



PRECISION
BIOSCIENCES

PRECISION BIOSCIENCES: A Gene Editing Company Dedicated to Improving Life (DTIL)

January 11, 2022

Forward Looking Statements

This presentation (together with any other statements or information that we may make in connection herewith) contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation (together with any other statements or information that we may make in connection herewith) that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding the development of our product candidates involving our ARCUS genome editing platform, the timing of trials, including clinical updates and interim data, and results therefore of our “off-the-shelf” CAR T immunotherapy candidates PBCAR0191, PBCAR19B, PBCAR269A in combination with nirogacestat, anti-CD19 CAR T combinations with foralumab, and our in-vivo gene editing product candidates including PBGENE-PCSK9, PBGENE-PH1, PBGENE-HBV and product candidates partnered with Eli Lilly including PBGENE-DMD, expected milestones for 2022, 2023 and 2024, including, without limitation, updates regarding the Company’s ex vivo CAR T and in vivo gene editing pipeline. In some cases, you can identify forward-looking statements by terms such as “aim,” “anticipate,” “believe,” “expect,” “should,” “plan,” “intend,” “estimate,” “target,” “mission,” “goal,” “may,” “will,” “would,” “could,” “project,” “predict,” “contemplate,” “potential,” 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 or greenhouse studies and clinical or field trials; public perception about genome editing technology and its applications; competition in the genome editing, biopharmaceutical, biotechnology and agricultural 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 subjects; 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 the outbreak of COVID-19, 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, 2021, 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 Events and Presentations at investor.precisionbiosciences.com.

Agenda

- **ARCUS® premier gene editing platform**
- *ex vivo* applications of ARCUS focused on **first-in-class and best-in-class allogeneic CAR T programs**
- *in vivo* applications of ARCUS expect to deliver **3 INDs/CTAs in 3 YEARS**

Building on 2021 Progress to Further Validate ARCUS in 2022

2021 Accomplishments:

- Closed ≤6 target *in vivo* gene editing deal with Lilly
- Announced phase 1 data for PBCAR0191 supporting trial expansion
- Advanced PBCAR19B stealth cell into the clinic
- Expedited clinical PBGENE-PCSK9 development plan for Familial Hypercholesterolemia
- Fortified management team (CEO, CMO, CFO) and board
- Completed spin-out of Elo to focus on human therapeutics

Looking ahead to 2022 and beyond:

- Further **validate ARCUS clinically** to positively impact human health

ARCUS: Advanced Genome Editing Platform for *ex vivo* and *in vivo* Editing

PRECISION

- Safety
- Specificity

VERSATILITY

- Small Size Allows Tailored Tissue Delivery (via LNP and AAV delivery)
- Performs Complex Edits
(Gene Insertion & Gene Repair)

ARCUS: Custom Engineered for Genome Editing

Versatility Precision

	ARCUS	Zinc Finger Nuclease or TALENs	CRISPR Sa/SpCAS9	BASE EDITOR
Origin	Eukaryotic homing endonuclease, evolved for gene insertion	Bacterial restriction enzyme, evolved for defense	Bacterial restriction enzyme, evolved for defense	Derived from CRISPR
Resting state	Inactive	Active	Active	Active
Cut type	Consistent 3' overhang	Variable: Blunt or 5' overhang	Blunt	N/A
• <i>Repair mechanism</i>	Primarily HDR	Primarily NHEJ	Primarily NHEJ	Only single base edits
• <i>Ability to track off-target edits</i>	Very High	Low	Low	Very low
Size	Small	Large	Large	Very large
• <i>Delivery with single AAV</i>	✓	✗	✓ / ✗	✗

Two Applications for Delivering on the Promise of Therapeutic Genome Editing

ARCUS[®] Genome Editing

Derived from natural homing
endonuclease for *ex vivo* and *in vivo*
applications



***Ex Vivo* ARCUS Editing for Allogeneic CAR T Immunotherapy**

*Single Gene edit, donor derived
CAR T cells*



***In Vivo* ARCUS Editing for Genetic Diseases**

*Potentially curative,
one-time treatment*

The Promise of *ex vivo* Gene Editing for Allogeneic CAR T Therapy



- Auto-CAR T potentially curing 3.5 out of 10 patients
 - ~4 weeks required to manufacture auto-CAR T cells
 - Up to 20% of intended auto-CAR T patients never receive treatment
- Precision's **off-the-shelf allogeneic CAR T reduces complexity** and increases likelihood for patients to receive treatment without delay
- Cells from healthy donors with **novel manufacturing process and single gene edit to prevent chromosomal abnormalities**

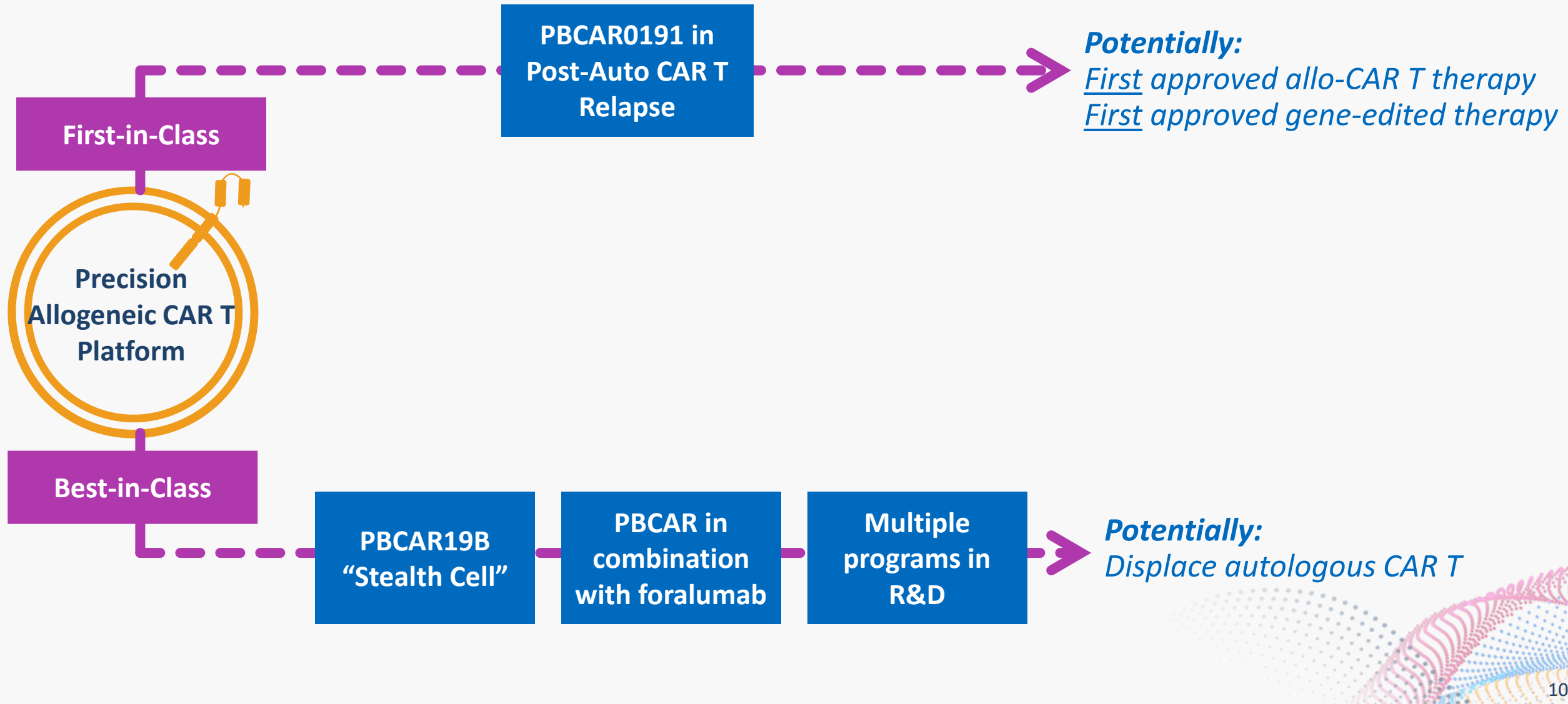
ex vivo CAR T Pipeline

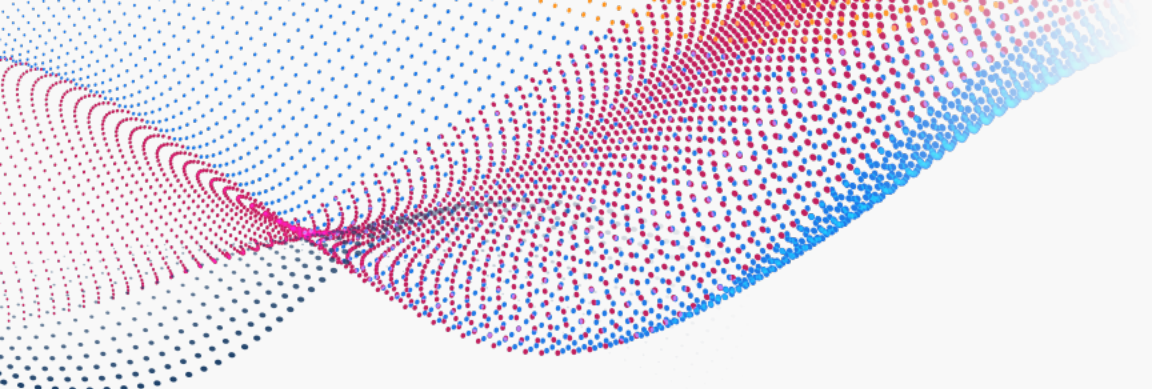
Program	Indication	Target	Preclinical	Clinical	Next Milestone
PBCAR0191	Post-auto CAR T relapse NHL	CD19			Mid-2022
PBCAR19B	NHL	CD19			Mid-2022
PBCAR269A ¹ in combination with GSI	Multiple Myeloma	BCMA			Mid-2022
CD19 combination with foralumab ² (anti-CD3 mAb)	TBD	CD19			2022 IND amendment

