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):
April 17, 2024

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 April 17, 2024, 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 genetic medicine 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 & Media" 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 April 17, 2024
99.2	Corporate Presentation, dated April 17, 2024
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: April 17, 2024

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

Poseida Therapeutics Hosts Gene Therapy R&D Day Highlighting New Scientific Advancements and Pipeline Focus

Fully non-viral approach to genetic medicine employs differentiated gene delivery, gene editing and gene insertion technology

Progressing two fully non-viral programs in rare disease with significant unmet patient need

Virtual R&D Day featuring academic experts and Poseida's leadership and scientific teams to be held today at 10:00am ET / 7:00am PT

SAN DIEGO, April 17, 2024 — Poseida Therapeutics, Inc. (Nasdaq: PSTX), a clinical-stage cell therapy and genetic medicines company advancing a new class of treatments for patients with cancer and rare diseases, today announced that the Company plans to highlight progress across its proprietary non-viral genetic engineering and delivery platform and rare disease pipeline during a virtual R&D Day to be held today at 10:00am ET / 7:00am PT.

"Poseida is forging ahead with a renewed focus on our genetic medicine portfolio. Our system of proprietary, non-viral tools used individually or together has the capacity to treat rare genetic diseases as well as address much more prevalent diseases," said Kristin Yarema, Ph.D., President & Chief Executive Officer of Poseida Therapeutics. "In the short-term, we are laser-focused on progressing our two lead non-viral candidates within areas of significant opportunity: P-KLKB1-101 for Hereditary Angioedema, and P-FVIII-101, which utilizes our fully non-viral stable gene insertion technique to treat Hemophilia A, a condition affecting approximately 30,000 adults and children in the U.S. alone."

"Poseida has developed a broad suite of fully non-viral, differentiated genetic engineering technologies, including stable, potentially site-specific insertion of whole genes, high-fidelity gene editing, and strength in delivery systems including lipid nanoparticles," said Blair Madison, Ph.D., Chief Scientific Officer of Gene Therapy at Poseida Therapeutics. "We believe this uniquely positions us in the industry to deliver on the hope and promise of genetic medicines and bring much-needed therapies to patients in need."

The event will highlight the Company's proprietary genetic engineering and delivery platform, including its non-viral gene insertion and gene editing programs. External expert speakers will include:

- Marc Riedl, M.D., M.S., Professor of Medicine and Clinical Director of the U.S. HAEA Angioedema Center at University of California, San Diego; and
- Steven W. Pipe, M.D., Professor of Pediatrics and Pathology, University of Michigan

Key Gene Therapy R&D Day Topics and Highlights

Gene Therapy Programs

The Company will present advancements in fully non-viral liver-directed gene therapies highlighting the potential for functional cures across commercially viable indications.

- **P-KLKB1-101** is the Company's lead liver-directed investigational gene therapy program for the treatment of hereditary angioedema (HAE), a rare, inherited disorder which results in the swelling of the limbs, intestinal tract, and airways which can be both debilitating and life-threatening. The Company will share data highlighting durable disease correction and high fidelity in pre-clinical studies using the Company's enhanced editing technology, Cas-CLOVER™.
- **P-FVIII-101**, the Company's second non-viral gene therapy program, is a liver-directed investigational in vivo gene therapy for the treatment of Hemophilia A, a hereditary disorder caused by a deficiency in Factor VIII (FVIII) production resulting in excessive bleeding occurring either spontaneously or due to trauma. The Company will share data demonstrating durability and restoration of FVIII deficiency to near-normal levels in adult mouse models.

Technology Innovation in Gene Therapy

The Company will highlight significant advancements in its emerging platform technologies.

- **Site-specific Super piggyBac®** is a single enzyme fusion system for site-specific integration, executing clean DNA gene insertion without double strand breaks, unintended mutations, or the need for DNA repair. The Company will announce that the current molecular evolution of its platform yields a 30-fold improvement of DNA expression and efficient targeted cargo integration at single- and multi-copy sites. These data support the potential for the Company's non-viral insertion technology as an efficient and safe approach to achieve sustained DNA integration and expression to remediate disease.
- **Cas-CLOVER** is a proprietary high-fidelity nuclease for enabling clean site-specific gene editing that is engineered for high specificity. The Company will present data confirming and validating the benefits and advantages of Cas-CLOVER in multiple applications and disease areas.
- **Novel Lipids and DNA Delivery**: The Company is leveraging proprietary lipids notable for their low immunogenicity, dose titration potential, and ability to be manufactured at scale and favorable cost. The Company has achieved multiple breakthroughs in its delivery technology, including novel lipids for in vivo delivery of its technology as well as innovations enabling improved in vivo non-viral DNA delivery.

Video Webcast and Replay

This virtual event and access to the live webcast is available to through the following registration link: https://wsw.com/webcast/cc/pstx6/1466622.

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

About Poseida Therapeutics, Inc.

Poseida Therapeutics is a clinical-stage biopharmaceutical company advancing differentiated cell therapies and genetic medicines with the capacity to cure certain cancers and rare diseases. The Company's pipeline includes investigational allogeneic CAR-T cell therapies for both solid tumors and hematologic cancers as well as investigational in vivo genetic medicines that address patient populations with high unmet medical need. The Company's approach is based on its proprietary genetic editing platforms, including its non-viral piggyBac® DNA Delivery System, Cas-CLOVER™ Site-Specific Gene Editing System, Booster Molecule and nanoparticle gene delivery technologies, as well as in-house GMP cell therapy manufacturing. The Company has formed a global strategic collaboration with Roche to unlock the promise of cell therapies for patients with hematologic malignancies. Learn more at www.poseida.com and connect with Poseida on X 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 and manufacturing activities and capabilities; the potential capabilities and benefits of the Company's technology platforms and product candidates, including the efficacy and safety profile of such product candidates; the quotes from Drs. Yarema and Madison; and the Company's plans and strategy with respect to developing its technologies and product candidates. 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; 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.

# # #

Poseida Investor and Media Relations:
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Senior Vice President, IR & Corporate Communications
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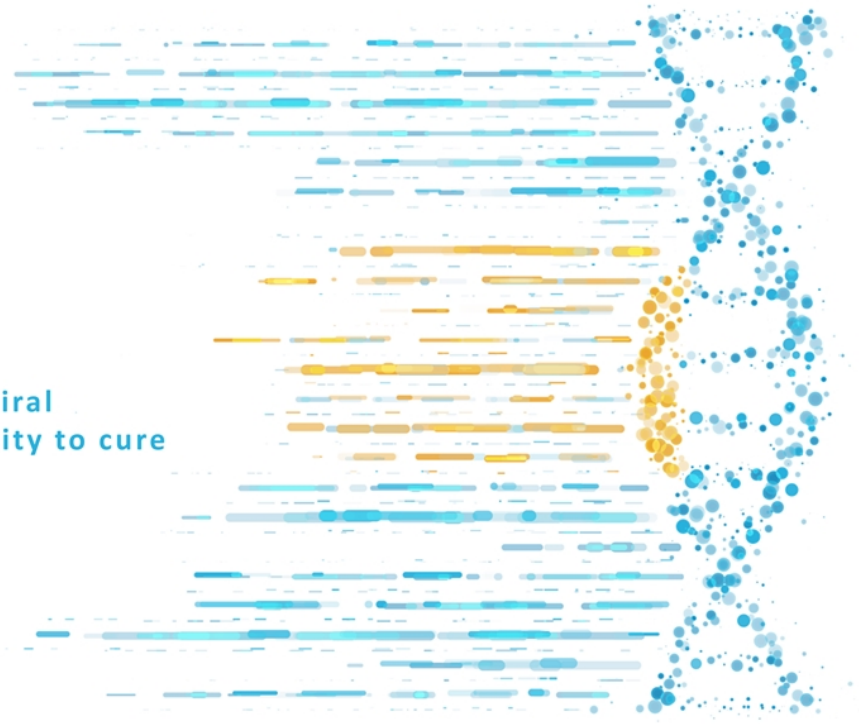
Senior Director, IR & Corporate Communications
PR@poseida.com

Exhibit 99.2

POSEIDA THERAPEUTICS



Gene Therapy R&D Day

Advancing next-generation non-viral genetic medicines with the capacity to cure

APRIL 17th, 2024

Disclaimer

This presentation and any accompanying oral commentary contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts and include, without limitation, statements related to future events; our future financial performance or condition; business strategy; expected timing and plans with respect to development milestones, clinical trials, and regulatory and manufacturing activities; estimated market opportunities for product candidates; potential capabilities and benefits of our technology platforms and product candidates, including the efficacy and safety profile of such product candidates; the quotes from Peter Marks; our plans and strategy with respect to developing our technologies and product candidates; our ability to exploit and consummate additional business development opportunities; and future results of anticipated development efforts. Words such as "expect(s)," "feel(s)," "believe(s)," "will," "may," "anticipate(s)", “potentially” or negative of these terms or similar expressions are intended to identify forward-looking statements. These forward-looking statements are based on management's current expectations of future events only as of the date of this presentation and are subject to a number of important risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: risks associated with conducting clinical trials; whether any of our product candidates will be shown to be safe and effective; our ability to finance continued operations; our reliance on third parties for various aspects of our business; competition in our target markets; our ability to protect our intellectual property; our ability to retain key scientific or management personnel; risks and uncertainties associated with development and regulatory approval of novel product candidates in the biopharmaceutical industry; and other risks and uncertainties described in our filings with the Securities and Exchange Commission, including under the heading “Risk Factors”. Except as required by law, we assume no obligation to update these forward-looking statements, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

POSEIDA THERAPEUTICS

Welcome & Introduction

Presenter:

Kristin Yarema, PhD

Agenda

Introduction	*Kristin Yarema, PhD*
P-KLKB1-101	
Program / Platform	*Marc Riedl, MD, MS / Blair Madison, PhD / Bonnie Jacques, PhD*
Non-viral system	*Jack Rychak, PhD*
P-FVIII-101	
Program / Platform	*Steven Pipe, MD / Blair Madison, PhD*
Site specific SPB™	*Blair Madison, PhD*
Conclusion	*Kristin Yarema, PhD*
Q&A	*Executive and Scientific Leadership*

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

ALLOGENEIC CAR-T

The future of cell therapy is allo

GENETIC MEDICINES

Non-viral delivery of genetic editing and gene therapies to enable access for all patients

OUR PEOPLE

Passionate and dedicated team working on treatments for patients with cancer and genetic diseases

OUR PLATFORMS

Innovating with powerful and differentiated genetic engineering technologies using an integrated systems approach

Early technologies for genetic medicines have presented many challenges

Gene replacement

AAV
Lentivirus
Other viral vectors
mRNA therapy

- Safety & immune challenges
- Low cargo capacity
- Lack of durability (non-integrating virus)
- Not appropriate for all patients
- mRNA replacement = lower durability

Gene modification

TALEN
Zinc Fingers
Cas9
BE/PE

- Low fidelity, low activity, or low cargo capacity
- Unintended edits when pursuing nuclease-mediated insertion
- Potential for safety issues (e.g., genotoxicity, translocations)

Manufacture and delivery

AAV manufacture
Conventional lipids

- AAV (high-cost manufacturing with high titer needs)
- High cost and complexity
- Empty capsid impurities
- Lack of reliability

Better tools are imperative to unlock the promise of genomic medicines


"We are enthusiastic to see the development of non-viral vectors for gene therapy and look forward to working with sponsors on these programs as they work to achieve the necessary efficiency needed for effective gene transfer."
– Peter Marks, Director of the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration
POSEIDA THERAPEUTICS

Poseida's vision for genetic medicine

Effective – capacity to cure*

Safe – non-viral, low immunogenicity lipid nanoparticles

Durable – stable genome editing/insertion

Patient-friendly – single or short course of treatment

Scalable – can be produced at scale and cost-effectively

Broad applicability – treat patients of all types & ages

Versatile – insert genes of any size, remove genes or signals, across cell types

*By inserting, deleting or modifying genes

POSEIDA THERAPEUTICS

This product vision requires an entirely new suite of technologies

Whole gene insertion

DNA transposon

- ✓ Integrated, stable expression
- ✓ Large cargo capacity for whole genes
- ✓ Safe harbor insertion, including in non-dividing cells
- ✓ Re-dosable, reversible and scarless

High fidelity gene editing

RNA-guided DNA nuclease

- ✓ Exceptional fidelity
- ✓ Efficient
- ✓ Applicable to different cell types
- ✓ Multiplexing potential

Manufacture and delivery

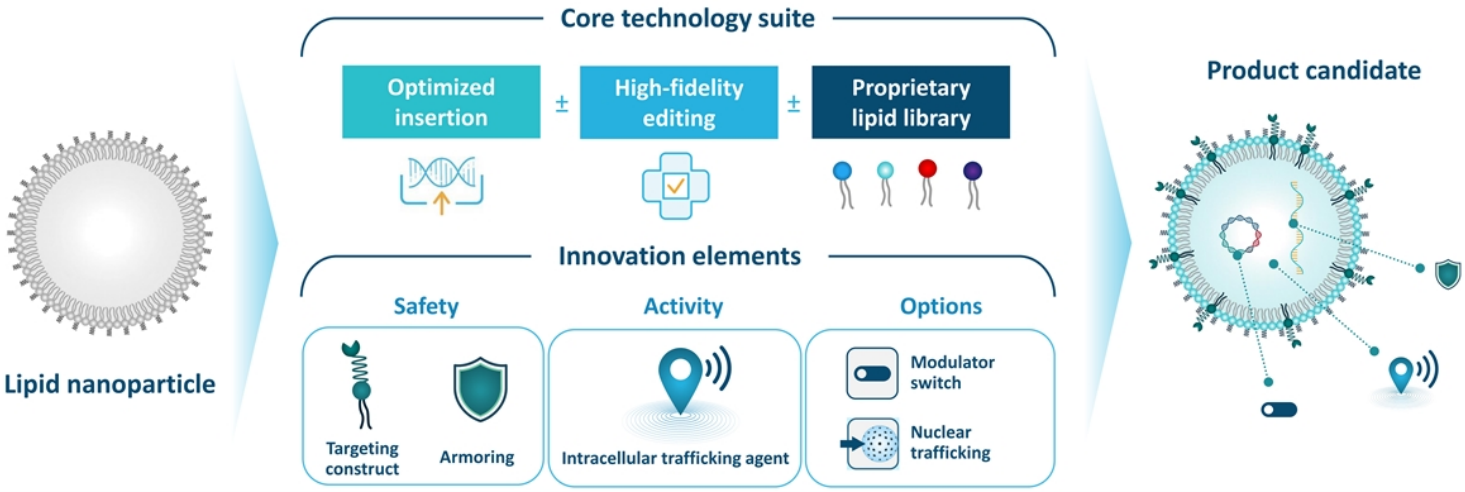
LNP

- ✓ Low immunogenicity
- ✓ Titrate-to-efficacy dosing
- ✓ Scalable
- ✓ Favorable cost of goods

Our technologies could be used individually or together to deliver transformational therapies

Versatility in developing products tailored to therapeutic need

Potential to add proprietary innovation elements onto core technology components



Launching into in vivo gene editing and insertion, building upon ex vivo expertise

Deploying our genetic engineering technologies to address serious diseases

	Gene editing	Gene insertion
In vivo (genetic disease)	**P-KLKB1-101:** Non-viral Cas-CLOVER editing of disease-relevant gene (Hereditary Angioedema)	**P-FVIII-101:** Non-viral whole gene insertion for functional correction (Hemophilia A)

Focus for today

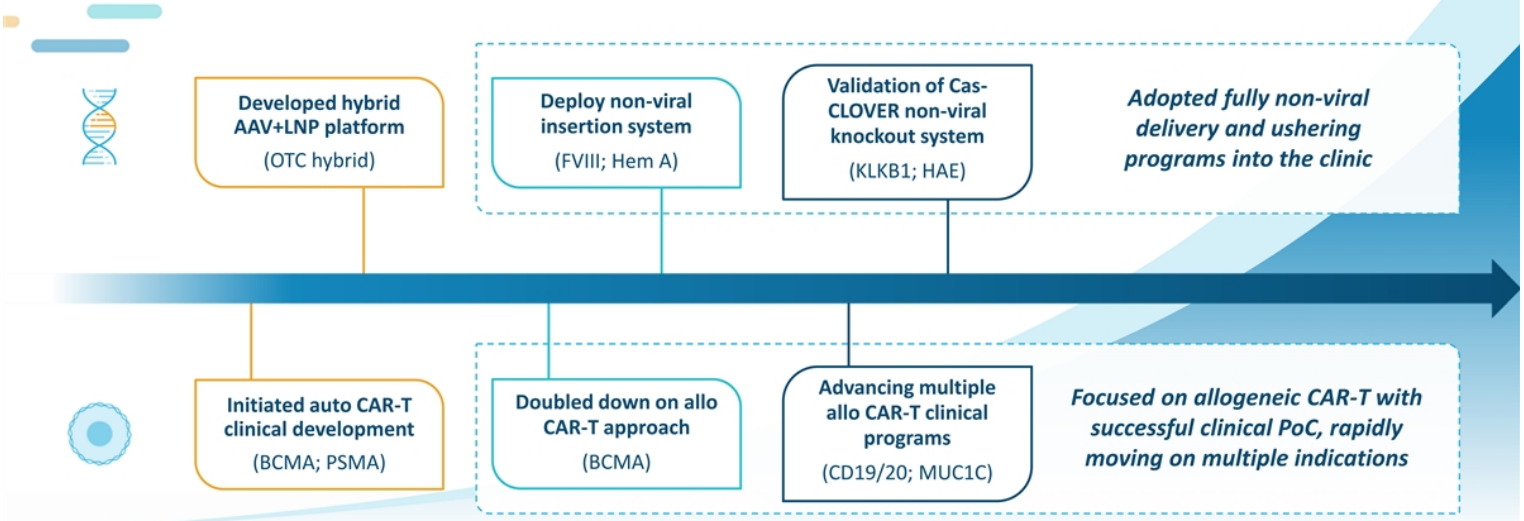
Ex vivo (oncology)

Clinically validated allogeneic CAR-T portfolio

- P-BCMA-ALLO1 (multiple myeloma)
- P-CD19CD20-ALLO1 (B-cell malignancies)
- P-MUC1C-ALLO1 (solid tumors)

Advancing forward with our proprietary non-viral systems with strategic focus

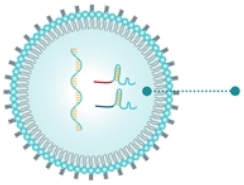
Building from foundational learnings to advance a highly differentiated approach across gene and cell therapy



Focused development of key programs within areas of significant opportunity

P-KLKB1-101: Hereditary Angioedema

RESEARCH | PRECLINICAL | IND-ENABLING



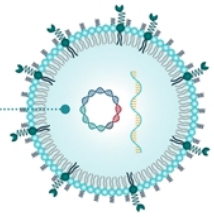
Non-viral Cas-CLOVER editing of disease-relevant gene

- Rare, inherited disorder resulting in swelling in limbs, face, intestinal tract and airways
- ~6,000[1] people with HAE in the U.S., with estimated $2.6B and growing[2] market

P-FVIII-101: Hemophilia A

RESEARCH | PRECLINICAL | IND-ENABLING

Non-viral whole gene insertion for functional correction



- Hereditary disorder resulting in excessive bleeding either spontaneously or due to trauma
- ~30,000[3] people with hemophilia in the U.S., with estimated $7.6B and growing[4] market

1. NIH HAE Epidemiology https://pubmed.ncbi.nlm.nih.gov/21549036/ 2. Evaluate Pharma, 2022 estimate 3. hemophilia.org 4. Clarivate, 2024 estimate.

