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# *Precision BioSciences Corporate Presentation*

May 2023

# Forward-Looking Statements

This presentation contains forward-looking statements, as may any related presentations, within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this herein and in any related presentation that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding our growth strategy, research advancement, clinical development and regulatory review of our product candidates, the expected timing of updates regarding our CAR T and in vivo gene editing programs and research, the expected timing of our communications with regulators, the expected advancement toward and timing of IND and CTA filings, expected efficacy and benefit of our platform, programs, product candidates, and manufacturing improvements and optimizations, the progress and success of collaborations with Lilly, Novartis, and other partners, including the receipt of any milestone, royalty, or other payments pursuant to and satisfaction of obligations under collaboration agreements, the goal of displacing autologous CAR T therapy, the goal of providing a one time, potentially curative treatment for genetic diseases, the goal of complex edits of the genome, the potential of "safe harbor" gene insertion, the ability of AAV and LNP delivery capabilities, the ability of our product candidates, if approved, to become best-in-class or first-in-class, expectations about our operational initiatives and business strategy, achieving key milestones and additional collaborations, and expectations regarding our liquidity and ability to fund operating expenses and capital expenditures requirements. In some cases, you can identify forward-looking statements by terms such as "aim," "anticipate," "approach," "believe," "contemplate," "could," "estimate," "expect," "goal," "intend," "look," "may," "mission," "plan," "possible," "potential," "predict," "project," "should," "target," "will," "would," or the negative thereof and similar words and expressions.

Forward-looking statements are based on management's current expectations, beliefs and assumptions and on information currently available to us. Such statements are subject to a number of known and unknown risks, uncertainties and assumptions, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various important factors, including, but not limited to: our ability to become profitable; our ability to procure sufficient funding and requirements under our current debt instruments and effects of restrictions thereunder; risks associated with raising additional capital; our operating expenses and our ability to predict what those expenses will be; our limited operating history; the success of our programs and product candidates in which we expend our resources; our limited ability or inability to assess the safety and efficacy of our product candidates; our dependence on our ARCUS technology; the initiation, cost, timing, progress, achievement of milestones and results of research and development activities, preclinical studies and clinical trials; public perception about genome editing technology and its applications; competition in the genome editing, biopharmaceutical, and biotechnology fields; our or our collaborators' ability to identify, develop and commercialize product candidates; pending and potential liability lawsuits and penalties against us or our collaborators related to our technology and our product candidates; the U.S. and foreign regulatory landscape applicable to our and our collaborators' development of product candidates; our or our collaborators' ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations and/or warnings in the label of an approved product candidate; our or our collaborators' ability to advance product candidates into, and successfully design, implement and complete, clinical or field trials; potential manufacturing problems associated with the development or commercialization of any of our product candidates; our ability to obtain an adequate supply of T cells from qualified donors; our ability to achieve our anticipated operating efficiencies at our manufacturing facility; delays or difficulties in our and our collaborators' ability to enroll patients; changes in interim "top-line" and initial data that we announce or publish; if our product candidates do not work as intended or cause undesirable side effects; risks associated with applicable healthcare, data protection, privacy and security regulations and our compliance therewith; the rate and degree of market acceptance of any of our product candidates; the success of our existing collaboration agreements, and our ability to enter into new collaboration arrangements; our current and future relationships with and reliance on third parties including suppliers and manufacturers; our ability to obtain and maintain intellectual property protection for our technology and any of our product candidates; potential litigation relating to infringement or misappropriation of intellectual property rights; our ability to effectively manage the growth of our operations; our ability to attract, retain, and motivate key executives and personnel; market and economic conditions; effects of system failures and security breaches; effects of natural and manmade disasters, public health emergencies and other natural catastrophic events; effects of COVID-19 pandemic and variants thereof, or any pandemic, epidemic or outbreak of an infectious disease; insurance expenses and exposure to uninsured liabilities; effects of tax rules; risks related to ownership of our common stock and other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2022, as any such factors may be updated from time to time in our other filings with the SEC, which are accessible on the SEC's website at www.sec.gov and the Investors page of our website under SEC Filings at investor.precisionbiosciences.com.

The 2022 financial results included in presentation are unaudited and preliminary, and this presentation does not present all information necessary for an understanding of the Company's financial condition as of December 31, 2022 and its results of operations for the three months and year ended December 31, 2022. The Company's actual results may differ from the preliminary estimates above due to the completion of the Company's year-end accounting procedures, including execution of the Company's internal control over financial reporting, and audit of the Company's financial statements for the year ended December 31, 2022 by the Company's independent registered public accounting firm, which are ongoing.

# Precision's Growth Strategy:

*Leverage the ARCUS gene editing platform in oncology and genetic diseases*

**1** **Advance a first-in-class and a best-in-class allogeneic CAR T treatment for hematologic cancer**

- Lead anti-CD19 allogeneic candidate, azercabtagene zapreleucel (azer-cel) potential first-in-class for CAR T relapsed patient population with DLBCL.
- Next-generation anti-CD19 allogeneic candidate, PBCAR19B stealth cell, potential best-in-class CAR T therapy for patients with relapsed or refractory (r/r) non-Hodgkin lymphoma (NHL), with primary focus on DLBCL.

**2** **Unlock full potential of ARCUS *in vivo* gene editing platform**

- **Differentiate ARCUS** on safety, gene insertion and complex edits
- **Advance first *in vivo* gene editing programs to the clinic** to address serious genetic diseases and chronic hepatitis B

**3** **Secure selective premium *in vivo* gene editing collaborations**

- Unlock additional development opportunities, reach more patients and provide capital for advancing wholly owned programs

Building an end-to-end gene editing company, spanning research through commercialization

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* relapsed/refractory non-Hodgkin lymphoma

# **Precision BioSciences:** A Clinical Stage Gene Editing Company Built on Wholly Owned ARCUS Genome Editing Platform

## ARCUS® Platform
for therapeutic drug development

Diversified Pipeline

***Ex Vivo***:

*Allogeneic CAR T immunotherapies*
- Single-gene edit, donor-derived, single-dose

***In Vivo***:

*Gene editing for complex genetic diseases*
- Potentially curative, one-time treatment

- Pioneers in genome editing technology development
- Scalable in-house manufacturing capabilities
- ARCUS platform and nucleases are unencumbered by third-party IP; control of over 100 issued patents related to ARCUS and its applications
- Strong balance sheet provides 2+ years of runway[1]

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[1] Based on cash and cash equivalents of approximately $190 million as of December 31, 2022, expected operational receipts and available credit.

# Agenda

- 2022 Accomplishments
- Allogeneic CAR T Program Update
- Differentiating the ARCUS Platform
- ARCUS *In Vivo G*ene Editing Program Highlights
- 2023 Priorities & Milestones

# 2022 Accomplishments

- Presented **compelling clinical allogeneic CAR T data to date; 100% ORR 73% CR**[1]
- **Secured $75M for *in vivo* gene editing collaboration with Novartis** for hemoglobinopathies
- **Raised $50M in equity financing** from new and existing investors
- **Extended the cash runway**; Runway greater than 2 years[2]
- **Optimized CAR T manufacturing process** designed to improve attributes for safety and efficacy
- **Published first NHP proof-of-concept data supporting HBV** *in vivo* gene editing program
- **Progressed Lilly and Novartis** preclinical *in vivo* gene editing programs, including DMD and SCD
- **Received favorable Type C feedback from FDA** regarding CMC plan for azer-cel

[1] Results announced on June 8, 2022 (n=12) were as of May 31, 2022

[2] As of December 31, 2022, Precision had approximately $190 million in cash and cash equivalents. The Company expects that existing cash and cash equivalents, expected operational receipts, and available credit will be sufficient to fund its operating expenses and capital expenditure requirements into 2025.

# *Allogeneic CAR T Programs*

## Potential first-in-class and best-in-class approaches

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# Executive Summary

## Azer-cel: Potential First-In-Class Opportunity for CAR T Relapsed CD19+ DLBCL

### Azer-cel is Precision's Lead CAR T Program Demonstrating Efficacy and Improved Safety Across Hematologic Malignancies

- Precision has amassed a robust data package (n = 84) for Azer-cel in NHL and ALL, with clinically meaningful efficacy and an acceptable safety profile
- Azer-cel data is most compelling in the Diffuse Large B Cell Lymphoma (DLBCL) CAR T relapse setting (n=18) with 83% ORR, 61% CR rates and 55% DoR ≥6 months[1]
- In latest cohort (n=7), Azer-cel safety profile ameliorated with 0% ≥ Grade 3 Allogeneic CAR T related AEs in fragile, relapse patient population

### Next Step is Regulatory Guidance for Azer-cel Clinical Development Plan

- FDA meeting expected in June
- 500M Cells + FluCy750 established as viable Phase 2 dose for safety and efficacy
- Upcoming meeting objective to guide potential Phase 2 study; focus on trial design, size and endpoints

## 19B Stealth Cell: Potential Best-In-Class Opportunity for Earlier Line CAR T Naïve CD19+ DLBCL

### 19B Stealth Manufacturing Optimization Resulted in Phase I Efficacy and Safety on Par With Autologous CAR T in R/R NHL Setting

- Achieved 71% ORR with no Grade ≥3 Allogeneic CAR T related adverse events; Most compelling signal achieved in DLBCL patients with 80% ORR, and 60% CR (MRD-)
- 540M Cells + FluCy750 established as ongoing investigational dose based on Phase I therapeutic index
- 19B Stealth construct proof of concept achieved; enabling expansion and persistence by delaying host rejection through immune cloaking

## Building On Strong Cell Therapy Foundation

- Optimization of manufacturing platform using ARCUS for CAR T insertion now clinically validated across two clinical candidates
- Precision CAR T platform has broad applicability beyond hematologic malignancies, including solid tumors and autoimmune diseases

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Note: Azer- cel = Precision's lead clinical candidate, Azercabtagene zapreleucel; NHL = Non-Hodgkin's Lymphoma (NHL) & ALL= Acute Lymphoblastic Leukemia

1. N=11 patients evaluable for ≥ 6 months duration on response, 6 durable responders past 6 months or longer with 431 (> 1 year) median days on response; DoR measured from D0

# Total Body of Evidence:
## Azer-cel Has Meaningful Clinical Activity Across B Cell Malignancies

**84**

Patients Treated With Azer-cel

| **61** NHL Patients | **23** B-ALL Patients |
|---|---|
| **58% ORR** | **61% ORR** |
| 41% CR | 61% CR/CRi |

**All Doses / All LD Regimens**

★ **Tailoring Azer-cel for the right patient, with right dose, right product attributes and right lymphodepletion**

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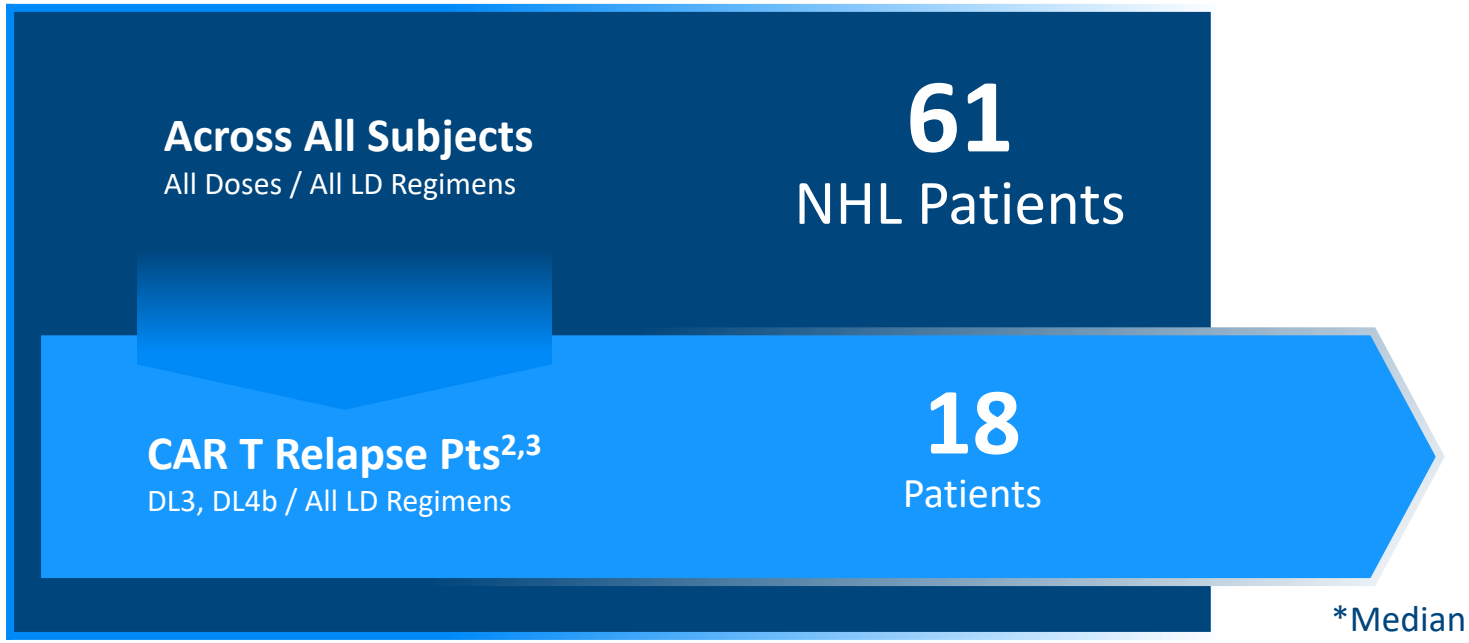
Note: Based on Patients Evaluable for Efficacy

# Azer-cel is Active in CAR T Relapsed Patients:

## Demonstrated High Response Rates and Durability




**83% ORR**

61% CR Rate

55% DoR ≥ 6-months[1]

*Median duration in ≥ 6-month responders is 431 days

★ **Azer-cel has the potential to provide new standard of care for this high-risk population with unmet need**

Note: Based on Patients Evaluable for Efficacy

1. N=11 patients evaluable for ≥ 6 months duration on response, 6 durable responders past 6 months or longer with 431 (> 1 year) median days on response; DoR measured from D0
2. N = 2 CAR T Relapse Patients patients were also treated at sLD and observed a 50% ORR
3. CAR T relapse Includes 17 NHL and 1 ALL patient from ASH Cohort; only sLD patients receiving optimized product attributes included

