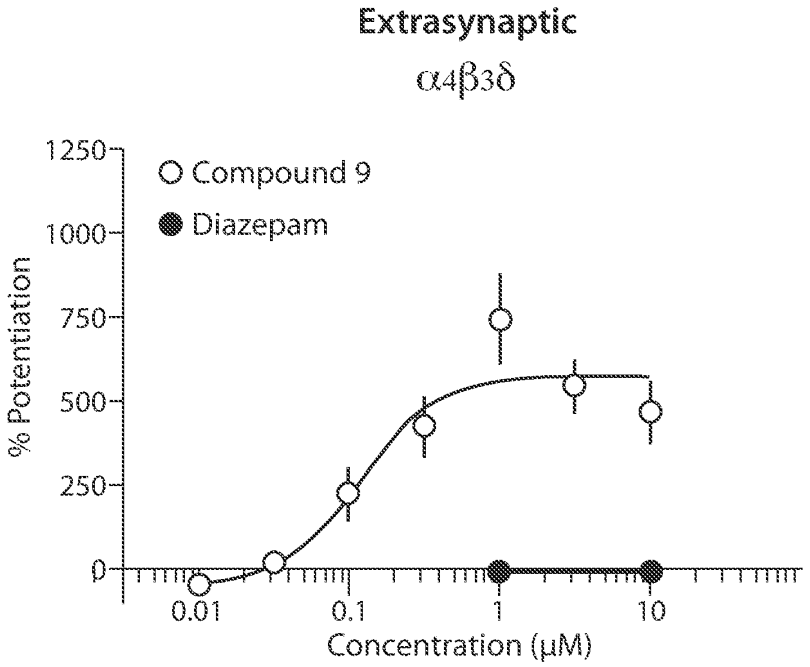

Extrasynaptic
α4β3δ
Compound 9
Diazepam
% Potentiation
1250
1000
750
500
250
0
0.01
0.1
1
10
Concentration (μM)

FIG. 1A

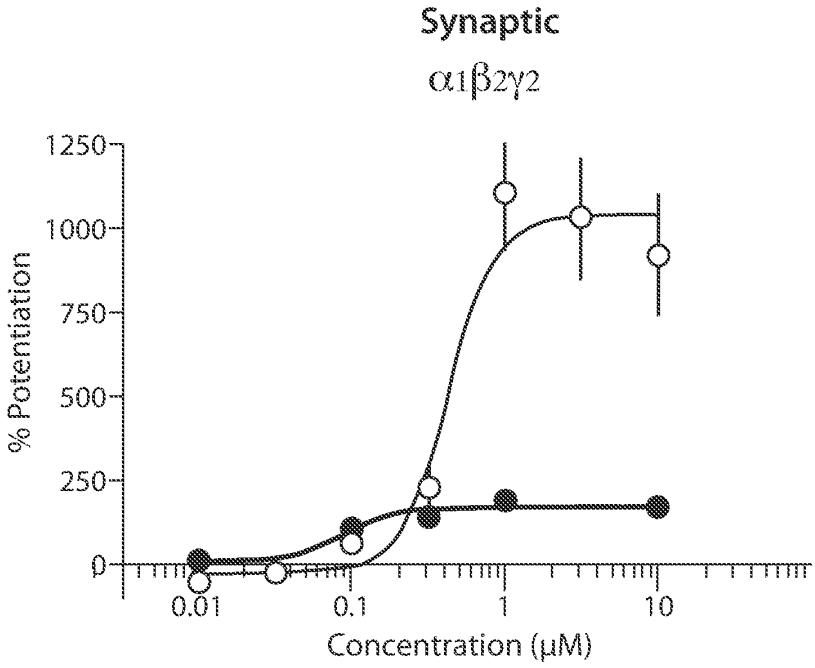

Synaptic
α1β2γ2
% Potentiation
1250
1000
750
500
250
0
0.01
0.1
1
10
Concentration (μM)

