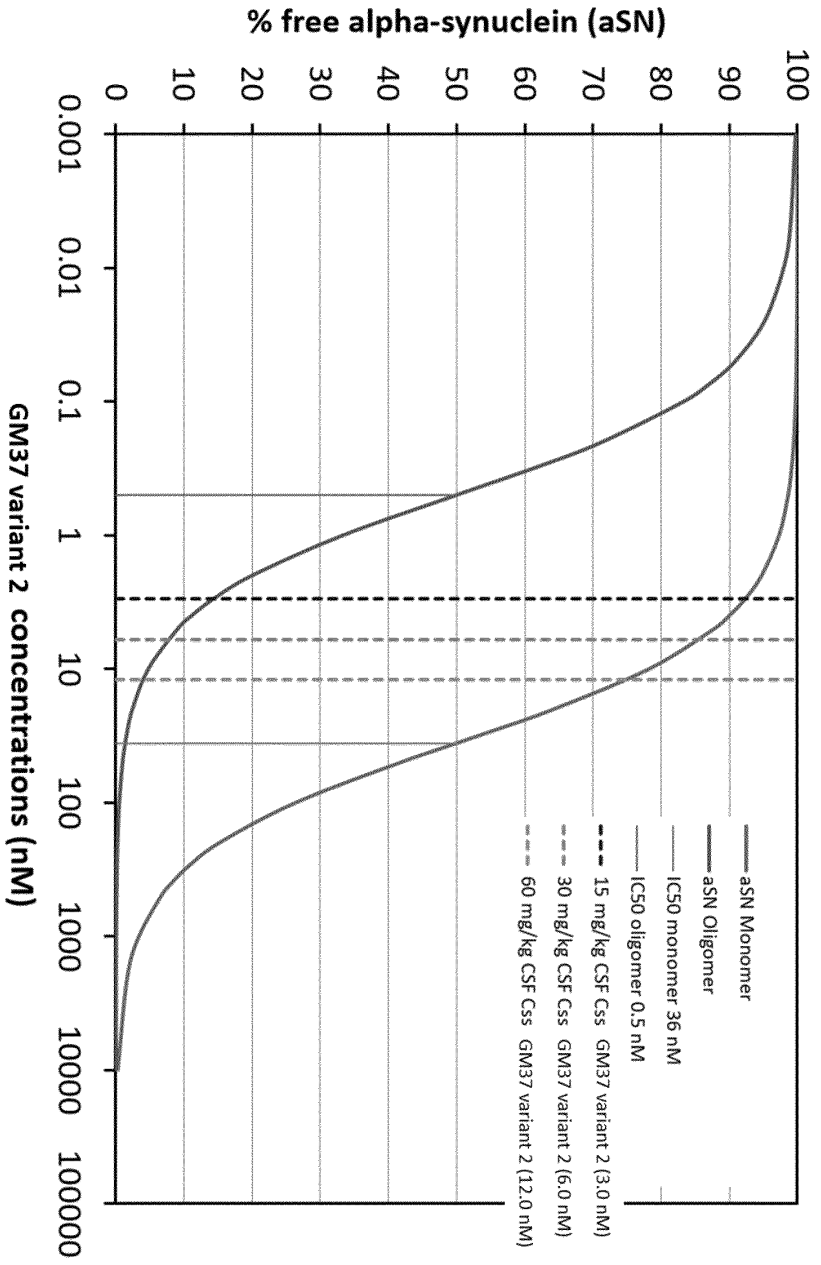
Figure 1


% free alpha-synuclein (aSN)
100
90
80
70
60
50
40
30
20
10
0
0.001
0.01
0.1
1
10
100
1000
10000
100000
GM37 variant 2 concentrations (nM)
aSN Monomer
aSN Oligomer
IC50 monomer 36 nM
IC50 oligomer 0.5 nM
15 mg/kg CSF Css GM37 variant 2 (3.0 nM)
30 mg/kg CSF Css GM37 variant 2 (6.0 nM)
60 mg/kg CSF Css GM37 variant 2 (12.0 nM)

5

Figure 2

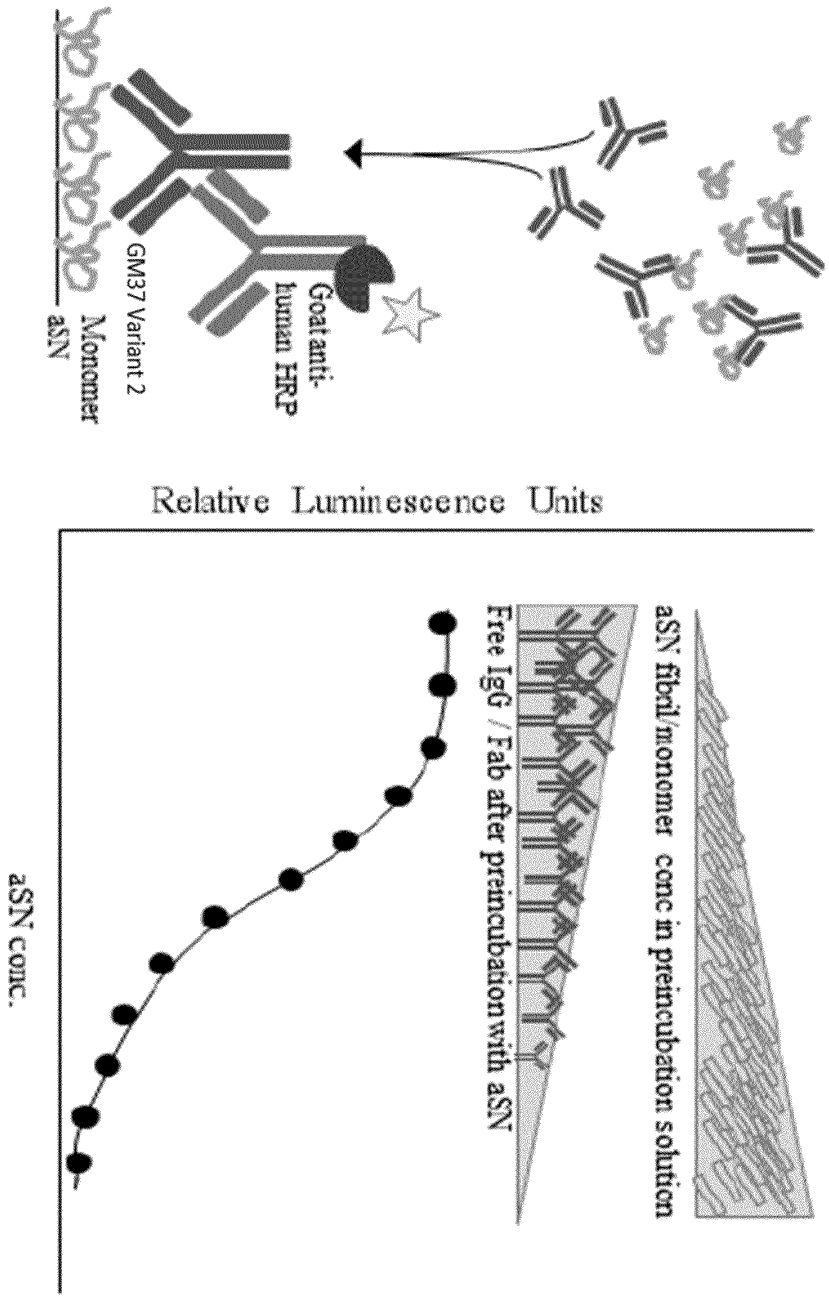

Monomer aSN
GM37 Variant 2
Goat anti-human HRP
Relative Luminescence Units
aSN conc.
Free IgG / Fab after preincubation with aSN
aSN fibril/monomer conc in preincubation solution

