

Structure and Receptor Affinity for High Mannose and
Phosphorylated Oligosaccharides

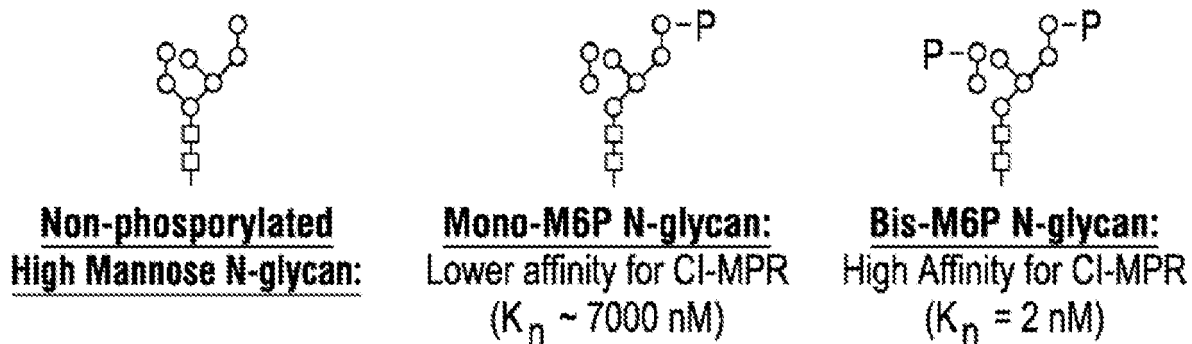


FIG. 1A

Mannose 6-phosphate (M6P)