1. PBCAR269A is being evaluated in combination with gamma secretase inhibitor, nirogacestat from SpringWorks Therapeutics

2. Exclusive license agreement with Tiziana Life Sciences to evaluate foralumab with allogeneic CAR T candidates for cancer treatment

ex vivo CAR T Pipeline Focused on First-in-Class and Best-in-Class Approaches

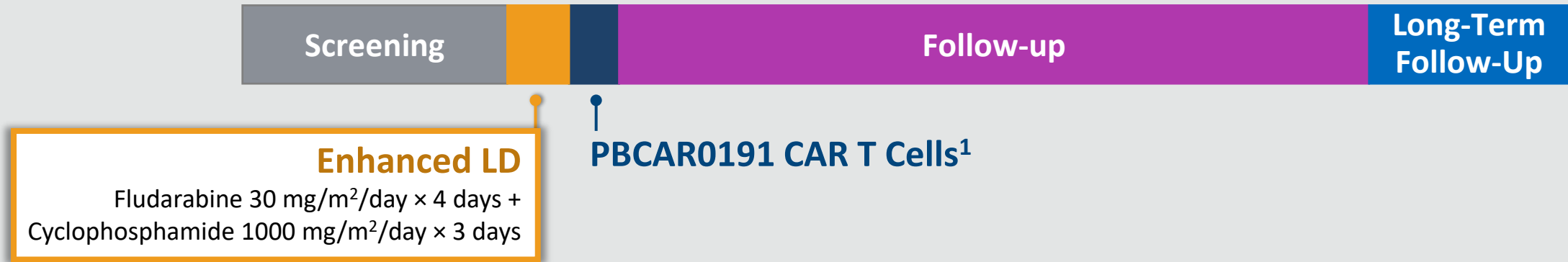




Precision BioSciences Allogeneic CAR T Portfolio Going Forward: Our Focused Path to First-in-Class

- Population with **highest unmet need**
- **No clear standard-of-care**
- Potential **rapid path to market**
- Potential for **first allogeneic CAR T** to reach the market

PBCAR0191 with Enhanced Lymphodepletion in R/R CD19+ B-Cell Malignancies



Objectives

- Mitigate host immune rejection to improve PBCAR0191 expansion and persistence
- Increase frequency and durability of Complete Responses (CRs)
- Assess safety (e.g., Grade ≥3 CRS or ICANS)
- Evaluate activity in subjects with and without prior autologous CD19-directed CAR therapy

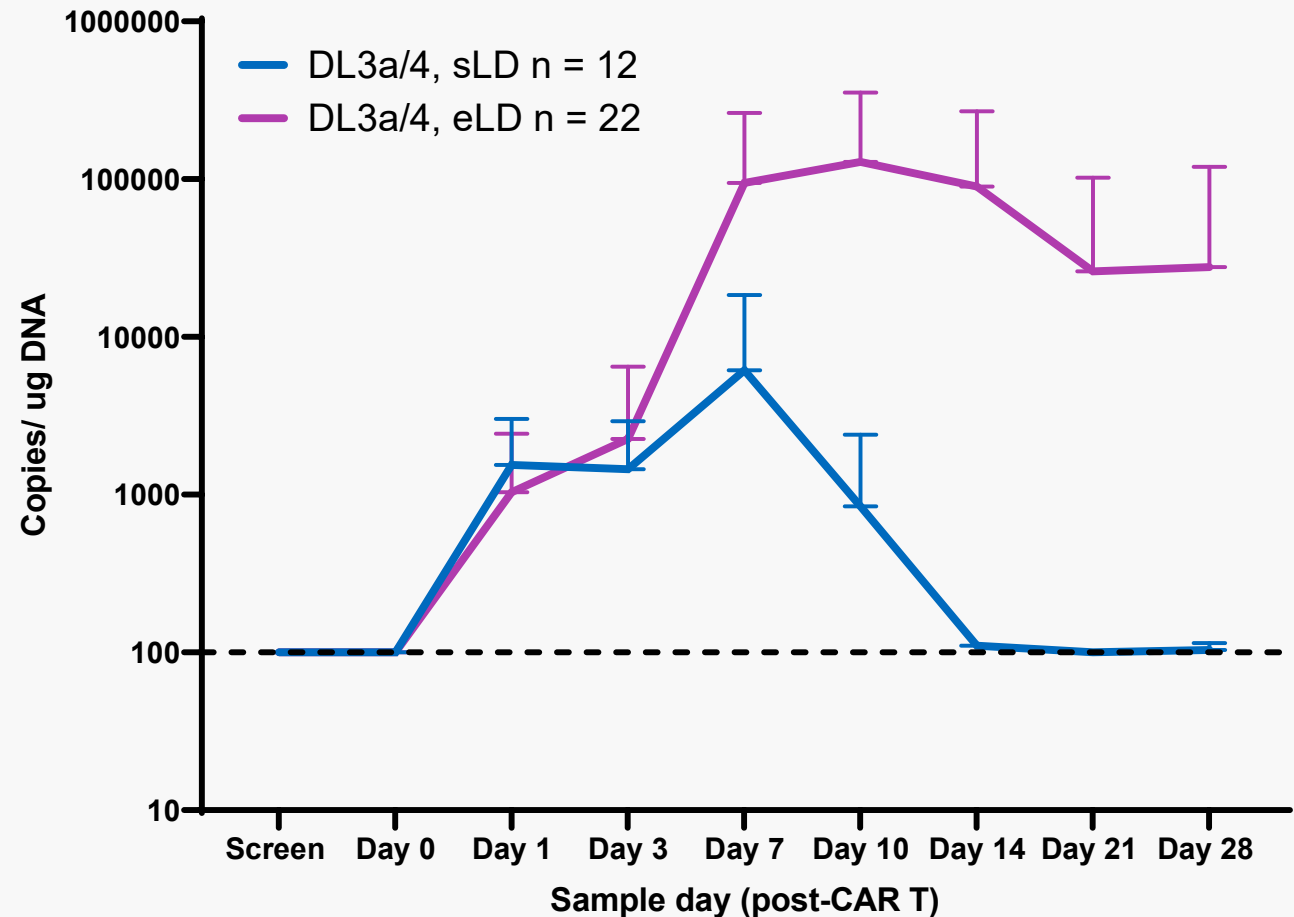
1. PBCAR0191 Dosed at Dose Level 3 (3×10^6 cells/kg Day 0) or Dose Level 4a (3×10^6 cells/kg Day 0 plus 3×10^6 cells/kg Day 10; DL's 3/4a combined due to lack of expansion upon 2nd infusion w/out LD in split dosing

