



# Pioneering and Delivering the Future of Genomic Medicines

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February 2023

## Forward-Looking Statements

This presentation contains forward-looking statements regarding our current expectations. These forward-looking statements include, without limitation, statements relating to the potential to develop, obtain regulatory approvals for and commercialize durable, safe and effective therapies to treat certain diseases and the timing, availability and costs of such therapies, the potential to use ZFP, ZFP-TR, CAR-Treg and other technologies to develop durable, safe and effective therapies, the potential for us to benefit and earn milestone and royalty payments from our collaborations and the timing of any such benefits and payments, our plans to halt our investment in, and seek a new partner for, our sickle cell disease program, our cell therapy strategy, including expansion to additional indications, plans and timing regarding our financial resources, including the sufficiency thereof and plans to reduce our operating expenses, anticipated plans and timelines for us and our collaborators to enroll patients in and conduct clinical trials, dose and screen patients, present clinical data and make regulatory submissions, the anticipated advancement of our product candidates to late-stage development, including potential future Phase 3 trials, execution of our corporate strategy, our pipeline, the identification of additional targets, and the advancement of preclinical programs to the clinic, key milestones and catalysts, and other statements that are not historical fact. These statements are not guarantees of future performance and are subject to certain risks and uncertainties that are difficult to predict. Our actual results may differ materially and adversely from those expressed. Factors that could cause actual results to differ include, without limitation, risks and uncertainties related to the effects of the evolving COVID-19 pandemic and the impacts of the pandemic and other macroeconomic factors, including as a result of the ongoing conflict between Russia and Ukraine, on the global business environment, healthcare systems and business and operations of us and our collaborators, including the initiation and operation of clinical trials; the research and development process; the uncertain timing and unpredictable results of clinical trials, including whether preliminary or initial clinical trial data will be representative of final clinical trial data and whether final clinical trial data will validate the safety, efficacy and durability of product candidates; the impacts of clinical trial delays, pauses and holds on clinical trial timelines and commercialization of product candidates; the unpredictable regulatory approval process for product candidates across multiple regulatory authorities; the manufacturing of products and product candidates; the commercialization of approved products; the potential for technological developments that obviate technologies used by us and our collaborators; the potential for us or our collaborators to breach or terminate collaboration agreements; the potential for us to fail to realize our expected benefits of our collaborations; and the uncertainty of our future capital requirements, financial performance and results. There can be no assurance that we and our collaborators will be able to develop commercially viable products. These risks and uncertainties are described more fully in our Annual Report on Form 10-K for the fiscal year ended December 31, 2022, as supplemented by our future reports filed with the Securities and Exchange Commission. Forward-looking statements contained in this presentation speak only as of the date hereof, and we undertake no duty to update such information except as required under applicable law. This presentation concerns investigational product candidates that are under preclinical and/or clinical investigation and which have not yet been approved for marketing by any regulatory agency. They are currently limited to investigational use, and no representations are made as to their safety or efficacy for the purposes for which they are being investigated. Any discussions of safety or efficacy are only in reference to the specific results presented here and may not be indicative of an ultimate finding of safety or efficacy by regulatory agencies.

**We are a genomic medicines company dedicated to translating ground-breaking science into medicines that transform the lives of patients and families afflicted with serious disease**



**Four Clinical-Stage Programs  
Advancing Towards Potential  
Commercialization**



**Advanced Research and  
Scientific Platform  
Fueling Value Creation**



**In-House  
Manufacturing Provides  
Flexibility and Control**

# Sangamo in 2023: Value Thesis

## ① First wave of value-driving programs advancing to/through late-stage development

- Compelling proof-of-concept data supporting future pivotal development.
- **Fabry disease:** Ph I/2 results support potential best-in-class product profile. Phase 3 start expected by YE2023 following regulatory guidance.
- **Hemophilia A (with Pfizer):** pivotal data readout expected 1H 2024. BLA submission anticipated 2H 2024, generating potential milestones and, if approved, royalties.

## ② Second wave of potentially transformative autoimmune and neurology programs advancing into the clinic

### Pioneer in CAR-Tregs

- We believe we are the first company to dose patients with engineered CAR-Tregs.
- TX200 renal transplant Ph I/2 study progresses, with possible acceleration to prove biology and platform value.
- Disciplined progress of pre-clinical candidates in MS and IBD. First IND submission expected 2024.

### Genome Engineering in the CNS

- Portfolio of pre-clinical wholly owned and partnered programs advancing.
- Second of four wholly-owned programs expected to be disclosed Q2 2023. IND submission expected 2024 based on advances in delivery.
- Investments partially offset by partner programs.

## ③ Powerful research platform continually innovates to support value creation, including in delivery



## ④ In-house cGMP manufacturing facilities provide control over quality, supply, timelines and cost



## ⑤ Demonstrated track record of partnerships results in non dilutive funding, expands the portfolio, provides access to domain expertise and offsets cost

# Demonstrated progress across wholly owned and partnered programs

## Wholly Owned Programs

INDICATION	TECHNOLOGY	PRECLINICAL	PHASE 1/2	PIVOTAL
<b>Fabry Disease</b> (Israltagene civalparovec)	Gene Therapy	Clinical data presented Feb 2022. Phase 3 expected to begin in 2023.		
<b>Sickle Cell Disease</b> (BIVV003)	Cell Therapy	Seeking partner to advance.		
<b>Renal Transplant</b> (TX200; Auto)	T <sub>REG</sub> Cell Therapy	First two patients dosed.		
<b>Renal Transplant</b> (Allogeneic)	T <sub>REG</sub> Cell Therapy			
<b>Inflammatory Bowel Disease</b>	T <sub>REG</sub> Cell Therapy			
<b>Multiple Sclerosis</b>	T <sub>REG</sub> Cell Therapy			
<b>Prion</b>	ZF Genome Engineering			
<b>Neurology</b> (3 Undisclosed)	ZF Genome Engineering			

## Partnered Programs

INDICATION	TECHNOLOGY	PRECLINICAL	PHASE 1/2	PIVOTAL
<b>Hemophilia A</b> (Giroctogene fitelparvovec)	Gene Therapy			
<b>Oncology</b> (Kite-037)	Cell Therapy			
<b>Oncology</b> (Undisclosed)	Cell Therapy			
<b>Neurodevelopmental Disorders</b>	ZF Genome Engineering			
<b>ALS/FTD</b>	ZF Genome Engineering			
<b>Huntington's Disease</b>	ZF Genome Engineering			
<b>a-Synuclein</b> (ST-502)	ZF Genome Engineering			
<b>Tauopathies</b> (ST-501)	ZF Genome Engineering			
<b>Neurology</b> (DMI)	ZF Genome Engineering			
<b>Neurology</b> (1 Undisclosed)	ZF Genome Engineering			

WAVE ONE

WAVE TWO

## Recent business updates

### Fabry Disease

- Compelling Phase I/2 data update being presented at *WORLD Symposium* showed extended benefit on ERT withdrawal,  $\alpha$ -Gal A levels, kidney biopsy data and SF-36 health scores.
- First available kidney biopsy data showed 78% Gb3 substrate clearance at 6-months.
- Phase 3 planning, with US and EU strategies, progressing.

### Hemophilia A

- Patient dosing resumed November 2022.
- Dosing to support Phase 3 primary analysis largely complete.
- Pfizer announced at Q4 earnings that this remains one of their most promising assets.

### CAR-Treg Immune Regulation

- TX200 in renal transplant continues to be generally well tolerated in both patients dosed.
- Manufactured dose for the final patient in the first cohort. Dosing expected early 2Q23.
- Opportunities to accelerate dose escalation timelines are being explored with regulators.

### Sickle Cell Disease

- Presented promising data from Phase I/2 PRECIZN-I study at ASH in December.
- Believe the product is competitive with new manufacturing process, but we are not taking this program forward.
- Seeking a potential partner who would be able to progress this promising asset to Phase 3.

### Financial Results

- As of December 31, 2022 we had approximately \$308M in cash, cash equivalents and marketable securities.



# Looking Ahead: Anticipated Milestones



## Fabry Disease

- Conclude dosing in Phase I/2 expansion by end of 2023 (not expected to be a gating factor to Ph3).
- Commence Phase 3 trial by YE2023.



## Hemophilia A

- Dosing to support primary analysis expected to be complete in Q1 2023.
- Pivotal data readout estimated in 1H 2024. BLA submission in 2H 2024.



## CAR-Treg in Immune Regulation

- Complete Cohort 1 dosing in renal transplant in early Q2 2023.
- Initiate Cohort 2 dosing during summer 2023 with potential for dose escalation acceleration.
- Complete *in vivo* studies in MS and Inflammatory Bowel Disease.



## Wave Two Pipeline

- Targets and data from next wholly owned CNS genome engineering program to be revealed in 2023.
- Two new IND submissions in 2024 (CAR-Treg and CNS).

## Our current financial resources are focused on pipeline progression and value creation

### Key Financial Metrics

**\$~308m**

Cash and Marketable  
Securities Balance  
as of 12/31/22

**\$815m**

Cash Received from  
Partners to date

**\$6.7bn**

In Potential  
Milestones

**Additional  
Potential  
Royalties**

### Q4 2022 Financial Performance / Financial Guidance for 2023

**\$27.2m**

Revenues -  
Q4 2022

**\$74.3m**

Non-GAAP OpEx\* -  
Q4 2022

**\$275 – \$295m**

Non-GAAP OpEx Guidance\*\* -  
FY 2023

**Our resources are tightly allocated in line with our business priorities**

\* GAAP total operating expenses were \$82.6 million for Q4 2022, compared to \$67.9 million for Q4 2021 and included stock-based compensation expense (“SBC”) of \$8.3 million and \$8.1 million, respectively.

\*\* On a GAAP basis we expect our 2023 operating expenses to be in the range of \$310 - \$330 million including anticipated SBC of approximately \$35 million.



# 1. Wave One Clinical Programs

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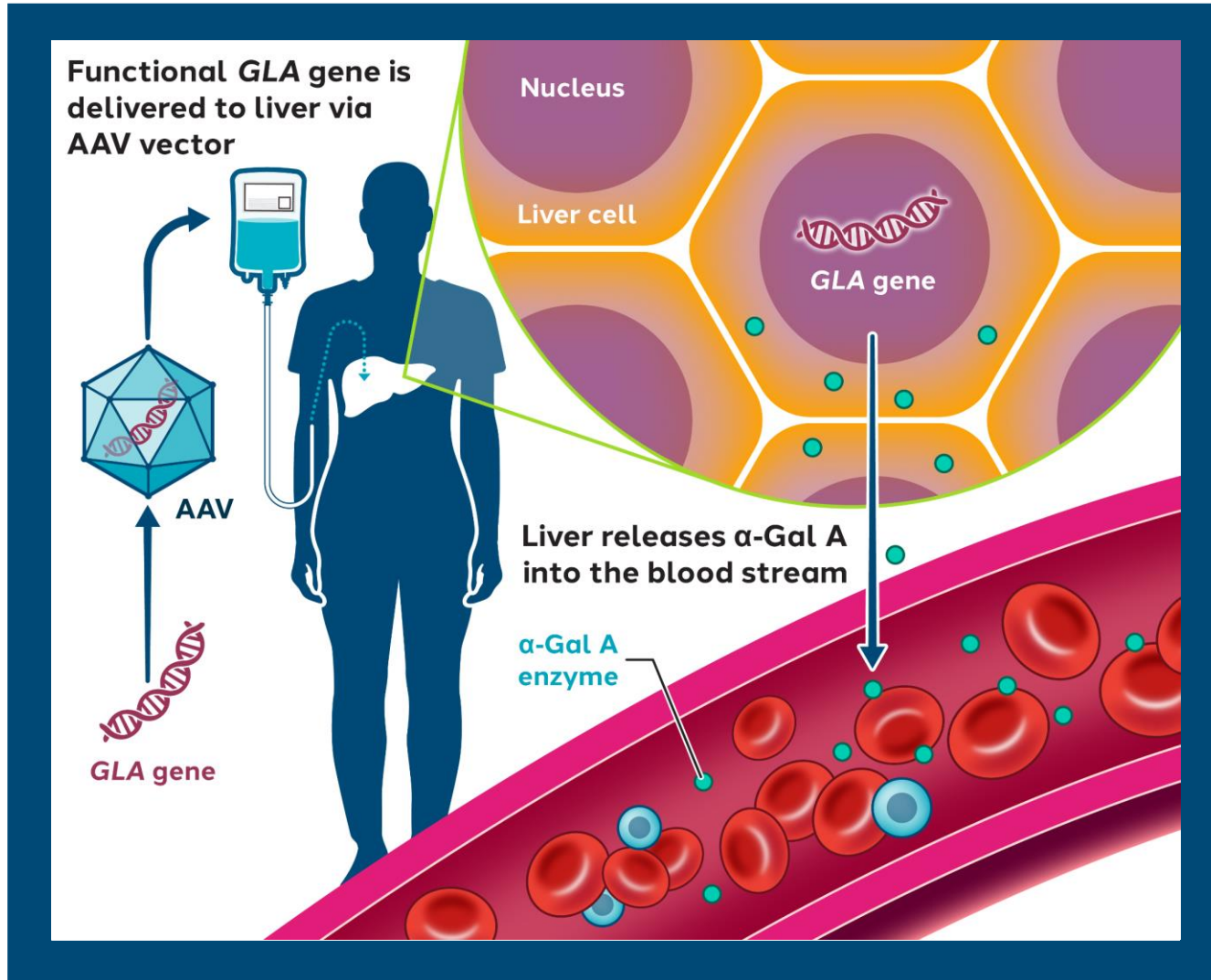
Portfolio of Late- and Near Late-Stage Assets with Compelling Proof-of-Concept Clinical Data and Clinical Execution