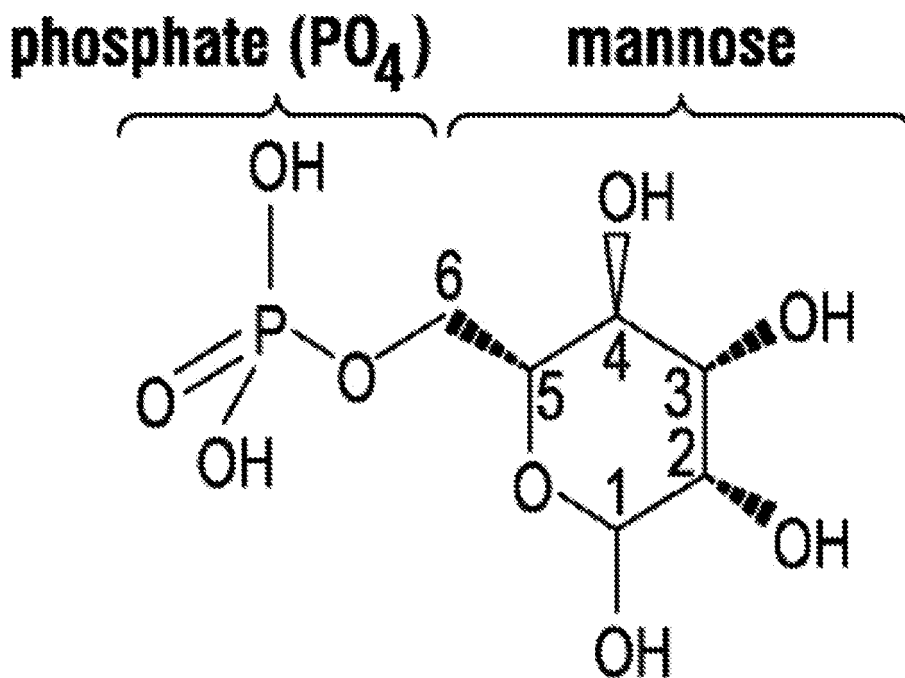


FIG. 1B

Comparison of Productive and Non-Productive Targeting Glycan Specific Receptors

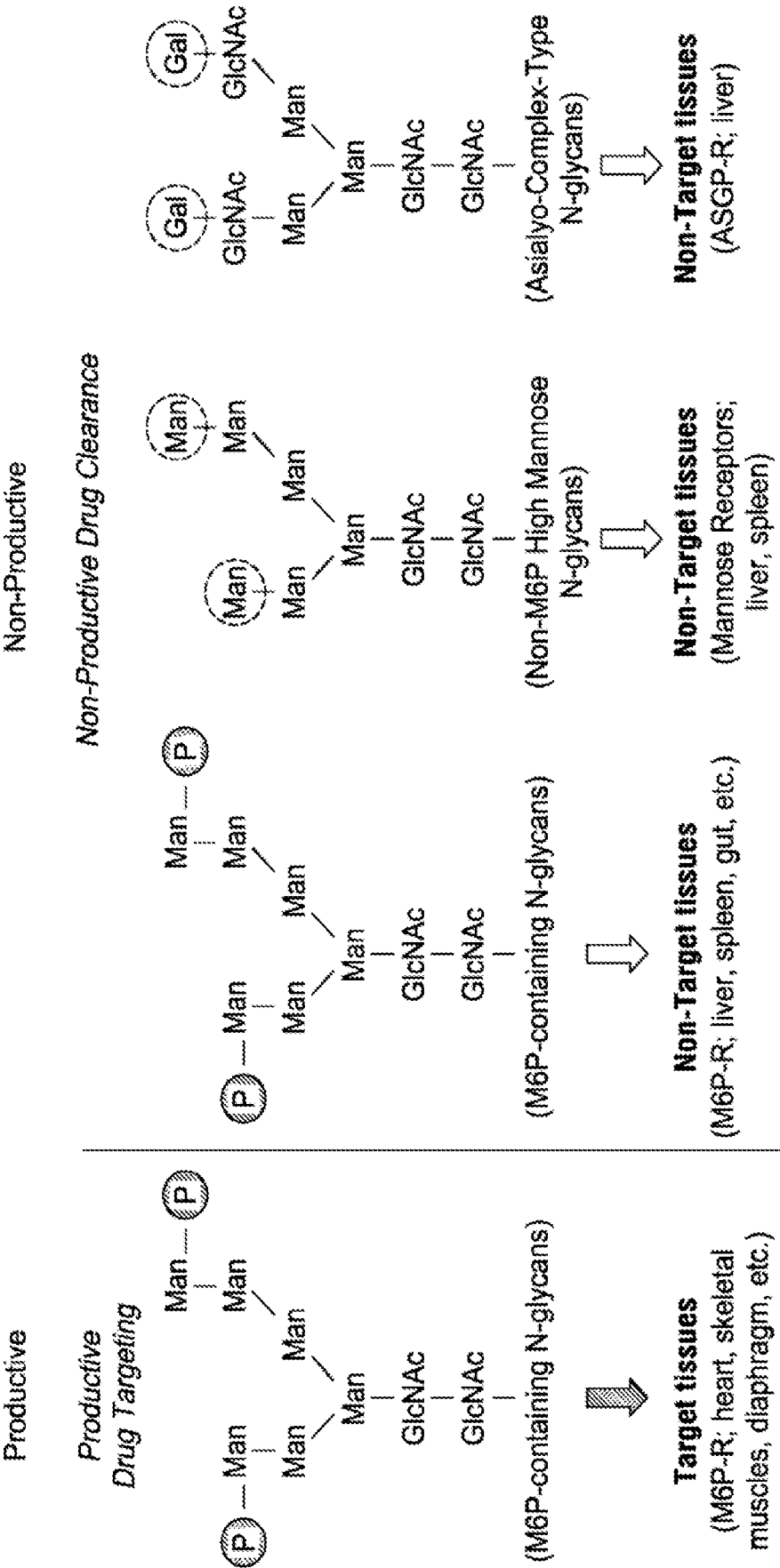


Fig. 2B

Fig. 2A

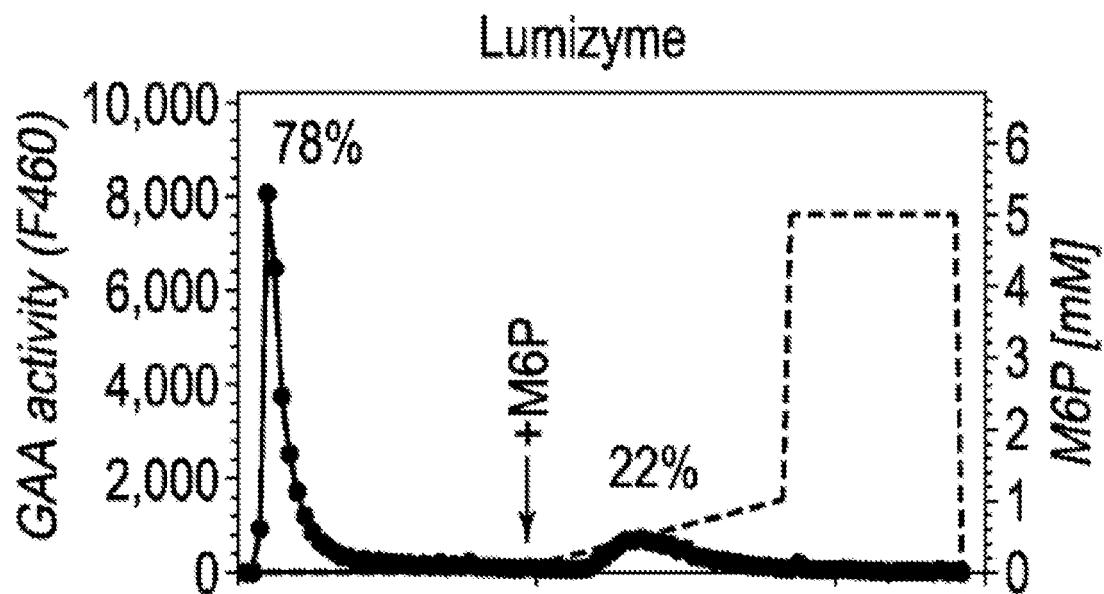


FIG. 3A

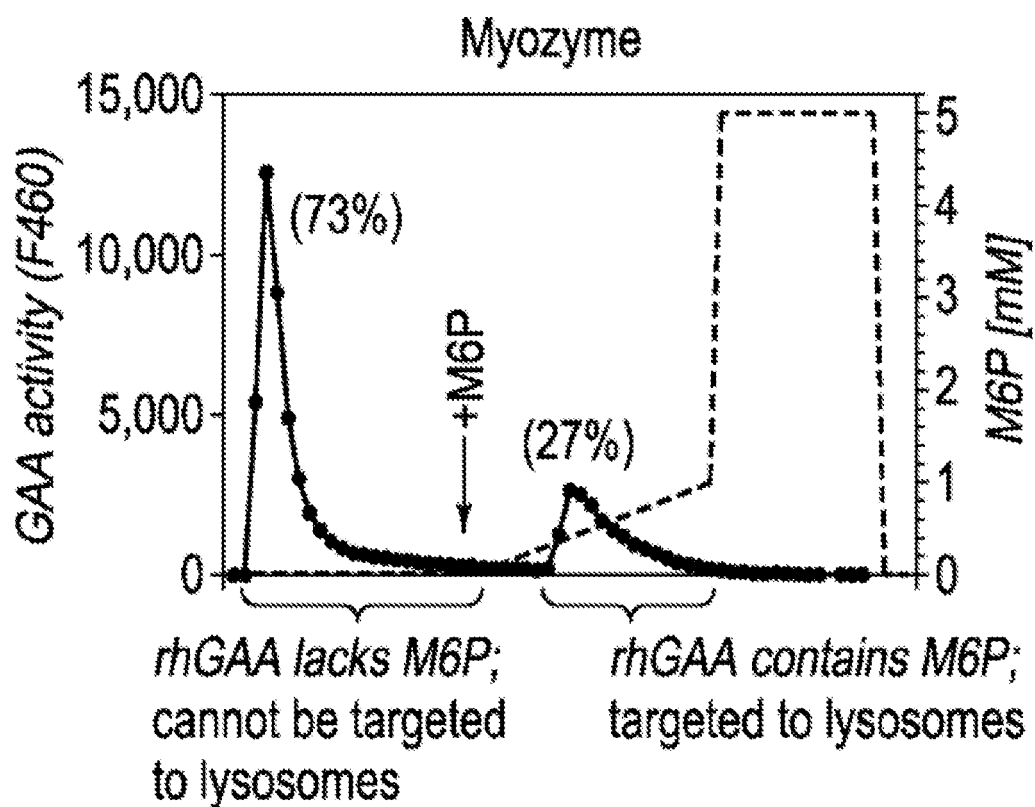


FIG. 3B

ATB200 Vector Construction

◆ Host Cell: DG44

◆ Vector: pOptivec-110

□ Invitrogen vector

□ 952 aa, native signal peptide

◆ Screening Pressure: -HT, 500nM MTX

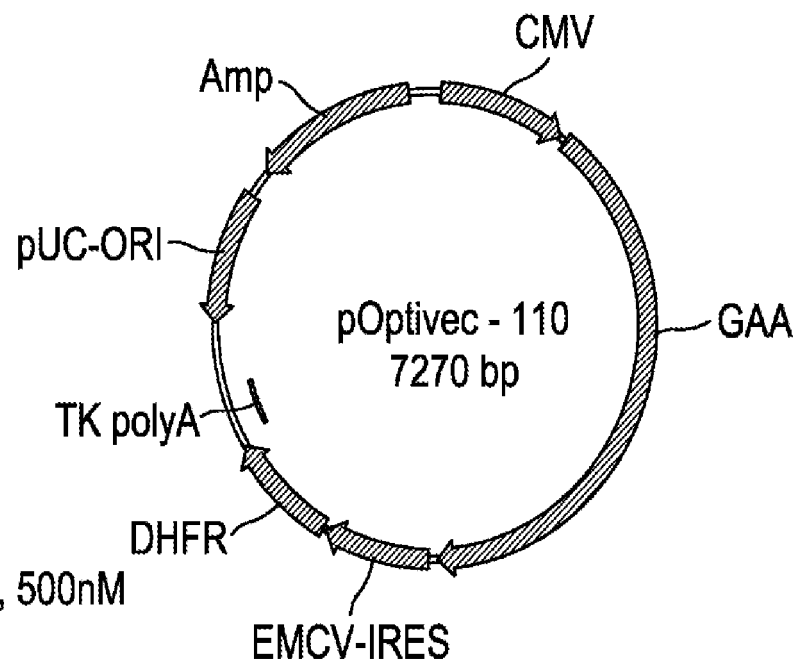


FIG. 4

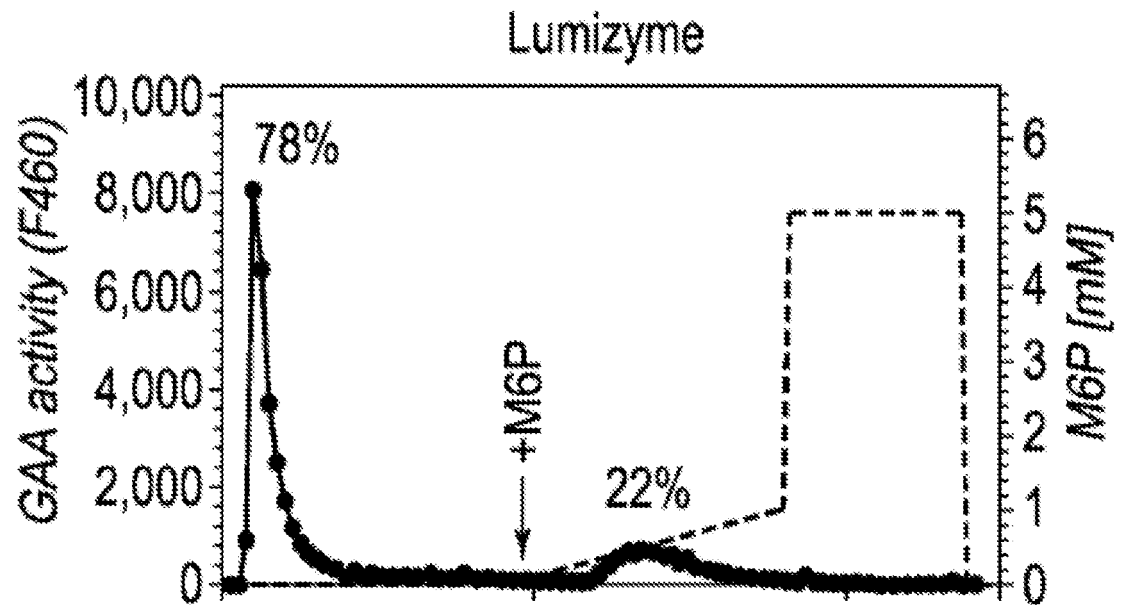


FIG. 5A

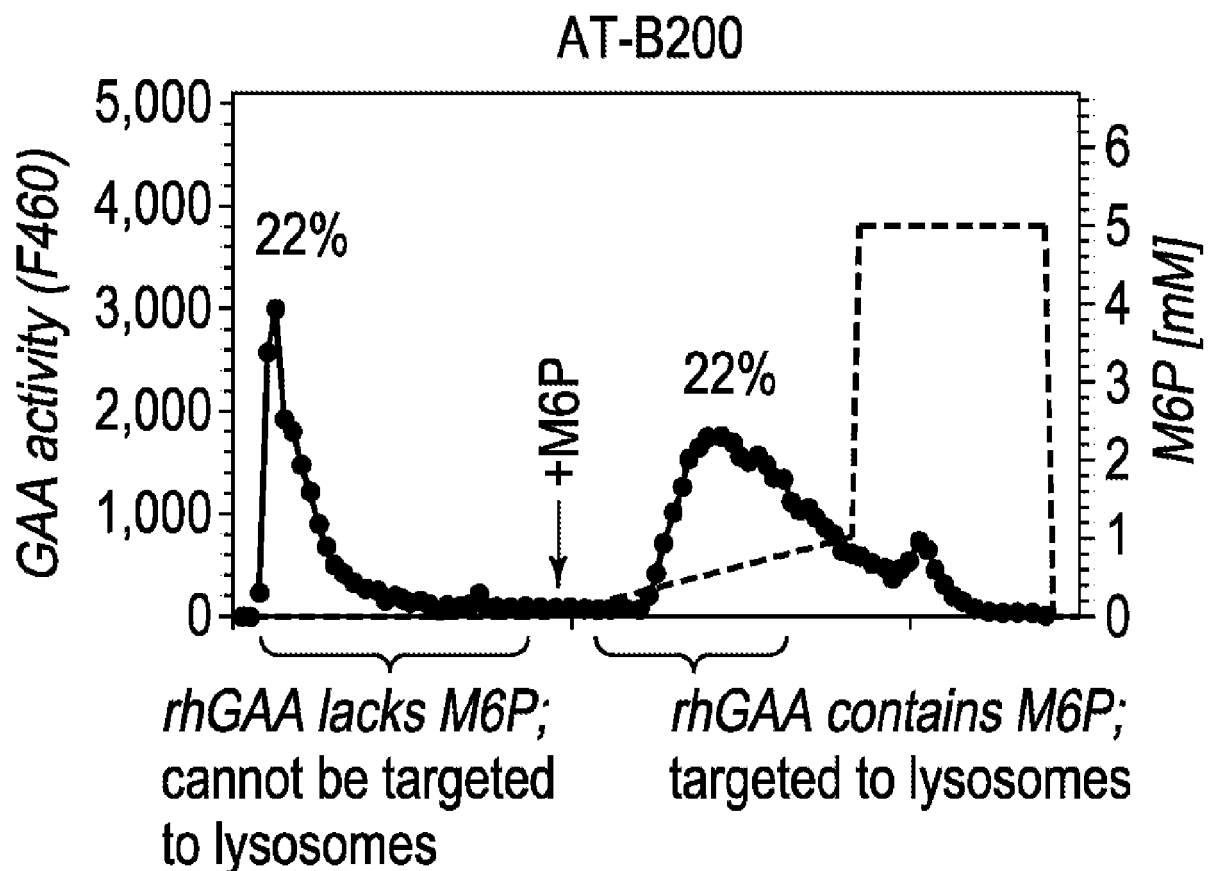
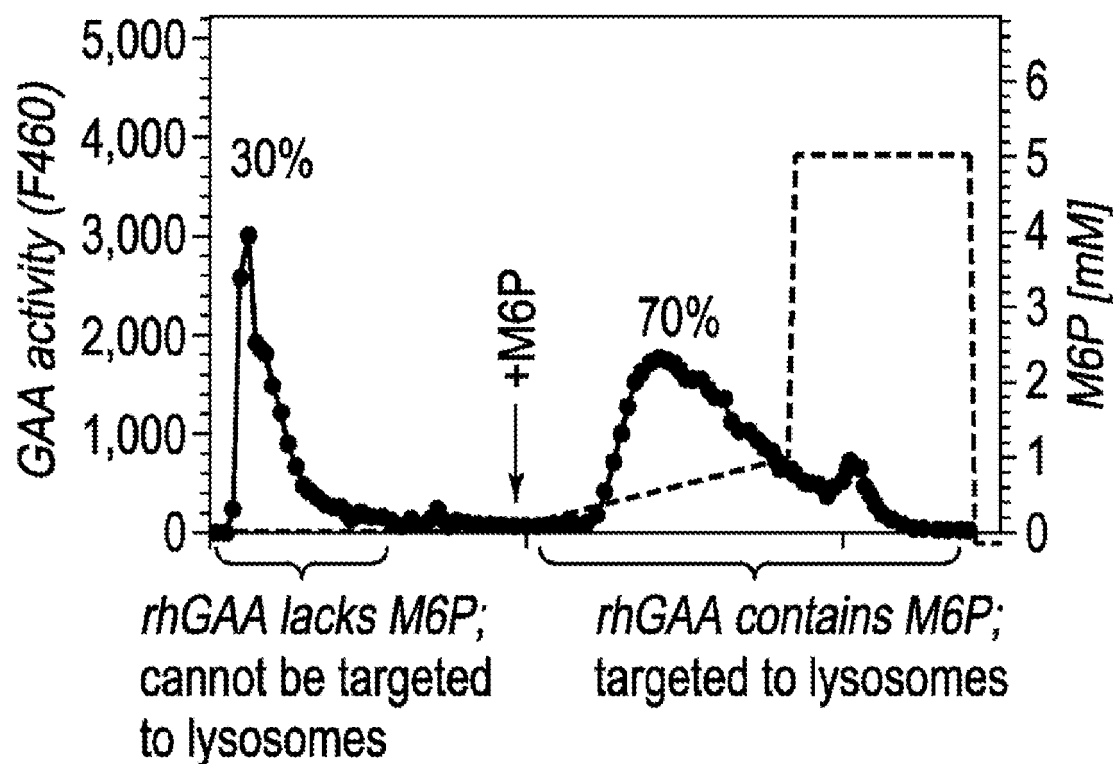


FIG. 5B

Embodiment 1



Embodiment 2

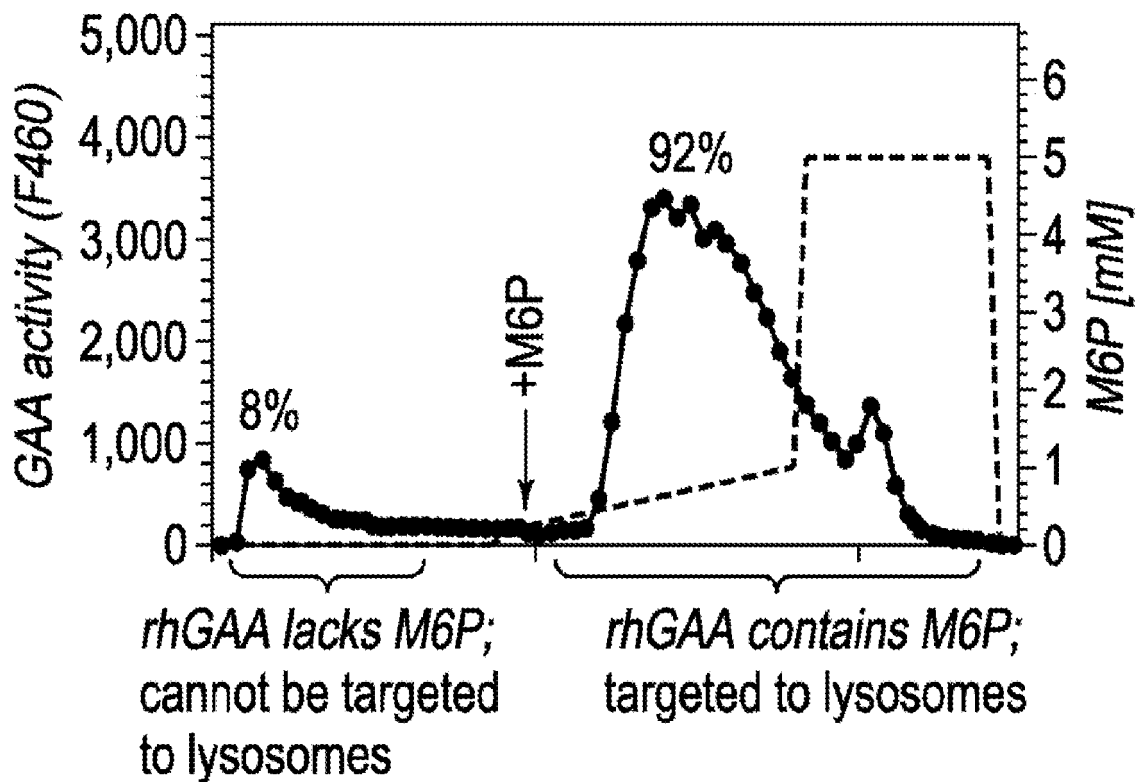


FIG. 6

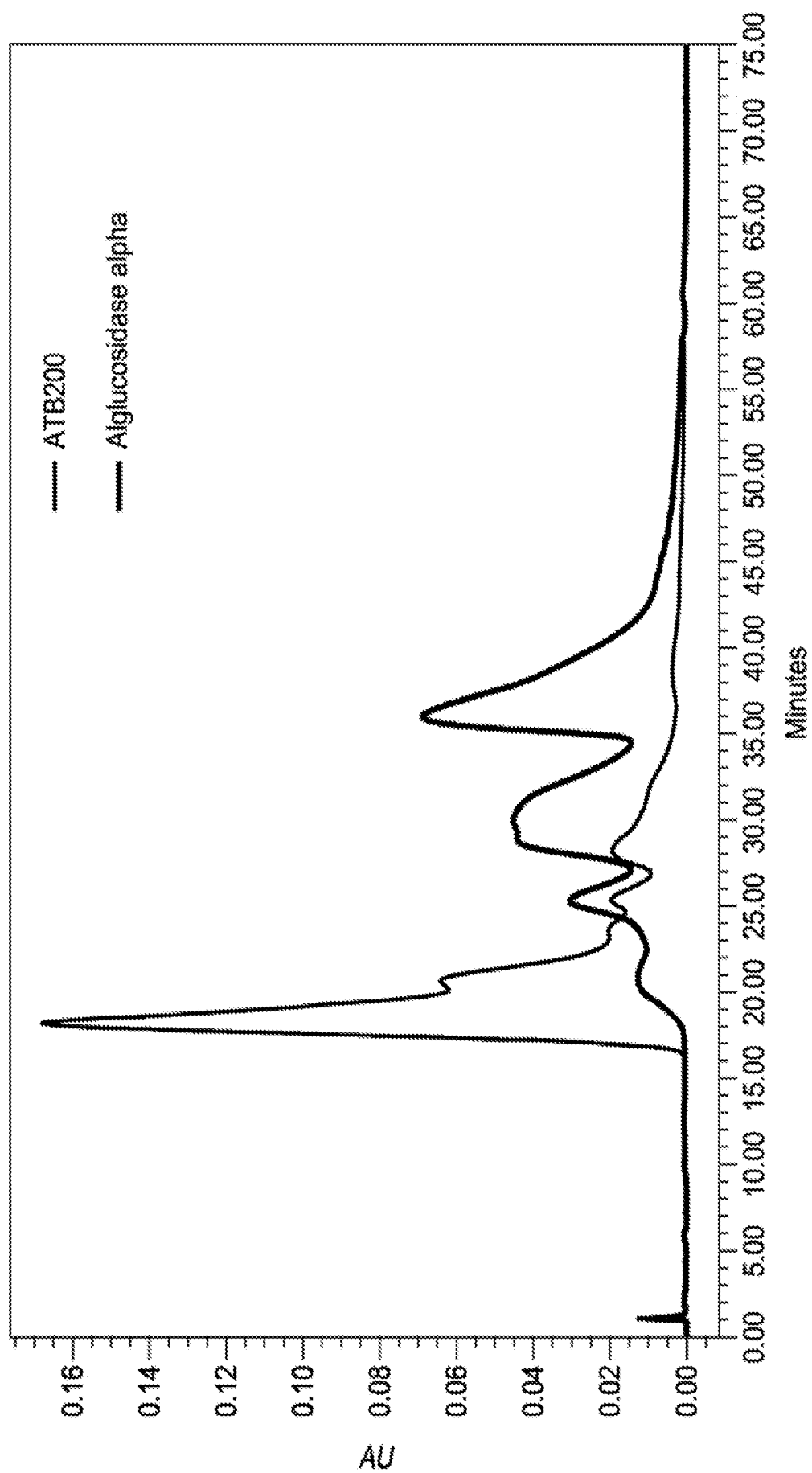


FIG. 7

Distribution of N-Glycans on rhGAA Preparations

	Lumizyme	BP-rhGAA*	ATB200	
			1	2
Complex Type N-Glycans	70.7%	48.9%	51.0%	47.5%
Hybrid Type N-Glycans	6.7%	9.7%	4.4%	3.7%
High Mannose Type N-Glycans:				
Non-phosphorylated	15.8%	23.7%	14.0%	9.9%
Mono-M6P	5.2%	10.4%	13.4%	14.2%
Bis-M6P	1.6%	6.8%	17.2%	24.7%

