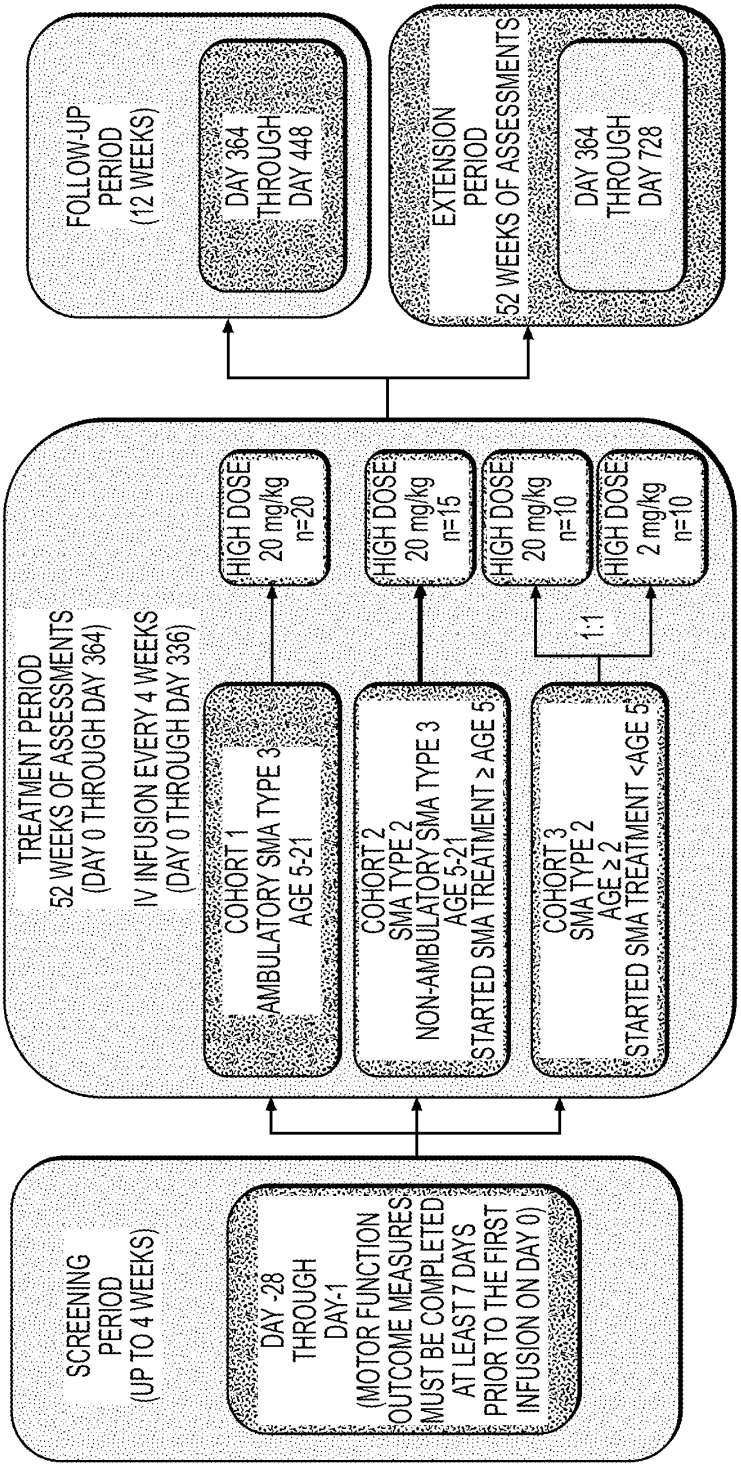

SCREENING PERIOD (UP TO 4 WEEKS)
DAY -28 THROUGH DAY-1 (MOTOR FUNCTION OUTCOME MEASURES MUST BE COMPLETED AT LEAST 7 DAYS PRIOR TO THE FIRST INFUSION ON DAY 0)
TREATMENT PERIOD 52 WEEKS OF ASSESSMENTS (DAY 0 THROUGH DAY 364)
IV INFUSION EVERY 4 WEEKS (DAY 0 THROUGH DAY 336)
COHORT 1 AMBULATORY SMA TYPE 3 AGE 5-21
COHORT 2 SMA TYPE 2 NON-AMBULATORY SMA TYPE 3 AGE 5-21 STARTED SMA TREATMENT ≥ AGE 5
COHORT 3 SMA TYPE 2 AGE ≥ 2 STARTED SMA TREATMENT <AGE 5
1:1
HIGH DOSE 20 mg/kg n=20
HIGH DOSE 20 mg/kg n=15
HIGH DOSE 20 mg/kg n=10
HIGH DOSE 2 mg/kg n=10
FOLLOW-UP PERIOD (12 WEEKS)
DAY 364 THROUGH DAY 448
52 WEEKS OF ASSESSMENTS EXTENSION PERIOD
DAY 364 THROUGH DAY 728

FIG. 1

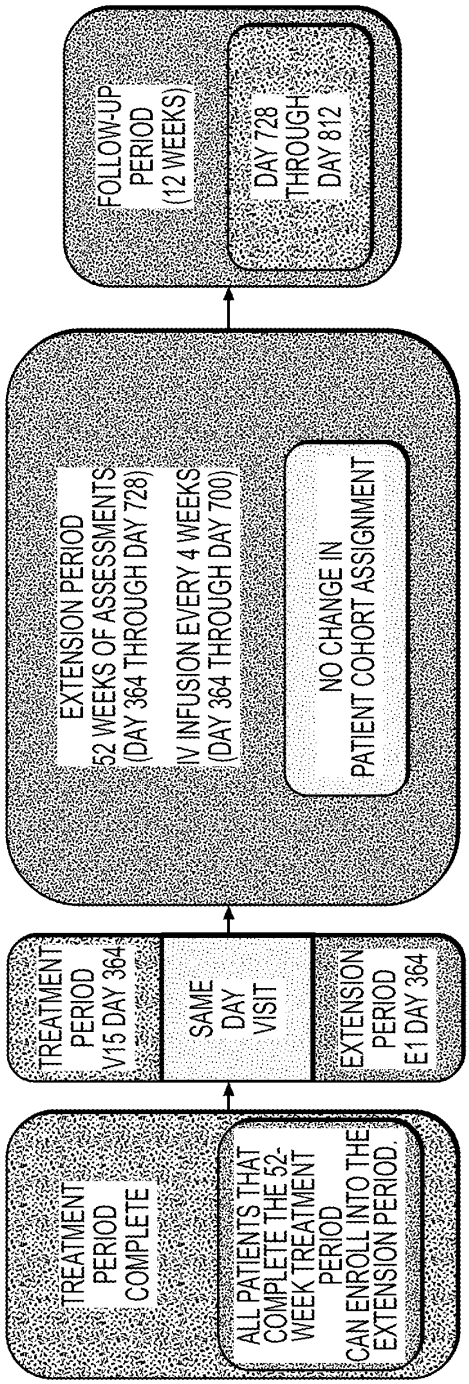

TREATMENT PERIOD COMPLETE
ALL PATIENTS THAT COMPLETE THE 52-WEEK TREATMENT PERIOD CAN ENROLL INTO THE EXTENSION PERIOD.
TREATMENT PERIOD V15 DAY 364
SAME DAY VISIT
EXTENSION PERIOD E1 DAY 364
EXTENSION PERIOD
52 WEEKS OF ASSESSMENTS (DAY 364 THROUGH DAY 728)
IV INFUSION EVERY 4 WEEKS (DAY 364 THROUGH DAY 700)
NO CHANGE IN PATIENT COHORT ASSIGNMENT
FOLLOW-UP PERIOD (12 WEEKS)
DAY 728 THROUGH DAY 812

FIG. 2

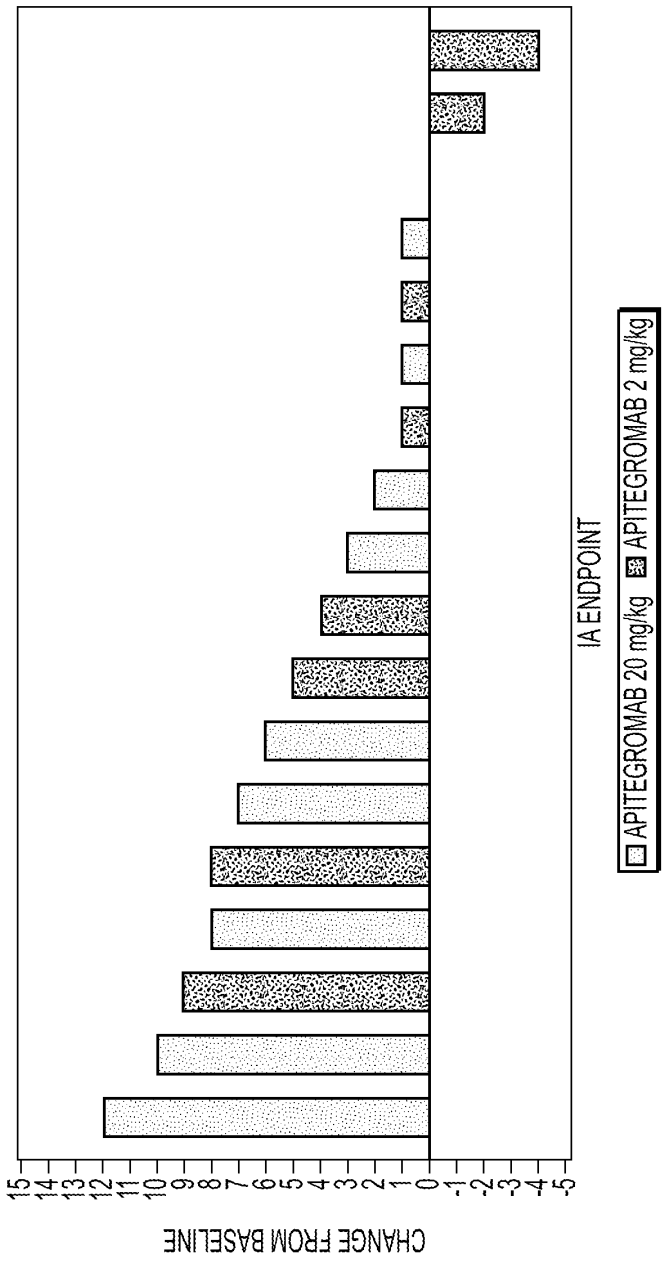

CHANGE FROM BASELINE
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
-5
IA ENDPOINT
APITEGROMAB 20 mg/kg
APITEGROMAB 2 mg/kg

FIG. 3A

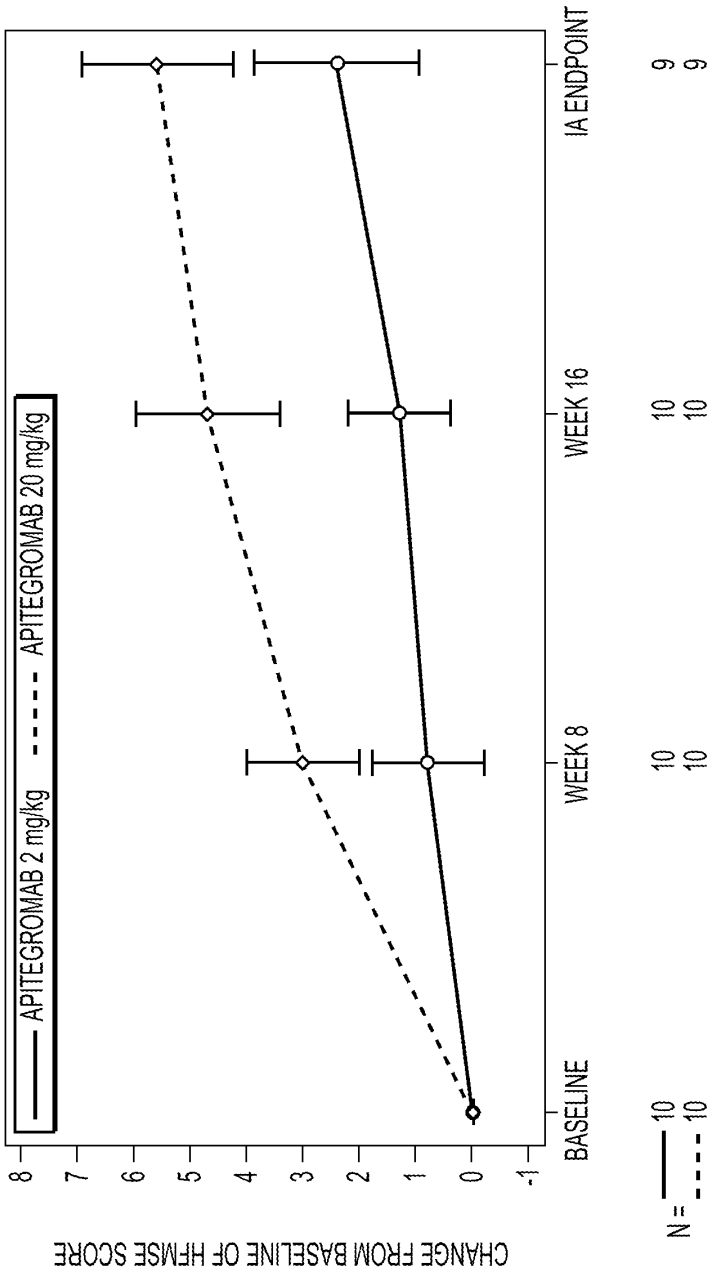

APITEGROMAB 2 mg/kg
APITEGROMAB 20 mg/kg
CHANGE FROM BASELINE OF HFMSE SCORE
8
7
6
5
4
3
2
1
0
-1
BASELINE
WEEK 8
WEEK 16
IA ENDPOINT
N =
10
10
10
10
10
10
9
9

FIG. 3B

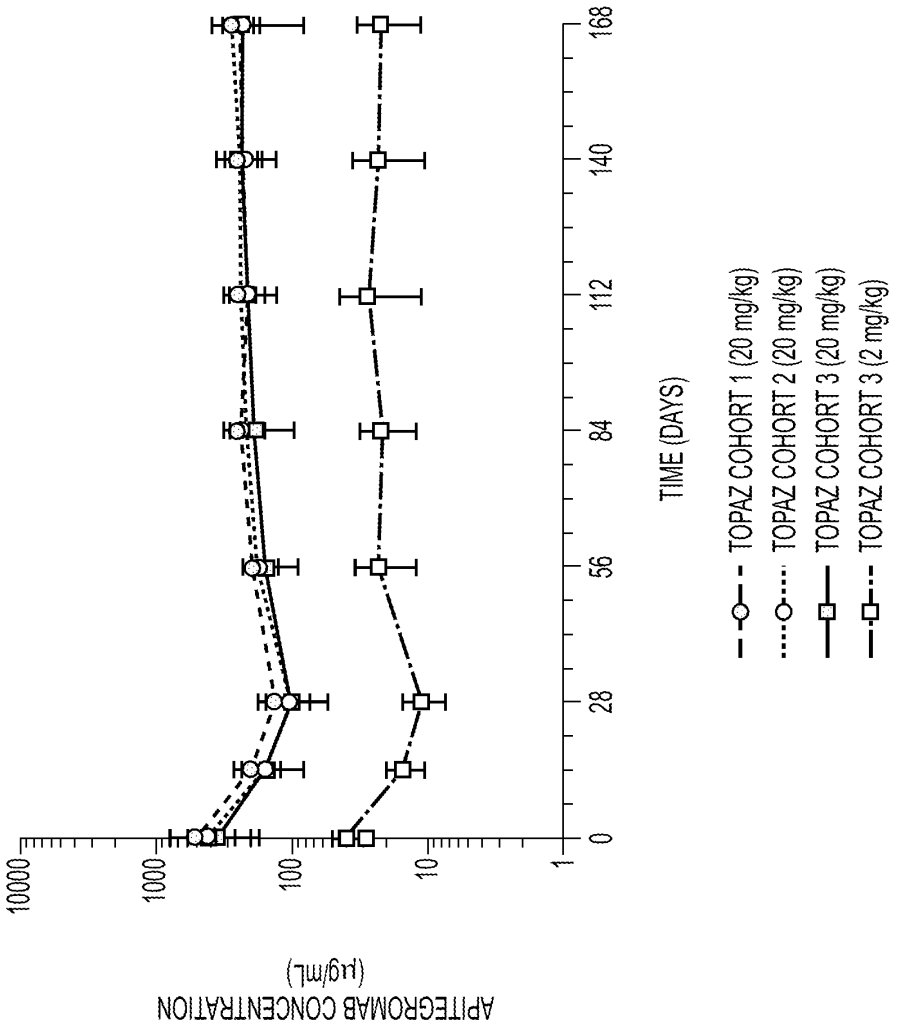

APITEGROMAB CONCENTRATION
(µg/mL)
10000
1000
100
10
1
0
28
56
84
112
140
168
TIME (DAYS)
TOPAZ COHORT 1 (20 mg/kg)
TOPAZ COHORT 2 (20 mg/kg)
TOPAZ COHORT 3 (20 mg/kg)
TOPAZ COHORT 3 (2 mg/kg)

