UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported):
February 23, 2022

Poseida Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-39376**	**47-2846548**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

9390 Towne Centre Drive, Suite 200, San Diego, California	**92121**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (858) 779-3100

N/A
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	**PSTX**	**Nasdaq Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On February 23, 2022, members of management of Poseida Therapeutics, Inc. (the "Company") and external advisors are providing an update on the Company's research and development programs and making available the corporate presentation attached as Exhibit 99.1 to this report. The presentation is also available under the "Investors" section of the Company's website.

The information in this Item 7.01 of this report (including Exhibit 99.1) is furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended. The information shall not be deemed incorporated by reference into any other filing with the Securities and Exchange Commission made by the Company, whether made before or after today's date, regardless of any general incorporation language in such filing, except as shall be expressly set forth by specific references in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Corporate presentation, dated February 23, 2022
104	Cover Page Interactive Data File

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Poseida Therapeutics, Inc.

Date: February 23, 2022

By: /s/ Harry J. Leonhardt, Esq.
Name: Harry J. Leonhardt, Esq.
Title: General Counsel, Chief Compliance Officer & Corporate Secretary

Exhibit 99.1

POSEIDA THERAPEUTICS

The Next Wave of Cell and Gene Therapies with the Capacity to Cure

R&D Day

February 23, 2022

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 activities; estimated market opportunities for product candidates; 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: risks 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; 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.

R&D Day Agenda and Speakers

Poseida Programs and Technologies

- Welcome
- Introduction and Overview
- Platform Technologies
  - Super PiggyBac® DNA Delivery System
  - CAS-CLOVER™ Gene Editing
  - Biodegradable Nanoparticle Delivery
- T_{SCM} Phenotype in CAR-T
  - The Importance of T_{SCM}
  - Stemness and Our Differentiation
- T_{SCM}-Based CAR-T Therapies
  - P-PSMA-101 Autologous CAR-T for mCRPC
  - Allogeneic CAR-T Platform and Programs
  - Advantages of Dual CAR
- Innovative Gene Therapies
  - Partnering with Takeda on Gene Therapies
  - P-FVIII-101 for Hemophilia A
  - P-OTC-101 for OTCD
- Emerging Technologies
  - Site-Specific piggyBac® (SS-SPB)
  - Cas-CLOVER™ in vivo
  - TCR-T platform update
  - CAR 3.0 update
- Business Strategy and Mission
- Conclusion
- Audience Q&A

POSEIDA THERAPEUTICS

R&D Day 2022

Eric Ostertag, MD, PhD
Founder & Executive Chairman

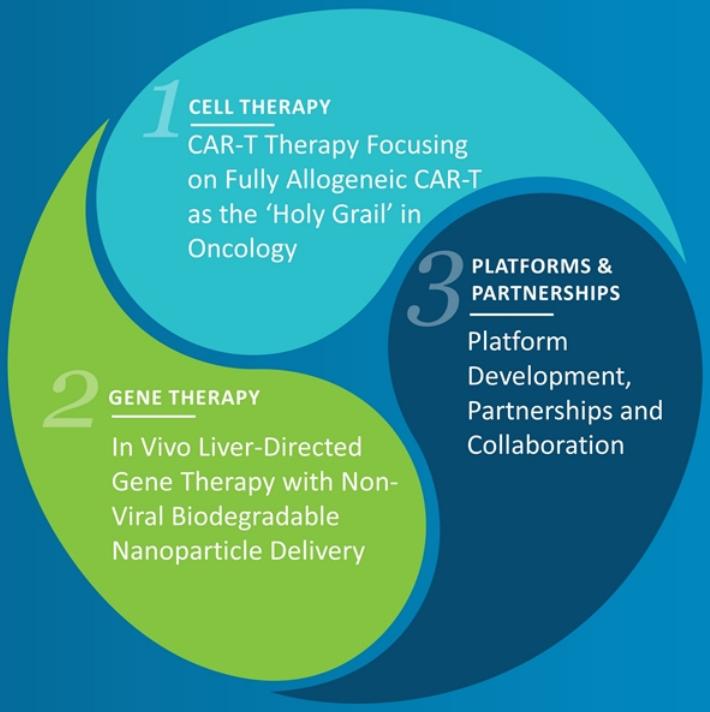
On a Mission to Redefine Cell and Gene Therapy

NASDAQ: **PSTX**

260+ Employees

Headquartered in **San Diego, CA**

Strong and **Broad IP** Portfolio



POSEIDA THERAPEUTICS

Powerful Platform Technologies Drive Our Strategy

Proprietary In-house Technology Platforms for Gene Insertion, Gene Editing, and Gene Delivery

Super piggyBac®

- Non-viral system
- Highly efficient technology to add DNA to genome
- Large genetic cargo capacity
- Broad range of cells
- Advantages in tolerability, potency, speed to clinic and costs

GENE INSERTION

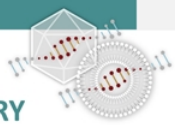
Cas-CLOVER™

- Highly precise site-specific nucleases
- Ability to edit resting T cells while maintaining desirable T_{SCM} characteristics
- Major advantages:
  - tolerability
  - ease of design
  - low cost
  - multiplexing ability

GENE EDITING

Nanoparticles AAV Vectors

- Delivers long-term stable gene expression
- Non-viral and viral delivery of DNA and proteins both ex vivo and in vivo
- Ability to deliver to multiple cell types and target specific tissues



GENE DELIVERY

Individually or in combination, our core technologies enable us to engineer a portfolio of product candidates designed to overcome the limitations of current cell and gene therapeutics

Our Platform Technologies Have Broad Reach

Various combinations our innovative platform technologies create unique opportunities across the cell and gene therapy landscape

*Poseida has listed companies it believes are representative of those active in cell and gene therapy.

POSEIDA THERAPEUTICS

Powerful Platform Technologies Drive Our Strategy

Proprietary In-house Technology Platforms for Gene Insertion, Gene Editing, and Gene Delivery

Super piggyBac®

- Non-viral system
- Highly efficient technology to add DNA to genome
- Large genetic cargo capacity
- Broad range of cells
- Advantages in tolerability, potency, speed to clinic and costs

GENE INSERTION

Cas-CLOVER™

- Highly precise site-specific nucleases
- Ability to edit resting T cells while maintaining desirable T_{SCM} characteristics
- Major advantages:
  - tolerability
  - ease of design
  - low cost
  - multiplexing ability

GENE EDITING

Nanoparticles AAV Vectors

- Delivers long-term stable gene expression
- Non-viral and viral delivery of DNA and proteins both ex vivo and in vivo
- Ability to deliver to multiple cell types and target specific tissues

GENE DELIVERY

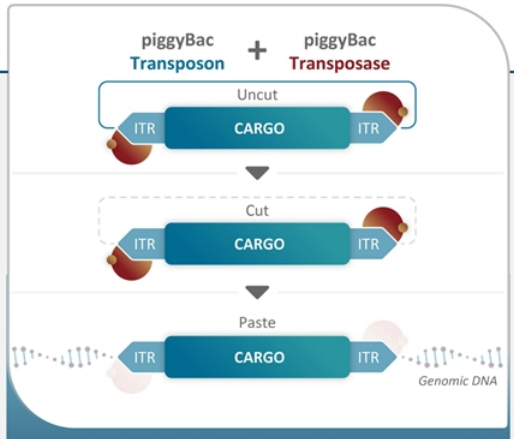
Individually or in combination, our core technologies enable us to engineer a portfolio of product candidates designed to overcome the limitations of current cell and gene therapeutics

PiggyBac®: Versatility in DNA Delivery

BENEFITS IN
CELL THERAPY

Generating CAR-T Products with Desirable High Percentage of T_{SCM} Cells

- Preferentially favors **stem cell memory T cells (T_{SCM})** and works well in **resting T cells** for potentially improved tolerability and more durable responses
- **Large cargo capacity** enables multi-CAR products, addition of safety switch and selection gene



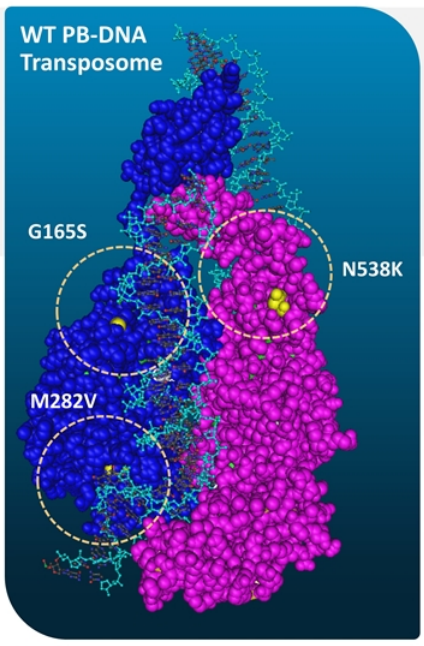
- Enables DNA integration
- Non-viral gene insertion technology
- Works in a wide variety of cell types
- Multiple safety and cost benefits

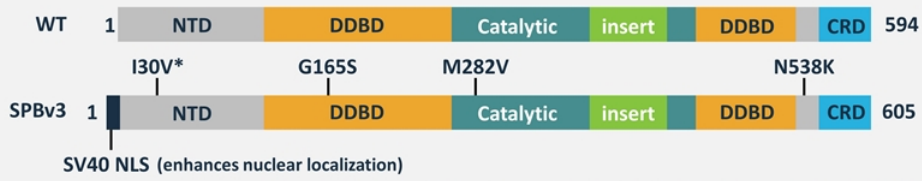
BENEFITS IN
GENE THERAPY

Integrates Into DNA Delivering Stable Long-Term Expression

- Ideal for use in **dividing tissues** like those in juvenile liver
- **Highly efficient** integration may allow **reduced dosing and single treatment cures**
- **Large cargo** for delivering larger genes
- **Delivered using AAV + nanoparticle** or in vivo EP

piggyBac®: Wild Type (WT) vs. Super piggyBac® (SPB)



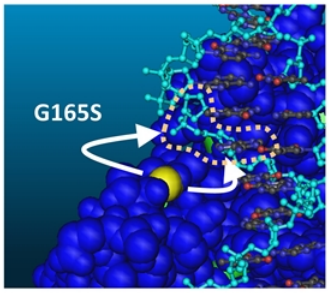


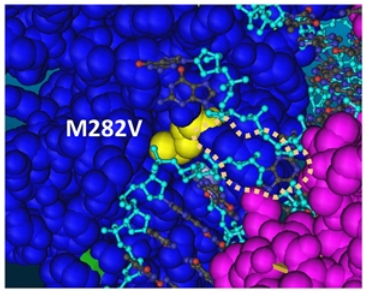
NTD: N-terminal domain | **DDBD:** Dimerization & DNA binding domain | **CRD:** Cysteine-rich domain
***unknown mechanism underlying hyperactive effect of I30V**

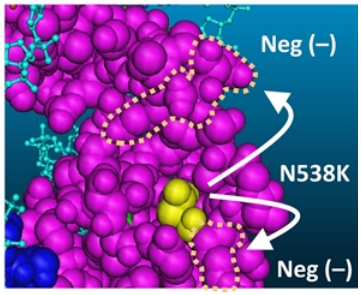
DNA-BINDING
G165S: Enhances DNA binding (H-bonds w/ PO4 and Adenine)

CATALYSIS
M282V: Enhances pi-stacking b/t Tyr283 and Adenine in TTAA

STABILIZATION
N538K: Electrostatic stabilization in linker between DDBD and CRD





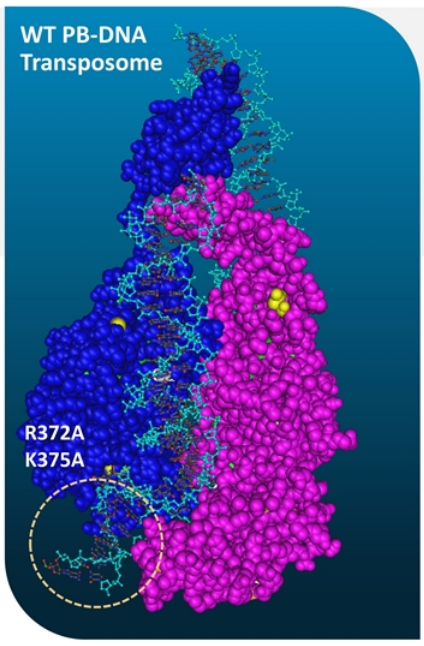


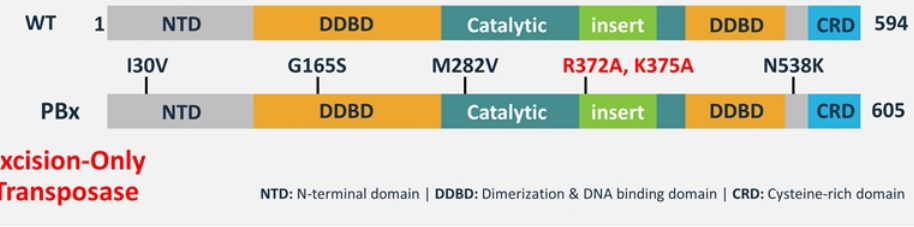
*Structure from **Chen et al. Nat Commun, 2020 Jul 10;11(1):3446***

*Hyperactive mutations from **Yusa et al. PNAS, 2011 Jan 25;108(4):1531-6***

POSEIDA THERAPEUTICS

piggyBac®: Wild Type (WT) vs. Excision-Only piggyBac® (PBx)



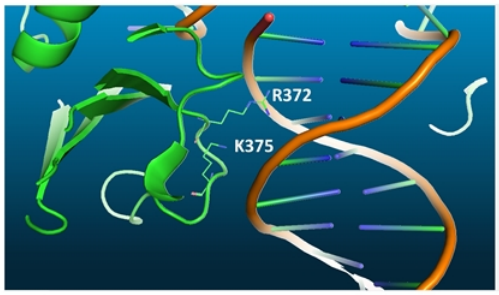


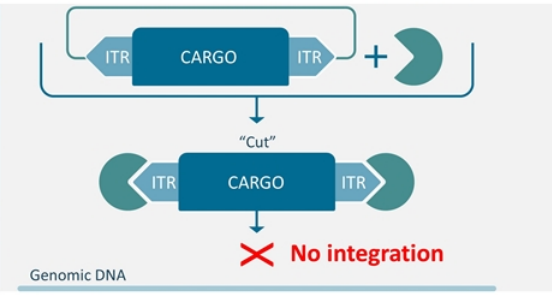
Excision-Only Transposase

NTD: N-terminal domain | **DDBD:** Dimerization & DNA binding domain | **CRD:** Cysteine-rich domain

TARGET DNA-BINDING

R372 & K375: Critical because of interaction with target DNA (H-bonds w/ PO4 in backbone)





Structure from ***Chen et al. Nat Commun, 2020 Jul 10;11(1):3446***

PBx mutations from ***Li et al. PNAS, 2013 Jun 18;110(25):E2279-87***

POSEIDA THERAPEUTICS

Powerful Platform Technologies Drive Our Strategy

Proprietary In-house Technology Platforms for Gene Insertion, Gene Editing, and Gene Delivery

Super piggyBac®

- Non-viral system
- Highly efficient technology to add DNA to genome
- Large genetic cargo capacity
- Broad range of cells
- Advantages in tolerability, potency, speed to clinic and costs

Cas-CLOVER™

- Highly precise site-specific nucleases
- Ability to edit resting T cells while maintaining desirable T_{SCM} characteristics
- Major advantages:
  - tolerability
  - ease of design
  - low cost
  - multiplexing ability

Nanoparticles AAV Vectors

- Delivers long-term stable gene expression
- Non-viral and viral delivery of DNA and proteins both ex vivo and in vivo
- Ability to deliver to multiple cell types and target specific tissues

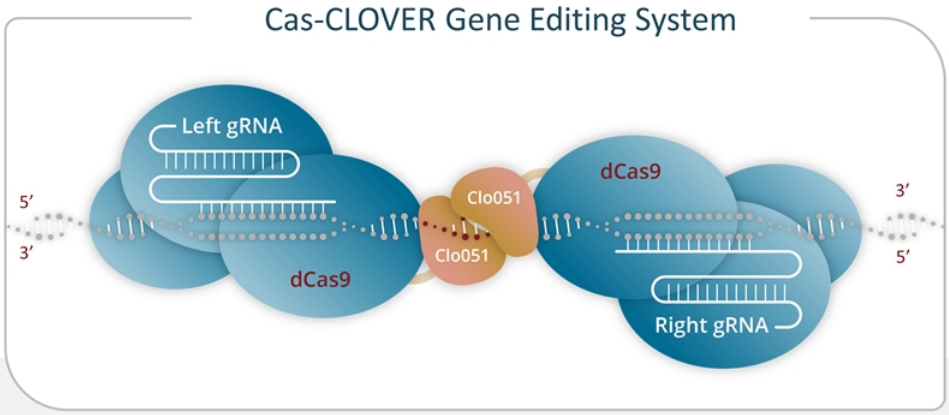
Individually or in combination, our core technologies enable us to engineer a portfolio of product candidates designed to overcome the limitations of current cell and gene therapeutics

GENE INSERTION

GENE EDITING

GENE DELIVERY

Cas-CLOVER™: Ultra-Clean Gene Editing



- **Low-to-no off-target cutting**
- **High Editing Efficiency** in resting T-cells resulting in high % of T_{SCM} cells
- Ease of use/design
- Multiplexing ability
- High specificity
- Lower cost

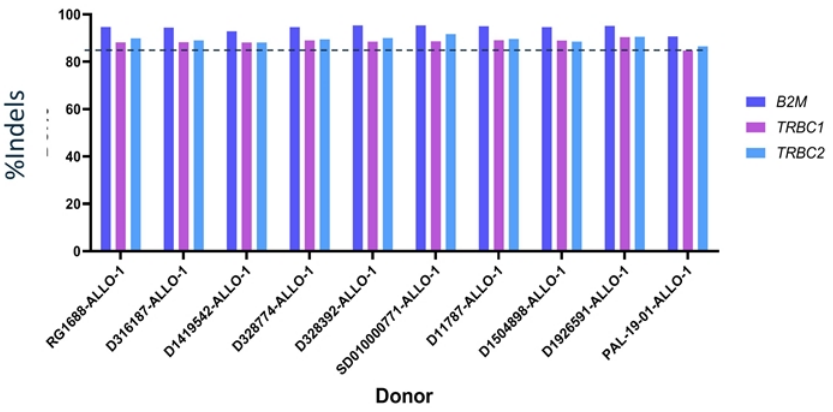
Potentially the Cleanest Gene Editing Platform

with important ability to efficiently edit resting cells enables fully **Allogeneic CAR-T** products and **Gene Therapy** applications including ongoing development for non-viral in vivo gene editing

Highly Efficient On-target Knock-out in the P-BCMA-ALLO1 Product, at Both *TRBC* and *B2M* Sites Using Multiplexed Cas-CLOVER™ Editing

- Multiple products (10) were tested by NGS to determine editing (% Indels) at the *TRBC1*, *TRBC*2 and *B2M* sites
- Single step multiplexed editing is highly efficient: Editing at *B2M* and *TRBC* is >85% across multiple donors (by NGS)
- Functional protein knock-out confirmed by FACS, other functional assays

TRBC and *B2M* Mutation (by NGS)

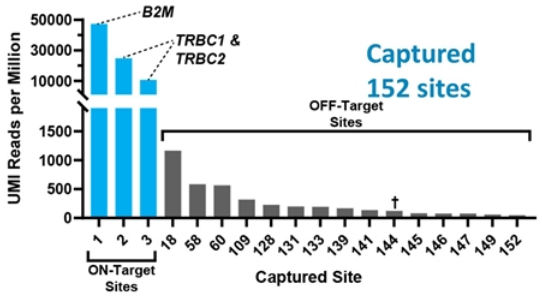


POSEIDA THERAPEUTICS

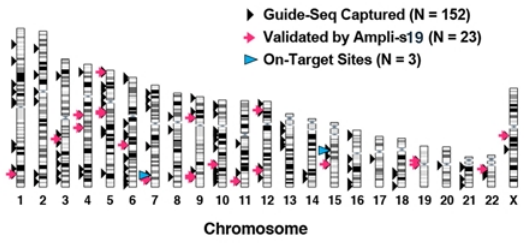
Cas-CLOVER™: Low to No Off-Target Cutting

Guide-Seq

Sites Captured in ≥ 2 Donors by Guide-Seq



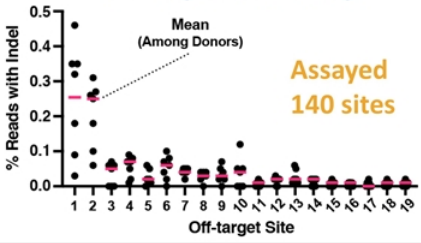
Captured and Validated OTE Sites



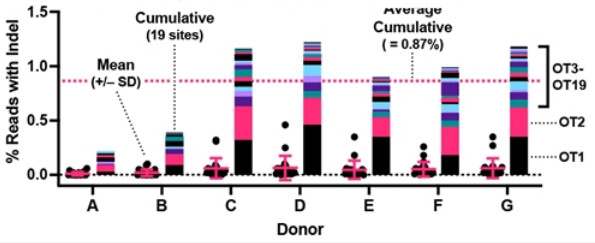
No hits in oncogenes or tumor suppressors (COSMIC database)

Ampli-Seq

Off-target Site Editing



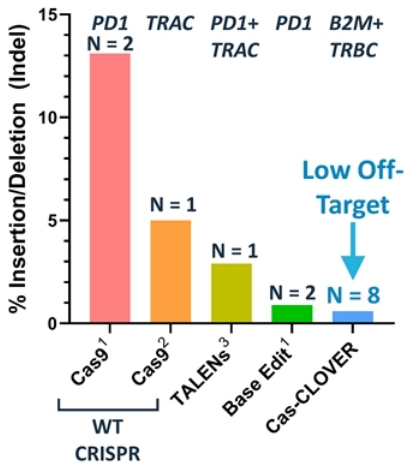
Off-target Mutations Per Donor



POSEIDA THERAPEUTICS

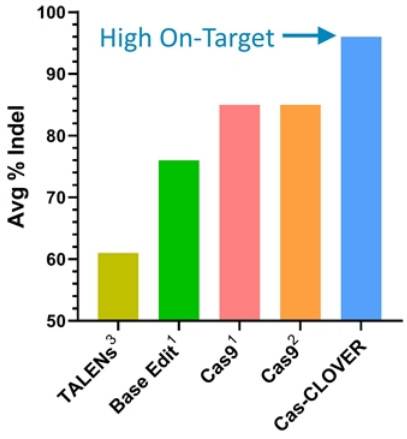
Cas-CLOVER™: Fidelity in T Cells vs. Competing Technology

Maximum observed off-target frequency



- Other studies examine few (10 to 25) candidate off-target sites[1-3]
- Our Cas-CLOVER off-target study is ~10x broader and includes 8 donor lots

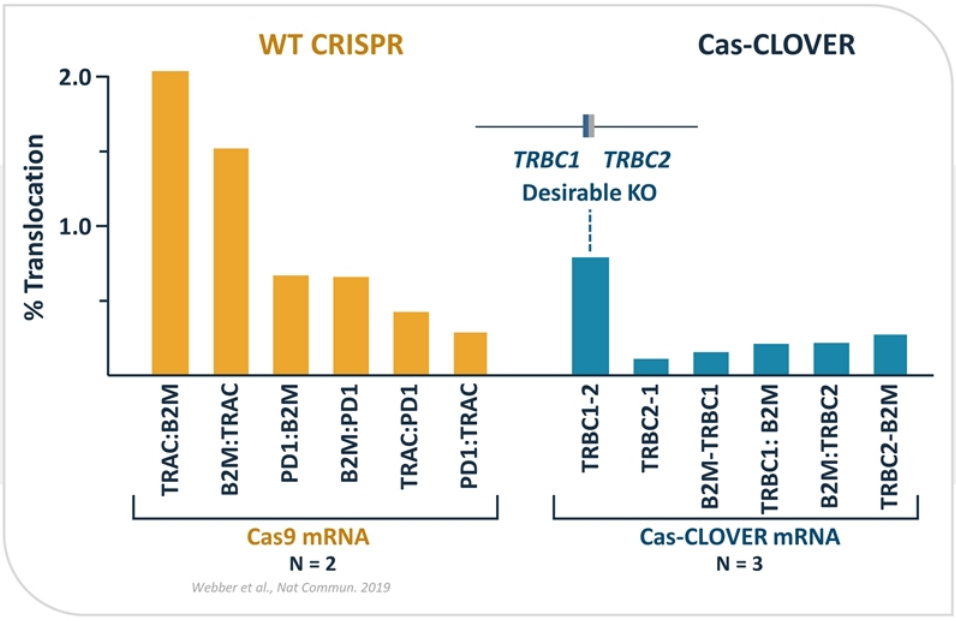
High Fidelity in the context of High Efficiency



1. Webber et al., Nat Commun. 2019 Nov 19;10(1):5222 2. Ren et al., Oncotarget. 2017 Mar 7; 8(10): 17002–17011 3. Gautron et al., Mol Ther Nucleic Acids. 2017 Dec 15;9:312-321

POSEIDA THERAPEUTICS

Cas-CLOVER™: Very Low Translocation Frequency in T Cells vs. CRISPR



Webber et al., Nat Commun. 2019

Cas-CLOVER Allogeneic CAR-T translocation rate <0.4%

Other studies (CRISPR & TALENs):

- **4% cells have *TRAC* translocation (FISH)**
  Qasim et al., *Sci Trans Med*. 2017
- **2-2.5% with *TRAC-B2M* translocation**
  Giannoukos et al., *BMC Genomics.* 2018
- **Up to 2% with *TRAC-CD52* translocations**
  Poirot et al., *Cancer Res*. 2015

With Cas-CLOVER, the avg. rate of translocation with off-target sites <0.01%

Powerful Platform Technologies Drive Our Strategy

Proprietary In-house Technology Platforms for Gene Insertion, Gene Editing, and Gene Delivery

Super piggyBac®

- Non-viral system
- Highly efficient technology to add DNA to genome
- Large genetic cargo capacity
- Broad range of cells
- Advantages in tolerability, potency, speed to clinic and costs

Cas-CLOVER™

- Highly precise site-specific nucleases
- Ability to edit resting T cells while maintaining desirable T_{SCM} characteristics
- Major advantages:
  - tolerability
  - ease of design
  - low cost
  - multiplexing ability

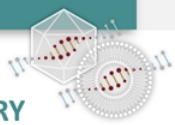
Nanoparticles AAV Vectors

- Delivers long-term stable gene expression
- Non-viral and viral delivery of DNA and proteins both ex vivo and in vivo
- Ability to deliver to multiple cell types and target specific tissues

Individually or in combination, our core technologies enable us to engineer a portfolio of product candidates designed to overcome the limitations of current cell and gene therapeutics

GENE INSERTION

GENE EDITING



GENE DELIVERY

Delivery: Moving Toward Non-Viral Biodegradable Nanoparticles

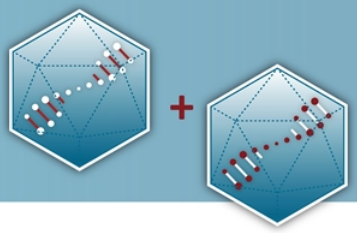
OUR GOAL:

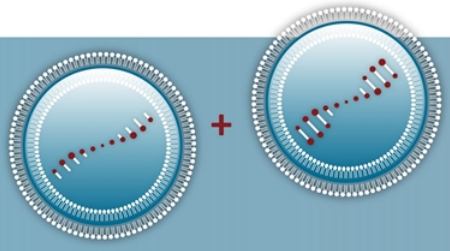
Develop Single Treatment Cures Utilizing Our In Vivo Gene Therapy Technologies

Potential for Single-Treatment Cures

VIRAL

AAV (SPB-DNA)
AAV (PB-DNA)





NON-VIRAL

Nanoparticle (SPB – RNA)
Nanoparticle (PB – DNA)

In pre-clinical studies piggyBac+AAV enabled **permanent and stable DNA integration** and **long-term expression**

Ability to effectively **work in dividing tissues** including the juvenile liver

Ability to **deliver larger genes** with nanoparticle+piggyBac than AAV

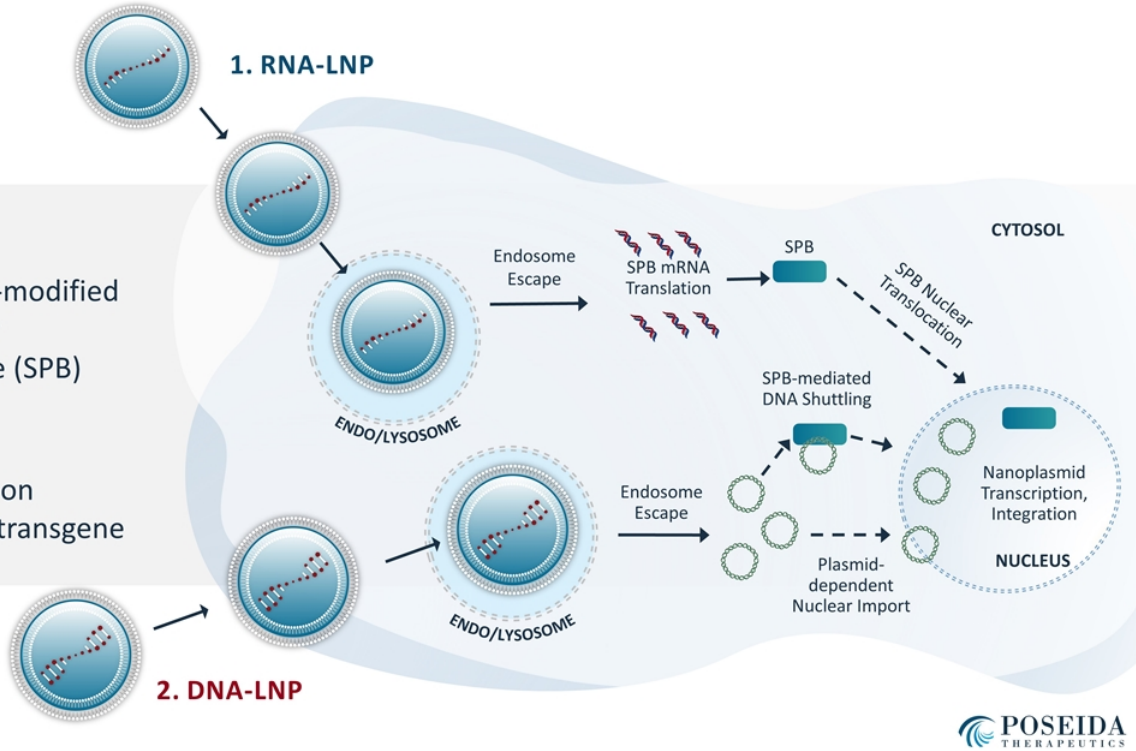
General Mechanism of LNP Co-Delivery of RNA and DNA

1. RNA-LNP

Delivers capped, base-modified mRNA encoding super piggyBa®c transposase (SPB)

2. DNA-LNP

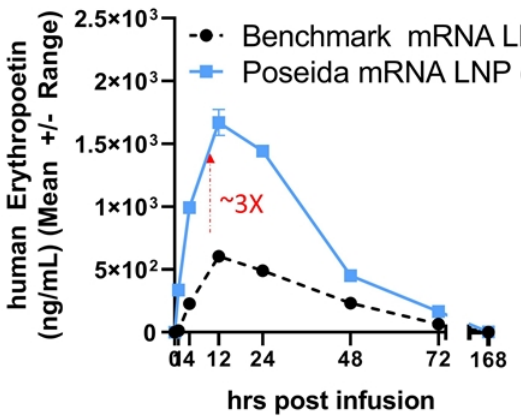
Delivers DNA transposon encoding therapeutic transgene



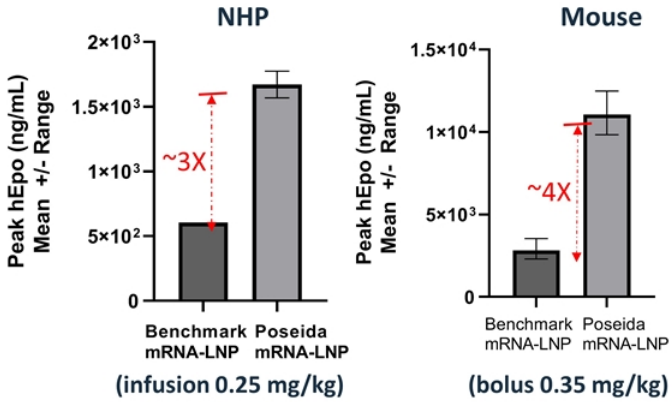
POSEIDA THERAPEUTICS

Poseida Biodegradable RNA LNP Works in Non-Human Primates

>3X More Potency Compared With Benchmark



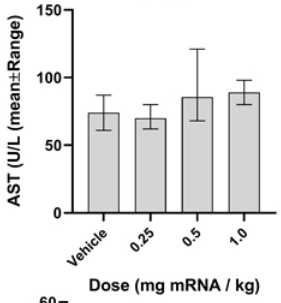
Cmax (0.25 mg/kg):
~1,500 ng/mL

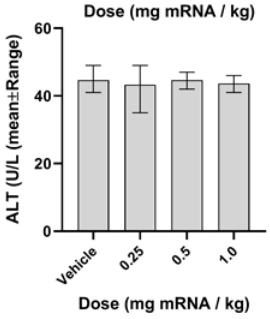


POSEIDA THERAPEUTICS

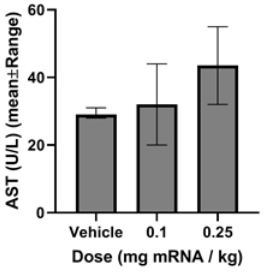
Poseida Biodegradable RNA LNP is Well Tolerated

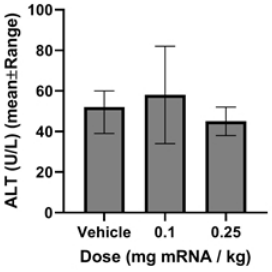
Rat





NHP



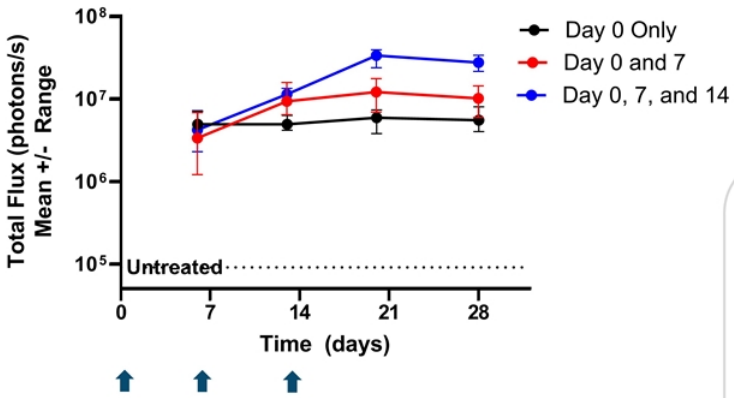


No meaningful elevation of liver enzymes 7 days following LNP treatment

POSEIDA THERAPEUTICS

piggyBac® Nanoparticle System can be Dosed Repeatedly

Repeat Dosing of DNA+SPB

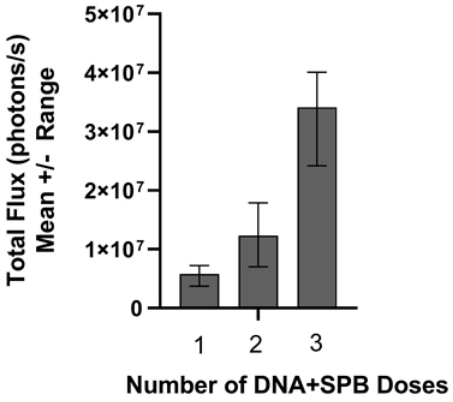


Dose 1 Dose 2 Dose 3

0.25 mg/kg DNA + 0.5 mg/kg SBP-5MeC
Adult/WT Mice
Nano.pB-HLP-fLuc2 **NT-01-009-201**

