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 22, 2023

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 22, 2023, Poseida Therapeutics, Inc. (the "Company") issued a press release announcing that members of its management and external advisors are providing an update on the Company's research and development programs and making available a corporate presentation. A copy of the press release and the corporate presentation are attached as Exhibit 99.1 and Exhibit 99.2, respectively, to this report. The corporate presentation will also be available under the "Investors" section of the Company's website.

The information in this Item 7.01 of this report (including Exhibits 99.1 and 99.2) 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	Press Release, dated February 22, 2023
99.2	Corporate Presentation, dated February 22, 2023
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 22, 2023

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

Poseida Therapeutics Hosts Third Annual Virtual R&D Day Highlighting Novel Pipeline Assets and Latest Technology Innovations

Virtual R&D Day featuring key opinion leaders and Poseida's leadership and scientific team members to be held today at 10:00am ET / 7:00am PT

SAN DIEGO, February 22, 2023 — Poseida Therapeutics, Inc. (Nasdaq: PSTX), a clinical-stage cell and gene therapy company advancing a new class of treatments for patients with cancer and rare diseases, today announced that the Company plans to highlight its clinical and preclinical pipeline progress during a virtual R&D Day to be held today at 10:00am ET / 7:00am PT.

"R&D Day is our annual showcase for the innovative and exciting science we are advancing at Poseida that continues to drive our leadership in the field of cell and gene therapies," said Mark Gergen, Chief Executive Officer of Poseida Therapeutics. "Today, we will announce our second liver-directed preclinical gene therapy program partnered with Takeda: P-PAH-101 for the in vivo treatment of Phenylketonuria, or PKU. We are excited to share the progress we have made with our site-specific Super piggyBac platform to enable highly targeted site-specific editing and insertion, one of the most sought-after characteristics of genetic engineering. Finally, in our cell therapy portfolio, we continue to differentiate ourselves, expanding our capabilities for our allogeneic T cell platform to deploy TCRs in combination with CARs in solid tumors. We are thankful for the continued dedication of our scientists, partners and collaborators as we work together to unlock the potential of our technologies to treat patients with cancer and rare genetic diseases."

The Company's third-annual R&D Day will feature its executive leadership and scientists for a morning of presentations and fireside chats with special guest speakers exploring the future of cell and gene therapy. The program will highlight the Company's proprietary genetic engineering platform technologies, differentiated allogeneic CAR-T programs, and novel approaches to gene therapy as well as ongoing collaborations with Roche and Takeda.

External speakers will include:

- George M. Church, Ph.D., a pioneer in the fields of genetics and synthetic biology and Chair of the Company's Gene Therapy Scientific Advisory Board;
- Madhu Natarajan, Ph.D., Head of the Rare Diseases Drug Discovery Unit at Takeda;
- Christine Brown, Ph.D., Professor, City of Hope, a CAR-T cell expert and member of the Company's Immuno-Oncology Scientific Advisory Board.

Key R&D Day Topics and Highlights

In Vivo Gene Therapy Programs

The Company will present advancements in hybrid technology highlighting the potential for single treatment cures across multiple diseases.

- P-OTC-101 is the Company's liver-directed gene therapy program for the in vivo treatment of urea cycle disease caused by a deficiency in the ornithine transcarbamylase (OTC) enzyme, a defect that impairs the body's ability to detoxify ammonia, a byproduct of protein metabolism. The Company will show data highlighting disease correction and evaluation in non-human primates, with the Company's lead lipid nanoparticle formulation that has demonstrated favorable tolerability.
- The Company will announce P-PAH-101, its second Takeda-partnered gene therapy program. P-PAH-101 is a liver-directed gene therapy to treat PKU, an inherited genetic disorder caused by mutations in the phenylalanine hydroxylase (PAH) gene resulting in buildup of phenylalanine in the body. If left untreated, PKU can affect a person's cognitive development. P-PAH-101 utilizes Super piggyBac technology combined with a hybrid adeno-associated virus (AAV) and nanoparticle delivery system. Preclinical data has demonstrated the potential to resolve phenylalanine to normal levels following a single treatment in juvenile and adult mice.

Emerging Technologies in Gene Therapy

The Company will highlight its continuing focus on innovation in its emerging platform technologies at today's event.

- Site-specific Super piggyBac DNA Delivery, first unveiled at the Company's R&D Day in February 2022, has continued to advance. The Company has made significant enhancements to efficiency and site-specific transposition, with up to 60% of haploid genomes modified.
- The Company has made key enhancements to its non-viral gene delivery system resulting in nearly 10-fold improvements in DNA expression in the past 12 months on a pathway towards realizing the full potential of non-viral gene delivery.

Allogeneic Cell Therapy Programs

- The Company will recap early clinical data presented at the European Society for Medical Oncology Immuno-Oncology Annual Congress in December 2022 (ESMO I-O) on both of its Phase 1 allogeneic cell therapy programs: P-MUC1C-ALLO1, a wholly-owned CAR-T product candidate targeting solid tumors derived from epithelial cells, including breast and ovarian cancers, and P-BCMA-ALLO1, a CAR-T product candidate partnered with Roche targeting relapsed/refractory multiple myeloma. The Company plans to present additional updates on both trials at a medical conference in 2023.
- The Company will present preclinical data on additional emerging allogeneic CAR-T programs including P-CD19CD20-ALLO1, P-CD70-ALLO1 and P-ckit-ALLO1.

Emerging Technologies in Cell Therapy

- The Company will share early preclinical data highlighting progress made towards developing dual-targeting CAR-TCR-T therapies capable of recognizing extracellular and intracellular solid tumor antigens for potential improved clinical outcomes.

R&D Day Webcast Information

Registration for this virtual event and access to the live webcast will be available on the Investors & Media section of the Company's website, www.poseida.com. A replay of the webcast will be available for 90 days following the presentation.

About Poseida Therapeutics, Inc.

Poseida Therapeutics is a clinical-stage biopharmaceutical company advancing differentiated cell and gene therapies with the capacity to cure certain cancers and rare diseases. The Company's pipeline includes allogeneic CAR-T cell therapy product candidates for both solid and liquid tumors as well as in vivo gene therapy product candidates that address patient populations with high unmet medical need. The Company's approach to cell and gene therapies is based on its proprietary genetic editing platforms, including its non-viral Super piggyBac® DNA Delivery System, Cas-CLOVER™ Site-Specific Gene Editing System and nanoparticle and hybrid gene delivery technologies. The Company has formed global strategic collaborations with Roche and Takeda to unlock the promise of cell and gene therapies for patients. Learn more at www.poseida.com and connect with Poseida on Twitter and LinkedIn.

Forward-Looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements include statements regarding, among other things, expected plans with respect to clinical trials, including timing of clinical data updates; anticipated timelines and milestones with respect to the Company's development programs; the potential capabilities and benefits of the Company's technology platforms and product candidates; the Company's plans and strategy with respect to developing its technologies and product candidates; and future contributions of the Company's scientists, partners and collaborators. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. These forward-looking statements are based upon the Company's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, the Company's reliance on third parties for various aspects of its business; risks and uncertainties associated with development and regulatory approval of novel product candidates in the biopharmaceutical industry; the Company's ability to retain key scientific or management personnel; the fact that the Company will have limited control over the efforts and resources that its strategic partners devote to advancing development programs under their respective collaboration agreements and the ability of its strategic partners to early terminate the collaborations, such that the Company may not receive the potential fees and payments under the collaboration agreements or fully realize the benefits of such collaborations; and the other risks described in the Company's filings with the Securities and Exchange Commission. All forward-looking statements contained in this press release speak only as of the date on which they were made. The Company undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made, except as required by law.

Investor Contact:
Alex Lobo
Stern Investor Relations
IR@poseida.com

Media Contact:
Sarah Thailing
Senior Director, Corporate Communications and IR
Poseida Therapeutics, Inc.
PR@poseida.com

Exhibit 99.

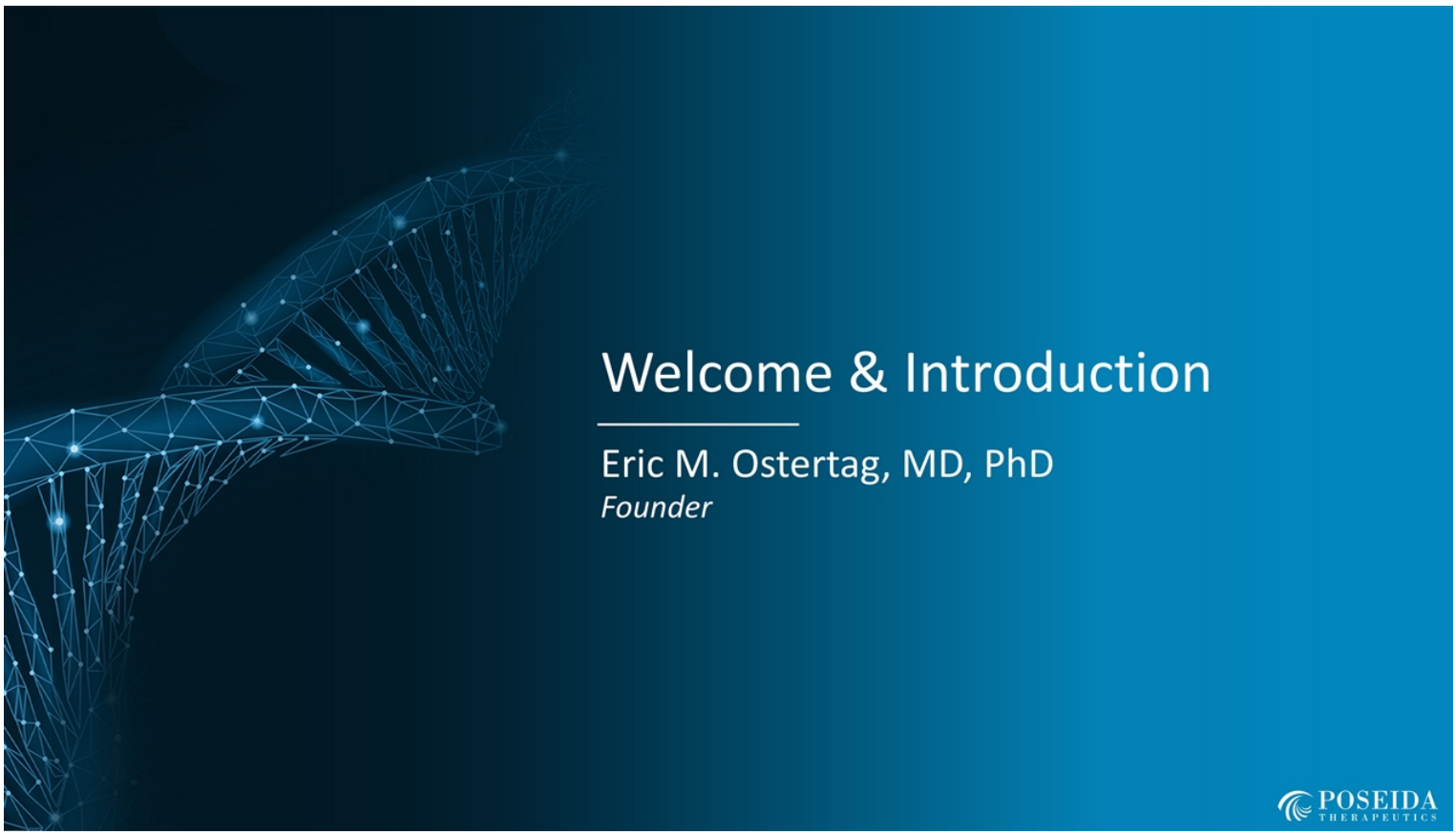
POSEIDA THERAPEUTICS

A New Class of Cell & Gene Therapies With the Capacity to Cure

February 22, 2023

Disclaimer

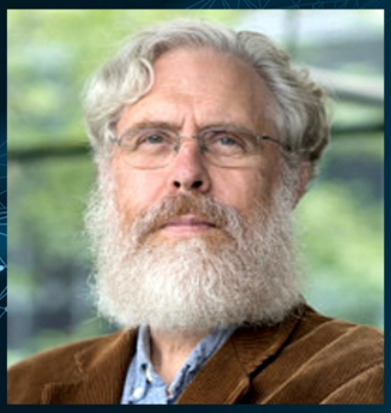
This presentation and any accompanying oral commentary contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts and include, without limitation, statements related to future events; our future financial performance or condition; business strategy; expected timing and plans with respect to development milestones, clinical trials, and regulatory and manufacturing activities; estimated market opportunities for product candidates; statements regarding potential fees, milestone and royalty payments we may receive pursuant to our collaboration agreements; and future results of anticipated development efforts. Words such as "expect(s)," "feel(s)," "believe(s)," "will," "may," "anticipate(s)", “potentially” or negative of these terms or similar expressions are intended to identify forward-looking statements. These forward-looking statements are based on management's current expectations of future events only as of the date of this presentation and are subject to a number of important risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: the fact that collaboration agreements may be terminated early; the fact that we will have limited control over the efforts and resources our collaborators devote to advancing development programs under our collaboration agreements; 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.


Welcome & Introduction
Eric M. Ostertag, MD, PhD
Founder
POSEIDA
THERAPEUTICS

Agenda

Introduction	*Eric M. Ostertag, MD, PhD, Founder*
Fireside Chat	*George Church, PhD, Gene Editing Pioneer & Chair, Poseida Gene Therapy SAB*
Gene Therapy	*Brent Warner, President, Gene Therapy*
Fireside Chat	*Madhu Natarajan, PhD, Head, Rare Diseases Drug Discovery Unit, Takeda*
Pipeline Programs	*Jack Rychak, PhD & Bernard Kok, PhD*
Emerging Technology	*Blair Madison, PhD; Oscar Alvarez, PhD & Alex Schudel, PhD*
Cell Therapy	*Devon J. Shedlock, PhD, Chief Scientific Officer, Cell Therapy*
Fireside Chat	*Christine Brown, PhD, Professor, City of Hope; CAR-T Cell Expert & Member, Poseida Immuno-Oncology SAB*
Clinical Programs	*Rajesh Belani, MD*
Preclinical	*Stacey Cranert, PhD; Julia Coronella, PhD; Nina Timberlake, PhD & Devon J. Shedlock, PhD*
Conclusion	*Mark Gergen, CEO*
Q&A	*Executive and Scientific Leadership*

Fireside Chats: *Guest Speakers*



George Church, PhD

Gene Editing Pioneer and Chair, Poseida Gene Therapy SAB

Madhu Natarajan, PhD

Head, Rare Diseases Drug Discovery Unit – Takeda

Christine Brown, PhD

Professor, City of Hope; CAR-T Expert; and Member, Poseida Immuno-Oncology SAB

POSEIDA THERAPEUTICS

POSEIDA THERAPEUTICS

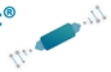
Gene Therapy (GTx)

Brent Warner
President, Gene Therapy

February 22, 2023

Robust Platform Technologies Supporting Our GTx Pipeline Programs

Current Platforms

Super piggyBac® (SPB)  Non-viral transposon gene insertion technology

SPB Hybrid AAV + LNP  Gene insertion technology utilizing AAV as DNA donor

Lipid Nanoparticles (LNP)  Proprietary lipid nanoparticles built to deliver DNA

Cas-CLOVER™  High fidelity gene editing system for knock-out / knock-in

Site-Specific Super piggyBac® (ssSPB)  Next generation programmable gene targeting/editing system

Current Programs

P-OTC-101
SPB Hybrid AAV + LNP
Poseida Owned

- Pre-clinical program
- Capsid / construct selected
- Finalizing pathway to IND
- New data presented today

P-PAH-101
SPB Hybrid AAV + LNP
Partnered with Takeda

- New pre-clinical program
- New data presented today

P-FVIII-101
SPB Non-viral
Partnered with Takeda

- Pre-clinical program
- Data presented at ASH 2022
- Best of ASH 2022 selection
- New data presented today

Future Pipeline

Liver Directed Knock-out
Cas-CLOVER

Liver Directed Metabolic Disease
SPB Non-viral

Focus on Accelerating Programs and Platforms

Poseida's strong platform technologies are enabling a new class of Gene Therapies potentially overcoming many of the hurdles of first generation / standard Gene Therapies

2023 GTx Focus

1. **Efficiency in accelerating** our programs
2. **Enhance our platforms** and pipeline
3. **Emergence as a leader** in Gene Therapy

2023 GTx Priorities

Accelerate Programs

- Advance current programs towards IND / clinical readiness
- Disseminate data at upcoming congresses

Enhance Platforms

- Accelerate ssSPB to become a leading Gene Editing Platform
- Breadth and depth across proprietary LNP portfolio

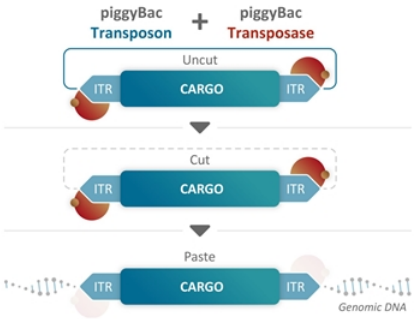
Strengthen Pipeline

- Accelerate next programs to pipeline
- Deepen focus in liver directed diseases + exploratory in next tissue / disease


GTx Pipeline Programs
Jack Rychak
Vice President, Research and Development – GTx
POSEIDA
THERAPEUTICS

Powerful Platforms Enabling Innovative Gene Therapy Products

SPB Gene Insertion



Highly efficient integration of therapeutic transgene into genome

Non-Viral Delivery System

Transposon + Transposase

Nanoparticle system to enable delivery of large cargo and repeat dosing

Hybrid Delivery System

Transposon + Transposase

Leverage mature AAV and LNP delivery technology for challenging diseases

POSEIDA THERAPEUTICS

SPB Non-Viral and Hybrid Advantages Over Standard AAV

	POSEIDA THERAPEUTICS		
	Non-Viral Delivery System	**Hybrid Delivery System**	Standard AAV Delivery
			
Durability:	**Permanent**	**Permanent**	Unstable Episome
Insertion Profile:	**Open Chromatin**	**Open Chromatin**	Random / hotspots (e.g., @Rian)[1-6]
Delivery Effectiveness:	Moderate	**High**	**High**
Neonate:	High Efficiency	High Efficiency	Higher vector dilution
VCN:	Low (<1/dg)	1-4 (Integrated)	1-1000 (dep. on dose, serotype, cell)
Re-Dosing:	**Demonstrated Data**	Early Feasibility	Difficult

1) Kang et al., *Mol. Ther. Methods Clin.* 2019; 2) Zhong et al., *Hum. Gene Ther.* 2013; 3) Donsante et al., *Science* 2007; 4) Chandler et al., *J. Clin. Invest.* 2015; 5) Walia et al., *Mol. Ther.* 2015; 6) Li et al., *Mol. Ther.* 2021

Robust Platform Technologies Supporting Our GTx Pipeline Programs

Current Platforms

Super piggyBac® (SPB)	Non-viral transposon gene insertion technology
SPB Hybrid AAV + LNP	Gene insertion technology utilizing AAV as DNA donor
Lipid Nanoparticles (LNP)	Proprietary lipid nanoparticles built to deliver DNA
Cas-CLOVER™	High fidelity gene editing system for knock-out / knock-in
Site-Specific Super piggyBac® (ssSPB)	Next generation programmable gene targeting/editing system

Current Programs

P-OTC-101
SPB Hybrid AAV + LNP
Poseida Owned

- Pre-clinical program
- Capsid / construct selected
- Finalizing pathway to IND
- New data presented today

P-PAH-101
SPB Hybrid AAV + LNP
Partnered with Takeda

- New pre-clinical program
- New data presented today

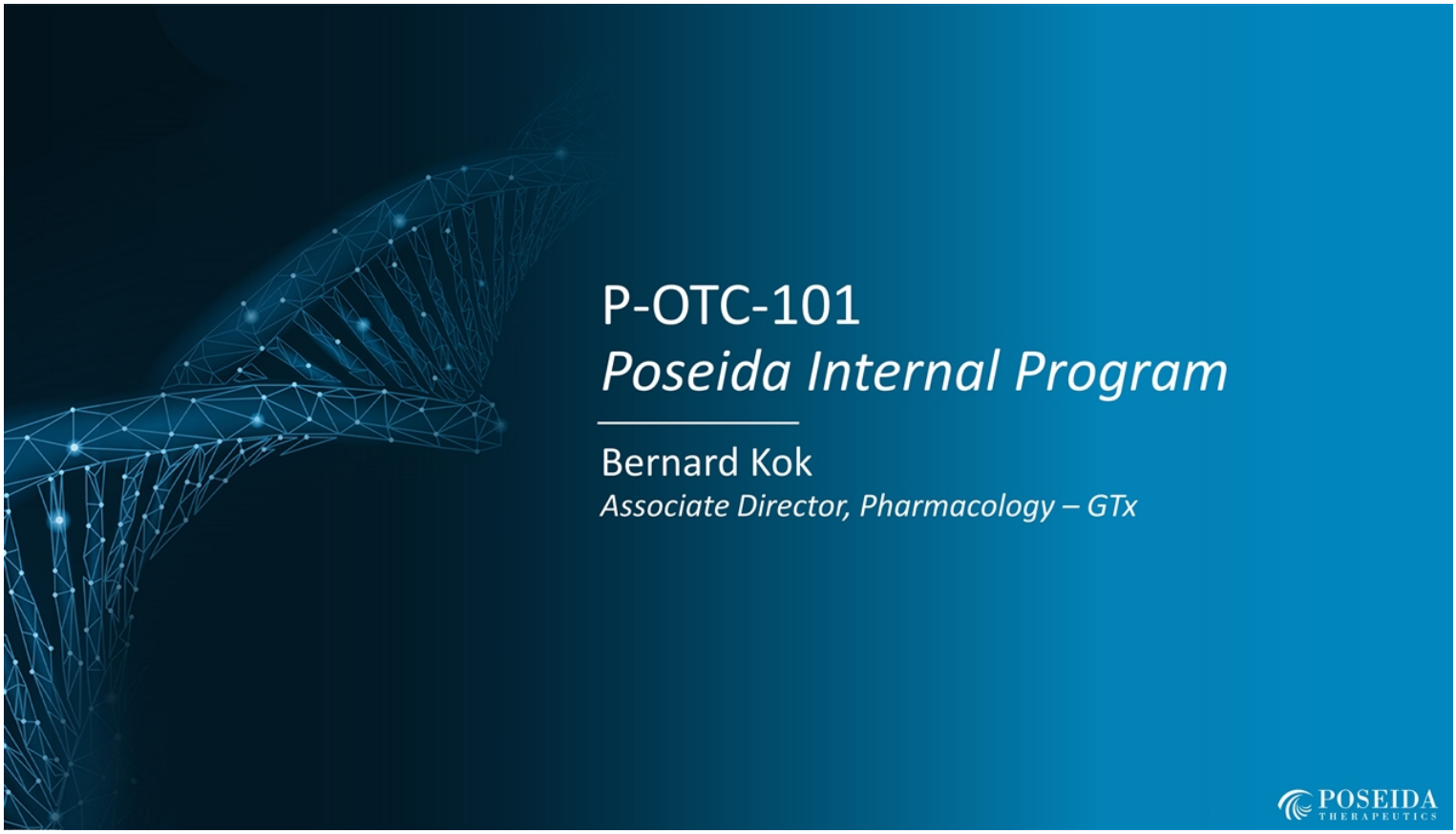
P-FVIII-101
SPB Non-viral
Partnered with Takeda

- Pre-clinical program
- Data presented at ASH 2022
- Best of ASH 2022 selection
- New data presented today

Future Pipeline

Liver Directed Knock-out
Cas-CLOVER

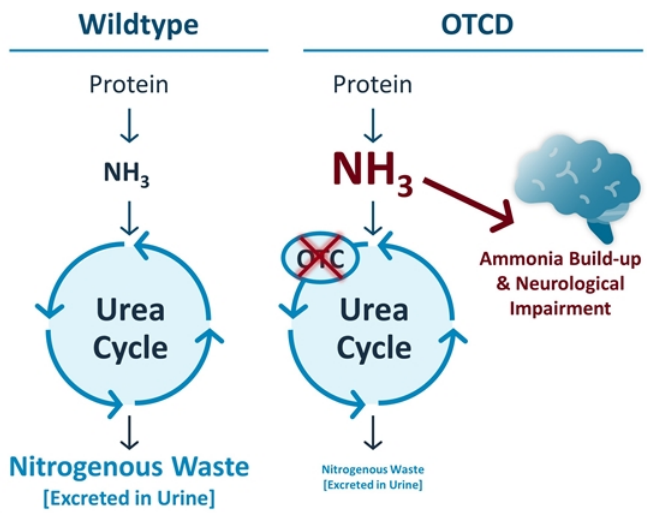
Liver Directed Metabolic Disease
SPB Non-viral


P-OTC-101
Poseida Internal Program
Bernard Kok
Associate Director, Pharmacology – GTx
POSEIDA
THERAPEUTICS

Ornithine Transcarbamylase Deficiency (OTCD) – High Unmet Need

- X-linked metabolic liver disorder causing toxic ammonia build-up
- Most common urea cycle disorder and most common cause of 'early onset' illness[1]
- NH3 build-up -> neurological impairment / death
- Dietary protein restriction & alternative pathway drugs inadequate for early onset illness
- Mortality and morbidity in severe patients
- Liver transplantation can be corrective, but
  - Inaccessible to many
  - Lifetime immunosuppression
  - Significant unmet need for functional cure

Mechanism

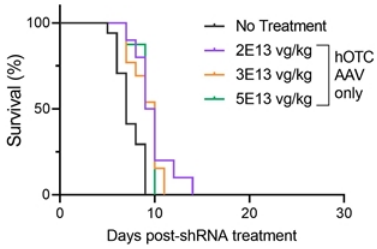


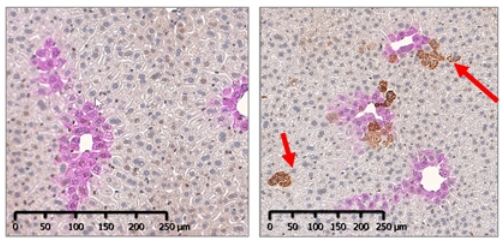
1. Summar et al. 2008 Acta Paediatrica

AAV Alone is Not Effective or Durable to Rescue Severe OTCD

Experimental Design:

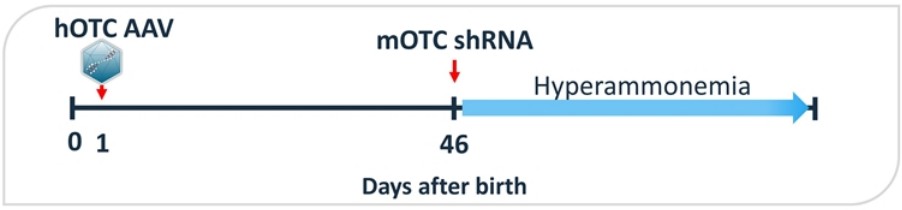
- Neonatal OTCD mice (residual 5-10% OTC activity) treated at birth (day 1) with various doses of human OTC (hOTC) AAV
- Severe disease induction on Day 46 by reducing mouse OTC expression





OTC (**brown**), central vein marker (**purple**)

hOTC AAV alone failed to rescue severe OTCD at all doses due to lack of durability from non-integrating AAV