eLD¹ Markedly Increased PBCAR0191 Peak Expansion vs. sLD²

PBCAR0191 Expansion by PCR

Mean Peak ~21X

Mean Area Under the Curve (AUC) ~47X



* All eligible subjects began LD within 1 day of eligibility determination

1. Enhanced LD (eLD) = Fludarabine 30 mg/m²/day × 4 days + Cyclophosphamide 1000 mg/m²/day × 3 days

2. Standard LD (sLD) = Fludarabine 30 mg/m²/day × 3 days + Cyclophosphamide 500 mg/m²/day × 3 days

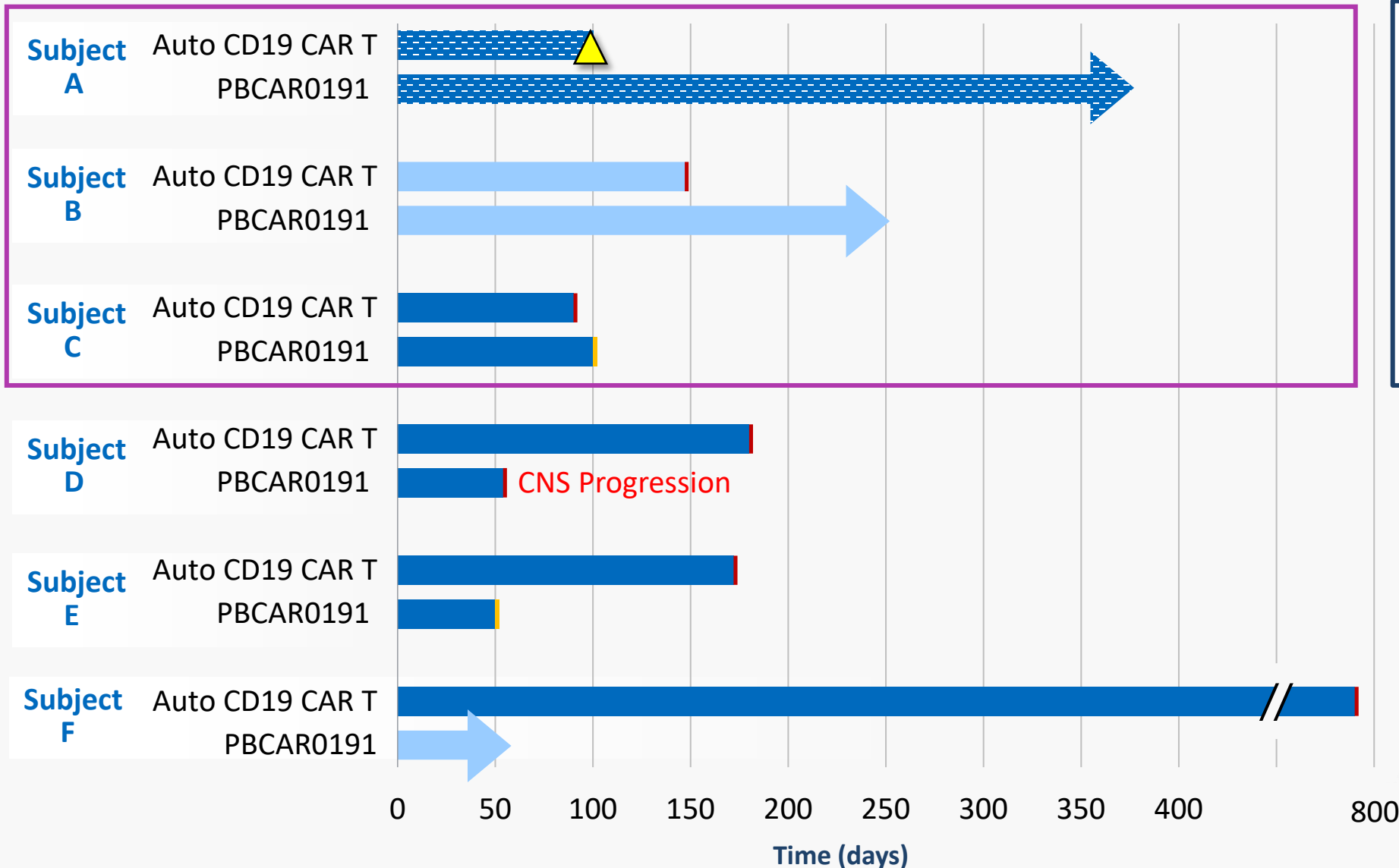
3. Dose Level 3 = 3 × 10⁶ cells/kg Day 0; Dose Level 4a = 3 × 10⁶ cells/kg Day 0 and Day 10)

Best Response to PBCAR0191 with eLD Comparable Between Auto-CAR T Relapsed & Auto-CAR T Naïve Subjects

n (%)	All evaluable subjects (N=22) ¹	CAR T naïve (n=16) ²	CAR T experienced (n=6)
Overall Response Rate (ORR) ≥Day 28	16 (73%)	10 (63%)	6 (100%)
Complete Response (CR) ≥Day 28	13 (59%)	9 (56%)	4 (66%)

1. One subject non-evaluable for efficacy at Day 28 assessment due to death related to cardiac arrest after choking incident
2. One subject received CD19 NK-CAR therapy

Depth & Duration of Response to PBCAR0191 in CD19 Auto-CAR T Relapsed Subjects

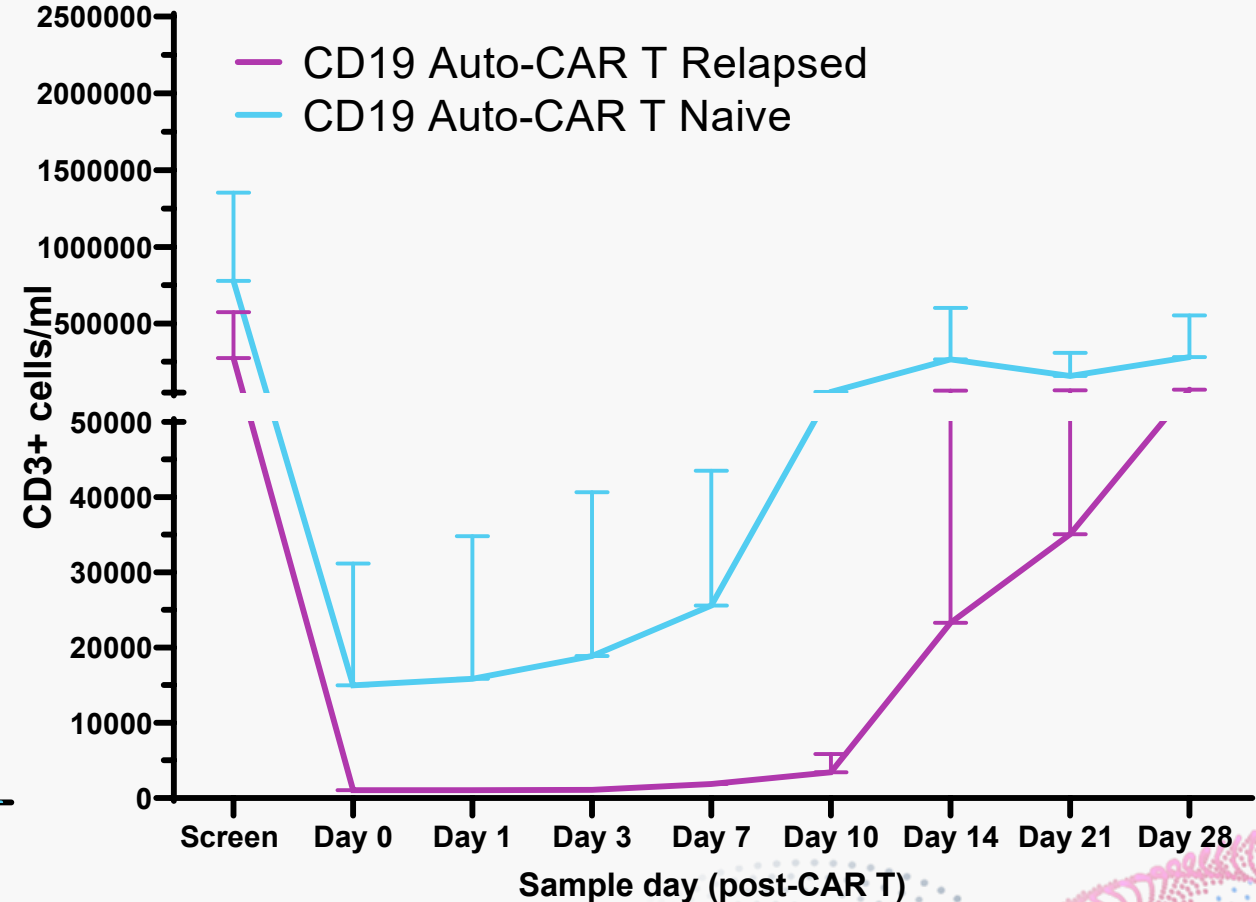
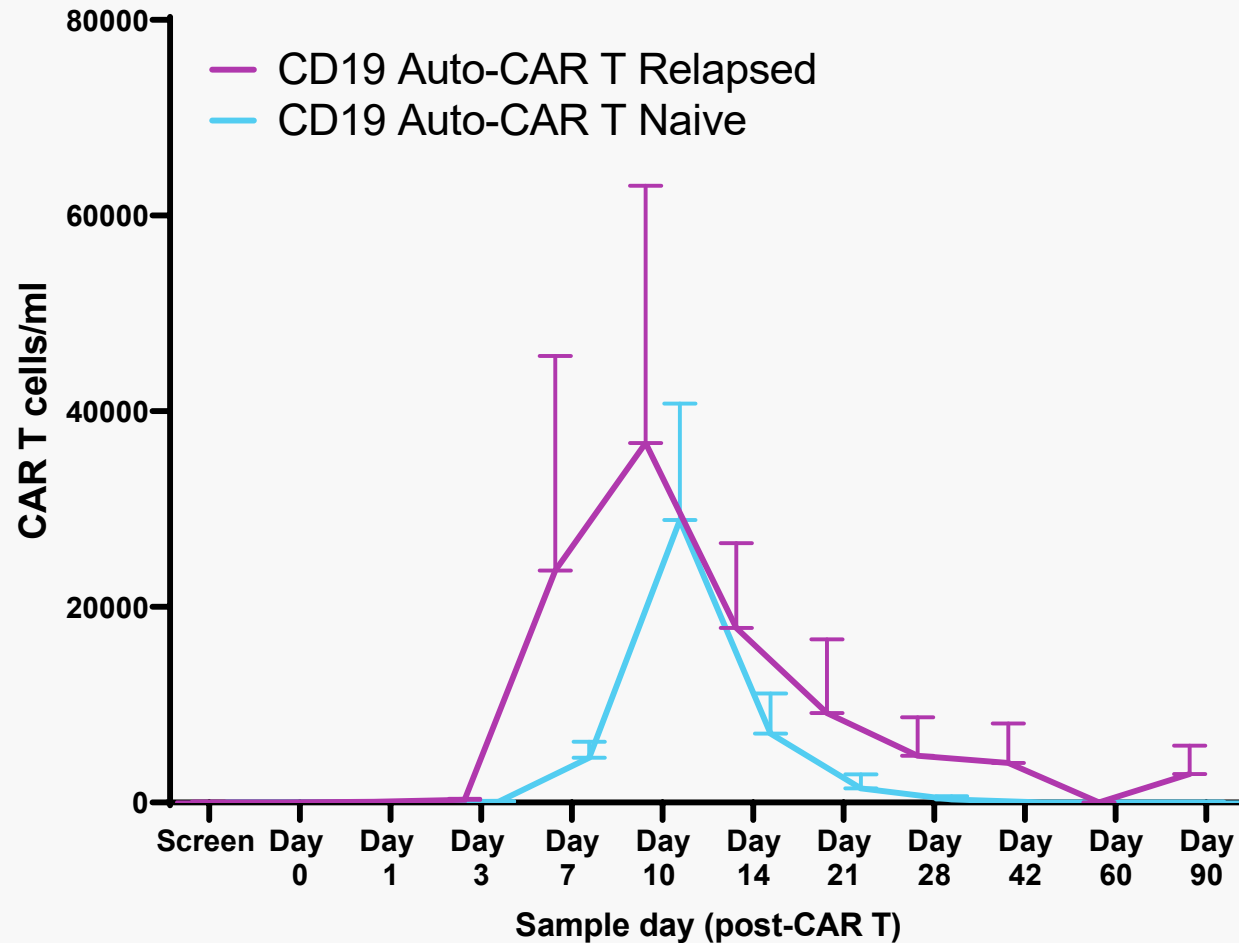