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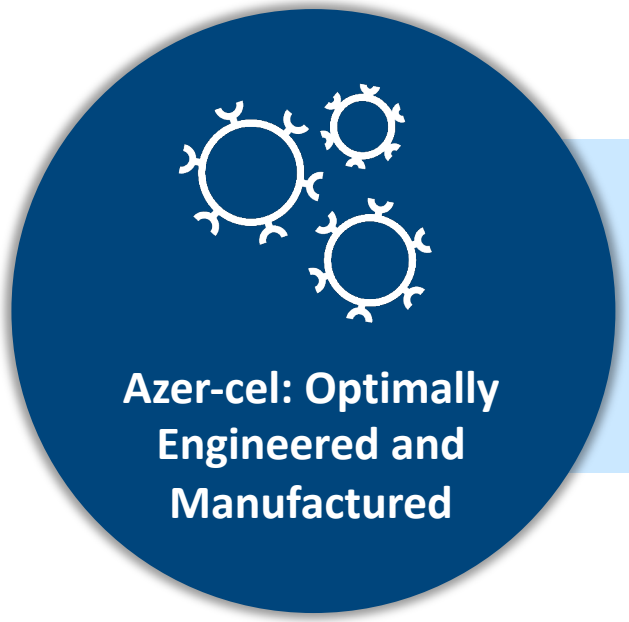
# Azer-cel Approach is Biologically Rational for CAR T Relapse Population




- **Azer-cel from healthy donor may be more effective than an autologous product**
- **Autologous products made from cancer patients with impaired immune system may result in suboptimal product attributes[1-4]**

1. Jacobson CA, et. al. J Clin Oncol 2020; 38:3095., Nastoupil LJ, et. al. J Clin Oncol 2020; 38:3119.
2. Das RK, et. al. Blood Adv 2020; 4: 4653.
3. T cell quantity and function impaired by prior therapy precluding generation of high-quality Auto CAR T product
4. Prior Chemotherapy adversely impacts surviving T cells and reduces early-lineage T cells necessary for CAR T cell expansion

# Majority of CAR T Relapse Patients Continue to Have CD19+ Disease

**~85%** **of patients[1]**
**continue to have CD19+ disease**

**In our prospective data, patients continue to have antigen positive disease**


Note: Retrospective Literature states that 12-28% of patients have antigen negative relapse (CD19-)
1. Precision Internal Clinical Data
2. Precision data; Spiegel US Consortium data

# CAR T Relapse Setting Has No Approved Standard of Care and Poor Prognosis

| | CAR T Relapse Outcomes U.S. Consortium Actual Data / RWD[1,2,3] | Proposed TPP For CAR T Relapse Patients |
|---|---|---|
| Overall Response Rate (ORR) | ~20-30% | > 50% |
| Progression Free Survival (mPFS) | ~1.8 months | > 3 months |
| Overall Survival (mOS) | Drug tx: 4-6 months<br>Palliative Care: <1 month | > 6 months |
| Safety | Manageable safety profile in this fragile patient population | ★ No treatment related Grade 5 events |
| Potential Regulatory Path | No therapy currently indicated/approved | Single-arm study with historical control<br>*(e.g., U.S. Consortium Data)* |

Notes: TPP = Target Product Profile

1. Barriers to enrollment in clinical trials of patients with aggressive.., Bezzera, E. Mayo Clinic, 2021
2. US CAR T Consortium Study - https://pubmed.ncbi.nlm.nih.gov/33156925/
Note: Other therapies included targeted treatments such as venetoclax, brentuximab vedotin or ibrutinib, novel therapies, steroids, second CAR-T on clinical trial, and allogeneic stem cell transplant. In total, 8 patients proceeded to allogeneic stem cell transplant after axi-cel PD, 3 of whom remain in CR.
3. University of Washington study shows CAR T early relapsers only have mOS of 3.8 months; https://onlinelibrary.wiley.com/doi/10.1002/ajh.25505

# CAR T Relapse Market is Large and Growing

YESCARTA

Breyanzi

KYMRIAH® (tisagenlecleucel) Dispersion for IV infusion

**60-65%**

**of patients currently treated with Auto CAR T will relapse[1]**

**★ By 2025, Global CAR T Relapse Patient Pool Is Expected To Grow ~4x as Auto CAR T Drugs become the SoC in 2L+**

→ Estimate total Global G8 markets to be ~18k patients per year[2]

1. Estimated from ZUMA 1 and ZUMA 7 EFS rates
2. G8 includes US, Japan, Canada and EU5 assuming equal access to CAR T therapies; market research, CancerMPact

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# Azer-cel: Allogeneic CAR T

## For CD19+ CAR T Relapsed Patients

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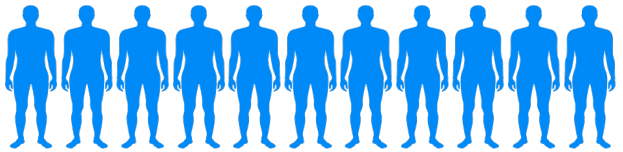
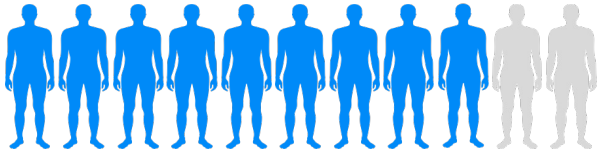
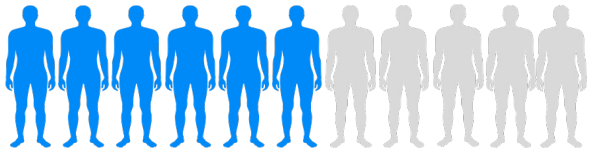
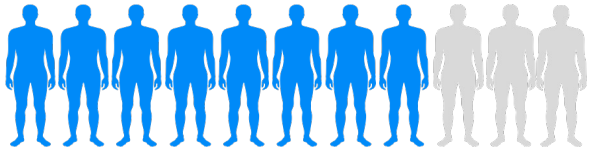
# One Year Ago, Precision Showed Compelling Data in the CAR T Relapse Setting



**CAR T relapsed**
**Median 5 lines**
**(n = 11)**

| | | n (%) |
|---|---|---|
| **ORR ≥ Day 28** |  | **11 (100%)** |
| **CR ≥ Day 28** |  | **9 (82%)** |
| **≥ 6 mo. Duration of Response** |  | **6 (55%)** *of evaluable* |
| **PFS > 2 months**<br>U.S. Consortium/RWD Threshold |  | **8 (73%)** |

ClinicalTrials.gov identifier: NCT03666000;
11 of 12 patients were evaluable

**Data cutoff 01May2023**

**Despite compelling response and durability data** → **Safety profile needed to be ameliorated** given treatment related events

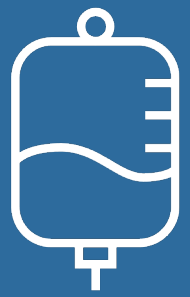
Note: ORR = Overall Response Rate, CR = Complete Remission, PFS = Progression Free Survival, LD = Lymphodepletion, DoR is calculated from Day 0

# Significant Progress Made to Improve Azer-cel Therapeutic Index

- Optimized manufacturing process using ARCUS leading to improved product attributes resulting in improved potency and control
- Received favorable CMC feedback from the FDA for ongoing development path
- Reduced lymphodepletion dose intensity with goal to improve safety

# Two Levers Designed to Improve Therapeutic Index

## 1 Reduced LD Dose Intensity:
Reducing the Fludarabine Dose in Lymphodepletion



Reduce total fludarabine exposure during lymphodepletion

**4 days**

**3 days**

Fludarabine dose of **30 mg/m$^2$ per day**

## 2 Potency with Control:
Improving Product Attributes

**Process improvement led to improved fitness measured by non apoptotic cell fraction**

**In optimized manufacturing process, reduced CD4+/CD8+ ratio to minimize inflammatory toxicities**

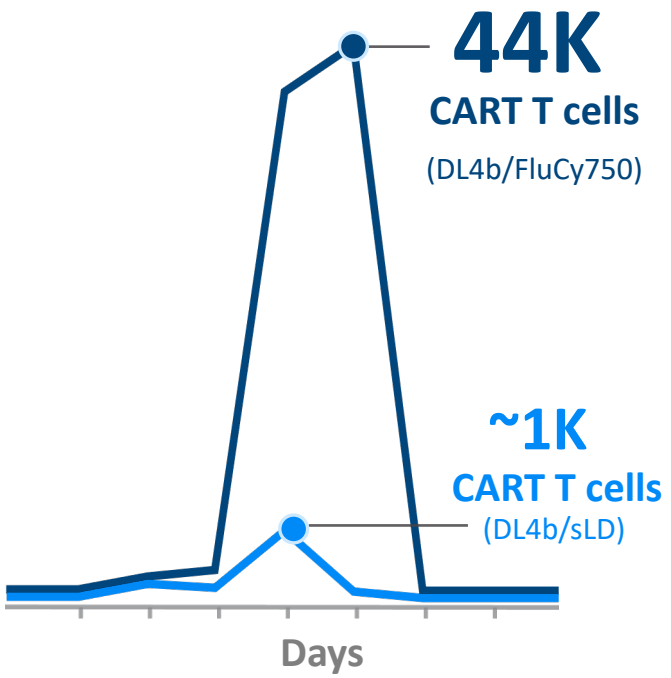
- Total CD4+ CAR T effective cell dose is a key contributor of CD8+ CAR T cell peak expansion, inflammatory cytokines and inflammatory toxicities such as ICANS

# Optimizing Lymphodepletion Regimen to Drive CAR T Expansion:
## An Important Factor to Drive Molecular Remission (MRD-)

### Reduced to sLD to Improve Safety

Outcome: Modest Expansion[1]

*Mean CAR T Peak*




**Durable responders for Yescarta - ZUMA 1 had CAR T levels in range 21k to 92k CAR T Cells per mL**

Transitioned To

### FluCy750

Outcome: Increased Expansion

**FluCy750 vs. sLD:**

- Increased homeostatic cytokines to drive expansion: 58x Peak and 51x AUC
- Similar inflammatory cytokine profile to maintain safety

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Note: 2 patients treated with azer-cel 500M cells with sLD achieved lower peak and 50% ORR/CR

1. DL4b/sLD showed 0.8k CAR T cells

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# Azer-cel Safety Update

## CD19+ CAR T Relapsed Patients

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# Optimized Product Attributes and Reduced Fludarabine Exposure Significantly Improves Safety Profile

Azer-cel

Data Update

| Number (%) of subjects experiencing events with max grade | | | DL3a/eLD Cohort (n=6) | DL4b/mLDCohort (n=6) | Latest Cohort (DL4b FluCy750 or sLD) (n=7) | Latest Cohort (DL4b FluCy750) (n=5) |
|---|---|---|---|---|---|---|
| **AE of special interest[1]** | **CRS** | *Grade 1 or Grade 2* | 5 (83%) | 4 (67%) | **4 (57%)** | **3 (60%)** |
| | | *Grade 3 or higher* | 0 | 0 | **0** | **0** |
| | **ICANS** | *Grade 1 or Grade 2* | 2 (33%) | 1 (17%) | **0** | **0** |
| | | *Grade 3 or higher[2]* | 1 (17%) | 2 (33%) | **0** | **0** |
| | **GvHD** | | 0 | 0 | **0** | **0** |
| **Other notable AEs** | **Infection** | *Grade 1 or Grade 2* | 0 | 1 (17%) | **0** | **0** |
| | | *Grade 3 or higher* | 4 (67%) | 2 (33%) | **0** | **0** |
| | **Grade 5 events[3]** | | 2 (33%)[3] | 3(50%)[4] | **0** | **0** |

Note: In Latest cohort, 500M cells is DL4b

1. AESI-Adverse Events of Special Interest
2. Median duration of Grade 3 ICANS was 4 days (2-24days)
3. Two deaths in the DL3a/ eLD Cohort related to infections and suspected fludarabine associated neurotoxicity
4. Three deaths in DL4b/ mLD Cohort were suspected fludarabine associated neurotoxicity

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# In Latest Cohort, n = 5, Azer-cel CAR T Specific AE Profile is Comparable to Approved Autologous CAR T

| Number (%) of subjects experiencing events with max grade | | | Autologous CAR T | | | Allogeneic CAR T |
|---|---|---|---|---|---|---|
| | | | Yescarta[1] (r/r LBCL) | Kymriah[2] (r/r DLBCL) | Breyanzi[3] (r/r LBCL) | **Azer-cel** (n=5) **(CAR T Relapse DLBCL) (500M Cells + FluCy750)** |
| **AE of special interest** | **CRS** | *Grade 1 or Grade 2* | 84% | 51% | 43% | **60%** |
| | | *Grade 3 or higher* | 9% | 23% | 3% | **0** |
| | **Neurologic toxicities (including ICANS)** | *Grade 1 or Grade 2* | 56% | 41% | 23% | **0** |
| | | *Grade 3 or higher* | 31% | 19% | 10% | **0** |

**FOR ILLUSTRATIVE PURPOSES ONLY**: no head-to-head clinical trial has been conducted evaluating Azer-cel or other products. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies.

