

Structure and Receptor Affinity for High Mannose and Phosphorylated Oligosaccharides

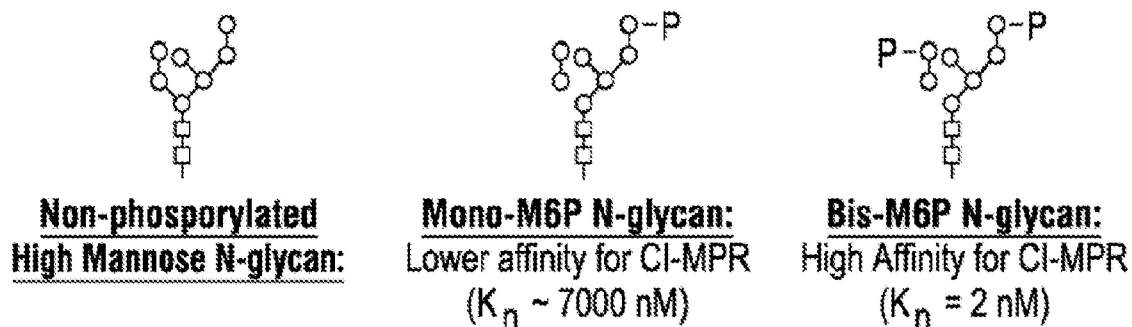


FIG. 1A

Mannose 6-phosphate (M6P)

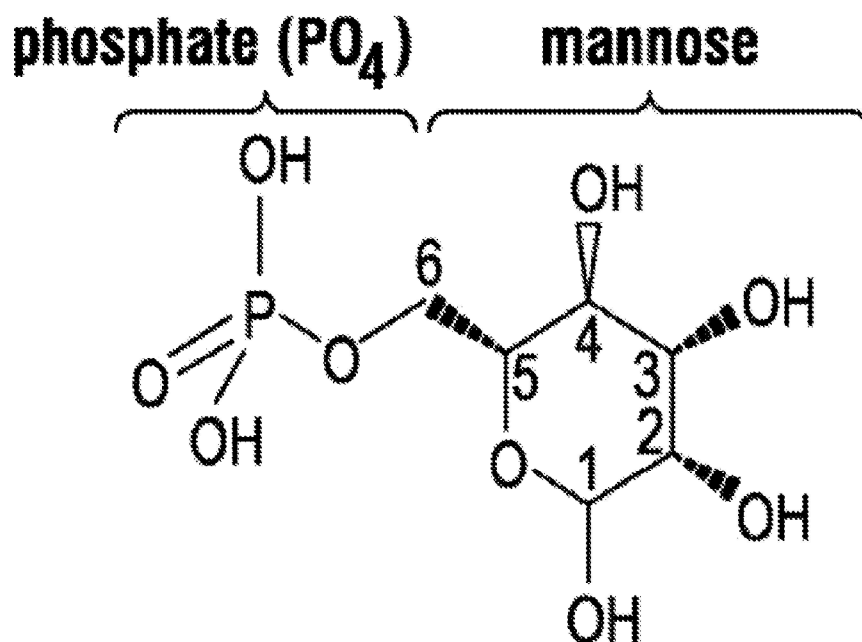


FIG. 1B

Comparison of Productive and Non-Productive Targeting Glycan Specific Receptors

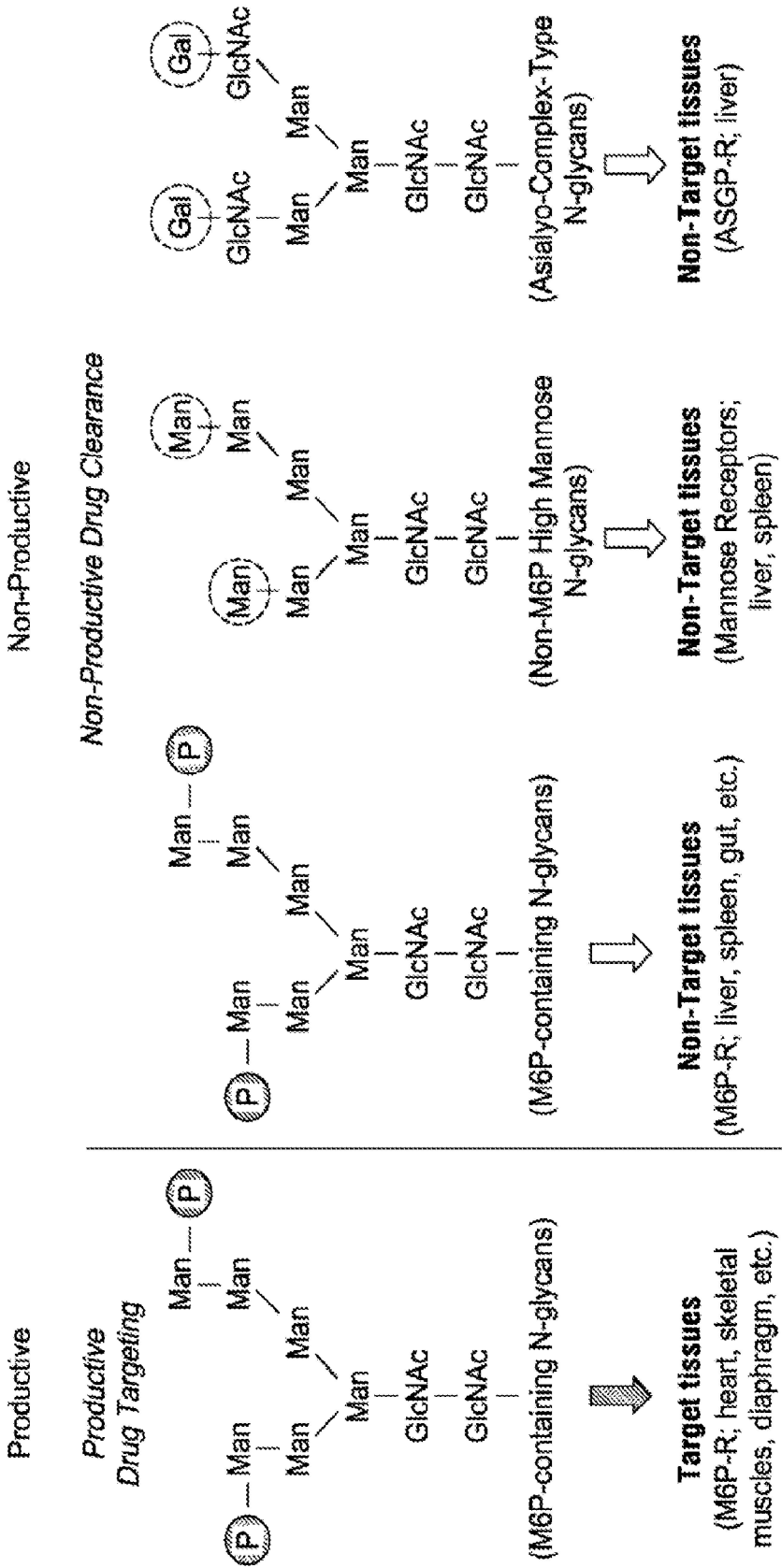


Fig. 2B

Fig. 2A

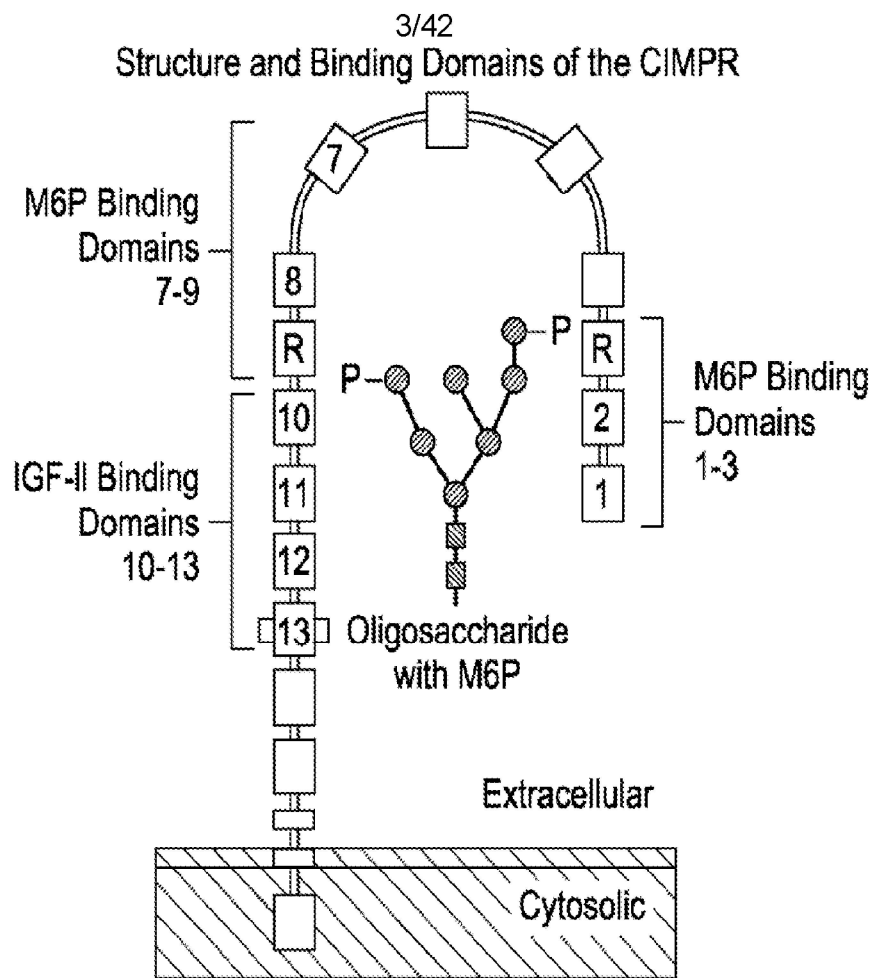


Fig. 3A

Ligands; Affinity and In Vivo Location of Three Glycoprotein Receptors

Ligand	Receptor	Affinity (nmolar)	Location
Bis-Phosphorylated Glycan	CIMPR	2	All Cells
Mono-Phosphorylated Glycan		7,000	
High Mannose Glycan	Mannose Receptor	20 ^b	Macrophages Dendritic Cells
De-sialylated Complex Glycan	Asialoglycoprotein Receptor	7 ^c	Hepatocytes

Reference: ^aTong *et al* 1989; ^bTaylor *et al* 1992; ^cSchwartz *et al* 1981

Fig. 3B

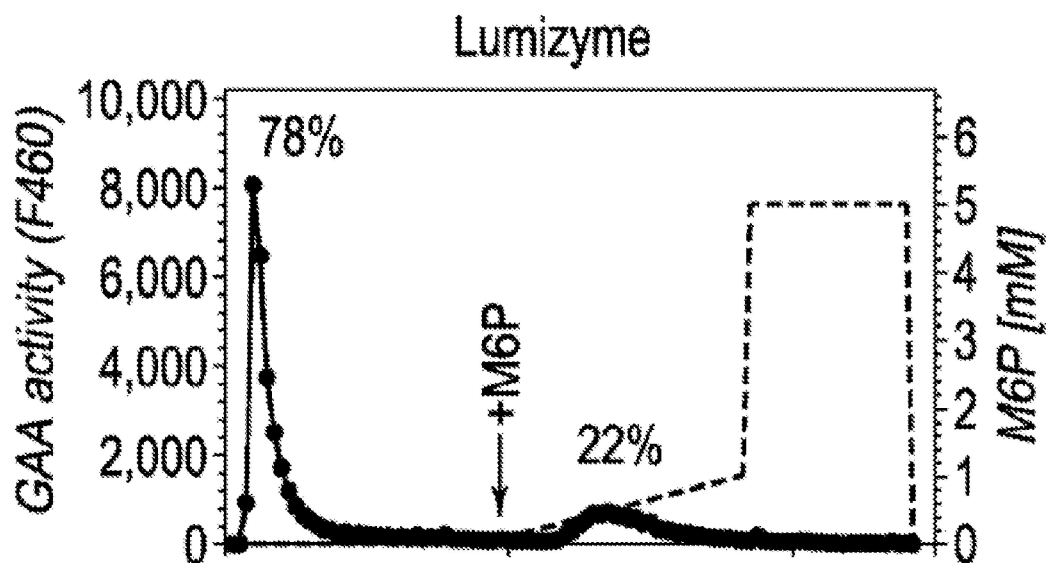


Fig. 4A

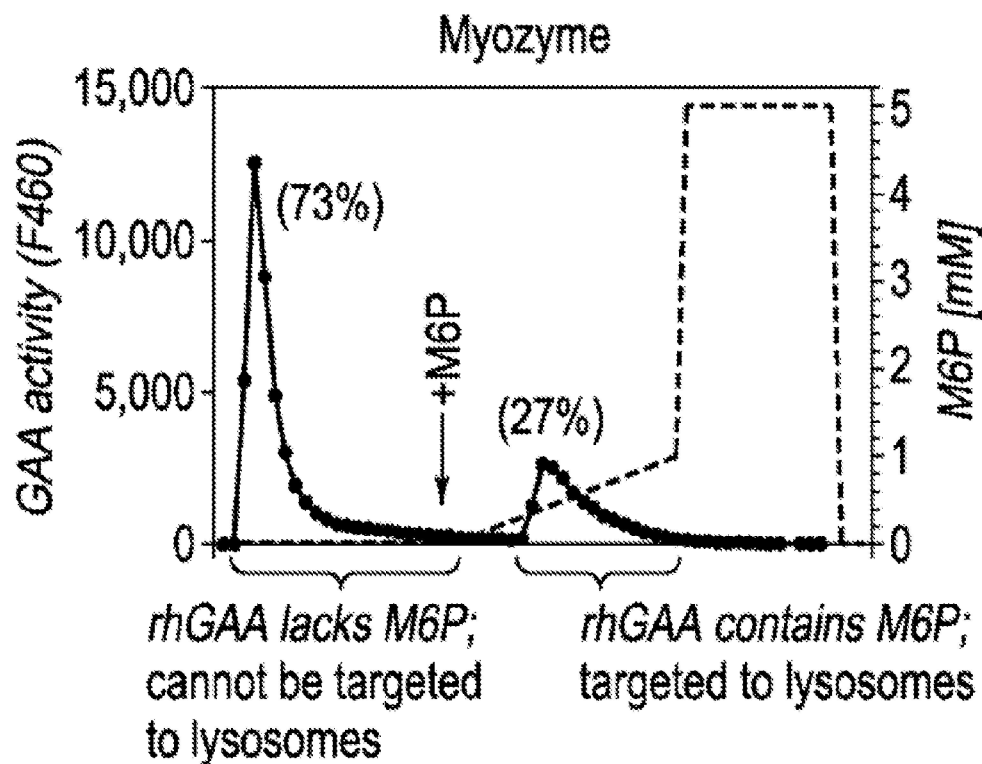
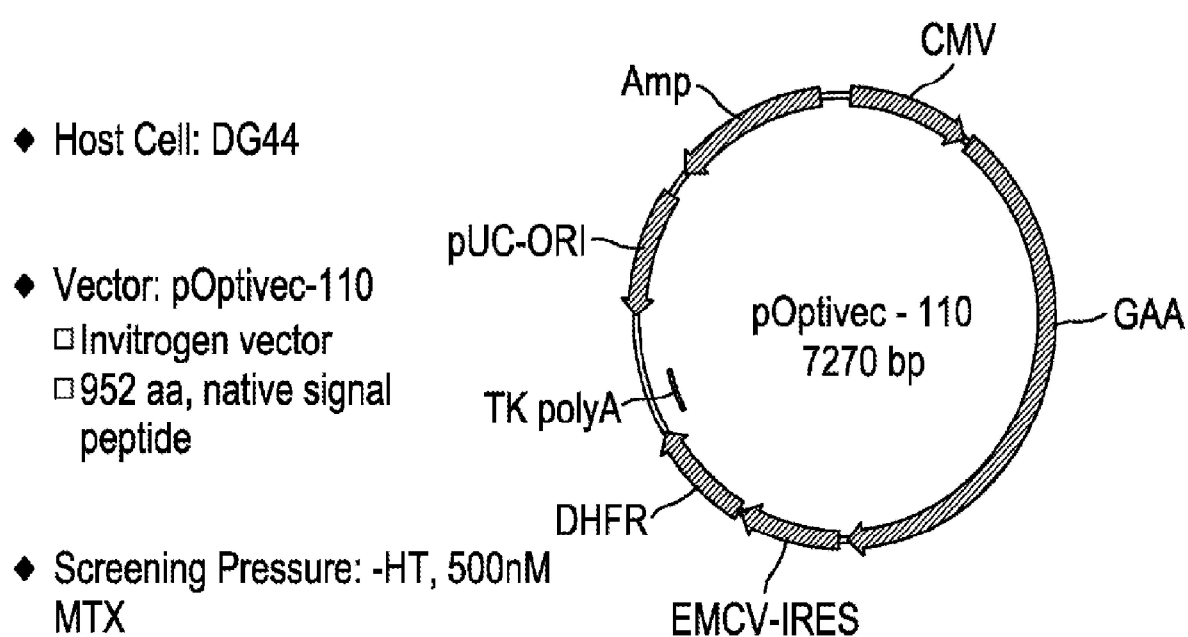