FIG. 1B

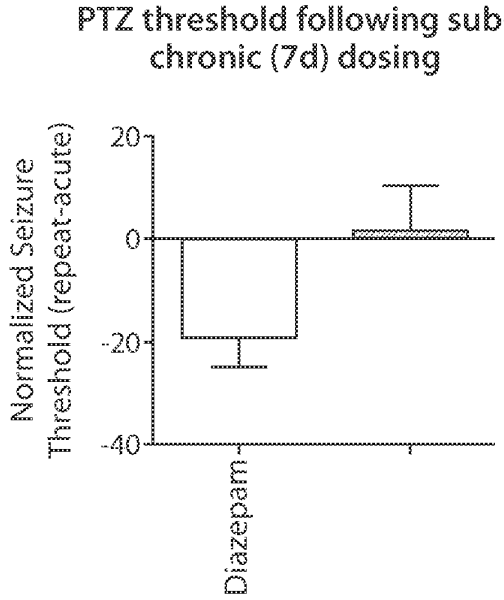

PTZ threshold following sub-chronic (7d) dosing
Normalized Seizure Threshold (repeat-acute)
20
0
-20
-40
Diazepam

FIG. 2A

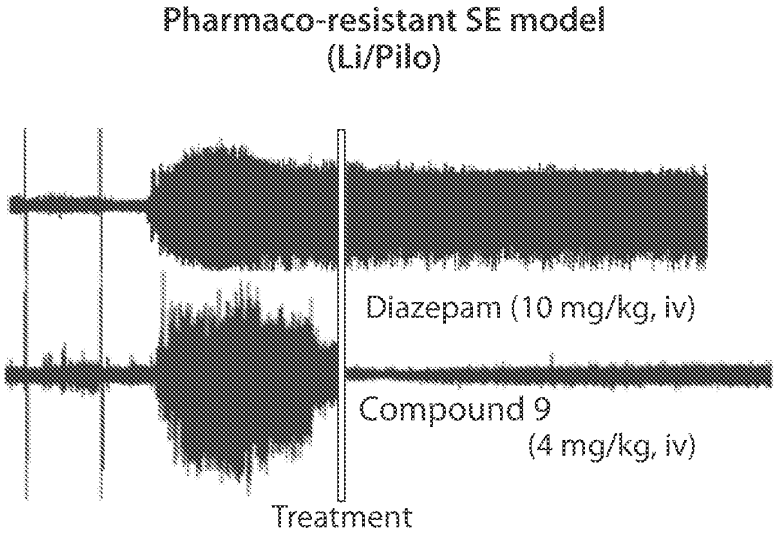

Pharmaco-resistant SE model (Li/Pilo)
Diazepam (10 mg/kg, iv)
Compound 9
(4 mg/kg, iv)
Treatment

FIG. 2B

Seizure Model		mg/kg (IP)
Mouse	MES *	Active
	PTZ (sc)	MED = 0.3 (IP/PO)
	6Hz (32 mA)	ED_{50} = 1.9
	6Hz (44 mA)*	ED_{50} > 10
	Audiogenic	MED ≤ 0.1
	Corneal Kindling *	ED_{50} = 1.22
	mTLE	MED ≤ 1.0
Rat	MES *	Active
	LTG-resistant AMG Kindled*	ED_{50} = 0.47
	Li-pilocarpine SE	MED = 3 (IV)

