P-BCMA-ALLO1 — a non-viral allogeneic anti-BCMA CAR T therapy with potent anti-tumor function for the treatment of multiple myeloma

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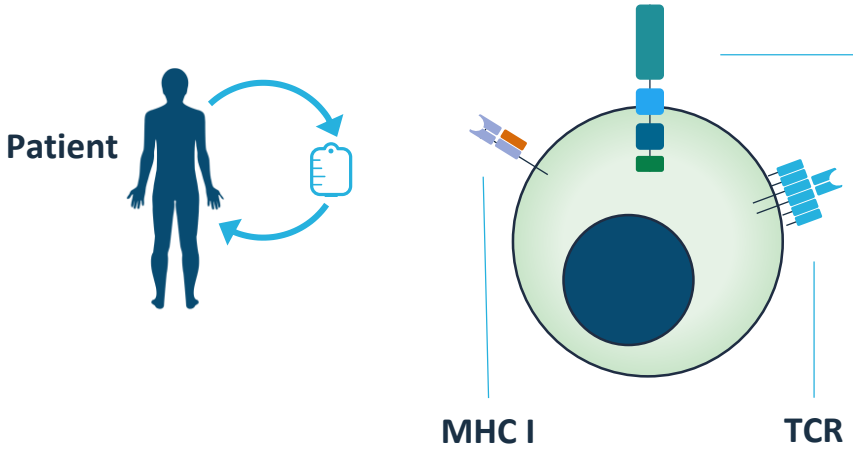
POSEIDA THERAPEUTICS

Allogeneic CAR-T – The Holy Grail of Cell Therapy

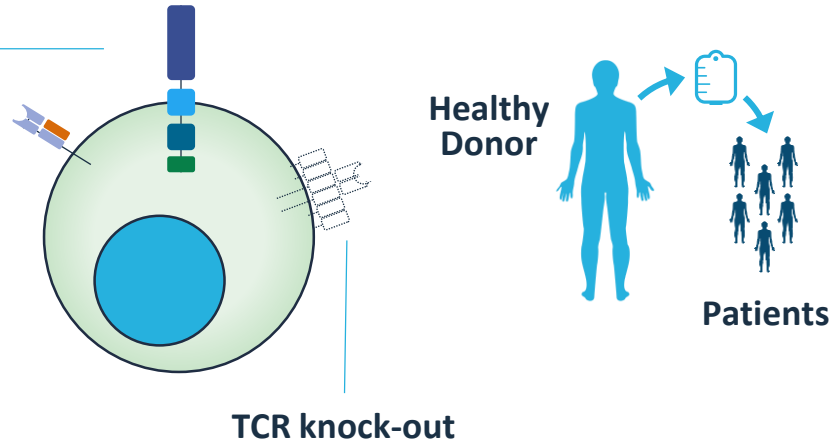
AUTOLOGOUS/PATIENT-DERIVED CAR-T



EXPERIENCE TO DATE

- Good efficacy in liquid tumor indications including Poseida's P-BCMA-101
- Outstanding safety driven by non-viral product with T stem cell memory (T_{SCM}) phenotype
- Relatively high production cost of an individualized product