Figure 3

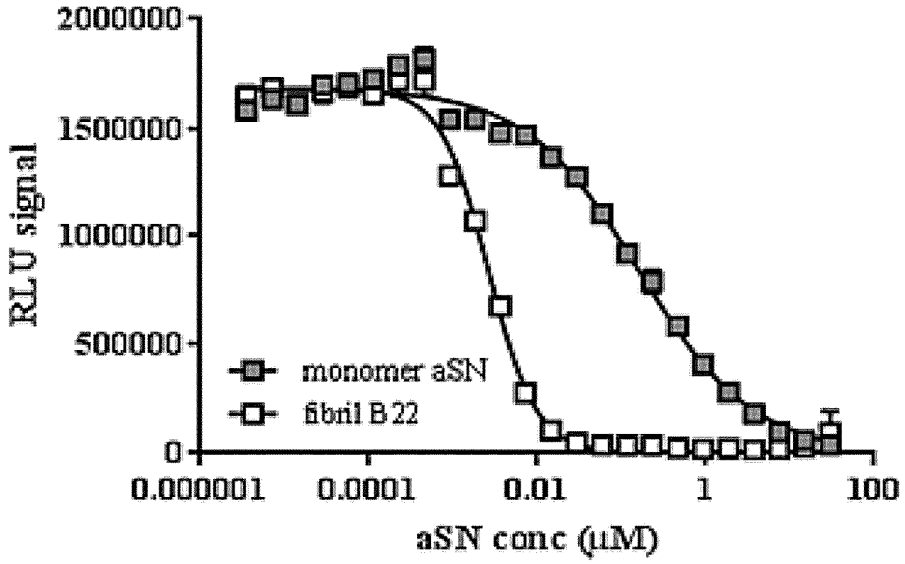
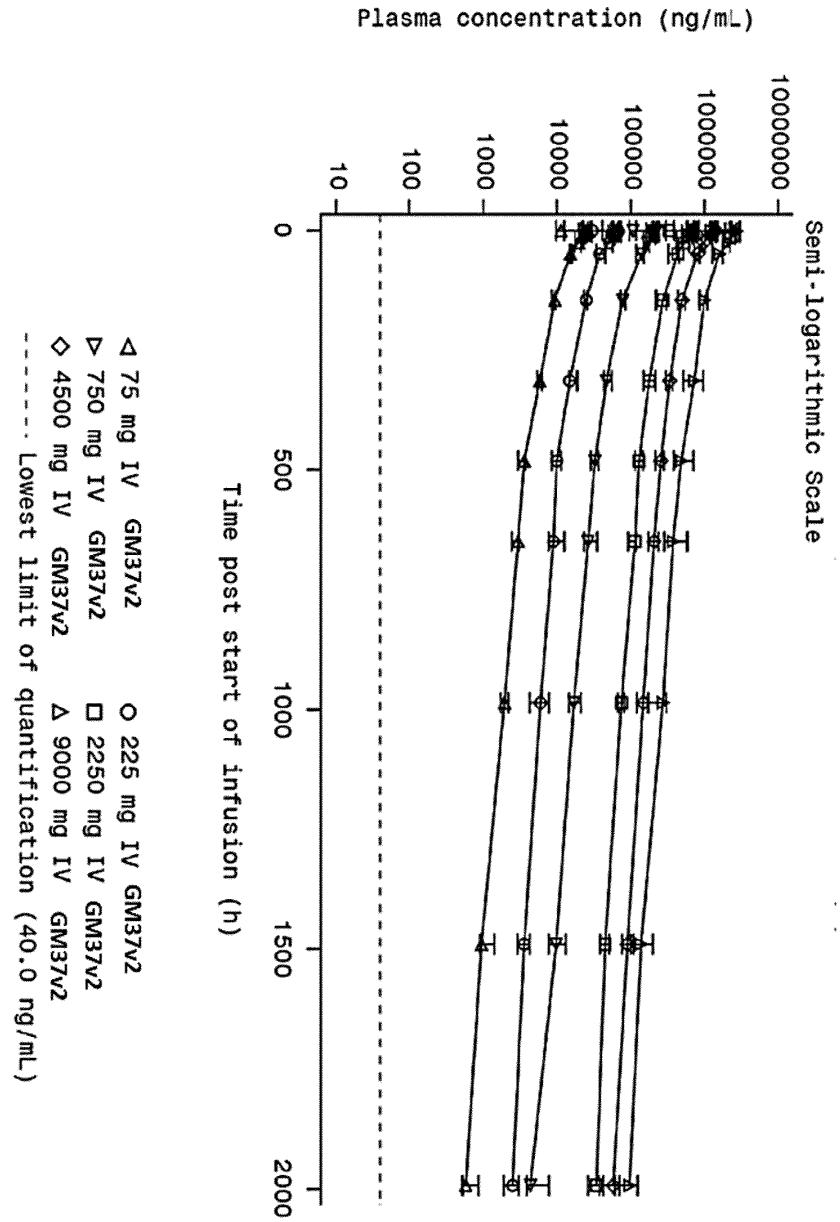
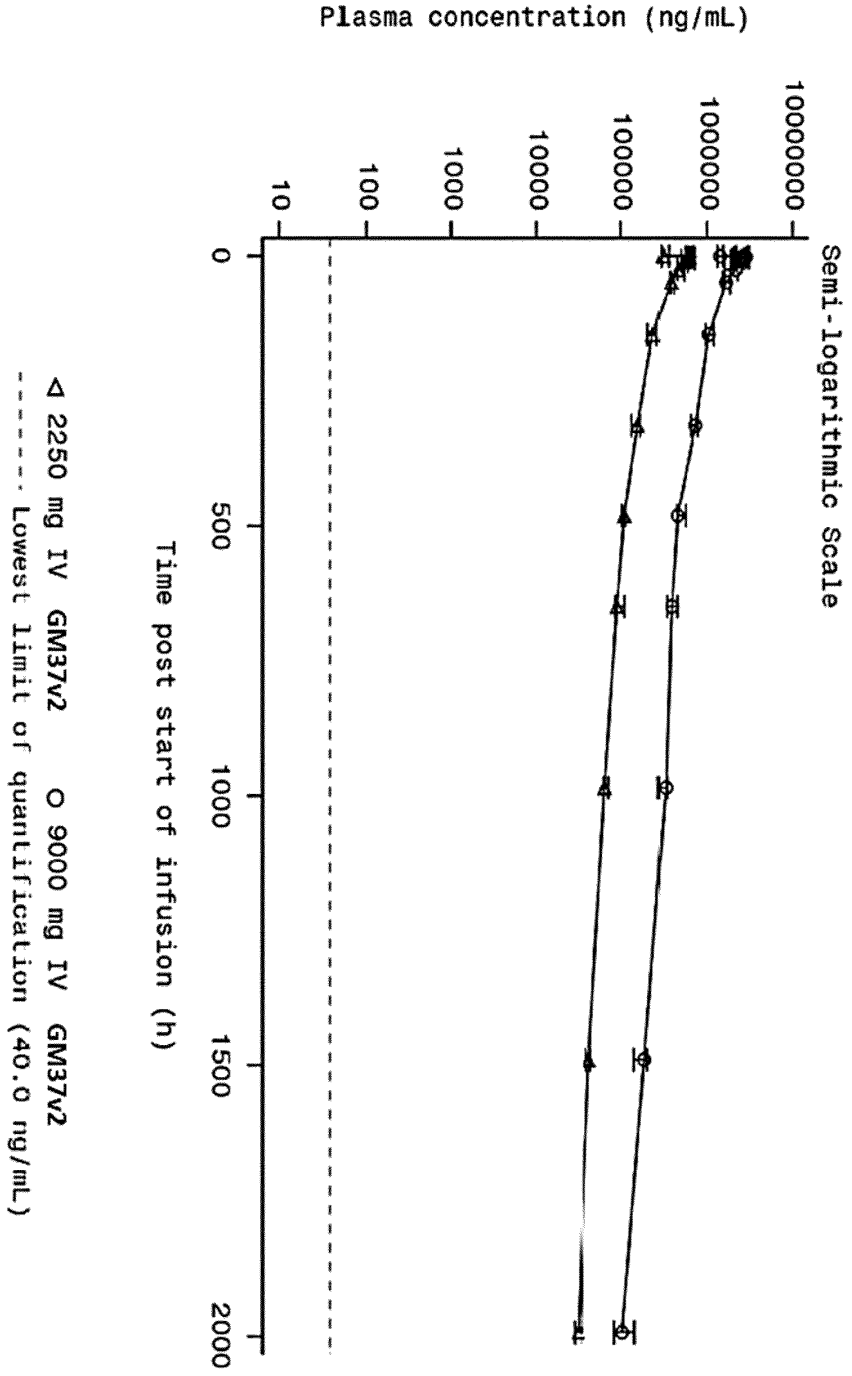

2000000
1500000
1000000
500000
0
RLU signal
monomer aSN
fibril B22
0.000001
0.0001
0.01
1
100
aSN conc (µM)

Figure 4 a


Plasma concentration (ng/mL)
Semi-logarithmic Scale
10000000
1000000
100000
10000
1000
100
10
0
500
1000
1500
2000
Time post start of infusion (h)
◁ 75 mg IV GM37v2
○ 225 mg IV GM37v2
▷ 750 mg IV GM37v2
□ 2250 mg IV GM37v2
◇ 4500 mg IV GM37v2
△ 9000 mg IV GM37v2
Lowest limit of quantification (40.0 ng/mL)

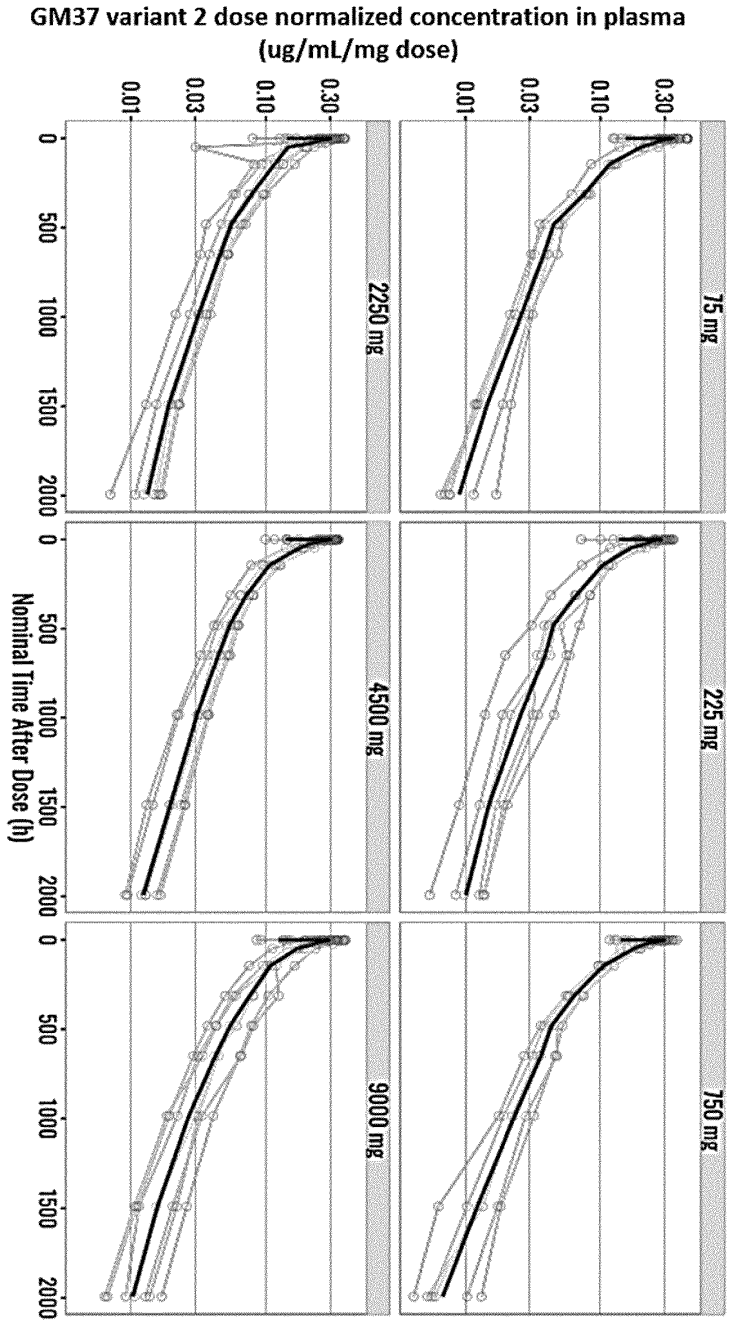
5

Figure 4 b


Plasma concentration (ng/mL)
Semi-logarithmic Scale
10000000
1000000
100000
10000
1000
100
10
0
500
1000
1500
2000
Time post start of infusion (h)
Δ 2250 mg IV GM37v2
O 9000 mg IV GM37v2
Lowest limit of quantification (40.0 ng/mL)

5

Figure 5


GM37 variant 2 dose normalized concentration in plasma
(ug/mL/mg dose)
0.01
0.03
0.10
0.30
0
500
1000
1500
2000
Nominal Time After Dose (h)
75 mg
225 mg
750 mg
2250 mg
4500 mg
9000 mg