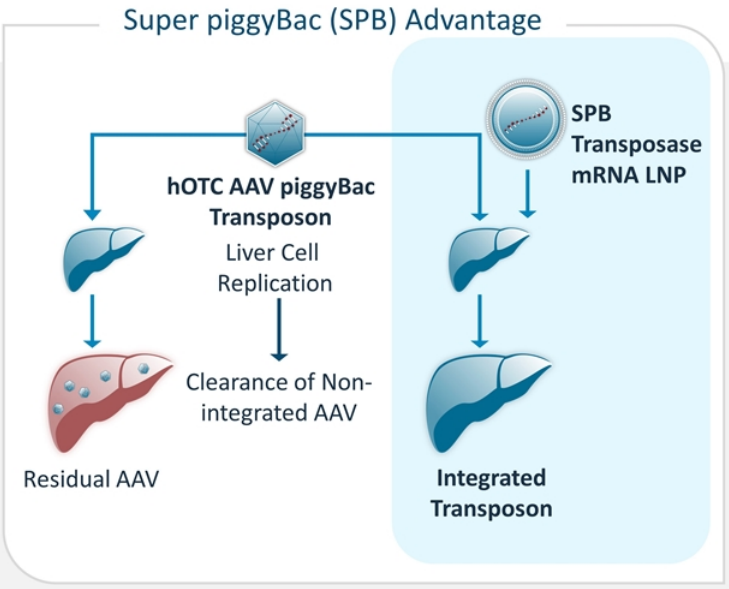


POSEIDA THERAPEUTICS

Goal is to Deliver Functional Cures with Hybrid P-OTC-101

hOTC AAV + **SPB mRNA LNP**

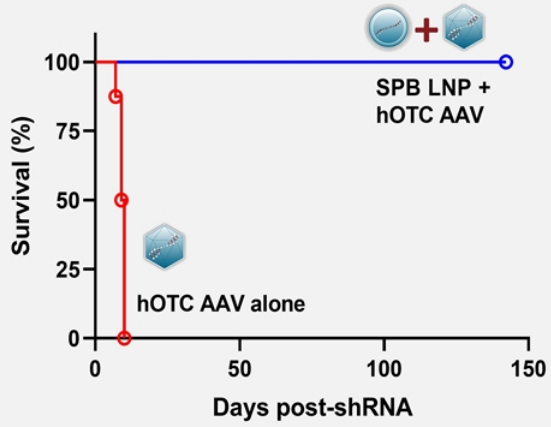
- Biodegradable nanoparticle transiently delivers SPB
- Efficient integration in growing liver enables:
  - Durable OTC expression
  - Potentially a functional cure
  - Potential for neonatal/juvenile patients
- Therapeutic protein levels with 1/10th the AAV dose to reduce AAV toxicity
- Low (2-4) integrated vector copy numbers per cell
- Option of re-dosing SPB, to titrate hOTC level

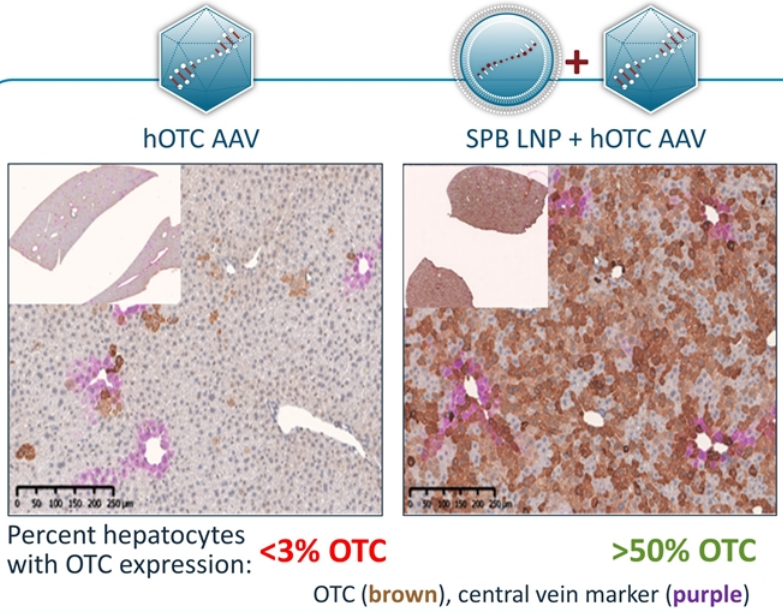


POSEIDA THERAPEUTICS

P-OTC-101 Achieved Expression of OTC Leading to Functional Cure

100% Rescue of Mortality in OTCD Model

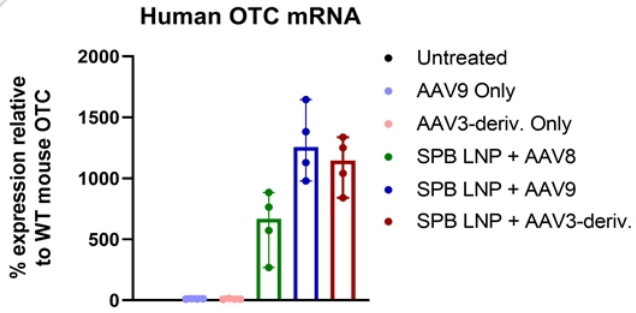


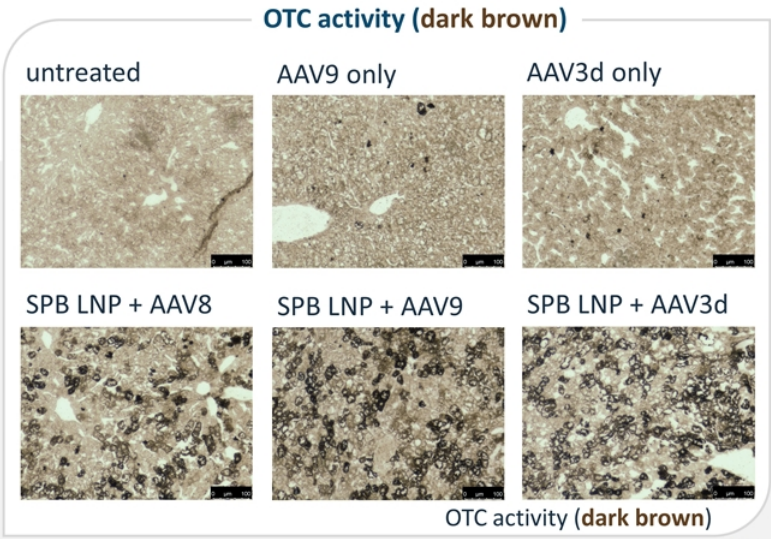


- 0.2 mg/kg SPB transposase LNP + 2E13 vg/kg hOTC AAV or AAV alone administered on day 1 of life to spf^{ash} OTCD mice
- IHC for glutamine synthetase (pink), human OTC (brown) in liver on day 83 post-treatment

POSEIDA THERAPEUTICS

SPB LNP Enables “Plug ‘n Play” with Different AAV Capsids





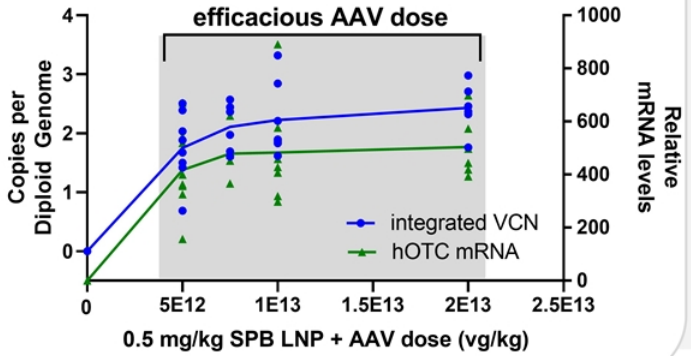
- SPB mRNA LNPs were co-administered with AAV serotypes encapsulating hOTC transgenes to newborn WT mice
- Human OTC mRNA and distribution of OTC activity were measured at study termination (Day 28 post-Tx)

POSEIDA THERAPEUTICS

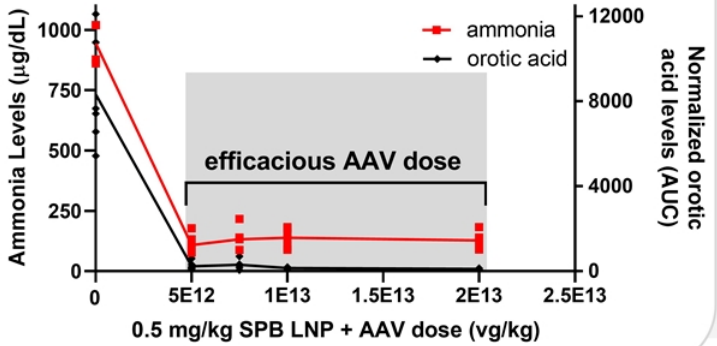
Strong Efficacy Seen Across Wide AAV Dose Range for P-OTC-101

- 0.5 mg/kg SPB mRNA LNP + dose titration of hOTC AAV administered to neonatal OTCD mice
- Molecular and biomarker analysis was performed 40 to 70 days post-treatment

Molecular Readouts



Disease Biomarkers



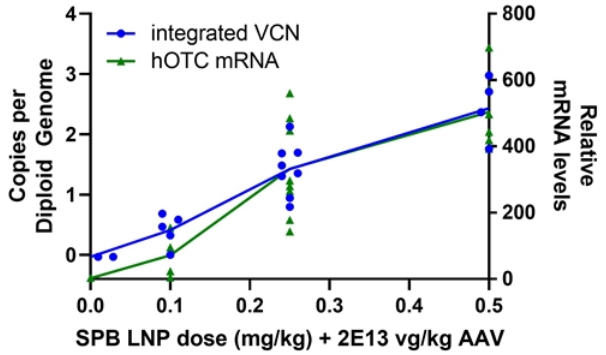
- Over a wide AAV dose range, Poseida's AAV-LNP system provides high transgene levels and efficacy (decreased disease biomarkers)

POSEIDA THERAPEUTICS

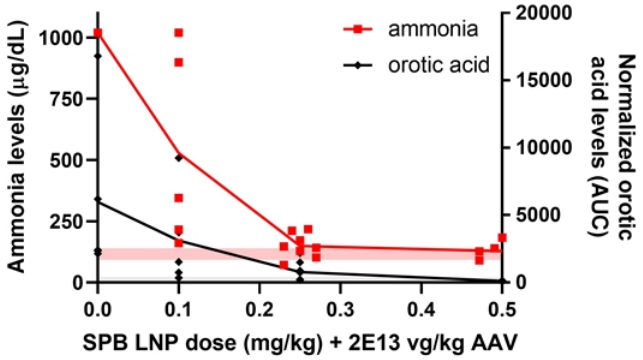
SPB mRNA LNP Dose Response Enabled Titrated Correction

- Dose titration of SPB mRNA LNP + 2E13 vg/kg hOTC AAV administered to neonatal OTCD mice
- Molecular and biomarker analysis was performed 40 to 70 days post-treatment

Molecular Readouts



Disease Biomarkers



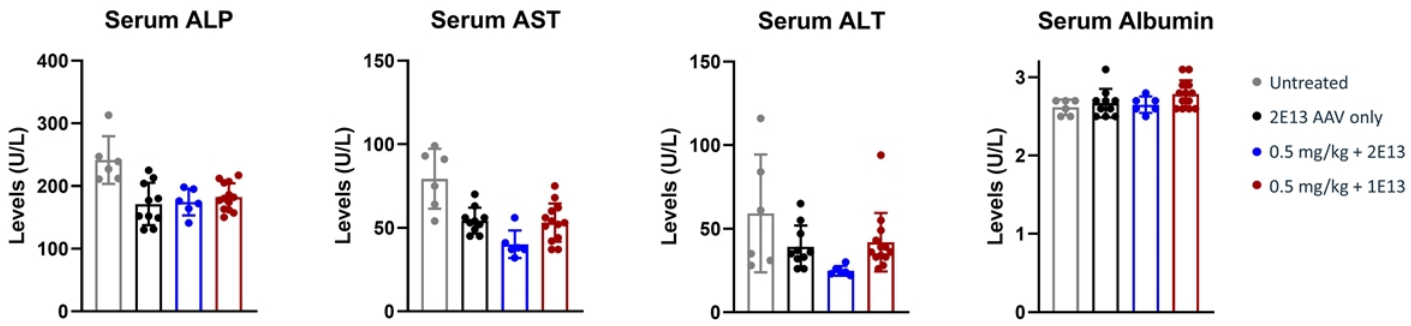
- SPB LNP levels are the primary driver of dose titratability for transgene levels and disease correction

POSEIDA THERAPEUTICS

P-OTC-101 Demonstrated Favorable Tolerability

- 0.5 mg/kg SPB mRNA LNP + 1E13 or 2E13 vg/kg hOTC AAV administered to neonatal OTCD mice

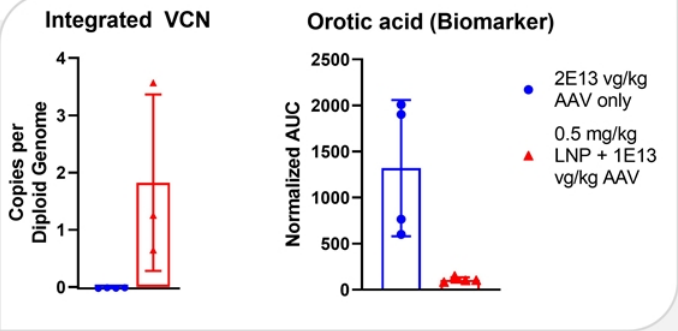
Clinical Chemistry – Liver Tox Markers

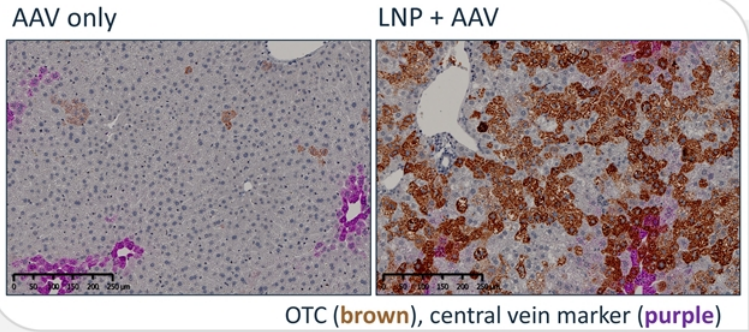


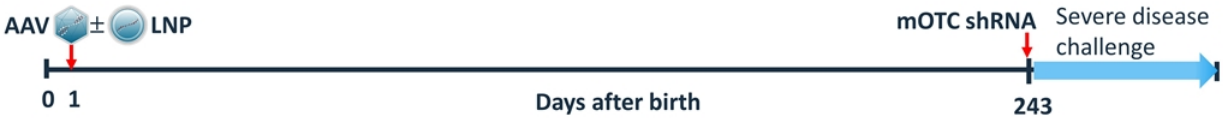
- Minimal impact on clinical chemistry at high SPB mRNA LNP and hOTC AAV doses 40 days post-treatment in OTCD mice compared to hOTC AAV alone or untreated

POSEIDA THERAPEUTICS

P-OTC-101 Provided a Durable Response in OTCD Mouse Models







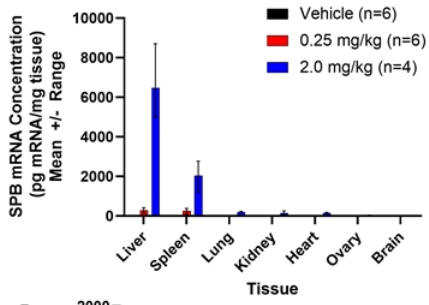
- hOTC AAV +/- 0.5 mg/kg SPB mRNA LNP administered to neonatal OTCD mice and analysis performed 243 to 278 days post-treatment
- Durable responses in integrated VCN, disease biomarker and distribution were observed

POSEIDA THERAPEUTICS

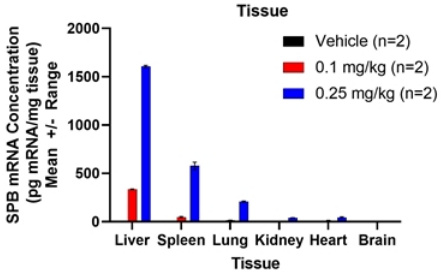
P-OTC-101 SPB LNP Well Tolerated in Non-Human Primate Study

Biodistribution

Mouse



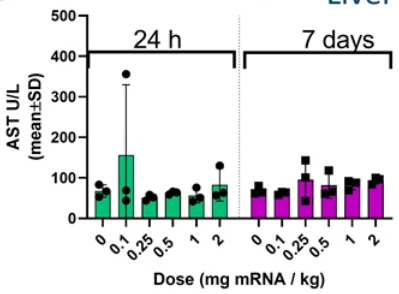
NHP

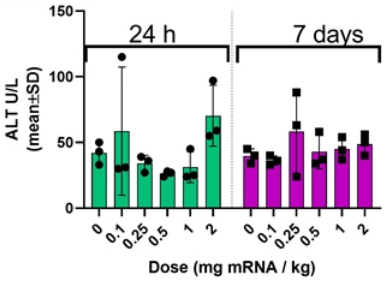


Comparable SPB mRNA biodistribution in rodent and NHP

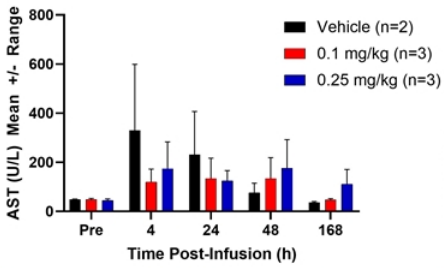
Liver Enzymes

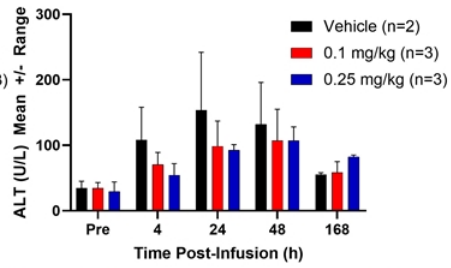
Mouse





NHP





No meaningful liver enzyme elevations above vehicle observed in rodent nor NHP

POSEIDA THERAPEUTICS

P-OTC-101: Summary and Key Takeaways

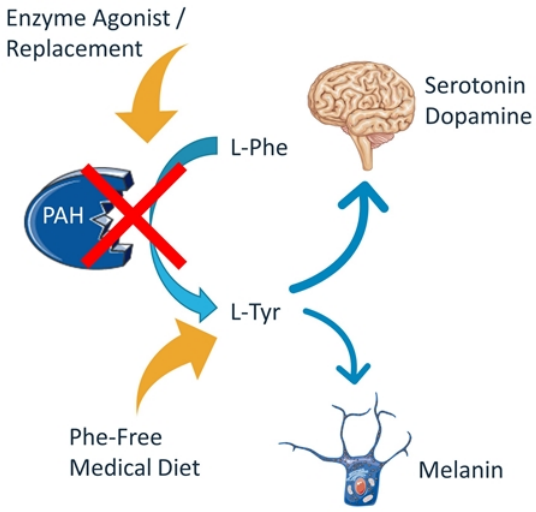
- P-OTC-101 (hybrid SPB LNP + AAV) rescues OTCD with a durable response
  - Proof-of-concept for a functional cure of OTCD
  - Provides pathway for early onset / severe OTCD, unlike standard AAVs
  - Highlights use as a “plug-and-play” system with different AAV capsids
  - Improvements in disease biomarkers across wide AAV dose ranges with favorable tolerability
  - Highlights final therapeutic design on pathway towards clinic
- Poseida’s SPB mRNA LNP highlights encouraging profile
  - Demonstrates consistent and comparable data across two species (rodents and NHPs)
  - Highlights mRNA LNP potential for future programs
- Key next steps
  - Finalization of pathway to IND


P-PAH-101
Partnered with Takeda
Jack Rychak
Vice President, Research and Development – GTx
POSEIDA
THERAPEUTICS

Phenylketonuria – Rare Disorder Without an Approved Gene Therapy

- Rare genetic metabolic disorder that increases the body's levels of Phenylalanine
  - Phenylalanine is one of the building blocks (amino acids) of proteins
  - Phenylketonuria (PKU) is caused by a change in the phenylalanine hydroxylase (PAH) gene
- PKU occurs in 1 in 10,000 to 15,000 newborns[1]
  - In the U.S., about 17,500 people are living with PKU[2]
- Most cases of PKU are detected after birth by newborn screening[1]
- Current PKU therapies require lifelong management[2]
  - No approved Gene Therapies to treat PKU

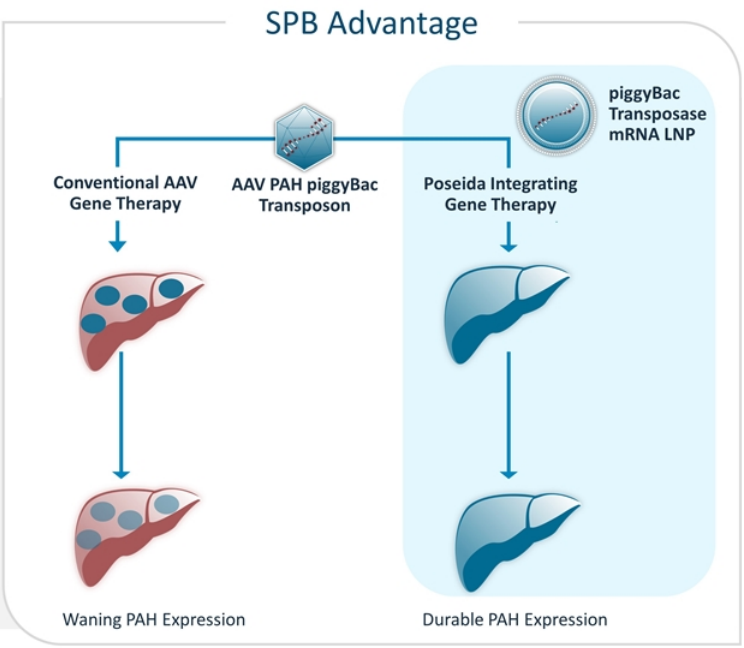
Mechanism



1. https://medlineplus.gov/genetics/condition/phenylketonuria/ 2. https://www.pku.com/about-pku/phe-in-the-brain

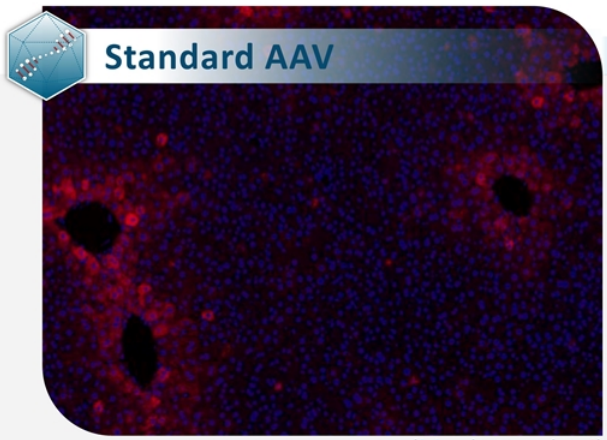
P-PAH-101 Aims to Transform Standard of Care for PKU

- AAV delivers therapeutic transgene, Phenylalanine hydroxylase expression cassette
- Biodegradable nanoparticle delivers SPB as mRNA
- SPB mRNA rapidly translated into protein and integration of PAH transgene into genome
- Significant increase in PAH transgene expression and distribution in liver compared to AAV alone
- Possibility of lifelong durability from integrated PAH transgene

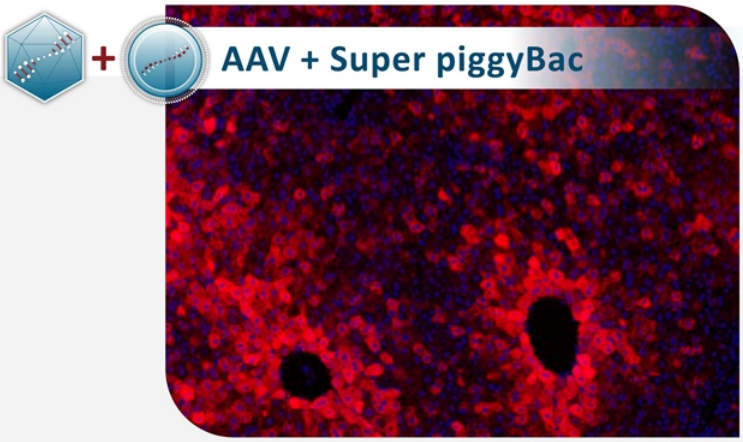


POSEIDA THERAPEUTICS

P-PAH-101 Delivers Superior Hepatocyte Transduction Over AAV



DAPI (**blue**), PAH (**red**)



DAPI (**blue**), PAH (**red**)

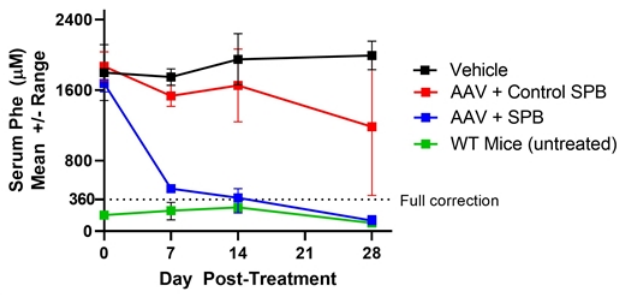
- Immunofluorescence: therapeutic PAH protein stained in red; cell nuclei (DAPI) stained in blue
- Adult wild type mice administered 3E12 vg/kg AAV +/- 0.5 mg/kg SPB-LNP
- Livers collected for analysis on day=14 post dosing

POSEIDA THERAPEUTICS

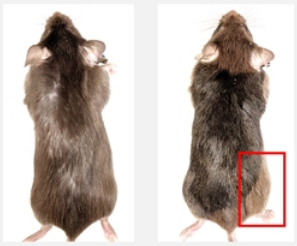
P-PAH-101 Resolved Disease in Adult Mouse Model of PKU

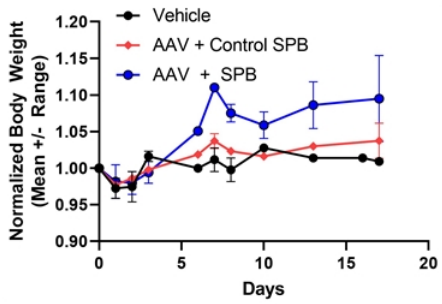
STUDY OVERVIEW

- Adult male Enu2 treated on day=0 of study by single IV dose
- AAV comprising PAH transposon co-administered with mRNA-LNP with functional SPB or inactive SPB (control)
- Low AAV dose (1E12 vg/kg)