POSEIDA THERAPEUTICS

Guest speakers

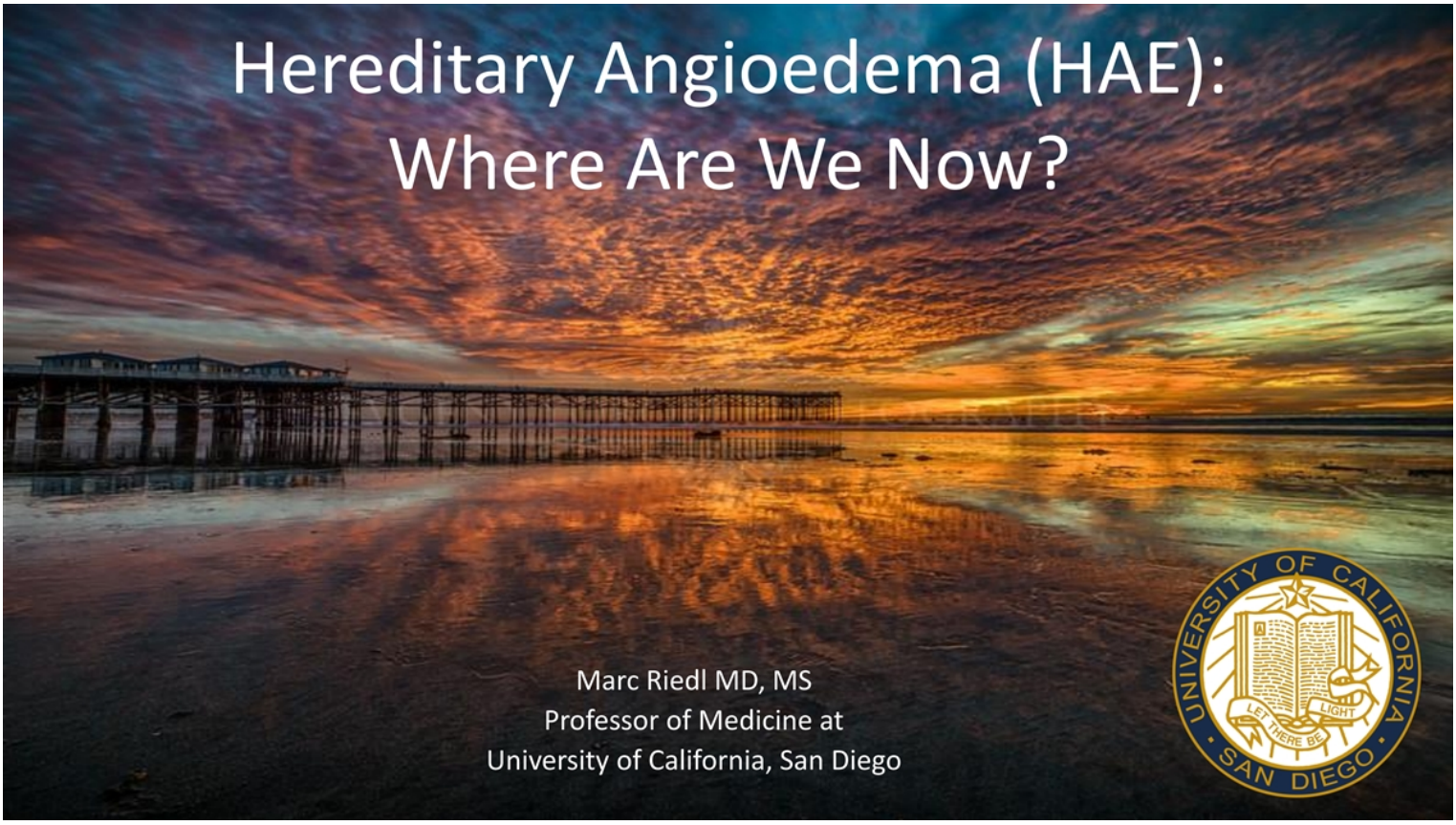
Marc Riedl, MD, MS

Professor of Medicine at
University of California, San Diego

Steven W. Pipe, MD

Professor of Pediatrics and
Pathology, University of Michigan

Hereditary Angioedema (HAE): Where Are We Now?

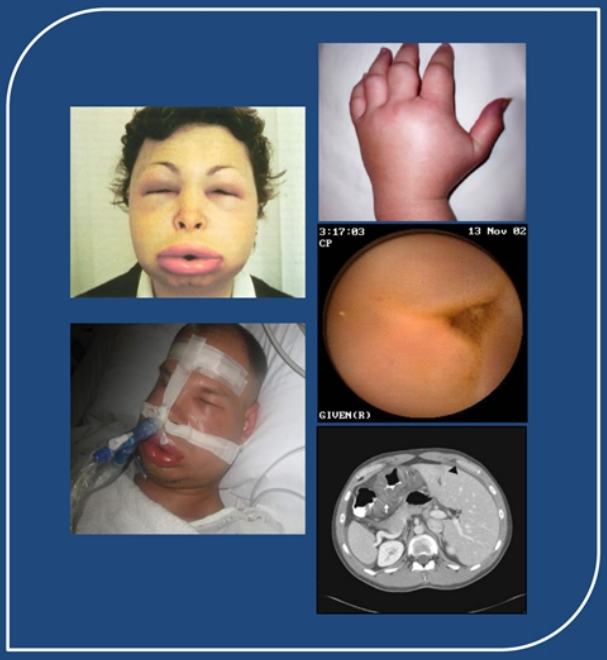


Marc Riedl MD, MS
Professor of Medicine at
University of California, San Diego

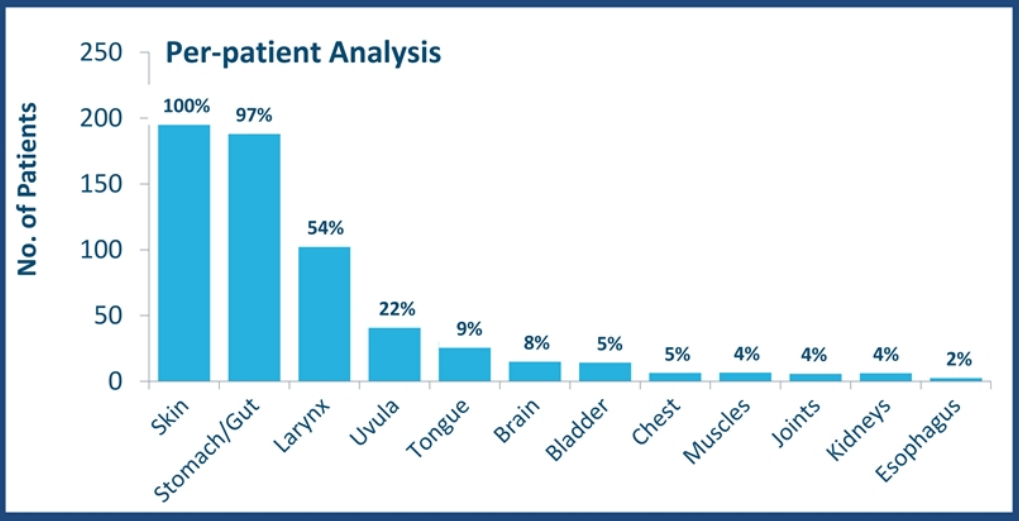
HAE Clinical Features

Angioedema without urticaria: Severe and unpredictable

- **Affected areas**: Face, oropharynx, extremities, GI, genitourinary tract
  - Risk of death by asphyxiation
  - Prolonged attacks, intensifying over 24 hours, lasting 2-4 days
- **Unresponsiveness to traditional therapies**: antihistamines, corticosteroids, epinephrine
- **Triggers**: trauma, stress, estrogen-containing oral contraceptives, hormone replacement therapy
- **Often familial**: Autosomal dominant inheritance



Incidence and anatomical location of HAE Symptoms



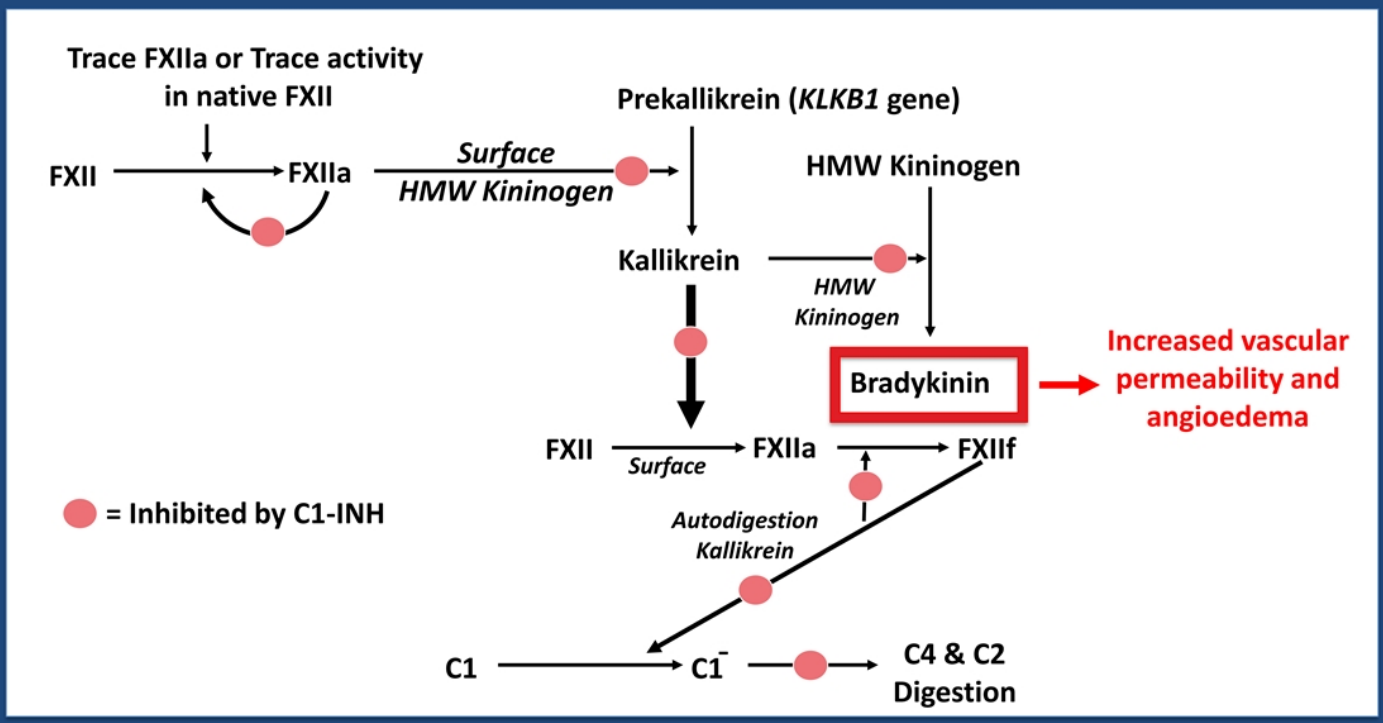
Longitudinal assessment*

- 221 patients with HAE
- 5736 patient-years of observation
- 131,110 angioedema episodes
- 1,229 laryngeal edema episodes; impacted 108 of 209 patients (51.7%)
- Mean number of attacks/year: 22.9
  - Females 24.0
  - Males 20.1

- ~1:50,000; no ethnic predominance; females generally more severe phenotype
- Minimal barriers to newer therapies besides unknown safety risks for pregnant women and pediatric patients

*Bork K, et al. *Am J Med*. 2006;119:267-274.

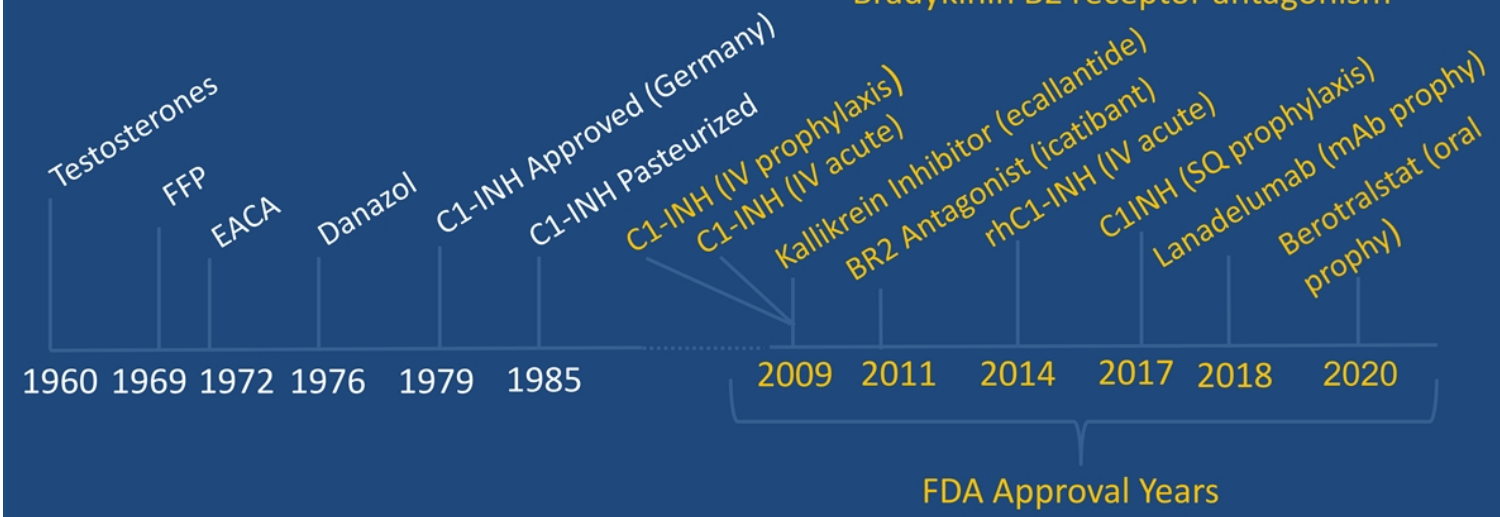
HAE pathophysiology



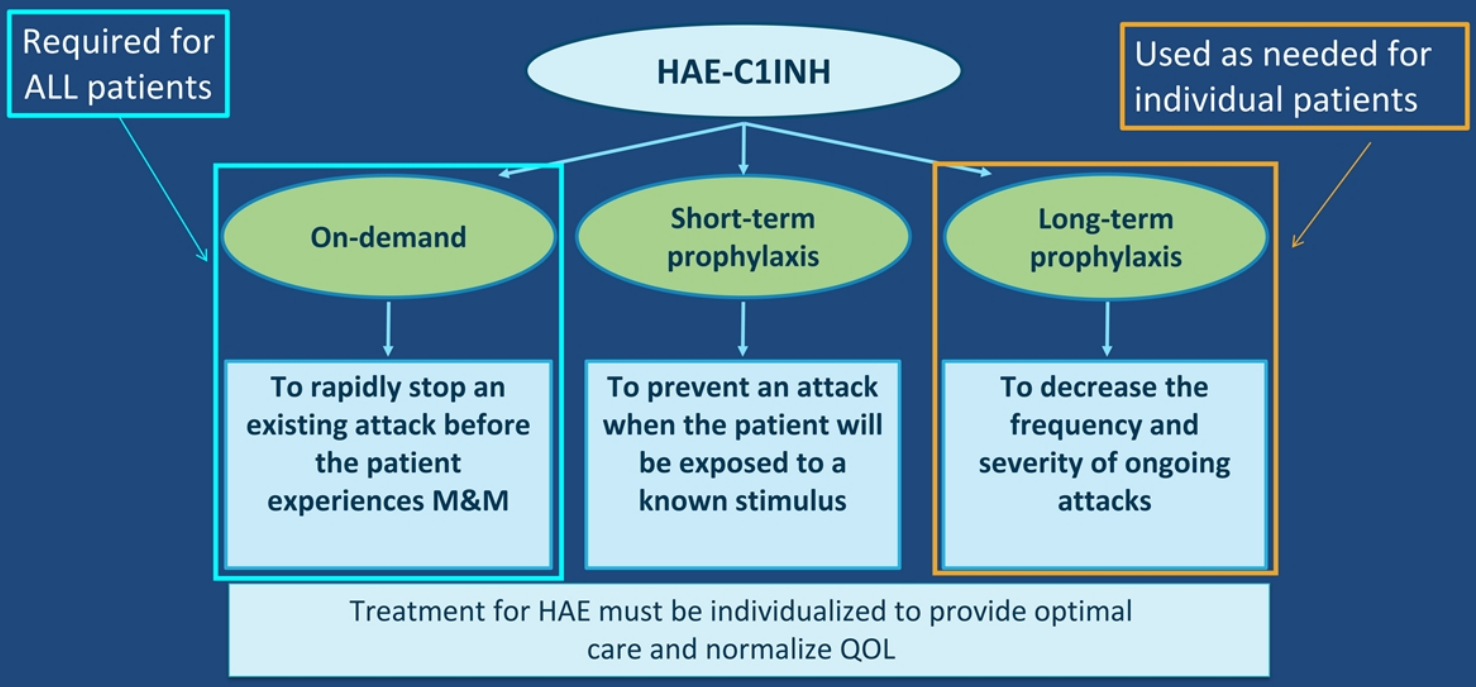
History of HAE therapies

Common Mechanisms of Action in 21st century:

- C1-INH replacement therapy
- Kallikrein inhibition (from *KLKB1* gene)
- Bradykinin B2 receptor antagonism

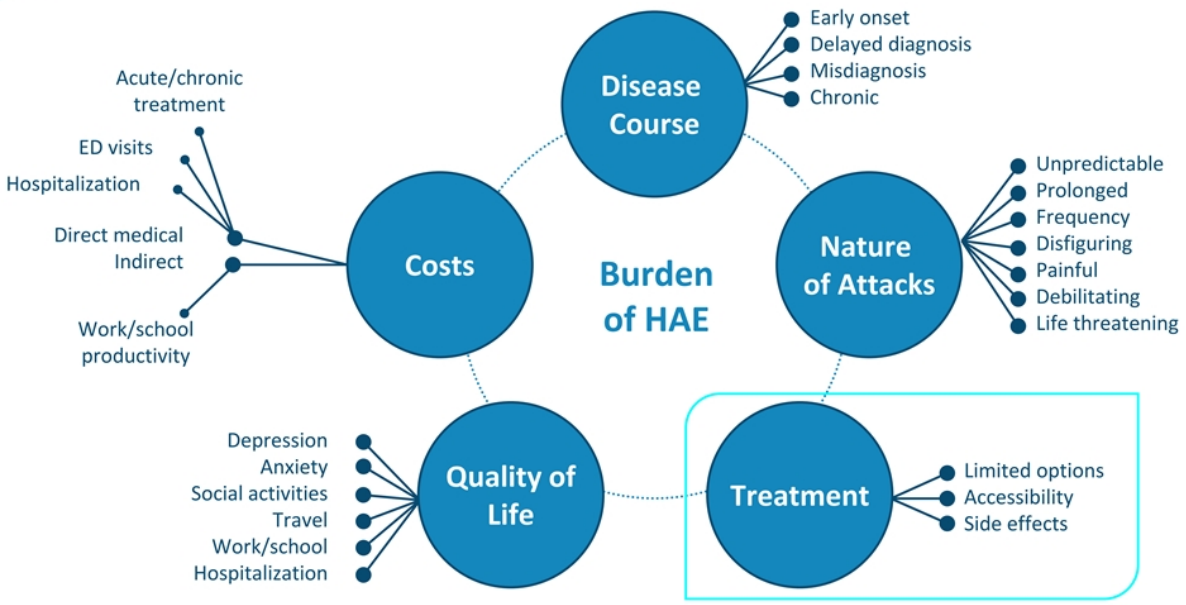


Current treatment strategies for HAE



Busse P, et al. *J Allergy Clin Immunol Pract.* 2020:

Impact of HAE on patient lives



Banerji A, et al *Ann Allergy Asthma Immunol*. 2013

Consensus on treatment goals in HAE

- Global Delphi Initiative: Panel of 23 international HAE experts
  - Consensus agreement of >75%
- **Key Ultimate Goals**
  - **Normalize the patient's life (100%)**
  - **Achieve total control of the disease (95%)**
- Patient input on how they or their physician should assess whether HAE is well-controlled or their life is normalized (100%)
- Patients and treating physicians would benefit from novel tools to help assessment of HAE control or normalization of life (89%)

Unanswered Questions for Future HAE therapies:

- Safety
- Efficacy
- Tolerability (Burden of Treatment)
- Quality of Life
- Accessibility

Maurer M, et al. J Allergy Clin Immunol. 2021 May 25;S0091-6749(21)00821-6.

The road forward for unmet needs

- **Current state of patient management**:
  - Prevention of death and excessive pain
  - Reduced hospitalizations and disability
- **Unmet Needs:**
  - Reduced treatment burden and frequency
  - Life without interference from HAE
- **Potential Next-Generation Therapies**
  - KLKB1-targeting gene editing (e.g. Poseida)
  - KLKB1-targeting anti-sense oligonucleotides (e.g. Ionis)
  - C1-INH AAV-based gene therapy (e.g. BioMarin)
  - Targeted oral therapies (kallikrein inhibition, B2 receptor antagonism)

Thank you

POSEIDA THERAPEUTICS

P-KLKB1-101 for the treatment of Hereditary Angioedema (HAE)

Application of Cas-CLOVER

Presenter:

Blair Madison, PhD

HAE patients have an unmet need for a safe therapy with durable efficacy

P-KLKB1-101: Potential technology advantages

Safety

- ✓ High fidelity editing of *KLKB1* gene using Cas-CLOVER
- ✓ ~20x higher fidelity than Cas9, across multiple tissues/targets[1-12]
- ✓ Greatly minimized unintended edits
- ✓ Potential titration to individual patient needs

Durability

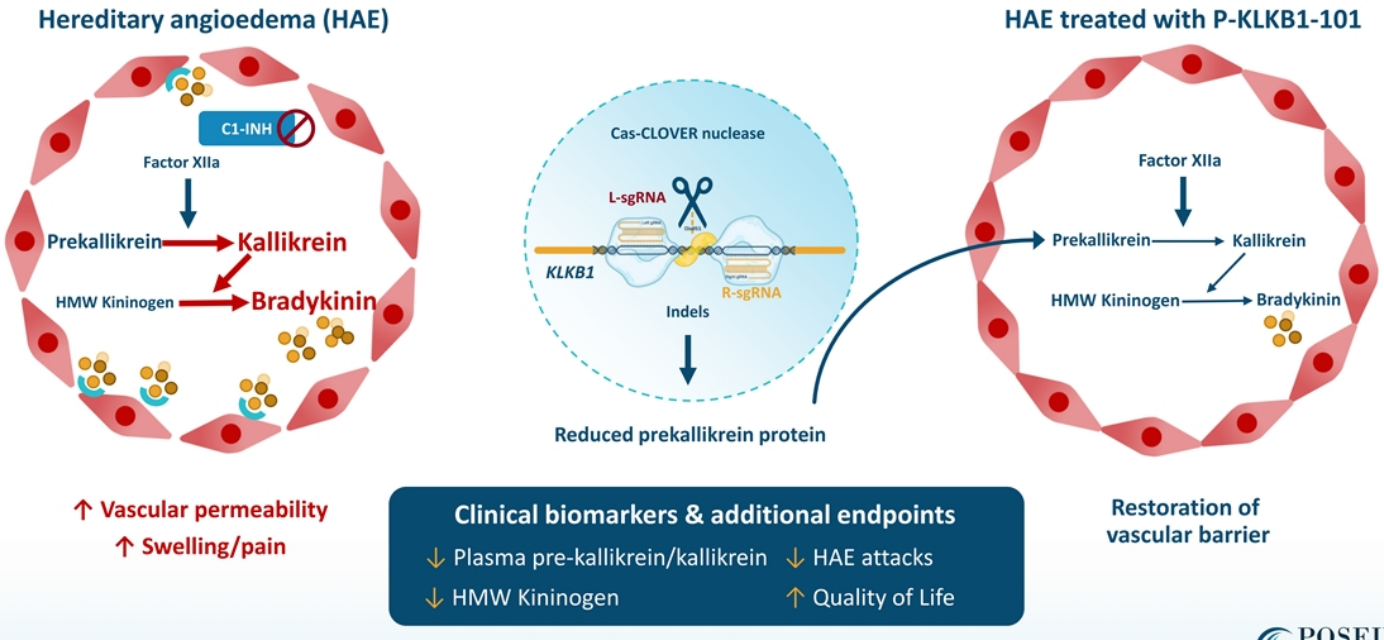
- ✓ Sustained efficacy via *KLKB1*/kallikrein inactivation for long-term relief
- ✓ Relief from treatment burden and anxiety of chronic prophylaxis
- ✓ Non-viral approach enables follow-up treatment if ever needed

Holistic approach to addressing unmet patient need

1. Ren et al., *Clin Cancer Res*., 2017; 2. Antoniani et al., *Blood*. 2018; 3. Georgiadis et al., *Mol Ther*. 2018; 4. Webber et al., *Nature Comm*., 2019; 5. Gilmore et al., *NEJM* 2021; 6. Fix et al., *J Immunother Cancer*. 2022; 7. Ottaviano et al. *Sci. Trans. Med*., 2022; 8. Zhang et al., *Nature*., 2022; 9. Cancellieri et al., *Nature Genetics* 2023; 10. Longhurst et al., *NEJM* 2024. 11. Madison et al., *Mol Ther Nucleic Acids*. 2022; 12. Data on file, *Manuscript in preparation (Poseida Therapeutics)*

POSEIDA THERAPEUTICS

Our gene editing approach to durable correction for hereditary angioedema

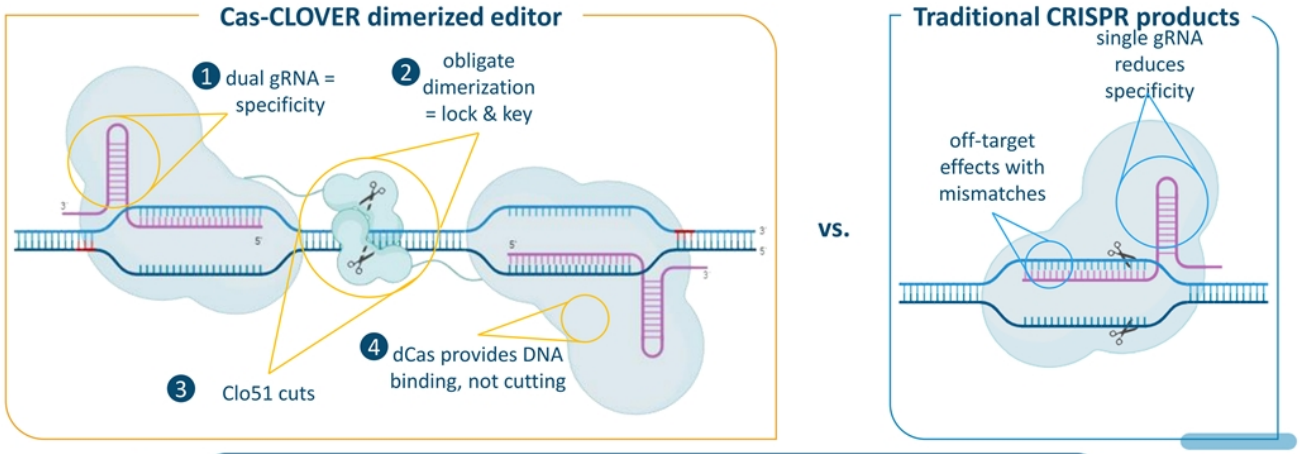


Clinical biomarkers & additional endpoints

- ↓ Plasma pre-kallikrein/kallikrein
- ↓ HAE attacks
- ↓ HMW Kininogen
- ↑ Quality of Life

Cas-CLOVER provides clean gene editing: engineered for high specificity

High-fidelity Poseida system via a dual guide RNA approach for a highly specific "molecular address"



Technical advantages

- Dual gRNA increases molecular specificity by **12 orders** of magnitude
- Obligate dimerization ensures spatial restriction of each edit
- High fidelity editing at *KLKB1*, with 100% primate-conserved gRNAs

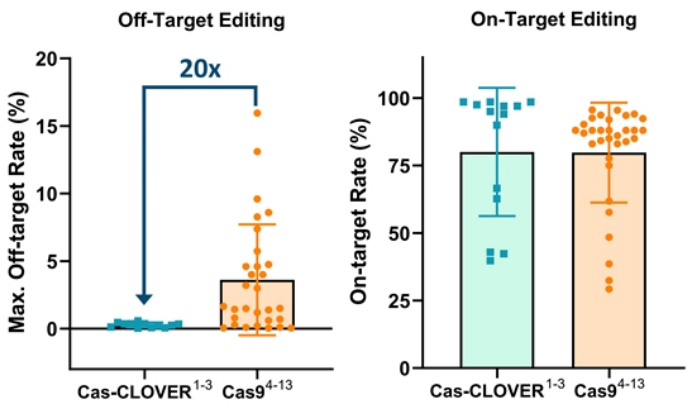
Cas-CLOVER gene editing system yields 20x higher fidelity than Cas9

Differentiated system with low to no off-target editing across multiple cells/targets

Cas-CLOVER technology:

- **20x** higher fidelity than Cas9 nuclease
- High on-target performance
- Clinical product: Poseida allo CAR-T
- Enhanced Clo51 nuclease

The difference



Cas9 targets: *KLKB1, TTR, TRAC, TRBC, HBB/HBD, B2M, PDCD1, TGFBR2, BCL11A, CD52*
Cas-CLOVER targets: *KLKB1, Pcsk9, B2M, TRBC1, TRBC2;* **Cells:** hepatocytes, HSPCs, T cells, HUDEP-2

1. Madison et al., *Mol Ther Nucleic Acids*. 2022; 2. Alvarez et al., *Mol Ther*. 31(4), Supp. 1, S1-794. 2023. 3. Data on file, *Manuscript in preparation (Poseida Therapeutics)* 4. Gilmore et al., *NEJM* 2021; 5. Longhurst et al., *NEJM* 2024; 6. Ren et al., *Clin Cancer Res*., 2017; 7. Antoniani et al., *Blood*. 2018; 8. Georgiadis et al., *Mol Ther*. 2018; 9. Webber et al., *Nature Comm*., 2019; 10. Fix et al., *J Immunother Cancer*. 2022; 11. Ottaviano et al. *Sci. Trans. Med*., 2022; 12. Zhang et al., *Nature*., 2022; 13. Cancellieri et al., *Nature Genetics* 2023.

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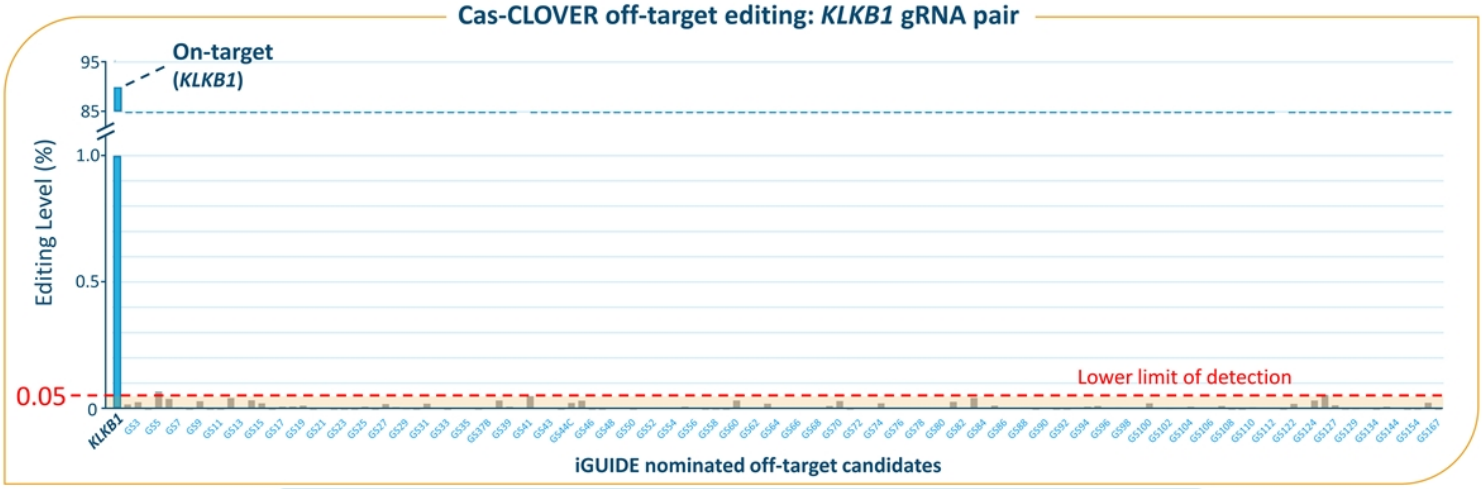
Unrivaled high fidelity at *KLKB1* locus, yielding <0.1% off-target editing

KLKB1 off-target evaluation in liver (primary human hepatocytes) in the context of 90% on-target editing