5

Figure 6 a

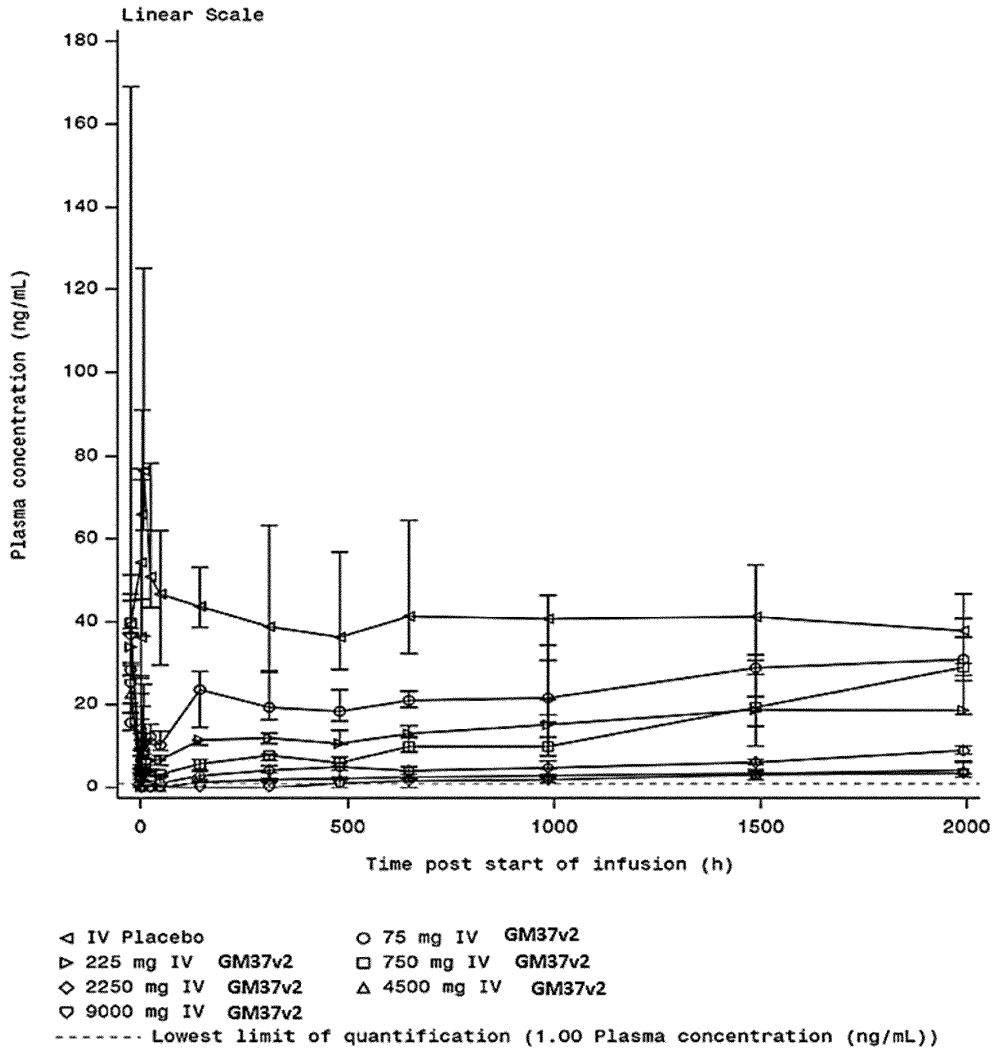
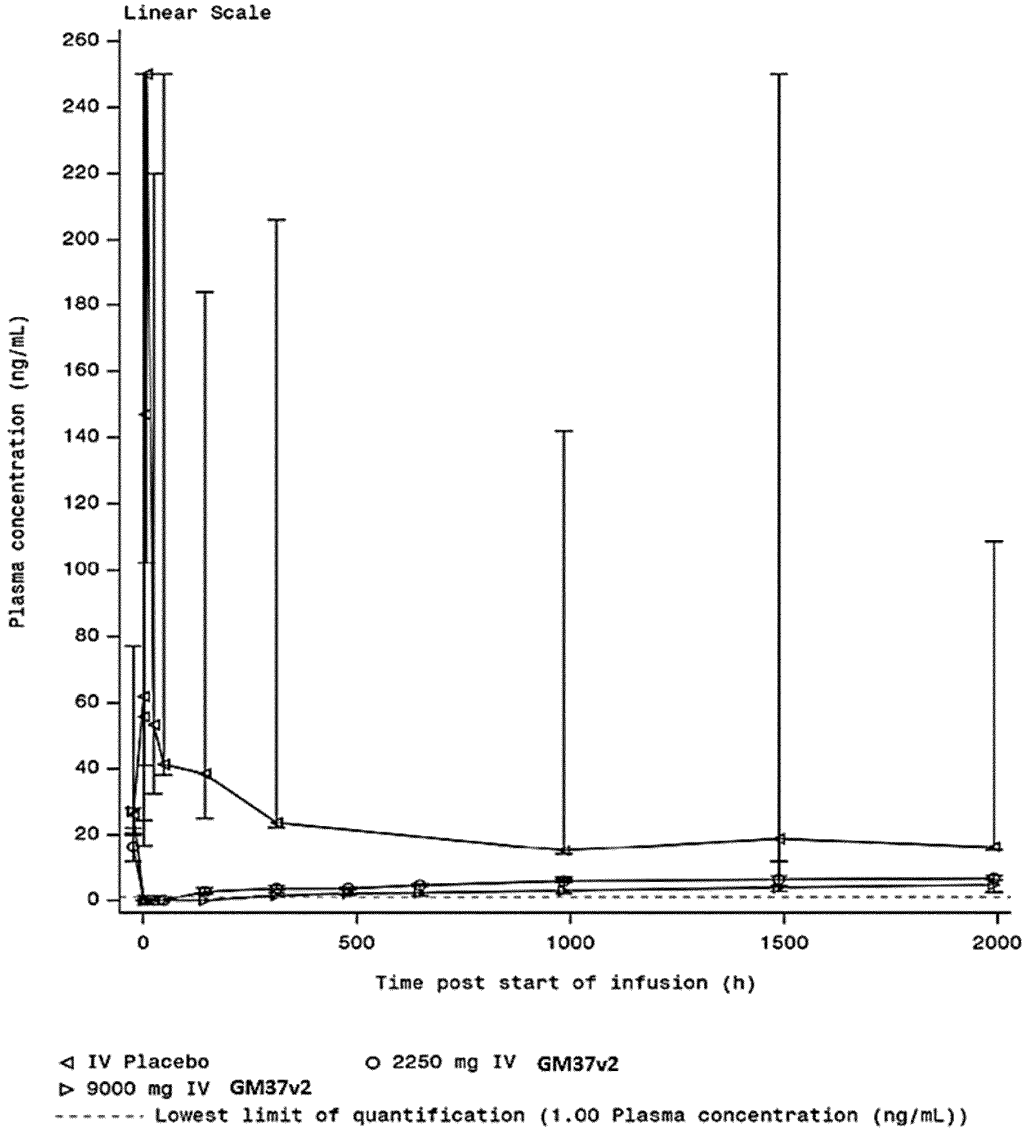
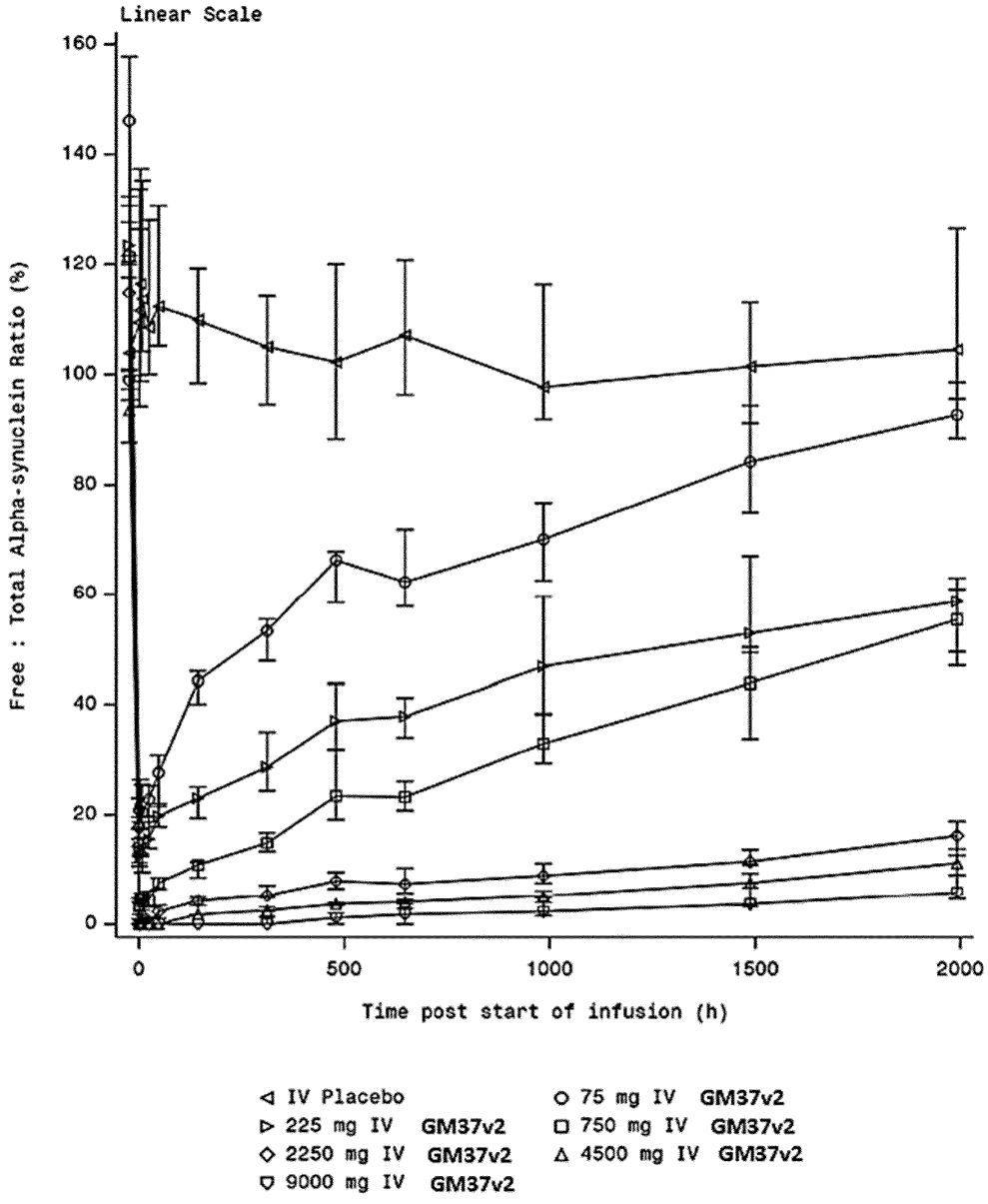

Linear Scale
Plasma concentration (ng/mL)
180
160
140
120
100
80
60
40
20
0
0
500
1000
1500
2000
Time post start of infusion (h)
IV Placebo
75 mg IV GM37v2
225 mg IV GM37v2
750 mg IV GM37v2
2250 mg IV GM37v2
4500 mg IV GM37v2
9000 mg IV GM37v2
Lowest limit of quantification (1.00 Plasma concentration (ng/mL))

Figure 6 b


Linear Scale
Plasma concentration (ng/mL)
260
240
220
200
180
160
140
120
100
80
60
40
20
0
0
500
1000
1500
2000
Time post start of infusion (h)
◁ IV Placebo
○ 2250 mg IV GM37v2
▷ 9000 mg IV GM37v2
Lowest limit of quantification (1.00 Plasma concentration (ng/mL))

5

Figure 7 a


Linear Scale
Free : Total Alpha-synuclein Ratio (%)
160
140
120
100
80
60
40
20
0
0
500
1000
1500
2000
Time post start of infusion (h)
IV Placebo
75 mg IV GM37v2
225 mg IV GM37v2
750 mg IV GM37v2
2250 mg IV GM37v2
4500 mg IV GM37v2
9000 mg IV GM37v2

