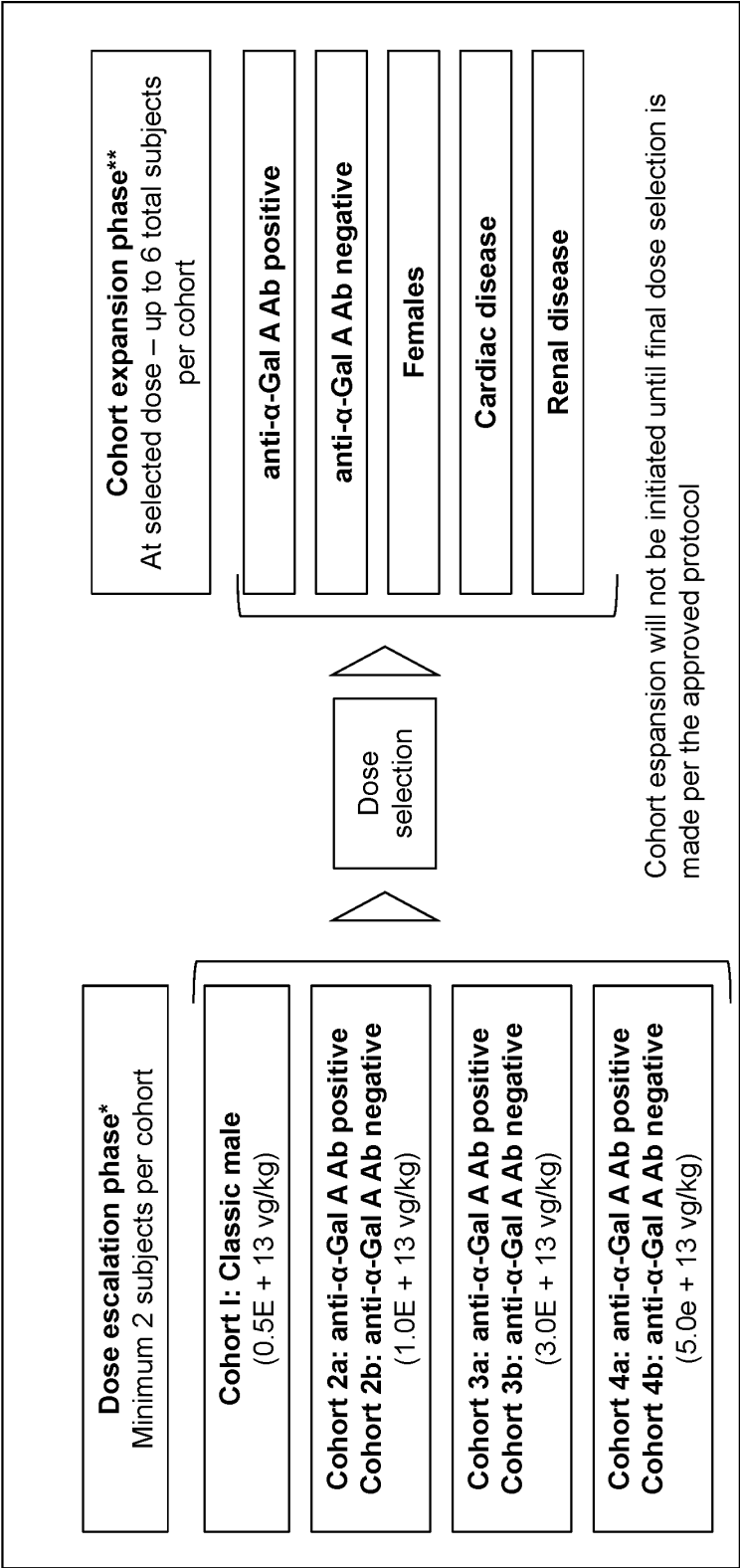


FIG. 1

Phase 1/2 STAAR Study Design and Objectives



* Safety and efficacy data of each cohort was/will be reviewed by a safety monitoring committee (SMC) prior to dose escalation.
** The dose for the expansion cohorts may be reassessed if there are emerging safety considerations

FIG. 2

Phase 1/2 STAAR Study: Baseline Patient Characteristics

	Cohort 1 (n=2) 0.5e13 vg/kg		Cohort 2 (n=2) 1.0e13 vg/kg		Cohort 3 (n=3) 3.0e13 vg/kg			Cohort 4 (n=2) 5e13 vg/kg		Expansion (n=1) 5e13 vg/kg
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	
Age (years)	48	25	42	22	39	42	51	49	40	34
On ERT	Yes	No; pseudo-naïve	No; pseudo-naïve	Yes	Yes	Yes	Yes	No (Naïve)	No (Naïve)	No; pseudo-naïve
Plasma α-Gal A activity (nmol/h/mL)	1.54	0.92 (Mosaic)	Below LOQ	2.44	0.85	Below LOQ	Below LOQ	1.9	Below LOQ	Below LOQ
Plasma lyso-Gb3 (ng/mL)*	22.1	18.1	83.2	11.1	32.7	1.91	16.4	16.9	213	169
Primary disease signs and symptoms	• Hypohidrosis • Tinnitus and vertigo • Left ventricular hypertrophy • Palpitations • Anemia • Leg edema	• Anhidrosis • Tinnitus • Acroparesthesia† • Sinus bradycardia • Left ventricular hypertrophy	• Hypohidrosis • Tinnitus and vertigo • Acroparesthesia† • ECG sinus arrhythmia	• Hypohidrosis • Neuropathic pain • Aortic root dilation	• Tinnitus • High frequency hearing loss • Acroparesthesia† • Sinus bradycardia	• Hypohidrosis • Tinnitus • Neuropathic pain • Acroparesthesia	• Depression • Ventricular tachycardia • Hearing loss • Neuropathic pain	• Tinnitus • Mild ventricular hypertrophy • Acroparesthesia	• Mild ventricular wall thickness	• Hearing loss • Tinnitus • Ventricular hypertrophy • Acroparesthesia
Renal function (eGFR)*, ‡	101.4	111.4	112.9	100	91.5	80	76	42	75	116
Pre-existing α-Gal A Abs	Positive (1280)	Negative	Positive (160)	Positive (320)	Positive (20480)	Negative	Negative	Negative	Negative	Positive (80)
Mutation	G261D	C422T	W340R	S297Y	Q283X	D215S	IVS5/c.801+3A>G	P362L	C422T	N34S

Ab= antibody; CKD-EPI= Chronic Kidney Disease Epidemiology Collaboration, eGFR= estimated glomerular filtration rate; LOD= limit of detection.

*Baseline values were considered the timepoint immediately preceding AAV-001 administration.

†Burning, tingling, or numbness in the extremities.

‡ eGFR measured as CKD-EPI (mL/min/1.73m²).

FIG. 3

Phase 1/2 STAAR Study: Safety and Tolerability

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
Any AEs related to AAV-001	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

*There were no AEs leading to study discontinuation, hospitalization, or death.

FIG. 4A

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)		Cohort 3 (3.0e13 vg/kg) (n=1)		Overall (N=5)	
	n	Events	n	Events	n	Events	n	Events
Treatment-related adverse events (total)	1	3	1	2	1	6	3	11
Hemoglobin decreased	1	1	0	0	0	0	1	1
Platelet count increased	1	1	0	0	0	0	1	1
Rash	1	1	0	0	0	0	1	1
Pyrexia	0	0	1	2	1	1	2	3
Headache	0	0	0	0	1	1	1	1
Myalgia	0	0	0	0	1	1	1	1
Fatigue	0	0	0	0	1	1	1	1
Abdominal pain	0	0	0	0	1	1	1	1
Frequent bowel movents	0	0	0	0	1	1	1	1

FIG. 4B

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)		Cohort 3 (3.0e13 vg/kg) (n=1)		Cohort 4 (5.0e13 vg/kg) (n=2)		Overall (N=6)	
	n	Events	n	Events	n	Events			n	Events
Treatment-related adverse events (total)	1	3	1	2	1	6	2	5	5	16
Hemoglobin decreased	1	1	0	0	0	0	0	0	1	1
Platelet count increased	1	1	0	0	0	0	0	0	1	1
Rash	1	1	0	0	0	0	0	0	1	1
Pyrexia	0	0	1	2	1	1	1	1	3	4
Chills	0	0	0	0	0	0	1	1	1	1
Headache	0	0	0	0	1	1	1	1	2	2
Myalgia	0	0	0	0	1	1	0	0	1	1
Arthralgia	0	0	0	0	0	0	1	1	1	1
Fatigue	0	0	0	0	1	1	0	0	1	1
Abdominal pain	0	0	0	0	1	1	0	0	1	1
Frequent bowel movements	0	0	0	0	1	1	0	0	1	1
Diarrhea	0	0	0	0	0	0	1	1	1	1