Fig. 4B

ATB200 Vector Construction

***Fig. 5***

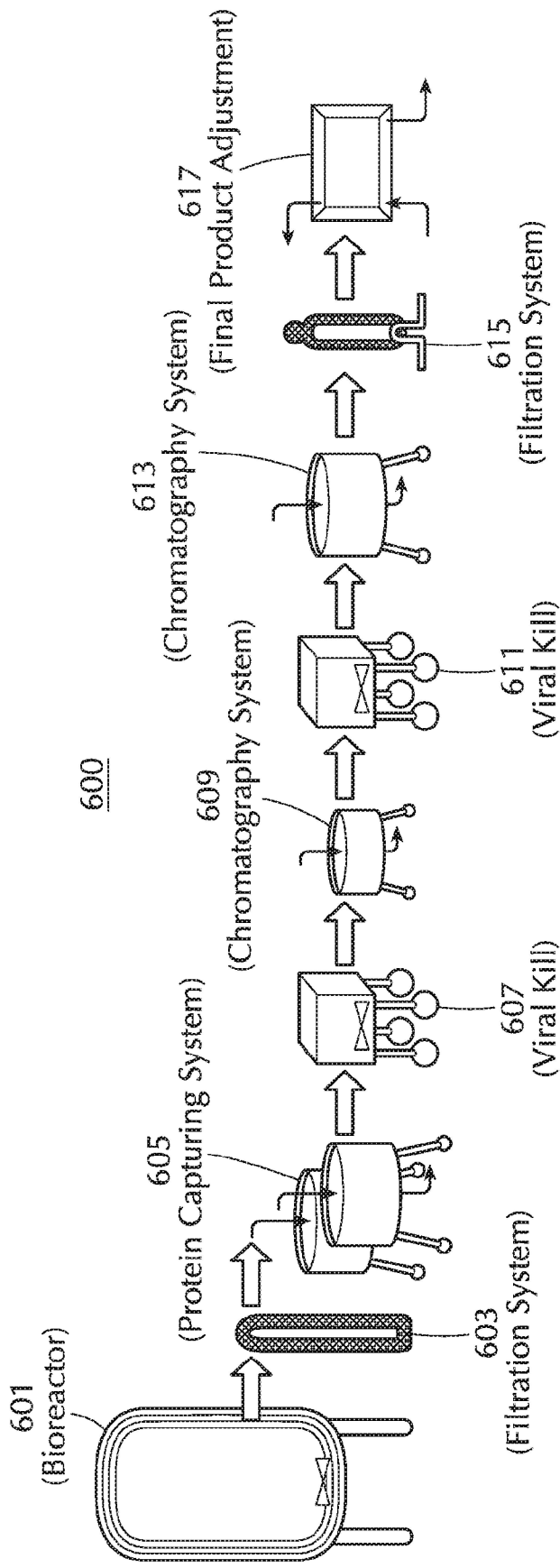


FIG. 6

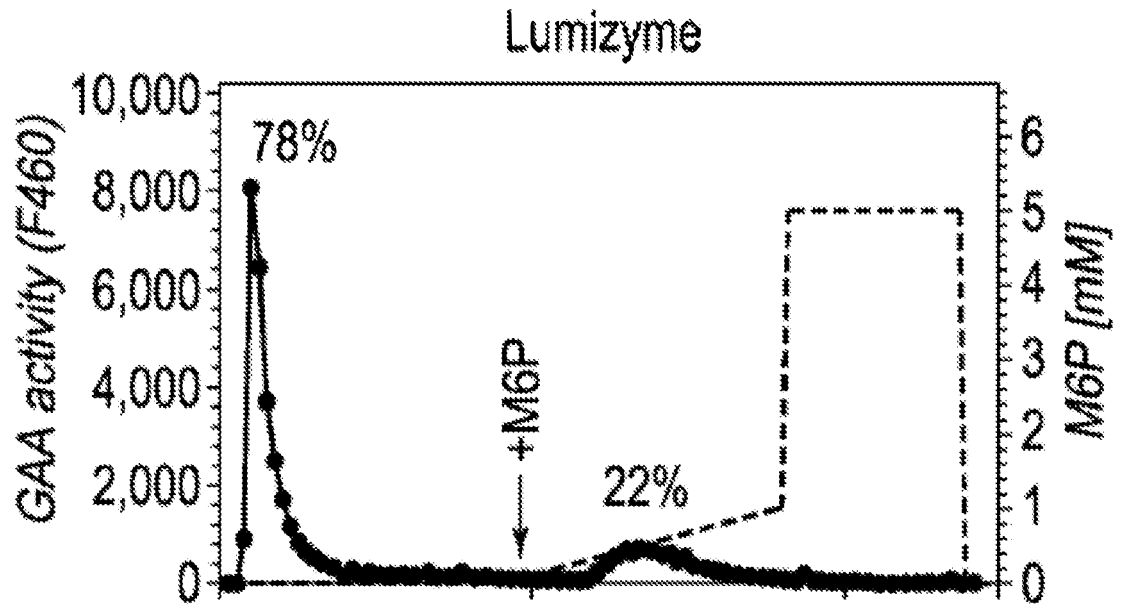


FIG. 7A

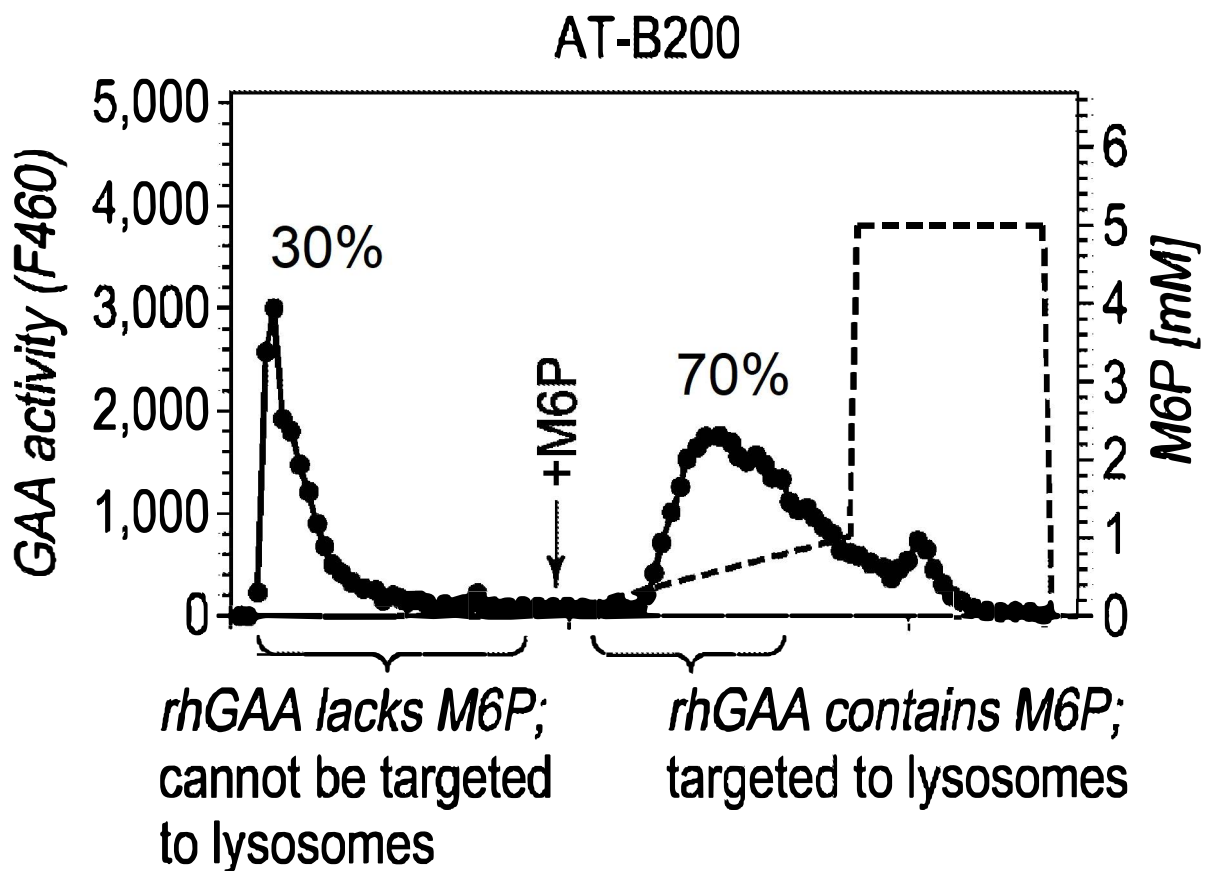
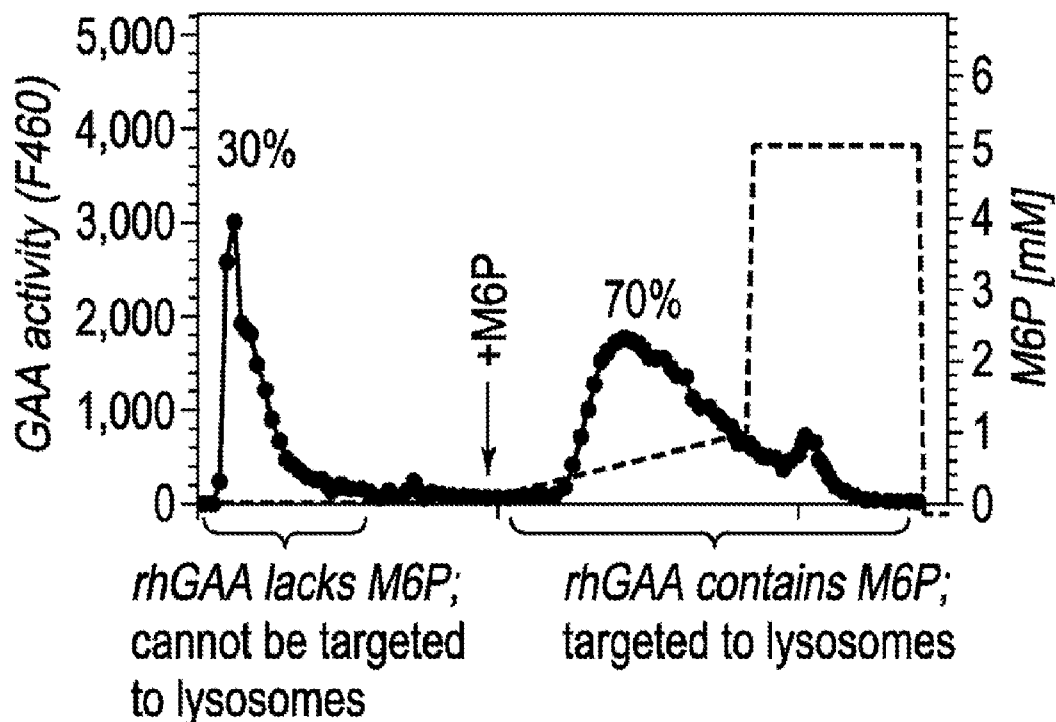