5

Figure 7 b

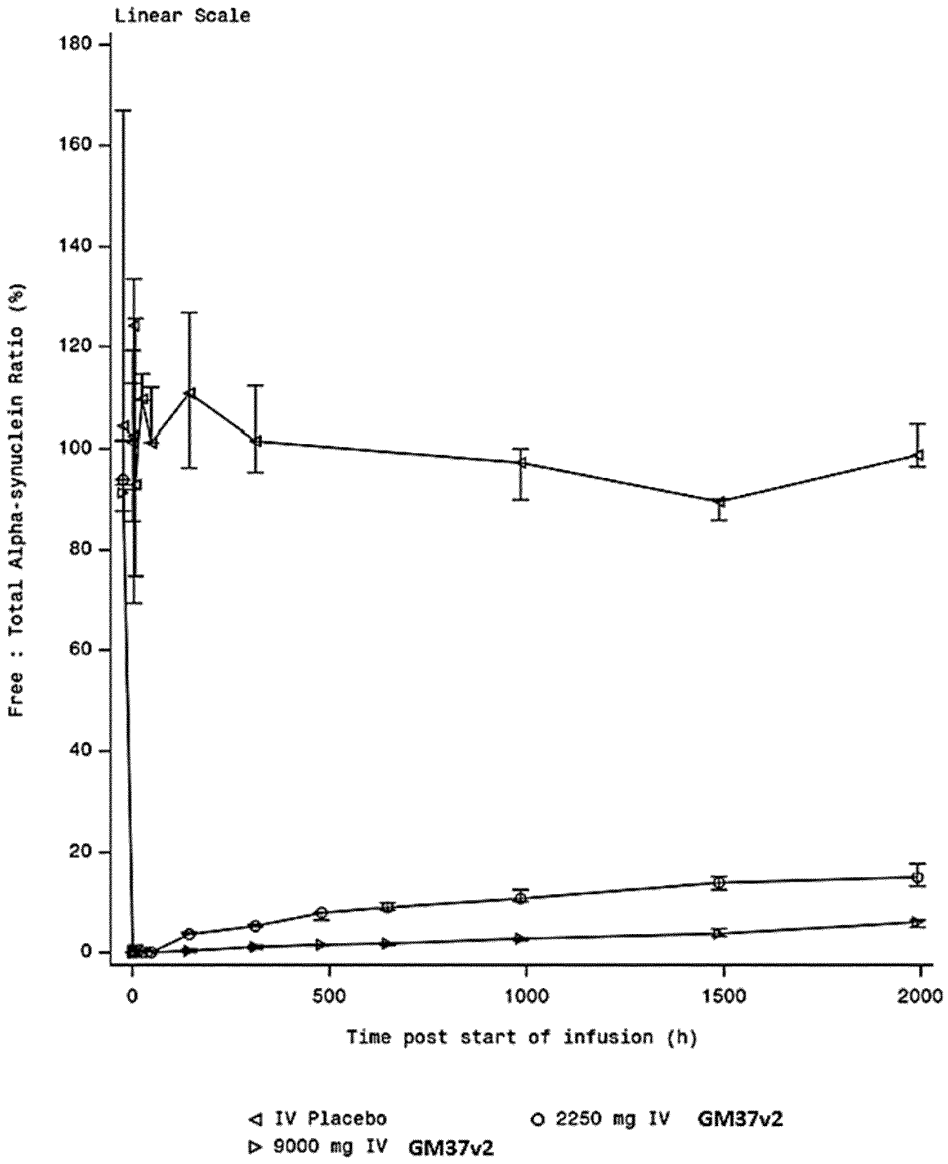

Linear Scale
Free : Total Alpha-synuclein Ratio (%)
180
160
140
120
100
80
60
40
20
0
0
500
1000
1500
2000
Time post start of infusion (h)
◁ IV Placebo
○ 2250 mg IV GM37v2
▷ 9000 mg IV GM37v2

Figure 8

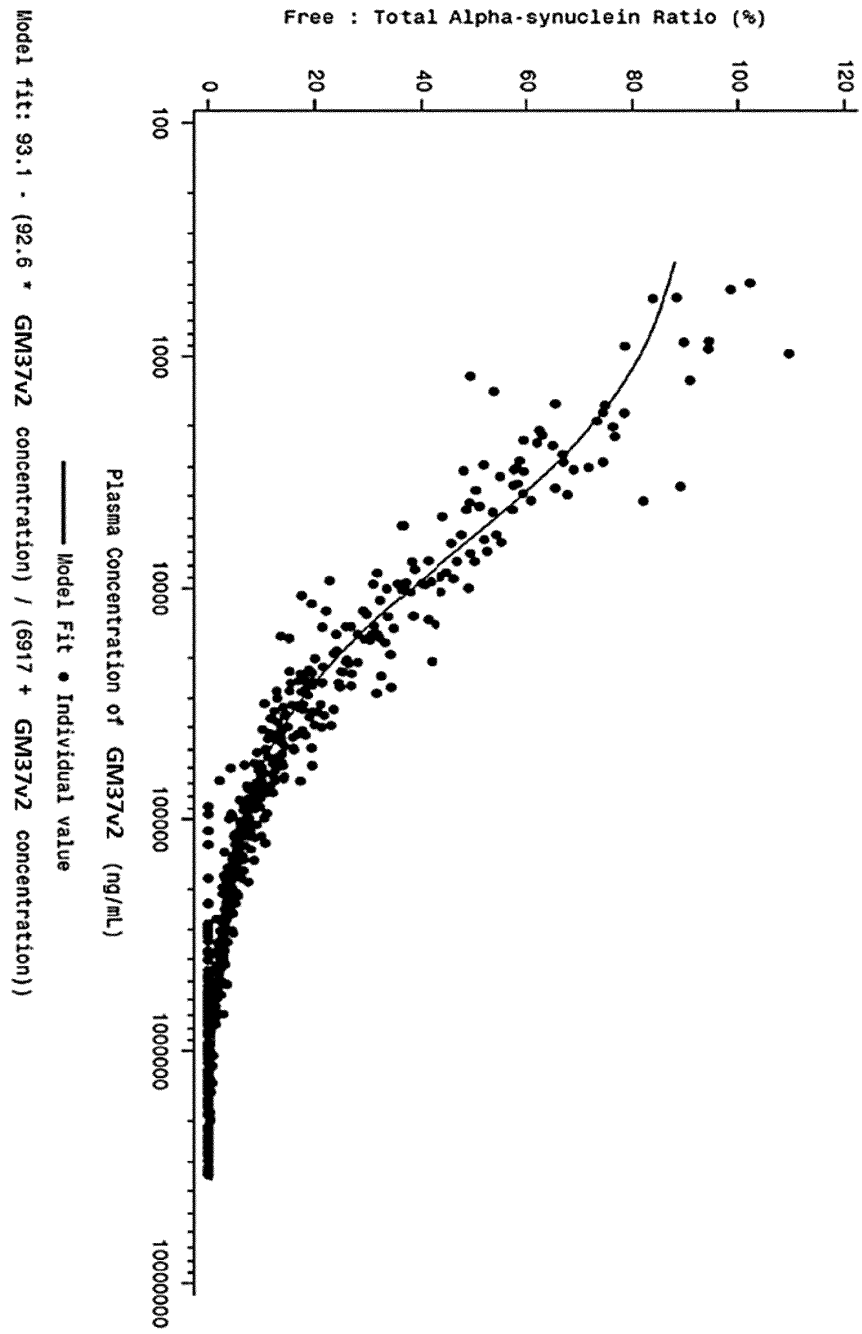
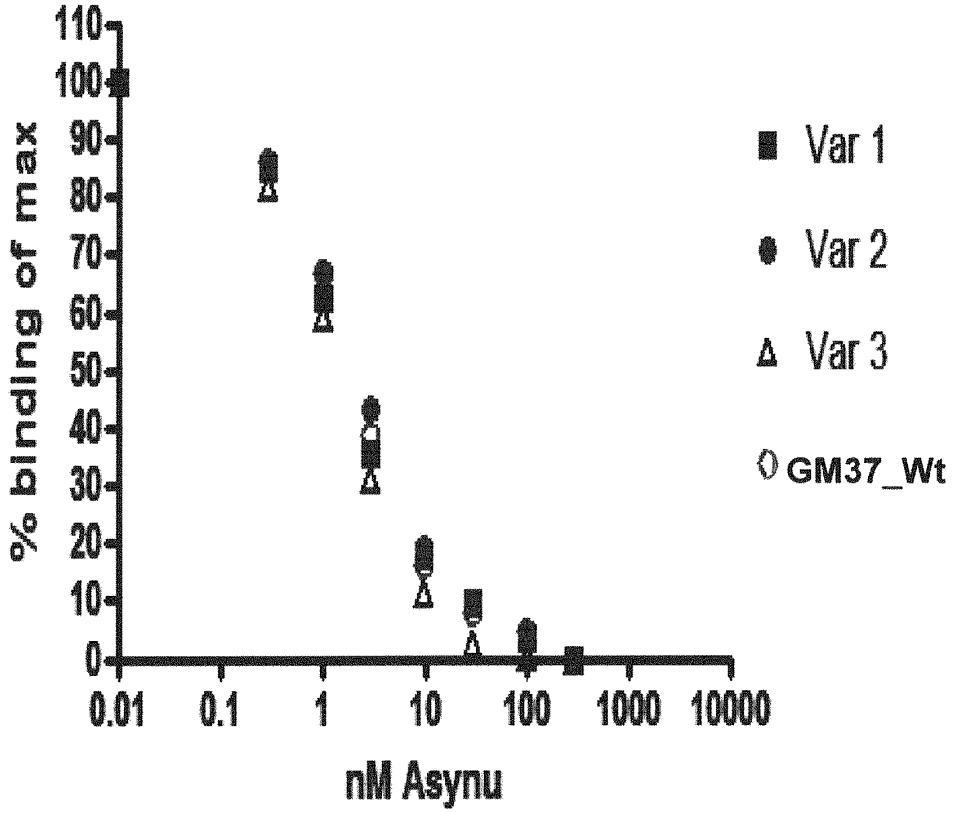

Free : Total Alpha-synuclein Ratio (%)
0
20
40
60
80
100
120
100
1000
10000
100000
1000000
10000000
Plasma Concentration of GM37v2 (ng/mL)
Model Fit
Individual value
Model fit: 93.1 - (92.6 * GM37v2 concentration) / (6917 + GM37v2 concentration))

Figure 9


% binding of max
110
100
90
80
70
60
50
40
30
20
10
0
0.01
0.1
1
10
100
1000
10000
nM Asynu
Var 1
Var 2
Var 3
GM37_Wt

5

Figure 10

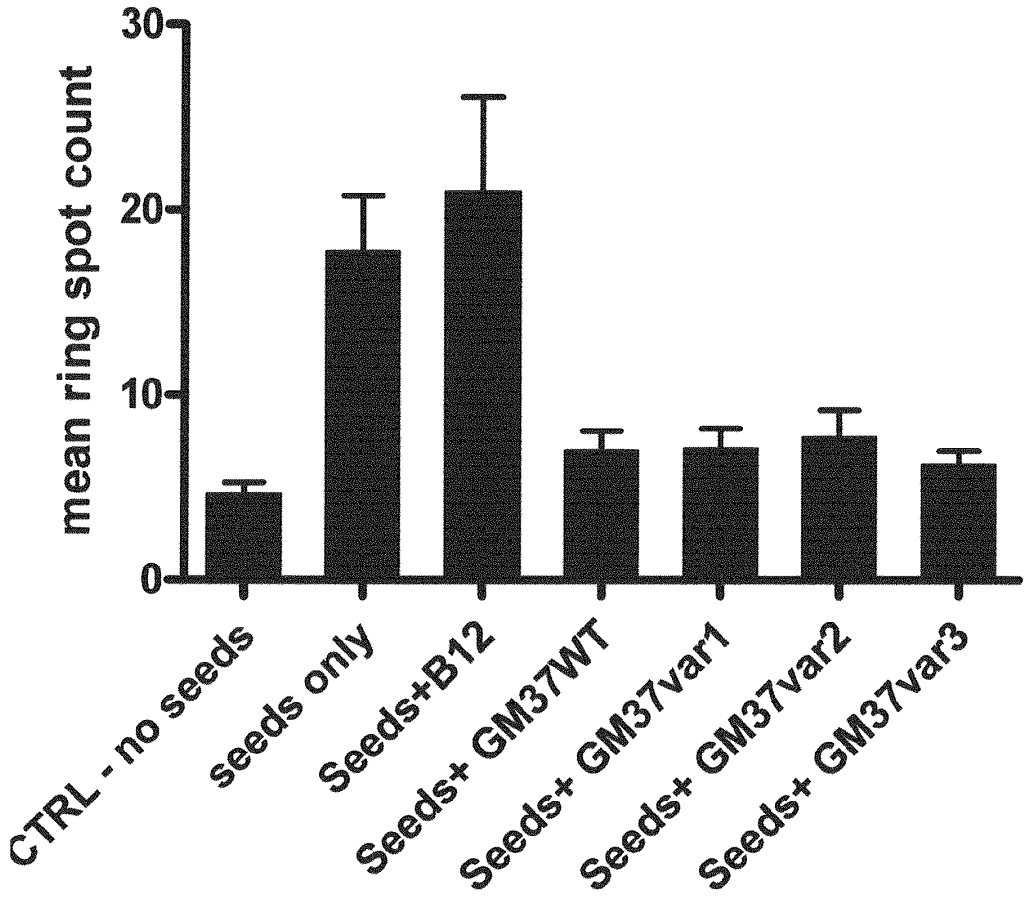
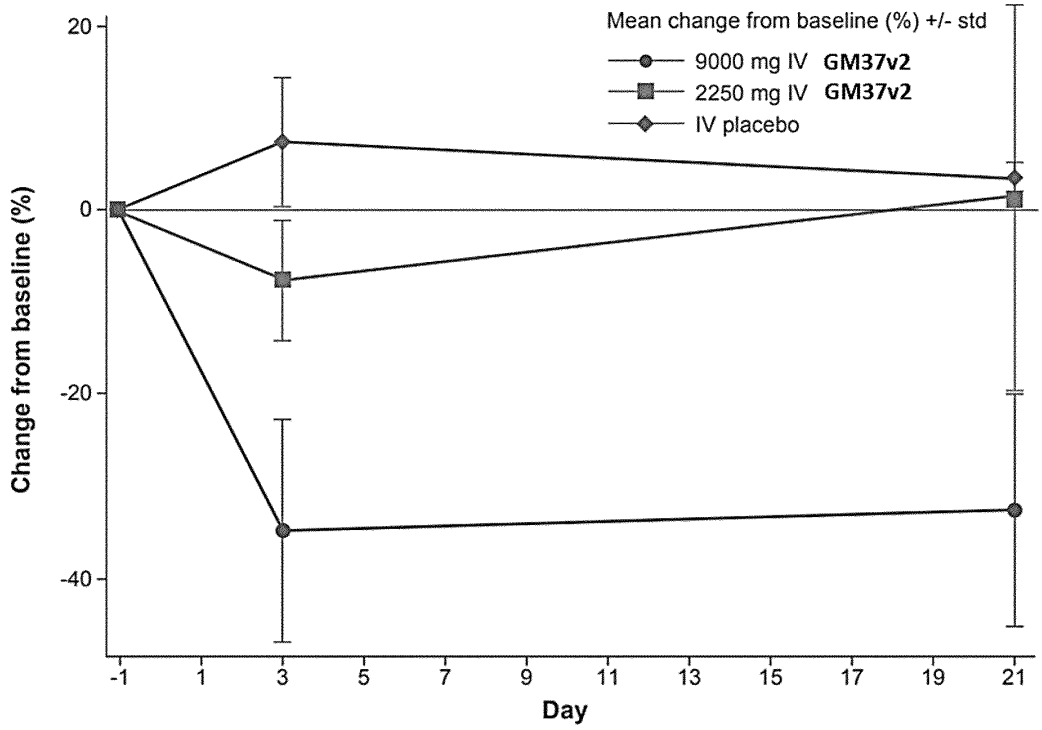