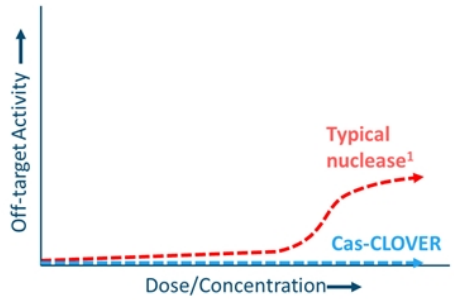
- Off-target editing at background level, below 0.1%
- Vast majority of sites show no editing – only 3 sites above LLOD
- 40x lower than rate observed in liver-directed Cas9 applications[1,2]

1. Gilmore et al., *NEJM* 2021; 2. Longhurst et al., *NEJM* 2024

POSEIDA THERAPEUTICS

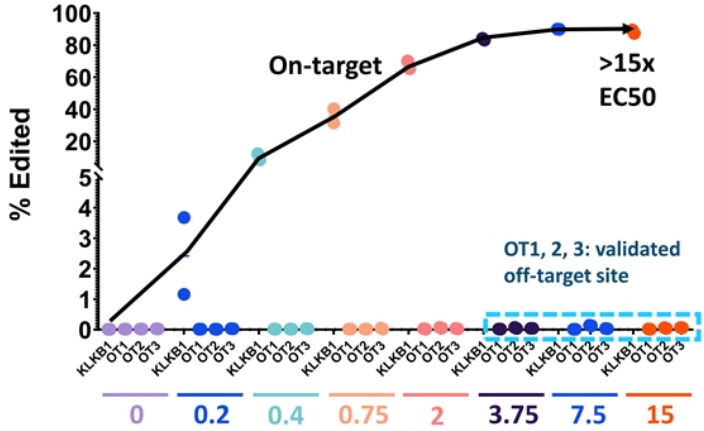
Cas-CLOVER maintains high fidelity even at 75x dose escalation

Off-target editing rate



- Cas9 yields compromised fidelity at higher doses
- No escalated off-target editing with Cas-CLOVER

Cas-CLOVER editing in primary human hepatocytes



Relative LNP Concentration (1 = EC50)

1. Gilmore et al. 2021, *NEJM*

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P-KLKB1-101 for the treatment of Hereditary Angioedema (HAE)

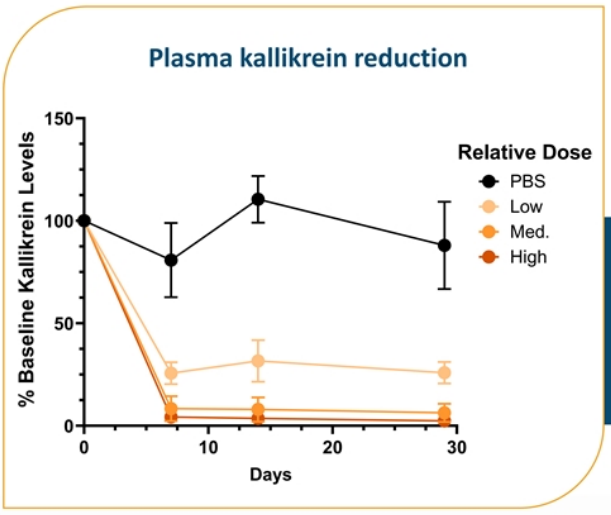
In vivo application of Cas-CLOVER: Pharmacology studies

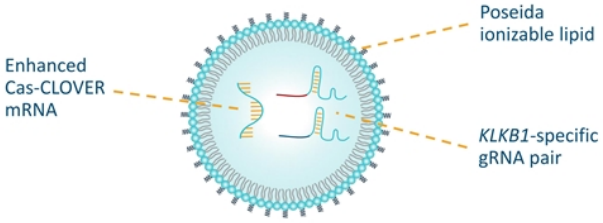
Presenter:

Bonnie Jacques, PhD

Stable targeted reduction of HAE biomarker with KLKB1 gene editing

Dose-responsive reduction with candidate LNP exceeds performance target in mice



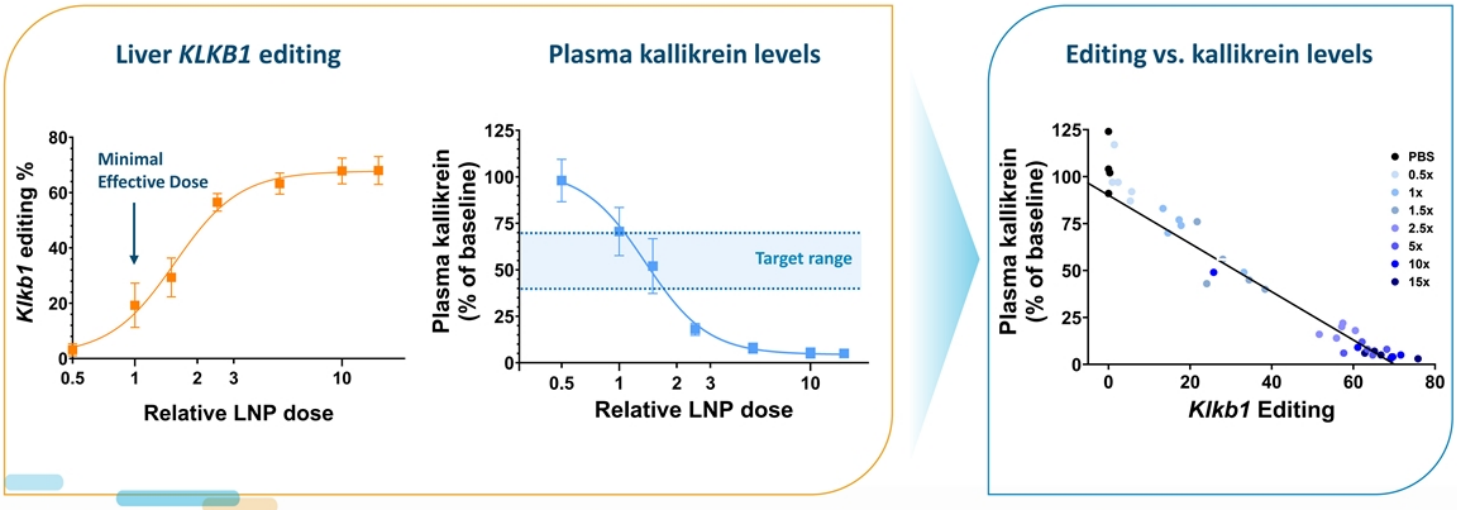


Lead LNP candidate yields target reduction:

- Target kallikrein reduction of 30-60%
- Maintenance of plasma kallikrein depletion

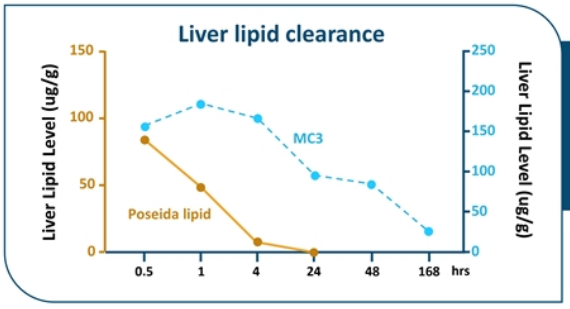
Wide effective dose range provides opportunity for titrating doses

Candidate yields controlled dose-dependent reduction in targeted kallikrein protein



Favorable safety and tolerability supports a wide therapeutic index

Rapid lipid clearance with no acute liver toxicity concerns



- *Rapid* clearance of Poseida ionizable lipid
  - *Key for minimizing liver toxicity*
- 7x faster than MC3 lipid (external FDA-approved)

Mouse dose escalation:

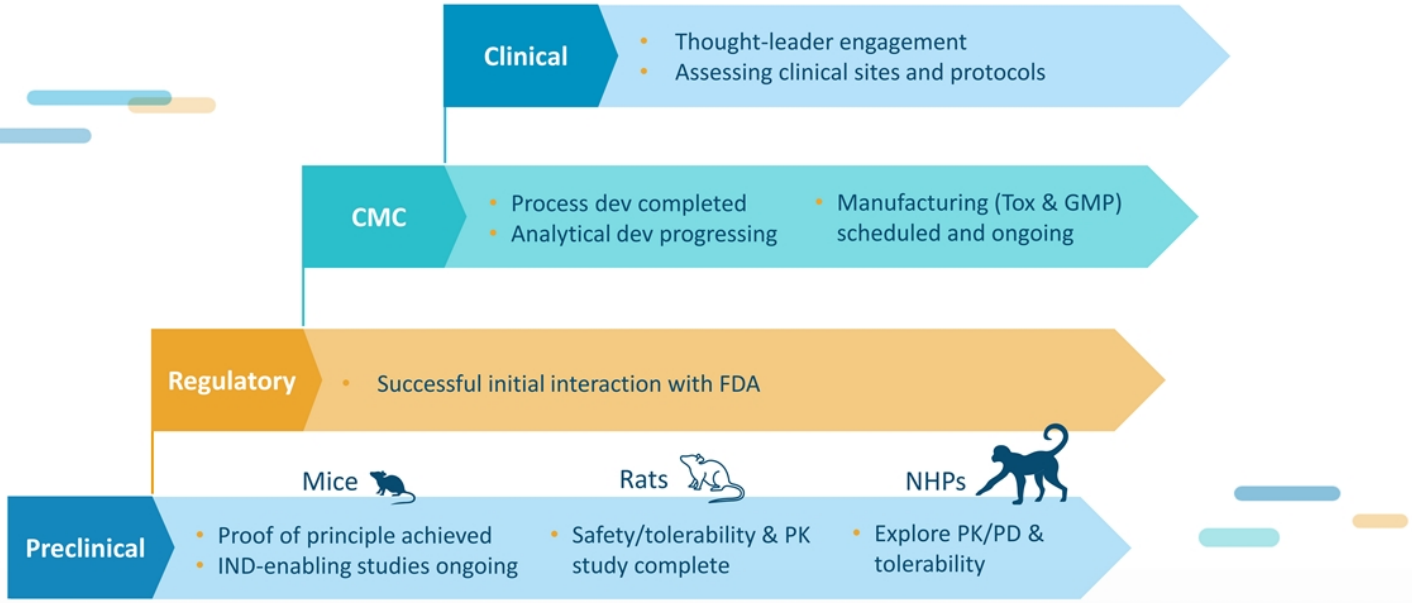
- At 2.5x to 15x minimum effective dose (MED)
  - ✓ No signs of liver toxicity
  - ✓ No elevation of GGT or CK
- No dose limiting toxicity up to >20x MED

Liver toxicity markers (24 hrs)

- ☑ AST
- ☑ ALT
- ☑ ALP
- ☑ T Bil

Within normal range

Validation across multiple species, progress towards clinical readiness



POSEIDA THERAPEUTICS

Poseida's non-viral gene insertion system

Presenter:

Jack Rychak, PhD

Transformative genetic medicines require sophisticated delivery and insertion technologies

The problem:

- Loss of gene function underpins many addressable genetic diseases
- Insertion of whole, functional genes needed to address these diseases with a single product across patient types
- Titrate-to-efficacy dosing needed for safe and efficacious delivery

Our solution

Optimal system can both **insert sizeable DNA** cargo and deliver it via a safe, **non-viral** approach such as engineered nanoparticles

Molecular platform

Poseida transposon

Insertion of whole genes into human genome

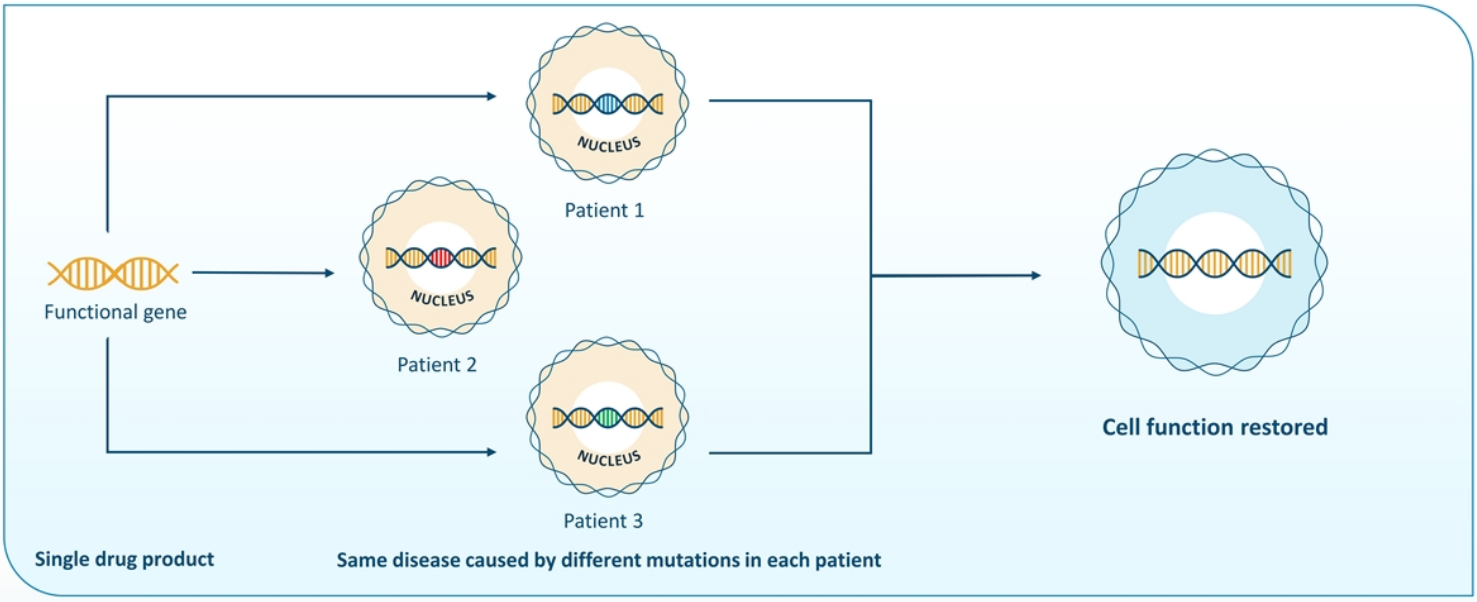
Delivery platform

Lipid nanoparticle

Repeat-dose delivery of molecular platform to desired cells

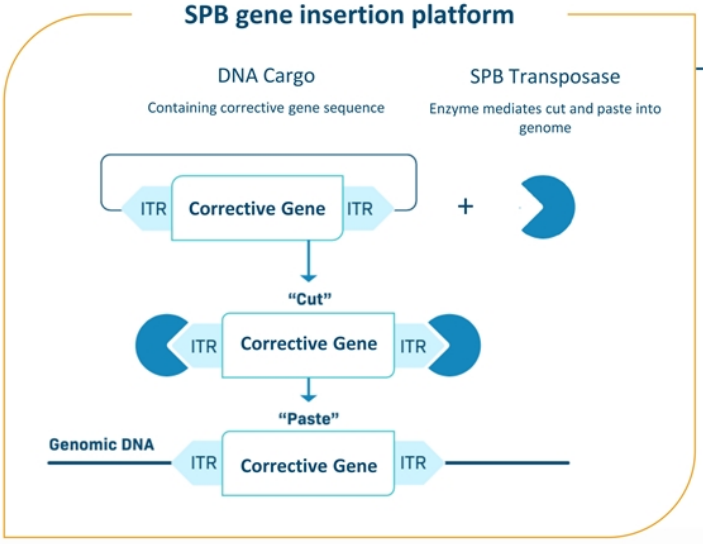
Efficient large DNA delivery unlocks the potential of genetic medicines

Poseida approach entails insertion of whole-gene DNA cargo for universal correction



Poseida molecular platform enables cut-and-paste insertion of large DNA cargo

Super piggyBac (SPB) is a high-efficiency transposon system for inserting genes into the genome



Why SPB?

- **Unique product versatility**
  - Single molecular platform can insert any therapeutic gene
- **SPB catalyzes direct gene insertion**
  - Highly efficient transposase enables in vivo use
- **Compact transposase (<2 kbp)**
  - Enables robust non-viral formulation for in vivo delivery
- **Large cargo capacity**
  - Supports whole-gene sized cargo
- **SPB platform clinically validated in 5 Poseida ex-vivo programs**

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

POSEIDA THERAPEUTICS

Our non-viral delivery technology is poised to unlock the field of genetic medicine

Why non-viral?