AAV + SPB Treatment

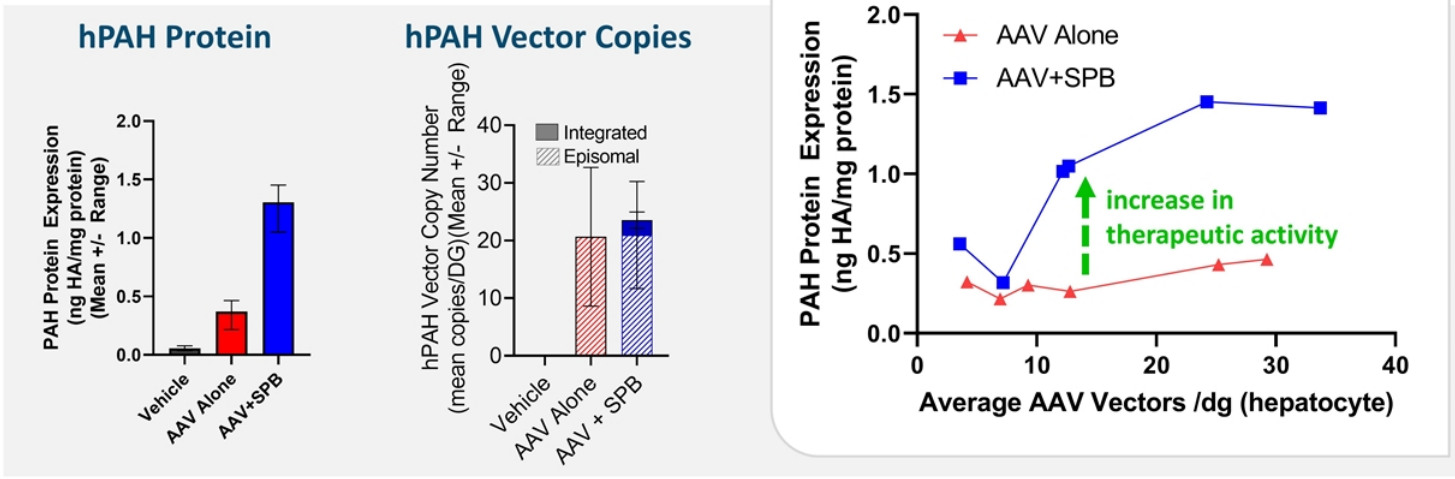




- Normalization of serum phenylalanine to wild type levels 14 days following single IV dose
- Reversion of fur color and increased weight gain over untreated and control animals

POSEIDA THERAPEUTICS

SPB-Mediated Integration Enables Efficacy at Lower AAV Doses



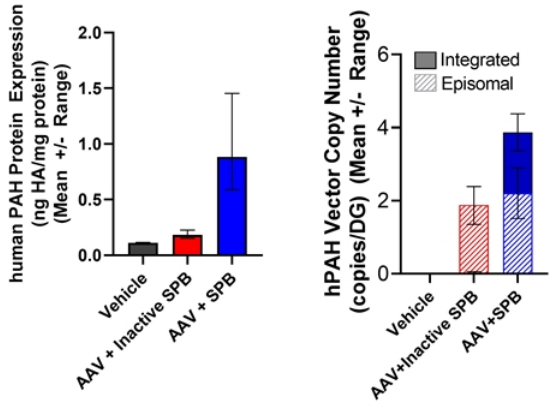
- Integration potentiates PAH transgene copies delivered by AAV in adult mouse model
- SPB hybrid system offers potential to significantly reduce AAV dose versus standard AAV therapies

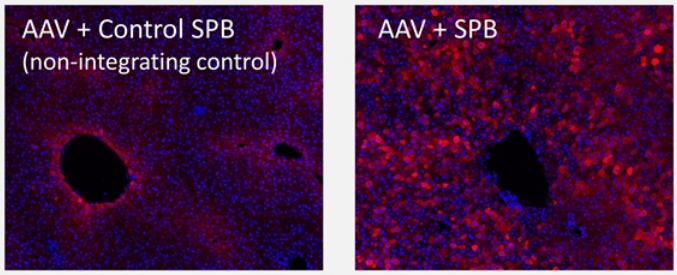
POSEIDA THERAPEUTICS

P-PAH-101 Demonstrates Potential to Treat Juvenile PKU Patients

STUDY OVERVIEW

- Juvenile mice treated on day=21 of life by IV single dose
- AAV comprising PAH transposon co-administered with mRNA-LNP with functional SPB or inactive SPB (control)
- Low AAV dose (1E12 vg/kg) with analysis 4 weeks post-treatment





SPB-mediated integration maintains PAH protein expression in juvenile setting

POSEIDA THERAPEUTICS

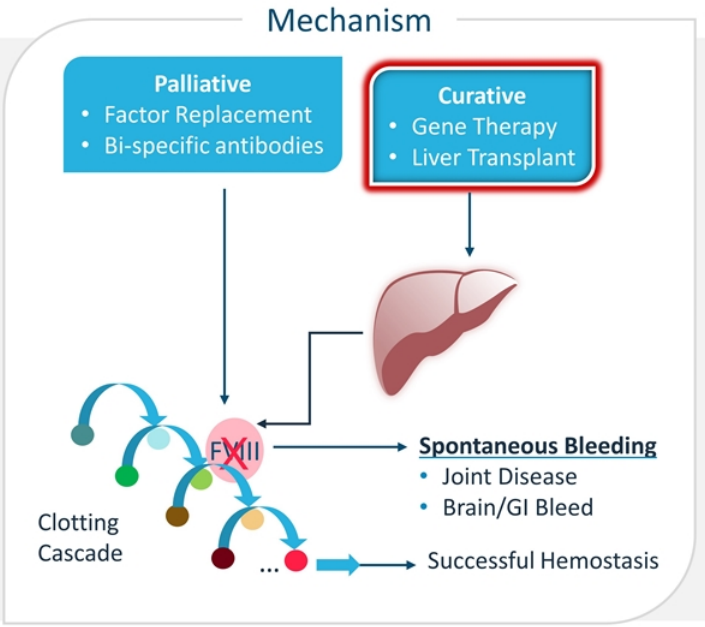
P-PAH-101: Summary and Key Takeaways

- P-PAH-101 (SPB LNP + AAV) demonstrates ability to rescue disease
  - Provides early proof of concept to deliver a functional cure for PKU
  - Demonstrates ability to reduce serum PHE to normal levels following a single IV dose
  - Highlights early ability to significantly reduce AAV titers versus standard AAVs
  - Improvements in additional biomarkers such as coat color
- Poseida's SPB mRNA LNP continues to demonstrate favorable profile
  - Consistent data across two hybrid programs with potential platform use
- Key next steps
  - Continue pre-clinical work on P-PAH-101 in collaboration with Takeda


P-FVIII-101
Partnered with Takeda
Jack Rychak, PhD
Vice President, Research and Development – GTx
POSEIDA
THERAPEUTICS

Hemophilia A is a Rare Disease Amenable to Gene Therapy

- X-linked bleeding disorder caused by deficiency in coagulation factor VIII
  - Large cDNA (~7.1 kb) and complex protein
- Severity of hemorrhagic episodes tends to correlate directly with the plasma FVIII concentration, majority of patients have severe disease (<1% FVIII activity)
- Gene Therapy has the potential to deliver functional cures for Hemophilia A, however, current solutions only treat a subset of patients:
  - Utilize Adeno-associated virus (AAV)
  - Inability to re-dose with current technology
  - Not appropriate for use in juvenile patients
  - Challenges with safety, toxicity and immunogenicity

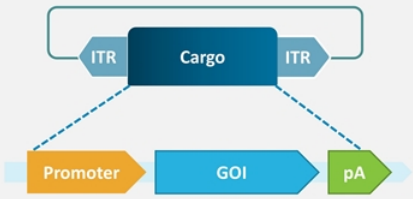


POSEIDA THERAPEUTICS

Non-viral SPB May Be a Highly Efficient System for Transposing Transgenes

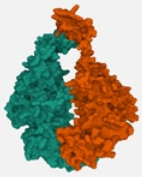
Co-delivery of Both Transposon and Transposase Required for Genomic Insertion

Transposon

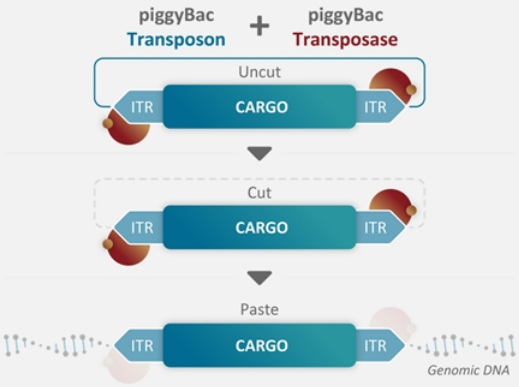


- Formulated as double-stranded DNA
- Cargo comprises promoter, gene(s) of interest (ORF), and regulatory elements

3rd Generation SPB Transposase



- Formulated as mRNA
- Transient expression is adequate for high-efficiency transposition; no concerns from persistent transposase expression



- SPB-mediated genomic insertion of genetic cargo to address early-onset genetic deficiencies

POSEIDA THERAPEUTICS

Lipid Nanoparticles Enable In Vivo Use of SPB for Gene Therapy

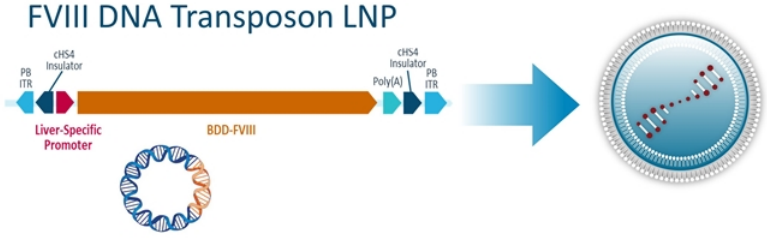
SPB Dual LNP Approach

hFVIII Transposon LNP

Super piggyBac Transposase LNP

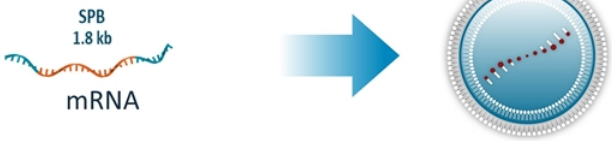
- Biodegradable lipid nanoparticles (LNPs) deliver SPB transposase and human FVIII (hFVIII) transposon (therapeutic transgene)
- Very large cargo capacity for SPB and LNP
- Stable integration of functional hFVIII gene into genome
- Durable hFVIII expression in growing liver
- Possibility of repeated dosing to efficacy

FVIII DNA Transposon LNP



Therapeutic Transgene (DNA)

SPB mRNA Transposase LNP

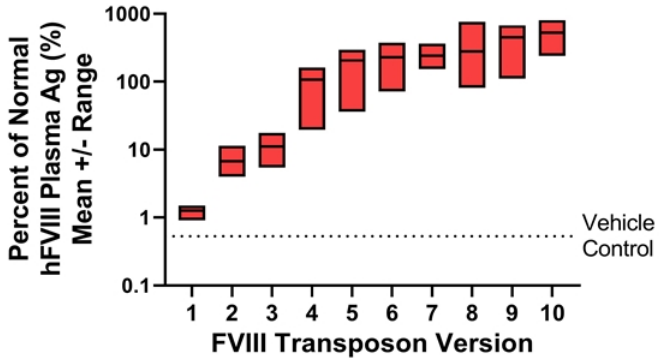


POSEIDA THERAPEUTICS

LNP Platform is Unconstrained by Cargo Capacity Limitations

- Panel of hFVIII transposons with variable promoter, UTR, coding sequence, and other regulatory elements (>7Kb)
- Transposons formulated as LNP
- Transposon LNP co-administered with SPB LNP as single dose IV to juvenile mice (n=5-7)
- hFVIII plasma levels measured by ELISA after 1 week

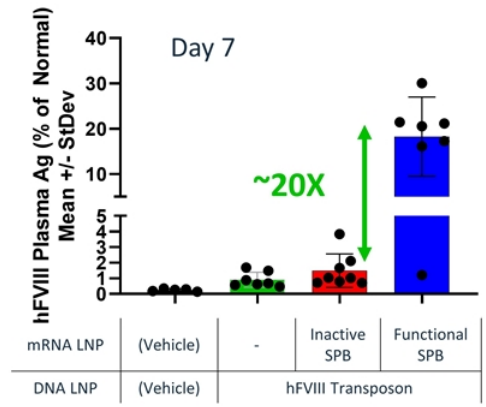
Optimization of hFVIII Sequence in Mice



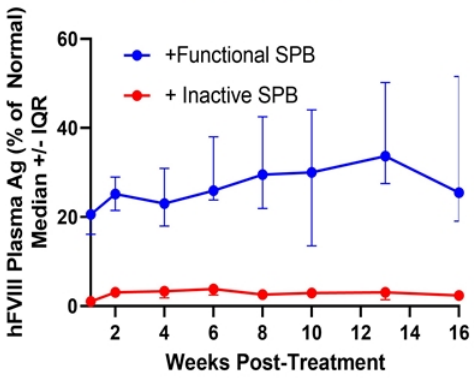
POSEIDA THERAPEUTICS

Durable FVIII Expression in Adult HemA Mouse With Single LNP Dose

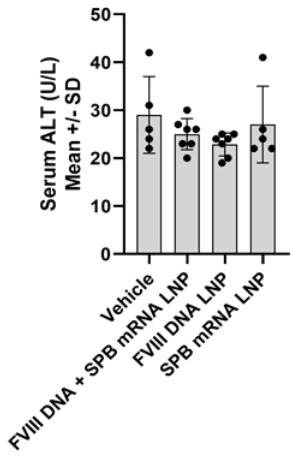
Significant Increase in hFVIII Expression Over Non-Integrating Control



Stable hFVIII Expression Over 16 Weeks



Liver Enzymes (17 Week)



LNP administered as single dose IV to adult mice deficient in FVIII and tolerized to human FVIII

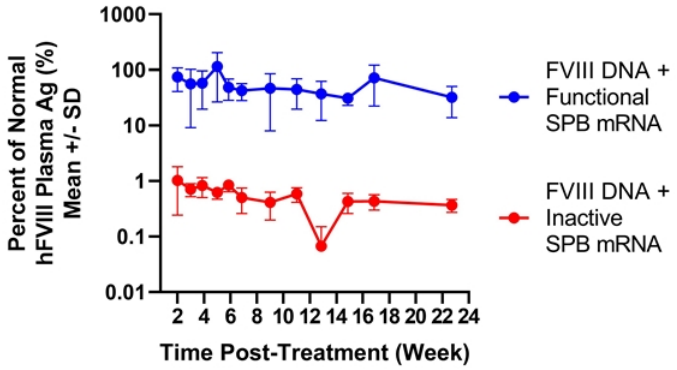
POSEIDA THERAPEUTICS

Favorable Durability Following Single Dose in Neonatal Mice

- Dual-LNP co-administered as single dose IV to neonatal (day 1 of life) BALB/c mice (n=6-9)
  - Transposon DNA-LNP: 0.25 mg/kg
  - Transposase mRNA-LNP: 1.0 mg/kg
- Human FVIII expression (protein concentration in plasma) measured by ELISA

RESULTS: Durable expression of human FVIII maintained over 5 months

FVIII Expression in Neonatal WT Mice



POSEIDA THERAPEUTICS

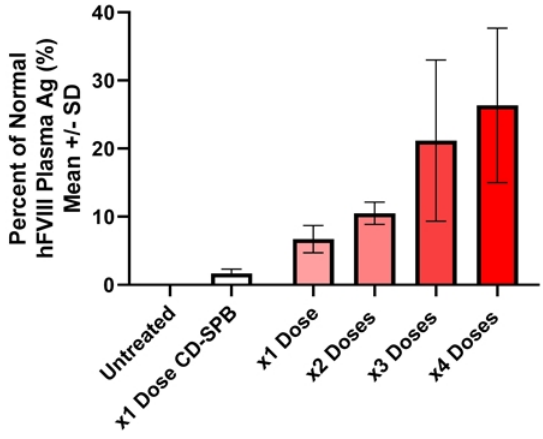
Non-Viral Nanoparticle Delivery System Facilitates Repeat Dosing

- Dual-LNP co-administered as single dose IV to adult (10wk) BALB/c mice on day 0, 3, 8, and 10
  - Transposon DNA-LNP: 0.25 mg/kg
  - Transposase mRNA-LNP: 0.5 mg/kg
- hFVIII plasma levels measured by ELISA on day 13

RESULTS:

- Dose-proportional increase in hFVIII antigen level was observed
- Data supports concept of repeat dosing of non-viral piggyBac system

FVIII Expression in Adult WT Mice



POSEIDA THERAPEUTICS

P-FVIII-101: Summary and Key Takeaways

- A non-viral, liver-specific gene therapy utilizing SPB achieved and sustained normalized (>50%) hFVIII activity following a single dose
  - Demonstrated repeat dosing, indicating potential for dose titration in mice
  - Delivered therapeutic FVIII activity in mice following single and repeat doses
  - Durability observed at least 6 months following a single dose in mice
- Data establishes proof of concept for treating Hemophilia A across all ages, which could lead towards a functional cure
- Key next steps:
  - Continue pre-clinical work on P-FVIII-101 in collaboration with Takeda


GTx Emerging Technology
Blair Madison
Chief Scientific Officer – GTx
POSEIDA
THERAPEUTICS

Robust Platform Technologies Supporting Our GTx Pipeline Programs

Current Platforms

Super piggyBac® (SPB)		Non-viral transposon gene insertion technology
SPB Hybrid AAV + LNP		Gene insertion technology utilizing AAV as DNA donor
Lipid Nanoparticles (LNP)		Proprietary lipid nanoparticles built to deliver DNA
Cas-CLOVER™		High fidelity gene editing system for knock-out / knock-in
Site-Specific Super piggyBac® (ssSPB)		Next generation programmable gene targeting/editing system

Current Programs

P-OTC-101 SPB Hybrid AAV + LNP Poseida Owned	• Pre-clinical program • Capsid / construct selected • Finalizing pathway to IND • New data presented today
P-PAH-101 SPB Hybrid AAV + LNP Partnered with Takeda	• New pre-clinical program • New data presented today
P-FVIII-101 SPB Non-viral Partnered with Takeda	• Pre-clinical program • Data presented at ASH 2022 • Best of ASH 2022 selection • New data presented today

Future Pipeline

Liver Directed Knock-out
Cas-CLOVER

Liver Directed Metabolic Disease
SPB Non-viral

POSEIDA THERAPEUTICS

Emerging Platform Technologies

Non-viral LNP Delivery Platform

- Proprietary in-house nanoparticle technology
- For delivery of RNA and/or DNA
- Includes biodegradable ionizable lipids
- Coupled with optimized nucleic acid formats for maximal efficacy
- Enables delivery to neonatal liver, where SPB excels

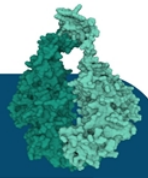
GENE DELIVERY

Cas-CLOVER™

- Highly precise site-specific nucleases[1]
- Ability to edit human and mouse hepatocytes with high efficacy
- Major advantages:
  - Tolerability
  - Ease of design
  - Low cost
  - Multiplexing ability

GENE EDITING

Site-specific Super piggyBac



- In-house proprietary site-specific genome targeting platform
- Programmable to integrate at specific sites, while maintaining core SPB advantages:
  - Active in non-dividing cells
  - Large cargo capacity
  - No/little DNA DSBs
  - Reversible & scarless

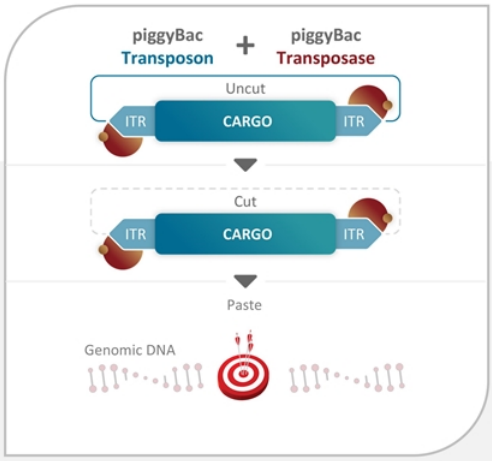
GENE INSERTION

1. Madison et al., Molecular Therapy – Nucleic Acids, 2022. (https://www.sciencedirect.com/science/article/pii/S216225312200155X)


Site-Specific Super piggyBac
Blair Madison
Chief Scientific Officer – GTx
POSEIDA
THERAPEUTICS

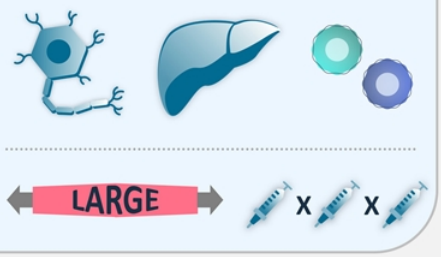
Programmable Editing Platform With Site Specificity

What Advantages Would Site-specific piggyBac Provide Over CRISPR Knock-ins?



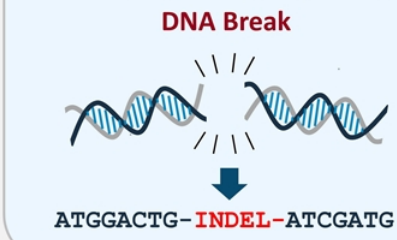
ssSPB Advantages

- Active in non-dividing cells
- Large cargo capacity
- Simple 2-component system
- Re-dosable, reversible[1], scarless[1]



CRISPR Challenges

- Double-strand breaks[2]
- DNA repair needed[3]
- Unintended mutations[4]
- Irreversible (one shot)[2-4]



1. Yusa et al. *Proc Natl Acad Sci U S A.* 2011; 2. Jinek et al., *Elife.* 2013; 3. Cong et al., *Science.* 2013; 4. Ran et al., *Cell.* 2013

Developing Site-specific Transposition With ssSPB

GENOME
- Desirable
- Less Desirable
- Intended target

Super piggyBac (SPB)

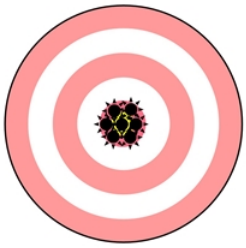
Desirable profile but not site-specific

External Attempts to Make Site-specific SPB[1-7]

3-5-fold
Greater site-specificity

POSEIDA THERAPEUTICS

Site-specific SPB

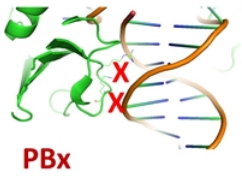


>500-fold
Greater site-specificity

1. Maragathavally, K. J., et al., *FASEB J.* 2006 2. Wang, W., et al., *PNAS* 2008 3. Kettlun, C., et al., Mol Ther. 2011 4. Owens, J.B., et al., *Nucleic Acids Res.* 2012
5. Li, X., et al., *PNAS* 2013 6. Owens, J.B., et al., *Nucleic Acids Res.* 2013 Ye, L., et al., *Sci Rep.* 2015 7. Hew, B.E., et al., *Synth Biol* 2019

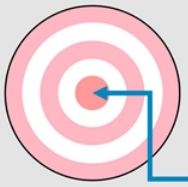
PBx Rescue Swaps Non-Specific With Specific DNA-Binding

Rescuing PBx Integration-Defective Transposase



Excision ✓

No Integration



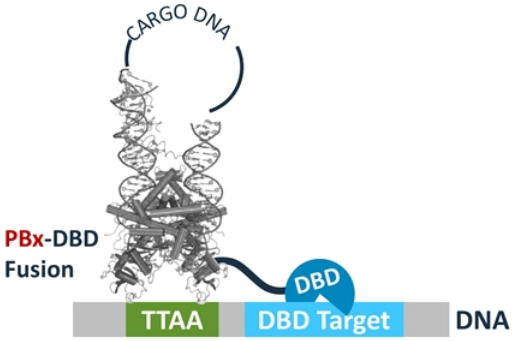
− Non-specific binding

+ Specific binding

Bind only here

Remove Non-specific Binding

- Fuse sequence-specific DBD to PBx
- PBx enables low/no off-target background



Our Strategy

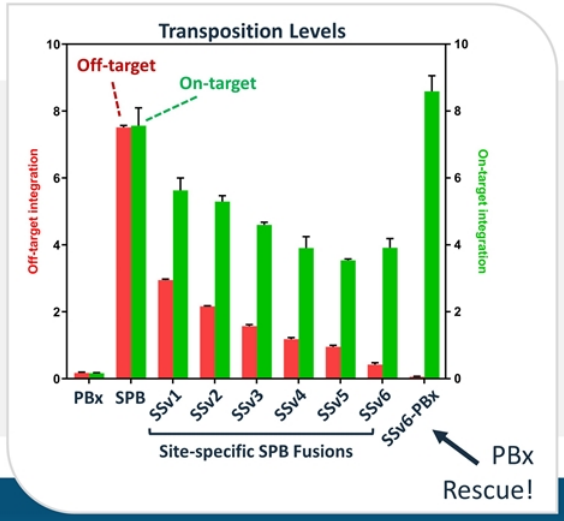
- Exploit structure data
- Computational modeling
- Iterative screen
- Pursue rescue of PBx

POSEIDA THERAPEUTICS

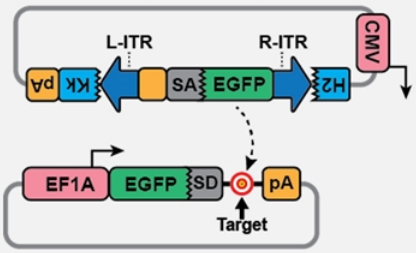
Our Strategy Yields Rescue of Excision-Only PBx

Our Strategy

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



Split GFP Episomal Site-specific Reporter



Results:

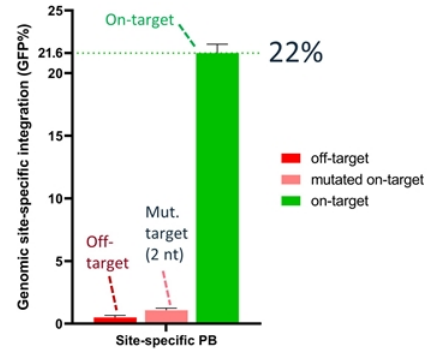
1. First demonstrated rescue of integration-defective PBx mutant
2. Unprecedented level of site-specificity: >500-fold
3. Data here are from un-optimized SPB fusion protein

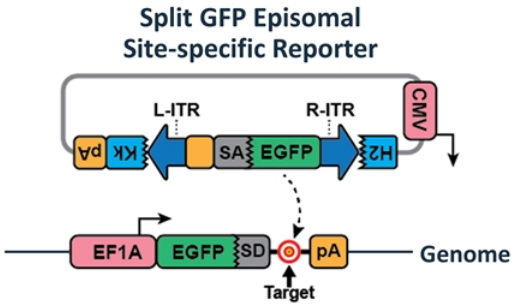
POSEIDA THERAPEUTICS

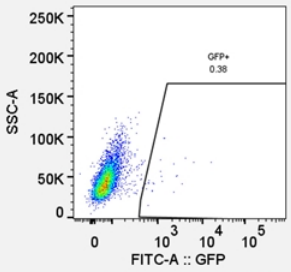
First Generation ssSPB Yields Site-specific Transposition into Genome

Genomic Target

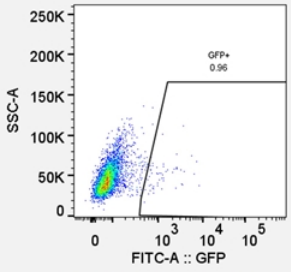
- Synthetic reporter delivered via lentivirus in HEK293T
- Site-specific delivery reconstitutes split GFP reporter
- Over 20% of cells GFP+



