

# Pioneering and Delivering the Future of Genomic Medicines

April 2023

## **Forward-Looking Statements**

This presentation contains forward-looking statements regarding our current expectations. These forward-looking statements include, without limitation, statements relating to our focus on key strategic priorities, 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 ZF, ZF-TR, CAR-Treg, SIFTER 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 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, the impact of our announced restructuring, 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 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, disruptions in access to bank deposits and lending commitments due to bank failure, 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 Quarterly Report on Form 10-Q for the guarter ended March 31, 2023 to be filed with the Securities and Exchange Commission, or SEC, and future reports filed with the SEC. 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



First wave of value-driving programs advancing to/through late-stage development Second wave of potentially transformative neurology and autoimmune programs advancing into the clinic Powerful research platform continually innovates to support value creation, including in delivery

Demonstrated track record of partnerships results in non dilutive funding, expands the portfolio, and offsets cost

#### 2023 VALUE THESIS



# 1Q23 Key Takeaways



Clinical Momentum Continues Strong clinical momentum continues in **Phase I/2 STAAR study in Fabry disease** with 20 patients dosed in total. We are preparing to meet with the FDA on the proposed Phase 3 trial design this summer.

Dosed third patient in cohort I of **Phase I/2 CAR-Treg STEADFAST study for TX200** in HLA A2 mismatched kidney transplantation.

Established **Nav I.7 for chronic neuropathic pain** as flagship program of wholly owned neurology epigenetic regulation pipeline, with IND submission expected in 2024.



# 1Q23 Key Takeaways



Pipeline prioritization and sharpened strategic focus



### **Financial Highlights**

Announced **strategic pipeline prioritization** and **corporate restructuring**, including US workforce reduction of approximately 27%.

#### Pipeline being prioritized to focus on three key areas:

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Nav 1.7 and Prion as cornerstones to the neurology epigenetic regulation portfolio Advancing Fabry program towards potential Phase 3 trial

# 03

Progressing Phase I/2 CAR-Treg study of TX200 through the clinic

Announced pausing of select pre-clinical programs, and the significant reduction in internal manufacturing and allogeneic research footprints in California.

- Approximately **\$241 million in cash, cash equivalents, and marketable securities** as of March 31, 2023.
- Previously announced 2023 non-GAAP operating expense guidance of \$275-295 million no longer valid. Updated range is \$240-260 million for 2023 (as of April 26, 2023).
- Continue to assess ways to further reduce our annual operating expenses consistent with the prioritized objectives and progress of the company.

# **Sharpened Strategic Focus**

### Neurology Epigenetic Regulation

- Led by Nav 1.7 and Prion programs.
- Innovative zinc finger epigenetic regulation technology, underpinned by strong capsid delivery capabilities.
- Expected to deliver one IND submission in 2024 and one in 2025.

### Advancing Fabry to Potential Phase 3 Trial

- First-in-class and best-inclass Fabry gene therapy candidate.
- Favorable safety profile, evidence of clinical benefit in Phase1/2 study.
- Progressing planning for potential Phase 3 trial.
- Potential to dramatically reduce the reliance on ERT.

### Progressing Phase I/2 Study of TX200

- Leader in CAR-Treg cell therapy development.
- Advancing TX200 in renal transplant through Phase 1/2 study, with plans for dose escalation acceleration.
- Advanced Treg research and development capabilities.

Hemophilia A in Phase 3 with Pfizer progresses with up to \$240m in potential milestones

Capsid discovery platform SIFTER<sup>™</sup> is addressing the challenge of delivery with additional potential partnership value



# **Prioritized Pipeline and Delivery Platform**

WHOLLY OWNED PROGRAMS				
Indication	Technology	Preclinical	Phase I/2	Pivotal
Fabry Disease (Isaralgagene civaparvovec)	Gene Therapy	Clinical data presented Feb 2022. P	hase 3 expected to begin in 2023	
Renal Transplant (TX200; Auto)	Treg Cell Therapy	First three patients dosed in Phase	e 1/2 study	
Chronic Neuropathic Pain (Nav 1.7)	ZF Genome Engineering	Preclinical data at ASGCT		
Prion	ZF Genome Engineering	Preclinical data at ASGCT		
Neurology (undisclosed)	ZF Genome Engineering			
Inflammatory Bowel Disease	Treg Cell Therapy			
Multiple Sclerosis	Treg Cell Therapy			
PARTNERED PROGRAMS				
Indication	Technology	Preclinical	Phase I/2	Pivotal
Hemophilia A (Giroctogene fitelparvovec)	Gene Therapy			<b>P</b> fizer
Oncology (Kite-037)	Cell Therapy	Kite		
Oncology (Undisclosed)	Cell Therapy	Kite		
ALS/FTD	ZF Genome Engineering	<b>P</b> fizer		
Huntington's Disease	ZF Genome Engineering	Takeda		



