Fabry Disease: Preliminary Data Readout for Isaralgagene Civaparvovec (ST-920)

Data cutoff September 17, 2021

Forward-Looking Statements

This presentation contains forward-looking statements regarding our current expectations. These forward-looking statements include, without limitation, statements relating to the therapeutic potential of isaralgagene civaparvovec (ST-920), including its potential clinical benefit to patients with Fabry disease, plans and timelines for screening, enrolling and dosing patients in the Phase 1/2 STAAR clinical study, plans and timelines for conducting a Phase 3 clinical trial of isaralgagene civaparvovec, 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, the uncertain timing and unpredictable nature of clinical trials and clinical trial results, including the risks that therapeutic effects observed in preliminary clinical trial results will not be durable in patients and that final Phase 1/2 STAAR study data will not validate the safety and efficacy of isaralgagene civaparvovec; reliance on results of early clinical trials, such as the Phase 1/2 STAAR study, which results are not necessarily predictive of future clinical trial results, including the results of any Phase 3 trial of isaralgagene civaparvovec; risks and uncertainties related to the evolving COVID-19 pandemic and its impact on the global business environment, healthcare systems and our business and operations, including the initiation and operation of clinical trials; the research and development process; 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; and the uncertainty of our future capital requirements, financial performance and results. There can be no assurance that we 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 year ended December 31, 2020 as supplemented by our Quarterly Report on Form 10-Q ended September 30, 2021. 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 an investigational product candidate that is under clinical investigation and which has not yet been approved for marketing by any regulatory agency. It is currently limited to investigational use, and no representations are made as to its safety or efficacy for the purposes for which it is 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. The information contained in this presentation is as of November 4, 2021, and Sangamo undertakes no duty to update forward-looking statements contained in this presentation except as required by applicable laws.

Executive Summary

- Isaralgagene civaparvovec (ST-920) was generally well tolerated; no treatment-related adverse events higher than Grade 1 occurred
- All four patients treated in the first two dose cohorts are exhibiting above-normal and sustained α-Gal A activity which was maintained for up to one year for the first patient treated
- The first 3 patients dosed all reported improvements in ability to sweat
- Investigators withdrew Patient 4 from ERT and are planning to withdraw Patient 1 based on the stability of their α-Gal A activity following treatment
- The fifth patient has been dosed, in Cohort 3, and the sixth patient is in screening
- Based on these data, Phase 3 planning has been initiated

Cutoff date: September 17, 2021

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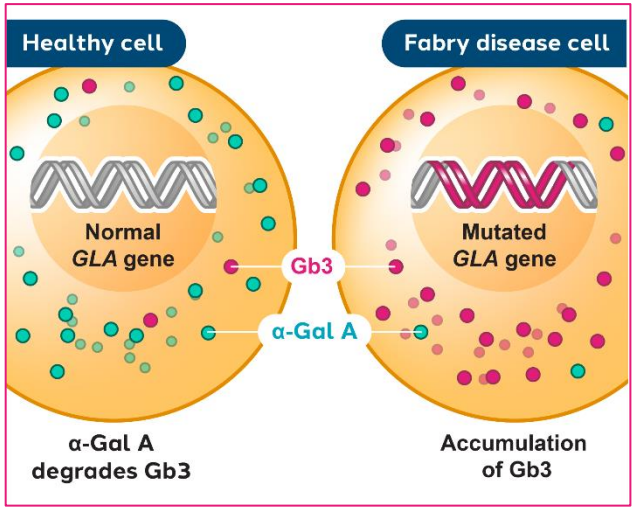
Fabry Disease Overview

Mechanism of disease and biomarkers



Clinical biomarkers:
α-Gal A activity, lyso-Gb3

Organs and systems impacted

Kidney
Progressive kidney disease

Cardiovascular
Heart failure, strokes/TIA

Skin
Rashes, temperature sensitivity, abnormal sweating

Neuropathic pain
Burning/tingling commonly in extremities

Other
GI disturbances, hearing loss, vision problems, mood disorders

Reduced patient quality of life

Physical health impacts

- Chronic pain
- Shortened lifespan
- Inability/difficulty performing normal daily activities
- Temperature intolerance due to inability to sweat

Mental health impacts

- Depression and anxiety
- Change in sleep patterns
- Social functioning

α-Gal A, alpha-galactosidase A; Gb3, globotriaosylceramide; GI, gastrointestinal; GLA, galactosidase alpha; lyso-Gb3, globotriaosylsphingosine; TIA, transient ischemic attack.