Delivery of gene-size DNA

- Nanoparticle cargo capacity enables delivery of full genes to address all patient mutations

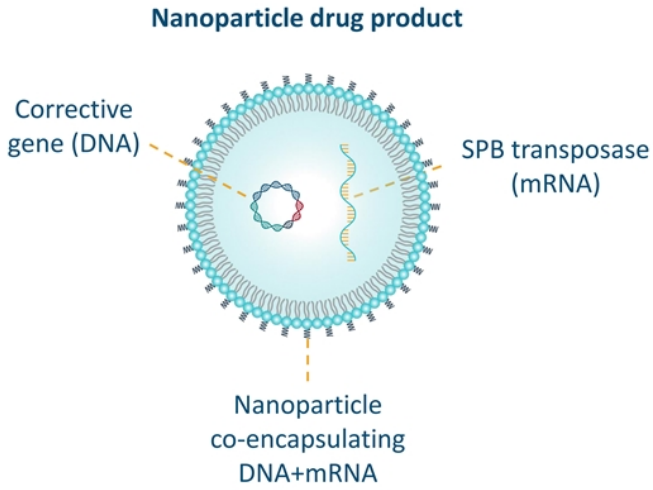
Safety / Efficacy

- Non-immunogenic nanoparticle enables repeated titrate-to-efficacy dosing

Manufacturability

- Nanoparticle platform built on chemistry, rather than biology, offers CMC advantages

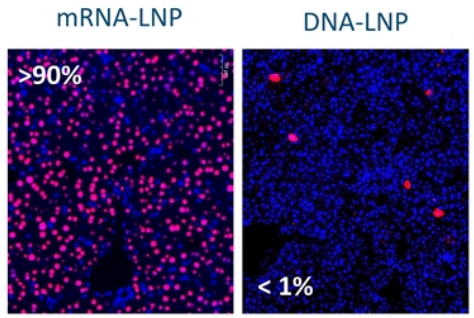
Nanoparticle drug product



Conventional mRNA-LNP platforms are not suitable for DNA delivery

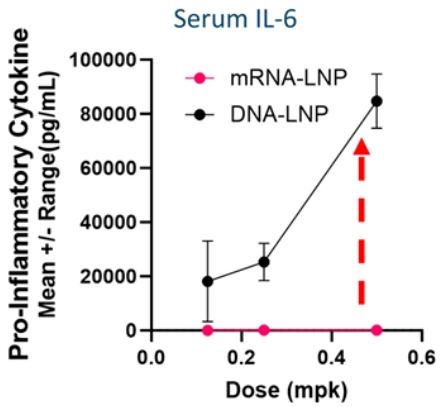
LNP provides a strong foundation upon which to build a non-viral DNA delivery system

Efficiency barrier



Immunocompetent adult mice administered conventional mRNA- or DNA-LNP intravenously

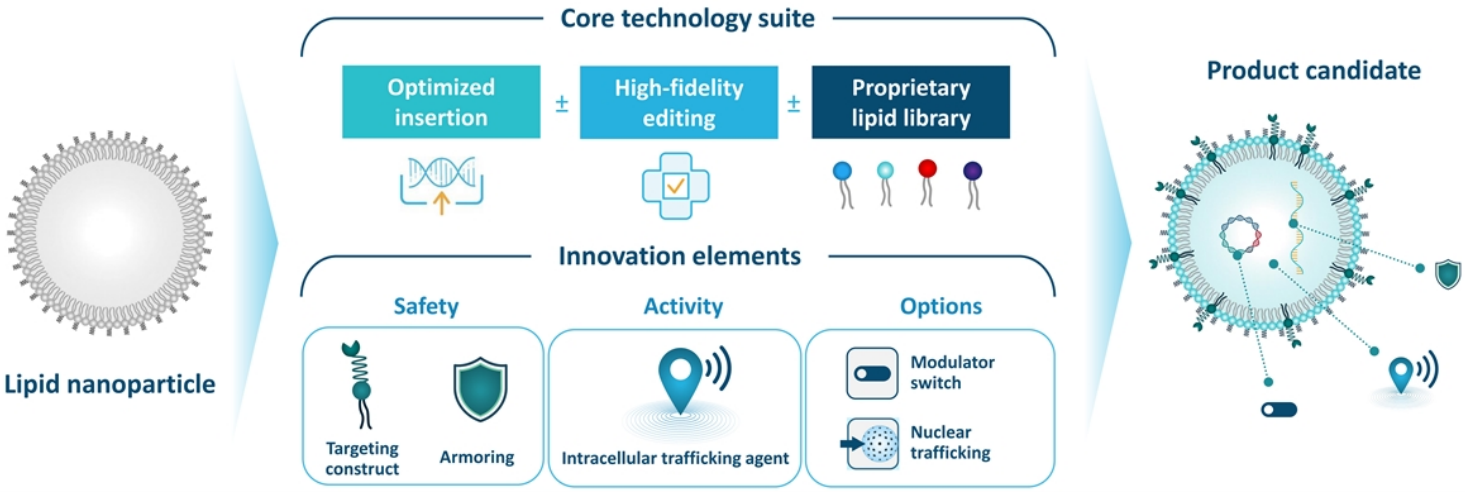
Safety challenge



Immunocompetent adult mice administered conventional mRNA- or DNA-LNP intravenously; Interleukin-6 (IL-6) measured at 4h post-dose

Poseida non-viral technology goes beyond the conventional lipid nanoparticle

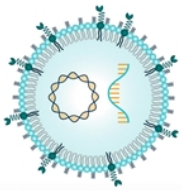
Incorporates the best of our proprietary technologies to enable powerful product candidates



Designed to enable the clean delivery of DNA

- Unintended immune cell uptake leads to release of pro-inflammatory cytokines
  - Can result in cell dysfunction and death
- Platform de-targets immune cells and armors hepatocytes from pro-inflammatory cytokines

Hepatocyte safety toolkit

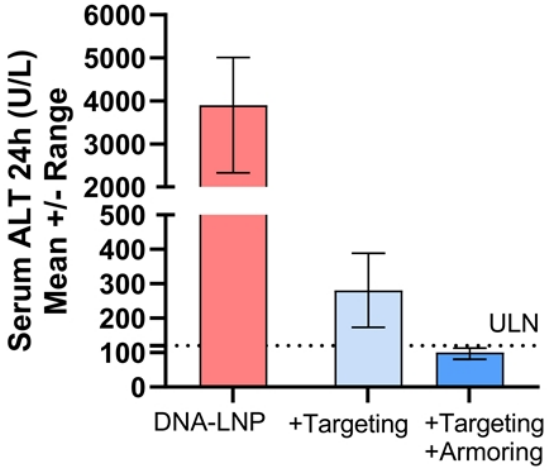


Non-viral system

Targeting construct

Armoring

Hepato-safety for FVIII DNA Delivery

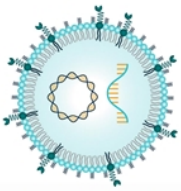


Adult immunocompetent mice administered 0.5 mg/kg Poseida nanoparticle comprising SPB transposase and hFVIII transposon.

Engineered for efficient hepatocyte transduction

- Poseida-invented ionizable lipids exhibit unique functionality for packaging large DNA molecules
- Targeting construct enables active targeting of hepatocytes
- Intracellular trafficking agent (ICTA) is a proprietary molecule that boosts activity of non-virally delivered DNA payloads

Hepatocyte transduction toolkit

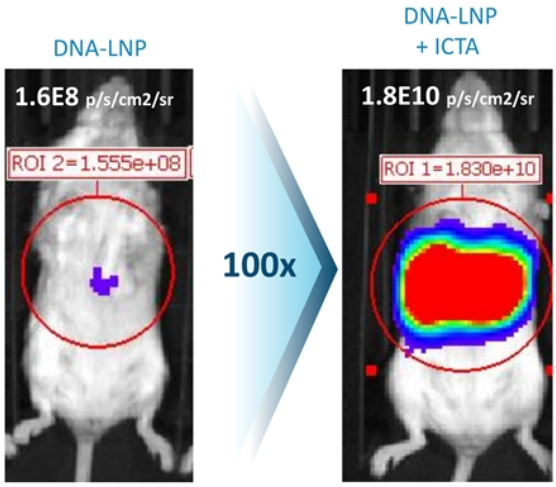


Non-viral system

Intracellular trafficking agent (ICTA)

Ionizable lipids

Significant increase in DNA activity with ICTA



Adult immunocompetent mice administered 0.5 mg/kg DNA –LNP intravenously; whole-body bioluminescence imaging performed at +7 days post-treatment

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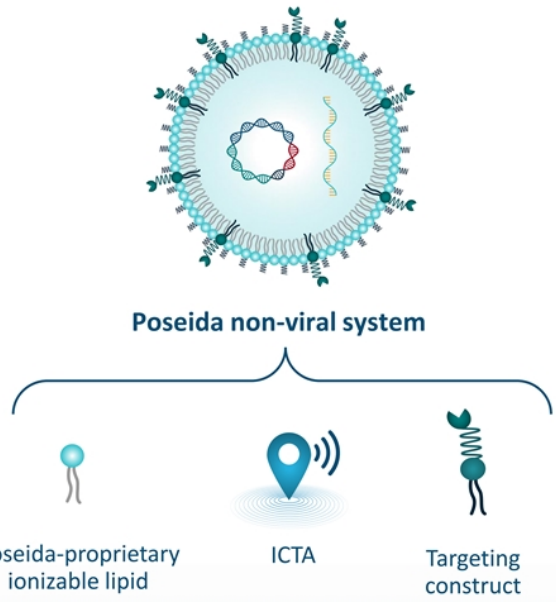
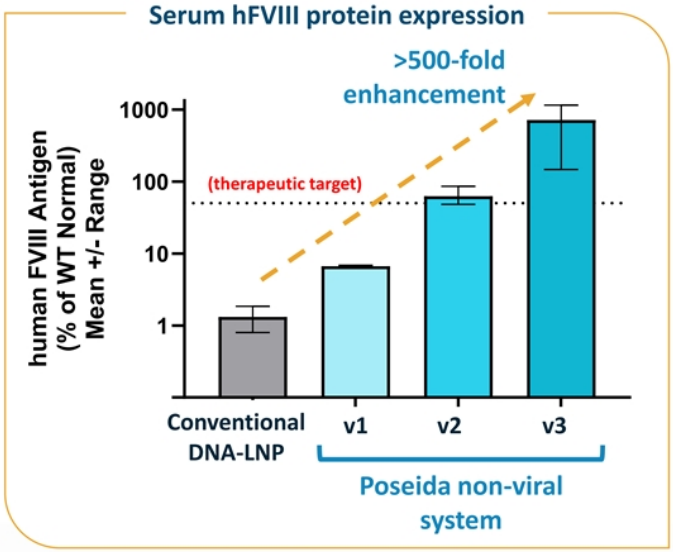
Exponential enhancement of secreted transgene expression for max efficacy

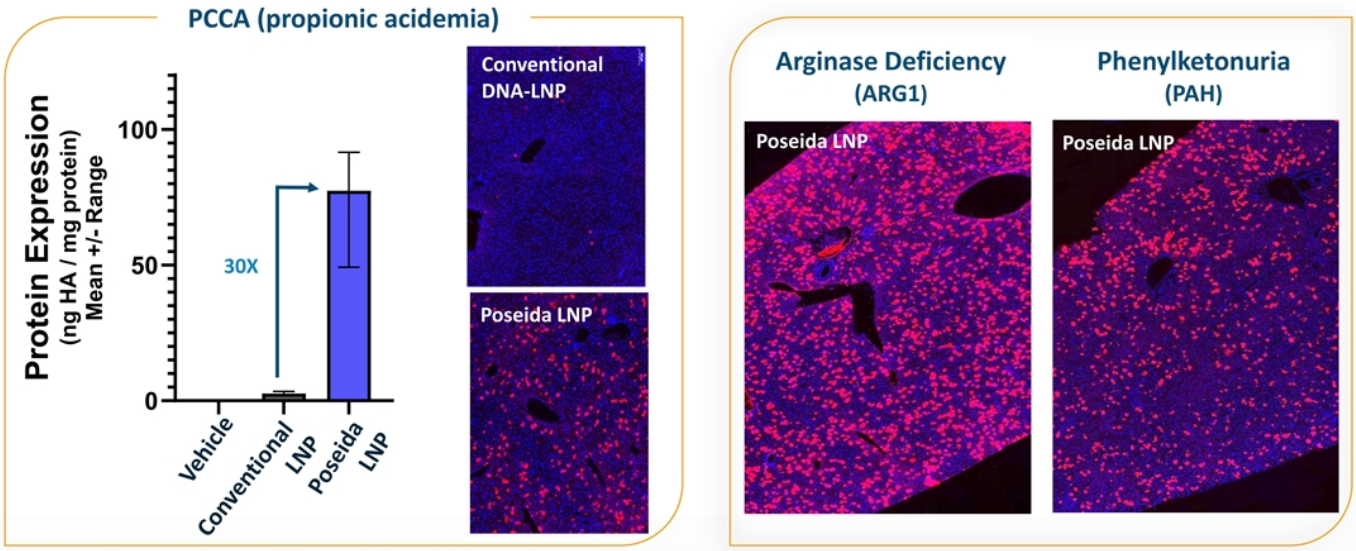




Adult immunocompetent mice administered single dose of LNP; human FVIII expression in serum measured by ELISA at +7-14 days

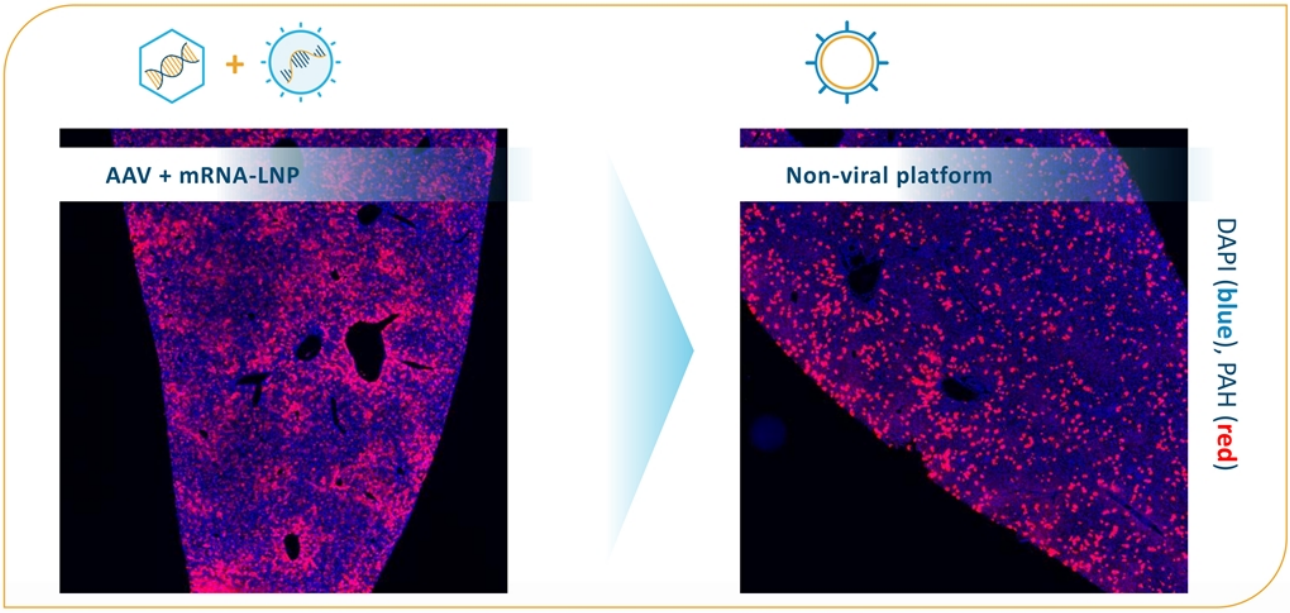
Significant increase in hepatocyte transduction with cell trafficking agent

Progression toward non-viral treatment of metabolic diseases



Juvenile immunocompetent mice single dose of LNP intravenously; immunostaining for transgene protein (pink).

Poseida’s non-viral platform achieving AAV efficiency



Juvenile immunocompetent mice co-administered AAV-PAH donor and mRNA–LNP (left) or administered single dose of Poseida LNP (right) intravenously; immunostaining for PAH protein.

Poseida's non-viral transposon technology uniquely addresses needs of an optimal product

Gene delivery technologies

- Delivery technologies that are non-integrating, (AAV, mRNA and episomal DNA) lack durability
- Additional immunogenicity challenges faced by AAV

Gene editing and insertion technologies

	Base/prime editor	Nuclease (knock-in)	Non-viral transposon
Single product coverage *(ability to address all mutation types)*			✓
Correction permanence			✓
Ease of redosing			✓
Deliverability *(compact enzyme size)*			✓

Note: Comparison is of representative technologies in each category and may not reflect all the most recent advances.