FIG. 4C

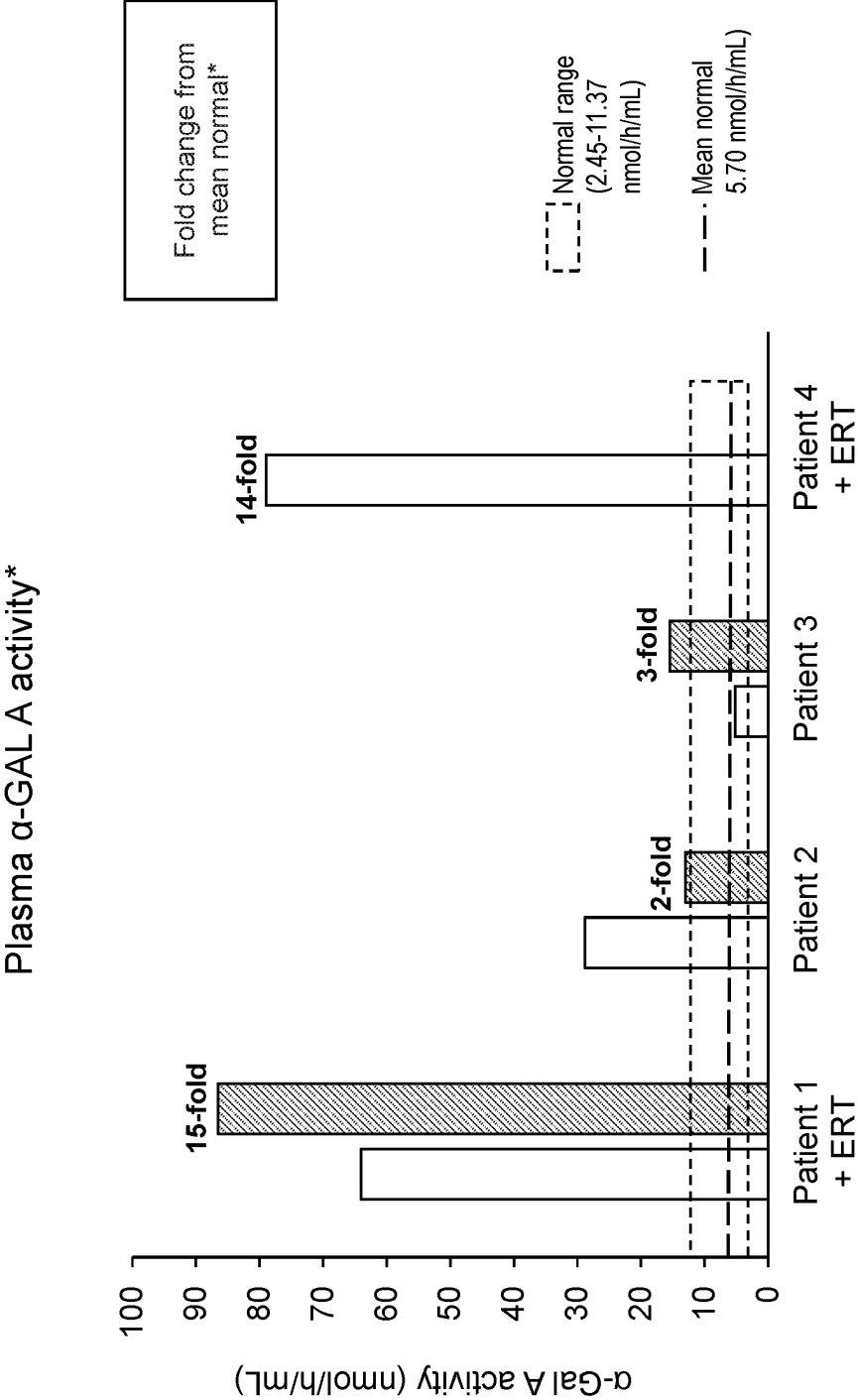
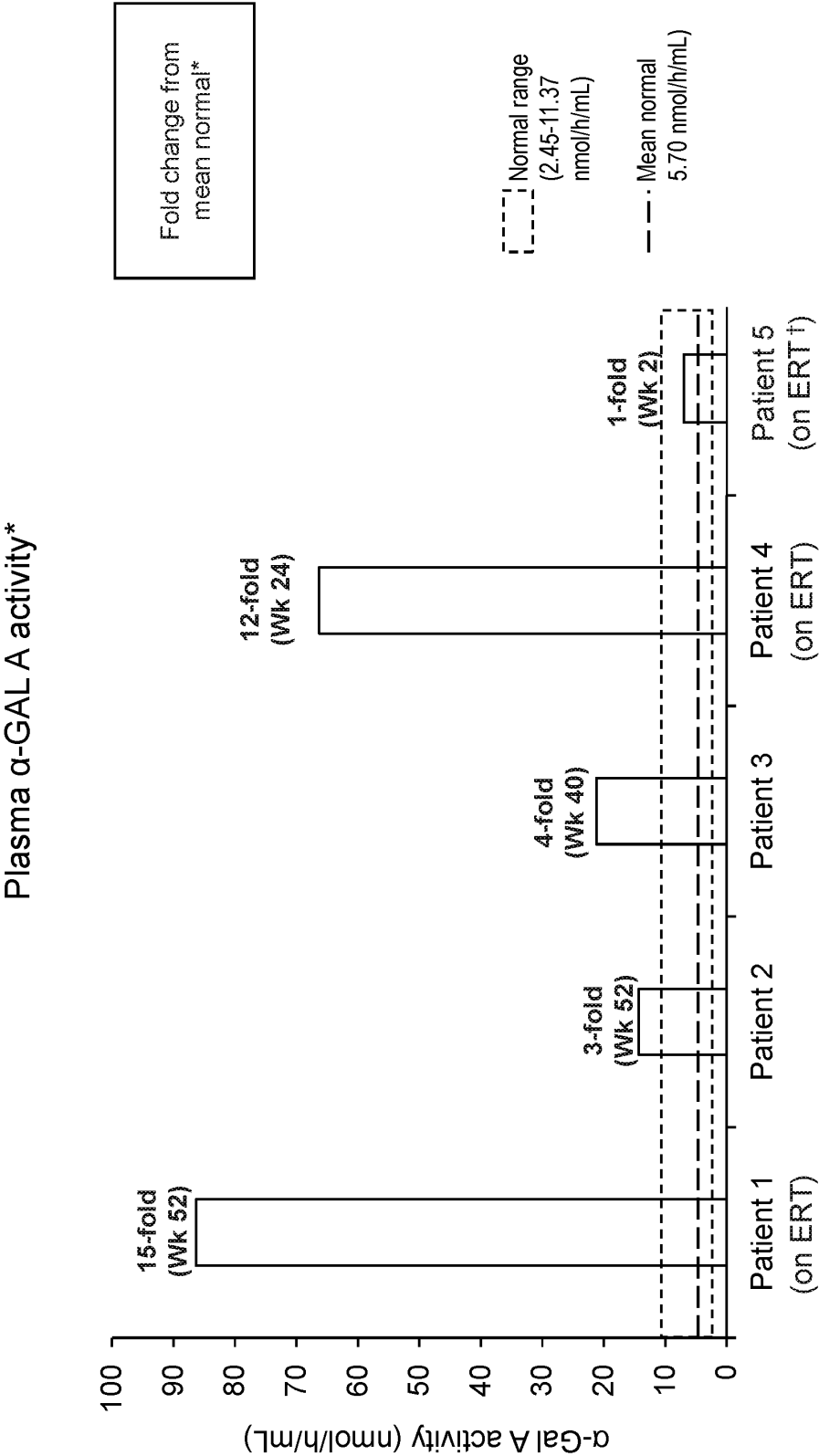


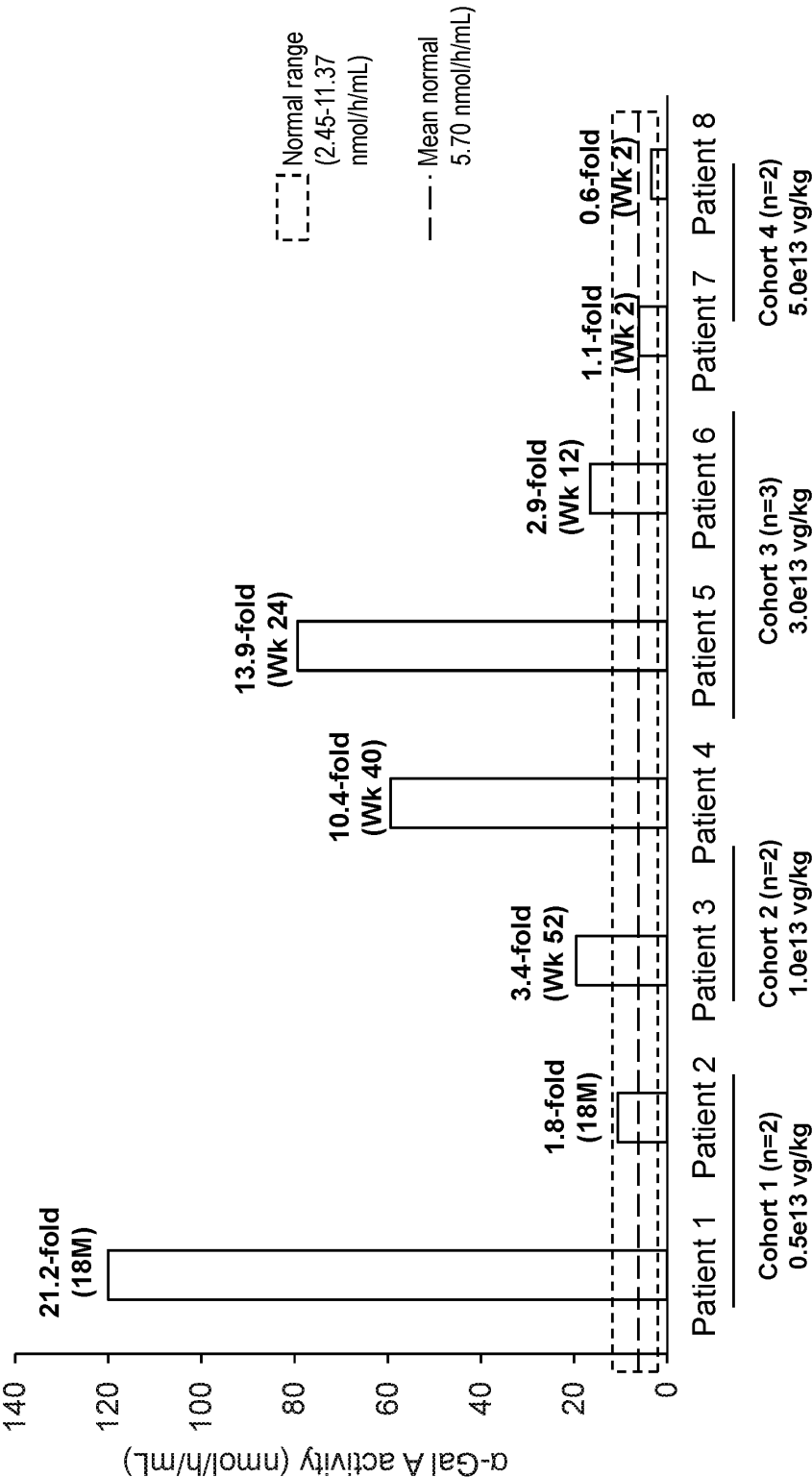
FIG. 5A



[†]Subject was withdrawn from ERT at week 24.

FIG. 5B

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



Biomarker results were evaluated from 9 patients in 4 dose cohorts (0.5e13 vg/kg, 1.0e13 vg/kg, 3.0e vg/kg and 5.0313 vg/kg) as of 19May22/ SMC4 Datacut .

*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 subjects on ERT this was sampled at ERT trough. Normal range and mean were determined based on healthy male individuals.