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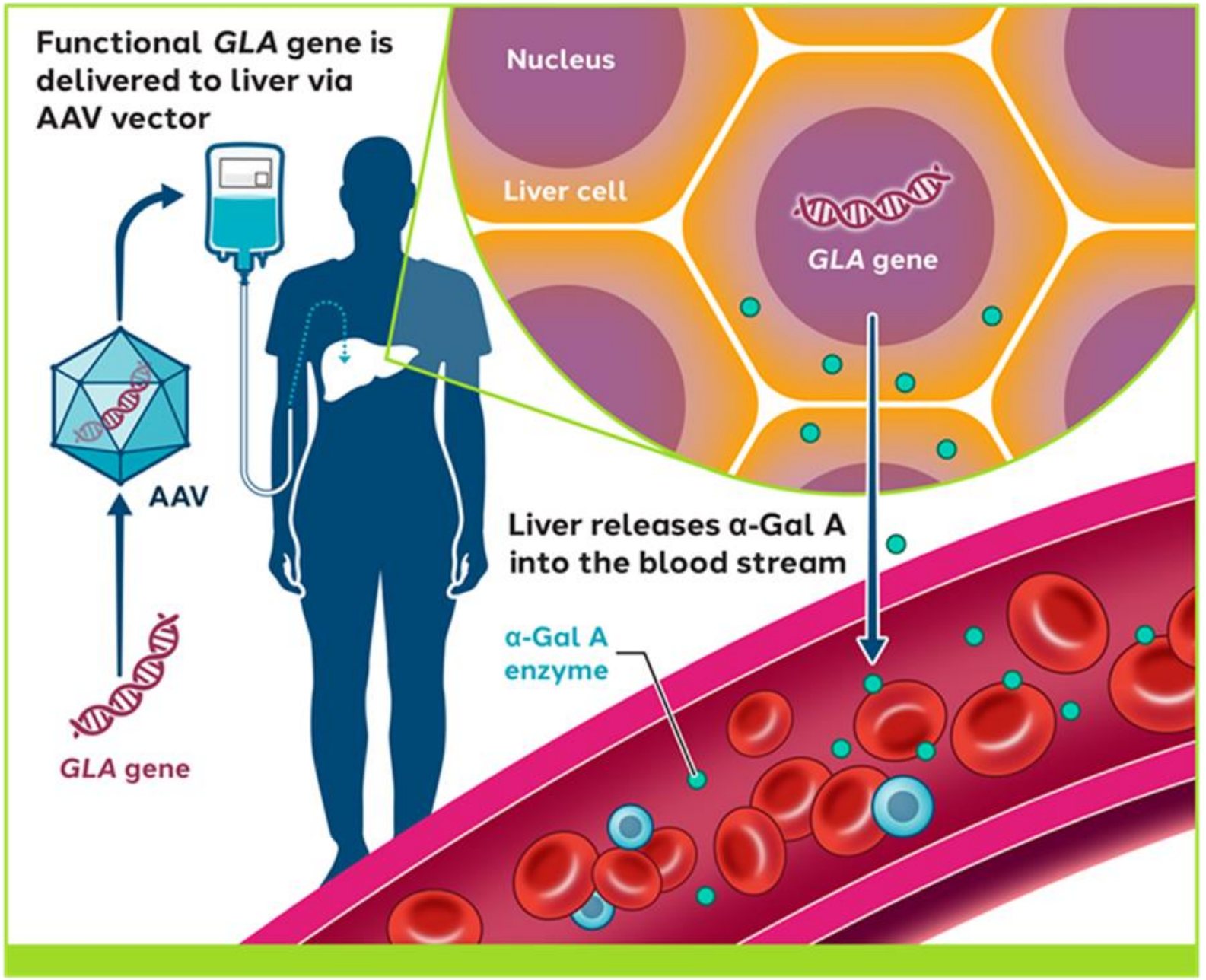
ST-920: One-time, Liver-directed Gene Therapy Candidate for the Treatment of Fabry Disease



AAV, adeno-associated virus.

Goals of Treatment With Isaralgagene Civaparvovec (ST-920)

A one-time infusion, without the need for preconditioning

Deliver long-lasting improvement of symptoms most important to patients

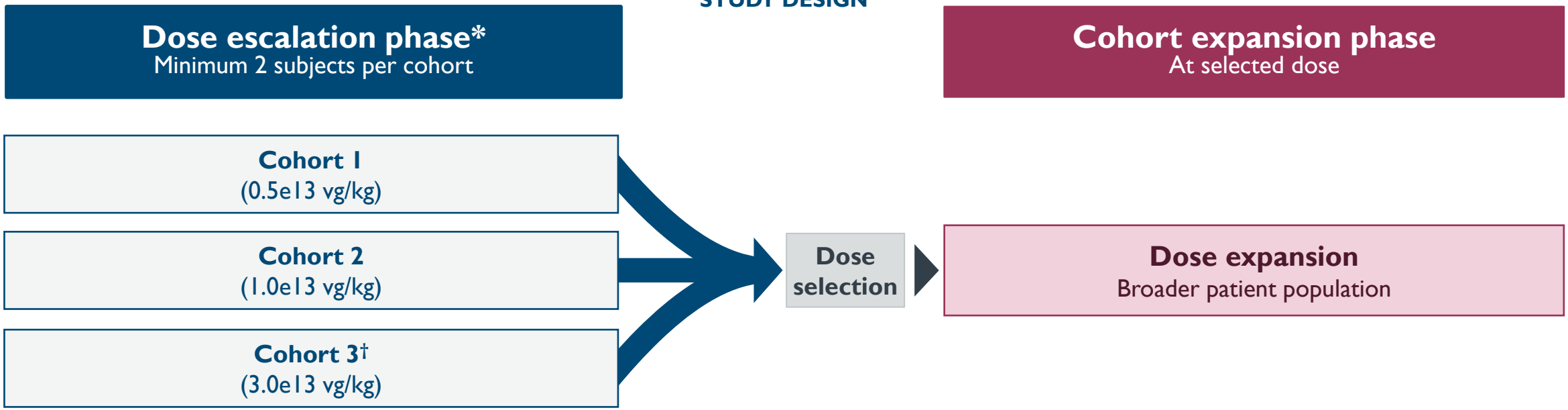
Eliminate the need for biweekly ERT infusions

Phase 1/2 STAAR Study Design and Objectives

STAAR

A Phase 1/2, global, open-label, single-dose, dose-ranging multicenter study to assess the safety and tolerability of ST-920, an AAV2/6 human α-Gal A gene therapy in patients with Fabry disease

STUDY DESIGN



*Safety and efficacy data of each cohort were reviewed by an independent safety monitoring committee prior to dose escalation.
†Protocol supports an additional cohort at a higher dose level, if required.