- 100% ORR in subjects who received prior auto-CAR T
- *PBCAR0191 response duration exceeded original response to auto-CAR T in 3 of 5 evaluable subjects*

- CR/CrI (MRD-)
- CR
- PR
- PD
- Death on study in ongoing response
- Allo-transplant

PBCAR0191 with eLD: Earlier Expansion, Higher Peak, Prolonged Persistence, Delayed CD3 Recovery in Relapsed Auto-CAR T Setting

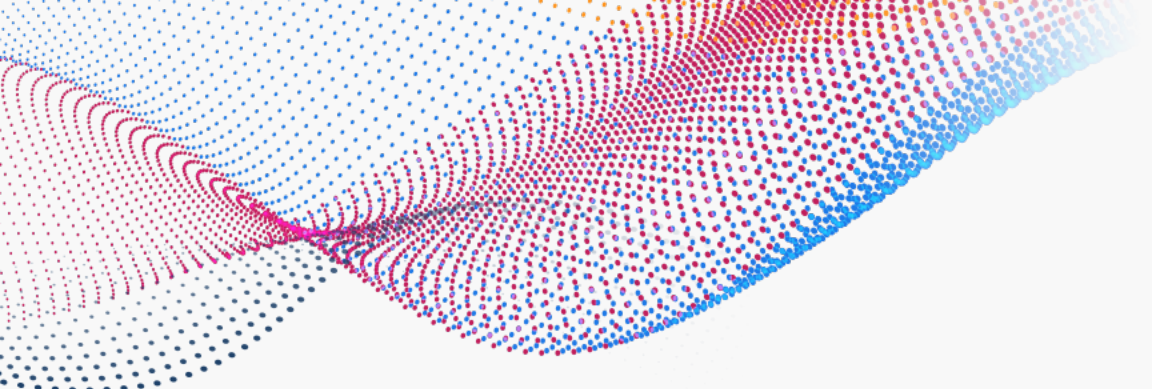
PBCAR0191 expansion and CD3+ cells measured by flow cytometry



Evidence for PBCAR0191 + eLD in Auto-CAR T Relapsed

- Auto-CAR T has changed the landscape for 3rd line lymphoma; ~65% of patients relapse¹
- As auto-CAR T moves to second line, the number of patients requiring salvage increases
- No FDA approved therapeutics for patients who progress following auto-CAR T therapy; median overall survival of 3+ months¹
- PBCAR0191 + eLD may offer effective treatment for relapsed auto-CAR T patients
- All 6 subjects who progressed following CD19 auto-CAR T therapy responded to PBCAR0191 following eLD with 66% CR rate
- Duration of response exceeded auto-CAR T response in 3 of 5 evaluable subjects

Next Steps for Precision: Further investigate CD19 auto-CAR T relapsed lymphoma subjects to validate activity and safety in this growing population with highest unmet need

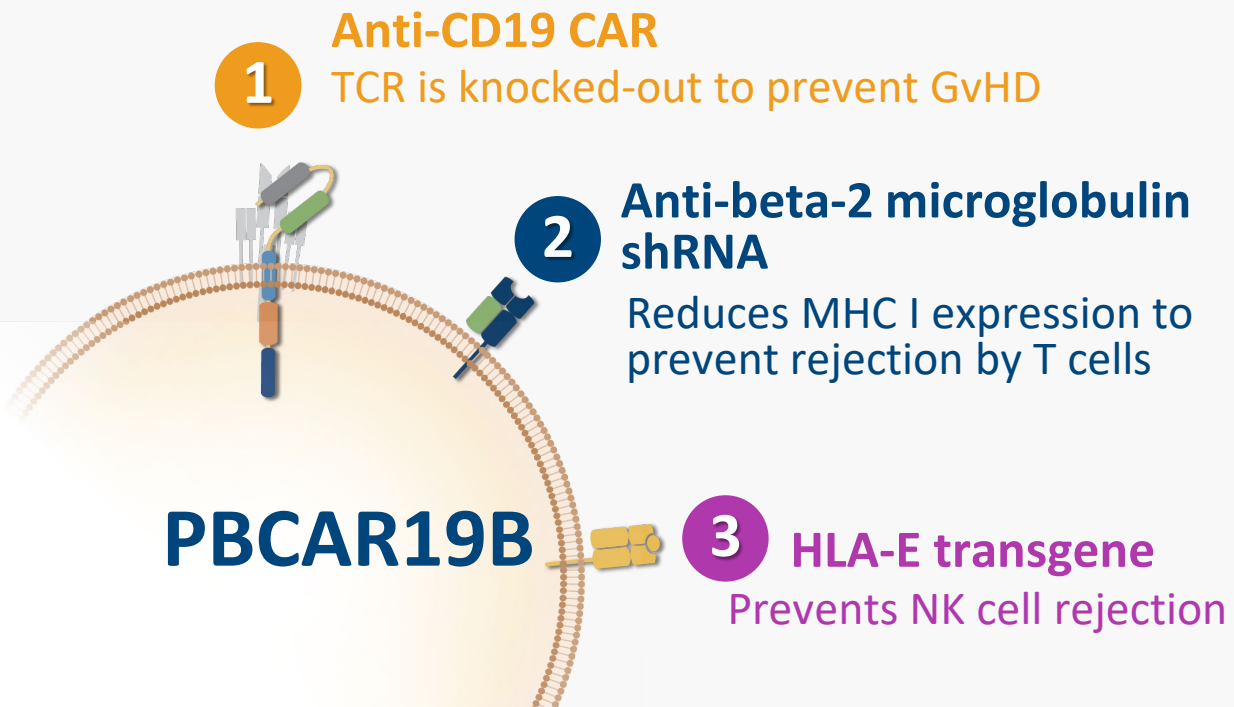


Best-in-Class: Allogeneic PBCAR T Cell Products for Subjects with Relapsed/Refractory B-Cell Malignancies

- **Single dose**
- **ARCUS single-gene edit** minimizing translocation safety concerns
- Therapeutic index **as good as, or better than**, approved auto-CAR T product profiles
- **Overcome rejection** of allogeneic CAR T cells by patient immune system

PBCAR19B Stealth Cell Progress in Clinic

Accomplished with a single-step gene edit to minimize risk of chromosome abnormalities