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# **Recent business updates**

Neurology Epigenetic Regulation

**Fabry Disease** 

CAR-Treg Immune Regulation

Hemophilia A

ASGCT

- Announced NavI.7 to treat chronic neuropathic pain as flagship program in Sangamo's newly prioritized wholly owned neurology pipeline, with an IND submission expected in 2024.
- Decided to pause further development of programs previously partnered with Biogen and Novartis, pending the identification of a suitable capsid for delivery for those specific indications.
- Dosed an additional 3 patients in Phase 1/2 study to achieve a total of 20 patients dosed.
- Progressed plans to meet with the FDA on proposed Phase 3 study design in the summer.
- Dosed third patient in cohort 1 in the Phase 1/2 study.
- Product candidate continues to be generally well tolerated in all three patients dosed.
- Received positive regulatory feedback for accelerated dose escalation protocol from two European agencies to date.
- Dosing of patients in Phase 3 AFFINE trial complete to support primary analysis.
- Pivotal data read-out expected in mid-2024.
- BLA and MAA submissions anticipated in second half of 2024.
- 14 Sangamo abstracts accepted for presentation at ASGCT on May 16-20, 2023, in Los Angeles, California.

# Looking Ahead: Anticipated Milestones



#### **Fabry Disease**

- Plan to meet with the FDA on proposed Phase 3 trial design in summer 2023.
- Conclude dosing in Phase 1/2 expansion by YE2023.
- Commence Phase 3 trial by YE2023.



#### **Neurology Epigenetic Regulation Programs**

- IND submission for Nav 1.7 expected in 2024.
- Data from Nav 1.7 and broader neurology pipeline to be presented at ASGCT 26<sup>th</sup> Annual Meeting in May 2023.
- IND submission for wholly owned prion disease program anticipated in 2025.



#### **CAR-Treg in Immune Regulation**

- Commence dosing in cohort 2.
- Provide update on TX200 accelerated dose escalation protocol.
- Share initial data from cohort I by YE2023.
- In vivo studies in MS and Inflammatory Bowel Disease.



#### Hemophilia A (Pfizer)

- Pivotal data readout estimated in 1H 2024.
- BLA and MAA submissions in 2H 2024.



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



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



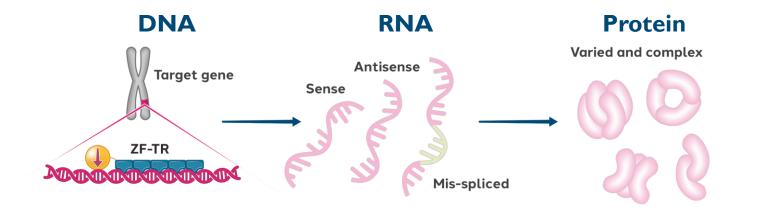
\* Currently in process of completing the customary quarter-end close and review procedures, including the evaluation of non-cash charges related to impairment of long-lived assets. The final results for Q1 2023 could materially differ from the preliminary expected results disclosed in this deck. The full first quarter 2023 financial results will be reflected in a Quarterly Report on Form 10-Q which is expected to be filed no later than May 10, 2023.

\*\* On a GAAP basis we expect our 2023 operating expenses to be in the range of \$315 - \$335 million, including Goodwill impairment expense of \$38 million, impairment of long-lived assets of up to \$20 million, and stock-based compensation expense of approximately \$35 million.

# Zinc Finger Genomic Engineering for Neurology

Led by Nav 1.7 and Prion

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







# ZF transcriptional regulators in neurology

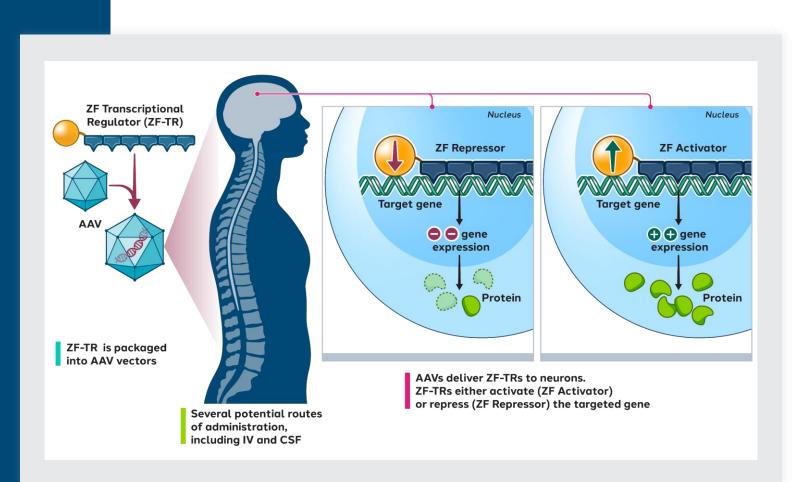
## ZF Transcriptional Regulators can be designed to:

#### **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

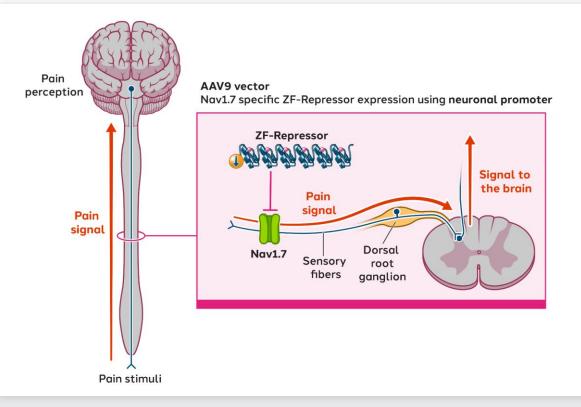
• Activate the expression of genes that are inadequately expressed





# Nav 1.7 specific Zinc Finger repressor to treat neuropathic pain

Given the high unmet need and lack of effective treatments, there is an urgent need to develop novel therapeutics for the treatment of chronic neuropathic pain

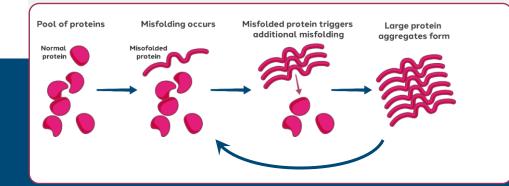


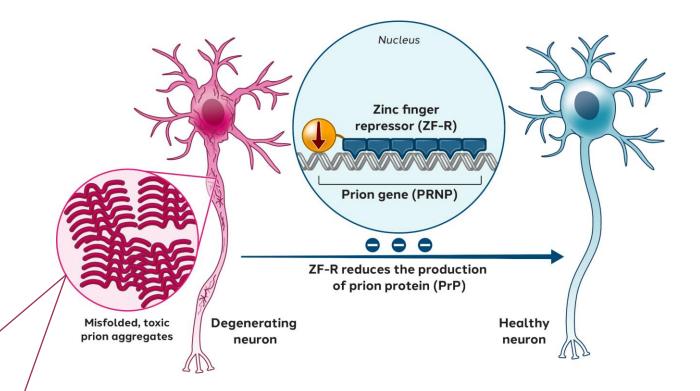
- Nav 1.7 is a voltage gated sodium channel expressed in the Dorsal Root Ganglion (DRG)
- Alterations in Nav 1.7 activity directly regulate pain levels in several genetic disorders
- Blocking NavI.7 in the DRG is expected to prevent the **transmission of nociceptive pain signals** to the brain
- This allows us to target multiple **neuropathic pain indications**, regardless of the cause of the pain
- Reducing pain by inhibiting NavI.7 is not predicted to be associated with **any neurological side effects**



# 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

Maddox et al, 2020	
Mead et al, 2022	

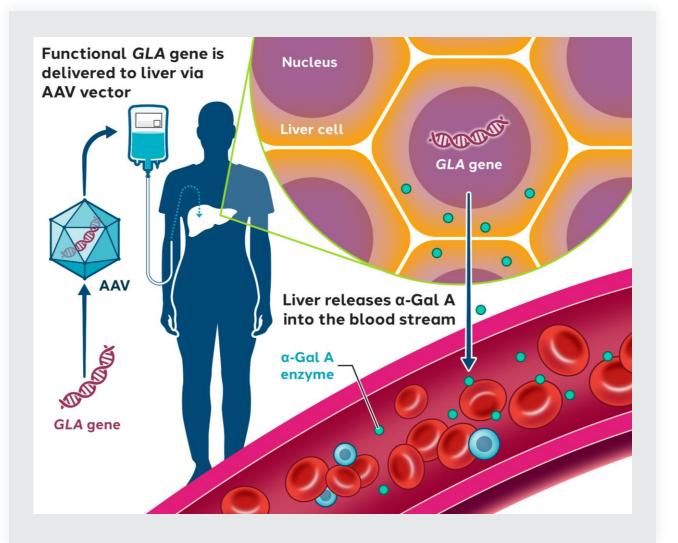
Bueler et al., 1993 Fischer et al., 1996

Mallucci et al., 2003 Safar et al., 2005



# Fabry Disease (isaralgagene civaparvovec or ST-920)

# Isaralgagene 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



# Isaralgagene civaparvovec (ST-920) in Fabry disease previously presented at WORLDSymposium 2023, February 2023

#### **Evidence of clinical effect in Fabry disease**

- Sustained expression of α-Galactosidase A (α-Gal A) activity in
   I3 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 (0.5×10<sup>13</sup> 5×10<sup>13</sup> vg/kg).
- No requirement for prophylactic corticosteroids or other immune modulating agents.