ENTRY CRITERIA

- Patients ≥18 years of age with Fabry disease
- On ERT regimen, or ERT-naïve, or ERT-pseudo-naïve (no ERT treatment in the prior six months)

PRIMARY OBJECTIVE

- Assess safety and tolerability of ST-920

SECONDARY OBJECTIVES

- Assess α-Gal A activity and the presence of its substrates in plasma over time
- Assess impact of ST-920 on ERT administration required for subjects on ERT
- Assess impact of ST-920 on renal and cardiac function
- Assess clinical impact of ST-920 on Fabry disease (including QoL)

ERT, enzyme replacement therapy; QoL, quality of life.

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Phase 1/2 STAAR Study: Baseline Patient Characteristics

	Cohort 1 (n=2) 0.5e13 vg/kg		Cohort 2 (n=2) 1.0e13 vg/kg	
	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)	48	25	42	22
On ERT	Yes	No; pseudo-naïve	No; pseudo-naïve	Yes
Plasma α-Gal A activity (nmol/h/mL)*	1.54	0.92	Below LOQ	2.44
Plasma lyso-Gb3 (ng/mL)*	22.1	18.1	83.2	11.1
Primary disease signs and symptoms	• Reduced ability to sweat • Tinnitus and vertigo • Left ventricular hypertrophy • Palpitations • Anemia	• Inability to sweat • Tinnitus • Acroparesthesia† • Sinus bradycardia • Left ventricular hypertrophy	• Reduced ability to sweat • Tinnitus and vertigo • Acroparesthesia† • ECG sinus arrhythmia	• Neuropathic pain • Aortic root dilation • Decreased libido
Renal function (eGFR)*,‡	101.4	111.4	112.9	100
Pre-existing α-Gal A Abs	Positive	Negative	Positive	Positive
Mutation	G621D	C422T	W340R	S297Y

All patients had classic Fabry disease.

Ab, antibody; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; LOQ, limit of quantitation.
*Baseline values were considered the time point immediately preceding ST-920 administration.
†Burning, tingling, or numbness in the extremities.
‡eGFR (mL/min/1.73 m^2) was calculated using the CKD-EPI.

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Phase 1/2 STAAR Study: Safety and Tolerability

MedDRA Preferred Term	Cohort 1 (0.5e13 vg/kg) (n=2)		Cohort 2 (1.0e13 vg/kg) (n=2)		Overall (N=4)	
	n	Events	n	Events	n	Events
Treatment-related adverse events (total)	**1**	**3**	**1**	**2**	**2**	**5**
Hemoglobin decreased	1	1	0	0	1	1
Platelet count increased	1	1	0	0	1	1
Rash	1	1	0	0	1	1
Pyrexia	0	0	1	2	1	2

Safety data were evaluated from the 4 patients in the first 2 dose cohorts (0.5e13 vg/kg and 1.0e13 vg/kg) as of the cutoff date of September 17, 2021.

Isaralgagene civaparvovec (ST-920) was generally well tolerated

No liver enzyme elevations requiring steroid treatment

No treatment-related serious adverse events were reported

All treatment-related adverse events were Grade 1 (mild)