FIG. 7B

Embodiment 1



Embodiment 2

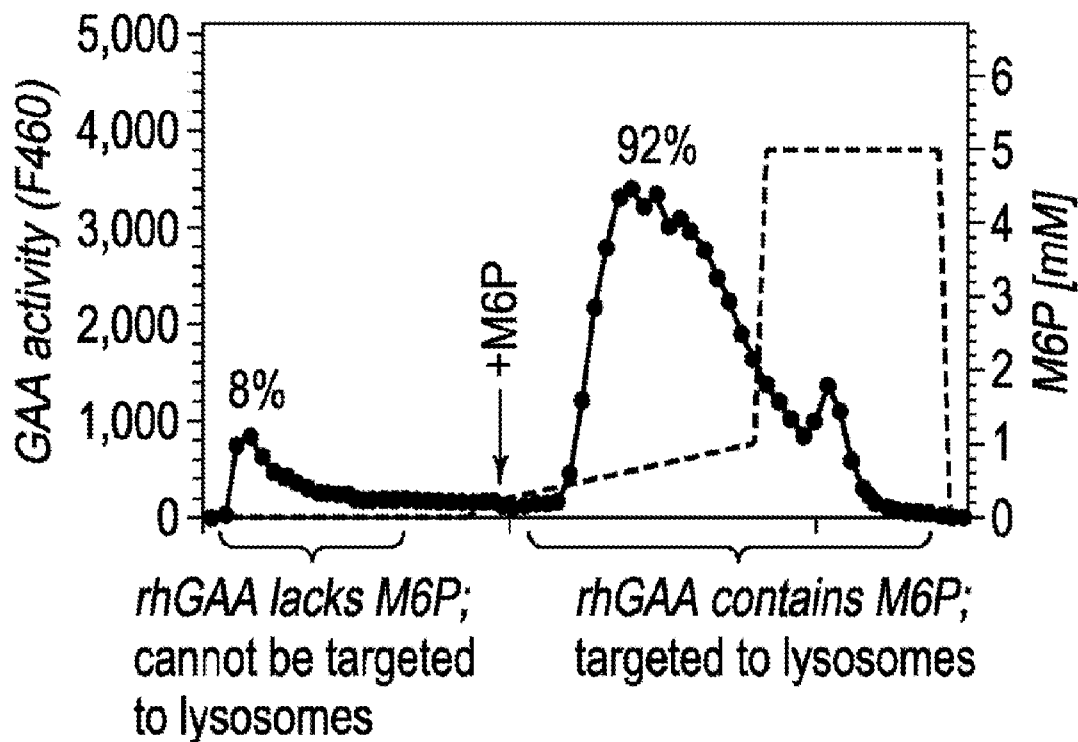


FIG. 8

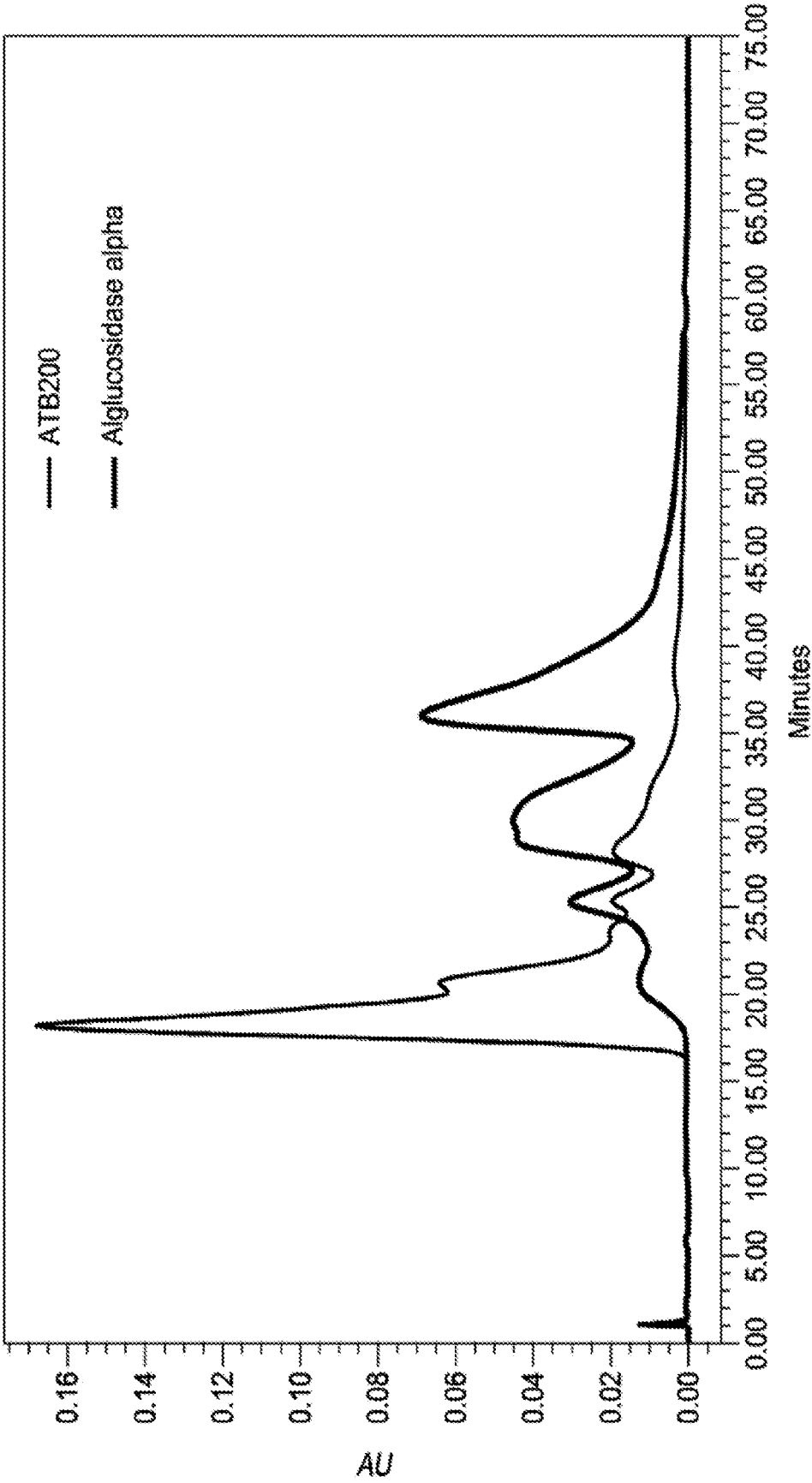


FIG. 9

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. 10

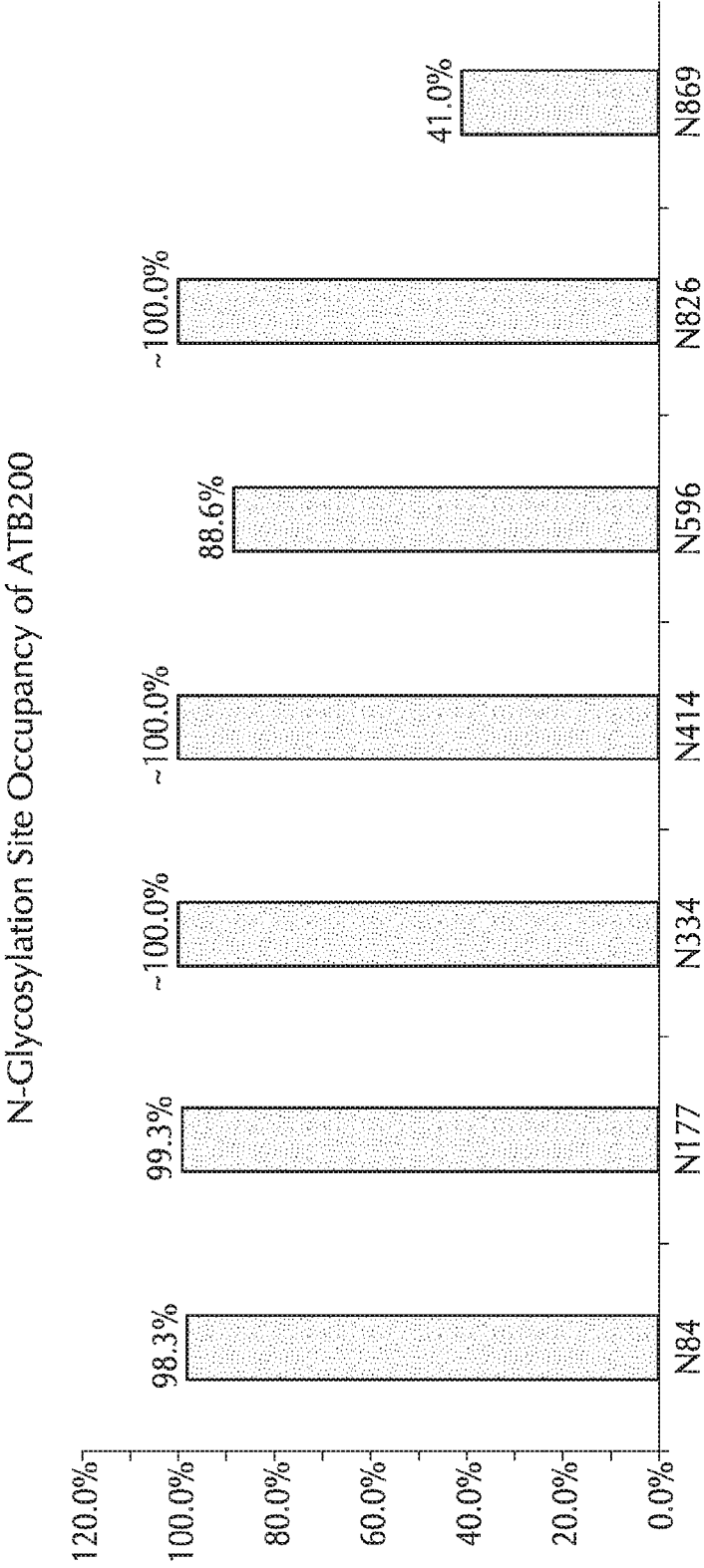


FIG. 11A

N-Glycosylation Profile of N84

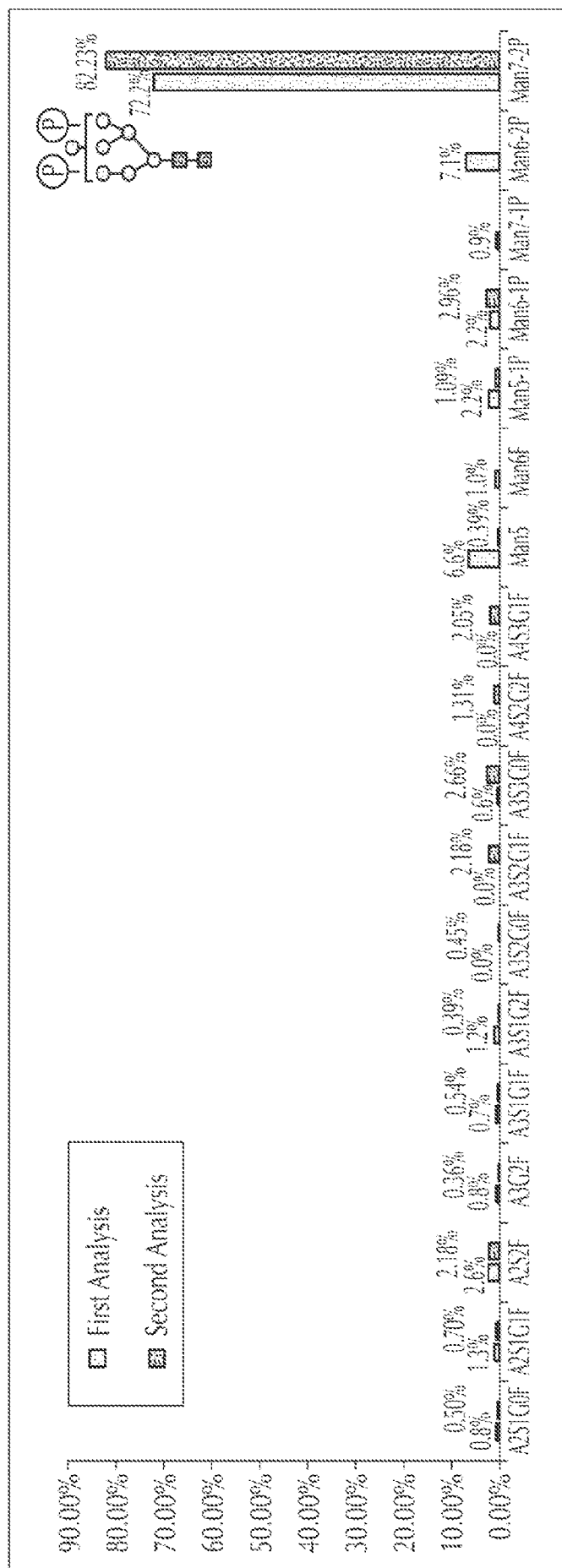


FIG. 11B

N-Glycosylation Profile of N177

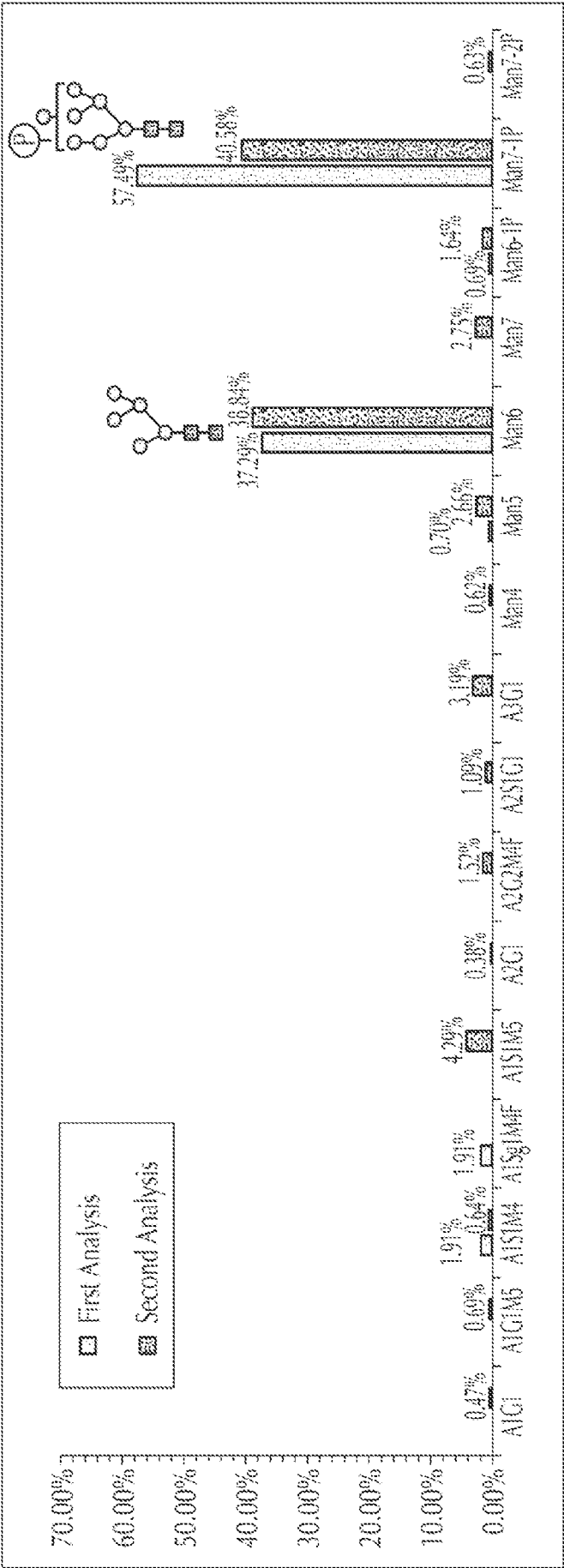


FIG. 11C

N-Glycosylation Profile of N334

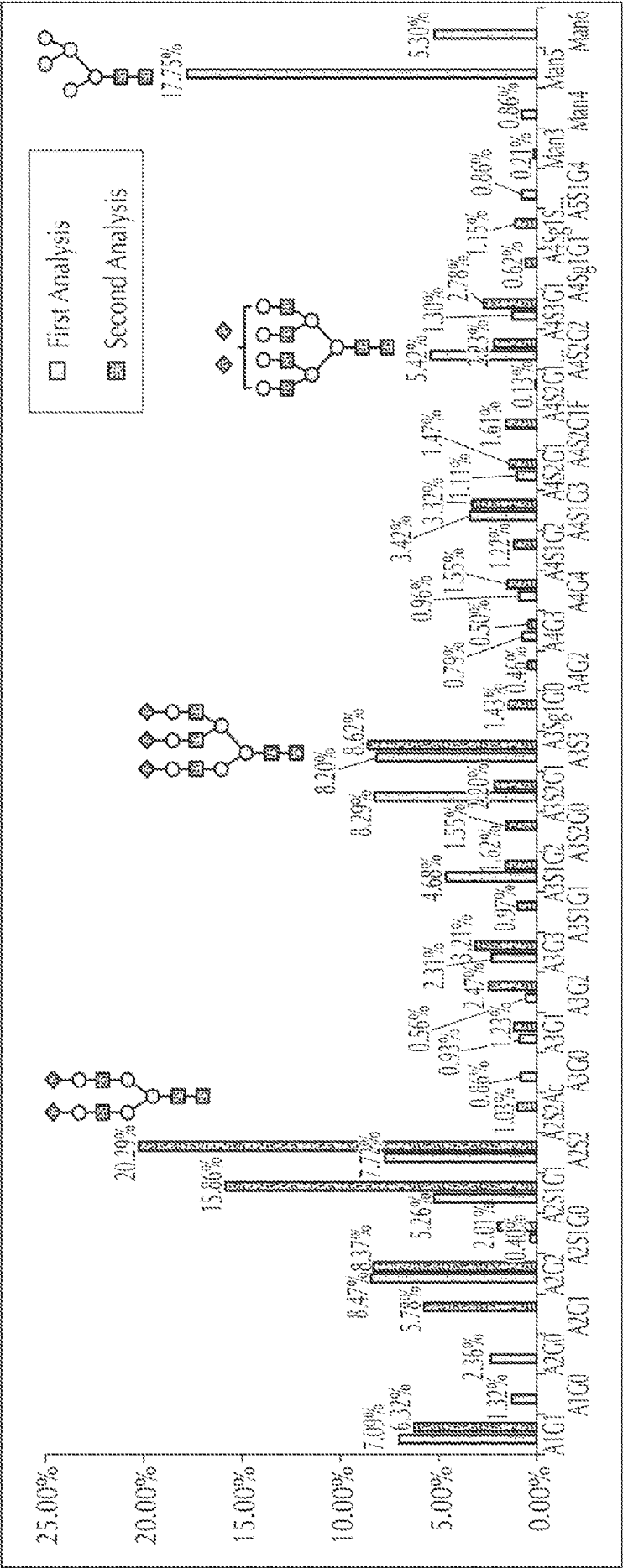


FIG. 11D

N-Glycosylation Profile of N414

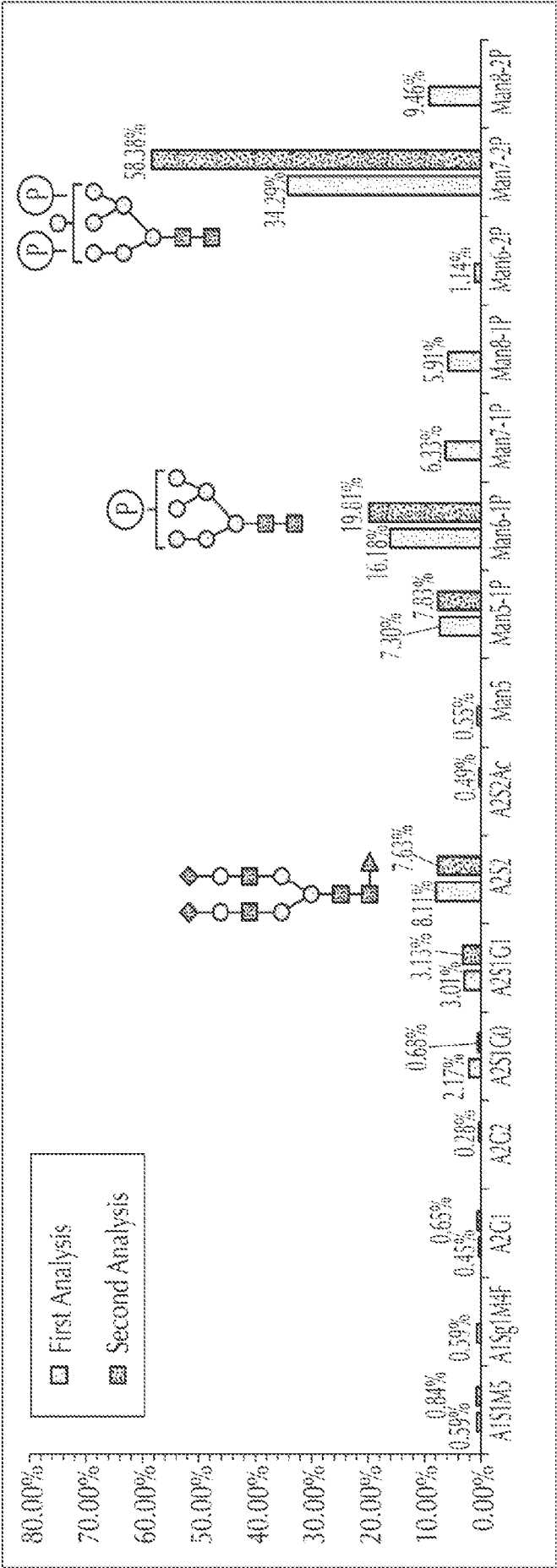


FIG. 11E

N-Glycosylation Profile of N596

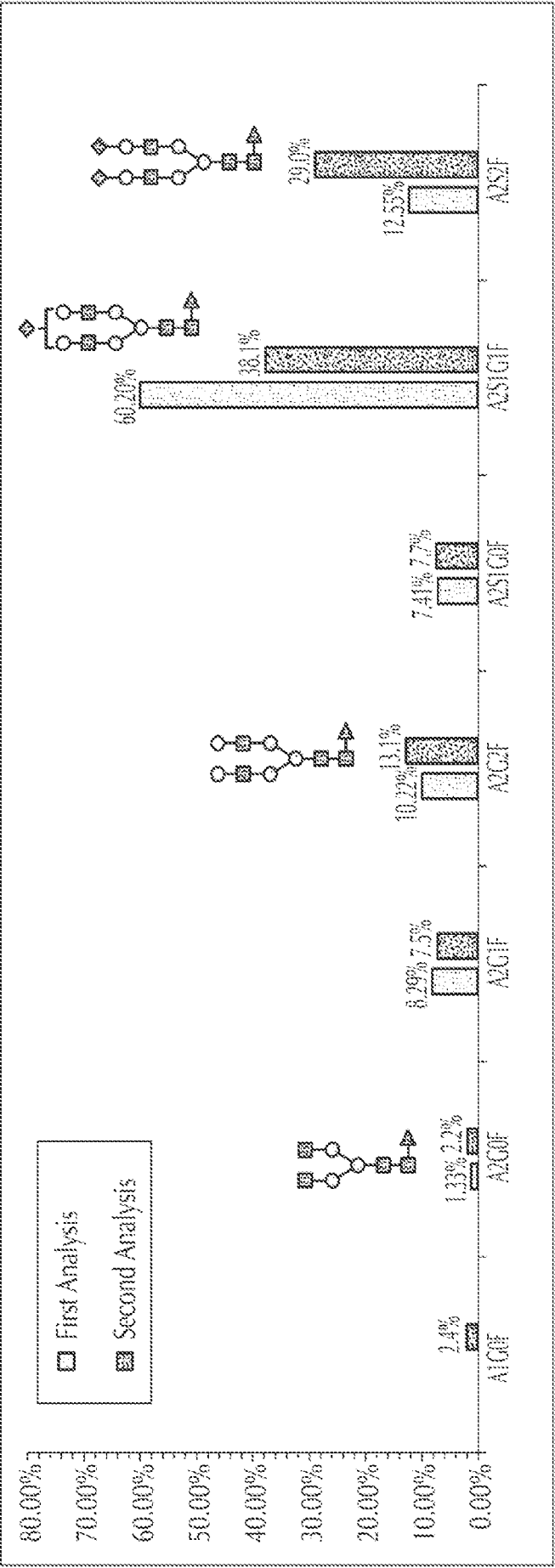


FIG. 11F

N-Glycosylation Profile of N826