FIG. 5C

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

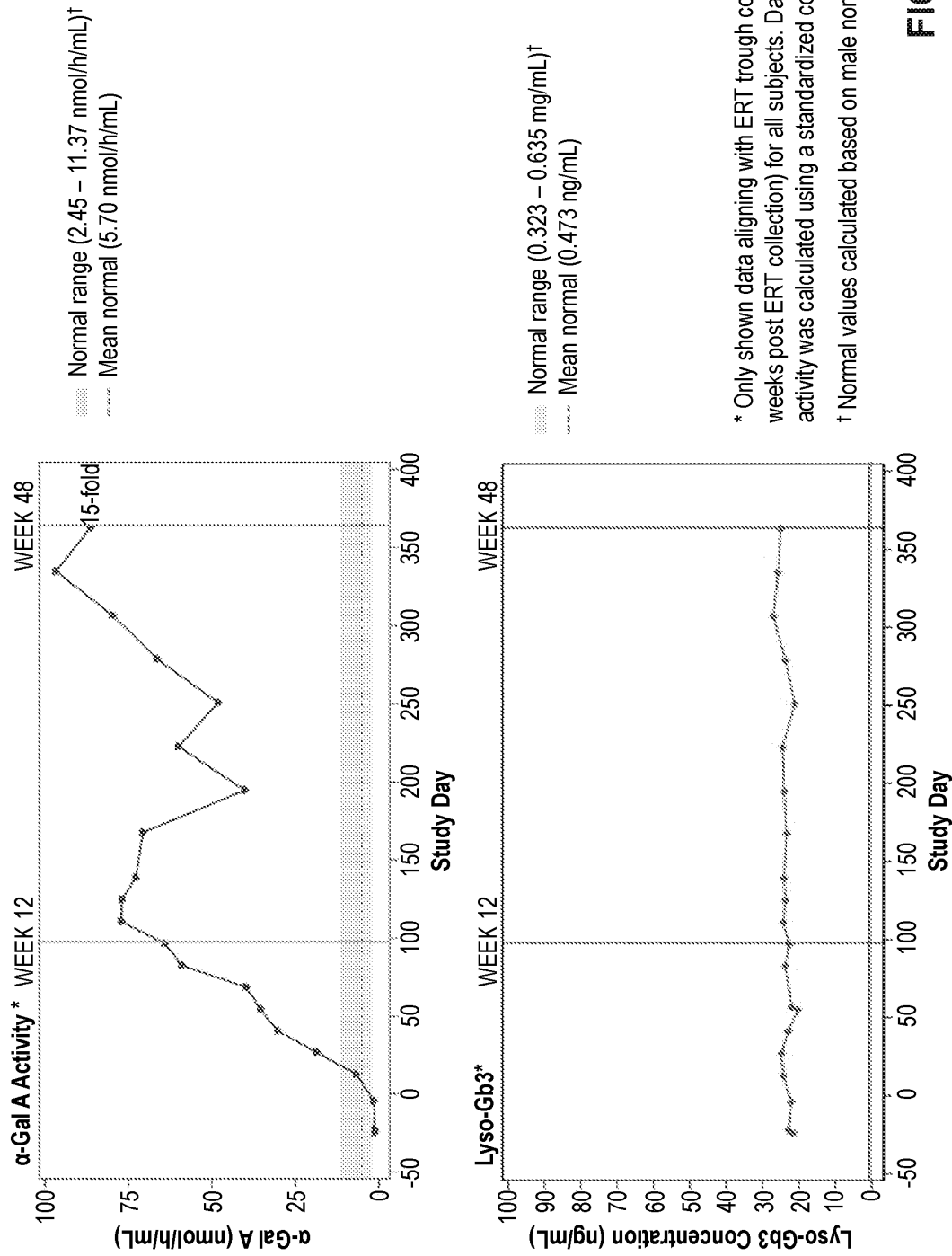
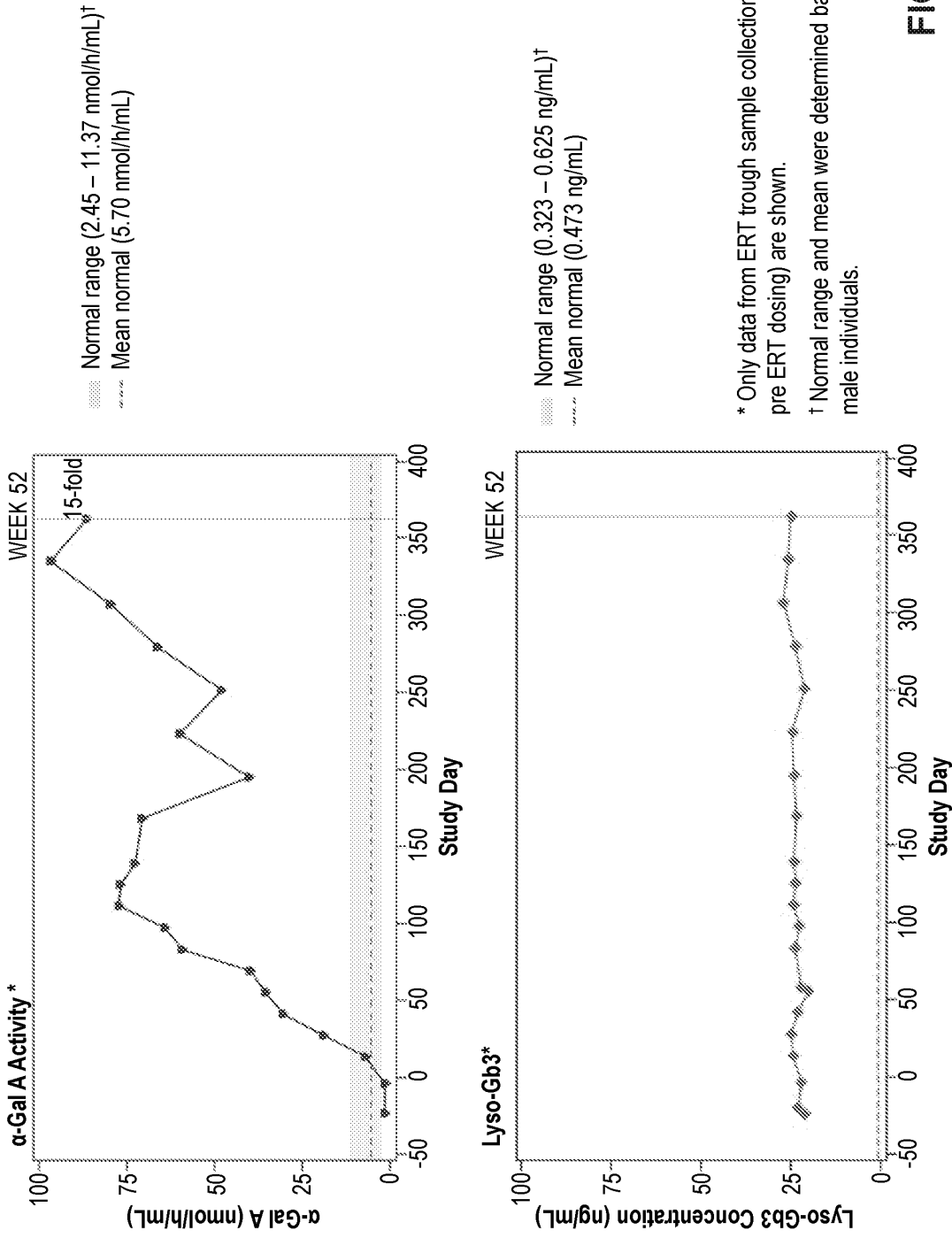


FIG. 6A

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



* 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 1: Plasma A-Gal activity and Lyso-Gb3

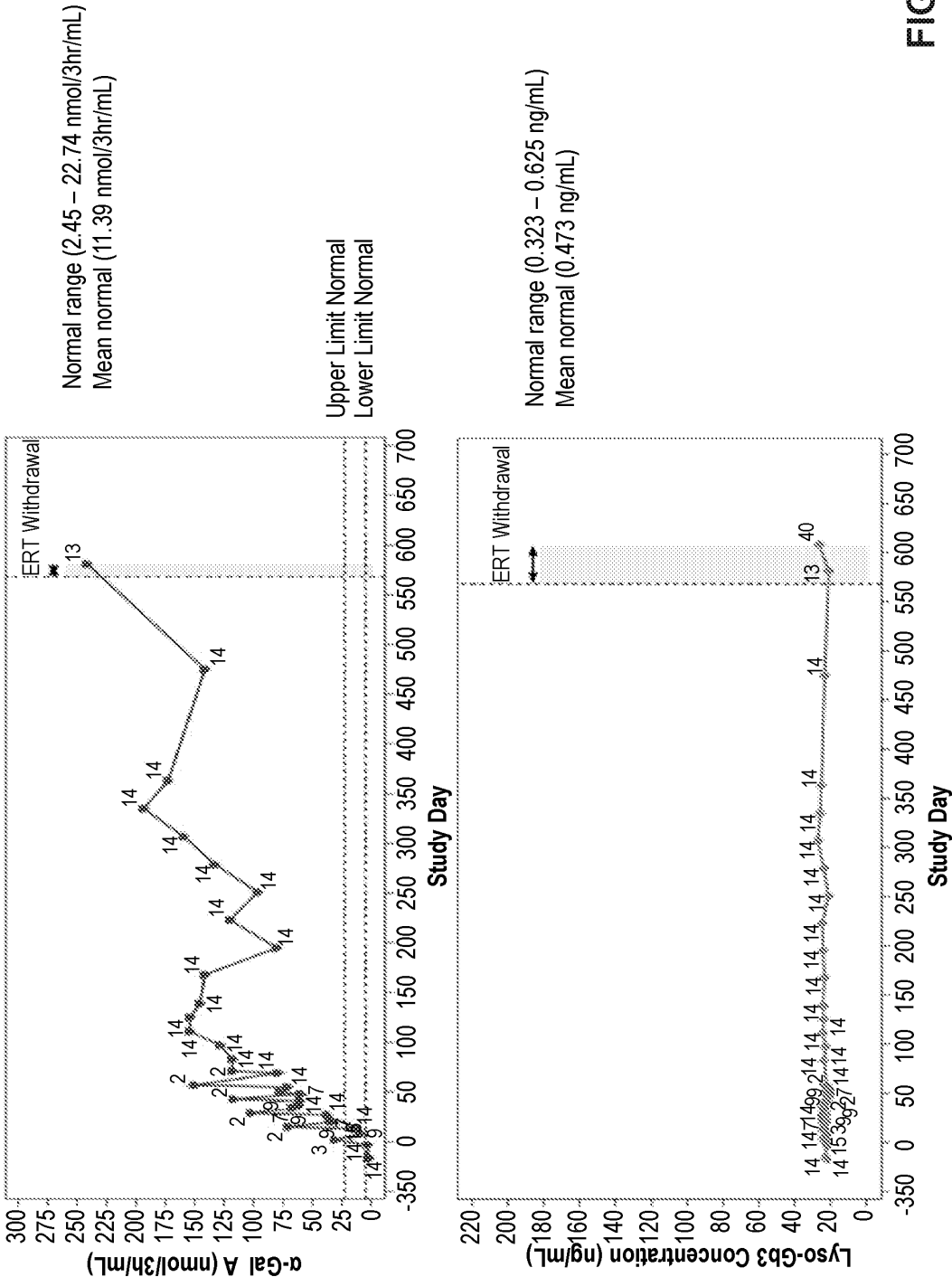
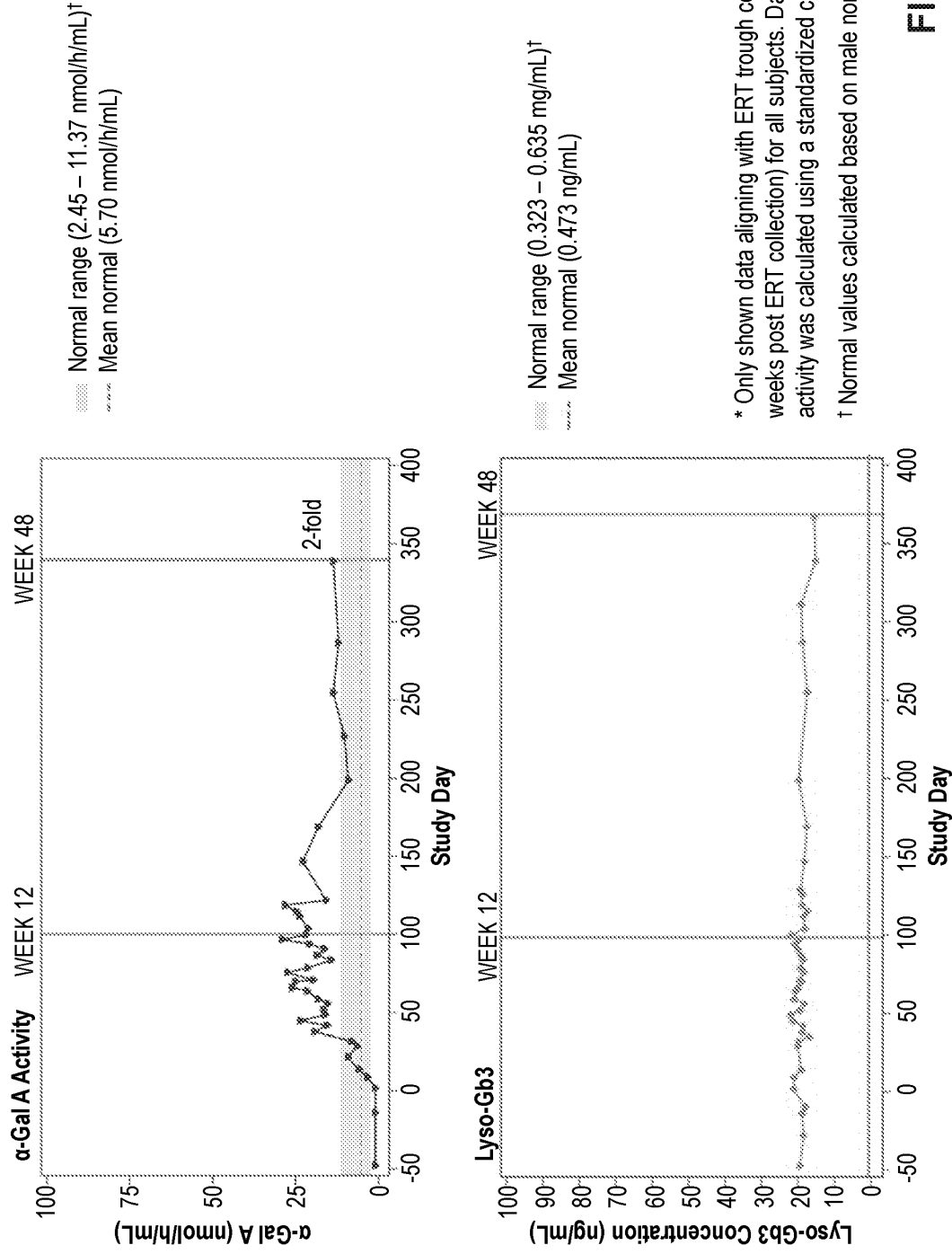