mean ring spot count
30
20
10
0
CTRL - no seeds
seeds only
Seeds+B12
Seeds+ GM37WT
Seeds+ GM37var1
Seeds+ GM37var2
Seeds+ GM37var3

Figure 11



Low dose = 2250 mg (cohort B1); high dose = 9000 mg (cohort B2).

aSyn, alpha-synuclein; CSF, cerebrospinal fluid; PD, Parkinson's disease; std, standard deviation.

Figure 12

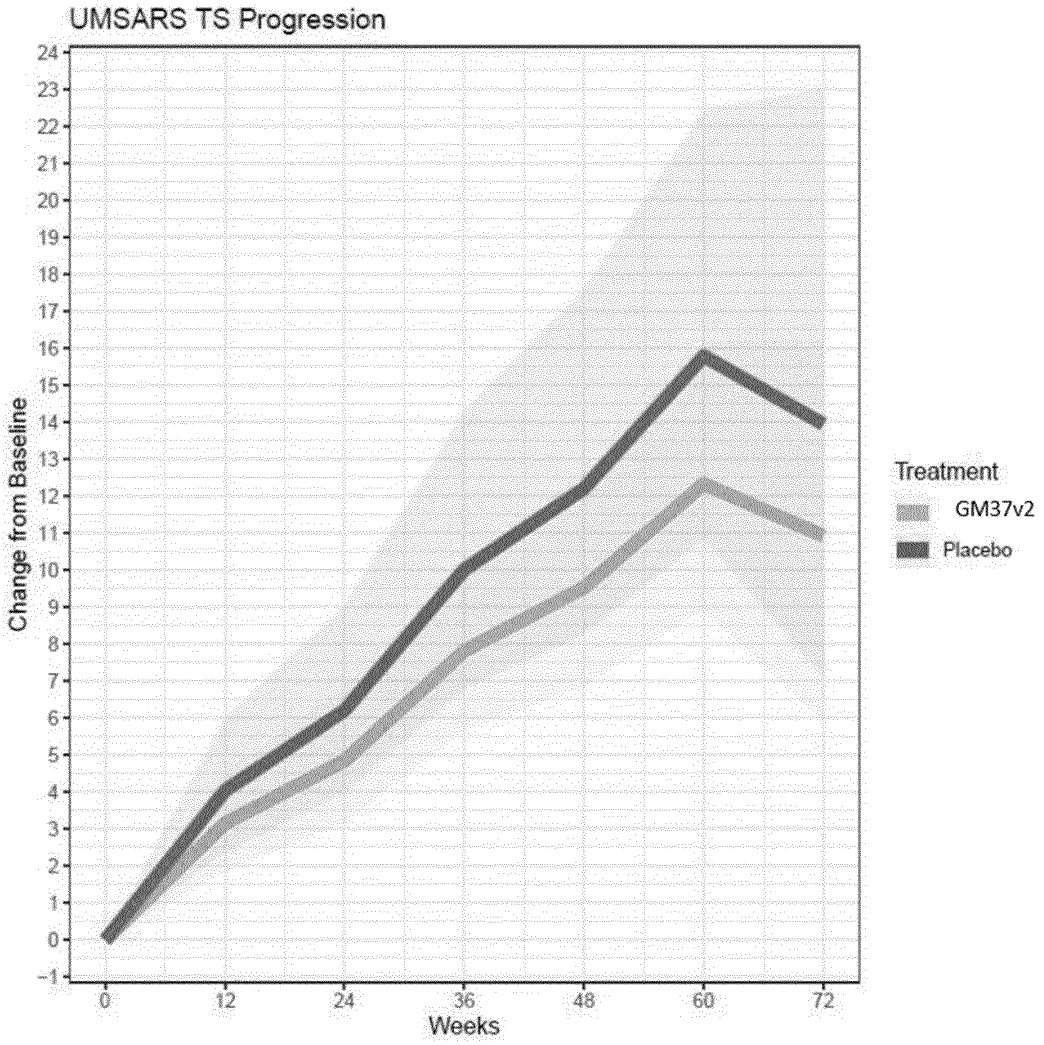

UMSARS TS Progression
Change from Baseline
Weeks
0
12
24
36
48
60
72
Treatment
GM37v2
Placebo

Figure 13

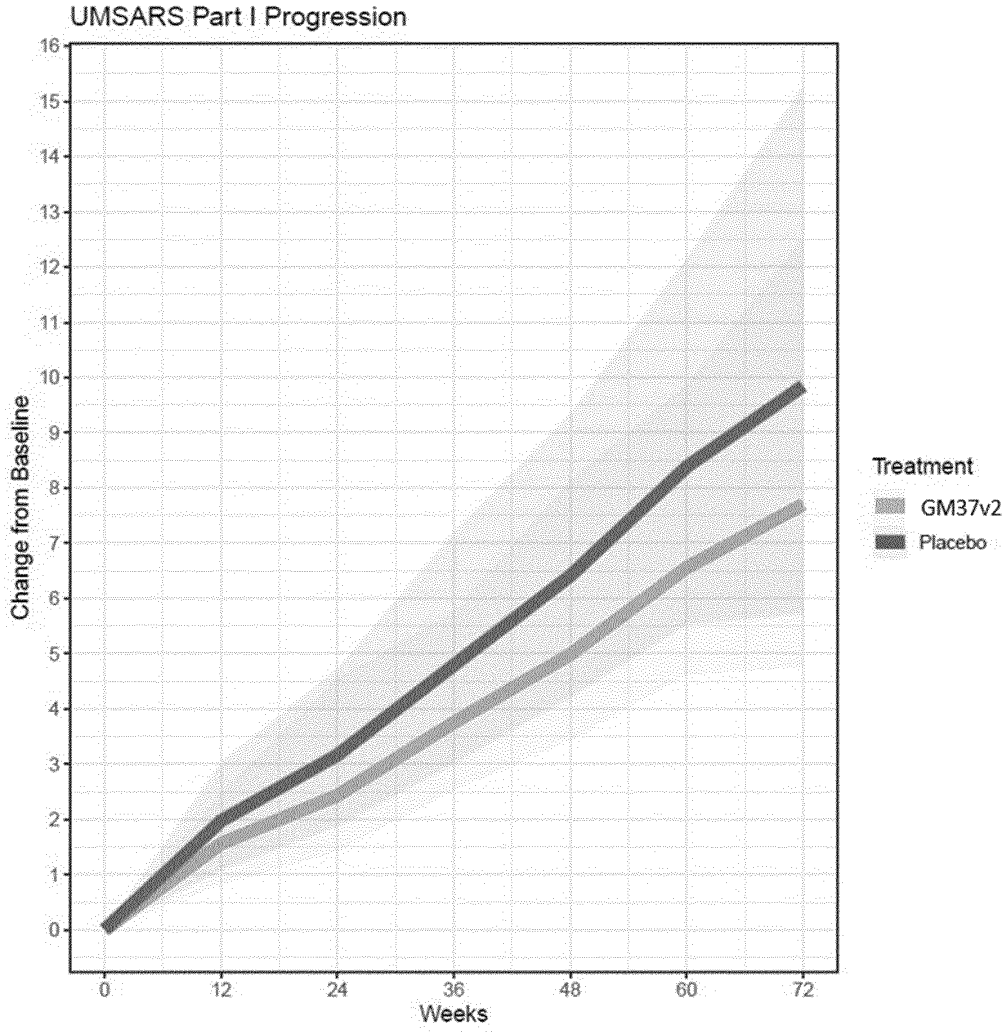

UMSARS Part I Progression
Change from Baseline
Weeks
0
12
24
36
48
60
72
Treatment
GM37v2
Placebo