Poised for the next wave of non-viral gene therapies

Summary

- Non-viral delivery of gene-size DNA may enable treatment of broad patient populations safely and cost-effectively
- DNA is a difficult payload to deliver due to transduction challenges and unique immune-safety hurdles
- Builds on conventional LNP platform to enable delivery of whole-gene DNA cargos and genome insertion machinery
- Poseida immune cell de-targeting and armoring has the potential to overcome inherent toxicities from DNA
- Establishes a holistic systems approach to enable powerful programs in hematology and metabolic diseases

Next steps

- Go-forward focus on non-viral platform
- Selection of development candidate to support P-FVIII-101
- Ongoing refinement of platform elements in translational animal species

Treatment landscape for Hemophilia A: Available Therapies and Unmet Needs

Steven W. Pipe, MD
Professor of Pediatrics and Pathology,
University of Michigan

MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

Clinical classification of Hemophilia

30,000-33,000 persons with Hemophilia in the USA

- 85% with Hemophilia A (factor VIII deficiency)
- 15% with Hemophilia B (factor IX deficiency)

Classification	Severe (40%- 50%)	Moderate (10%)	Mild (30%- 40%)
FVIII or FIX activity	<1%	1%–5%	6%–30%
Pattern of bleeding episodes	2–4 per month approx.	4–6 per year approx.	Uncommon
Cause of bleeding episodes	Spontaneous	Minor trauma	Major trauma Surgery

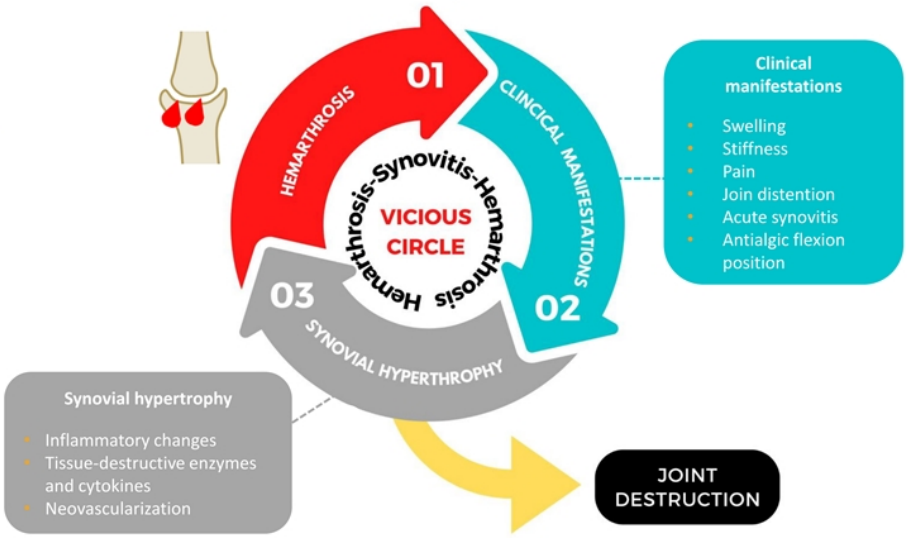
Adapted from Arun B, Kessler CM. In: Coleman RW, et al, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice.* 4th ed. Philadelphia, Pa: Lippincott, Williams & Wilkins; 2000:815-824.
https://www.cdc.gov/ncbddd/hemophilia/data.html

A single hemarthrosis (joint bleed) can result in joint disease later in life

The risk of joint damage increases with each subsequent hemarthrosis[1]

- Musculoskeletal bleeding episodes, including hemarthrosis (joint bleeding), make up approximately 80% of all bleeds in patients with hemophilia
- Joint bleeds can cause a high degree of joint damage and functional limitations if there is no rehabilitation

The hemarthrosis-synovitis-hemarthrosis vicious circle in hemophilia[2]

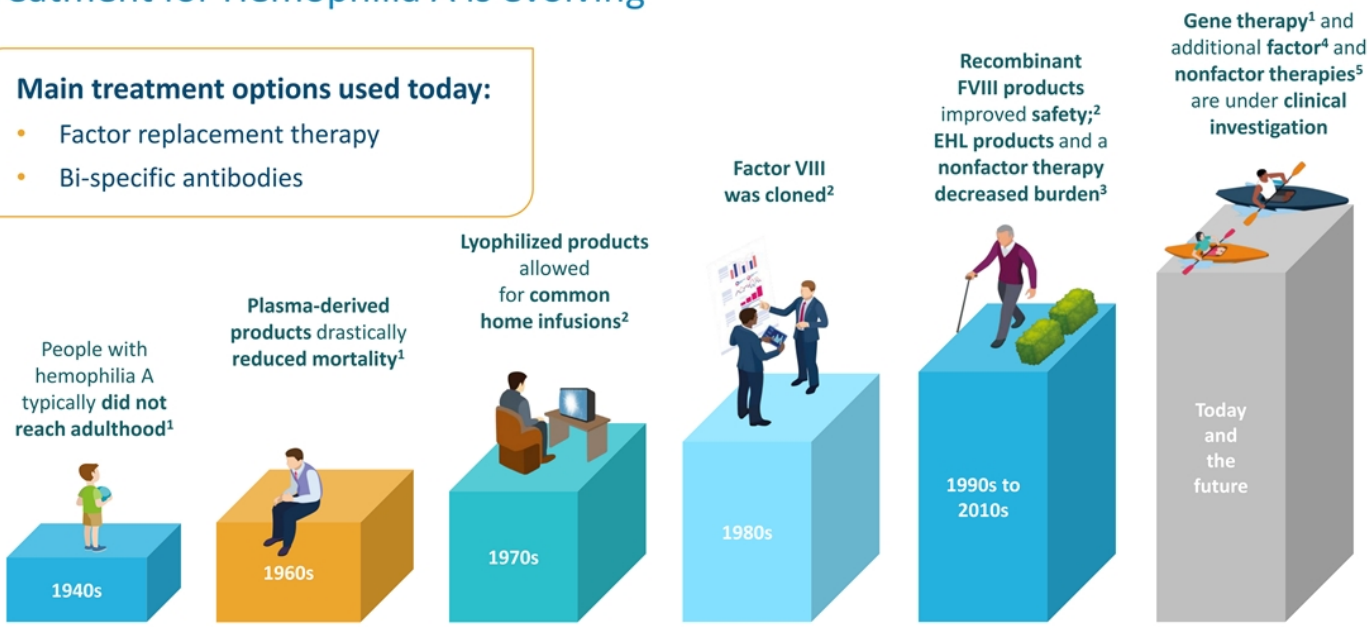


1. Angela Forsyth et al. Health 2020:12, 158-179
2. Ruben Cuesta-Barriuso et al. Journal of Blood Medicine 2022:13, 589-601

Treatment for Hemophilia A is evolving

Main treatment options used today:

- Factor replacement therapy
- Bi-specific antibodies



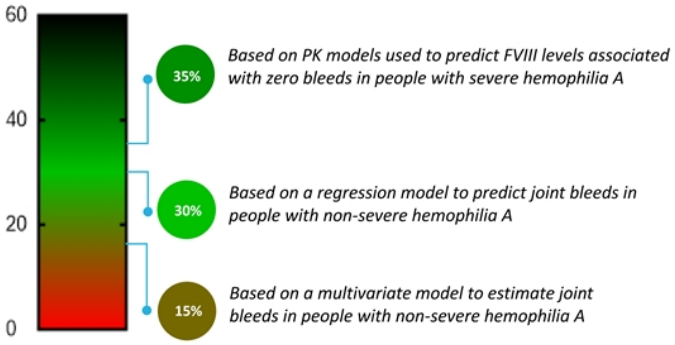
EHL, extended half-life; FVIII, factor VIII.

1. Skinner MW, et al. *Haemophilia*. 2020;26(1):17-24. 2. Lusher JM. In: Kaushansky K, Berliner N, eds. *50 Years in Hematology: Research That Revolutionized Patient Care*. Washington, DC: American Society of Hematology; 2008:25-27. 3. Berntorp E, et al. *Blood Reviews*. 2021;50:100852. 4. Konkle A, et al. *N Engl J Med* 2020;383(11):1018-1027. 5. Lenting PJ. *Blood Adv*. 2020;4: 2111–2118.

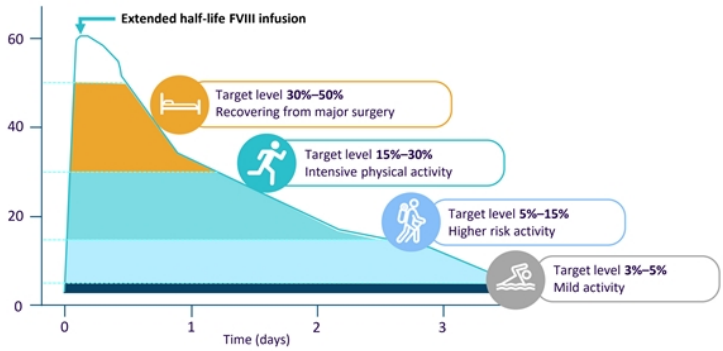
Current prophylaxis regimens are inadequate to safeguard individuals with Hemophilia

- ***Unmet need for hemophilia patients*** *requiring treatments that* ***improve Quality of Life***
- Factor replacement **disadvantageous** for **QoL** due to treatment **peaks/troughs** and lack of constant FVIII levels over time

FVIII levels associated with Zero Joint bleeds[1, 2, 3]

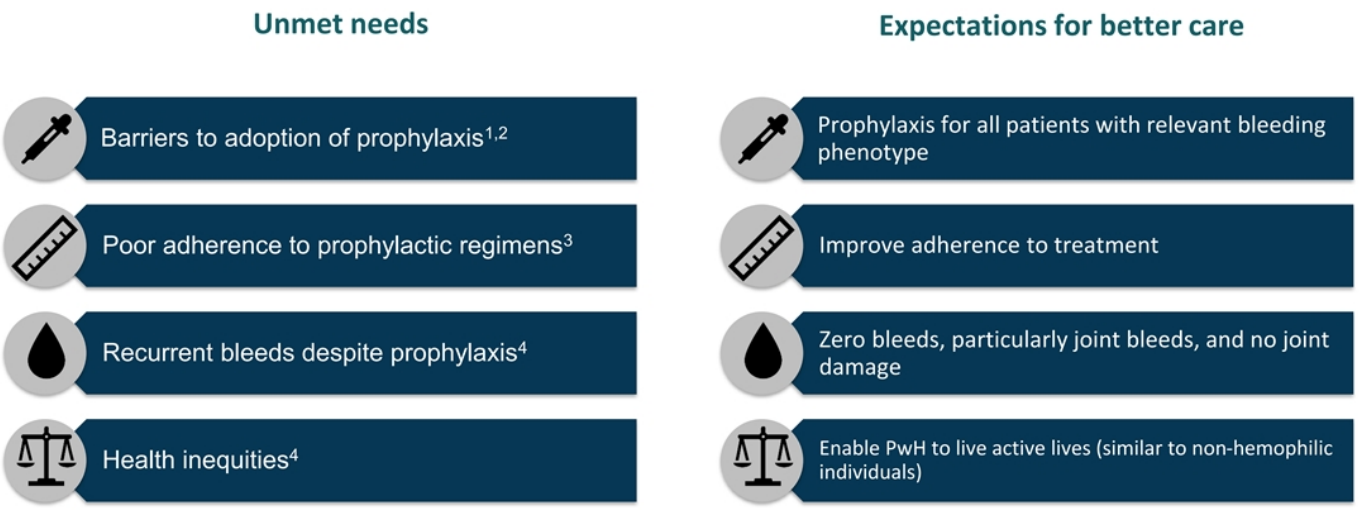


Recommended target FVIII levels after treatment infusion for various physical activities[4]



1. den Uijl I, et al. Haemophilia. 2011;17(1):41-44; 2. Soucie J, et al. Blood Adv. 2018;2(16):2136-2144; 3. Chowdary P, et al. Thromb Haemost. 2020;120(5):728-736; 4. Berntorp E, et al. Blood Rev. 2021;50:100852.

Despite many advances, unmet needs in Hemophilia remain



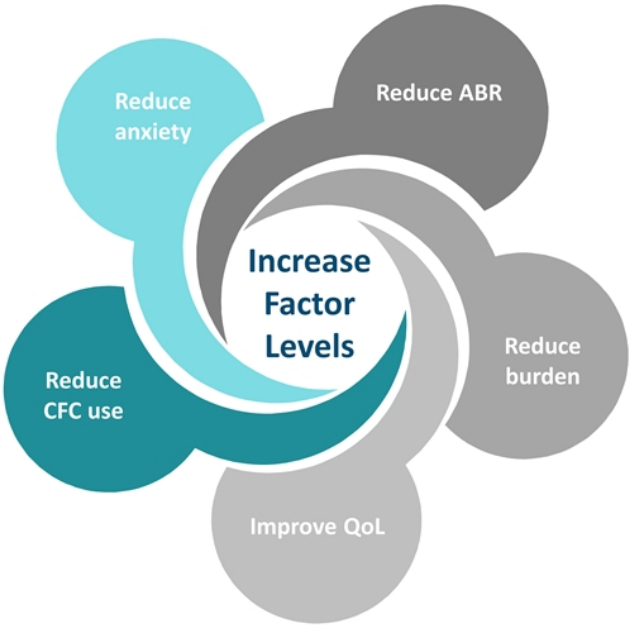
1. Berntorp E et al. *Haemophilia*. 2017;23:105-114. 2. Ay C et al. *Ann Hematol*. 2020;99:2763-2771. 3. Thornburg CD and Duncan NA. *Patient Prefer Adher*. 2017;11:1677-1686 4. Warren B et al. *Blood Adv*. 2020;4:2451.

Current and future approaches to care for Hemophilia A

	Pre-replacement Therapy	Replacement Therapy[1,2]	Non-replacement Therapy[1–3]	Viral Gene Therapy[1–3]	Future Therapy
		On demand Prophylaxis Standard half-life Extended half-life	Mimetics / agonists *Substitution therapy* Antagonists *Haemostatic rebalancing*	rAAV vector-mediated *Liver-directed* Lentivirus-mediated *Bone marrow-targeted*	Non-viral technologies *Liver-directed* Therapeutic Modality X
Tools of Our Trade	Supportive care only	Plasma-derived clotting factors Recombinant clotting factors Unmodified Bioengineered	Bispecific antibodies siRNA knockdown mAb inhibitors Bioengineered serpins	Gene addition Gene editing Cellular therapy	Gene addition Gene editing Cellular Therapy
Safety Concerns	Consequences of no Tx: • Mortality • Crippling joint disease	• Infections (bloodborne)* • Inhibitors, anaphylaxis • Anti-drug antibodies • Thrombosis • Assay challenges	• Thrombosis • Thrombotic microangiopathy • Anti-drug antibodies • Allergic reactions • Assay challenges	• Immune response to rAAV • Liver toxicity • Inhibitors? • Vector integration effects	• Immune response • Liver toxicity • Inhibitors • Integration considerations

*With plasma-derived clotting factors only.
mAb: Monoclonal antibody; rAAV: Recombinant adeno-associated virus; siRNA: Small interfering RNA; Tx: Treatment.
1. Srivastava A, et al. *Haemophilia* 2013;19:e1–47. 2. Mannucci PM. *Haematologica* 2020;105:545–53. 3. Weyand AC, Pipe SW. *Blood* 2019;33:389–98.

Goals and risks of gene therapy in Hemophilia



Potential safety issues for all gene therapies in development for hemophilia

Liver toxicity
Transaminitis, liver toxicity

Impaired immunity
Immunosuppressive therapy often required

Thrombosis
Consequences of increased factor expression

Oncogenesis
Requires monitoring

ABR, annualized bleeding rate; CFC, clotting factor concentrate; QoL, quality of life.
Pipe SW, et al. Expert Opin Biol Ther. 2022;22:1099-1115.

Potential pros and cons of current gene therapy for Hemophilia

Viral Gene Therapy

Pros	Cons	Ideal
Single-infusion event Liberation from prophylaxis burden	Some patients currently ineligible (children, NAb, factor inhibitors)	Pediatric to adult patients Individualized titration Repeat administration
Steady-state hemostasis (reduced ABR)	Known/unknown risks Liver toxicity, impaired immunity	Non-viral
Reduced anxiety	Long-term safety and durability?	Acute and long-term safety
Annual cost savings	High initial cost	Stable durability of effect
		Lower cost

ABR: Annualized bleed rate

Pipe SW, et al. Expert Opin Biol Ther. 2022;22:1099-1115.

Thank you

POSEIDA THERAPEUTICS

P-FVIII-101 for the treatment of Hemophilia A

In vivo application of non-viral system

Presenter:

Blair Madison, PhD

Key challenges for AAV and episomal approaches to Hemophilia A

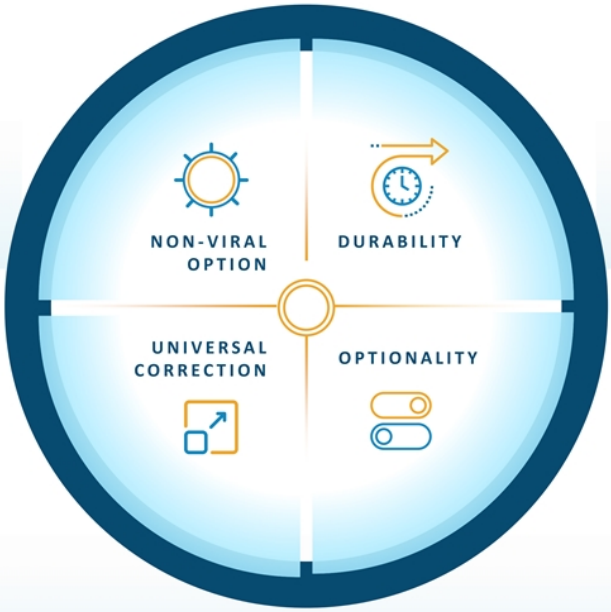
Desirable feature	AAV	Episomal	Poseida non-viral insertion system
No long-term immune suppression:	X	✓	✓
Potential re-dosing:	X	✓	✓
Large cargo capacity:	X	?	✓
Juvenile efficacy:	X	X	✓
Low vector copy number:	X	X	✓
Durability:	X	X	✓

Potential added non-viral advantages:

- Technology overcomes critical limitations and stalled uptake of AAV
- Avoids issue of seroprevalence against certain AAV vectors
- Provides a complete system of features, vs. episomal methods

Poseida's non-viral system has potential to address unmet needs for Hemophilia A patients

- Non-viral lipid nanoparticle (LNP) delivery less immunogenic
- Greater access without concerns of prior viral exposure
- Titrate-to efficacy, or re-dosing, for a personalized therapy



- Transposition in hepatocytes for potential long-term durability
- 13 months of FVIII expression with potential for longer
- Key advantages in adolescents, for early intervention

- Large transposon cargo capacity enables whole gene restoration
- Optimally suited for both FVIII gene along with key *cis*-regulatory elements

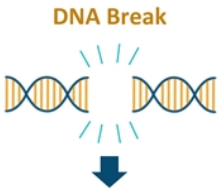
- Flexibility: modulate through an inducible off-switch
- Titrate down, switch off, or swap out therapies

DNA insertion technology enables whole gene functional correction

Key advantages of our gene insertion approach over Cas9 knock-ins and episomal strategies

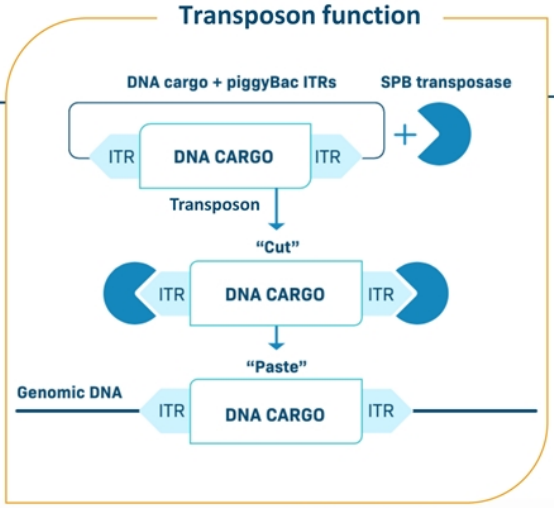
Cas9 knock-in challenges

- Double-strand breaks[1]
- DNA repair needed[2]
- Irreversible (one shot)[1-3]



