivo screen of PSMA binder candidates




## Reactivity of Lead Dual CAR with PSMA isoforms




- Dual biparatopic PSMA CAR-T outperforms tandem and single VH CAR-T in vivo
- Optimal combination of ICDs (E.g. CAR1-ICD1 + CAR2-ICD2) will be determined for PSMA dual CAR

- CAR-T with selected binders do not bind alternative PSMA isoforms (expressed extratumorally)




PSMA, prostate-specific membrane antigen; VH, heavy chain variable; PBS, phosphate buffered saline; ICD, intracellular domain

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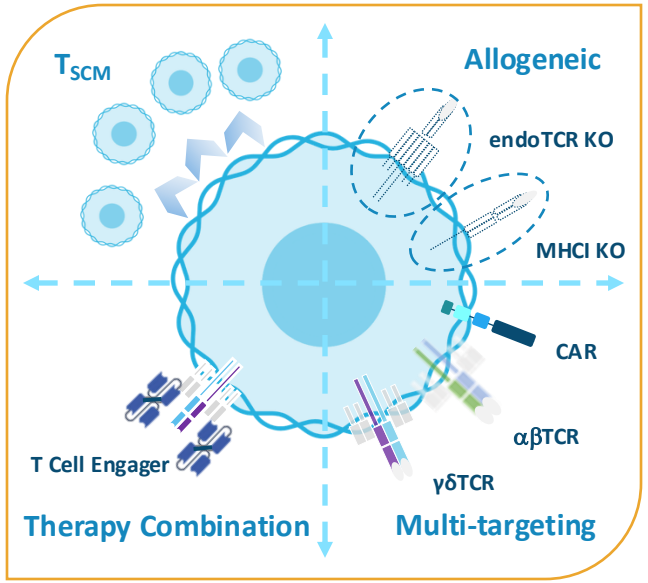
# Concept of Xyphos/Poseida Research collaboration for convertible Allo CAR-$T_{SCM}$



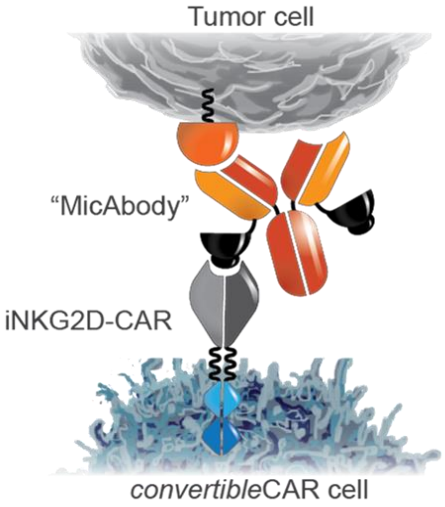

Key features of the Allo-T platform, with the range of possible modifications shown

*Combine the Allo-T and ACCEL™ platform to target solid tumors*

Poseida's Allo-T cell platform

Xyphos' ACCEL™ Platform w/ MicAbody™ library

***convertibleCAR™ expressing Allo-T cells***




ACCEL™ platform, consisting of a modified mAb with engineered ligand (MicAbody™) and iNKG2D-based convertibleCAR™

- ✓ Combination of ACCEL™ and $T_{SCM}$ aims to create a long lasting, highly active, but exquisitely controlled cancer killing CAR-T
- ✓ The collaboration will provide us with the opportunity to utilize clinical stage allogenic T-cells to maximize the value of the ACCEL™ platform
- ✓ Xyphos' MicAbody™ Library will be used in conjunction with Poseida's ALLO-T platform
- ✓ **Single T-cell design (iNKG2D T) with efficient manufacturing process**




$T_{SCM}$, stem memory T cell; endoTCR, endogenous T cell receptor; KO, knock out; MHCI, major histocompatibility complex class I; Allo, allogneic; cCAR, convertible CAR; mAb, monoclonal antibody; iNKG2D, inert natural killer group 2 member D receptor

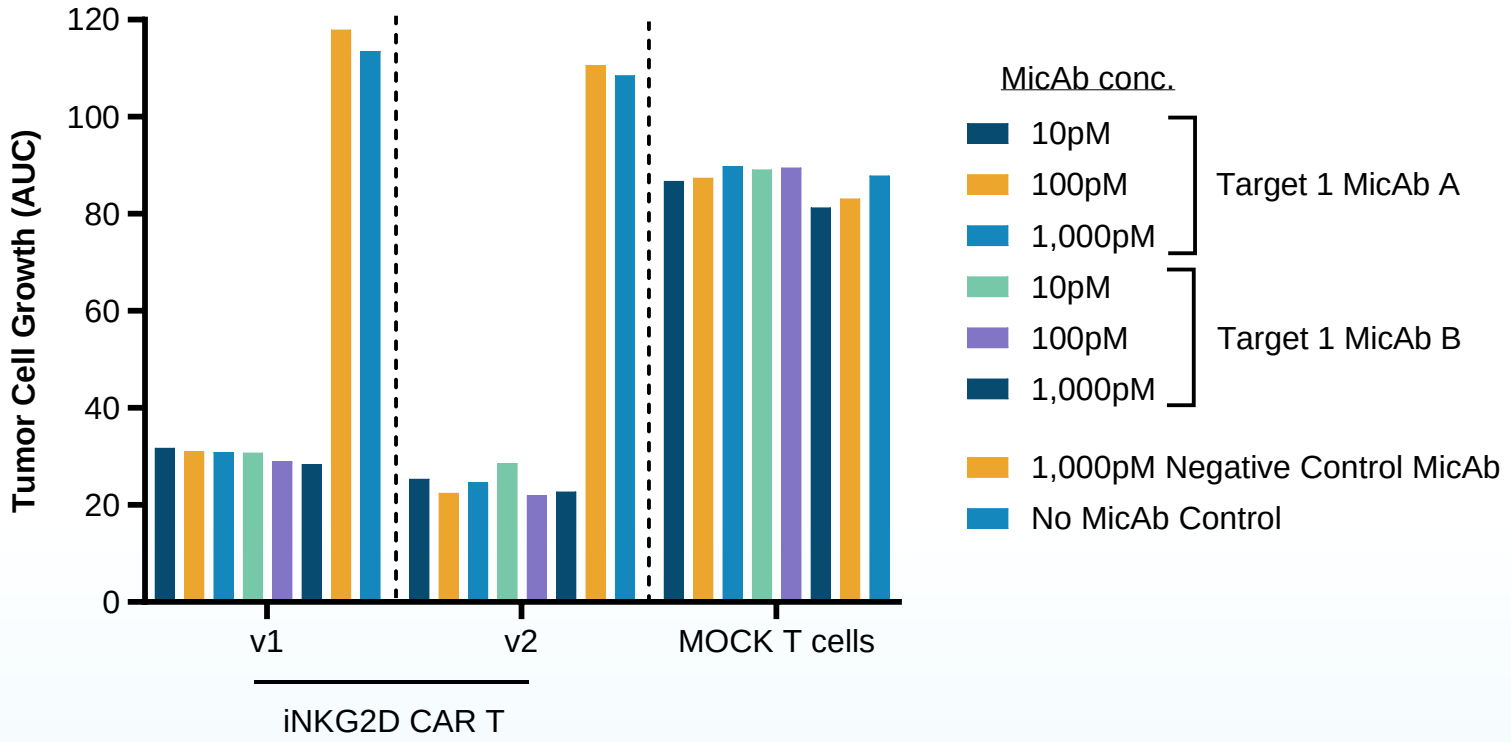
POSEIDA THERAPEUTICS

NEW DATA

# Allogeneic universal cCAR-T and solid tumor-targeting MicAbody™ demonstrate compatibility of Poseida, Xyphos platforms

- Allogeneic universal iNKG2D cCAR-$T_{SCM}$ in the presence of solid tumor antigen-targeting MicAbody™ demonstrates potent, specific in vitro cytotoxicity
- Demonstrates potential to develop a highly flexible family of drug products consisting of a single off-the shelf Allo CAR-TSCM matrixed with multiple MicAbodies™

**Allogeneic iNKG2D CAR-T + Target 1 MicAbody™ in vitro cell killing assay (5:1 E:T ratio)**







$T_{SCM}$, stem memory T cell; cCAR, convertible CAR; iNKG2D, inert natural killer group 2 member D receptor; AUC, area under the curve; pM, picomolar; POC, proof-of-concept