Figure 14

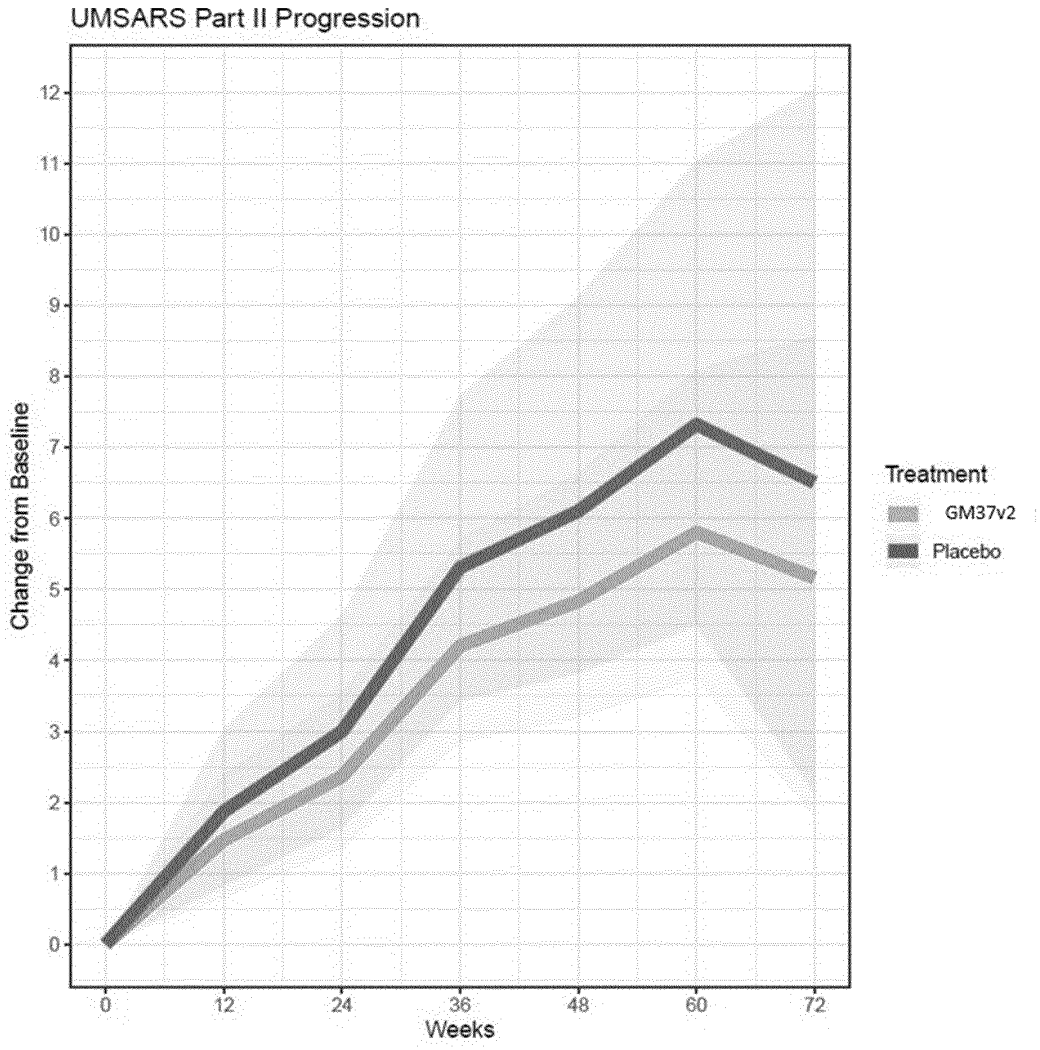

UMSARS Part II Progression
Change from Baseline
0
1
2
3
4
5
6
7
8
9
10
11
12
0
12
24
36
48
60
72
Weeks
Treatment
GM37v2
Placebo

Figure 15

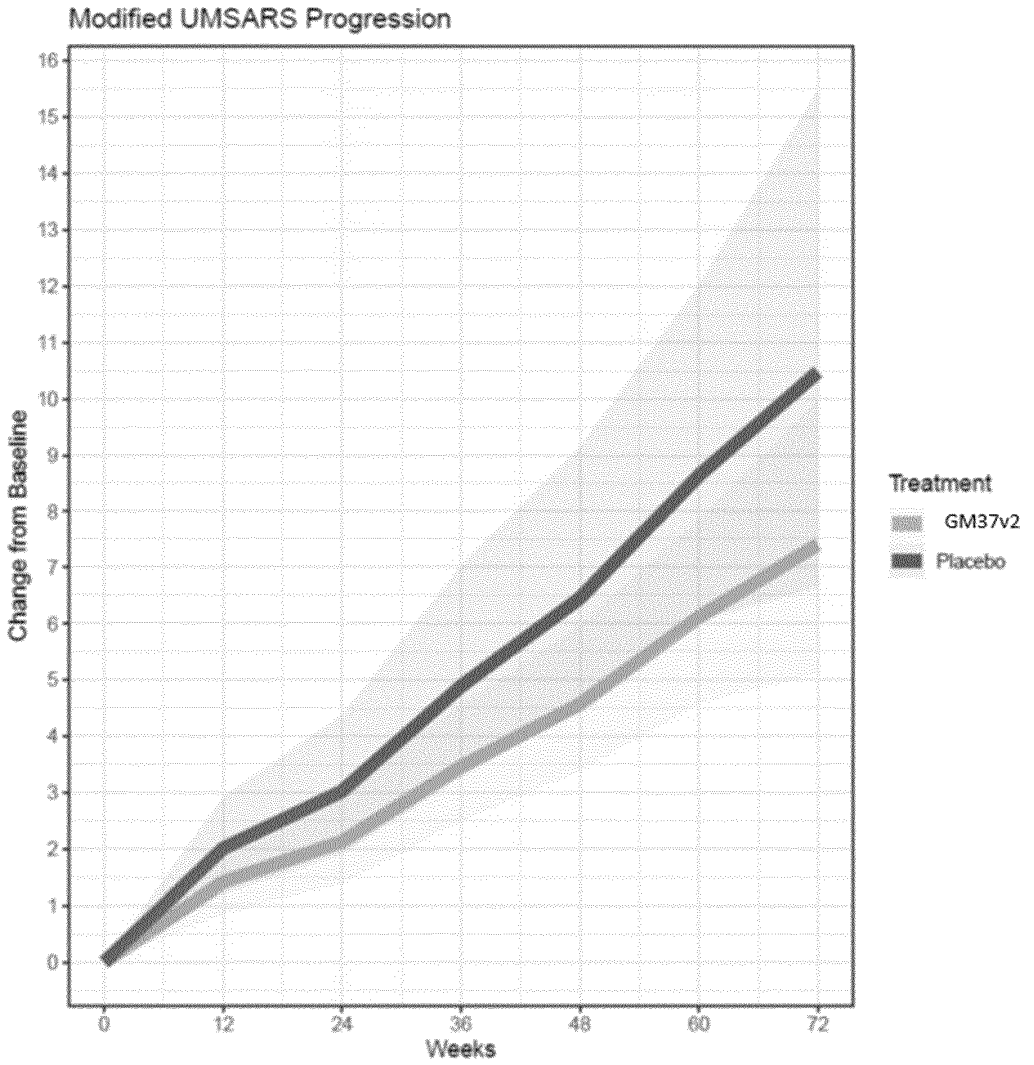

Modified UMSARS Progression
Change from Baseline
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
0
12
24
36
48
60
72
Weeks
Treatment
GM37v2
Placebo

Figure 16a

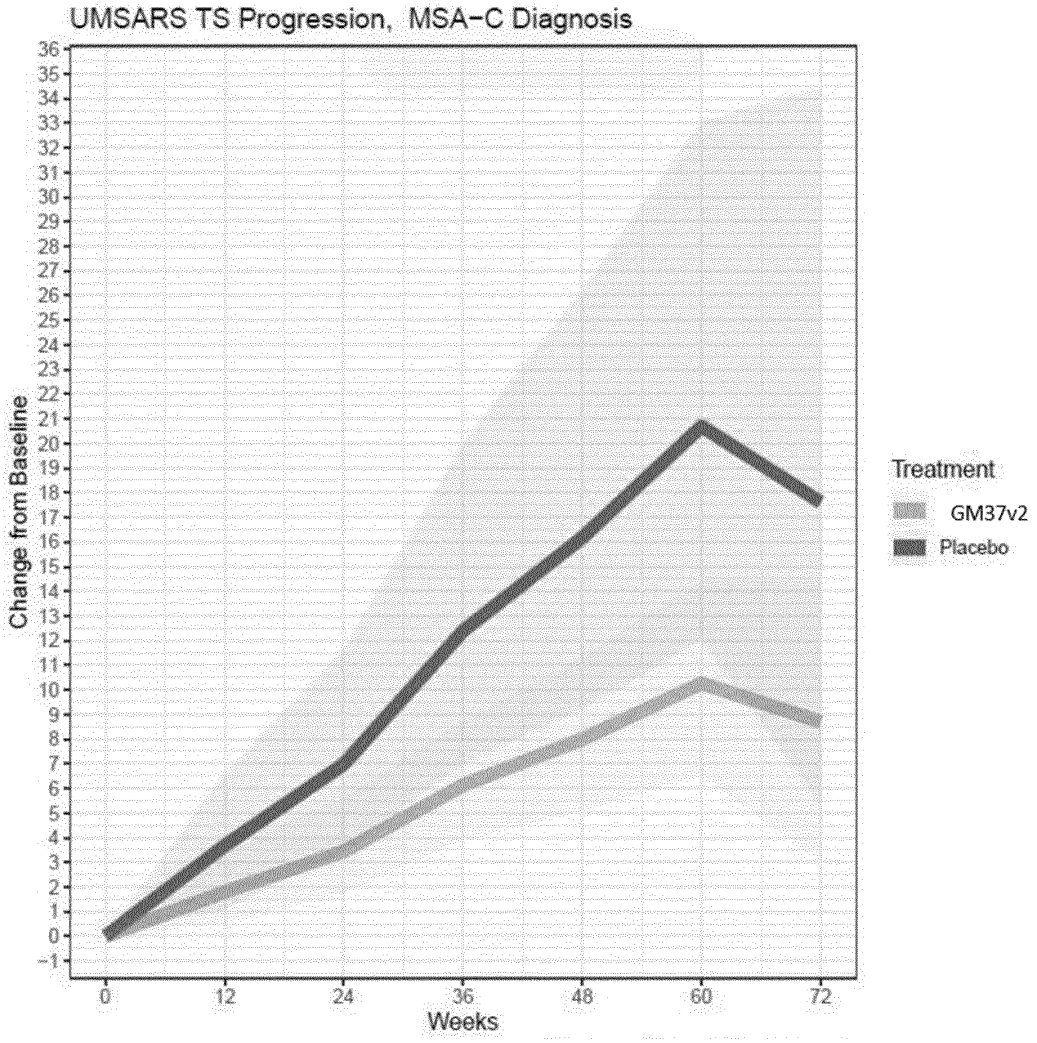

UMSARS TS Progression, MSA-C Diagnosis
Change from Baseline
Weeks
0
12
24
36
48
60
72
Treatment
GM37v2
Placebo

Figure 16b

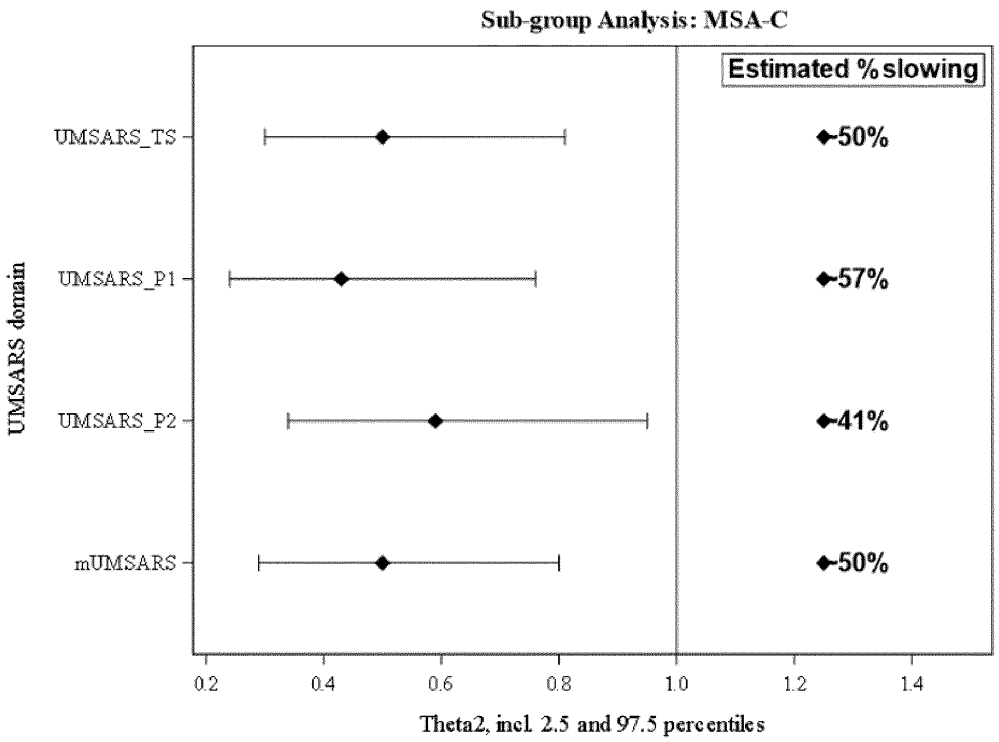

Sub-group Analysis: MSA-C
Estimated % slowing
UMSARS_TS
UMSARS_P1
UMSARS_P2
mUMSARS
50%
57%
41%
50%
UMSARS domain
0.2
0.4
0.6
0.8
1.0
1.2
1.4
Theta2, incl. 2.5 and 97.5 percentiles