- Sequential transposon + SPB results in essentially dose-proportional transgene expression

Repeat Dosing (Day 28)

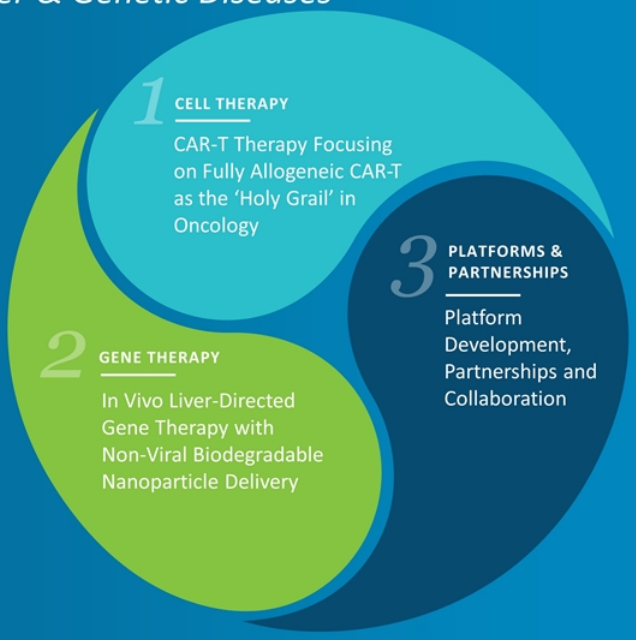


POSEIDA THERAPEUTICS

Multiple Avenues to Significant Value Creation

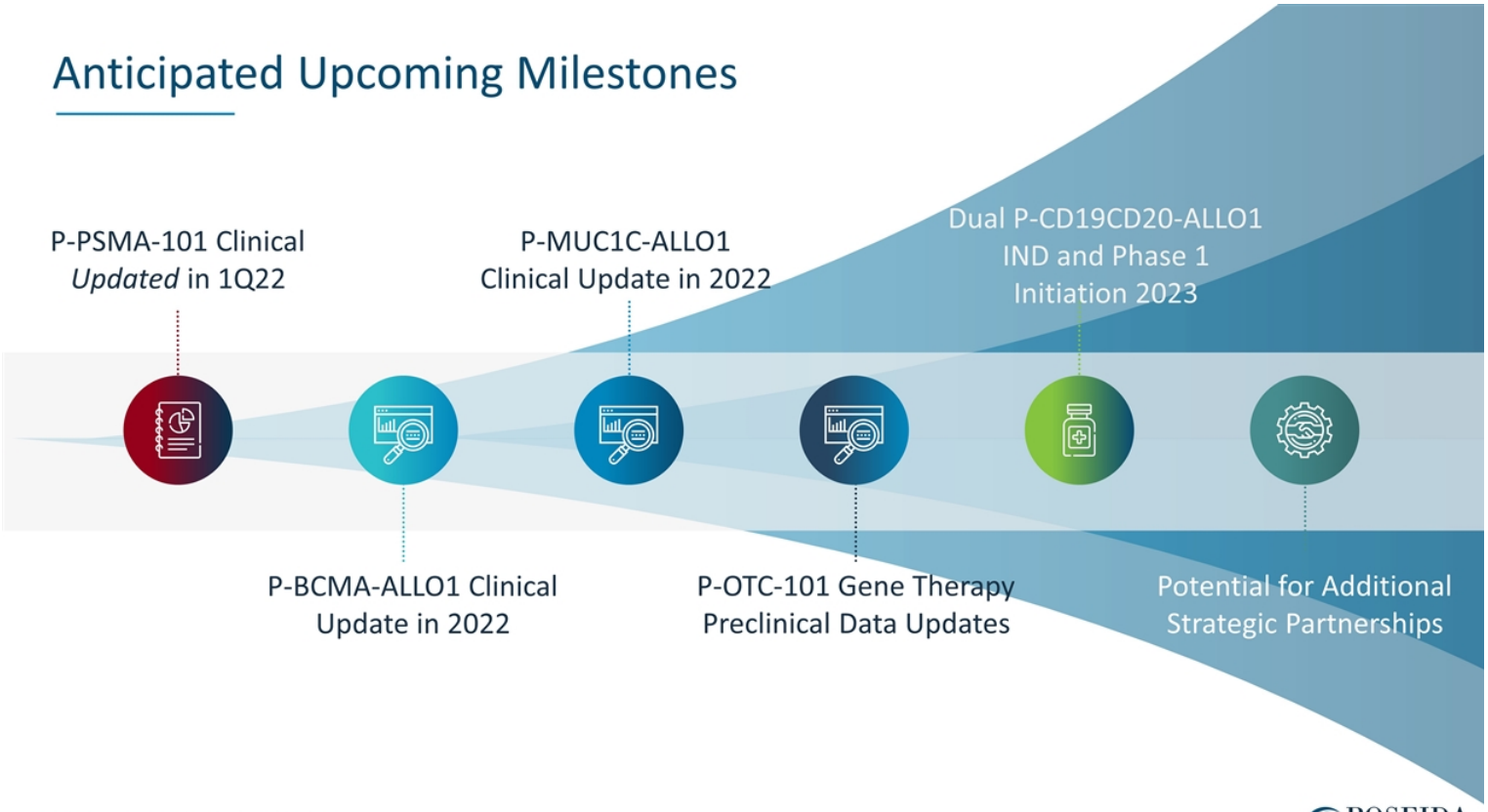
Working to Engineer Single-Treatment Cures for Cancer & Genetic Diseases

- **Broad innovative genetic engineering technology platforms**
- **Novel fully allogeneic high-T_{SCM} CAR-T approach** as well as Autologous CAR-T targeting PSMA
- **Gene therapy focus on** single treatment cures with non-viral delivery and **strategic partnership with Takeda**



POSEIDA THERAPEUTICS

Anticipated Upcoming Milestones



POSEIDA THERAPEUTICS

Luca Gattinoni, MD
Director of the Division of
Functional Immune Cell Modulation
Leibniz Institute for Immunotherapy (LIT)

The Importance of Stem Cell Memory (T_{SCM}) Cells

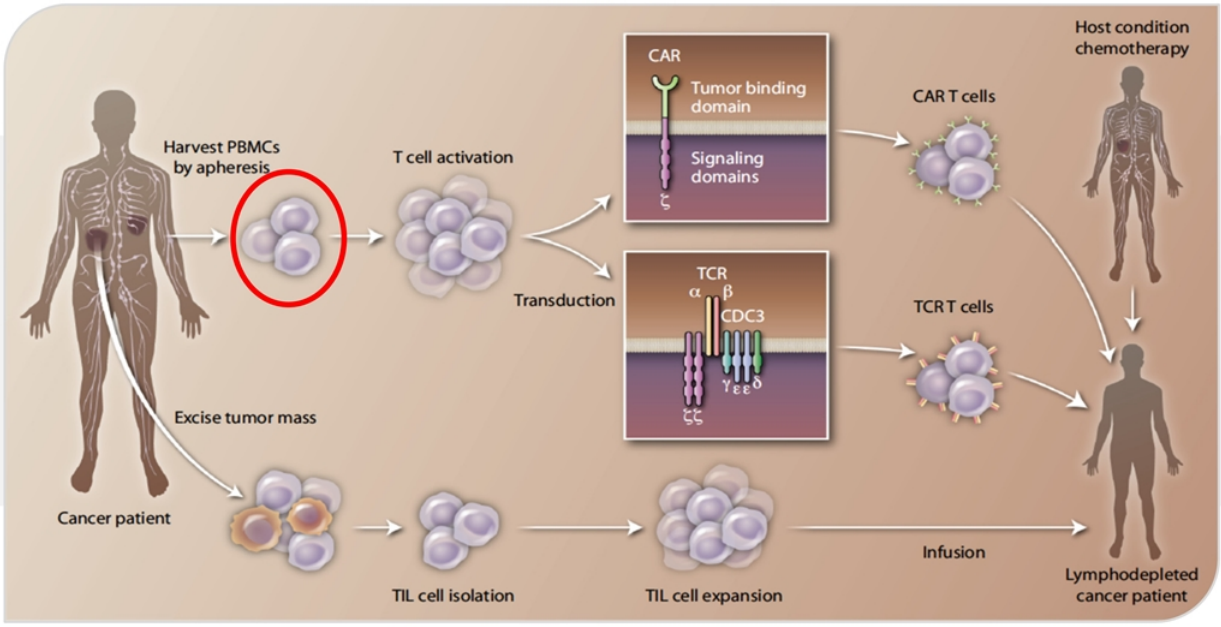
- Postdoc in Dr. Restifo's lab at National Cancer Institute
- Identified human T stem cell memory (T_{SCM}) cells
- Pioneer in use of T_{SCM} cells for adoptive immunotherapy
- Major contributor to understanding of T_{SCM} biology
- Over 100 publications and numerous academic awards
- Member of Poseida's Immuno-Oncology Scientific Advisory Board

POSEIDA THERAPEUTICS

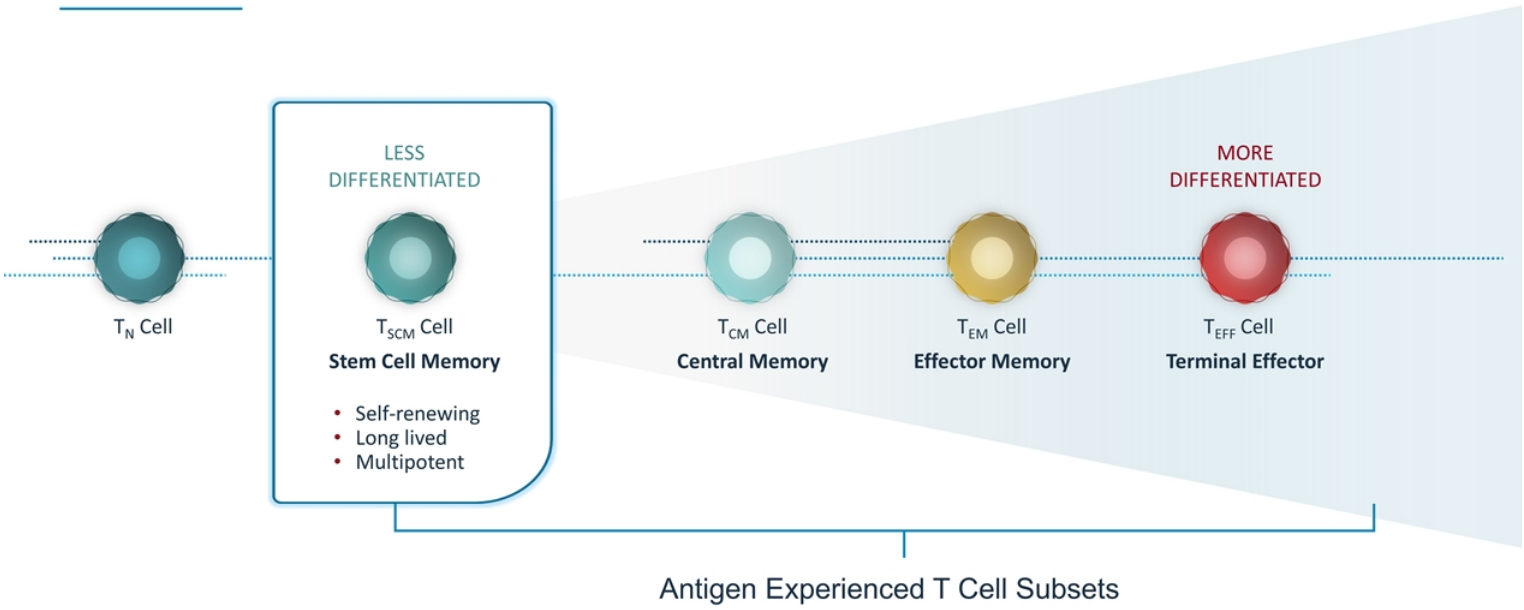
The Importance of Stem Cell Memory T (T_{SCM}) Cells

Luca Gattinoni, MD
Director of the Division of Functional Immune Cell Modulation
Leibniz Institute for Immunotherapy (LIT)

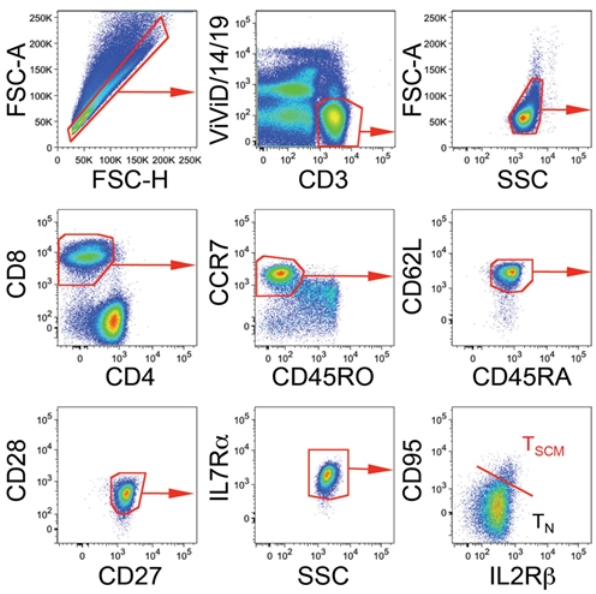
Adoptive Immunotherapy Strategies

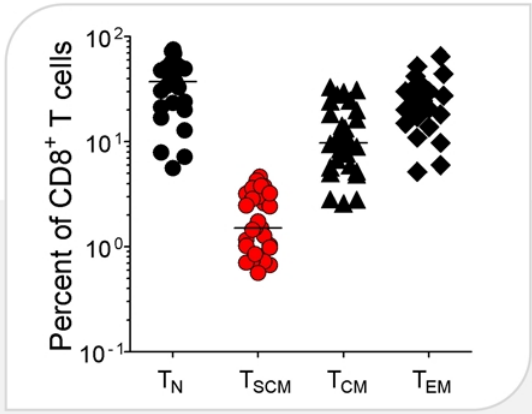


Not All T Cells are Created Equally



T_{SCM} Cells Largely Display a Naïve-like Phenotype



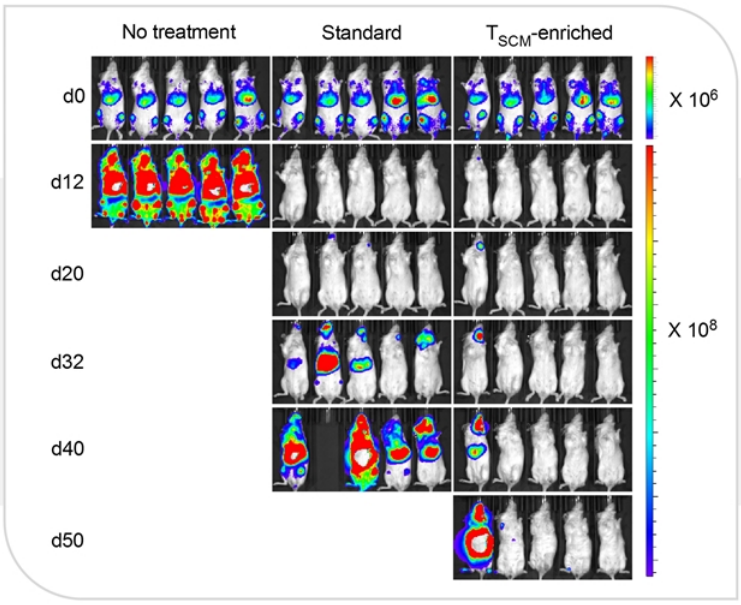


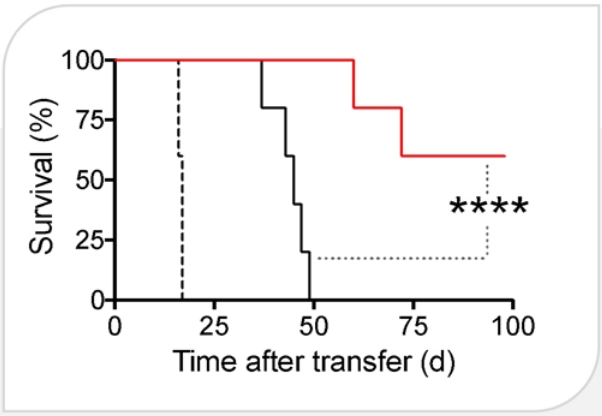
Gattinoni et al. Nat Med 2011

CXCR3 and **CD58** can also be used to identify human T_{SCM} cells within naïve-like T cells

T_{SCM} Are Key to CAR-T Efficacy in Pre-clinical Studies

CD19 CAR-modified T_{SCM} Cells Mediate Long-lasting Antitumor Responses Against ALL

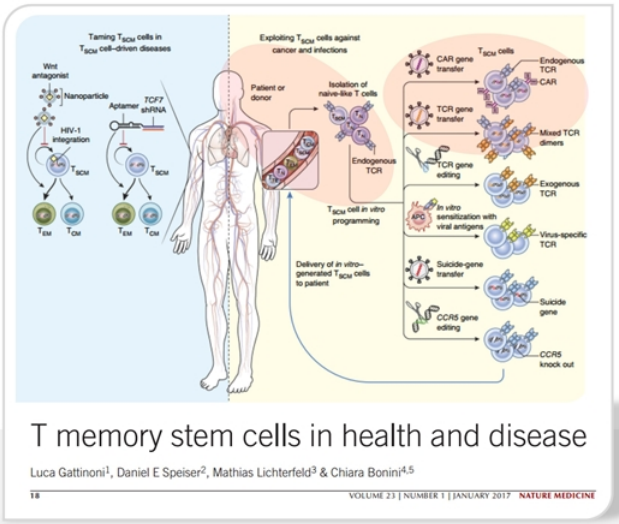




Sabatino et al., Blood 2016

T_{SCM} Are the Key to CAR-T Efficacy & Safety

- P-BCMA-101 data shows correlation of T_{SCM} and efficacy:
  - Preclinical: Barnett et al; Hermanson et al, Poseida (2016) 58th ASH
  - Clinical: Spear et al, Poseida (2019) 4th CAR-TCR Summit
- T_{SCM} is shown to correlate with CAR-T clinical response:
  - Melenhorst et al, UPenn (2017) Pre-manufactured cells, 20th ASGCT
  - Basu et al, Adaptimmune (2017) Persistent clones, 2nd CAR-TCR Summit
  - T_{CM}: Larson, Juno (2018) PK, safety and durability, AACR
  - T_{SCM}-like TIL: Beatty, Moffitt (2018) response & survival, 33rd SITC
  - Bot et al, Kite (2018) 33rd SITC & (2019) 4th CAR-TCR Summit
  - T_{CM}: Fraietta, UPenn (2018) responses and memory-related genes, Nat Med PMID: 29713085
  - T_{CM}: Deng et al, MDACC/axi-cel (2020) Nat Med PMID: 33020644
  - T_{SCM}-like TILS: Krishna, S et al. Science (2020), CR and TSCM gene set enrichment



T memory stem cells in health and disease

Luca Gattinoni[1], Daniel E Speiser[2], Mathias Lichterfeld[3] & Chiara Bonini[4,5]

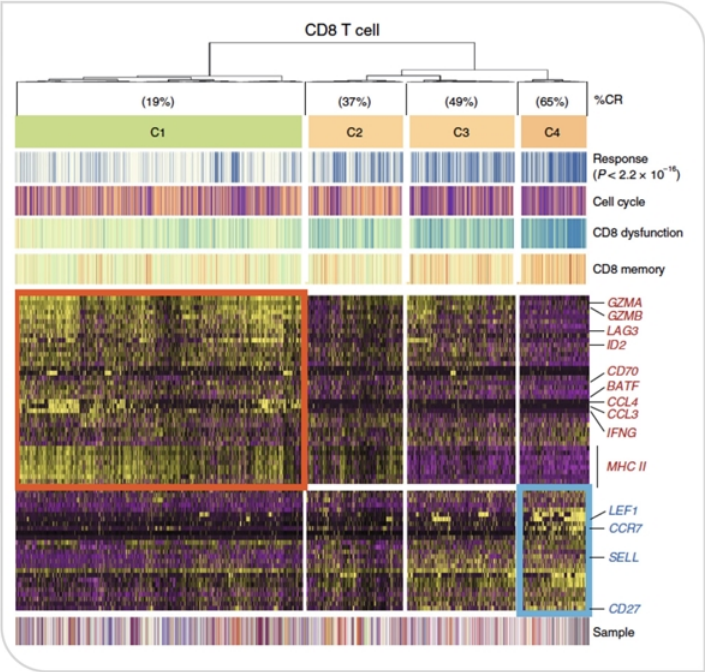
18 VOLUME 23 | NUMBER 1 | JANUARY 2017 NATURE MEDICINE

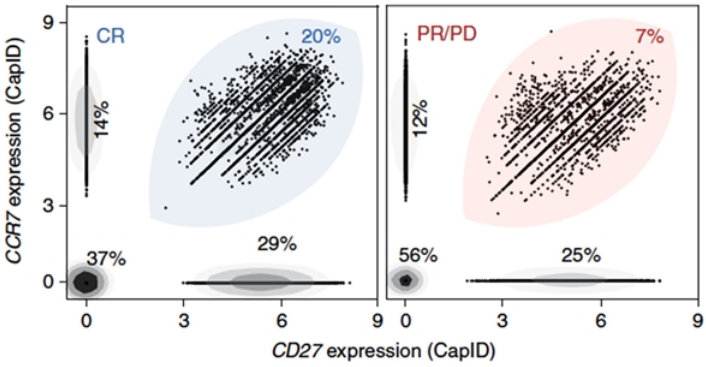
"The extreme longevity, the robust proliferative potential and the capacity to reconstitute a wide-ranging diversity of the T cell compartment make the TSCM cell type an ideal cell population to employ in adoptive immunotherapy"

Luca Gattinoni[1], Daniel E Speiser[2], Mathias Lichterfeld[3] & Chiara Bonini[4,5]
Volume 23 | Number 1 | January 2017 | NATURE MEDICINE

POSEIDA THERAPEUTICS

Early Memory Gene-Signature Correlates with CAR-T Efficacy



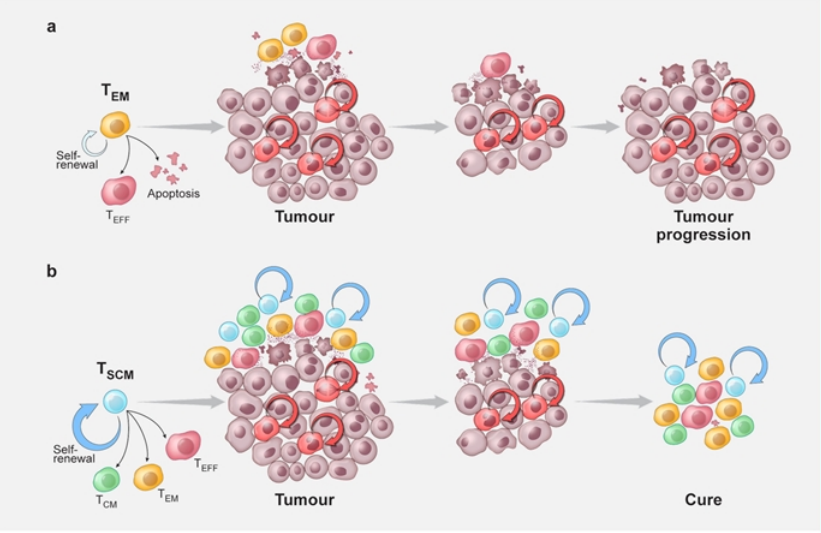


Deng Q et al., Nature Med 2020

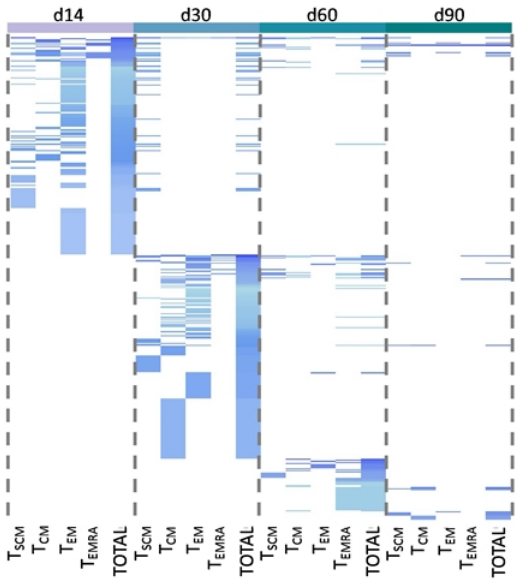
POSEIDA THERAPEUTICS

Self-renewal and Multipotency are Key to CAR-T Efficacy

T_{SCM} Clones Contribute Substantially to the Circulating CAR T Cell Pools, During Both Early Expansion and Long-term Persistence



Gattinoni et al., Nat rev cancer 2012

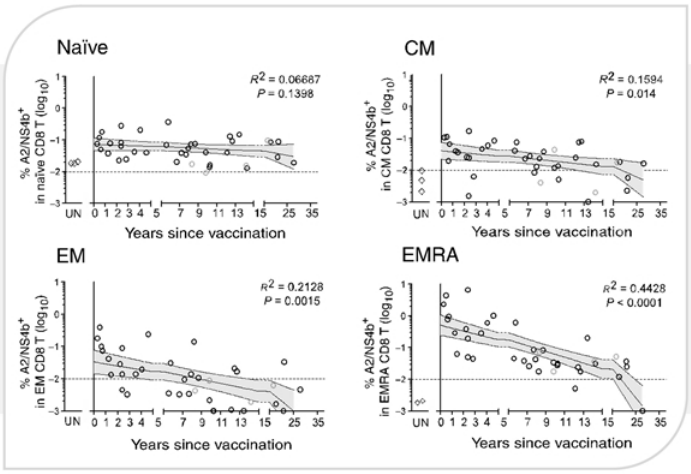


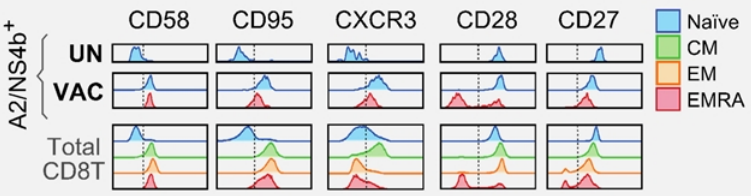
NCI/LIT unpublished

POSEIDA THERAPEUTICS

T_{SCM} Are Key to CAR-T Duration of Response

T_{SCM} Cells are Stably Maintained for > 25 Years Following Yellow Fever Vaccination

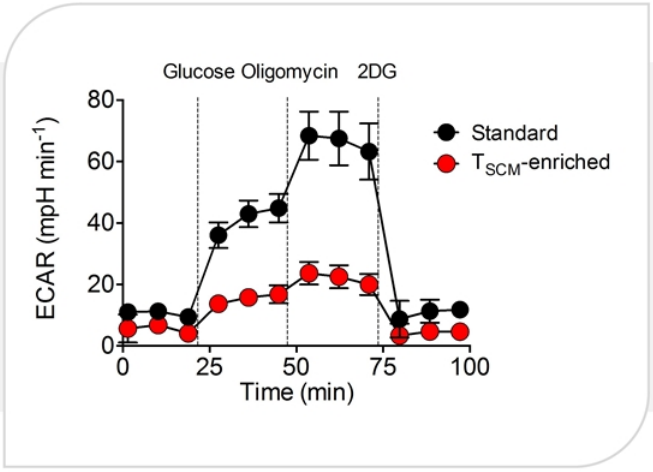


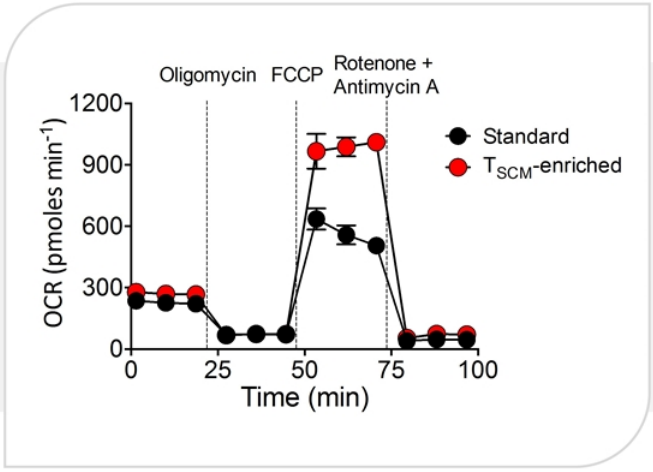


Fuertes Marraco et al., *Science TM 2015*

T_{SCM} Metabolic Fitness is Key to CAR-T Duration of Response

Low Glycolytic Metabolism and High Mitochondrial Respiratory Capacity are Associated with Long-lived Memory Cells





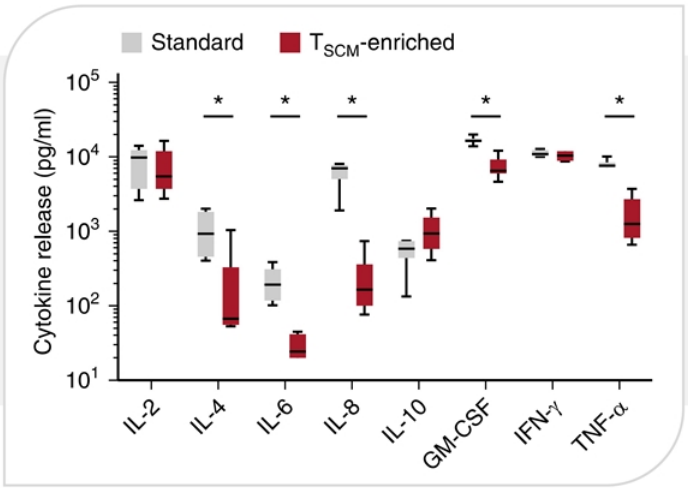
EACR: Extracellular Acidification rate
FCCP: Carbonyl cyanide-4 (trifluoromethoxy) phenylhydrazone = uncoupler
OCR: Oxygen consumption rate

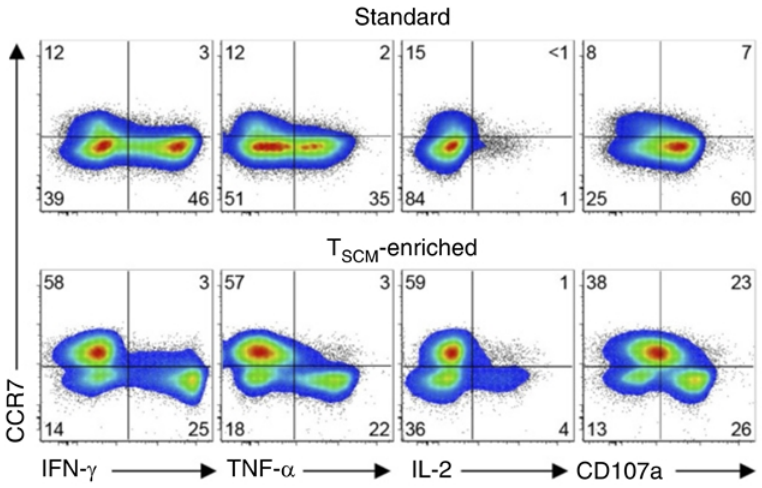
Sabatino et al., Blood 2016 | Sukumar et al., J Clin Invest 2013 | van der Windt et al., Immunity 2016

POSEIDA THERAPEUTICS

T_{SCM} Are the Key to CAR-T Safety

Reduced Release of Inflammatory Cytokines by Allogeneic CD19 CAR-modified T_{SCM} Cell Products





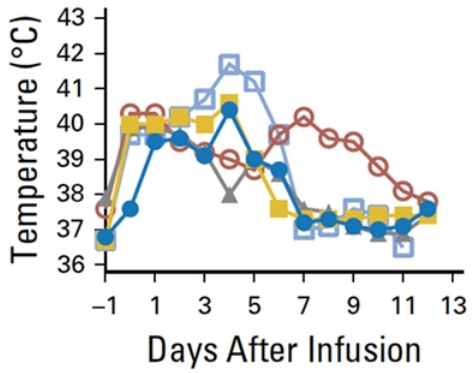
Sabatino et al., Blood 2016

POSEIDA THERAPEUTICS

T_{SCM} Are the Key to CAR-T Safety

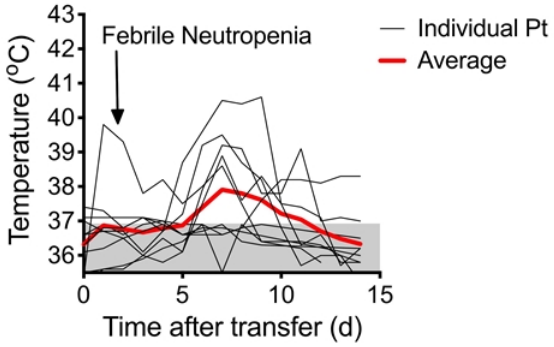
Delayed Kinetic and Milder Inflammatory Responses by Allogeneic CD19 CAR-modified T_{SCM}

Standard CD19-CAR T Cells



Brudno et al. *J Clin Oncol, 2016*

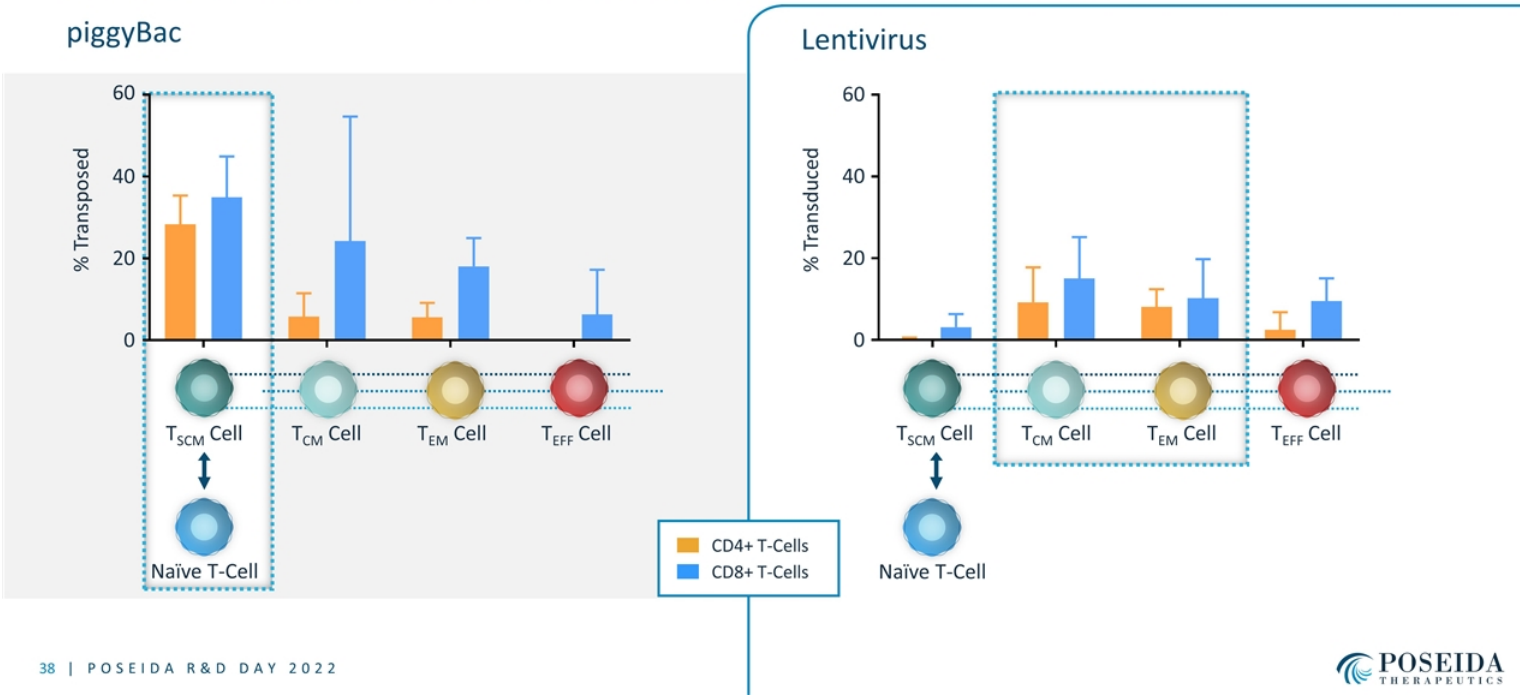
CD19-CAR T_{SCM}-enriched cells



NCI/LIT Unpublished

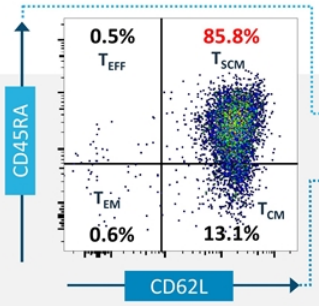
Poseida's piggyBac® Preferentially Transposes T_{SCM} Cell and Naïve Precursors

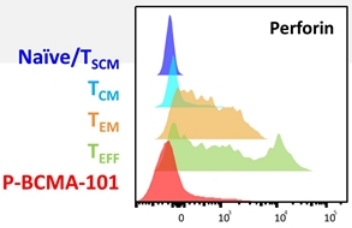
Lentivirus Transduces More Differentiated T-Cells In Preclinical Studies



POSEIDA THERAPEUTICS

Poseida's CAR-T Products are Comprised of a High-Percentage of T_{SCM} Cells





	T_N	T_{SCM}	T_{CM}	T_{EM}	T_{TE}	P-BCMA-101
CD45RA	+	+	-	-	+	+
CD45RO	-	-	+	+	-	-
CCR7	+	+	+	-	-	+
CD62L	+	+	+	-	-	+
CD28	+	+	+	+/-	-	+
CD27	+	+	+	+/-	-	+
IL-7Rα	+	+	+	+/-	-	+
CXCR3	-	+	+	-	-	+
CD95	-	+	+	+	+	+
CD11a	-	+	+	+	+	+
IL-2Rβ	-	+	+	+	+	+
CD58	-	+	+	+	+	+
CD57	-	-	-	+/-	+	-

Stemness
Proliferative potential
Lymphoid homing
Antigen independence
Lipid metabolism
Low Δψm

Senescence
Cytotoxicity
Tissue tropism
Antigen addiction
Gylcolytic metabolism
Oxidative stress

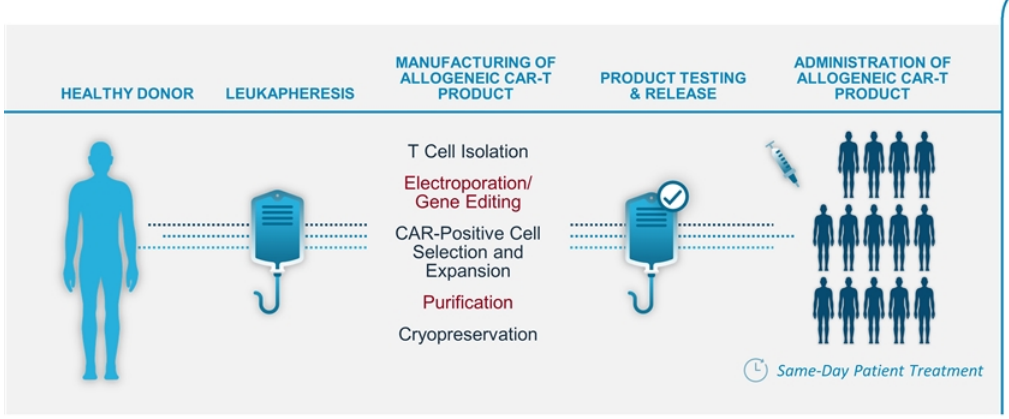
Adapted from Gattinoni et al. (2017) Nat. Med.