POSEIDA THERAPEUTICS

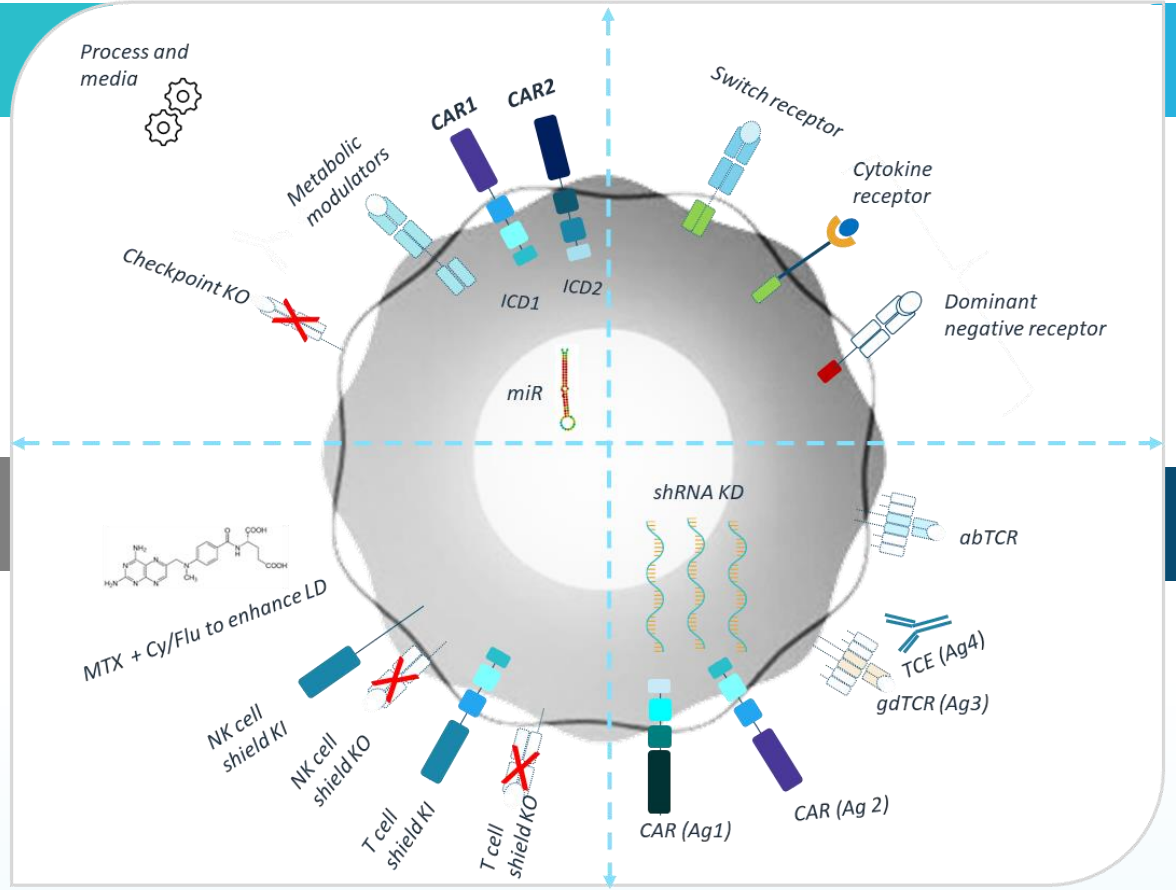
# Poseida is systematically exploring next-generation improvements for solid tumors to be used in ‘third-wave’ innovation

## Potency and persistence

- Cell health, cell activation, and pathway utilization for maintenance of stemness and optimal potency

## Immune escape

- T cell and NK cell shields can increase drug exposure via decreasing rejection by host immune cells




## Armoring

- Armoring can block TME suppressive signals or co-opt for activation and expansion

## Multi-Antigen targeting

- Transposon transgene can express multiple CARs, $\gamma\delta/\alpha\beta$ TCR, enables use of TCE for targeting up to 4 unique antigens with a single CAR-T

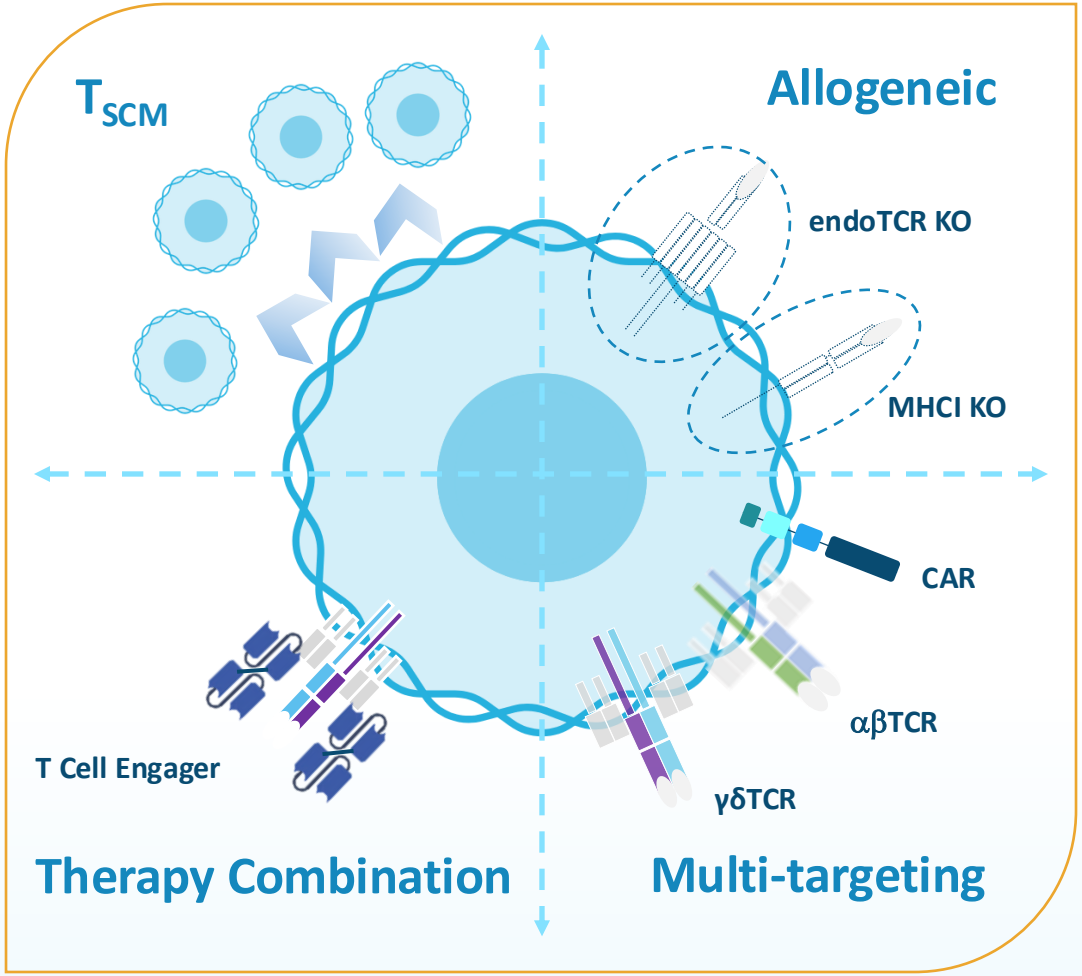



TME, tumor microenvironment; NK, natural killer; KO, knock out; KI, knock in; ICD, intracellular domain; miR, microRNA; MTX, methotrexate; Ag, antigen; abTCR, alpha-beta T cell receptor; gdTCR, gamma-delta T cell receptor; shRNA, short hairpin RNA; TCE, T cell engager

POSEIDA THERAPEUTICS

# A new platform for tough tumors: Poseida's combination CAR-TCR technology is designed to address the challenges of adoptive cell therapy for solid tumors

- Inclusion of one or more CARs and TCRs simultaneously (CAR-TCR technology) is enabled by large transposon cargo capacity
- Can combine classic CAR + γδTCR or αβTCR in single products
- CAR-TCR addresses the heterogeneity of solid tumor antigen expression:
  - Recognize both cell-membrane (CAR) and cytoplasmic (TCR) antigens
  - Capable of engaging TCE therapeutic against a 3rd target
  - Potential to be used with TCR-T-priming reagent or vaccine
- CAR-TCR potency and persistence:
  - TCR provides additional survival signal for cell persistence
  - TCR maintains high memory, low exhaustion phenotype for longer duration
  - γδTCR may have advantages for trafficking, without need for HLA matching or GVHD risk







$T_{SCM}$, stem memory T cell; endoTCR, endogenous T cell receptor; KO, knock out; MHCI, major histocompatibility complex class I; TCE, T cell engager; GVHD, graft-versus-host disease; TCE, T cell engager; HLA, human leukocyte antigen