Figure 17a

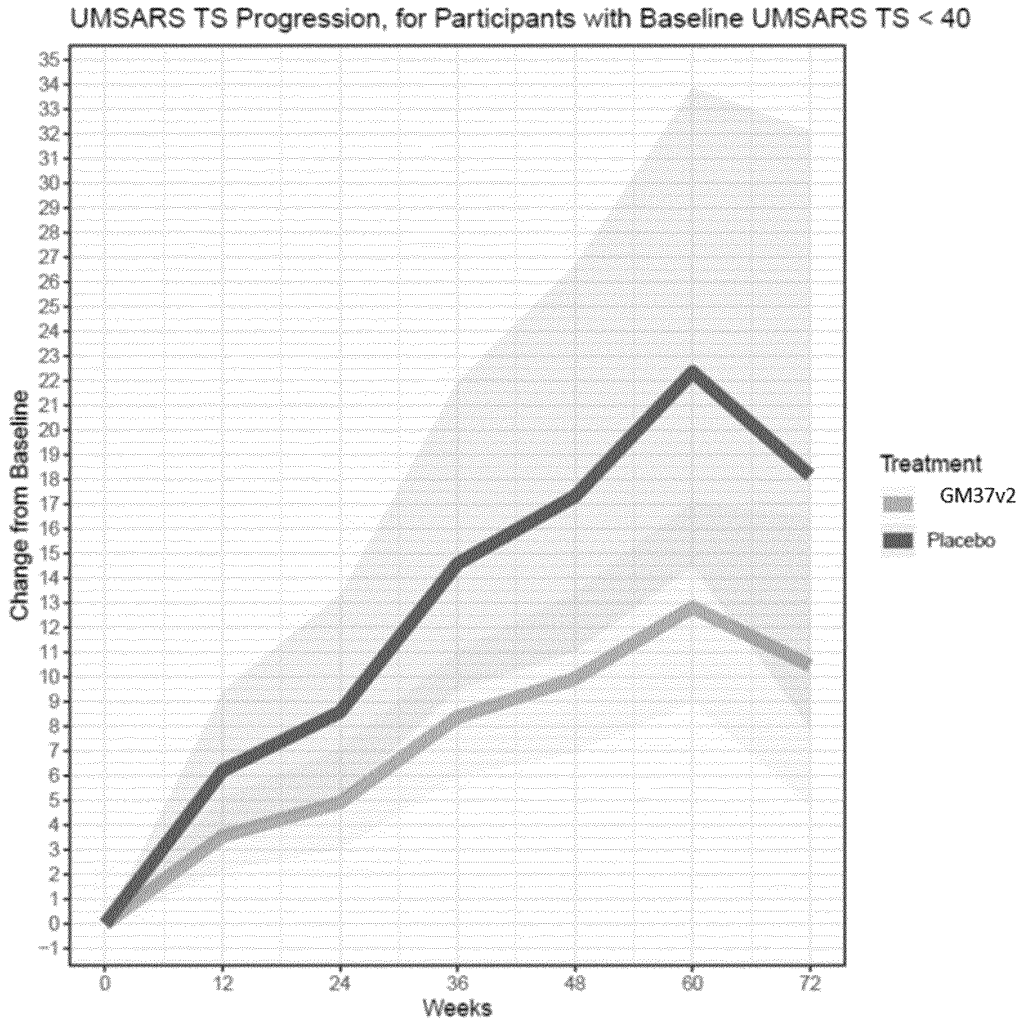

UMSARS TS Progression, for Participants with Baseline UMSARS TS < 40
Change from Baseline
Weeks
0
12
24
36
48
60
72
Treatment
GM37v2
Placebo

Figure 17b

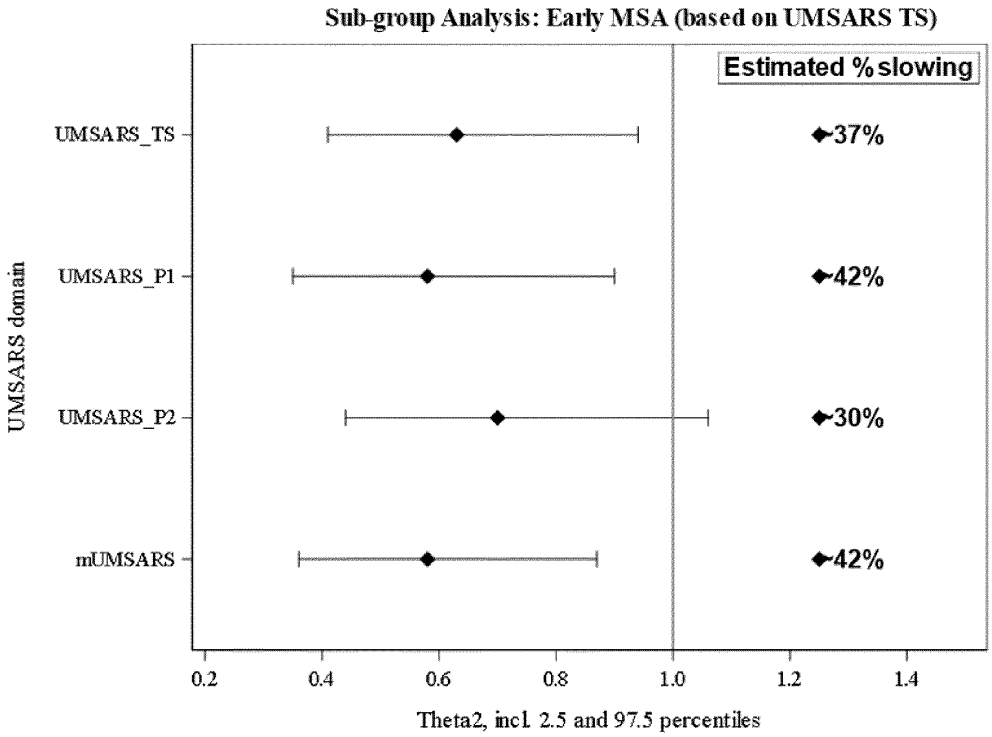

Sub-group Analysis: Early MSA (based on UMSARS TS)
Estimated % slowing
UMSARS_TS
UMSARS_P1
UMSARS_P2
mUMSARS
37%
42%
30%
42%
UMSARS domain
0.2
0.4
0.6
0.8
1.0
1.2
1.4
Theta2, incl 2.5 and 97.5 percentiles

Figure 18a

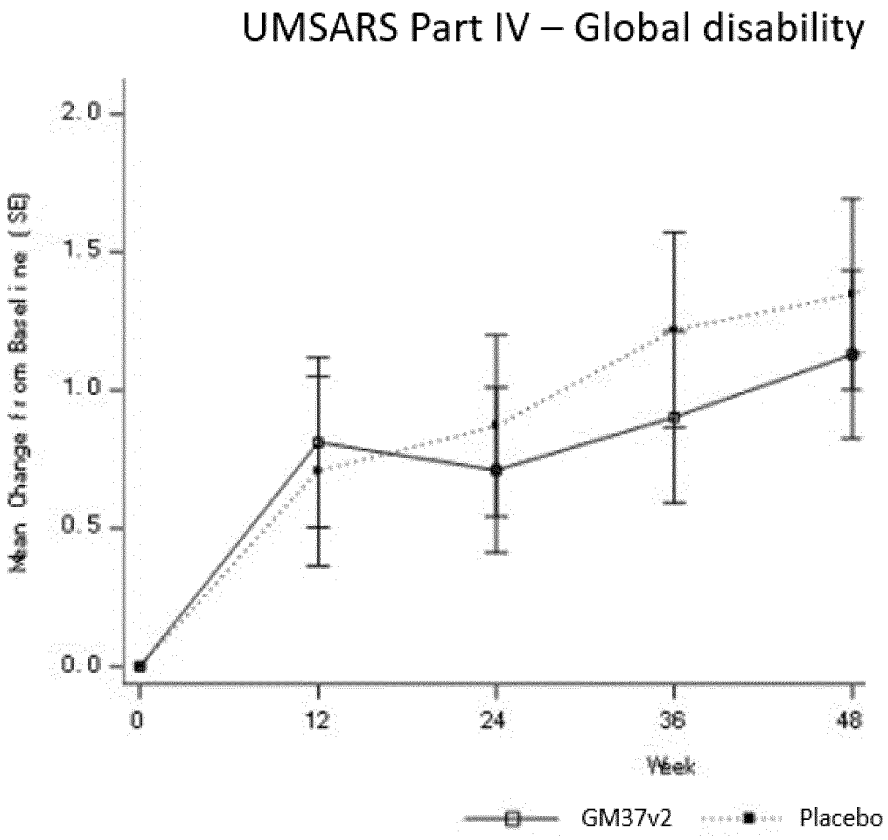

UMSARS Part IV – Global disability
Mean Change from Baseline (SE)
2.0
1.5
1.0
0.5
0.0
0
12
24
36
48
Week
GM37v2
Placebo

Figure 18b

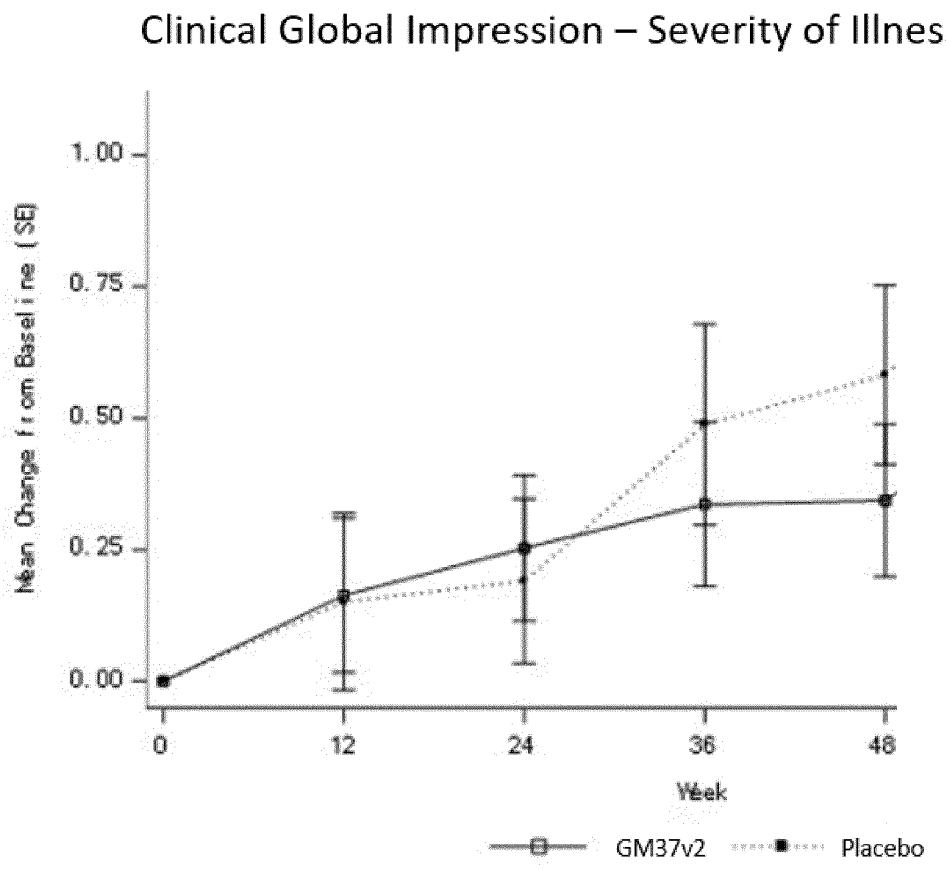

Clinical Global Impression – Severity of Illness
Mean Change from Baseline (SE)
1.00
0.75
0.50
0.25
0.00
0
12
24
36
48
Week
GM37v2
Placebo