FIG. 4

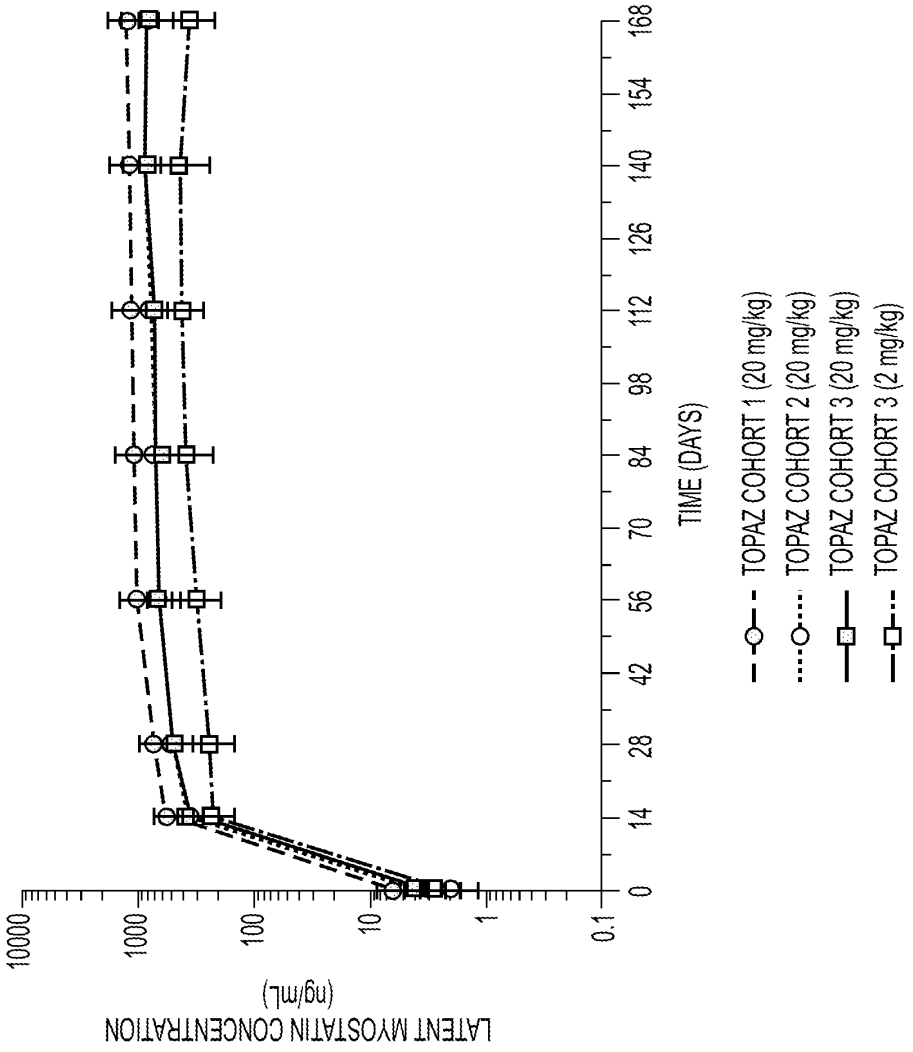

LATENT MYOSTATIN CONCENTRATION
(ng/mL)
10000
1000
100
10
1
0.1
0
14
28
42
56
70
84
98
112
126
140
154
168
TIME (DAYS)
TOPAZ COHORT 1 (20 mg/kg)
TOPAZ COHORT 2 (20 mg/kg)
TOPAZ COHORT 3 (20 mg/kg)
TOPAZ COHORT 3 (2 mg/kg)

FIG. 5

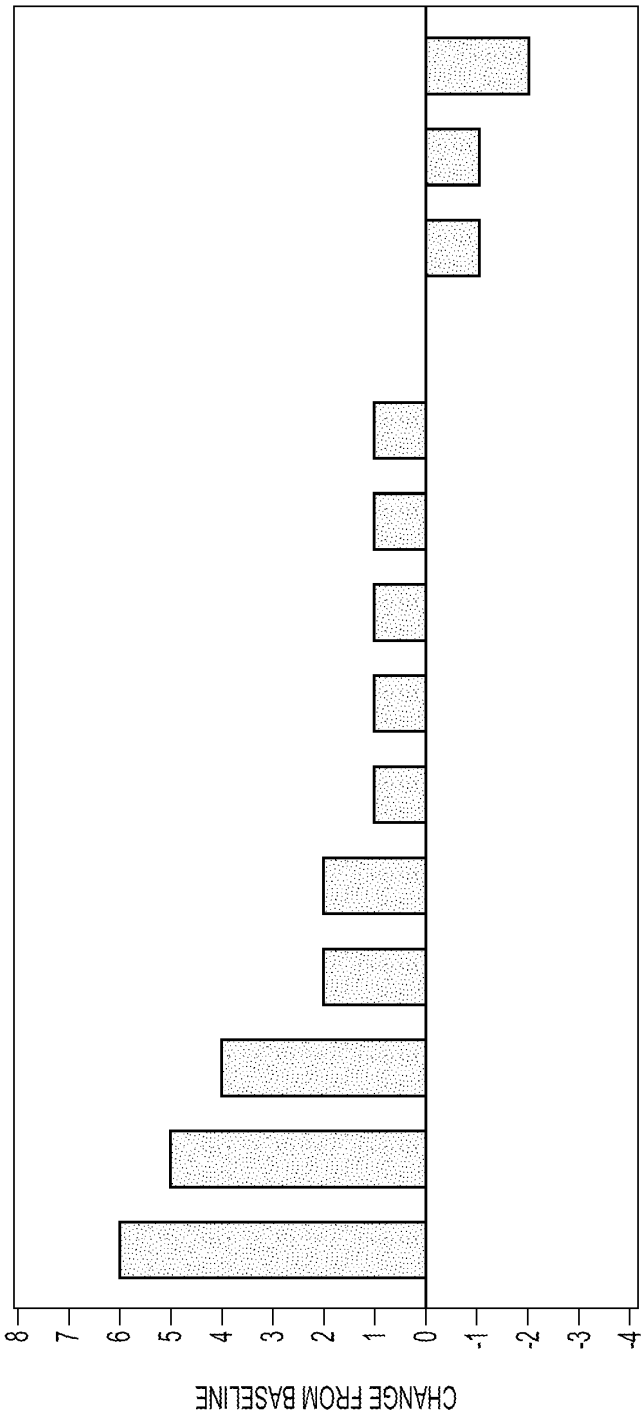

CHANGE FROM BASELINE
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
IA ENDPOINT
APITEGROMAB 20 mg/kg

FIG. 6A

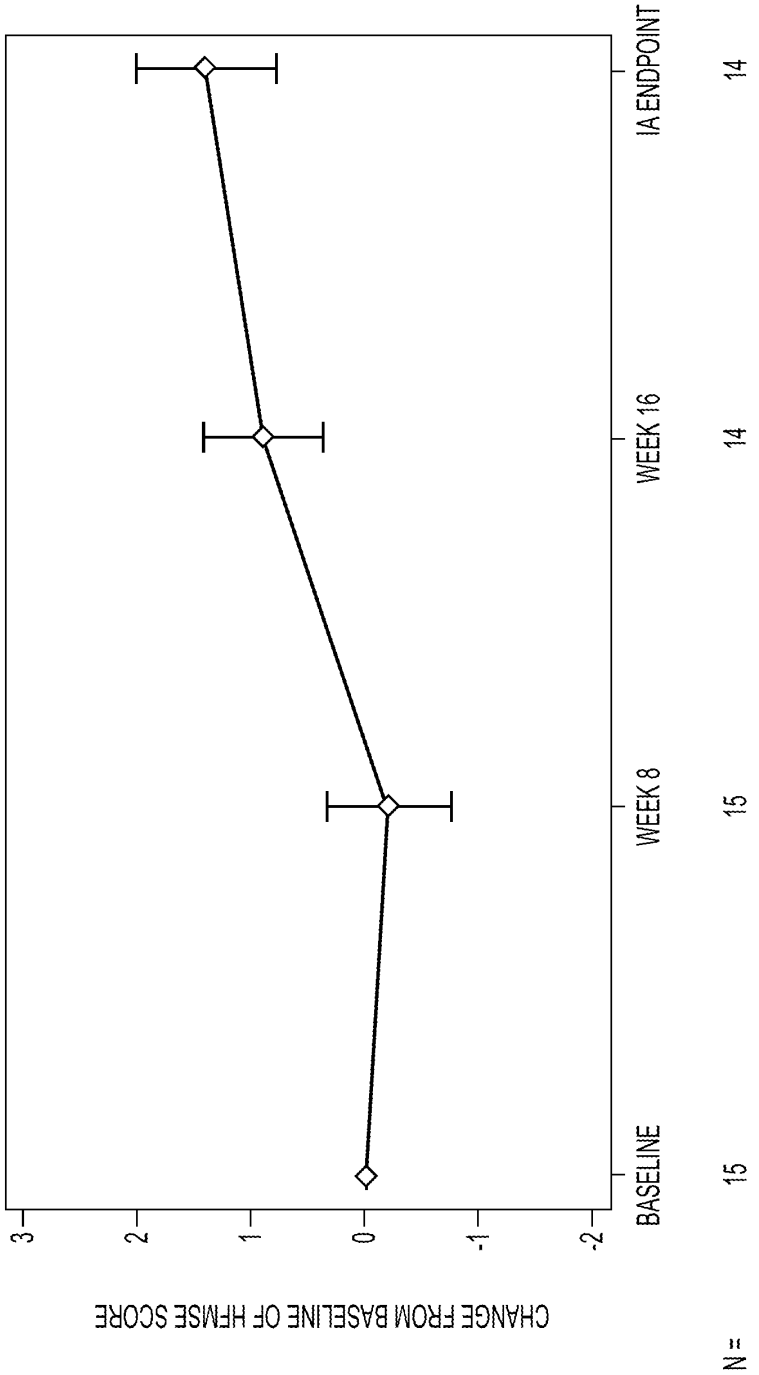

CHANGE FROM BASELINE OF HFMSE SCORE
3
2
1
0
-1
-2
BASELINE
WEEK 8
WEEK 16
IA ENDPOINT
N =
15
15
14
14

FIG. 6B

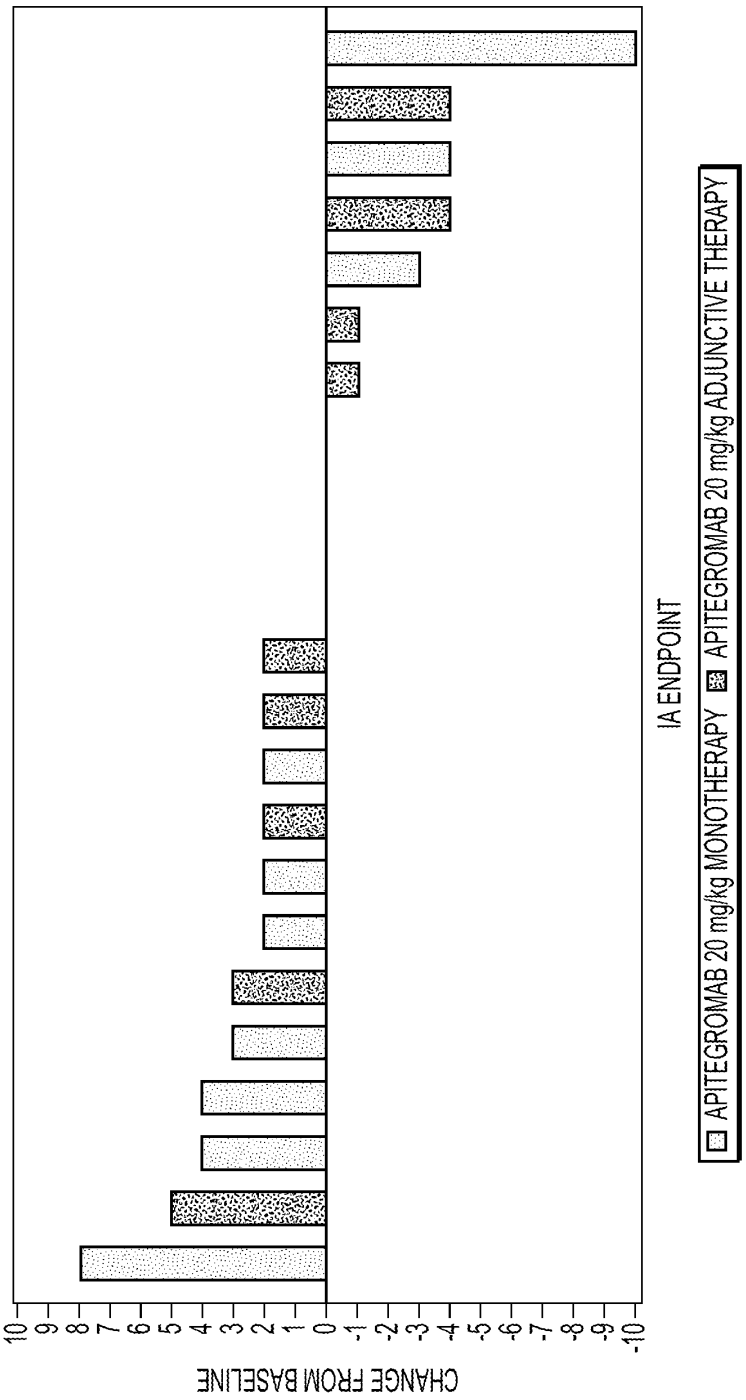

CHANGE FROM BASELINE
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
-5
-6
-7
-8
-9
-10
IA ENDPOINT
APITEGROMAB 20 mg/kg MONOTHERAPY
APITEGROMAB 20 mg/kg ADJUNCTIVE THERAPY

FIG. 7A

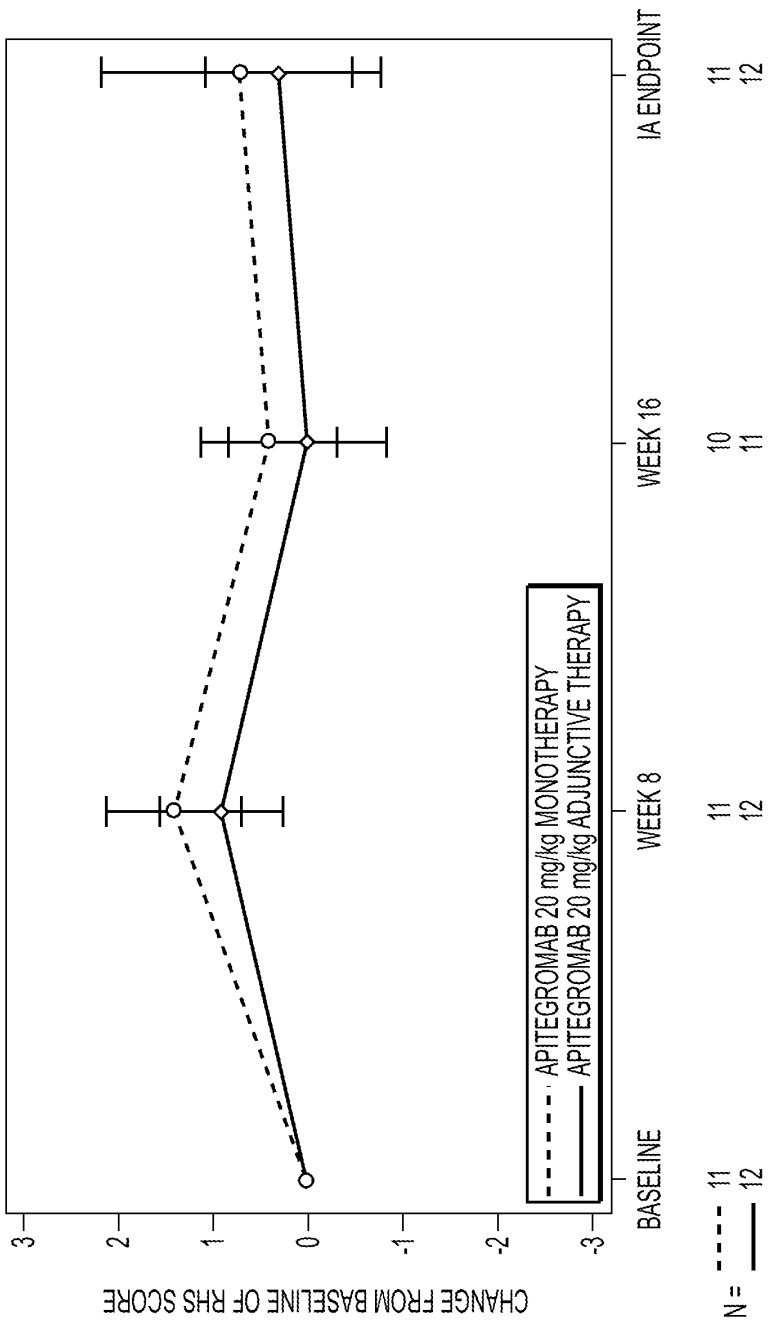
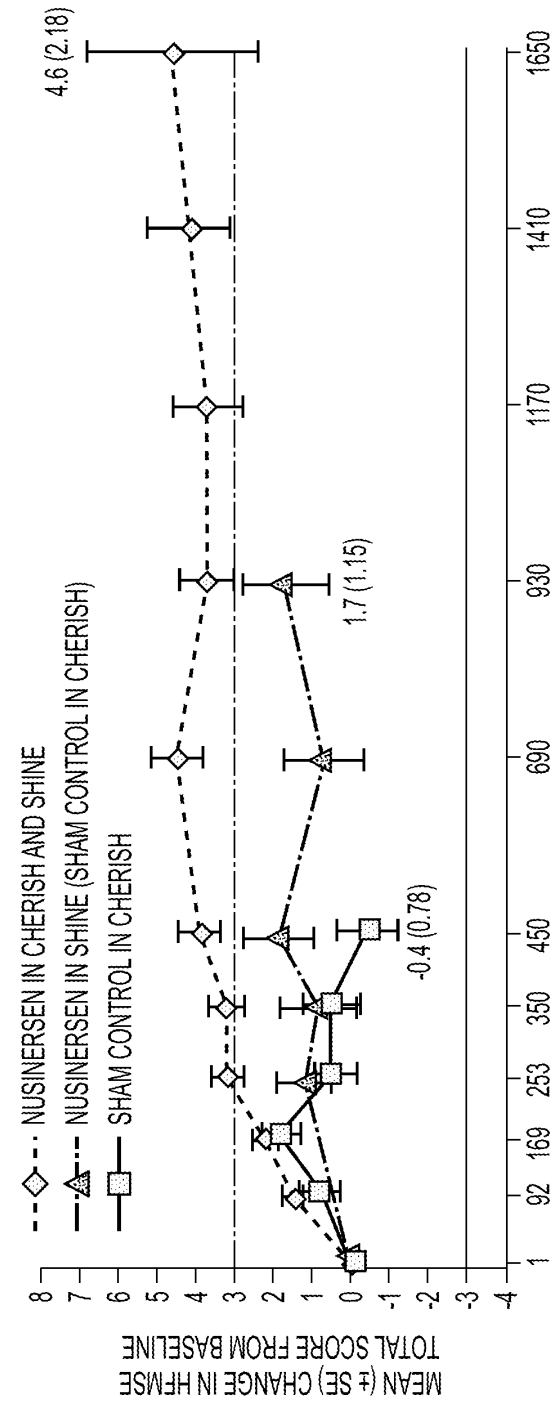