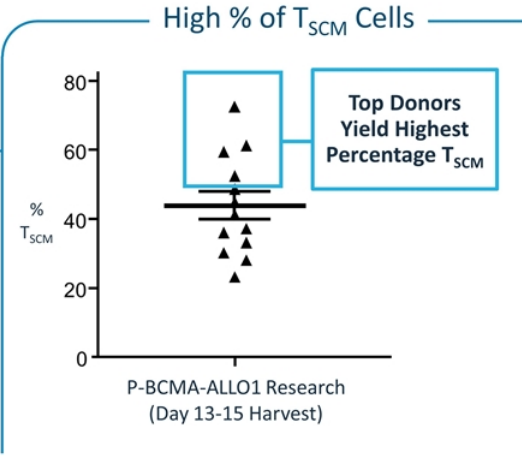
Poseida products closely match a T_{SCM} phenotype when using extensive cell surface markers and even intracellular markers

POSEIDA THERAPEUTICS

Poseida's CAR-T Products are Comprised of a High-Percentage of T_{SCM} Cells

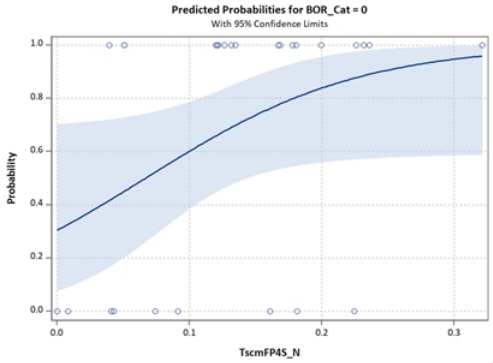
Allogeneic Product Have Final T_{SCM} Percentages Reaching ~80%



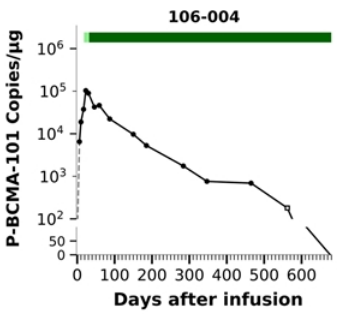


Efficacy, Durability and Safety of Poseida's High-T_{SCM} Auto Product P-BCMA-101

TSCM Correlates with Best Responses



Can Persist In Vivo



And Offers A Superior Safety Profile

- **Over 100 patients** dosed
- 28 patients dosed **fully outpatient**
- All CRS was Grade 1/2
- No to v**ery low neurotoxicity**
- **No patient admitted to the ICU**
- **No patient death due to P-BCMA-101**

- T_{SCM} in P-BCMA-101 is directly **correlated with best responses in the clinic**
- **Long-term persistence of T_{SCM} cells** in some patients
  - **Detectable product and sCR at >22 months post-infusion**
  - Ability to **re-expand without re-administration of product**
- Potentially best-in-class safety profile allows for fully outpatient dosing

POSEIDA THERAPEUTICS

The Importance of T_{SCM} Metabolism to Survival in the Tumor Microenvironment (TME)

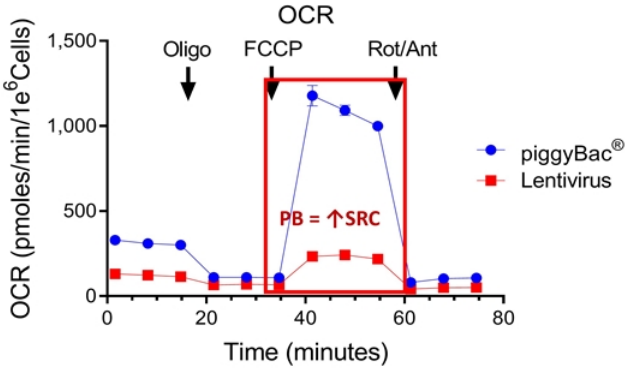
Oxidative phosphorylation avoids dependency on glucose and other metabolites that are lacking in the solid tumor microenvironment

BBζ CAR

↑Persistence
↑ Central Memory
↑ SRC
↑ Mitochondrial biogenesis
↑ Oxidative metabolism

Carl June et al., Ideal Metabolic Signature of CAR-T cells

Poseida CAR-T cells exhibit the '**ideal metabolic signature**' hypothesized to achieve durable responses



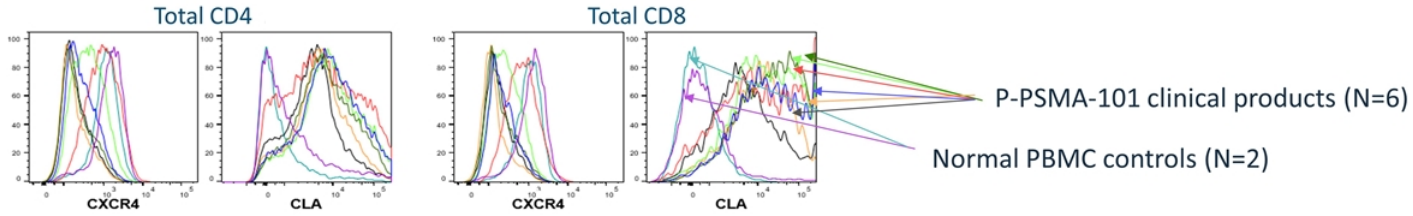
FCCP: Carbonyl cyanide-4 (trifluoromethoxy) phenylhydrazone = uncoupler
Rot/Ant: Rotenone + Antimycin A
OCR: Oxygen consumption rate

POSEIDA THERAPEUTICS

The Importance of T_{SCM} Trafficking for Clinical Efficacy in Solid Tumor Indications

- Poseida CAR-T and TSCM express a variety of trafficking molecules
- May facilitate trafficking to marrow, tumor
- P-PSMA-101 robust clinical activity against bone marrow metastases

Trafficking Molecule	T_{SCM}/T_{CM}	T_{EFF}	P-PSMA-101
CD62L (L-selectin)	+	-	+
CXCR4	+	-	+
CXCR3	+	-	+
CLA (Cutaneous lymphocyte antigen)	+	-	+
CCR7	+	-	+
CD11a (LFA-1-a)	+	-	+



POSEIDA THERAPEUTICS

Summary

- T_{SCM} is the most desirable cell type for creating CAR-T products
  - Associated with best responses in the clinic
  - Unprecedented duration of response in some patients
  - Unique and potentially best-in-class safety profile
  - A key to CAR-T success against solid tumor indications

- Poseida has a unique manufacturing platform that created CAR-T products with exceptionally high percentages of T_{SCM} cells
  - Typical range of 50-80% T_{SCM} cells in allogeneic products
  - T_{SCM} cells have elevated bone homing markers, which is highly relevant in bone predominant cancers

POSEIDA THERAPEUTICS

T_{SCM} Based CAR-T Product Candidates

Matt Spear, MD
Chief Medical Officer

Not All T Cells Are Created Equally

The Importance of Stem Cell Memory T Cells (T_{SCM})

LESS DIFFERENTIATED

T_{SCM} Cell
Stem Cell Memory

- Self-renewing
- Long lived
- Multipotent

T_{CM} Cell
Central Memory

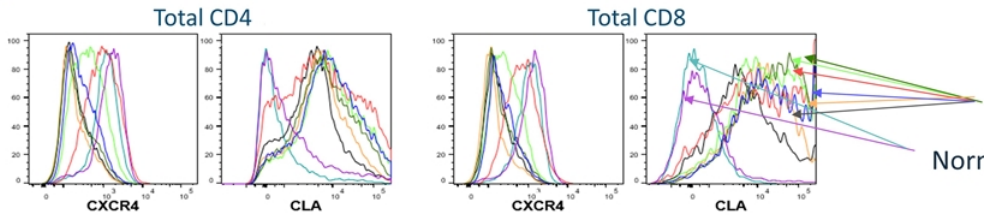
T_{EM} Cell
Effector Memory

MORE DIFFERENTIATED

T_{EFF} Cell
Effector T Cell

STEMNESS MATTERS
Products with High % of T_{SCM} Cells

- Strong correlation with best responses in the clinic
- More gradual tumor killing with less toxicity
- Better duration of response and potential for re-response
- **T_{SCM} engrafts in bone marrow – key to CAR-T success in solid tumors**



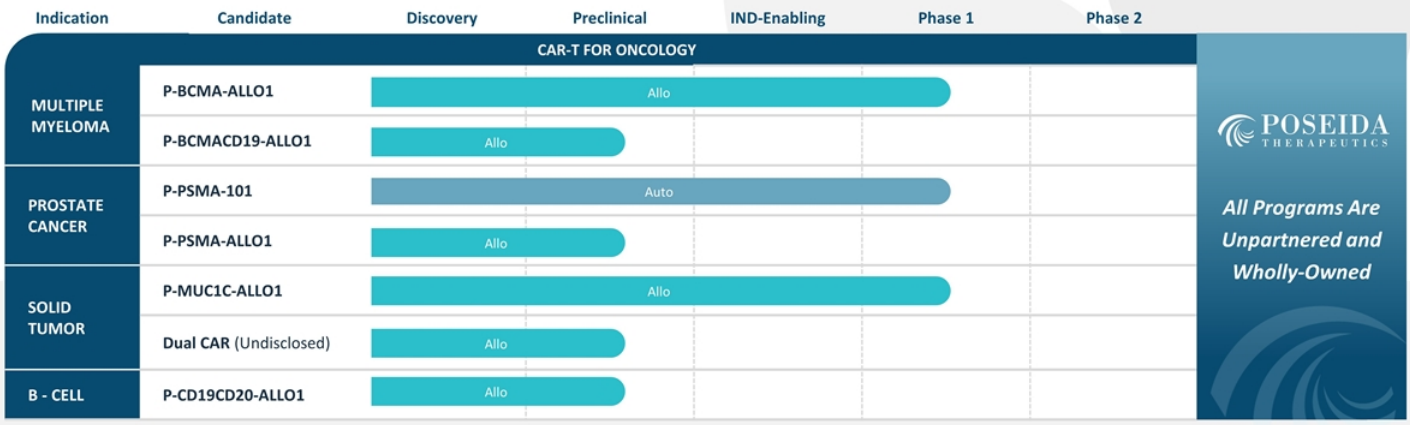
P-PSMA-101 clinical products (N=6)

Normal PBMC controls (N=2)

POSEIDA THERAPEUTICS

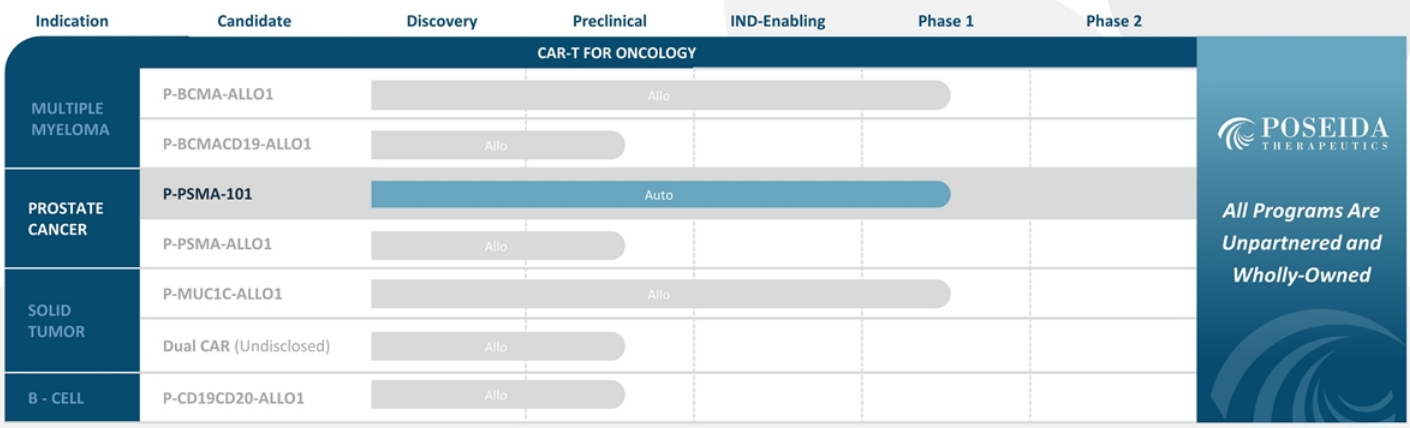
Cell Therapy Pipeline

CAR-T for Oncology and Beyond



Cell Therapy Pipeline

CAR-T for Oncology and Beyond



P-PSMA-101: PSMA Targeted CAR-T Cells for Metastatic Castrate-Resistant Prostrate Cancer (mCRPC)

Population

- **~2.8M** prostate cancer patients in US
- **~40K** new cases of mCRPC in US per year
- **27.5K** US patient deaths per year

Proven Target

- **PSMA** expressed on most prostate cancers also many salivary gland cancers
- **PSMA** targeted successfully
- Radioligand therapy in advanced development
- 7 bispecifics in early development
- **P-PSMA-101- only CAR-T in development with marked response data**

Unmet Need

- **High unmet need** for mCRPC
- Minimal effective options after taxane chemotherapy and 2nd generation anti-androgen agents
- **~25%** 5-yr survival for mCRPC patients

[1]*https://globenewswire.com/news-release/2017/02/02/913304/0/en/Prostate-Cancer-Market-Study-2017-Market-Size-of-Prostate-Cancer-Drugs-to-7b-in-2016-from-2-5b-in-2011.html*
[2]*https://www.researchandmarkets.com/research/wxtf93/global_prostate*

Susan F. Slovin, MD, PhD
Memorial Sloan Kettering Cancer Center

- Professor of Medicine, Department of Medicine at Weill Medical College of Cornell University
- Attending Physician in the Genitourinary Oncology Service, Sidney Kimmel Center for Prostate and Urologic Cancers, Department of Medicine, Memorial Sloan-Kettering Cancer Center
- Medical degree from Jefferson Medical College
- Doctorate in pathobiology from Columbia University
- Research fellowship in clinical immunology at Scripps Clinic & Research Foundation
- Hematology/oncology fellowship, Memorial Sloan-Kettering Cancer Center
- Leadership of the Prostate Immunotherapy Group
- Chair, MSK Data Safety and Monitoring Committee, Associate Vice Chair, Dept of Medicine, Academic Administration

POSEIDA THERAPEUTICS

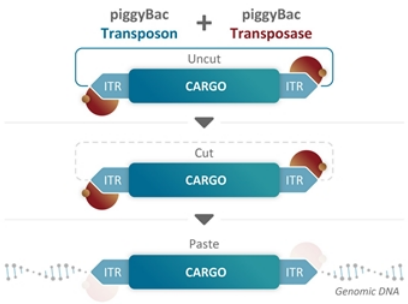
Phase 1 Study of P-PSMA-101 CAR-T Cells in Patients with Metastatic Castration-resistant Prostate Cancer (mCRPC)

Susan Slovin, MD, PhD
Memorial Sloan Kettering Cancer Center, New York, NY

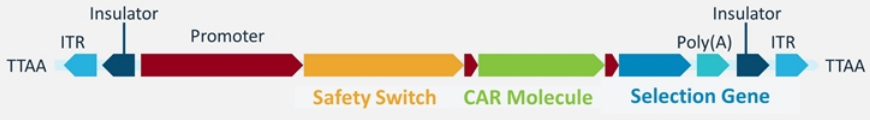
Overview

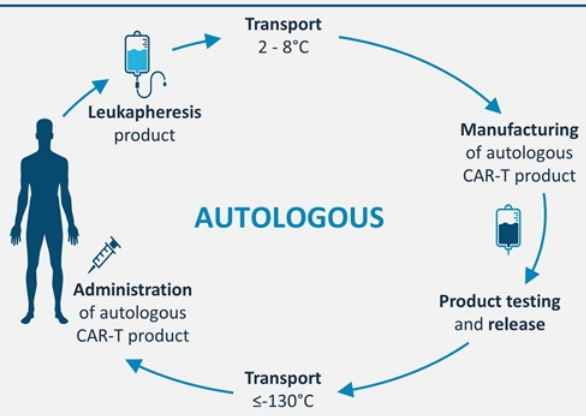
- P-PSMA-101 is made using a unique CAR-T platform that results in a product comprised of a high percentage of T stem cell memory (T_{SCM}) cells that targets Prostate-Specific Membrane Antigen (PSMA)
- T_{SCM} cells have bone marrow homing capability that may be particularly relevant to specific solid tumors, such as prostate adenocarcinoma
- At very low doses, P-PSMA-101 induces deep and durable responses in heavily pretreated mCRPC patients
- P-PSMA-101 demonstrates a reasonable safety profile with early management of CRS prodromes

piggyBac®: A Non-viral DNA Delivery System That Creates High-T_{SCM} CAR-T Products



- Non-viral gene insertion technology
- Enables efficient DNA integration & stable expression
- Multiple safety, timeline and cost benefits
- Very large cargo capacity (>20X viral systems)
- Works in a wide variety of cell types (T_{SCM} cells)

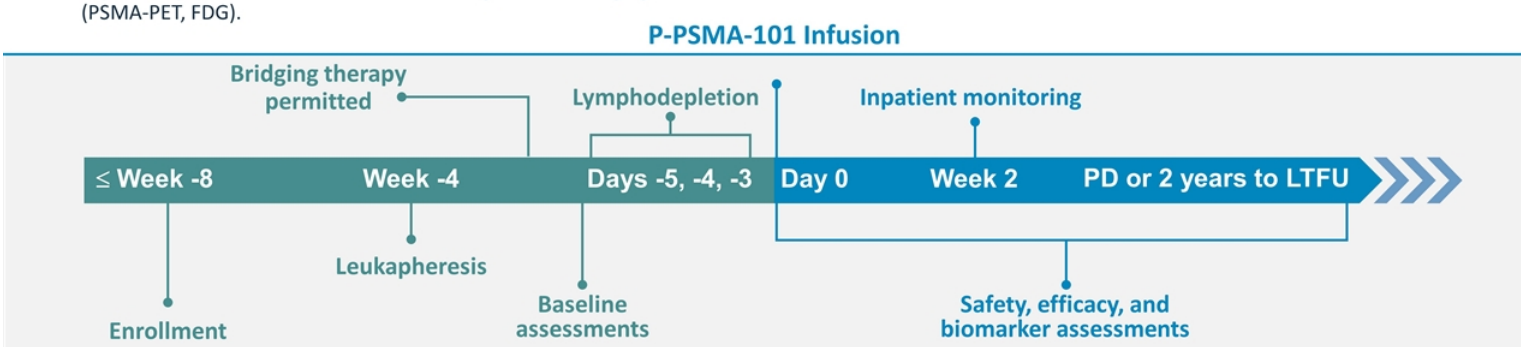




POSEIDA THERAPEUTICS

Phase 1 mCRPC Clinical Trial: P-PSMA-101-001

- P-PSMA-101 is an autologous CAR-T therapy targeting PSMA and is made using a unique non-viral transposon system (piggyBac) that results in a CAR-T product composed of a high percentage of stem cell memory T cells (T_{SCM}).
- Open label, 3+3 design, dose escalation + recommended Phase 2 dose expansion, 60 patients.
- Standard 3-day lymphodepletion regimen: fludarabine 30 mg/m^2 and cyclophosphamide 300 mg/m^2.
- Standard response criteria as per PCWG3: PSA, bone scans/CT, and exploratory biomarkers and novel tumor-targeted PET imaging (PSMA-PET, FDG).
- PET imaging was dependent on institutional availability.
- Key inclusion criteria: mCRPC, measurable disease, received a CYP17 inhibitor or second-generation anti-androgen therapy and a taxane, and adequate organ function.
- Subjects with advanced salivary gland cancers now eligible to enroll under Amendment 4 (12 Nov 21).
- Key exclusion criteria: second malignancy, active infection, or significant autoimmune, central nervous system, cardiac, ocular, or liver disease.



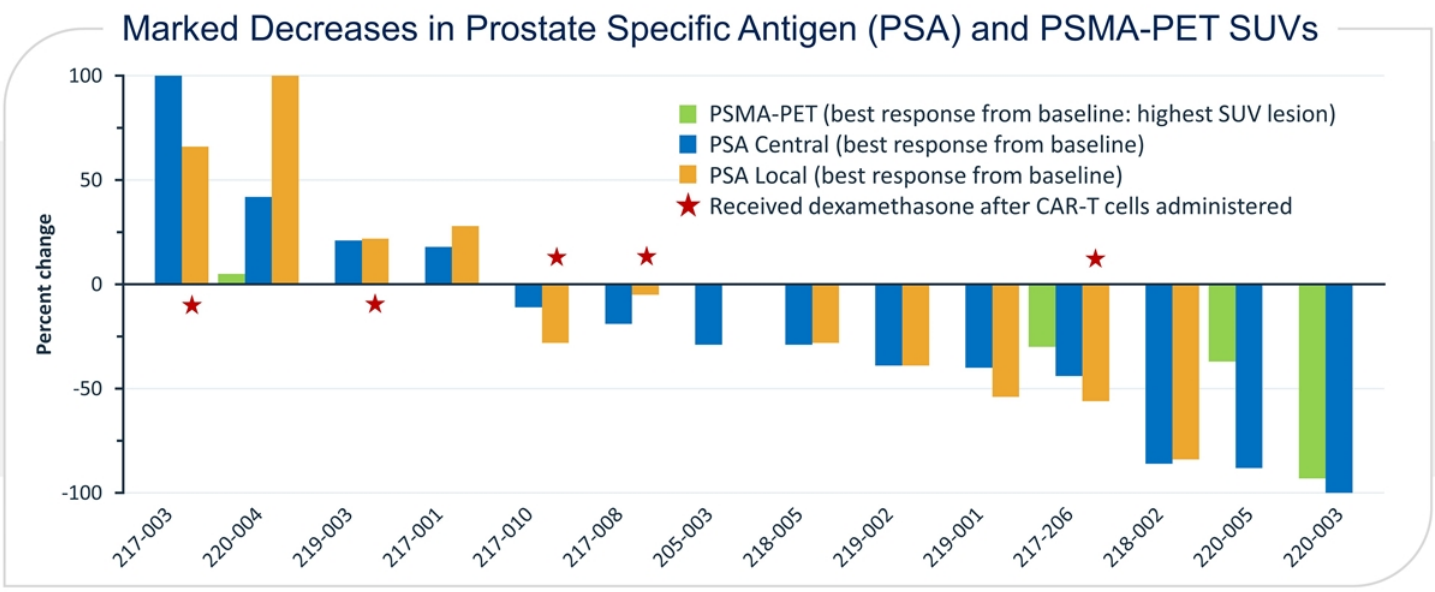
CAR = chimeric antigen receptor; CT = computed tomography; FDG = fluorodeoxyglucose; LTFU = long-term follow-up; mCRPC = metastatic castration-resistant prostate cancer; PCWG3 = Prostate Cancer Working Group 3; PD = progressive disease; PET = positron emission tomography; PSA = prostate-specific antigen; PSMA = prostate membrane-specific antigen.

Demographics & Characteristics (Heavily Pretreated mCRPC Patients)

CAR-T cells administered: Cells/kg	Mean (Min/Max) x 10^6	Patients (#)
Cohort -1: 0.25 x 10^6 single infusion	21.6 (19/24)	6
Cohort 1: 0.75 x 10^6 single infusion	61.3 (37/73)	7
Cohort 2: 2.0 x 10^6 single infusion	112.0 (112/112)	1

Parameter (n=14)	
Median (min, max) age, y	71 (57, 79)
Median (min, max) time since diagnosis, y	6.4 (1, 23)
ECOG (Baseline) PS, 0/1, n (%)	7 (50) / 7 (50)
Prior regimens, median (min, max)	**7 (3, 15)**
LHRH agonist/antagonist, n (%)	12 (86)
bicalutamide / flutamide, n (%)	8 (57)
Enzalutamide, n (%)	12 (86)
Abiraterone, n (%)	12 (86)
Taxane, n (%)	11 (79)
PSMA bispecific, n (%)	**3 (21)**
PSMA radioligand therapy, n (%)	0

High Rates of Anti-Tumor Activity Demonstrated with Multiple Methods



[a] Central or local results. [b] CTC0 (n=5) defined as patients with CTCs >0 at enrollment and CTC = 0 during a post-infusion CTC assessment (12–13-week follow-up). [c] CTC_{conv} (n=5) defined as patients with CTCs ≥5 at enrollment, then CTCs ≤4 measured at a post-infusion assessment. [d] Patient 219-001. [e] Patient 217-206.
CAR = chimeric antigen receptor; CTC = circulating tumor cells; PET = positron emission tomography; PSA = prostate-specific antigen; PSMA = prostate membrane-specific antigen; SUV = standardized uptake value.

PSA and Circulating Tumor Cells (CTC) Response Rates

PSA responses (n=14)[a]

Response	n (%)
PSA response (≥30% decrease)	6 (42.9)
PSA response (≥50% decrease)	5 (35.7)
CTC0[b]	1[d] (20.0)
CTC_{conv}[c]	1[e] (20.0)

[a] Central or local results. [b] CTC0 (n=5) defined as patients with CTCs >0 at enrollment and CTC = 0 during a post-infusion CTC assessment (12–13-week follow-up).
[c] CTC_{conv} (n=5) defined as patients with CTCs ≥5 at enrollment, then CTCs ≤4 measured at a post-infusion assessment. [d] Patient 219-001. [e] Patient 217-206.

Treatment-Emergent Adverse Events

TEAEs (n=14)

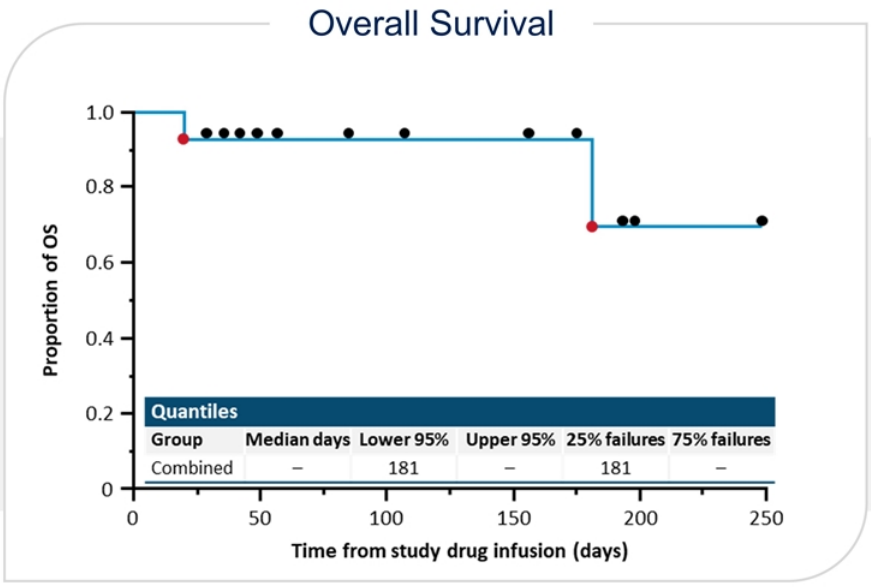
TEAE, n (%)	Overall	Grade ≥3
Dose-limiting toxicity (at dose 0.75 x 10^6 cells/kg)	1 (7)	1 (7)
CRS[a]	8 (57)	2 (14)
ICANS	2 (14)	1 (7)
Neutropenia/neutrophil count decreased[b]	5 (36)	5 (36)
Thrombocytopenia/platelet count decreased[b]	5 (36)	4 (27)
Anemia	5 (36)	5 (36)
Infection		
Overall	2 (14)	1 (7)
First month	2 (14)	1 (7)

TRAEs (n=14)

TRAE, n (%)	With >20% incidence	Grade ≥3
CRS	7 (50)	2 (14)
Headache	7 (50)	0 (0)
Fatigue	6 (43)	1 (7)
Chills	5 (36)	0 (0)
AST increased	5 (36)	3 (21)
Vision blurred	4 (29)	0 (0)
ALT increased	4 (29)	1 (7)
Pyrexia	3 (21)	0 (0)
aPTT prolonged	3 (21)	0 (0)

[a] Grade ≥3 events were 2 cases of macrophage activation syndrome/CRS, one fatal after non-compliance in follow-up. CRS was frequently associated with transaminitis and intermittently with ocular symptoms/inflammation.
[b] Patient counted once for either term.
ALT = alanine aminotransferase; aPTT = activated partial thromboplastin time; AST = aspartate aminotransferase; CRS = cytokine release syndrome; ICANS = immune effector cell–associated neurotoxicity; TEAE = treatment-emergent adverse event; TRAE = treatment-related adverse event.

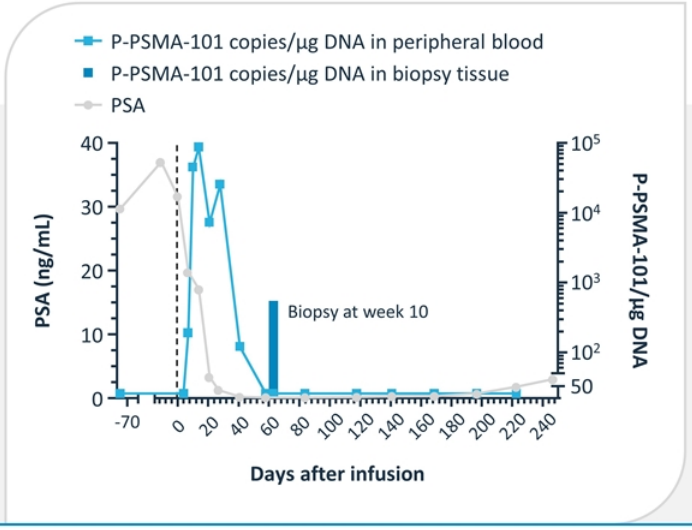
Overall Survival (OS)

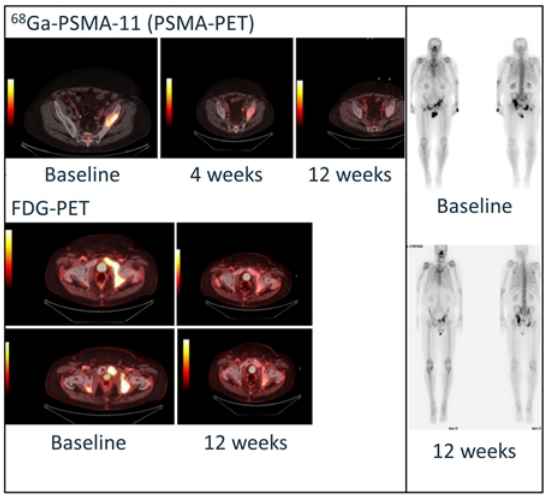


POSEIDA THERAPEUTICS

Patient 220-003: Evidence of Near Complete Tumor Elimination

PK, PSA, PSMA-PET, FDG-PET, Bone Scan, and Pathology Correlate in Response



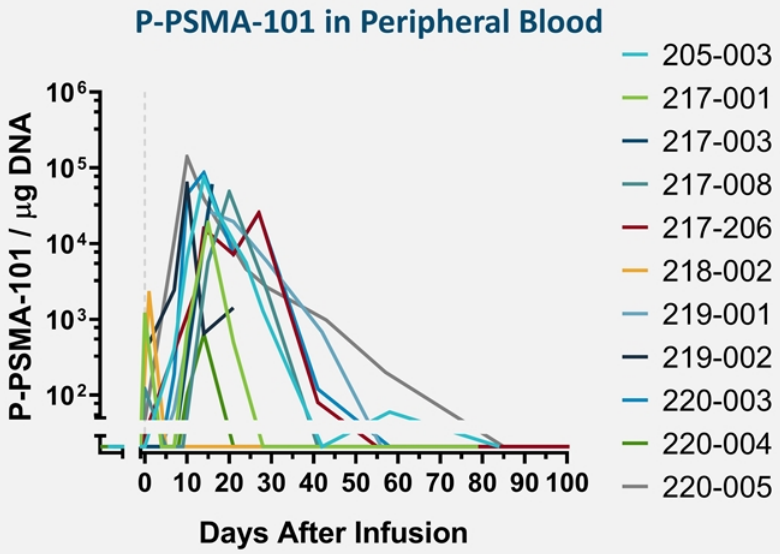


Biopsy at week 10 of prior bone metastasis showed CAR-T cells, bone remodeling, and bone marrow but no tumor cells.