FIG. 8

N-Glycosylation Site Occupancy of ATB200

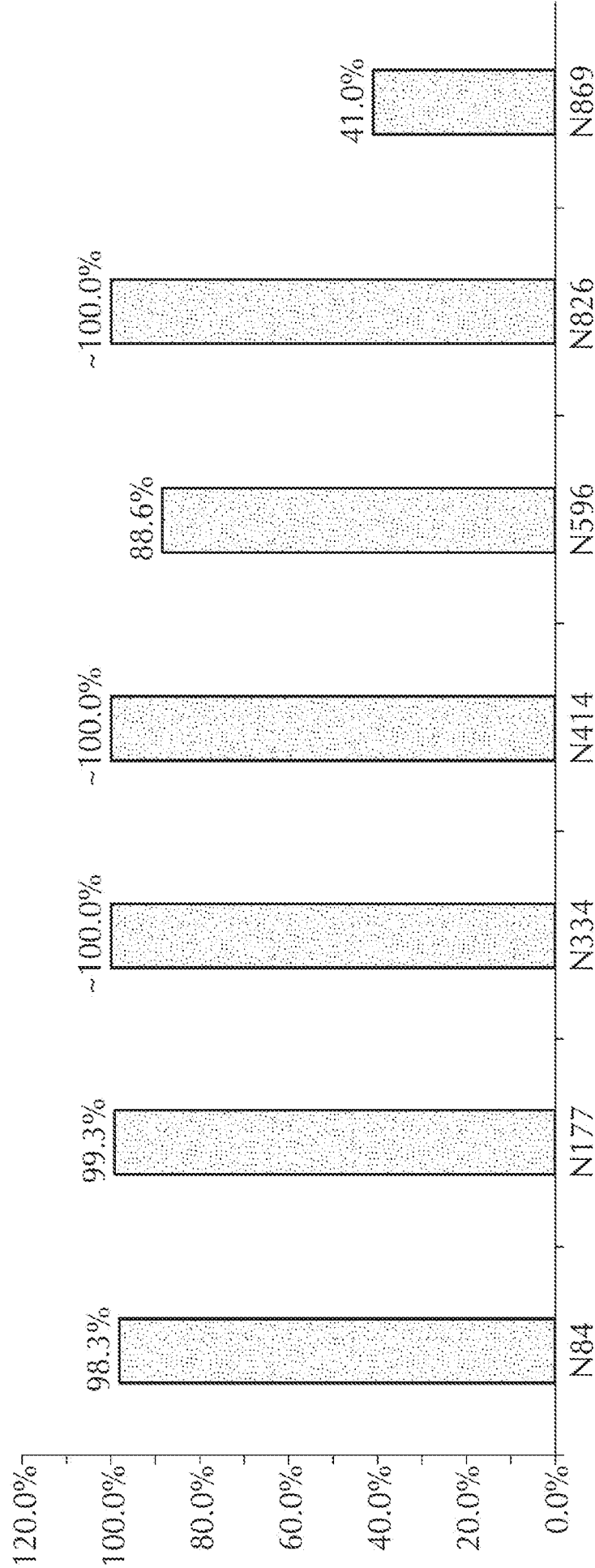


FIG. 9A

N-Glycosylation Profile of N177

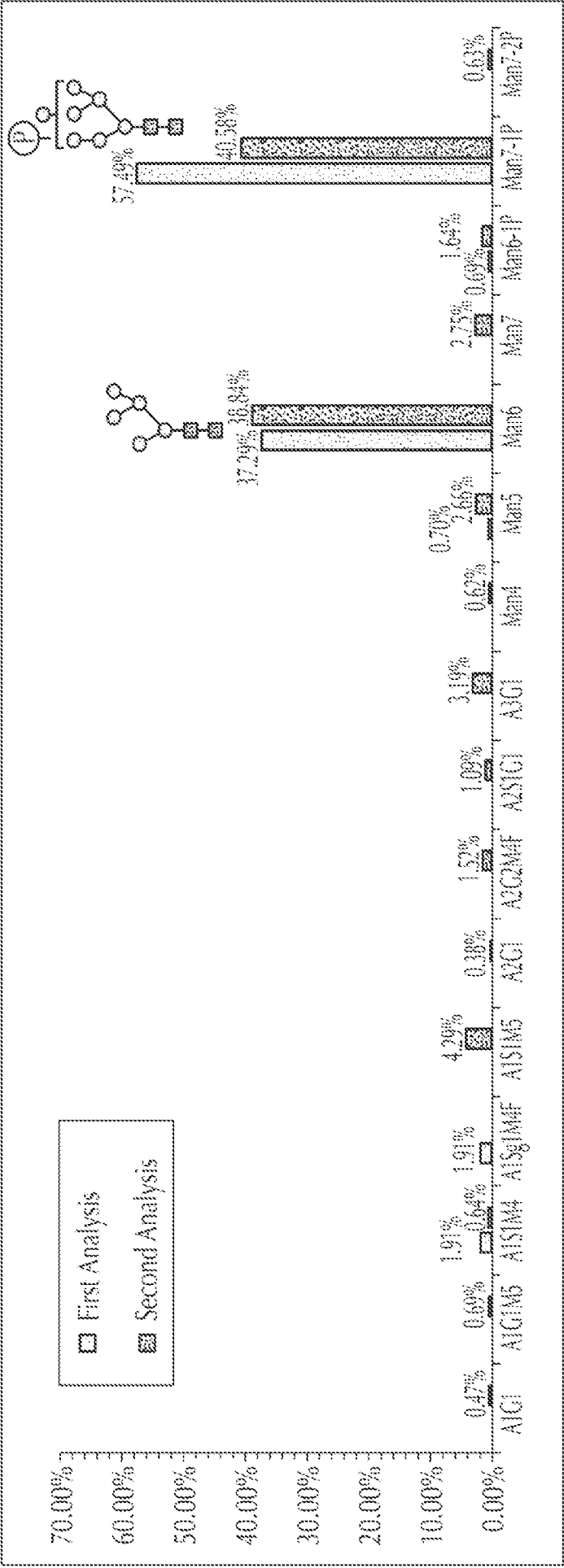


FIG. 9C

N-Glycosylation Profile of N334

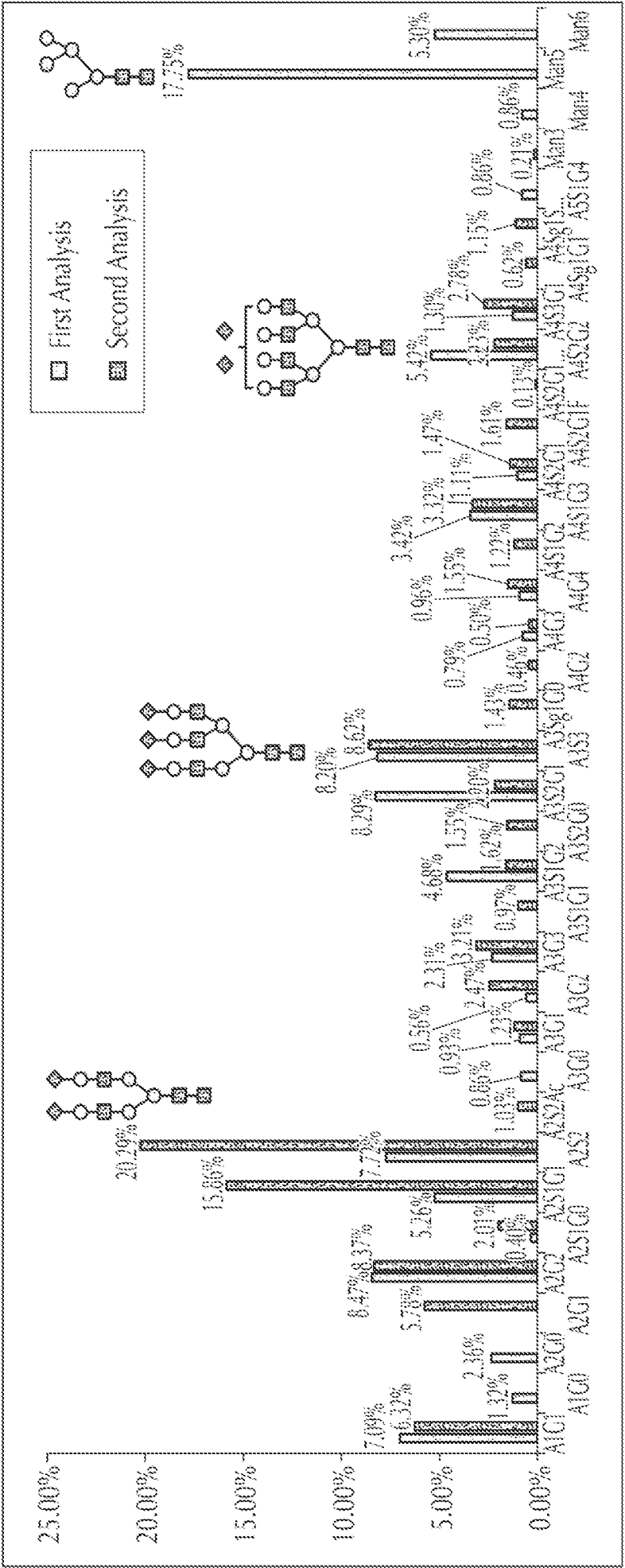


FIG. 9D

N-Glycosylation Profile of N414

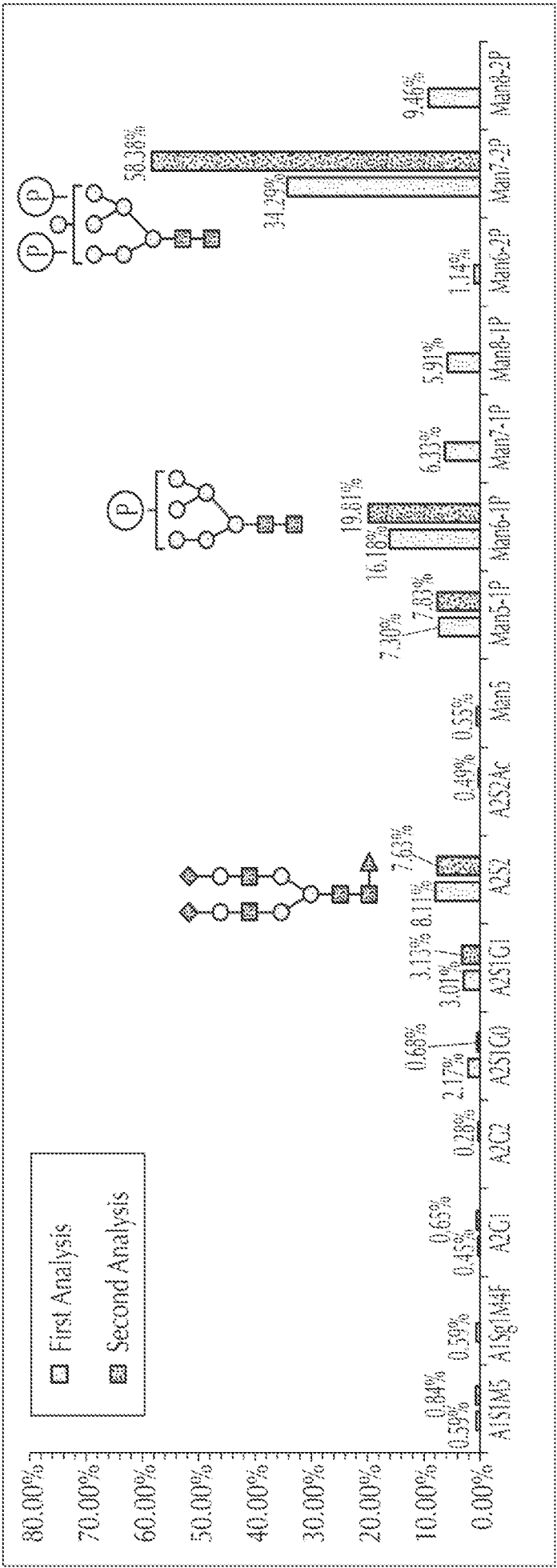


FIG. 9E

N-Glycosylation Profile of N596

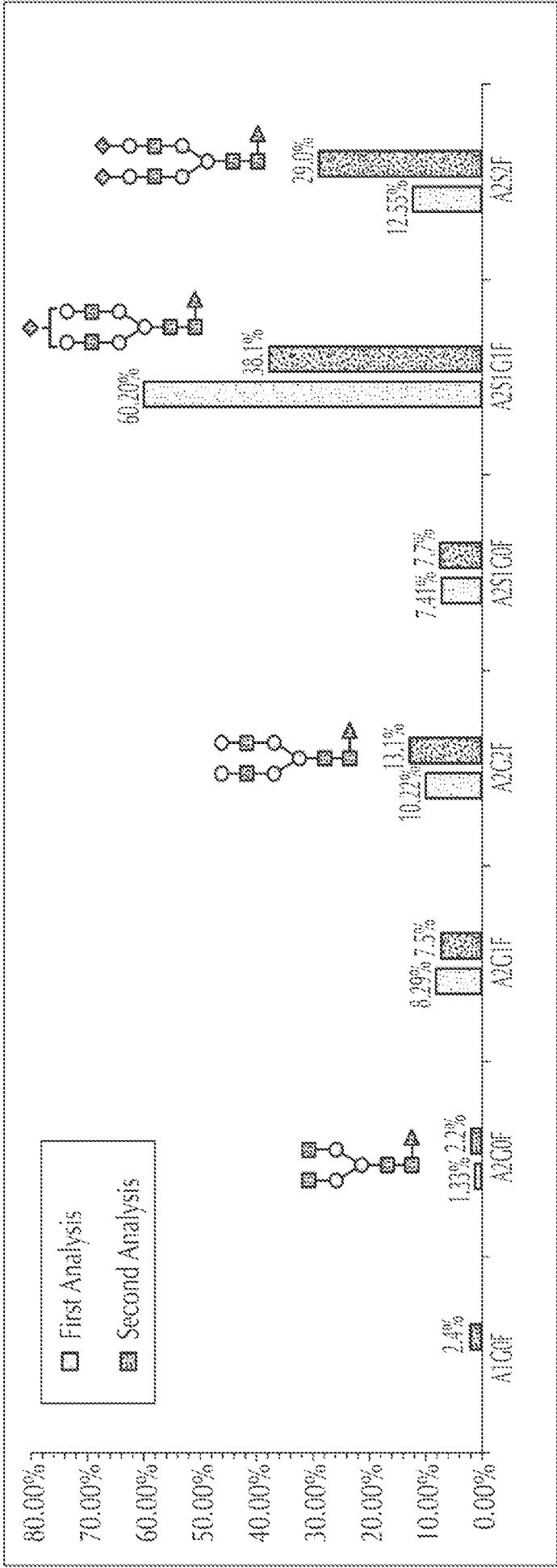


FIG. 9F

N-Glycosylation Profile of N826

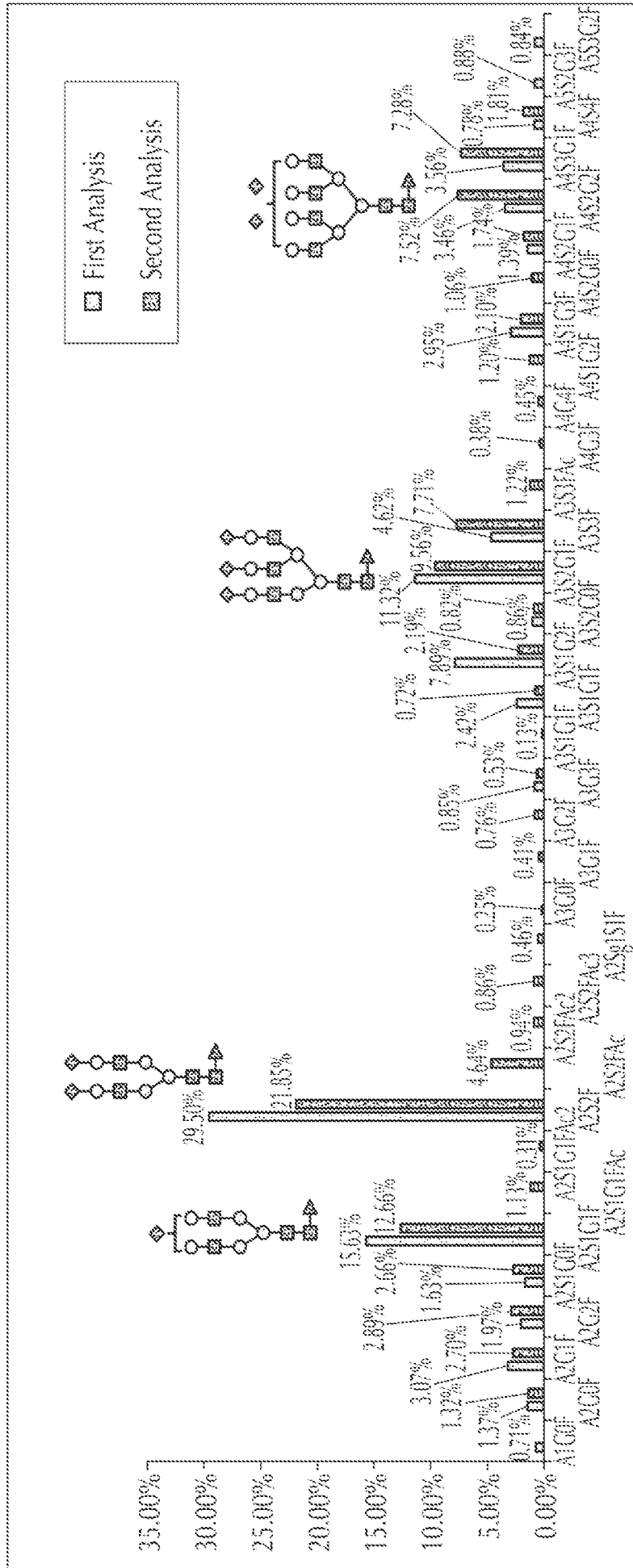


FIG. 9G

Relative Percent Bis-M6P and Mono-M6P in Each N-glycosylation Site

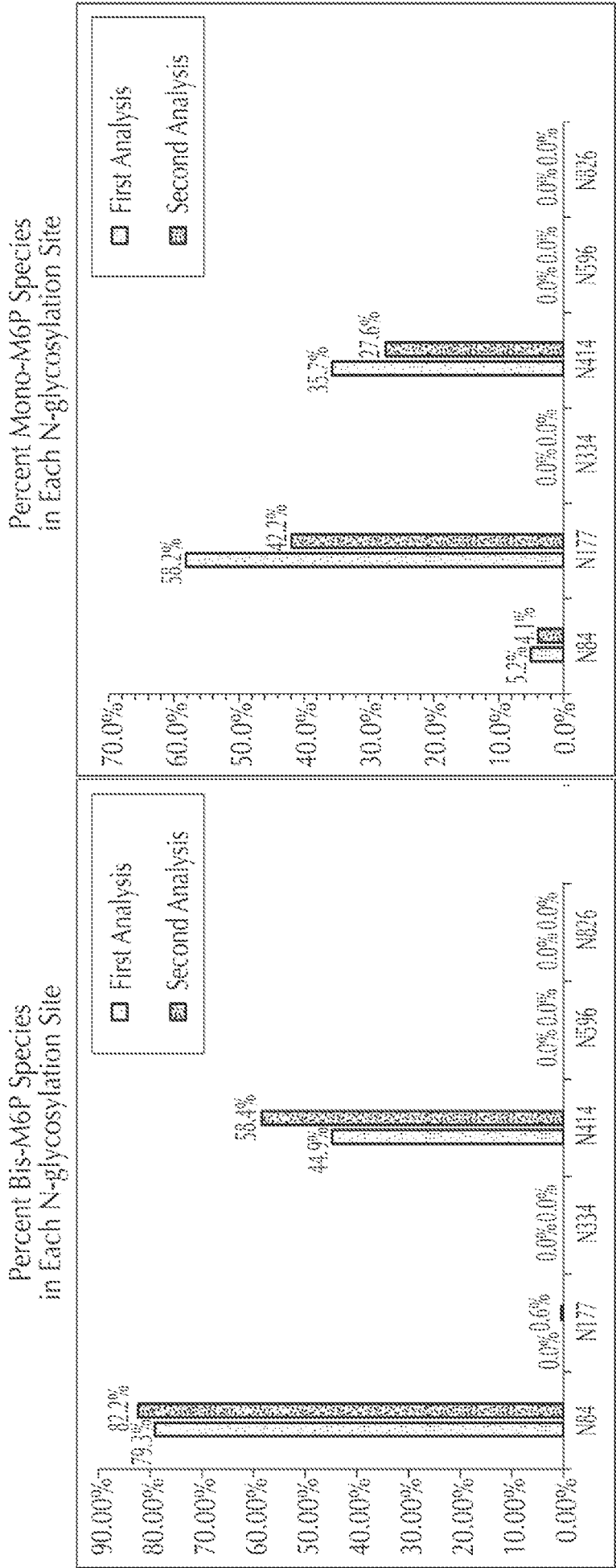


FIG. 9H

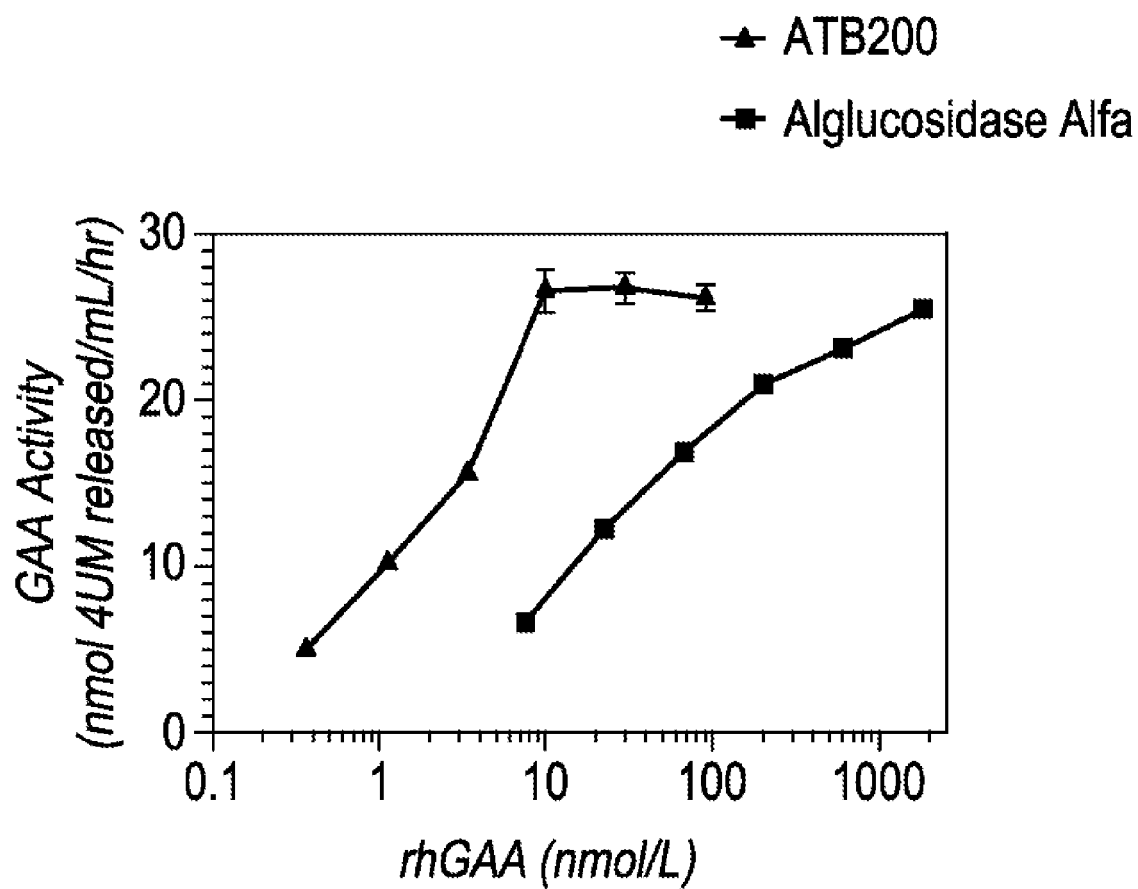


FIG. 10A

Glycan	Alglucosidase Alfa (mol bis-glycan/ mol protein)	ATB200 (mol bis-glycan/ mol protein)
Bis-M6P	0.1	1.3