 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 1/2 expansion phase.

Phase 3 planning actively progresses

• We expect dosing of the Phase 1/2 expansion phase to **conclude by the end of 2023.** 



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

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

	Dose Escalation Cohorts						:					
	0.5 ×	<b>hort  </b> 10 <sup>13</sup> vg/kg N = 2	×	n <b>ort 2</b> 0 <sup>13</sup> vg/kg I = 2	3 × 1	<b>hort 3</b> 0 <sup>13</sup> vg/kg ↓ = 3	5 × 1	h <b>ort 4</b> 0 <sup>13</sup> vg/kg I = 2	<b>G</b> r 5 × 10	ansion oups 0 <sup>13</sup> vg/kg   = 4		otal = 13
	N	Events	N	Events	N	Events	N	Events	N	Events	N (%)	Events
Adverse Events	2	30	2	20	3	29	2	10	4	18	3 (100%)	107
Treatment Related Adverse Events	I	3	2	3	I	6	2	6	4	12	10 (77%)	30
Serious Adverse Events (Unrelated)	0	0	0	0	I	I	0	0	0	0	l (7.7%)	I

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

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

#### **Serious Adverse Events (Unrelated)**

• Unrelated Sepsis (Cohort 3, I participant)

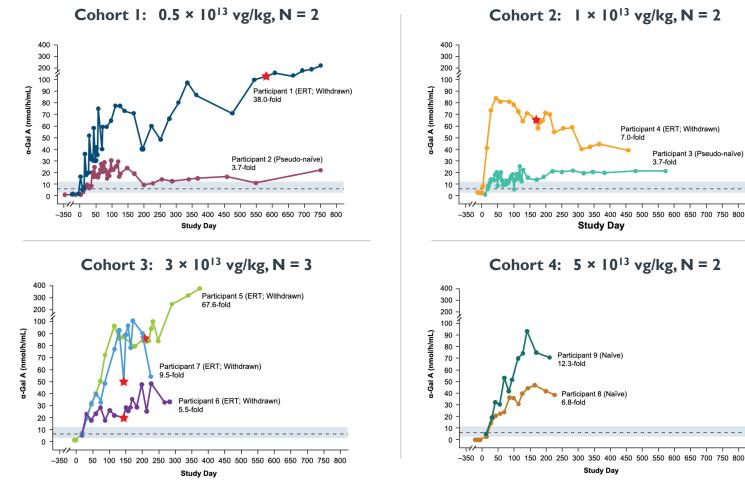


#### No Treatment Related Adverse Events greater than a Grade 2 as of the cut-off date

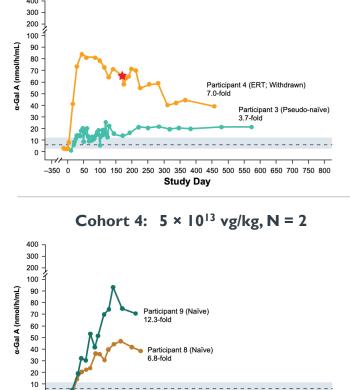
- Hepatic Enzymes No administration of corticosteroids for transaminase elevations
- **Platelets** No clinically significant decreases in platelets observed
- Cardiac Events
   Not observed
- Allergic reaction One expansion phase participant experienced a Grade I allergic reaction treated with diphenhydramine

# 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.

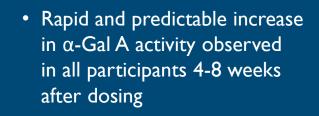


Cohort 2:  $1 \times 10^{13}$  vg/kg, N = 2



Study Day

Normal range (2.45 - 11.37) --- Mean Normal 5.70 ERT Withdrawa



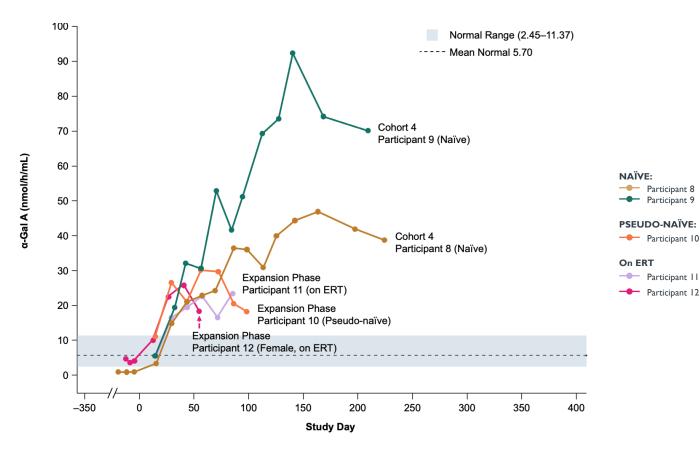
- Supraphysiological α-Gal A activity maintained in all participants
- ERT withdrawal completed for all 5 participants – with continued supraphysiological activity following withdrawal
- ST-920 expression observed was durable, with  $\alpha$ -Gal A activity at supraphysiological levels maintained in all participants, up to 2+ years