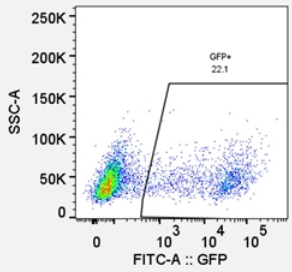




off-target TTAA site



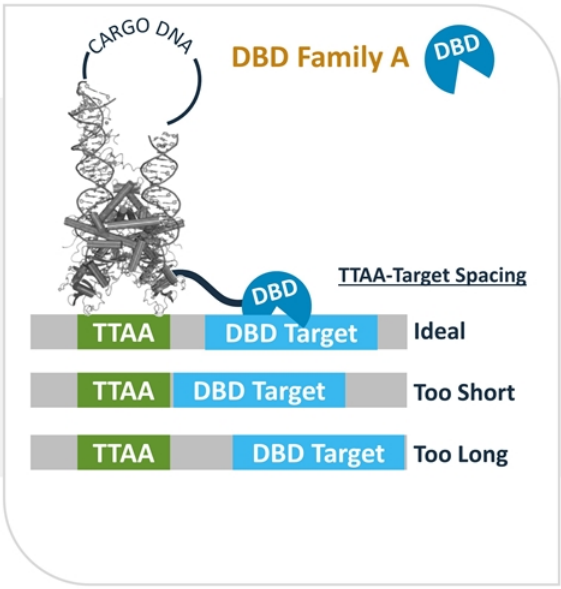
mutated on-target TTAA site

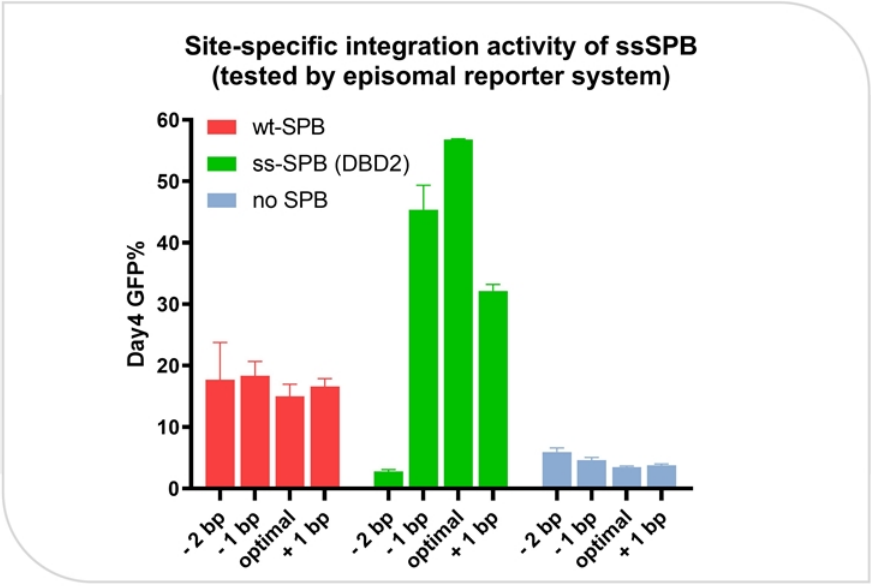


on-target TTAA site

POSEIDA THERAPEUTICS

Fine Tuning Identifies Ideal Spacing Between DBD Target and TTAA

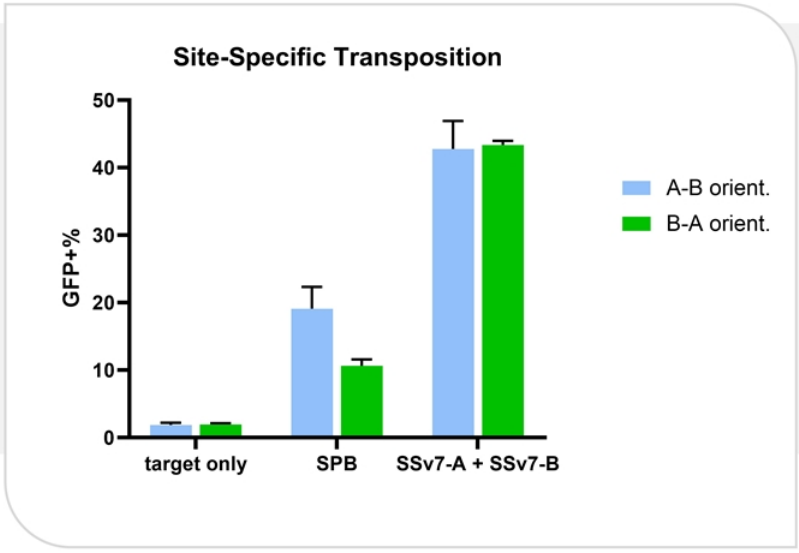


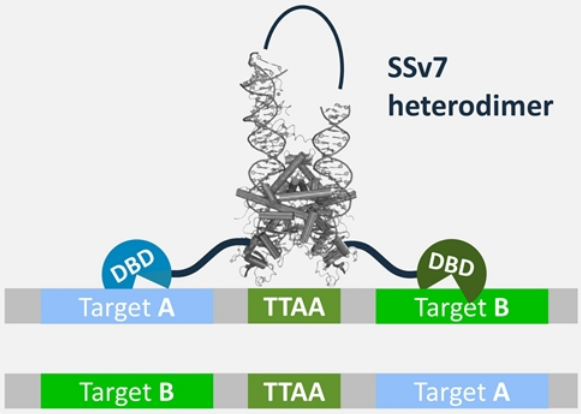


POSEIDA THERAPEUTICS

ssSPB Functions as Heterodimer for Bipartite Targets

Non-palindromic Targets Validated With Heterodimeric ssSPB: Yields ~40% GFP+





- High efficiency maintained as heterodimer
- GFP episomal reporter in HEK293T

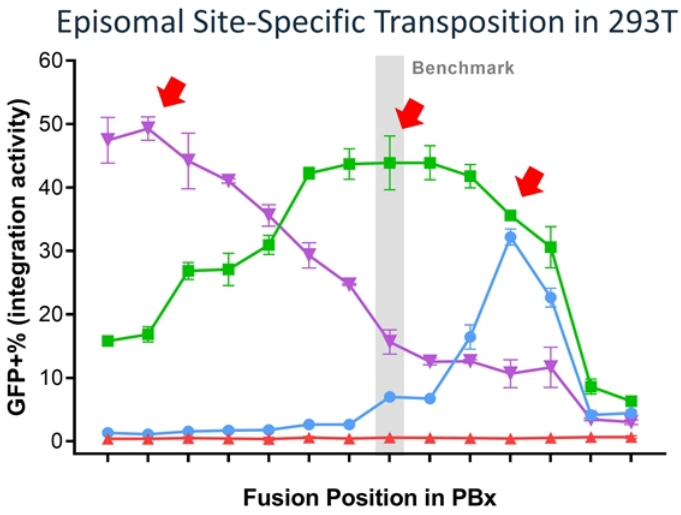
POSEIDA THERAPEUTICS

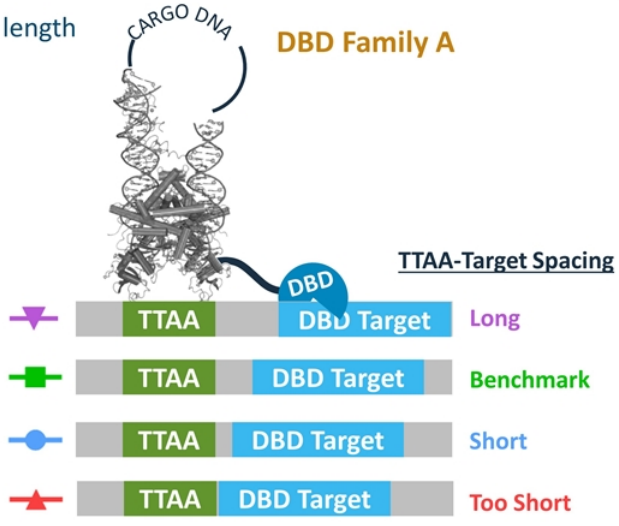
Varying Spacing and Fusion Location Reveals 3 Ideal Combinations

Alternative Fusion Designs Expand Targeting Range of Family A ssSPB

Design Trend Identified

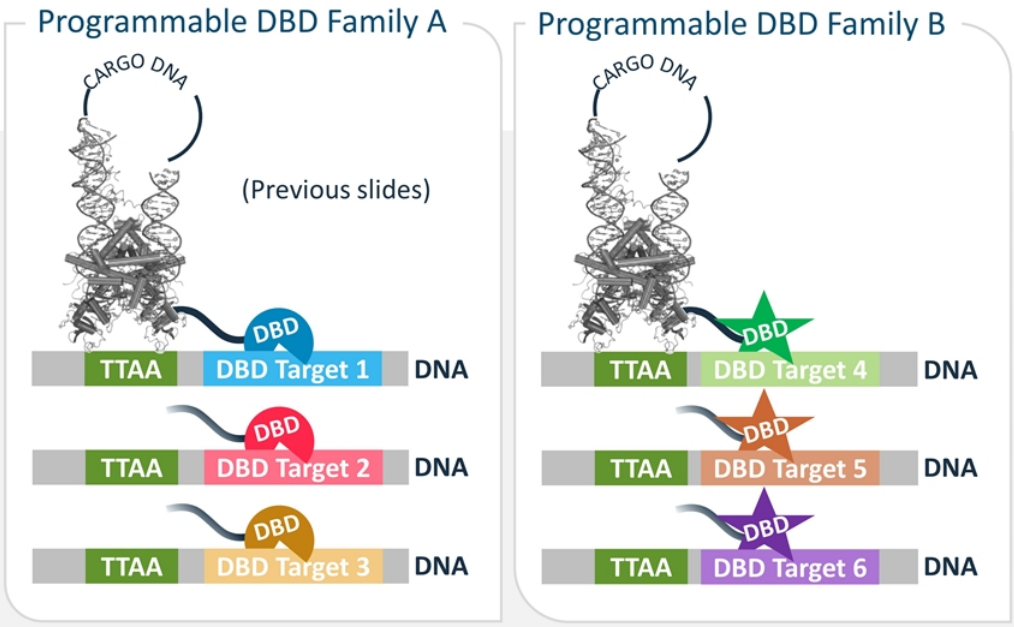
Correlation between PBx fusion site and TTAA-DBD target spacer length





POSEIDA THERAPEUTICS

Expanding The Programmability of ssSPB With Additional DBD Family



Wide Range of Targetable Sequences

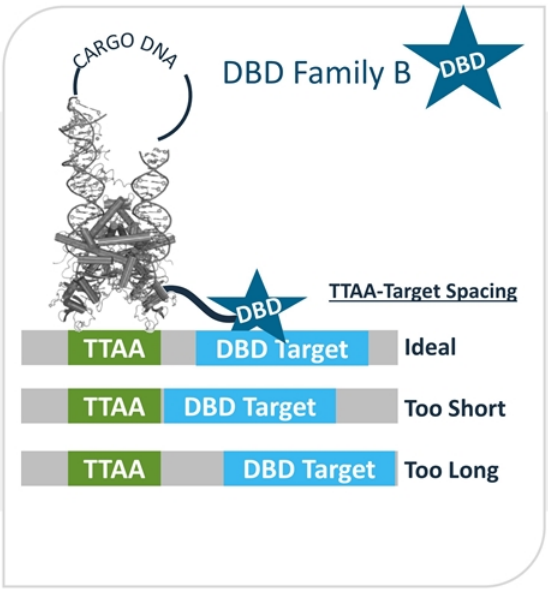
- Rational design used to generate ssSPB with distinct families of programable DBDs
- Distinct DBD families prefer sequences with different characteristics (e.g., GC content)
- Greatly expands range of sites that can be targeted

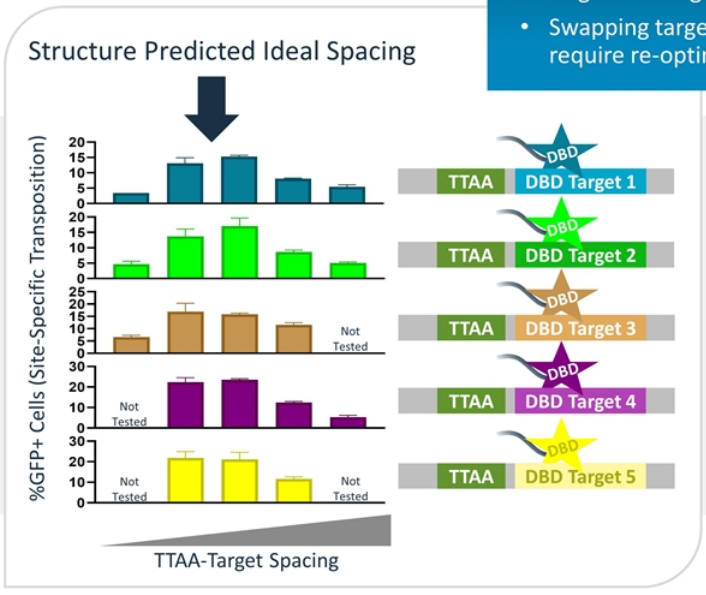
POSEIDA THERAPEUTICS

Plug and Play Programmability With ssSPB

Consistent and Predictable

- Consistent spacing between DBD binding site at TTAA makes target ID straight-forward
- Swapping target sites doesn't require re-optimization

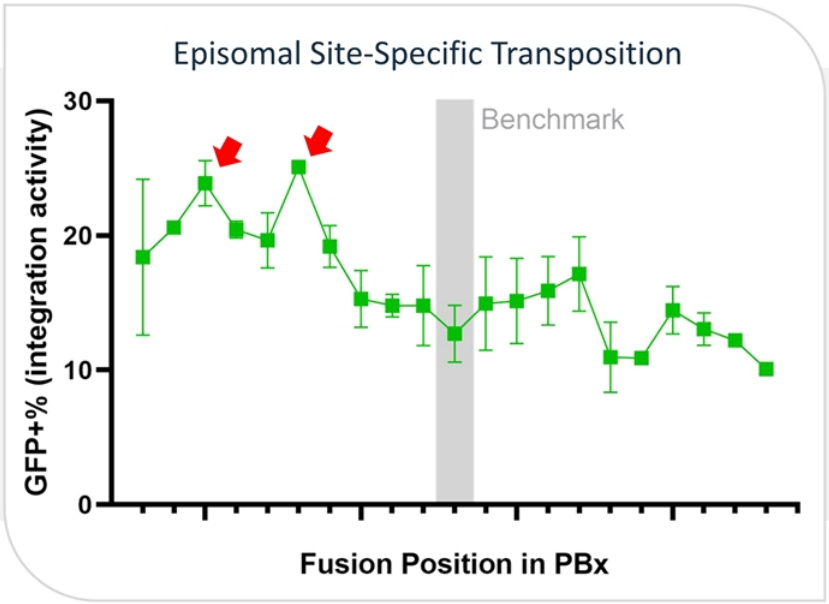




POSEIDA THERAPEUTICS

Varying Spacing Reveals Enhanced Activity of ssSPB

Fine-Tuning the PBx Fusion Position with DBD-B

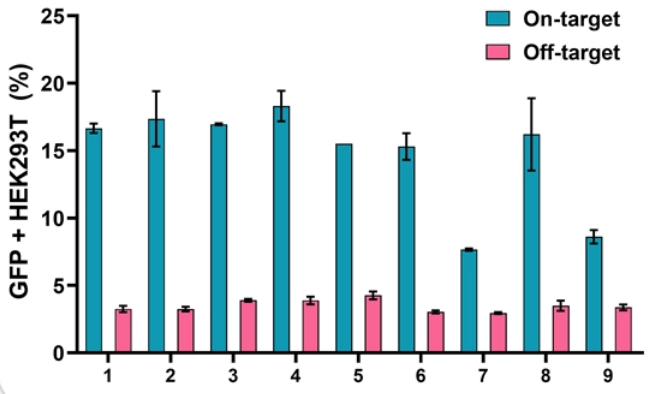


Room For Improvement on Fusion Design

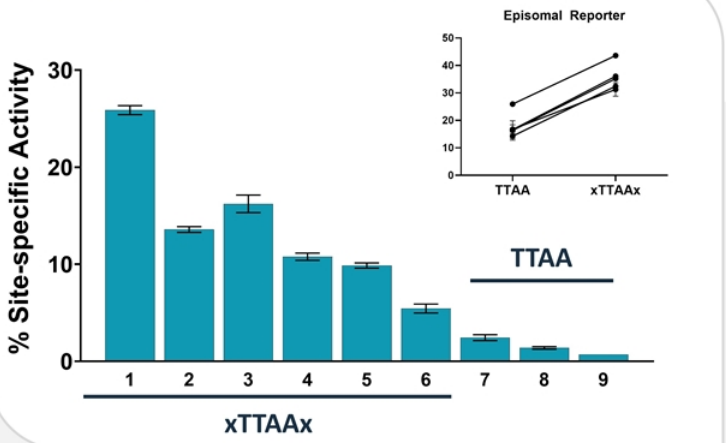
- Twenty additional fusion sites on PBx tested with our current target spacer length
- Several new fusions outperform benchmark
- Panel of new PBx fusions were tested with alternative target spacers

Robust Genome Editing Achieved at Tooling Site

Episomal Site-Specific Transposition



Genomic Site-Specific Transposition at Site-X



Robust site-specific transposition characterized:

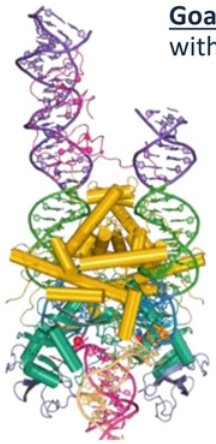
- High editing at target sites 1, 2, and 3
- ID'd xTTAAx as new feature for optimal target site

POSEIDA THERAPEUTICS

Approach: Alter Interactions With DNA to Enhance Transposition

Titrating Activity For Optimal Integration, Without Compromising Fidelity

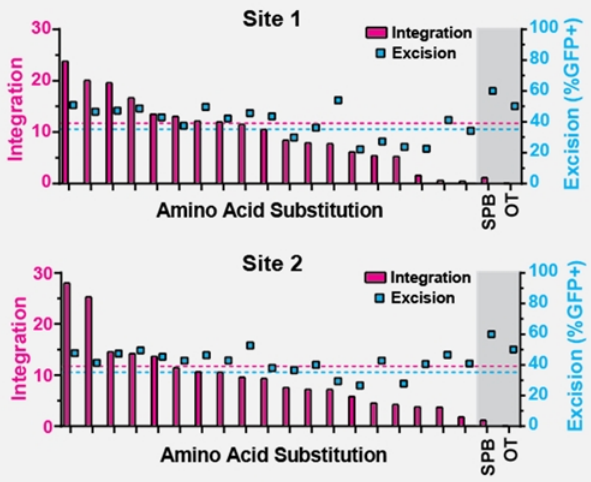
SPB Structure-Based SSM



Goal: Boost on-target integration without increasing off-target events

Strategy:

- Site-saturation mutagenesis
- Multiple positions targeted within SPB



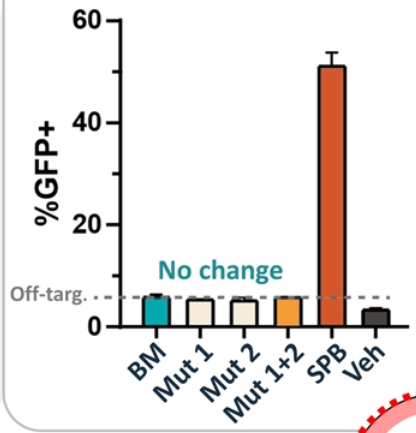
- 6 mutants increase site-specific integration (episomal)
- Tested a subset of hits for genomic DNA editing

POSEIDA THERAPEUTICS

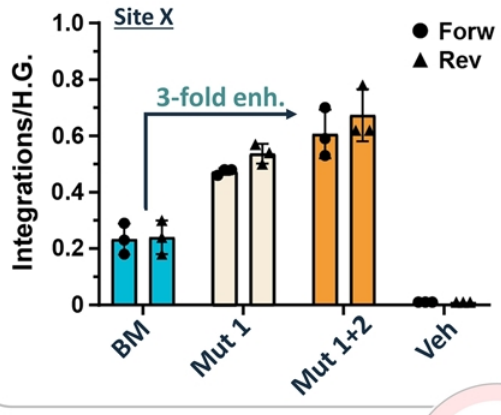
Success: Altering Interactions With DNA Enhances Transposition

Mutations That Enhance Integration Preserve Fidelity

Off-target/Random Integration

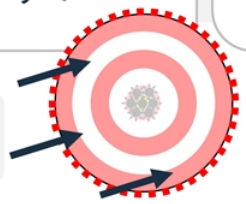


On-Target Genomic Integration (ddPCR)



1. Mutations assessed for effects on random (off-target) integration
2. Evaluate genomic on-target integration
3. Two mutations <u>increase</u> integration without raising off-target rate

1st, check off-target rate



2nd, check on-target rate

POSEIDA THERAPEUTICS

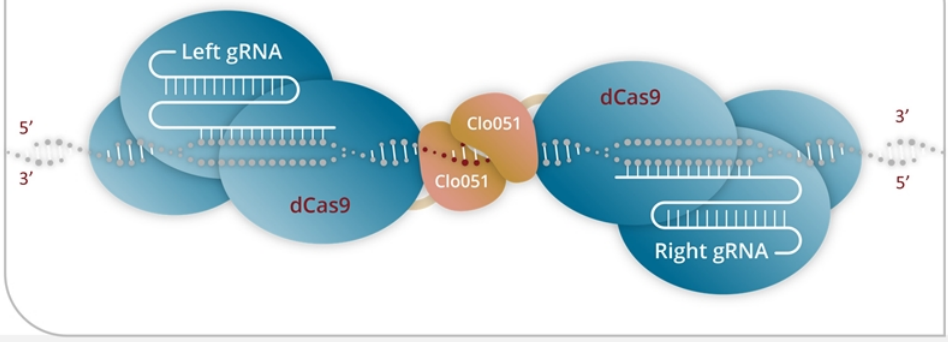
ssSPB: Summary and Key Takeaways

- Site-specific transposition attained an impressive rate with up to 60% of haploid genomes
- Specific context at TTAA reveal key features for enhanced transposition
- Optimization reveals new favorable fusion locations within PBx
- Enhancing integration is attainable without increasing off-target integration
- Key next steps:
  - Transitioning to other cells: integration beyond tooling cell lines (293T, K562, HepG2)
  - Stacking: optimizations proving fully stackable, with even some synergy
  - Dimer/transpososome modifications: 3 strategies in progress


Liver-Directed Gene Editing and Insertion with Cas-CLOVER™
Oscar Alvarez
Associate Director, Genetic Engineering
POSEIDA THERAPEUTICS

Cas-CLOVER: Clean Gene Editing

Cas-CLOVER Gene Editing System



- Low-to-no off-target cutting
- Ease of use/design
- Multiplexing ability
- High specificity
- Lower potential costs
- High efficiency editing in liver (>80% with Poseida LNPs)
- Greater knock-in rate than Cas9

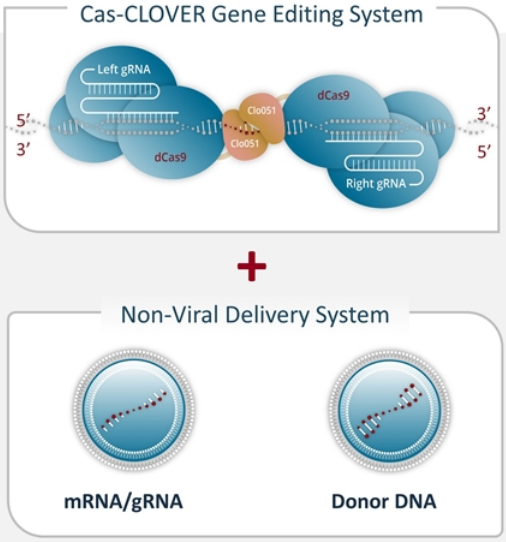
Potentially the Cleanest Gene Editing Platform

- Extensively vetted for off-target effects in peer-reviewed publication[1]
- Key ability to efficiently edit single or multiple genes
- Fully non-viral approach for *in vivo* gene editing
- Diverse toolbox of variants for expanded targeting (e.g., PAM diversity)

1. Madison et al., Molecular Therapy – Nucleic Acids, 2022. (https://www.sciencedirect.com/science/article/pii/S216225312200155X)

Combining Poseida Platforms to Enable Potentially Curative Therapies

Advantages of Fully Non-viral Cas-CLOVER for In Vivo Gene Therapies



- High fidelity
- High editing efficiency
- Multiplexing ability
- Multiple payload delivery
- Transient mRNA expression
- Low immunogenicity
- Redosing capability
- Delivery to multiple tissues

Knock-out

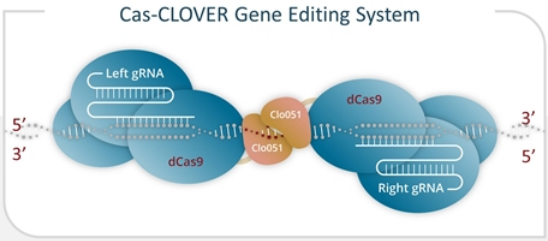
- Precise editing of single or multiple genes
- Disruption of dysfunctional genes to reduce disease severity

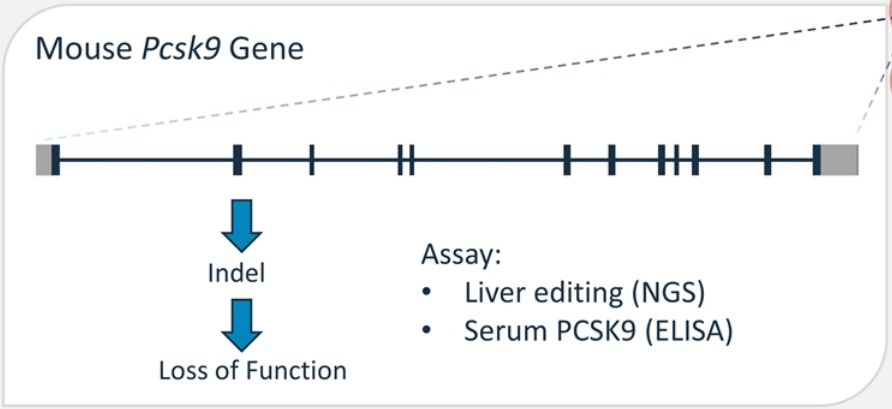
Knock-in

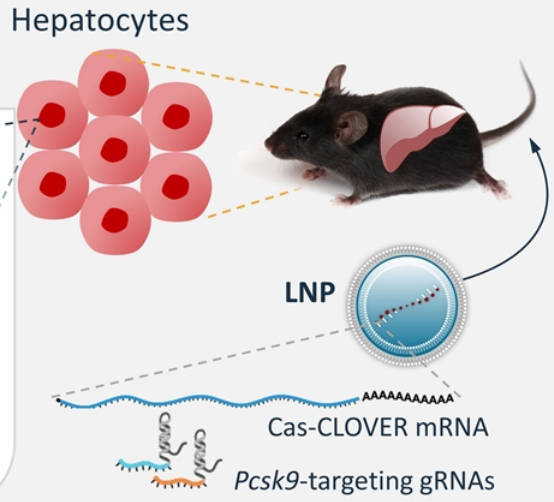
- Site-specific integration of a therapeutic transgene
- Functional disease correction