FIG. 10B

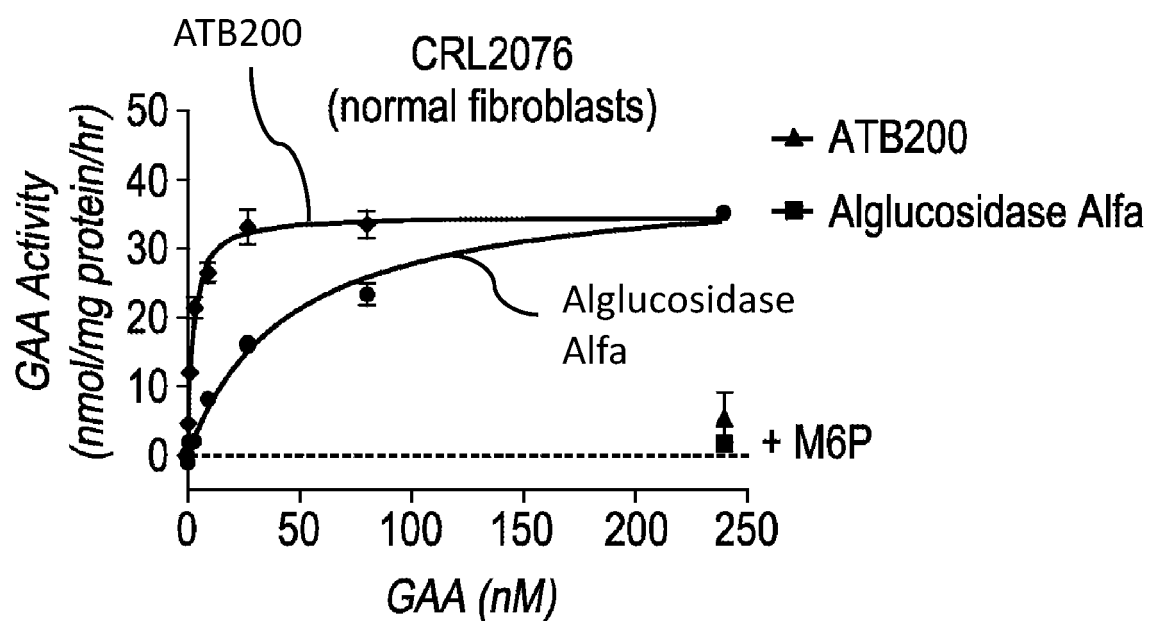


FIG. 11A

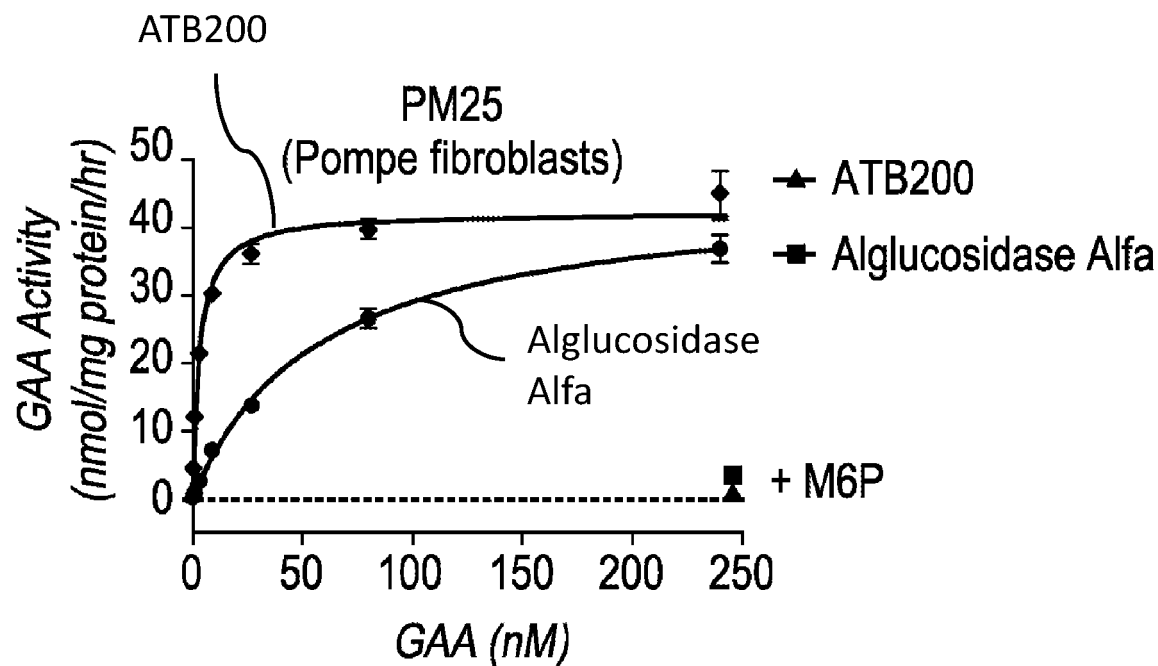


FIG. 11B

Cell Line	K_{uptake} (nM)	
	AT200	Lumizyme
normal	2	56
Pompe	3	57

FIG. 11C

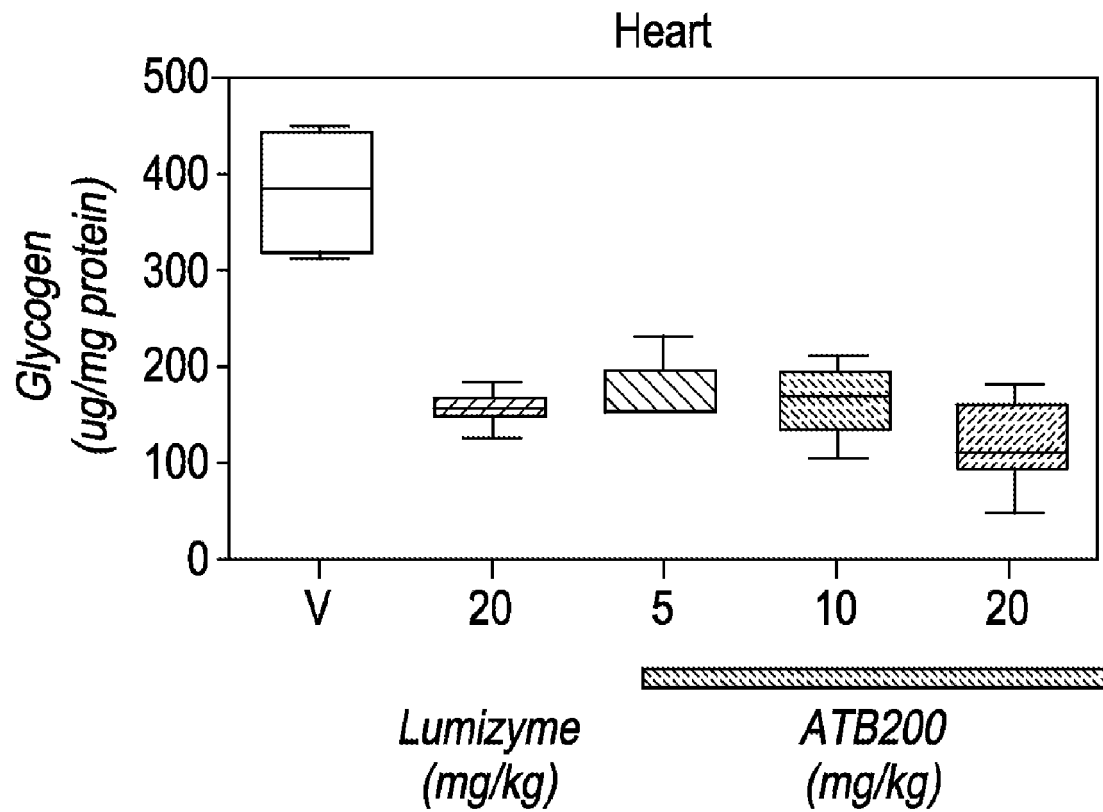


FIG. 12A

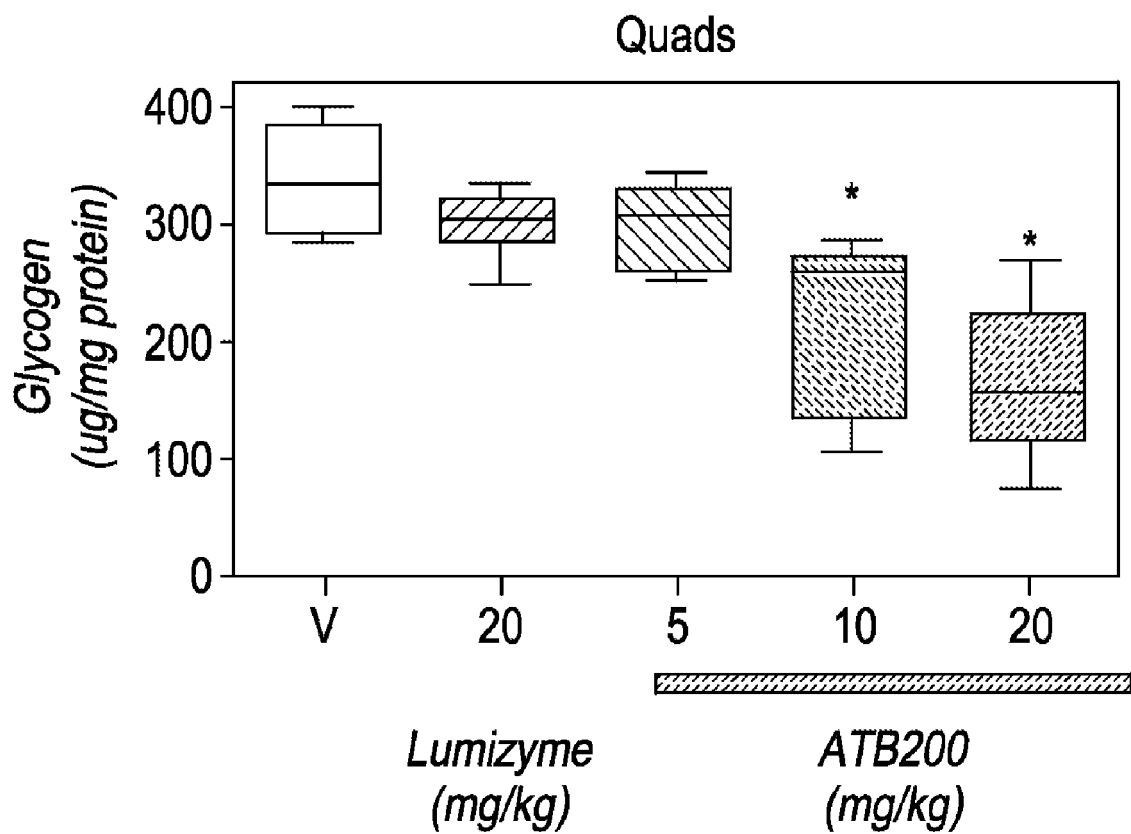


FIG. 12B

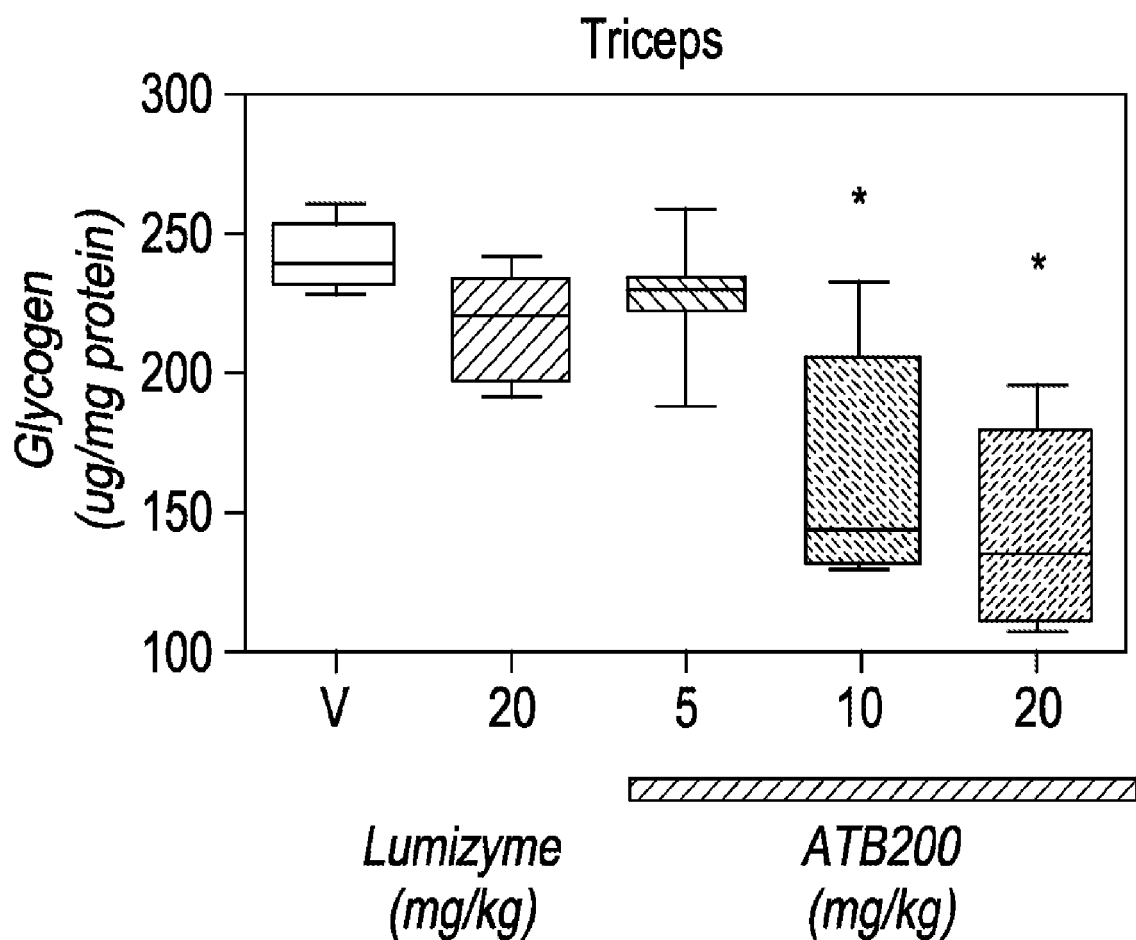


FIG. 12C

Comparison of % glycogen reduction in <i>Gaa</i> KO mice after Lumizyme or ATB200 administration (with or without miglustat)		
Enzyme ± Chaperone	Quadriceps	Triceps
Lumizyme alone (20 mg/kg)	14	14
ATB200 alone (20 mg/kg)	74	62
ATB200 + Miglustat (20 mg/kg) + (10 mg/kg)	94	73