α-Gal A activity measured using 3-hour reaction time. Normal range determined in healthy males. Fold change from normal mean was calculated at last measured time point. Long Term Follow-up Data: Data points > Study Day 365. α-Gal A, alpha-galactosidase A; ERT, enzyme replacement therapy

# The proposed Phase 3 clinical trial dose (5 × $10^{13}$ 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

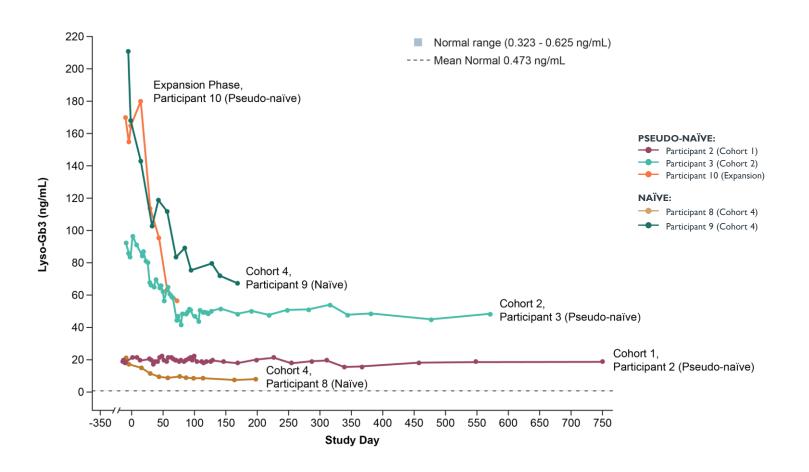
   (5 × 10<sup>13</sup> vg/kg) produced rapid, predictable and durable increases in plasma α-Gal A activity across all participants as of the data cut-off
- The female participant has demonstrated a similar response profile to males as of the data cut-off



Participant I 3: Week 6: 3.97 nmol/h/mL.  $\alpha$ -Gal A activity measured using 3-hour reaction time. Normal range determined in healthy males. Long Term Follow-up Data: Data points > Study Day 365  $\alpha$ -Gal A, alpha-galactosidase A; ERT, enzyme replacement therapy

## 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

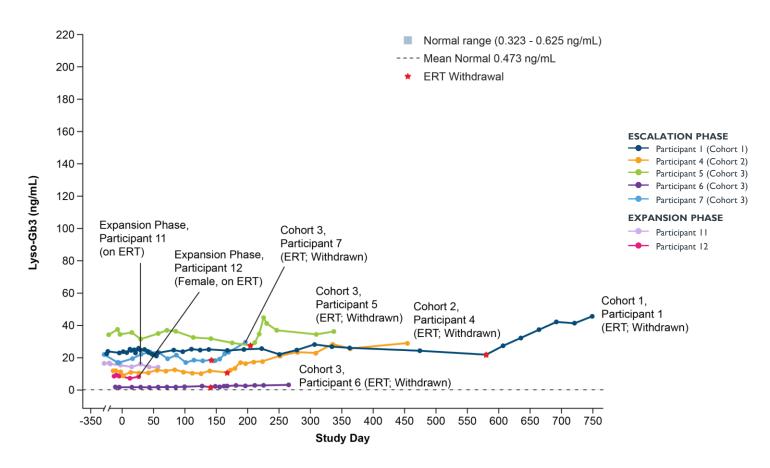
- For the first time, at the high dose, we observed a further reduction (54%) in Lyso-Gb3 where baseline plasma levels started lower (<25 ng/mL)</li>
- Plasma Lyso-Gb3 continued to decrease in two participants
- Plasma Lyso-Gb3 levels
   were stable up to 25 months



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

# 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.



# Sangame

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.

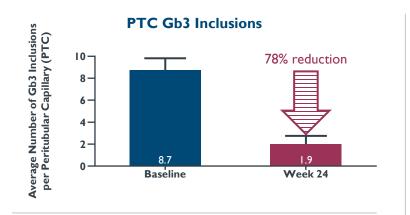
#### **Dose Escalation Phase**

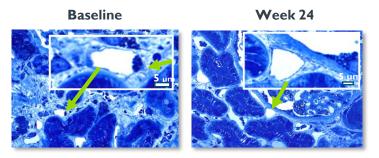
- ERT withdrawal was successful in all ERT-treated participants
- Lyso-Gb3 levels following ERT withdrawal remained within the range of levels and variability normally observed in participants treated with ERT<sup>1,2,3</sup>
- In these participants, α-Gal A activity remained elevated, and no participant has experienced symptoms requiring the resumption of ERT
- Expansion Phase
- At this data cut, ERT withdrawal had not yet been initiated for any participant
- I. 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 podocyturia