ALLOGENEIC/HEALTHY DONOR-DERIVED CAR-T



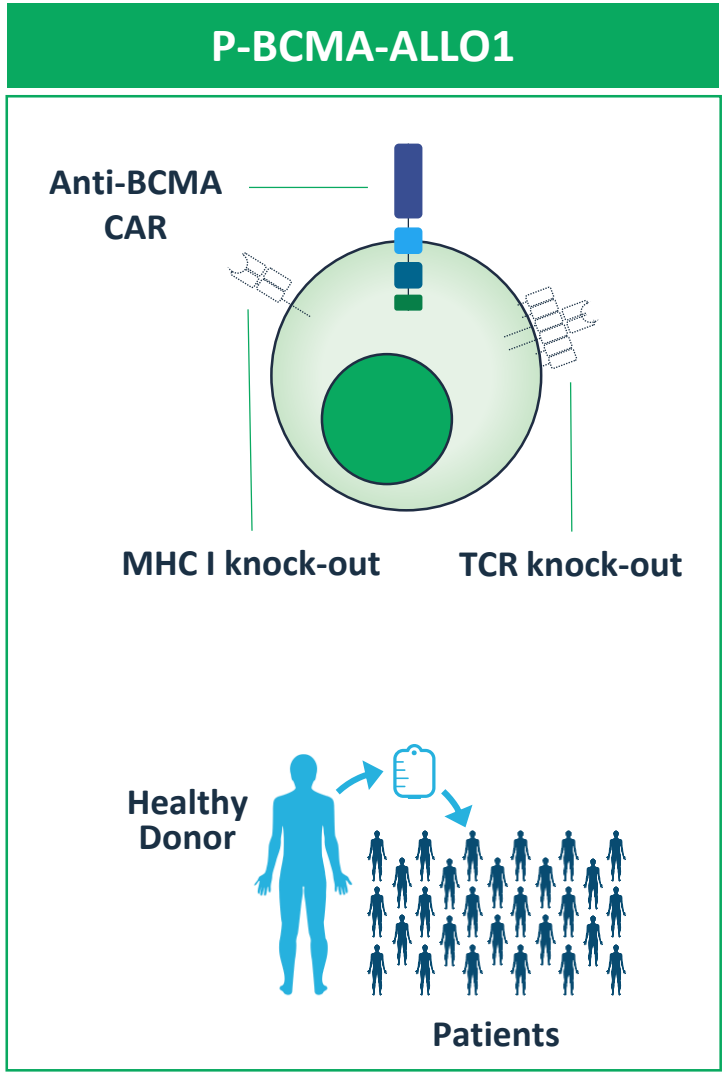
PROMISES AND ADVANTAGES

- Healthy donor material promises better product characteristics
- Off the shelf access and convenience
- Dramatically reduced cost

POSEIDA THERAPEUTICS

P-BCMA-ALLO1 – Creating a New Standard for Allogeneic CAR-T

- **High % of T_{SCM}** Phenotype through use of piggyBac® technology
  - Growing evidence that T_{SCM} is the desired phenotype for CAR-T
- **Fully allogeneic** approach with Cas-CLOVER gene editing
  - TCR KO to prevent graft versus host disease
  - MHC I KO to prevent host versus graft reaction
- Addressing TCR deletion liability with **Booster Molecule technology**
  - Creating gene edited CAR-T without a loss in functionality
- Robust manufacturing process with the ability to generate **hundreds of doses** per manufacturing run
- Bring our **superior safety profile** from autologous to allogeneic CAR-T



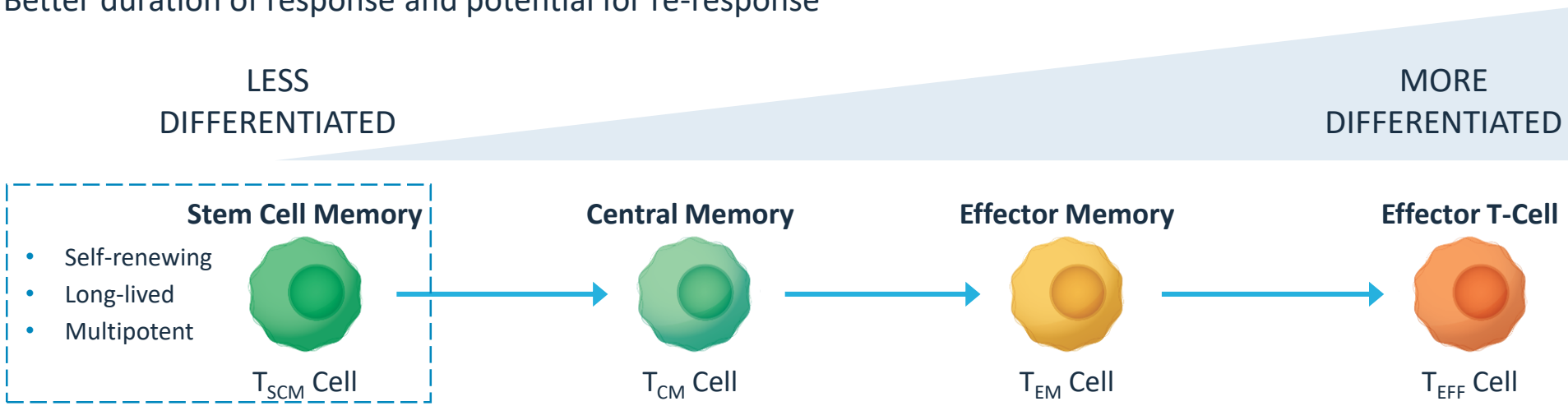
POSEIDA THERAPEUTICS

T_{SCM} – The Ideal T Cell for Adoptive Immunotherapy

> "The extreme longevity, the robust proliferative potential and the capacity to reconstitute a wide-ranging diversity of the T cell compartment make **the T_{SCM} cell type an ideal cell population to employ in adoptive immunotherapy**"