FIG. 13

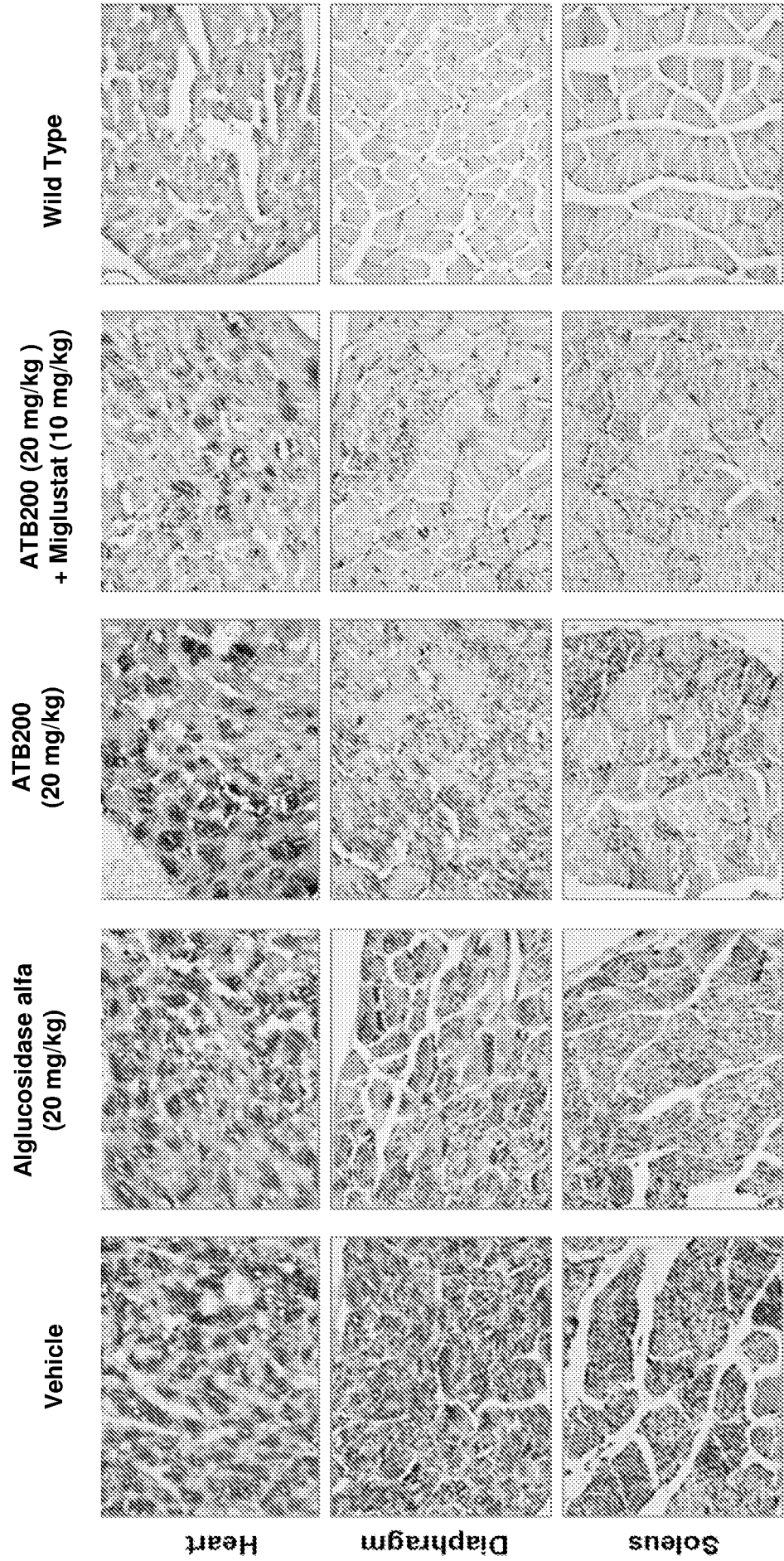


FIG. 14

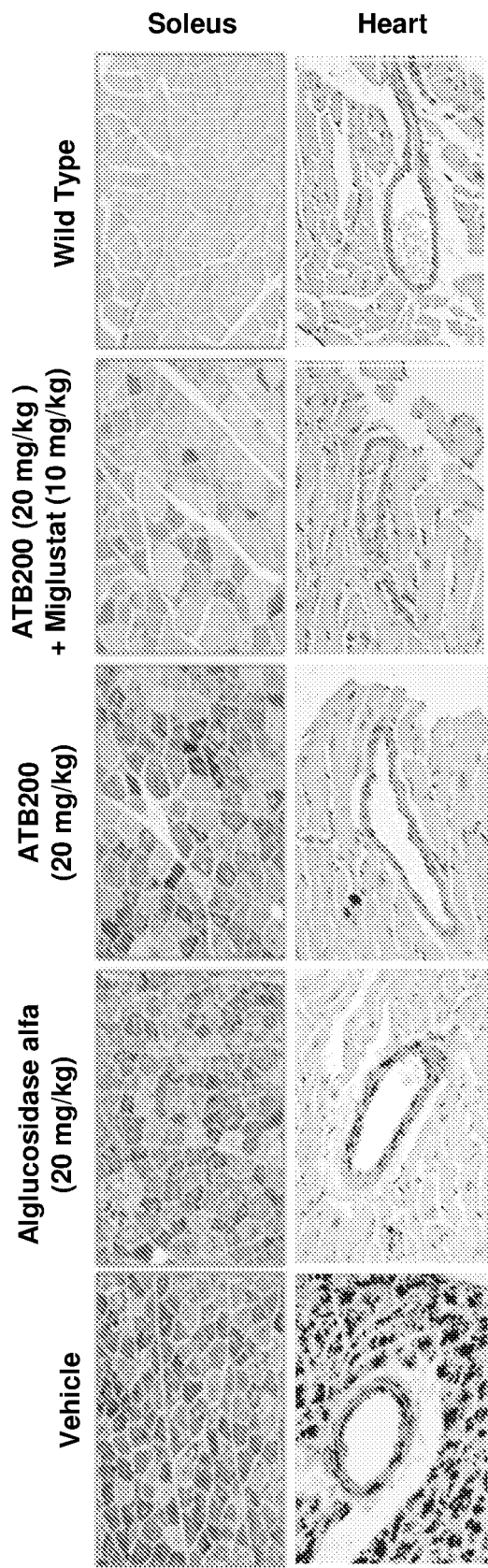


FIG. 15

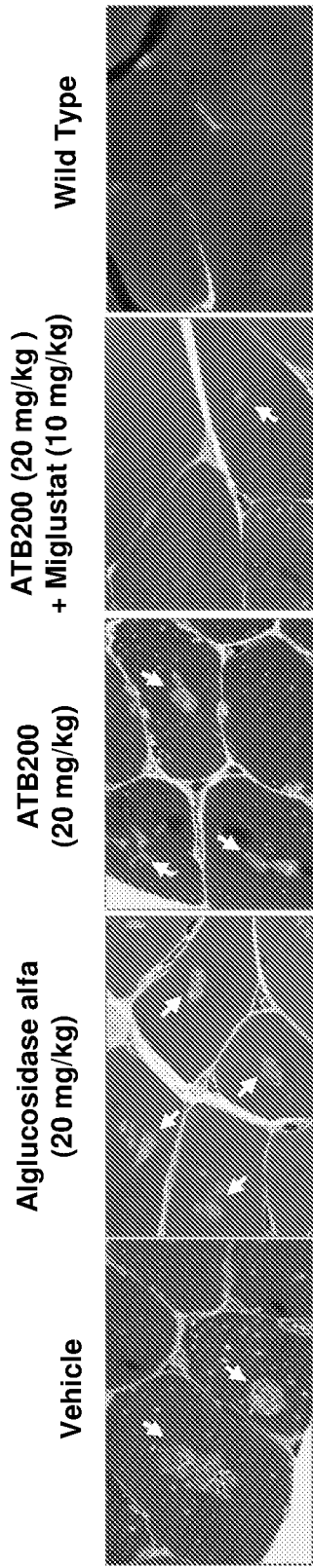


FIG. 16

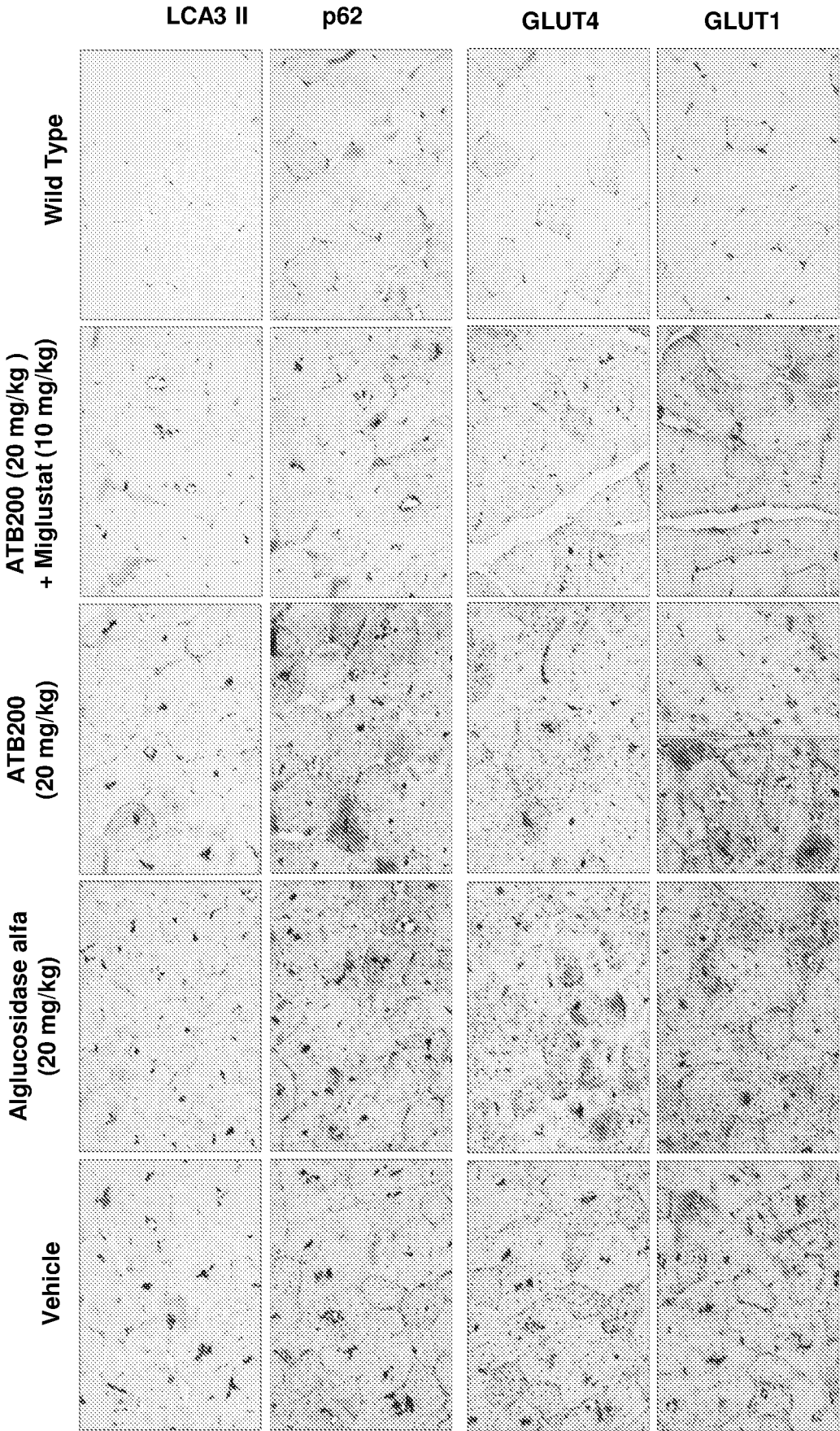


FIG. 17

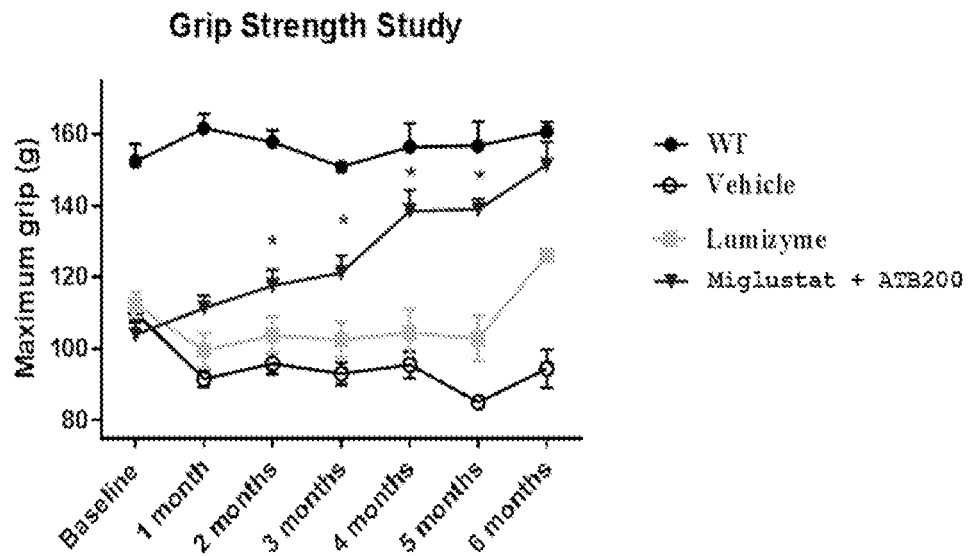


FIG. 18A

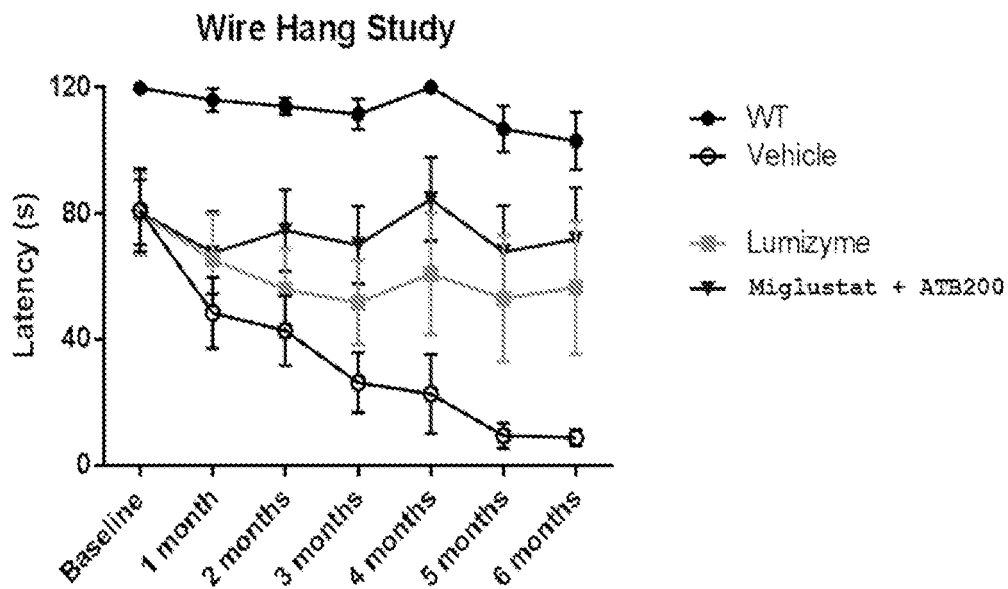


FIG. 18B

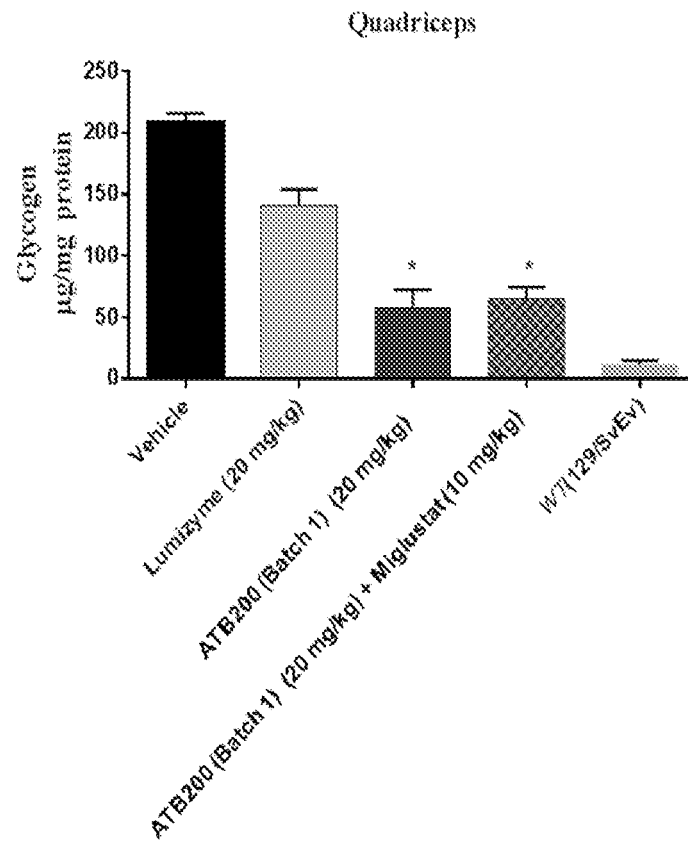


FIG. 19A