POSEIDA THERAPEUTICS

PCSK9 Knock-out Use to Demonstrate Cas-CLOVER Editing in Liver







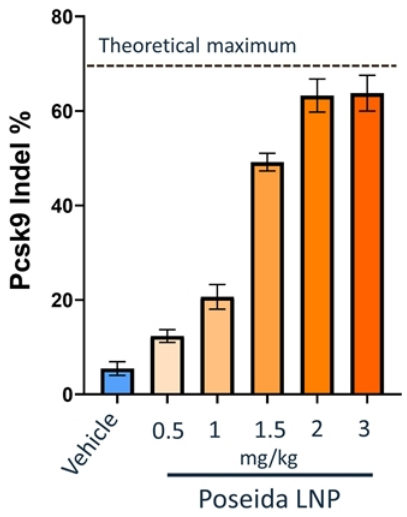
POSEIDA THERAPEUTICS

Efficient Cas-CLOVER Delivery and Editing in Mouse Liver

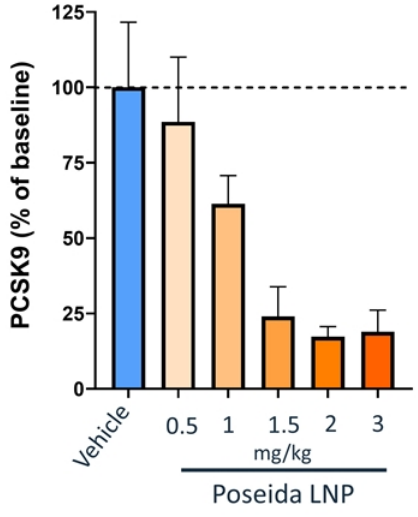
Cas-CLOVER in vivo liver editing with high efficiency

- Cas-CLOVER mRNA and gRNAs were delivered using Poseida proprietary LNP
- Clear dose response effect
- Poseida LNP efficacy is maximal at 2 mg/kg **(65% indels**)
- **>80-85%** decrease in PCSK9 protein with doses >1.5 mg/kg

DNA Editing (NGS)



Protein Serum Levels



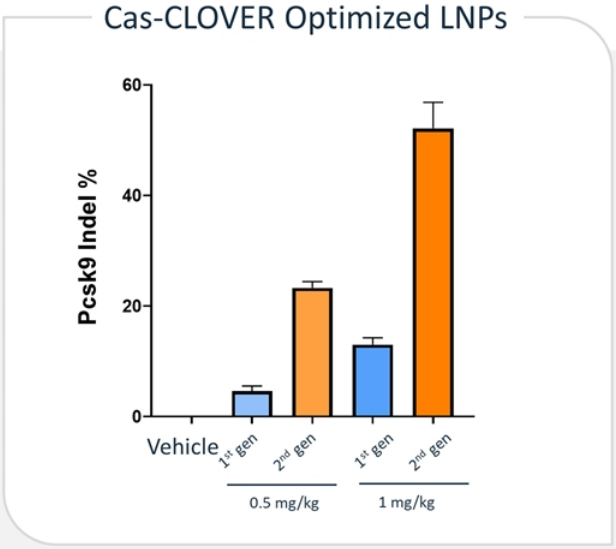
POSEIDA THERAPEUTICS

2nd Generation Cas-CLOVER LNPs Boost Editing by 4-fold

More potent LNP Enable Lower Doses While Maintaining Efficacy

Cas-CLOVER LNP process optimization:

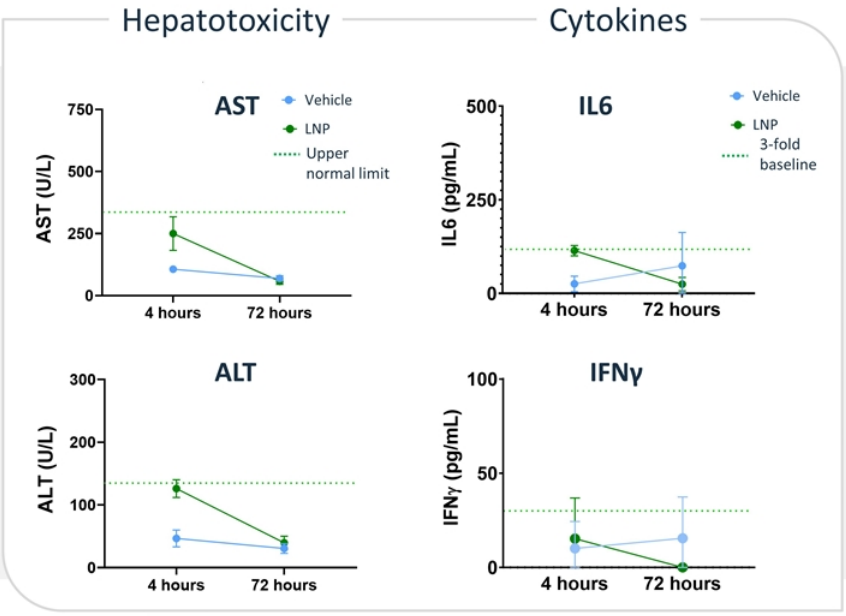
- 1st generation LNP
- 2nd generation LNP
  - Cas-CLOVER protein engineering
  - mRNA chemical and sequence optimization
  - gRNA chemical enhancement
  - Optimal mRNA/gRNA ratios
  - Optimized lipid composition



Cas-CLOVER Lipid Nanoparticles Have Favorable Toxicity Profile

Cas-CLOVER LNPs very low hepatotoxicity / immunogenicity

- Liver enzyme levels (AST/ALT) in serum after dosing are maintained within normal range
- Minimal elevation of IL6 and IFNγ serum levels after dosing that resolves within 72 hours



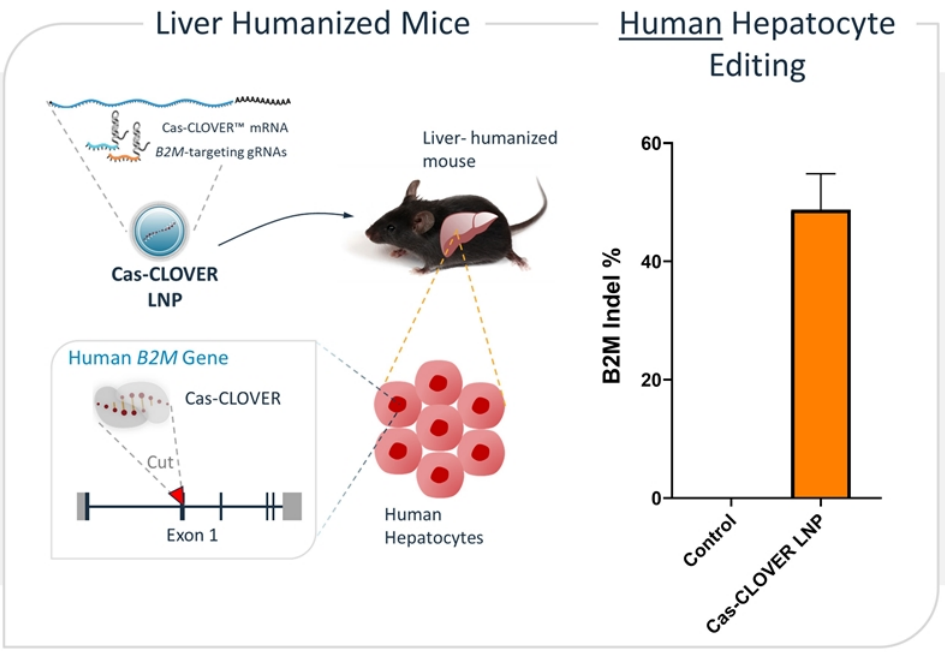
2 mg/kg RNA/LNP

POSEIDA THERAPEUTICS

Cas-CLOVER LNPs Enable Editing of Human Hepatocytes In Vivo

Cas-CLOVER edits human hepatocytes in mouse model

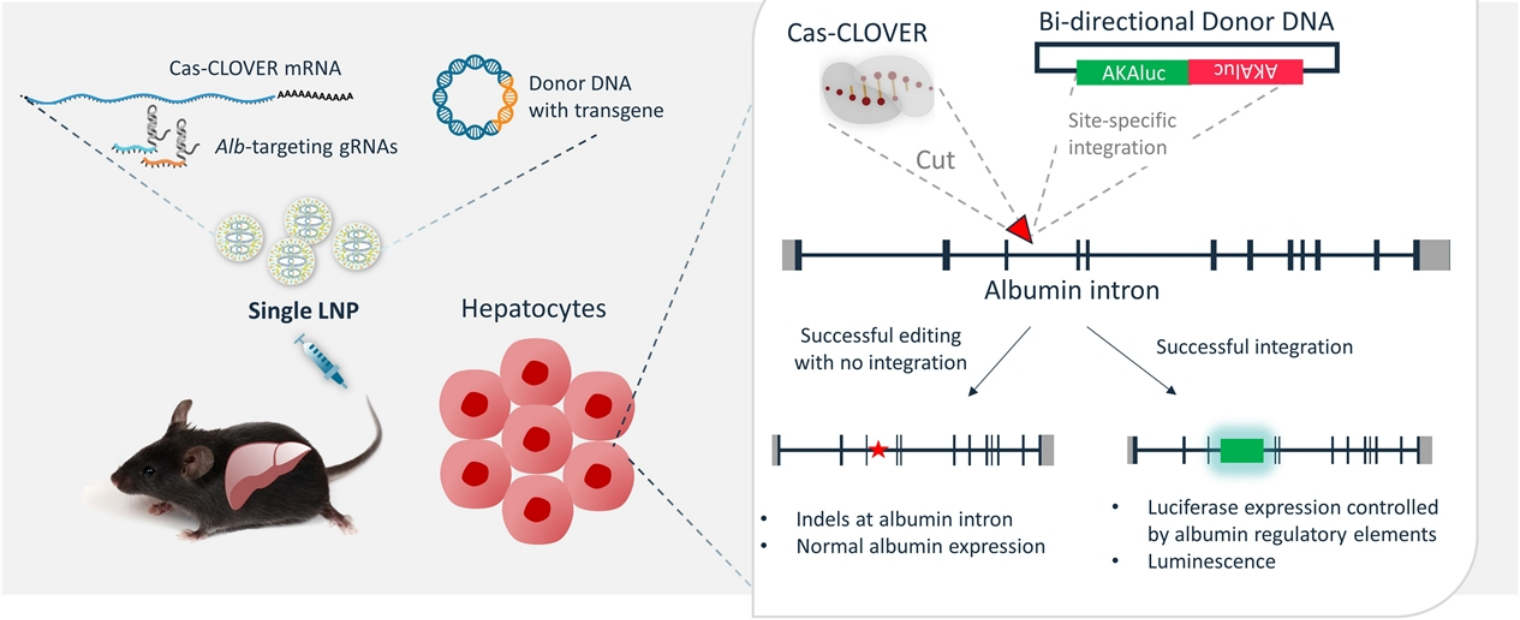
- Mice with **humanized-liver** (TK-Nog) were treated with a single injection Cas-CLOVER LNP targeting human *B2M*
- Treated mice show successful editing of *B2M* exon 1 – **45-50% indels by ddPCR (human-specific)**



POSEIDA THERAPEUTICS

Strategy for Cas-CLOVER Site-Specific Transgene Integration in Liver

Cas-CLOVER for Donor DNA Integration at Alb

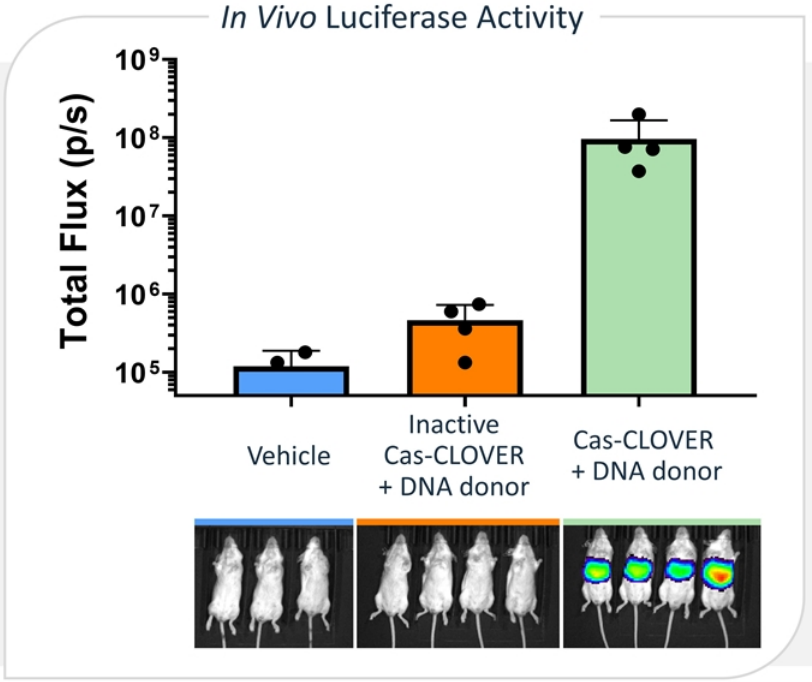


POSEIDA THERAPEUTICS

Non-viral Cas-CLOVER Achieves Site-Specific Integration / Expression

Cas-CLOVER enables precise genomic integration of large transgenes in vivo

- Fully non-viral delivery of Cas-CLOVER mRNA, gRNAs, and donor DNA using Poseida proprietary LNP
- Robust luciferase signal persisted > 3 mo
- Expression dependent on Cas-CLOVER activity
- Molecular analysis confirmed site-specific integration at albumin intron



POSEIDA THERAPEUTICS

Cas-CLOVER: Summary and Key Takeaways

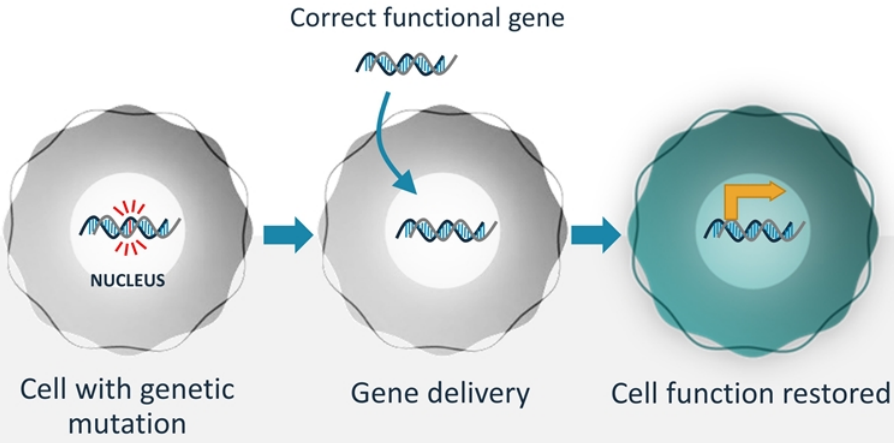
- Cas-CLOVER for site-specific non-viral knockouts
  - Cas-CLOVER is delivered using Poseida's proprietary biodegradable mRNA LNP
  - Gene editing efficiency (>60%) and protein reduction (~85%) at PCSK9 locus is approaching the theoretical maximum following single injection
  - Cas-CLOVER enables gene editing in human hepatocytes *in vivo*
- Cas-CLOVER for site-specific non-viral knock-ins
  - Fully non-viral delivery of Cas-CLOVER and donor DNA enables site-specific transgene integration in liver
- Key next steps:
  - Development of potential disease-specific gene knock-out pipeline programs
  - Continue optimization of site-specific integration platform


Non-viral Delivery Platform
Alex Schudel
Research Scientist II – GTx
POSEIDA
THERAPEUTICS

Delivering DNA is Necessary for High Impact Gene Therapy

DNA Gene Therapy

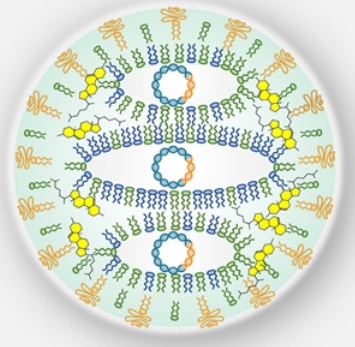
- Need to deliver DNA to nucleus for:
  - Function (transcription)
  - Genome integration (for stability)
- AAV and other viral-enabled systems have performed well, but are limited
- Non-viral delivery has benefits:
  - Repeat dosing feasibility
  - Large transgene cargo
  - Durability with integration



POSEIDA THERAPEUTICS

LNPs Use Several Lipid Types to Efficiently Encapsulate Nucleic Acid

LNP Structure



Lipid nanoparticle (LNP) encapsulating nucleic acid

Formulation Composition

Cargo

Nucleic acid

Helper Lipids

Cholesterol

PEG Lipid

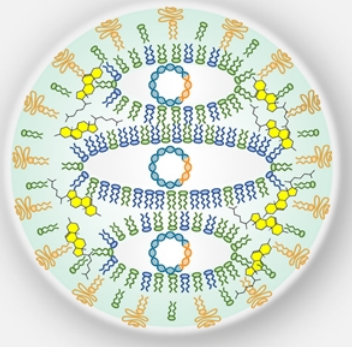
Structural Lipid

Cationic Lipid

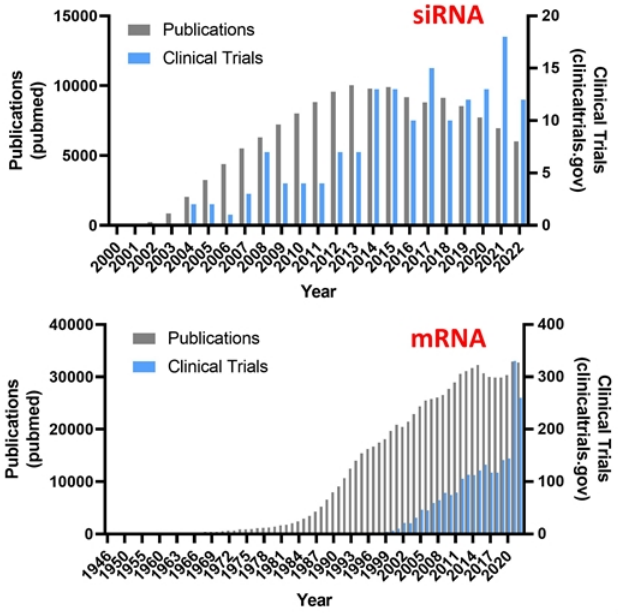
Ionizable lipid

LNPs Are a Mature Nucleic Acid Delivery Platform (mRNA, siRNA)

LNP Structure



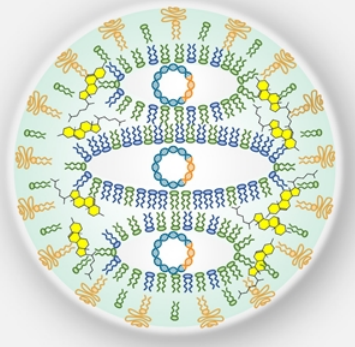
Lipid nanoparticle (LNP) encapsulating nucleic acid



1. Publication data from pubmed.gov, clinical trial data from clinicaltrials.gov; keywords "siRNA" or "mRNA"

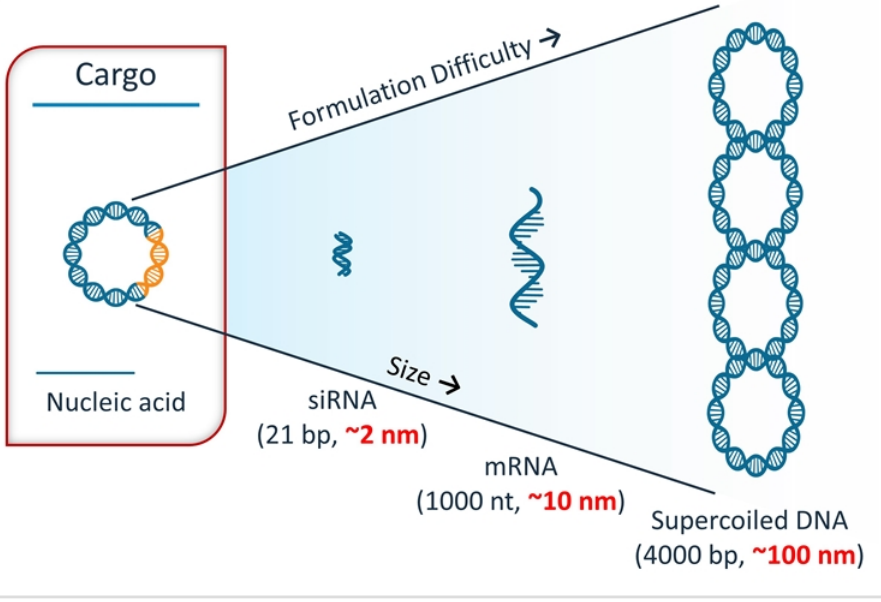
DNA is a Formulation Challenge for LNPs Due to Large Size

LNP Structure



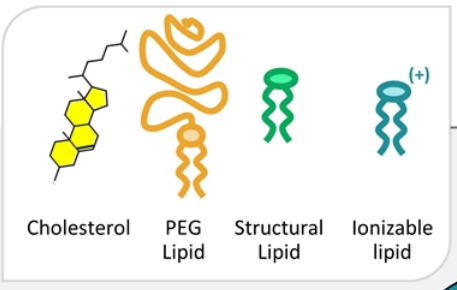
LNP
(**~80-120 nm**)

Size Scale of Nucleic Acid: siRNA → mRNA → DNA

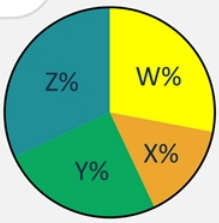


POSEIDA THERAPEUTICS

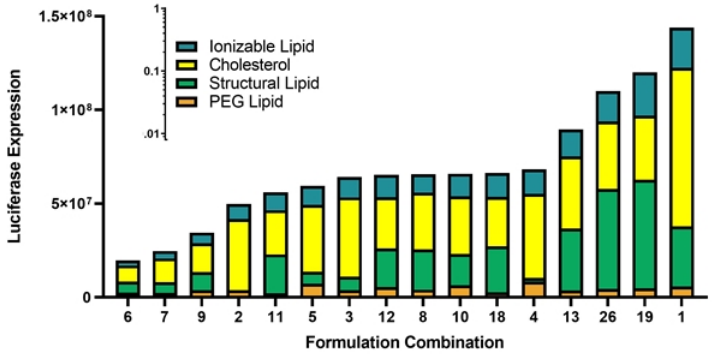
LNP Formulations Can be Optimized For DNA Delivery



Complexity of LNPs:
Compositional diversity by varying 4 key components



Novel Lipid Formulation Discovery



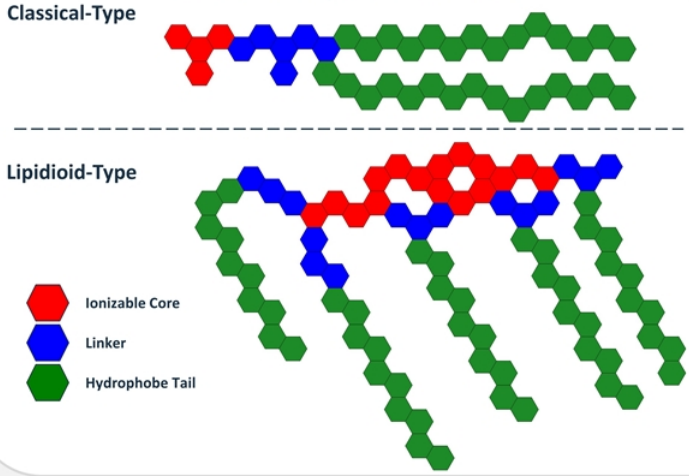
LNP-Mediated DNA Delivery using Design of Experiments

This mathematical approach is the same for making LNPs for siRNA and mRNA and doesn't require new technology

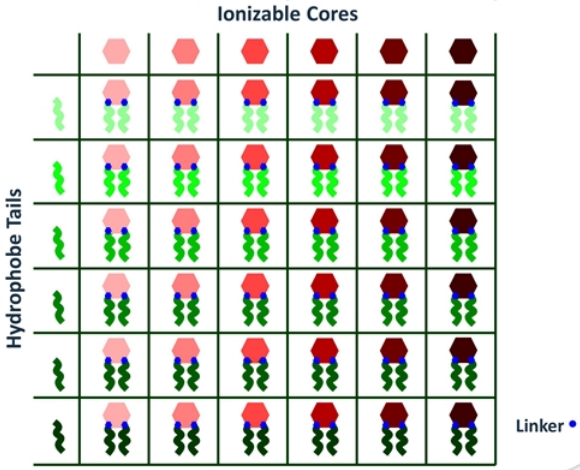
POSEIDA THERAPEUTICS

We Have the Capability of Designing a Wide Array of Lipids

General Lipid Structure



Combinatorial Synthesis Library



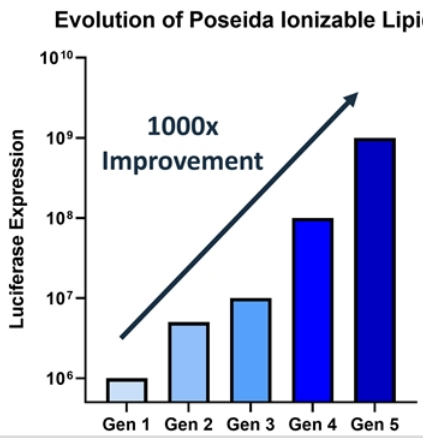
Inventing New Lipids for DNA Delivery

- Our approach has covered a wide range of lipid structures
- Combined with our formulations efforts we have screened hundreds of lipids

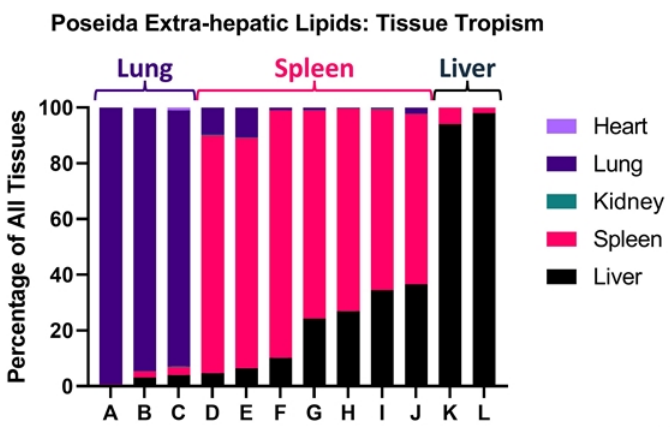
POSEIDA THERAPEUTICS

Next Generation Potent DNA and Extra-hepatic Lipids

Lipid Discovery Progress



Lipid Tissue Tropism



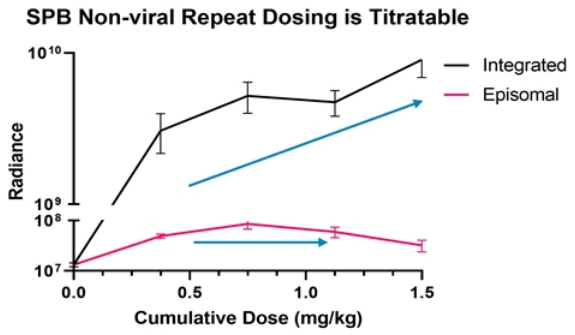
Inventing New Lipids for DNA Delivery

- We improved our lipid potency by over 1000x for in vivo delivery of luciferase DNA
- Built proprietary lipids which have extra-hepatic tissue tropism