- Gattinoni *et al.* T memory stem cells in health and disease. *Nat. Med* .(2017).

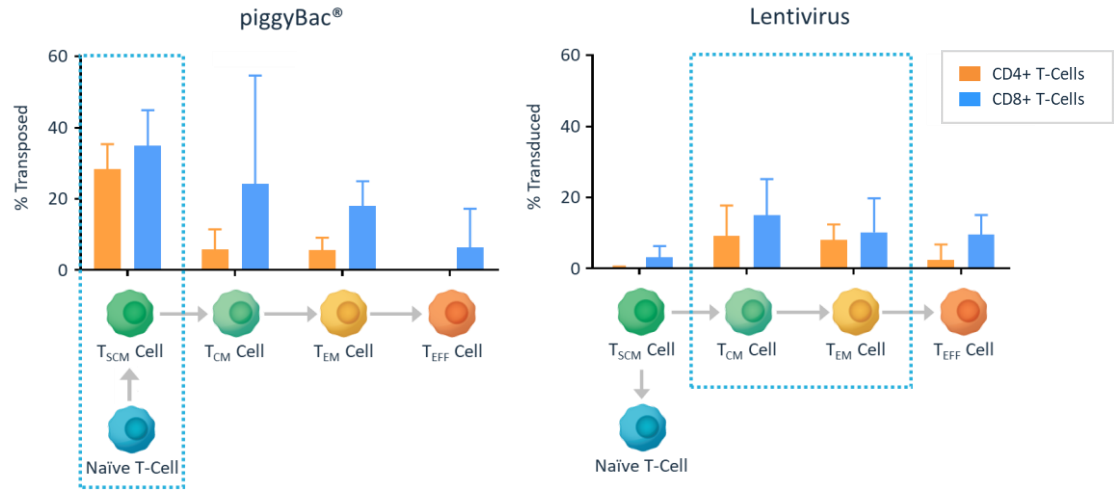
- **P-BCMA-101 – an autologous T_{SCM} CAR-T**
  - $\%T_{SCM}$ correlates with response in patients
  - Gradual expansion of T_{SCM} CAR-T with less toxicity
  - Better duration of response and potential for re-response



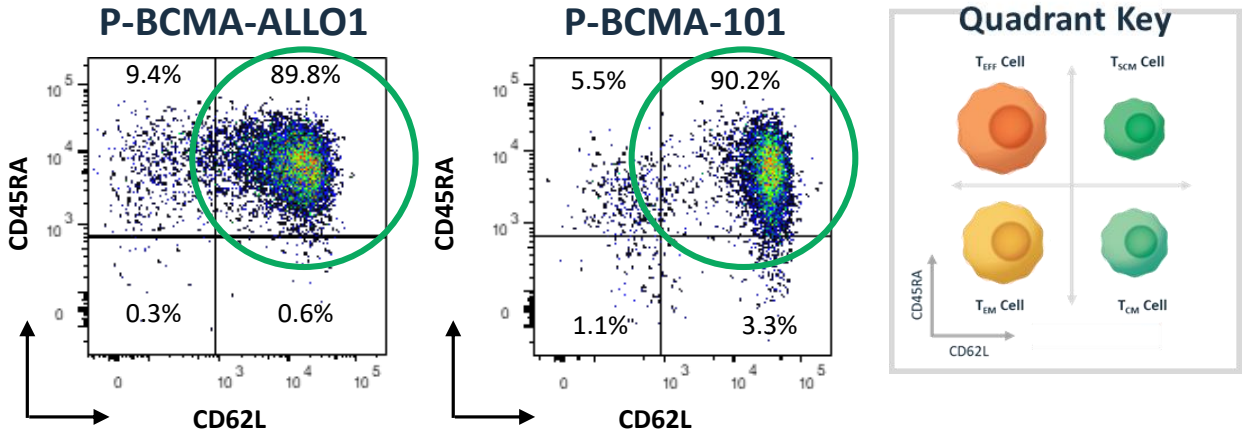
POSEIDA THERAPEUTICS

PiggyBac® Produces an Allogeneic CAR-T Product rich in T_{SCM}

- **PiggyBac® preferentially transposes naïve/T_{SCM} cells**
  - Lentivirus transduced a more differentiated cell population