ATGGACTG-INDEL-ATCGATG

Transposon function



ITR = inverted terminal repeat

Transposon advantages

- Stability & durability (vs. episome)
- No double-strand breaks[4]
- Large cargo capacity
- Active in non-dividing cells
- Simple 2-component system
- Re-dosable and reversible[5]

1. Jinek et al., *Elife*. 2013; 2. Cong et al., *Science*. 2013; 3. Ran et al., *Cell*. 2013; 4. Saha et al., *Nucleic Acids Res*. 2015; 5. Yusa et al. *Proc Natl Acad Sci U S A*. 2011

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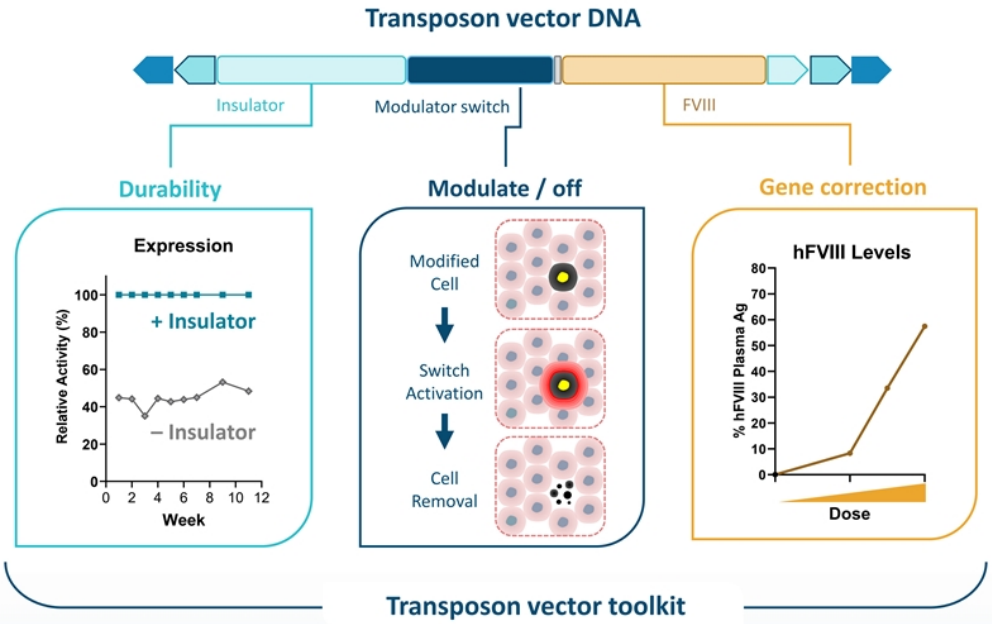
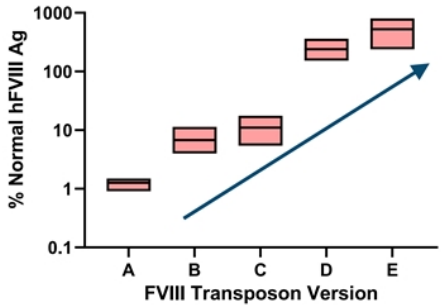
Large cargo capacity transposon provides optimal FVIII levels and optionality



Next-gen DNA/mRNA drives efficient insertion for maximal FVIII expression

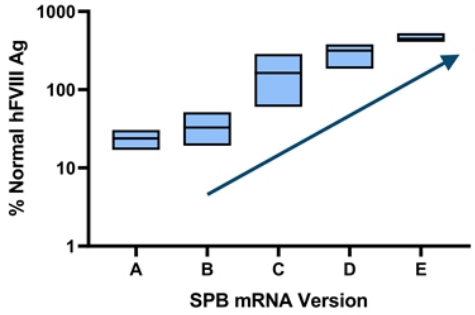
Iterative engineering of both transposon and transposase yields key advantages for robust FVIII levels

Transposon DNA



- Enhanced vector engineering
- Large vector cargo capacity for multiple key components

Transposase mRNA

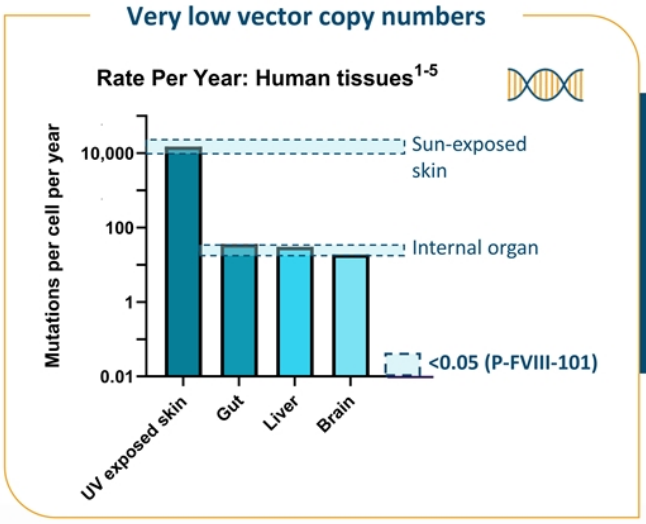


- Next generation optimized SPB
- Stabilizer boosts integration in target cells
- Immune evasion element dampens anti-drug response, especially in context of **repeat** dosing

Data plotted as peak elevations, current as of 03/12/2024. Data verification pending

Hemophilia A only requires minimal integration in small proportion of liver cells

Key safety advantage with fewer vector copies per cell, for minimizing insertional mutagenesis



How much is needed for therapeutic levels of FVIII?

- Insertion in <5% of liver cells more than sufficient
- **1,000-fold** lower than internal organ mutation rate
- **1 million-fold** lower than sun-exposed skin rate[6]

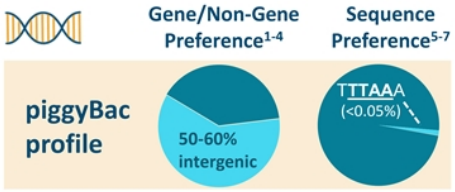
1. Werner and Sottoriva, *PLoS Comput Biol.* 2018; 2. Martincorena et al., *Science*. 2015; 3. Bae et al., *Science*. 201; 4. Blokzijl et al., *Nature*. 2016; 5. Lodato et al., *Science*. 2018; 6. At a VCN of 0.015 per diploid genome for P-FVIII-101.

POSEIDA THERAPEUTICS

Poseida gene insertion technology has a favorable integration profile

No safety findings following extensive in vivo studies

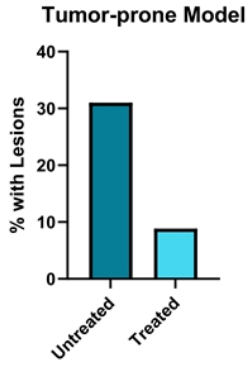
Favorable integration profile



***Restricted** integration, favoring expression*

- No liver lesions associated with transposition[8]
- Consistent with academic studies[9, 10]
- No clonal expansion observed in any lot of Poseida clinical CAR-T cells[11]

No transformation

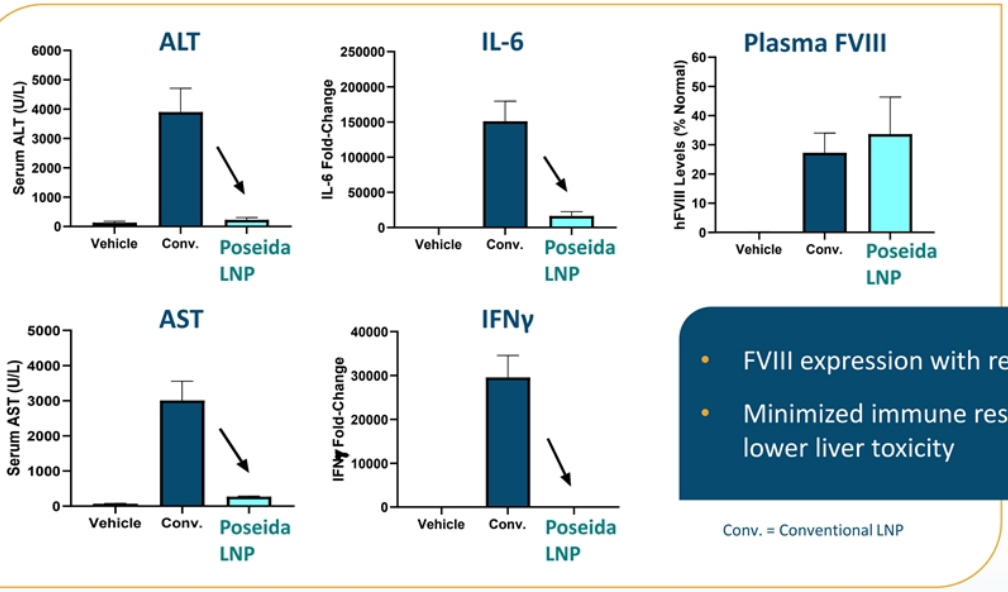


1. Liang et al., *Genesis*. 2009. 2. Galvan et al., *J Immunother*. 2009. 3. Gogol-Doring et al., *Mol Ther*. 2016 4. Yoshida et al., *Sci Rep*. 2017. 5. Li et al., *Insect Mol Biol*. 2005; 6. Ding et al., *Cell*. 2005; 7. Wilson et al., *Mol Ther*. 2007; 8: Data on file: among >200 mice in ≥6-month studies (amounting to >136 mouse-years) for 3 transgenes. 9: Siew et al., *Hepatology* 2019. 10: Rad et al. *Nat Genetics* 2015. 11: Data on file: 105 patients, 41.8 billion cells, avg VCN=1.7, with 128 person-years LTFU8-11, Madison and Shedlock. *Mol Ther*. 2023; NCT03288493; NCT04249947; NCT03741127.

POSEIDA THERAPEUTICS

Poseida non-viral system provides FVIII expression with low immunogenicity

Key delivery technology provides high tolerability in mice without compromising FVIII expression



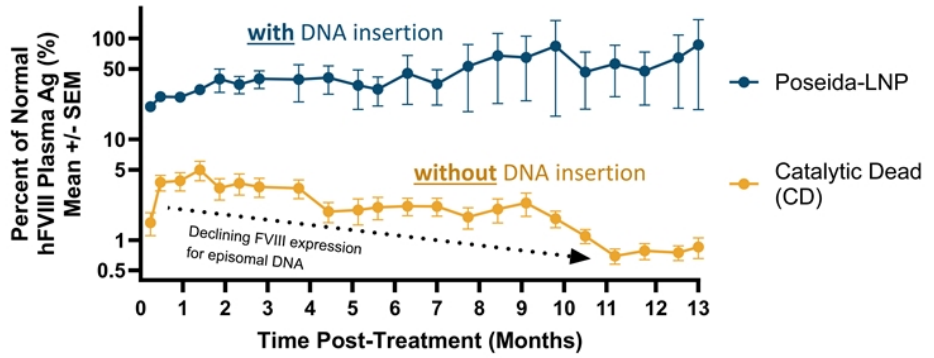
- FVIII expression with reduction of key cytokines
- Minimized immune response, in turn, provides lower liver toxicity

Conv. = Conventional LNP

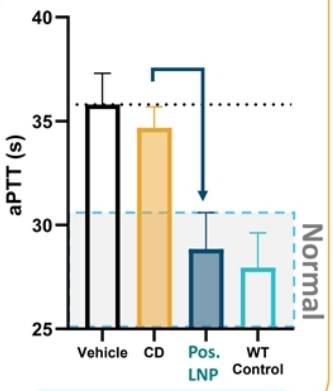
Durable FVIII expression achieved in adult mouse model across 13 months

Target levels achieved throughout study, providing key markers for success

FVIII expression in adult Hemophilia A mice



Clotting efficacy
13 months



Hemostasis achieved

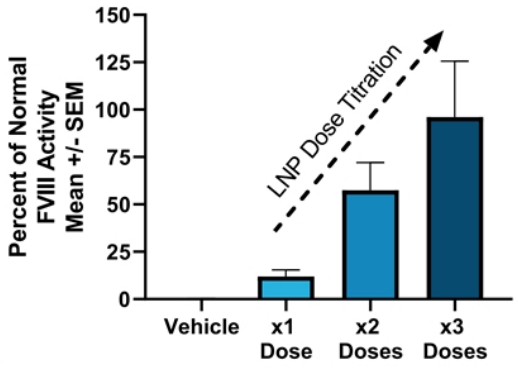
Study results

- hFVIII levels maintained throughout study (tolerized mouse model)
- No lesions or liver pathology in any animal at 13-month take-down

Titrating to efficacy via repeat dosing achieved in multiple studies

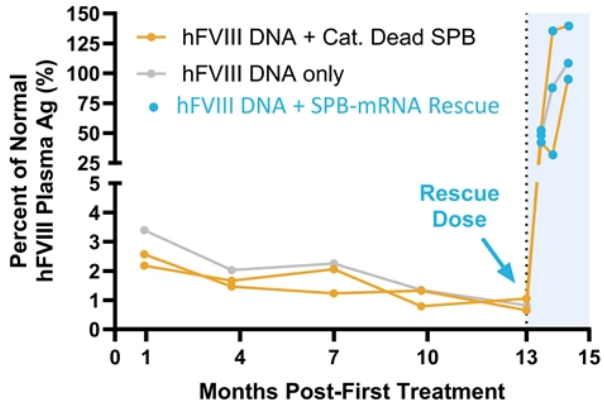
Additional repeat dosing experiments highlight ability to provide a rescue dose

FVIII activity in adult hemophilia A mice



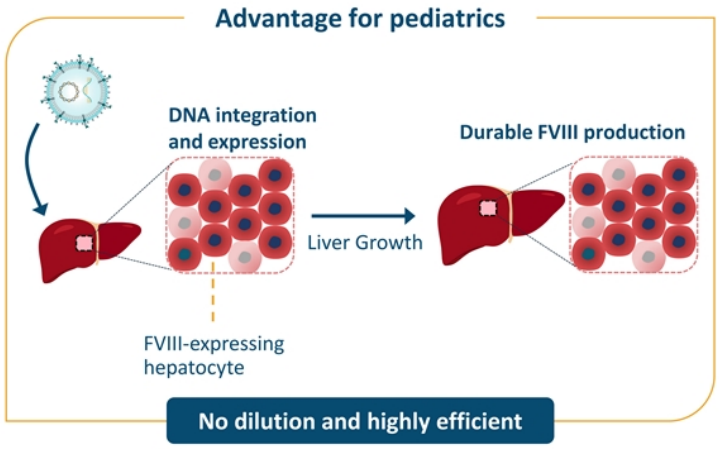
Repeat dosing yields stepwise increase of FVIII levels

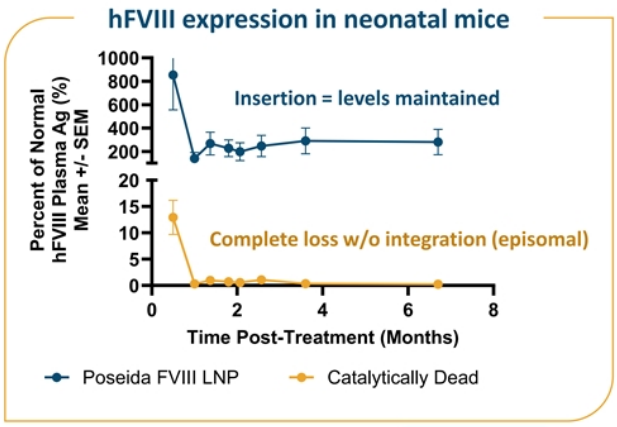
FVIII rescue in adult hemophilia A mice



Prior exposure to transposase + LNP components does not pose a barrier

Performance in growing liver supports principle of early intervention

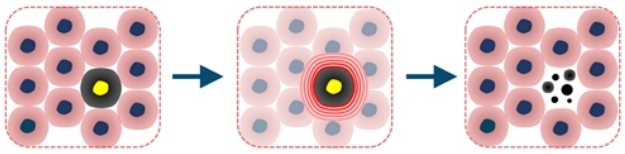




New options enabled to down-regulate / remove expression

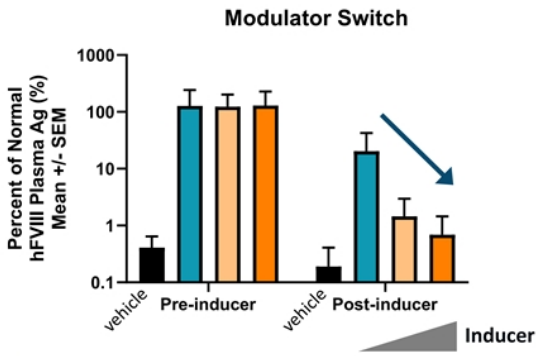
Large cargo capacity with our non-viral system enables added optionality

- Capable of “dialing down” FVIII levels
- Very small minority of hepatocytes impacted
- Provides option to switch off or down-regulate