- Phase 1 **study initiated on June 30, 2021**
- Subjects receive increasing flat dose levels (2.7×10^8 - 8.1×10^8 CAR T cells) plus standard lymphodepletion¹
- **First three patients dosed** at Dose Level 1
- Currently enrolling at multiple sites
- Expect initial **clinical updates mid-year 2022**

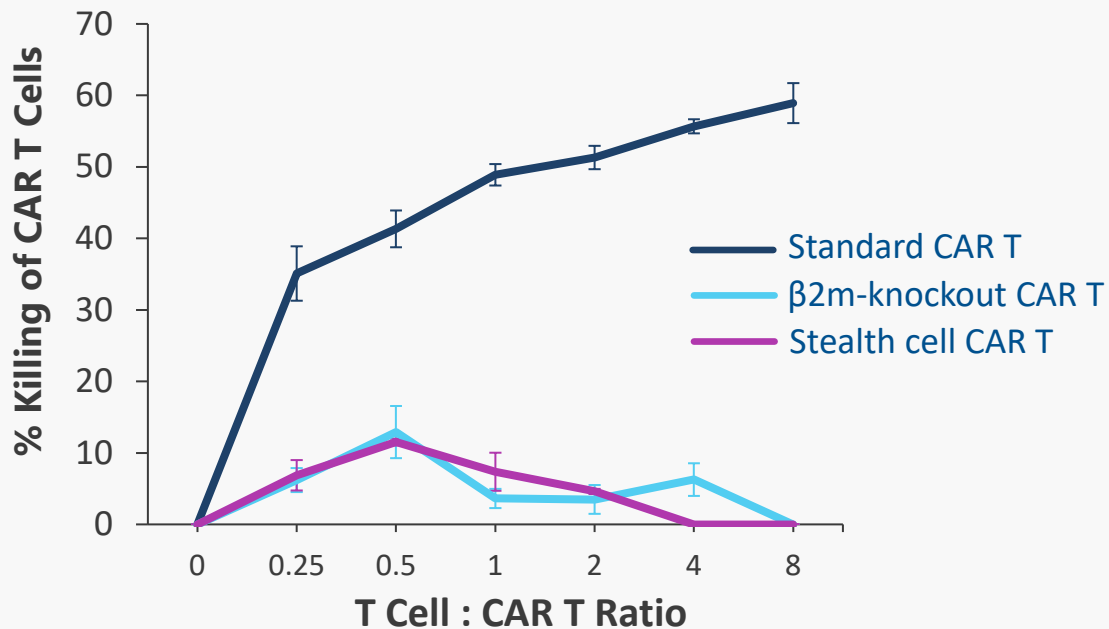
1. Standard LD (sLD) = Fludarabine $30 \text{ mg/m}^2/\text{day} \times 3 \text{ days}$ + Cyclophosphamide $500 \text{ mg/m}^2/\text{day} \times 3 \text{ days}$

Second-Generation “Stealth Cell” CAR T Platform

- The Stealth Cell vector incorporates an anti- β 2m shRNA and an HLA-E transgene
- Stealth Cell CAR Ts resist rejection by T cells & NK cells in mixed-lymphocyte reactions

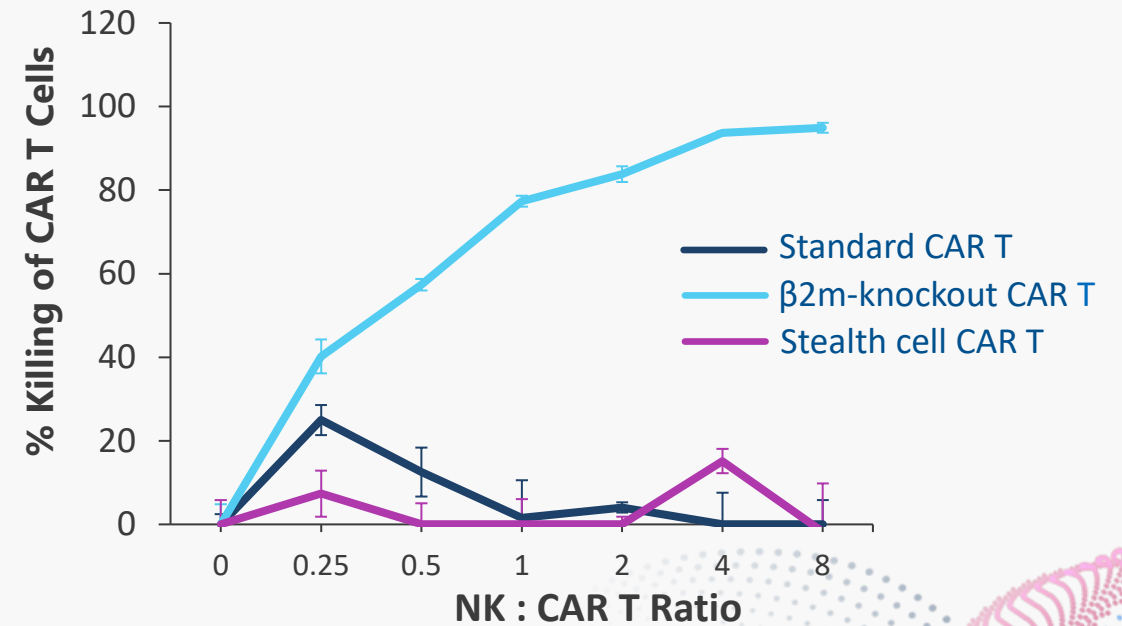
Rejection by T cells

(n=4 mismatched donors)

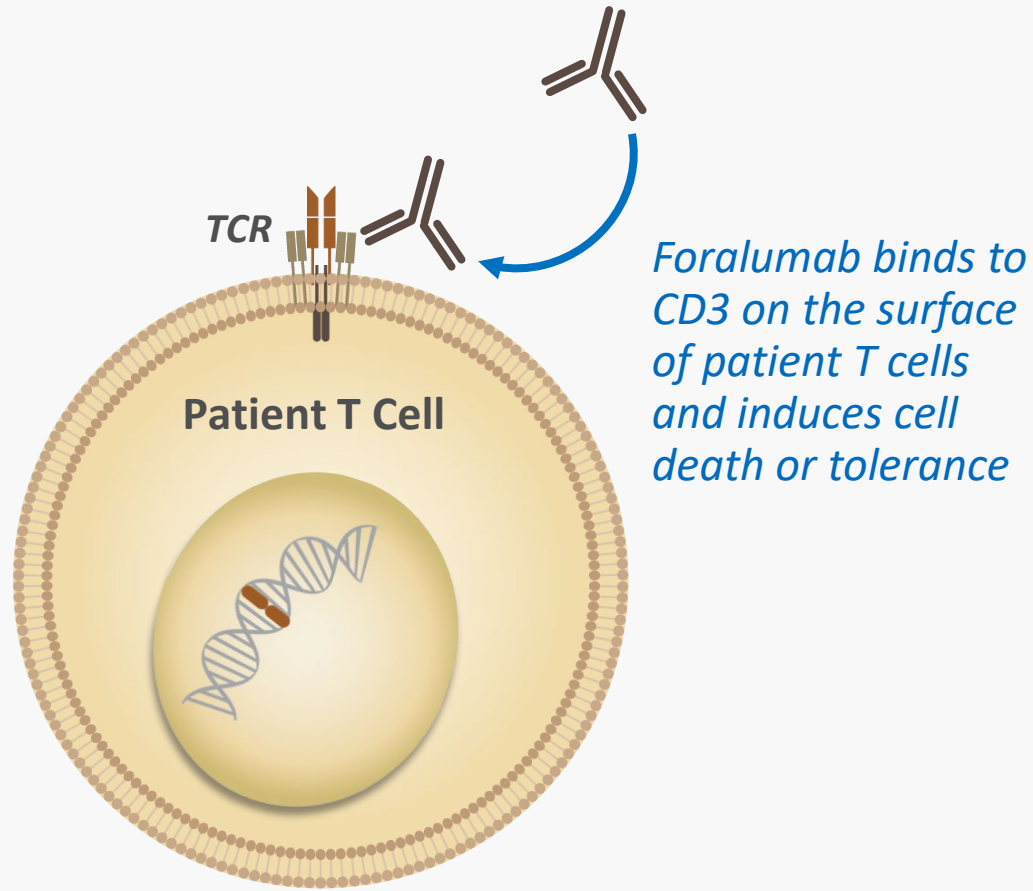


Rejection by NK cells

(n=3 mismatched donors, strong activation protocol)



Foralumab¹ is an Anti-CD3 Antibody for Selective Depletion of Patient T Cells



- Foralumab **may prevent CAR T cell rejection** by eliminating the anti-CAR T response
- **PBCAR T cells are resistant to foralumab** because foralumab cannot bind allogeneic CAR T cells when the TCR complex is deleted
- Foralumab **can be used in combination with any PBCAR therapy**
- Investigate foralumab in combination with **anti-CD19 CAR T; update IND in 2022**
- **Exclusive partnership** with Tiziana