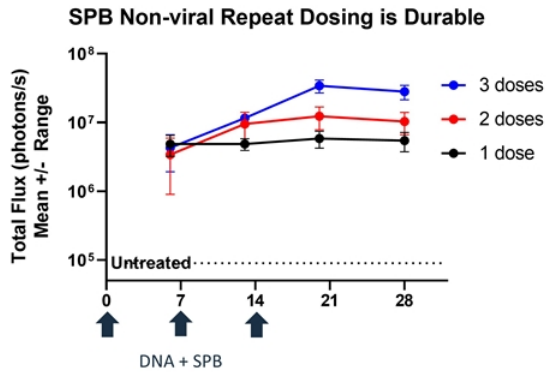
POSEIDA THERAPEUTICS

Repeat Dosing Capabilities of SPB Non-viral System

Dose Titration



Dose Durability



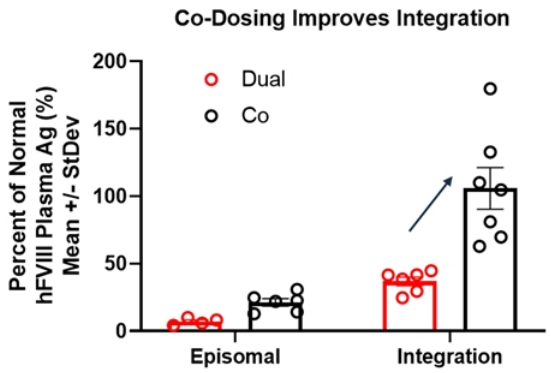
Key advantages of non-viral approach:

- Repeat Dosing: Non-viral DNA delivery allows for precise tailoring of gene expression

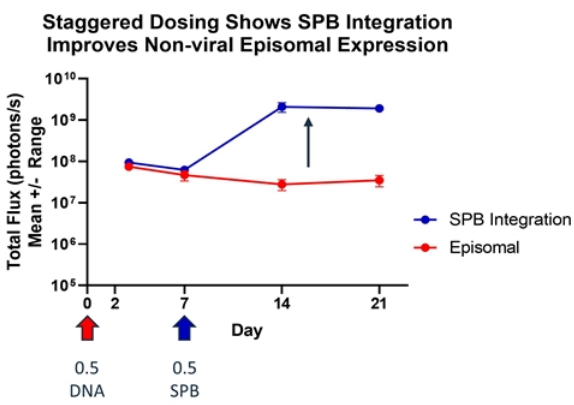
POSEIDA THERAPEUTICS

SPB Enhances Expression of Gene Through Integration

mRNA and DNA Co-Encapsulation



SPB Expression Enhancement



Key advantages of Non-viral approach:

- Versatility of dosing paradigm: co-encapsulation vs dual administration with timing flexibility
- Co-encapsulation of mRNA SPB and DNA improves integration and transgene expression
- SPB-enabled integration of episomal DNA significantly improves expression and durability

POSEIDA THERAPEUTICS

Growing Liver Platform/LNPs While Expanding to Other Tissues

2022 — **LNP Liver Depth**
- Depth in Liver LNP Portfolio
- HSC Early Development
- Lung Early PoC

2023 — **LNP Lung Expansion**
- Continued Expansion in Liver
- Continued HSC Development
- Expansion of Lung LNPs
- Next Tissue Early PoC

2024 — **LNP Next Tissue Expansion[1]**
- Continued Expansion in Liver
- Continued HSC Development
- Continued Expansion in Lung
- Expansion of Next Tissue LNPs

Highlights

- Continued focus on expanding proprietary liver focused LNPs – building suite of different lipids available to tackling most liver-directed diseases
- Early Feasibility data showing ability to utilize SPB Non-Viral Delivery to Lung targets
- In 2023, further development work on expanding platform in lung and exploring other tissue targets

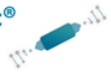
Non-viral Delivery Platform: Summary and Key Takeaways

- Significant advancement for DNA delivery and activity (expression)
  - 10-fold improvement in DNA expression in the last 12 months
  - Broad applicability of DNA delivery system to treat liver-relevant diseases
- Advancement of Poseida Proprietary LNP portfolio in past ~12 months
  - Significant acceleration of proprietary liver LNP portfolio
  - First proprietary lung directed LNP developed and tested
- Demonstrated ability to re-dose / dose titrate to therapeutic levels using SPB
- Next steps:
  - Expand on potential for DNA delivery to other tissues
  - DNA expression improvements anticipated in 2023 via our proprietary non-viral delivery system


GTx Wrap Up
Brent Warner
President, Gene Therapy
POSEIDA
THERAPEUTICS

Robust Platform Technologies Supporting Our GTx Pipeline Programs

Current Platforms

Super piggyBac® (SPB)		Non-viral transposon gene insertion technology
SPB Hybrid AAV + LNP		Gene insertion technology utilizing AAV as DNA donor
Lipid Nanoparticles (LNP)		Proprietary lipid nanoparticles built to deliver DNA
Cas-CLOVER™		High fidelity gene editing system for knock-out / knock-in
Site-Specific Super piggyBac® (ssSPB)		Next generation programmable gene targeting/editing system

Current Programs

P-OTC-101 SPB Hybrid AAV + LNP Poseida Owned	• Pre-clinical program • Capsid / construct selected • Finalizing pathway to IND • New data presented today
P-PAH-101 SPB Hybrid AAV + LNP Partnered with Takeda	• New pre-clinical program • New data presented today
P-FVIII-101 SPB Non-viral Partnered with Takeda	• Pre-clinical program • Data presented at ASH 2022 • Best of ASH 2022 selection • New data presented today

Future Pipeline

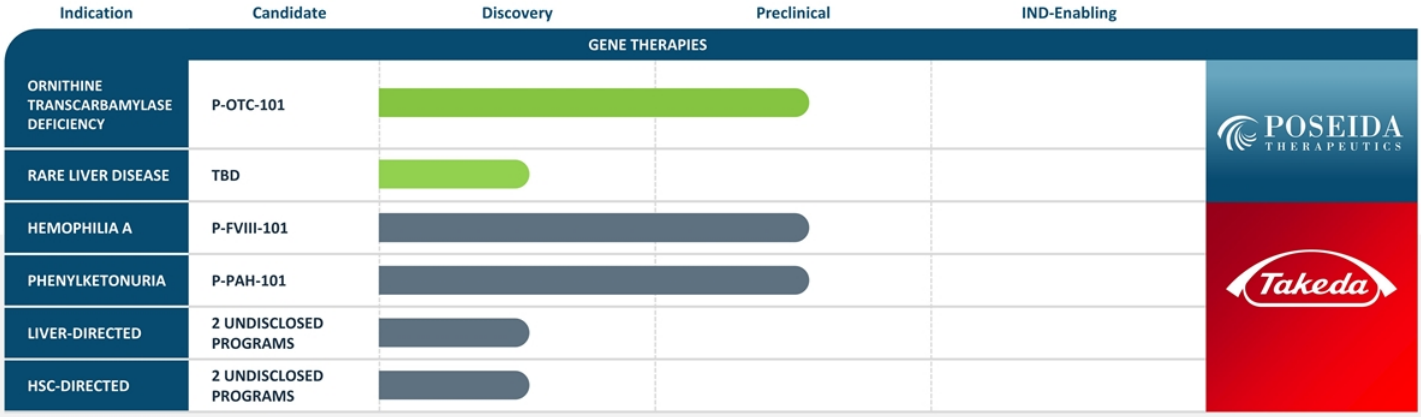
Liver Directed Knock-out
Cas-CLOVER

Liver Directed Metabolic Disease
SPB Non-viral

POSEIDA THERAPEUTICS

Our In Vivo Gene Therapy Pipeline

Initial Focus on Liver-Directed Gene Therapy



POSEIDA THERAPEUTICS

Cell Therapy

Devon J Shedlock, PhD
CSO, Cell Therapy

February 22, 2023

Innovation in Allogeneic CAR-T Cell Therapy

A New Class of Allogeneic CAR-T Therapy for Oncology

Cell Type Matters

T_{SCM} Cell

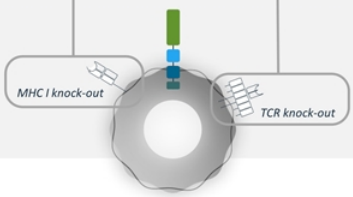
Stem Cell Memory

- Self renewing
- Long lived
- Multipotent

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

Super piggyBac® (SPB) is the ideal nonviral gene insertion technology

Fully Allogeneic CAR-T



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

Cost, Scale & Reach

Booster Molecule technology with the potential to deliver up to 100's of doses translating into low cost and broader patient and commercial reach

POSEIDA THERAPEUTICS

Powerful Platform Technologies Enable Our Allo CAR-T Pipeline

Super piggyBac

- Non-viral system
- Highly efficient technology to integrate DNA in 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

Allo CAR-T Solutions

- Booster molecule to overcome “allo tax”
- Transgene positive selection
- Safety switch
- Armoring ability
- In-house GMP manufacturing
- High T_{SCM} final product

CELL SOLUTIONS

Our suite of technologies are the basis for highly differentiated allogeneic CAR-T products

While our current focus is T cells – these technologies have the potential to work in many cell types including NK Cells, Tregs, HSCs, iPSCs and others

Super piggyBac Delivery of a Highly Functional Multicistronic CAR Transgene

Safety Switch

INCORPORATES PROPRIETARY SAFETY SWITCH

- Rapid, dose-dependent **elimination** of engineered T- cells as needed
- Potential **management of** Cytokine Release Syndrome (**CRS**) or other Adverse Effects **(AEs)**

CAR Molecule

DIFFERENTIATED BINDING CAR-T MOLECULE

- VH or scFv molecule with **high-specificity binding**
- Fully human with no **toxic signaling observed to date**

Selection Gene

DRUG RESISTANCE GENE PERMITS POSITIVE SELECTION

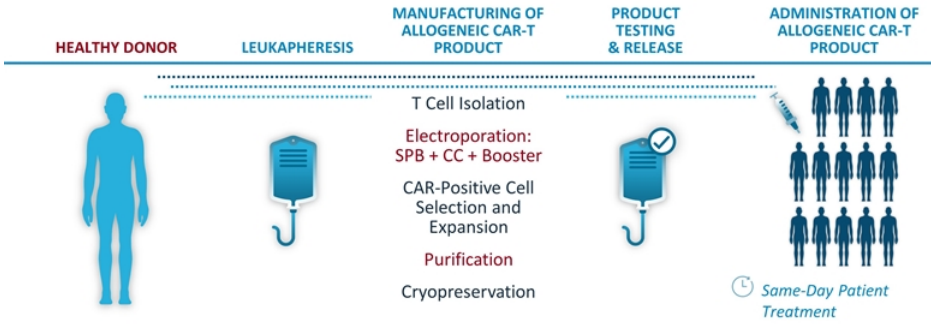
- **~100% of T-cells** in final product express the CAR molecule
- Predicted to result in **greater therapeutic index**

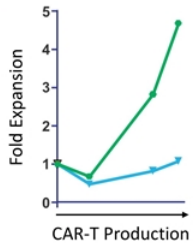
- SPB integration into T cell genome is a permanent and stable event
- Allogeneic CAR-T products harbor on average ~2-3 vector copies (VCN) per cell

POSEIDA THERAPEUTICS

Strategic Focus on Improved Allogeneic CAR-T Manufacturing

P-BCMA-ALLO1 and P-MUC1C-ALLO1 Phase 1 Studies On-going





With Booster

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

Unique Allogeneic Platform

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

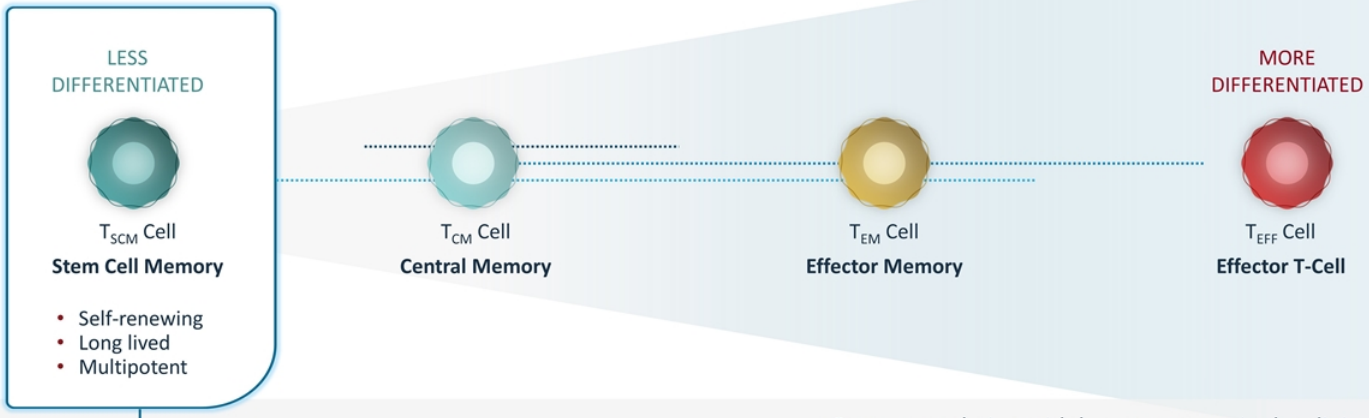
Booster Molecule

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

POSEIDA THERAPEUTICS

Not All T Cells Are Created Equally

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



Super piggyBac
Preferentially Transposes Naïve and T_{SCM} Cells

STEMNESS MATTERS

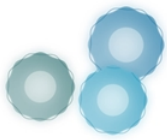
Products with High % of T_{SCM} Cells:

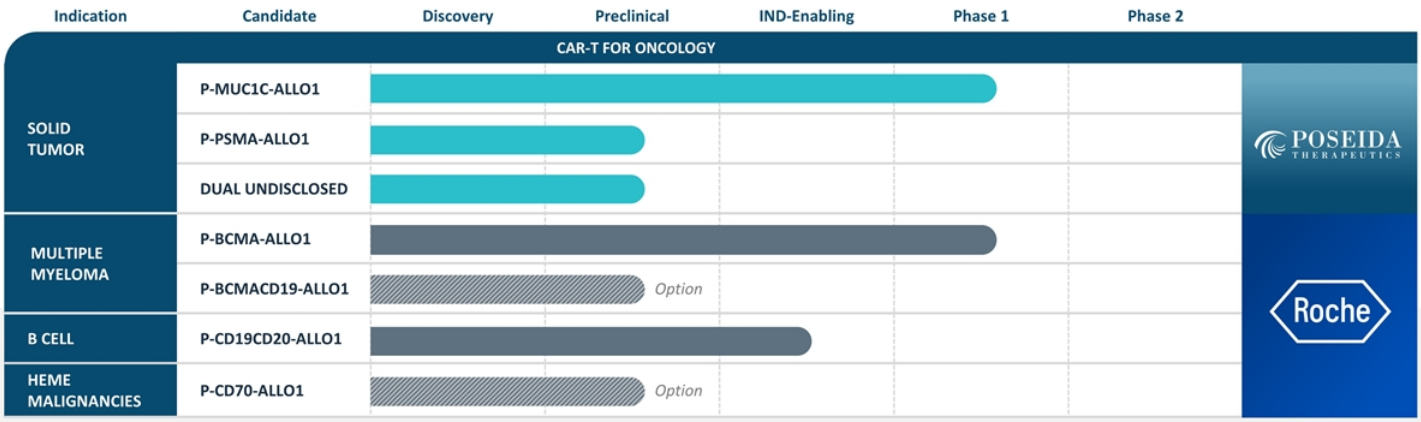
- Strong correlation with best responses in the clinic
- More gradual tumor killing with less toxicity
- Better duration of response and potential for re-response
- T_{SCM} engrafts in bone marrow – key to CAR-T success in solid tumors

POSEIDA THERAPEUTICS

Our Allogeneic CAR-T Pipeline

Focused on Off-the-Shelf Cell Therapies for Both Solid and Liquid Tumors






P-MUC1C-ALLO1 Clinical Update
Rajesh Belani, MD
Vice President, Clinical Development
POSEIDA
THERAPEUTICS

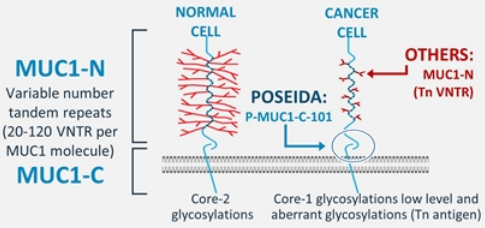
P-MUC1C-ALLO1-001 Phase 1 Trial in Solid Tumors

- MUC1C a unique binding target
  - Different than other MUC1 programs
- Large potential patient population
  - Strong preclinical data in breast cancer (TNBC) and ovarian cancer
- Ongoing dose escalation
- Outpatient administration allowable
- Early clinical data presented at ESMO-IO (Dec 2022)

KEY ELIGIBILITY

- Advanced treatment-resistant solid tumors, including but not limited to breast, ovarian, pancreatic, NSCLC and other epithelial solid tumors
- Measurable Disease per RECIST criteria
- ECOG status of 0 to 1

Our MUC1-C Approach vs Others



Study Schematic: Trial Design

PRIMARY ENDPOINTS

- Assess safety and MTD based on DLT

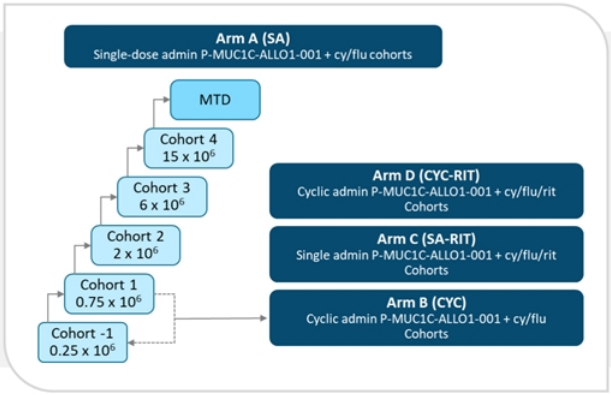
SECONDARY OUTCOMES

- Safety/feasibility: AE, Cytokine Release Syndrome (CRS), neurotoxicity, Graft vs Host Disease (GVHD)
- Efficacy: RECIST criteria: ORR, TTR, DOR, PFS, OS will be analyzed

POSEIDA THERAPEUTICS

P-MUC1C-ALLO1-001 Study Schematic

Phase 1 3+3 Dose Escalation



Planned Dose Escalation*

If the Maximum Tolerated Dose (MTD) has not been reached in Arm A following completion of Cohort 4, the dose of P-MUC1C-ALLO1 may be increased by 5-10 x10^6 cells/kg for the subsequent dose levels as agreed upon with the safety committee and the FDA

- Doses are weight-based (cells/kg)
- Amending protocol to allow fixed dosing

POSEIDA THERAPEUTICS

P-MUC1C-ALLO1 Cellular Product is Comprised Primarily of Stem Cell Memory T-cells

Manufacturing Characteristics

Mean (Range)	Clinical Lots (n = 6)
CD4/CD8 Ratio	0.9 (0.3, 2.0)
Stem cell memory CD8 T cells, %	54.8 (32.9, 79.9)
Central memory CD8 T cells, %	44.4 (19.2, 66.7)
Effector memory CD8 T cells, %	0.6 (0.2, 1.8)
Effector CD8 T cells, %	0.2 (0, 0.6)
% CCR7 +	95.0 (94.0, 95.8)
% CAR +	98.3 (96.7, 98.9)

- Reliably high frequency of CAR+ cells (>95%) across clinical lots
- P-MUC1C-ALLO1 is largely comprised of early memory T cells, i.e., T_{SCM} and T_{CM} ($CD45RO^-$ $CD45RA^+CD62L^+$ or $CD45RO^+CD45RA^-CD62L^+$, respectively)
- Low composition of late memory T cells (<5%)
- Products are consistently >90% $CCR7^+$

P-MUC1C-ALLO1-001 Phase 1 Dose-escalation Clinical Results

Patient Demographics and Characteristics (Data Cutoff 11-14-2022)

CAR-T cells administered, cells/kg	Mean (min, max) x 10^6	Patients, n
Cohort 1: 0.75 x 10^6 single infusion	74.15 (47.93, 96.98)	3
Cohort 2: 2.0 x 10^6 single infusion	164.15 (103.88 / 203.56)	3

Parameter (n=6)	
Age, median (min, max), years	61 (59, 68)
Time since diagnosis, median (min, max), years	4.1 (1.08, 10.13)
Baseline ECOG performance status, 0/1, n (%)	3 (50%) / 3 (50%)

Prior therapy	
No. of prior regimens, all patients (n=6): median (min, max)	4 (2, 6)

Cohort	Patient #	Sex	Tumor Type	Lines of Prior Therapy, n	Last Therapy
1	1	M	Esophageal adenocarcinoma	3	Ramucirumab/Taxol
1	2	M	Colorectal	6	Investigational STING agonist
1	3	F	Breast (HR+, Her2-)	4	Eribulin
2	4	M	Pancreatic	3	FOLFOXIRI
2	5	F	Pancreatic	2	Capecitabine/Radiotherapy
2	6	M	Prostate	5	Docetaxel

P-MUC1C-ALLO1 Demonstrates Favorable Safety and Encouraging Efficacy

Data Cutoff 11-14-2022

				Safety		Response and Disposition		
Cohort/ cell dose	Patient #	Tumor type	Lines of prior therapy, n	Dose-limiting toxicities	Related Grade ≥3 SAEs	Best overall response (RECIST)	Days on study**	Status
Cohort 1 0.75×10^6 cells/kg	1	Esophageal adenocarcinoma	3	None	None	Progressive disease	178	LTFU
	2	Colorectal	6	None	None	Stable disease	121	PTFU
	3	Breast (HR+, Her2-)	4	None	None	Partial response	102	LTFU
Cohort 2 2×10^6 cells/kg	4	Pancreatic	3	None	None	Stable disease	43	PTFU
	5	Pancreatic	2	None	None	NE*	21	PTFU
	6	Prostate	5	None	None	NE*	8	PTFU

Safety

- No dose limiting toxicities or SAEs considered related to P-MUC1C-ALLO1 were observed
- No CRS, ICANS, or graft vs host disease were observed
- Grade 3-4 treatment-emergent AEs were anemia (n=1), leukopenia (n=1), neutropenia (n=5), lymphocyte count decreased (n=2) and subclavian vein thrombosis (n=1)

Efficacy

- Six heavily pretreated patients have been dosed with P-MUC1C-ALLO1
- Among the 4 evaluable patients, 1 had best overall response of PR and 1 had SD at the low starting dose of 0.75×10^6 cells/kg and additionally one subject had SD at the 2×10^6 cells/kg dose

P-MUC1C-ALLO1: Summary and Key Takeaways

- P-MUC1C-ALLO1 is largely comprised of early memory T cells, i.e., T_{SCM} and T_{CM}
- Ph1 was initiated in May 2022 and is estimated to treat up to 100 patients across 15 sites
- Three patients in cohort 1 and 3 patients in cohort 2 have been treated
- Both cohort 1 and cohort 2 were completed without dose-limiting toxicities, CRS or graft vs host disease
- Early signs of clinical activity were observed including 1 partial response in a breast cancer patient at the low dose and two other patients with gastrointestinal malignancies achieving stable disease
- Ph1 enrollment and dose escalation is on-going with subjects now enrolling in cohort 3 dose-level (Arm A) and cyclic dosing (Arm B)
- Previously treated subjects are eligible per protocol for re-treatment at the original dose given or at a higher dose-level that has cleared DLT period


P-BCMA-ALLO1 Clinical Update
Rajesh Belani, MD
Vice President, Clinical Development
POSEIDA
THERAPEUTICS

Background

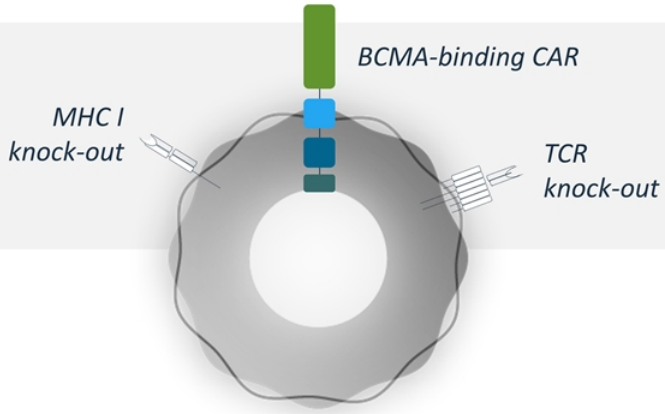
- Multiple myeloma (MM) is an incurable plasma cell malignancy with high expression of B-cell Maturation Antigen (BCMA)
- Two autologous CAR-Ts targeting BCMA are approved for relapsed refractory MM (RRMM)
- Autologous CAR-T are limited by:
  - The need for apheresis
  - Long manufacturing times and high manufacturing costs
  - Poor product quality because the T-cells are obtained from myeloma patients
- An allogeneic “off the shelf” CAR-T:
  - Eliminates the need for apheresis
  - Provides on demand therapy
  - Utilizes better-quality T-cells from healthy donors
- P-BCMA-ALLO1 is an allogeneic CAR-T targeting BCMA being developed for the treatment of RRMM

P-BCMA-ALLO1 Partnered with Roche

Allogeneic CAR-T Therapy for Multiple Myeloma

Optimized for safety, efficacy and to overcome autologous CAR-T limitations

- Produced from healthy donor T cells
- Numerous patients can be treated with each manufacturing run
- Nonviral transposition
- High fidelity gene editing
- High proportion T_{SCM} cells
- Available “on demand”



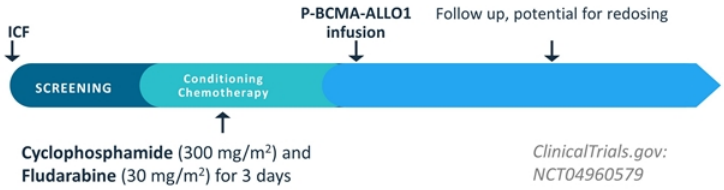
Phase 1 P-BCMA-ALLO1-001 Clinical Trial in Multiple Myeloma

- Multiple learnings from autologous program informed allogeneic approach
  - Even higher T_{SCM}
  - Better binder technology (utilizing VH binder)
  - Booster molecule (lower cost)
- Ongoing dose escalation
- Early clinical data presented at ESMO-IO (Dec 2022)

KEY ELIGIBILITY

- Relapsed Refractory Multiple Myeloma
- Received at least 3 lines of therapy that include a PI, IMiDs and CD38 mAb
- Measurable Disease
- ECOG status of 0 to 1

Study Schematic: Trial Design



PRIMARY ENDPOINTS

- Assess safety and MTD based on DLT

SECONDARY OUTCOMES

- Safety/feasibility: AE, Cytokine Release Syndrome (CRS), neurotoxicity, Graft vs Host Disease (GVHD)
- Efficacy: IMWG criteria: ORR, TTR, DOR, PFS, OS will be analyzed