FIG. 6C

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



* Only shown data aligning with ERT trough collections (every 2 weeks post ERT collection) for all subjects. Data for α-Gal A activity was calculated using a standardized conversion factor.

† Normal values calculated based on male normal ranges.

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

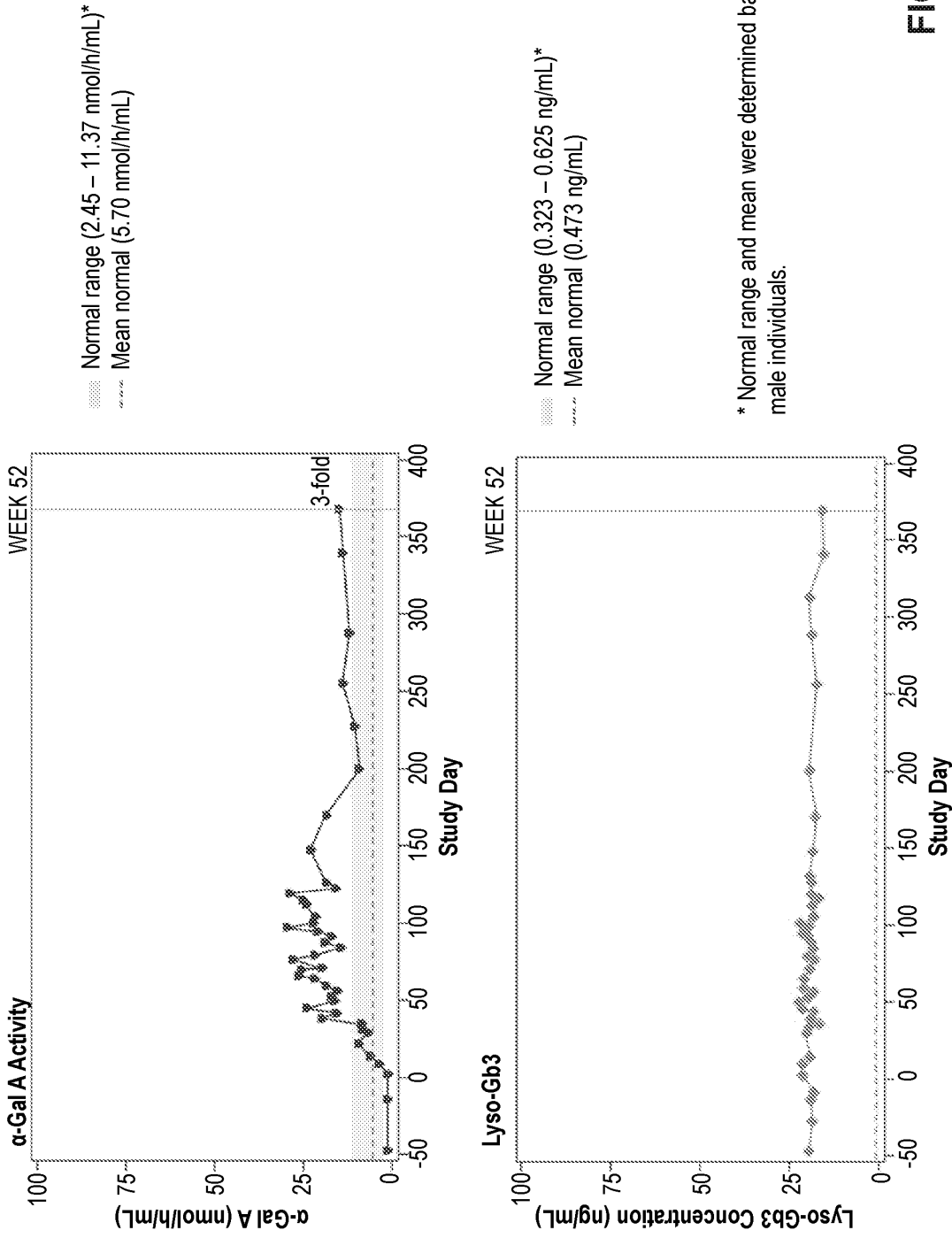


FIG. 6E

Patient 2: Plasma A-Gal activity and Lyso-Gb3

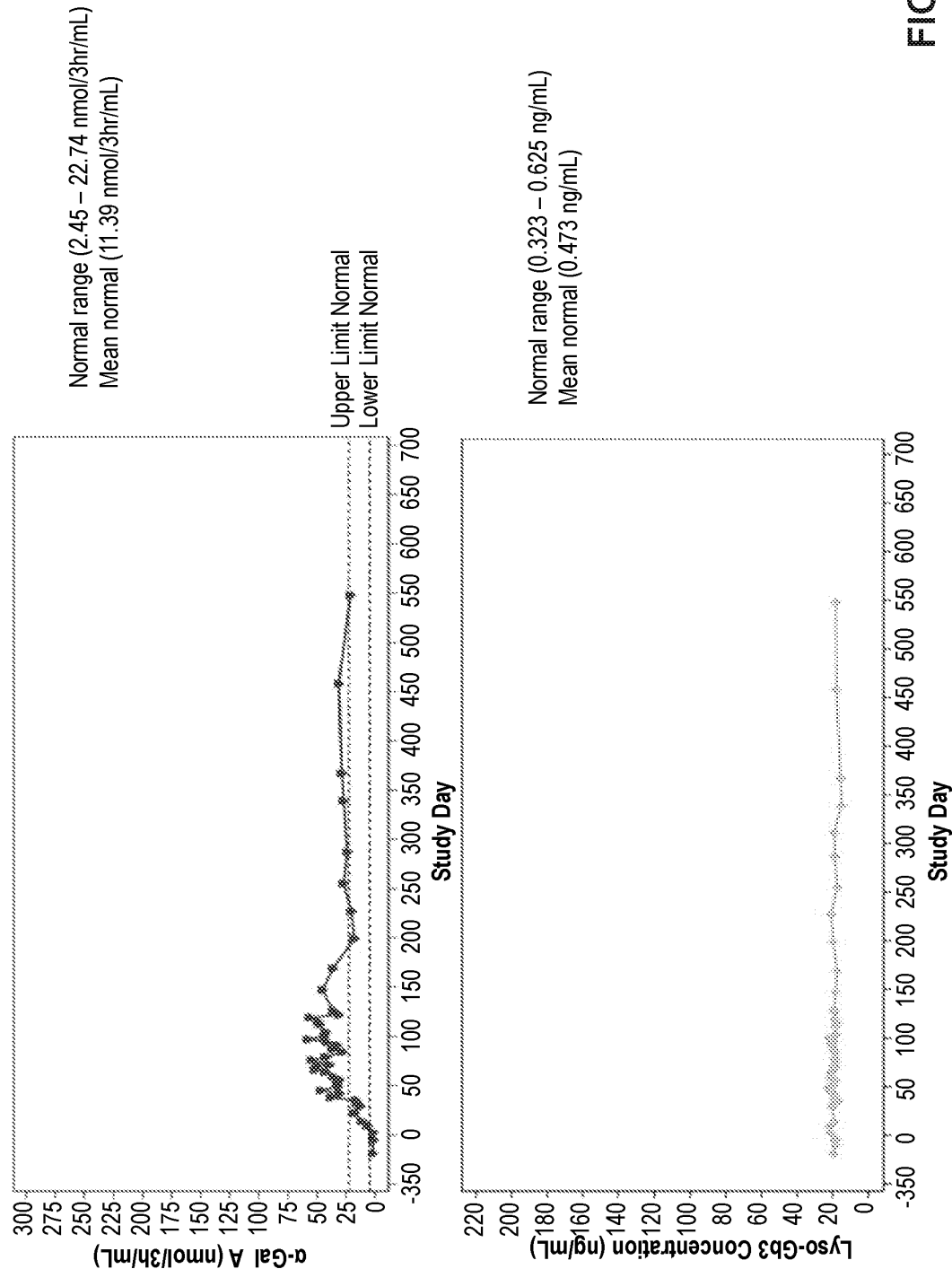
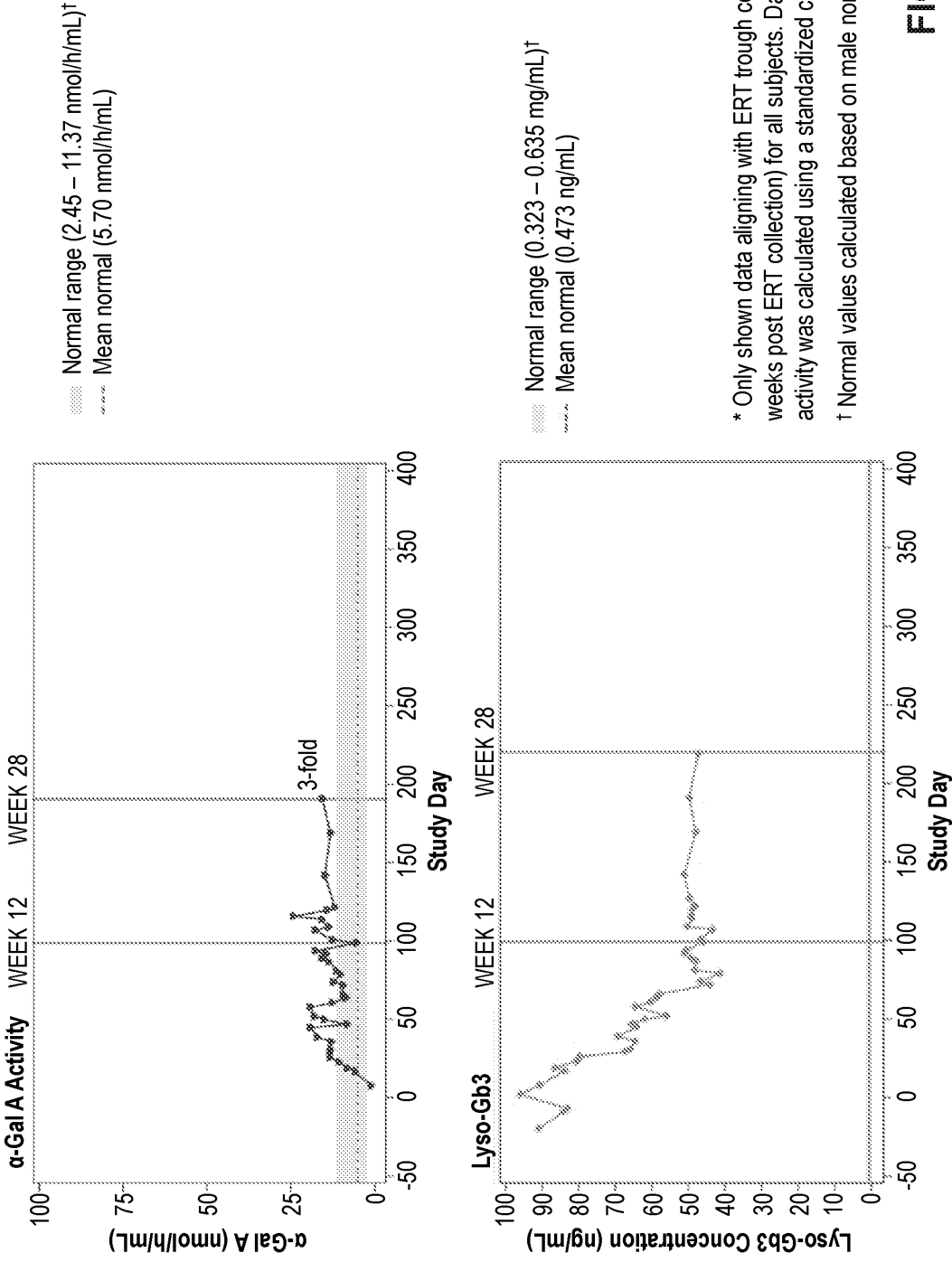
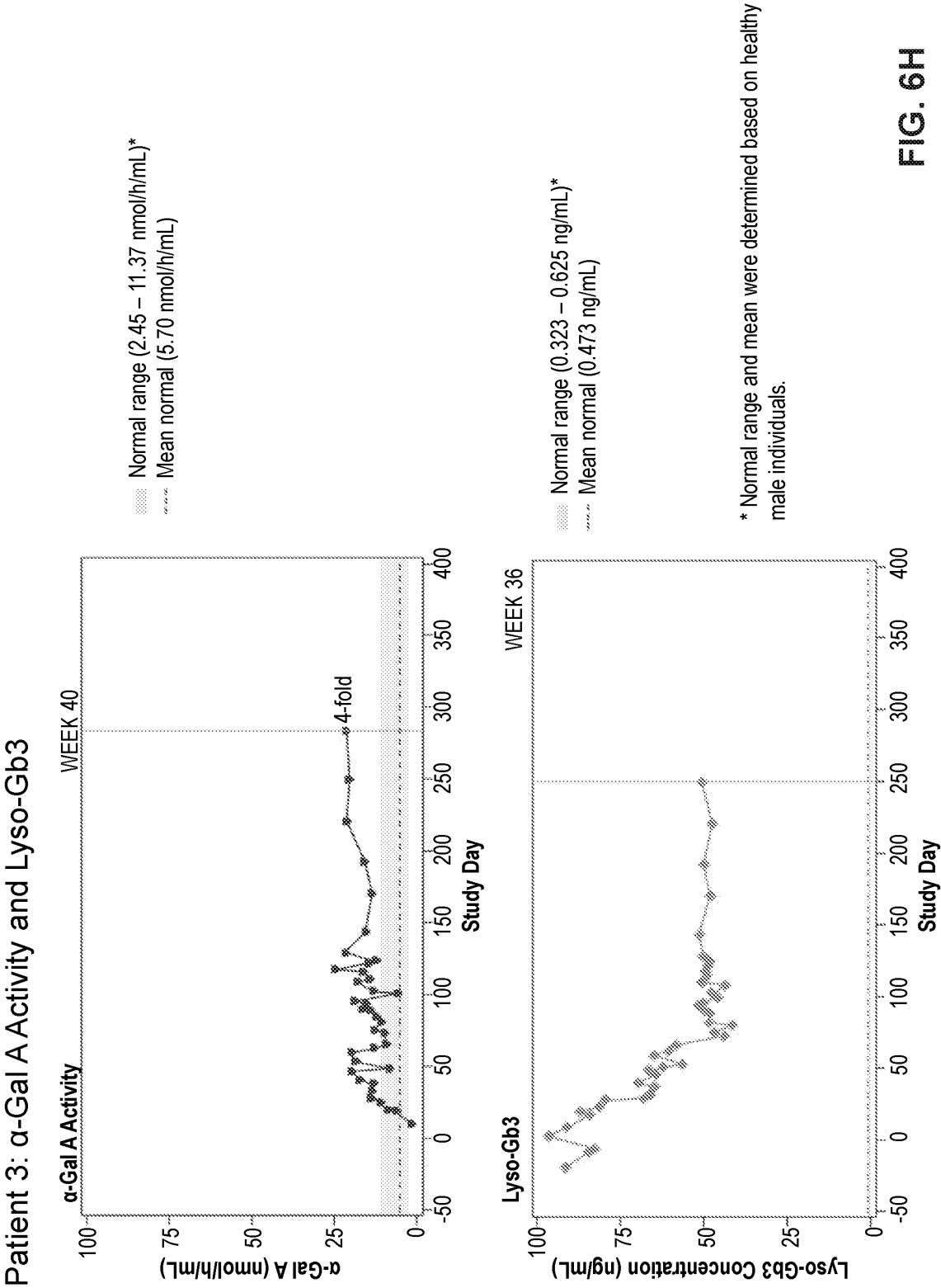