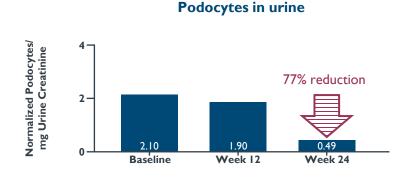
Cohort 4 ( $5 \times 10^{13}$  vg/kg) - high number of Gb3 inclusions and lyso-Gb3 at baseline

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





**Representative PTC Images** 



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

Podocyte quantification was performed via immunofluorescence with urine creatinine normalization. The Barisoni Lipid Inclusion Scoring System (BLISS) was used in a blinded manner by 3 independent pathologists to quantify PTC Gb3 inclusions. Lines above the bars indicate standard deviation. α-Gal A, alpha-galactosidase A; ERT, enzyme replacement therapy; PTC, peritubular capillary; lyso-Gb3, globotriaosylsphingosine; Gb3, globotriaosylceramide.

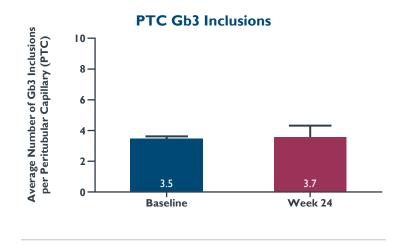
- ST-920 cleared 78% of Gb3 inclusions from peritubular capillaries
- ST-920 also reduced urinary podocyte loss by 77%
- This participant exhibited significant increase in a-Gal A activity and reduction in lyso-Gb3 after dosing with ST-920
- The significant decrease in renal Gb3 inclusions and the reduction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

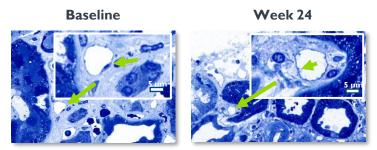


# Participant 8: stable renal Gb3 inclusions and reduced podocyturia

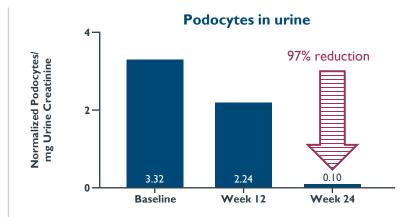
Cohort 4 ( $5 \times 10^{13}$  vg/kg) - lower number of Gb3 inclusions and lyso-Gb3 at baseline

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 × mean normal
Plasma lyso-Gb3 (ng/mL)	16.9	7.24	57% 🗸

Podocyte quantification was performed via immunofluorescence with urine creatinine normalization. The Barisoni Lipid Inclusion Scoring System (BLISS) was used in a blinded manner by 3 independent pathologists to quantify PTC Gb3 inclusions. Lines above the bars indicate standard deviation. α-Gal A, alpha-galactosidase A; ERT, enzyme replacement therapy; PTC, peritubular capillary; lyso-Gb3, globotriaosylsphingosine; Gb3, globotriaosylceramide.

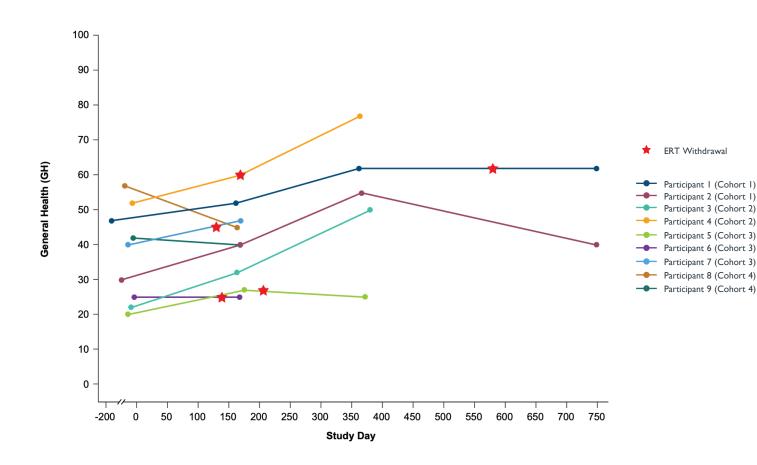
- Peritubular capillary (PTC) renal Gb3 inclusions were stable in this participant
- ST-920 reduced urinary podocyte loss by 97%
- This participant exhibited significant increases in a-Gal A activity and reductions in lyso-Gb3 after dosing with ST-920
- These data provide additional evidence of a potentially 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 ± SE, 95% CL
Baseline	
Week 24	2.9±2.57 [-3.2, 8.9]
(n=8)	p=0.2996
Week 52	<b>19.6±4.26 [7.8, 31.4]</b>
(n=5)	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