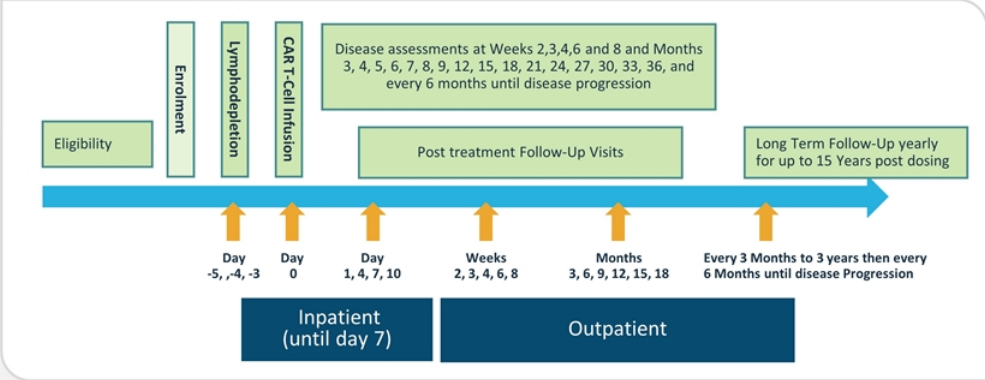
POSEIDA THERAPEUTICS

P-BCMA-ALLO1-001 Dose Escalation Plan and Study Schematic

Single infusion Dose Levels (cells/kg/dose)

Cohort minus 2:	0.0625×10^6
Cohort minus 1:	0.25×10^6
Cohort 1:	0.75×10^6
Cohort 2:	2×10^6
Cohort 3:	6×10^6
Cohort 4:	10×10^6
Cohort 5:	15×10^6

If cohort 5 is completed without concluding an MTD, the safety Committee may elect to assess further escalation cohorts in 5-10 X 10^6 P-BCMA-ALLO1 cells/kg increments



- Open label, multicenter, Phase 1, dose escalation study to assess the safety and efficacy of P-BCMA-ALLO1
- Administered intravenously as a single dose
- Dose levels will be tested in 3+3 escalation design in approximately 40 RRMM patients

POSEIDA THERAPEUTICS

P-BCMA-ALLO1-001 Patient Demographics and Characteristics

CAR-T Cells Administered: Cells/kg	Mean (Min/Max) x 10^6	Patients, n
Cohort 1: 0.75 x 10^6 single infusion	48 (37/ 64)	7
Cohort 2: 2.0 x 10^6 single infusion	162 (126/210)	3

Age / Gender/ Time Since Diagnosis / Performance Status (n=10)	
Median (min, max) age, y	75 (33, 85)
Male, n (%)	3 (30)
Median (min, max) time since diagnosis, y	5.17 (1.48, 18.85)
Diagnosis Subtype, n (%)*	IgG, 7 (70)
	IgA, 2 (20)
	Kappa FLC, 5 (50)
	Lambda FLC, 5 (50)
Cytogenetic High-risk, n (%)	5 (50)
ECOG (Baseline) PS, 0 (%) /1 (%)	3 (30) / 7 (70)

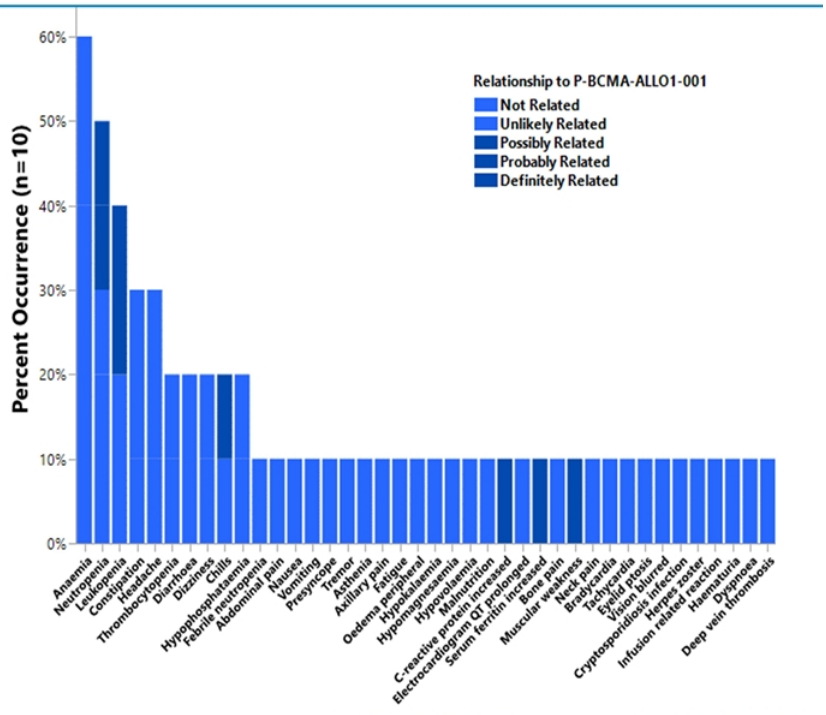
Prior Therapy Exposure (n=10)	
Median (min, max) # prior regimens	6.5 (4, 10)
Prior anti-BCMA therapy, n (%)	3 (30)

*No patients with IgM, IgE, IgD or Non-Secretory Diagnosis Subtypes

Data Cut Off 11-14-2022

P-BCMA-ALLO1 Demonstrates Favorable Safety Profile

- A total of 10 patients were treated with P-BCMA-ALLO1, 7 in cohort 1, and 3 in cohort 2
- Three SAE occurred in cohort 1 (G3 Febrile Neutropenia, G3 Disseminated Herpes Zoster, G3 Cryptosporidiosis infection)
- No SAE were related to P-BCMA-ALLO1
- No CRS, GVHD, neurotoxicity, DLT or Adverse Events of Special Interest (AESI) have been observed as of the data cutoff
- Six cohort 1 patients are available for response evaluation



Data Cut Off 11-14-2022

POSEIDA THERAPEUTICS

P-BCMA-ALLO1 Demonstrates Encouraging Efficacy

- All enrolled patients are heavily treated having received 6.5 median prior lines of therapy
- 3 out of 6 evaluable cohort 1 patients had received prior BCMA targeted therapy
- 4 out of 6 evaluable cohort 1 patients had high risk cytogenetics
- ORR for Cohort 1 is 50%
- ORR in patients who have received prior BCMA targeting therapy is 66%
- ORR in patients with high-risk cytogenetics is 50%

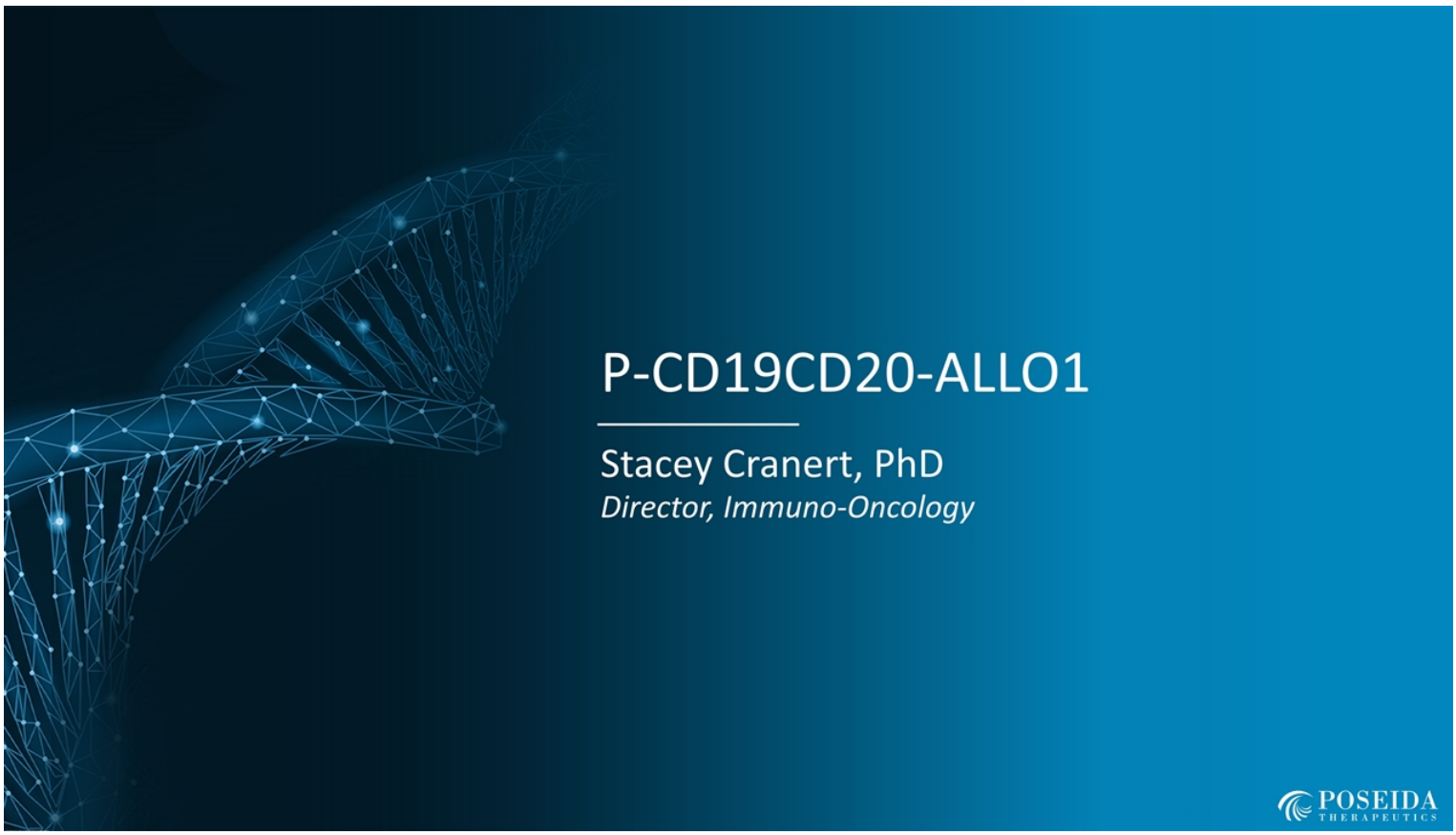
Patient	Cohort	Age	Prior Lines of Therapy	Cytogenetic Risk	Prior BCMA Targeting Therapy	Best Response
1	1	79	8	Standard	Yes (Belantamab)	SD
2	1	69	5	High	Yes (Belantamab)	VGPR
3	1	75	5	High	No	PR
4	1	33	10	Standard	Yes (Bispecific Ab)	PR
5	1	75	4	High	No	SD
6	1	66	4	High	No	SD

Data Cut Off 11-14-2022

POSEIDA THERAPEUTICS

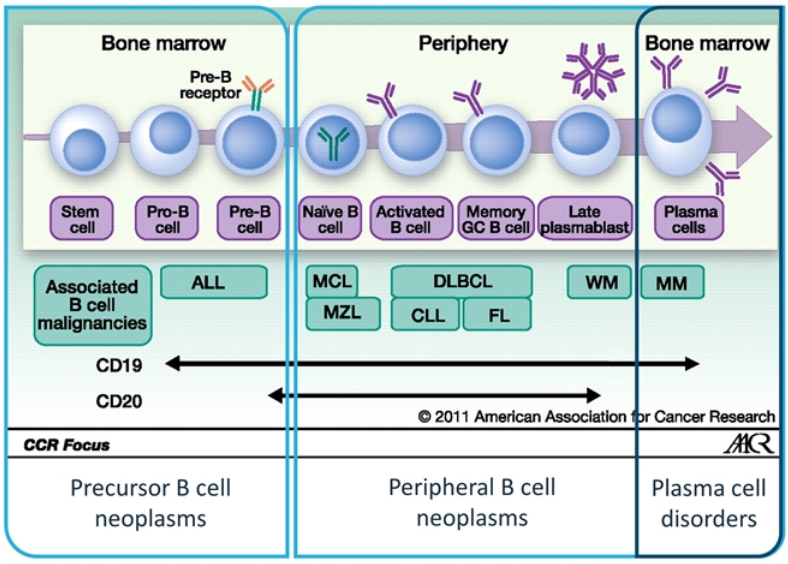
P-BCMA-ALLO1: Summary and Key Takeaways

- P-BCMA-ALLO1 is an allogeneic “off the shelf” BCMA targeting CAR-T therapy that demonstrates compelling anti-myeloma activity, in a heavily pretreated patient population, at the lowest dose tested, while demonstrating excellent tolerability
- It is active in patients who have failed prior BCMA targeted therapy and in patients with high-risk myeloma
- The clinical activity is seen without CRS, GVHD or neurotoxicity
- Dose escalation is ongoing
- Additional treatment regimens to be explored following a protocol amendment including cyclic dosing, repeat dosing, fixed (non-weight based) dosing, alternate lymphodepletion strategies and Rituximab combination
- P-BCMA-ALLO1 represents an important cellular therapy advance and could represent an attractive treatment option for MM


P-CD19CD20-ALLO1
Stacey Cranert, PhD
Director, Immuno-Oncology
POSEIDA
THERAPEUTICS

CD19/CD20 Dual CAR for Peripheral B Cell Malignancies

- Highly validated therapeutic targets for B cell malignancies
- Expression of both markers is highly restricted to the B cell lineage
- CD19 is a transmembrane glycoprotein of the Ig superfamily
  - Expressed during all stages of B cell development
- CD20 is membrane bound B cell marker thought to act as an ion channel
  - Expressed on late pro-B cells > memory B cells
- 4 FDA-approved CD19-targeting CAR-T for B cell malignancies
- **~30% of patients treated with CD19-targeting CAR-T relapse with CD19 Ag loss or downregulation**

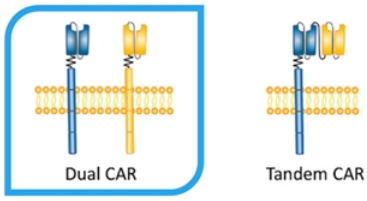


POSEIDA THERAPEUTICS

P-CD19CD20-ALLO1 Dual CAR-T

- Licensed to Roche
- Poseida Project Stage: IND planned 2023
- Early competitor data suggests excellent clinical activity for CD19/CD20 targeting
- Dual targets address limitations of single Ag loss and tumor heterogenicity, while dual CAR expression addresses structural limits of tandem configuration
- CD19 / CD22 tandem CAR-T demonstrated obstructed activity for 2nd binder

Poseida's advantage: Large PB cargo capacity allows for Dual CAR expression from a single transgene



CD19/CD20 CAR-T On-going Clinical Trials

OWNER	PRODUCT	INDICATION
Lentigen/Medical College of Wisconsin	LV20.19 Tandem-Auto	NHL Phase 1 (**82% ORR** and **64% CR**, D28)
Chinese PLA General Hospital	TanCAR	r/r NHL Phase 1/2a (**79% ORR** and **71% CR**)
UCLA	CD19/CD20 Bispecific (Tandem)	r/r NHL, CLL Phase 1 (**90% ORR, 70% CR; 7/10**)
Miltenyi	CD19/CD20 DUAL CAR	r/r NHL Phase 1 (**75% ORR; 9/12** and **42% CR; 5/12**)
Shanghai Children's Medical Center	Coadministration of CD19- and CD22- CAR-T cells	B-ALL (**99% CR** of 194 patients ≤ 20 yo)

Preclinical and clinical advances in dual-target chimeric antigen receptor therapy for hematological malignancies. Cancer Sci, 2021
CD19/CD20 Bispecific Chimeric Antigen Receptor (CAR) in Naïve/Memory T Cells for the Treatment of Relapsed or Refractory Non-Hodgkin Lymphoma. Cancer Discovery, 2022
Phase I Trial of MB-CART2019.1 in Patients with Relapsed or Refractory B-Cell Non-Hodgkin Lymphma: 2 Year Follow-Up Report. Hemasphere, 2022

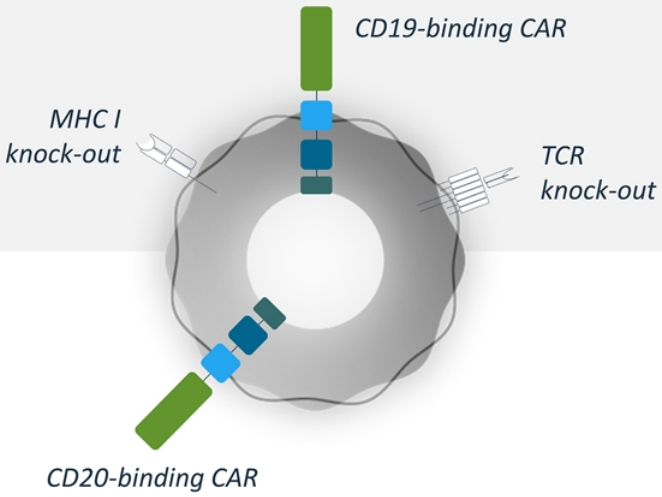
POSEIDA THERAPEUTICS

P-CD19CD20-ALLO1

Allogeneic CAR-T Therapy for B cell Malignancies

Optimized for Safety and Efficacy

- Produced from healthy donor T cells
- Nonviral transposition
- High fidelity gene editing
- High proportion T_{SCM} cells
- Targeted Indications: R/R DLBCL, CLL, MZL, MCL, FL, PMBCL
  - No FDA Approved CAR-T therapy for CLL and MZL

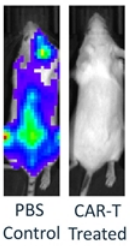


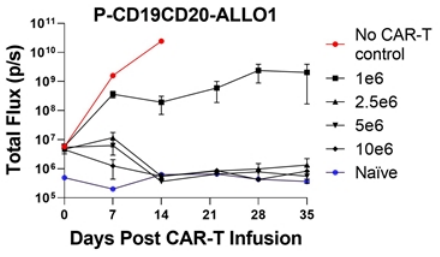
POSEIDA THERAPEUTICS

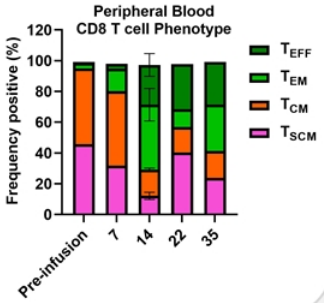
In Vivo Activity Against Leukemia and Lymphoma Xenografts

P-CD19CD20-ALLO1 demonstrates Ag-specific anti-tumor activity in a dose response against multiple tumor models in vivo

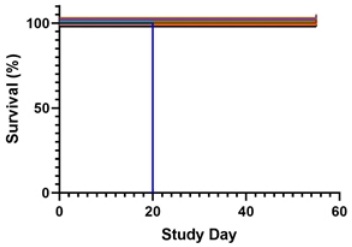
Raji (Burkitt's lymphoma)

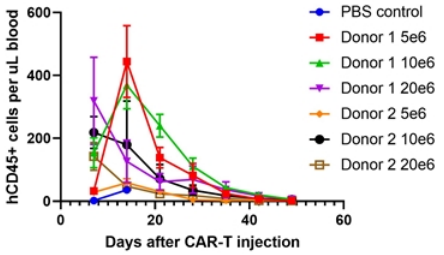






Mec1 (B-CLL)





Program on track for 2023 IND filing

POSEIDA THERAPEUTICS

P-CD19CD20-ALLO1: Summary and Key Takeaways

- P-CD19CD20-ALLO1 is a DUAL targeting CAR-T aiming to prevent relapse in B cell malignancies
- This Allogeneic CAR-T product demonstrates:
  - Strong in vivo cytotoxicity against xenograft models of CLL and lymphoma
  - High T_{SCM}
- IND filing planned 2023


P-CD70-ALLO1
Julia Coronella, PhD
Vice President, Immuno-Oncology
POSEIDA
THERAPEUTICS

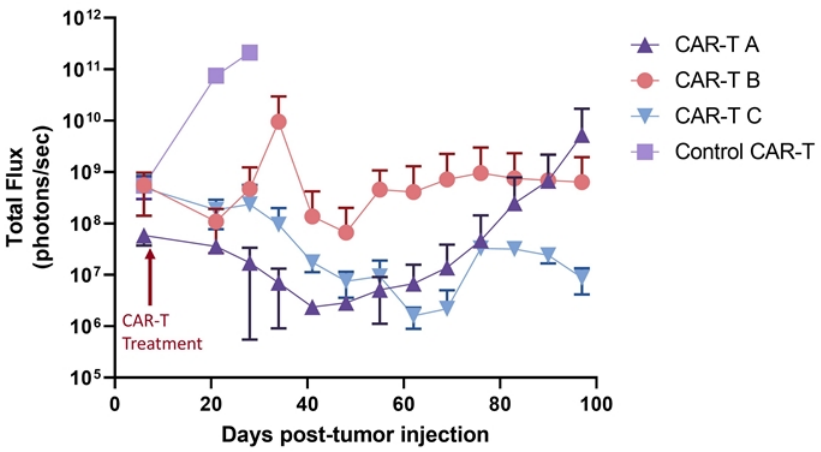
CD70 CAR-T for Hematologic Cancers

- Project stage: preclinical
- CD70 is highly expressed in AML (85%), NHL (90%), and RCC (80%)
- Highly expressed in Cutaneous T-cell lymphoma (CTCL); MF (95%), pcALCL (100%), PTCL (64%)
- Limited healthy tissue expression (APCs, activated T/B cells) and favorable safety record for other programs in development
- Roche holds an option to license

Anti-CD70 CAR-T/TCR-T/mAb/ADC Currently in Development

OWNER	PRODUCT	INDICATION
CRISPR Tx	Allo CAR-T (CTX-130)	**TCL (Phase I; 70% ORR and 30% CR)** RCC (Phase I)
Allogene Tx	Allo CAR-T (ALLO-316)	RCC (Phase I) AML (pre-clinical)
U of Florida	Auto CAR-T with IL-8R	GBM (Phase I)
NCI	Auto CAR-T	CD70+ solid tumors (Phase I/II)
TCR2 Tx	TCR-T with mbIL-15 (TC-520)	RCC (pre-clinical)
Argenx	mAb (Cusatuzumab)	AML (Phase I/II; **45% CR**)
Seagen	ADC (SEA-CD70)	MDS/AML (Phase I)
Ambryx	ADC (ARX305)	RCC (IND approved)

Anti-CD70 CAR-T Cells Effectively Control Tumors in a Xenograft Model of AML

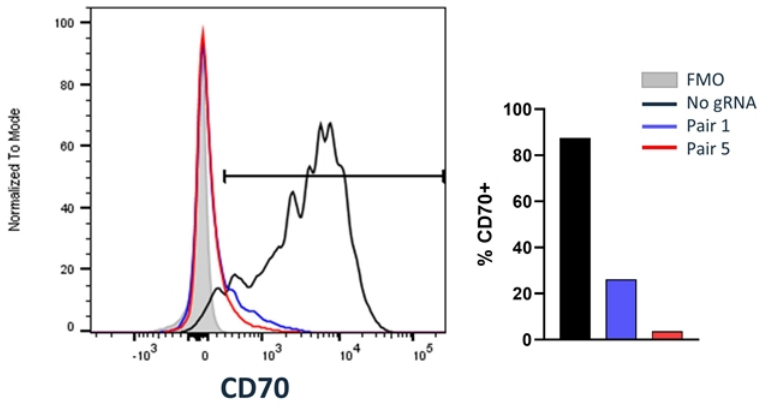


- Tool CAR-T cells expressing binders generated from published scFv sequences were used for target proof of concept in the Nomo-1 model of AML
- 6/12 tool CAR-T assessed effectively slowed or controlled tumor growth in this model

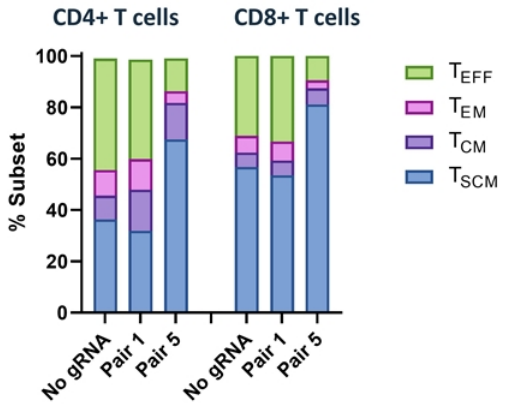
POSEIDA THERAPEUTICS

Cas-CLOVER Editing of CD70 Locus Yields 95% KO Efficiency and Increases % T_{SCM} in Anti-CD70 CAR-T Cells

CD70 Editing Efficiency



Final Product Phenotype

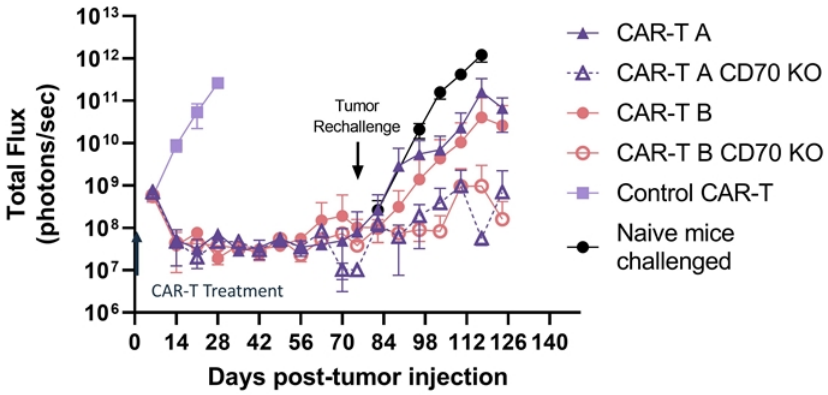


- Anti-CD70 CAR-T cells express CD70, which can lead to fratricide, activation, and/or impaired efficacy
- Cas-CLOVER gene editing ablates CD70 expression during CAR-T production yielding a final product with improved phenotype compared to unedited cells

POSEIDA THERAPEUTICS

Anti-CD70 CAR-T With CD70 KO Exhibit Improved Durability of Response Against AML Xenografts In Vivo

- Tool CAR-T cells with or without CD70 KO were rechallenged with a high dose of tumor after initial period of tumor control
- Only CD70 KO cells were able to control tumor rechallenge



POSEIDA THERAPEUTICS

P-CD70-ALLO1: Summary and Key Takeaways

- Super piggyBac is used to generate anti-CD70 CAR-T cells with high T_{SCM} and strong in vivo cytotoxicity against a xenograft model of AML
- Cas-CLOVER efficiently disrupts CD70 expression during CAR-T production, yielding a product with increased T_{SCM} cell content and improved in vivo durability
- Anti-CD70 single domain VH binders have been generated and lead candidate identification is underway


P-ckit-ALLO1
Nina Timberlake, PhD
Director, Immuno-Oncology
POSEIDA
THERAPEUTICS

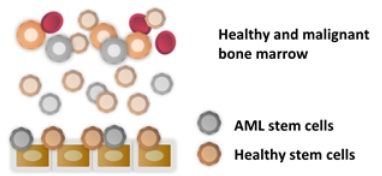
P-ckit-ALLO1 as a Bridge to Transplant in R/R AML

- Project stage: preclinical
- c-kit is expressed on >95% of HSCs and overexpressed in >80% of AML including on leukemic stem cells
- P-ckit-ALLO1 aims to increase transplant eligibility in relapsed/refractory AML patients and improve treatment efficacy and durability by specifically targeting AML stem cells