- Fabry Disease
- Hemophilia A
- Sickle Cell Disease



## Fabry Disease (isargalgene civaparvovec or ST-920)

# Isargagene civaparvovec (ST-920): one-time, liver-directed gene therapy candidate for the treatment of Fabry disease currently in Phase 1/2



## The patient promise: our goals for ST-920

- Safe, one-time administration
- Full physiologic enzyme replacement
- Eliminate ERT infusions
- Durable efficacy
- Low immunogenicity
- No prophylaxis with steroids or other immunomodulating agents

# Isargagene civaparvovec (ST-920) in Fabry disease at WORLDSymposium 2023

## Evidence of clinical effect in Fabry disease

- Sustained expression of  **$\alpha$ -Galactosidase A** ( $\alpha$ -Gal A) activity in **13 patients for over 2 years** for the longest treated patient.
- Clearance or stabilization of **renal Gb3 inclusions** along with reductions in **urine podocyte loss** suggests a favorable impact on progression of Fabry nephropathy and tissue absorption.
- All participants in the Dose Escalation phase who commenced the study on ERT have been **successfully withdrawn**.
- 40-65% plasma **Lyso-Gb3 reduction** in naïve/pseudo-naïve participants with high plasma Lyso-Gb3.
- Clinically meaningful and statistically significant increase in **SF-36 mean general health scores**.

## Favorable safety profile to date

- Generally **well tolerated** at all dose levels ( $0.5 \times 10^{13}$  -  $5 \times 10^{13}$  vg/kg).
- **No requirement for prophylactic corticosteroids** or other immune modulating agents.

## Phase 3 planning actively progresses

- Preparations for a potential Phase 3 trial actively progressing, with a **trial start anticipated by the end of 2023**. Not expected to be gated by completion of Ph I/2 expansion phase.
- We expect dosing of the Phase I/2 expansion phase to **conclude by the end of 2023**.

## ST-920 is generally well tolerated with a favorable safety profile: Overall summary of treatment-emergent AEs

Ph 1/2 STAAR data, WORLDSymposium, February 2023. Cut-off Oct 20, 2022.

	Dose Escalation Cohorts								Expansion Groups 5 × 10 <sup>13</sup> vg/kg N = 4		Total  N = 13	
	Cohort 1 0.5 × 10 <sup>13</sup> vg/kg N = 2		Cohort 2 1 × 10 <sup>13</sup> vg/kg N = 2		Cohort 3 3 × 10 <sup>13</sup> vg/kg N = 3		Cohort 4 5 × 10 <sup>13</sup> vg/kg N = 2					
	N	Events	N	Events	N	Events	N	Events	N	Events	N (%)	Events
Adverse Events	2	30	2	20	3	29	2	10	4	18	13 (100%)	107
Treatment Related Adverse Events	1	3	2	3	1	6	2	6	4	12	10 (77%)	30
Serious Adverse Events (Unrelated)	0	0	0	0	1	1	0	0	0	0	1 (7.7%)	1

### Most Common Treatment Related Adverse Events (All Grade 1 or Grade 2)

- Pyrexia, headache, chills
- Fabry disease (increased pain)

### Serious Adverse Events (Unrelated)

- Unrelated Sepsis (Cohort 3, 1 participant)

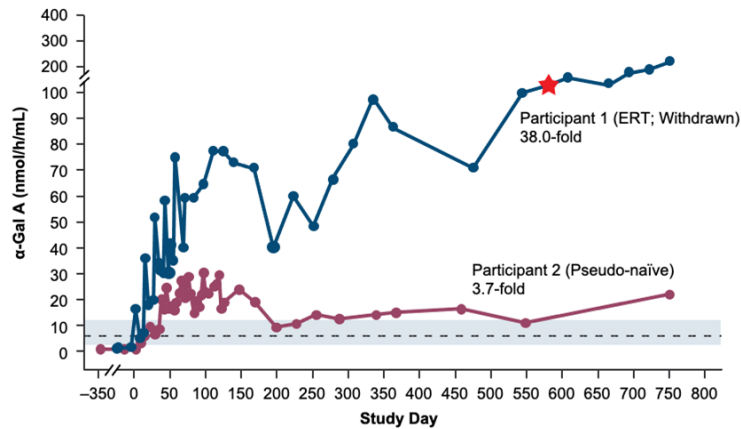
### No Treatment Related Adverse Events greater than a Grade 2 as of the cut-off date

- **Hepatic Enzymes**  
No administration of corticosteroids for transaminase elevations
- **Platelets**  
No clinically significant decreases in platelets observed
- **Cardiac Events**  
Not observed
- **Allergic reaction**  
One expansion phase participant experienced a Grade 1 allergic reaction treated with diphenhydramine

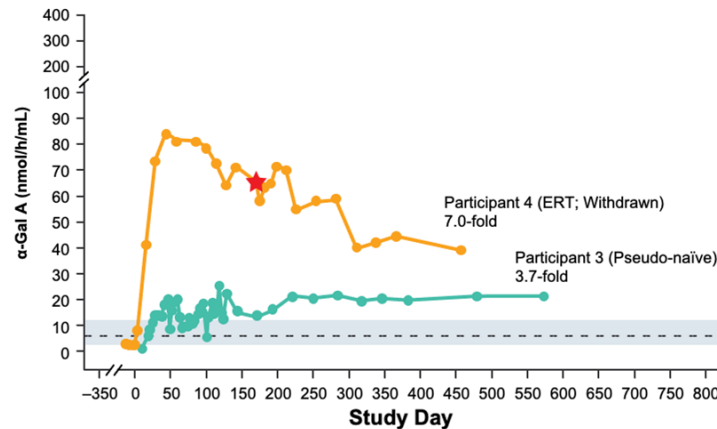
# Rapid, predictable and stable expression of $\alpha$ -Gal A activity occurred in all Dose Escalation cohorts

Ph 1/2 STAAR data, WORLDSymposium, February 2023. Cut-off Nov 15, 2022.

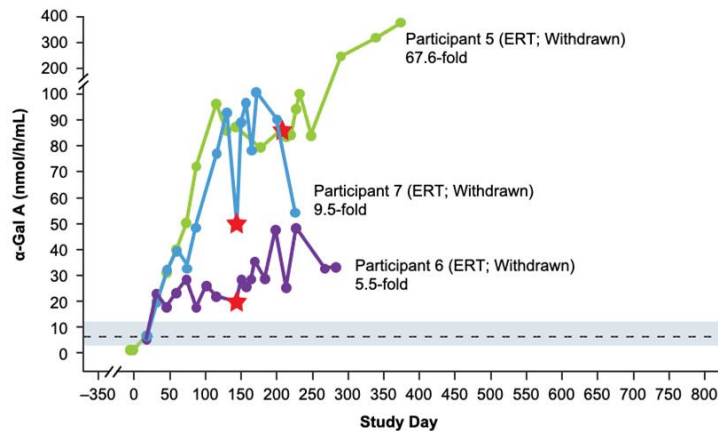
## Cohort 1: $0.5 \times 10^{13}$ vg/kg, N = 2



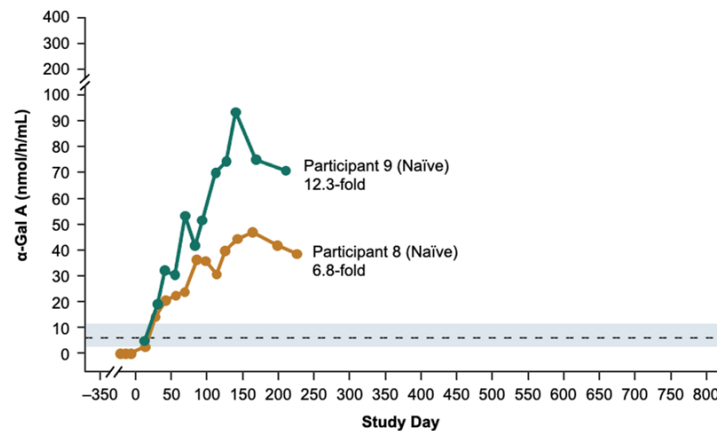
## Cohort 2: $1 \times 10^{13}$ vg/kg, N = 2