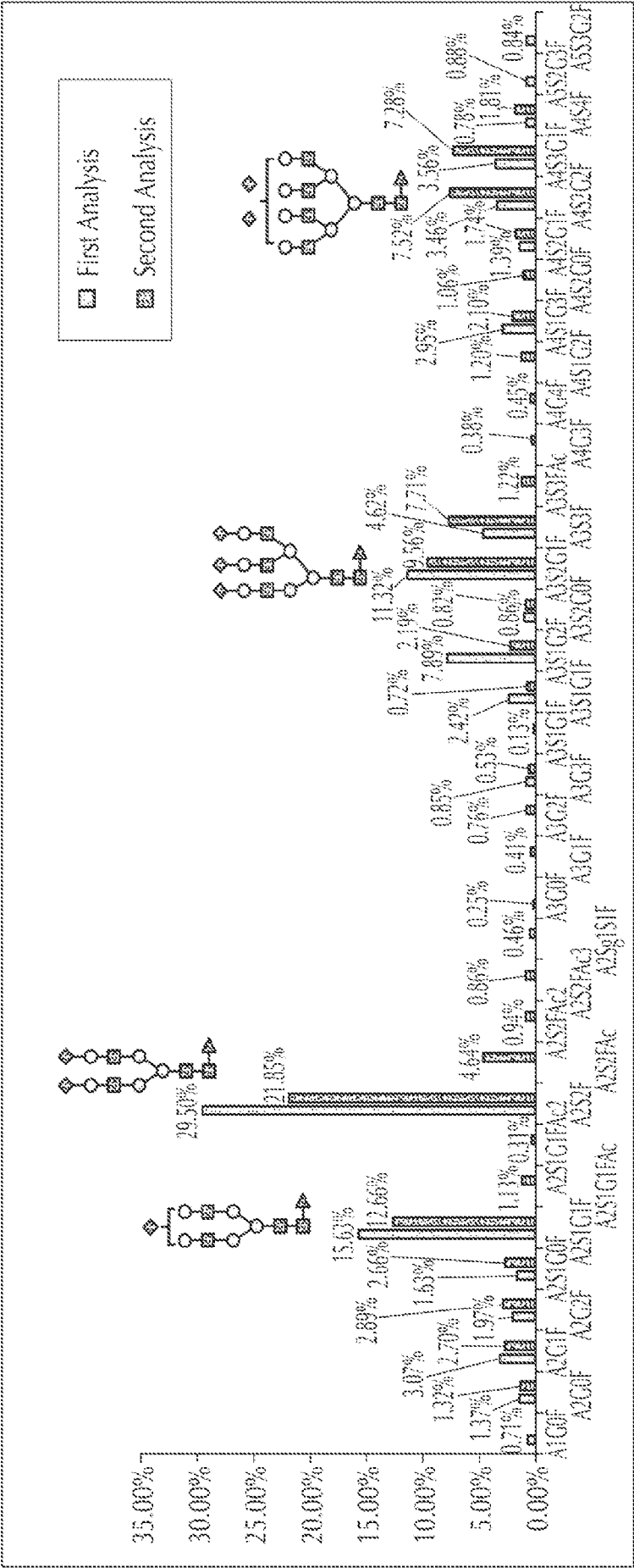


FIG. 11G

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

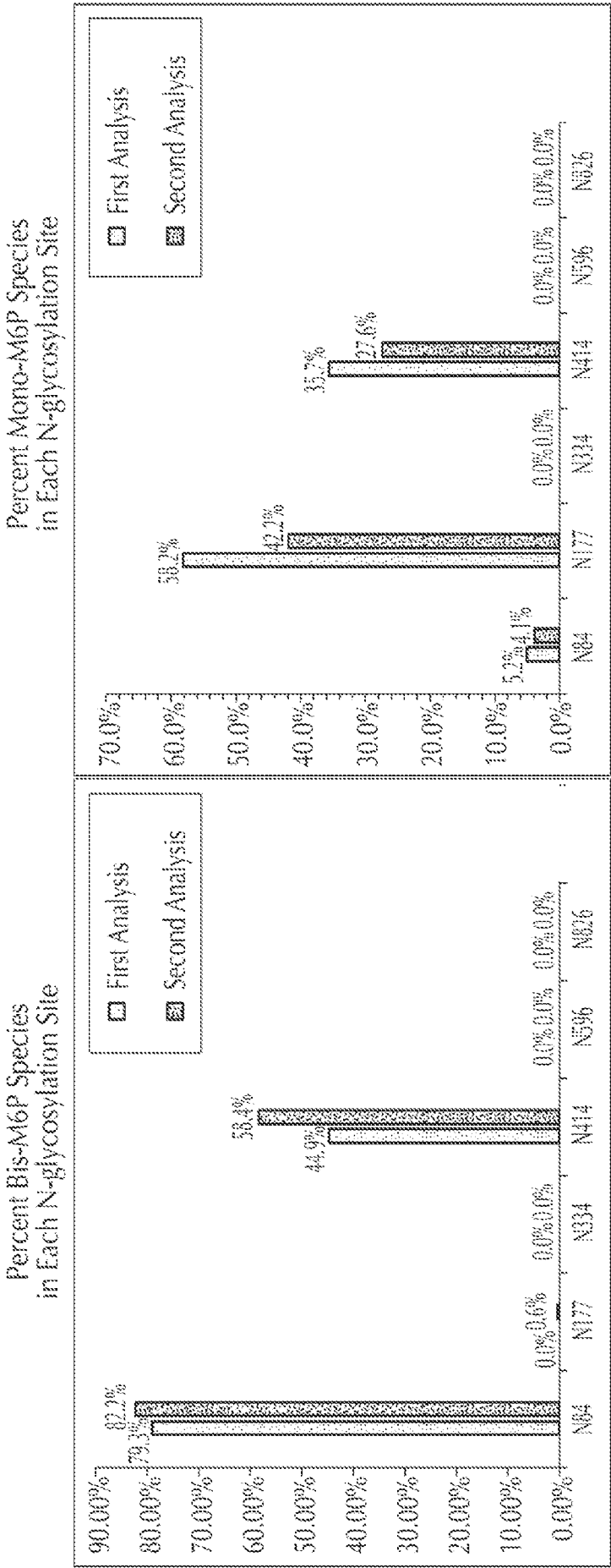


FIG. 11H

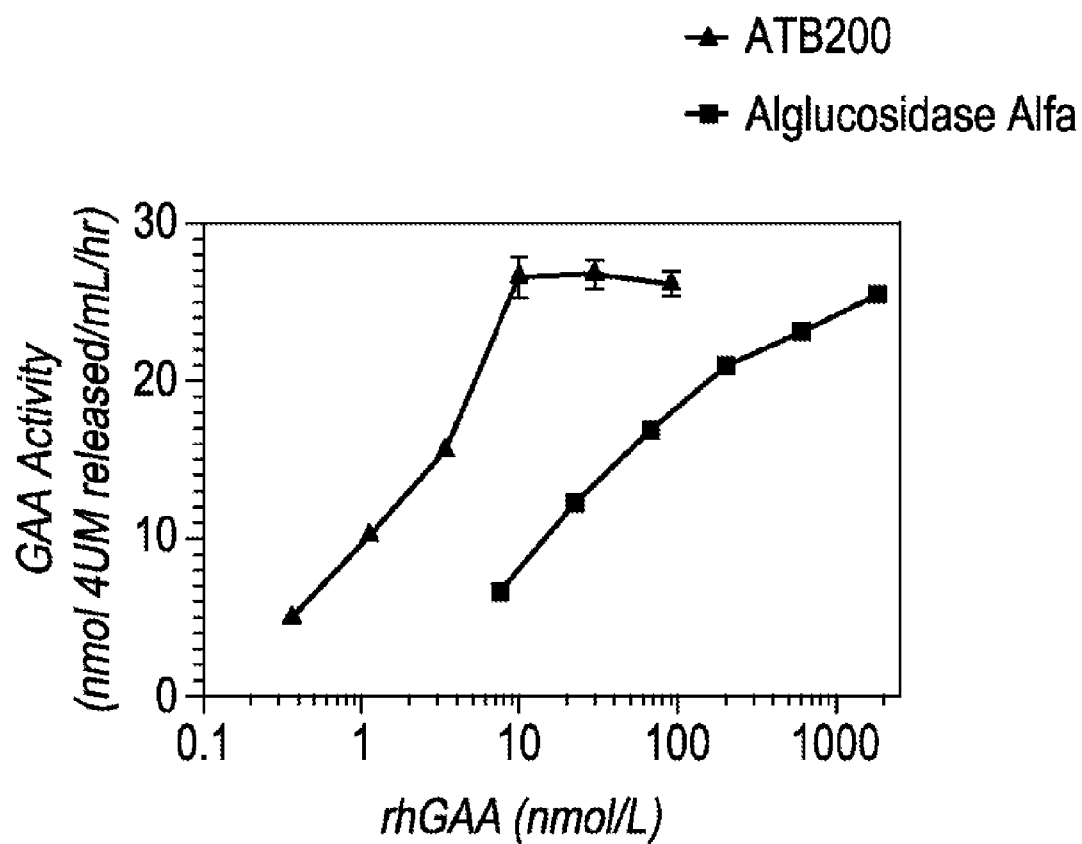


FIG. 12A

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

FIG. 12B

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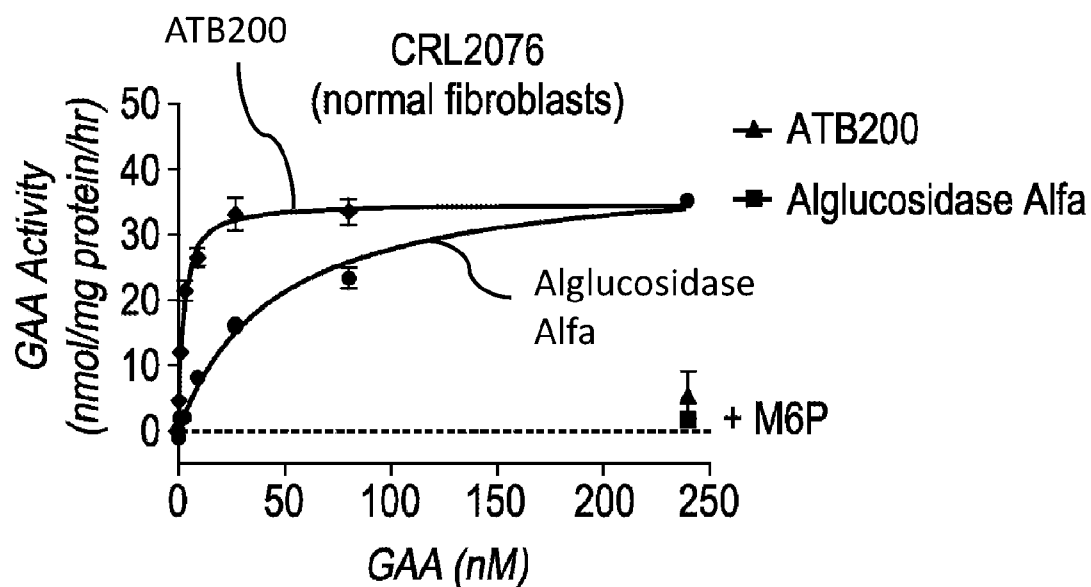


FIG. 13A

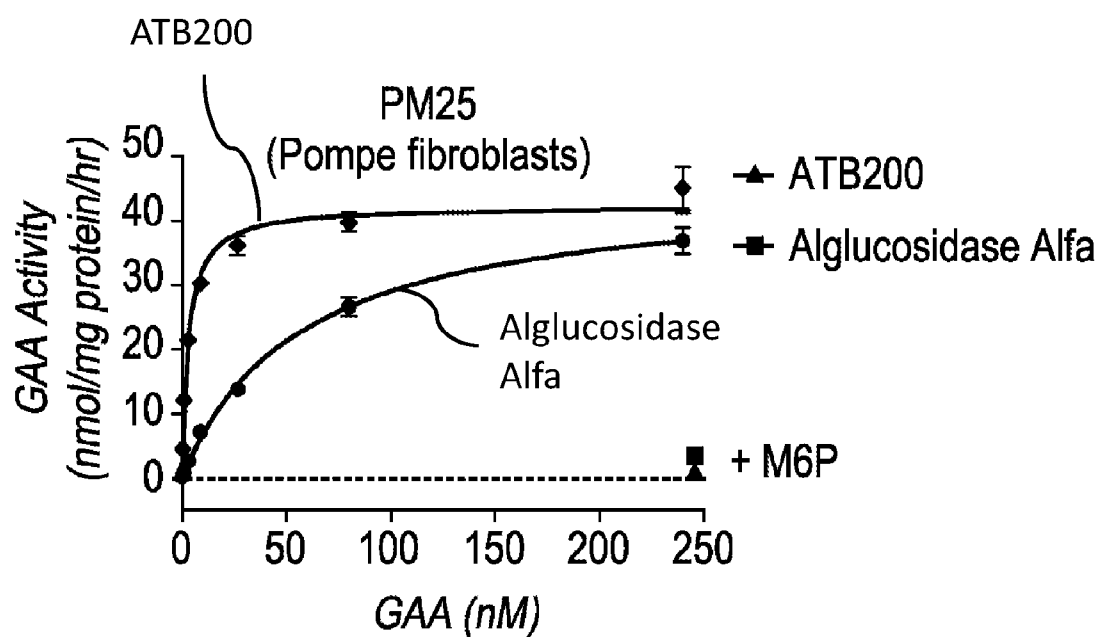


FIG. 13B

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

FIG. 13C

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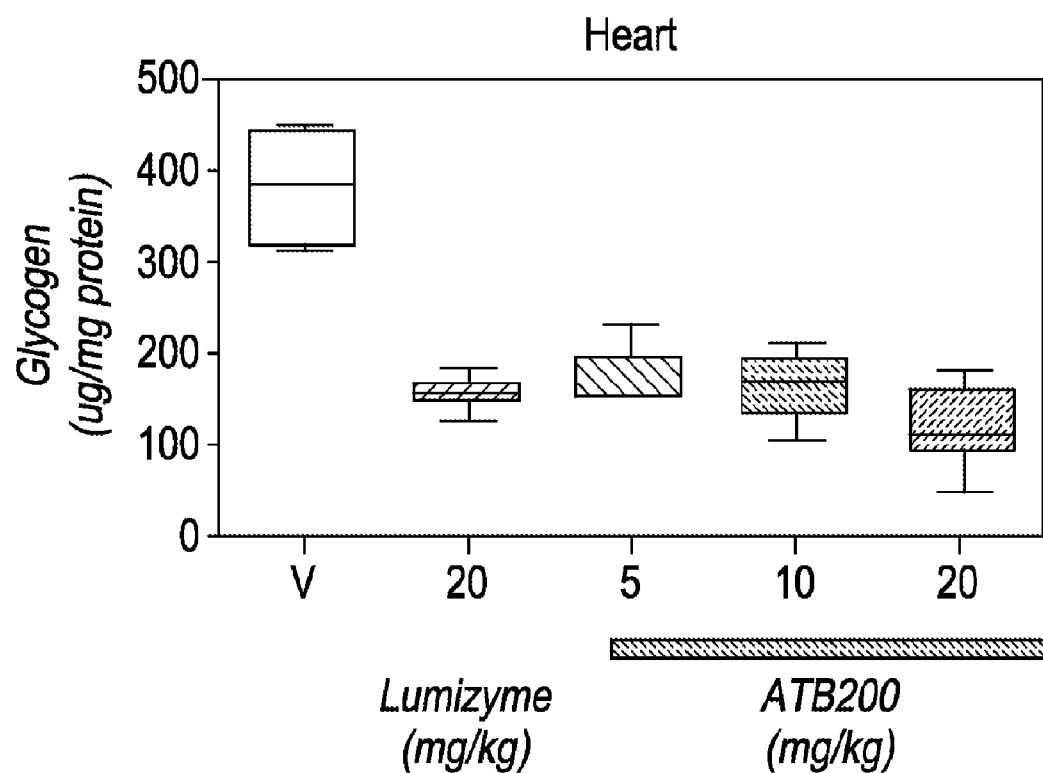


FIG. 14A

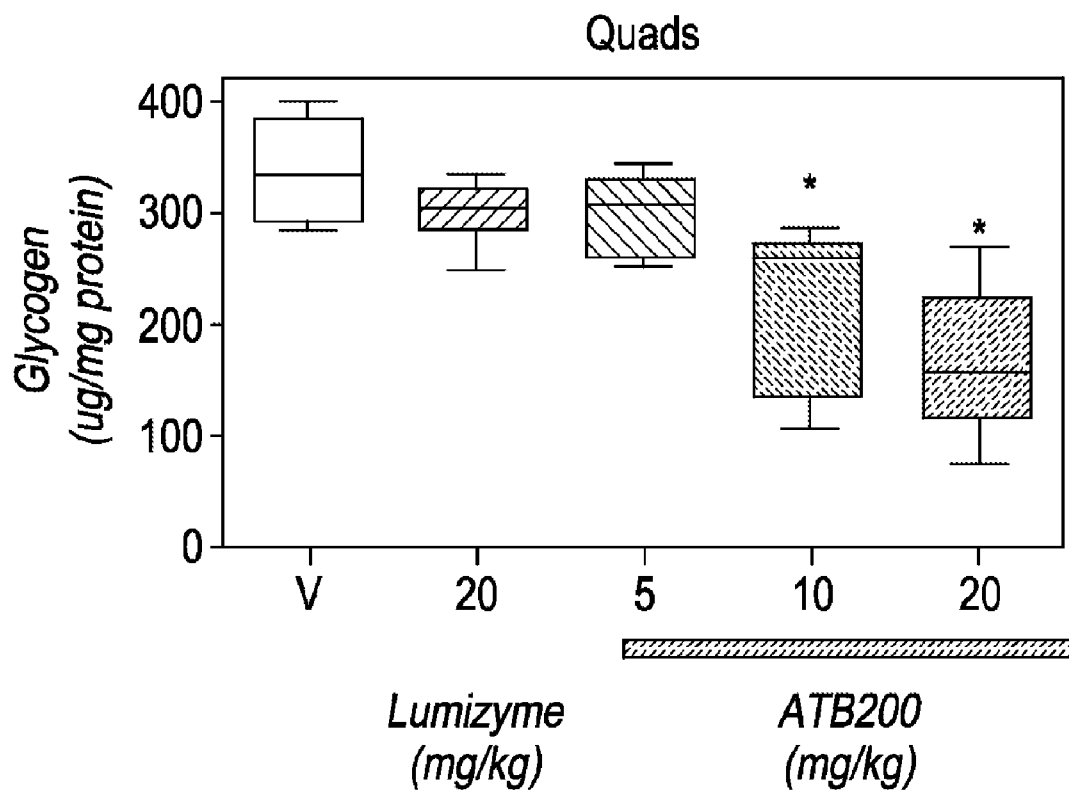


FIG. 14B

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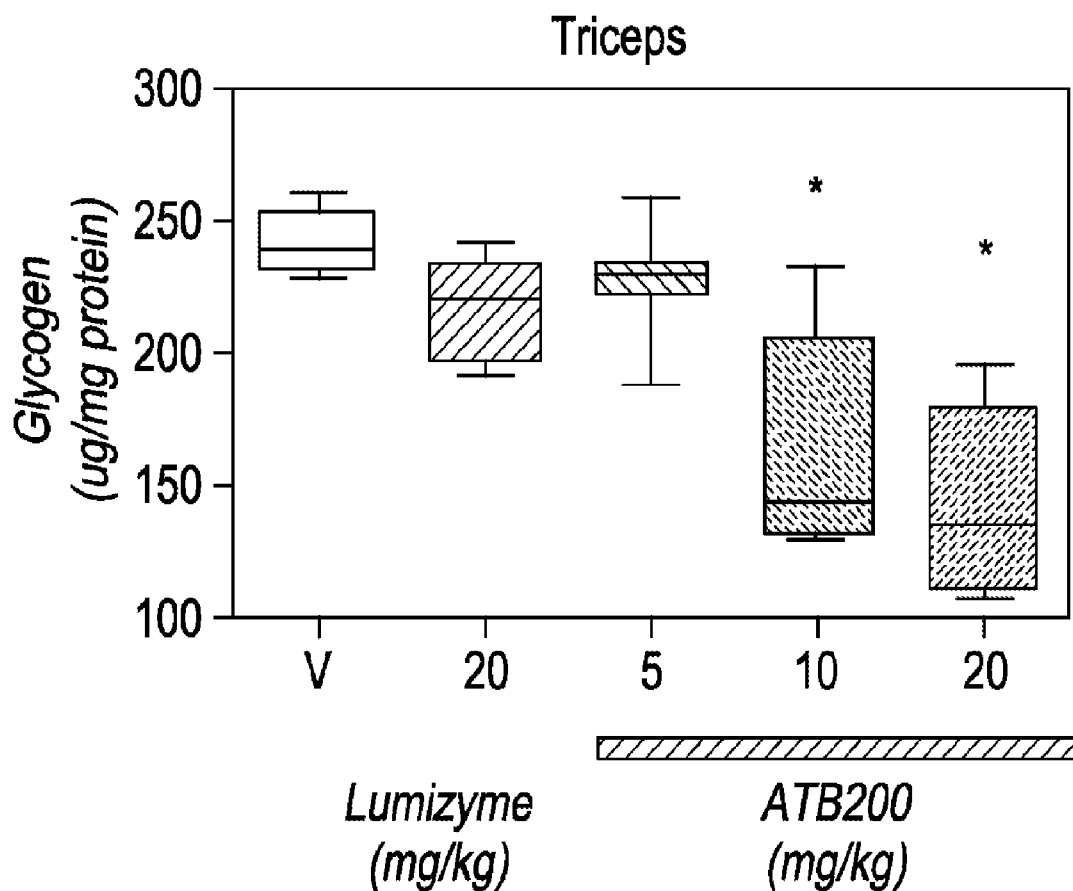