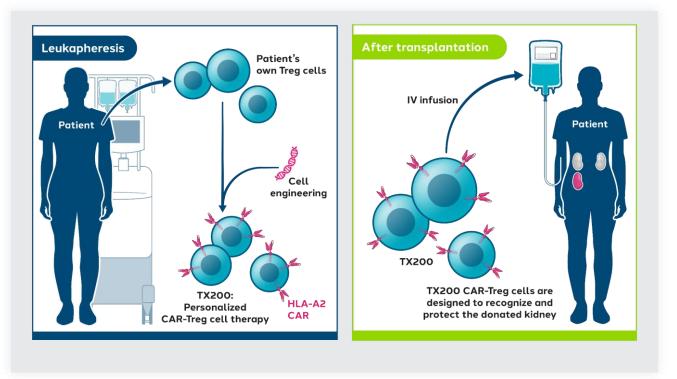
- Change from baseline at Week 52 is statistically significant with mean=9.6, 95% CL: [7.8, 31.4], p=0.010 (paired t-test)
- A 3-to-5-point change on any SF-36 score is the minimally clinically important difference (MCID)<sup>1</sup>

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



# CAR-Treg Cell Therapy in Immune Regulation

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



### The patient promise: Our goals for TX200

- 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>



# Phase 1/2 study evaluating TX200 in renal transplantation



Dosed third patient in Cohort I.The product candidate continues to be generally well tolerated.



Preparations for higher dose cohort underway.



Received positive regulatory feedback for accelerated dose escalation protocol. Plan to share initial data from cohort I by YE2023. **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

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.



### Pioneering TX200 program establishes manufacturing and Treg engineering experience for potential future expansion into major autoimmune indications

		Potential future autoimmune indications for expansion				
	Preclinical CAR-Treg	Autoimmune Hepatitis	Systemic Sclerosis			
Clinical CAR-Treg	Multiple Sclerosis	Crohn's Disease	Type I Diabetes Mellitus			
	Inflammatory Bowel Disease	Neuromyelitis Optica	Ulcerative Colitis			
Autologous Renal Transplant	Allogeneic Renal Transplant	Rheumatoid Arthritis				

#### **Cell Therapy Strategy**

#### CURRENT

- Seeks to provide potential proof-of-concept for CAR-Treg cell therapy
- Aims to establish key manufacturing and 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

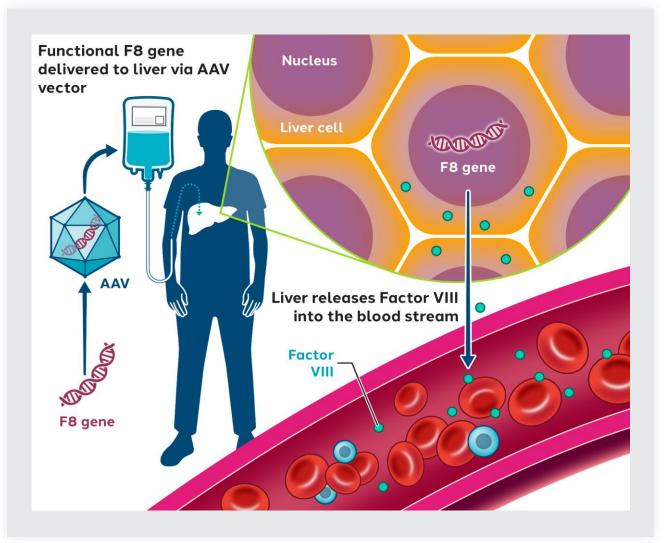


# Hemophilia A

(giroctocogene fitelparvovec)



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



#### The patient promise: Our goals for giroctocogene 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.

### Dosing to support primary analysis of AFFINE is now complete

A pivotal readout is expected in 1H 2024. BLA and MAA submissions 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\*\*