- Produces **P-BCMA-ALLO1** – an **allogeneic CAR-T rich in T_{SCM}** phenotype
  - Harness the potency and safety benefits already experienced with autologous P-BCMA-101



POSEIDA THERAPEUTICS

PiggyBac® – High Cargo Capacity Allows Delivery of Additional Safety Features

SAFETY SWITCH

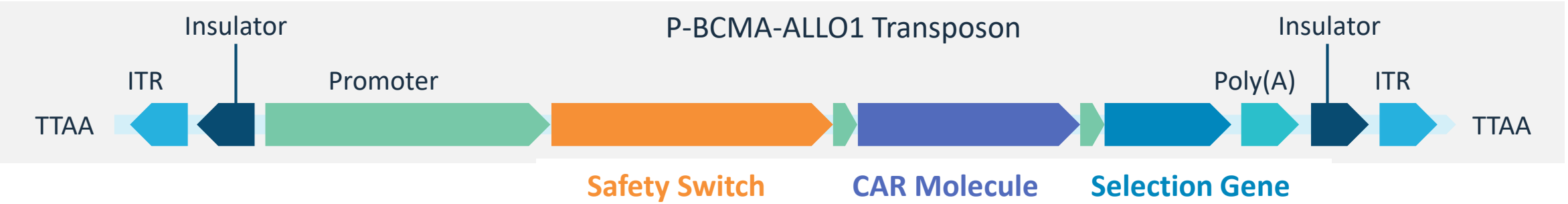
Incorporates proprietary safety switch

- Rapid, dose-dependent elimination of engineered T-cells if needed
- Management of Cytokine Release Syndrome (CRS) or other AEs

SELECTION GENE

Drug resistance gene permits positive selection

- **~100% of T cells** in final product express the CAR molecule
- Predicted to result in **better therapeutic index**



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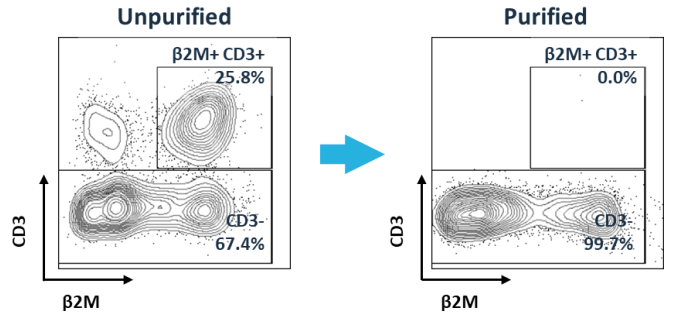
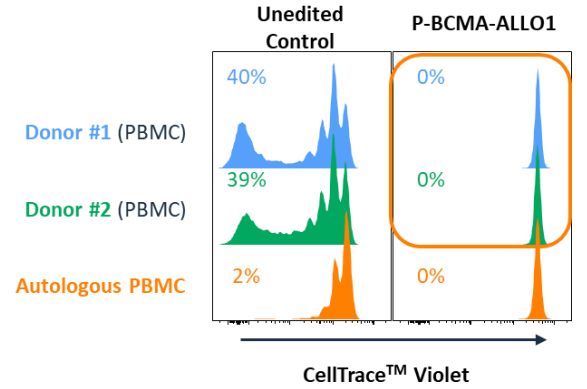
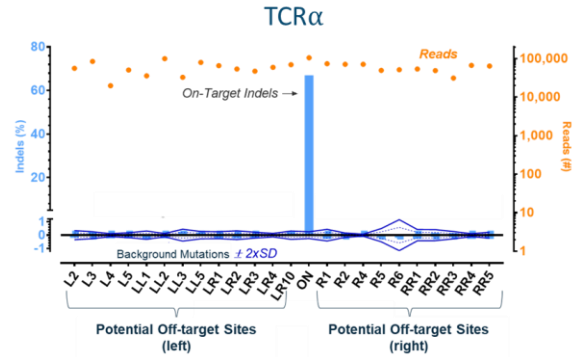
Cas-CLOVER Gene Editing for Improved Safety