CHANGE FROM BASELINE OF RHS SCORE
3
2
1
0
-1
-2
-3
BASELINE
WEEK 8
WEEK 16
IA ENDPOINT
APITEGROMAB 20 mg/kg MONOTHERAPY
APITEGROMAB 20 mg/kg ADJUNCTIVE THERAPY
N =
11 11 10 11
12 12 11 12

FIG. 7B



GROUP	MEAN (SD) HFMSE SCORES	
	BASELINE[b]	VISIT NOTED[c]
NUSINERSEN IN CHERISH AND SHINE (DAY 1650)	22.4 (8.33)	26.1 (13.75)
NUSINERSEN IN SUNSHINE (SHAM CONTROL IN CHERISH) (DAY 930)	19.8 (8.39)	21.3 (9.53)
SHAM CONTROL IN CHERISH (DAY 450)	19.9 (7.23)	19.5 (8.26)

FIG. 8

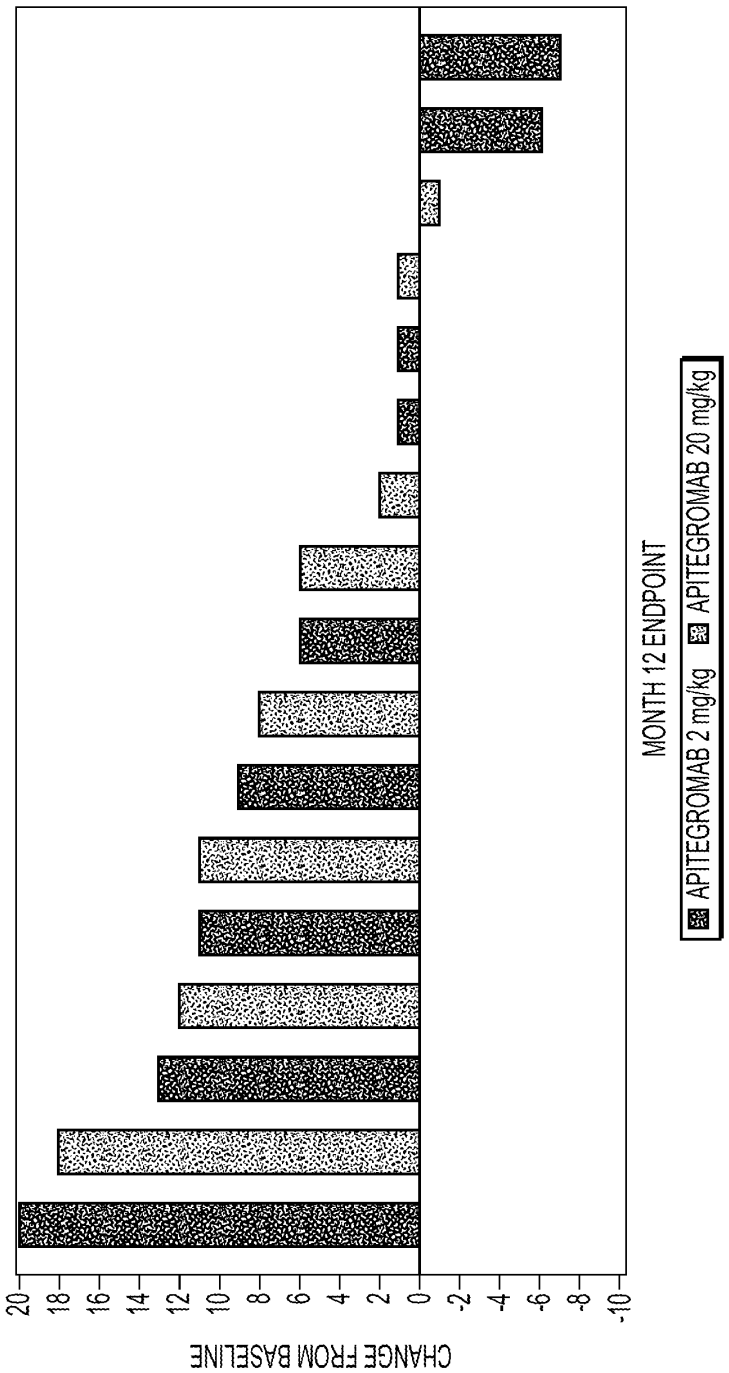

CHANGE FROM BASELINE
20
18
16
14
12
10
8
6
4
2
0
-2
-4
-6
-8
-10
MONTH 12 ENDPOINT
APITEGROMAB 2 mg/kg
APITEGROMAB 20 mg/kg

FIG. 9A

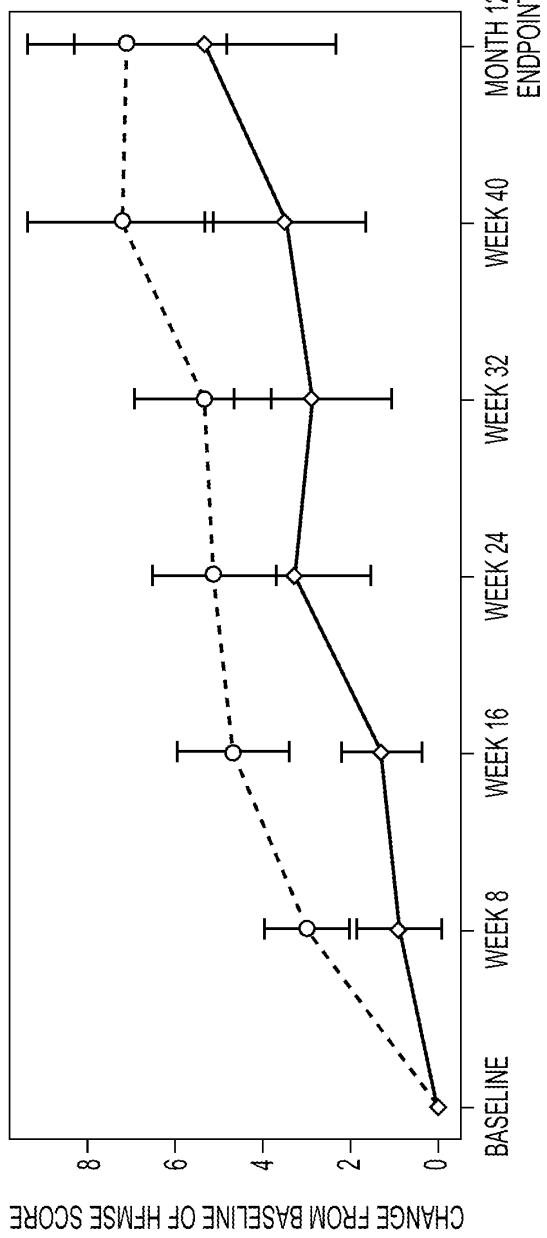

CHANGE FROM BASELINE OF HFMSE SCORE
0
2
4
6
8
BASELINE
WEEK 8
WEEK 16
WEEK 24
WEEK 32
WEEK 40
MONTH 12 ENDPOINT
APITEGROMAB 2 mg/kg
APITEGROMAB 20 mg/kg
SAMPLE SIZE AT EACH VISIT
APITEGROMAB 2 mg/kg 10 10 10 7 8 8 9
APITEGROMAB 20 mg/kg 10 10 10 8 8 8 8

FIG. 9B

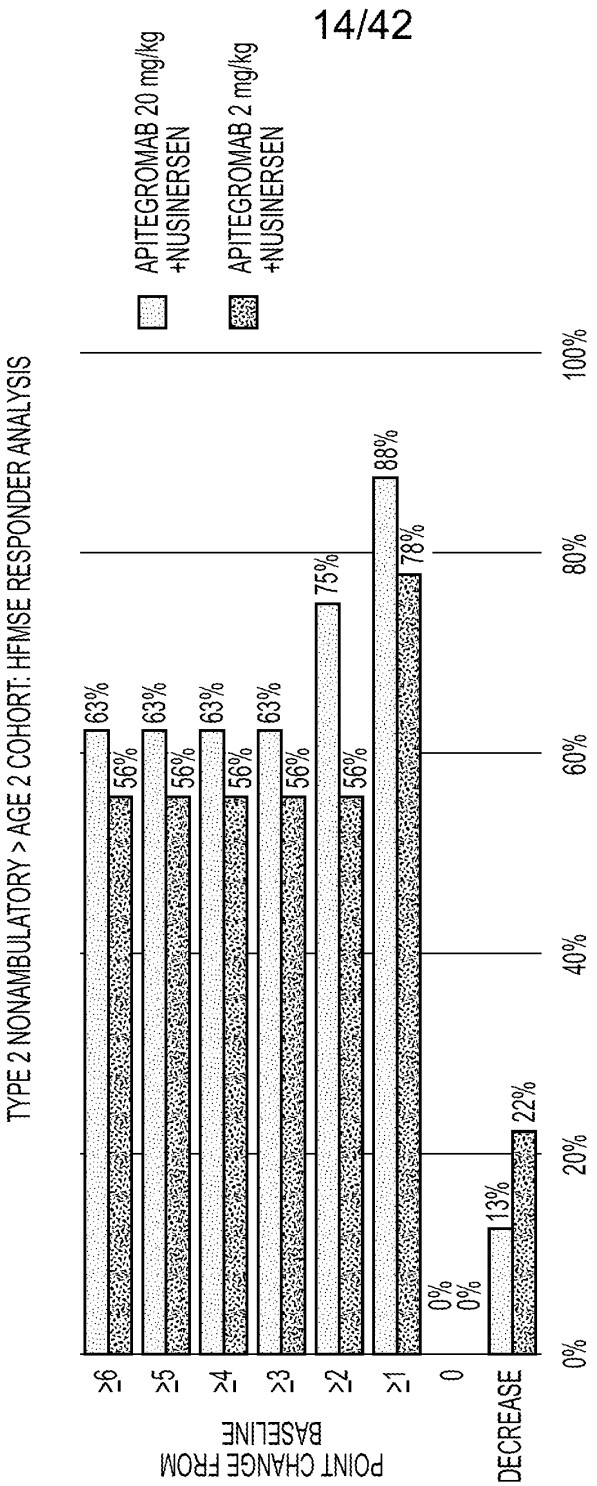

TYPE 2 NONAMBULATORY > AGE 2 COHORT: HFMSE RESPONDER ANALYSIS
APITEGROMAB 20 mg/kg +NUSINERSEN
APITEGROMAB 2 mg/kg +NUSINERSEN
POINT CHANGE FROM BASELINE
≥6
≥5
≥4
≥3
≥2
≥1
0
DECREASE
63%
56%
63%
56%
63%
56%
63%
56%
75%
56%
88%
78%
0%
0%
13%
22%
0%
20%
40%
60%
80%
100%

FIG. 9C

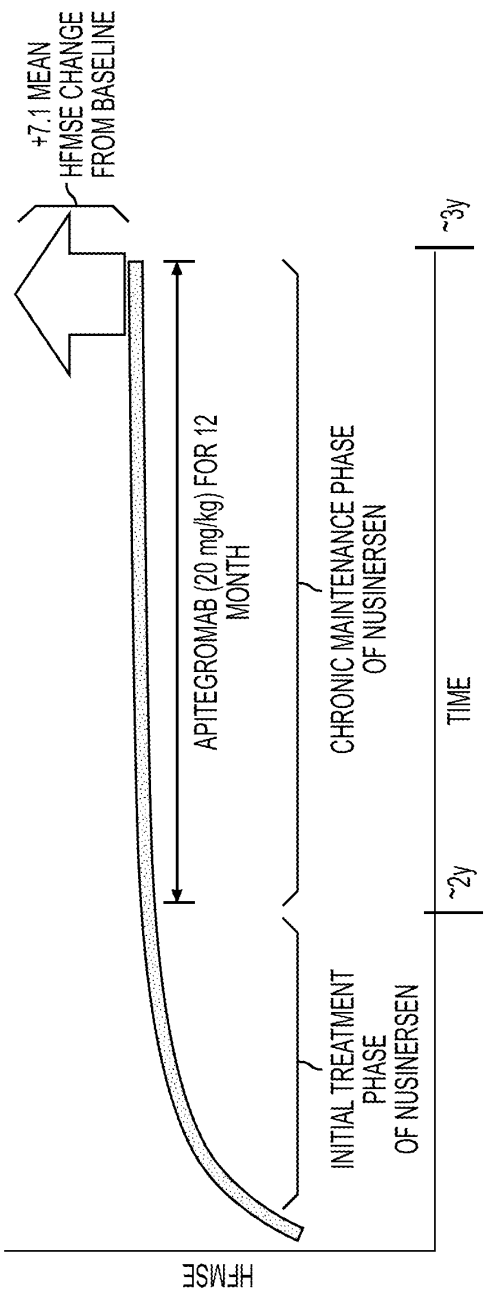

+7.1 MEAN
HFMSE CHANGE
FROM BASELINE
APITEGROMAB (20 mg/kg) FOR 12
MONTH
CHRONIC MAINTENANCE PHASE
OF NUSINERSEN
INITIAL TREATMENT
PHASE
OF NUSINERSEN
~2y
~3y
TIME
HFMSE