FIG. 14C

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. 15

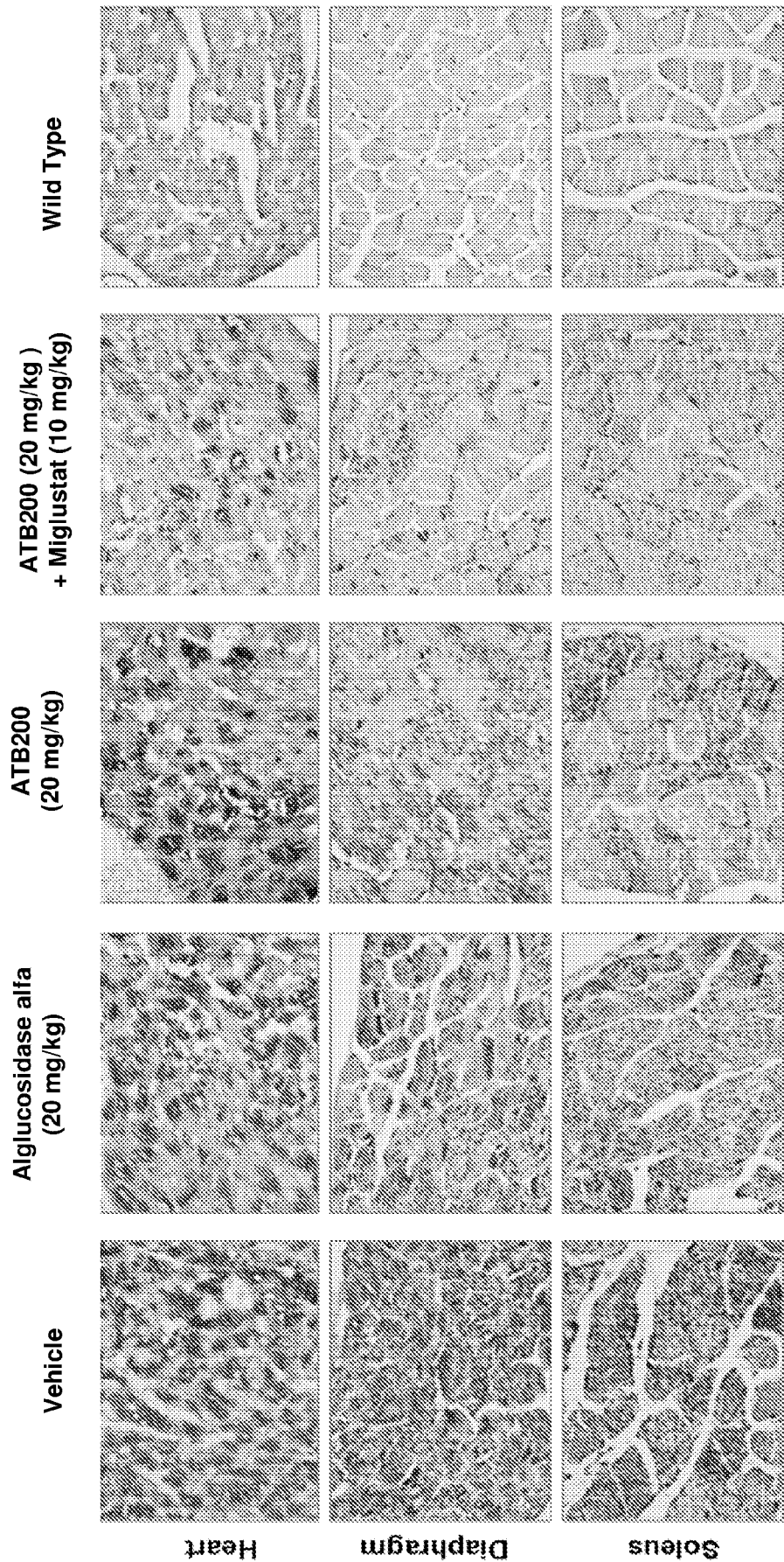


FIG. 16

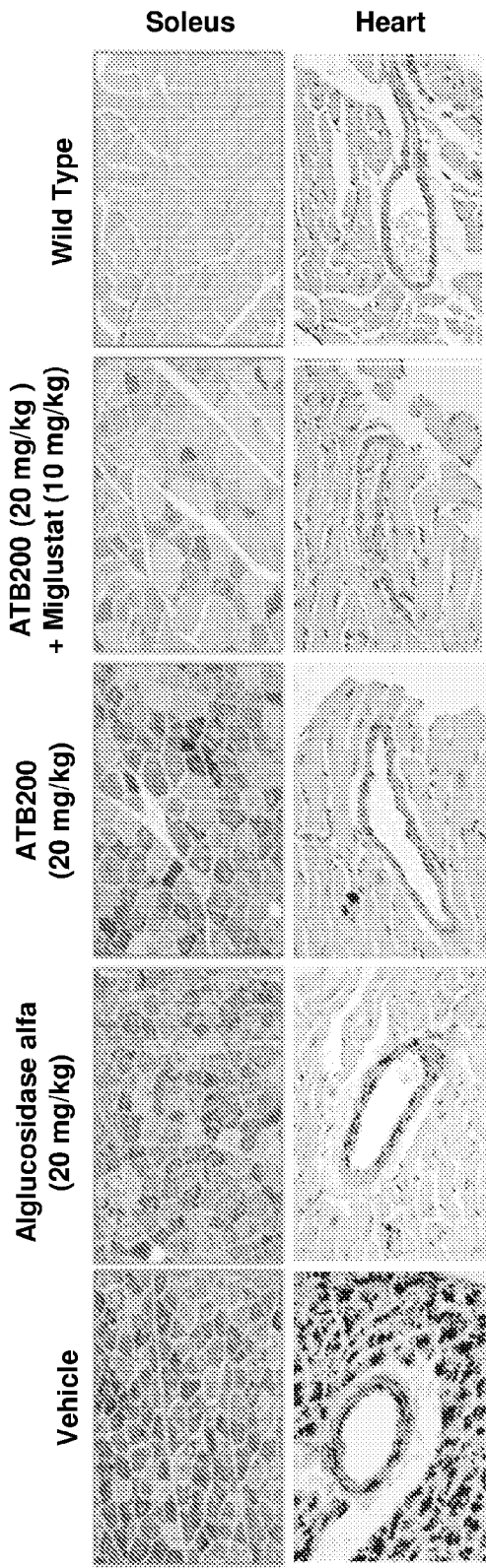


FIG. 17

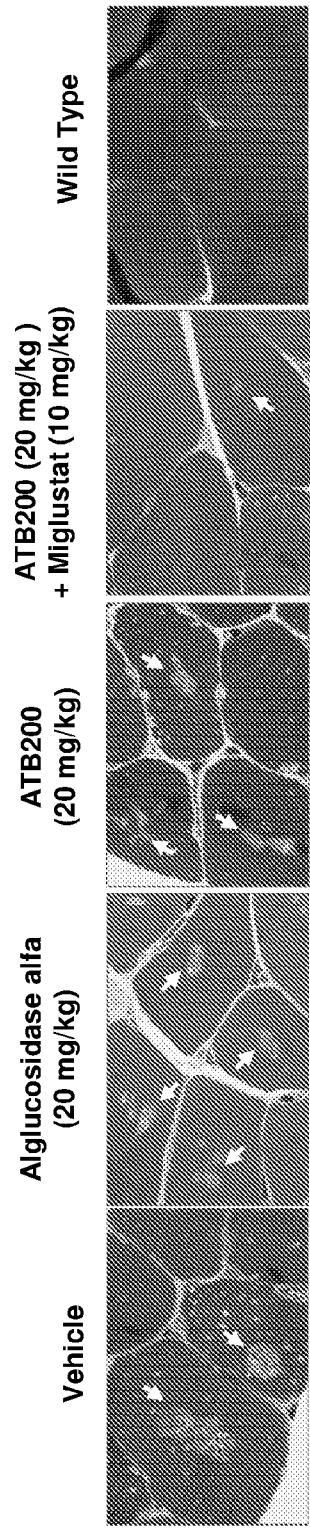


FIG. 18

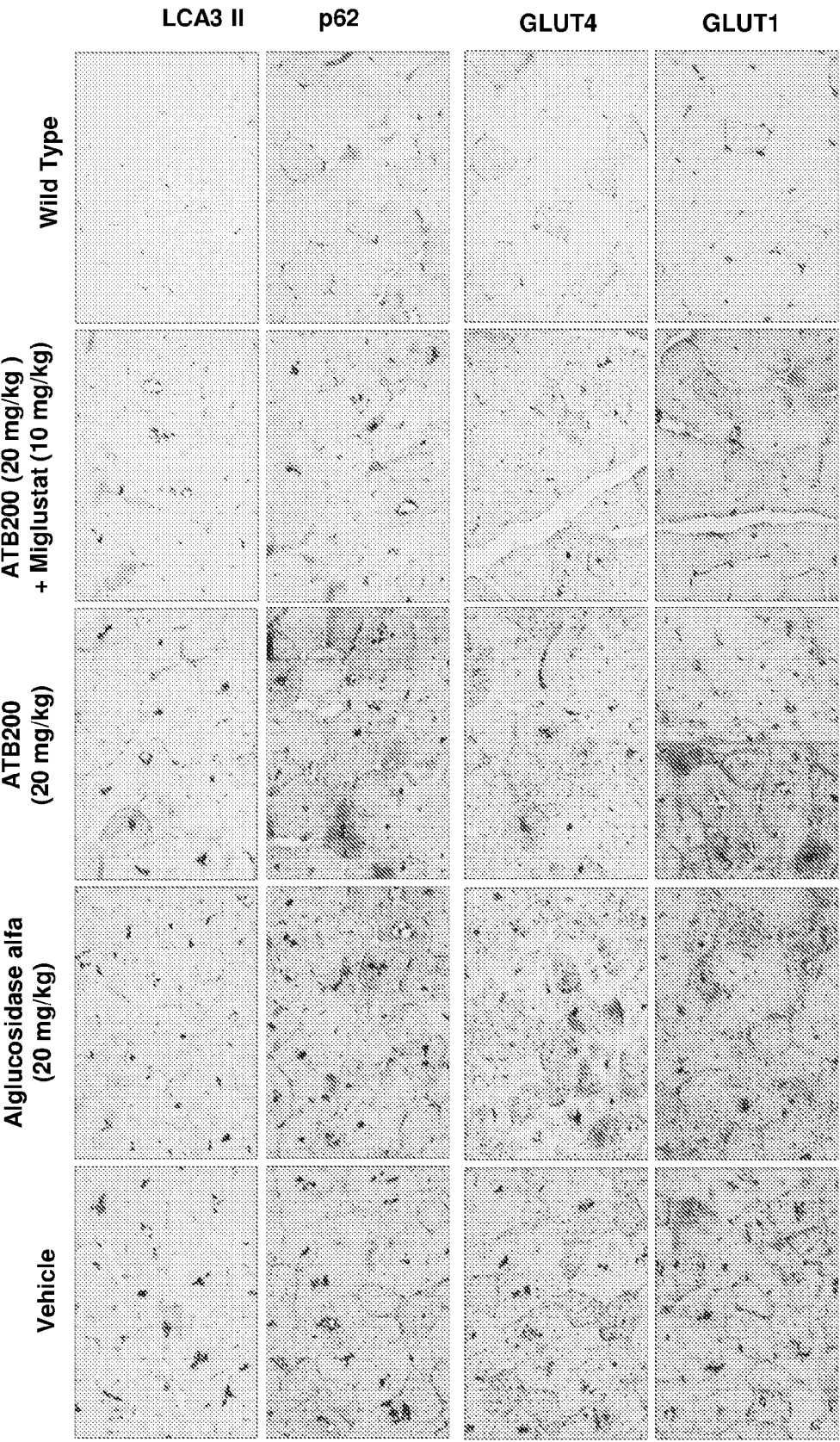
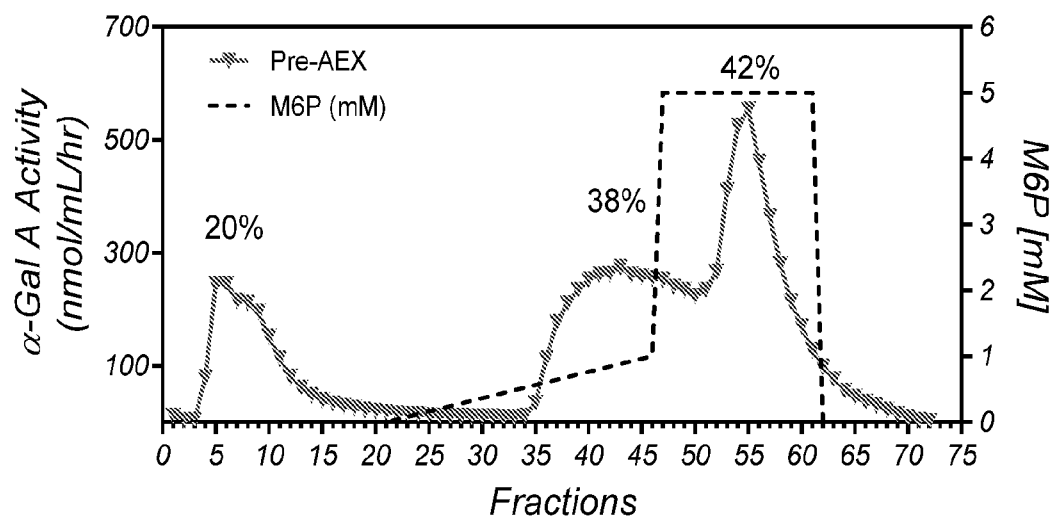