CAR = chimeric antigen receptor; FDG = fluorodeoxyglucose; PET = positron emission tomography; PK = pharmacokinetics; PSA = prostate-specific antigen; PSMA = prostate membrane-specific antigen.

POSEIDA THERAPEUTICS

Pharmacokinetics: Consistently High Expansion



- Most patients have **significant CAR-T cell** expansion in peripheral blood to levels generally associated with efficacy in CAR-T products
- Many CAR-T products show **peak expansion between 5-14 days**
- P-PSMA-101 shows **peak expansion between 10-28 days**

Summary & Conclusions

- This interim update shows the exceptional efficacy of novel anti-PSMA CAR-T-cell product
- P-PSMA-101 at very low doses induced durable biochemical, radiographic, and functional radiographic responses in heavily pretreated patients with mCRPC, including a pathologic complete response, with notable PFS and OS, and significant CAR-T-cell expansion to the 10^4 to 10^5 copies/ug range.
- Ten of 14 patients (71%) of patients demonstrated PSA declines, with 5 of 14 patients (36%) showing PSA declines of ≥50%.
- P-PSMA-101 expressed elevated bone and inflammation homing markers and demonstrated trafficking to bone tumor biopsies, highly relevant in bone-avid disease like prostate cancer.
- CRS rate was 57% and ICANS rate was 14%, which has been manageable when treated rapidly with steroids and anti-cytokine agents.
- 18 patients have now been treated, and additional data presentations are expected in 2022

Acknowledgements

With the greatest appreciation to the patients

P-PSMA-101-001 Investigators

Memorial Sloan-Kettering Cancer Center
Susan F. Slovin, M.D., Ph.D.

City of Hope
Tanya Dorff, M.D.

Sarah Cannon Research Institute - HealthOne Denver
Gerald Falchook, M.D.

Dana-Farber Cancer Institute
Xiao Wei, M.D.

Massachusetts General Hospital
Xin Gao, M.D.

University of California at San Francisco (UCSF)
David Oh, M.D.

University of California at San Diego (UCSD)
Rana Mckay, M.D.

We would particularly like to recognize the commitment and dedication of the scientists and professionals at Poseida who made this possible.

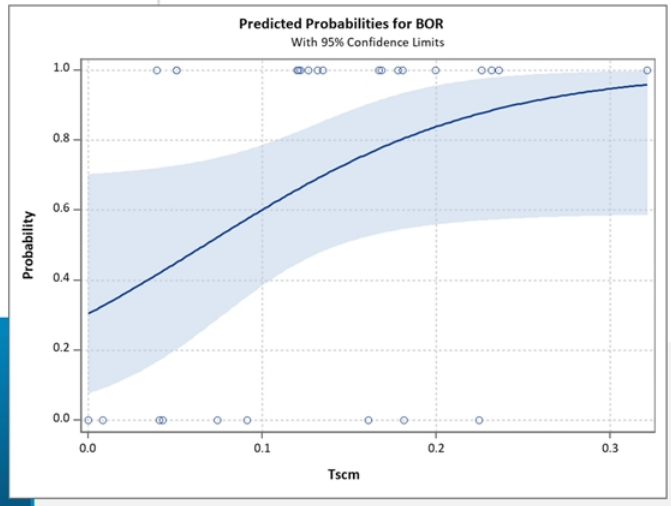
POSEIDA THERAPEUTICS

T_{SCM} Based Allogeneic CAR-T Platform and Product Candidates

Devon J. Shedlock, PhD
Chief Scientific Officer, Cell Therapy

T_{SCM} are the Key to CAR-T Efficacy & Safety

- P-BCMA-101 data shows correlation of T_{SCM} and efficacy:
  - Preclinical: Barnett et al; Hermanson et al, Poseida (2016) 58th ASH
  - Clinical: Spear et al, Poseida (2019) 4th CAR-TCR Summit
- T_{SCM} is shown to correlate with CAR-T clinical response:
  - Melenhorst et al, UPenn (2017) Pre-manufactured cells, 20th ASGCT
  - Basu et al, Adaptimmune (2017) Persistent clones, 2nd CAR-TCR Summit
  - T_{CM}: Larson, Juno (2018) PK, safety and durability, AACR
  - T_{SCM}-like TIL: Beatty, Moffitt (2018) response & survival, 33rd SITC
  - Bot et al, Kite (2018) 33rd SITC & (2019) 4th CAR-TCR Summit (2021) 7th CAR-TCR Summit
  - T_{CM}: Fraietta, UPenn (2018) TET2 Disruption, Nat Med PMID: 29849141
  - T_{CM}: Deng et al, MDACC/axi-cel (2020) Nat Med PMID: 33020644



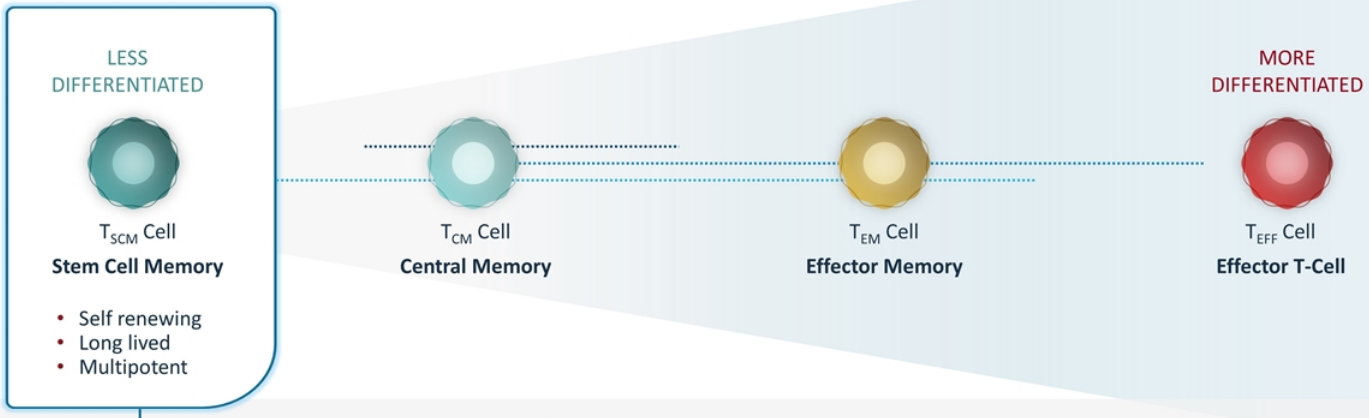
"The extreme longevity, the robust proliferative potential and the capacity to reconstitute a wide-ranging diversity of the T cell compartment make ***the T_{SCM} cell type an ideal cell population to employ in adoptive immunotherapy****"*

Luca Gattinoni[1], Daniel E Speiser[2], Mathias Lichterfeld[3] & Chiara Bonini[4,5]
Volume 23 | Number 1 | January 2017 | NATURE MEDICINE

POSEIDA THERAPEUTICS

Not All T Cells are Created Equally

The Importance of Stem Cell Memory T Cells (T_{SCM})



STEMNESS MATTERS

Products with High % of T_{SCM} cells:

- Strong correlation with best responses in the clinic
- More gradual tumor killing with less toxicity
- Better duration of response and potential for re-response
- T_{SCM} engrafts in bone marrow – key to CAR-T success in solid tumors

CAR-T_{SCM} Prodrug is Ideal for Treating Solid Tumors

We Believe T_{SCM} Hold the Potential to Engraft, Self-renew and Create Wave after Wave of More Differentiated Effector Cells with One Administration

Conventional Experience and Perception

- Poor CAR-T responses in solid tumors to date
- Rare instances with complete response (CR) have occurred (GBM, HCC) only after multiple administrations
- CAR-T can cause CRs in solid tumors, but **numerous doses of more differentiated cells are required**

Poseida's Approach

Our product candidates are comprised of a high percentage of T_{SCM} cells, which we believe hold the potential to engraft, self renew and **create wave after wave of more differentiated effector cells with one administration**

POSEIDA THERAPEUTICS

T_{SCM}-rich Allogeneic CAR-Ts Enabled by Poseida's Technologies

Innovation in Allogeneic CAR-Ts

Cell Type Matters

T_{SCM} Cell

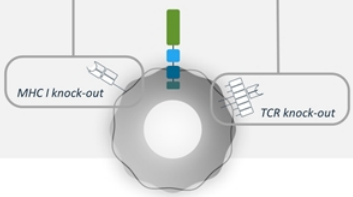
Stem Cell Memory

- Self-renewing
- Long lived
- Multipotent

T_{SCM} is the ideal cell type for CAR-T due to greater safety and durability

piggyBac® is the ideal nonviral gene insertion technology

Fully Allogeneic CAR-T



Addressing both Graft v Host and Host v Graft alloreactivity with **Cas-CLOVER™ Site-Specific Gene Editing**

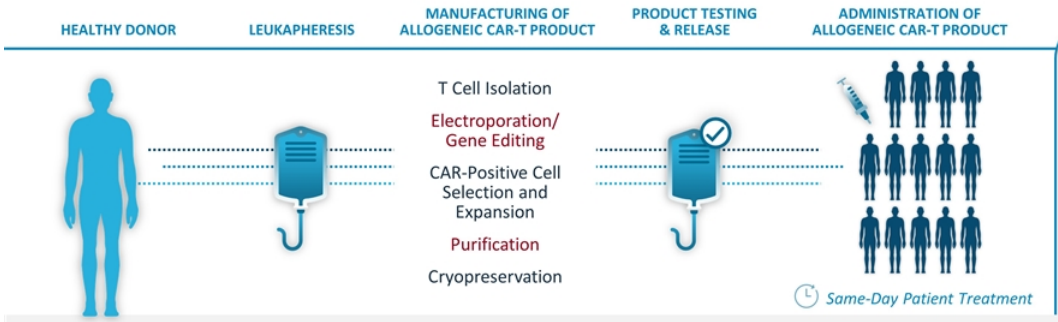
Cost, Scale & Reach

Booster Molecule technology delivers 100's of doses at low cost

Enables outpatient dosing and expanded patient reach

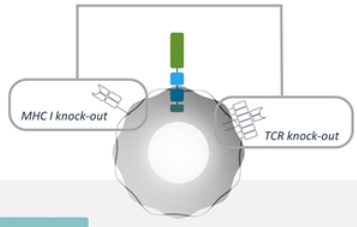
Poseida's Unique Allogeneic CAR-T Platform

P-BCMA-ALLO1 and P-MUC1C-ALLO1 INDs Cleared by FDA and Trial Start-up in Progress



FULLY ALLOGENEIC

Multiplex gene editing to address graft vs host (safety) and host vs graft (persistence)



Unique Allogeneic Platform

- Preserve/improve **high T_{SCM}**
- **Optimized dosing** regimens
- **Healthy donor** material
- **Robust manufacturing**
- Dramatic **cost reductions**
  - Up to **100s of doses**

Booster Molecule

- Our patented technology is designed to overcome the "Allo Tax" and **significantly increase production yield** while **preserving desirable T_{SCM} attributes** of P-BCMA-ALLO1

POSEIDA THERAPEUTICS

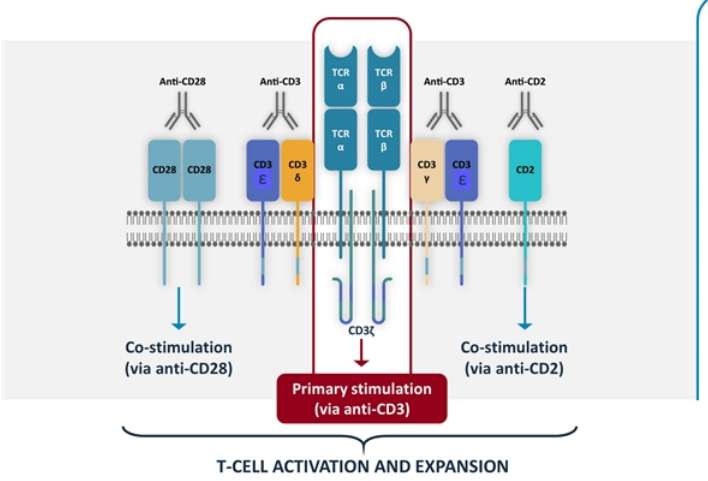
Booster Molecule Technology Overcomes the “Allo Tax”

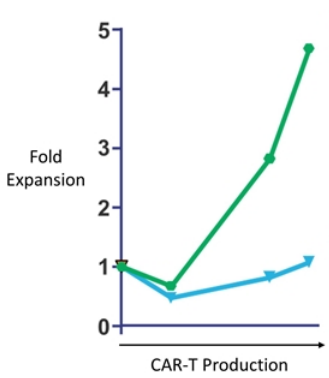
Other CAR-T Approaches Suffer from Impaired Allogeneic Manufacturing

THE PROBLEM:

Gene Editing of TCR Can Impair Allogeneic CAR-T Manufacturing

Compared to Unedited CAR-T = “Allo Tax”





With Booster

Our patented technology is designed to overcome these limitations, and **significantly increase production yield** while **preserving desirable T_{SCM} attributes** of P-BCMA-ALLO1

Without Booster

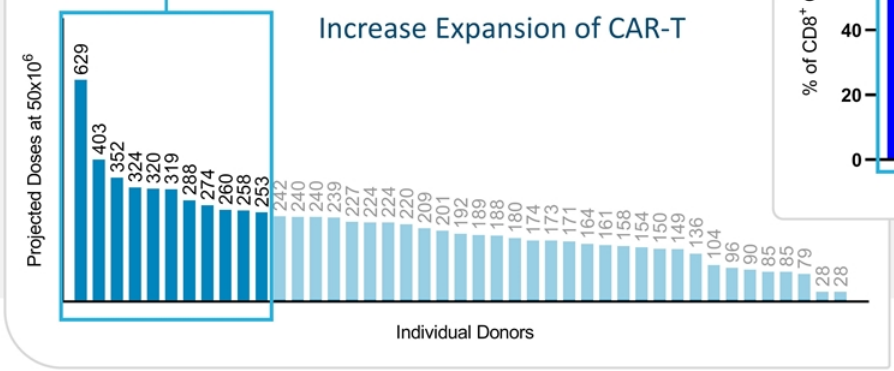
POSEIDA THERAPEUTICS

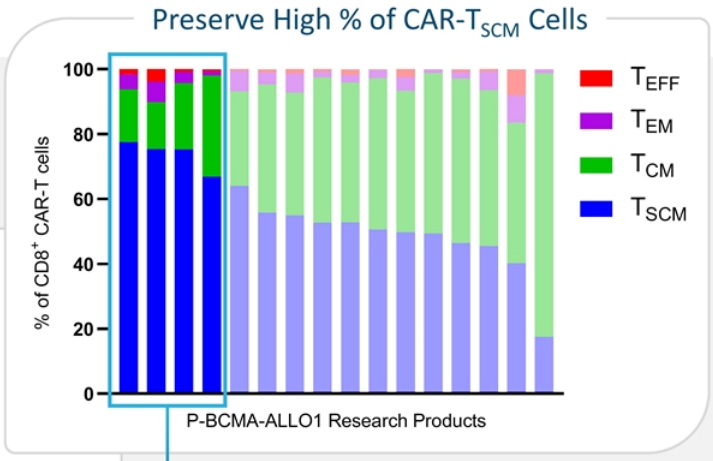
Booster in Action: Increased Expansion and High CAR-T_{SCM}

Preclinical Products Exhibit Favorable Expansion and Phenotype

Top Quartile Donors **Yield >250 Doses**

- >40 healthy donors screened
- >90% success in small scale production
- Clinical manufacturing with booster currently being optimized

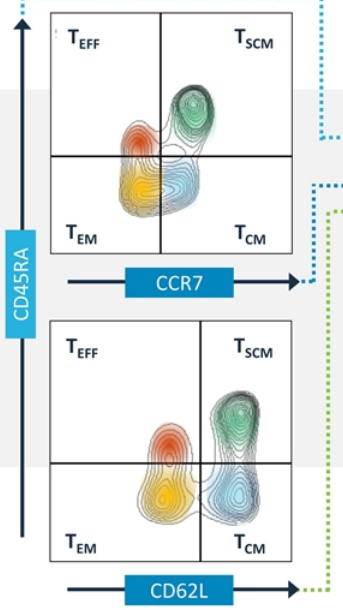




Top Quartile Products are **74% T_{SCM} and 94% T_{SCM} + T_{CM}**

POSEIDA THERAPEUTICS

Poseida's Allogeneic CAR-T Products are Rich in T_{SCM} Cells



- Gated on CD4/CD8+ T cells
- All T cells are CD95+

	T_N	T_{SCM}	P-BCMA-ALLO1	T_{CM}	T_{EM}	T_{TE}
CD45RA	+	+	+	-	-	+
CD45RO	-	-	-	+	+	-
CCR7	+	+	+	+	-	-
CD62L	+	+	+	+	-	-
CD28	+	+	+	+	+/-	-
CD27	+	+	+	+	+/-	-
IL-7Rα	+	+	+	+	+/-	-
CXCR3	-	+	+	+	-	-
CD95	-	+	+	+	+	+
CD11a	-	+	+	+	+	+
IL-2Rβ	-	+	+	+	+	+
CD58	-	+	+	+	+	+
CD57	-	-	-	-	+/-	+

Stemness
Proliferative potential
Lymphoid homing
Antigen independence
Lipid metabolism
Low Δψm

Senescence
Cytotoxicity
Tissue tropism
Antigen addiction
Gylcolytic metabolism
Oxidative stress

Adapted from Gattinoni et al. (2017) Nat. Med.

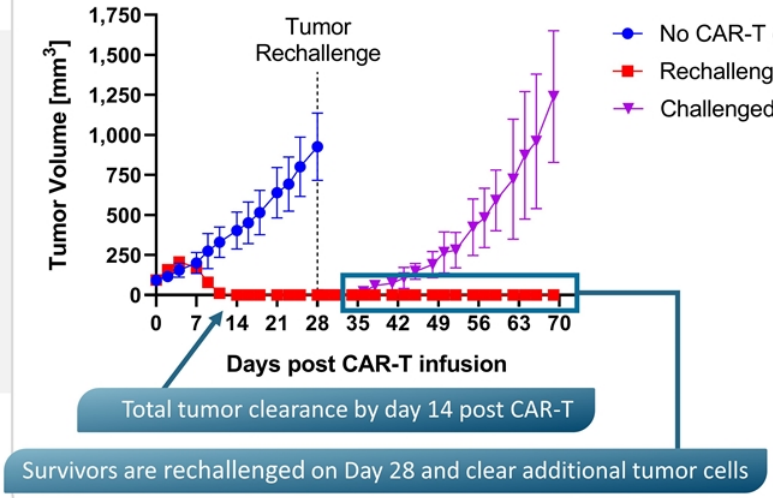
Poseida products closely match a T_{SCM} phenotype when using extensive cell surface markers by flow cytometry

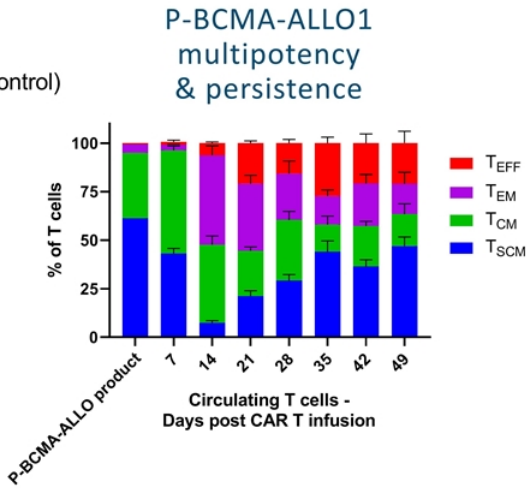
POSEIDA THERAPEUTICS

P-BCMA-ALLO1 Demonstrates Hallmarks of T_{SCM} Cells In Vivo

CAR-T_{SCM} Demonstrate Multipotency and Persistence in Tumor Rechallenge Model

Efficacy in Multiple Myeloma Cancer Model (RPMI-8226)





POSEIDA THERAPEUTICS

P-BCMA-ALLO1 Phase 1 r/r Multiple Myeloma Clinical Trial

Phase 1 Trial Design

- Open Label, 3+3 Dose Escalation
- 30 mg/m2 fludarabine + 300 mg/m2 cyclophosphamide x 3d lymphodepletion regimen
- P-BCMA-ALLO1 administered intravenously
  - Single dose cohorts
  - Multiple dose cohorts and Rituxan combinations considered for amendment (per FDA request)
- Up to 40 subjects

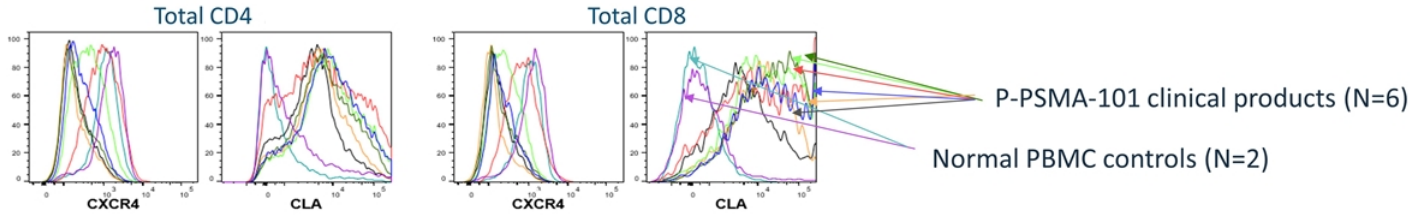
Clinical Trial Sites

- Advocate Aurora – Tulio Rodriguez, MD
- University of Oklahoma – Carrie Yuen, MD
- UCSD – Caitlin Costello, MD
- UCSF – Nina Shah, MD
- Johns Hopkins – Syed Abbas Ali, MD
- University of Maryland – Mehmet Kocoglu, MD
- University of Chicago – Ben Derman, MD

T_{SCM} Trafficking may be Important for Clinical Efficacy in Solid Tumors

- Poseida CAR-T and T_{SCM} express a variety of **trafficking molecules**
- May facilitate trafficking to marrow, tumor
- P-PSMA-101 robust clinical activity against bone marrow metastases

Trafficking Molecule	T_{SCM}/T_{CM}	P-PSMA-101	T_{EFF}
CD62L (L-selectin)	+	+	-
CXCR4	+	+	-
CXCR3	+	+	-
CLA (Cutaneous lymphocyte antigen)	+	+	-
CCR7	+	+	-
CD11a (LFA-1-a)	+	+	-

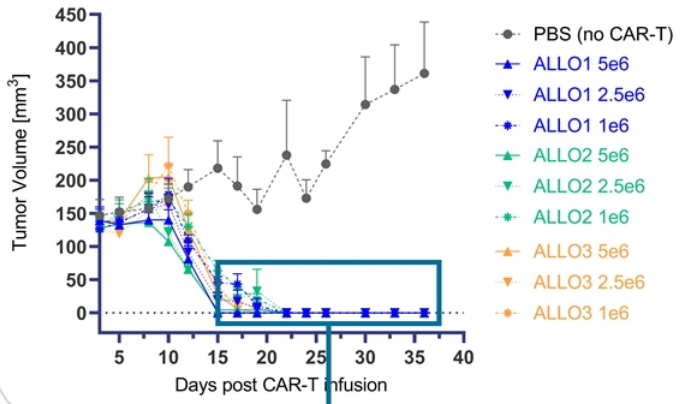


POSEIDA THERAPEUTICS

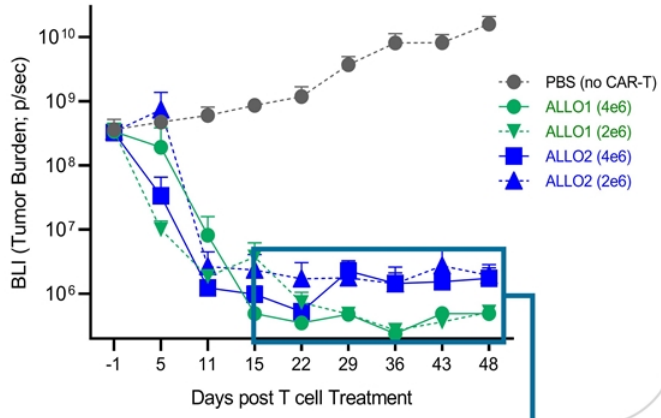
P-MUC1C-ALLO1 Potent Activity Against Solid Tumors In Vivo

Triple-negative Breast (MDA.MB.468) and Ovarian Cancer (OVCAR3) Models

Triple-Negative Breast Cancer Model



Ovarian Cancer Model



100% Tumor Elimination After ~2 Weeks

P-MUC1C-ALLO1 Phase 1 Clinical Trial

Phase 1 Trial Design

Phase 1 dose-finding and expansion study in advanced treatment-resistant solid tumors, including but not limited to ovarian cancer, pancreatic cancer, breast cancer (TNBC), non-small cell lung cancer (NSCLC) and others solid tumors

- Open Label, 3+3 Design, Single and cyclic Ascending Dose finding Study
- 30 mg/m2 fludarabine + 300 mg/m2 cyclophosphamide x 3d (Rituximab combination proposed)
- Up to 100 subjects; ~60 in dose-finding Part 1, with ~40+ in expansion cohort Part 2

Phase 1 Expansion (selected tumor types)

Single or cyclic dose with the selected dose in 10-15 subjects per indication

- **Cyclic dosing escalation cohorts proposed**
- **Outpatient** administration proposed

Study objectives

- Safety/Feasibility: AEs, Labs, CRS (Lee 2019) and CAR-T related toxicities and PK
- Dose finding: MTD and RP2D
- Efficacy: RECIST – ORR, TTR, DOR, PFS, OS etc. and PRO
- Exploratory: Biomarkers: P-MUC1 cells (vectors/clonality) and others

POSEIDA THERAPEUTICS

Aiming to Better Understand Biomarkers of Product Quality

Few Known Correlates of Preclinical / Clinical Activity, OR Biomarkers of Optimal Healthy Donors

Research Goals

- Identify biomarkers that:
  - Increase our knowledge of T cell fitness and function
  - Predict the best donors and products
- Identify best healthy donors for Allo production
- Utilize biomarker knowledge to make better CAR-T cells

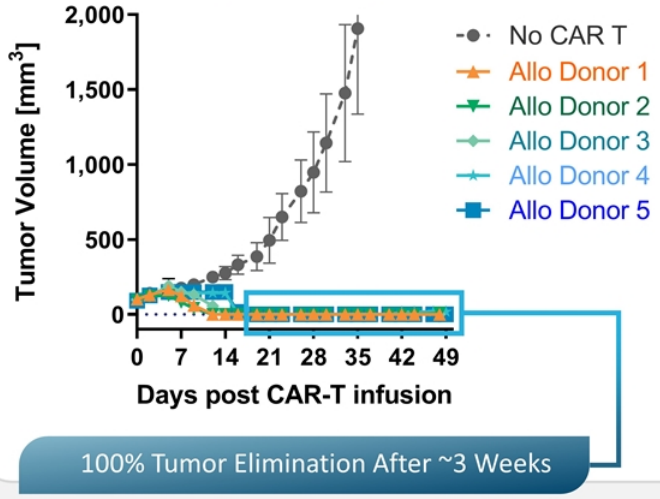
nCounter® Characterization Panels

POSEIDA THERAPEUTICS

Positive Predictive Value of Allogeneic CAR-T Product Quality

Stringent In Vivo Models Used to Measure Product Quality

Efficacy in Multiple Myeloma Cancer Model (RPMI-8226)



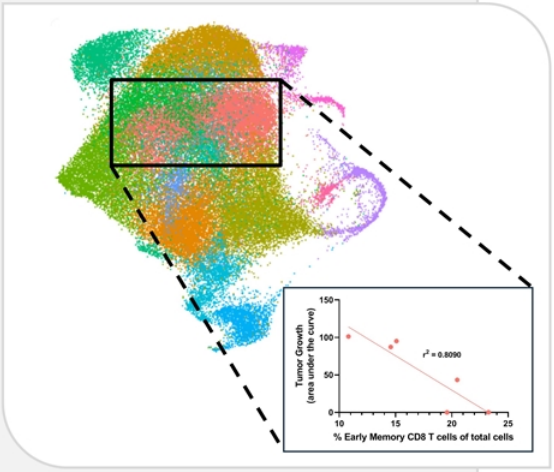
100% Tumor Elimination After ~3 Weeks

- Capacity for tumor control determined in vivo at 'stress' CAR-T doses
- Stringent myeloma model **fine-tuned using clinical samples of P-BCMA-101** with known clinical outcomes
  - **100% positive predictive value**: If clinical product completely killed tumor in the animal model, then it also had excellent activity in the clinical trial
- Correlative studies performed using preclinical lots (>25) of P-BCMA-ALLO1 that were extensively evaluated
  - Single cell approaches used allowing for deeper analysis of CAR-T functionality and heterogeneity unattainable by FACS or bulk RNA sequencing

P-BCMA-ALLO1 Early Memory Cells Correlate with Antitumor Efficacy

*Products with the Best In Vivo Activity Have **More T_{SCM} Memory Cells***

- **Presence of early memory cells** significantly correlated with in vivo efficacy
  - Inverse correlation between CD8+/ CCR7+/ CD27+/ CD62L+/ TCF7+ cells and tumor growth
- Also important:
  - **Viability** of product post-thaw
  - **Functional capacity** in serial restimulations assays (i.e. proliferative, multipotent, etc.)

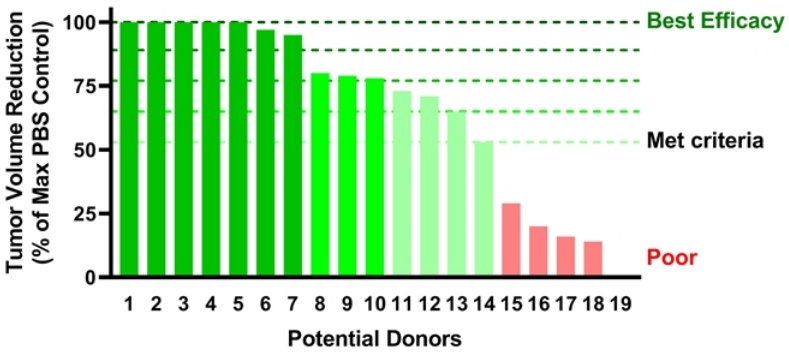


POSEIDA THERAPEUTICS

Screening Identifies Ideal Donors for Clinical Manufacturing

A Vast Majority of Healthy Donors Were Eligible for Clinical Lot Manufacture

- Healthy donors (>25) were **screened for manufacturability and function** (in vitro and in vivo tumor efficacy)
- Most donors (93%) met manufacturability criteria
- Of those, 74% (14 of 19) met activity release criteria and **are eligible for clinical lot manufacture**
  - 50% of those (7 of 14) demonstrated complete or near complete tumor elimination
- Top donors identified have the greatest chance of producing high-quality product



Summary: Poseida T_{SCM}-based Allogeneic CAR-T Platform

- CAR-T_{SCM} are the **key to efficacy and safety**
  - **Prodrug** is ideal for treating solid tumor indications
- Poseida's unique technology **enables fully allogeneic CAR-Ts rich in T_{SCM}**
  - **Booster molecule** facilitates potentially 100s of doses from a single manufacturing run
  - Pipeline candidates highly efficacious in stringent xenograft tumor models
    - P-BCMA-ALLO1 demonstrates complete tumor control in predictive model
    - P-MUC1C-ALLO1 has potent activity against a wide range of human tumors
  - IND Clearances in 3Q 2021 (P-BCMA-ALLO1) and 4Q 2021 (P-MUC1C-ALLO1)
- Understanding correlates of preclinical / clinical efficacy **can help to make better products**
  - **Product quality** is a measure of cell health, T cell fitness and function
  - The best products had more T_{SCM} and great functional capacity
  - Donor selection allows for generation of products with exceptionally high % T_{SCM}

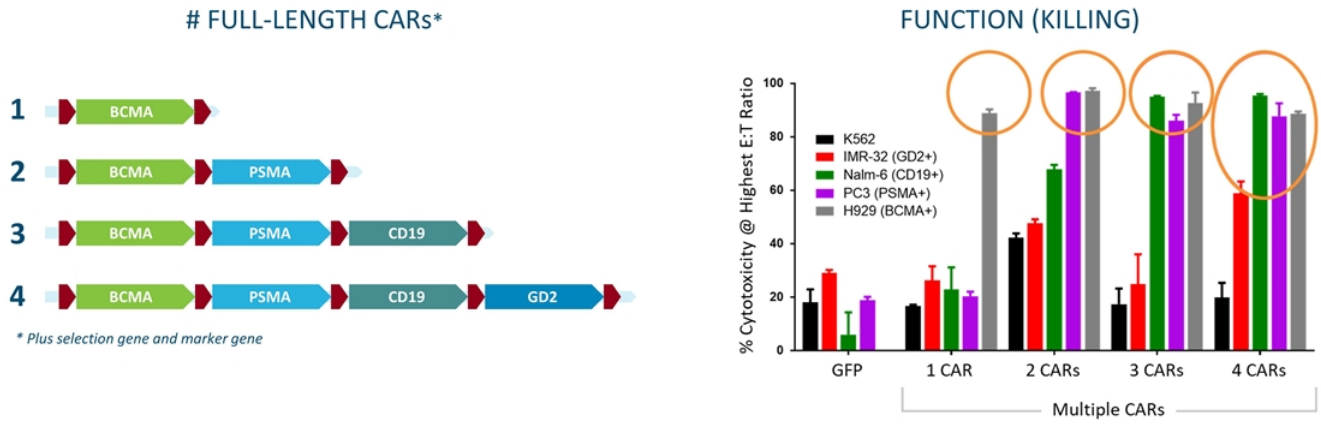
Dual CAR Programs

POSEIDA THERAPEUTICS

PiggyBac's Cargo Capacity Enables Multiple Antigen Targeting and More

Large Cargo Capacity Increases Optionality and Enables the Next Wave of Opportunity

Proof of Concept: PB Can Effectively Deliver Multiple Full-length CARs in Single Transposon System



Cargo capacity enables **multi-targeting, logic gating system, armoring or other strategies**, with additional capacity for safety switch, selection gene (and/or others)

Multiple Antigen Targeting with Dual CAR to Improve Efficacy

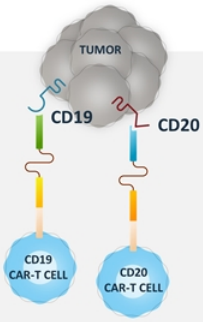
1. Overcome single antigen loss (heme)

CD19 CAR-T clinical trials: up to 40% of relapse is caused by loss of CD19 antigen

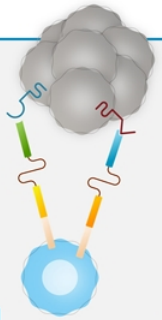
2. Target heterogeneous tumors (solid)

Highly heterogeneous antigen expression may contribute to poor CAR-T clinical responses against solid tumor

Single CAR
Co-administered



Dual CAR
Co-localized dual engagement



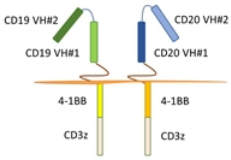
Tandem CAR
Conformation challenges?