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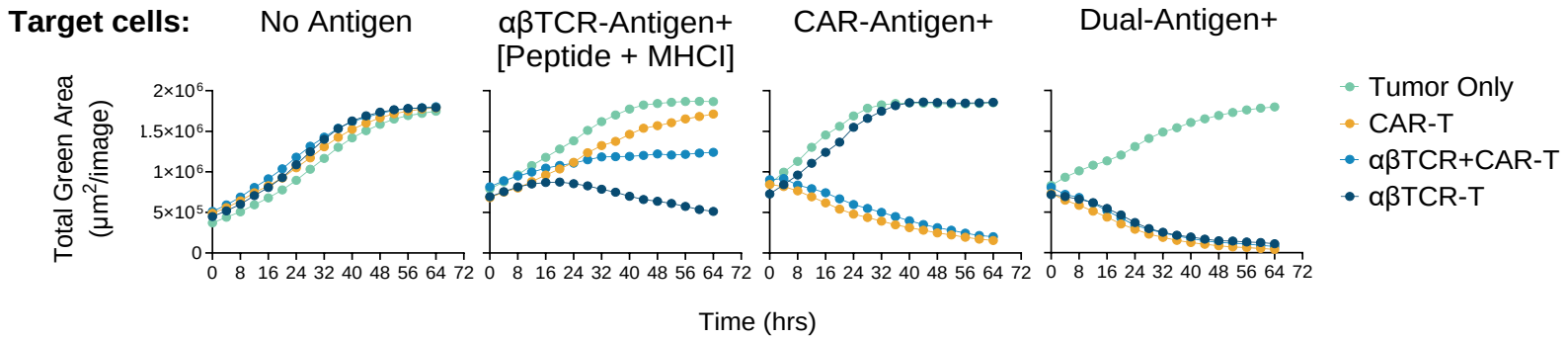
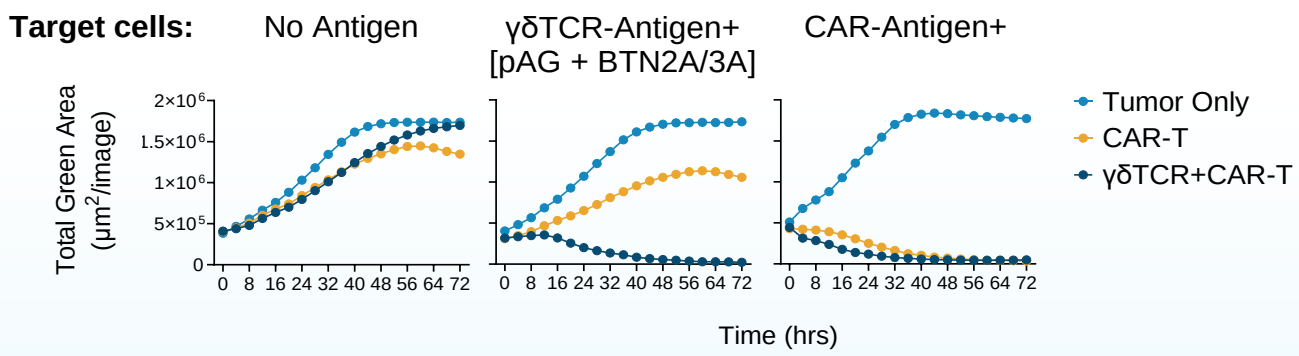
# CAR-TCR T cells exhibit strong functional capabilities against both cell surface CAR target and intracellular TCR target

## Allo CAR + abTCR or CAR + gdTCRTs kill single and double-Ag positive tumor cells

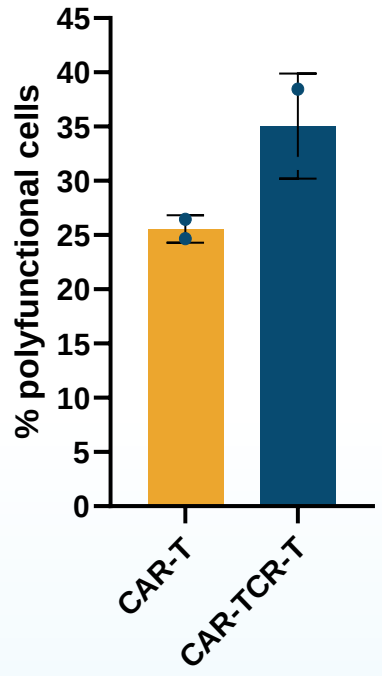
### MUC1C CAR + NY-ESO-I αβTCR




### MUC1C CAR + pAg γδTCR




When exposed to double Ag+ cells, a higher % of Allo CAR + αβTCR vs CAR-T express ≥ 2 immune mediator cytokines







TCR, T cell receptor; Allo, allogeneic; hrs, hours; Ag, antigen; MUC1C, C-terminal domain of Mucin 1; NY-ESO-1, New York esophageal squamous cell carcinoma 1; MHCI, major histocompatibility complex class 1; pAg, phosphoantigen; BTN, Butyrophilin

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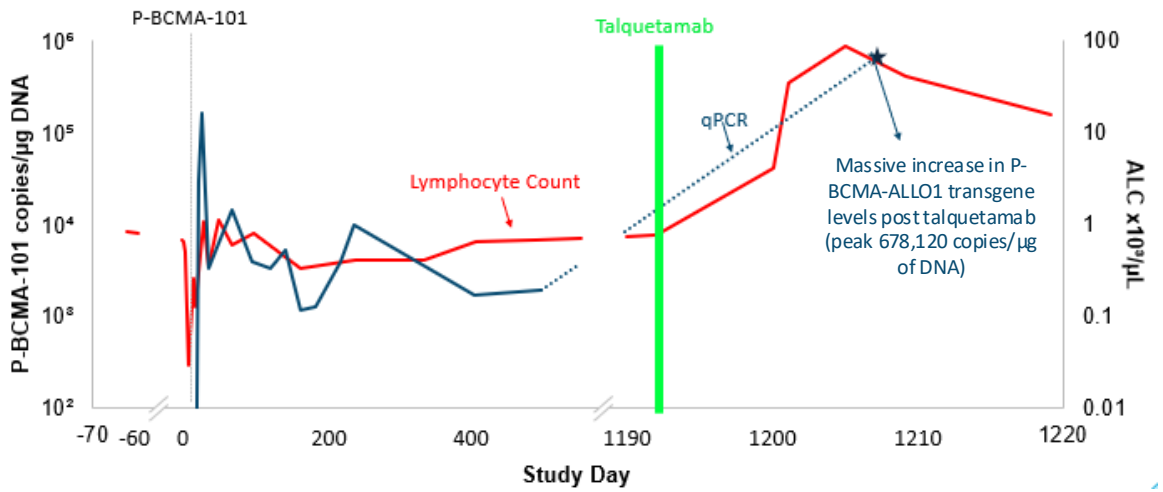
# Inspirational case study: T cell engager reactivation and redirection of CAR-Ts

## TCE talquetamab caused dramatic benign P-BCMA-101 reactivation years after CAR-T administration




- Pt received autologous P-BCMA-101, and achieved a sCR; in remission ~31 mo
- >3 years after P-BCMA-101, pt received 1 wk of GPRC5D TCE - talquetamab
- Dramatic benign polyclonal re-expansion of P-BCMA-101
- **sCR > 10 mo from last dose of TCE**
- Observation is possibly a unique feature of $T_{SCM}$-rich CAR-T products, such as P-BCMA-101, that demonstrate tropism for the bone marrow and are more likely to result in durable engraftment

"This case study demonstrates the remarkable potential of T stem cell memory-based therapies, providing a strong anti-myeloma response with a long-term remission and, notably, CAR-T cell persistence.

Most notably, we believe this is the first time that a T-cell engager has been seen to reactivate a CAR-T therapy, and the evidence suggests that this reactivation drove a second wave of CAR-T cell proliferation that led to another complete response three years after the initial successful CAR-T treatment. This patient is now off all anti-myeloma treatments and living in remission for more than nine months following 1 week of TCE therapy, a truly amazing outcome."

**Thomas G. Martin, M.D.**
Clinical Professor of Medicine, Adult Leukemia and Bone Marrow Transplantation Program and Director of Hematology, Blood and Marrow Transplantation and Cellular Therapy at UCSF





TCE, T cell engager; ALC, absolute lymphocyte count; qPCR, quantitative PCR;sCR, stringent complete response; pt, patient; GPRC5D, G protein-coupled receptor, class C, group 5, member D; $T_{SCM}$, stem memory T cells; UCSF, University of California San Francisco