1. Exclusive license agreement with Tiziana to evaluate foralumab with allogeneic CAR T candidates for cancer treatment

in vivo Application for Delivering on the Promise of Therapeutic Genome Editing

ARCUS® Genome Editing

Derived from natural homing
endonuclease for *ex vivo* and *in vivo*
applications



**Ex Vivo ARCUS Editing for
Allogeneic CAR T
Immunotherapy**
*Single Gene edit, donor derived
CAR T cells*



**In Vivo ARCUS Editing for
Genetic Diseases**
*Potentially curative,
one-time treatment*

Precision BioSciences *in vivo* Gene Editing Pipeline: Three INDs/CTAs in Next Three Years

Program	Indication	Tissue	Target	Delivery	Research	Candidate Selection	IND-Enabling	Expected IND/CTA	Partner
PBGENE-PCSK9 ¹	Familial Hypercholesterolemia	Liver	PCSK9	AAV				2022	
PBGENE-PH1	Primary Hyperoxaluria Type 1	Liver	HAO1	LNP				2023	
PBGENE-HBV	Chronic Hepatitis B	Liver	HBV	LNP				2024	
PBGENE-DMD	Duchenne Muscular Dystrophy	Muscle	DMD	AAV				--	<i>Lilly</i>
PBGENE-LLY2	Undisclosed	Liver	Undisclosed	Undisclosed				--	<i>Lilly</i>
PBGENE-LLY3	Undisclosed	CNS	Undisclosed	Undisclosed				--	<i>Lilly</i>

1. iECURE plans to develop PBGENE-PCSK9 through Phase 1 clinical trial. Precision retains rights to future development and commercialization of PBGENE-PCSK9.

Precision BioSciences: *in vivo* Gene Editing Strategy

Pipeline Validation & Expansion Creates Value

1

Clinical Validation

Knock-out Genes in Liver

AAV
LNP

PBGENE-PCSK9

PBGENE-PH1

PBGENE-HBV

IND/CTA
Submission

2022

2023

2024

2

Pipeline Expansion

Complex Edits &
Multiple Tissues

PBGENE-DMD
PBGENE-LLY2¹
PBGENE-LLY3¹

1. Precision has not disclosed the method of delivery or target for PBGENE-LLY2 and PBGENE-LLY3.

ARCUS for Familial Hypercholesterolemia (FH)

- One of the most common genetic diseases with pattern of severe hypercholesterolemia, cholesterol deposition and high risk of early onset coronary artery disease. Disorders all share decreased LDL clearance

Heterozygous FH (HeFH)

LDL-C >190mg/dl

1.3 – 1.5M in US

Family history of CAD, stroke

Homozygous FH (HoFH)

LDL-C >400mg/dl

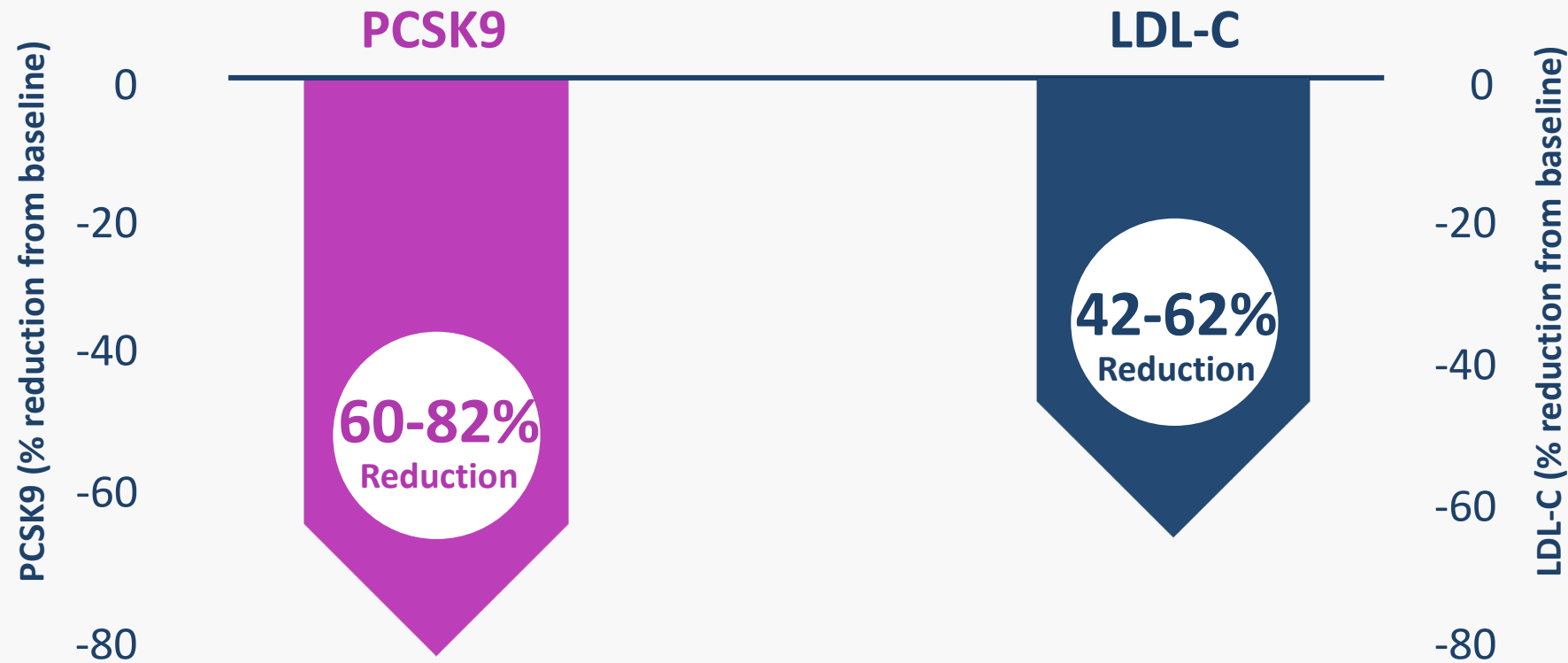
1,300 – 1,400 in US

Mortality common by 30 yrs

Goal of ARCUS Treatment:

Single treatment providing a stable and durable knock-out of PCSK9 and significant decrease in LDL-C for common, chronic, life-threatening condition

PBGENE-PCSK9: Single-Dose of AAV8-ARCUS Significantly Reduced Serum PCSK9 Levels & LDL-C Levels in NHPs for 3yr¹



1. Wang, et al. (2021) *Mol. Ther.* 29(6):2019-2029; M2PCSK9 dosed at 6e12 vg/kg

Overview of Primary Hyperoxaluria Type 1 (PH1)

- Rare genetic disease characterized by accumulation of calcium oxalate in kidneys, which leads to painful kidney stones and ultimately end-stage renal disease
- HAO1 encodes glycolate oxidase acts upstream of the formation of oxalate