- Efficient gene editing in **resting cells** is crucial for generation of **T_{SCM} rich allogeneic CAR-T**
- Multiplex gene knock out of TCR & MHC class I
- TCR KO purification to generate a safe product **unable to mediate GVHD**
- **No/low off-target cutting** increases safety of gene editing







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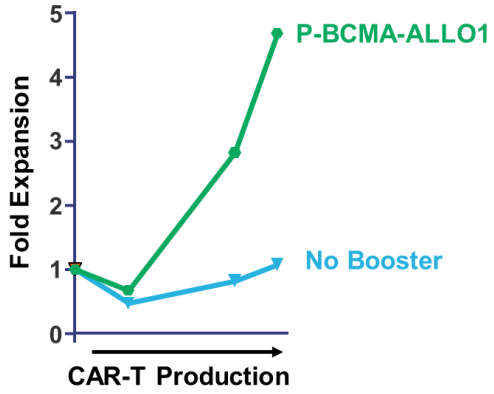
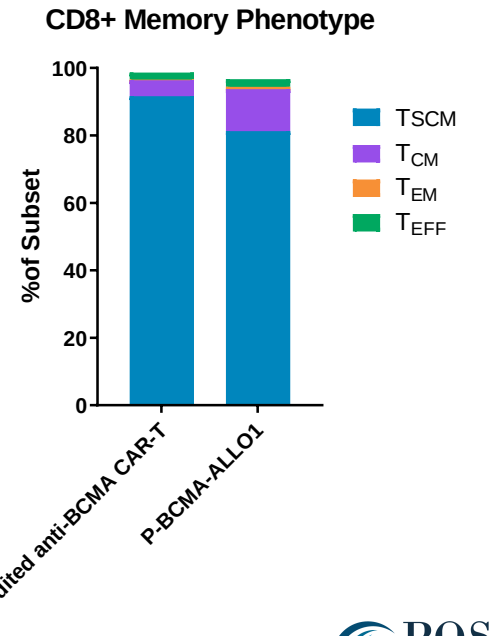
Booster Molecule Increases Yield and Preserves Desirable Attributes of P-BCMA-ALLO1

- Gene editing of TCR can impair allogeneic CAR-T products compared to unedited healthy donor CAR-T – The Allo Tax



- Booster Molecule technology overcomes these limitations, **significantly increases production yield** while **preserving desirable attributes** of P-BCMA-ALLO1



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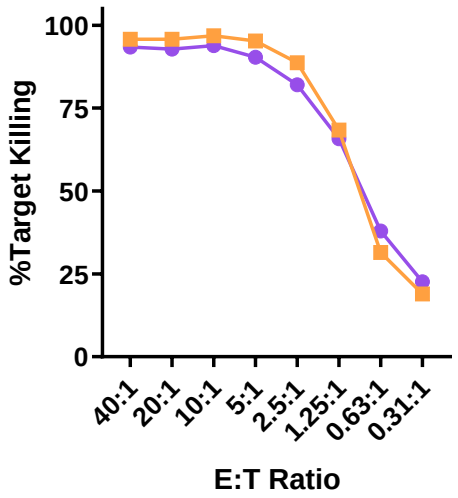
Booster-Produced P-BCMA-ALLO1 Functions at Least as well as Unedited Healthy Donor CAR-T Cells *in vitro*

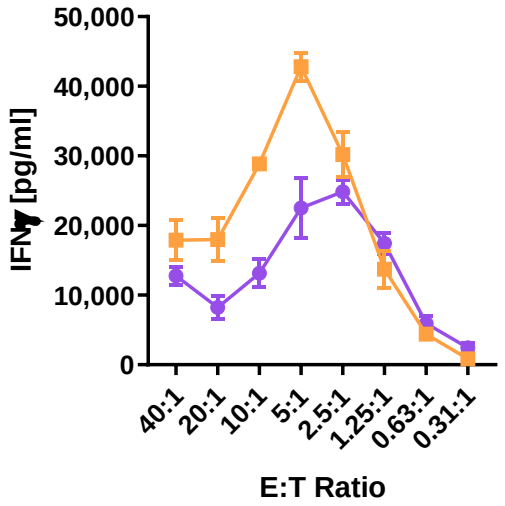
- Booster Molecule **preserves effector function and proliferative potential** even in TCR KO cells