Note: In Latest cohort, 500M cells is DL4b

1. https://www.yescartatecartusrems.com/
2. https://www.hcp.novartis.com/products/kymriah/diffuse-large-b-cell-lymphoma-adults/safety-profile/
3. https://www.breyanzi.com/receiving-breyanzi
4. Allogene 2023 10K

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# Azer-cel Efficacy Update

## Durability and Molecular Response

Update from ASCO ’22, n = 11 patients

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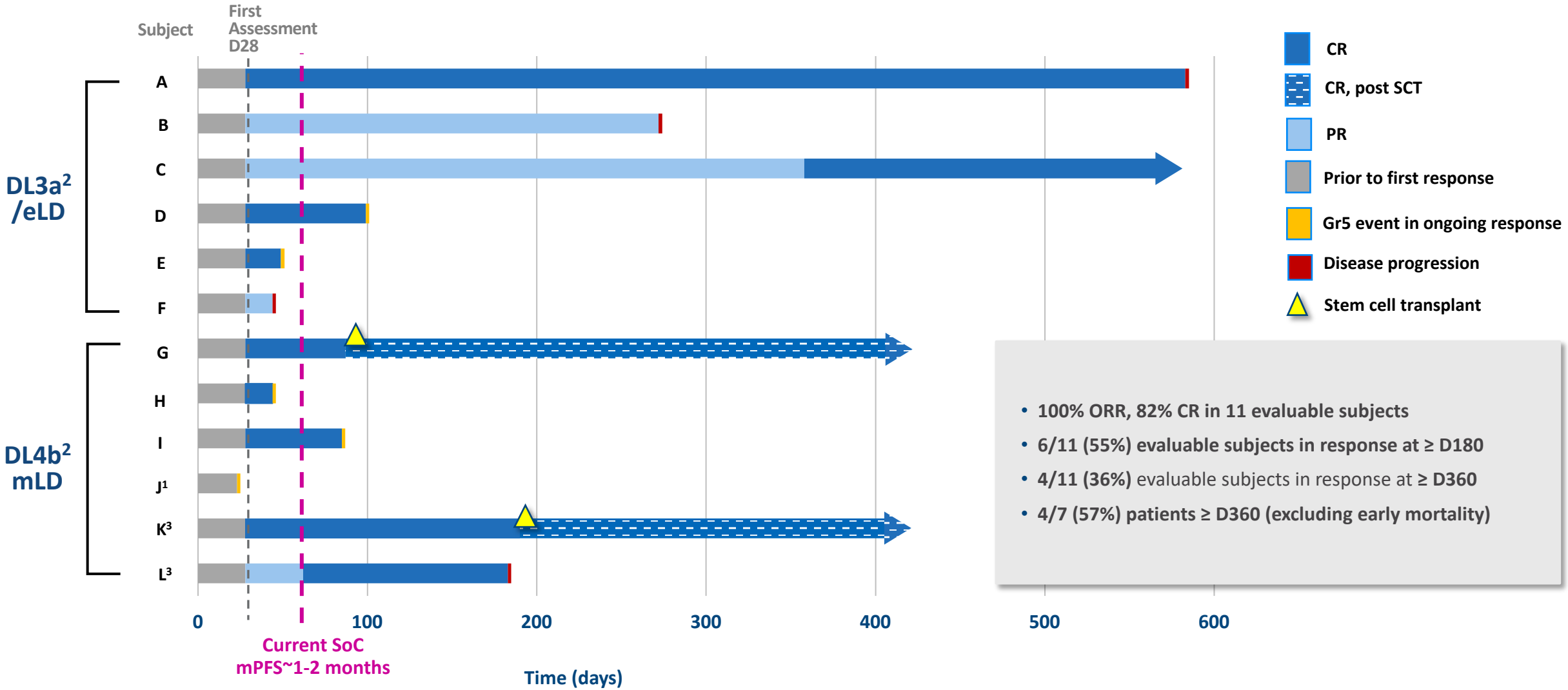
# Update Since ASCO 2022 Data: Durability Favorable vs. Current Treatment

## Current Treatment Defined in U.S. Consortium Data/RWD

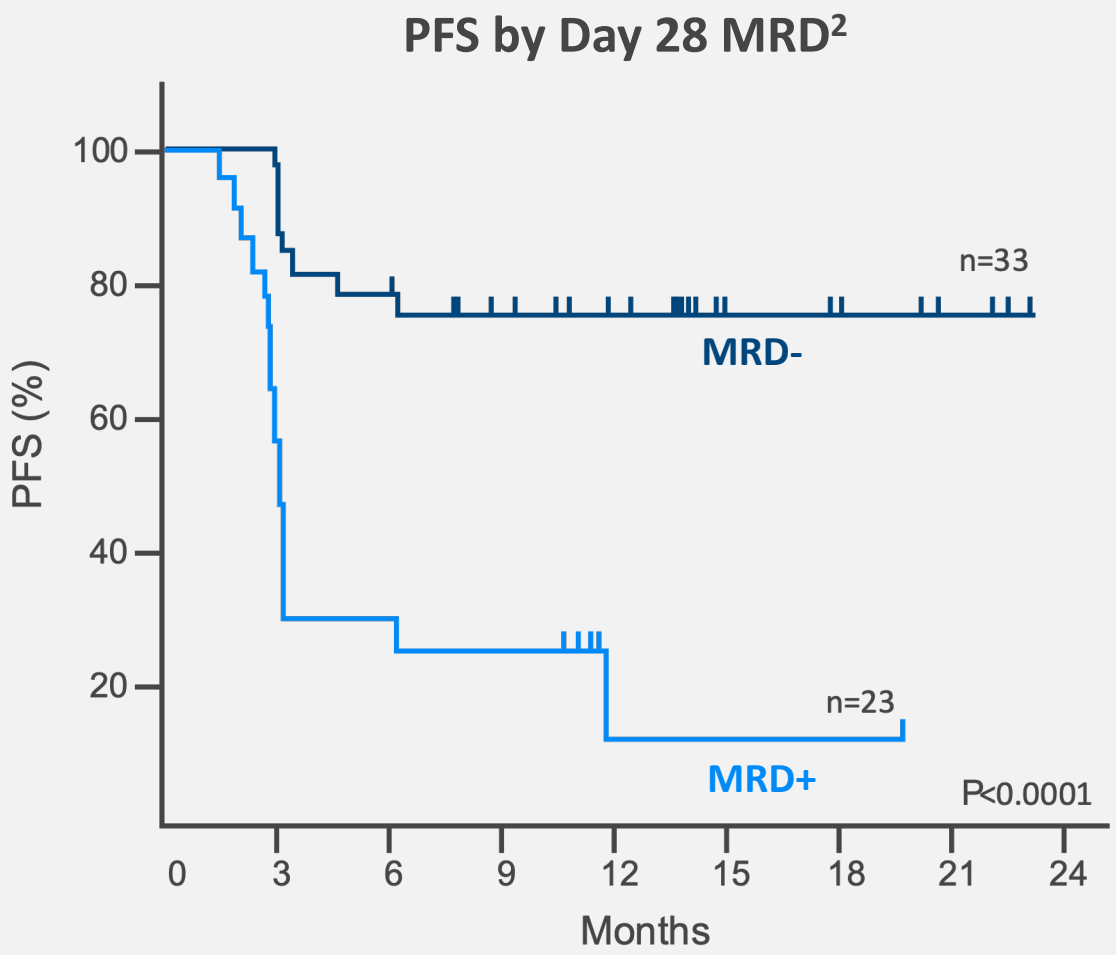



- 100% ORR, 82% CR in 11 evaluable subjects
- 6/11 (55%) evaluable subjects in response at ≥ D180
- 4/11 (36%) evaluable subjects in response at ≥ D360
- 4/7 (57%) patients ≥ D360 (excluding early mortality)

1. Subject J was non-evaluable for efficacy at Day 28 assessment due to death from suspected fludarabine (Flu)-associated neurotoxicity on Day 23.
2. DL3a dose – 3 x $10^6$ CAR T cells/kg; DL4b dose – 500 x $10^6$ CAR T cells/flat dose.
3. Subject K relapsed after Allo CAR T. Original response: K – CR for 150 days before PD . Subject L relapsed after Allo CAR T. Original response: L- PR for 14 days before PD.
Note: DoR calculated from Day 0 onwards

*Data cutoff 01May2023

# Molecular Remission (MRD-) Key Predictor of Durability




- Early Clearance of Circulating Tumor DNA (MRD-) measured by ClonoSEQ is Predictive for Relapse Free Interval After CAR T Treatment (per ZUMA-1)[1]
- PFS is Strongly Correlated with MRD Negative Status
- Molecular Remission (MRD-) is Predictive of Durable Response

1. MRD was evaluated via NGS-MRD assay to assess for ctDNA in plasma. Any detectable ctDNA was considered MRD-positive.
ctDNA - circulating tumor DNA,; MRD – measurable (minimal) residual disease; NGS – next-generation sequencing; PET-CT – positron emission tomography-computed tomography; PFS – progression-free survival
2. Frank MJ et al., *J Clin Oncol.* 2021 Jun 16 ; JCO2100377.

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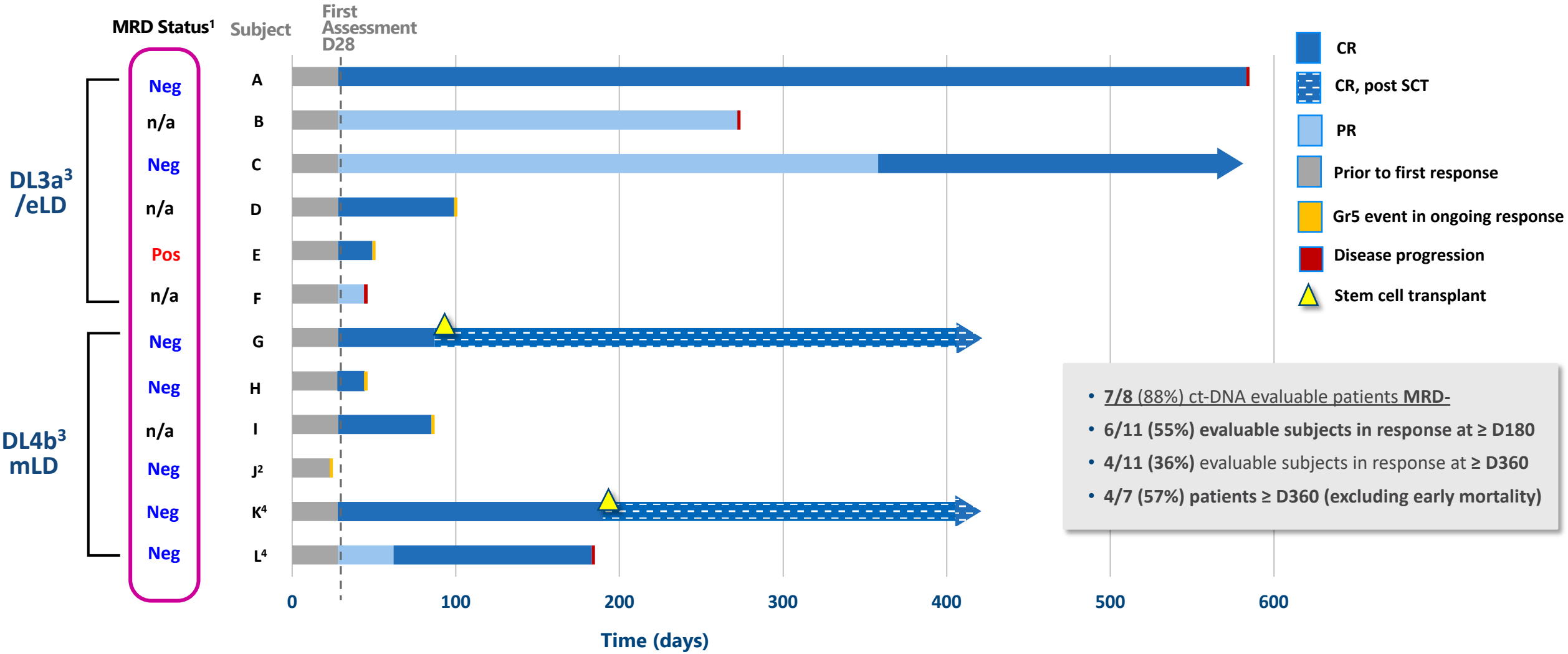
# Update Since ASCO 2022: MRD Negativity Correlated With Durability






1. MRD determination for subjects C, E, G, H, K, and L using clonoSEQ®MRD Detection Assay (Adaptive Biotechnologies) at D28. Assessment for subject J was on D14. MRD determination for subject A was performed using a flow-based MRD assay.
2. Subject J was non-evaluable for efficacy at Day 28 assessment due to death from suspected fludarabine (Flu)-associated neurotoxicity on Day 23.
3. DL3a dose – 3 x $10^6$ CAR T cells/kg; DL4b dose – 500 x $10^6$ CAR T cells/flat dose.
4. Subject K relapsed after Allo CAR T. Original response: K – CR for 150 days before PD . Subject L relapsed after Allo CAR T. Original response: L- PR for 14 days before PD.