Competitive Advantage

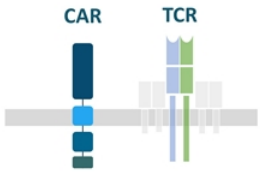
Shah et al., Front Oncol. 2019; 9: 146

Additional Approaches Beyond Single CARs

Dual-CAR Tandem



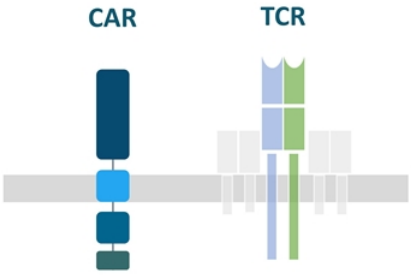
CAR-TCR



POSEIDA THERAPEUTICS

Multiple Antigen Targeting by Combining CAR-T and TCR-T Platforms

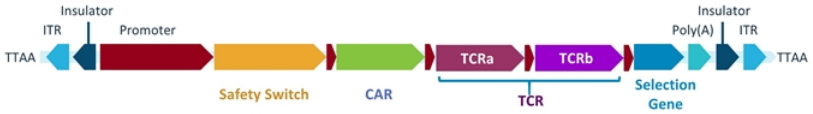
Simultaneous expression of CAR and TCR



POTENTIAL BENEFIT

Enable engineered T cell to **recognize both cell surface and intracellular antigen** presented by MHC

CAR+TCR Transposon

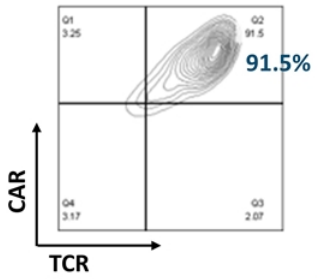


Integrate CAR and TCRα/β genes into one multi-cistronic cassette

piggyBac® can be leveraged to deliver CAR and TCR αβ in same product

- Over 90% of engineered T cells express both CAR and TCR

CAR+TCR co-expression



Hybrid CAR/TCR-T cells may exhibit **better killing and higher tumor infiltration** in solid tumor indications

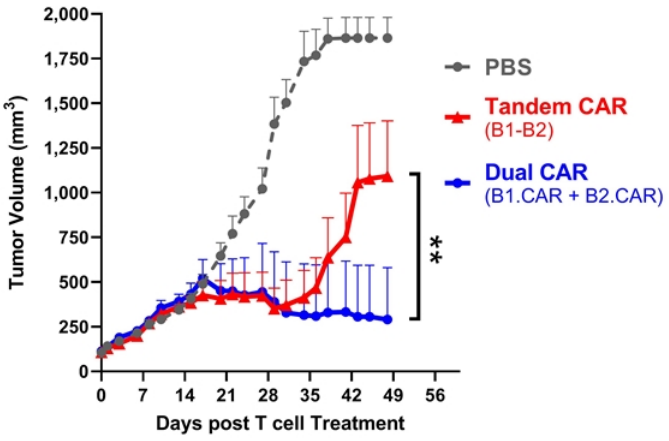
POSEIDA THERAPEUTICS

Dual CAR is More Effective Than a Tandem CAR

PiggyBac Provides Competitive Advantage with Dual CAR

- **We compared various formats** of our single-domain VH binders:
  - Single CAR
  - Single Tandem CAR
  - Dual CAR
- We have learned:
  - A tandem CAR is sometimes better than a single CAR
  - A **Dual CAR-T is almost always better than a single or tandem CAR-T**
- Lessons learned will be implemented in future pipeline programs

Dual CAR-T vs Single Tandem

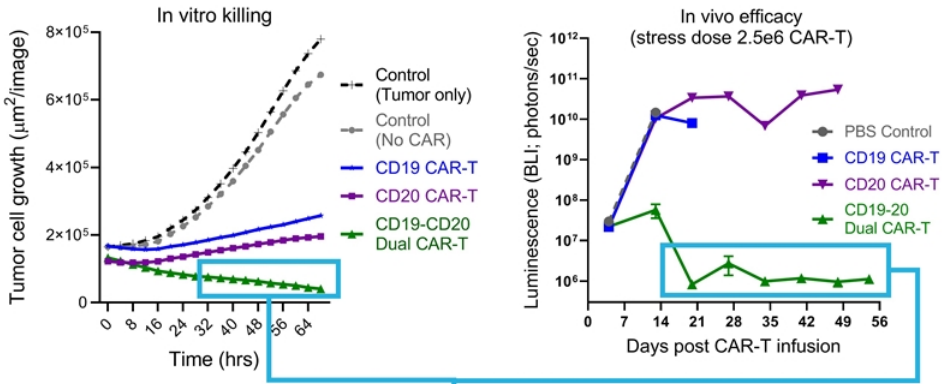


CD19/CD20 Dual CAR for B Cell Malignancies & Autoimmune Diseases

1. **ALLO CD19/CD20**
   B cell Leukemia and Lymphoma
2. **ALLO CD19/BCMA**
   Multiple Myeloma
3. **Dual ALLO (Undisclosed)**
   Solid Tumors

- CD19/CD20 Dual CAR-Ts kill (double positive target cells) better than either single CAR-T alone
  - Quad-cistronic vector
- Fully allogeneic
- Dual CAR-T maintain high % T_{SCM}
- Could also be used to treat autoimmune diseases

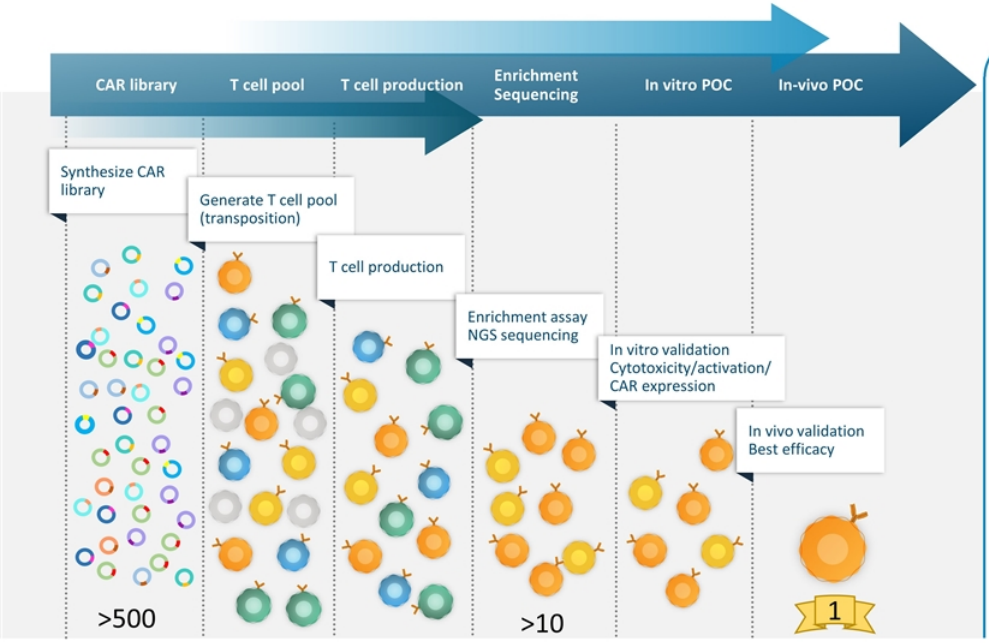
CAR-T Killing of Lymphoma Tumor Cells (Raji; $CD19^+$ and $CD20^+$)



Dual antigen targeting can increase efficacy

Binder Mutagenesis and Library Screening Platform

Capable of Improving Performance of any CAR Binder



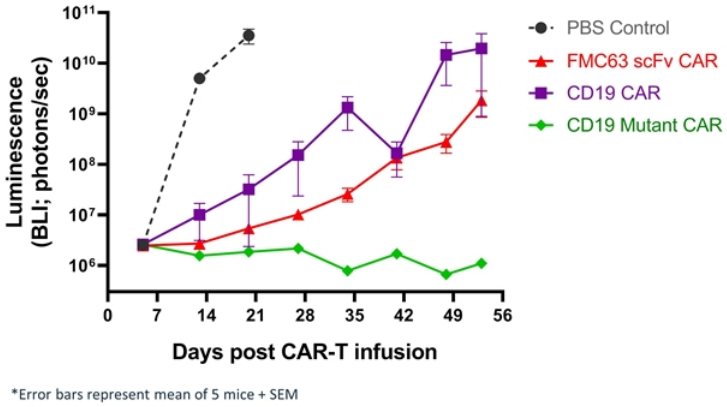
- **Powerful** binder mutagenesis platform
- Capable of **improving performance** of any CAR binder
- Developed at Poseida
- **In vivo screening** used for final determination of lead/s
  - Survival, tumor burden, T cell expansion (C_{max}), T cell exhaustion, etc.

POSEIDA THERAPEUTICS

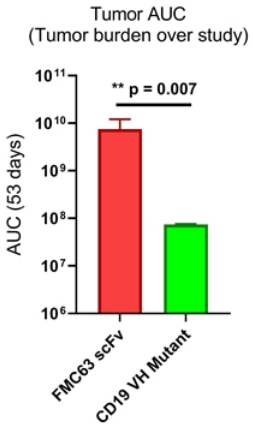
Improved CD19 VH Binder Performance

Proof-of-concept: Binder Enhanced Via Single Point Mutation to Outperform Canonical FMC63 scFv

Efficacy in Lymphoma Cancer Model (Raji)



*Error bars represent mean of 5 mice + SEM



Binder mutagenesis significantly improved final product function in a lymphoma cancer model

Summary: Poseida Dual CAR-T Programs

- PiggyBac's large cargo capacity enables delivery of **numerous therapeutic genes**
  - e.g., CAR, TCR, armor, safety switch, selection gene, etc.
- **Multiple antigen targeting** with Dual CAR-T or CAR-TCR cells can improve efficacy
  - Overcome single antigen loss (heme malignancies)
  - Target heterogenous tumors (solid tumor indications)
- Dual CAR is ***almost always*** **better** than a single or tandem CAR
- **Dual CAR (CD19/CD20)** is fully allogeneic, maintains a high % of T_{SCM}, and is more efficacious than either single CAR alone
- Poseida's Binder Mutagenesis and Library Screening Platform **can improve performance of any CAR binder**

POSEIDA THERAPEUTICS

Gene Therapy Product Candidates

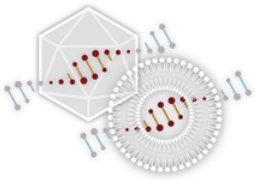
Eric Ostertag, MD, PhD
Founder & Executive Chairman

Disruption in Gene Therapy

In Vivo Gene Therapy for Rare Diseases

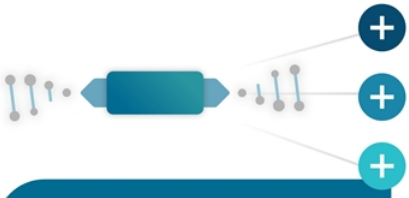
Fully Integrating

PiggyBac® integrates into DNA enabling the potential for single treatment cures



Addressing Challenges of Viral Delivery

piggyBac and **Nanoparticle** technology can address limitations of AAV

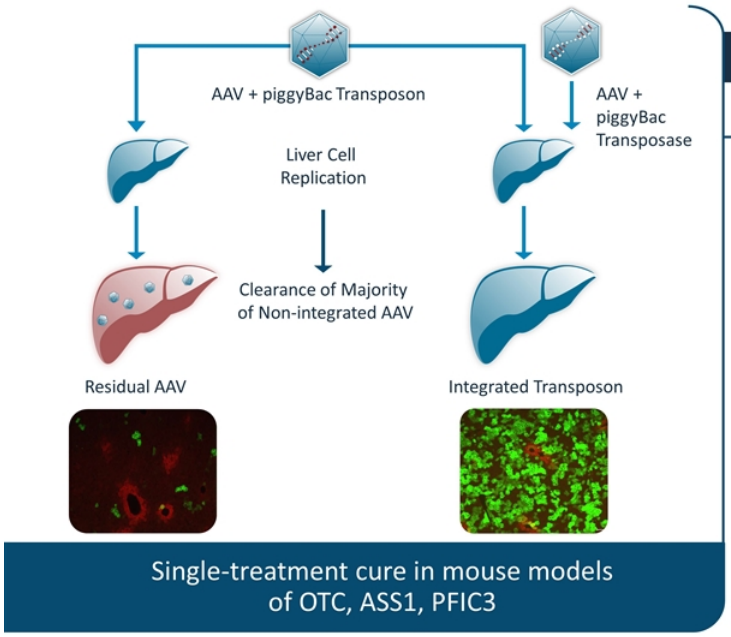


Broad Application

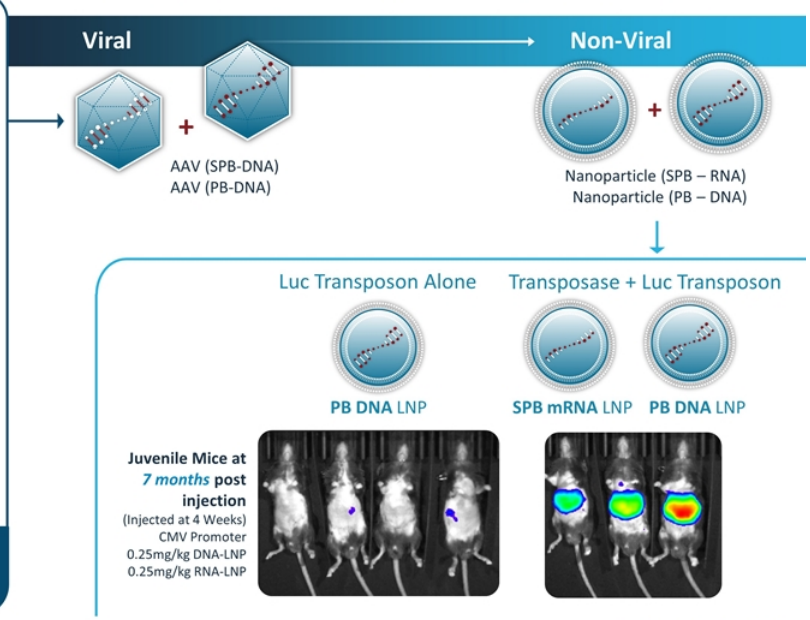
piggyBac cargo capacity addresses more indications and piggyBac can treat juvenile populations

Changing the Game in Liver-Directed Gene Therapy

piggyBac+AAV followed by piggyBac+Nanoparticle



Single-treatment cure in mouse models of OTC, ASS1, PFIC3



POSEIDA THERAPEUTICS

Announcing Our First Strategic Gene Therapy Partnership

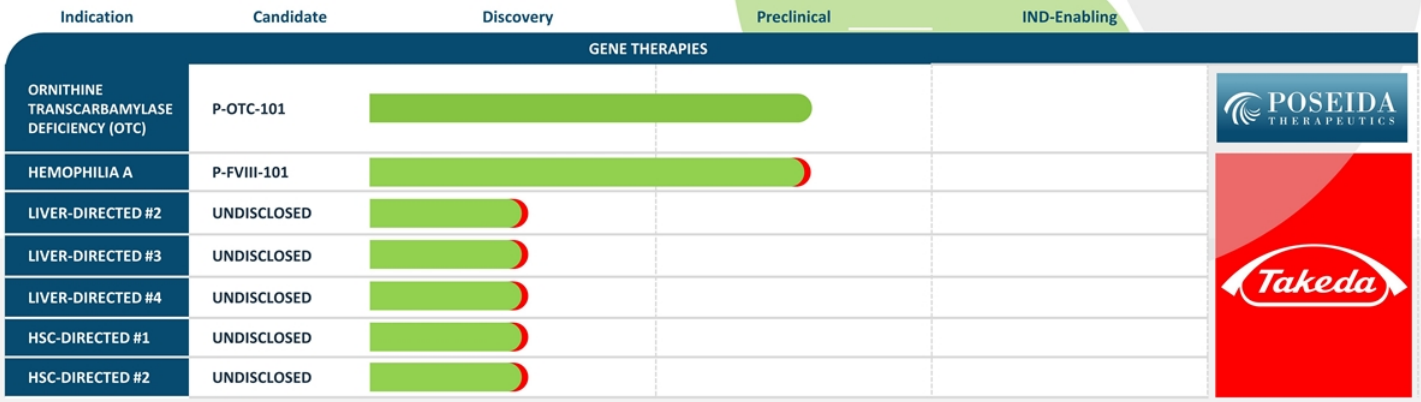
- Broad **non-viral in vivo gene therapy** research collaboration with Takeda
  - Liver-directed and HSC-directed indications
  - Six initial targets including **Hemophilia A**
    - Option for two additional targets
- Includes **all of Poseida's core technology platforms**
  - PiggyBac® gene insertion
  - Cas-CLOVER™ for gene editing
  - Biodegradable LNP nanoparticle for gene delivery
- Poseida responsible for research to candidate selection and Takeda has responsibility for development, manufacturing and commercialization

Takeda

- Financial Terms
- $45 million cash up front and pre-clinical milestones could exceed $125 million in the aggregate
- $435 million in clinical development, regulatory and commercial milestones per program
- Tiered royalties on commercial sales
- Takeda responsible for research program costs

Gene Therapy Pipeline

In Vivo Liver-Directed and HSC-Directed Gene Therapy



POSEIDA THERAPEUTICS

Emerging Technologies

Eric Ostertag, MD, PhD
Founder & Executive Chairman

POSEIDA THERAPEUTICS

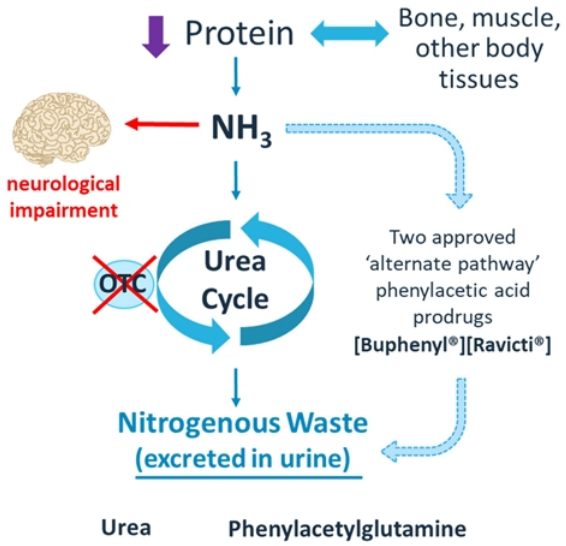
P-OTC-101 for Ornithine Transcarbamylase Deficiency

Jack Rychak, PhD
Vice President, Gene Therapy

Ornithine Transcarbamylase (OTC) Deficiency

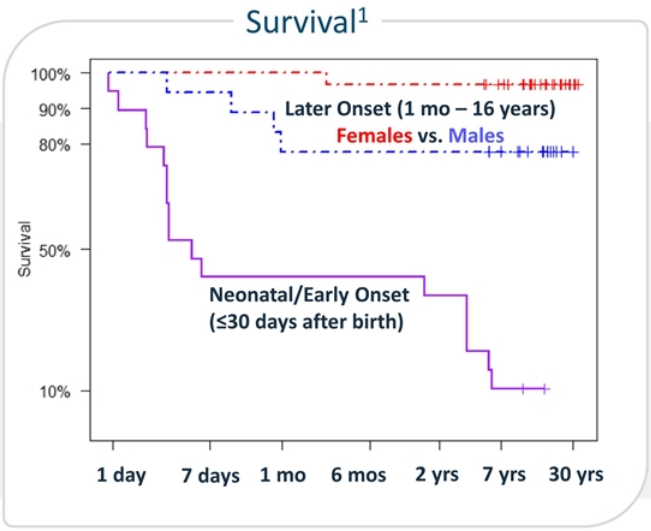
OTC Deficiency

- X-linked metabolic liver disorder
- Most common urea cycle disorder subtype and most common cause of 'early onset' illness
- Causes hyperammonemia crises which may result in neurological impairment or death
- Dietary protein restriction & alternative pathway drugs inadequate for early onset illness
  - Liver transplantation is standard care
    - Inaccessible to many
    - Morbidity and mortality
    - Lifetime immunosuppression



POSEIDA THERAPEUTICS

Early Onset/Severe OTC Deficiency: Major Unmet Need and Opportunity for Benefit



piggyBac® Benefits in OTC Disease

Integrates Into DNA Delivering Stable Long-Term Expression

- Ideal for use in **dividing tissues** like those in juvenile liver. **Not adequately treatable with standard non-integrating AAV gene therapies.**
- **Highly efficient** integration with piggyBac® may allow **reduced dosing and single treatment cures**
- **Delivered using AAV + nanoparticle**

[1] *Brassier et al., Orphanet Journal of Rare Diseases , 2015 (French series spanning 1971-2011)*

POSEIDA THERAPEUTICS

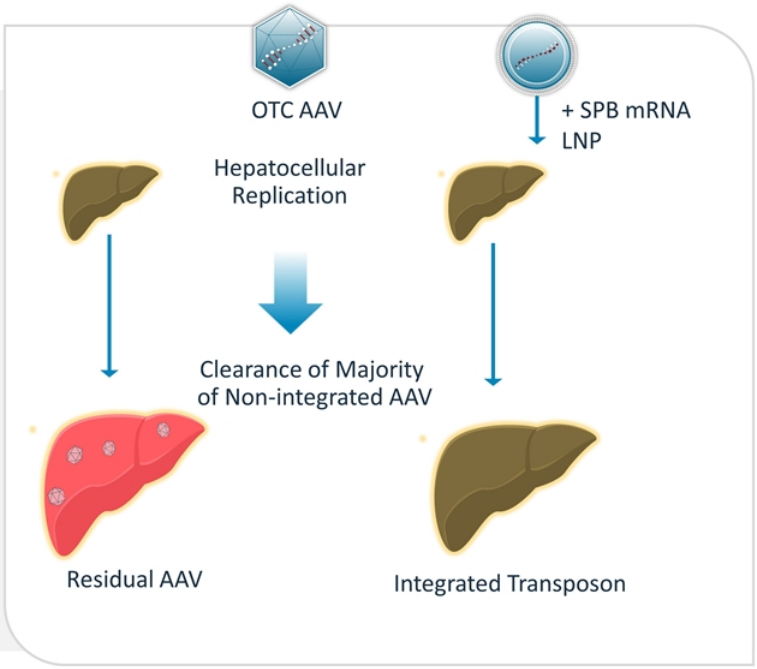
P-OTC-101

hOTC-AAV

+

piggyBac mRNA LNP

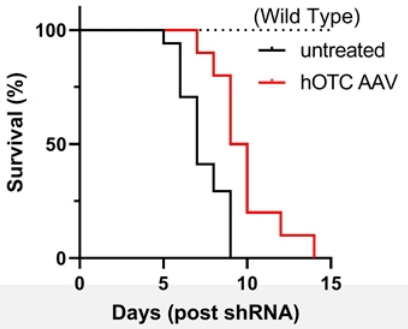
- Biodegradable nanoparticle transiently delivers Super piggyBac® transposase (SPB)
- Rapid and stable integration of functional OTC gene into the genome
- Durable OTC expression in growing liver enables single treatment cure
- Protein expression at therapeutic levels with order(s) of magnitude lower AAV doses
- Possibility of re-dosing SPB, if needed

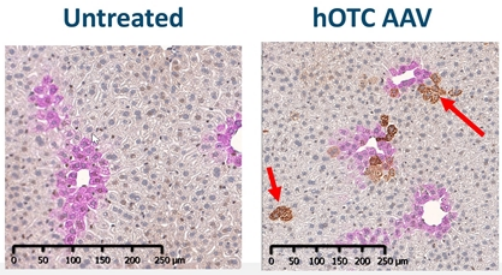


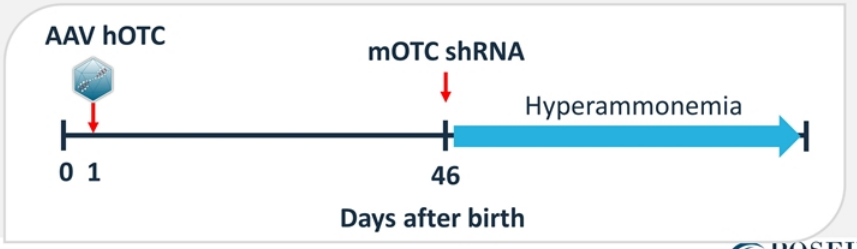
POSEIDA THERAPEUTICS

Standard AAV Approach is Insufficient to Rescue Severe Phenotype Following Neonatal Treatment

- Experimental Design
- SPFash treated on day=1 of life with 2E13 vg/kg of hOTC-AAV
- Mice challenged with shRNA (against mouse OTC) on day=46 to eliminate residual OTC expression to induce severe disease phenotype

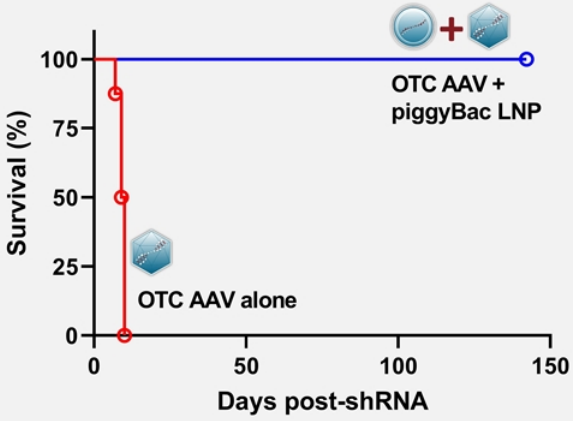


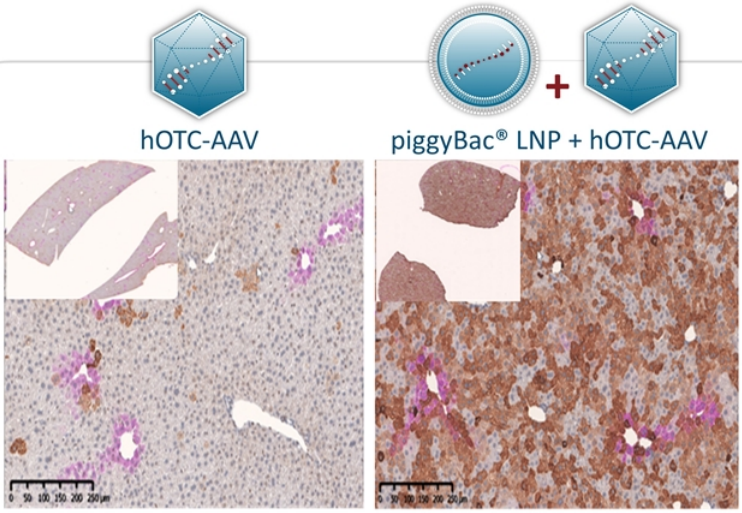




POSEIDA THERAPEUTICS

P-OTC-101 Enables Single Treatment Cure of OTC Disease Model



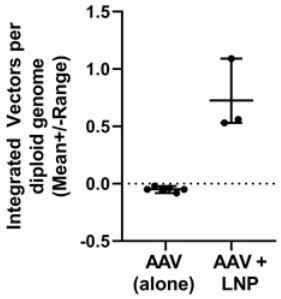


2E13 vg/kg hOTC-AAV +/- 0.2 mg/kg piggyBac transposase mRNA LNP administered on day=1 of life to spfash mice
IHC for glutamine synthetase (pink) human OTC (brown) in liver on day = 83

POSEIDA THERAPEUTICS

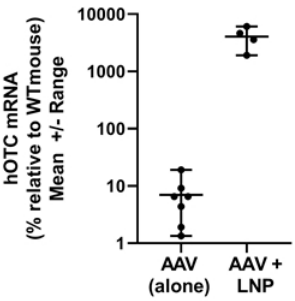
P-OTC-101 Enables Single Treatment Cure of OTC Disease

Integrated Vectors



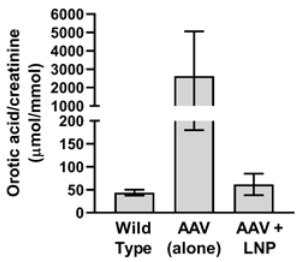
Integrated copies in liver measured by ddPCR on day 83 post-treatment

hOTC mRNA

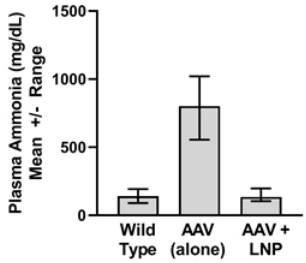


hOTC mRNA in liver measured by qRT-PCR on day 83 post-treatment

Urea Cycle Biomarkers



Urinary orotic acid measured by LC-MS/MS on day 35



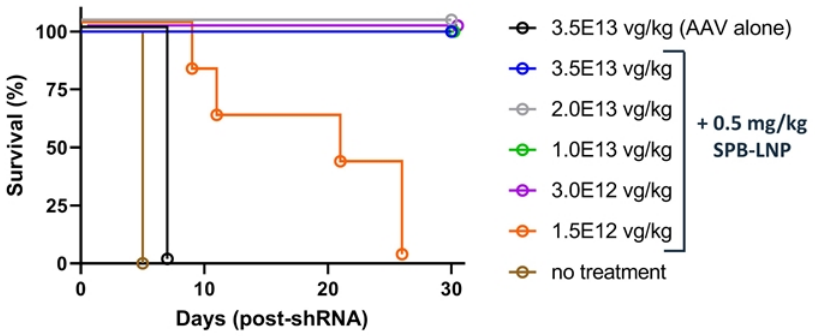
Plasma ammonia measured by clinical chemistry analyzer on day 83

2E13 vg/kg hOTC-AAV +/- 0.2 mg/kg piggyBac transposase mRNA LNP administered on day=1 of life to spfash mice

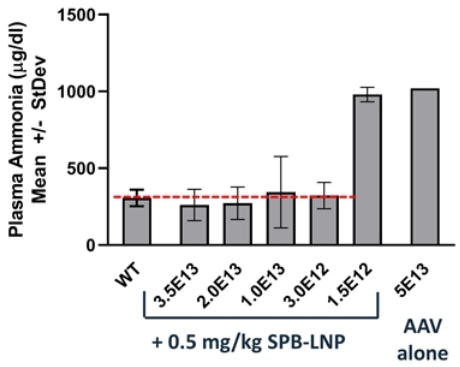
POSEIDA THERAPEUTICS

piggyBac® Reduces Therapeutic AAV Dose by Order(s) of Magnitude

Survival



Plasma Ammonia

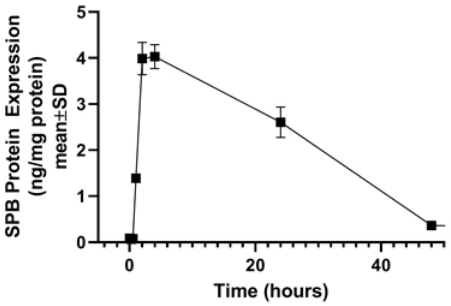


Plasma ammonia measured by clin. chemistry analyzer on day 77 post-treatment

0.5 mg/kg LNP + hOTC_AAV administered on day=1 of life to spfash mice

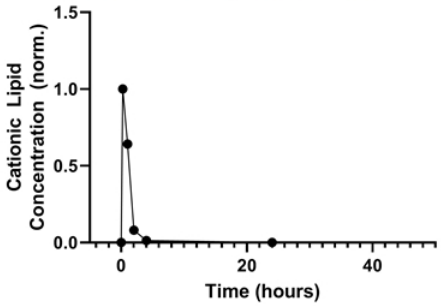
Transient mRNA Expression of piggyBac® Transposase from Biodegradable Nanoparticle

Transposase Expression



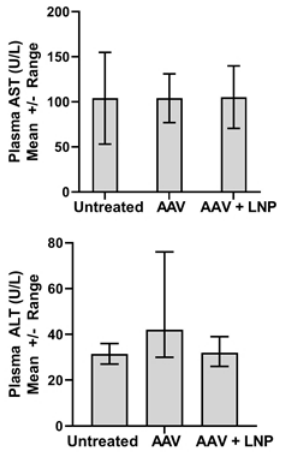
piggyBac transposase (SPB) expression in liver measured by ELISA in WT mice

Cationic Lipid Clearance



Cationic lipid concentration in liver measured by LC-MS/MS (0.5 mg/kg) in WT mice

Liver Enzymes



3.5E13 vg/kg hOTC-AAV +/- 2 mg/kg transposase LNP to juvenile spf-ash mice; liver enzymes measured on day=17 post treatment

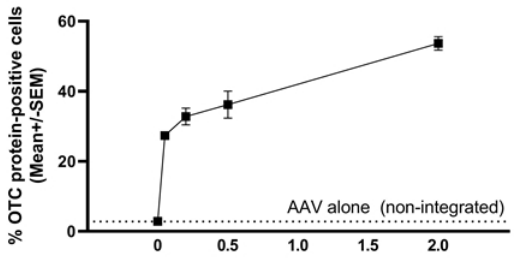
- Transient expression of transposase is effective in <24 hours
- No evidence of liver toxicity
- Greatly limits potential for immune response

POSEIDA THERAPEUTICS

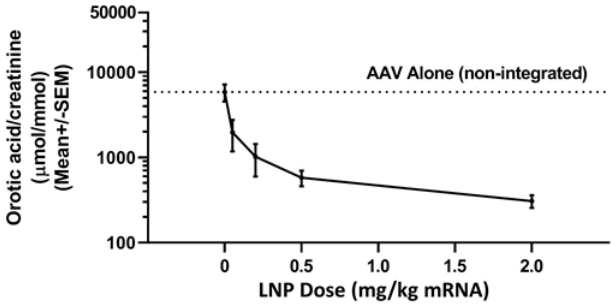
Transgene Activity is Responsive to LNP Dose

- hOTC-AAV + SPB transposase mRNA LNP administered on day=1; OTC expression and urinary orotic acid measured on day = 83
- Dose-proportional increase in hepatocytes expressing hOTC with transposase mRNA LNP dose
- Decrease in urinary orotic acid proportional to frequency of hOTC expressing hepatocytes

hOTC-Expressing Hepatocytes



Urinary Orotic Acid



POSEIDA THERAPEUTICS

Summary and Conclusions

- Single treatment of hybrid piggyBac® AAV+LNP enables cure in mouse model of severe OTC Disease
- piggyBac® hybrid LNP/AAV approach reduces required AAV dose for therapeutic efficacy by order(s) of magnitude
- The piggyBac® System **likely may be used with any AAV system** to greatly increase duration of transgene expression, reduce or eliminate toxicity and allow for treatment of pediatric patient populations
- P-OTC-101 shows does response and re-dosing of transposase is possible if necessary

POSEIDA THERAPEUTICS

P-FVIII-101 for Hemophilia A

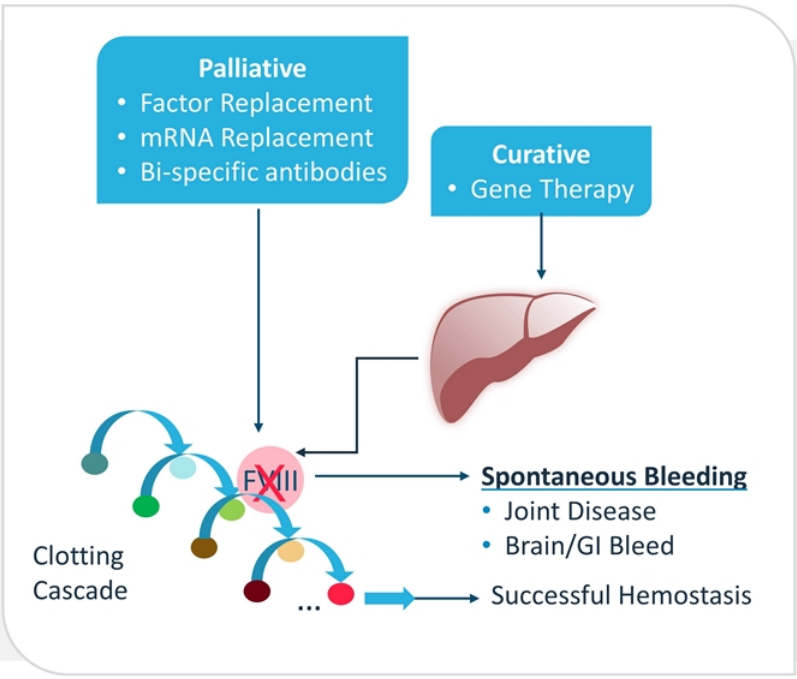
Jack Rychak, PhD
Vice President, Gene Therapy

Hemophilia A

- X-linked bleeding disorder caused by deficiency in factor VIII
  - Large cDNA (~7.1 kb) and complex protein
- Causes frequent bleeding episodes
- FVIII activity correlates with the severity of the disease

Classification	FVIII Activity	Relative Incidence
Severe	<1%	50%
Moderate	1-5%	30%
Mild	>5-40%	20%

- Current approaches not suitable for juvenile treatment (AAV gene therapy) or require lifelong treatment (protein replacement therapies)



P-FVIII-101

piggyBac® Dual LNP Approach

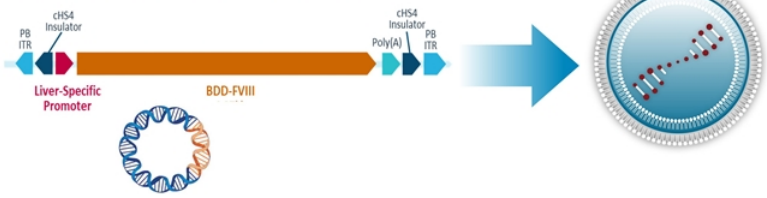
hFVIII Transposon LNP

+

piggyBac Transposase LNP

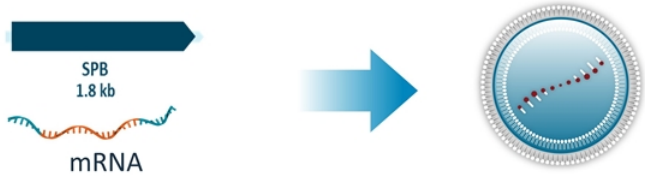
- Biodegradable lipid nanoparticles (LNPs) deliver Super piggyBac transposase (SPB) and FVIII transposon (therapeutic transgene)
- No known cargo capacity limits
- Stable integration of functional human FVIII gene into genome
- Durable FVIII expression in growing liver
- Possibility of repeated dosing, if required

FVIII DNA Transposon LNP



Therapeutic Transgene (DNA)

Super piggyBac (SPB) mRNA Transposase LNP

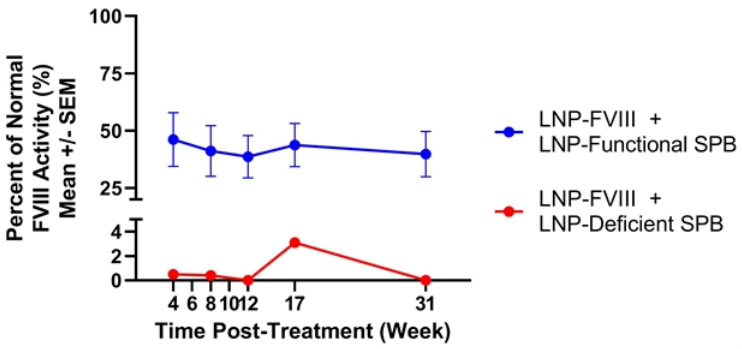


POSEIDA THERAPEUTICS

Durable FVIII Activity in Juvenile Mouse Model of HemA

- Dual-LNP co-administered as single dose IV to juvenile Hem A mice (n=7)
  - 0.25 mg/kg Transposon (DNA)
  - 0.50 mg/kg Transposase (mRNA)
- FVIII activity measured (tail vein collection) in 4-week intervals
- Therapeutic (25-83%) levels of FVIII activity observed
- Durable FVIII activity maintained over 7 months

FVIII Activity in Juvenile HemA Mouse

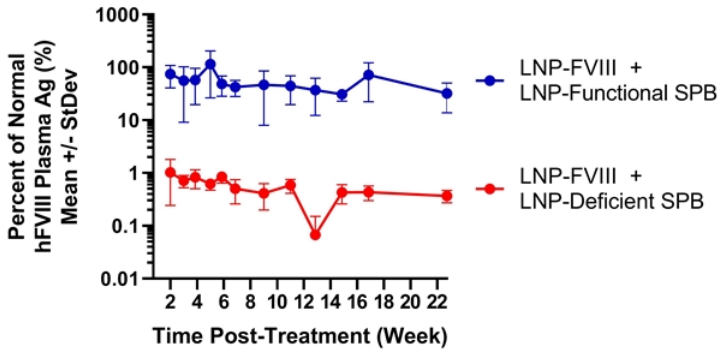


Sabatino, et al. "LNP delivery of piggyBac for gene delivery of FVIII for hemophilia A." National Hemophilia Foundation 16th Workshop on Novel Technologies and Gene Transfer for Hemophilia. 12-13 Nov 2021. Washington, D.C.