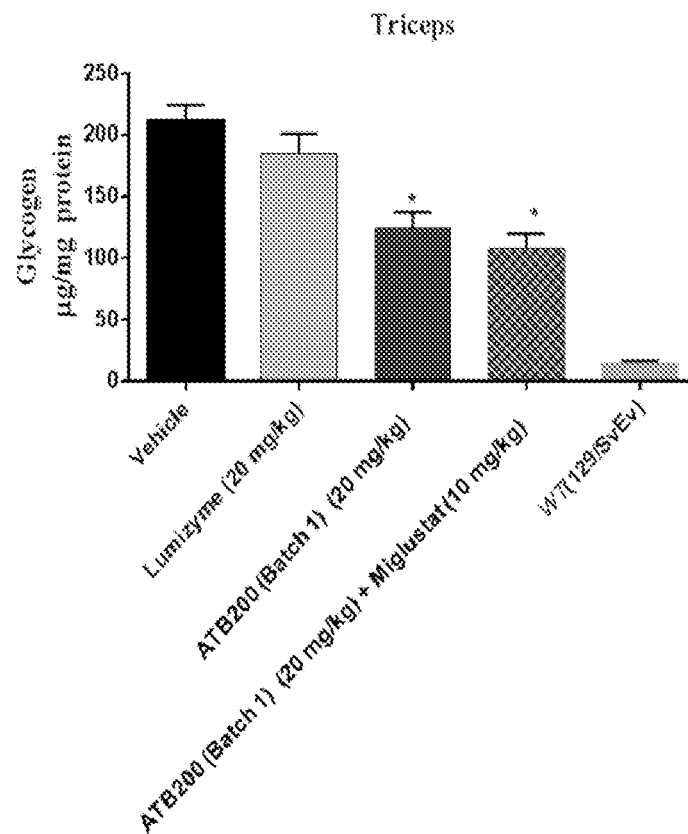


FIG. 19B

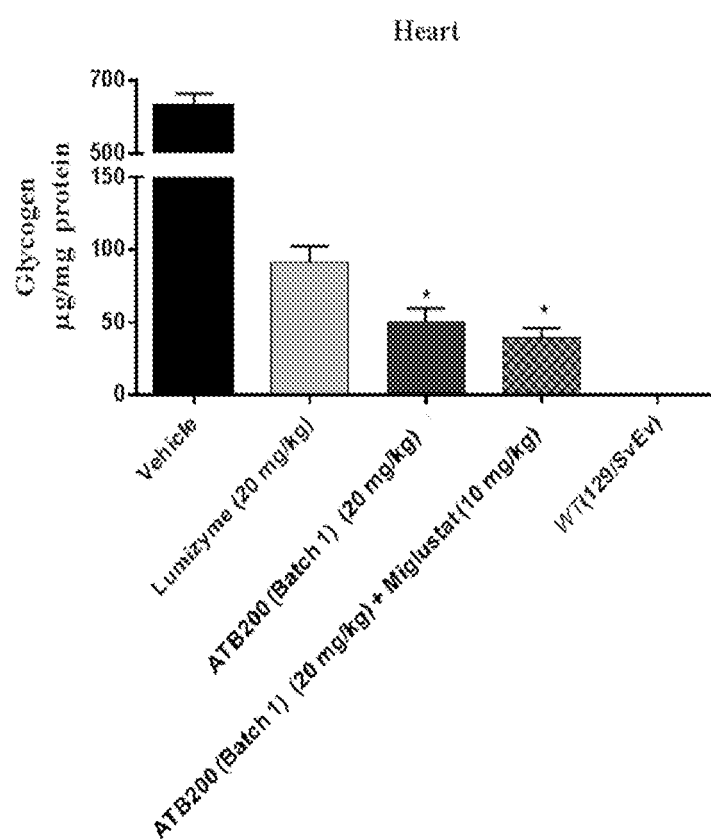


FIG. 19C

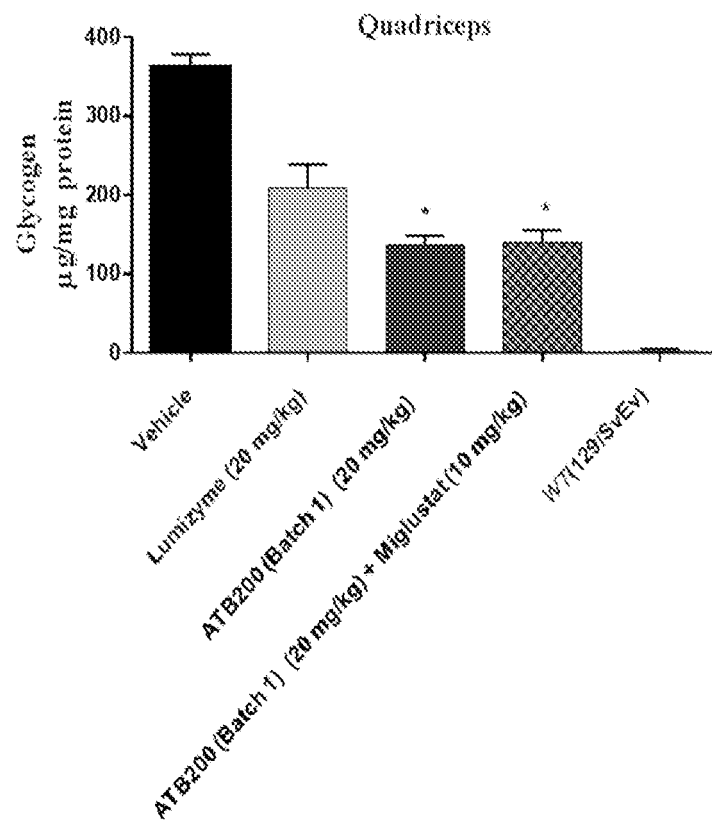


FIG. 19D

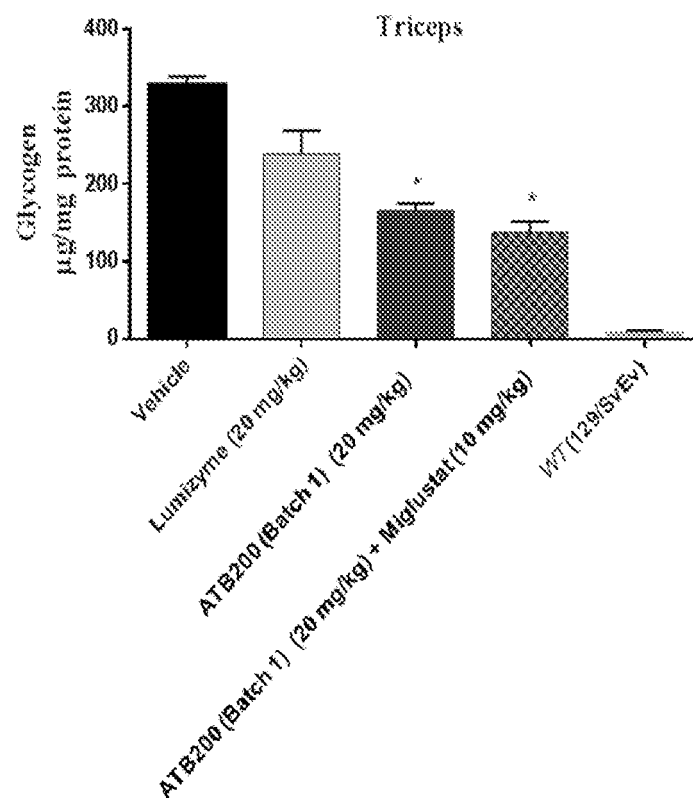


FIG. 19E

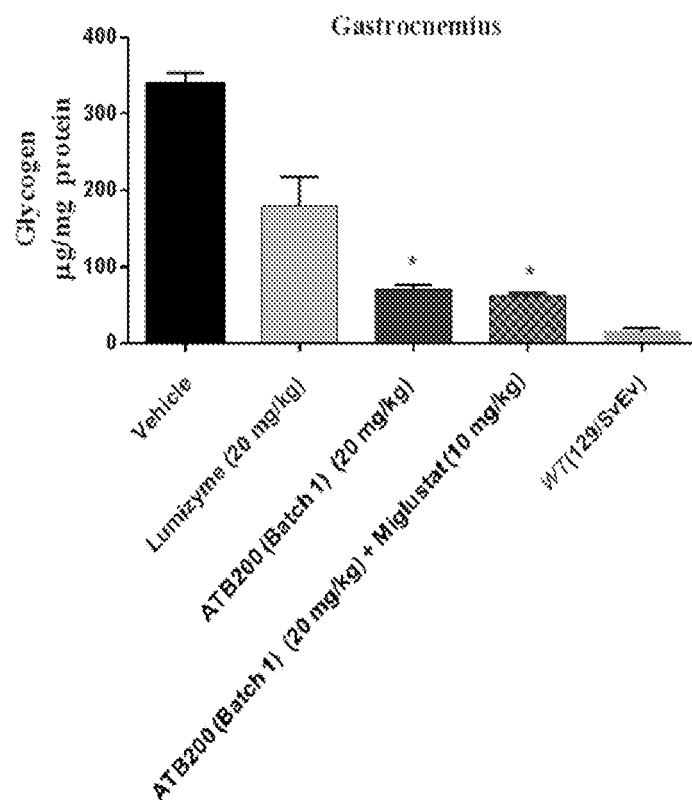


FIG. 19F

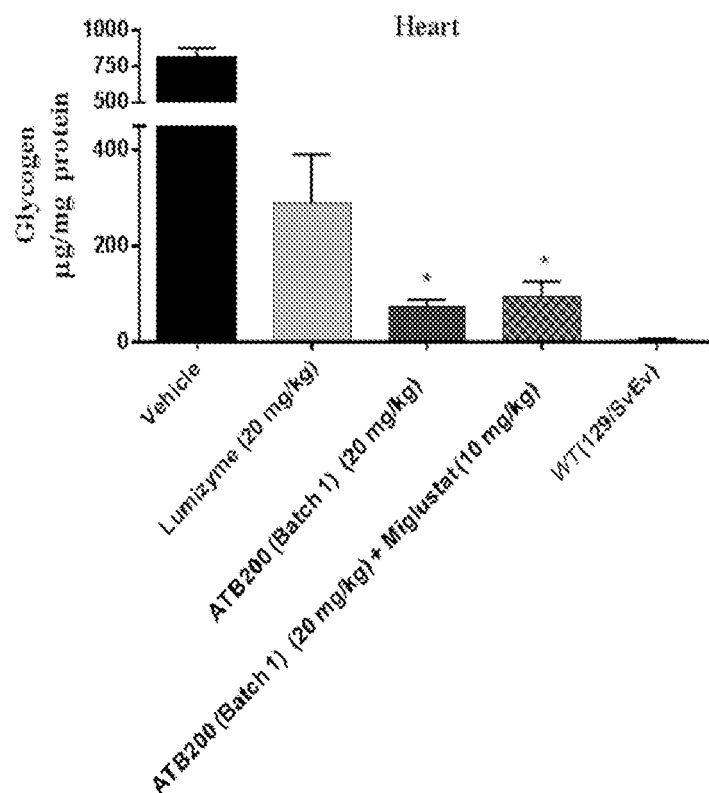


FIG. 19G

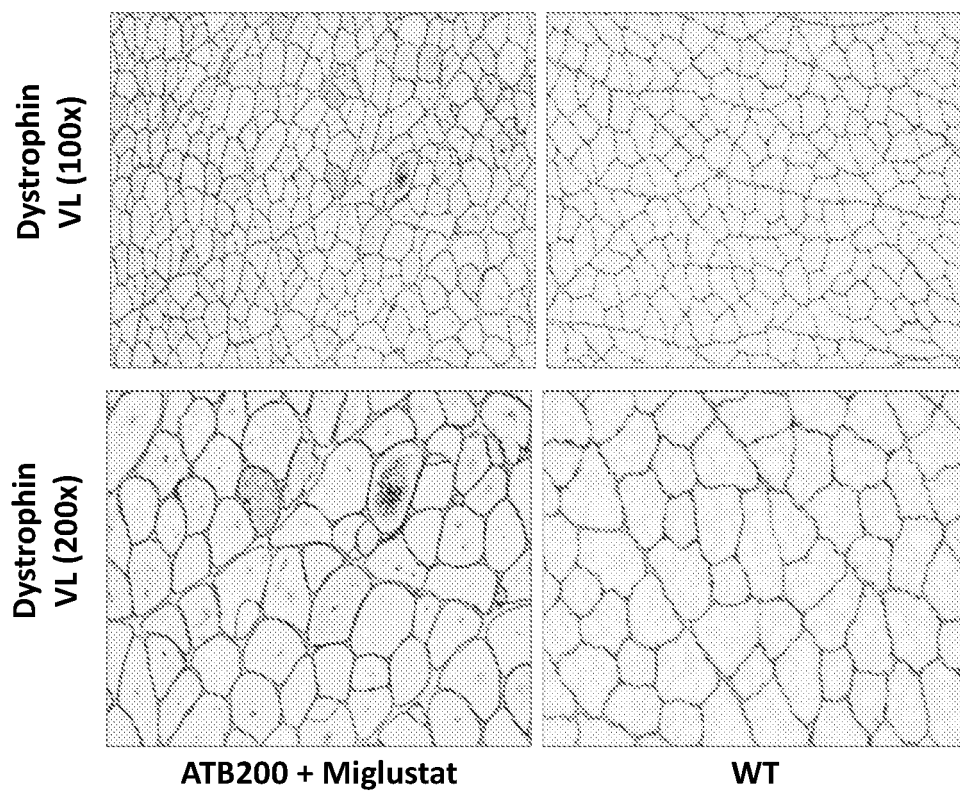
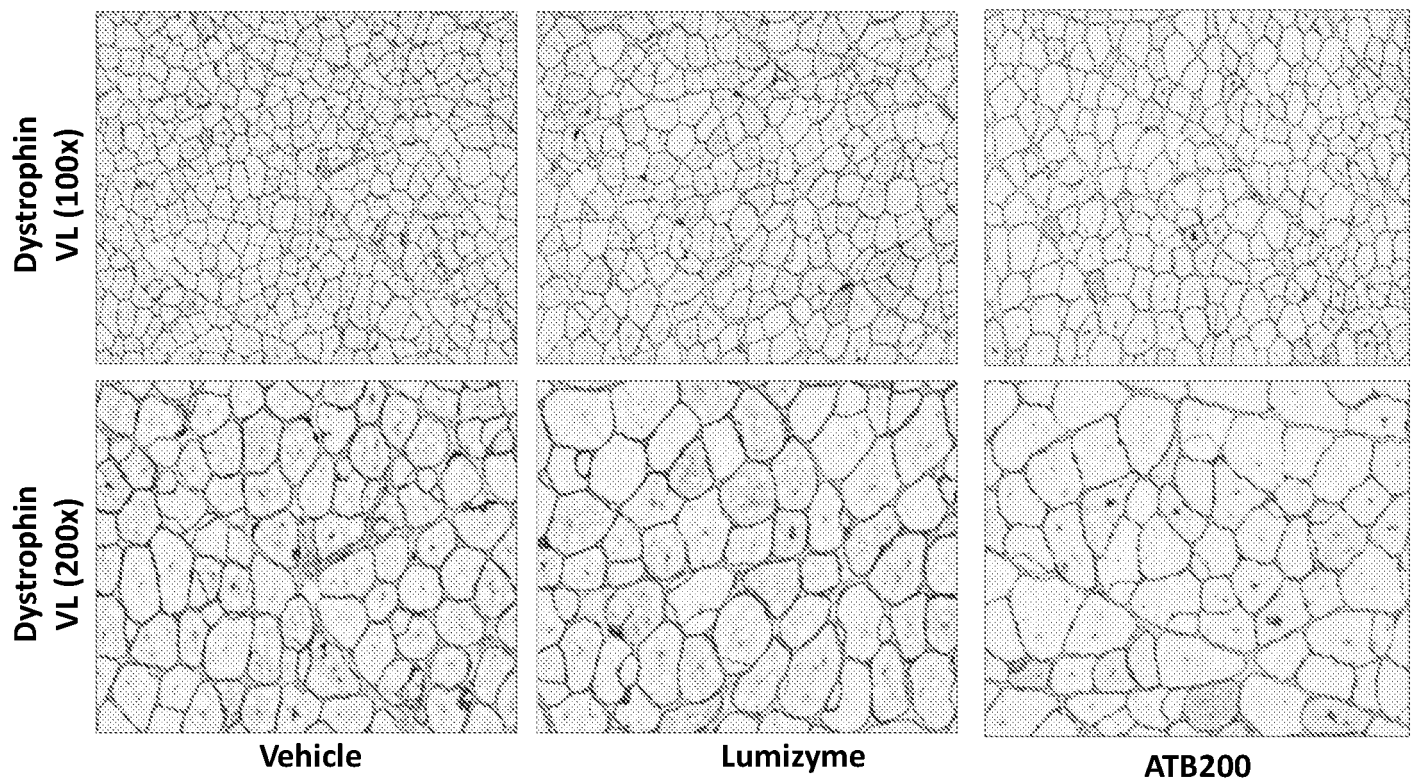