FIG. 9D

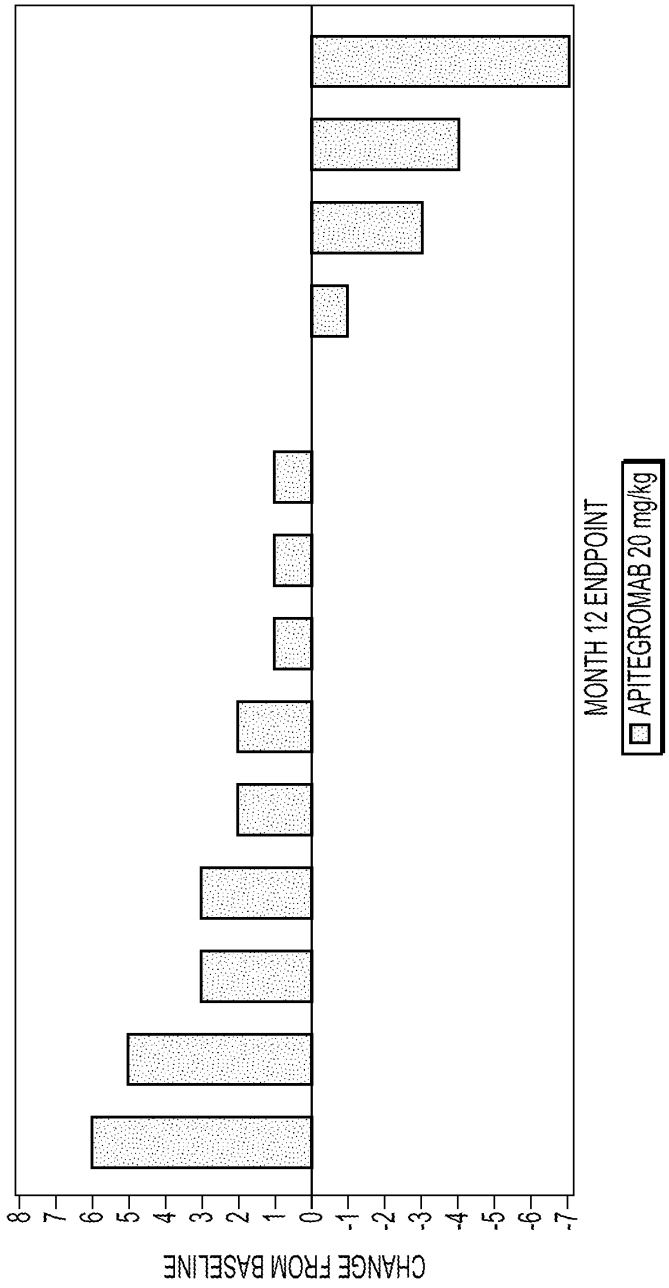

CHANGE FROM BASELINE
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
-5
-6
-7
MONTH 12 ENDPOINT
APITEGROMAB 20 mg/kg

FIG. 10A

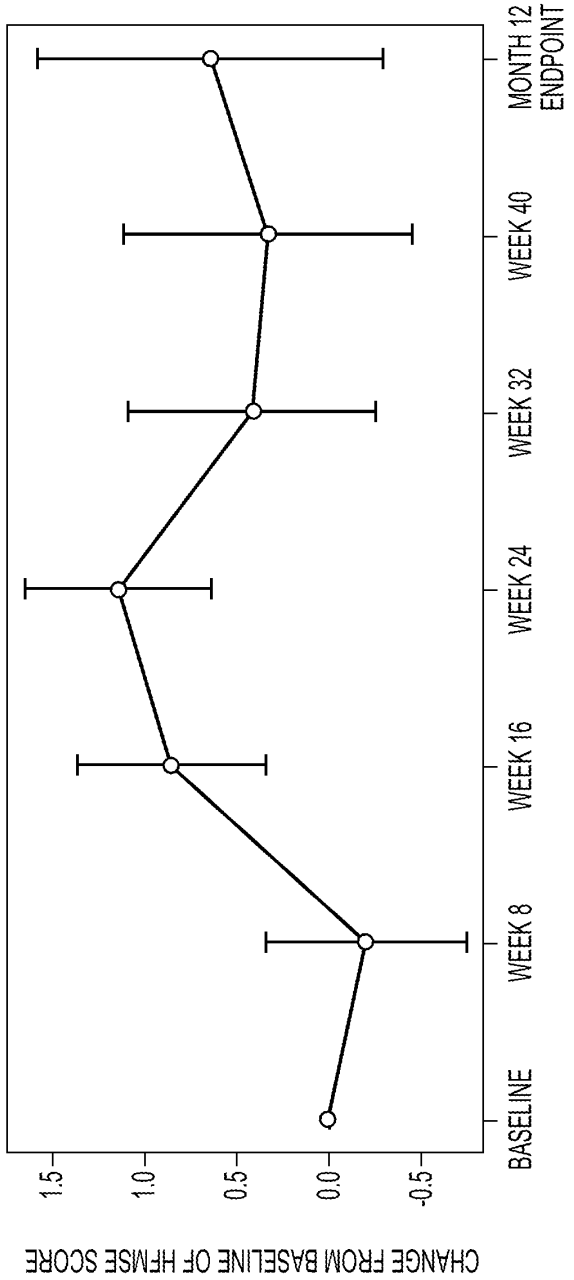

CHANGE FROM BASELINE OF HFMSE SCORE
1.5
1.0
0.5
0.0
-0.5
BASELINE
WEEK 8
WEEK 16
WEEK 24
WEEK 32
WEEK 40
MONTH 12 ENDPOINT
APITEGROMAB 20 mg/kg
SAMPLE SIZE AT EACH VISIT
APITEGROMAB 20 mg/kg 15 15 14 14 12 9 14

FIG. 10B

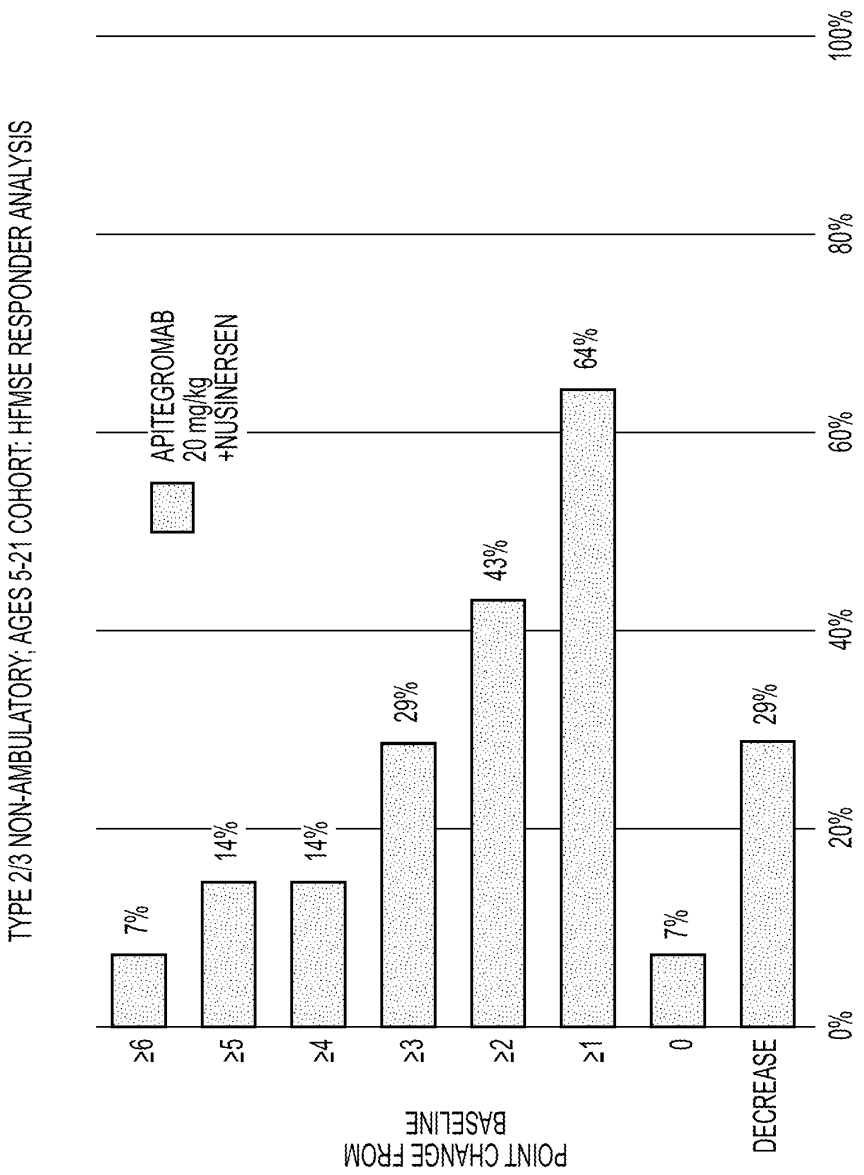

TYPE 2/3 NON-AMBULATORY; AGES 5-21 COHORT: HFMSE RESPONDER ANALYSIS
APITEGROMAB
20 mg/kg
+NUSINERSEN
POINT CHANGE FROM
BASELINE
≥6
≥5
≥4
≥3
≥2
≥1
0
DECREASE
7%
14%
14%
29%
43%
64%
7%
29%
0%
20%
40%
60%
80%
100%

FIG. 10C

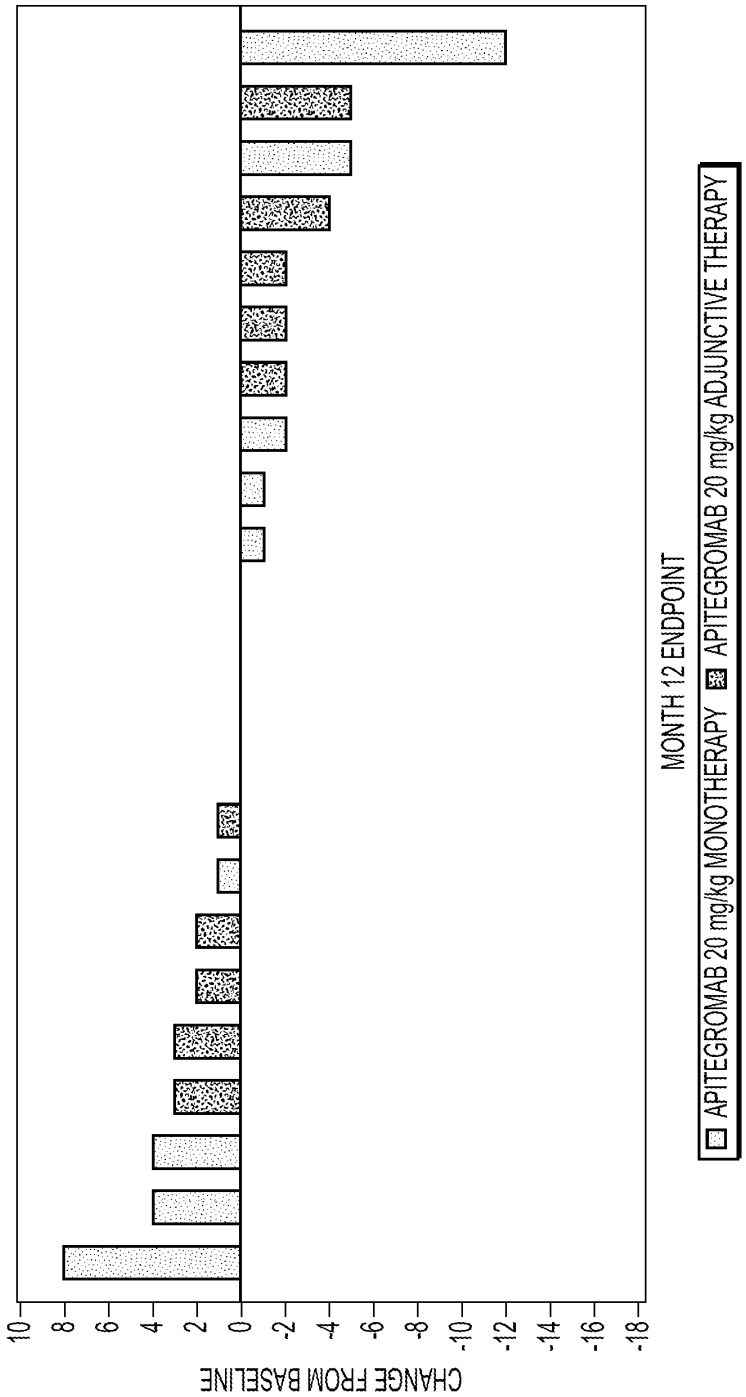

CHANGE FROM BASELINE
10
8
6
4
2
0
-2
-4
-6
-8
-10
-12
-14
-16
-18
MONTH 12 ENDPOINT
APITEGROMAB 20 mg/kg MONOTHERAPY
APITEGROMAB 20 mg/kg ADJUNCTIVE THERAPY

FIG. 11A

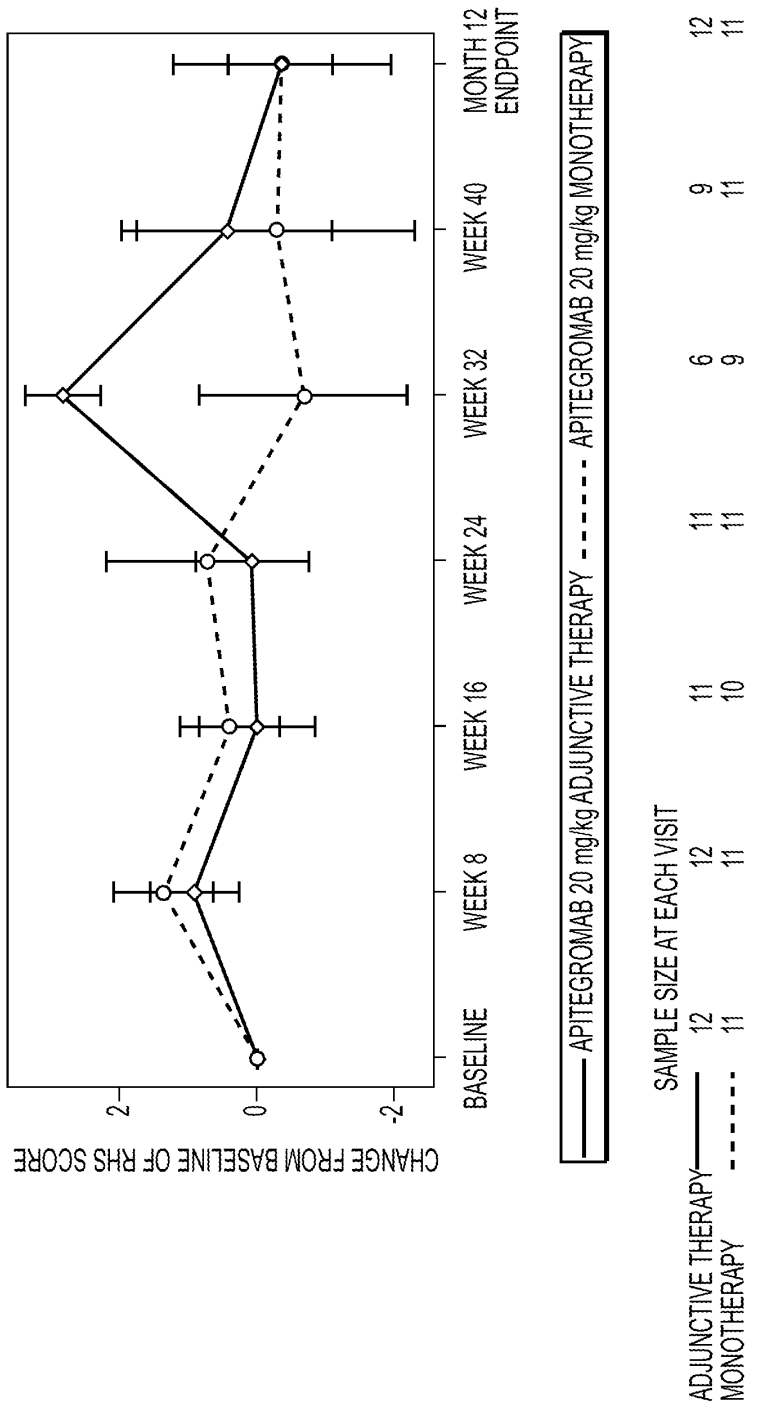

CHANGE FROM BASELINE OF RHS SCORE
2
0
-2
BASELINE
WEEK 8
WEEK 16
WEEK 24
WEEK 32
WEEK 40
MONTH 12 ENDPOINT
APITEGROMAB 20 mg/kg ADJUNCTIVE THERAPY
APITEGROMAB 20 mg/kg MONOTHERAPY
SAMPLE SIZE AT EACH VISIT
ADJUNCTIVE THERAPY 12 11 11 6 9 12
MONOTHERAPY 11 11 10 11 11 11 11

FIG. 11B

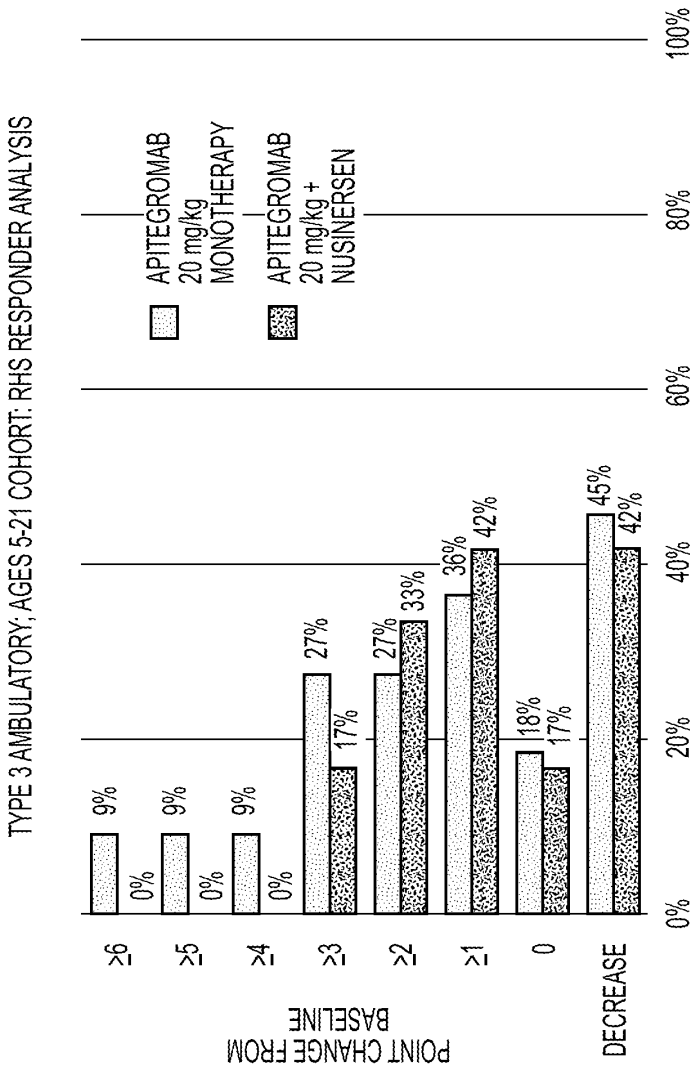

TYPE 3 AMBULATORY; AGES 5-21 COHORT: RHS RESPONDER ANALYSIS
APITEGROMAB 20 mg/kg MONOTHERAPY
APITEGROMAB 20 mg/kg + NUSINERSEN
POINT CHANGE FROM BASELINE
≥6
≥5
≥4
≥3
≥2
≥1
0
DECREASE
9%
0%
9%
0%
9%
0%
27%
17%
27%
33%
36%
42%
18%
17%
45%
42%
0%
20%
40%
60%
80%
100%