Durable Expression of Human FVIII Observed in Neonatal Mice

- Dual-LNP co-administered as single dose IV to neonatal (day 1 of life) healthy BALB/C mice (n=6-9)
  - 0.25 mg/kg Transposon (DNA)
  - 0.50 mg/kg Transposase (mRNA)
- Human FVIII expression (protein concentration) measured by ELISA bi-weekly
- Durable expression of human FVIII maintained over 5 months

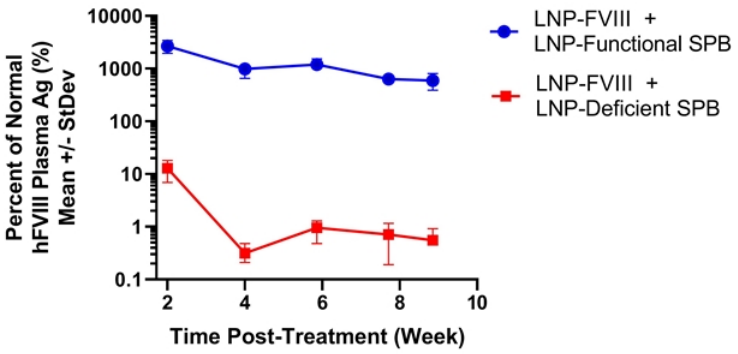
FVIII Expression in WT Neonatal Mouse



PiggyBac® Enables Supraphysiological FVIII Expression at Low Doses

- In-progress study evaluating ongoing FVIII transposon and SPB transposase sequence optimization
- Dual-LNP co-administered as single dose IV to neonatal (day 1 of life) healthy BALB/C mice (n=4)
  - 0.25 mg/kg Transposon (DNA)
  - 1.0 mg/kg Transposase (mRNA)
- Genome integration with piggyBac® enables massively supra-therapeutic FVIII expression levels at modest dose level in young liver

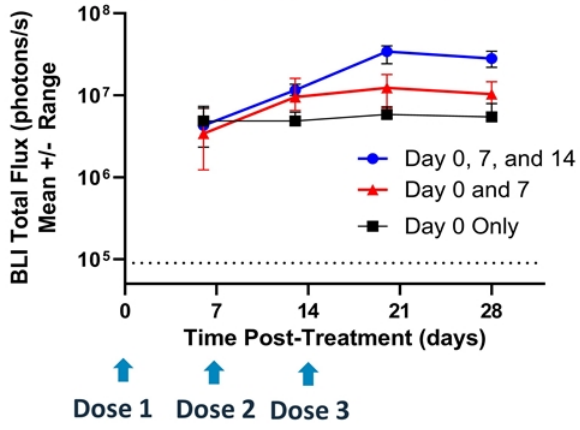
FVIII Expression in WT Neonatal Mouse



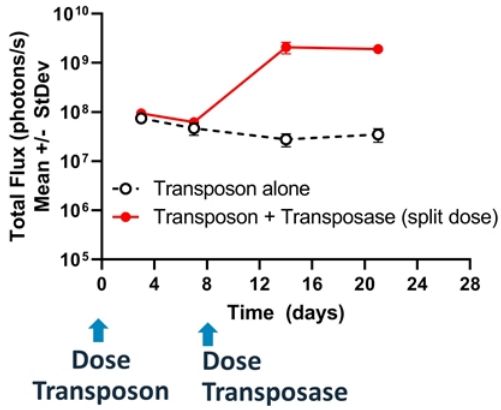
POSEIDA THERAPEUTICS

Dual LNP piggyBac® System Can be Repeatedly Dosed

Dual LNP, Repeat Dosing



Dual LNP, Split Dosing



- WT mice administered dual LNP with reporter (luciferase) transgene
- Controllable, dose-responsive pharmacology observed
- SPB transposase can be administered separately from transposon LNP

Summary

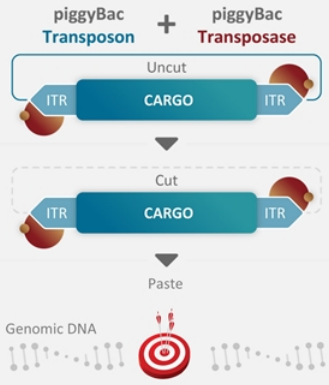
- P-FVIII-101 (fully biodegradable nanoparticle delivery) can achieve >100% of normal FVIII levels and durable expression with a single administration in a preclinical model.
- The biodegradable nanoparticle + Super piggyBac® DNA Delivery System may overcome the limitations of AAV-based systems.
  - Potential for single treatment cure
  - Ability to treat pediatric patients
  - No pre-existing immunity
  - Much larger cargo capacity
  - Dose proportional pharmacology
  - Ability to re-dose
  - Fewer safety concerns
  - Ease of manufacturing

POSEIDA THERAPEUTICS

Development of a Site-Specific Super piggyBac® Transposition System (ssSPB)

Blair Madison
Vice President, Genetic Engineering

The Next Wave in Gene Therapy: Site-specific Transposition



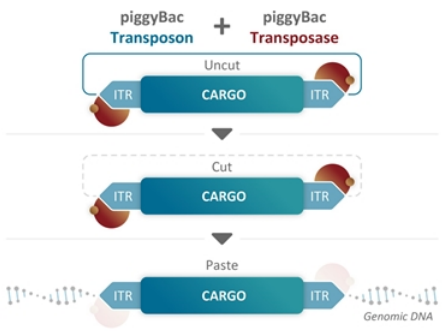
A site-specific piggyBac® platform would be revolutionary:

- Superb genotoxicity safety profile
- Enables simultaneous cargo knock-in and gene knock-out
- Programmability for targeting any site in the genome
- Simplicity: 2-component system (transposase and dsDNA)
- Agnostic to DNA repair pathways (no need for NHEJ, HDR, MMEJ, etc.)
- **Enables site-specific large cargo delivery in any cell type or tissue with nearly unlimited gene therapy applications:**
  - Site-specific delivery of entire genes with all regulatory elements!?

Tremendous implications for treating common genetic diseases:

Two Examples:	Gene Size	Protein Size	# of Mutations	Incidence
Muscular Dystrophy (*DMD*)	~2.1 Mb (!)	3685 aa (!)	>1800	~1 in 3,500 M births
Cystic Fibrosis (*CFTR*)	~187 Kb	1480 aa	>1700	~1 in 3,800 M/F births

piggyBac®: A Versatile DNA Delivery System for Developing Gene Therapy Products



- Non-viral gene insertion technology
- Enables DNA integration and stable expression
- High efficiency (Super piggyBac)
- Very large cargo capacity (~200 kB!)
- Works in a wide variety of cell types
- Multiple safety and cost benefits

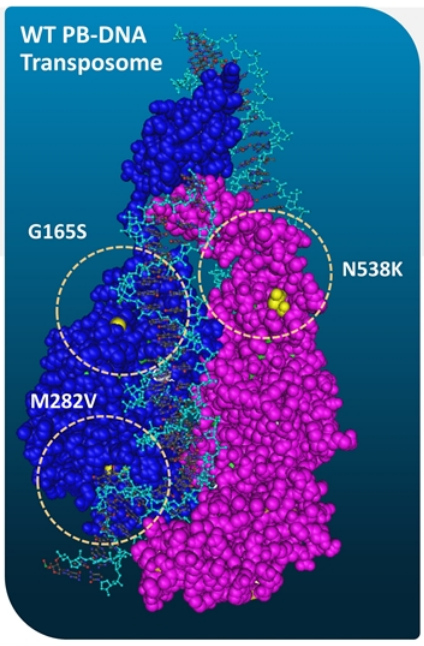
BENEFITS IN GENE THERAPY

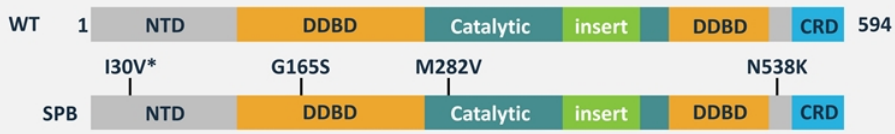
Integrates Into DNA Delivering Stable Long-Term Expression

- Ideal for use in **dividing tissues** like those in juvenile liver
- **Highly efficient** integration may allow **reduced dosing and single treatment cures**
- **Delivered using AAV + nanoparticle** or in vivo EP

POSEIDA THERAPEUTICS

piggyBac®: Wild Type (WT) vs. Super piggyBac® SPB



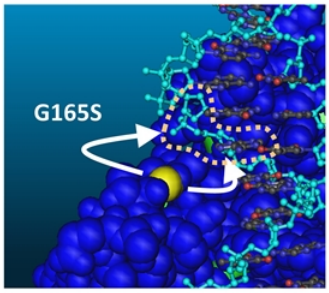


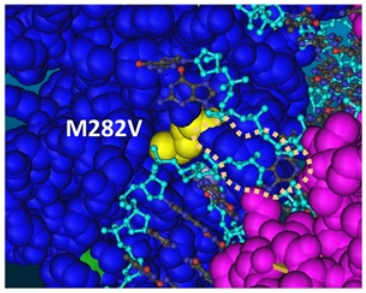
NTD: N-terminal domain | **DDBD:** Dimerization & DNA binding domain | **CRD:** Cysteine-rich domain
***unknown mechanism underlying hyperactive effect of I30V**

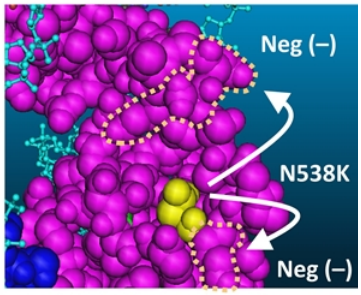
DNA-BINDING
G165S: Enhances DNA binding (H-bonds w/ PO4 and Adenine)

CATALYSIS
M282V: Enhances pi-stacking b/t Tyr283 and Adenine in TTAA

STABILIZATION
N538K: Electrostatic stabilization in linker between DDBD and CRD





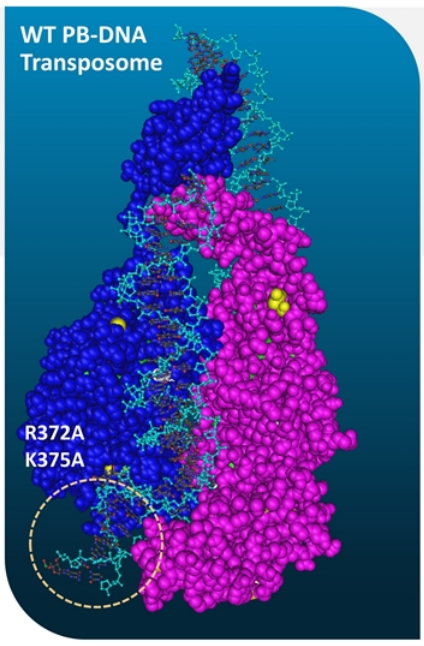


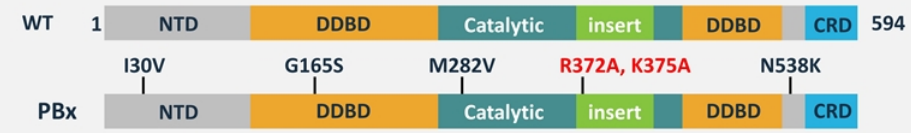
*Structure from **Chen et al. Nat Commun, 2020 Jul 10;11(1):3446***

*Hyperactive mutations from **Yusa et al. PNAS, 2011 Jan 25;108(4):1531-6***

POSEIDA THERAPEUTICS

piggyBac®: Wild Type (WT) vs. Excision-Only piggyBac® (PBx)



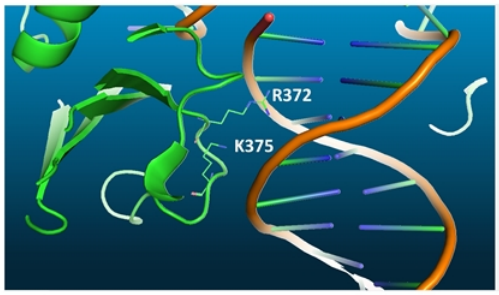


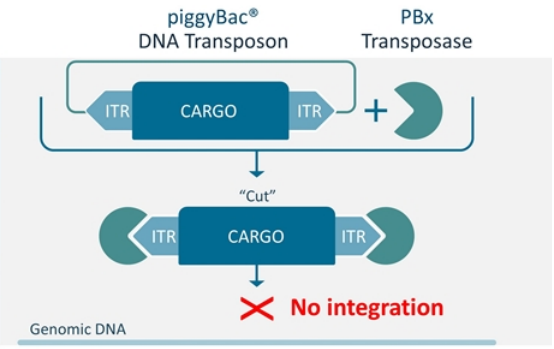
Excision-Only Transposase

NTD: N-terminal domain | **DDBD:** Dimerization & DNA binding domain | **CRD:** Cysteine-rich domain

TARGET DNA-BINDING

R372 & K375: Critical because of interaction with target DNA (H-bonds w/ PO4 in backbone)



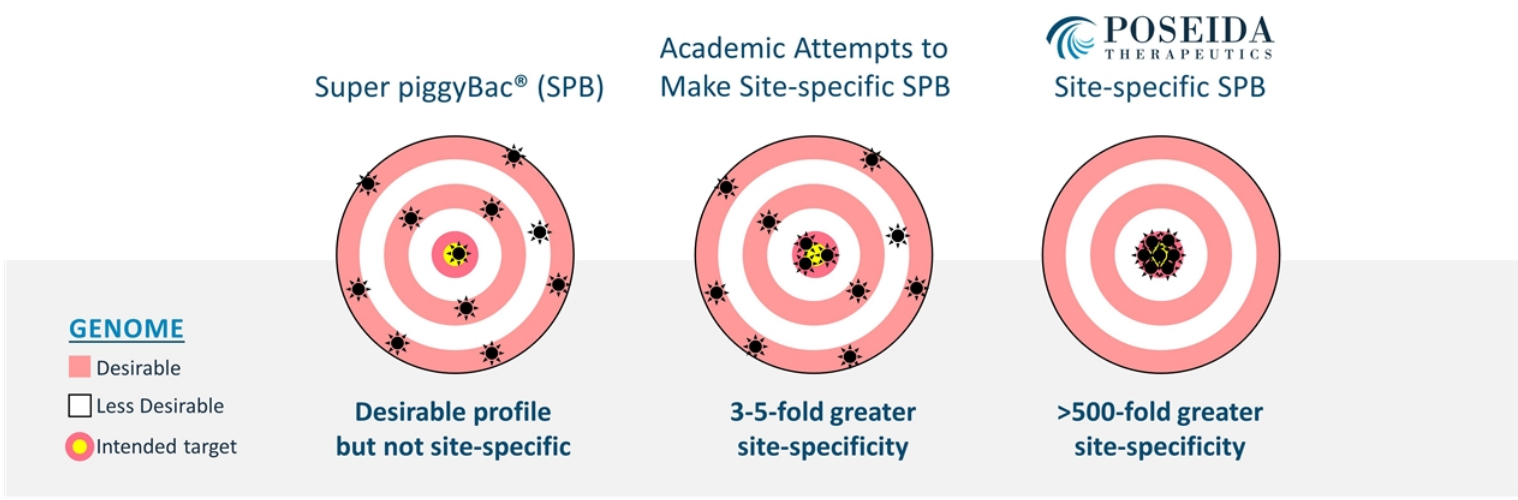


Structure from ***Chen et al. Nat Commun, 2020 Jul 10;11(1):3446***

PBx mutations from ***Li et al. PNAS, 2013 Jun 18;110(25):E2279-87***

POSEIDA THERAPEUTICS

Generating a Site-specific Super piggyBac® (ss-SPB) System

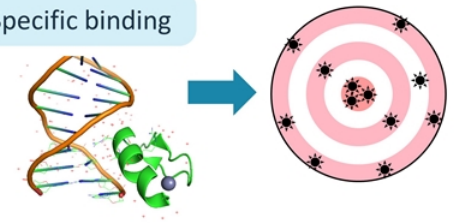


Maragathavally, K. J., et al., *FASEB J.* 2006 | Wang, W., et al., *PNAS* 2008 | Kettlun, C., et al., Mol Ther. 2011 | Owens, J.B., et al., *Nucleic Acids Res.* 2012 | Li, X., et al., *PNAS* 2013 | Owens, J.B., et al., *Nucleic Acids Res.* 2013
Ye, L., et al., *Sci Rep.* 2015 | Hew, B.E., et al., *Synth Biol* 2019

Strategies for Site-specific Transposition

PB Transposase-DNA-binding-domain Fusions

✚ Specific binding



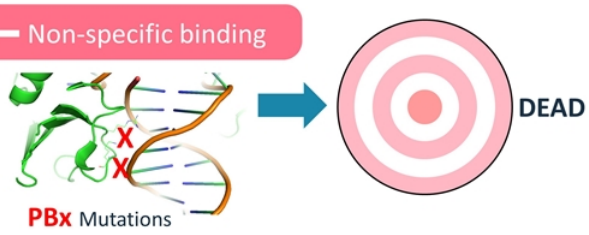
High Off-target Rate

Previous fusions of PB with:
- Gal4
- Zinc-finger
- TAL
- dCas9

Unimpressive Results:
- 3-5-fold enhancement at on-target site
- Predominantly off-target integration

Rescuing PBx Integration-Defective Transposase

— Non-specific binding



Previous fusions with PBx:
- Zinc-finger
- dCas9

Unimpressive Results:
- DBD could not rescue PBx integration at the on-target site

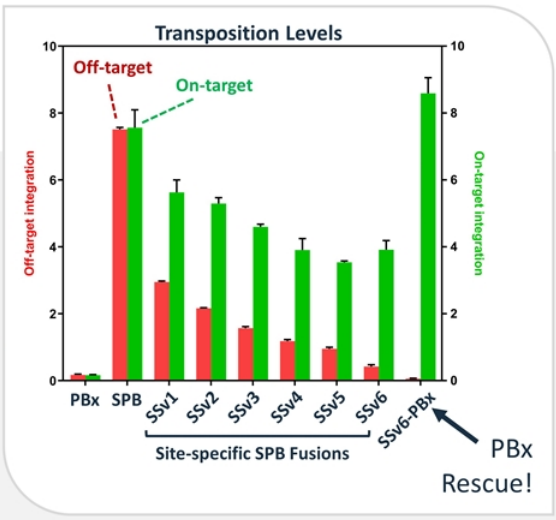
Li, X., et al., *PNAS* 2013
Hew, B.E., et al., *Synth Biol* 2019

POSEIDA THERAPEUTICS

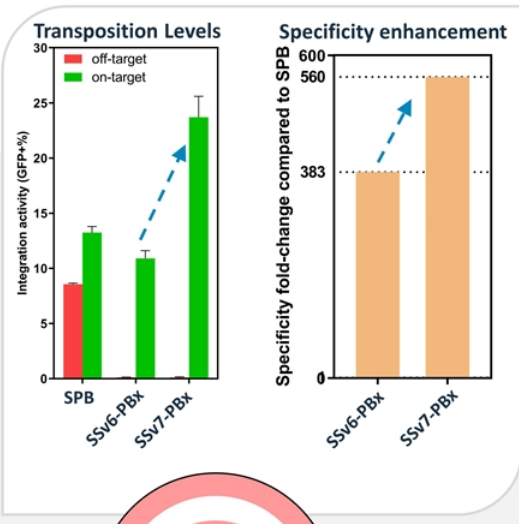
The Poseida Strategy

Our Strategy

- Exploit new structure data
- Computational modeling
- Iterative screen
- Pursue rescue of PBx

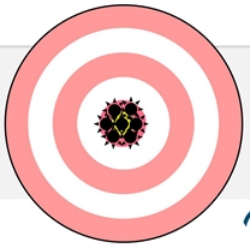


SSv7



Results:

1. First demonstrated rescue of integration-defective PBx mutant
2. Unprecedented level of site-specificity: **>500-fold** with SSv7
3. Data here are from un-optimized SPB fusion protein

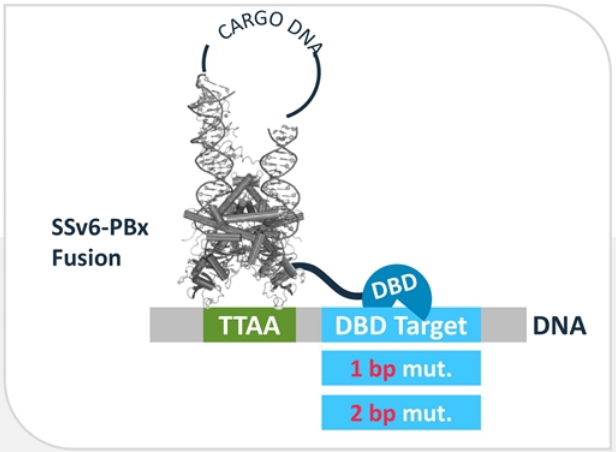


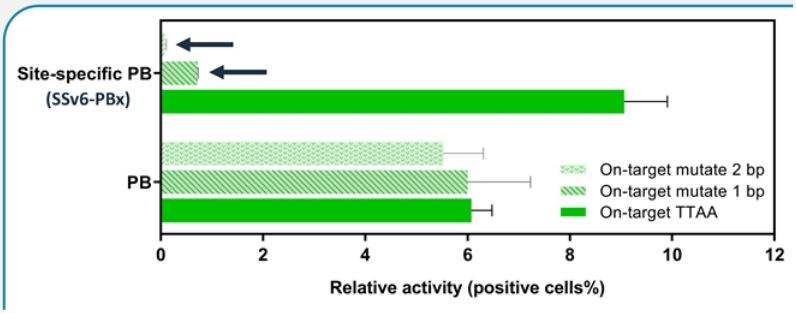
POSEIDA THERAPEUTICS

Off-target Tolerance of SSv6-PBx

Determining Specificity

- Mutate DBD target sequence to assay distinction of subtle alterations of 9-nt target
- Results show high level of discrimination for first-generation fusion
- Successive iterations/optimizations underway for increasing specificity



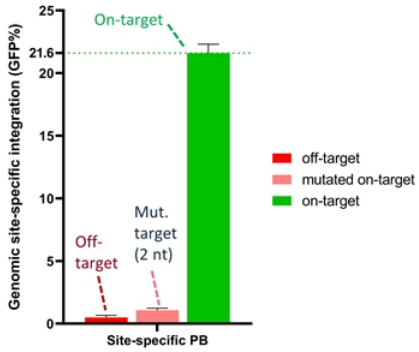


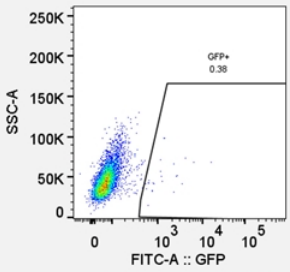
POSEIDA THERAPEUTICS

Site-specific Transposition into Genome

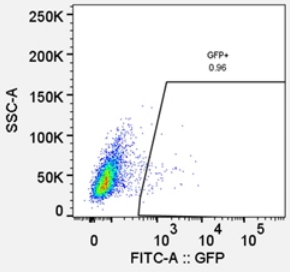
Genomic target

- Synthetic reporter delivered via lentivirus in HEK293T
- First assessed for SSv6-PBx
- Over 20% of cells GFP+

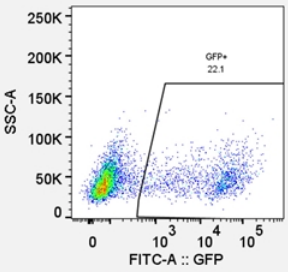




off-target TTAA site



mutated on-target TTAA site

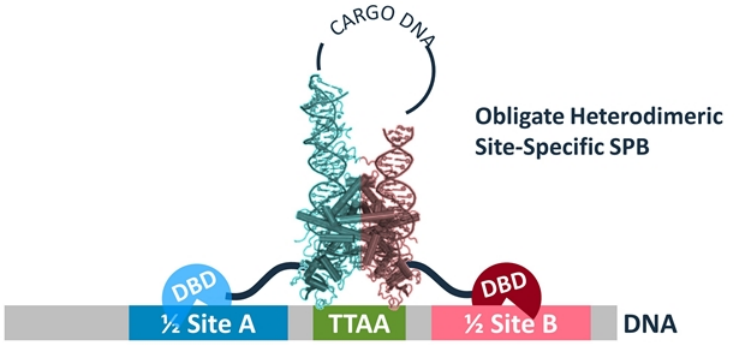


on-target TTAA site

Building Upon Site-specificity: Obligate SPB Heterodimer

Challenges with SPB-DBD Fusions

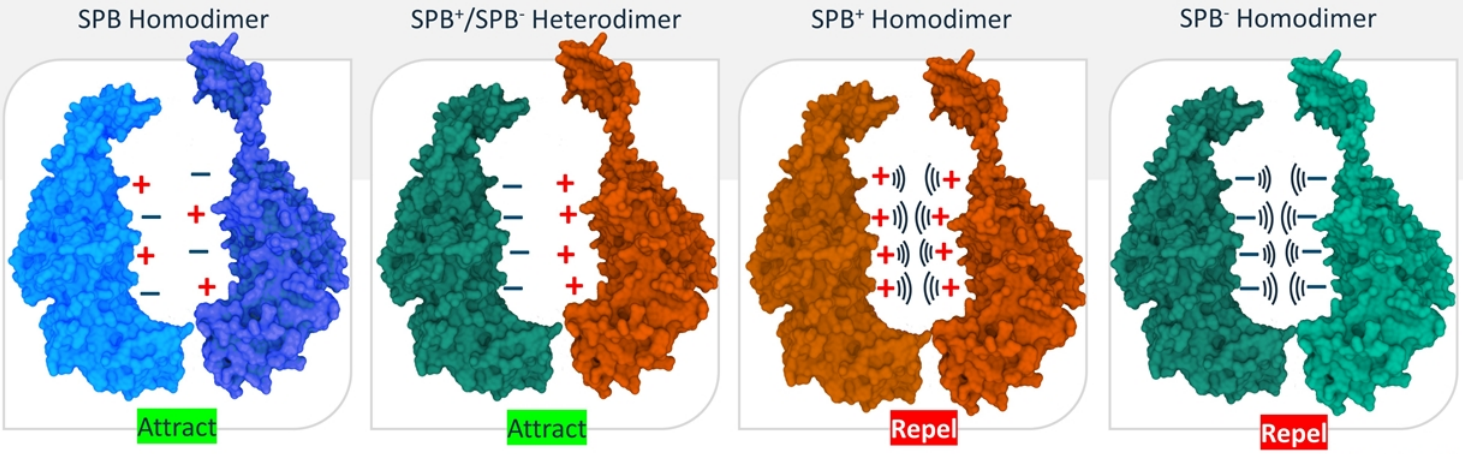
- Homodimeric nature of SPB complicates DBD fusion strategies;
  - Only one DBD can bind target site
- Bipartite (1/2 site) recognition sequences enables equal and balanced binding
- “Splitting” the recognition domains across 2 monomers enables more compact proteins



Key Characteristics of a SPB Obligate Heterodimer

- Each SPB contains both positive (+) and negative (-) charges in the dimerization interface
- Engineer two new versions of SPB protein:
  - SPB^{+} contains more (+) charge and SPB^{-} contain more (–) charge
- Transposition only occurs when SPB^{+} is mixed with SPB^{-}

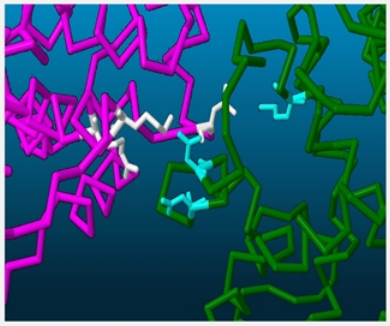
- SPB^{+} must be inactive as a homodimer
- SPB^{-} must be inactive as a homodimer

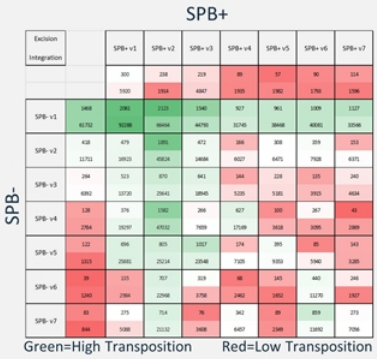


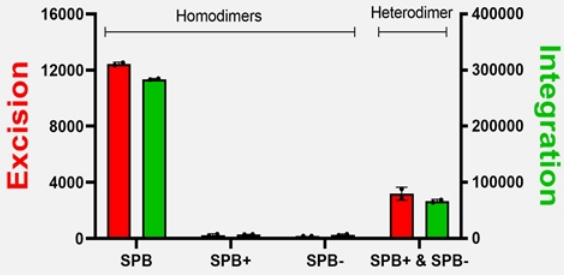
POSEIDA THERAPEUTICS

Rational Design of SPB Obligate Heterodimers

Structure Guided Design | Pairwise Activity Screen | SPB Obligate Heterodimer







- Cryo-EM structure of piggyBac® used to identify residues involved in dimerization
- Residues mutated individually or in combination to make 7 versions each of SPB^{+} and SPB^{-}
- SPB^{+} and SPB^{-} versions tested for transposition activity individually and in pairwise combinations
- Successfully created pairs with desired characteristics of an obligate heterodimer

POSEIDA THERAPEUTICS

Summary

- Poseida's first generation Site-Specific SPB (ss-SPB) is a major technological advance
- Complete and unprecedented rescue of the integration-defective PBx mutation
- Structure-informed design of site-specific DNA binding motif fusion achieves **>500-fold increase in site specificity**
- Proof of concept for **high efficiency site-specific integration established**
- Mutation analysis at target site indicates robust stringency/specificity
- Optimization of first-generation obligate heterodimer will enable "dual" site targeting

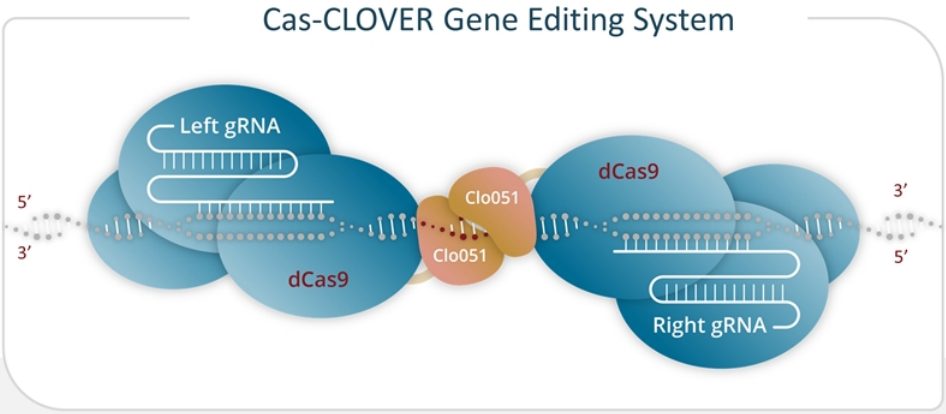
Site-specific piggyBac is poised for an enormous impact on gene therapy….