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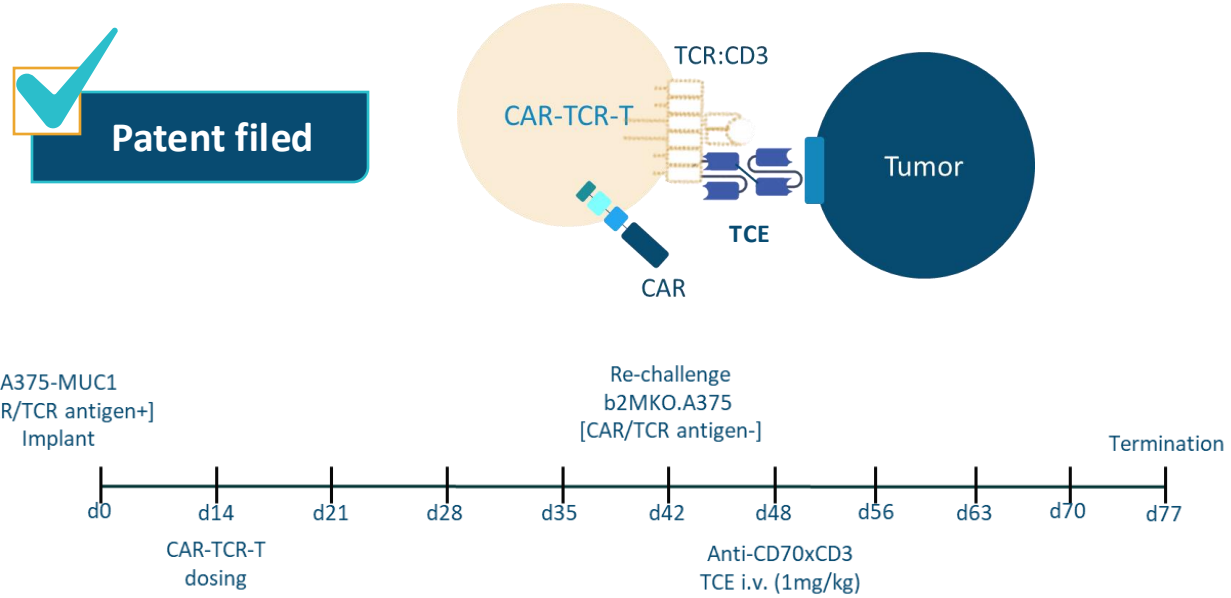
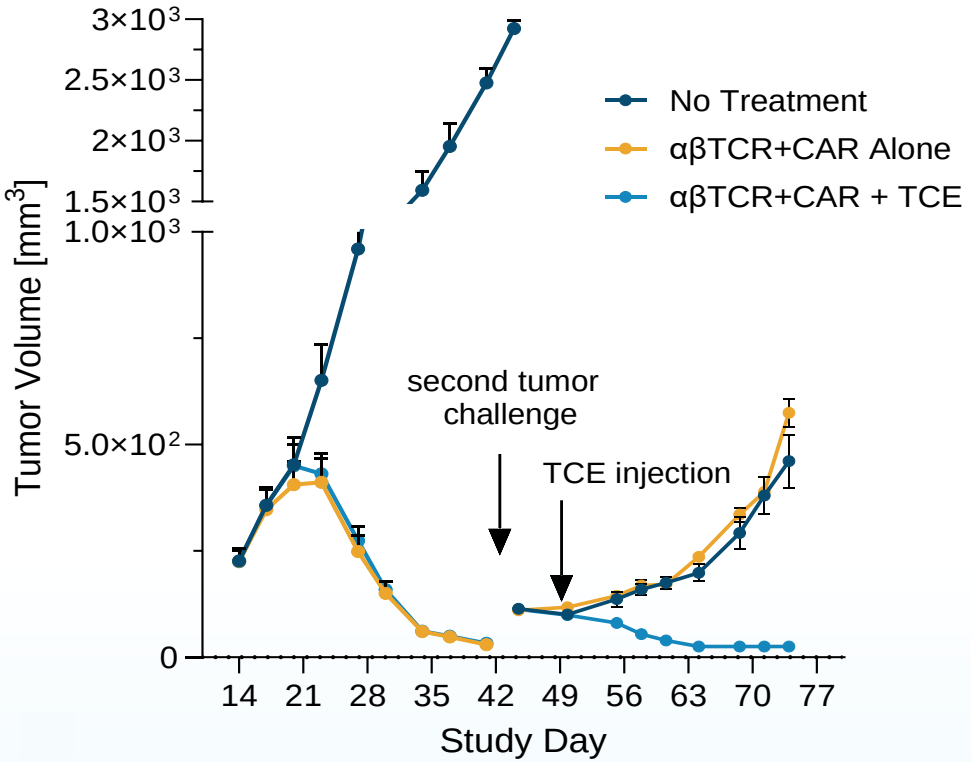
# Designing the CAR-TCR+TCE approach to work in allogeneic cell therapy: T cell engager reactivation and redirection of TCR+ CAR-Ts




- MUC1C-CAR + NY-ESO-1-TCR T cells:
  - controlled primary tumor (MUC1C$^{+}$/NY-ESO-1$^{+}$/CD70$^{-}$)
  - later, were **re-activated and re-directed** by administration of a CD70 T cell engager (TCE) to control challenge by a secondary tumor (MUC1C$^{-}$/NY-ESO-1$^{-}$/CD70$^{+}$)

**CAR+TCR-T synergized with TCE to control tumors expressing three unique antigens**







TCR, T cell receptor; MUC1C, C-terminal domain of Mucin 1; b2,Mbeta-2 microglobulin; KO, knock out; TCE, T cell engager; NY-ESO-1, New York esophageal squamous cell carcinoma 1

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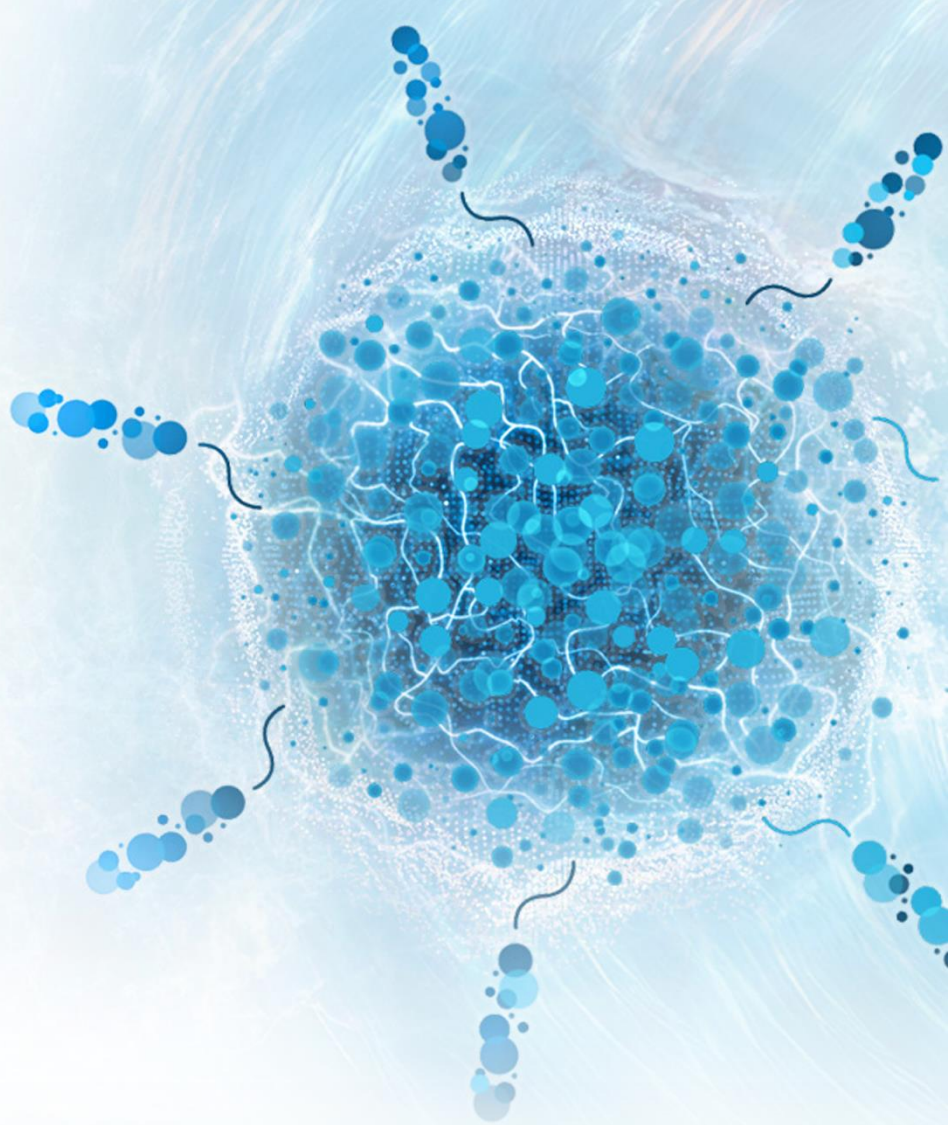
# The power of partnerships fireside chat



**Karen Basbaum**

*SVP, Business Development at Poseida Therapeutics*

**Peter Sandor, MD**

*EVP, Head of Corporate Strategy at Astellas Pharma*

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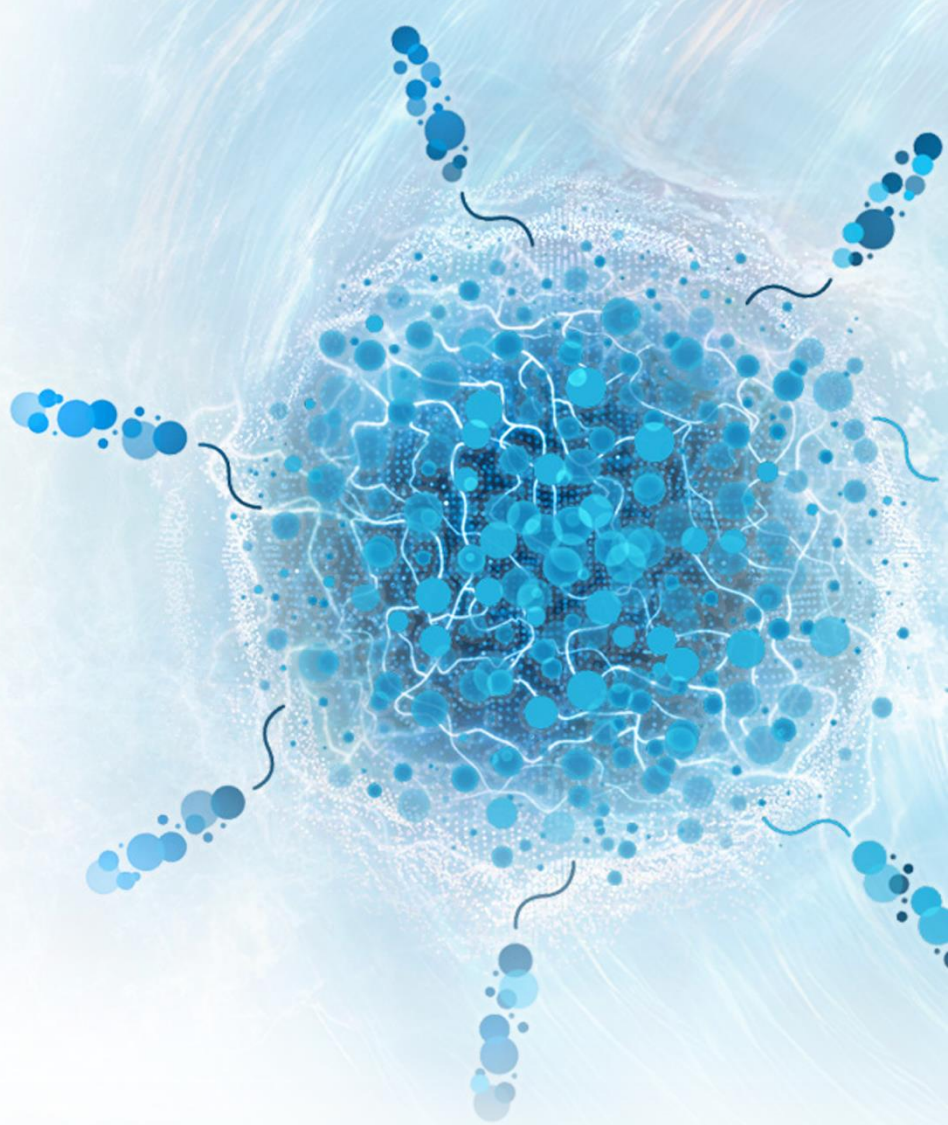
# In-house GMP manufacturing capabilities