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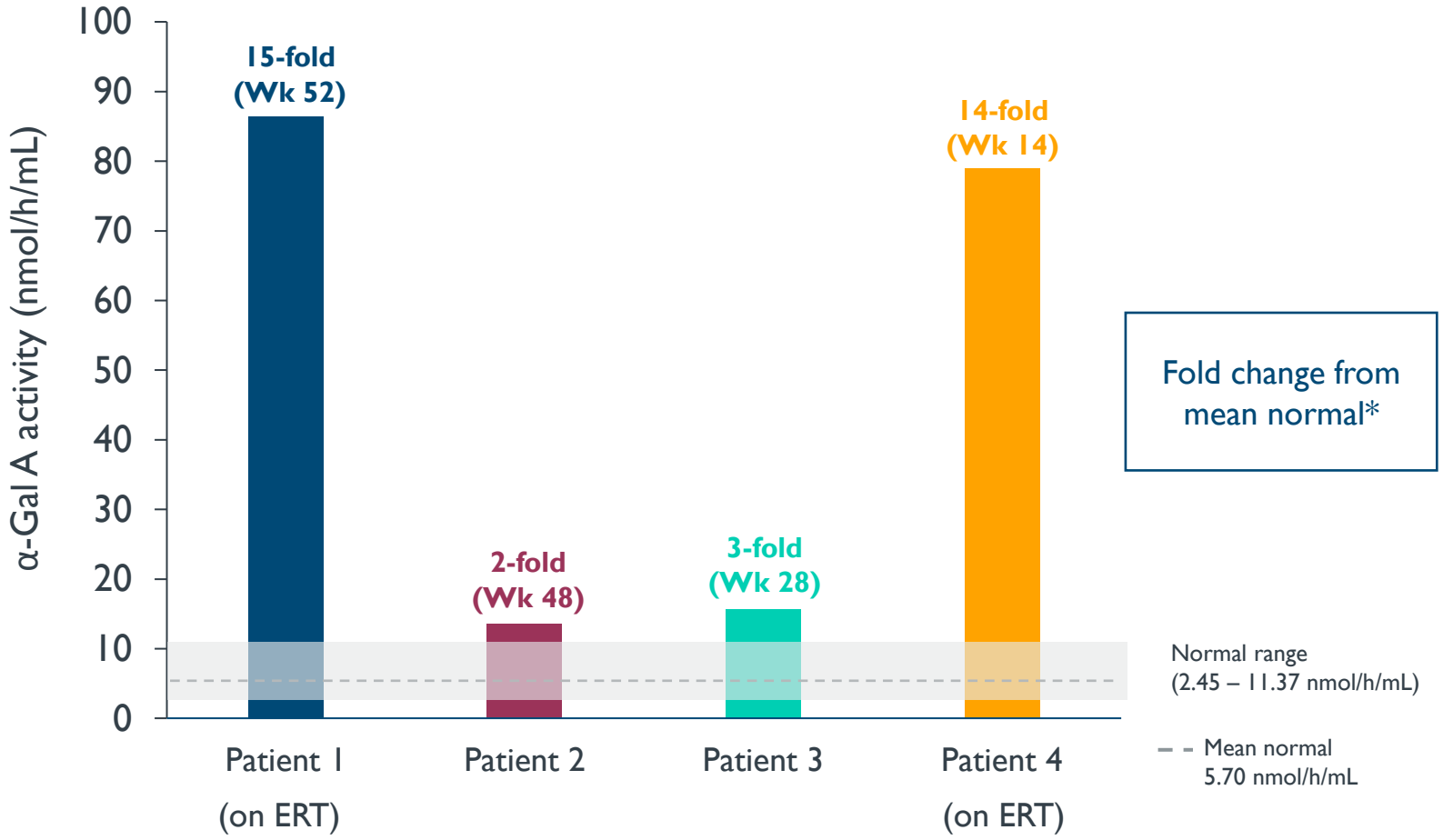
Phase 1/2 STAAR Study: Plasma α-Gal A Activity



Biomarker results were evaluated from the 4 patients in the first 2 dose cohorts (0.5e13 vg/kg and 1.0e13 vg/kg) as of the cutoff date of September 17, 2021.

*Fold change was calculated at last measured time point. α-Gal A activity was measured using a 3-hour reaction time and presented in nmol/h/mL. For Patients 1 and 4 this was sampled at ERT trough. Normal range and mean were determined based on healthy male individuals.

Elevated α-Gal A activity was maintained through the last sampling point for all patients: up to 1 year for the first patient treated and up to Week 14 for the fourth patient dosed

All subjects are exhibiting above-normal α-Gal A activity

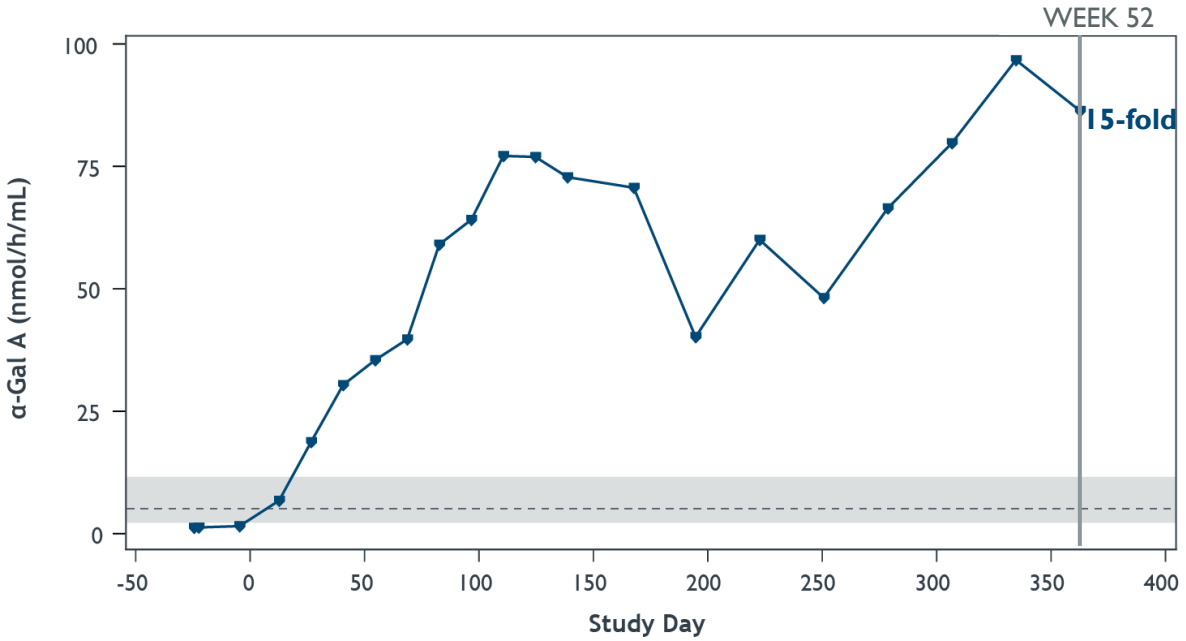
- Activity of 2-fold to15-fold above mean normal has been observed at last measured timepoint