FIG. 11C

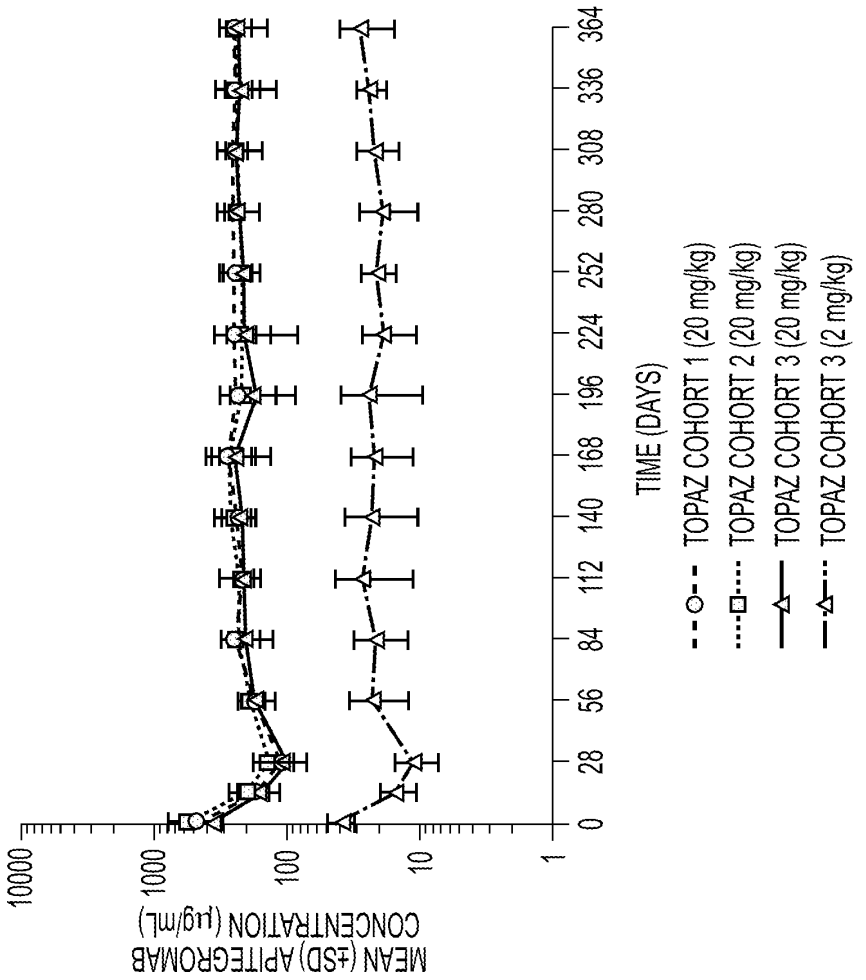

MEAN (±SD) APITEGROMAB CONCENTRATION (µg/mL)
10000
1000
100
10
1
0
28
56
84
112
140
168
196
224
252
280
308
336
364
TIME (DAYS)
TOPAZ COHORT 1 (20 mg/kg)
TOPAZ COHORT 2 (20 mg/kg)
TOPAZ COHORT 3 (20 mg/kg)
TOPAZ COHORT 3 (2 mg/kg)

FIG. 12A

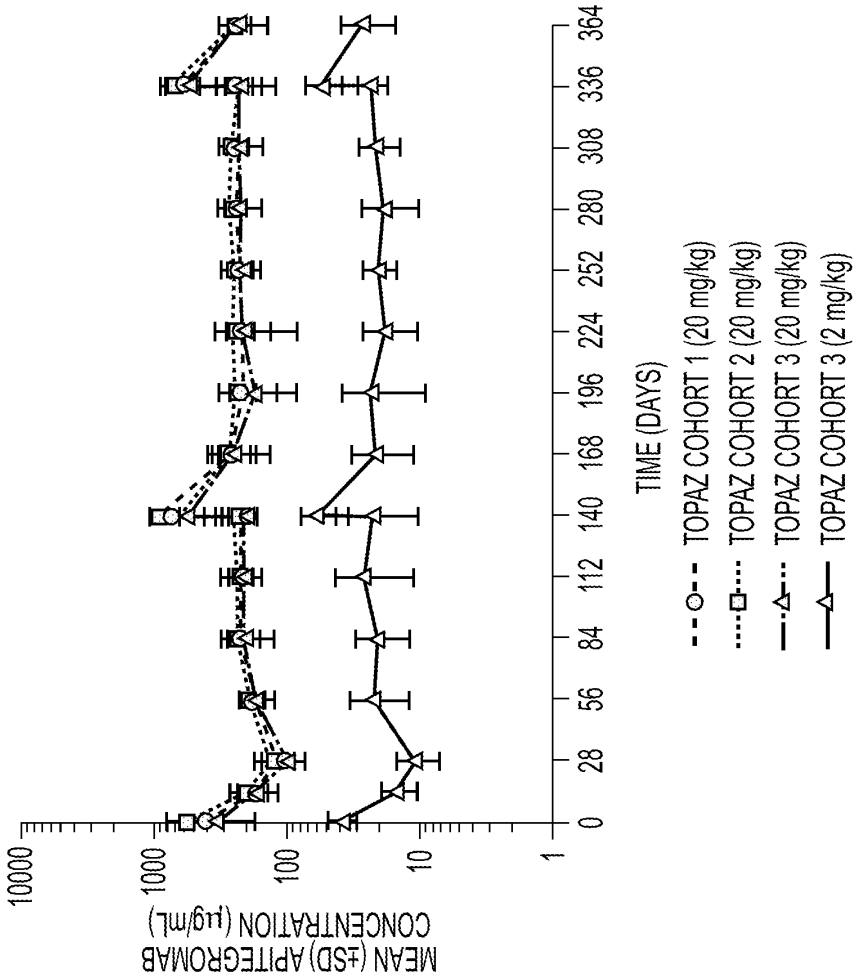

MEAN (±SD) APITEGROMAB CONCENTRATION (µg/mL)
10000
1000
100
10
1
0
28
56
84
112
140
168
196
224
252
280
308
336
364
TIME (DAYS)
TOPAZ COHORT 1 (20 mg/kg)
TOPAZ COHORT 2 (20 mg/kg)
TOPAZ COHORT 3 (20 mg/kg)
TOPAZ COHORT 3 (2 mg/kg)

FIG. 12B

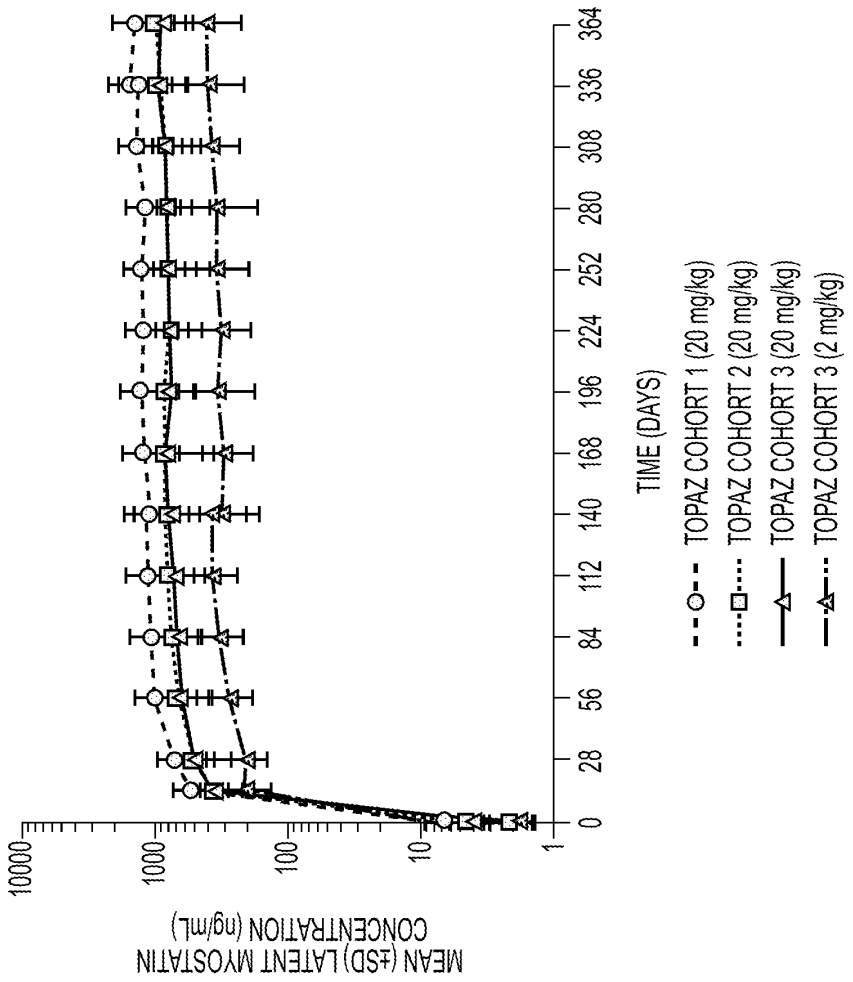

MEAN (±SD) LATENT MYOSTATIN CONCENTRATION (ng/mL)
10000
1000
100
10
1
0
28
56
84
112
140
168
196
224
252
280
308
336
364
TIME (DAYS)
TOPAZ COHORT 1 (20 mg/kg)
TOPAZ COHORT 2 (20 mg/kg)
TOPAZ COHORT 3 (20 mg/kg)
TOPAZ COHORT 3 (2 mg/kg)

FIG. 13

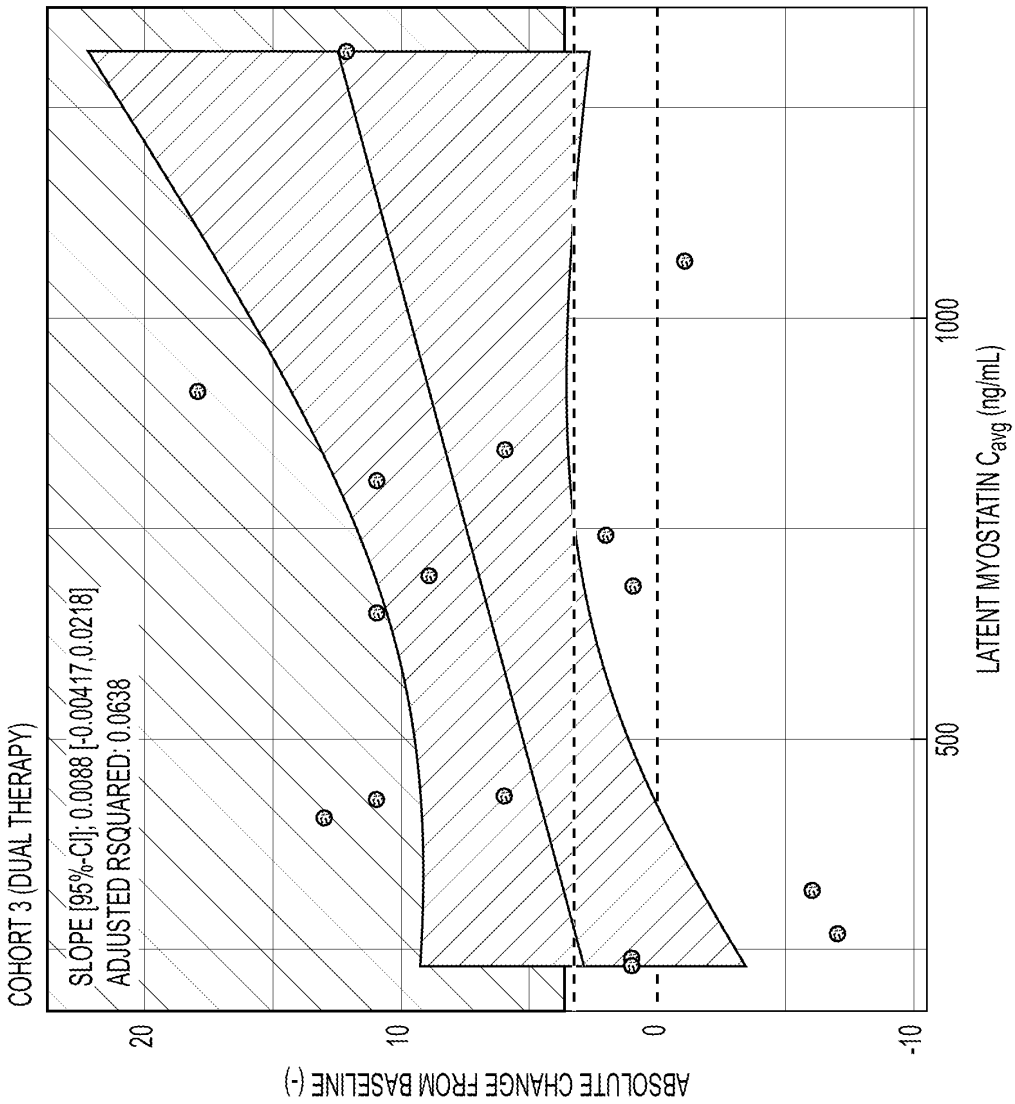

COHORT 3 (DUAL THERAPY)
SLOPE [95%-CI]: 0.0088 [-0.00417,0.0218]
ADJUSTED RSQUARED: 0.0638
ABSOLUTE CHANGE FROM BASELINE (-)
20
10
0
-10
500
1000
LATENT MYOSTATIN C_{avg} (ng/mL)