POSEIDA THERAPEUTICS

Liver-Directed Gene Editing with Cas-CLOVER™

Blair Madison
Vice President, Genetic Engineering

Cas-CLOVER™: Ultra-Clean Gene Editing



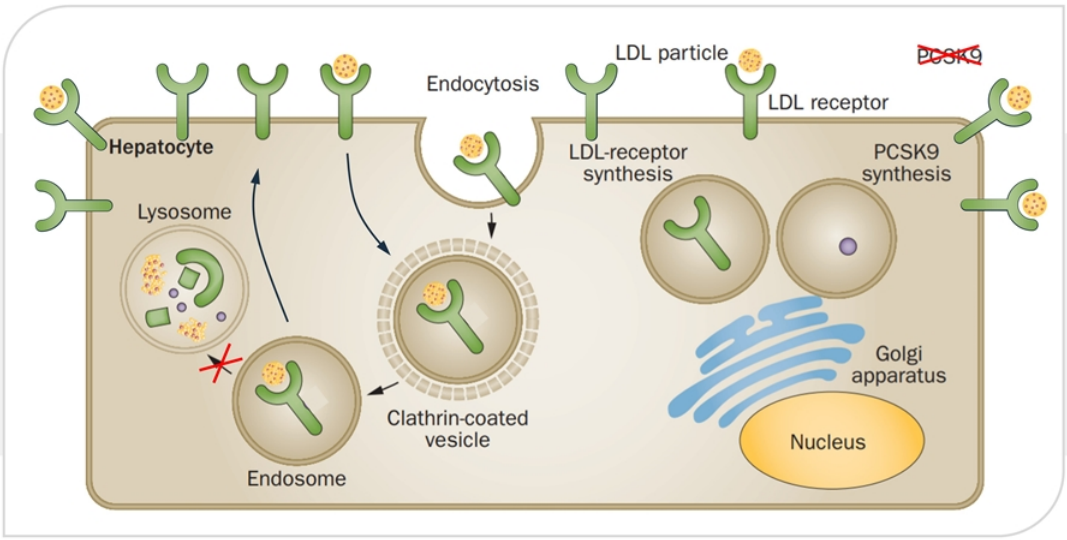
- **Low-to-no off-target cutting**
- **High Editing Efficiency** in resting T-cells resulting in high % of T_{SCM} cells
- Ease of use/design
- Multiplexing ability
- Lower cost

Potentially the Cleanest Gene Editing Platform

Efficiently edits resting cells - enables fully **Allogeneic CAR-T** products with profound implications for future non-viral **Gene Therapy** applications

Inhibition of PCSK9 to Lower LDL-Cholesterol Levels

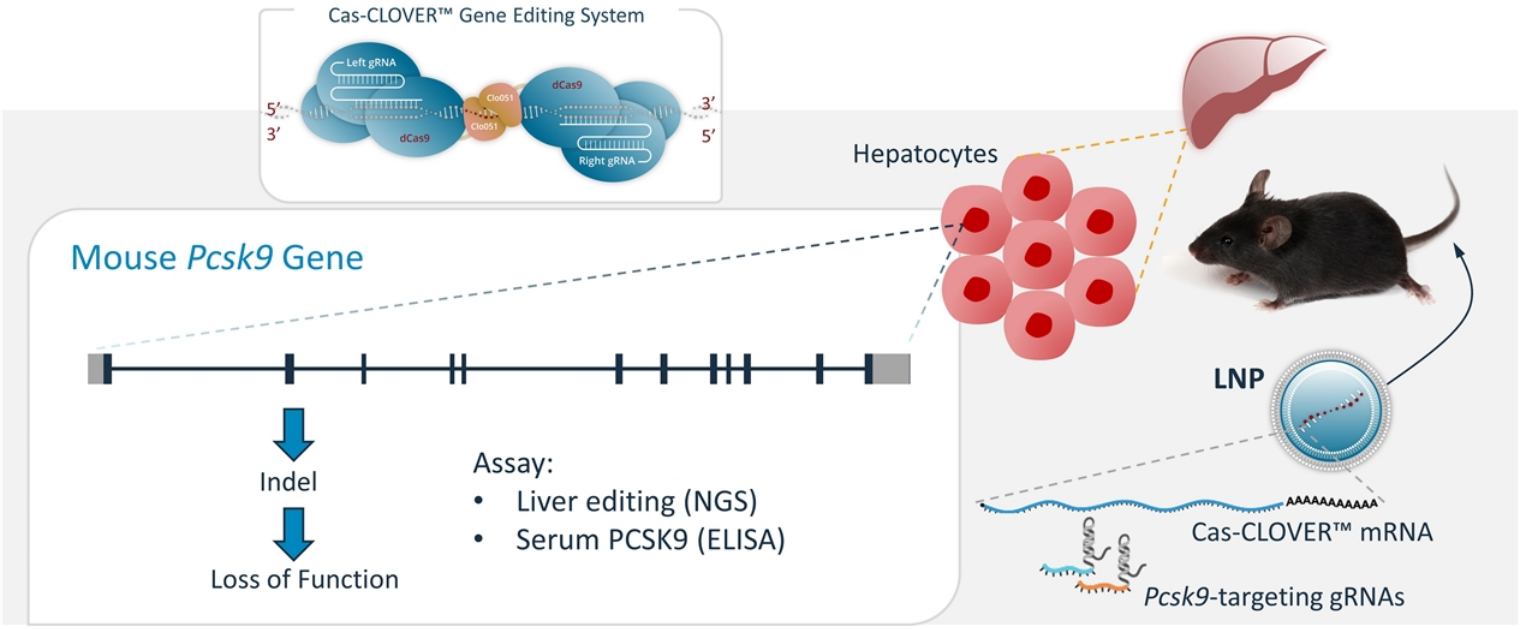
Reduction or elimination of PCKS9 protein results in endosomal recycling of LDL receptors, rather than degradation, causing an overall decrease in circulating levels of LDL-cholesterol.



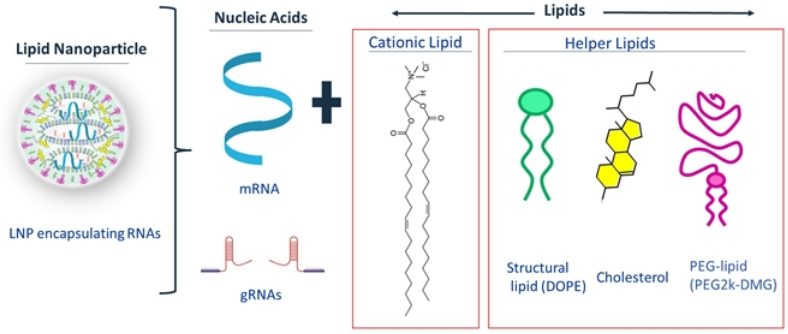
Adapted from Dadu, R. T. & Ballantyne, C. M. *Nat. Rev. Cardiol.*, 2014

POSEIDA THERAPEUTICS

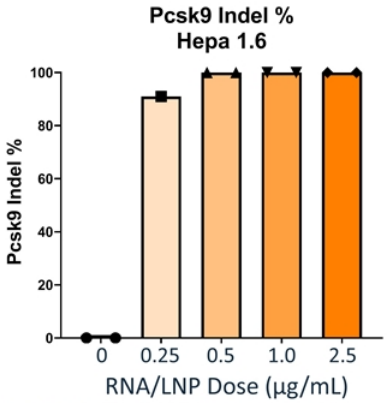
Strategy for Targeting PCSK9 in Liver Hepatocytes



In Vitro Delivery of Cas-CLOVER™ mRNA Results in 100% Editing



- Cas-CLOVER™ mRNA and gRNAs were encapsulated in single LNP with >96% encapsulation efficiency.

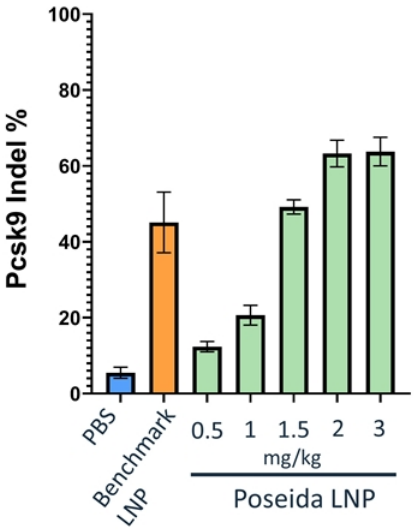


- Cas-CLOVER™ LNPs were used to transfect Hepa 1.6 cells.
- 100% editing with 500 ng RNA/LNP.
- Benchmark LNP used as POC

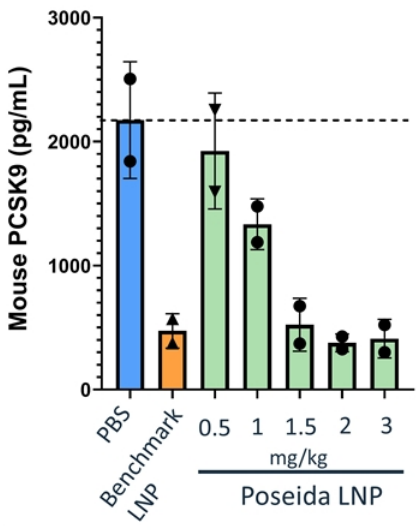
Efficient Cas-CLOVER™ Delivery and Editing with Poseida's Biodegradable LNPs

- Efficacy readouts show clear dose response effect. **Cas-CLOVER™ works for in vivo liver editing with high efficiency**
- Poseida LNP efficacy is maximal at 2 mg/kg **(>60% indels**)
- **>80-85%** decrease in PCSK9 protein with doses >1.5 mg/kg
- Poseida's proprietary biodegradable LNP used for delivery

DNA Editing (NGS)



Protein Serum Levels



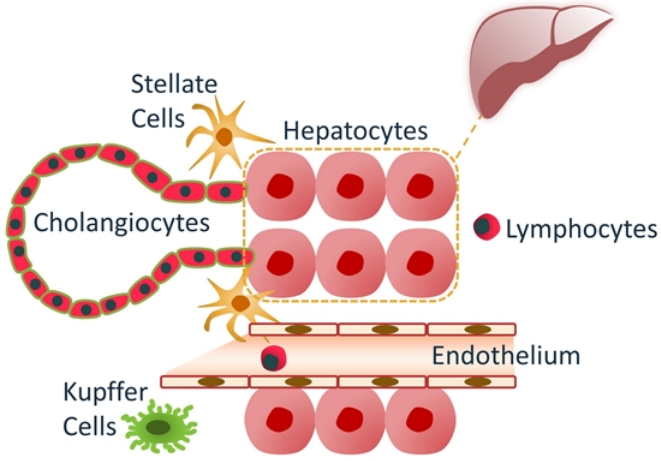
POSEIDA THERAPEUTICS

Cas-CLOVER™ is Approaching Maximal Gene Editing in Hepatocytes

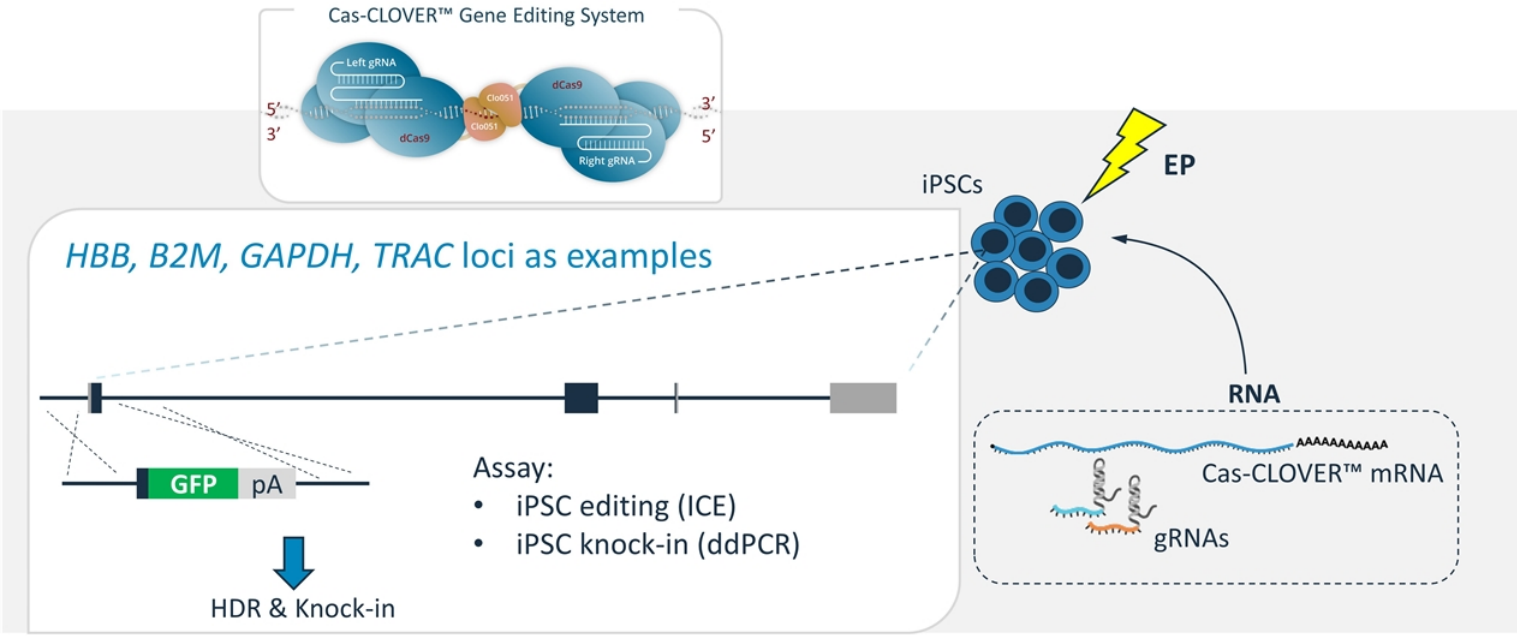
Liver biopsies consist of:

- Approximately 75% hepatocytes
- Remaining cells are stellate cells, Kupffer cells, cholangiocytes, endothelium, and lymphocytes, which do not express PCKS9

Suggests PCSK9 knockout rate of **>80% in hepatocytes**

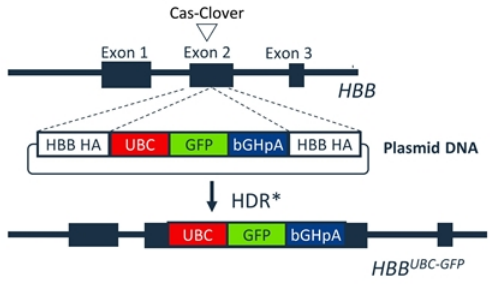


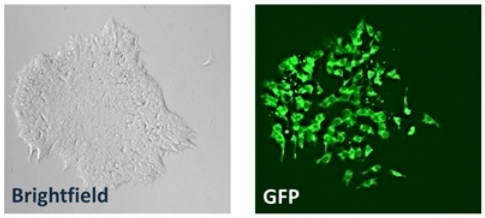
Cas-CLOVER™-mediated Knock-Ins in Induced Pluripotent Stem Cells (iPSCs)



Cas-CLOVER™ is More Efficient Than WT CRISPR for Knock-Ins

Site-specific Insertion of a Large Transgene

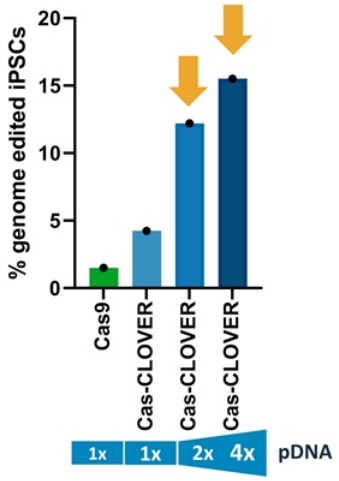




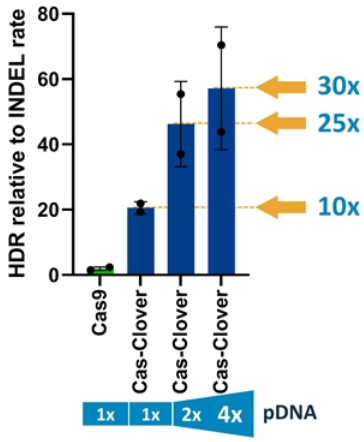
Bulk edited population of iPSCs

*Site-specific insertion confirmed by PCR

More DNA = More Editing



Cas-CLOVER™ 10-50x More Efficient

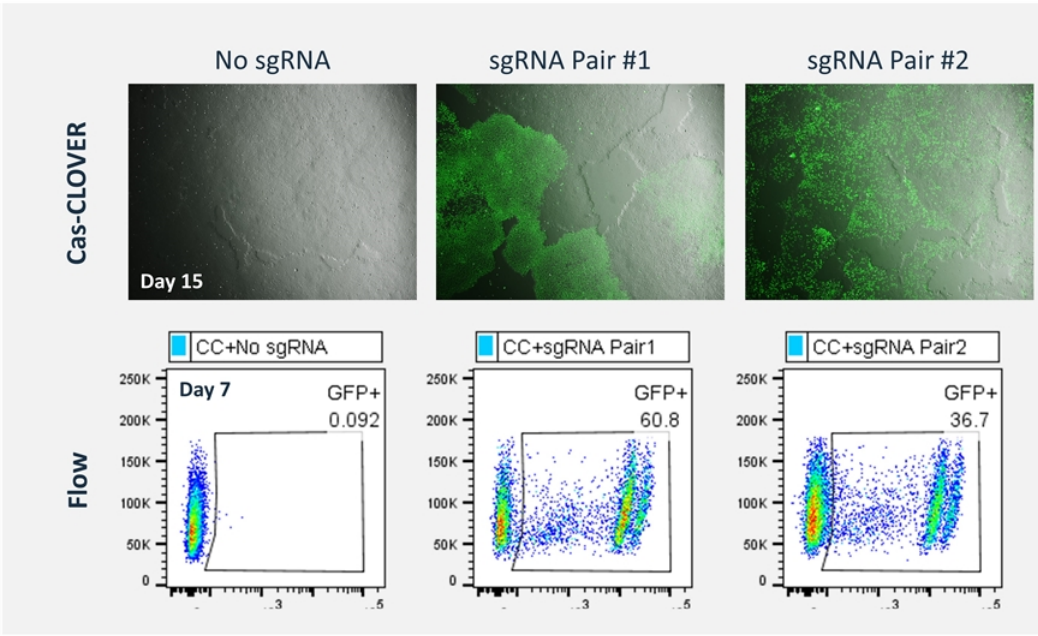


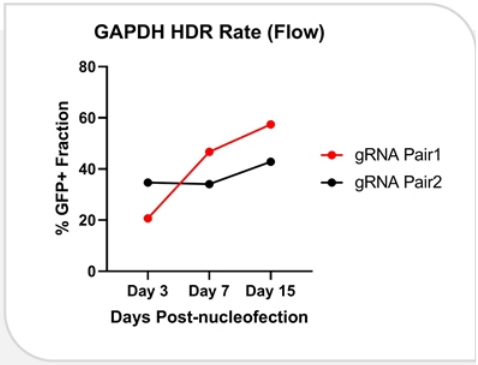
Cas-CLOVER vs. WT CRISPR

- ✓ More efficient plasmid-based gene insertion
- ✓ Confers higher tolerance to plasmid DNA

POSEIDA THERAPEUTICS

Ultra-High Efficiency Knock-Ins with Cas-CLOVER™: *GAPDH*

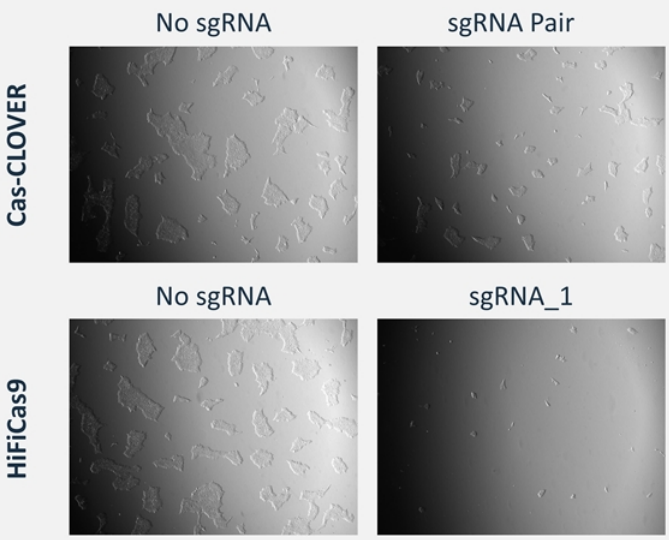


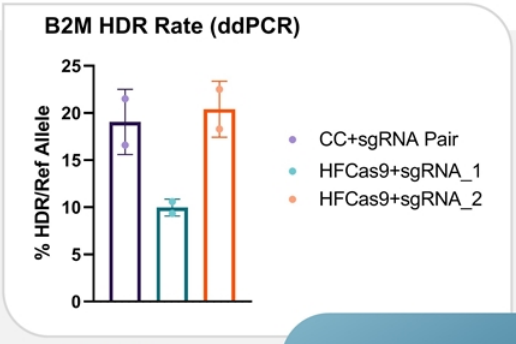


- Cas-CLOVER™ targeting at GAPDH yields ultra-high efficiency
- No selection/sorting
- Bi-allelic targeting evident

POSEIDA THERAPEUTICS

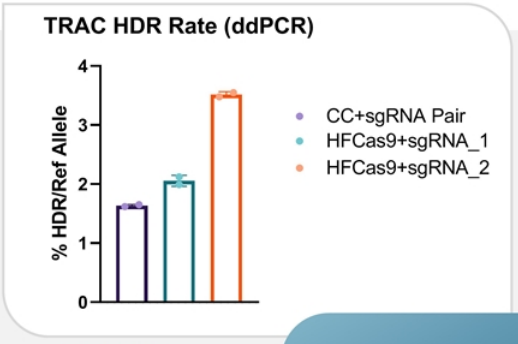
Highly Efficient and Low Toxicity Knock-Ins with Cas-CLOVER™: *B2M*





- HiFiCas9 vs. Cas-CLOVER™ yields similar efficiencies
- Cas-CLOVER™ exhibits significantly lower toxicity

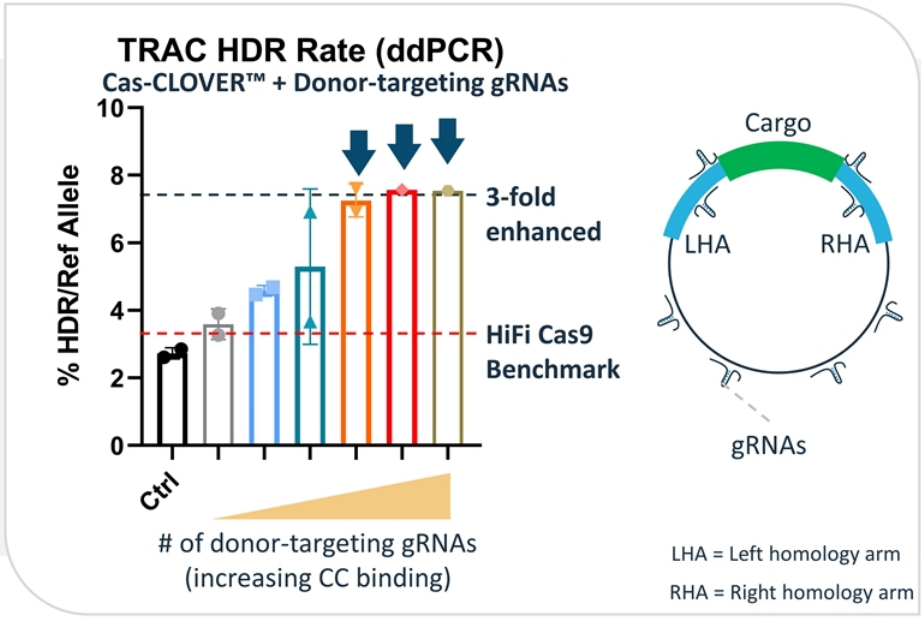
Highly Efficient and Low Toxicity Knock-Ins with Cas-CLOVER™: *TRAC*



- HiFiCas9 vs. Cas-CLOVER™ yields similar efficiencies
- Cas-CLOVER™ exhibits significantly lower toxicity

Cas-CLOVER™ Monomer Binding to Donor Enhances Homology Directed Repair (HDR)

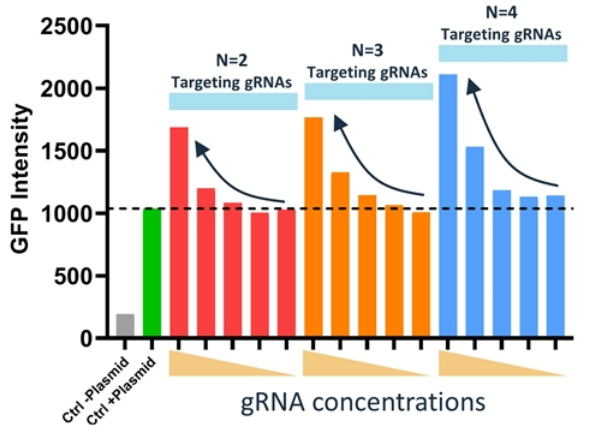
Frequent Outperformance of Cas9 Suggests Role for Cas-CLOVER™ in Enhancing HDR

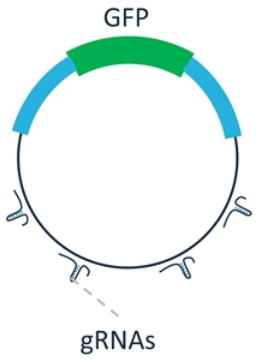


- With additional donor-targeting gRNAs, **HDR efficiency increases**
- Cas-CLOVER™ monomers cannot cut DNA, so role for nuclease unlikely
- Possibly due to enhanced nuclear translocation and/or protection of DNA from nucleases

Cas-CLOVER™ Monomer Binding to Plasmid Enhances Expression

Increased Episomal Expression Suggests Cas-CLOVER™ Enhances Nuclear Translocation

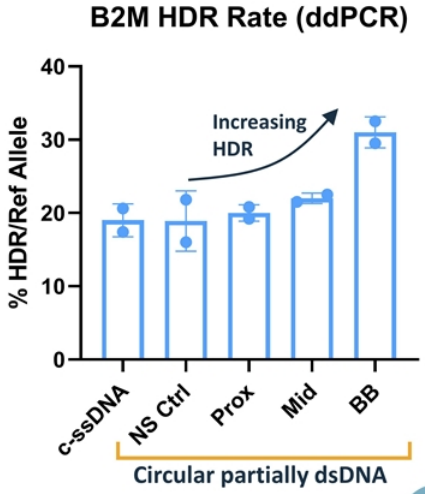


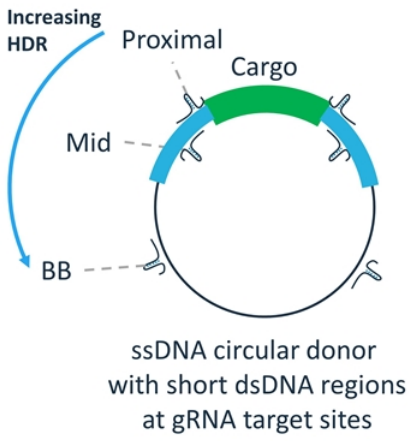


- With additional donor-targeting gRNAs, **GFP intensity increases**
- Cas-CLOVER™ monomers cannot cut → **nuclease independent**
- Likely due to **enhanced nuclear translocation**

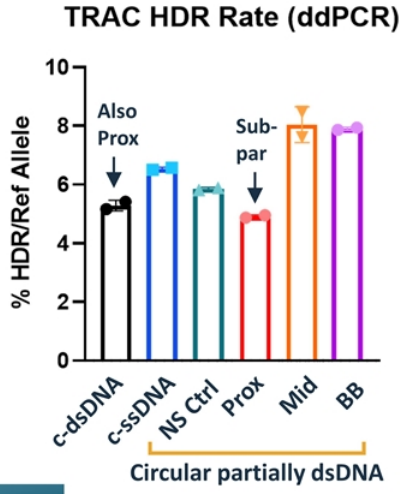
Benefits of Positioning gRNA Binding Away from HDR Region

Positioning May Help Reduce Interference with HDR Process (e.g., 3' strand invasion)





ssDNA circular donor with short dsDNA regions at gRNA target sites

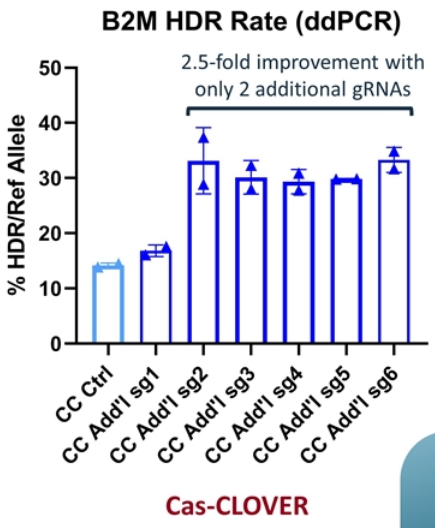


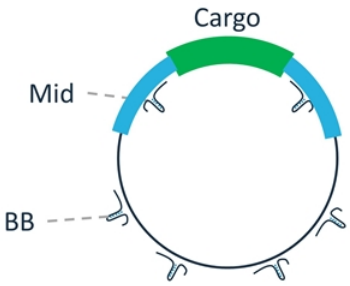
Implications for improved knock-ins:

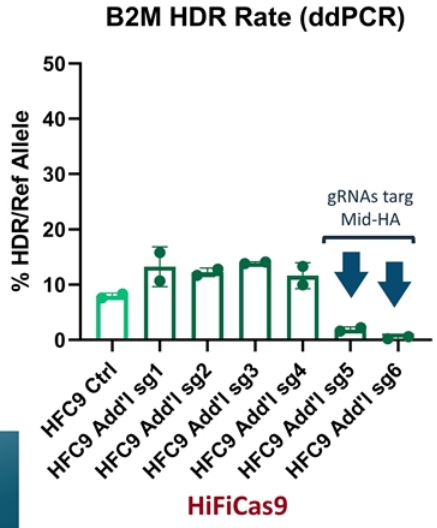
- Enhancement through add'l binding sites
- Only possible with dimeric system?

Enhanced HDR Only Observed with Cas-CLOVER™ Dimeric Platform

Targeting Cas9 nuclease to donor plasmid ineffective or detrimental







- Effects/benefit not observed with HiFiCas9, as expected
- Cutting of homology arms detrimental to HDR (HiFiCas9)

Summary

Cas-CLOVER™ works for high-efficiency site-specific gene editing

- Cas-CLOVER™ can be delivered using Poseida's proprietary biodegradable mRNA LNP
- Gene editing efficiency (>60%) and protein reduction (~85%) at Pcsk9 locus is approaching the theoretical maximum following single injection
- Cas-CLOVER™ enables high-efficiency knock-ins with low toxicity
- Cas-CLOVER™ binding acts as a Homology Directed Repair (HDR) enhancer by augmenting nuclear translocation

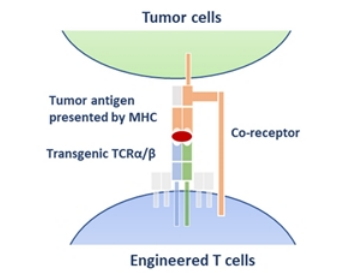
POSEIDA THERAPEUTICS

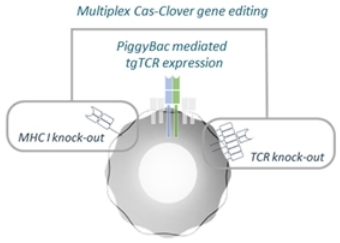
Fully Allogeneic TCR-T Program

Julia Coronella
Vice President, Immuno-Oncology

Platform Profile: Fully Allogeneic TCR-Engineered T cells (TCR-T)

Poseida TCR-T Platform



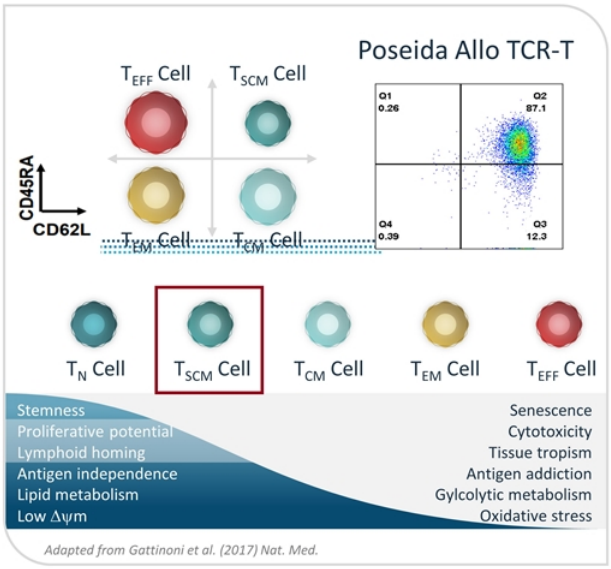


TCR-engineered T Cells

- **TCR-engineered T cells (TCR-T) express tumor-antigen-specific T cell receptors composed of α- and β-chains, which recognize antigen + MHC presented on the surface of target cells**
  - TCR-T access **intracellular** tumor antigens
  - TCR-T require **lower antigen density** than CAR-T
  - TCR-T may exhibit better cell persistence and tissue homing capability than CAR-T
- TCR-T have applications in oncology, infectious disease, autoimmunity
- Mechanistic advantages of TCR-T and CAR-T technology to address target heterogeneity and increase potency
- Potential combinations with antivirals

Poseida's Technology Offers Advantages in Developing Allogeneic TCR-T

Poseida technology platforms could address many of the limitations of current TCR-T therapies, including improving persistence, potency, manufacturing, and immune rejection



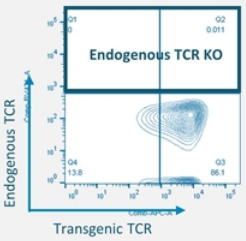
Adapted from Gattinoni et al. (2017) Nat. Med.