## Cohort 3: $3 \times 10^{13}$ vg/kg, N = 3



## Cohort 4: $5 \times 10^{13}$ vg/kg, N = 2

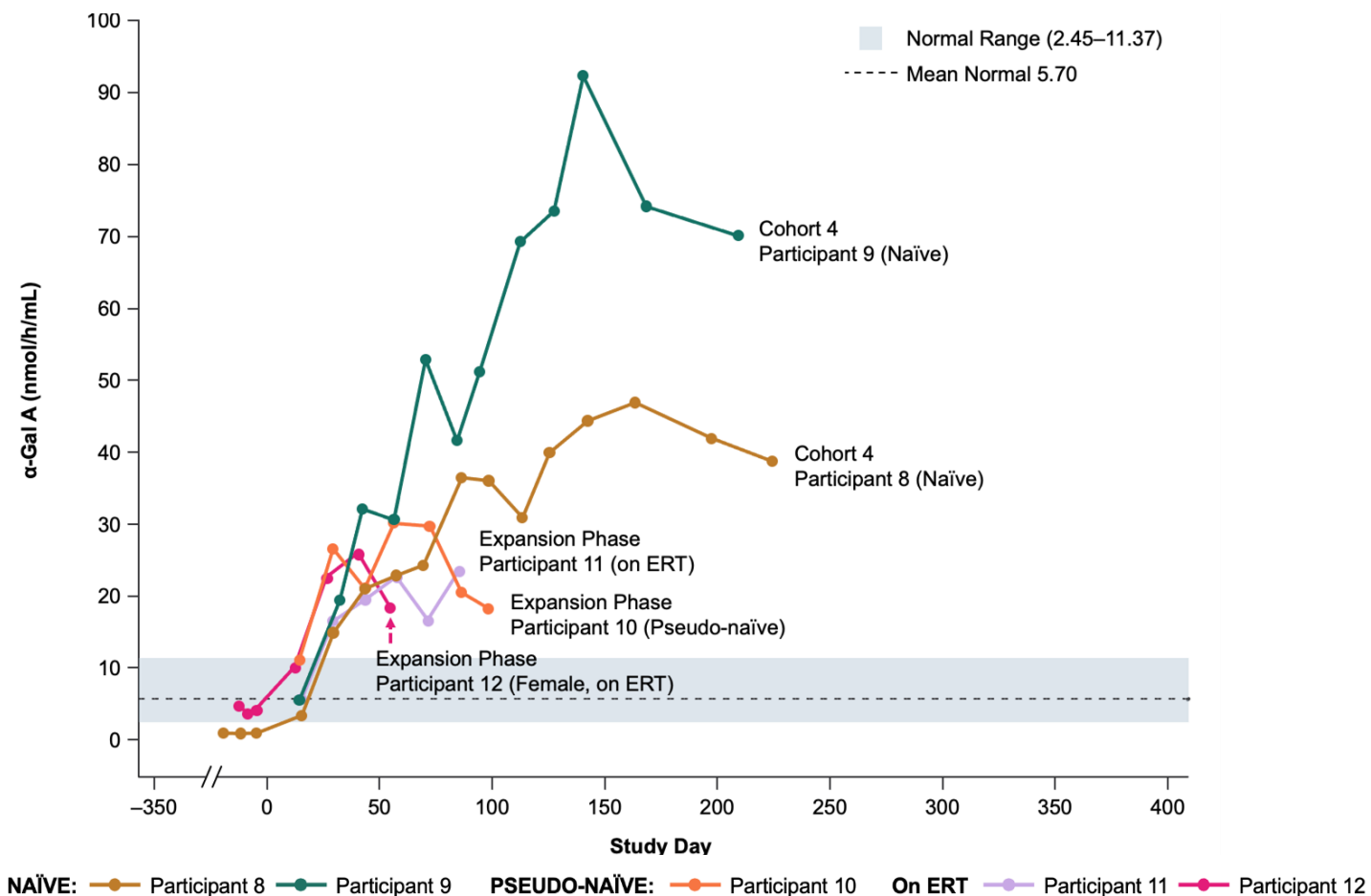


■ Normal range (2.45 - 11.37)    - - - Mean Normal 5.70    ★ ERT Withdrawal

- Rapid and predictable increase in  $\alpha$ -Gal A activity observed in all participants 4-8 weeks after dosing
- Supraphysiological  $\alpha$ -Gal A activity maintained in all participants
- ERT withdrawal completed for all 5 participants – with continued supraphysiological activity following withdrawal
- ST-920 expression observed was durable, with  $\alpha$ -Gal A activity at supraphysiological levels maintained in all participants, up to 2+ years

# The proposed Phase 3 clinical trial dose ( $5 \times 10^{13}$ vg/kg) produced rapid, sustained increases in $\alpha$ -Gal A activity in Dose Escalation (Cohort 4) and Expansion Phase participants

Ph 1/2 STAAR data, WORLDSymposium, February 2023. Cut-off Nov 15, 2022.

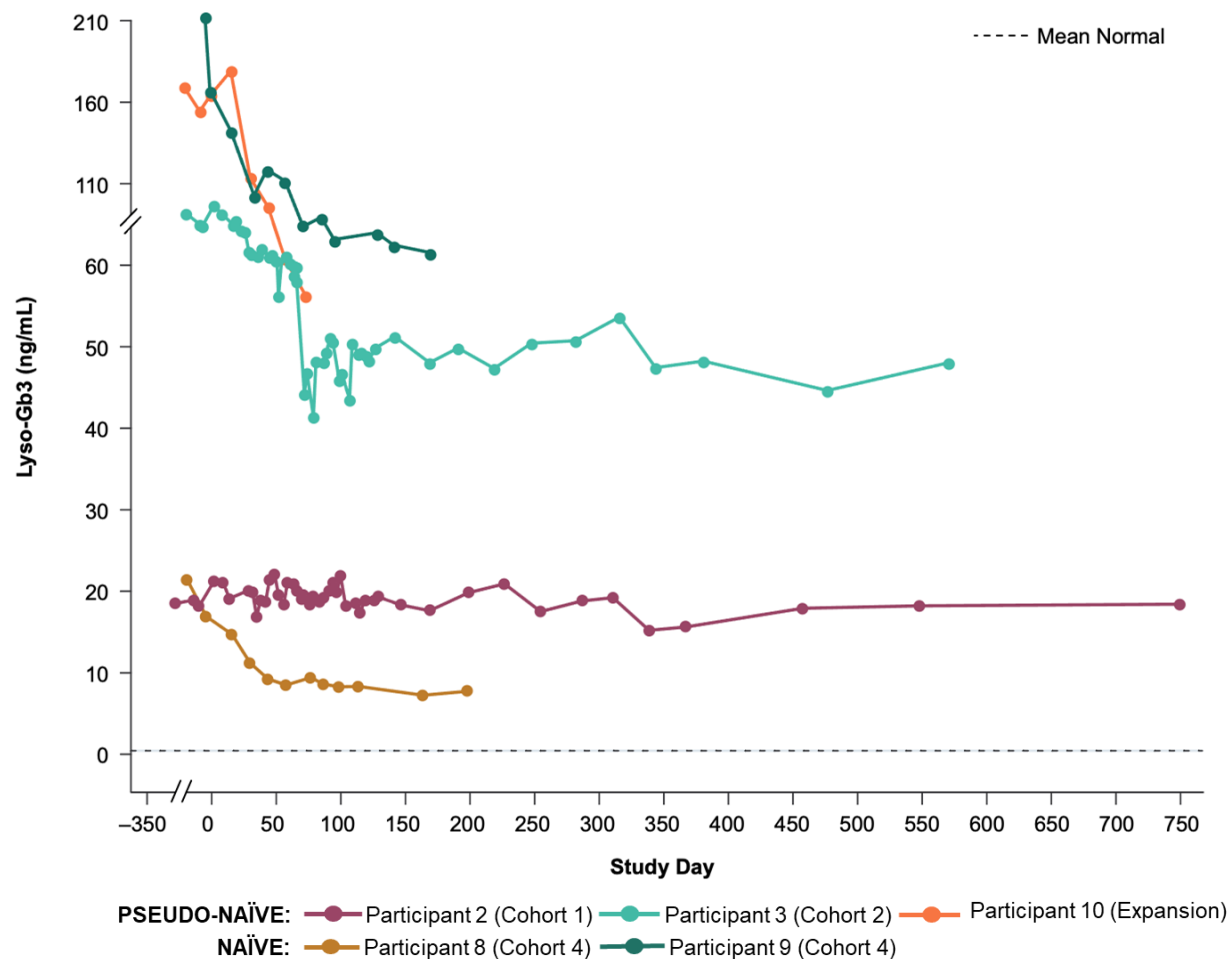


- The highest dose ( $5 \times 10^{13}$  vg/kg) produced rapid, predictable and durable increases in plasma  $\alpha$ -Gal A activity across all participants as of the data cut-off
- The female participant has demonstrated a similar response profile to males as of the data cut-off



# ST-920 effectively lowered plasma Lyso-Gb3 in naïve and pseudo-naïve participants across Dose Escalation and Expansion Phases

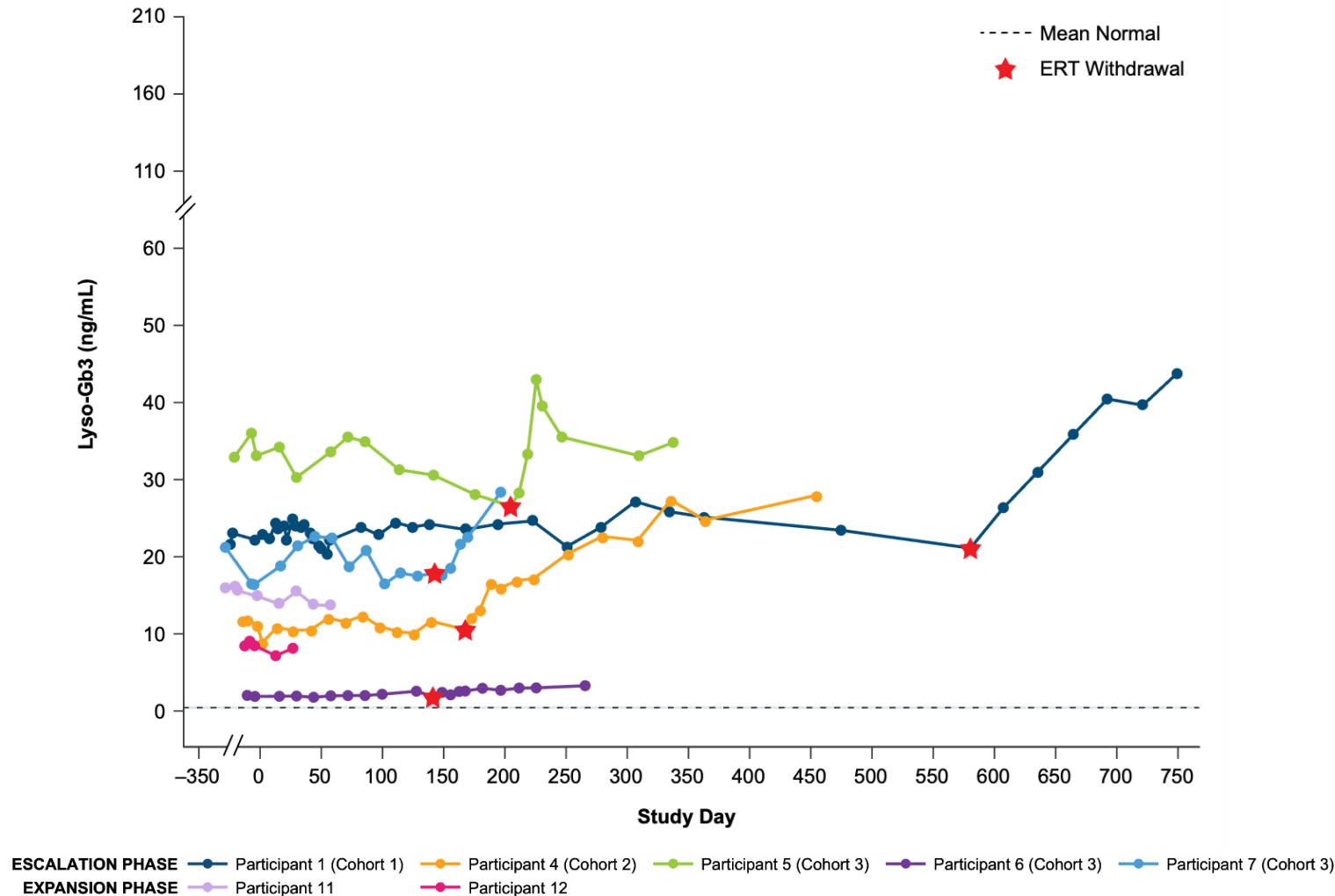
Ph 1/2 STAAR data, WORLDSymposium, February 2023. Cut-off Oct 20, 2022.



- Where baseline levels of Lyso-Gb3 started high (>80 ng/mL), participants experienced a 40% to 65% reduction in plasma levels
- For the first time, at the high dose, we observed a further reduction (54%) in Lyso-Gb3 where baseline plasma levels started lower (<25 ng/mL)
- Plasma Lyso-Gb3 continued to decrease in two participants
- Plasma Lyso-Gb3 levels were stable up to 25 months

# Plasma Lyso-Gb3 in ERT-treated dose escalation and expansion phase participants

Ph 1/2 STAAR data, WORLDSymposium, February 2023. Cut-off Oct 20, 2022.



Participant 13: Week 2 34.5 ng/mL Lyso-Gb3 normal range determined in healthy males and females. Normal range for males and females combined 0.32 to 0.63 ng/mL Long Term Follow-up Data: Data points > Study Day 365. Lyso-Gb3, globotriaosylsphingosine; ERT, enzyme replacement therapy.