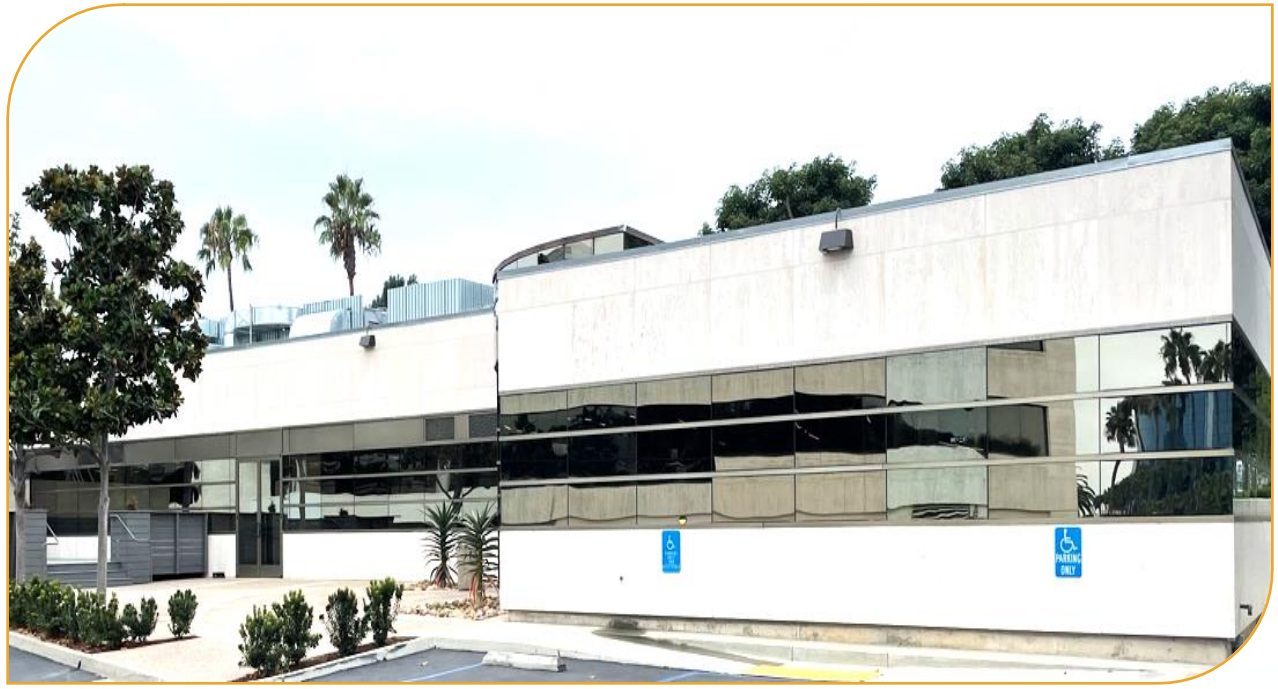


**Loren Wagner**

*Chief Operations Officer*

# Poseida manufactures GMP allogeneic CAR-T in house for higher yields and lower COGS

*Facility supports current needs for three allogeneic programs while simultaneously advancing our platform*



## POSEIDA'S ALLOGENEIC VS. AUTOLOGOUS PLANT

- **~1/10 facility size for comparable output[1]**
- **Far lower labor and operating costs[2]**
- **On demand product delivery to site of care**
- **Reach 100% of patients via stored inventory**
- **Targeting biologics-like COGS**

**Efficient | Accessible | Flexible | Cost Effective | Off-the-shelf**




*1. Assuming autologous facility size is 150,000 sq. ft.*
*2. Assumes an autologous facility workforce requires at least 900-1200 people*
*Data on file*

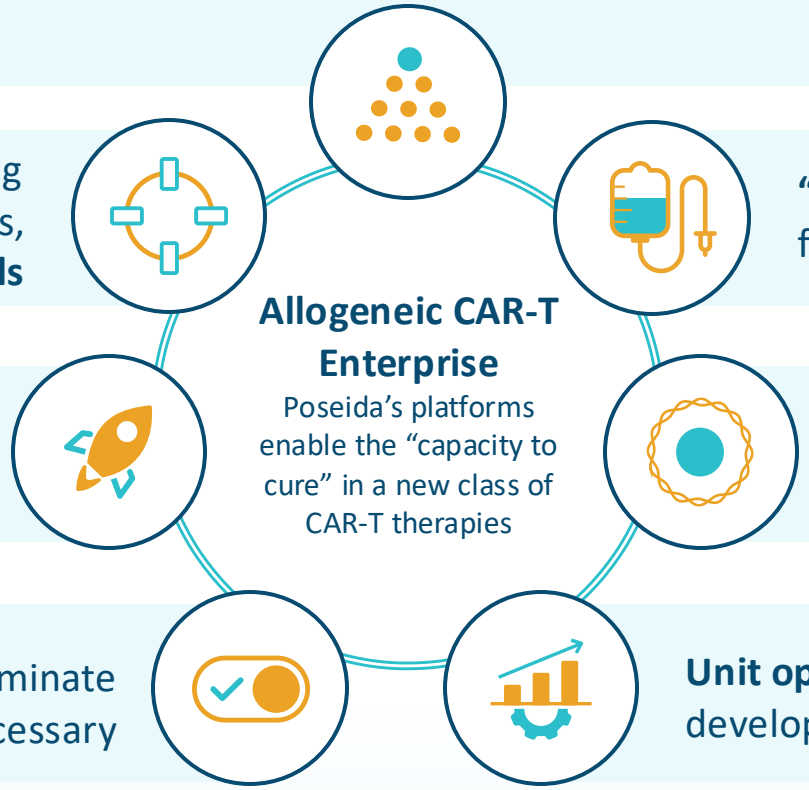
POSEIDA THERAPEUTICS

# Poseida's consistent platform reflects a holistic systems engineering approach to CAR-T set to deliver product after product

Robust healthy **donor screening system**

**Non-viral** gene insertion and gene editing approaches the same across all programs, and **customized for $T_{SCM}$ cells**

**"On-demand" delivery** of therapy from inventory through supply chain




Proprietary **Booster Molecule** improves manufacturing yield

**Selectable marker supports purification** so that nearly all cells are CAR-carrying, with the potential for optimal therapeutic index

**Safety "switch"** to selectively eliminate CAR-T cells in the patient, if necessary

**Unit operations optimization** across process development and quality, applied to all programs

**Poseida has taken a deliberate platform approach to develop a pipeline of allogeneic CAR-T programs that use the same proprietary technologies, the same manufacturing platform and reflect similar production methods**