1 High T_{SCM} TCR-T	piggyBac® CAR gene delivery generates a durable T_{SCM}-enriched cell therapy product for superior safety and efficacy
2 High fidelity multiplex gene editing	**Fully Allogeneic:** Cas-CLOVER™ editing of TCRA and TCRB to prevent GVHD and improve efficacy, reduce TCR mispairing, multiplex with B2M KO to reduce rejection **while retaining T cell robustness**
3 Multi-targeting	piggyBac® cargo capacity enables delivery of multiple genes for multi-targeting via CAR - TCR, and activation-gated expression
4 Platform versatility	Optimized platform for oncology, infectious disease, other applications

POSEIDA THERAPEUTICS

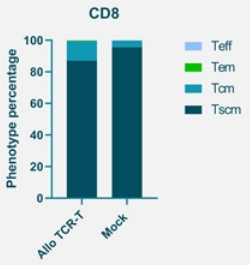
Fully Allogeneic TCR-T Produced with Poseida Platform Technology

Allogeneic



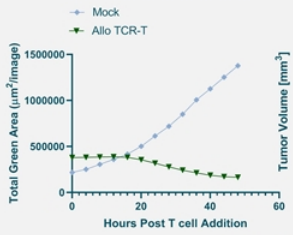
Efficient endogenous TCR KO reduces the potential for alloreactivity and GvHD

High % T_{SCM}



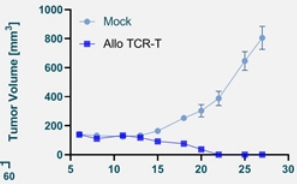
High T_{SCM} % in the final product is associated with improved safety/durability

Enhanced Cytotoxicity



Enhanced TCR avidity boosts TCR-T cytotoxicity

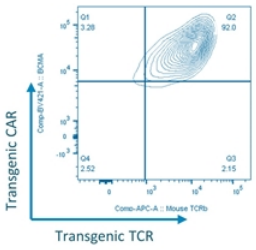
in vivo efficacy



Allo TCR-T exhibit promising in vivo anti-tumor efficacy

POC NY-ESO-1 TCR-T

CAR+TCR potential



Dual CAR+TCR expression enables targeting of multiple tumor antigens, reducing the potential for immune escape

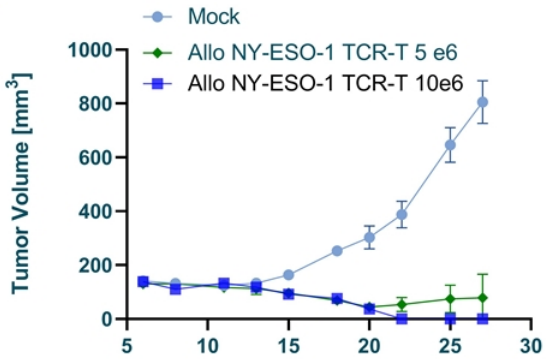
POSEIDA THERAPEUTICS

TCR-T for Immuno-Oncology (NY-ESO-1)

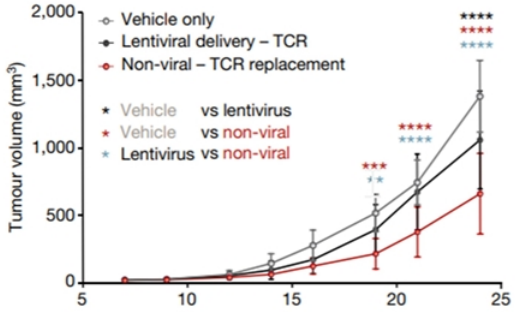
POSEIDA THERAPEUTICS

Optimized Allo NY-ESO-1 TCR-T Shows Robust In Vivo Activity

In vivo efficacy: A375-NSG model



Poseida data



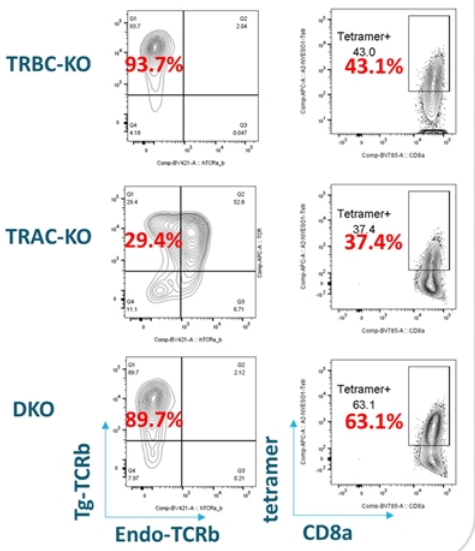
TCR: 1G4 Does@3e6 Tetramer+ cells

Roth, T.L., *et al. Nature* **559,** 405–409 (2018).

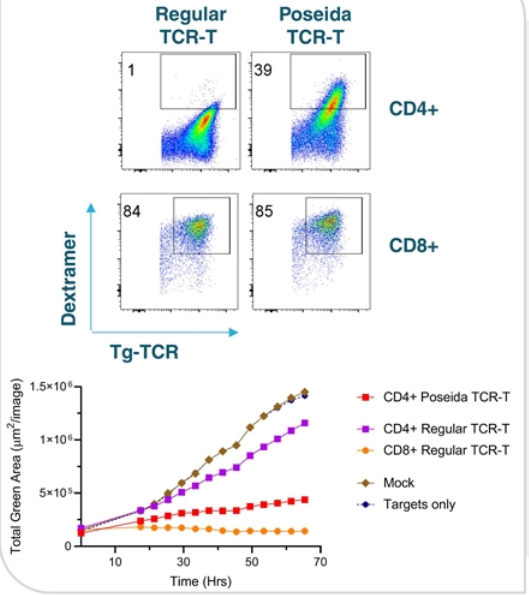
Proof-of-concept Allo TCR-T produced with optimized transposon demonstrated promising in vivo efficacy

Poseida Approaches to Enhance TCR-T Efficacy

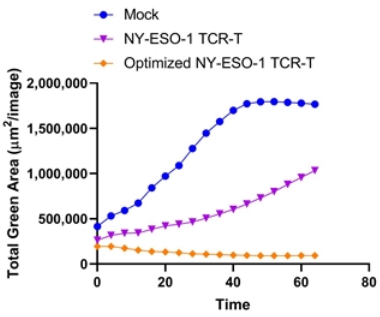
TRAC/TRBC DKO Prevents Mismatch Without Impairing T Cell Function



TCR Avidity Enhancement



Optimized TCR-T Exhibits Better Potency



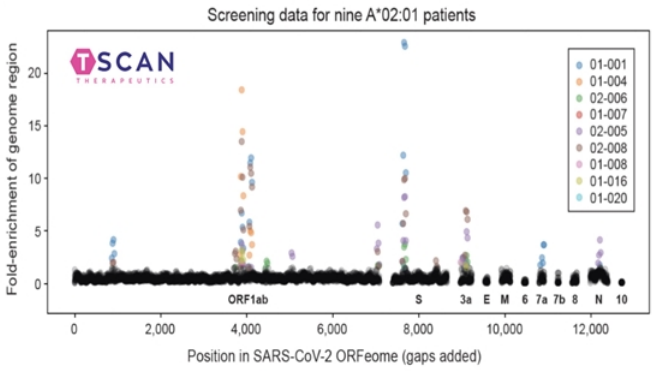
Optimized Allo TCR-T production process results more potent in vitro cell killing

POSEIDA THERAPEUTICS

TCR-T for Infectious Disease (COVID)

POSEIDA THERAPEUTICS

Collaboration with TScan to Identify and Sequence COVID-specific TCRs



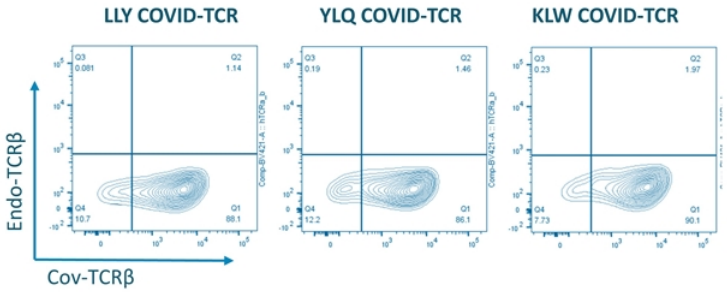
EPITOPE	PROTEIN	TCR CLONE	HLA
KLWAQCVQL	ORF1ab	63	A*02
YLQPRTFLL	S	31	A*02
LLYDANYFL	ORF3a	29	A*02

- At TScan, an epitope library of SARS-CoV-2 was screened against PBMC from convalescent patients
- Three dominant HLA-A2 restricted SARS-CoV-2 epitopes were identified (see table)
- TCR chains were sequenced and synthesized, for TCRs recognizing the dominant epitopes
- COVID-specific TCRs were expressed in engineered allogeneic TCR-T cells at Poseida

POSEIDA THERAPEUTICS

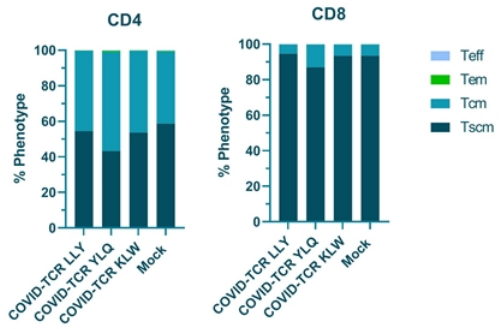
Characterization of Engineered Allo COVID TCR-T Product

Fully Allogeneic T cells with high expression of COVID-TCR



- Optimized engineering process yields final product with >80% expression of COVID TCR
- Optimized purification (chimeric TCRb chain of tgTCR) permits removal of unedited T cells

High % T_{SCM} in Final Product

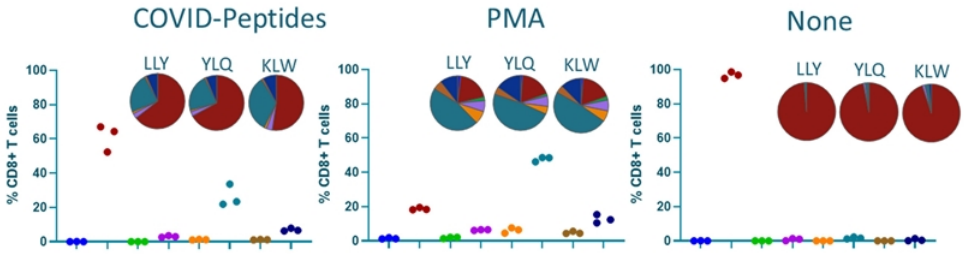


- High % T_{SCM} in final product

POSEIDA THERAPEUTICS

Allo COVID TCR-T Are Polyfunctional, Specific and Potent

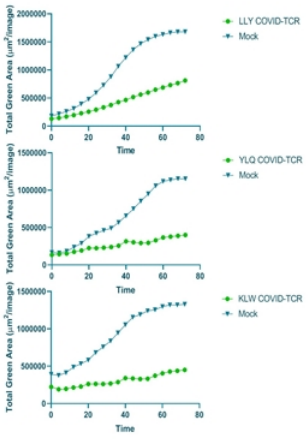
COVID-TCR T Polyfunctionality



IFNg-				IFNg+			
IL2-		IL2+		IL2-		IL2+	
TNFa+	TNFa-	TNFa+	TNFa-	TNFa+	TNFa-	TNFa+	TNFa-
IFNg-	IFNg-	IFNg-	IFNg-	IFNg+	IFNg+	IFNg+	IFNg+
IL2-	IL2-	IL2+	IL2+	IL2-	IL2-	IL2+	IL2+
TNFa+	TNFa-	TNFa+	TNFa-	TNFa+	TNFa-	TNFa+	TNFa-

- Robust induction of desired polyfunctional IFNg+ cells with viral peptide stimulation

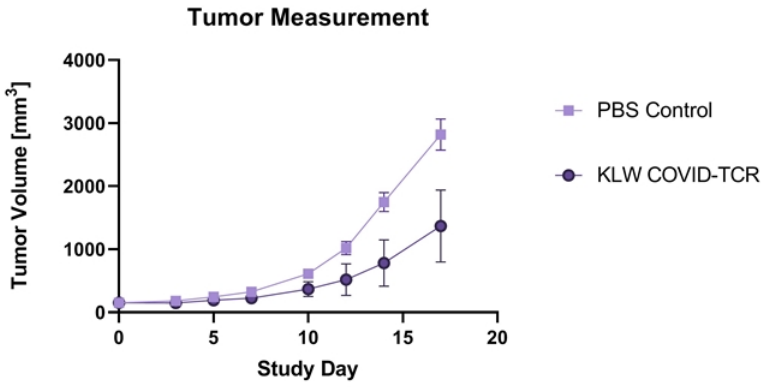
Effective and Specific Cytotoxic Response Against Cell Lines Presenting COVID Epitopes



POSEIDA THERAPEUTICS

Allogeneic TCR-T In Vivo Efficacy Against COVID Peptide+ Cells

Animal Model: COVID-epitope [KLW]-positive HEK293 Cells



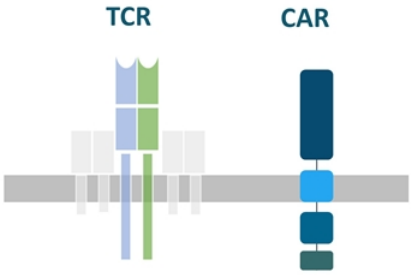
POC for Poseida TCR-T platform for infectious disease

Dual CAR/TCR T cells

POSEIDA THERAPEUTICS

Potential Therapeutic Benefits of CAR/TCR-T

Simultaneous Expression of CAR and TCR



- Enable engineered T cell to recognize both cell surface target and intracellular antigen presented by MHC

Poseida CAR/TCR-T: Best of Both Technologies

TCR

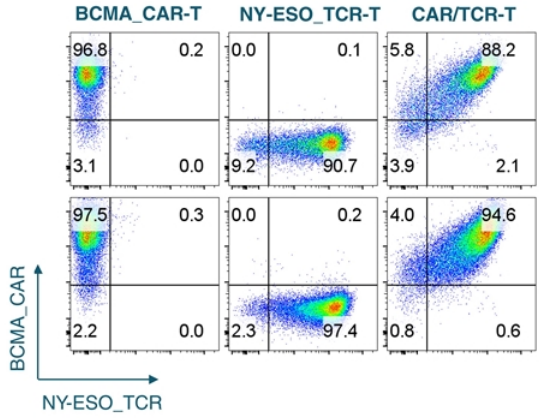
- Highly tumor-specific **intracellular antigens**
- Low antigen density requirement
- Polyfunctional CD4/CD8 **engagement of host immune system**
- Potential trafficking advantages in solid tumors

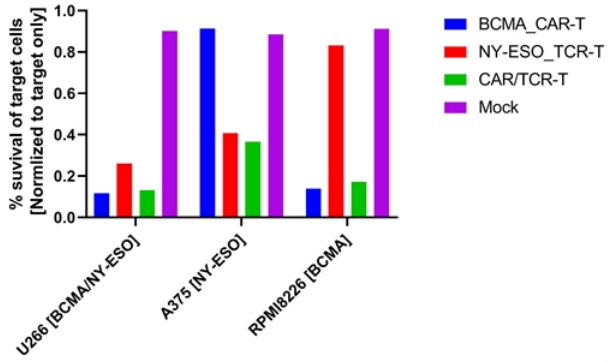
CAR

- **Cell surface antigens**
- **Validated process and platform**
- **Validated, robust anti-tumor activity**
- Tunable CAR binder and signaling domains
- Broad applicability

Allogeneic CAR/TCR-T Coexpression and Dual-Targeted Cell Killing

CAR/TCR-T Characterization





- CAR/TCR transposon comprised of both CAR and TCR gene into one expression cassette
- POC Allo CAR/TCR-T product exhibits **high % CAR/TCR expression** and **dual-antigen specificity, and potent in vitro cell killing**

Summary

- Poseida's TCR-T platform has numerous advantages, including a final product with a high percentage of stem cell memory (T_{SCM}) CD4 and CD8 cells
- Ultra-high fidelity Cas-CLOVER™ allows multiplex editing (TCRA, TCRB, B2M), while retaining robust T cell function in vitro and in vivo
- Proof-of-concept established for both oncology and infectious disease
- **Poseida's TCR-T platform can be combined with the CAR-T platform for dual targeting and potential additive activity**

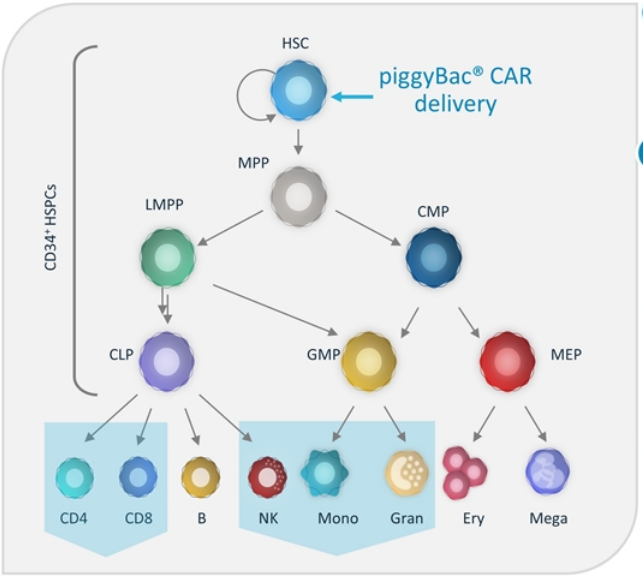
POSEIDA THERAPEUTICS

CAR 3.0 – Using Hematopoietic Stem Cells (HSCs) to Create CAR-based Cell Therapies

Nina Timberlake, PhD
Director, Ex Vivo Cell Therapy

CAR-HSC: The Next Wave in CAR Therapy

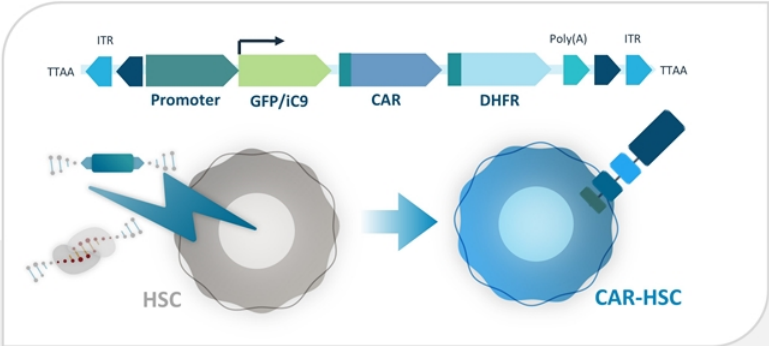
CAR-HSC could address many of the limitations of current CAR-T therapies, including improving persistence, potency, manufacturing, and immune rejection



1. **Unlimited T_{SCM} CAR-T** — piggyBac® CAR gene delivery to a small fraction of transplanted HSCs could provide an inexhaustible supply of T_{SCM} and differentiated CAR-T cells for continued eradication of recurring malignant cells
2. **Diverse CAR Effector Cells** — CAR gene delivery to the HSC makes CAR expression possible in any downstream cell type including T cells, NK cells, and macrophages for a multipronged, whole immune system approach
3. **Robust Expansion** — Gene delivery to a relatively small number of input HSCs lowers costs while dramatic cellular expansion during differentiation minimizes dosing limitations of mature cells
4. **Immune Tolerance** — Central immune tolerance achieved during stem cell transplant prevents rejection of CAR-effector cells derived from CAR-HSCs

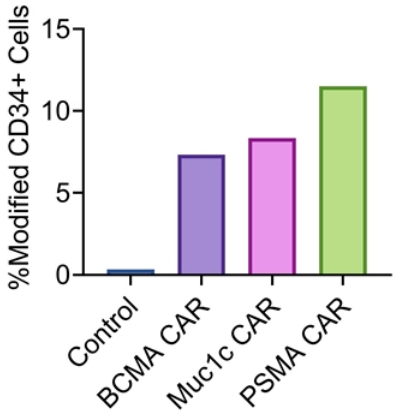
POSEIDA THERAPEUTICS

Translating Poseida's Platform Technologies to Modification of CD34+ Cells



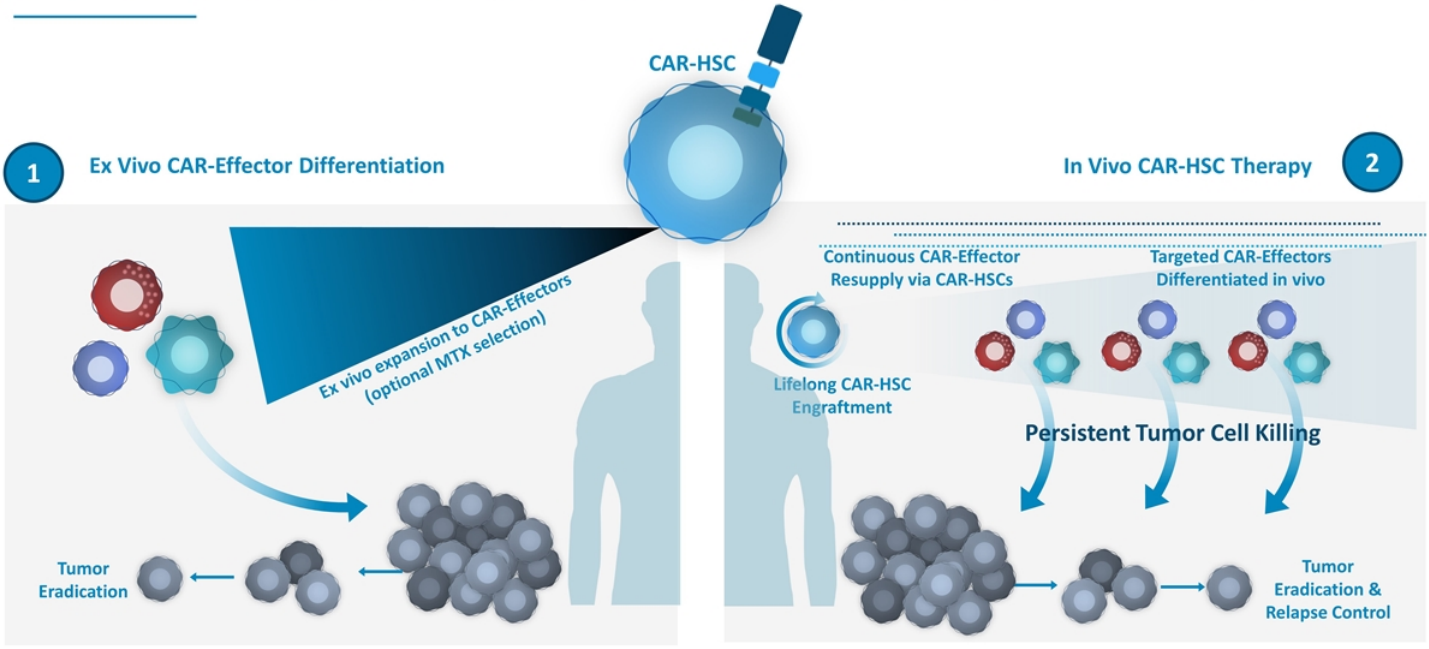
- Durable transgene expression in HSCs via piggyBac DNA Delivery System
- Efficient and high-fidelity KO using Cas-CLOVER™ Site-Specific Gene Editing System
- Availability of additional tools including safety switch and selection marker

Successful Modification of CD34+ Cells with Various CAR Vectors



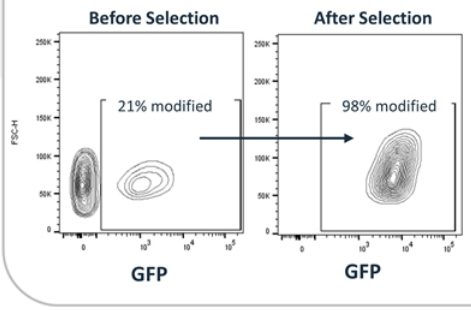
POSEIDA THERAPEUTICS

CAR-HSC Enables Multiple Pathways to Generate CAR-Effectors

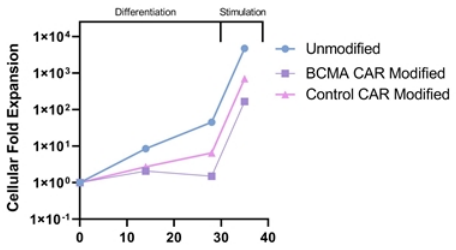


CAR-HSCs Undergo Efficient Ex Vivo Selection, Expansion and Differentiation

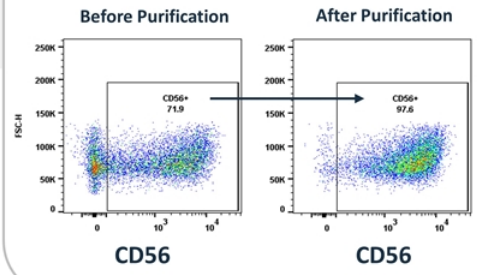
MTX Selection Yields Pure CAR-HSC Population



Robust Ex Vivo Expansion of HSCs to CAR-NK Cells

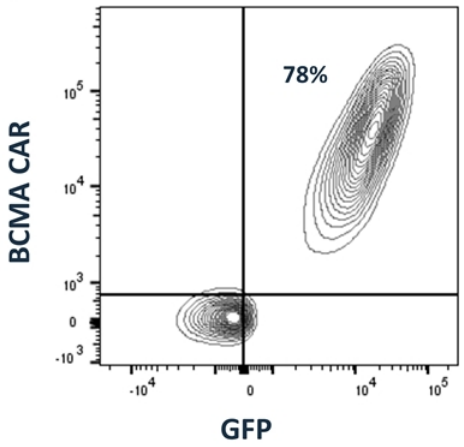


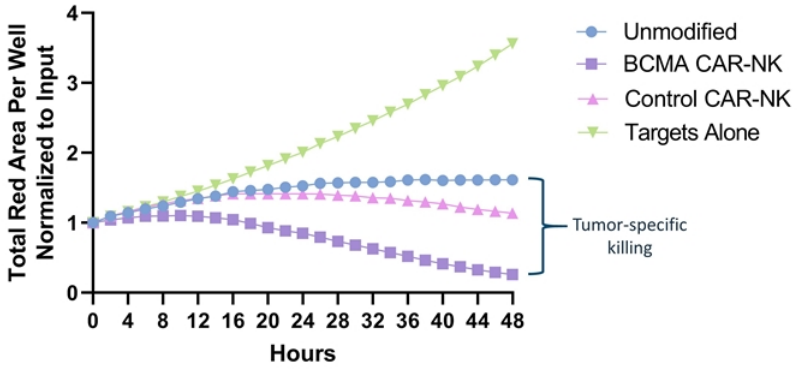
Efficient Differentiation and Purification of CD56+ Cells



POSEIDA THERAPEUTICS

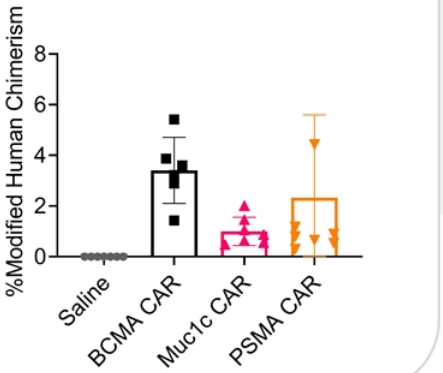
Ex Vivo Differentiated CAR-NK Cells Exhibit Target-Specific Cytotoxicity

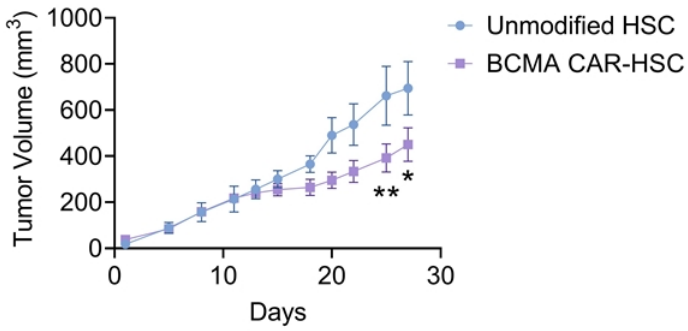




- CAR expression is effectively maintained during differentiation from CAR-HSCs to CAR-NK cells
- CAR-NK cells derived from CAR-HSCs have robust, tumor-specific killing capacity

CAR-modified HSCs can Engraft, Persist and Form Functional CAR-Effector Cells In Vivo





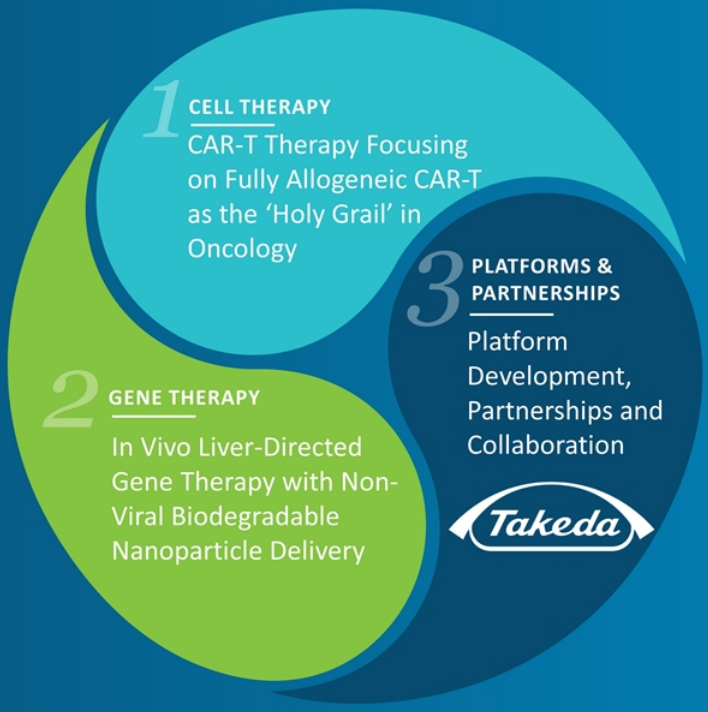
Summary

- HSCs can be modified via the piggyBac® DNA Delivery System and used to produce a variety of CAR-Effector cells either in vivo or ex vivo
- In vivo CAR-HSC therapy could provide an inexhaustible supply of effector cells (CAR-T, CAR-NK and CAR-macrophage) to eradicate tumor cells and prevent relapse
- CAR-HSCs can be differentiated in an ex vivo 'bioreactor' approach to generate high yields of CAR-Effector cells
- CAR-HSC may address many of the challenges currently facing the cell therapy field

POSEIDA THERAPEUTICS

R&D Day 2022
Closing Comments

Mark J. Gergen
Chief Executive Officer


1
CELL THERAPY
CAR-T Therapy Focusing on Fully Allogeneic CAR-T as the 'Holy Grail' in Oncology
2
GENE THERAPY
In Vivo Liver-Directed Gene Therapy with Non-Viral Biodegradable Nanoparticle Delivery
3
PLATFORMS & PARTNERSHIPS
Platform Development, Partnerships and Collaboration
Takeda

Innovation in CAR-T

Allogeneic CAR-T Therapy for Oncology

Cell Type Matters

T_{SCM} Cell

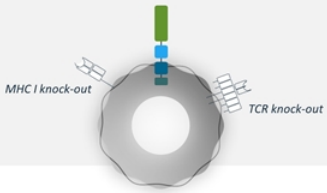
Stem Cell Memory

- Self-renewing
- Long lived
- Multipotent

T_{SCM} is the ideal cell type for CAR-T due to greater safety and durability

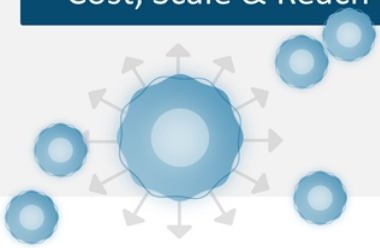
piggyBac® is the ideal non-viral gene insertion technology

Fully Allogeneic CAR-T



Addressing both Graft v Host and Host v Graft alloreactivity with **Cas-CLOVER™ Gene Editing**

Cost, Scale & Reach



Booster Molecule technology with the potential to deliver 100's of doses at low cost

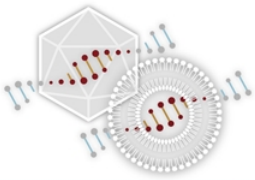
Enables outpatient dosing and expanded patient reach

Disruption in Gene Therapy

In Vivo Gene Therapy for Rare Diseases

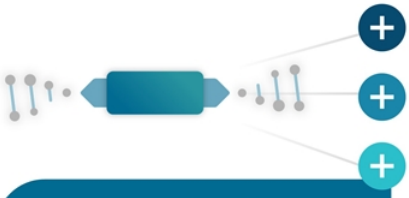
Fully Integrating

PiggyBac® integrates into DNA enabling the potential for single treatment cures



Addressing Challenges of Viral Delivery

piggyBac and **Nanoparticle** technology can address limitations of AAV



Broad Application

piggyBac® cargo capacity addresses more indications and piggyBac® can treat juvenile populations

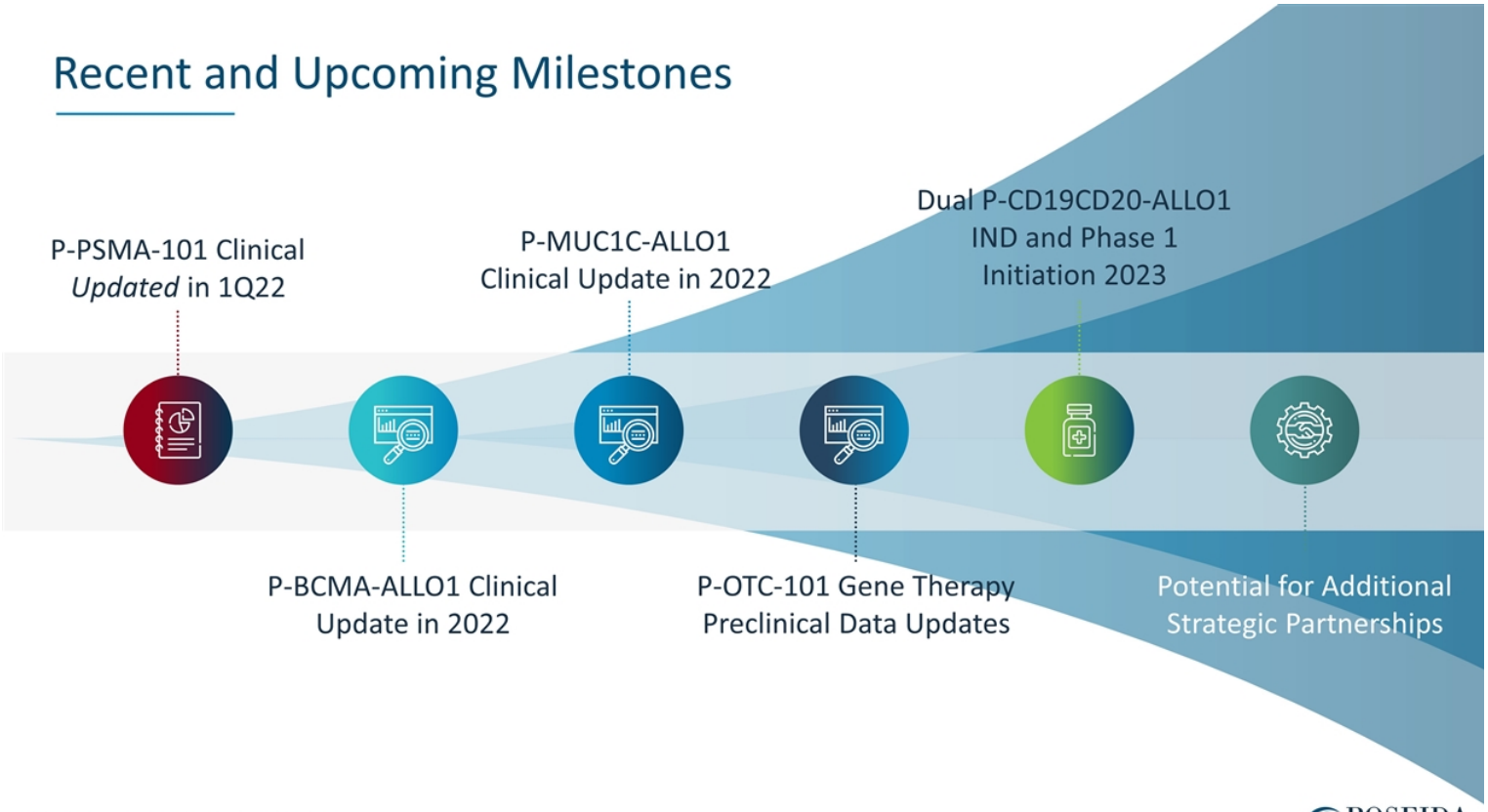
Our Platform Technologies Have Broad Reach

Various combinations our innovative platform technologies create unique opportunities across the cell and gene therapy landscape

*Poseida has listed companies it believes are representative of those active in cell and gene therapy.

POSEIDA THERAPEUTICS

Recent and Upcoming Milestones



POSEIDA THERAPEUTICS

Thank You

- Our Special Guests
  - Luca Gattinoni, MD
  - Susan Slovin, MD, PhD
- Presenters
  - Eric Ostertag, MD, PhD, Executive Chairman
  - Matthew Spear, MD, Chief Medical Officer
  - Devon Shedlock, PhD, CSO Cell Therapy
  - Julia Coronella, PhD, Vice President Immuno-oncology
  - Blair Madison, PhD, Vice President Genetic Engineering
  - Jack Rychak, PhD, Vice President Gene Therapy
  - Nina Timberlake, PhD, Director Ex Vivo Cell Therapy
- Poseida Employees
- Clinical Investigators
- Patients
- Investors
- Attendees

POSEIDA THERAPEUTICS

POSEIDA THERAPEUTICS

Q&A

The Next Wave of Cell & Gene Therapies
with the Capacity to Cure