Note: DoR calculated as response from Day 0 onwards

*Data cutoff 01May2023

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# Latest Azer-cel Cohort

## Additional Safety and Efficacy Data Supports Potential Phase 2 Recommended Dose

**500M CAR T Cells (DL4b) + FluCy750**

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FluCy750 = 30 mg/m$^2$ Flu × 3 days + 750 mg/m$^2$ Cy × 3 days

# Azer-cel + FluCy750 Preliminary Evidence of Efficacy:

## Overall Response Rate with Molecular Remissions in CAR T Relapse Setting

| Patient ID | Cell Dose[1] | LD Type[1] | MRD Status[2] | D28 Response[3] | Durability |
|---|---|---|---|---|---|
| O | 500M | FluCy750 | **Neg** | **CR** | PD (D90) **Antigen Escape** |
| P | 500M | FluCy750 | **Neg** | **PR** | D90+ |
| Q | 500M | FluCy750 | *Pending* | **PR** | D28+ |
| R | 500M | FluCy750 | Pos | SD | D28+ |
| S | 500M | FluCy750 | *n/a* | PD | n/a |

**60% ORR**

66% MRD-
(of evaluable n= 3)

**★ Latest cohort maintained efficacy with an ameliorated safety profile**

1. DL4b dose – 500 x $10^6$ CAR T cells/flat dose (500M Cells). FluCy750= 30 mg/$m^2$ Flu × 3 days + 750 mg/$m^2$ Cy × 3 days.
2. MRD determination using clonoSEQ®MRD Detection Assay (Adaptive Biotechnologies) at D28. Neg = negative, Pos = positive
3. N = 2 CAR T Relapse Patients were also treated at sLD and observed a 50% ORR

# Established Endpoints of Key Significance for Single Arm Hematologic Oncology Trials

| | | Proposed Endpoints For CAR T Relapse Patients | Azer-cel (500M cells + FluCy750) Interim Product Profile |
|---|---|---|---|
| *Potential Endpoints for FDA approval* | 1º Overall Response Rate (ORR) | > 50% | ✓ |
| | 2º Duration of Response (DoR) | > 50% @ 3 months | Not yet fully evaluable<br>66% MRD- |
| | 2º Safety Profile | ★ No Treatment Related Grade 5 Events | ✓ |
| | Potential Regulatory Path | Single-arm study with historical control<br>*(e.g., U.S. Consortium Data)* | Next step to be discussed with FDA |

Notes: 1º = Primary endpoint, 2º = secondary endpoint

# Azer-cel Potential First-In-Class Allogeneic Therapy for CAR T Relapsed Patients

- ☑ **In latest cohort, Azer-cel safety profile ameliorated with 0% ≥ Grade 3 Allogeneic CAR T related AEs in fragile CAR T relapse patient population**
- ☑ **Azer-cel highly active across CAR T relapsed patients (N=18), demonstrating 83% ORR, 61% CR rates with 55% DoR ≥ 6 months[1]**
- ☑ 〉 **Efficacy maintained at potential Phase 2 dose, 500M Cells + FluCy750 with 60% ORR and 66% MRD-**
- ☑ 〉 **Favorable CMC feedback from FDA on chemistry, manufacturing, and controls strategies support ongoing late-stage development for Azer-cel**
- ☑ 〉 **Clinical trial material ready from optimized manufacturing process**
- ☐ 〉 **Upcoming FDA clinical meeting to guide potential Phase 2 study; focus on trial design, size and endpoints**

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Note: DoR measured as response from Day 0

1. N=11 patients evaluable for 6-month DoR, 6 durable responders past Month 6 with 431 (> 1 year) median days on response

Best-In-Class Opportunity

# PBCAR19B Stealth Cell: Anti-CD19 Allogeneic CAR T

## Cloaked Design to Evade Immune Rejection and Potentially Displace 2nd Line Auto CAR T in CD19+ CAR T Naïve Patients

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# PBCAR19B Stealth Cell: Anti-CD19 Allogeneic CAR T Cloaked to Evade Immune Rejection

**Anti-CD19 CAR**
TCR is knocked-out to prevent GvHD

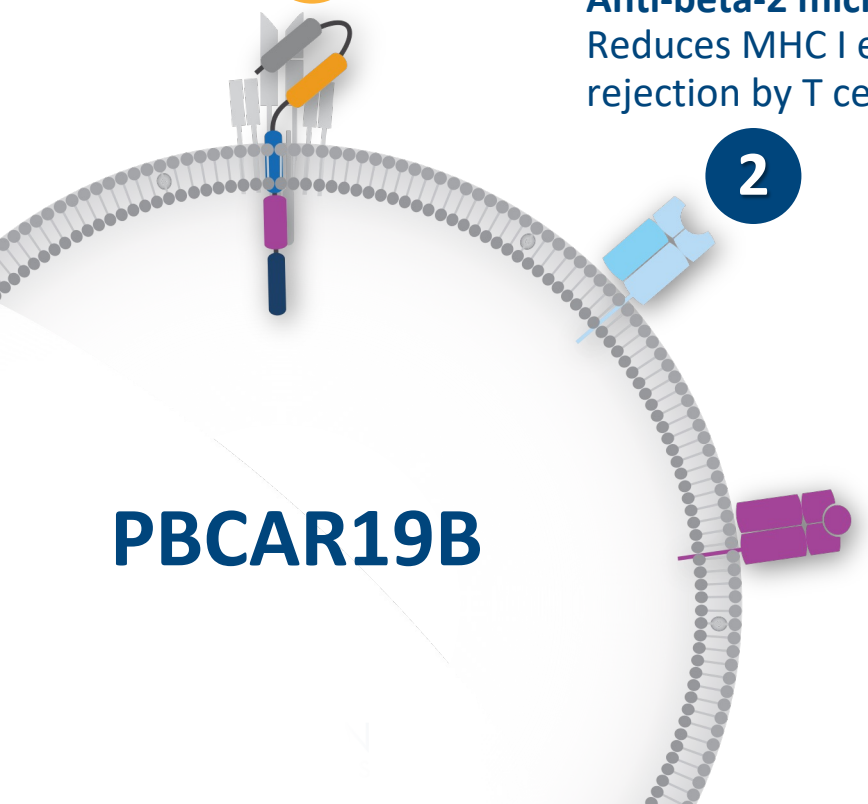
1

**Anti-beta-2 microglobulin (β2m) shRNA**
Reduces MHC I expression to prevent rejection by T cells

2

**HLA-E transgene**
Prevents rejection by NK cells

3



**PBCAR19B**

**Tx Goal/ Patient Population**

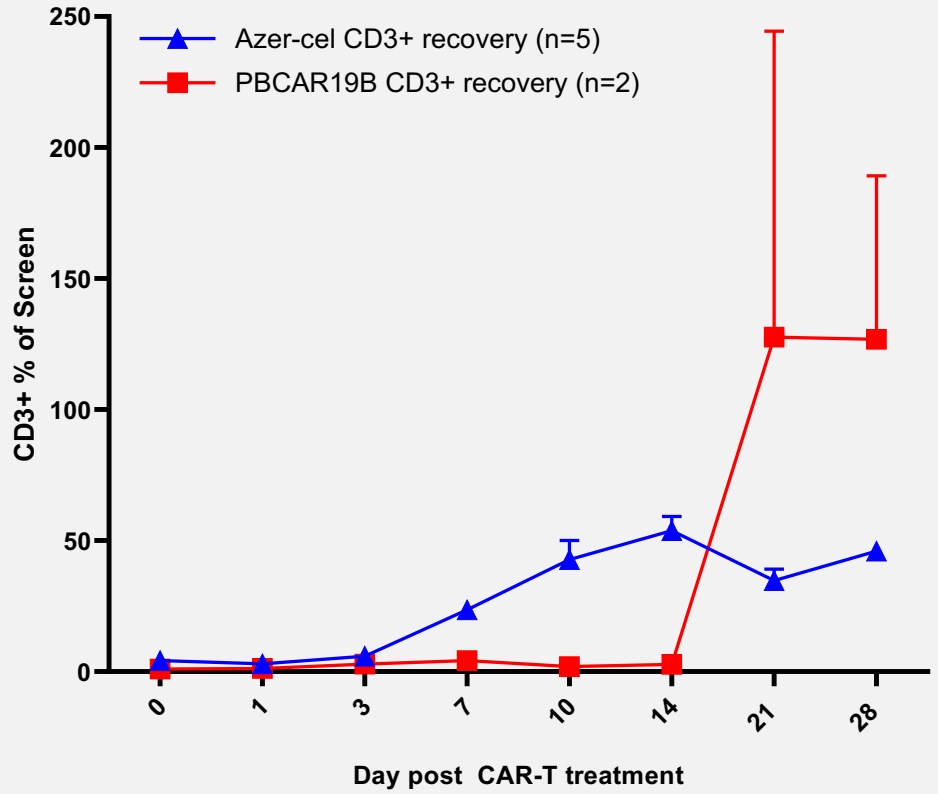
**Displace 2nd Line Auto CAR T in CD19+ CAR T Naïve Patients**

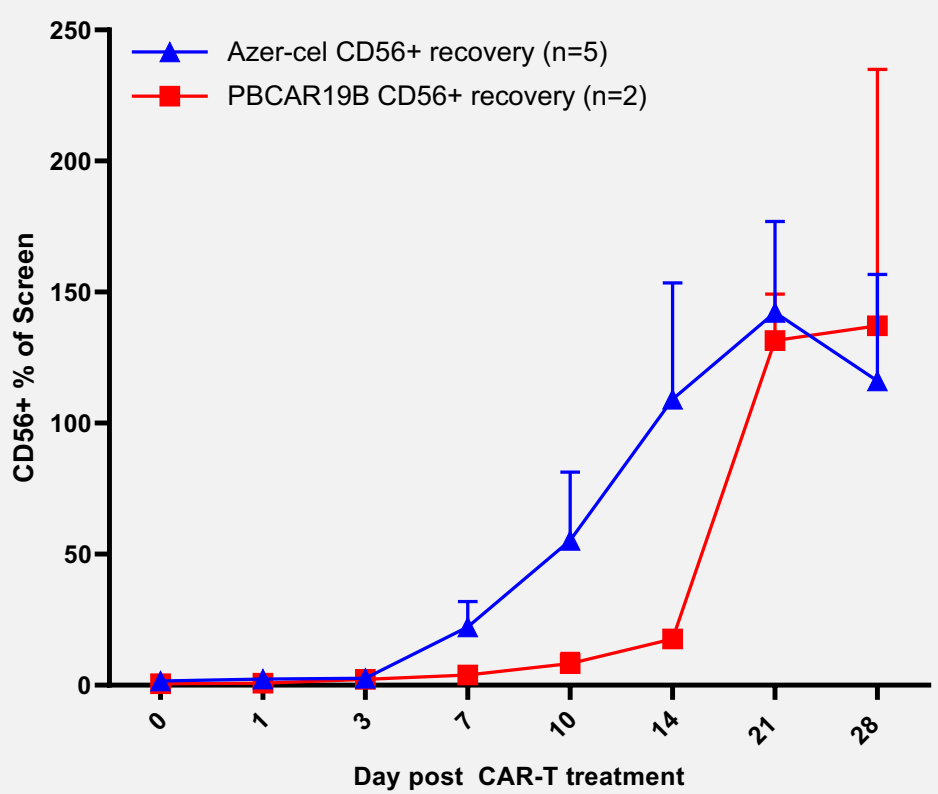
**Key Feature**

**PBCAR19B Stealth Cell**
Cloaked To Overcome Rejection by T Cells and NK Cells

# Delayed Immune Response By T Cells and NK Cells Demonstrates Proof of Principle For Stealth Construct in DLBCL






★ This strategy may further enhance efficacy profile to displace autologous CAR T in early line DLBCL

Note: Azer-cel DL4b dose – 500 x $10^6$ cells/flat dose per subject; 19B DL2 dose – 540 x $10^6$ cells/flat dose per subject.

# Allogeneic CAR T Related AE Profile in PBCAR19B Stealth Cell Treated Subjects



| Number (%) of subjects experiencing events with max grade | | | 540M Cells + sLD Cohort (n=3) | 540M Cells + FluCy750 Cohort (n=4) |
|---|---|---|---|---|
| AE of special interest | CRS | *Grade 1 or Grade 2* | 1 (33%) | 1 (25%) |
| | | *Grade 3 or higher* | 0 | 0 |
| | ICANS | *Grade 1 or Grade 2* | 1 (33%) | 0 |
| | | *Grade 3 or higher* | 0 | 0 |
| | GvHD | | 0 | 0 |
| Other notable AEs | Infection | *Grade 1 or Grade 2* | 0 | 0 |
| | | *Grade 3 or higher* | 0 | 0 |
| | Grade 5 events | | 0 | 0 |

**Data cutoff 01May2023*

Notes: FluCy750= 30 mg/m$^2$ Flu × 3 days + 750 mg/m$^2$ Cy × 3 days, Standard LD (sLD) = 30 mg/m$^2$ Flu × 3 days + 500 mg/m$^2$ Cy × 3 days; 540M Cells = DL2

# PBCAR19B Stealth Cell Dosed at 540M Cells Achieved 71% ORR with No Grade ≥3 Allogeneic CAR T Related Adverse Events

| Patient ID | Disease | LD Type[1] | MRD Status[2] | D28 Response | Durability |
|---|---|---|---|---|---|
| 1 | **DLBCL** | sLD | Pos | **PR** | PD (D60) |
| 2 | **DLBCL** | sLD | **Neg** | **CR** | D150+ |
| 3 | **DLBCL** | sLD | Pos | PD | n/a |
| 4 | **DLBCL** | FluCy750 | **Neg** | **CR** | D60+ |
| 5 | **DLBCL** | FluCy750 | **Neg** | **CR** | D28+ |
| 6 | MCL | FluCy750 | n/a | **PR** | D28+ |
| 7 | MCL | FluCy750 | Pos | PD | n/a |

**★ Most Compelling Signal: In DLBCL patients, 80% ORR with 60% CR (MRD-)**

**Data cutoff 01May2023*

Note: In DL1, 270M Cells, 1 PR out of 3 subjects treated

1. DL2 dose – 540 x $10^6$ CAR T cells/flat dose, sLD = 30 mg/$m^2$ Flu × 3 days + 500 mg/$m^2$ Cy × 3 days, FluCy750 = 30 mg/$m^2$ Flu × 3 days + 750 mg/$m^2$ Cy × 3 days
2. MRD determination using clonoSEQ®MRD Detection Assay (Adaptive Biotechnologies) at D28

# PBCAR19B Stealth Cell Potential Best-In-Class Allogeneic Therapy For CAR T Naïve Patients

- ☑ **Stealth Cell Proof of Concept Achieved:** Through immune cloaking, preliminary efficacy **in DLBCL patients enabling expansion and persistence** by delayed immune rejection

**Total Experience at 540M Cells**:

- ☑ Treatment with PBCAR19B 540M Cells showed encouraging safety profile with no ≥ Grade 3 Allogeneic CAR T related AEs
- ☑ PBCAR19B showed high ORR (71%) and CR rate (43%) in subjects with evidence of molecular remission (MRD-) and preliminary durability

**Compelling Signal of Interest:**

- ☑ Compelling signal in DLBCL patients, 80% ORR with 60% CR (MRD-); Long-term durability to be confirmed once evaluable
- ☐ 540M Cells + FluCy750 established dose for continued investigation in DLBCL patients

★ **Results achieved with new optimized manufacturing process further validate Precision's Cell Therapy Platform**

# Differentiating the ARCUS platform

## Highly differentiated genome editing platform for high unmet needs in genetic diseases

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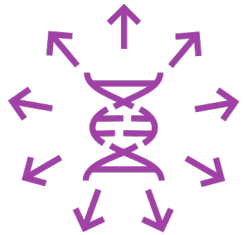
# Three Distinct Advantages of ARCUS Genome Editing Platform