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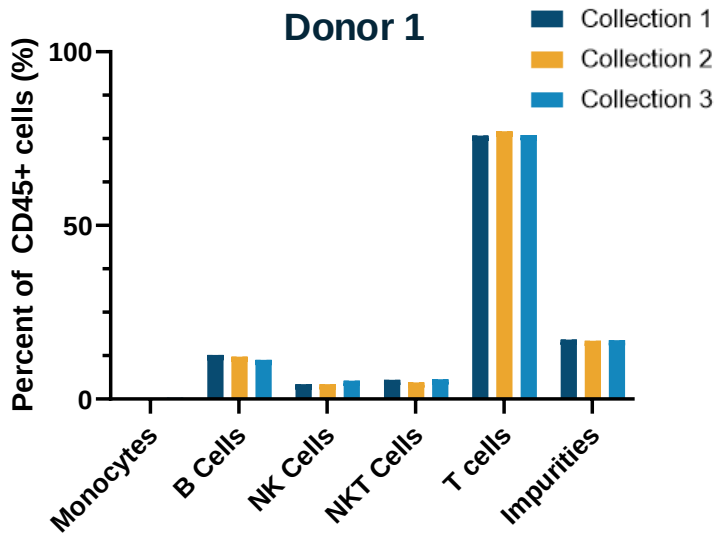
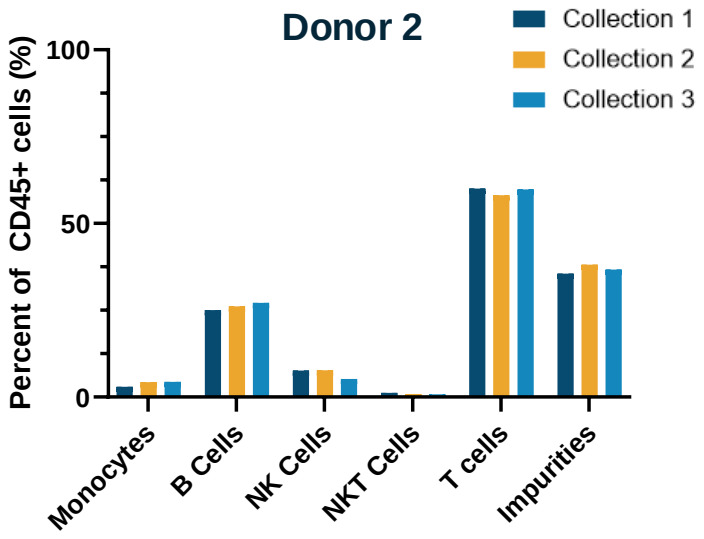
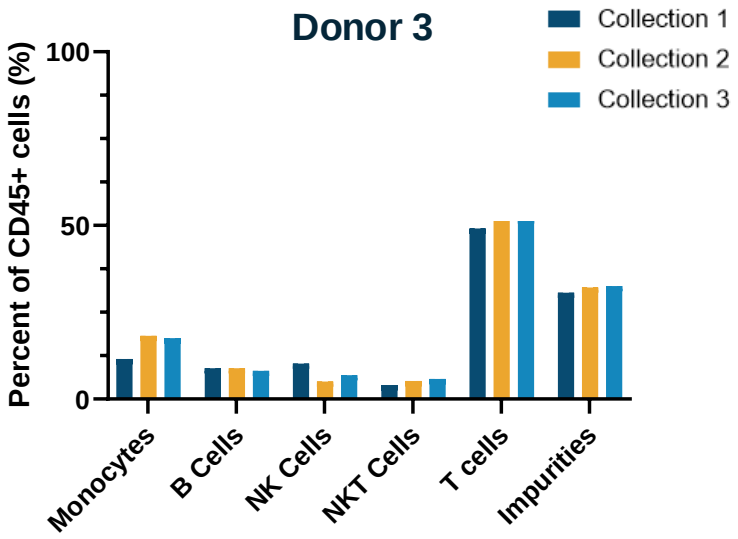
# Apheresis purity is variable among donors but consistent between collections

NEW DATA




Note: All cell types are % of CD45+ cells in apheresis

- All collections from a particular donor have similar cellular distributions in the apheresis
- Cell distribution in the apheresis is donor-dependent

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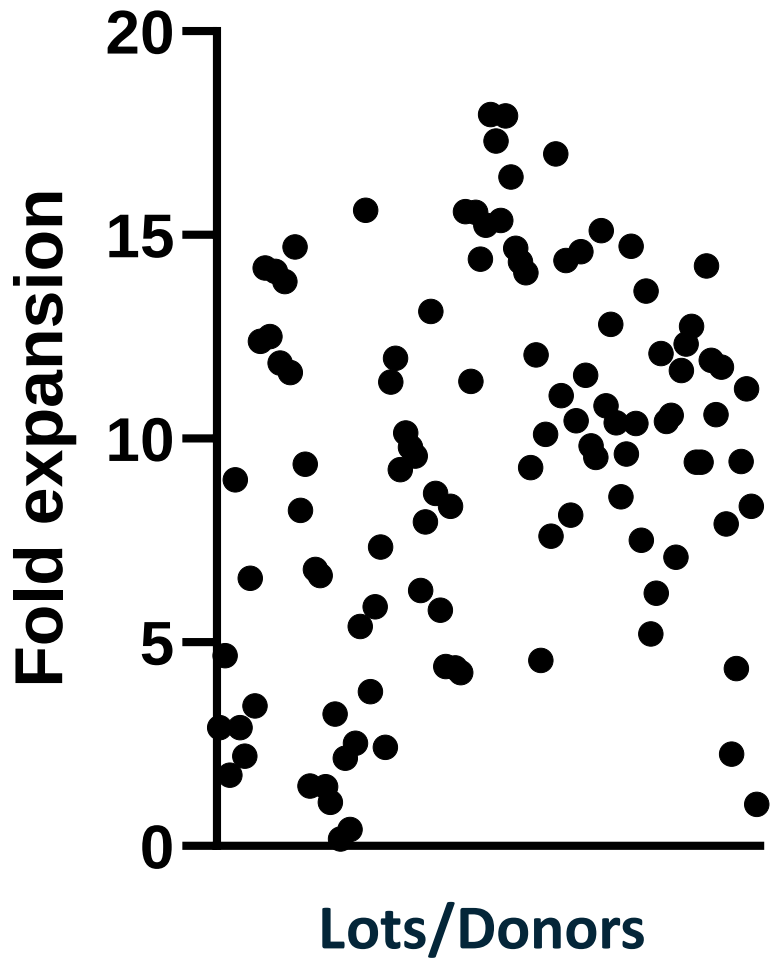
# Fold expansion during allogeneic CAR-T manufacturing is donor-dependent

NEW DATA




There is significant donor variability in fold expansion during CAR-T cell manufacturing

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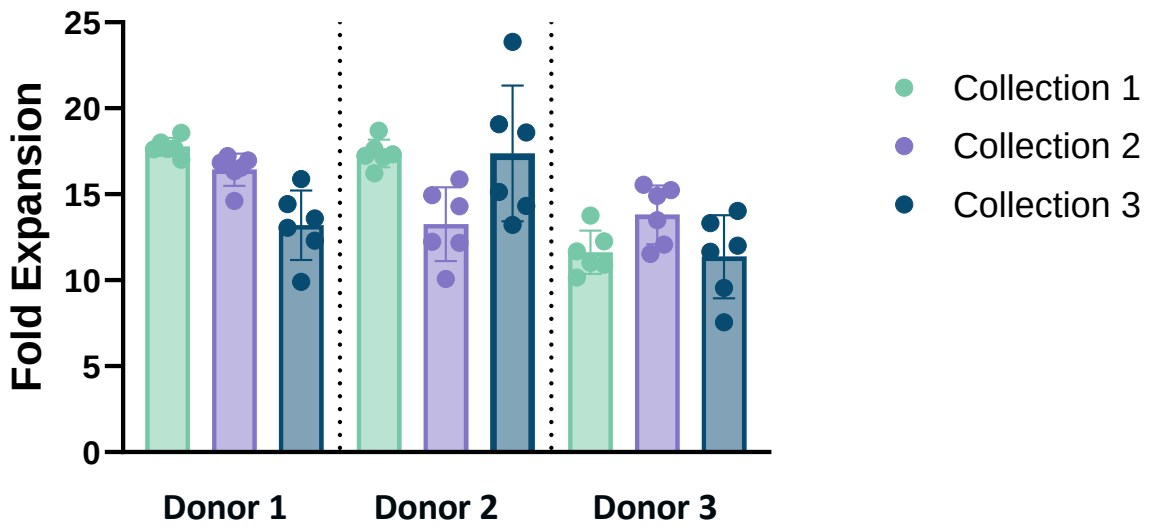
# Fold expansion is consistent across multiple collections from the same donor

NEW DATA

- Donors had slightly differential levels of expansion but were overall **within a consistent and predictable range**
- Donors had **consistent expansion** across **multiple collections**