FIG. 3A

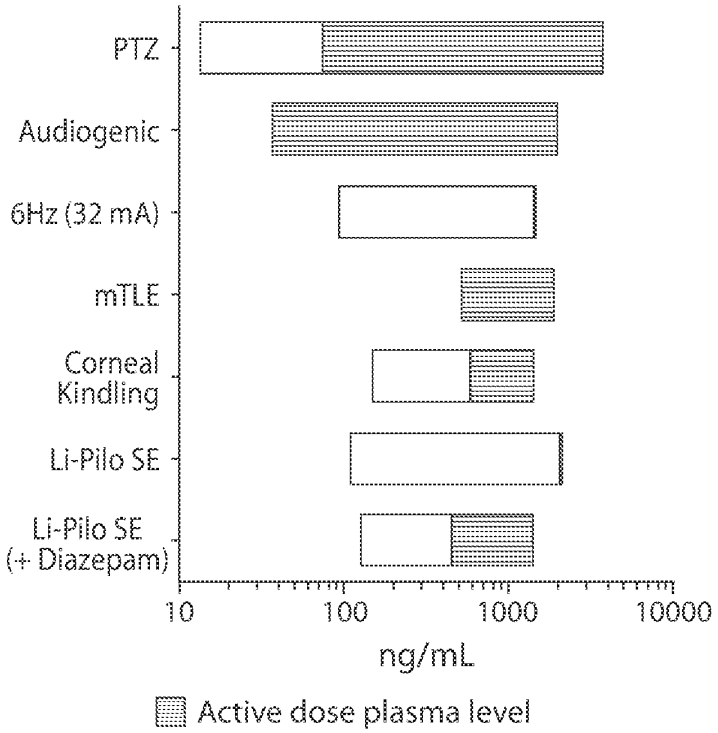


FIG. 3B

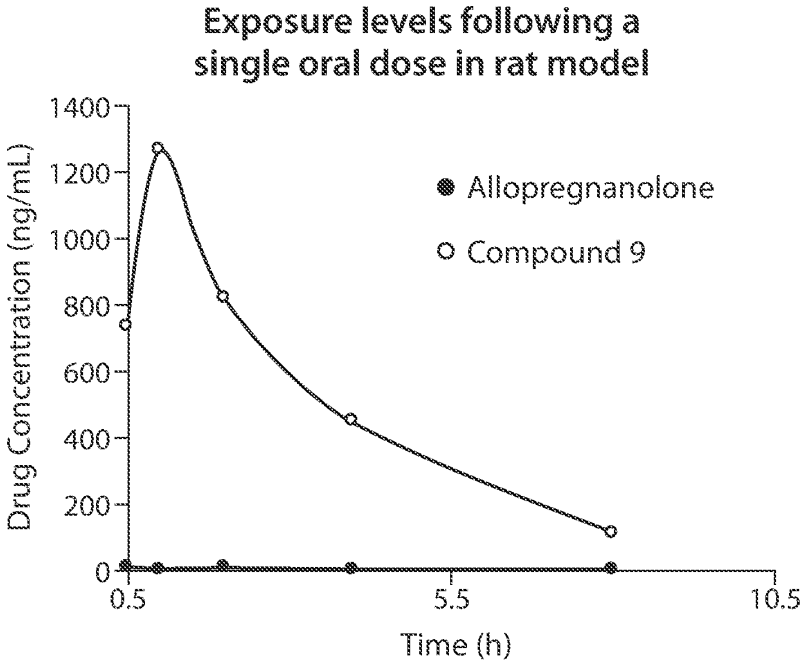

Exposure levels following a single oral dose in rat model
Drug Concentration (ng/mL)
1400
1200
1000
800
600
400
200
0
0.5
5.5
10.5
Time (h)
Allopregnanolone
Compound 9