FIG. 6F

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





Patient 3: Plasma A-Gal activity and Lyso-Gb3

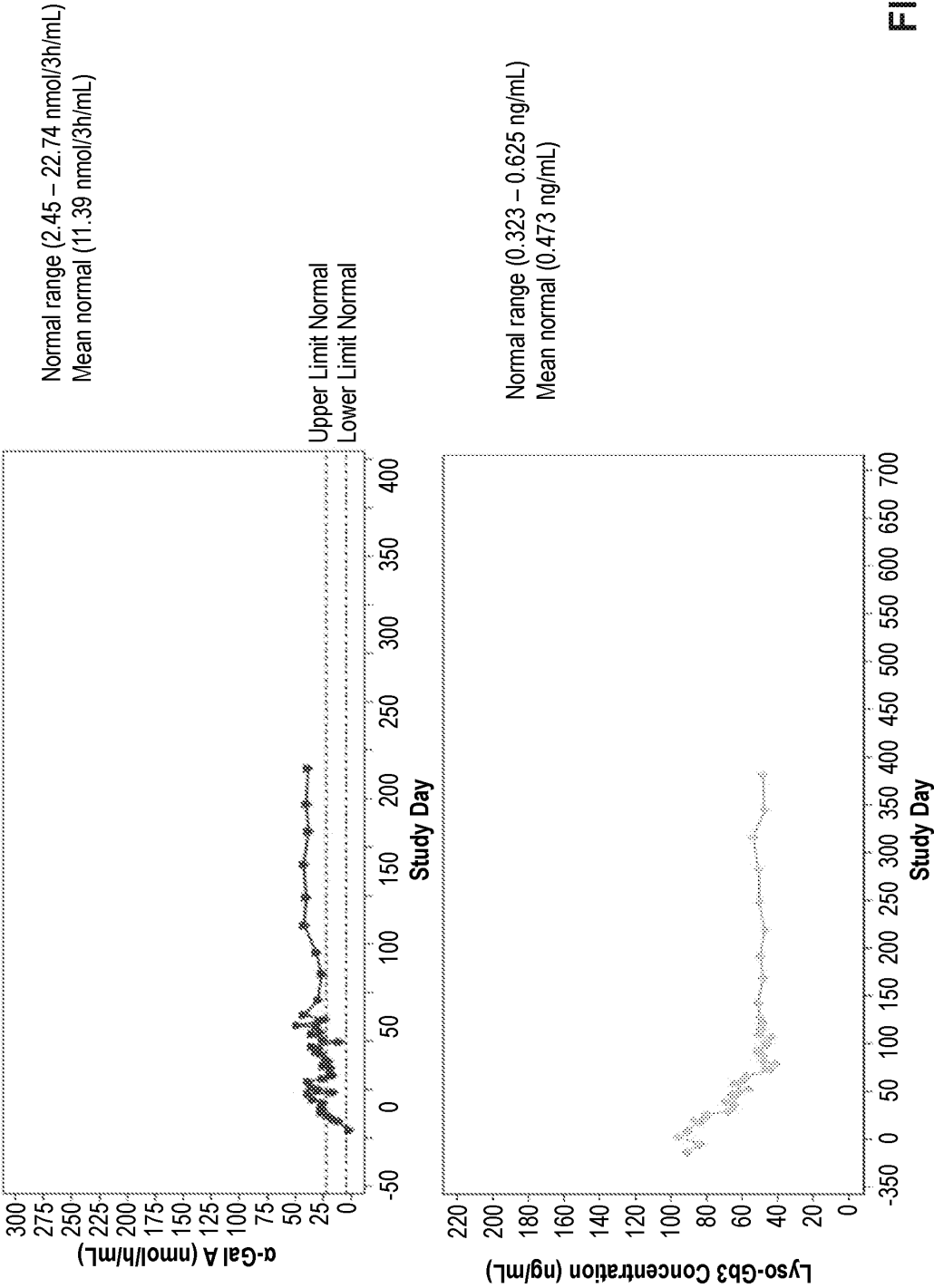
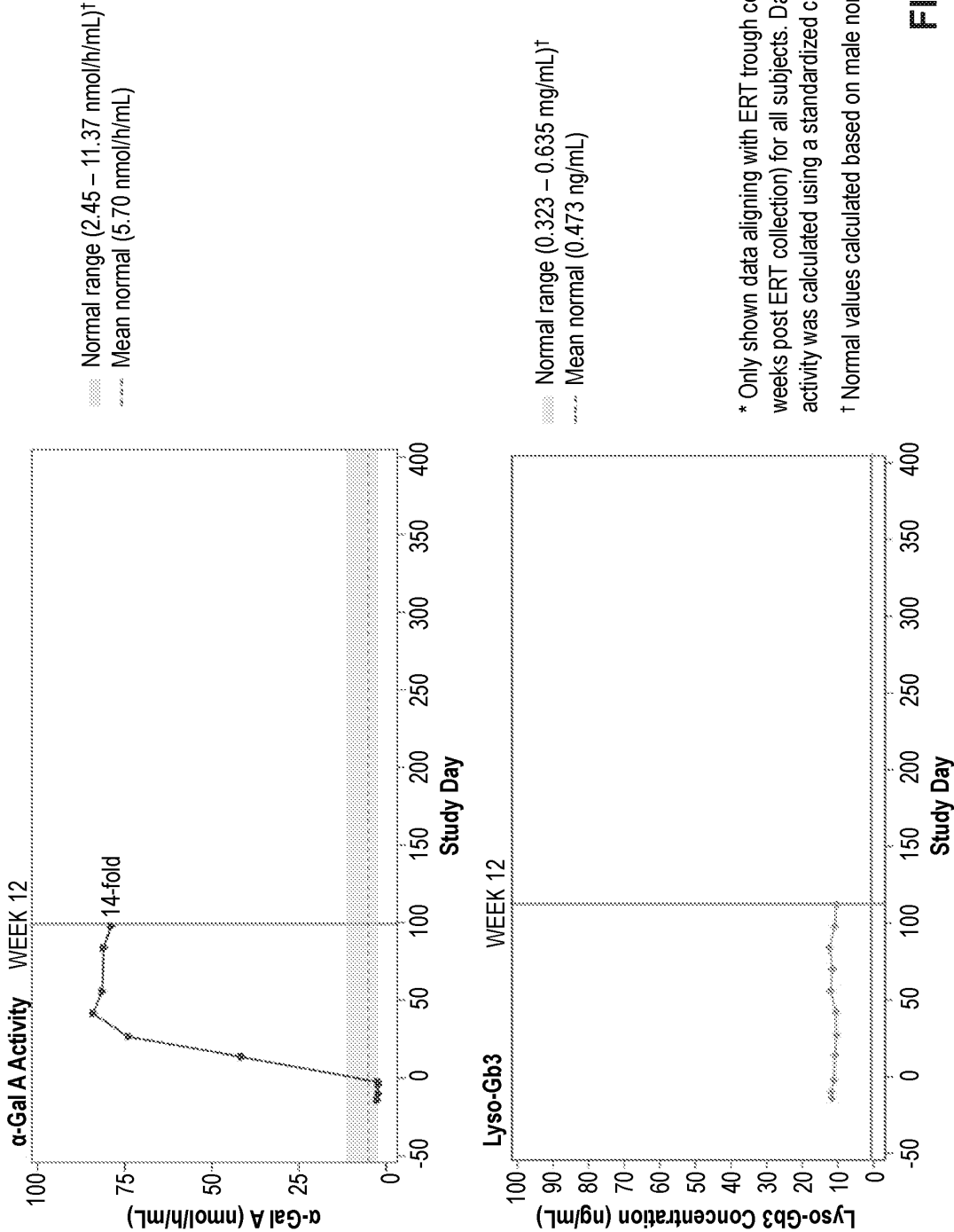


FIG. 6I

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



Patient 2: Plasma A-Gal activity and Lyso-Gb3

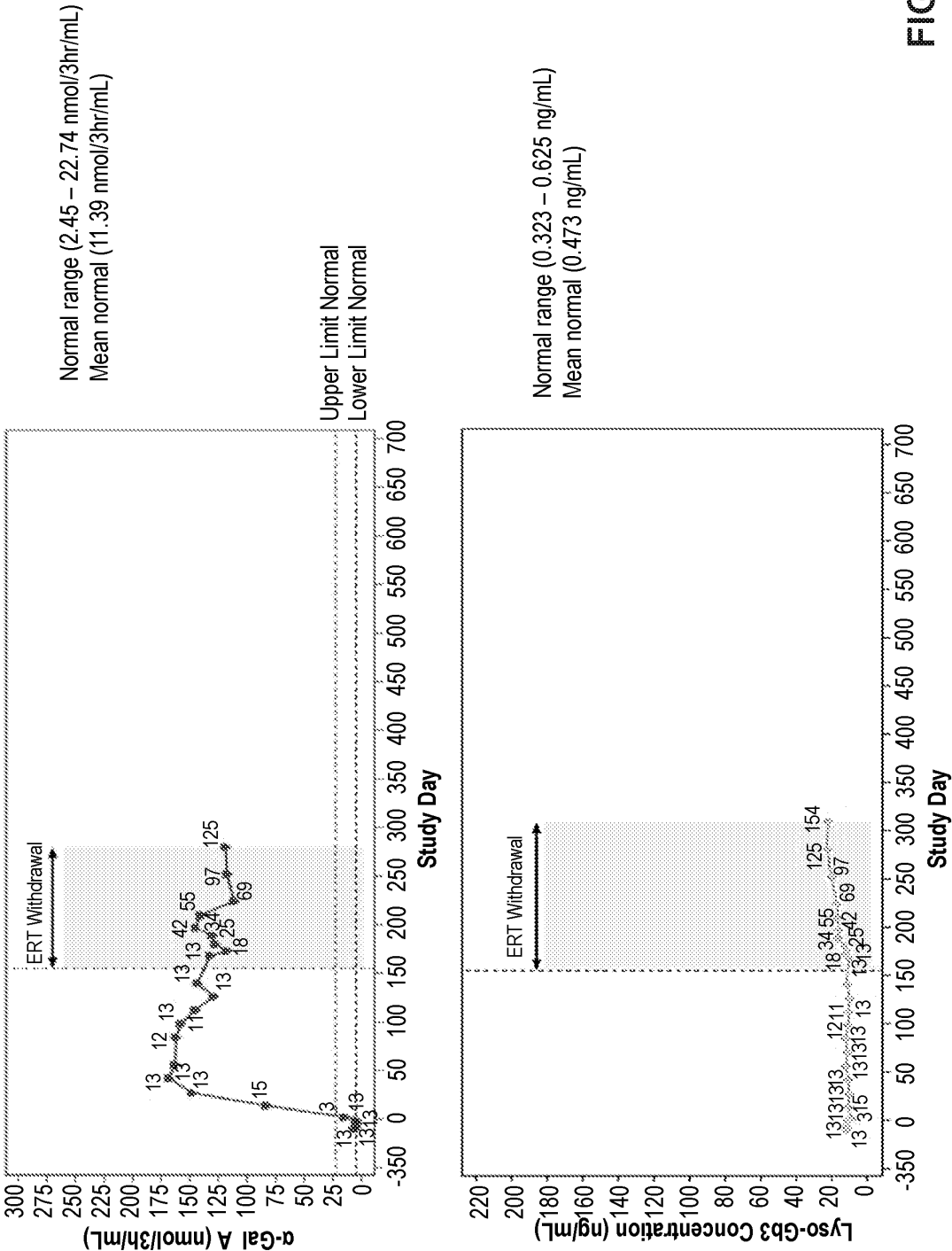
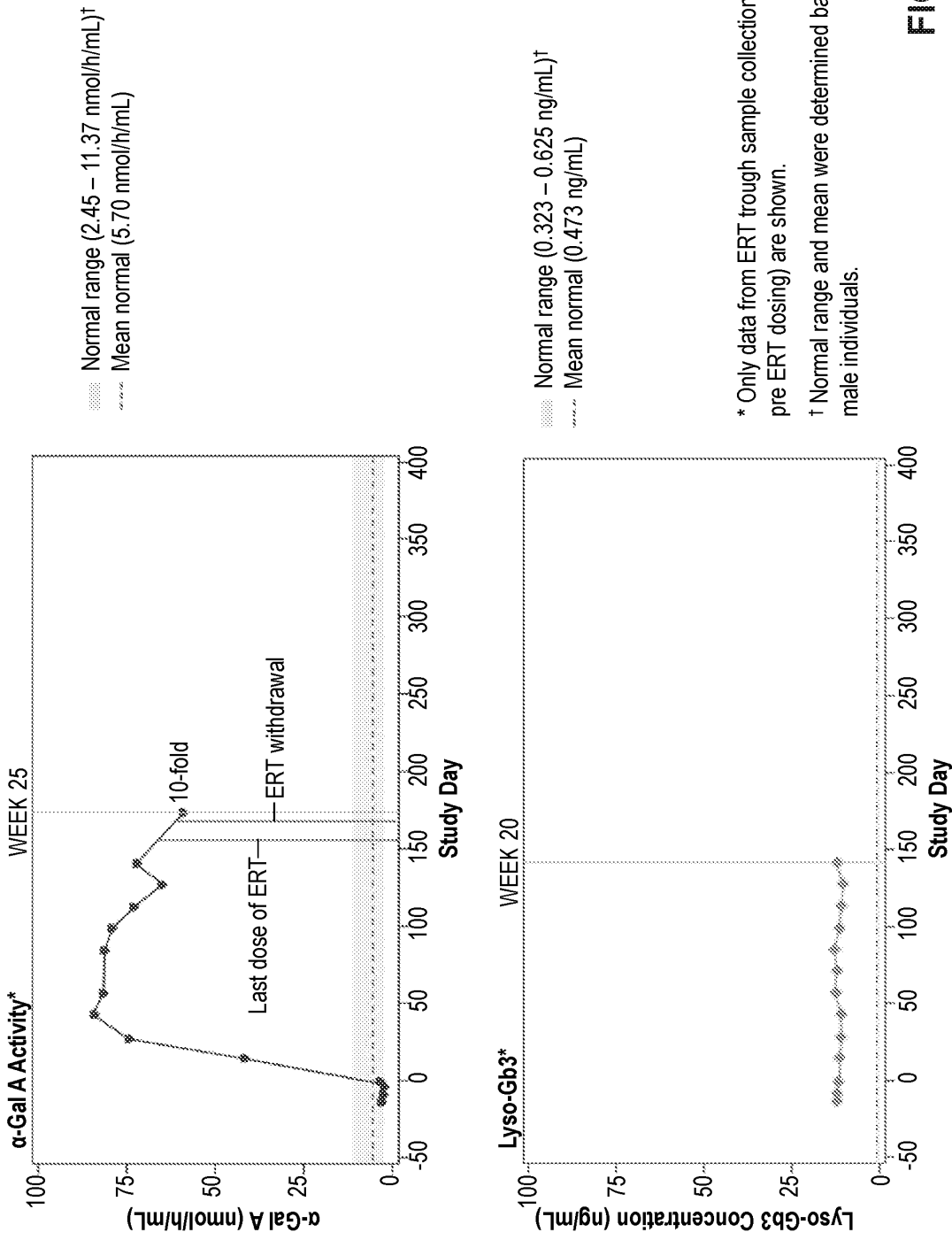