FIG. 14

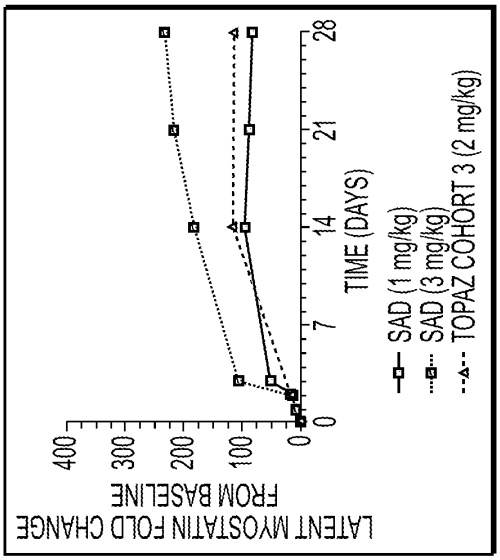


FIG. 15B

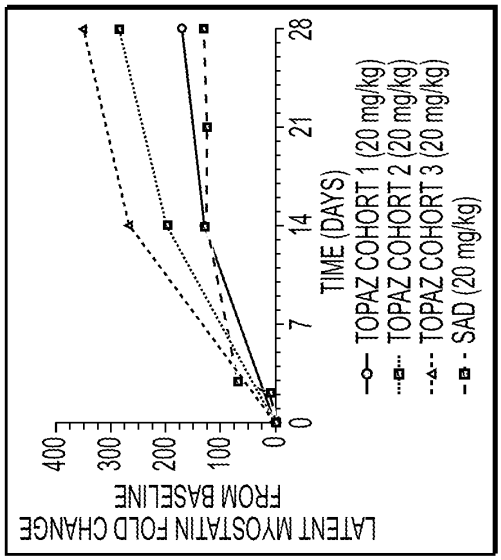


FIG. 15C

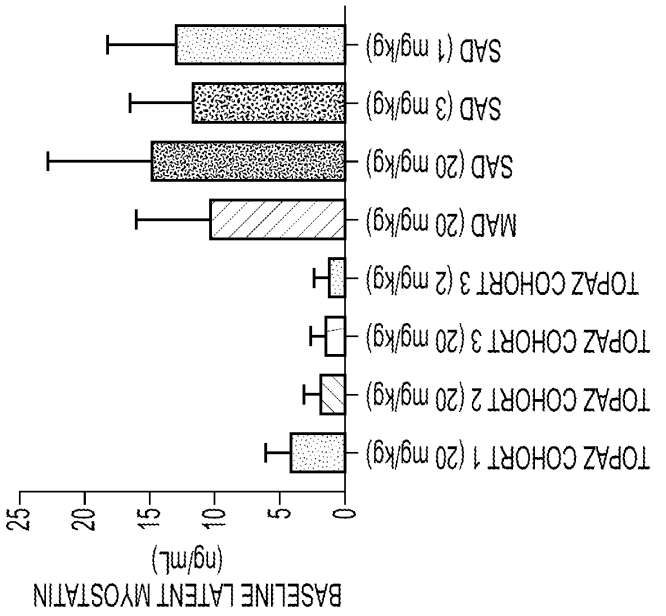


FIG. 15A

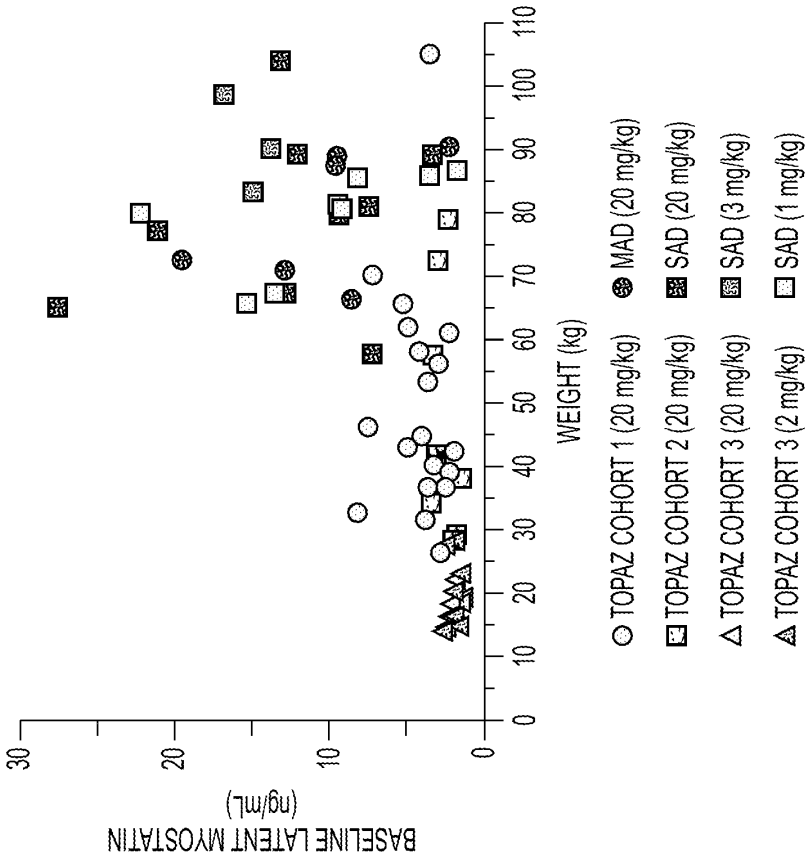

BASELINE LATENT MYOSTATIN (ng/mL)
0
10
20
30
WEIGHT (kg)
0
10
20
30
40
50
60
70
80
90
100
110
TOPAZ COHORT 1 (20 mg/kg)
MAD (20 mg/kg)
TOPAZ COHORT 2 (20 mg/kg)
SAD (20 mg/kg)
TOPAZ COHORT 3 (20 mg/kg)
SAD (3 mg/kg)
TOPAZ COHORT 3 (2 mg/kg)
SAD (1 mg/kg)

FIG. 16

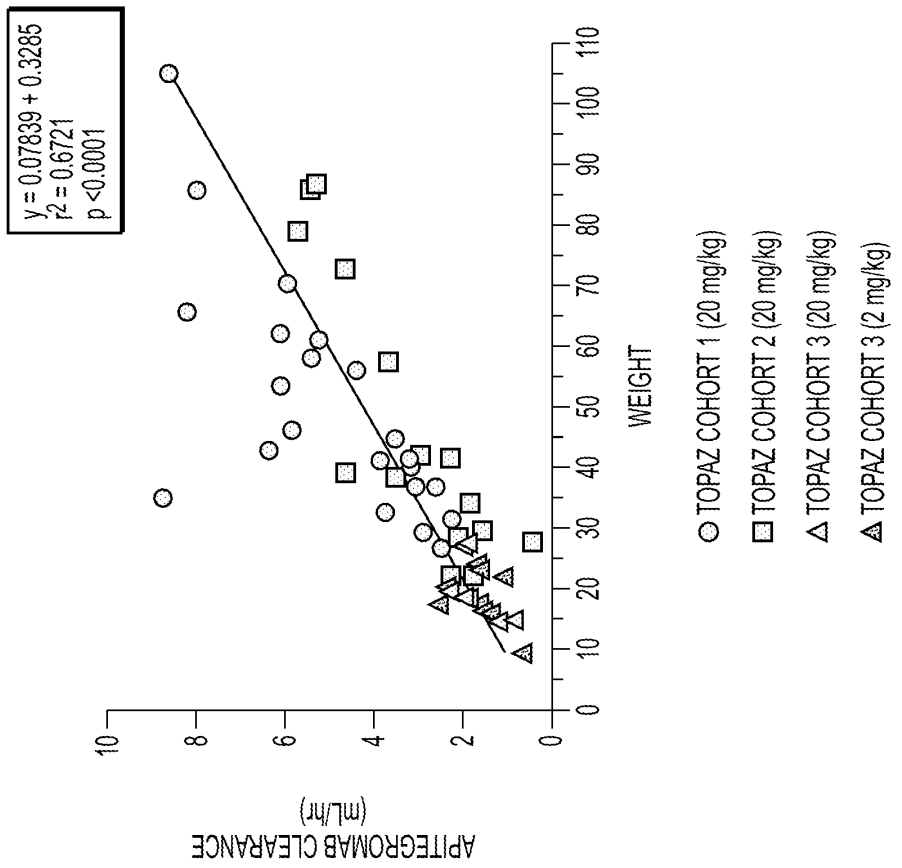

y = 0.07839 + 0.3285
r2 = 0.6721
p <0.0001
APITEGROMAB CLEARANCE
(mL/hr)
WEIGHT
TOPAZ COHORT 1 (20 mg/kg)
TOPAZ COHORT 2 (20 mg/kg)
TOPAZ COHORT 3 (20 mg/kg)
TOPAZ COHORT 3 (2 mg/kg)

FIG. 17

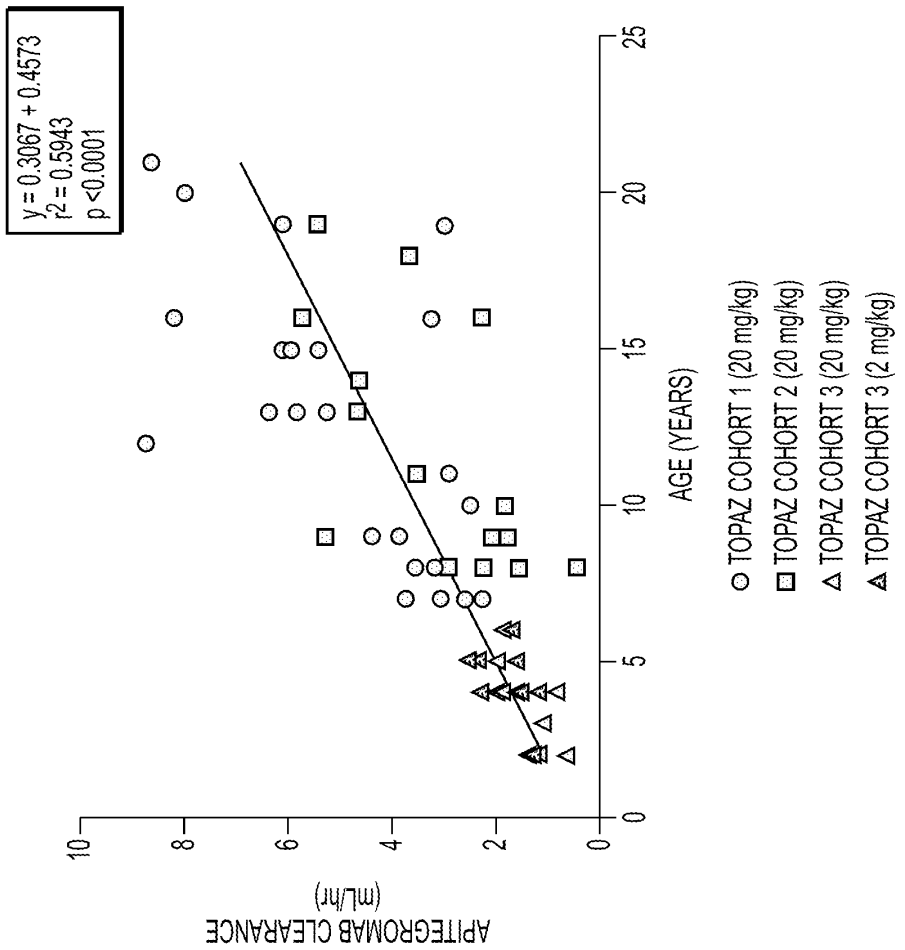

y = 0.3067 + 0.4573
r2 = 0.5943
p <0.0001
APITEGROMAB CLEARANCE
(mL/hr)
0
2
4
6
8
10
0
5
10
15
20
25
AGE (YEARS)
TOPAZ COHORT 1 (20 mg/kg)
TOPAZ COHORT 2 (20 mg/kg)
TOPAZ COHORT 3 (20 mg/kg)
TOPAZ COHORT 3 (2 mg/kg)

FIG. 18

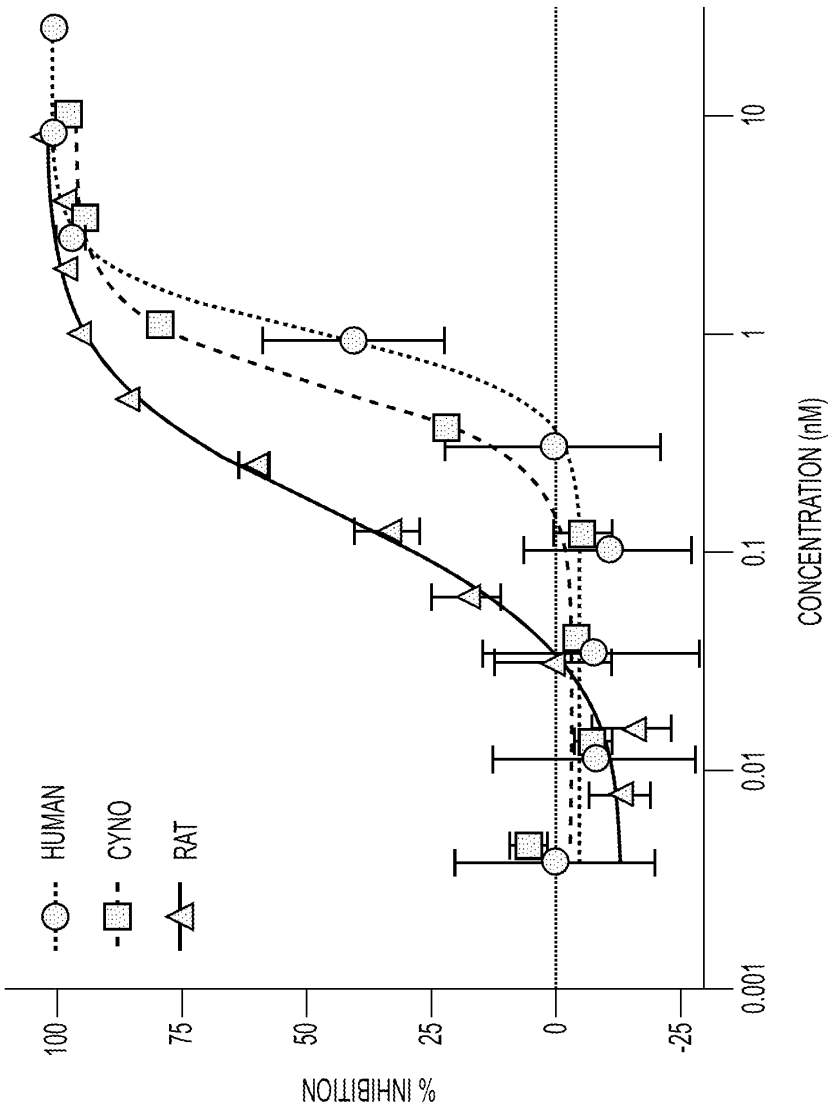

HUMAN
CYNO
RAT
% INHIBITION
100
75
50
25
0
-25
0.001
0.01
0.1
1
10
CONCENTRATION (nM)