40% of patients have
end-stage renal disease
at the time of diagnosis

Combined
liver-kidney
transplant often required



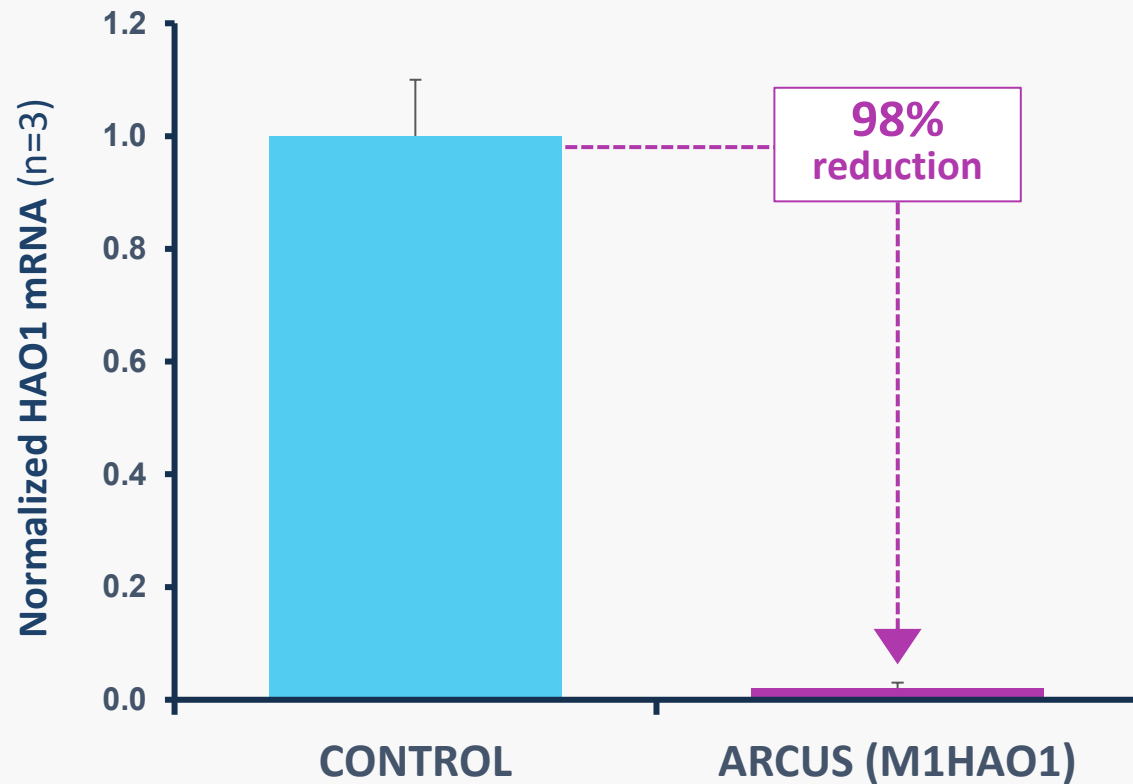
Affects adults
and young children



Prevalence of
1-3/1,000,000

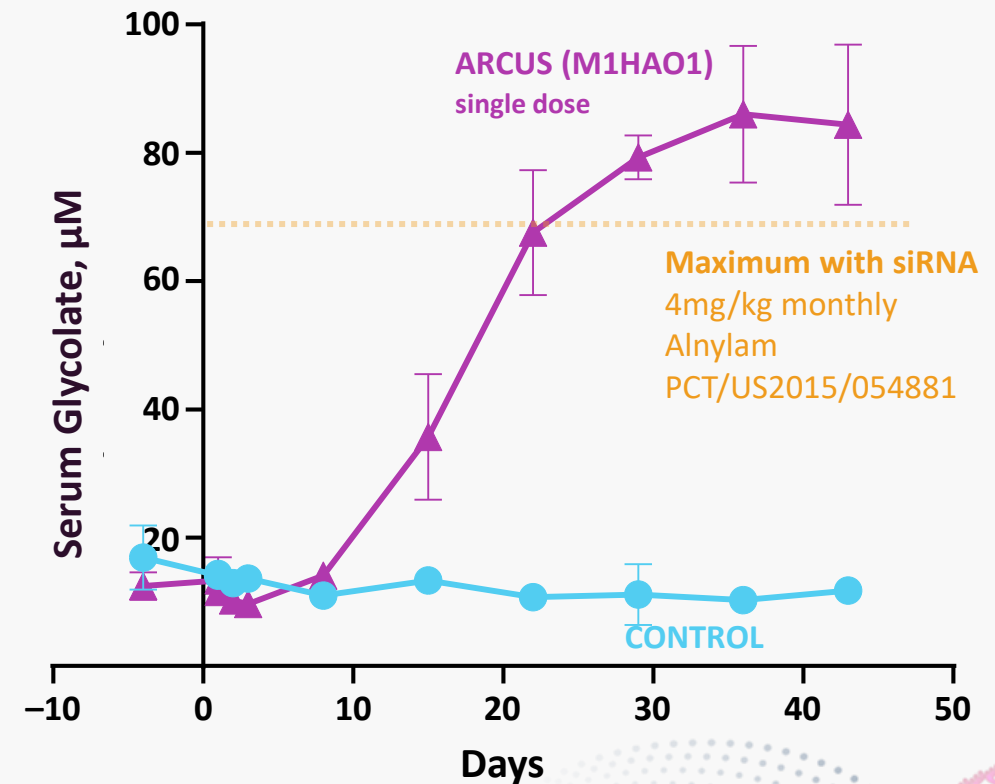
PBGENE-PH1 Decreased HAO1 mRNA by 98% and Increased Serum Glycolate in NHPs

ARCUS Reduced *HAO1* mRNA Levels



AAV Dose 3e13 vg/kg (n=3)

ARCUS Increased Serum Glycolate Levels



PBGENE-HBV Novel Approach to Chronic HBV (cHBV)

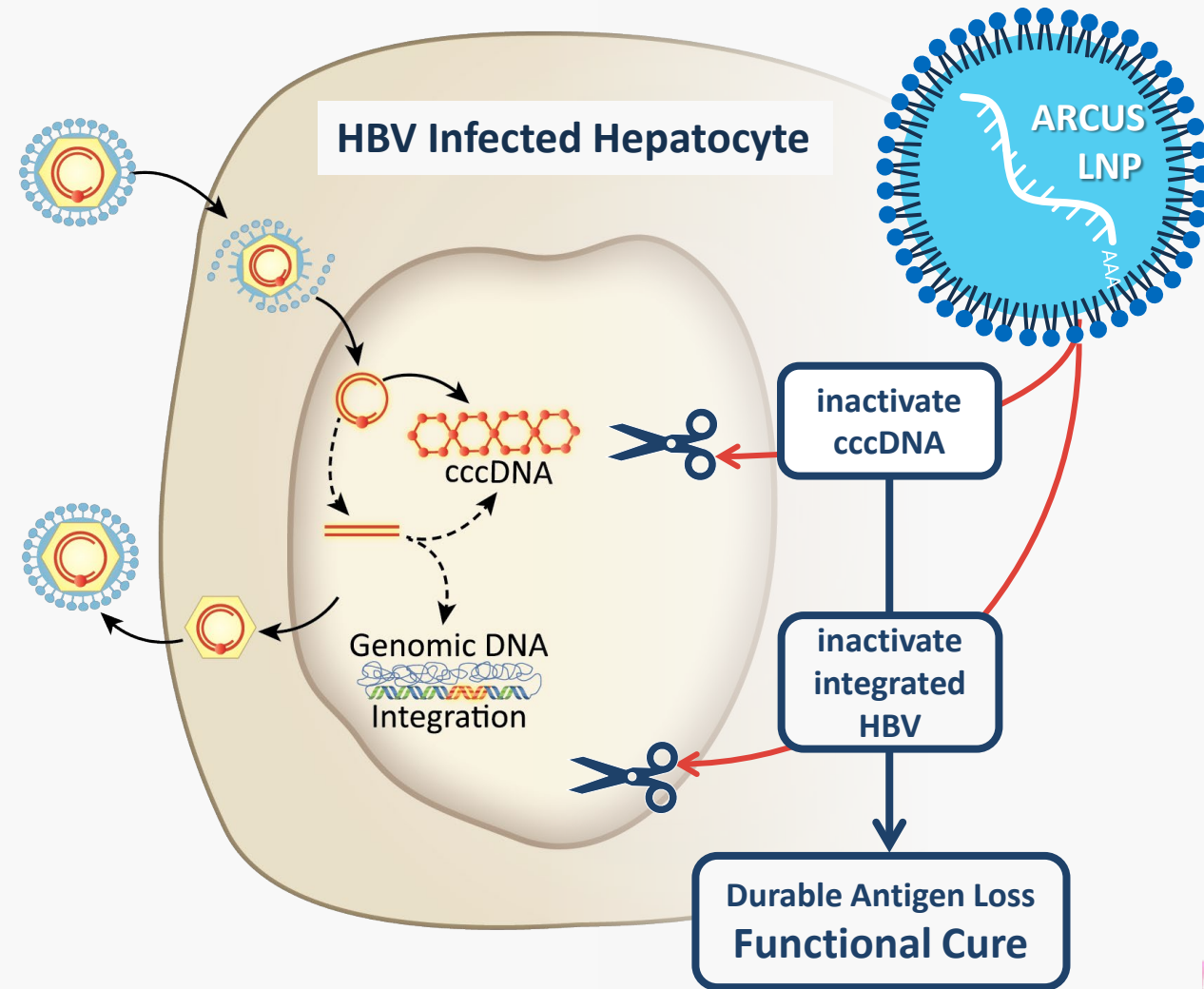
ARCUS-mediated **inactivation of cccDNA**
and **integrated HBV** could result in a
functional cure