Patient 4 was withdrawn from ERT, withdrawal is planned for Patient 1

Patient 1: Plasma α-Gal A Activity and Lyso-Gb3

Patient was on ERT and was anti–α-Gal A antibody positive

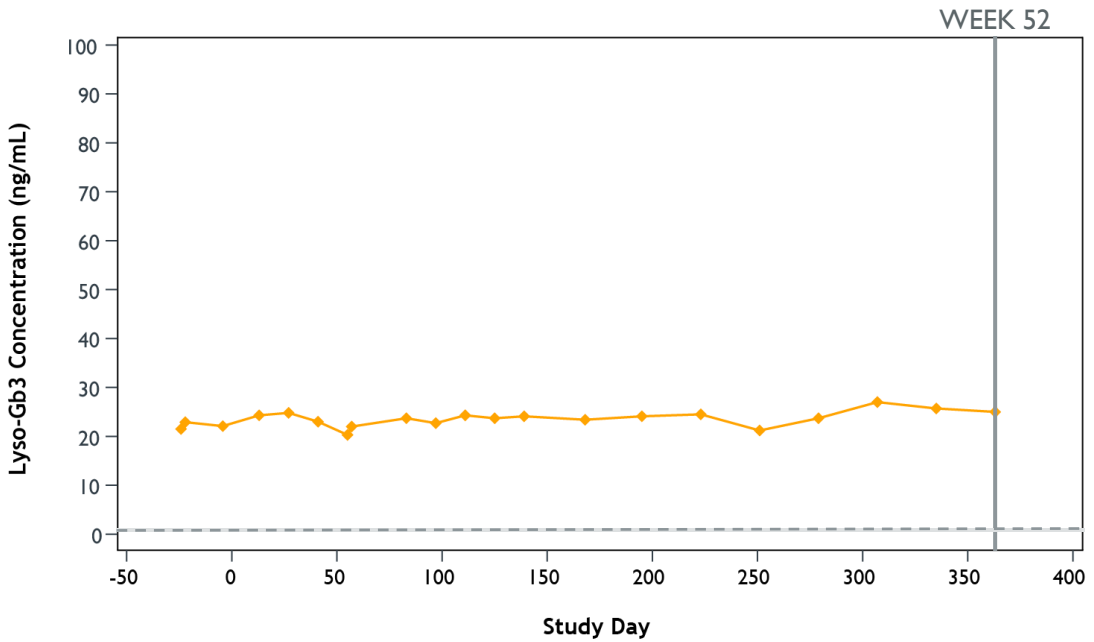
α-Gal A Activity*



Normal range (2.45 – 11.37 nmol/h/mL)†

Mean normal (5.70 nmol/h/mL)

Lyso-Gb3*



Normal range (0.323 – 0.625 ng/mL)†

Mean normal (0.473 ng/mL)

- Patient exhibiting above-normal α-Gal A activity that was sustained for 1 year
- Low baseline levels of plasma lyso-Gb3 remained steady over time
- Patient reported improvements in leg edema and ability to sweat
- Principal investigator noted stabilization of cardiac structure on serial assessments

*Only data from ERT trough sample collections (every 2 weeks pre ERT dosing) are shown.

†Normal range and mean were determined based on healthy male individuals.