## Dose Escalation Phase

- ERT withdrawal was successful in all ERT-treated participants
- Lyso-Gb3 levels following ERT withdrawal remained within the range of levels and variability normally observed in participants treated with ERT<sup>1, 2, 3</sup>
- In these participants,  $\alpha$ -Gal A activity remained elevated, and no participant has experienced symptoms requiring the resumption of ERT

## Expansion Phase

- At this data cut, ERT withdrawal had not yet been initiated for any participant

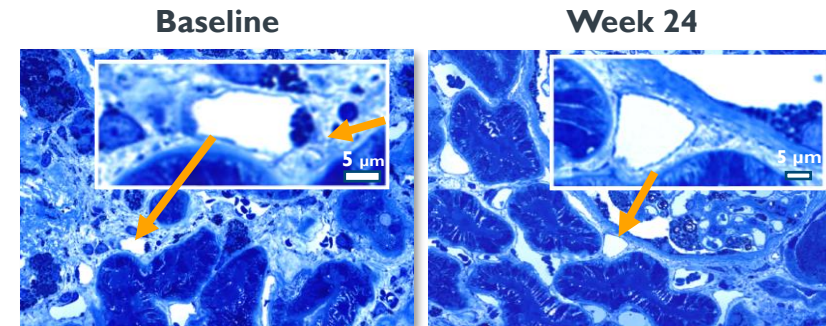
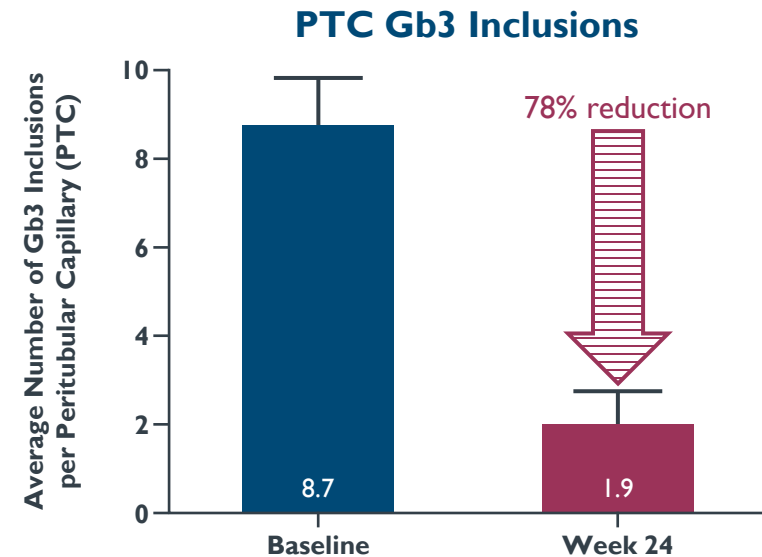
1. Arends, M., M et al. 2018. *J Med Genet*, 55: 351-58.
2. Nowak, A., F. et al. 2022. *J Med Genet*, 59: 287-93.
3. Kramer, J., M. et al. 2018. *Nephrol Dial Transplant*, 33: 1362-72.

# Participant 9: biomarkers of nephropathy significantly improved.

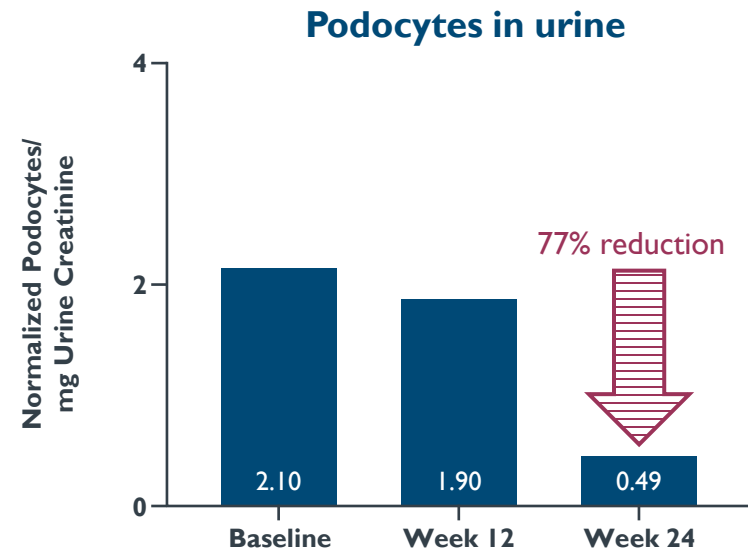
## Reduced renal Gb3 inclusions and podocytyuria

Cohort 4 ( $5 \times 10^{13}$  vg/kg) - high number of Gb3 inclusions and lyso-Gb3 at baseline

Ph 1/2 STAAR data, WORLDSymposium, February 2023. Cut-off Oct 20, 2022.



Representative PTC Images



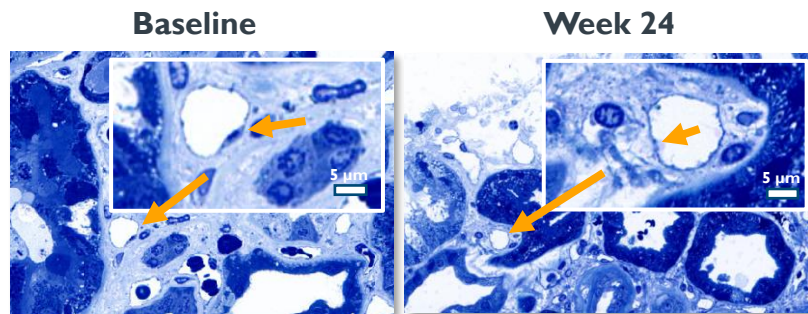
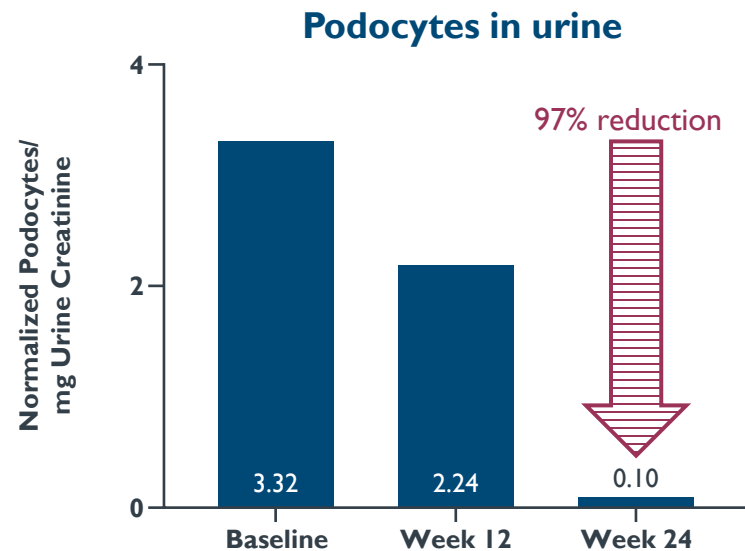
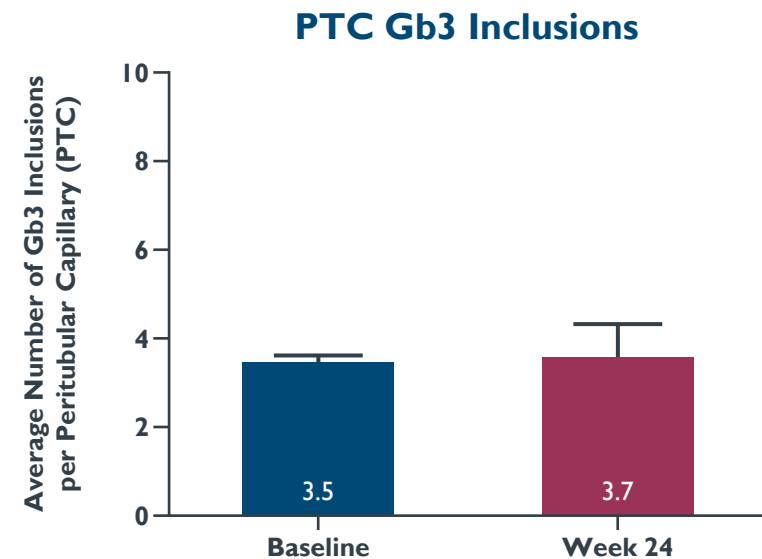
	Baseline	Week 24	Change
Plasma α-Gal A activity (nmol/h/mL)	Below LOQ	74.2	13 × Mean Normal
Plasma lyso-Gb3 (ng/mL)	167	66.8	60% ↓

- ST-920 cleared 78% of Gb3 inclusions from peritubular capillaries
- ST-920 also reduced urinary podocyte loss by 77%
- This participant exhibited significant increase in  $\alpha$ -Gal A activity and reduction in lyso-Gb3 after dosing with ST-920
- The significant decrease in renal Gb3 inclusions and the reduction in urine podocyte loss support a potential favorable impact on progression of Fabry nephropathy

# Participant 8: stable renal Gb3 inclusions and reduced podocytyria

Cohort 4 ( $5 \times 10^{13}$  vg/kg) - lower number of Gb3 inclusions and lyso-Gb3 at baseline

Ph 1/2 STAAR data, WORLDSymposium, February 2023. Cut-off Oct 20, 2022.



**Representative PTC Images**

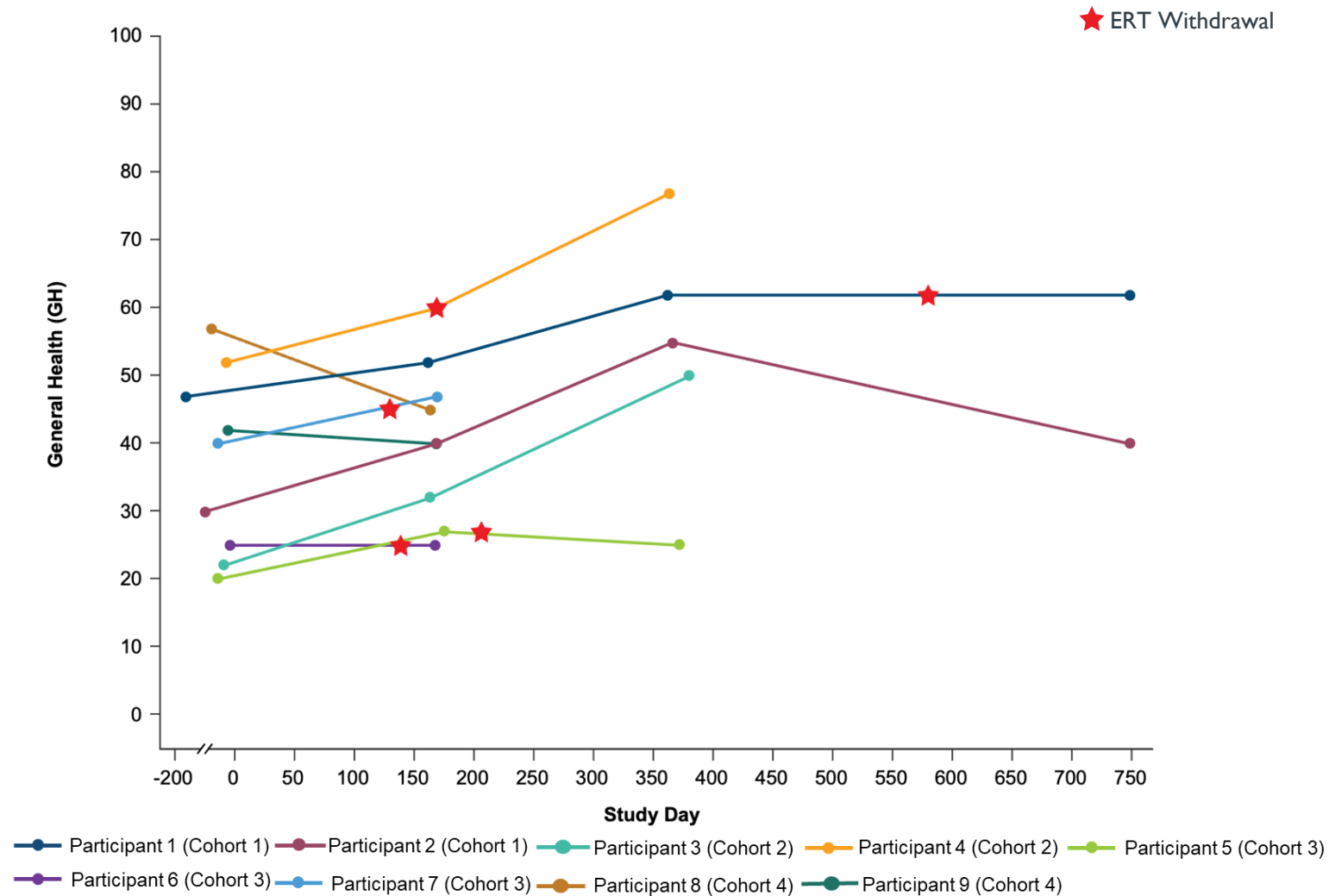
	Baseline	Week 24	Change
Plasma $\alpha$ -Gal A activity (nmol/h/mL)	0.96	46.89	8 $\times$ mean normal
Plasma lyso-Gb3 (ng/mL)	16.9	7.24	57% $\downarrow$

- Peritubular capillary (PTC) renal Gb3 inclusions were stable in this participant
- ST-920 reduced urinary podocyte loss by 97%
- This participant exhibited significant increases in  $\alpha$ -Gal A activity and reductions in lyso-Gb3 after dosing with ST-920
- These data provide additional evidence of a potentially favorable effect on Fabry nephropathy

In this participant chronic kidney disease may be multifactorial with possible contributions from hypertension and type 2 diabetes

## Dose escalation phase: clinically meaningful and statistically significant increase in mean SF-36 general health scores

Ph 1/2 STAAR data, WORLDSymposium, February 2023. Cut-off Oct 20, 2022.