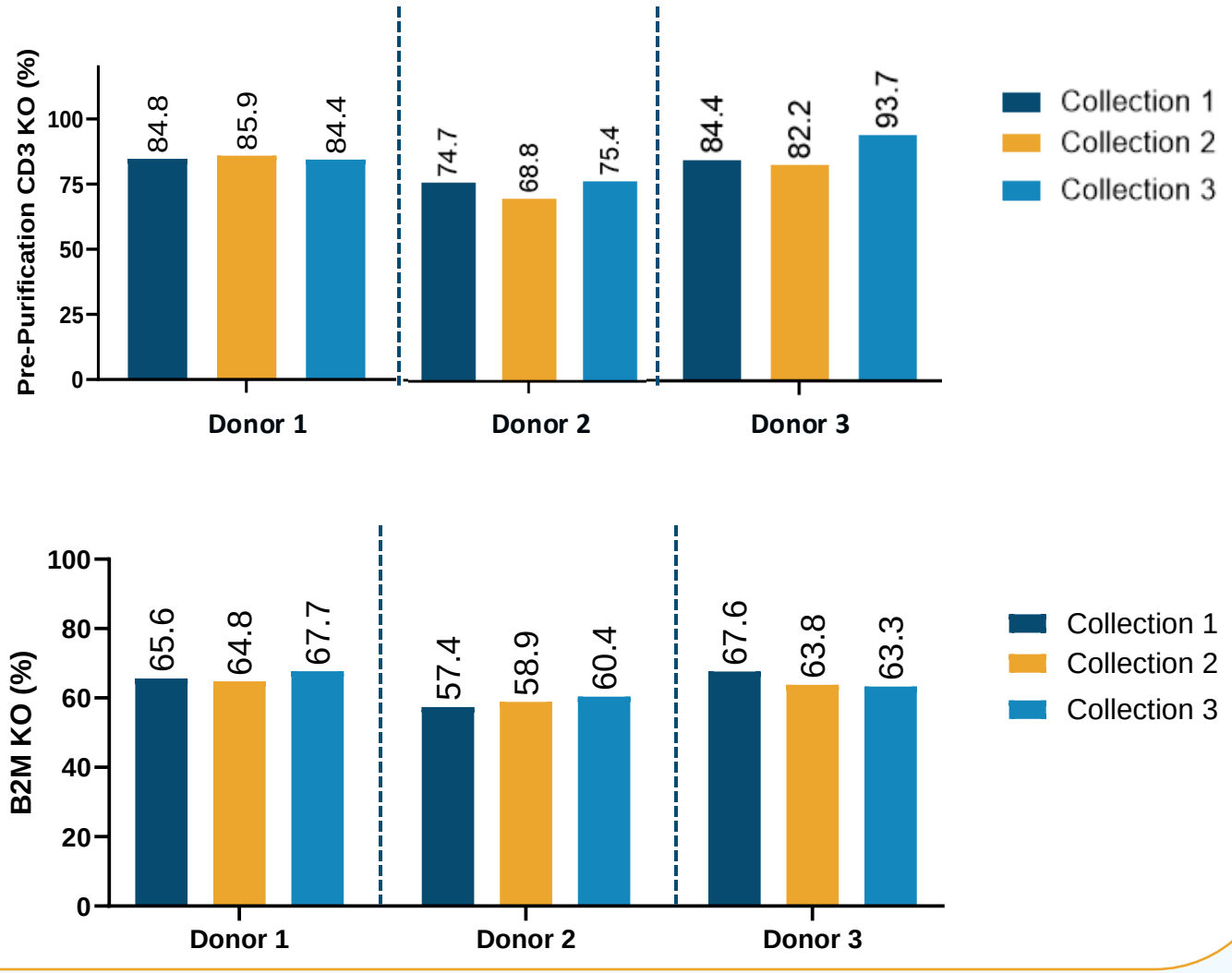




POSEIDA THERAPEUTICS

# Gene editing efficiency is donor-dependent but consistent across collections

NEW DATA




Pre-Purification CD3 KO and B2M KO is donor-dependent

- Donor 1 and Donor 3
  - ~80-90% (CD3 KO)
  - ~63-67% (B2M KO)
- Donor 2
  - ~68-75% (CD3 KO)
  - ~57-60% (B2M KO)

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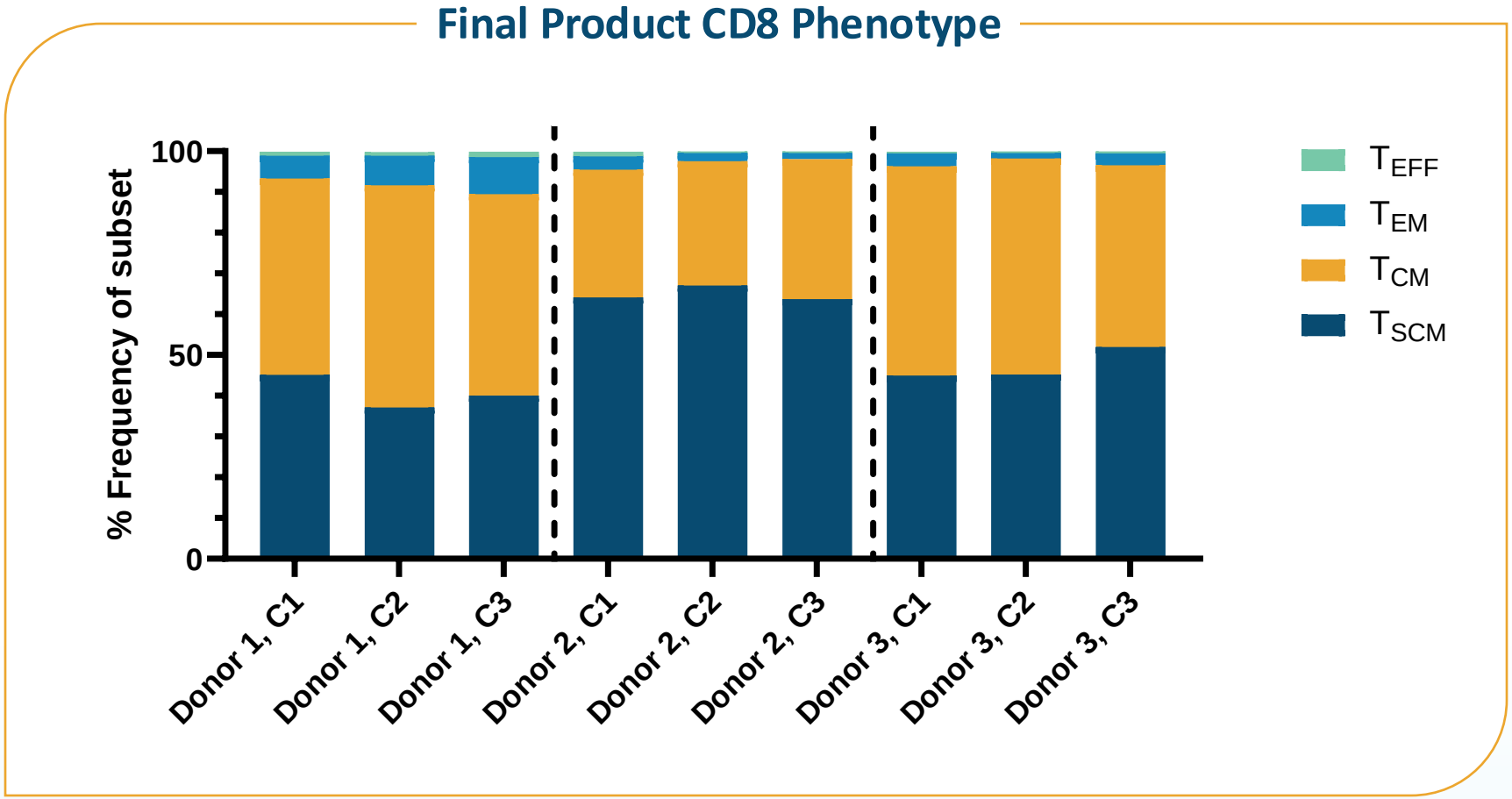
# Final product phenotype is donor-dependent but consistent across multiple collections

NEW DATA







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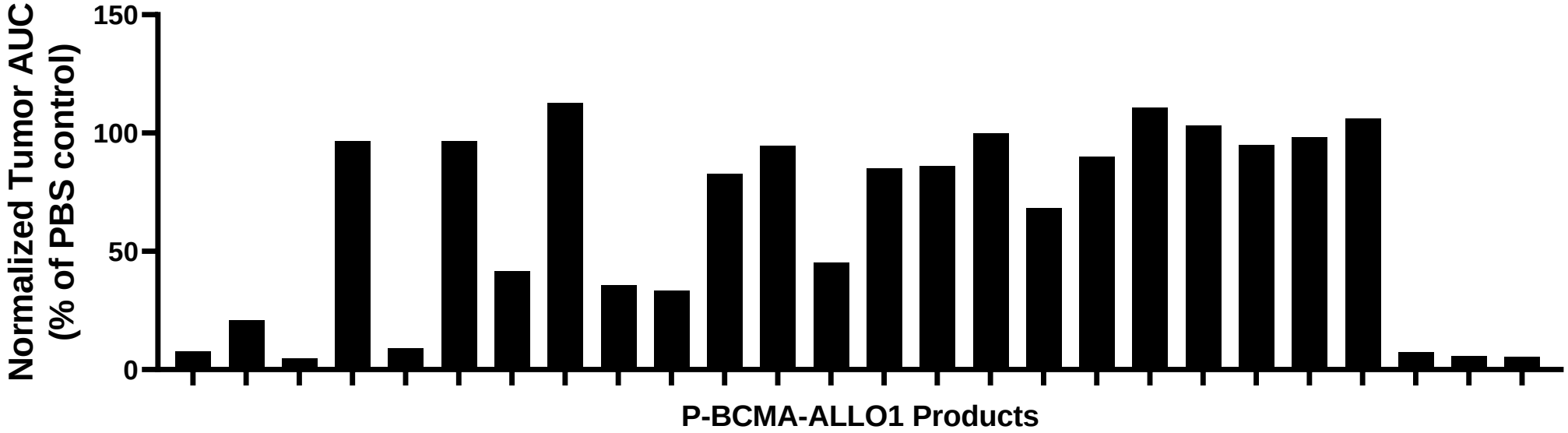
# Final product potency is donor-dependent but consistent for an individual donor

NEW DATA

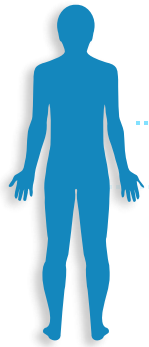
## In Vivo Potency



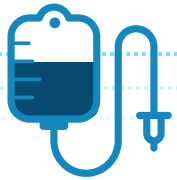

- There is donor-dependent variability for in vivo anti-tumor potency
  - This potency is relatively consistent with repeat donor collections and productions
  - Most variability in potency over repeat collections is due to changes in process/manufacturing