FIG. 19

A



B

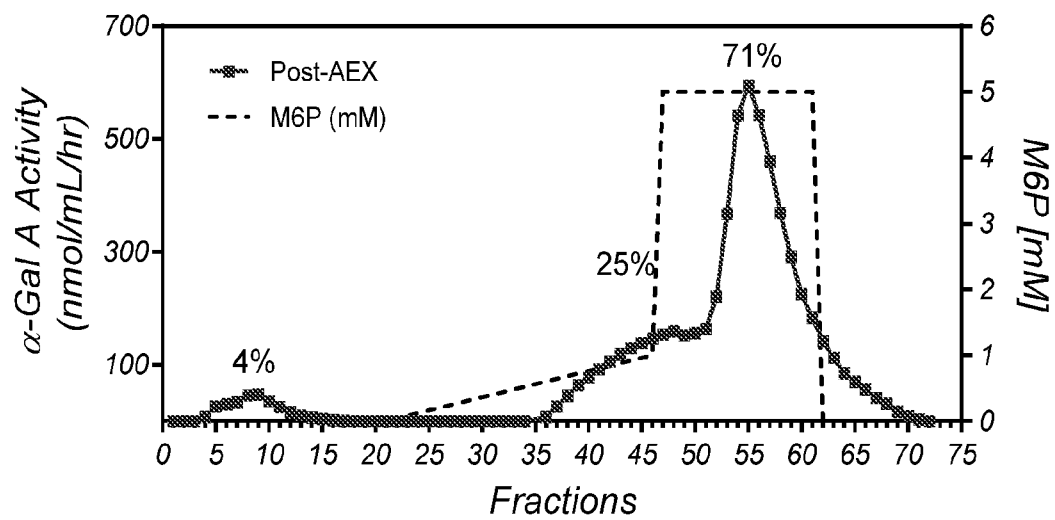


FIG. 20

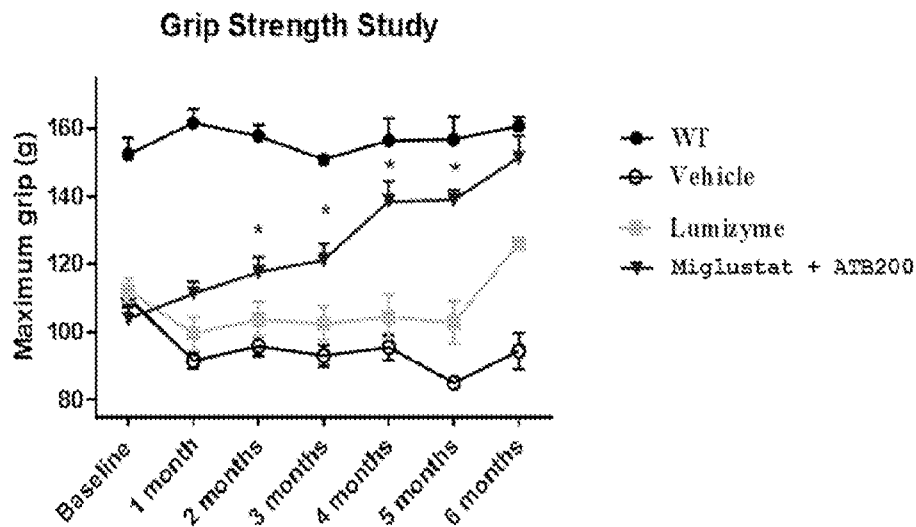


FIG. 21A

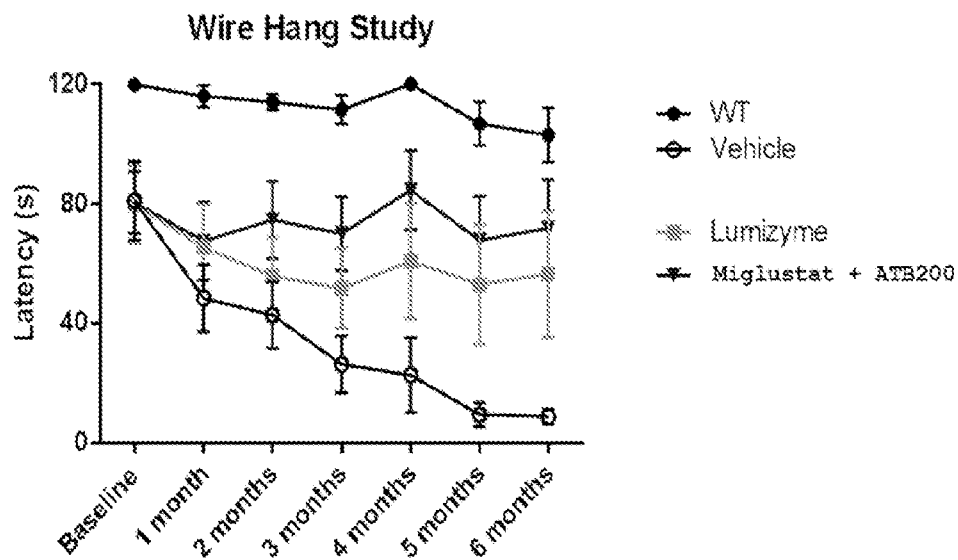


FIG. 21B

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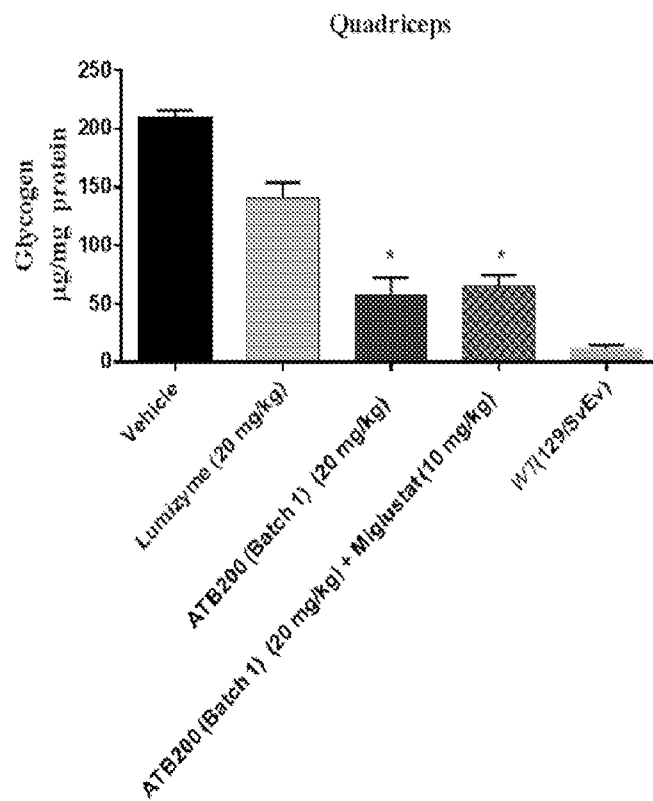


FIG. 22A

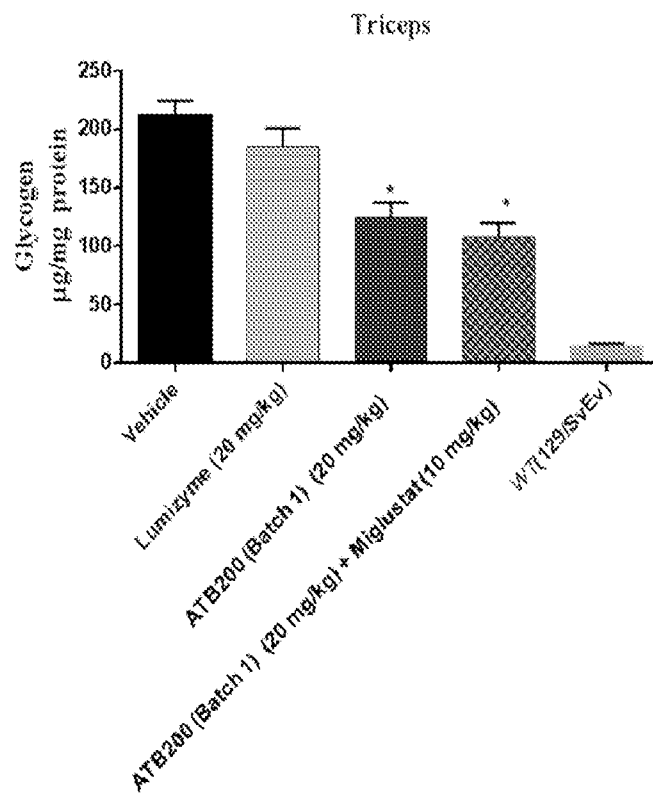


FIG. 22B

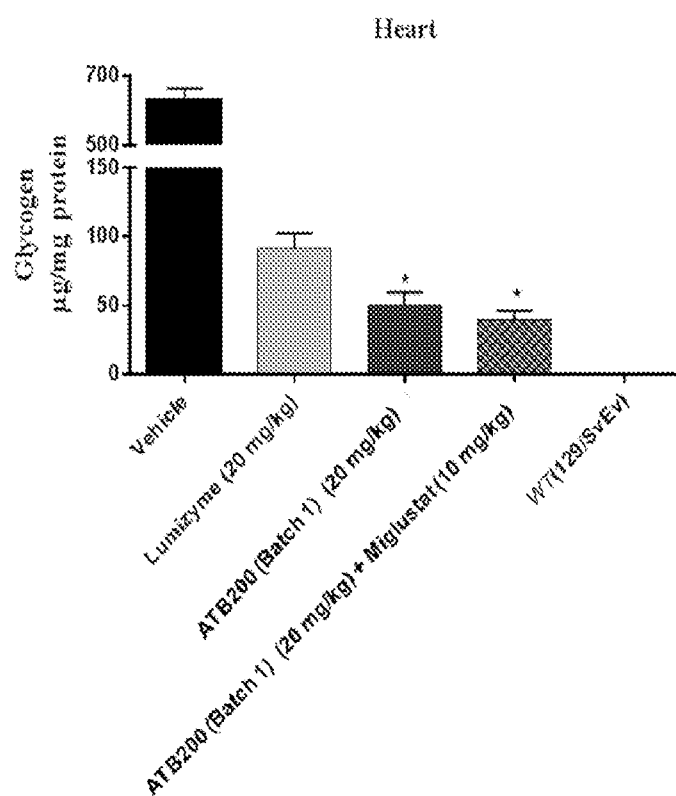


FIG. 22C

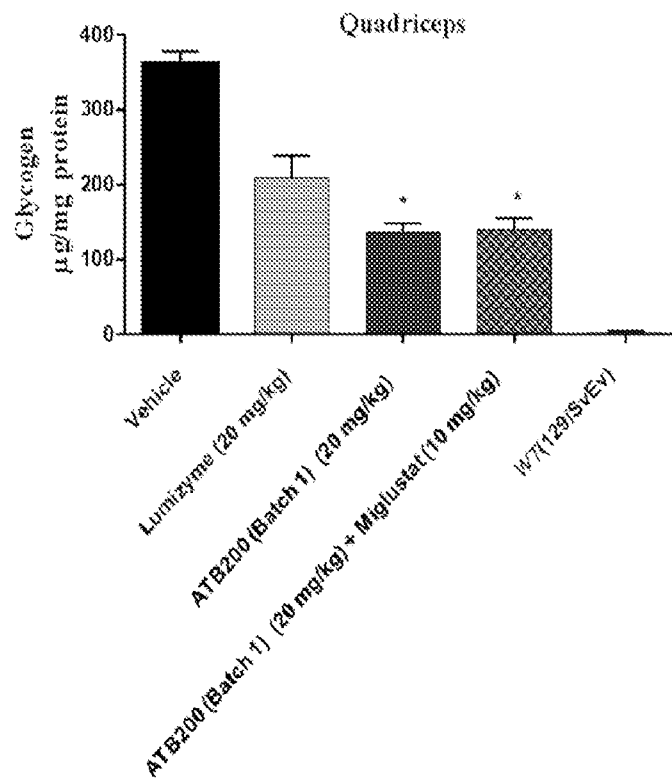


FIG. 22D

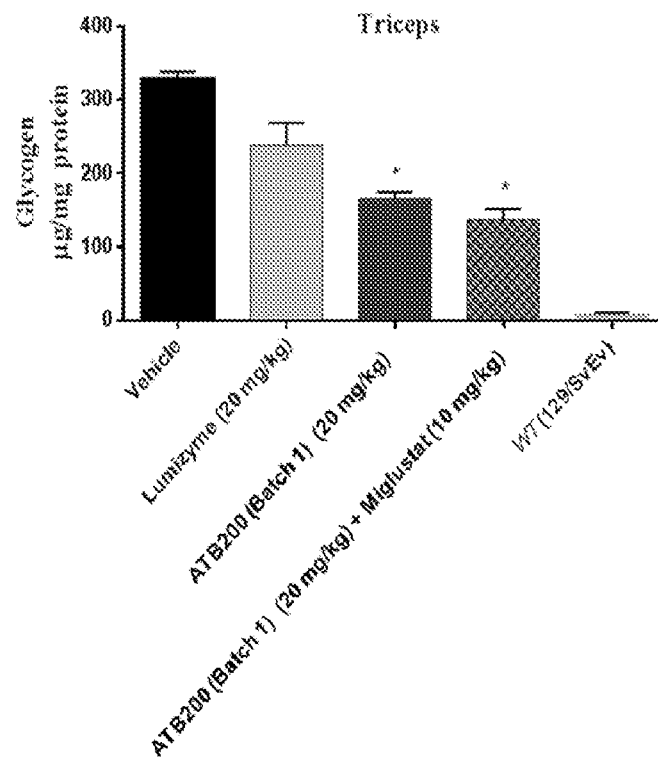


FIG. 22E

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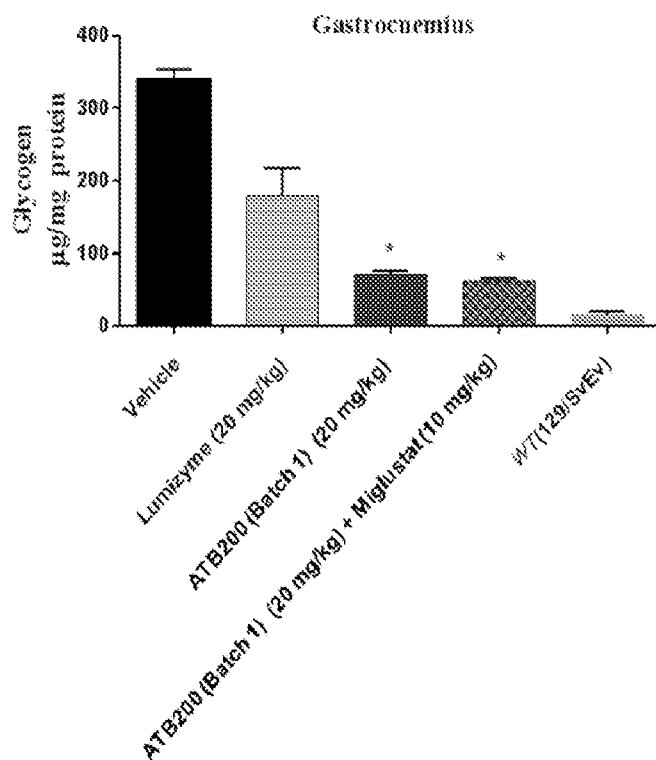