# 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



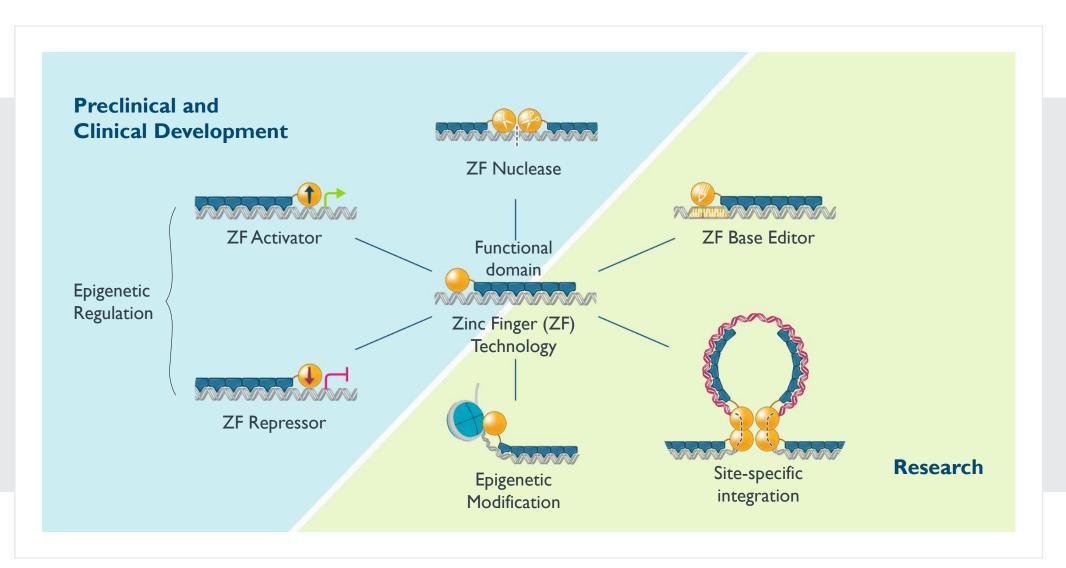
#### Compact

Improved delivery vector compatibility and genome accessibility



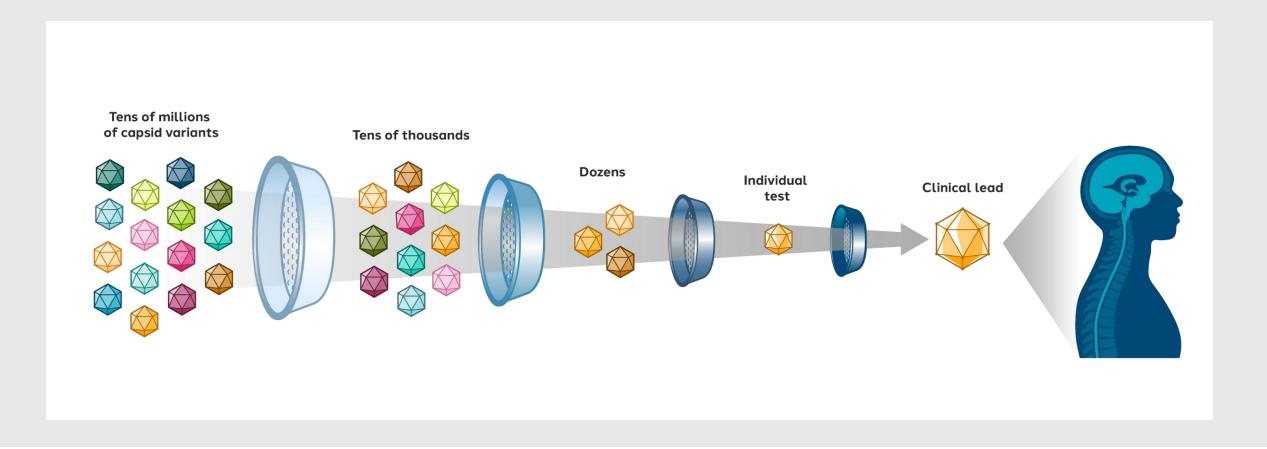


# A diverse set of functional domains can be appended to the ZF platform





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





# **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**

Social

### Governance

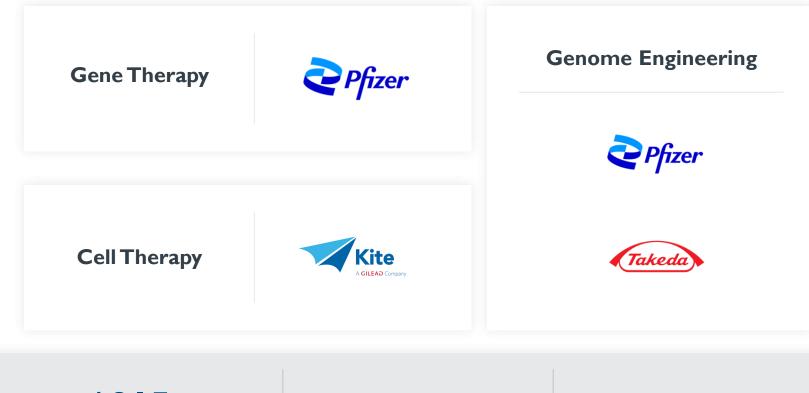
• Sangamo's headquarters in Brisbane is LEED certified, meaning it meets the requirements of a green building set by the U.S. Green Building Council

- Diversity, Equity and Inclusion (DEI) working group continues to advance internal initiatives
- Instituted DEI metrics to better track diversity initiatives and results
- Focus on DEI in recruitment and retention

- Majority independent Board oversees risk and strategy
- Separate Chair and CEO
- Three new independent directors added in the last three years
- Board is 29% female and 14% from underrepresented communities



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



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

\$815m cash received from partners to date Up to \$3.7b in potential future milestones Additional potential royalties

Promotes optimal resource allocation to advance late-stage clinical development