**Precision**
**(Safety & Specificity)**

- ARCUS is inactive until it binds to target DNA
- Off-target editing easier to detect and eliminate
- Iterative nuclease optimization process to customize safety and efficacy profile



**Versatility**

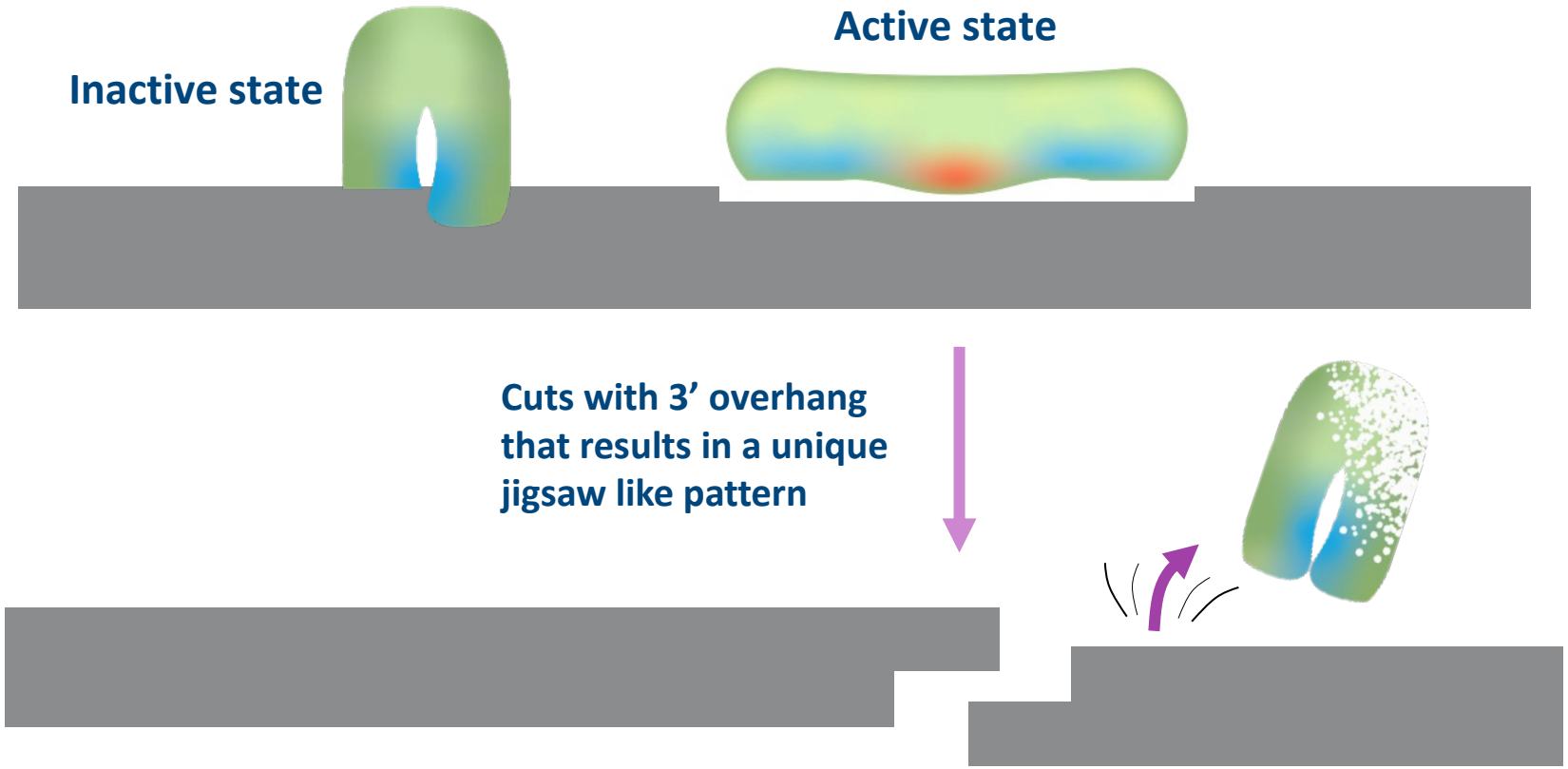
- Gene insertion, deletion or repair/complex edit
- DNA cuts are preferentially repaired by homology-directed repair (HDR)

**Delivery**

- ARCUS nucleases are small (364 amino acids)
- Delivery to broad array of tissues and cells using adeno-associated virus (AAV) and/or lipid nanoparticle (LNP)

# ARCUS: Engineering Nucleases that Mimic Nature's Genome Editing System

**The ARCUS nuclease is the only gene editor derived from a natural homing endonuclease**



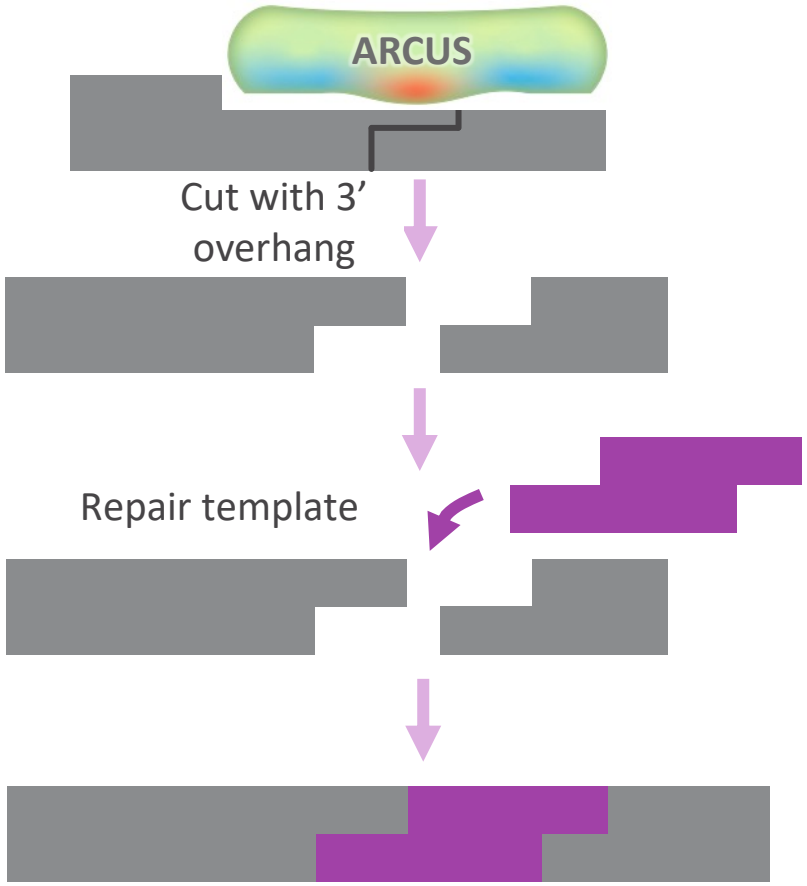

*The ARCUS nuclease cuts DNA at a specified site – can result in* ***simple and complex edits***

# ARCUS is Capable of Simple Edits and Optimally Suited for Complex Edits

| | | | |
|---|---|---|---|
| **Simple Edit** |  | **Deletion** | A deletion (also known as knock-out) is when **a gene is made inoperative** through a permanent change in the DNA; therefore, the gene **no longer expresses a functional protein** |
| **Complex Edits** |  | **Insertion** | An insertion (also known as knock-in) is when **a healthy copy of a gene is inserted into the genome** through a permanent change in the DNA |
| |  | **Excision** | An excision is when **a gene is altered** through permanent removal of a portion of the genome, **requiring multiple cuts** in the DNA |
| |  | **Replacement** | A replacement is when **a healthy copy of a gene is inserted into the genome at the same time as the defective gene is removed** from the genome |

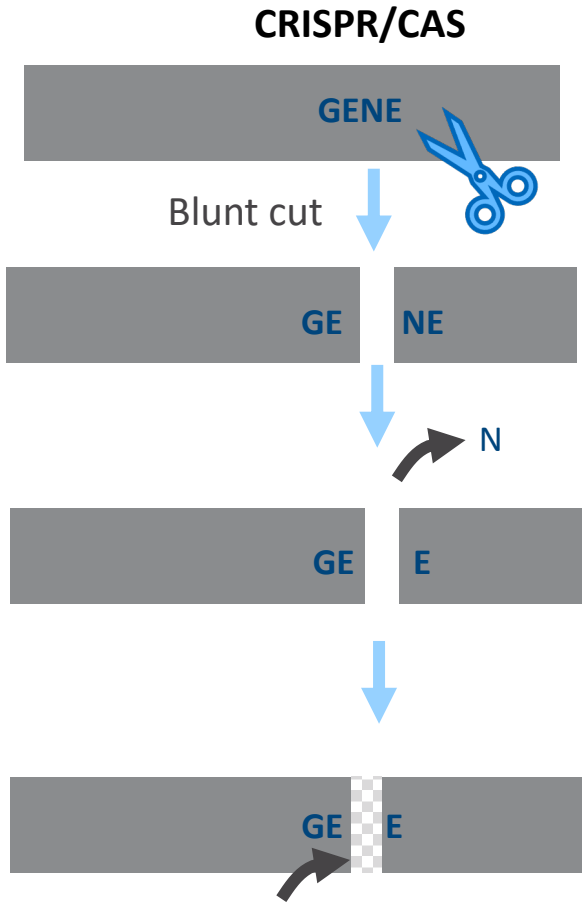
# Precise 3’ Overhang Cuts are Unique - Designed to Enable Gene Insertion and Complex Edits and Provide Identifiable Signature for On-Target Editing

## Complex/Homology-directed Repair (HDR)




*Incorporation of template sequence into genome*

## Simple/Non-Homologous End Joining (NHEJ)




*“indel” mutation*

# Effective Gene Editing Requires Both AAV and LNP Delivery Capabilities

*ARCUS can be effectively delivered with both AAV and LNP*

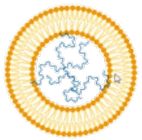
## AAV

**PROS**

- Sustained nuclease expression may provide increased efficacy
- **Gene insertion requires AAV to deliver DNA repair template**
- **AAV has been well-tolerated** in NHP studies to date
- **Tissue specificity:** target expression in target tissue only (via promoters)
- **Can deliver to broad tissue** (CNS, muscle, stem cells, etc.)

**CONS**

- **Pre-existing neutralizing antibodies** and prior **AAV based therapies** may limit patient access
- **Safety risk:** AAV integrations, risk of long-term immune response to long expression of the nuclease
- **Size limitations** on cargo capacity is a challenge for most gene editing technologies; **ARCUS is small and fits in AAV**



## LNP-mRNA

**PROS**

- **Potential to repeat dose** to maximize therapeutic impact
- **Scalability** for manufacturing
- **Transient (~48 hours)** nuclease expression **may have better safety profile**
- **No risk of insertion of the payload into the genome** since mRNA delivered by LNP cannot integrate into the genome

**CONS**

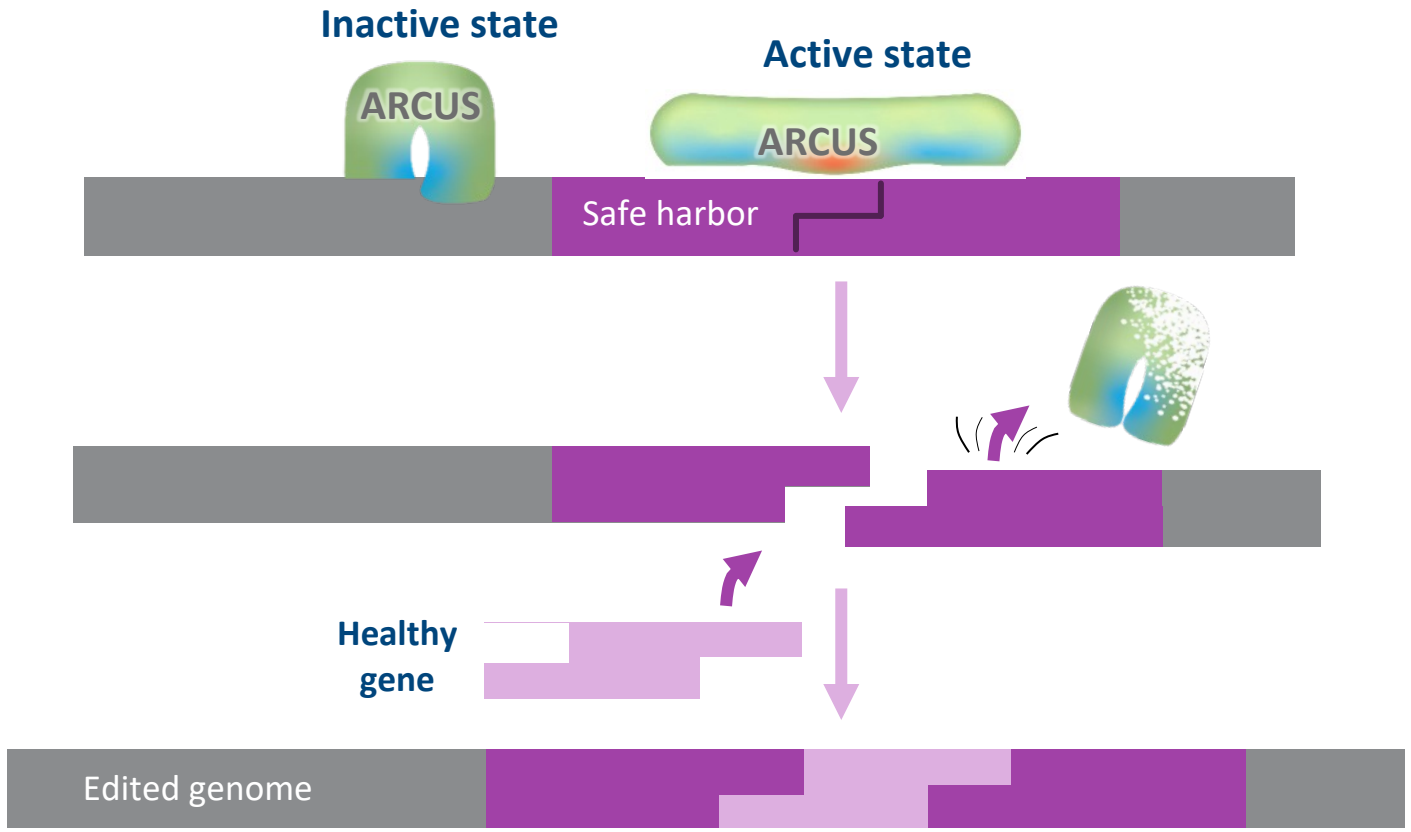
- **Transient (~48 hours)** nuclease expression **may limit efficacy**
- **Tolerability/Immunogenicity** of mRNA is a concern and high doses increase risk of complement activation
- **LNPs are largely restricted to use for liver** delivery today (novel approaches may permit LNPs beyond liver in future)
- **Payload (insertion) can not directly deliver DNA into the nucleus;** requires additional delivery system (e.g., AAV)