# Poseida's manufacturing platform, used across all products, delivers $T_{SCM}$-rich products with high purity

**Allogeneic manufacturing process enhanced with Booster Molecule technology to deliver high yields**



**ONE HEALTHY DONOR**



ONE LEUKOPAK

**Manufacturing**

T Cell Isolation

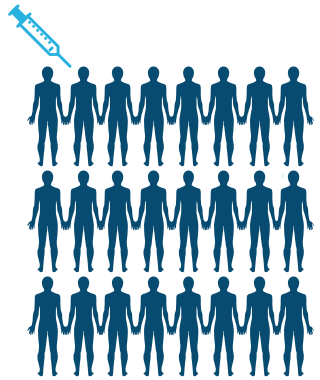
Non-viral Gene Editing

CAR-T Cell Selection and Expansion with Booster Molecule

Purification

Fill/finish

Storage in Inventory



**~100 DOSES**

- Production process preserves $T_{SCM}$ phenotype
- Nearly all CAR-carrying cells
- "On demand" delivery to site of care

**P-BCMA-ALLO1 interim Phase I study data presented at IMS 2024 illustrates our manufacturing capability, using product from 7 manufacturing lots and 6 different qualified donors**

Poseida Data on File




POSEIDA THERAPEUTICS

# Future manufacturing platform enhancement opportunities

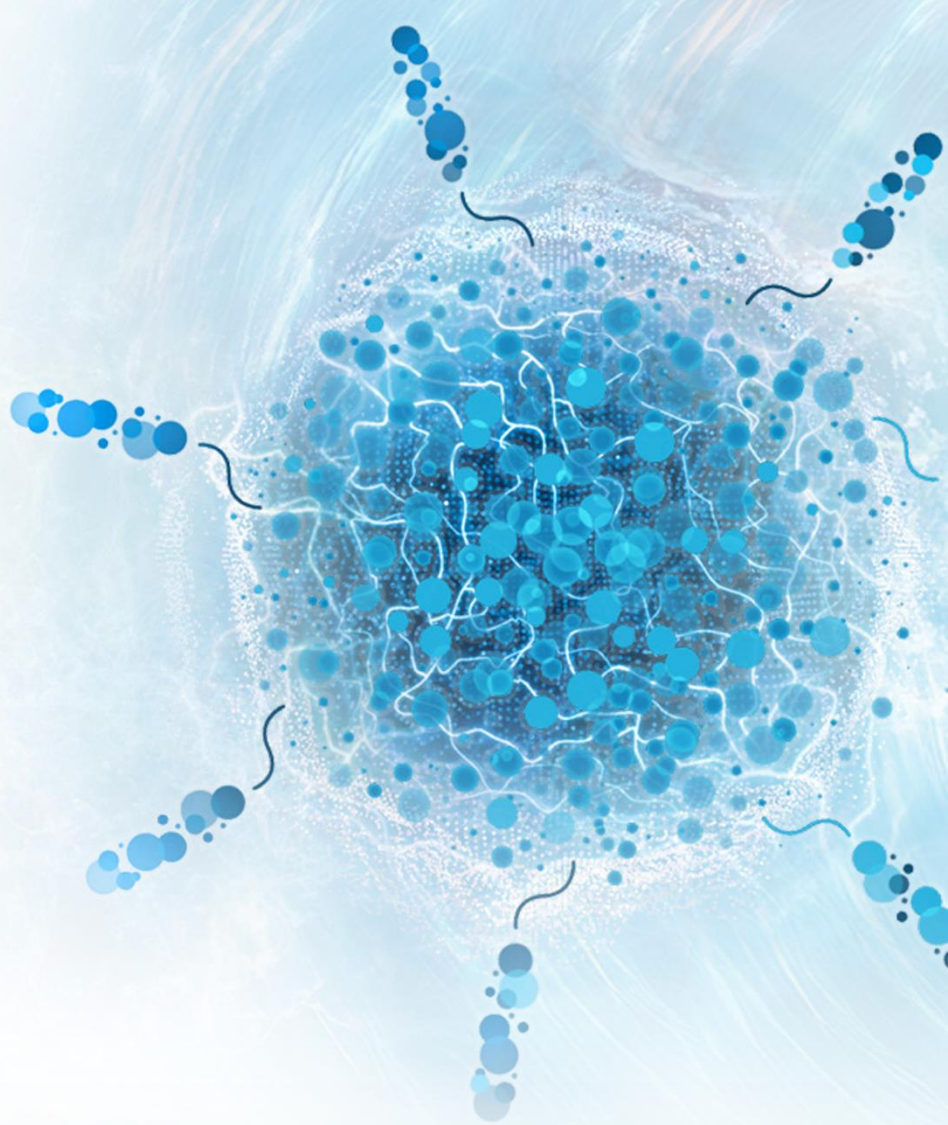
Donor screening data is a ripe space for cellular analysis via artificial intelligence. Advances in this space can create a faster and more economical way to assess potential donors.

Gene editing is the most sensitive and critical element of the manufacturing process. Advances in electroporation unit operations can improve editing, reduce the need for later depletion, and improve cell health throughout the process.

Poseida manufacturing processes to date have used static expansion flasks. Dynamic bioreactor environments and Booster Molecule enabling technology have the potential to unlock significantly higher yields, which results in lower cost of goods and a smaller required pool of donors.

POSEIDA THERAPEUTICS

# Concluding remarks

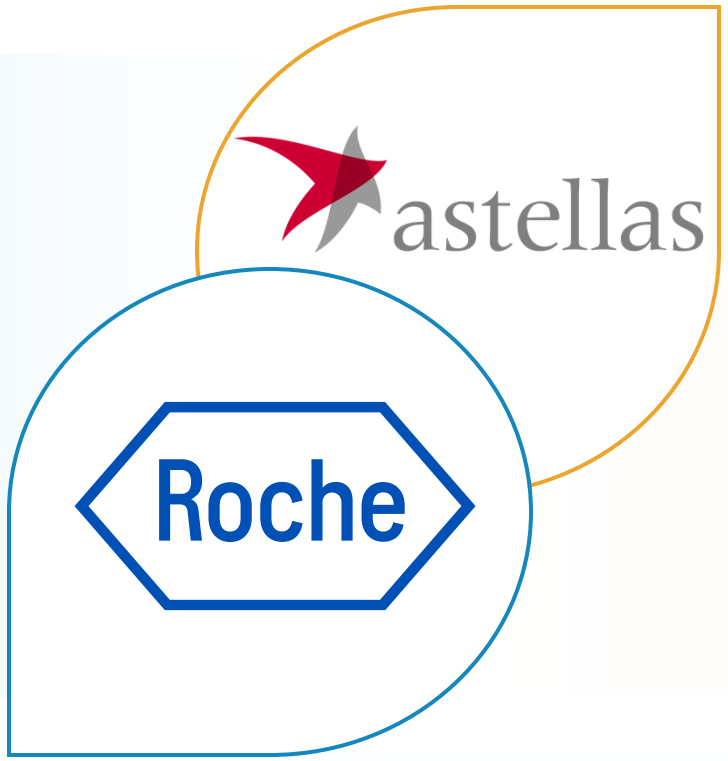


**Kristin Yarema, PhD**

*President & CEO*

# Strong partnerships with Roche and Astellas validate allogeneic platform and fund programs

- Deal worth up to **$6 billion** in aggregate value, plus royalties
- Currently **three heme malignancy** collaboration programs
- **$80 million** in milestone payments earned to date in 2024




- **$50 million** upfront plus up to **$550 million**, plus royalties
- Combines Poseida allogeneic platform with Astellas technology for up to two **'convertibleCARs™' for solid tumors**
- Follows an earlier **$50 million equity investment** in Poseida

**More than $400M generated through external partnership payments, upfronts and milestones over the past three years**

# Poseida's path to value creation in allogeneic cell therapy

*Presently heading into our second growth horizon*

*Build Foundation*

## VALIDATE PLATFORM

- Advance non-viral allogenic CAR-$T_{SCM}$ assets in the clinic
  - P-BCMA-ALLO1 in Phase 1b; RMAT designation
  - 3 clinical stage programs across liquid & solid tumors
- Establish partnerships with Roche and Astellas
- Manufacture GMP product in-house

*Extend Approach*

## DRIVE VALUE

- Enter autoimmune disease space
- Deepen and extend pharma partnerships
- Grow wholly-owned asset pipeline
- Refine next-generation tools & technologies
- Further strengthen manufacturing, healthy donor competencies

*Disrupt Cell Therapy*

## DELIVER FOR PATIENTS

- Stream assets from allogeneic CAR-$T_{SCM}$ product engine
- Launch new cell therapy platforms for greater reach (CAR-TCR and beyond)
- Manufacture high volume, low COGS products at scale
- Commercialize partnered and own assets that have strong value propositions

POSEIDA THERAPEUTICS

# Thank You

*To our patients, partners and dedicated Poseida teams for supporting our bold mission to redefine the future of cell therapy for life-threatening cancers and autoimmune diseases*