## General Health Score Dose Escalation Phase

Study Week	Change from Baseline Mean $\pm$ SE, 95% CL
Baseline	- - -
Week 24 (n=8)	2.9 $\pm$ 2.57 [-3.2, 8.9] p=0.2996
Week 52 (n = 5)	19.6 $\pm$ 4.26 [7.8, 31.4] p=0.010

Reference: ADQS, Listing 16.2.14, Table 14.3.4.5a  
Data points from the LTFU (Day 750) are not included  
CL: Confidence limit; SE, standard error

- Change from baseline at Week 52 is statistically significant with mean=19.6, 95% CL: [7.8, 31.4], p=0.010 (paired t-test)
- A 3-to-5-point change on any SF-36 score is the minimally clinically important difference (MCID)<sup>1</sup>

I. Arends, M., C. E. Hollak, and M. Biegstraaten. 2015. *Orphanet J Rare Dis*, 10: 77.

# Hemophilia A (giroctocogene fitelparvovec)

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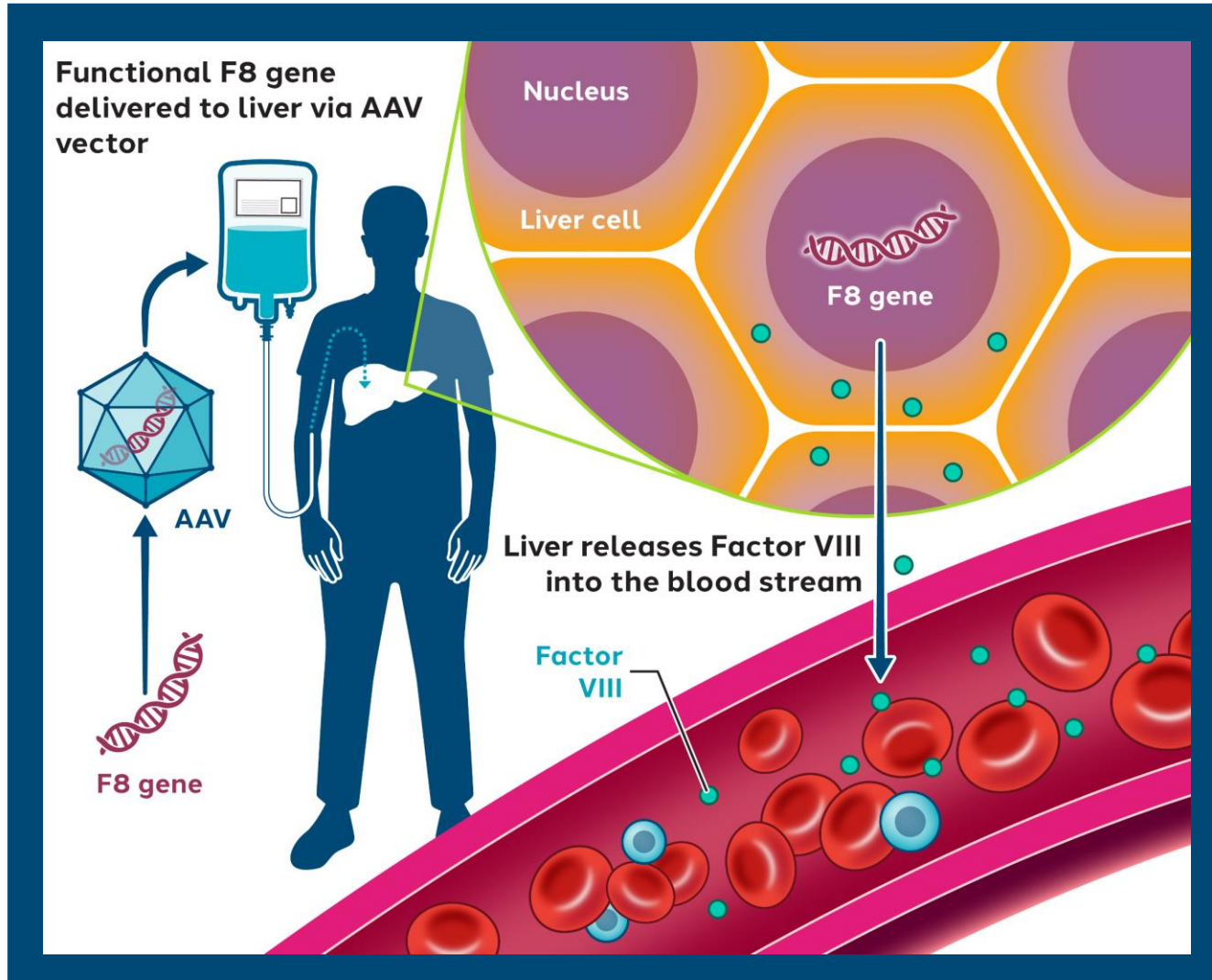
**Sangamo**  
THERAPEUTICS

+

 **Pfizer**



# Giroctogene fitelparvovec: one-time, liver directed gene therapy for treatment of Hemophilia A, currently in Phase 3



## Patient Promise: our goals for giroctogene fitelparvovec

- Administration of one-time infusion of liver-tropic rAAV6 vector carrying Beta domain deleted F8 gene
- Delivery of a working copy of the F8 gene to the liver so liver cells can start producing functional FVIII clotting factor



## Phase 3 AFFINE Study in Hemophilia A

### Program transitioned to Pfizer for phase 3 development

Open label, global, single-arm study of  
giroctocogene fitelparvovec gene therapy.

Primary endpoint is impact on annual bleed rate,  
or ABR, through 12 months following treatment.  
This will be compared to Factor VIII  
replacement therapy collected in the Phase 3  
lead-in study, which will provide a baseline for  
Phase 3 study participants.

Participants will be analyzed throughout the 5-  
year study period following the single infusion  
to further assess safety, durability and efficacy.

## AFFINE dosing is nearly complete


Dosing to support primary analysis  
expected to be complete by the end of  
Q1 2023.

A pivotal readout is expected in 1H 2024.  
BLA submission anticipated in 2H 2024.

Potential to generate up to \$240 million in  
remaining milestone payments\*, and 14-  
20% royalties on future product sales if  
approved\*\*

*\*from 2024*

*\*\*subject to customary reductions*

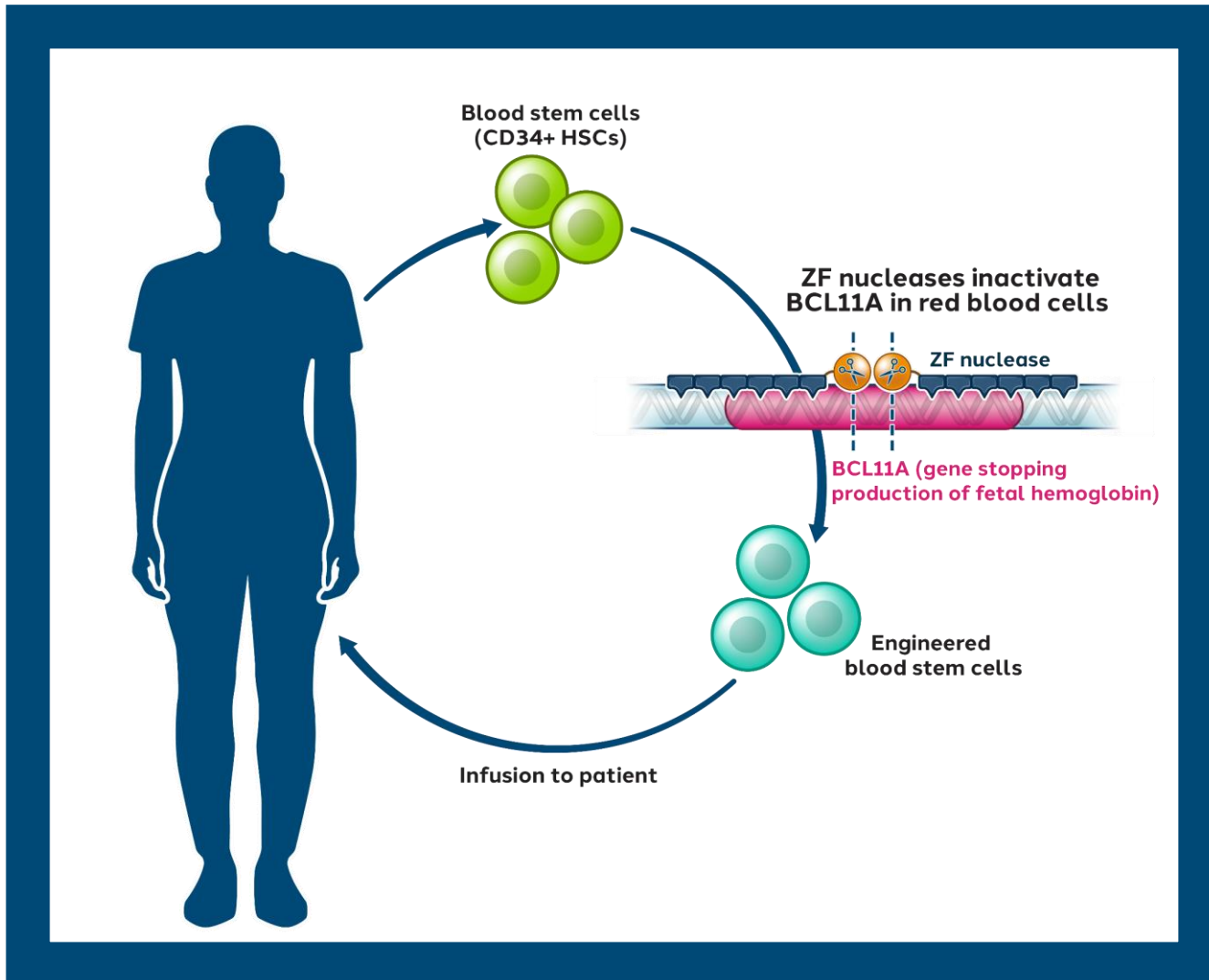


## Sickle Cell Disease (BIVV003)

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Strategic decision to prioritize SCD program  
for partnership