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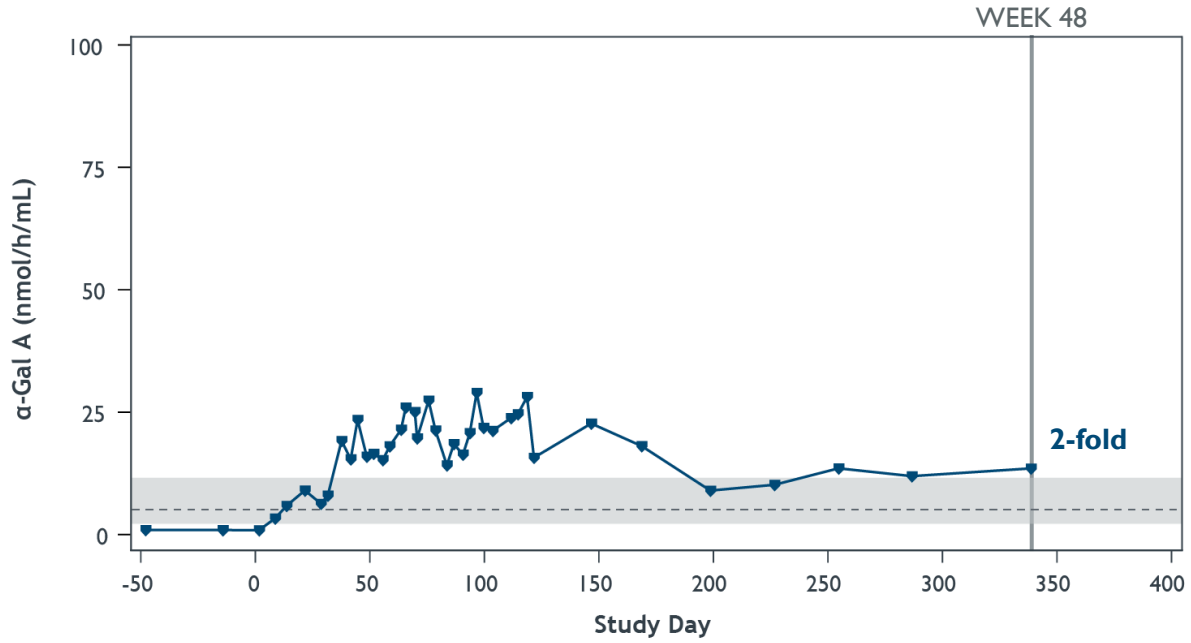
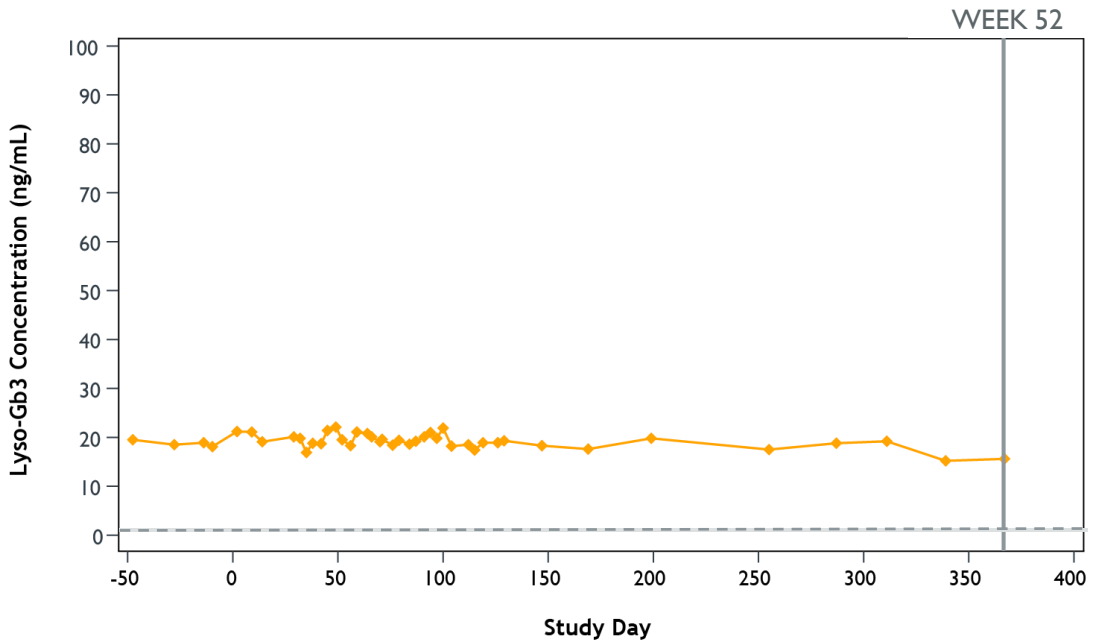
Patient 2: Plasma α-Gal A Activity and Lyso-Gb3

Patient was not on ERT (pseudo-naïve) and was anti–α-Gal A antibody negative

α-Gal A Activity



Lyso-Gb3



- Patient exhibiting above-normal α-Gal A activity that sustained through 48 weeks
- Low baseline levels of plasma lyso-Gb3 remained steady over time
- Patient reported improvement in ability to sweat

*Normal range and mean were determined based on healthy male individuals.