FIG. 4A

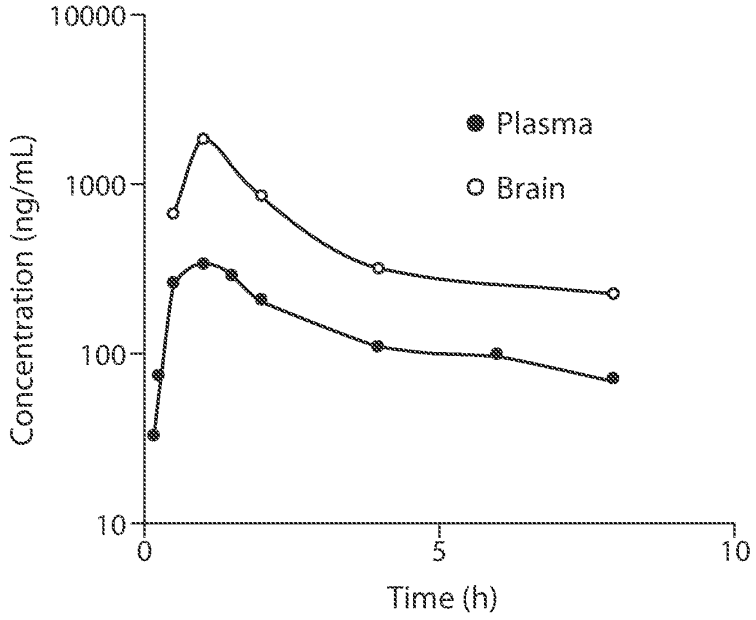

Concentration (ng/mL)
10000
1000
100
10
0
5
10
Time (h)
Plasma
Brain

FIG. 4B

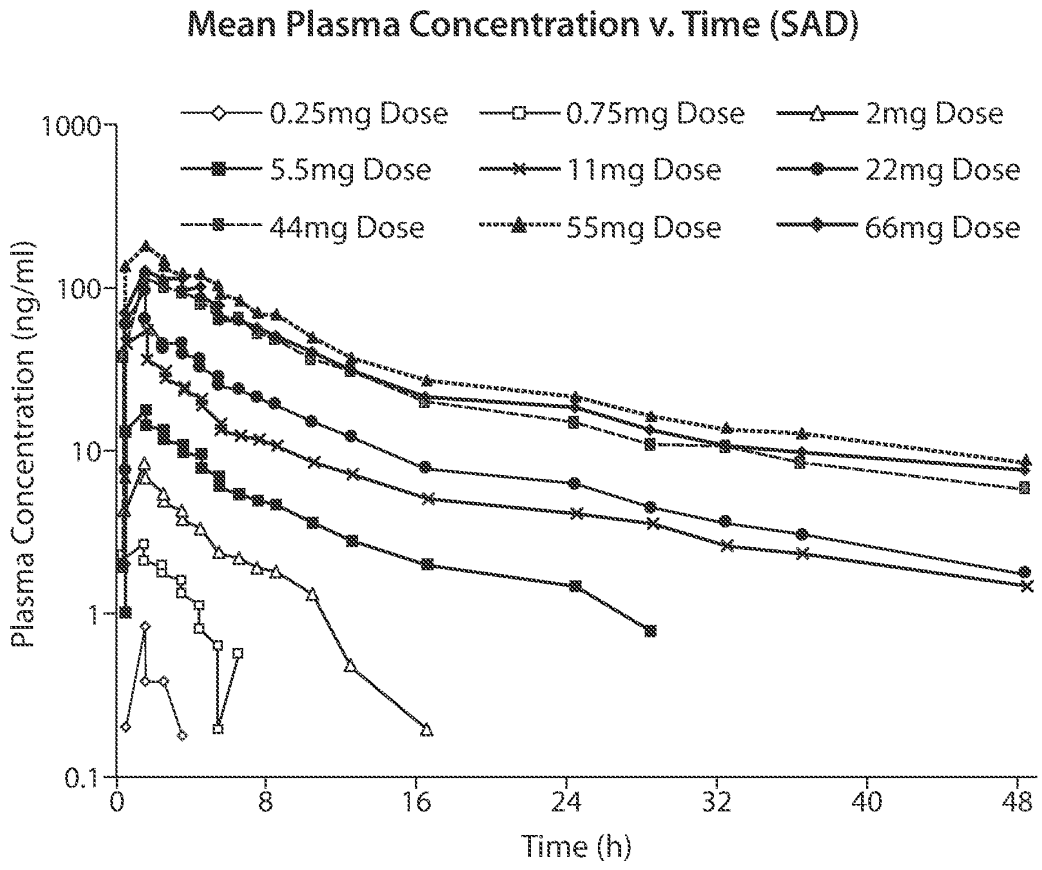

Mean Plasma Concentration v. Time (SAD)
0.25mg Dose
0.75mg Dose
2mg Dose
5.5mg Dose
11mg Dose
22mg Dose
44mg Dose
55mg Dose
66mg Dose
Plasma Concentration (ng/ml)
1000
100
10
1
0.1
0
8
16
24
32
40
48
Time (h)