FIG. 6K

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



* 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.

FIG. 6L

Patient 5: α-Gal A Activity and Lyso-Gb3

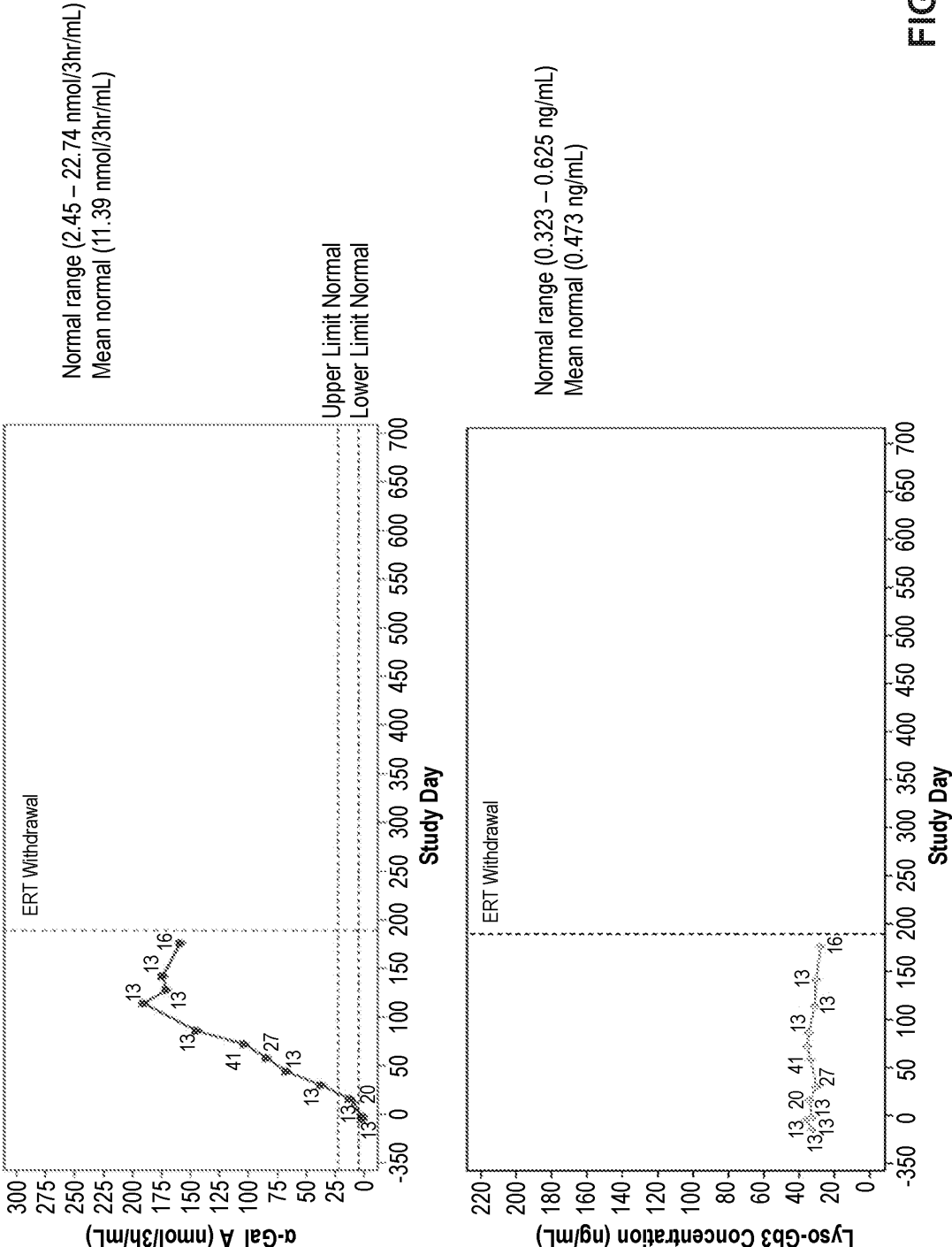
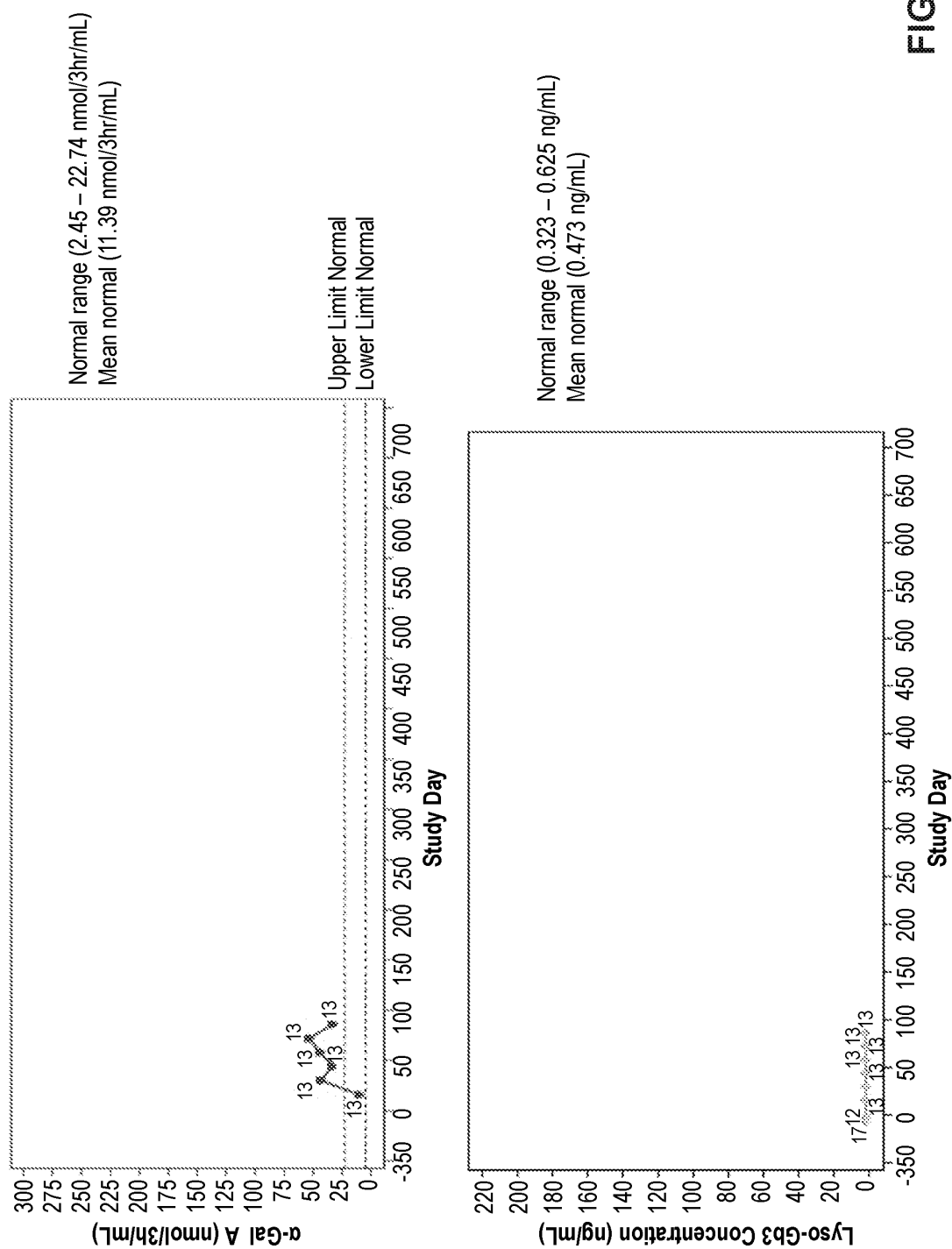