## BIVV003: Autologous cell therapy treatment for Sickle Cell Disease, currently in Phase 1/2

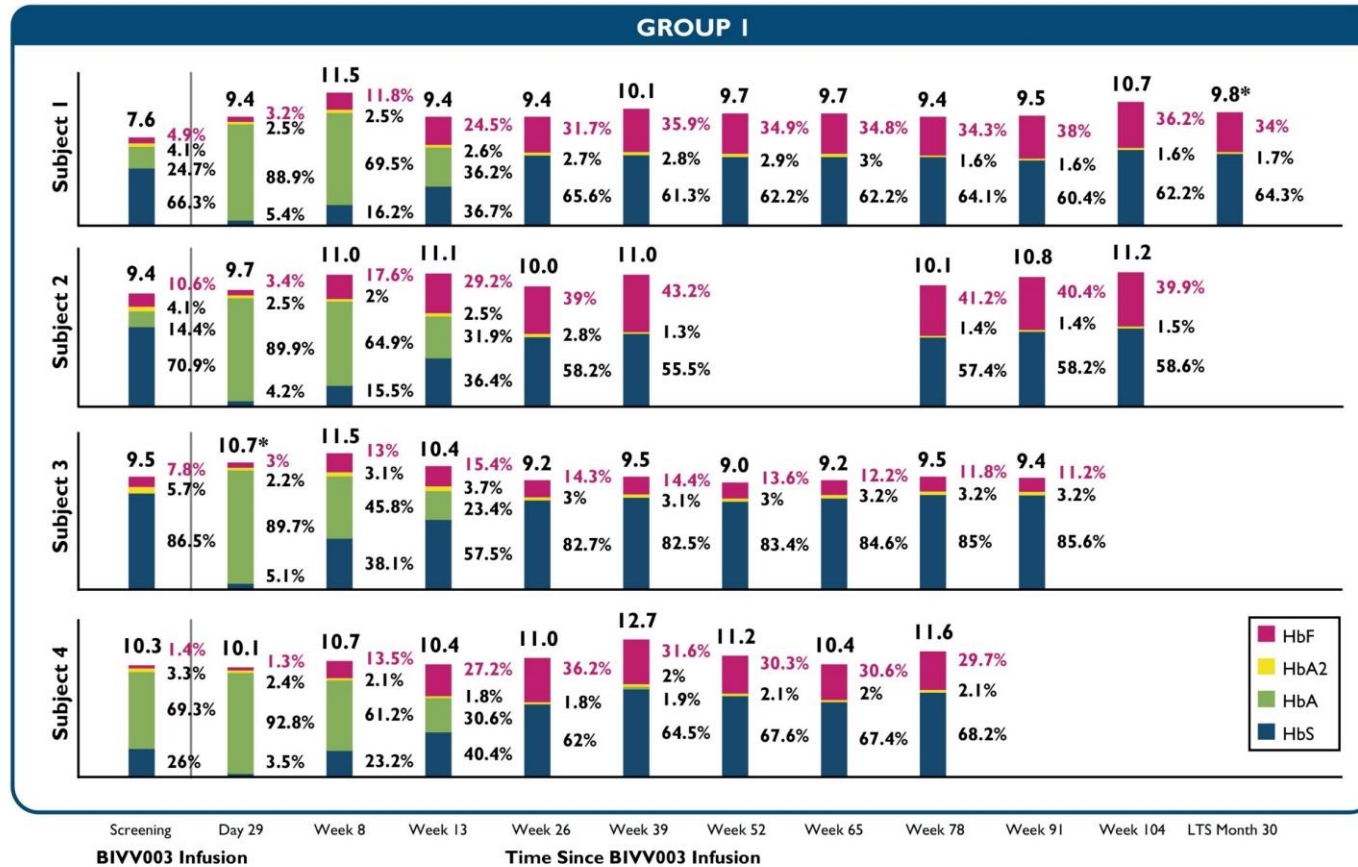


### Patient Promise: our goals for BIVV003

- Administration of autologous hematopoietic stem cells that are gene-edited *ex vivo* by zinc finger nuclease
- Target and disrupt the BCL11A enhancer in CD34+ HSPC, restoring the production of HbF and relieving SCD symptoms

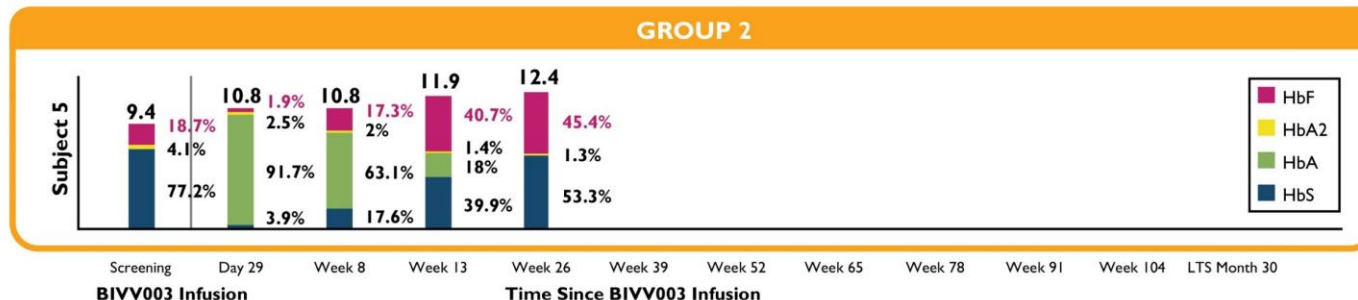
# Sickle Cell Disease: Preliminary Phase 1/2 data demonstrate therapeutic potential of BIVV003

PRECIZN-1 Data presented at ASH on December 10, 2022 (Abstract #2140). September 30, 2022, cutoff date.



## Group 1 (original manufacturing process):

Three of the four patients had HbF levels stabilized at  $\geq 30\%$  by 26 weeks which persisted for up to 30 months.



## Group 2 (improved manufacturing process):

Achieved HbF level of 45.4% and total Hb of 12.4 g/dL at week 26, showing greater efficacy than Group 1.

## Strategic decision made to halt further investments in Phase 3 planning

We expect to complete the Phase I/2 study but will make no material investments in the program going forward.

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Resources to be redeployed to Fabry and TX200 programs, to focus and drive forward our portfolio.

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Seeking a potential collaboration partner who would be able to progress this promising asset to a Phase 3 trial.

We believe BIVV003 is a competitive potential treatment, with an attractive safety profile and promising efficacy data thus far.

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Progressed additional manufacturing improvements which have the potential to further strengthen clinical outcomes, significantly reduce cost of goods and increase patient access.

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Learnings being applied to other parts of the business.

## 2. Wave Two Potentially Transformative Programs

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Autoimmune & Neurology

# Sangamo's Wave Two Programs

Innovative CAR-Treg program leverages extensive knowledge in ex vivo cellular engineering, manufacturing, and Treg biology to establish a leading position in Treg development

Neurology portfolio leverages knowledge of zinc finger genome engineering and domain expertise of partners to assemble a strong pipeline of CNS-targeted clinical candidates

## CAR-Treg Cell Therapy Platform

### Autologous Renal Transplant (TX200) Phase 1/2

FIRST TWO PATIENTS DOSED IN PROOF-OF-CONCEPT STUDY

### Inflammatory Bowel Disease *Preclinical*

### Multiple Sclerosis *Preclinical*



### Allogeneic Renal Transplant *Preclinical*

## Genome Engineering Platform

### Prion

*Preclinical*



### Neurology (3 Undisclosed)

*Preclinical*



### ALS / FTD

*Preclinical*



### Huntington's Disease

*Preclinical*



### Neuro-developmental Disorders

*Preclinical*



### Tauopathies, Synucleinopathies, DMI, Undisclosed

*Preclinical*

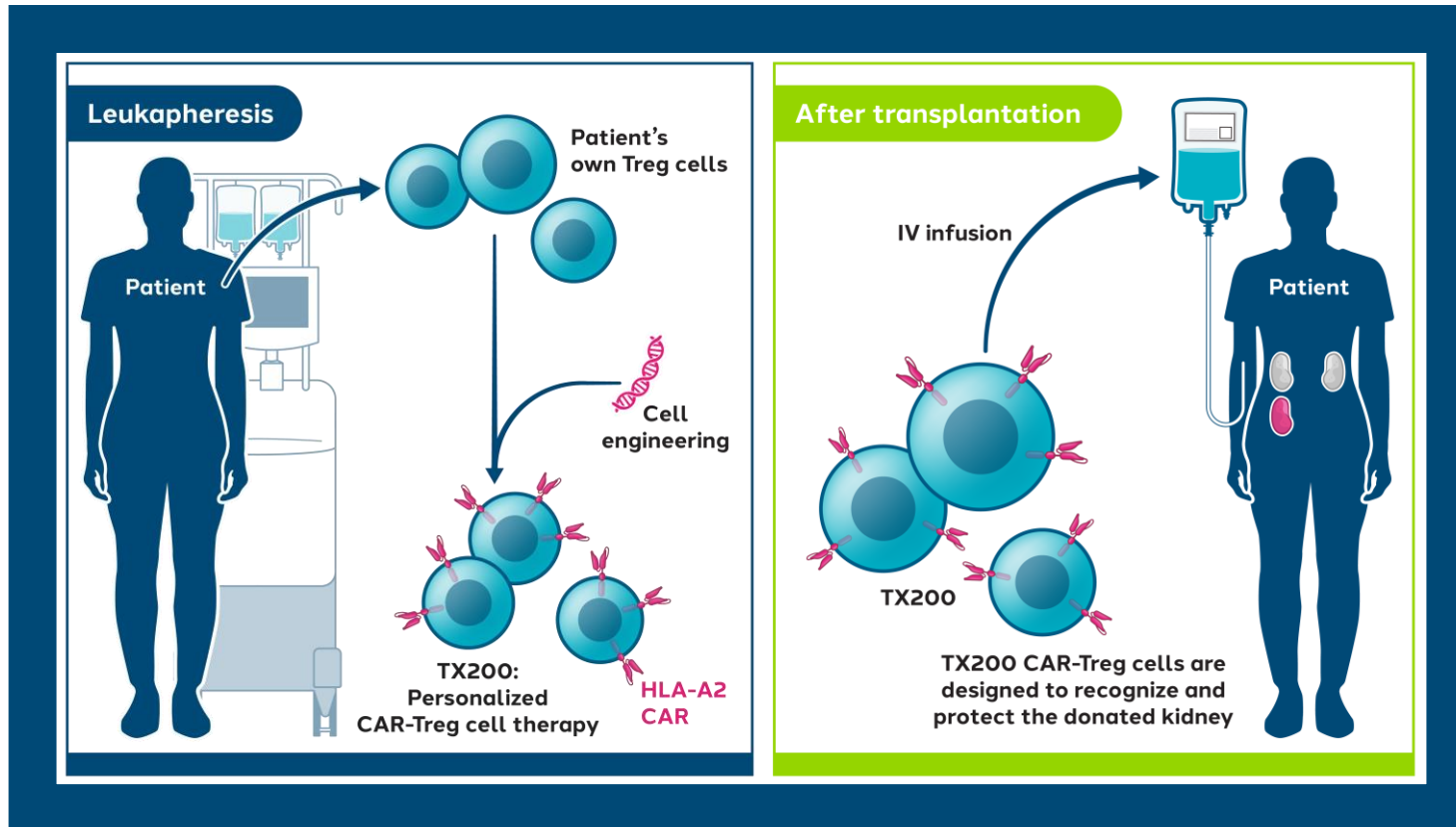






# CAR-Treg Cell Therapy in Immune Regulation

## TX200 (autologous): CAR-Tregs treatment in development for the prevention of immune-mediated rejection in HLA-A2 mismatched kidney transplantation from living donor currently in Phase 1/2



### The patient promise: goals of Treatment

- Administration of a one-time infusion of the patient's own Treg cells that have been engineered to express a CAR designed to recognize the HLA-A2 protein present on a transplanted kidney
- Protect the graft from immune-mediated rejection
- Reduce or eliminate the need for lifelong treatment with immunosuppressants

### HLA-A2 Mismatched Renal Transplant

**44,000 renal transplantations** in 2021 (US + EU)<sup>1</sup>

**21-26% of transplanted organs** are estimated to be HLA-A2 mismatched<sup>2</sup>

1. IROdat: <https://www.irodat.org>

2. Barocci et al. 2007; Marrari et al., 2010; Middleton et al., 1985; Schnitzler et al. 1997

# Phase 1/2 Study Evaluating TX200 in Renal Transplantation



Transplant and manufacturing for third patient successful, dosing expected in early 2Q23.



Progressing clinical and manufacturing activities for the first patient in the second cohort. Dosing expected summer 2023.



Exploring opportunities to accelerate dose escalation scheme.

## Entry Criteria

Male or female subjects aged 18-70 years, diagnosed with End Stage Renal Disease (ESRD) and waiting for a new kidney from an identified living donor.

HLA-A2 mismatch between kidney donor and kidney recipient.

## Primary Objective

Assess safety and tolerability of TX200.