# Unlocking Greater *In Vivo* Editing Potential via Safe Harbor, ARCUS Gene Insertion

A “safe harbor” ARCUS nuclease may be used to **develop multiple products to insert a different gene for each disease**

**Complex Edit**

Insertion



# *In Vivo Gene Editing Programs*

Precision *in vivo g*ene insertion and complex gene editing programs highlight unique ARCUS attributes

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# Broad and Deep *In Vivo* Pipeline Showcases ARCUS for Gene Insertion and Complex Edits

| PROGRAM | INDICATION | TISSUE | TARGET | COMPLEX EDIT TYPE / DELIVERY | RESEARCH | CANDIDATE SELECTION | IND-ENABLING | PARTNER |
|---|---|---|---|---|---|---|---|---|
| **PBGENE-HBV** | Chronic hepatitis B | Liver | *HBV* | Deletion/LNP | | | | |
| **PBGENE-HbE** | Sickle cell disease/ beta thalassemia | HSCs | — | Insertion/— | | | | NOVARTIS |
| **PBGENE-DMD** | Duchenne muscular dystrophy | Muscle | *DMD* | Excision/AAV | | | | Lilly |
| **PBGENE-LLY2** | Undisclosed | Liver | — | — | | | | Lilly |
| **PBGENE-LLY3** | Undisclosed | CNS | — | — | | | | Lilly |
| **iECURE-OTC** | Ornithine transcarbamylase deficiency | Liver | *OTC* | Insertion/AAV | | | | ECURE |
| **iECURE-PKU** | Phenylketonuria | Liver | *PAH* | Insertion/AAV | | | | ECURE |

# *ARCUS Safety Supported by Long-term Non-Human Primate Data*

Differentiated ability to track and minimize off-target editing

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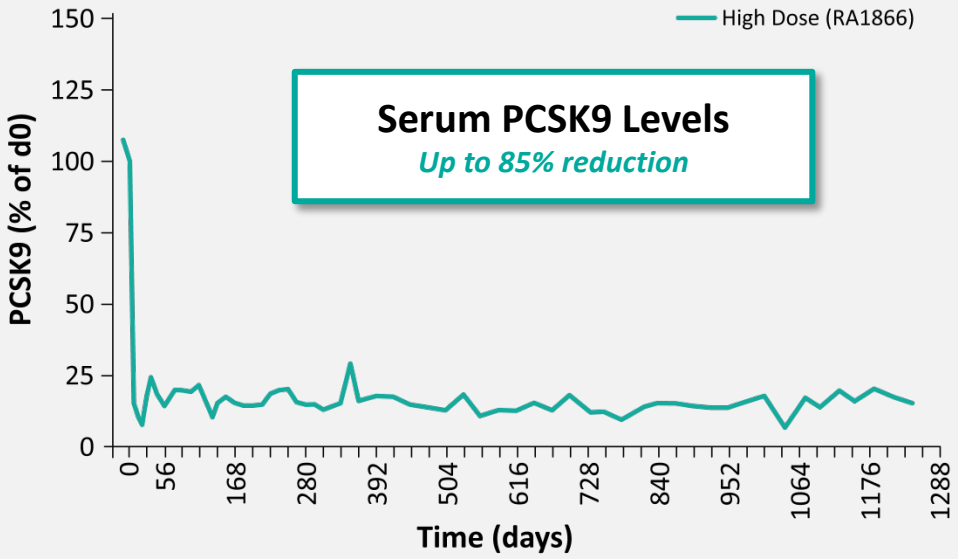
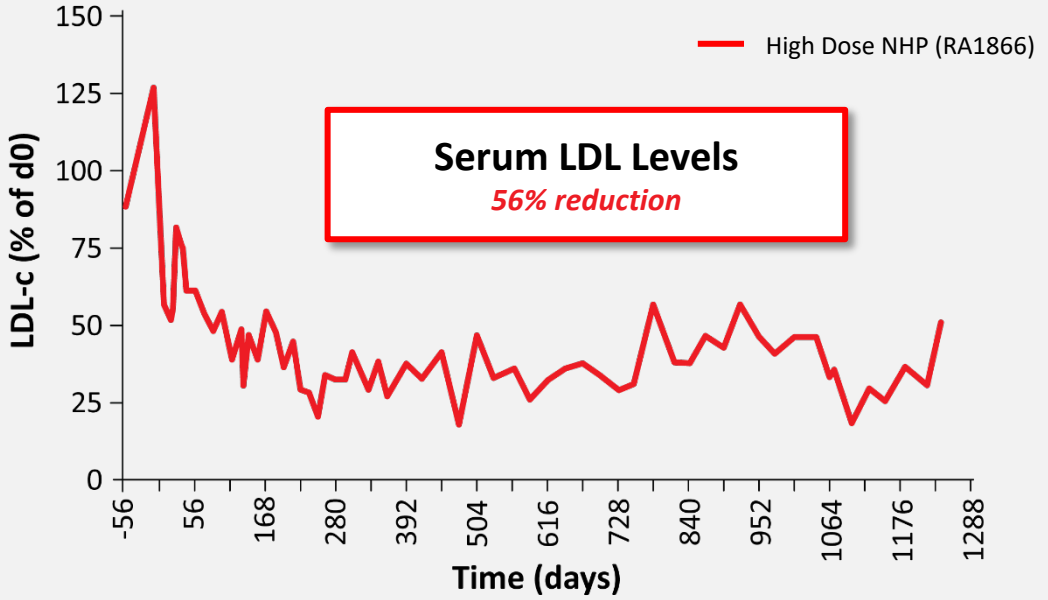
# Five Years of Follow-up for ARCUS in NHP; Longest, Publicly Known Gene Editing Data

## Non-Human Primate Animal Model

One-time delivery of an **AAV-ARCUS** vector into PCSK9 safe harbor for deletion resulted in long-term reductions of serum PCSK9 and LDL[1] (5-year timepoint approaching) with no additional safety concerns




**★ ARCUS delivered by AAV has been studied in the most extensive large animal data set of any gene editing tool showing sustained, safe deletion in long term NHP studies**

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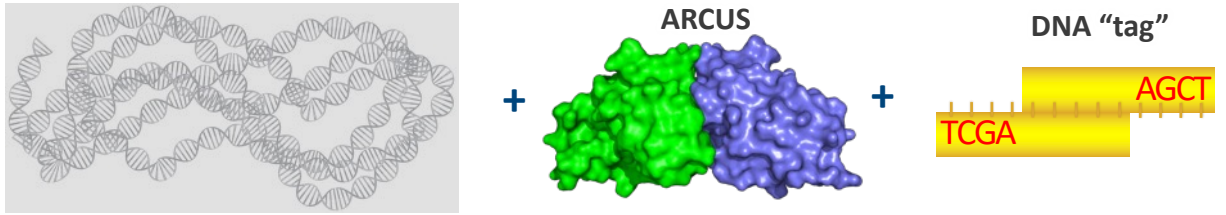
[1] Wang et al, *Molecular Therapy*, February 2021.

# ARCUS Safety and Specificity for Tracking Off-Target Editing

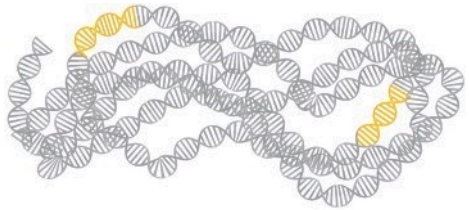
*Oligo Capture: A genome-wide assay for ARCUS off-target editing*

**Step 1**: Transfect cells with ARCUS and a DNA "tag"




**Step 2**: The "tag" is captured at DNA breaks resulting from ARCUS cleavage


**Step 3**: Genomic DNA is isolated from cells and evaluated on a next-gen sequencer to identify all sites where the "tag" was captured



**Step 4**: Sites of on- and off-target capture of the DNA "tag" are identified and deep sequenced to confirm editing

*ATGCTAGCTAGCTAGCTGATCGATGCTAGCTAGCTAGCTA*
*GTAGCTAGTAAGCTGATCGTAGCTGCCGCTGCTAGCTGA*
*TGCGCTAGTAGCTGCTAGTCGCTAGTCGGCAGTCGATGC*
*TGCTAGCTAGTAGCTGCATGCTAGCTAGTGTGTCGATGT*

# *ARCUS for Gene Insertion*

Wholly owned and partnered programs, including those for large gene insertions

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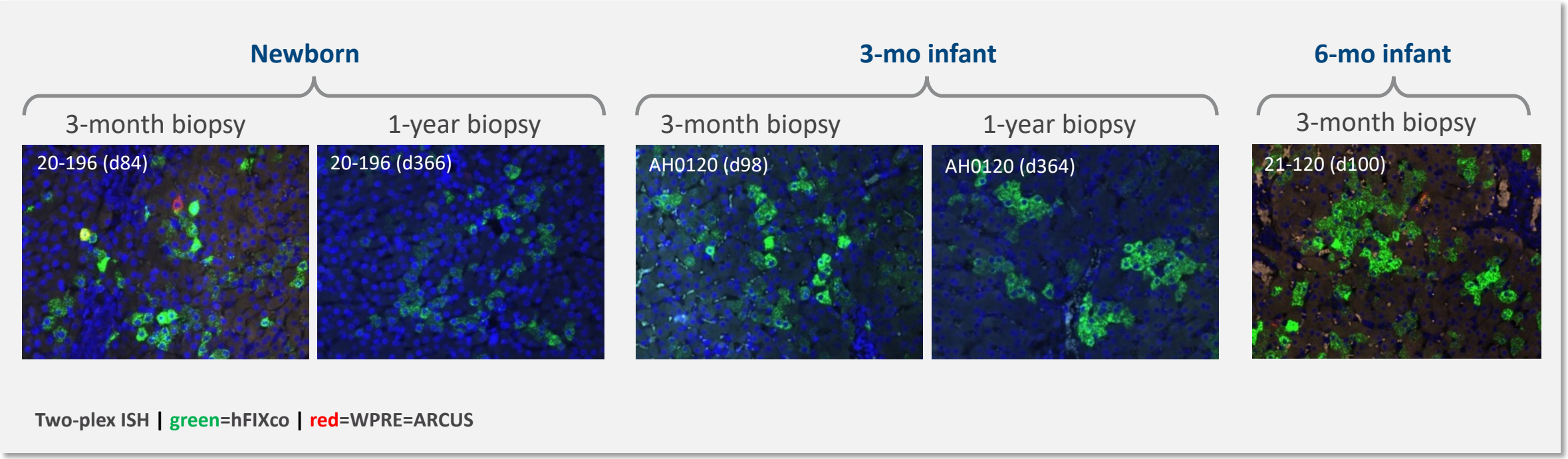
# Hemophilia B Gene Insertion: Stable Transduction of Factor IX in Newborn and Infant Macaque Liver (Non-Human Primates)[1]




**Green cells show that the Factor 9 (FIX) gene has been inserted and stable over 1 year**

**★ Factor 9 (FIX) gene insertion demonstrated in both newborn and infant NHPs to address Hemophilia B**

[1] Data Source: University of Pennsylvania's Gene Therapy Program

# Ornithine Transcarbamylase Deficiency (OTC) Clinical Candidate Shows Stable Gene Insertion at Year 1[1]



Delivery of twin AAV-based vectors carrying ARCUS nuclease vector (GTP-506A) and therapeutic donor vector (GTP-506D) via PCSK9 "safe harbor" site

Long-term stability of the edited genome in NHPs was demonstrated in newborn and infant macaques

- Efficient targeted insertion was achieved in NHPs up to three months of age, and studies of older infants are ongoing
- 12-month follow-up biopsies continued to demonstrate durability, with gene insertion efficiency up to 28.2%[2], well above the expected threshold for clinical benefit
- AAV delivery well tolerated; no evidence of liver histopathology in any ARCUS-treated animals

**★ Durable gene editing efficiency continues to be demonstrated in NHP studies using ARCUS**

[1] Data currently unpublished were presented at the International Conference on Ureagenesis Defects and Allied Conditions 2022 by researchers from the University of Pennsylvania's Gene Therapy Program in collaboration with iECURE. iECURE has a license to use of ARCUS for gene insertion for OTC. https://iecure.com/news/preclinical-data-from-iecures-gtp-506-demonstrates-potential-for-the-treatment-of-ornithine-transcarbamylase-otc-deficiency/