Figure 19a

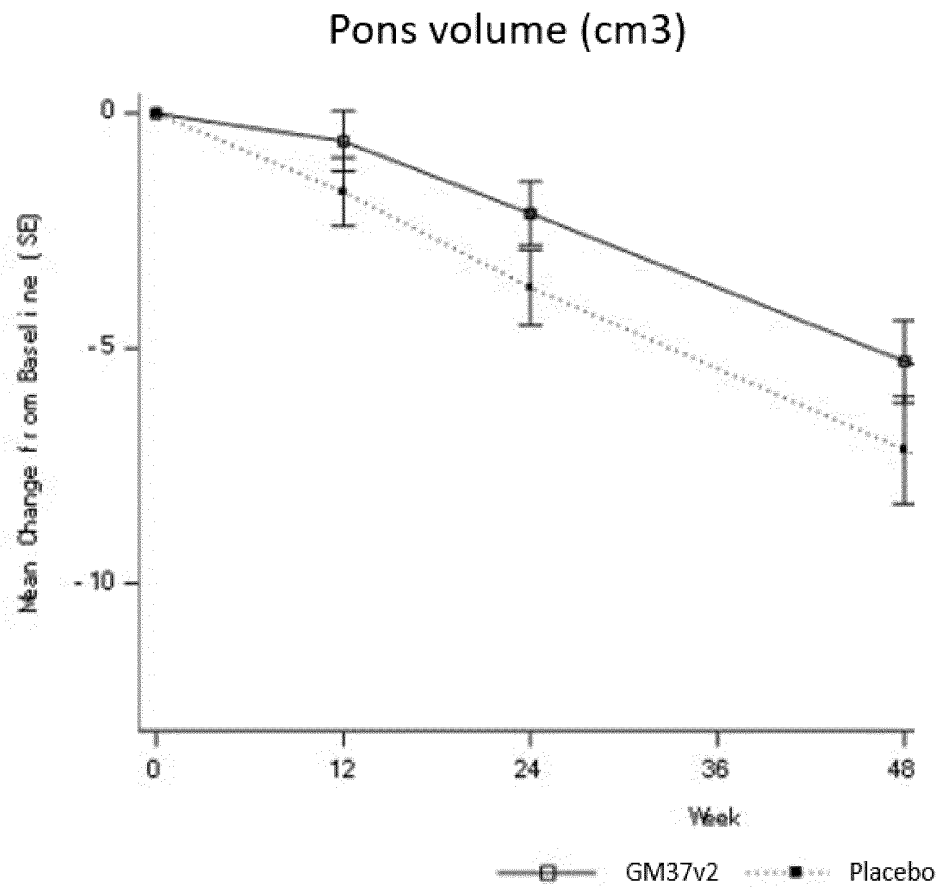

Pons volume (cm3)
Mean Change From Baseline (SE)
0
-5
-10
0
12
24
36
48
Week
GM37v2
Placebo

Figure 19b

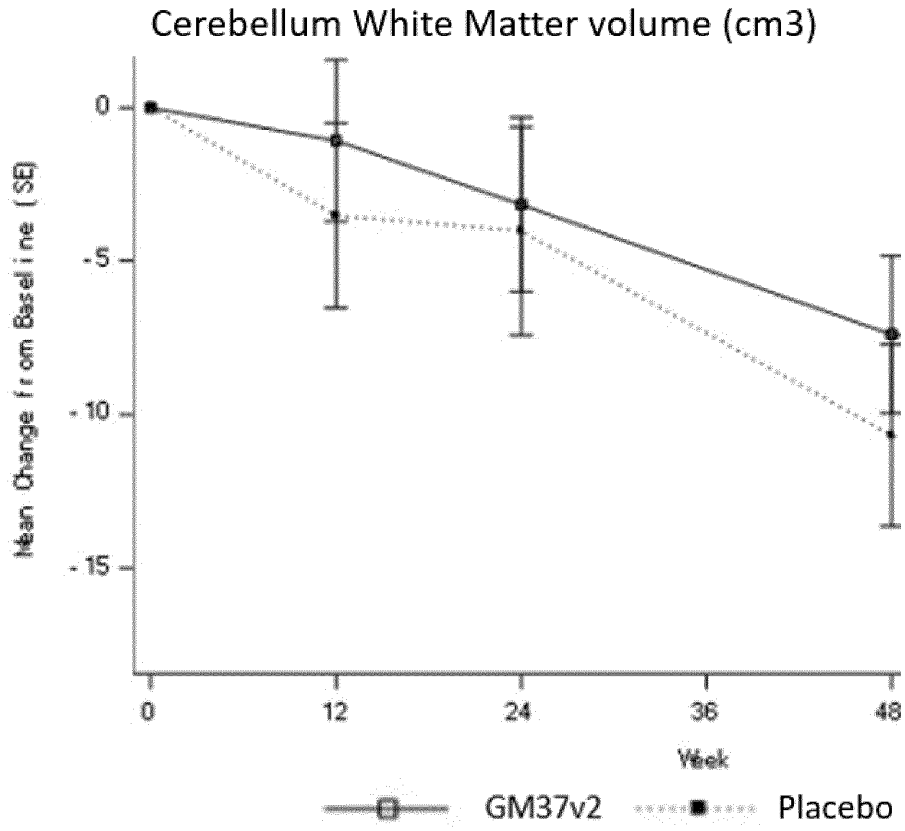

Cerebellum White Matter volume (cm3)
Mean Change from Baseline (SE)
0
-5
-10
-15
0
12
24
36
48
Week
GM37v2
Placebo

Figure 19c

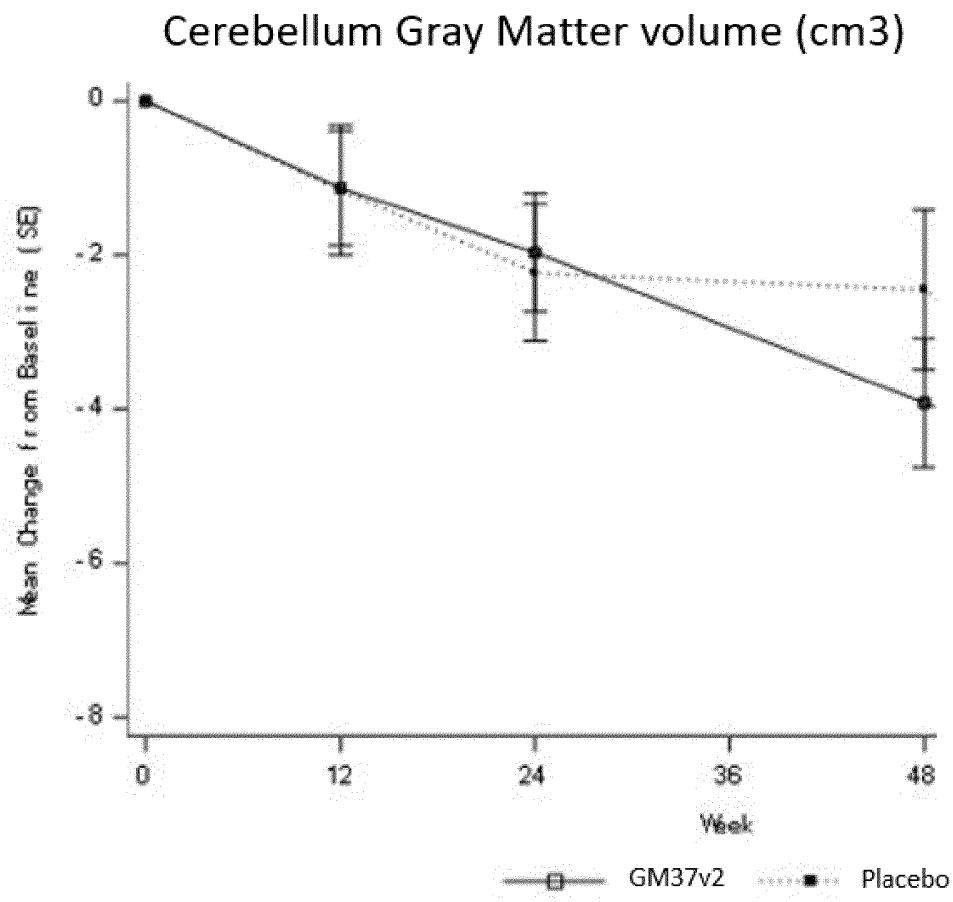
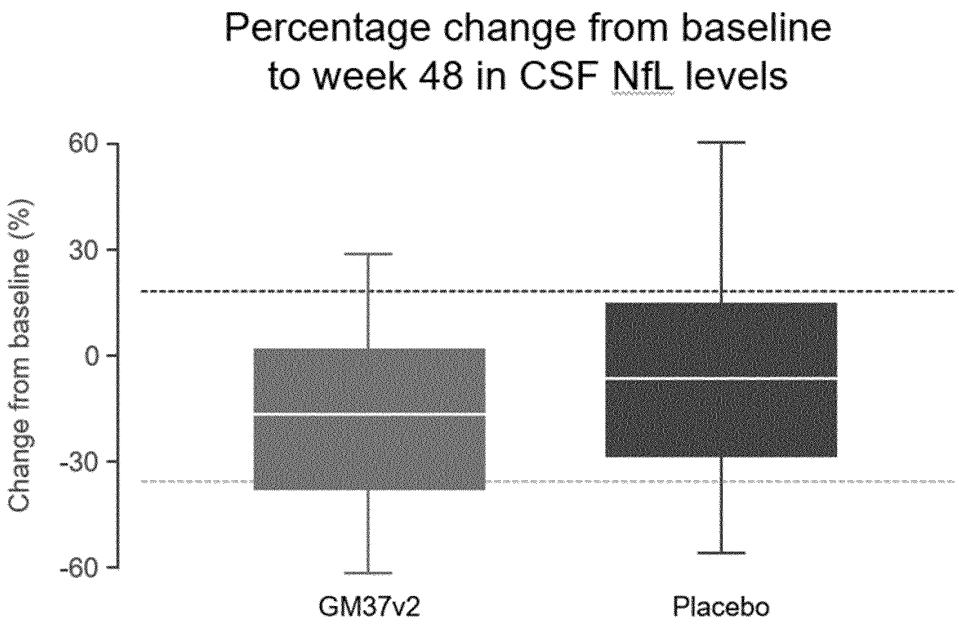

Cerebellum Gray Matter volume (cm3)
Mean Change from Baseline (SE)
0
-2
-4
-6
-8
0
12
24
36
48
Week
GM37v2
Placebo

Figure 20


Percentage change from baseline
to week 48 in CSF NfL levels
Change from baseline (%)
60
30
0
-30
-60
GM37v2
Placebo