FIG. 19

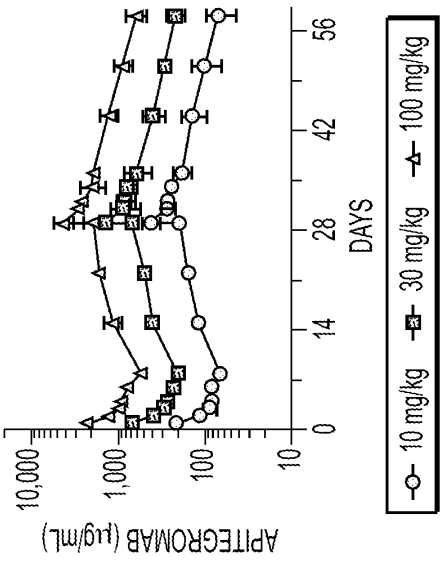


FIG. 20B

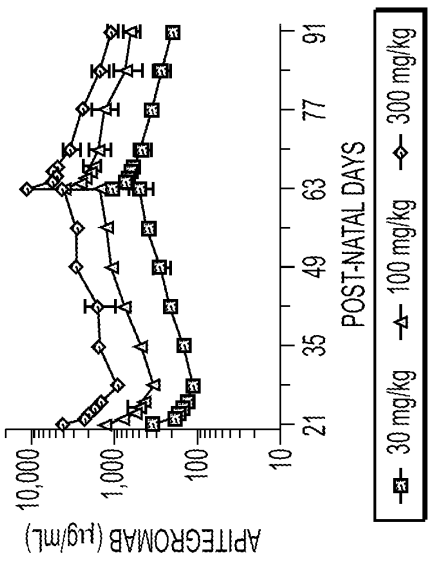


FIG. 20D

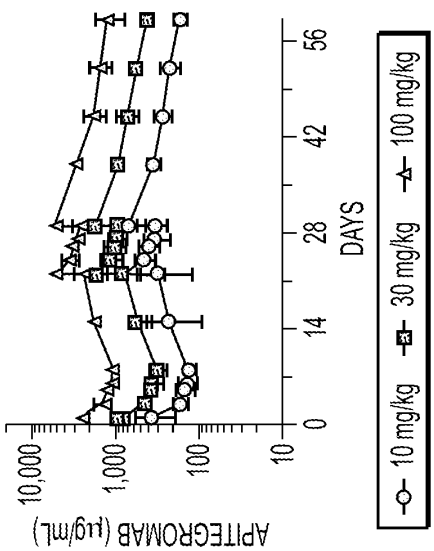


FIG. 20A

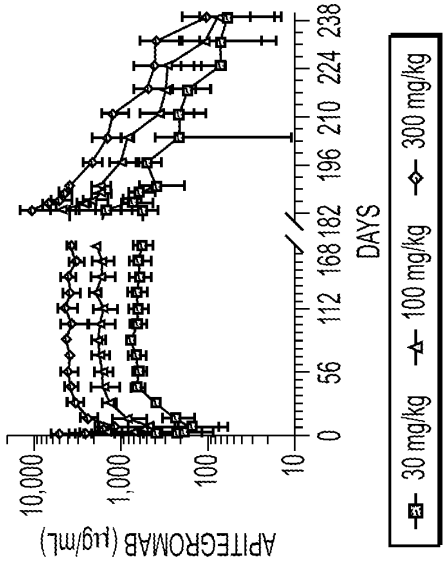


FIG. 20C



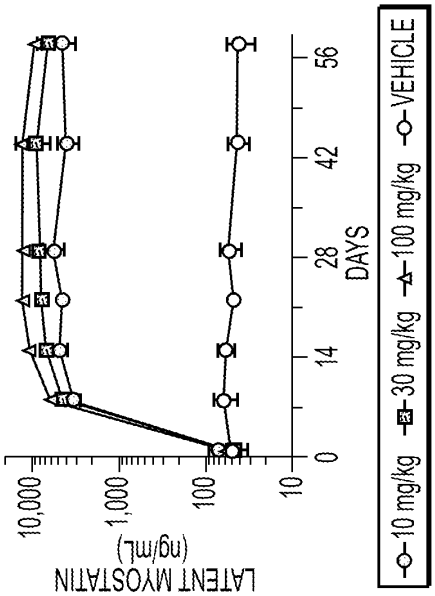


FIG. 21B

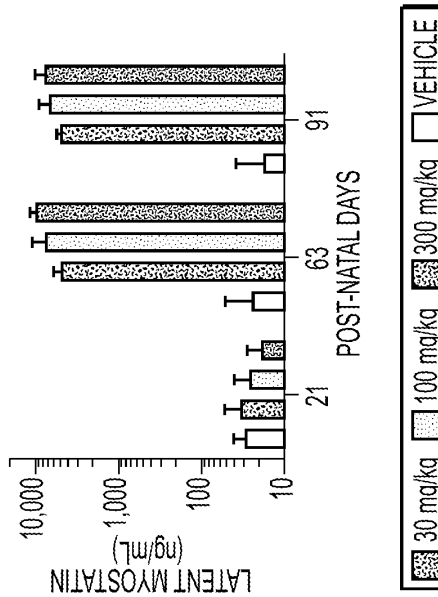


FIG. 21D

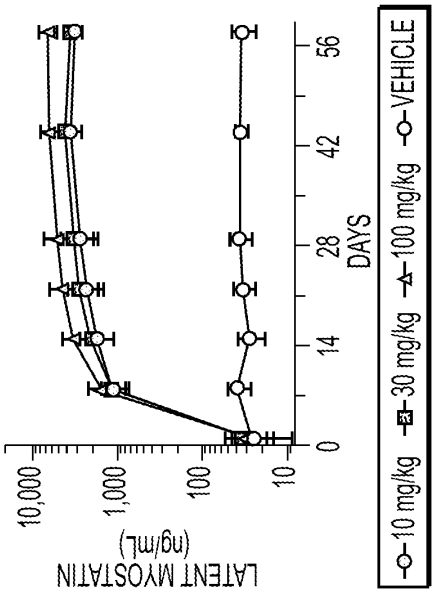


FIG. 21A

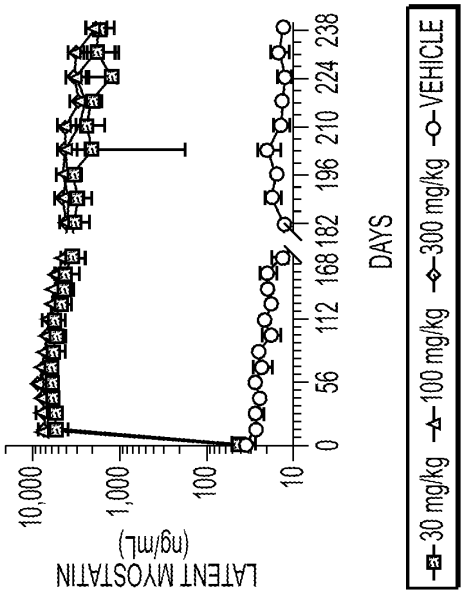


FIG. 21C

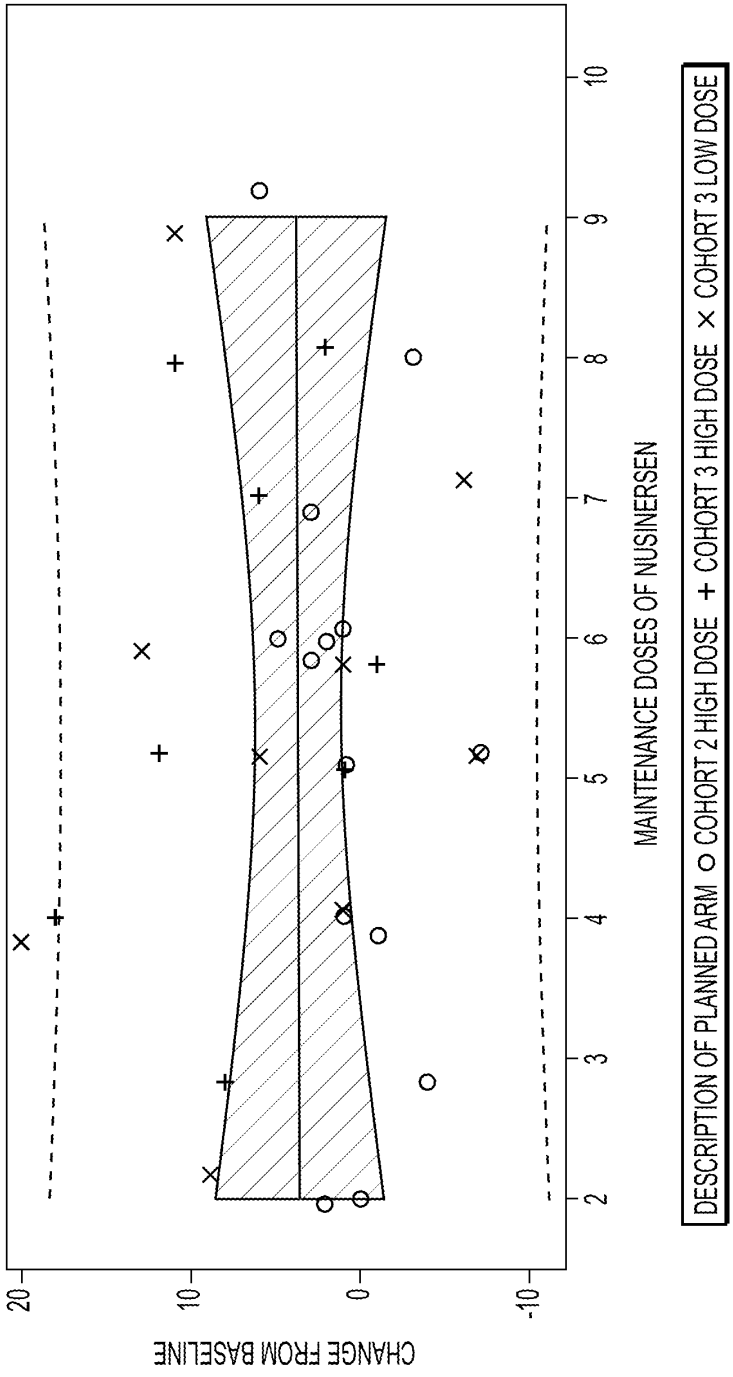

CHANGE FROM BASELINE
20
10
0
-10
2
3
4
5
6
7
8
9
10
MAINTENANCE DOSES OF NUSINERSEN
DESCRIPTION OF PLANNED ARM ○ COHORT 2 HIGH DOSE + COHORT 3 HIGH DOSE × COHORT 3 LOW DOSE

FIG. 22A

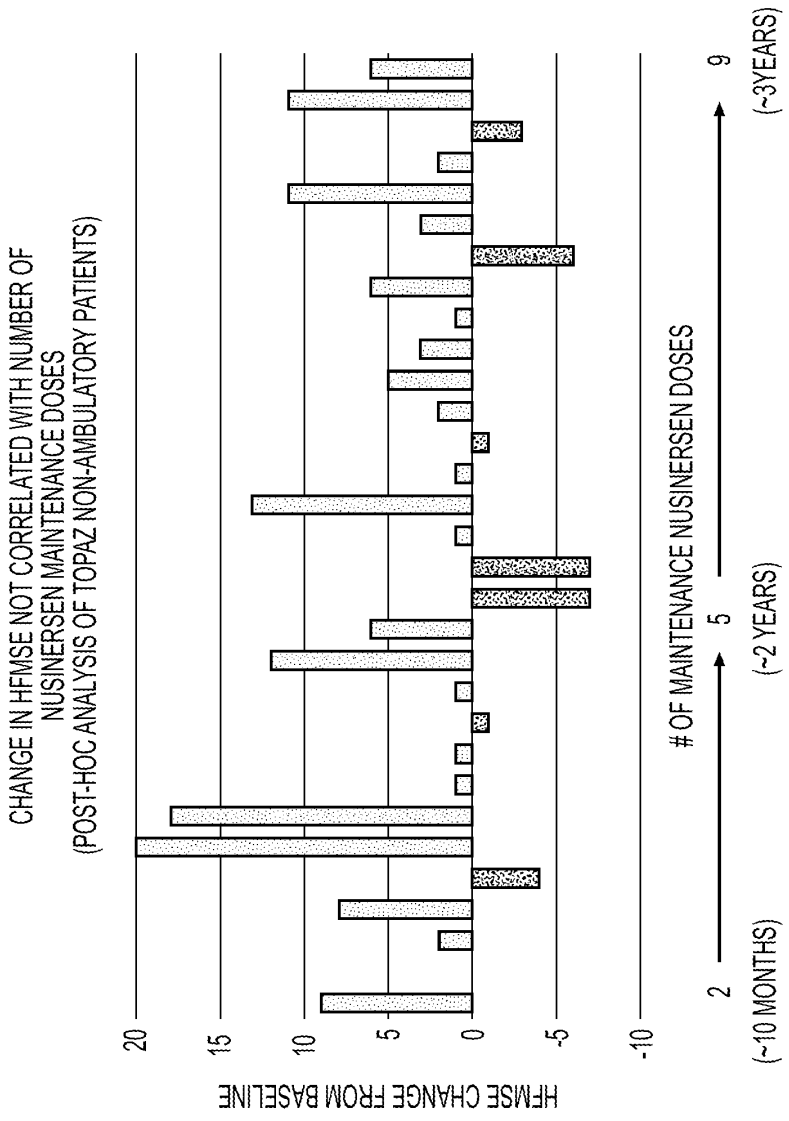

CHANGE IN HFMSE NOT CORRELATED WITH NUMBER OF NUSINERSEN MAINTENANCE DOSES
(POST-HOC ANALYSIS OF TOPAZ NON-AMBULATORY PATIENTS)
HFMSE CHANGE FROM BASELINE
20
15
10
5
0
-5
-10
OF MAINTENANCE NUSINERSEN DOSES
2
(~10 MONTHS)
5
(~2 YEARS)
9
(~3YEARS)

FIG. 22B

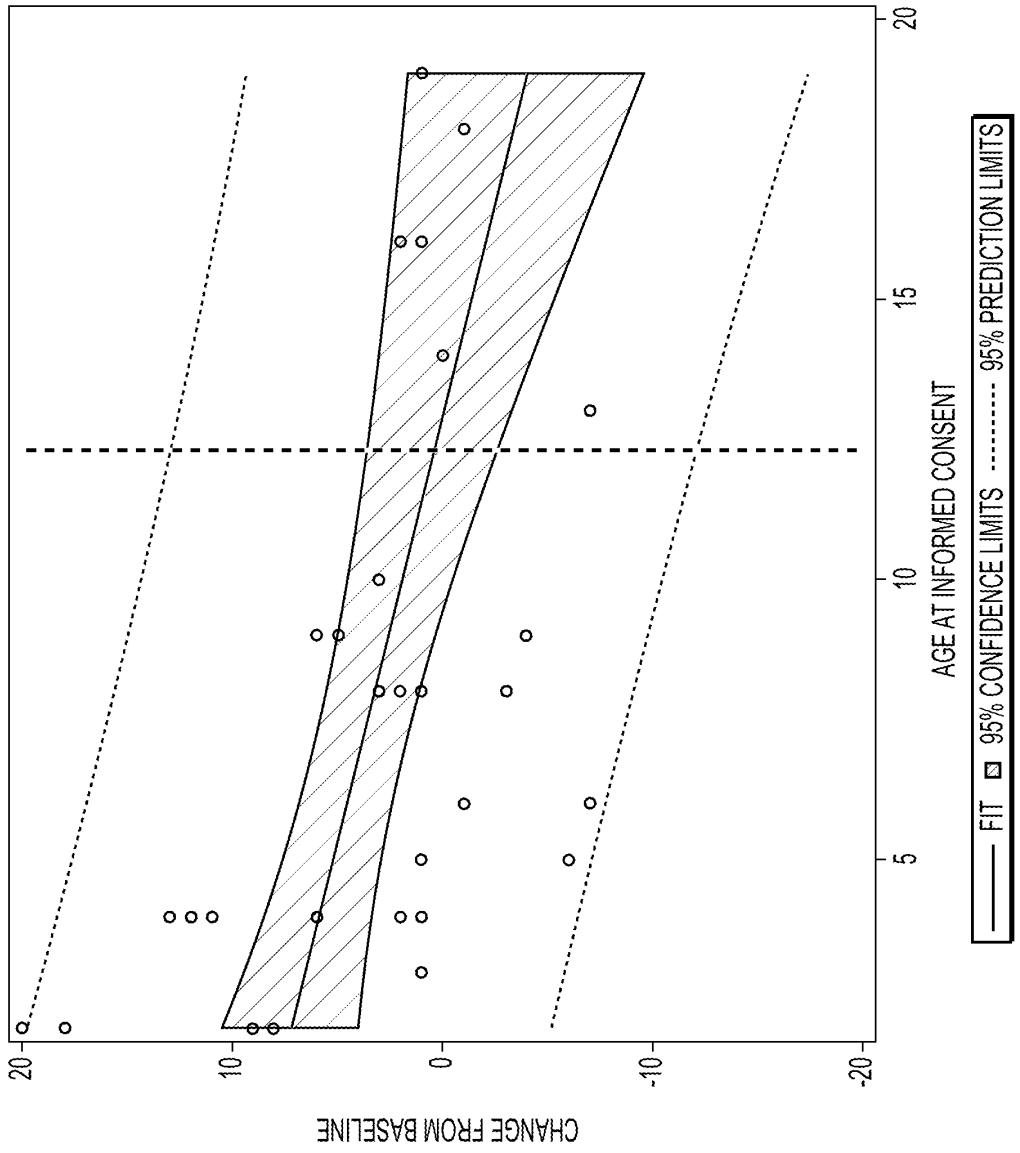

CHANGE FROM BASELINE
20
10
0
-10
-20
5
10
15
20
AGE AT INFORMED CONSENT
FIT
95% CONFIDENCE LIMITS
95% PREDICTION LIMITS

FIG. 23A

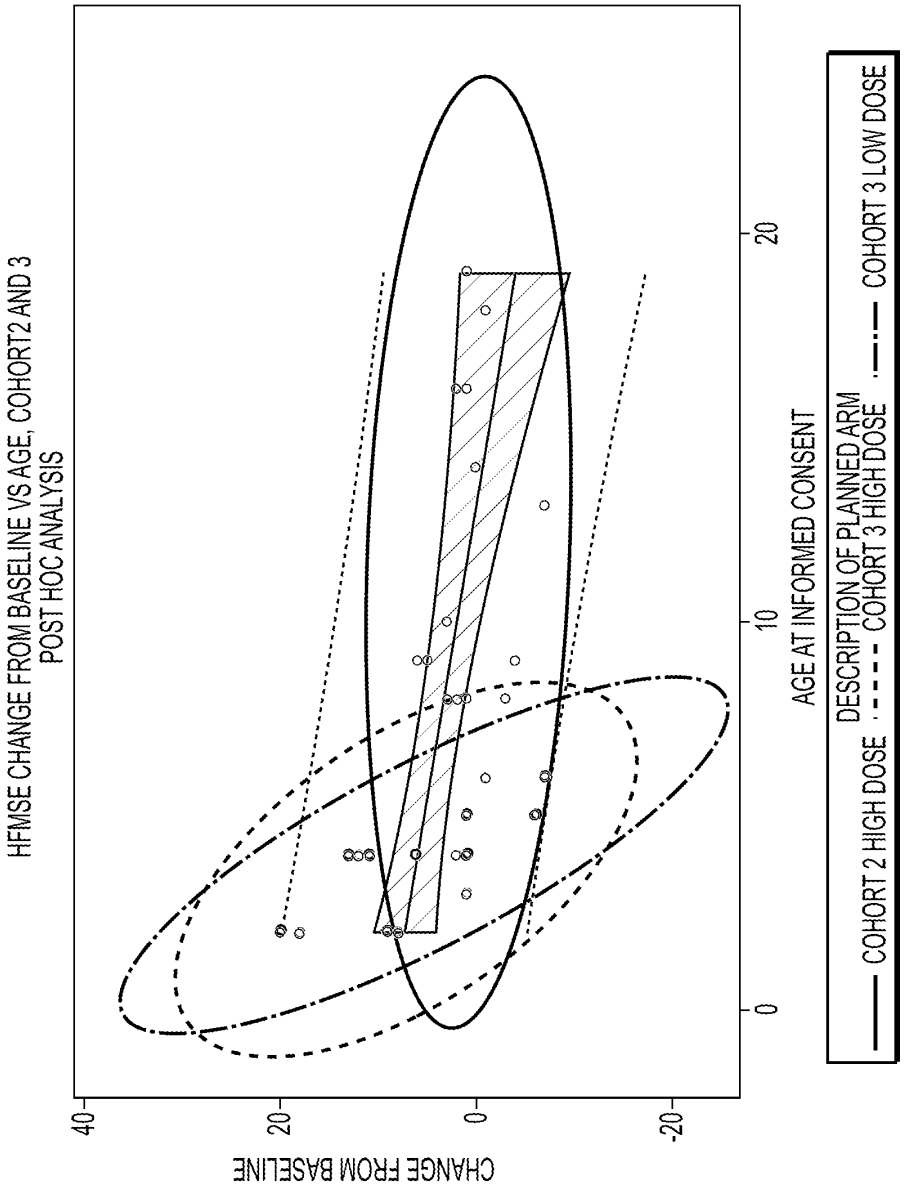

HFMSE CHANGE FROM BASELINE VS AGE, COHORT2 AND 3
POST HOC ANALYSIS
CHANGE FROM BASELINE
40
20
0
-20
0
10
20
AGE AT INFORMED CONSENT
DESCRIPTION OF PLANNED ARM
COHORT 2 HIGH DOSE
COHORT 3 HIGH DOSE
COHORT 3 LOW DOSE