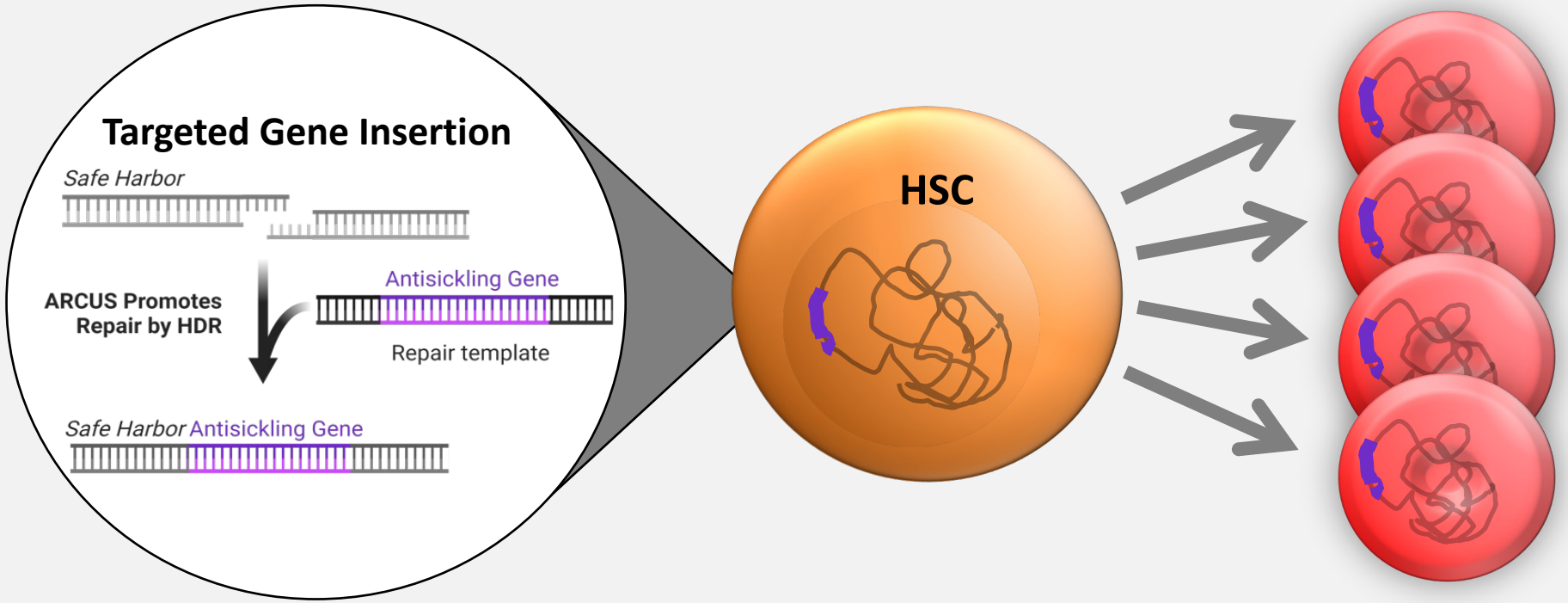
[2] Measured by in-situ hybridization (ISH)

# Gene Insertion to a “Safe Harbor” Locus in Hematopoietic Stem Cells



ARCUS will be used to add an antisickling gene to hematopoietic stem cells (HSCs)

Permanent integration of an antisickling gene into a “safe harbor” locus in HSCs is expected to prevent the sickle cell phenotype in mature erythrocytes.



# *ARCUS for Complex Edits*

- HBV approach edits DNA at two locations
- DMD approach makes a 500,000 base pair edit

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# Precision Approach in HBV: Excision in Two Locations in the Liver

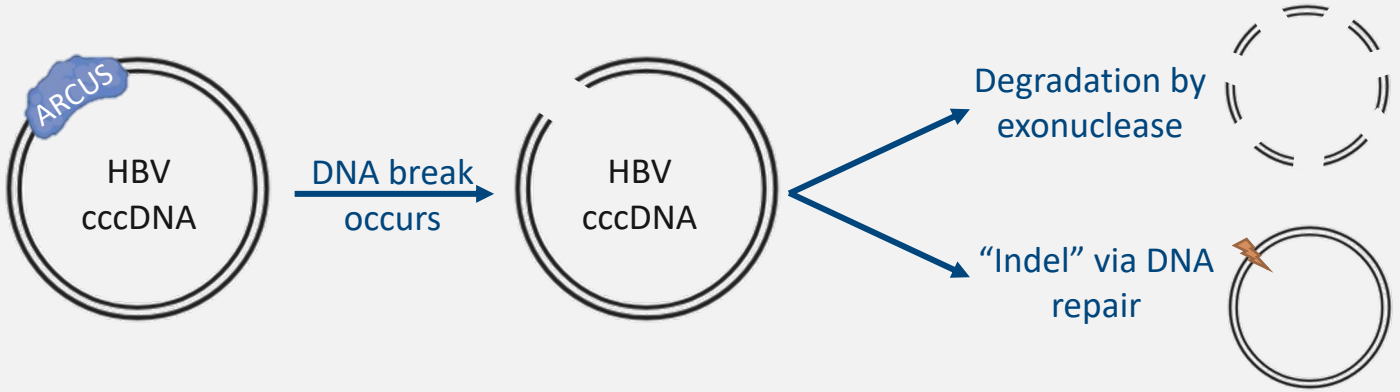
*Curing HBV requires targeting two key viral components – cccDNA and integrated HBV DNA*

**In Vivo**

Gene Excision for Chronic HepB >

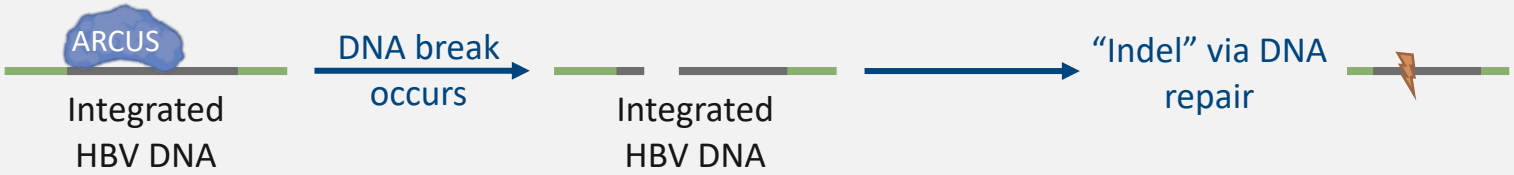
## 1. cccDNA

cccDNA is a pool of minichromosomes that hangs out in nucleus of liver cells and can re-establish infection




## 2. Integrated HBV DNA

Integrated HBV DNA attaches into the DNA and genome of liver cells




**★ Precision's therapeutic approach targets both HBV viral components enabling a path towards a potential cure**

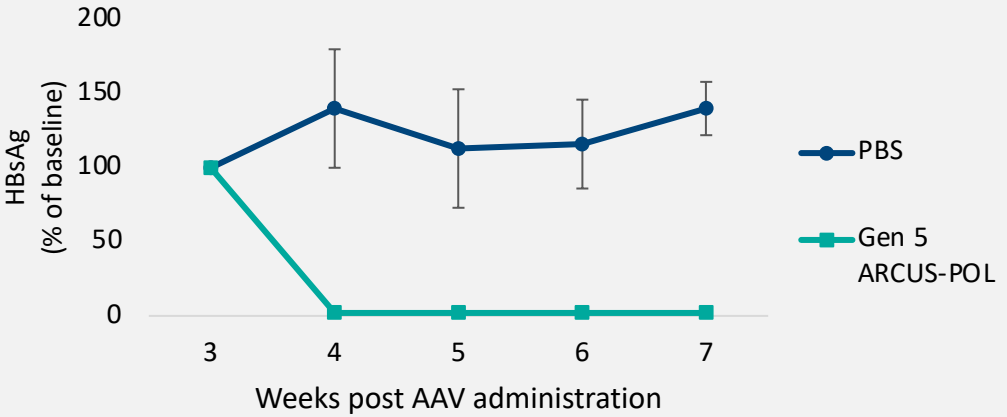
# ARCUS HBV Program has Shown Exciting Efficacy Data During *In Vivo* POC Studies Demonstrating Ability to Reduce Both HBV S-Antigen and HBV cccDNA

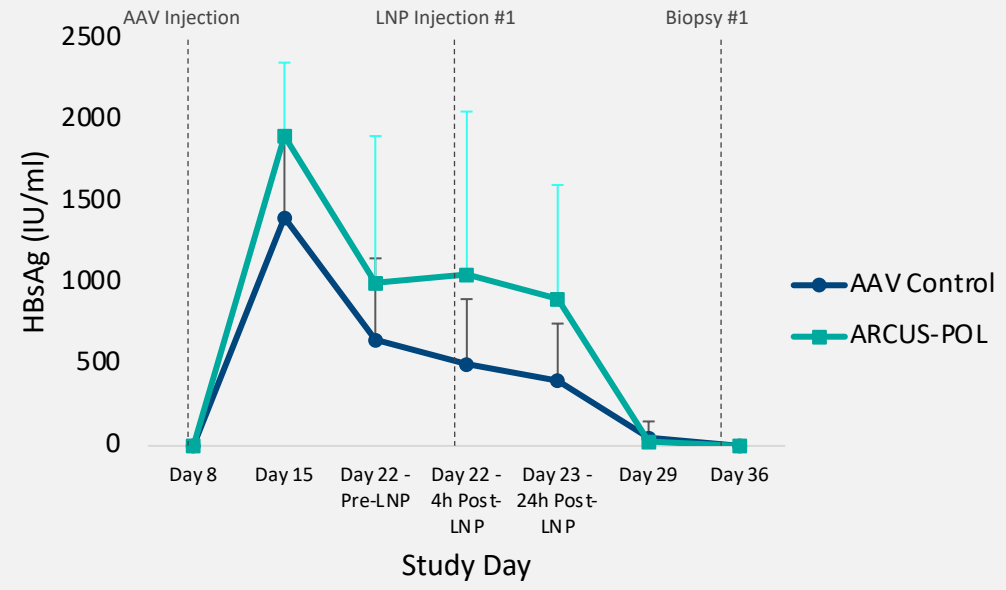


Data from *in vivo* models[1] treated **with ARCUS-HBV nuclease via LNP showed potential for delivering cures**

★ **96% reduction** in serum **HBsAg levels** and substantial reduction in the liver

★ **83% reduction** in HBV **cccDNA**




[1] *In vivo* models: episomal mouse model and episomal NHP model

# ARCUS to Restore Dystrophin Expression for Duchenne Muscular Dystrophy

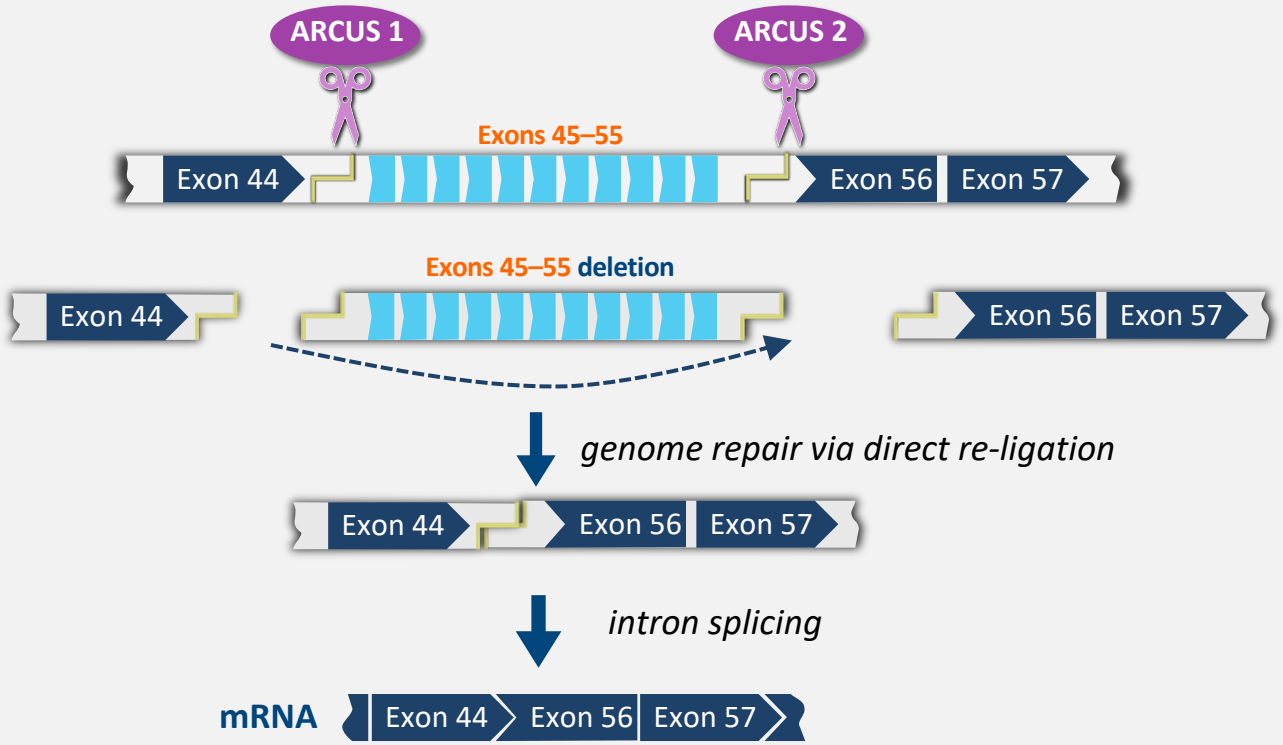


Restore dystrophin expression

Deleting exons 45-55 using a pair of ARCUS nucleases intended to remove a mutation hotspot responsible for >50% of DMD

## GOAL

ARCUS nucleases to make complex edit of the genome and make a variant of the dystrophin protein that is functionally competent