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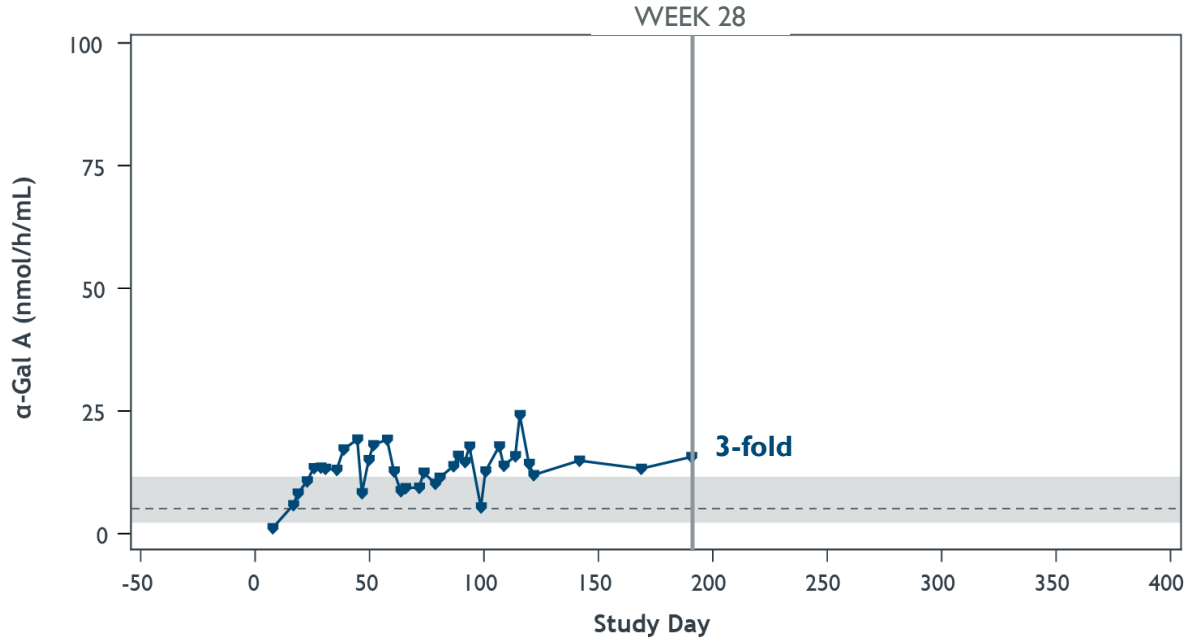
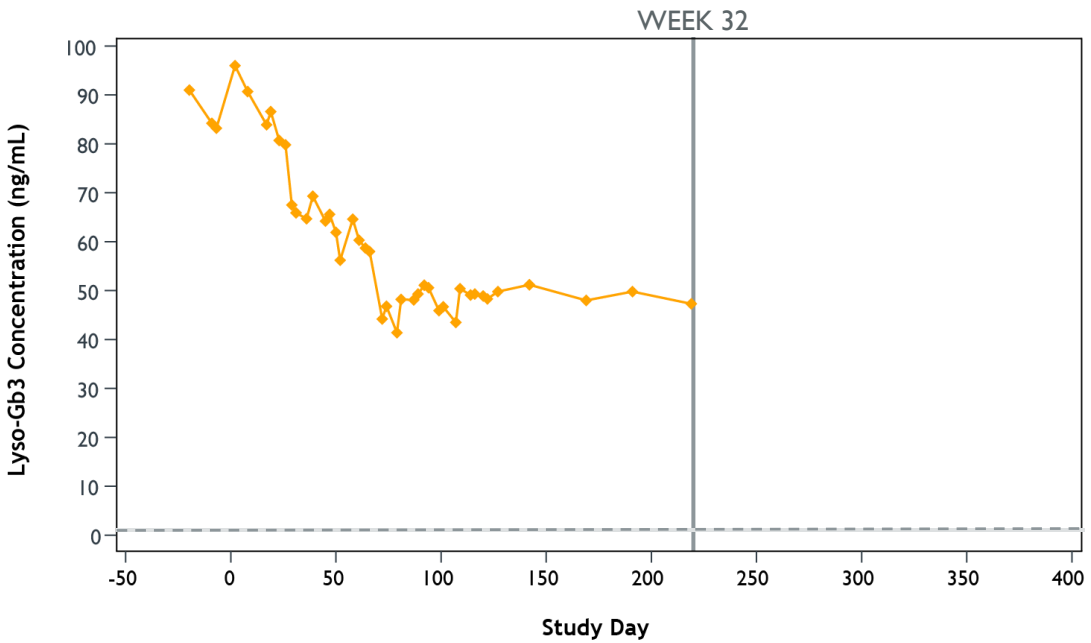
Patient 3: Plasma α-Gal A Activity and Lyso-Gb3

Patient was not on ERT (pseudo-naïve) and was anti–α-Gal A antibody positive

α-Gal A Activity



Lyso-Gb3



- Patient exhibiting above-normal α-Gal A activity that was sustained up to the last measured point at week 28
- Patient's plasma lyso-Gb3 levels were elevated at baseline
- Patient showed ~40% reduction in plasma lyso-Gb3 from baseline within 10 weeks after dosing, maintained through Week 32
- Patient reported improvement in ability to sweat

*Normal range and mean were determined based on healthy male individuals.