- P-BCMA-ALLO1 at least as potent as donor-matched, unedited CAR-T cells

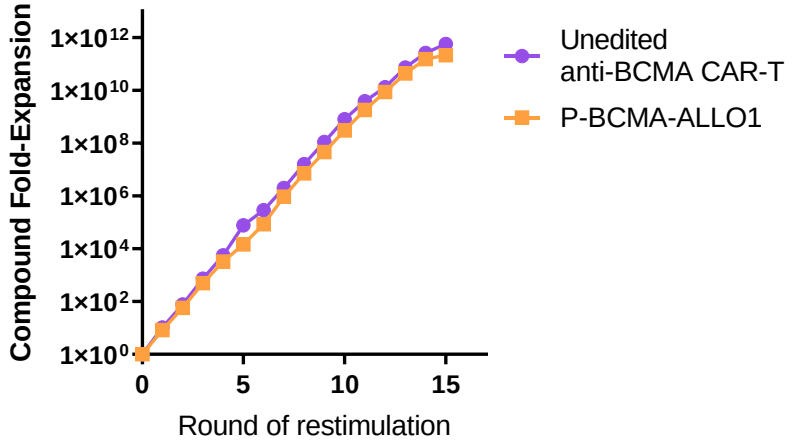
Target Cell Killing



Cytokine Secretion



High Proliferative Capacity



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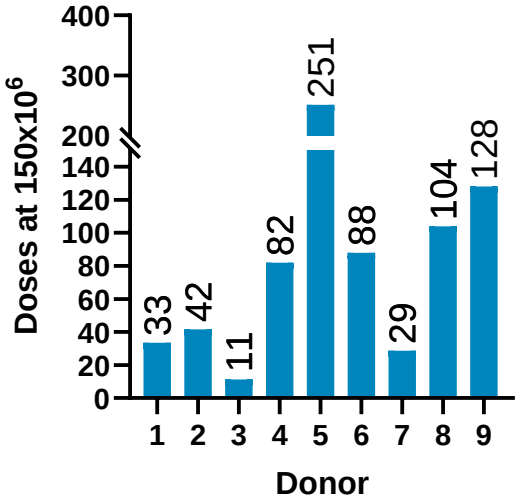
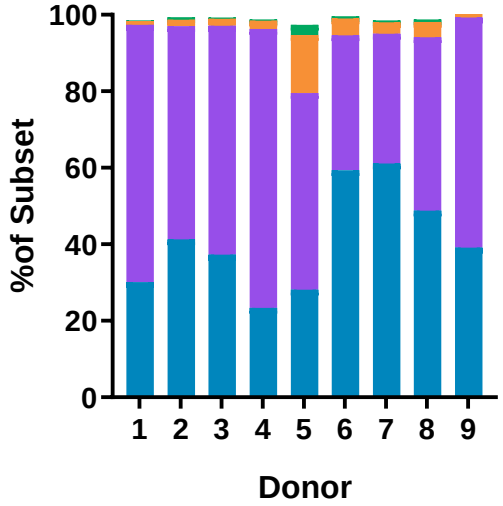
P-BCMA-ALLO1 Manufacturing Process is Robust Across a Wide Range of Healthy Donors

- **piggyBac®** gene delivery, **Cas-CLOVER** gene editing, and **Booster Molecule** result in highly robust P-BCMA-ALLO1 manufacturing process
- **Tens to hundreds of doses per manufacturing run** produced from a group of minimally pre-selected donors
- **High %T_{SCM}** achieved across all donors