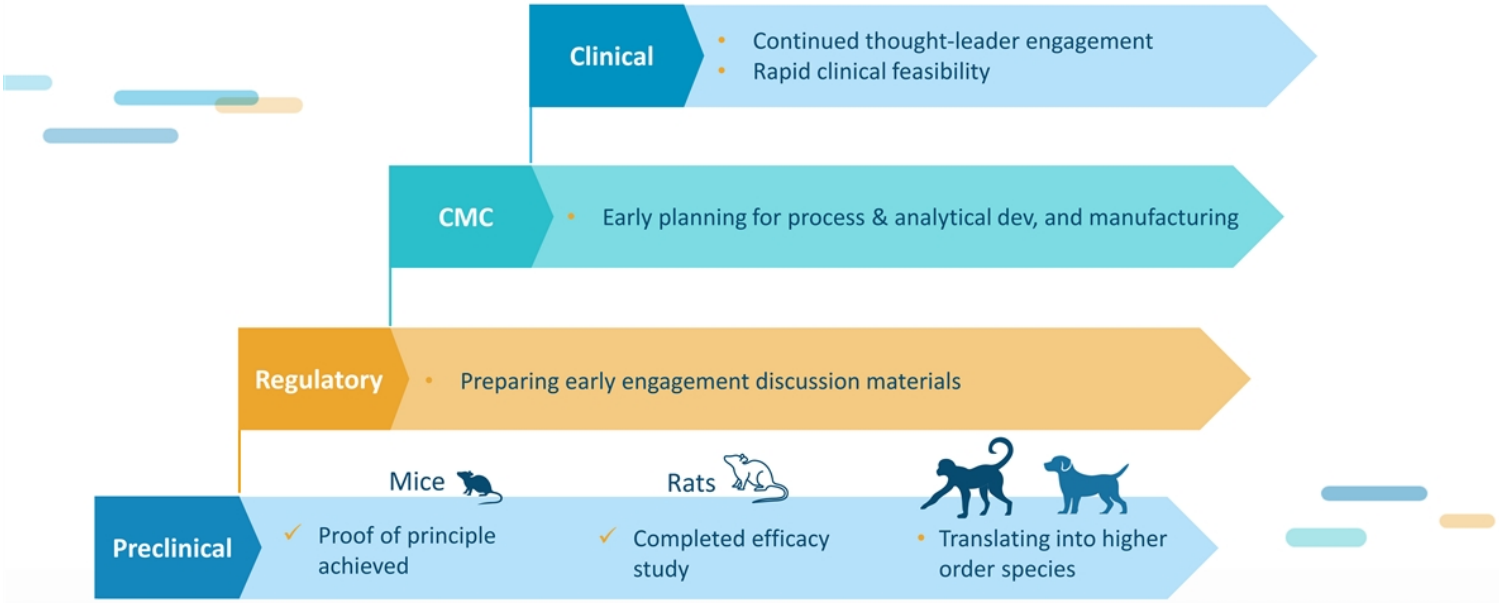


FVIII-expressing cell | Switch activation | Cell removal

Proof of concept results



Validation across multiple species, progress towards clinical readiness



POSEIDA THERAPEUTICS

Site-Specific Super piggyBac (ssSPB) Advancements

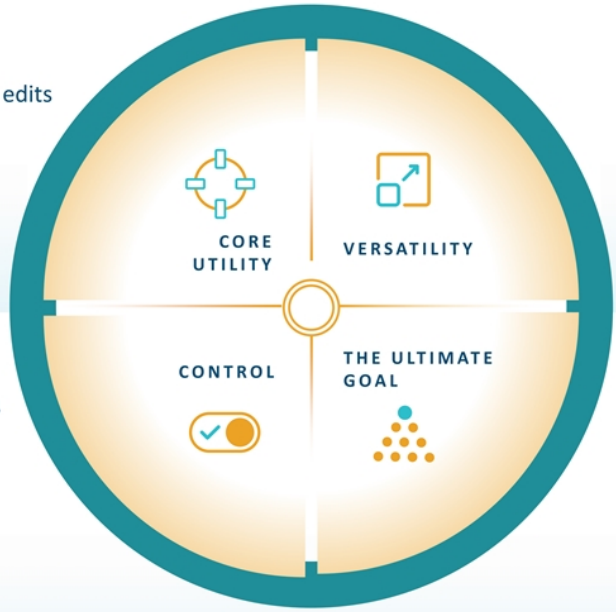
Update on site-specific gene insertion approach

Presenter:

Blair Madison, PhD

Unlocking the ideal traits of site-specific gene insertion with site specific SPB

- High-fidelity, yielding only desired edits
- Efficient integration rates
- Simplicity



- Reprogrammability
- Whole gene integration
- Targeting any genomic region
- Gene knock-out and knock-in
- Promoterless approach

- Reproducible integration pattern
- Uniform expression across all cells
- Predictable effects among edited cells

- Treat a broad range of genetic diseases with precision and efficiency

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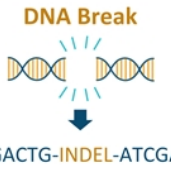
Site-specific SPB technology provides a simple system for targeted gene insertion

Cas9 and nucleases: the wrong fit

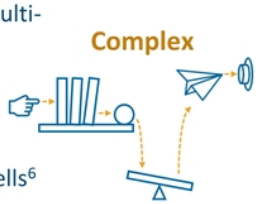
- Double-strand breaks[1]
- DNA repair needed[2]
- Unintended mutations[3]
- Irreversible (one shot)[1-3]



Other editors are complex or ineffective

e.g., TwinPE, PASTE, CAST, PRINT, Multi-component[5,6], multi-step[5]

- Byproduct edits[4,5,7]
- Limited cargo capacity[4]
- Require nickase cutting[4,5,7]
- Lower efficiency in mammalian cells[6]
- No re-programmability[7]



Site-specific SPB

Simple single enzyme fusion system for site-specific integration

Double-strand-break-free

1. Jinek et al., *Elife*. 2013; 2. Cong et al., *Science*. 2013; 3. Ran et al., *Cell*. 2013; 4. Anzalone et al., *Nat Biotechnol*. 2022; 5. Yarnall et al., *Nat Biotechnol*. 2023; 6. Lampe et al., *Nat Biotechnol*. 2024; 7. Zhang et al., *Nat Biotechnol*. 2024; 8. Yusa et al. *Proc Natl Acad Sci U S A*. 2011.

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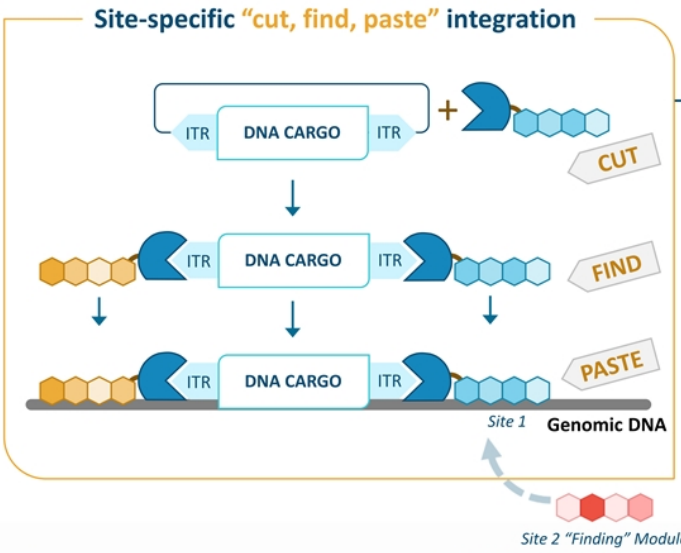
Site-specific SPB executes each “cut-find-paste” step with a single enzyme fusion protein



Site-specific SPB for additional control

CUT

- **Excision** from the donor vector/plasmid DNA

FIND

- **DNA-finding** modules direct integration to desired location

PASTE

- **Integration** at target site, double-strand-break-free (DSB-free)

Early version of site-specific SPB yields in vivo targeted transposition in mouse liver

Site-specific integration toolkit

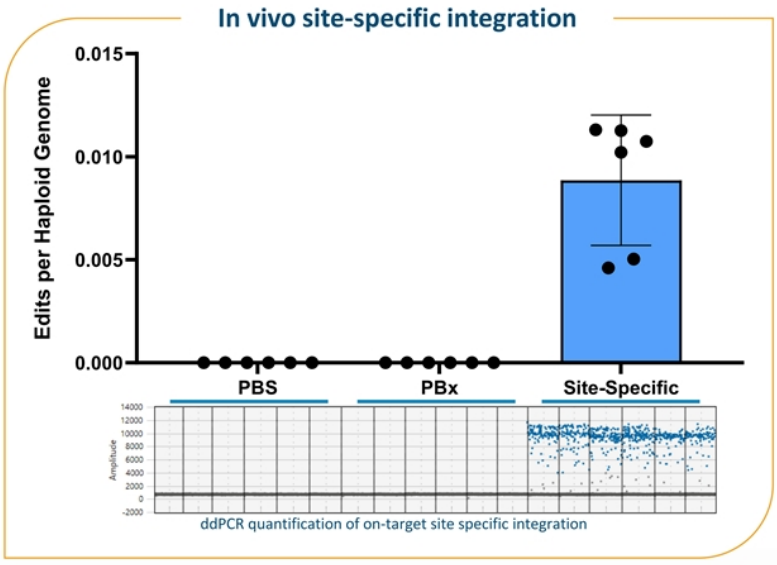
Transposase

Target finding

ITR DNA CARGO ITR

DNA Donor

- In vivo site-specific integration of cargo detected in liver
- Potential for gene therapy applications



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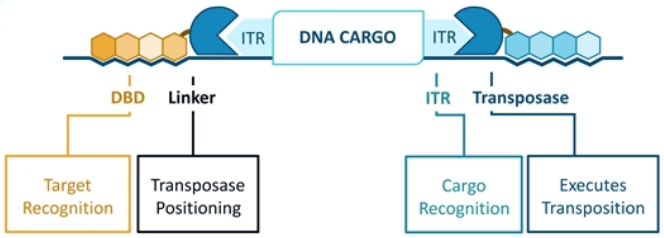
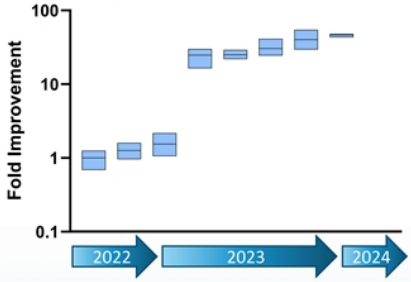
Further site-specific SPB engineering boosts on-target insertion rate at single-copy sites

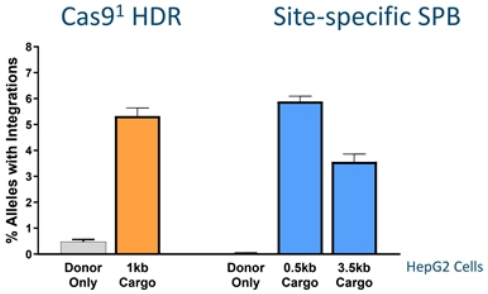
Points of optimization



Molecular Evolution



Integration at single copy target site



- Comparable integration efficiency to Cas9 HDR
- Difference: **no double-strand breaks or indels** with site-specific SPB

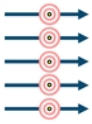
***Challenge**: DNA integration at 1 among millions of genomic positions (a hurdle for any technology)*

1. Cas9 delivered in RNP format

Site-specific SPB enables the targeting of repetitive sites, where nucleases would likely fail

Targeting repeats

Site specific transposase



Enhanced efficiency

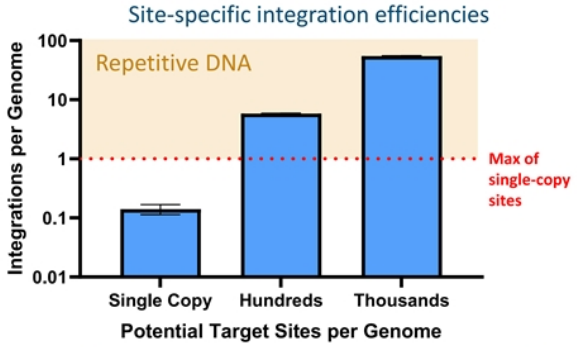
CRISPR/ nuclease

Cell death[1] (>100 cuts)

Why target multi-copy sites?

- Enhanced efficiency without compromising safety
  - Repetitive DNA largely devoid of protein-coding genes
- Infeasible with a nuclease (toxicity)

Breaching limit of single-copy target sites



Success with site-specific SPB

1. Smith et al. *Nucleic Acids Research*, 2020

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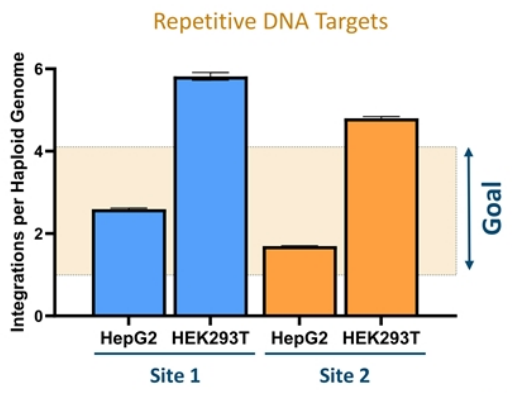
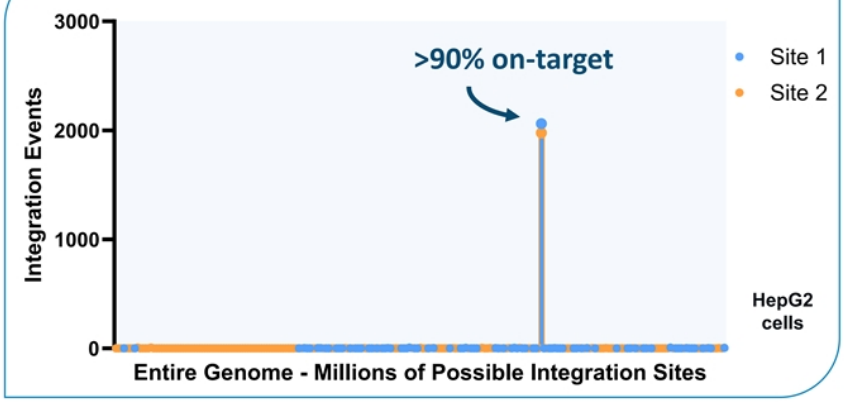
Predictable and reproducible integration with >90% on target fidelity

Efficiency data



Fidelity data



- Efficient, site-specific integration at repetitive target site
- Surpassing efficiency goal may allow reduced dosing
- Promising efficiency data observed at 9 additional sites

Site-specific SPB provides a foundational toolkit for targeted gene insertion

Summary

- Molecular evolution of site-specific SPB technology enhanced 30-fold over early generation
- Site-specific SPB technology efficient for targeted cargo integration at single- and multi-copy sites
- Validated benefit of targeting multi-copy sites, consistent with expectations and low toxicity of a **double-strand-break-free** approach

Next steps

- Continued refinement to engineering design, increasing fidelity beyond >90%
- In vivo optimization in context of non-viral LNP at repetitive safe harbor sites
- Identification and programmed targeting of additional repetitive safe harbor sites

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Conclusion

Presenter:

Kristin Yarema, PhD


"If we don't lean into accelerated approval, we're going to leave a lot of patients behind"
"I think the possibility of genome editing… could be an incredible game changer, not just for rare diseases but more common disease."
– Peter Marks, Director of the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration
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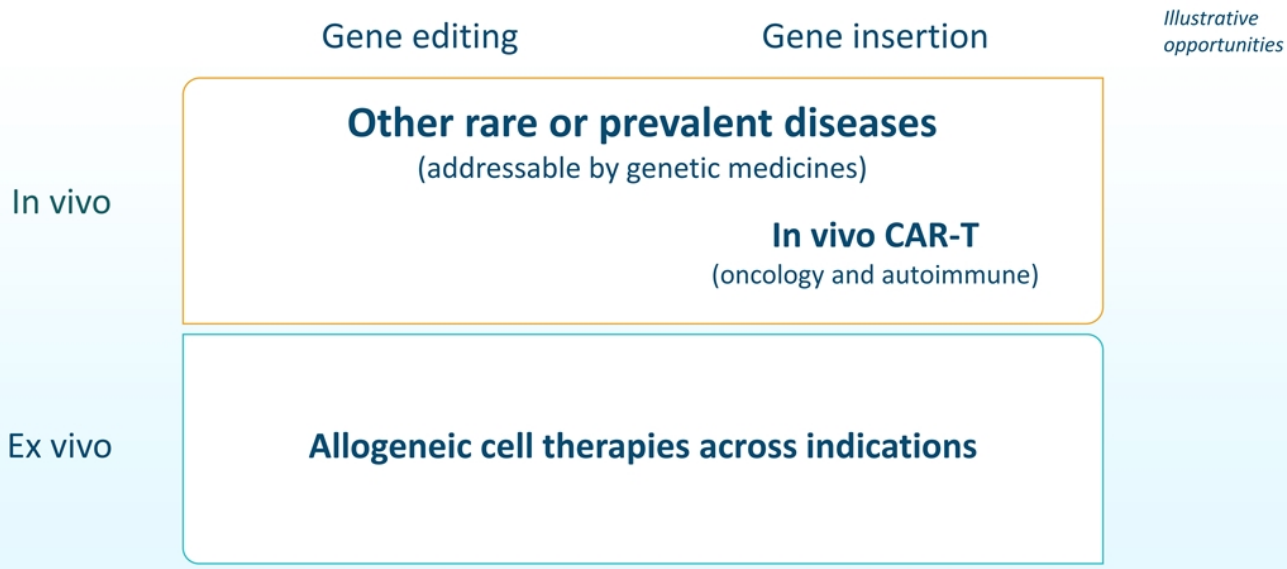
This is just the beginning…

Our powerful toolkit has the potential to unlock significant opportunities to address areas of unmet medical need



With a broad suite of differentiated gene editing technologies, Poseida is positioned to deliver on the promise of genetic medicines

Whole gene insertion

DNA transposon

High fidelity gene editing

RNA-guided DNA nuclease

Manufacture and delivery

LNP

We will continue to evaluate the right opportunity with the right partner to expand our impact for patients in serious need