FIG. 20

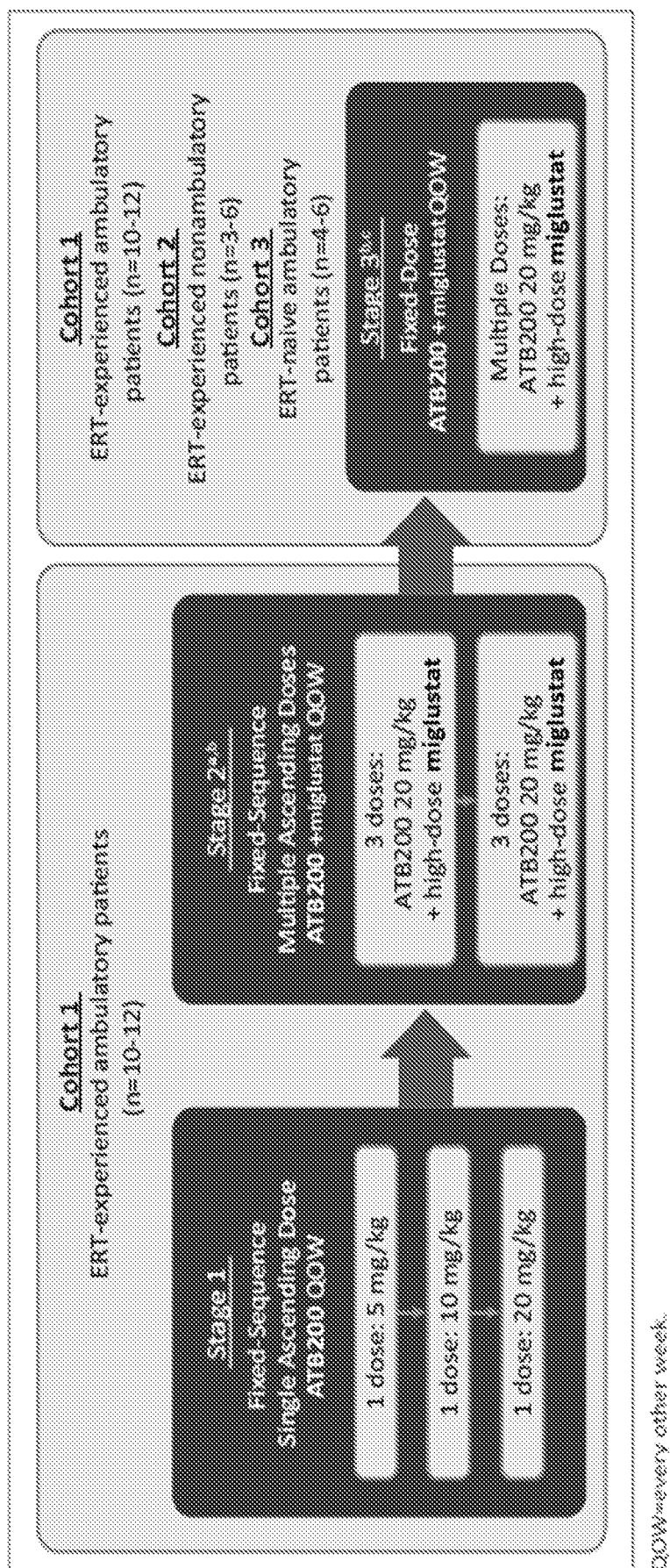


FIG. 21

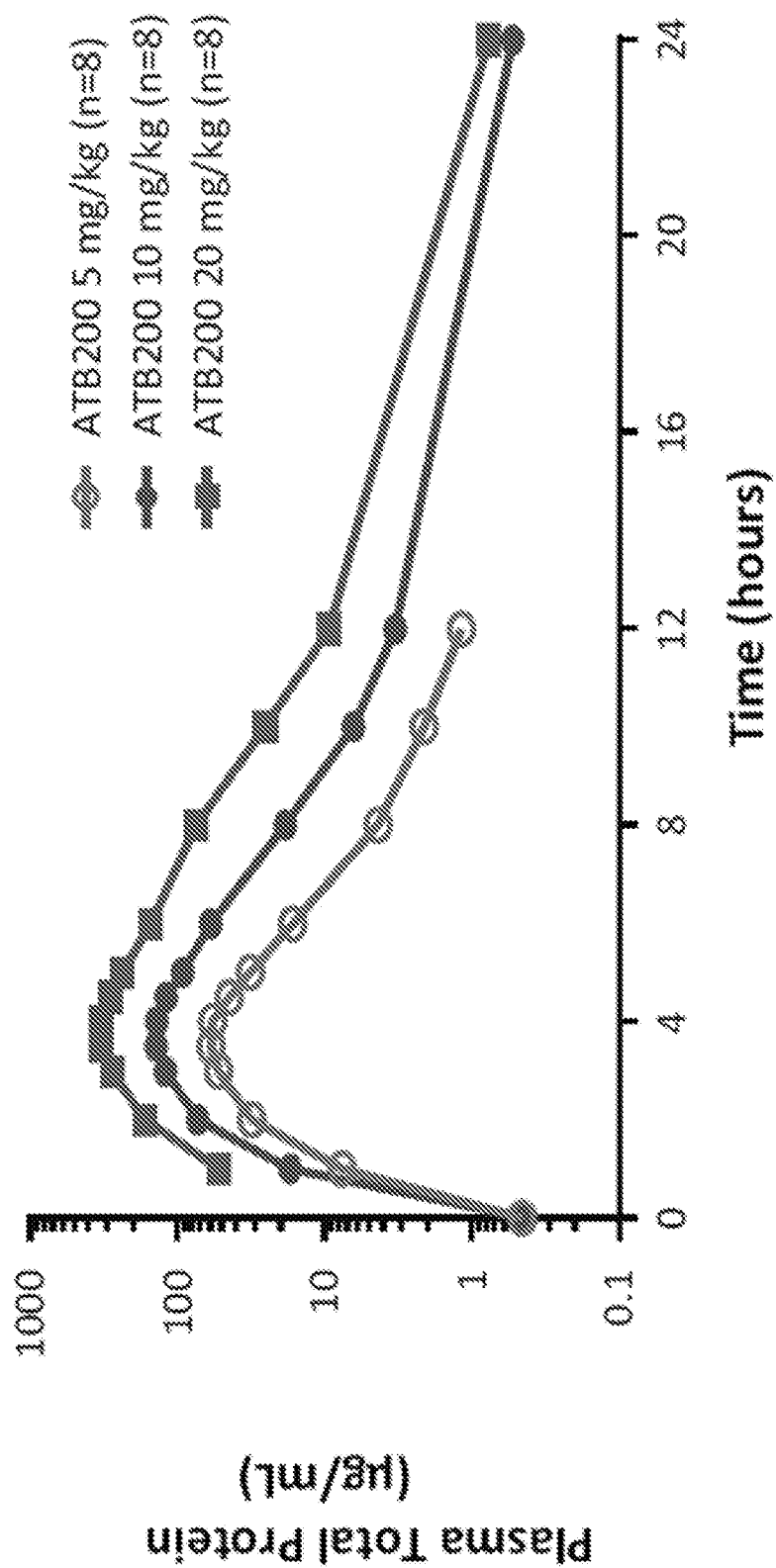


FIG. 22A

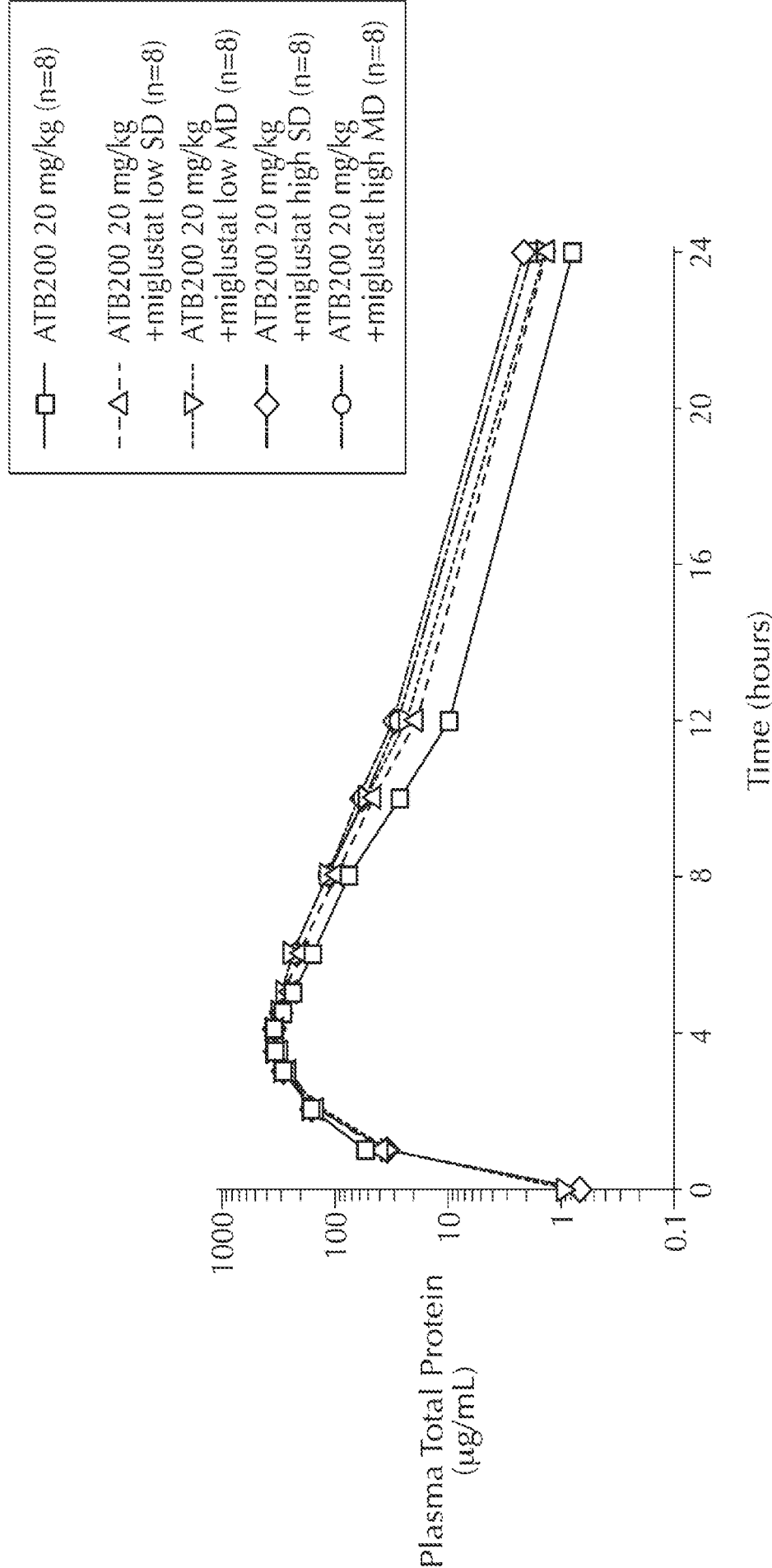


FIG. 22B

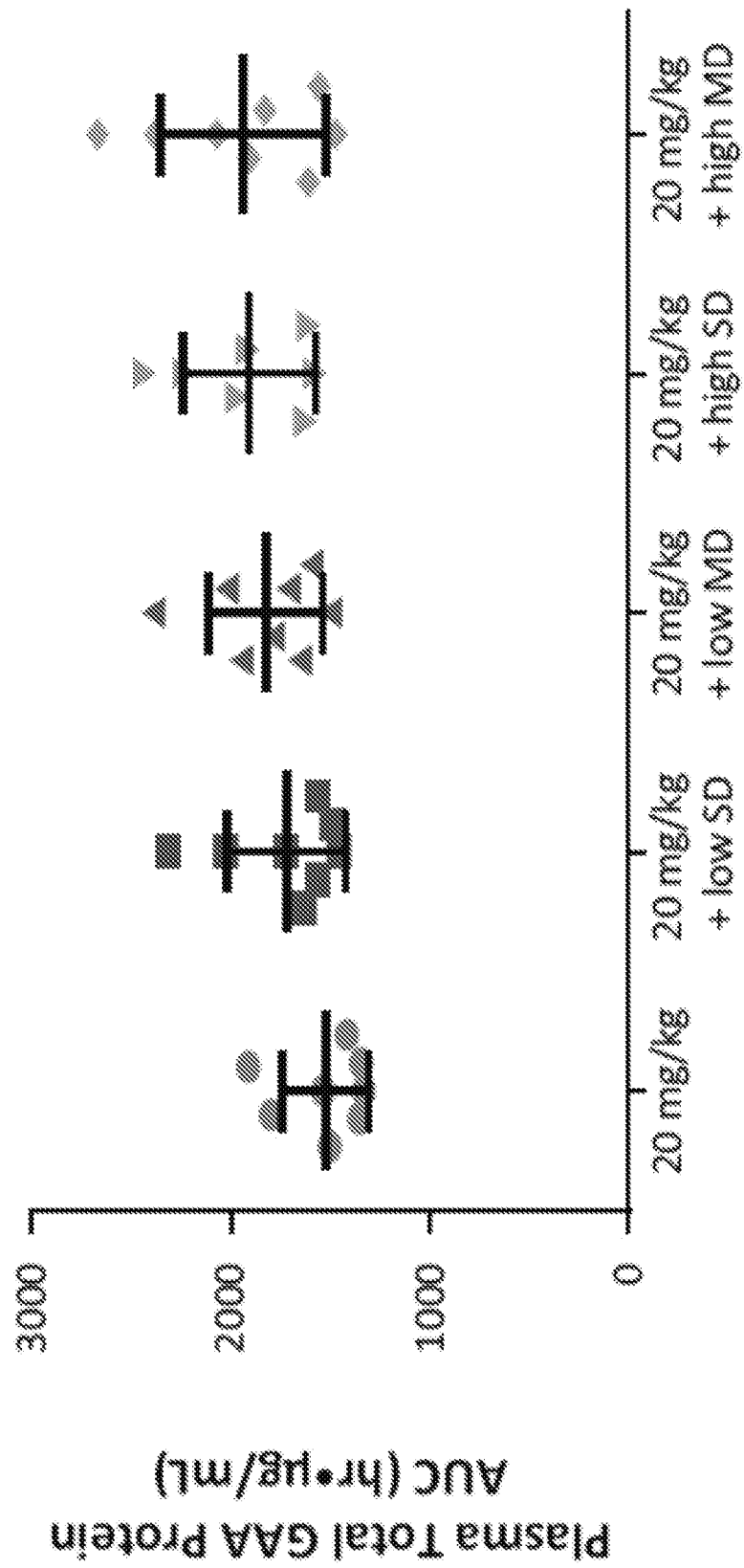


FIG. 22C

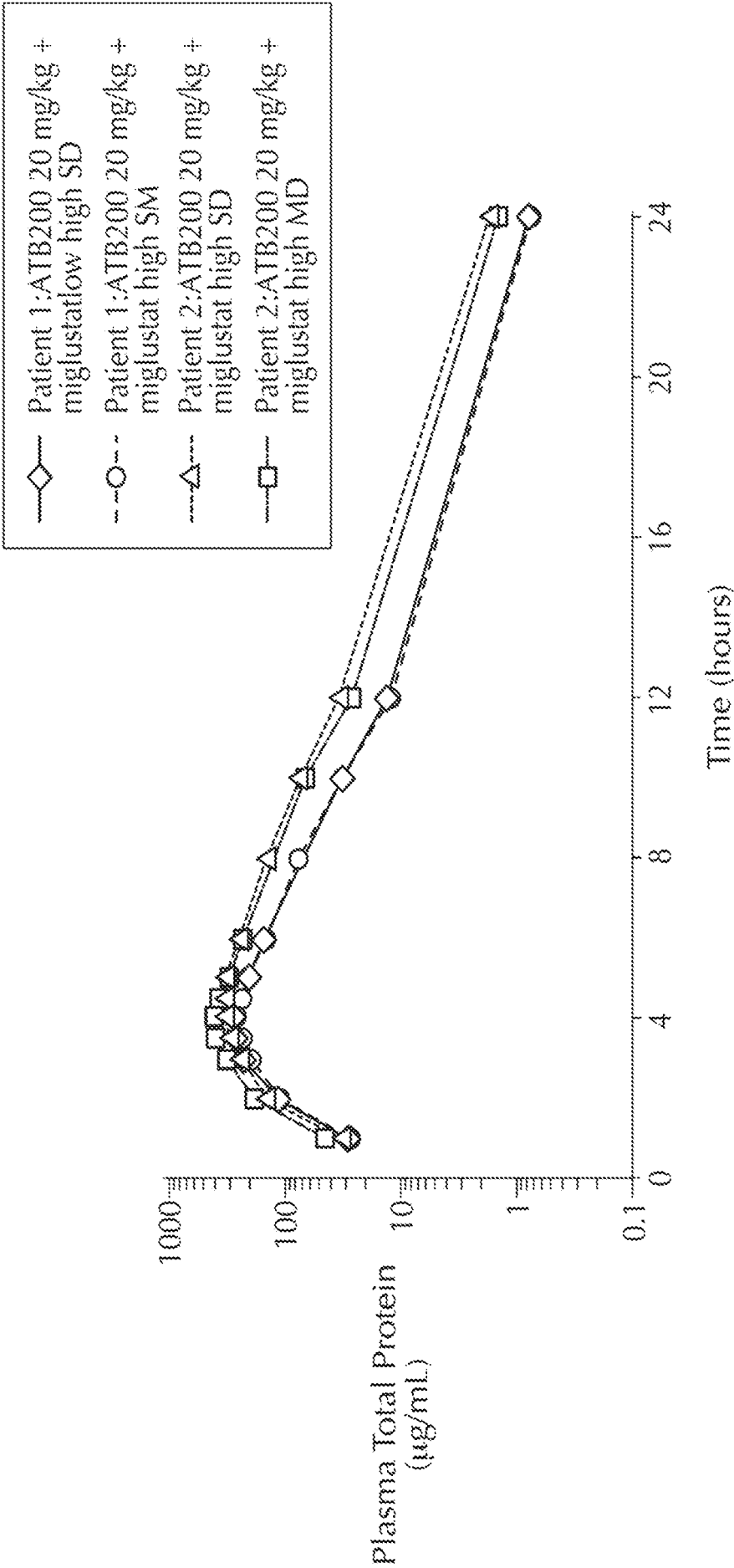


FIG. 22D

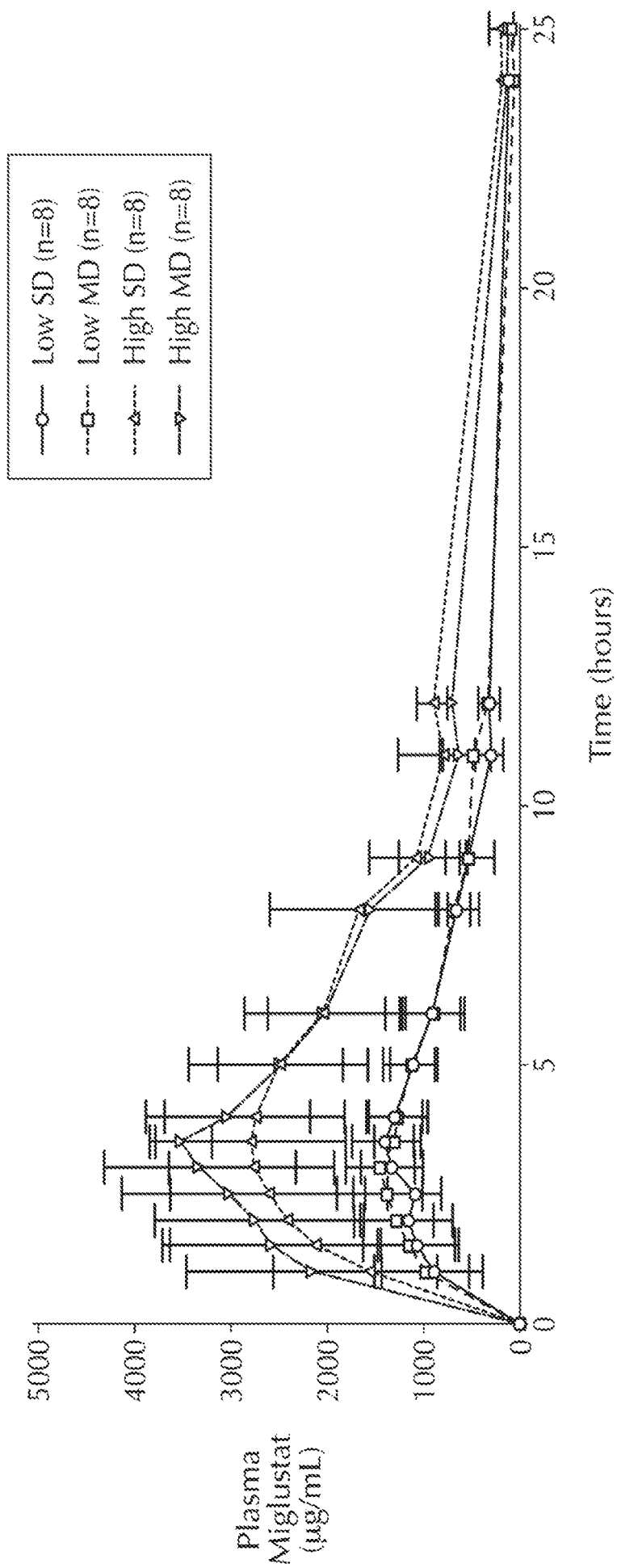


FIG. 23

Cohort 1: Percentage Change from Baseline for ALT, AST, and CPK