## Secondary Objectives

**Assess** incidence of acute graft rejection (confirmed by biopsy) and chronic graft rejection.

**Assess** ability of TX200 to reduce need for immunosuppressive therapy up to 84 weeks.

**Assess** localization of TX200 cells in the transplanted kidney.

**Assess** impact of TX200 on chronic graft-related outcomes.

**TX200 is designed to help the recipient accept their donated kidney and prevent their immune system from rejecting it, thereby reducing the need for systemic immunosuppressive therapy**

# Pioneering TX200 Program Establishes Manufacturing and Treg Engineering Experience for Potential Future Expansion into Major Autoimmune Indications

## Clinical CAR-Treg

Autologous Renal Transplant

## Preclinical CAR-Treg

Allogeneic Renal Transplant

Multiple Sclerosis

Inflammatory Bowel Disease

## Potential future autoimmune indications for expansion

Autoimmune Hepatitis

Crohn's Disease

Neuromyelitis Optica

Rheumatoid Arthritis

Systemic Sclerosis

Type I Diabetes Mellitus

Ulcerative Colitis

## Cell Therapy Strategy

### CURRENT

Seeks to provide potential proof-of-concept for CAR-Treg cell therapy

Aims to establish key manufacturing & QC processes

### FUTURE

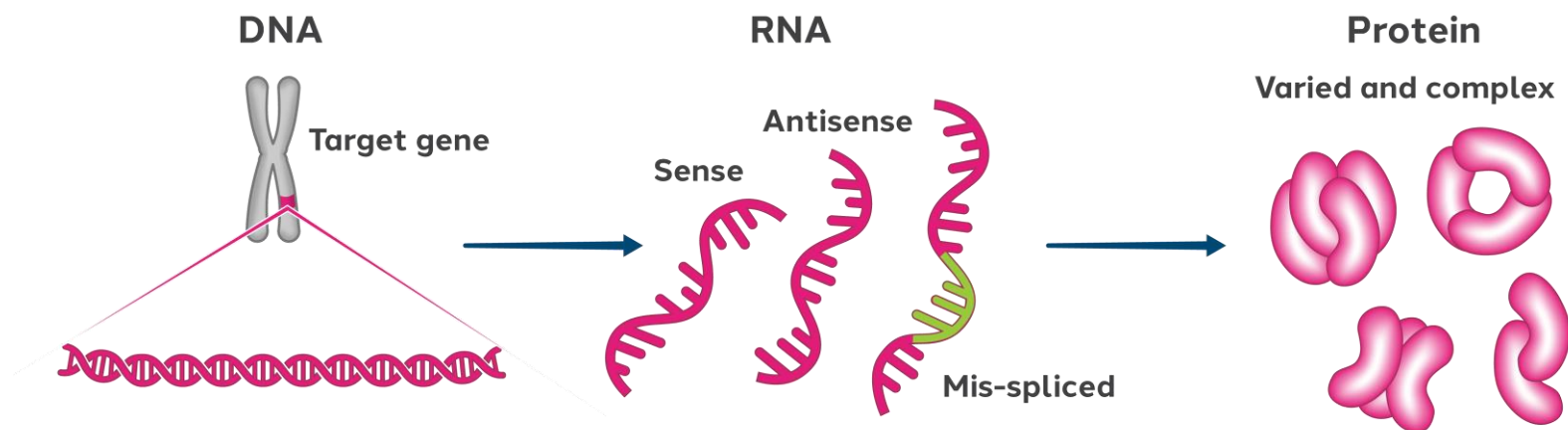
Leverage ZF genome engineering knowledge to potentially advance allogeneic and functionally-enhanced CAR-Tregs

Foundation upon which to potentially expand the addressable market

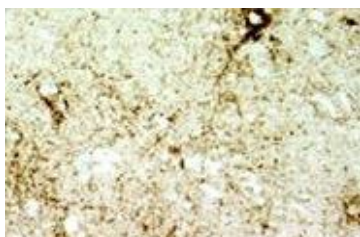


# Zinc Finger Genomic Engineering for Neurology

# ZF Transcriptional Regulators target upstream at the source of mutant protein isoforms and complexes, offering advantages over today's symptomatic approaches



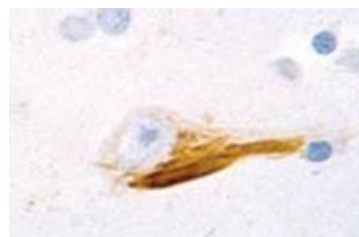
## PRION DISEASE



Prion



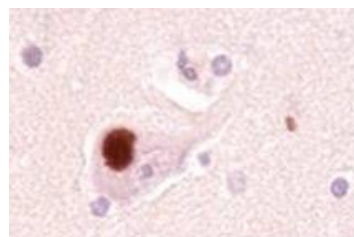
## TAUOPATHIES



Tau



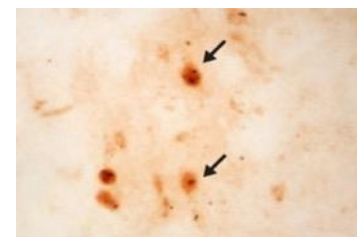
## PARKINSON'S DISEASE



$\alpha$ -Synuclein



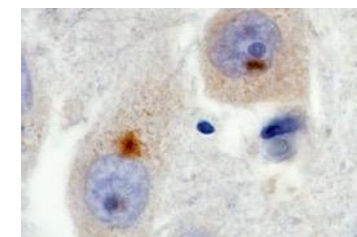
## HUNTINGTON'S DISEASE



Huntingtin



## ALS



C9orf72



Hill et al., 2003

Jucker & Walker 2013

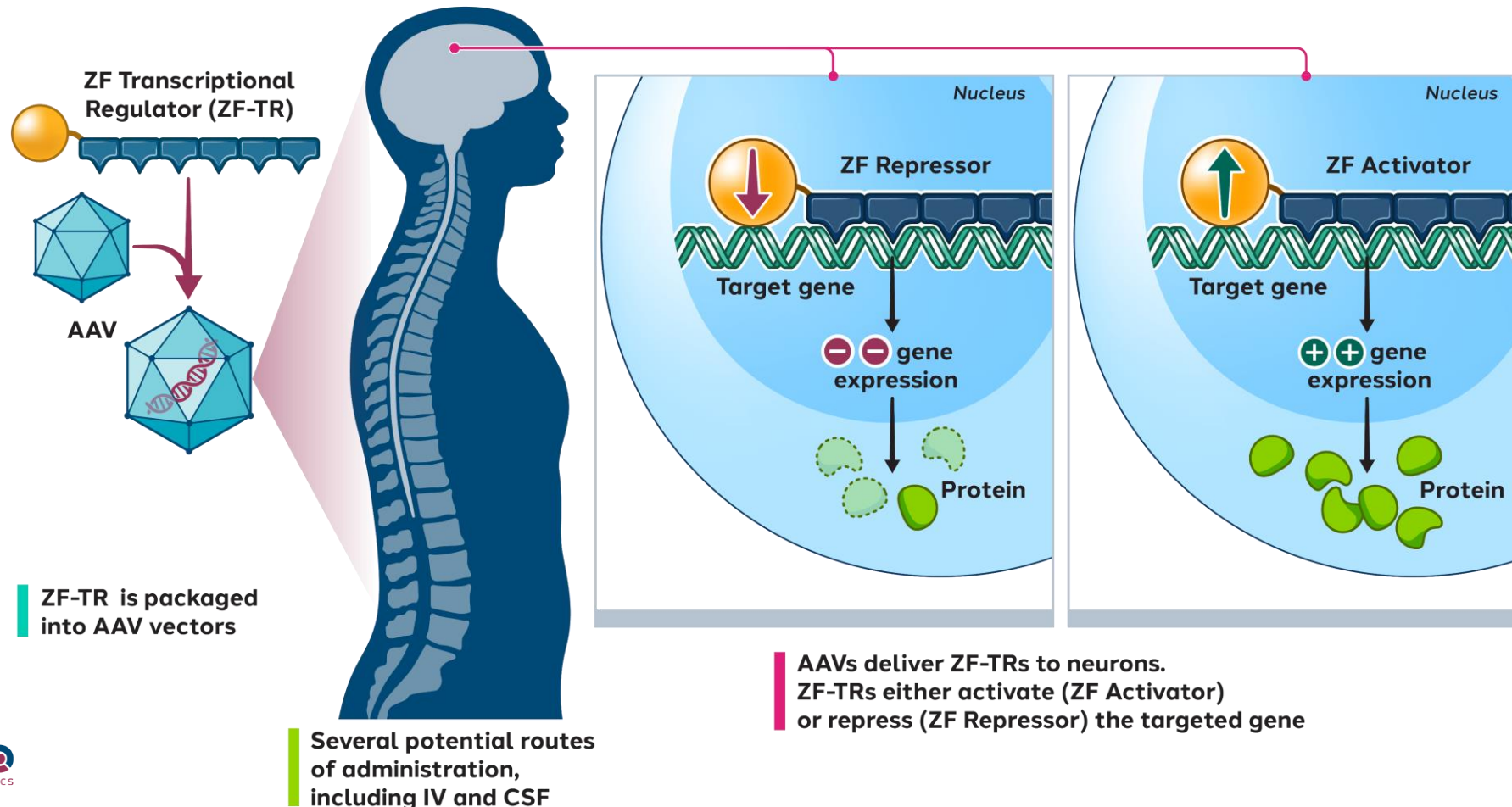
Irwin et al., 2015

Waldvogel et al., 2014

# ZF transcriptional regulators in the CNS

ZF Transcriptional Regulators can be designed to:

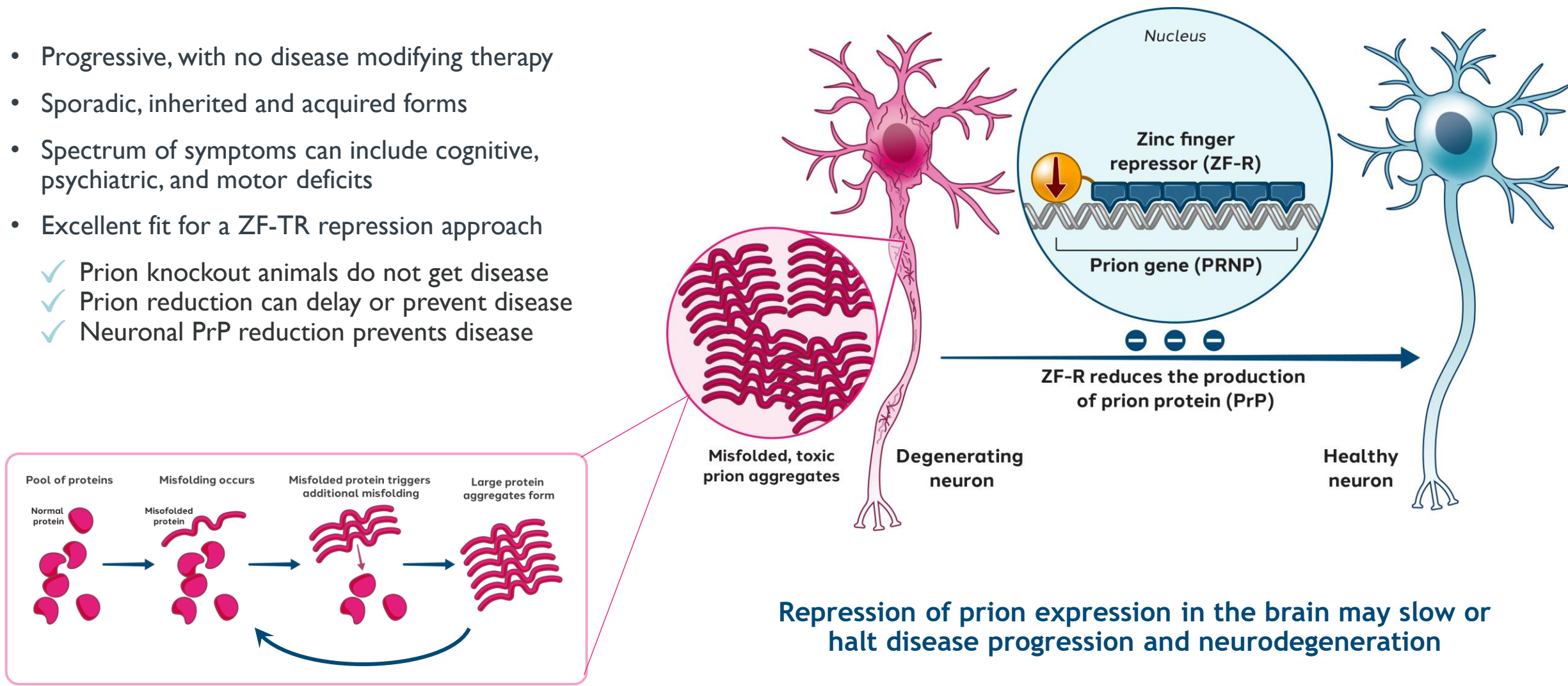
- ZF Repressors** {
  - Reduce the expression of a pathogenic gene
  - Selectively repress expression of a mutant allele while allowing for the expression of the healthy allele
- ZF Activators** {
  - Activate the expression of genes that are inadequately expressed