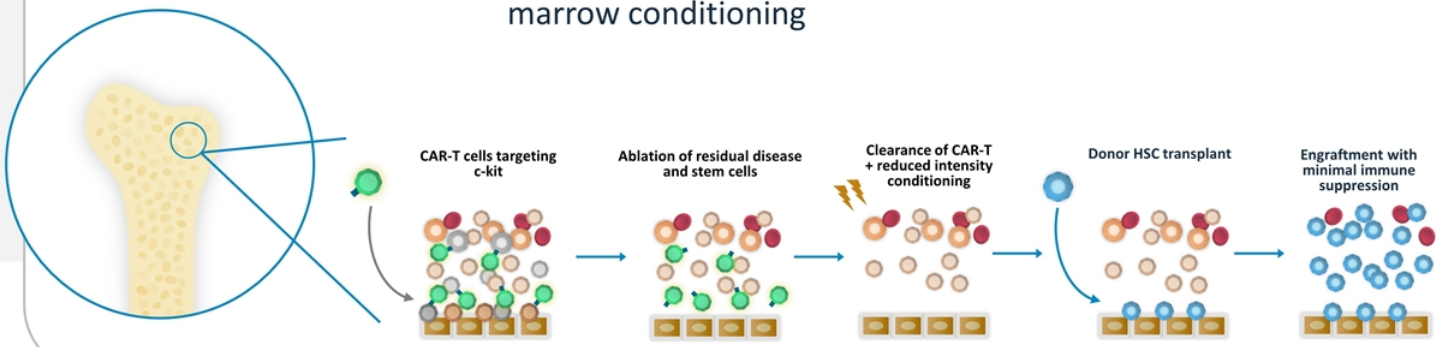
Anti-c-kit mAbs and ADCs Currently in Development

COMPANY	PRODUCT	INDICATION
Magenta Tx	anti-CD45 and anti-c-kit ADCs	Conditioning (preclinical) AML/MDS (Phase 1)
Jasper Tx	anti-c-kit mAb (JSP 191)	SCID and AML (Phase I)
Forty-Seven	anti-c-kit + anti-CD47 mAb	Conditioning (preclinical)

P-ckit-ALLO1 as a Bridge to Transplant in R/R AML



- Many AML patients do not qualify for transplant
- P-ckit-ALLO1 aims to increase the pool of transplant eligible patients by simultaneously clearing residual disease (bridging therapy) and providing highly specific reduced intensity bone marrow conditioning



POSEIDA THERAPEUTICS

Potential Advantages of P-ckit-ALLO1

P-ckit-ALLO1

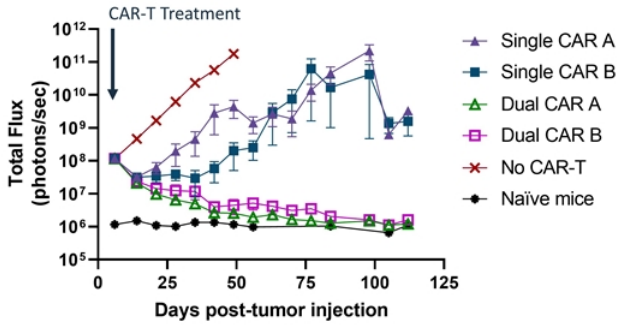
- Bone marrow homing and preferential expansion at the site of target cells
- Rapid and controllable clearance of CAR-T cells using embedded safety switch
- Direct target cell killing with potent cytotoxic activity

Antibody Reagents

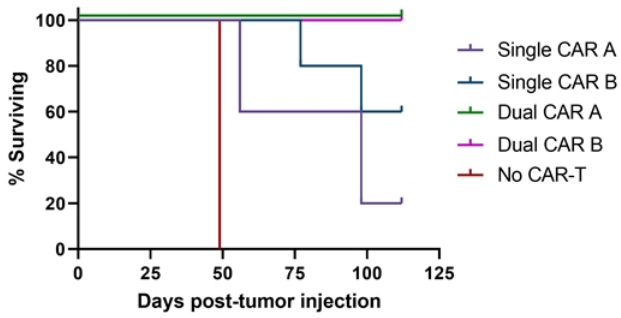
- High systemic drug concentration may increase risk of off-tumor toxicity
- Long serum half-life limits ability to transplant until reagent clears naturally
- Rely on ADCC, growth factor blockage, or complexed immunotoxins for killing—kinetics may be slow or lowered in stem cells

Dual Anti-c-kit CAR-T Cells Significantly Outperform Single CARs

Tumor Growth



Overall Survival



Dual anti-c-kit CAR-T cells exhibit increased potency compared to matched single CAR-T cells, resulting in complete tumor elimination, achieving 100% survival for more than 100 days in a xenograft model of AML

POSEIDA THERAPEUTICS

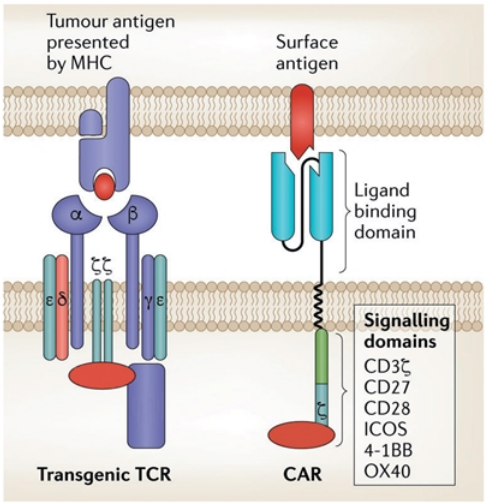
P-cKit-ALLO1: Summary and Key Takeaways

- Targeting c-kit^{+} cancer stem cells may improve the durability of responses in AML, which is known to originate from early bone marrow progenitors
- Super piggyBac enables delivery and expression of two full length c-kit targeting CARs from a single transgene
- Dual c-kit CAR-T cells have potent in vivo efficacy in a xenograft model of AML and reduce the incidence of antigen escape and T cell exhaustion in long term survival studies
- Targeting of normal, healthy stem cells by c-kit CAR-T cells may:
  - Provide a safer, less toxic conditioning regimen
  - Greatly reduce transplant-related morbidity and mortality
  - Improve patient outcomes
  - Expand pool of patients and indications where stem cell transplant can be applied


CAR-TCR-T for Solid Tumors
Devon J Shedlock, PhD
Chief Scientific Officer, Cell Therapy
POSEIDA
THERAPEUTICS

Engineered TCRs for Targeting Intracellular and Lipid Ags, and HSPs

TCR & CAR



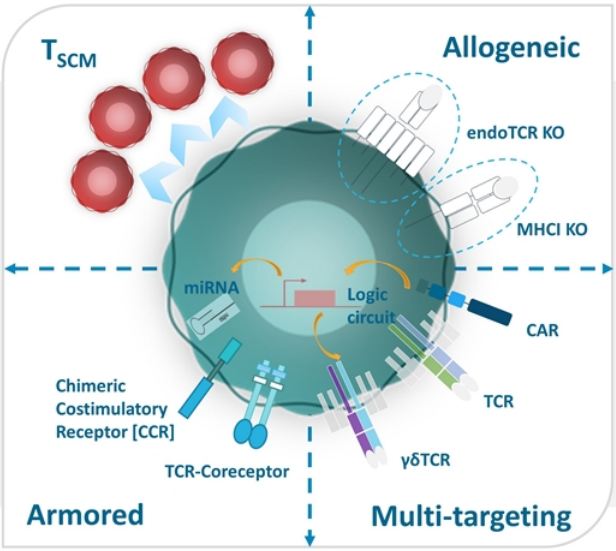
Nature Biotechnology **volume 36**, pages215–219 (2018)

- TCR-engineered cells express tumor-Ag-specific TCRs comprised of α- and β-, or γ- and δ-chains, which recognize **Ag + MHC or lipid Ags and heat shock proteins**
  a) TCRs access **intracellular** tumor antigens
  b) TCRs may require **lower antigen density** than CAR-T
  c) TCRs may exhibit **tissue homing and persistence advantages**
- TCR-engineered cells have **diverse applications**: oncology, infectious disease, autoimmunity, etc.
- Co-expression of a **TCR and a CAR may synergize to address target heterogeneity** and increase potency

POSEIDA THERAPEUTICS

Poseida's Development of Versatile Allogeneic CAR-TCR-T Cell Products

Enabled by Our Platform Technologies and Addresses Key Limitations of Current CAR-T and TCR-T Therapies, Including Improved Manufacturing, Engraftment, Potency, and Persistence

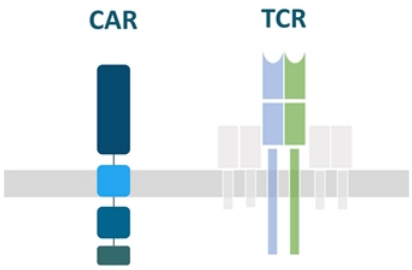


1. **T_{SCM} Rich** — Poseida's Allo platform generates a durable T_{SCM}-enriched cell therapy product
2. **Allogenic** — Combination of piggyBac®, Cas-CLOVER™ Booster molecule, and our proprietary Allo process
3. **Multi-targeting** — Large cargo enables delivery of multiple genes for multi-targeting via CAR, αβTCR, γδTCR, and/or activation-gated expression
4. **Armored** — Optimized platform with multiple molecular "armors" to enhance efficacy

POSEIDA THERAPEUTICS

Multiple Antigen Targeting by Combining CAR and TCR Platforms

Simultaneous Expression of CAR and TCR



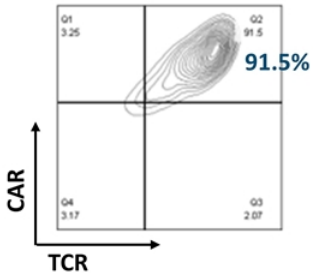
POTENTIAL BENEFIT

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

Allogeneic CAR-TCR-T

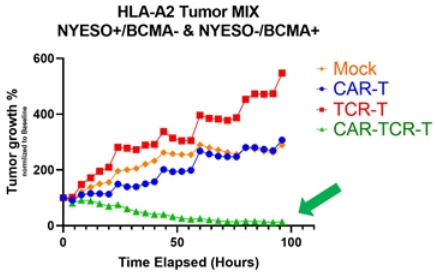
piggyBac® can be leveraged to deliver CAR and TCR in same product

CAR-TCR Co-Expression



A majority of engineered T cells express both CAR and TCR

Heterogeneous Tumor



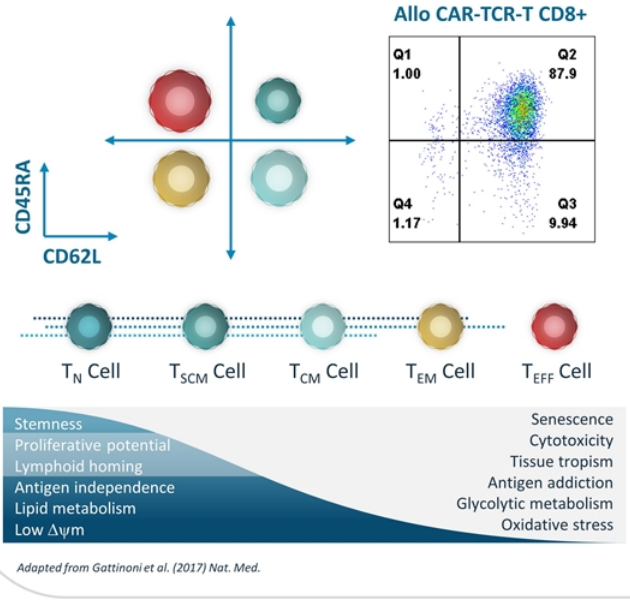
CAR-TCR-T exhibit dual-ag. specificity and their co-exp. synergizes to eliminate heterogenous tumors

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

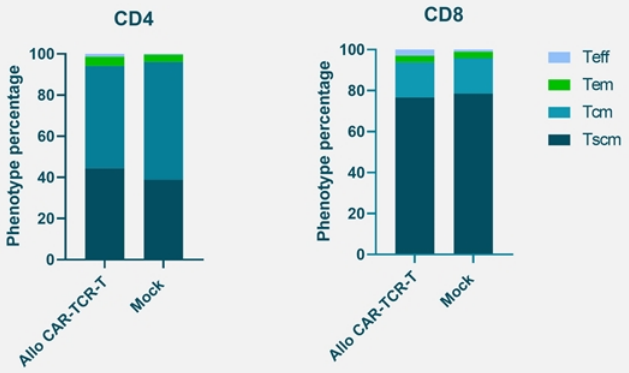
POSEIDA THERAPEUTICS

Super piggyBac®-produced CAR-TCR-T characterized by High %T_{SCM}

High %T_{SCM} Allogeneic CAR-TCR-T



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

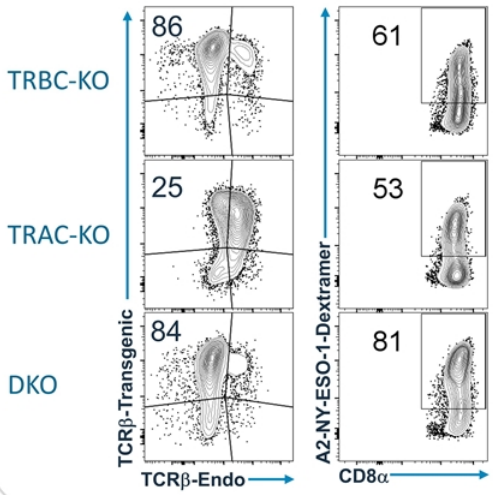


- SPB preferentially modifies early memory T cells resulting in high %T_{SCM} product
- In the clinic, T_{SCM} % is associated with greater safety / efficacy / durability

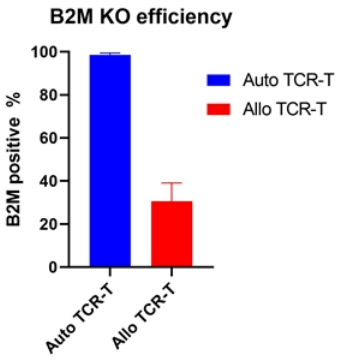
POSEIDA THERAPEUTICS

Multiplex Gene-editing Generates “Off-the-shelf” Allogeneic TCR-T

TRAC/TRBC DKO eliminates endogenous (Endo)-TCR and prevents TCR mismatching

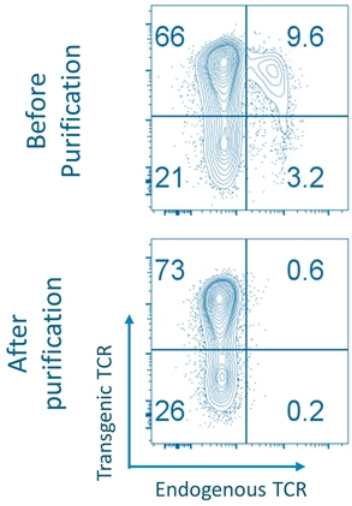


β2M KO disrupts MHC-I expression



- Cas-CLOVER™ mediated multiplex TCR & MHC-I KO with robust efficacy

Allogeneic CAR-TCR-T



POSEIDA THERAPEUTICS

Poseida's CD8 Co-receptor Enhances TCR Activity in Both CD4+ and CD8+ T cells

Poseida's Design

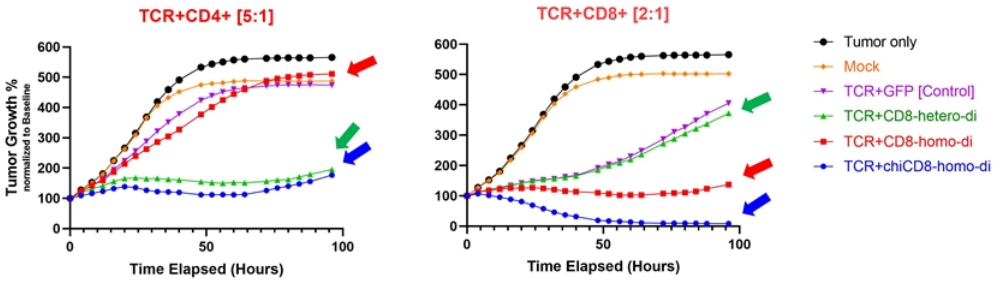
Chimeric CD8 homodimer (chiCD8-homo-di)

Competitors' Designs

CD8 heterodimer (CD8-hetero-di)

CD8 homodimer CD8-homo-di

De novo chimeric homodimer CD8 co-receptor incorporates both palmitoylation domain, a *lipid anchor facilitating coreceptor localization*, and high-affinity Lck binding domain which recruits *tyrosine Kinase to phosphorate TCR-CD3 complex*

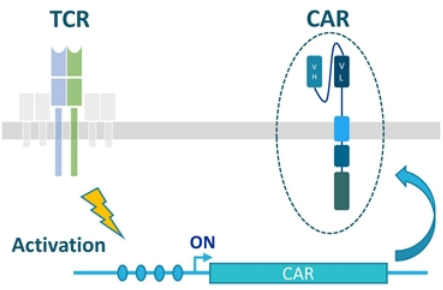


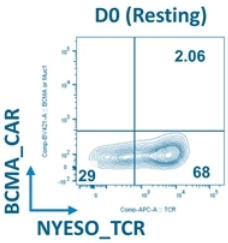
Our design **improved TCR activities in both CD4+ and CD8+ cells**

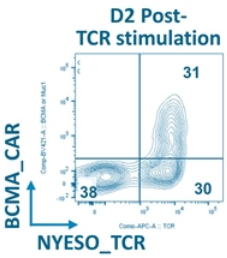
POSEIDA THERAPEUTICS

TCR-AIGES-CAR: TCR-Mediated CAR Expression for Improved Safety

TCR-activation Regulated CAR Expression





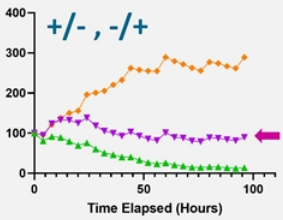


Potential of TCR-AIGES-CAR

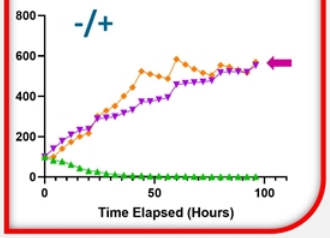
- Limit off-tumor activity of the CAR
- Decrease T cell expression burden

- CAR activity **restricted to TCR-Ag positive tumors**
  - TCR-AIGES-CAR-T shows **no cytotoxicity against single CAR-target positive tumors**
- TCR-AIGES-CAR-T exhibit **dual-antigen specificity following TCR activation**
  - TCR-mediated activation required for CAR expression

Heterogenous Tumor



Car-target Only Tumor



Mock TCR-AIGES-CAR-T CAR-TCR-T

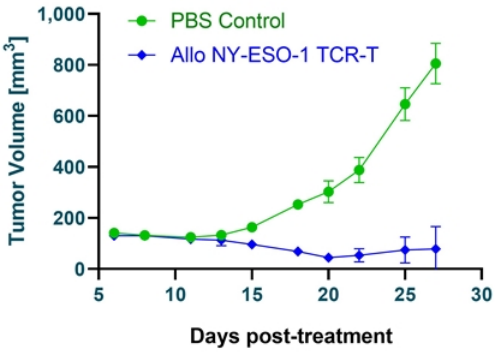
POSEIDA THERAPEUTICS

Versatile Platform Can be Adapted for Oncology, Infectious Disease, Autoimmune, and Other Indications

Allo TCR-T In Vivo Efficacy in Xenograft NSG Model

- **Oncology**: allogeneic TCR-T (no armors) exhibit remarkable in vivo efficacy in xenografted melanoma tumor model
- **Infectious Disease**: in vivo efficacy in COVID-19 infectious disease model as reviewed at Poseida's 2022 R&D Day (TScan)

NY-ESO-1+ A375-melanoma Tumor



POSEIDA THERAPEUTICS

CAR-TCR-T: Summary and Key Takeaways

- Poseida's non-viral technologies enabled development of our Allogeneic CAR-TCR-T Platform
  - Many advantages including **multi-targeting** and a **high % of T_{SCM}**
  - αβ and γδ TCRs recognize intracellular Ag-MHC and lipid Ags, respectively, providing key advantages over CAR alone
  - CAR and TCR co-expression may be **synergistic and improve activity against heterogeneous solid tumors**
- Armored CAR-TCR-Ts with functional enhancements exhibited **improved activity**
  - Chimeric CD8α co-receptor & Co-stimulatory molecule **increased TCR avidity and prolonged tumor control**
- This versatile platform can be adapted for oncology and beyond
  - **Preclinical proof-of-concept established** for both multiple oncology targets and viral infections

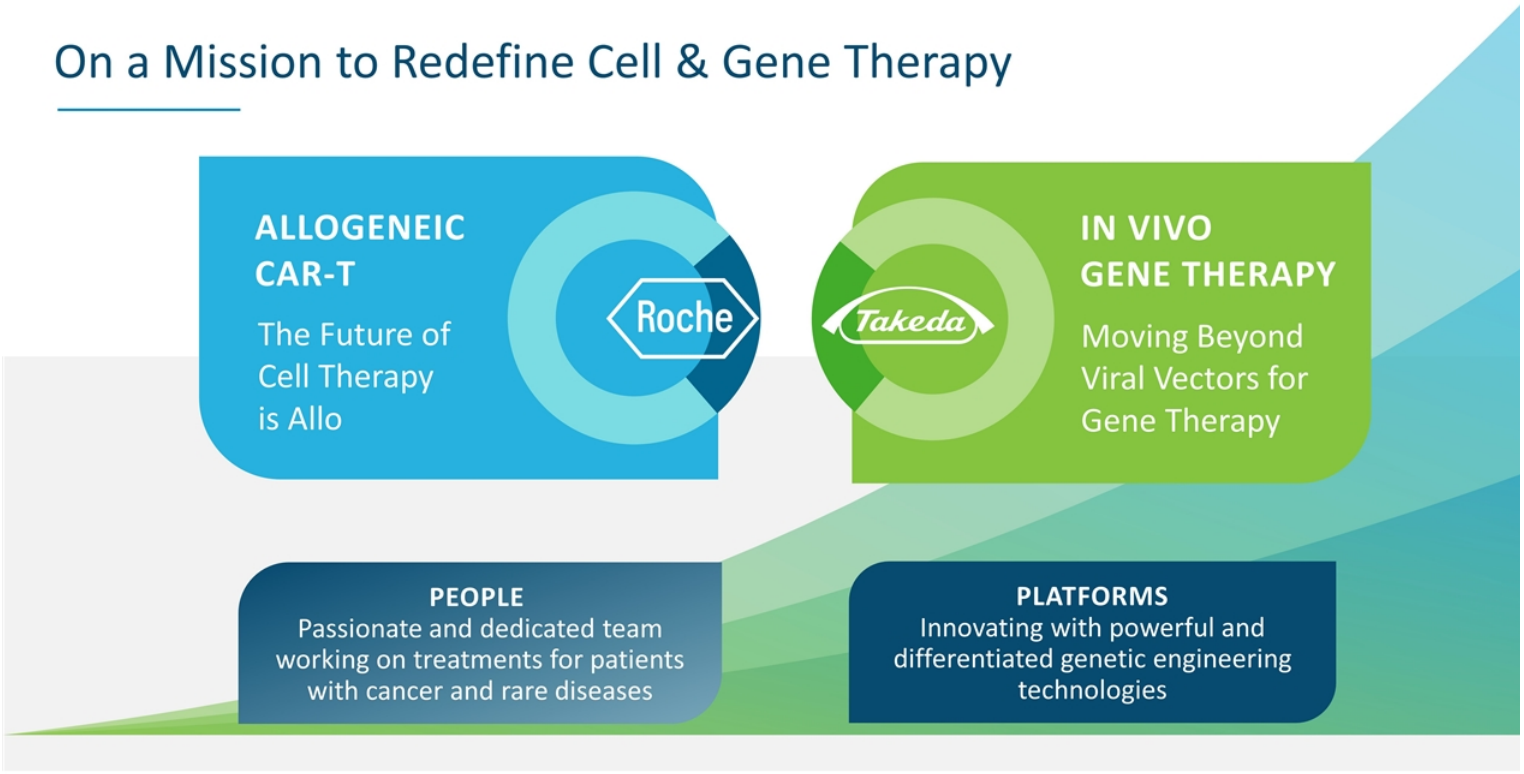

Conclusion and Summary
Mark J. Gergen
CEO
POSEIDA
THERAPEUTICS

Acknowledgements & Thank You

Introduction	*Eric M. Ostertag, MD, PhD, Founder*
Fireside Chat	*George Church, PhD, Gene Editing Pioneer & Chair, Poseida Gene Therapy SAB*
Gene Therapy	*Brent Warner, President, Gene Therapy*
Fireside Chat	*Madhu Natarajan, PhD, Head, Rare Diseases Drug Discovery Unit, Takeda*
Pipeline Programs	*Jack Rychak, PhD & Bernard Kok, PhD*
Emerging Technology	*Blair Madison, PhD; Oscar Alvarez, PhD & Alex Schudel, PhD*
Cell Therapy	*Devon J. Shedlock, PhD, Chief Scientific Officer, Cell Therapy*
Fireside Chat	*Christine Brown, PhD, Professor, City of Hope; CAR-T Cell Expert & Member, Poseida Immuno-Oncology SAB*
Clinical Programs	*Rajesh Belani, MD*
Preclinical	*Stacey Cranert, PhD; Julia Coronella, PhD; Nina Timberlake, PhD & Devon J. Shedlock, PhD*

Poseida employees, partners, collaborators, investors, analysts, investigators and especially the patients we serve.

On a Mission to Redefine Cell & Gene Therapy



Genetic Engineering Platforms Designed to Perform

Novel Technologies that Deliver Differentiated Products

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

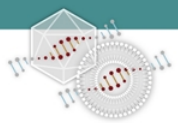
Cas-CLOVER

- 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

Our focus on innovation continues with ongoing improvements to all our platforms including progress on site-specific Super piggyBac for precise gene editing and insertion

Highly Differentiated Innovation in CAR-T

A New Class of Allogeneic CAR-T for Oncology

Cell Type Matters

T_{SCM} Cell

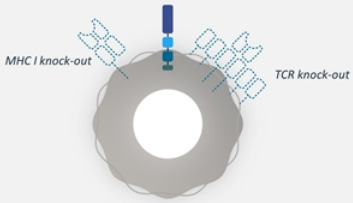
Stem Cell Memory

- Self-renewing
- Long lived
- Multipotent

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

Super 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**

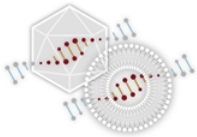
Cost, Scale & Reach

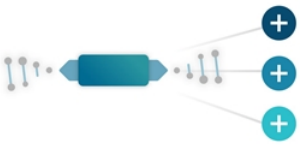
Booster Molecule technology with the potential to deliver 100's of doses translating into low cost and broader patient and commercial reach

POSEIDA THERAPEUTICS

Disruption in Gene Therapy

A New Class of Products for Rare Diseases and Hard-to-Treat Populations





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

*Focused on Genetic Correction and Improved Delivery with the **Capacity to Cure***

Advancing a New Class of Cell Therapy and Gene Therapy Products

Leveraging the Power of Products, Partnerships, People and Platforms

CELL THERAPY FOR ONCOLOGY

GENE THERAPY / GENE EDITING

Strong innovation engine, dedicated people and powerful differentiated platform technologies drive our opportunities


Q&A
POSEIDA
THERAPEUTICS