*Includes both T_{CM} and T_{SCM} cells in transistion

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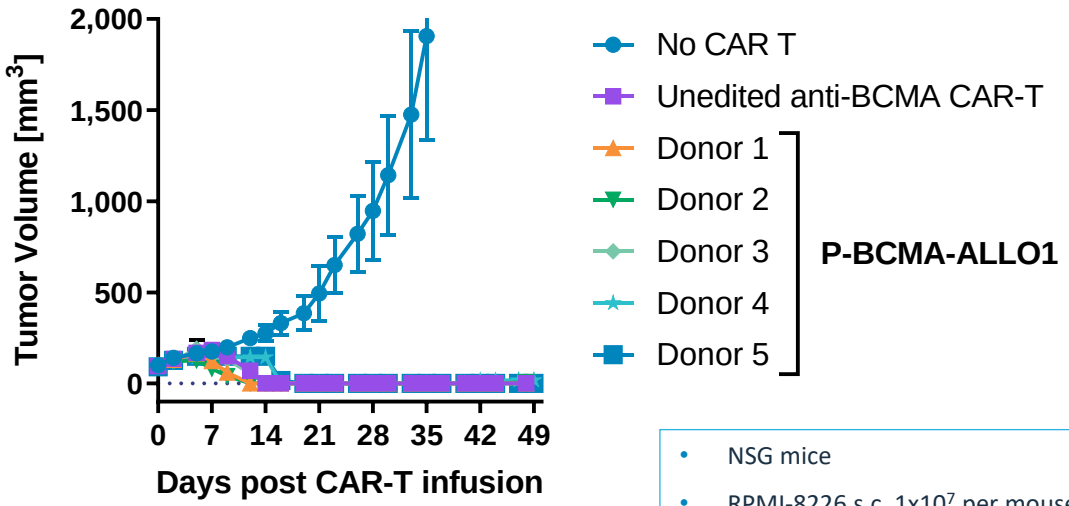
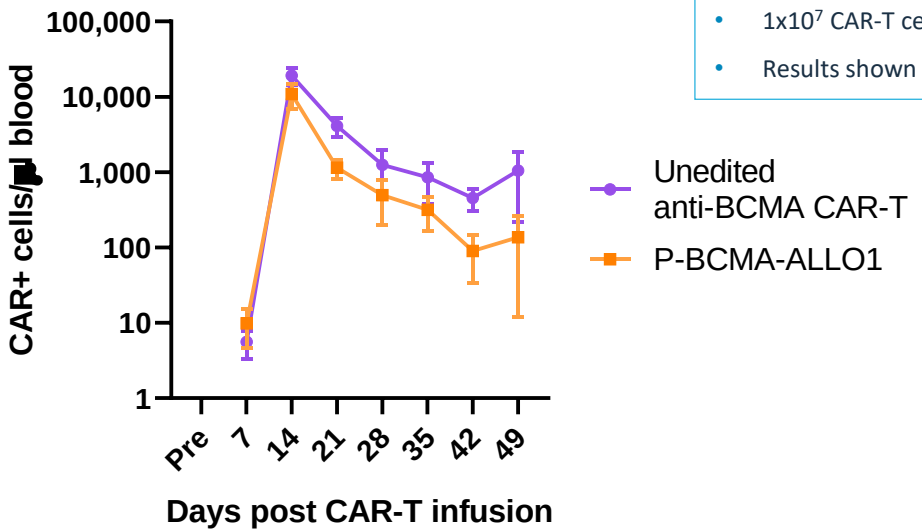
P-BCMA-ALLO1 from Various Donors Shows *in vivo* Activity

- P-BCMA-ALLO1 produced from five healthy donors showed **rapid and durable anti-tumor response** in MM xenograft model across all donors

- **Anti-tumor effect**, CAR-T **expansion**, and CAR-T **persistence** of P-BCMA-ALLO1 was comparable to unedited anti-BCMA CAR-T cells



- NSG mice
- RPMI-8226 s.c. $1x10^7$ per mouse
- $1x10^7$ CAR-T cells per mouse
- Results shown as mean ± SD



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Summary

- Highly desirable T_{SCM}-rich product phenotype
- Allogeneic CAR-T equivalent or better than unedited healthy donor CAR-T *in vitro* & *in vivo*
- Robust non-viral manufacturing process compatible with majority of healthy donors & ability to generate hundreds of doses per manufacturing run
- Superior safety due to T_{SCM} phenotype, no/low off-target gene editing, and safety switch
- Results support rapid advancement of P-BCMA-ALLO1 into the clinic for treatment of MM