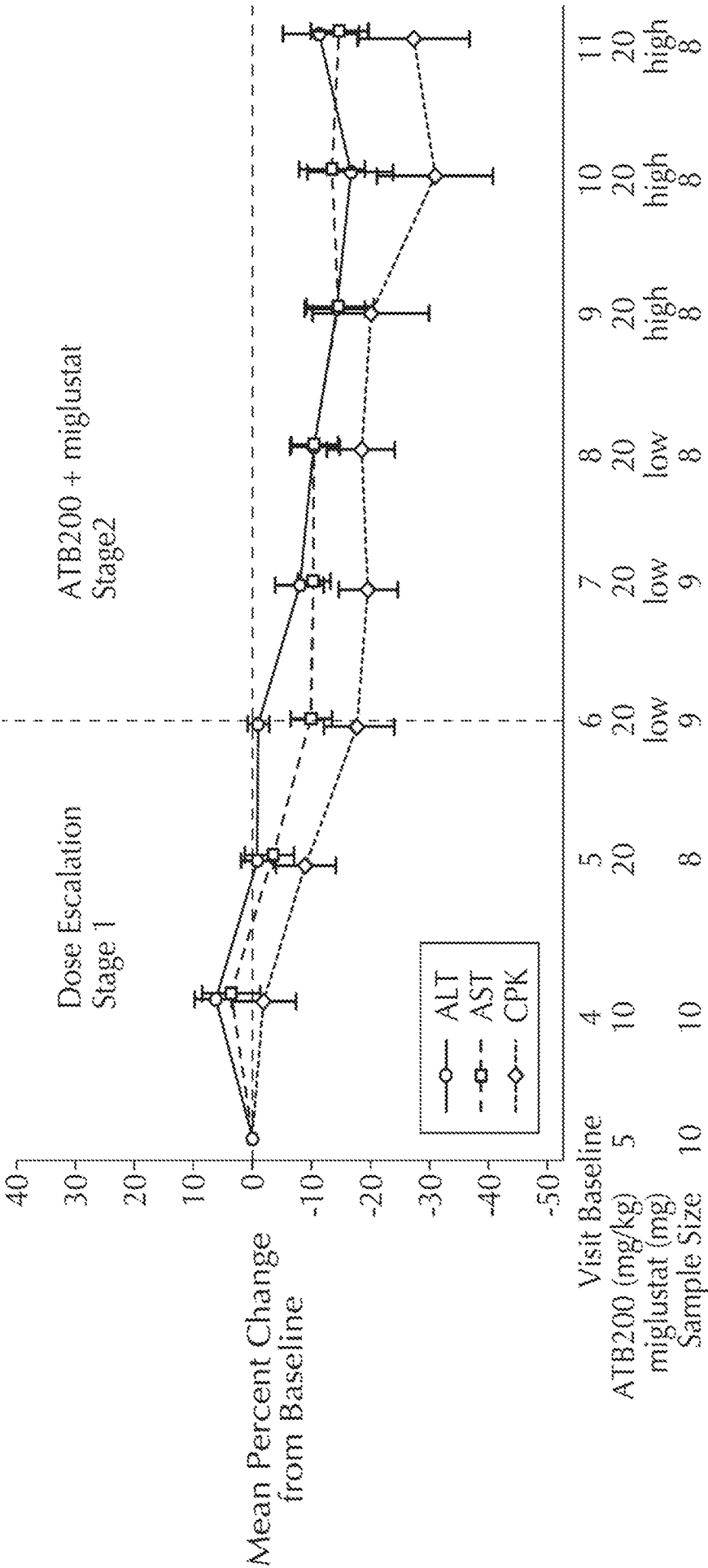


FIG. 24A

Cohort 1: Percentage Change from Baseline for HEX4

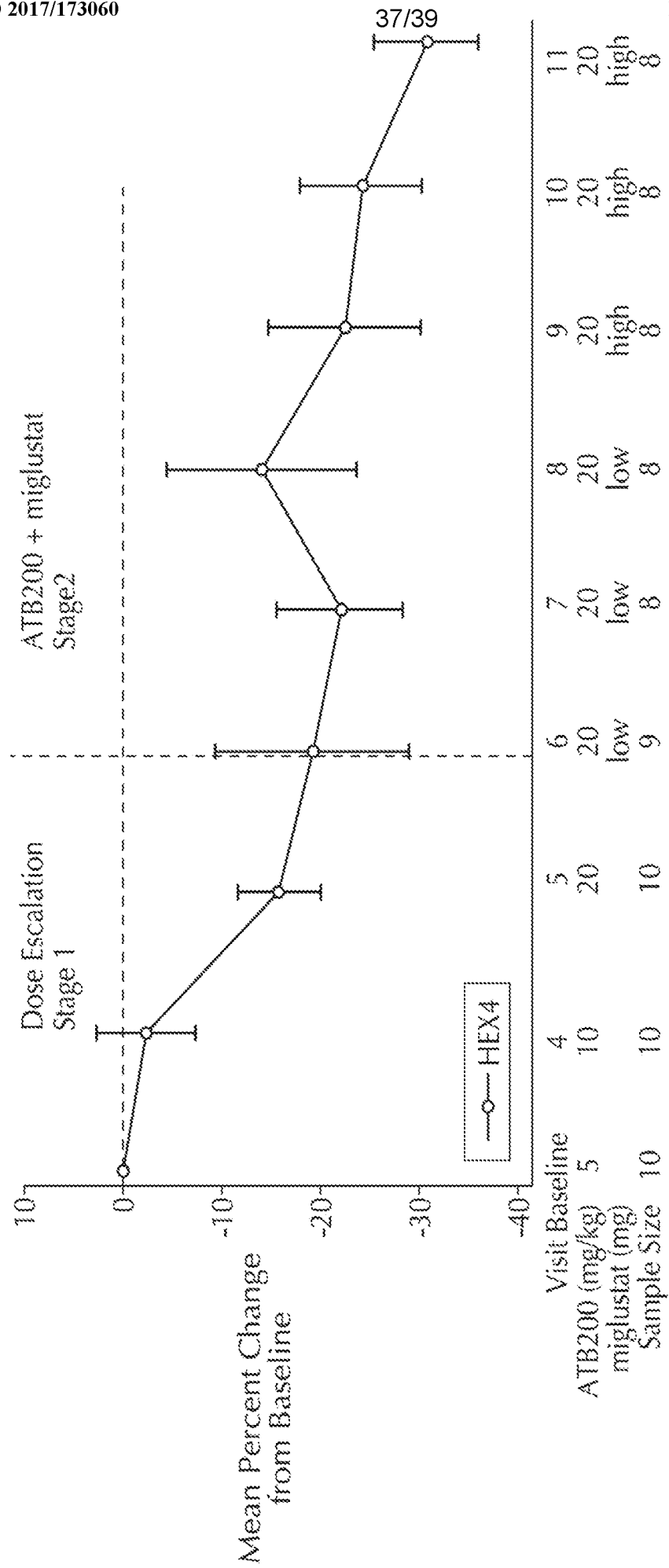


FIG. 24B

Cohort 3: Percentage Change from Baseline for ALT, AST, and CPK

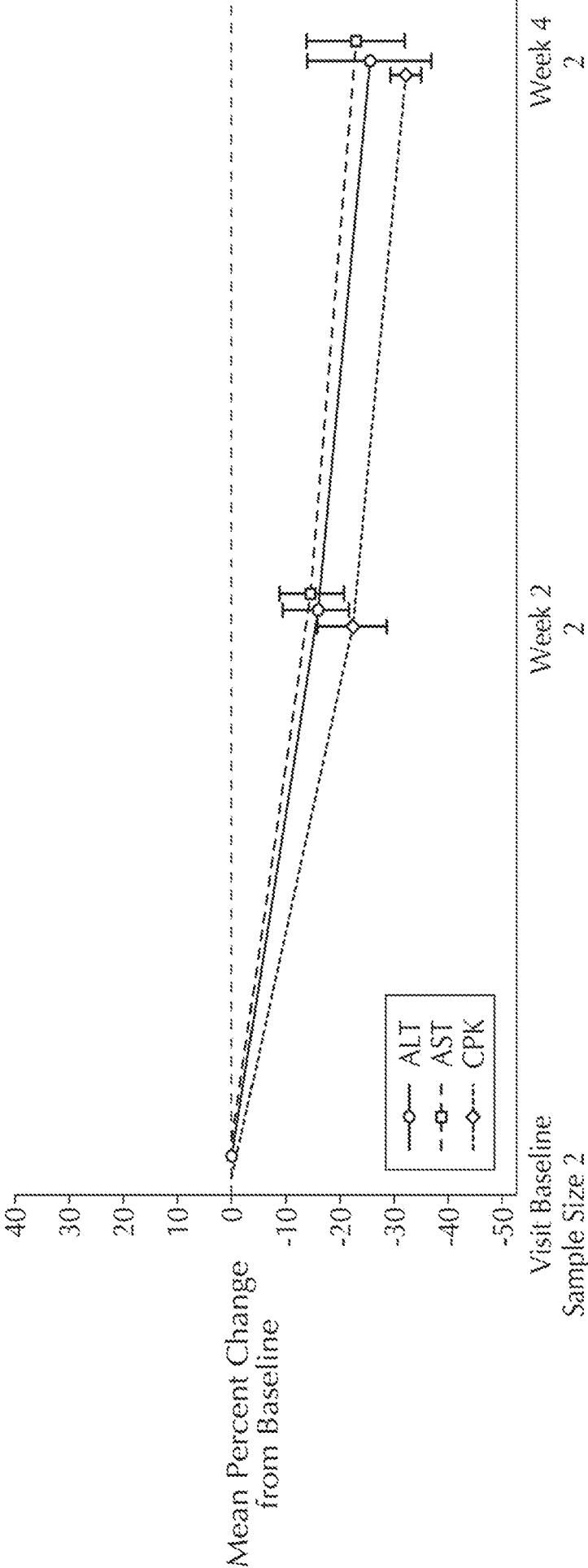


FIG. 24C

Cohort 3: Percentage Change from Baseline for HEX4

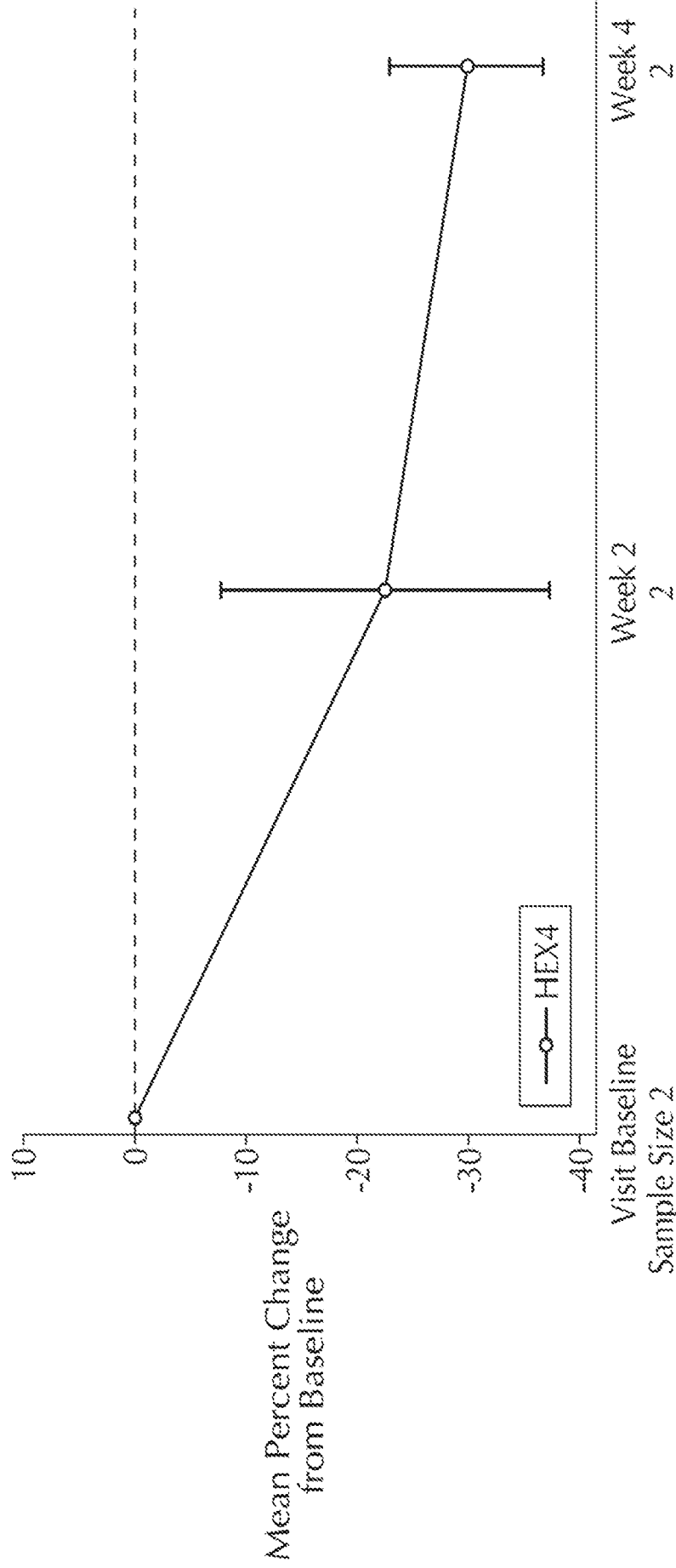


FIG. 24D