FIG. 23B

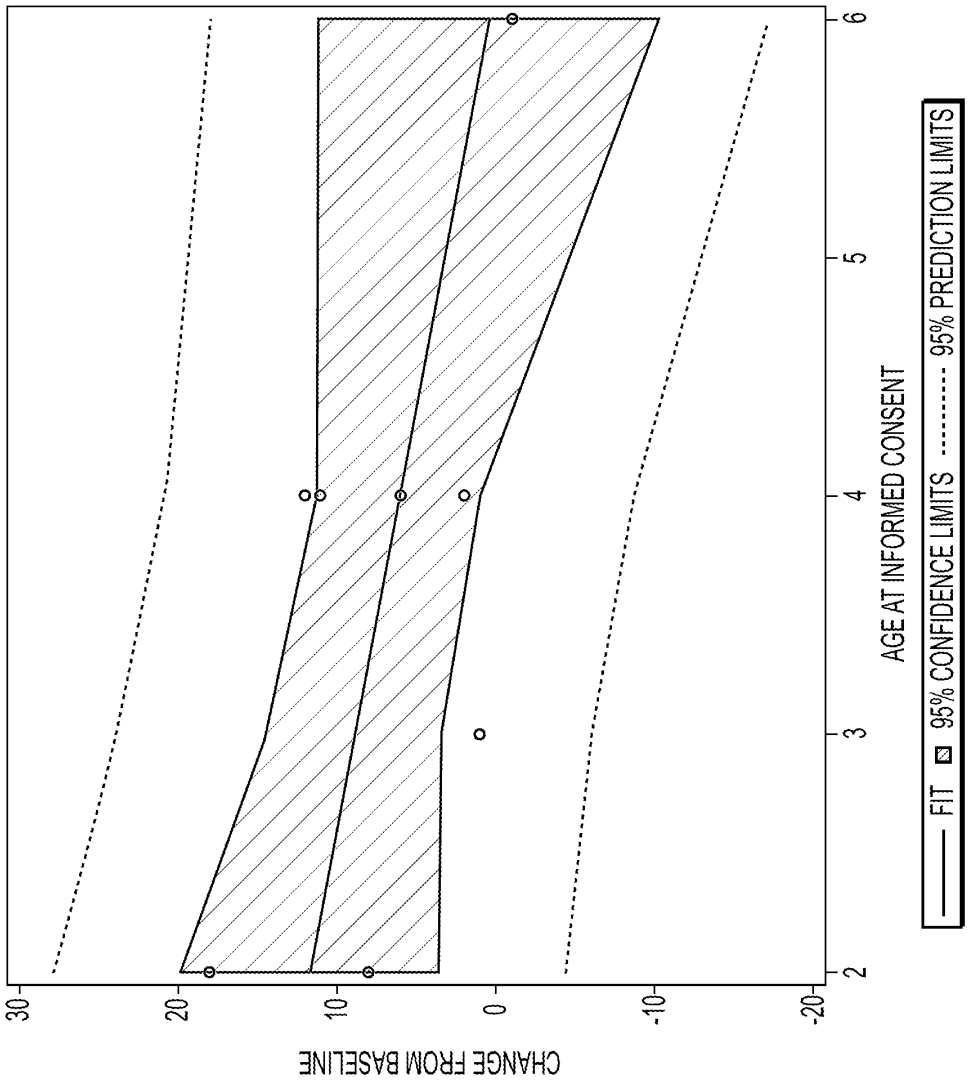

CHANGE FROM BASELINE
30
20
10
0
-10
-20
2
3
4
5
6
AGE AT INFORMED CONSENT
FIT
95% CONFIDENCE LIMITS
95% PREDICTION LIMITS

FIG. 23C

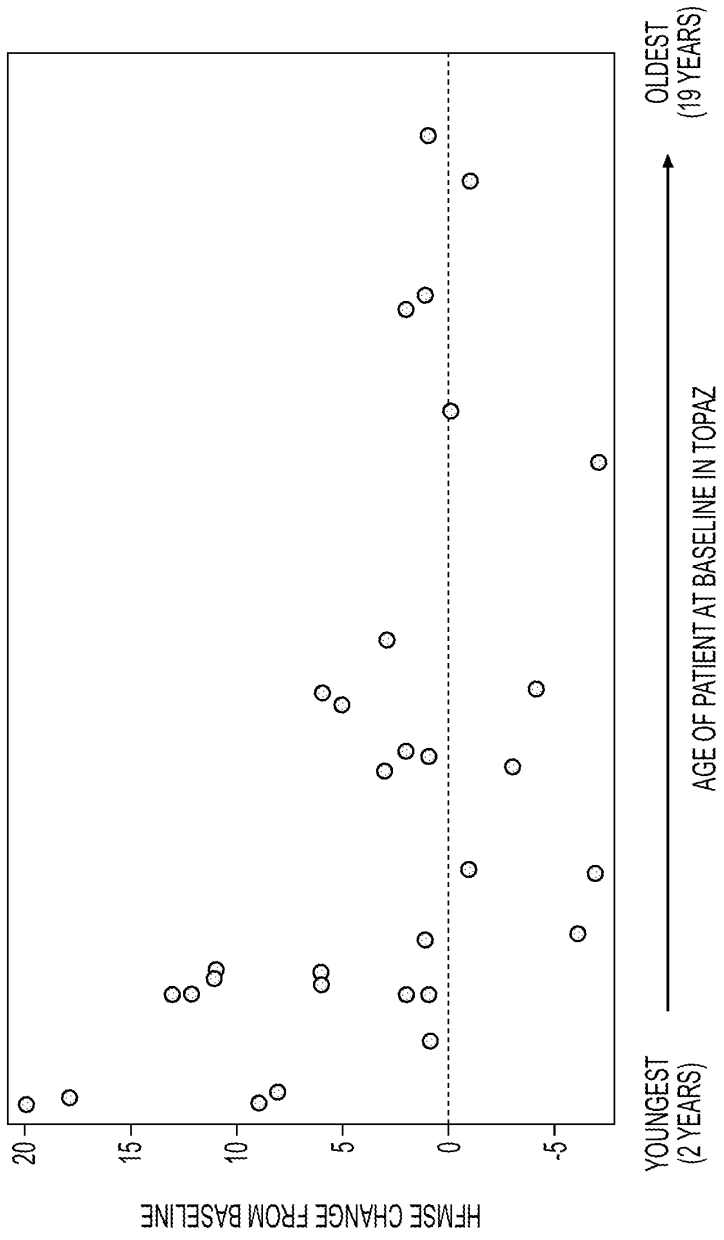

HFMSE CHANGE FROM BASELINE
20
15
10
5
0
-5
YOUNGEST (2 YEARS)
AGE OF PATIENT AT BASELINE IN TOPAZ
OLDEST (19 YEARS)

FIG. 23D

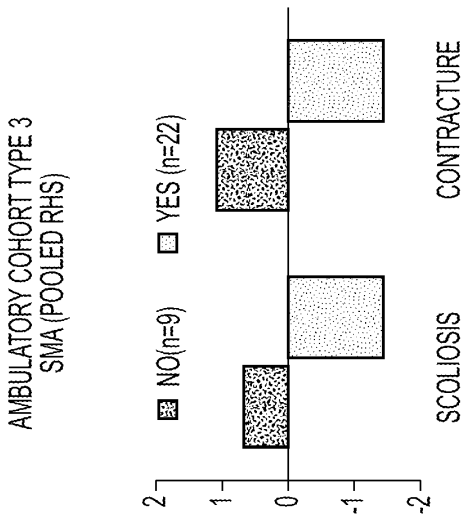


FIG. 24B

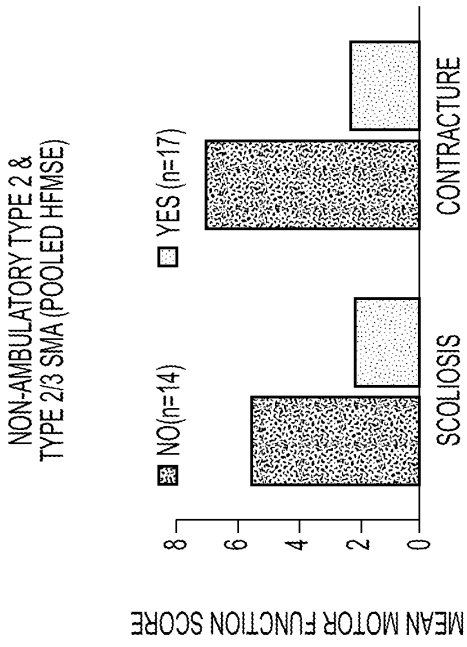


FIG. 24A

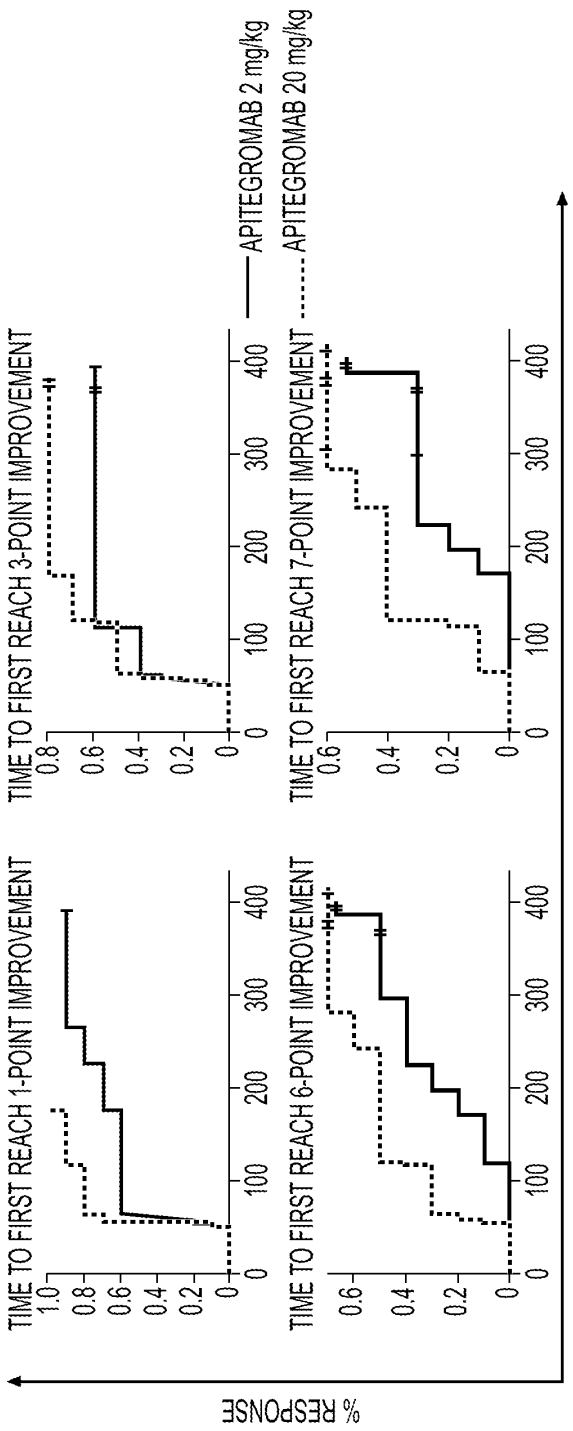

TIME TO FIRST REACH 1-POINT IMPROVEMENT
TIME TO FIRST REACH 3-POINT IMPROVEMENT
TIME TO FIRST REACH 6-POINT IMPROVEMENT
TIME TO FIRST REACH 7-POINT IMPROVEMENT
APITEGROMAB 2 mg/kg
APITEGROMAB 20 mg/kg
% RESPONSE
STUDY DAY

FIG. 25

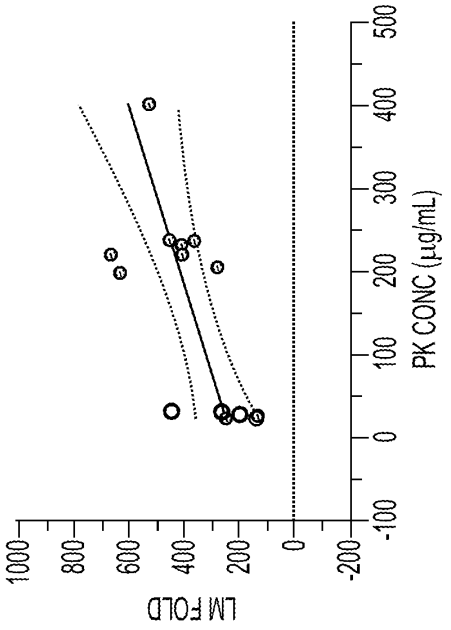


FIG. 26A

FIG. 26B

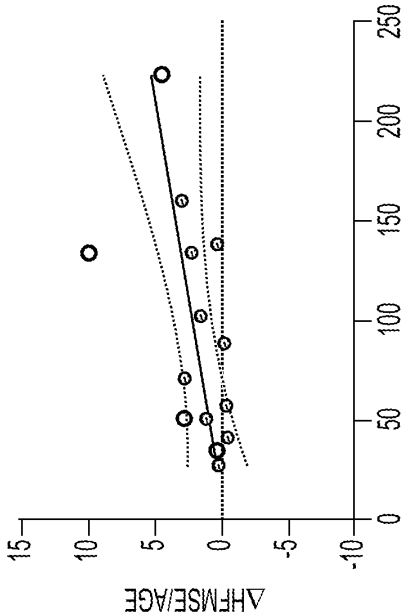


FIG. 26C

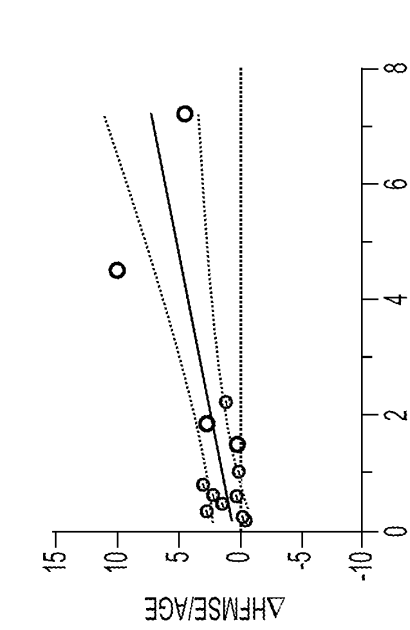


FIG. 26D

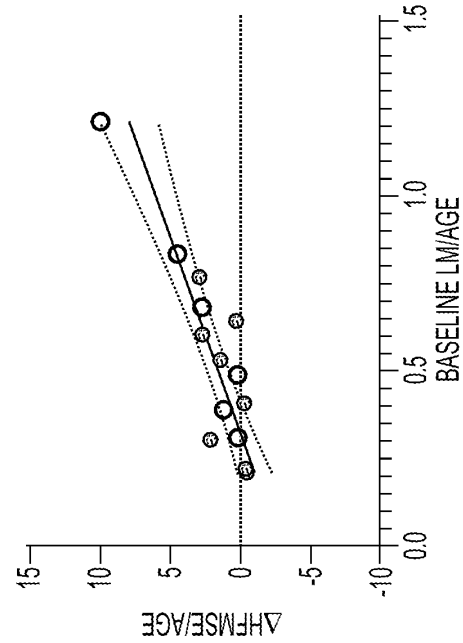


FIG. 27B

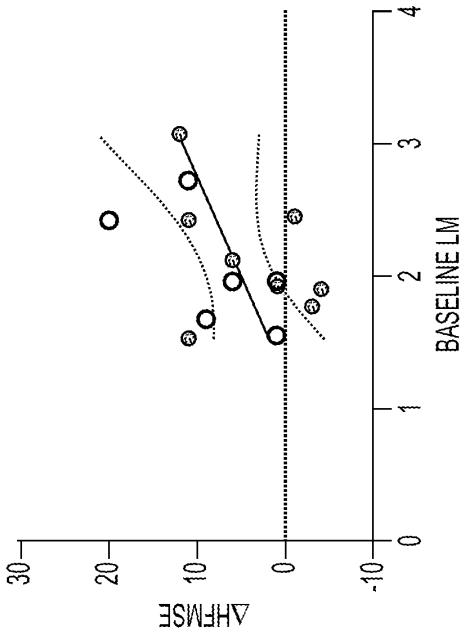


FIG. 27A