Chronic HBV unmet need is massive

US >860,000 cHBV infections

Globally >200 million cHBV infections

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



Transformative Gene Editing Partnership for Precision



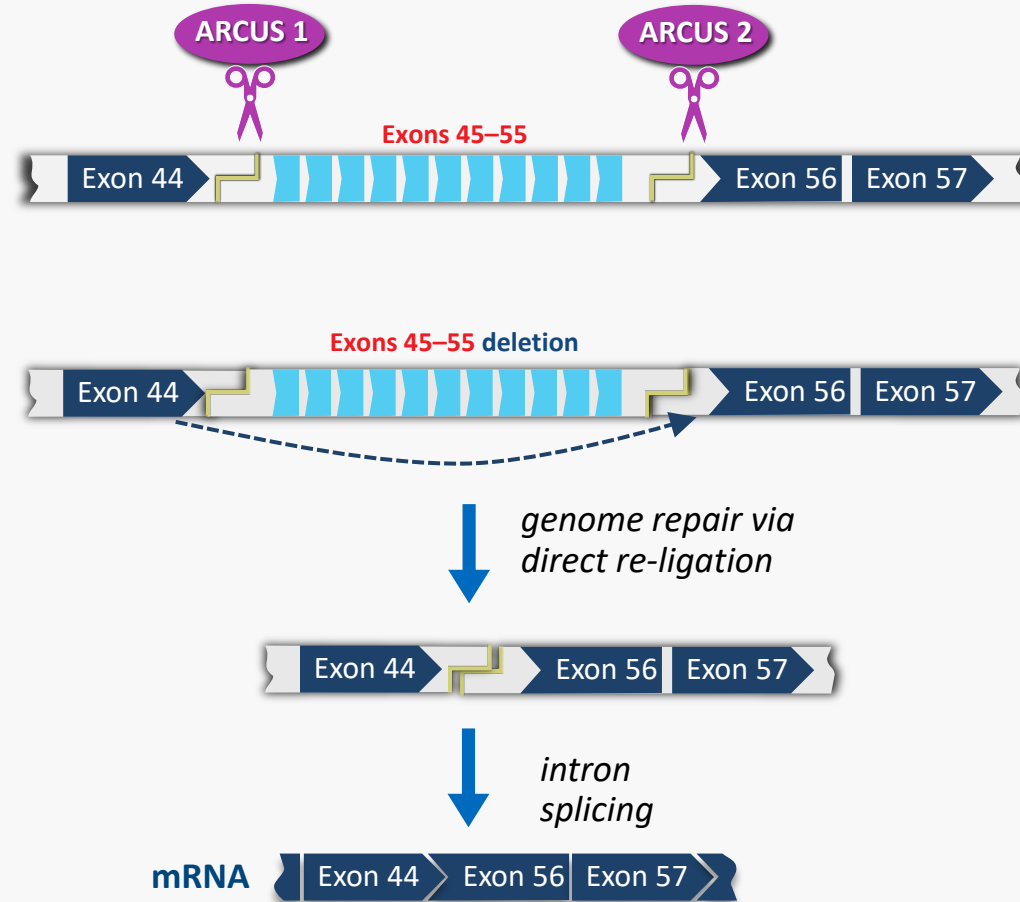
Research collaboration and license agreement aimed at treating challenging genetic diseases

- 3** Initial collaboration for 3 programs, including DMD
- +**
- 3** Lilly retains right to select up to 3 additional gene targets

- Precision:** Pre-IND R&D; **Lilly:** IND to commercial
- Upfront payment of **\$135 million including \$35 million equity stake**
- Up to \$420M per target** in development and commercialization milestones
- Mid-single digit to low-teens** tiered royalties

ARCUS for Therapeutic Treatment of DMD

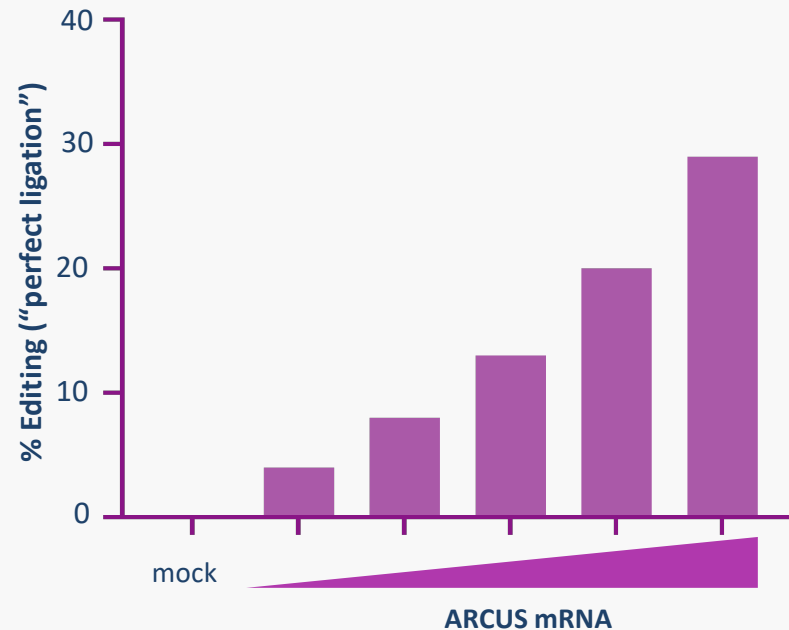
Goal: Restore dystrophin expression by deleting exons 45-55 using a pair of ARCUS nucleases intended to remove a mutation hotspot responsible for >50% of DMD



Dystrophin Gene Correction Observed in DMD Patient Myoblasts

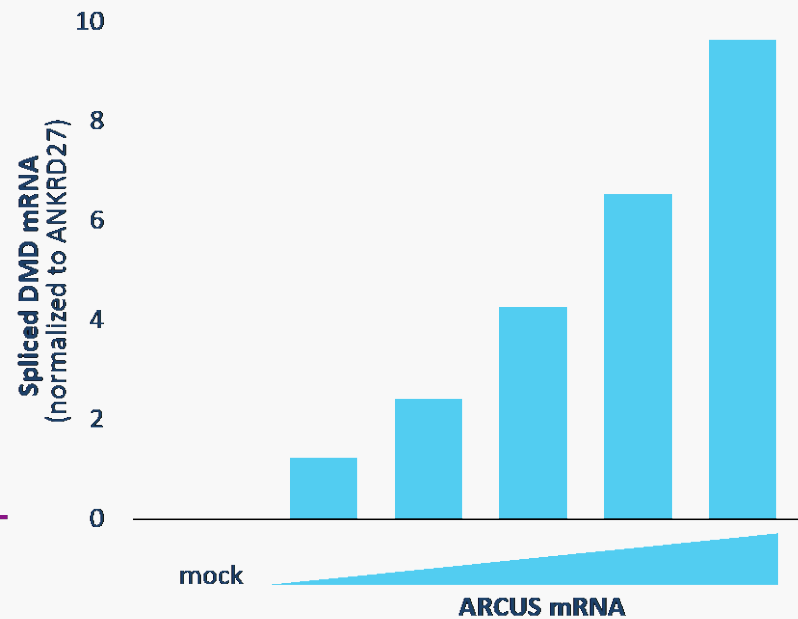
Corrected DNA

Exons 45-55 deleted



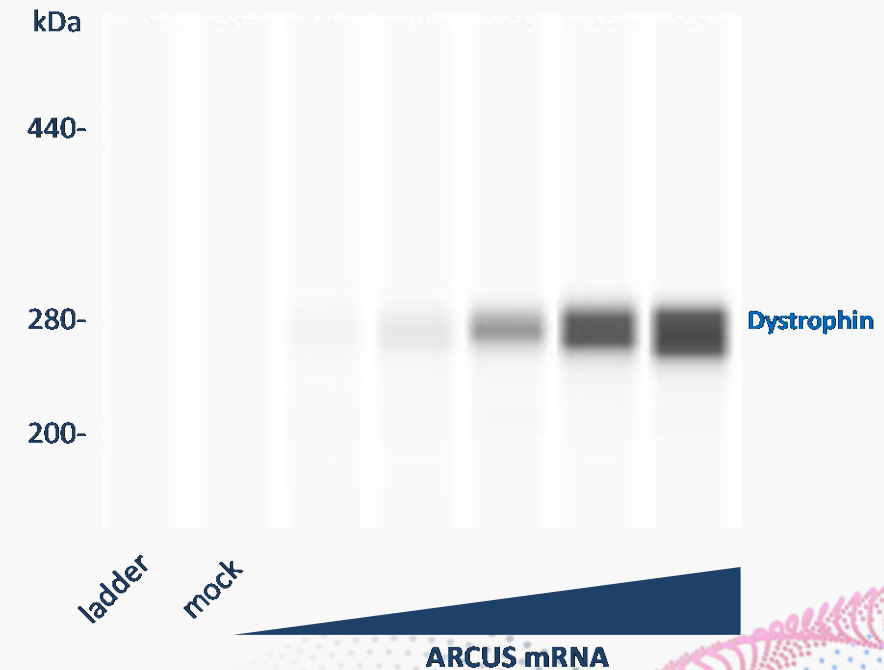
Corrected mRNA

Exon 44 spliced to Exon 56



Corrected Protein

Dystrophin protein expressed



Precision BioSciences Focused Execution in 2022 to Clinically Validate ARCUS

ex vivo CAR T Pipeline:

- PBCAR0191 with eLD: Potential first-in-class allogeneic CAR T – **update in mid-2022**
- PBCAR19B stealth cell: Potential best-in-class – **update in mid-2022**
- PBCAR269A combination with nirogacestat in Multiple Myeloma – **update in mid-2022**
- Develop CD19 combination with foralumab – **update IND in 2022**

in vivo Gene Editing Pipeline:

- Advance PBGENE-PCSK9 to IND/CTA **in 2022**
- Progress PBGENE-PH1 and PBGENE-HBV to enable IND/CTA **in 2023 & 2024**, respectively
- Progress PBGENE-DMD toward candidate selection

Overcome cancer.
Cure genetic disease.