# Zinc finger-mediated gene repression for Prion disease

- Progressive, with no disease modifying therapy
- Sporadic, inherited and acquired forms
- Spectrum of symptoms can include cognitive, psychiatric, and motor deficits
- Excellent fit for a ZF-TR repression approach
  - ✓ Prion knockout animals do not get disease
  - ✓ Prion reduction can delay or prevent disease
  - ✓ Neuronal PrP reduction prevents disease



Repression of prion expression in the brain may slow or halt disease progression and neurodegeneration

# 3. Powerful Research Platform

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Continually innovates to support value creation, including in delivery

# Sangamo's Differentiated ZF Genomic Engineering Platform

## Versatile, modular, customizable

Flexible configuration and  
multiple functionalities

## High activity and specificity

Tunable and optimizable  
DNA:protein interface

## High-resolution targeting

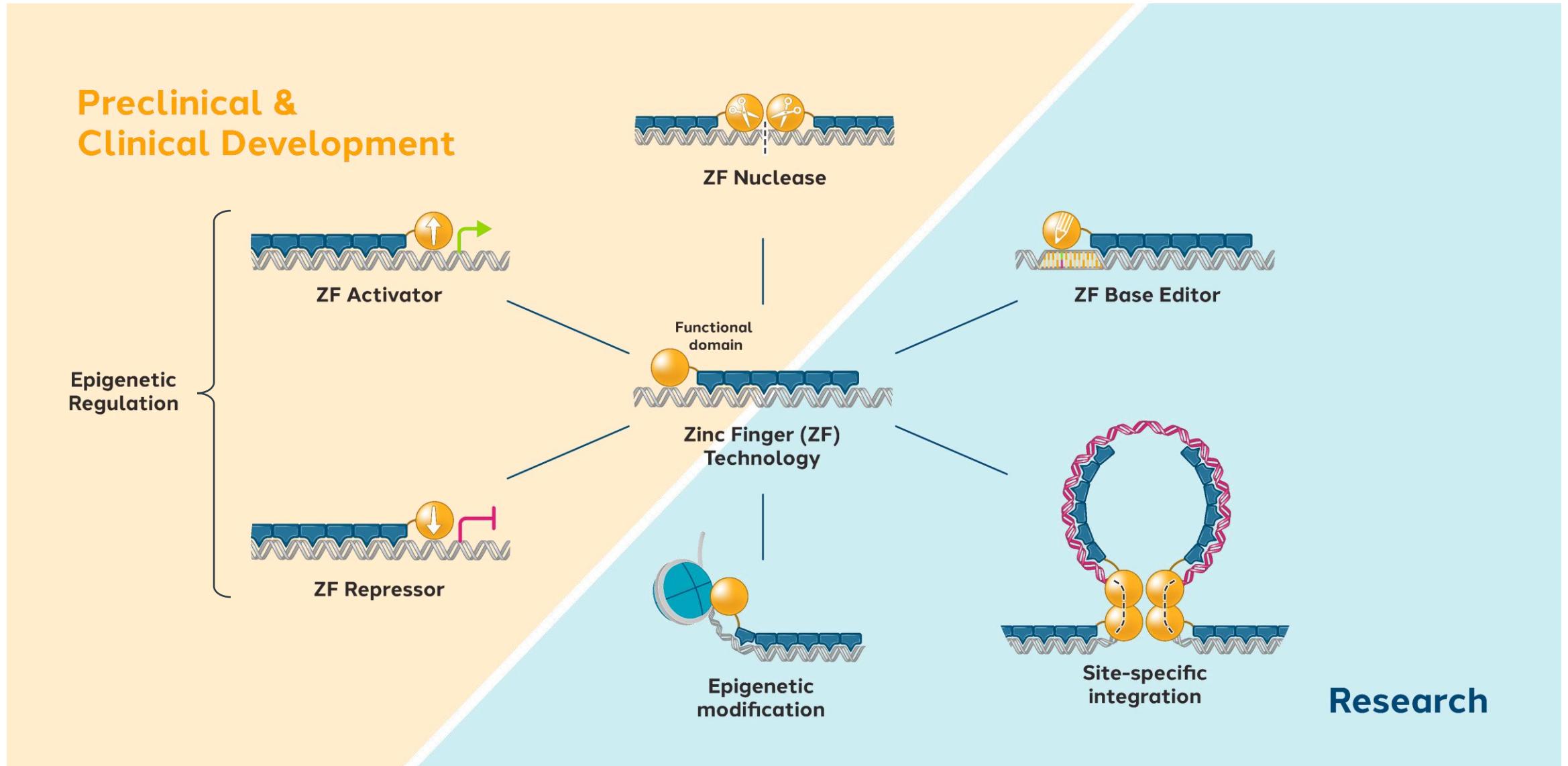
Genome-wide coverage, no restrictions

## Compact

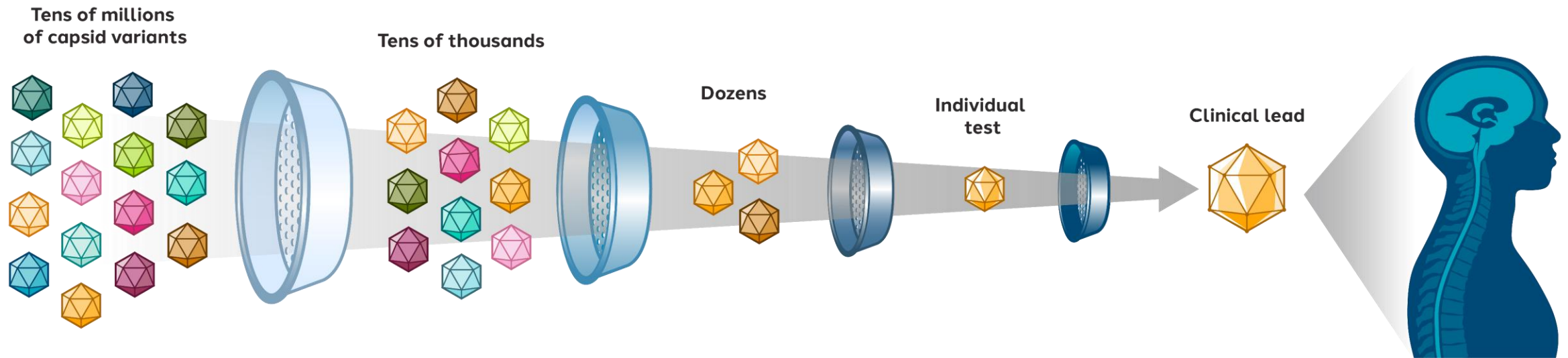
Improved delivery vector  
compatibility and genome accessibility



# A diverse set of functional domains can be appended to the ZF platform



# Our SIFTER™ platform enables selection of CNS-tropic AAV capsids to advance our innovative preclinical programs to the clinic



## 4. In-house cGMP Manufacturing Facilities

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Provide control over quality, supply,  
timelines and cost



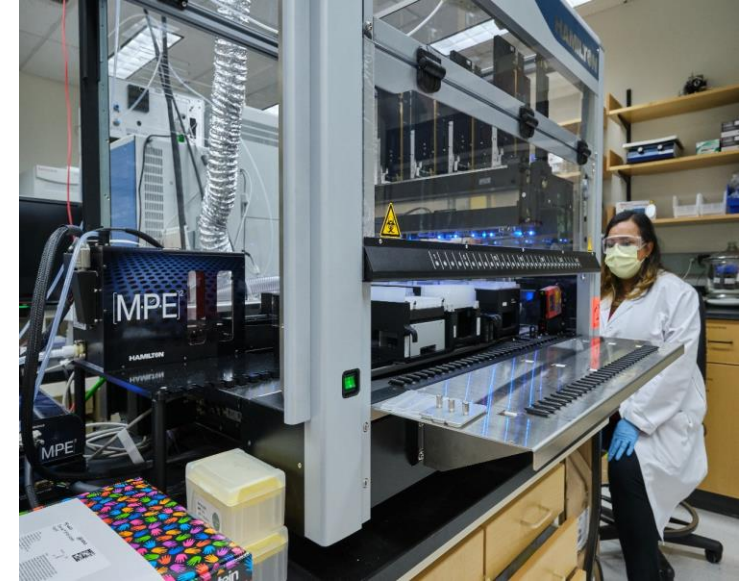
## In-house cell therapy and AAV manufacturing GMP facilities & deep manufacturing knowledge provide the infrastructure to execute on our clinical strategy



AAV and Cell  
Therapy manufacturing  
capabilities in-house



Opened new  
state-of-the-art GMP  
facilities in 2021



Dedicated access to AAV capacity up  
to 2000-L bioreactor scale with  
CDMO partners provides flexibility  
in manufacturing scale

In-house capabilities in US and France, and line of sight across manufacturing operations from procurement to release designed to enable greater control over quality, supply, cost, timeline and IP



# Key Highlights of Sangamo's Manufacturing Capabilities



## **Flexibility and control**

High degree of quality control for vector and cell therapy applications



## **Capacity to support R&D needs**

Balanced infrastructure designed to support achievement of critical milestones



## **Process knowledge**

Supported by highly experienced technical operations team



## **Geographic diversification**

US and EU sites designed to provide supply chain resiliency



## **Deep intellectual property portfolio**

Proprietary archive of ZFP modules, ~170 patent families, and trade secrets / know-how

## Our ESG Commitment

Sangamo strives to mitigate the environmental impact of our operations, promote diversity and inclusion in our workforce and govern our company responsibly and transparently

### Environment

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Sangamo's headquarters in Brisbane is LEED certified, meaning it meets the requirements of a green building set by the U.S. Green Building Council

### Social

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Diversity, Equity and Inclusion (DEI) working group continues to advance internal initiatives

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Instituted DEI metrics to better track diversity initiatives and results

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Focus on DEI in recruitment and retention

### Governance

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Majority independent Board oversees risk and strategy

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Separate Chair and CEO

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Three new independent directors added in the last three years

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Board is 29% female and 14% from underrepresented communities

## 5. Proven Track Record of Partnerships

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Results in non dilutive funding, provides access to domain expertise, expands the portfolio and offsets costs

## Multiple biopharma collaborations demonstrate the platform's potential and provide significant economics for Sangamo

### GENETHERAPY



### CELL THERAPY



### GENOME ENGINEERING



**\$815m**

cash received from  
partners to date

**Up to \$6.7b**

in potential future  
milestones

**Additional  
potential royalties**

Data as of December 31, 2022

## Numerous Benefits of Partnerships:

Large Pharma buy-in validates the potential of wave two mechanistic approach

Provides non-dilutive capital to advance pipeline

Leverages partner domain expertise

Promotes optimal resource allocation to advance late-stage clinical development

# Sangamo in 2023: Value Thesis

## ① First wave of value-driving programs advancing to/through late-stage development

- Compelling proof-of-concept data supporting future pivotal development.
- **Fabry disease:** Ph I/2 results support potential best-in-class product profile. Phase 3 start expected by YE2023 following regulatory guidance.
- **Hemophilia A (with Pfizer):** pivotal data readout expected 1H 2024. BLA submission anticipated 2H 2024, generating potential milestones and, if approved, royalties.

## ② Second wave of potentially transformative autoimmune and neurology programs advancing into the clinic

### Pioneer in CAR-Tregs

- We believe we are the first company to dose patients with engineered CAR-Tregs.
- TX200 renal transplant Ph I/2 study progresses, with possible acceleration to prove biology and platform value.
- Disciplined progress of pre-clinical candidates in MS and IBD. First IND submission expected 2024.

### Genome Engineering in the CNS

- Portfolio of pre-clinical wholly owned and partnered programs advancing.
- Second of four wholly-owned programs expected to be disclosed Q2 2023. IND submission expected 2024 based on advances in delivery.
- Investments partially offset by partner programs.

## ③ Powerful research platform continually innovates to support value creation, including in delivery



## ④ In-house cGMP manufacturing facilities provide control over quality, supply, timelines and cost



## ⑤ Demonstrated track record of partnerships results in non dilutive funding, expands the portfolio, provides access to domain expertise and offsets cost