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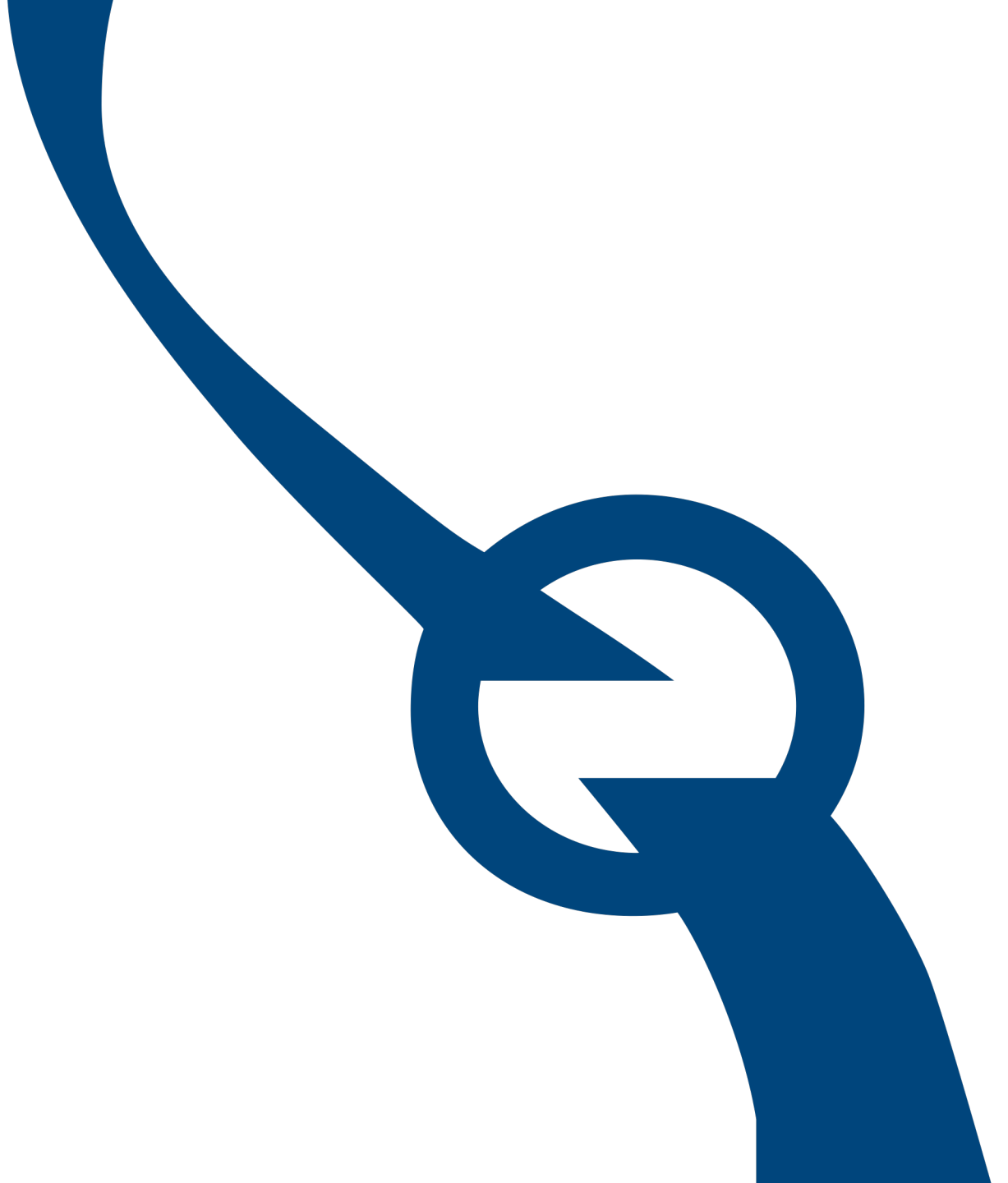
# *2023 Priorities*



# 2023 Priorities and Milestones

- Complete Phase 1b for azer-cel to support decision point for Phase 2
- Complete Phase 1 dosing trial for PBCAR19B
- Host CAR T update in first quarter of 2023
- Nominate the final drug candidate for HBV *in vivo* program
- Advance the first ARCUS *in vivo* nuclease to CTA through a partner
- Publish new preclinical data to further support *in vivo* gene editing programs
- Host *in vivo* gene editing R&D Day around mid-2023
- Further extend the cash runway

**Building the leading therapeutic gene editing company** focused on high unmet needs in oncology and genetic diseases

**Technology:** ARCUS, a premier genome editing platform

**People:** Fortified Senior Leadership Team with 15+ years perfecting ARCUS protein engineering

**Focus & Discipline:** Fiscal resources support 2+ years runway

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# Precision BioSciences: Senior Leadership Team

**Michael Amoroso**
*Since Sep 2021*
President &
Chief Executive Officer

Abeona Therapeutics · Celgene · Kite

**Derek Jantz, Ph.D.**
*Since Mar 2006*
Chief Scientific Officer,
Co-Founder

Johns Hopkins University & Medicine · Duke University

**Jeff Smith, Ph.D.**
*Since Mar 2006*
Chief Research Officer,
Co-Founder

Johns Hopkins University & Medicine · Duke University

**Alex Kelly**
*Since Oct 2020*
Chief Financial Officer

Allergan · Merck · Pharmacia

**Cindy Atwell**
*Since Apr 2019*
Chief Business Officer

Halozyme · abbvie · Amylin

**Alan List, M.D.**
*Since Apr 2021*
Chief Medical Officer

Moffitt Cancer Center

**Juli Blanche**
*Since May 2022*
Chief People Officer

Bristol Myers Squibb · Celgene · Merck

**Dario Scimeca**
*Since Jun 2019*
General Counsel

Genentech · Elan

**Neil Leatherbury**
*Since Mar 2017*
VP, CMC

miRNA Therapeutics · Azaya Therapeutics

PRECISION BIOSCIENCES

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# *Appendix*

# ARCUS for Chronic Hepatitis B Virus (cHBV) Targeting cccDNA



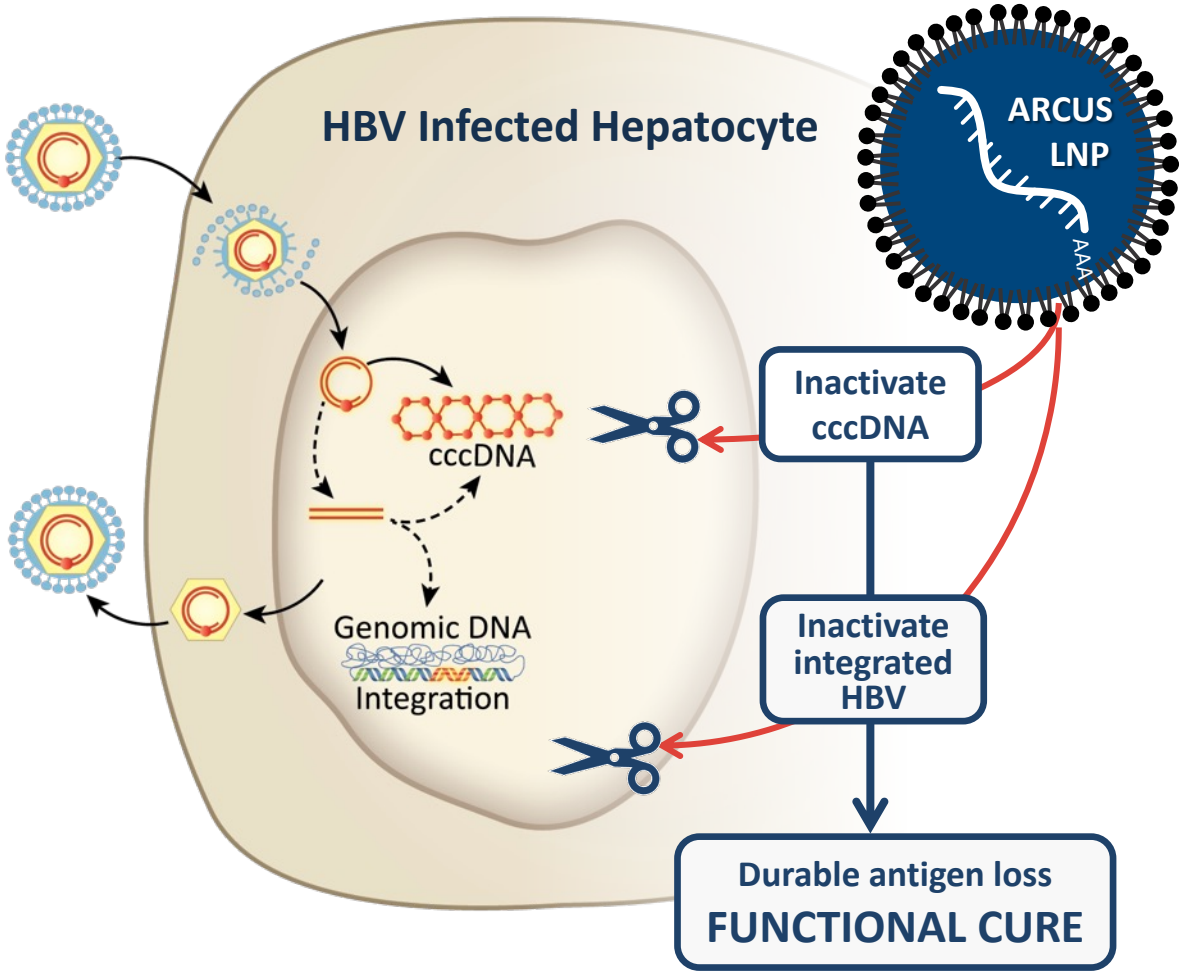
ARCUS-mediated **inactivation of cccDNA and integrated HBV** could result in a functional cure

**Chronic HBV is one of greatest racial health disparities in the U.S.**

**> 860,000**
**cHBV infections in the US**

**> 290 million**
**cHBV infections globally**

- > 90% of infected infants develop cHBV
- ≤ 50% of infected children 1-5 years develop cHBV
- 5-10% of infected healthy adults develop chive




https://www.hhs.gov/hepatitis/learn-about-viral-hepatitis/hepatitis-b-basics/index.html#:~:text=Risk%20for%20chronic%20infection%20is,liver%20failure%2C%20and%20premature%20death

# Novartis Collaboration Complementary to Precision's Existing *In Vivo* Gene Editing Partnership with Lilly



Research collaboration and license agreement aimed at treating challenging genetic diseases


**3** Initial collaboration for **three targets**, including Duchenne muscular dystrophy and **two other undisclosed programs targeting the liver and CNS**

**+**

**3** Lilly retains right to select up to **three additional gene targets**

- Upfront payment of $135M including $35M equity
- Up to $420M per target in development and commercialization milestones
- Mid-single digit to low tweens tiered royalties

# Duchenne Muscular Dystrophy Currently Lacks a Curative Treatment




**Mutation on the X chromosome interferes with dystrophin protein production, which is needed to form and maintain healthy muscle**

Affects approximately
**1 in 3,500**
live male births

# *In Vivo* Gene Insertion Collaboration with Novartis for Hemoglobinopathies



Builds on the unique gene insertion capabilities of ARCUS® and further validates ARCUS as a premium genome editing platform


**Collaboration with Novartis,** a global gene therapy leader

**Precision to develop a single ARCUS nuclease** for certain hemoglobinopathies such as sickle cell disease and beta thalassemia

**Goal to design ARCUS nuclease for safe and efficient *in vivo* gene insertion**

- Precision receives $75M upfront for a single target/single nuclease
- Eligible to receive up to an additional $1.4B in milestones and tiered royalties on sales of licensed products
- Collaboration adds hematopoietic stem cells (HSCs) to existing *in vivo* gene editing programs targeting the liver, muscle and central nervous system
- One-time, treatment for hard-to-treat genetic blood disorders such as sickle cell disease (SCD) and beta thalassemia

# Hemoglobinopathies are a Major World Health Problem



## Sickle Cell Disease (SCD)

**Affects the structure/function of hemoglobin, reducing the ability of red blood cells to transport oxygen**

- Acute sicklecell pain crises and life-threatening complications

## Beta Thalassemia

**One of the most common genetic diseases caused by a disruption of normal hemoglobin production**

- Complications: Overproduction of red blood cells inside and outside of the bone marrow, heart disease, chronic liver hepatitis, defects of the reproductive system, diabetes, and rare skin disorders

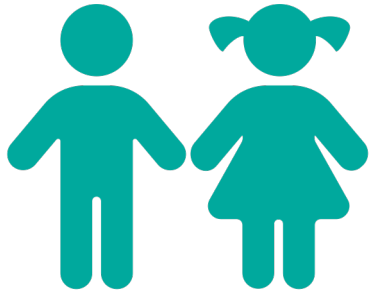
**Sickle Cell Disease Affects**

**>300,000**

**newborns annually**

**~1,000 children**

in Africa are born with SCD **every day** and > 50% will not reach their 5th birthday



**~68,000**

children born with thalassemia each year

Sedrak A, Kondamudi NP. Sickle Cell Disease. [Updated 2021 Nov 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-.
Needs T, Gonzalez-Mosquera LF, Lynch DT. Beta Thalassemia. [Updated 2022 May 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-.

# OTC is a Severe, Ultra Rare Genetic Condition With Extremely High Unmet Medical Needs Across Phenotypes



## Ornithine Transcarbamylase (OTC) Deficiency

- OTC deficiency is the most common **urea cycle disorder**
- Disease prevalence is between **1 in 60,000 and 1 in 72,000**
- Neonatal onset has been associated with **mortality rates as high as 74%**[1]
- A **liver transplant** is typically required by six months of age and is the only known curative treatment
- OTC deficiency is also associated with numerous **neuropsychological complications**
- **High ammonia levels** can lead to development delays, learning and intellectual disabilities, ADHD and executive function deficits, seizures, coma and death

## ~ 4,200 People with OTC in the US[2]

| **Neonatal-onset** *(<30 days since birth)* | **Late-onset Symptomatic** *(>30days to 16yo)* | **Late-onset Asymptomatic Adult** *(>16yo)* |
|---|---|---|
| Majority male X-linked / No enzymatic activity | Majority females w/skewed X-inactivation / Limited enzymatic activity | Majority female, asymptomatic |
| Catastrophic disease managed by liver transplants & aggressive medical mgt. / Significant neurocognitive problems and lower life expectancy | Severe disease managed by medical mgt. High risk for neurocognitive problems<br>Liver transplant / mortality risks exist | Usually manifest during stress situation (surgery, post-childbirth)<br>Rare but high mortality at initial event |

[1] Complete removal of OTC activity results in severe neonatal disease, while decreased OTC results in late-onset.
[2] Onset may occur at any age though is more common in infancy. HAC: Hyperammonemic Crisis, defined as plasma ammonia levels ≥ 150 µmol/L together with clinical symptoms probably related to hyperammonemia. OTC: Ornithine Transcarbamylase. Source: UpToDate; Orphanet; Hasegawa et. Al. J Pediatr Surg. 1995. Ah et. Al. GeneReviews. 2017. NORD; Lamb et. Al. BJM. 2016. Brassier et. Al. Orphanet Journal of Rare Disease 2015.; Unsinn et. Al. Orphanet Journal of Rare Diseases. 2016; Summar et al. NIH. 2008; Buerger et. Al. J. Inherit. Metab. Dis. 2013; ClearView Analysis.