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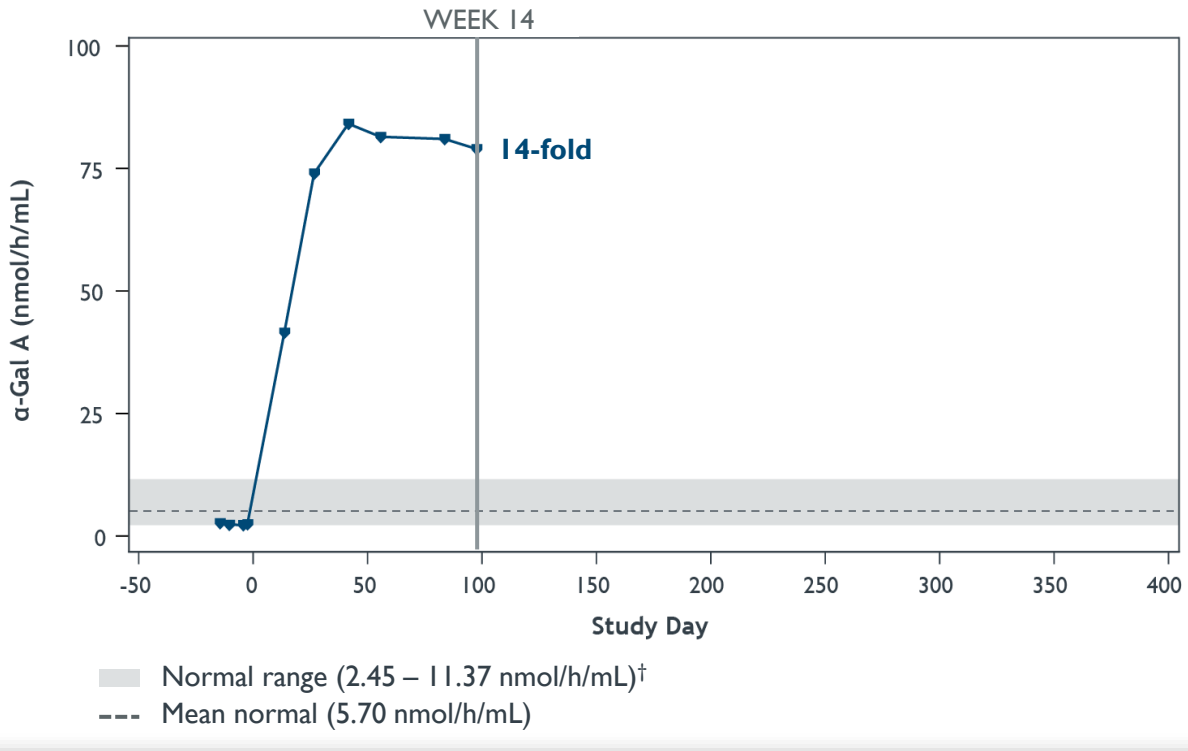
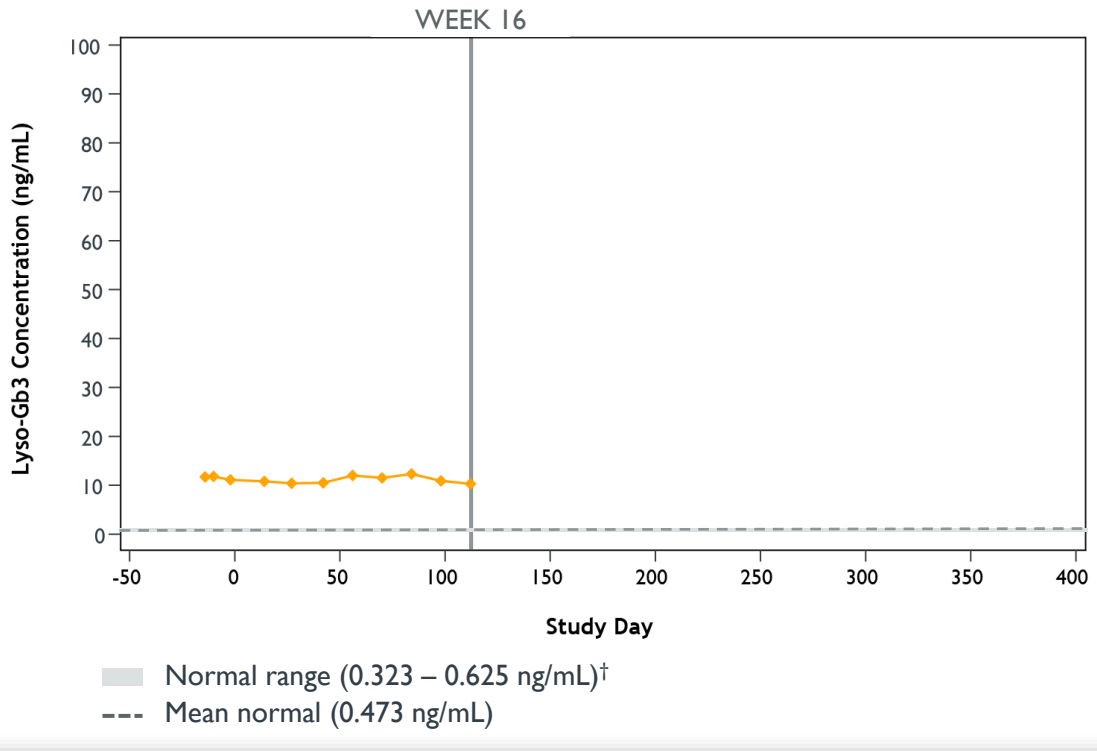
Patient 4: Plasma α-Gal A Activity and Lyso-Gb3

Patient was on ERT and was anti–α-Gal A antibody positive

α-Gal A Activity*



Lyso-Gb3*



- Patient exhibiting above-normal α-Gal A activity that sustained through 14 weeks
- Low baseline levels of plasma lyso-Gb3 remained steady over time
- Patient was withdrawn from ERT after the cutoff date

*Only data from ERT trough sample collections (every 2 weeks pre ERT dosing) are shown.
†Normal range and mean were determined based on healthy male individuals.

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Conclusions

- Isaralgagene civaparvovec (ST-920) was generally well tolerated
- No treatment-related adverse events higher than Grade 1 occurred
- All subjects are exhibiting above-normal and sustained α-Gal A activity
- Elevated α-Gal A activity was maintained through the last sampling point for all patients: up to 1 year for the first patient treated and up to Week 14 for the fourth patient dosed
- Patient with significant elevation in plasma lyso-Gb3 pre-treatment showed significant reduction after treatment
- Patients with low baseline levels of plasma lyso-Gb3 maintained steady levels through latest follow-up date
- The first 3 patients dosed all reported improvements in ability to sweat

Program Anticipated Next Steps

- Patients 1 and 2 have enrolled in the long-term follow-up study
- Patient 4 was withdrawn from ERT, withdrawal is planned for Patient 1
- 5th patient, in Cohort 3, was successfully dosed,
- 6th patient is in screening for potential dosing in Cohort 3
- Phase 1/2 results will continue to be updated in 2022 including being presented at a medical meeting
- Based on these data, Phase 3 planning has been initiated

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Thank you to the patients, families, and investigators for their participation in this study.