FIG. 22F

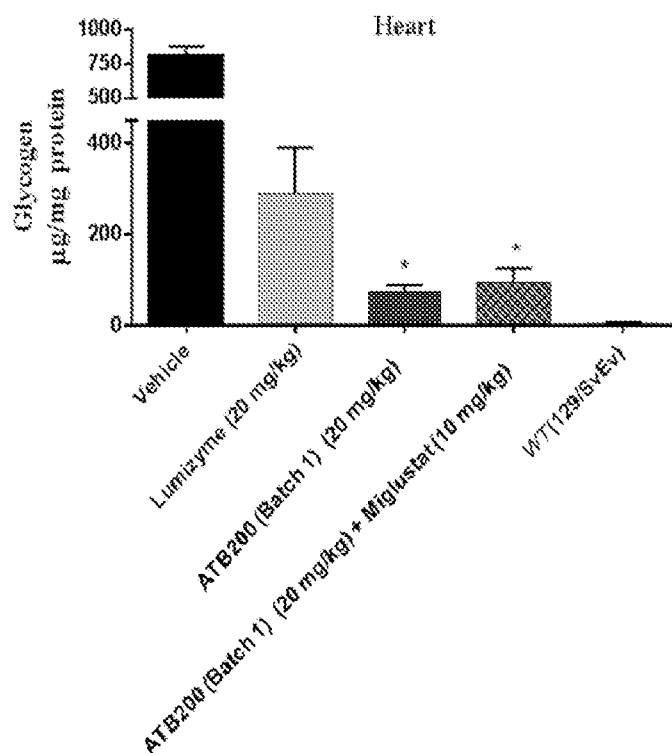


FIG. 22G

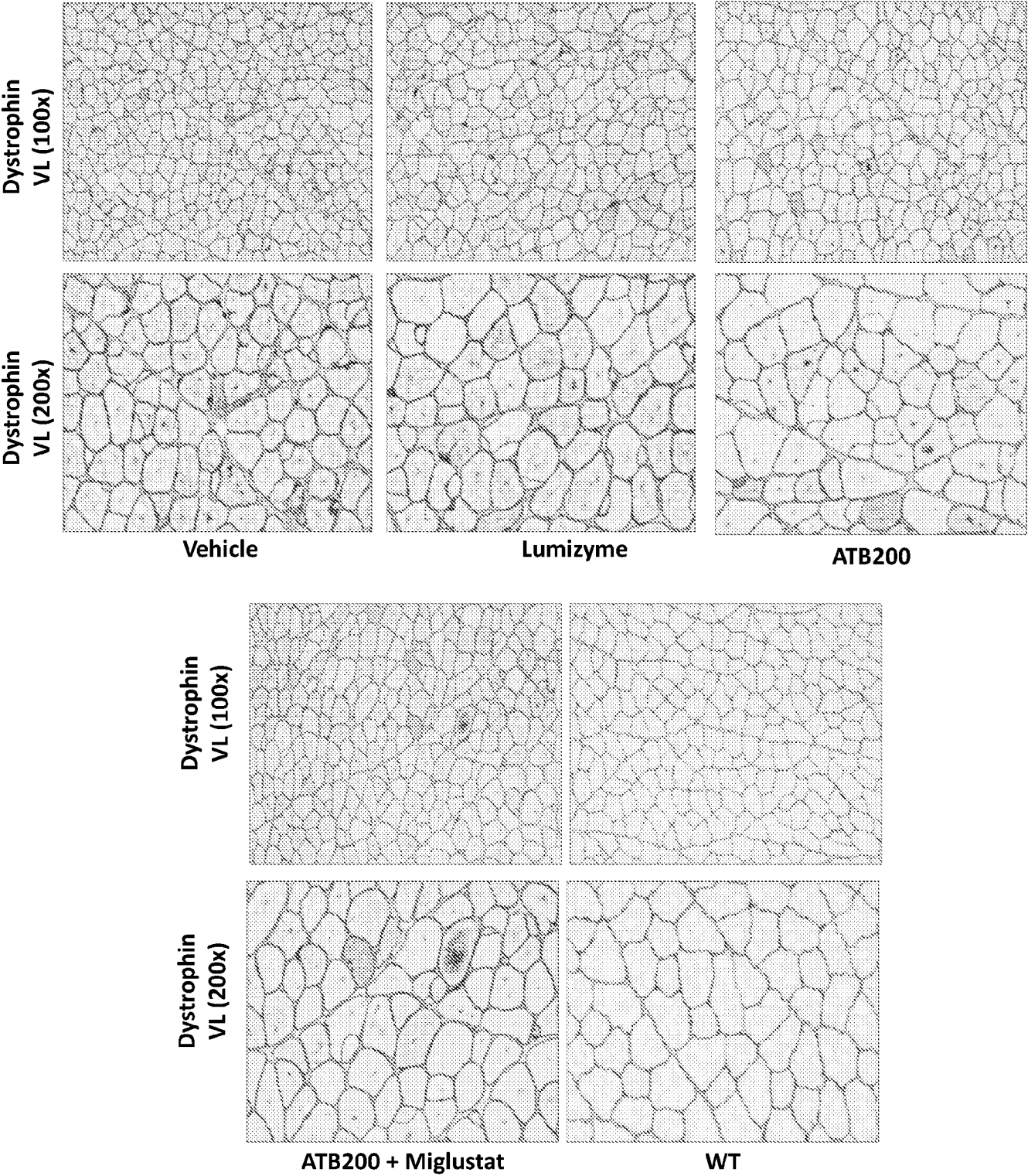


FIG. 23

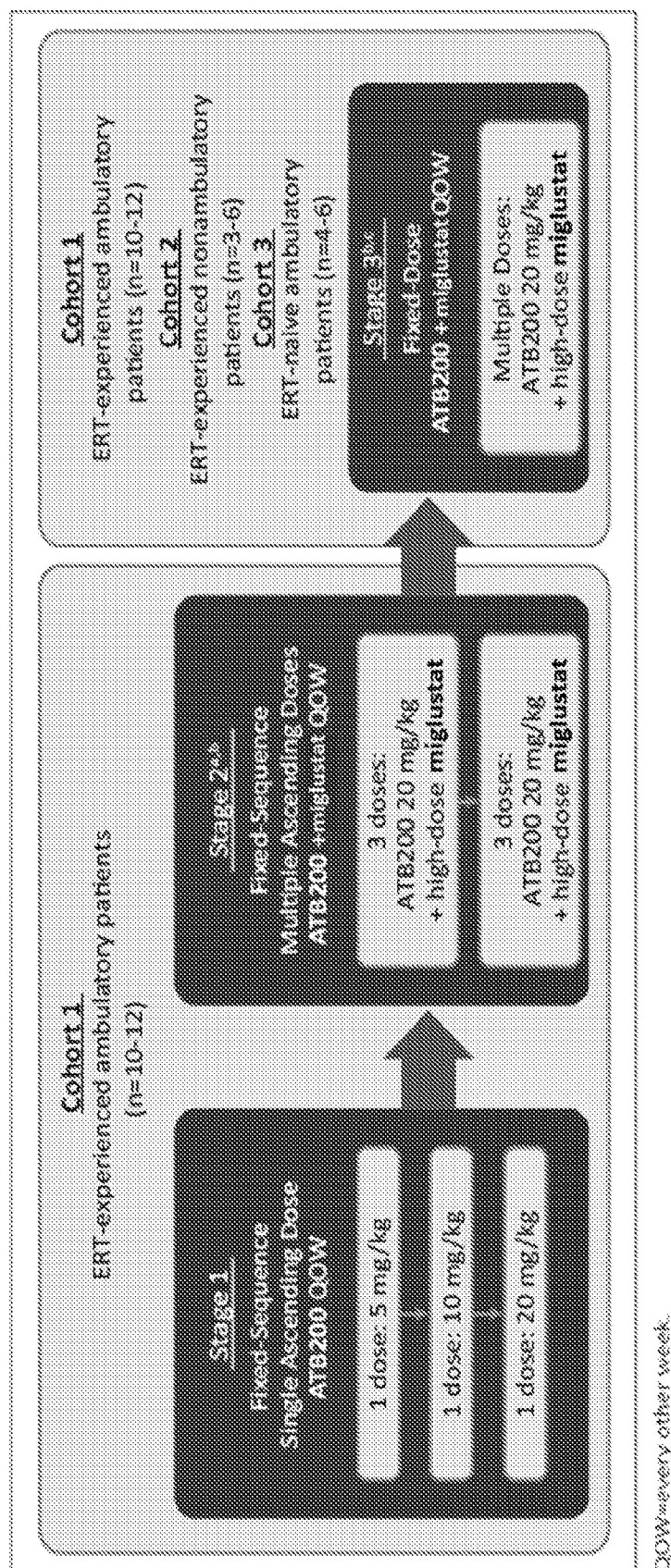


FIG. 24

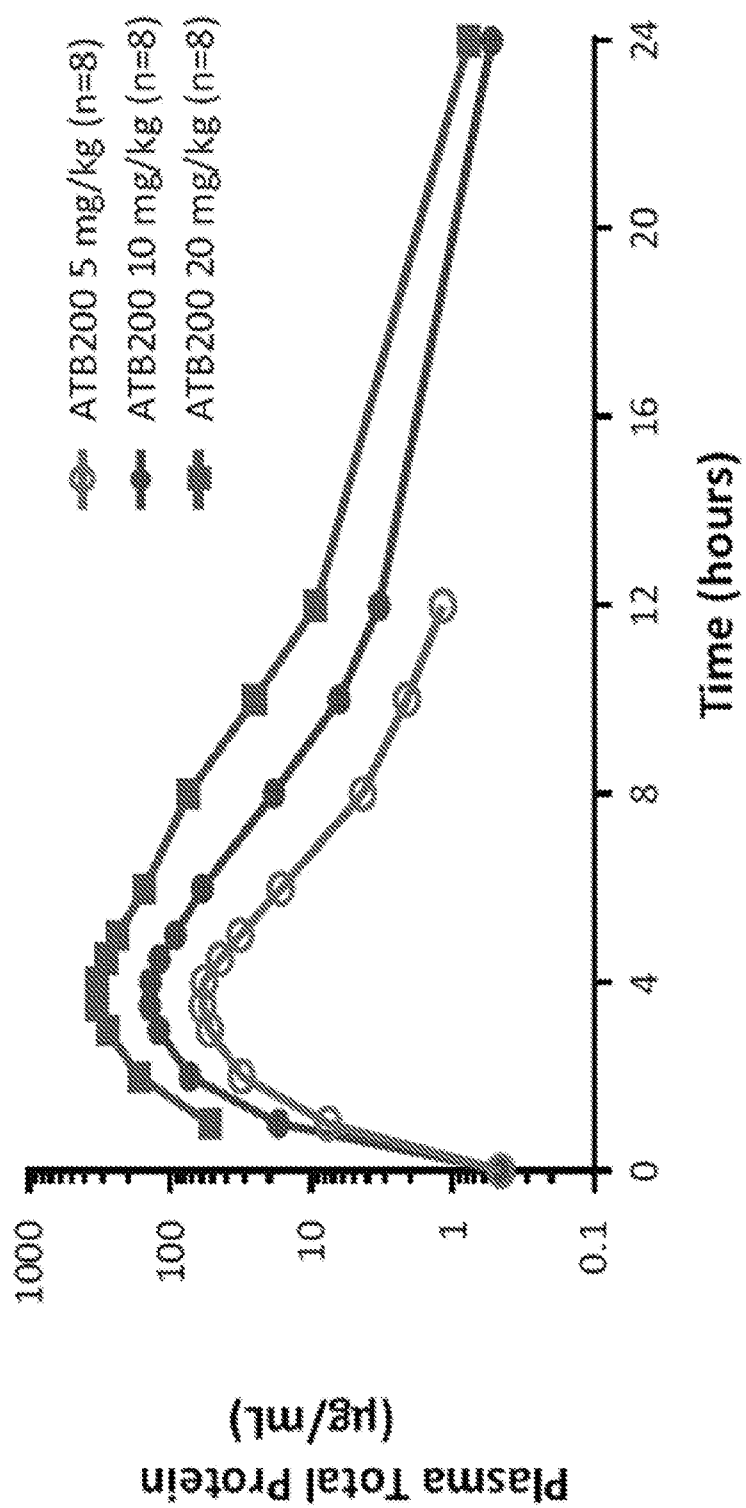


FIG. 25A

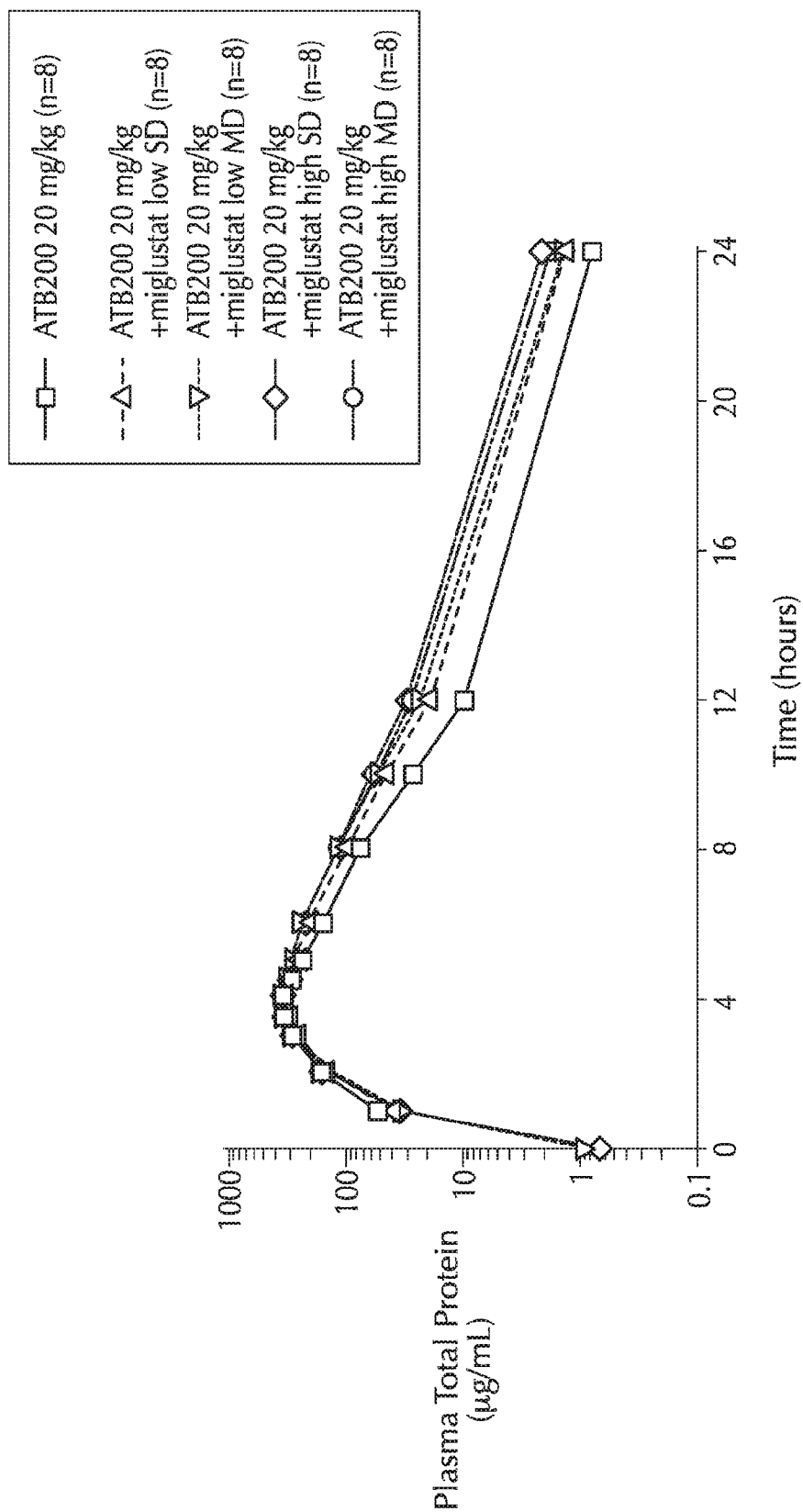


FIG. 25B

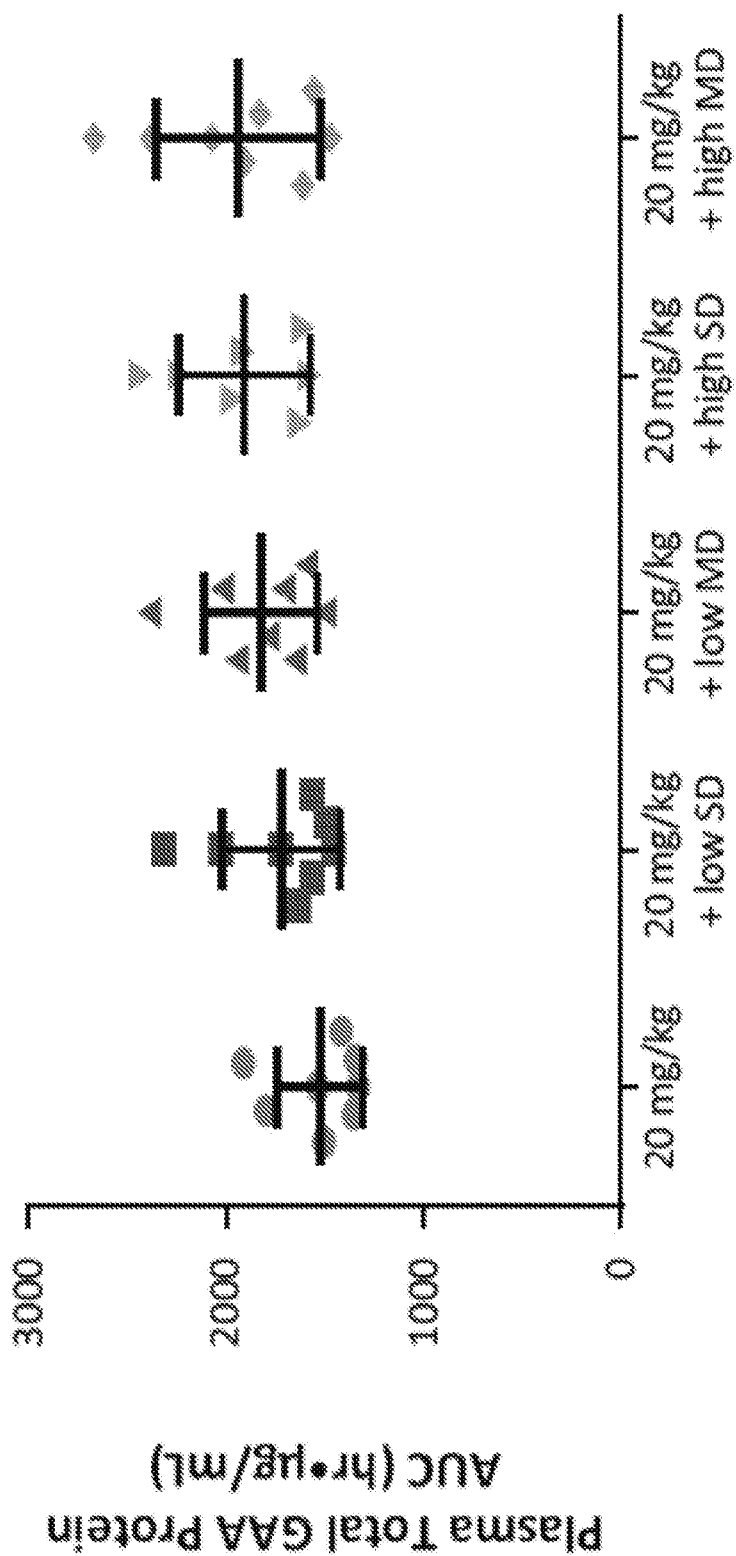


FIG. 25C

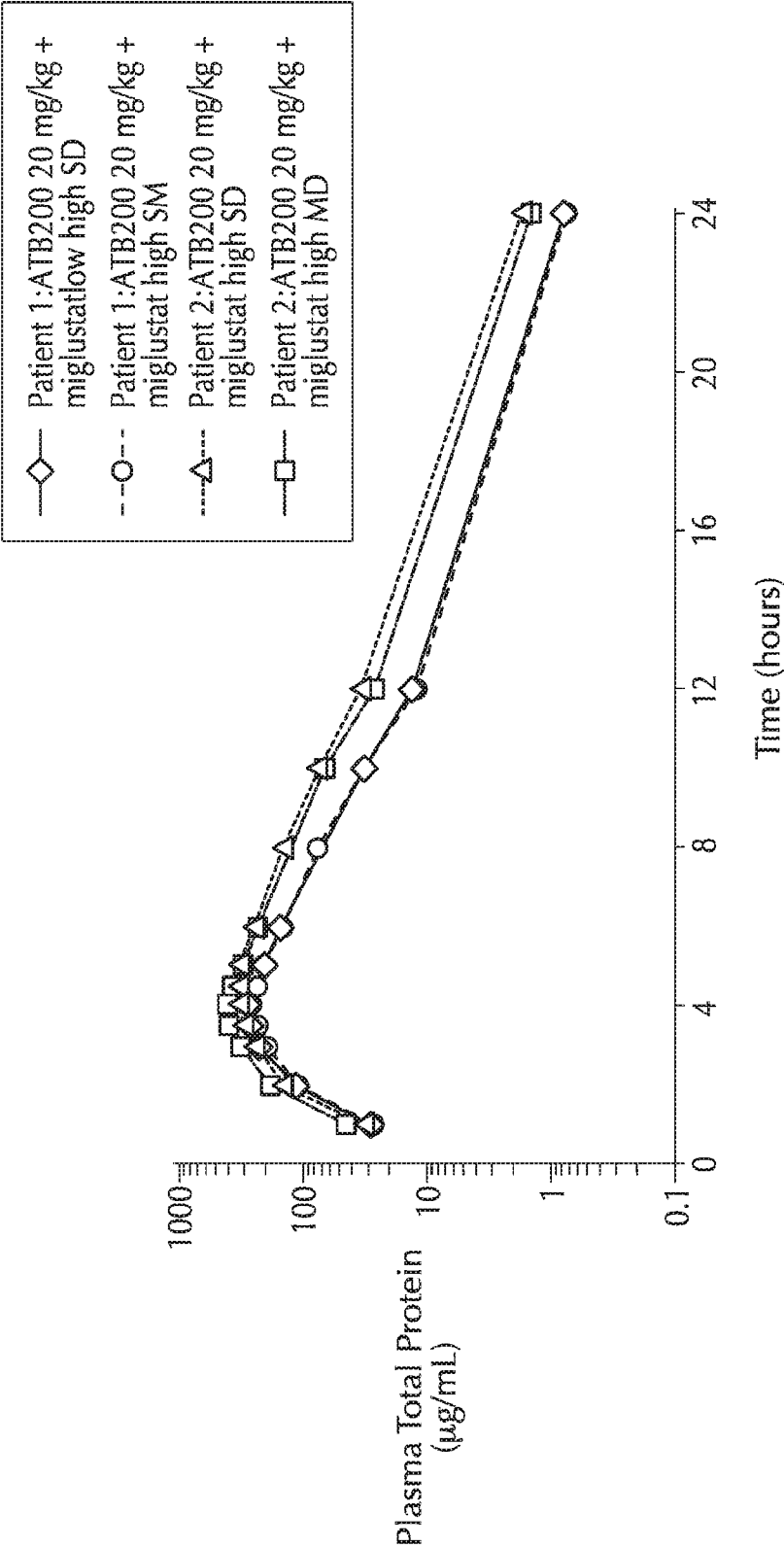