FIG. 6M

Patient 6: Plasma A-Gal activity and Lyso-Gb3



Patient 7: Plasma A-Gal activity and Lyso-Gb3

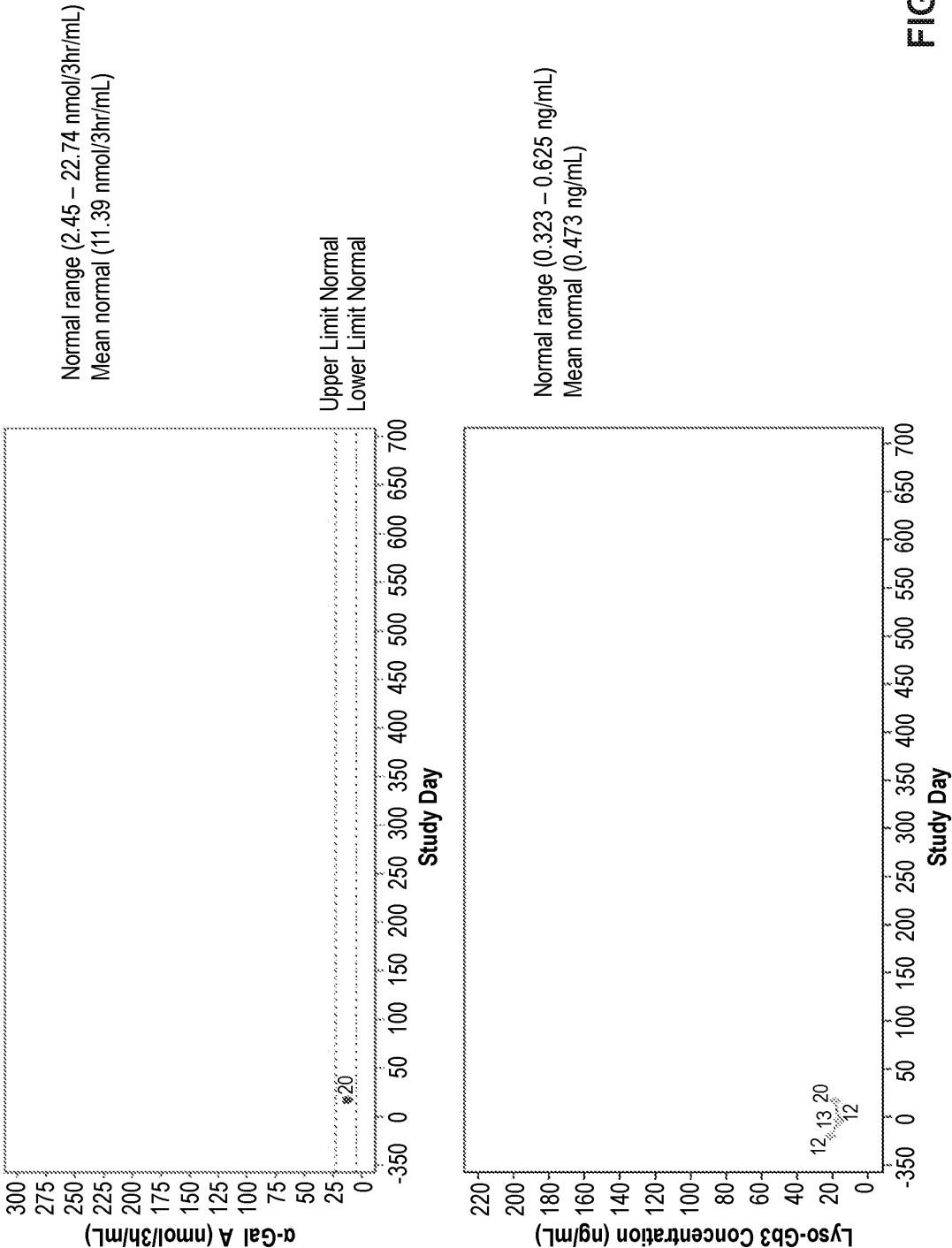


FIG. 60

Patient 8: Plasma A-Gal activity and Lyso-Gb3

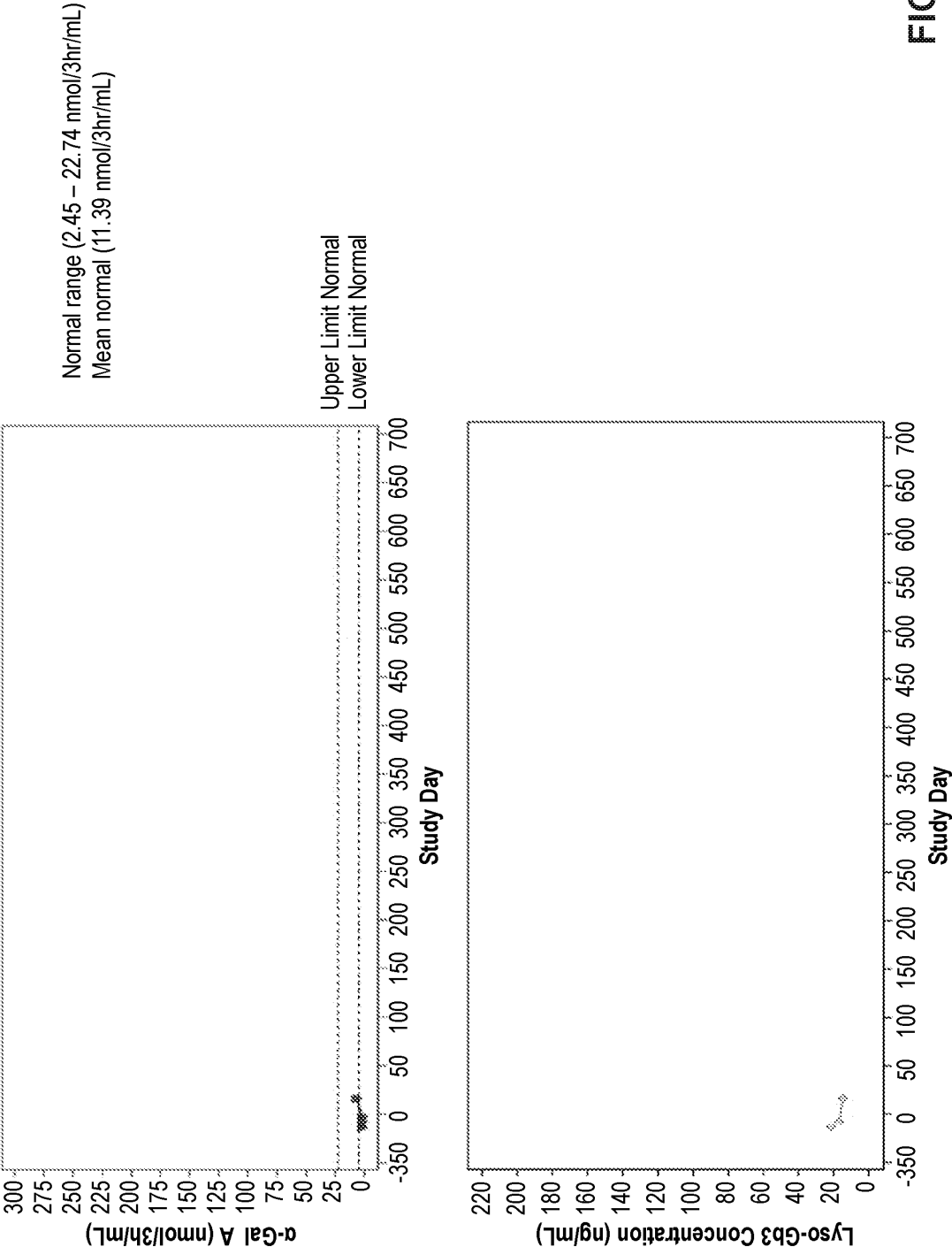


FIG. 6P

Patient 9: Plasma A-Gal activity and Lyso-Gb3

No Plasma A-Gal
available data at
this data cut.

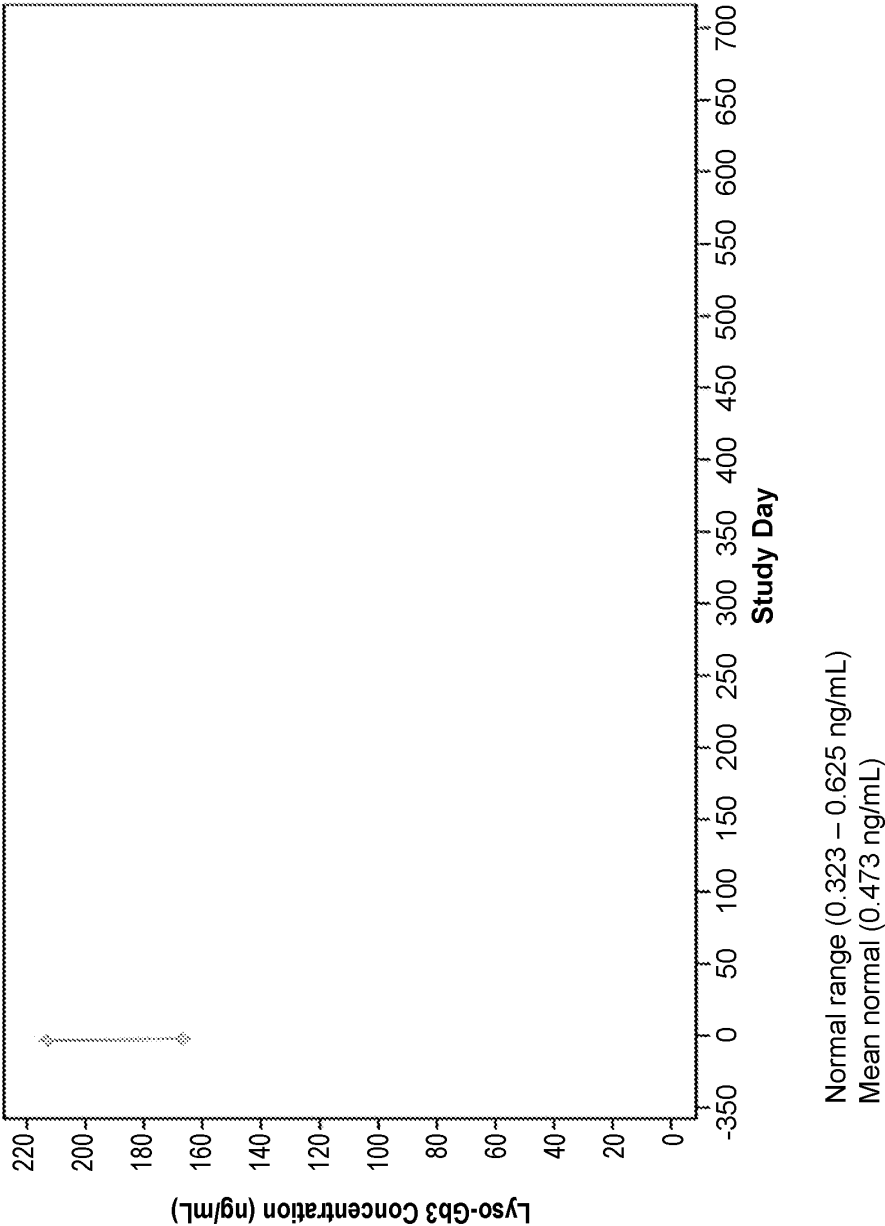


FIG. 6Q