FIG. 25D

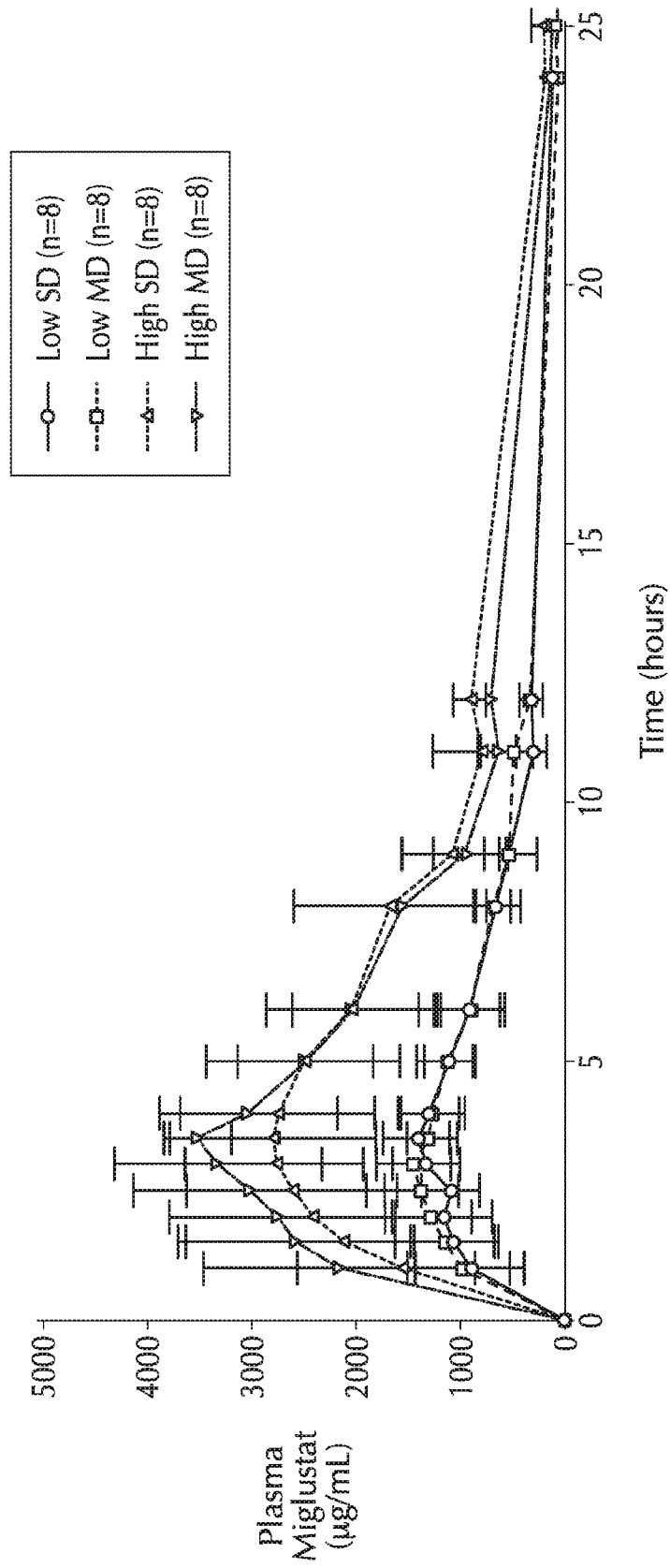


FIG. 26

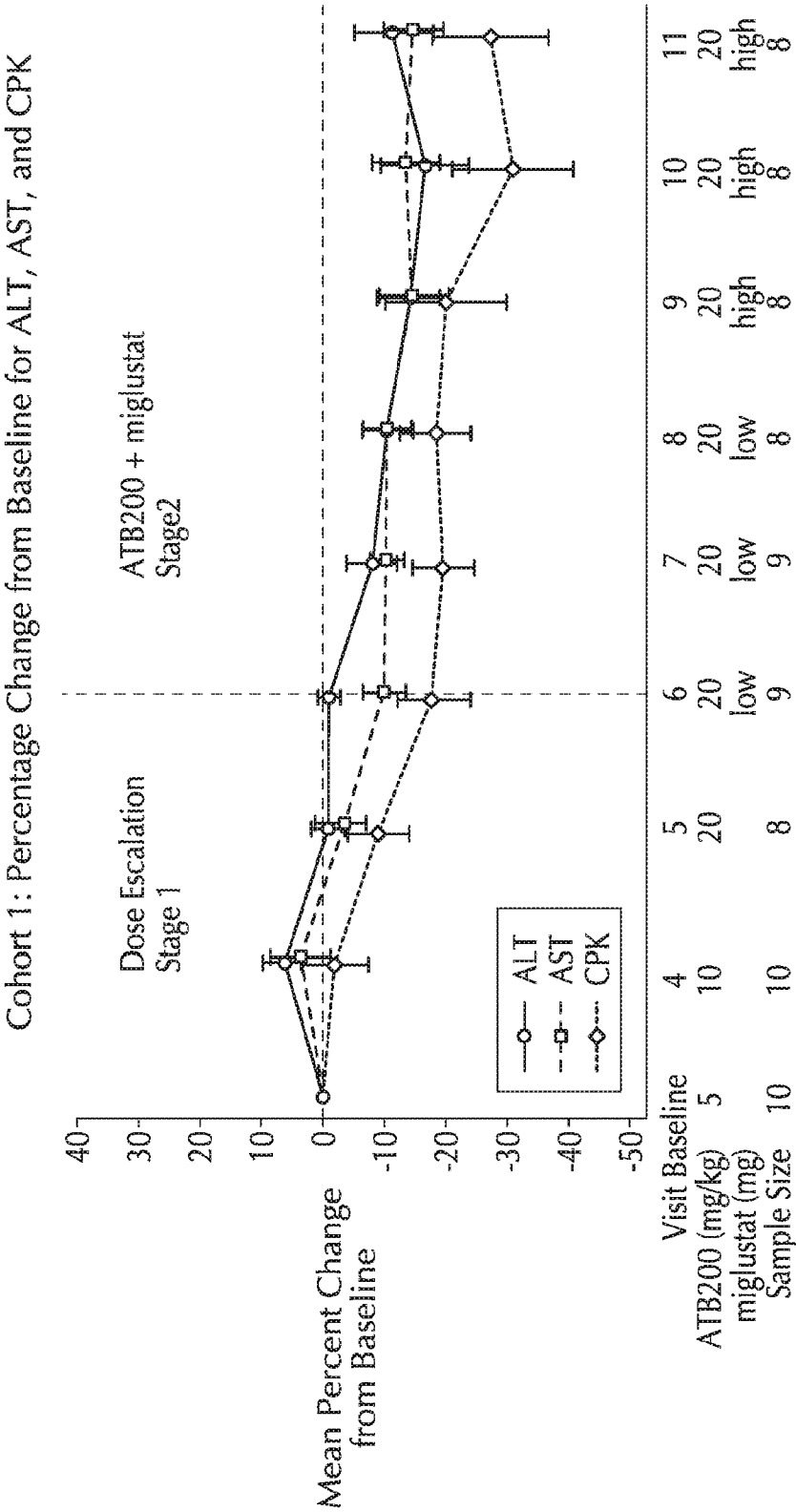


FIG. 27A

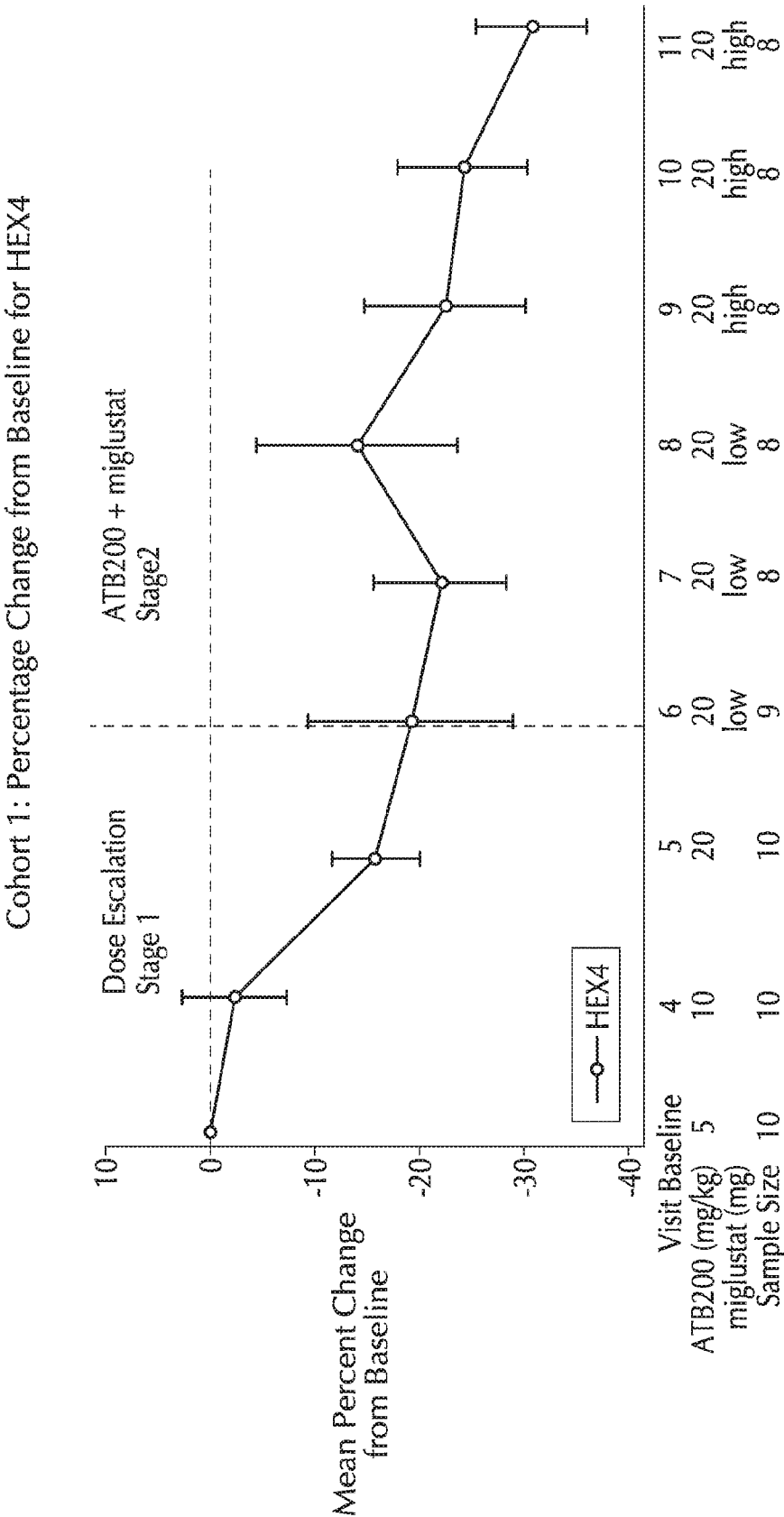


FIG. 27B

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

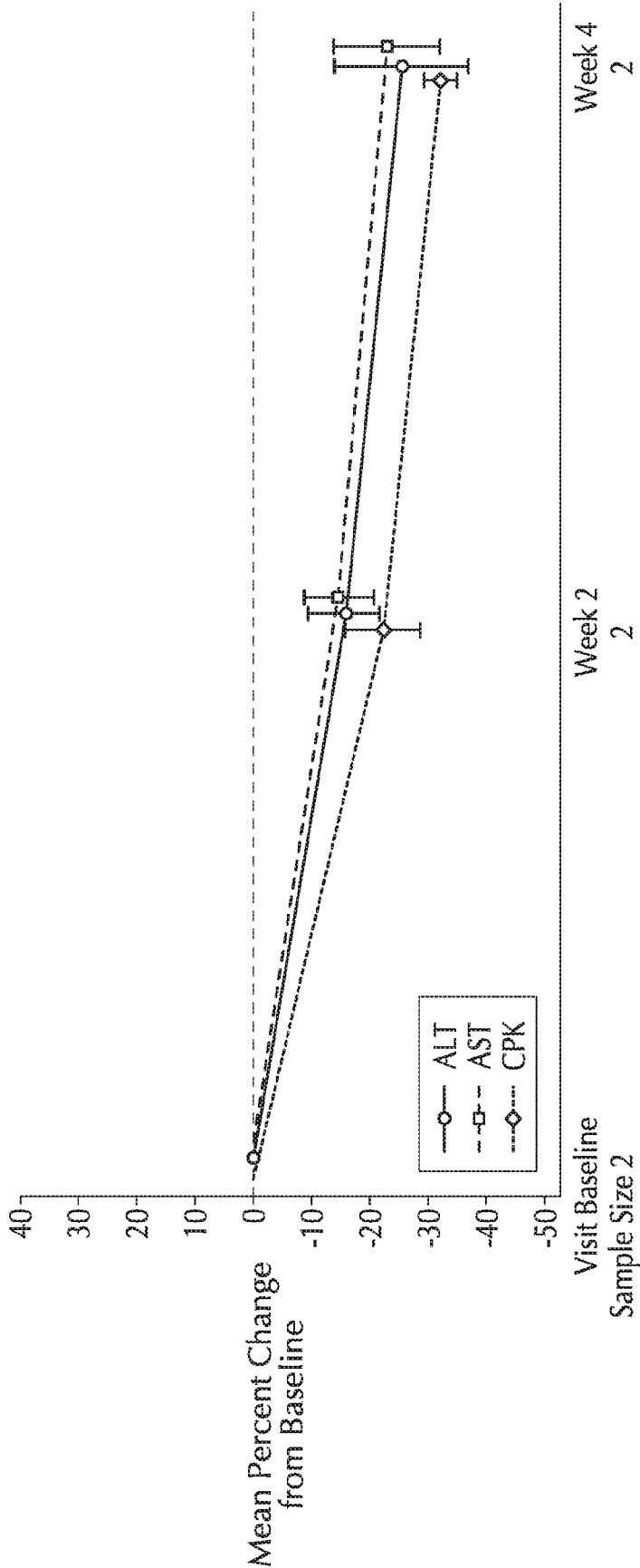


FIG. 27C

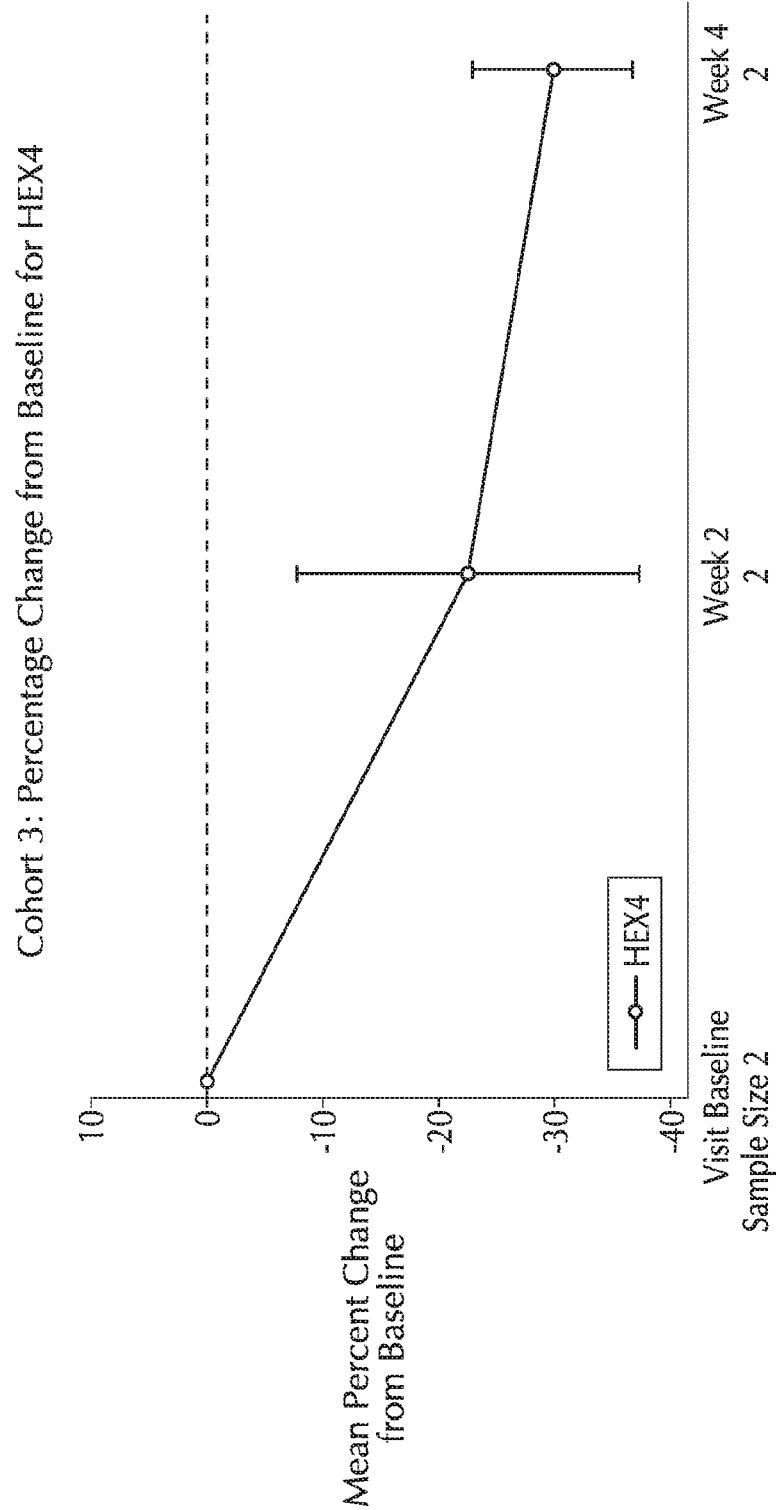


FIG. 27D