FIG. 5

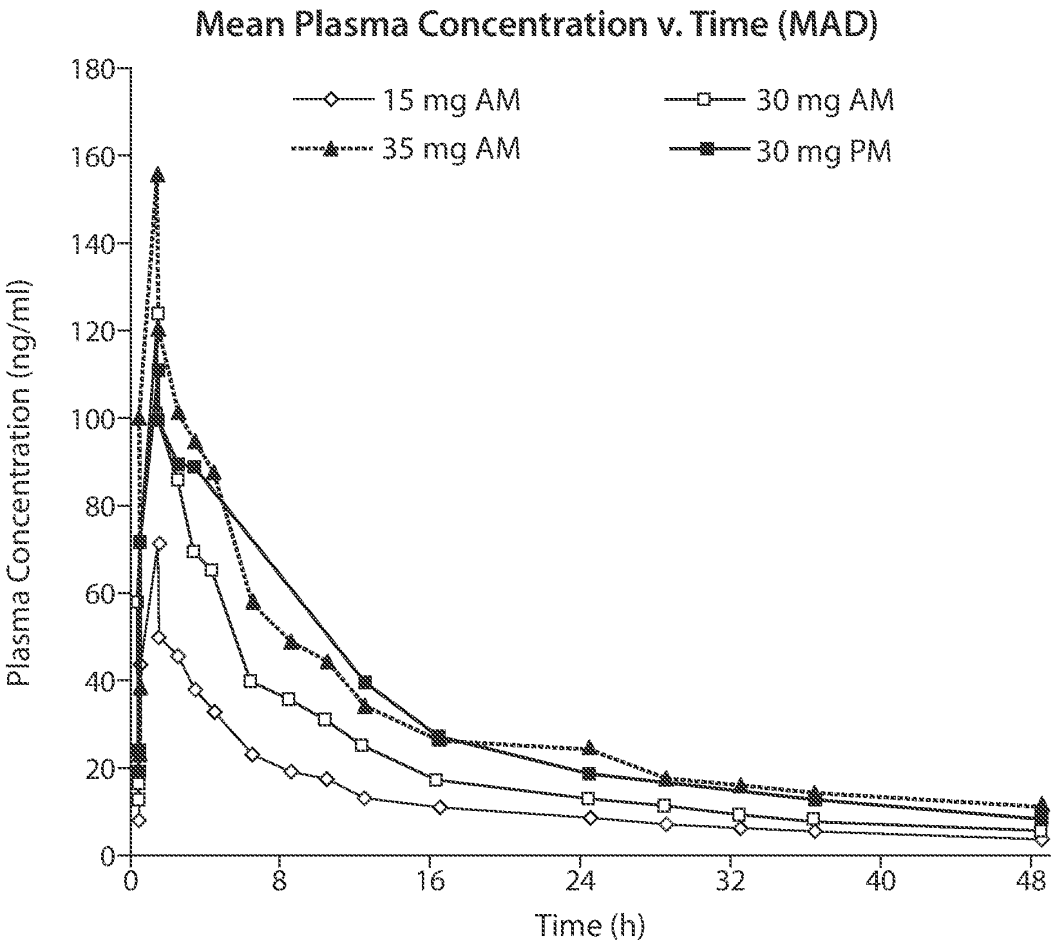

Mean Plasma Concentration v. Time (MAD)
15 mg AM
30 mg AM
35 mg AM
30 mg PM
Plasma Concentration (ng/ml)
180
160
140
120
100
80
60
40
20
0
0
8
16
24
32
40
48
Time (h)

FIG. 6

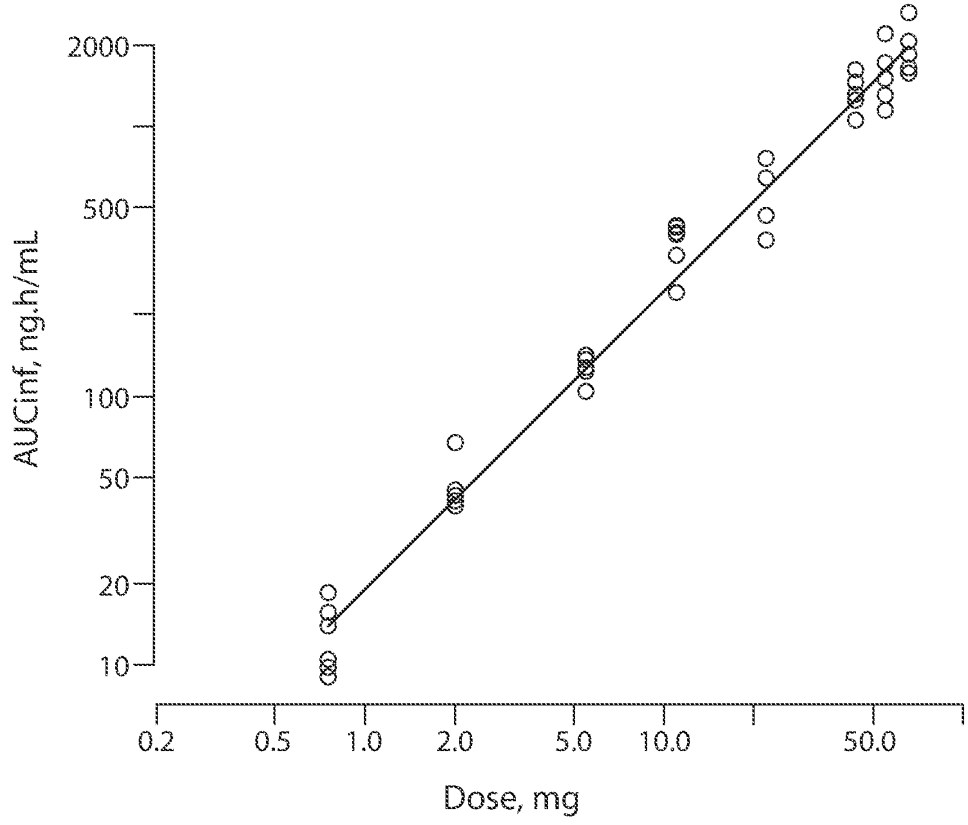


FIG. 7

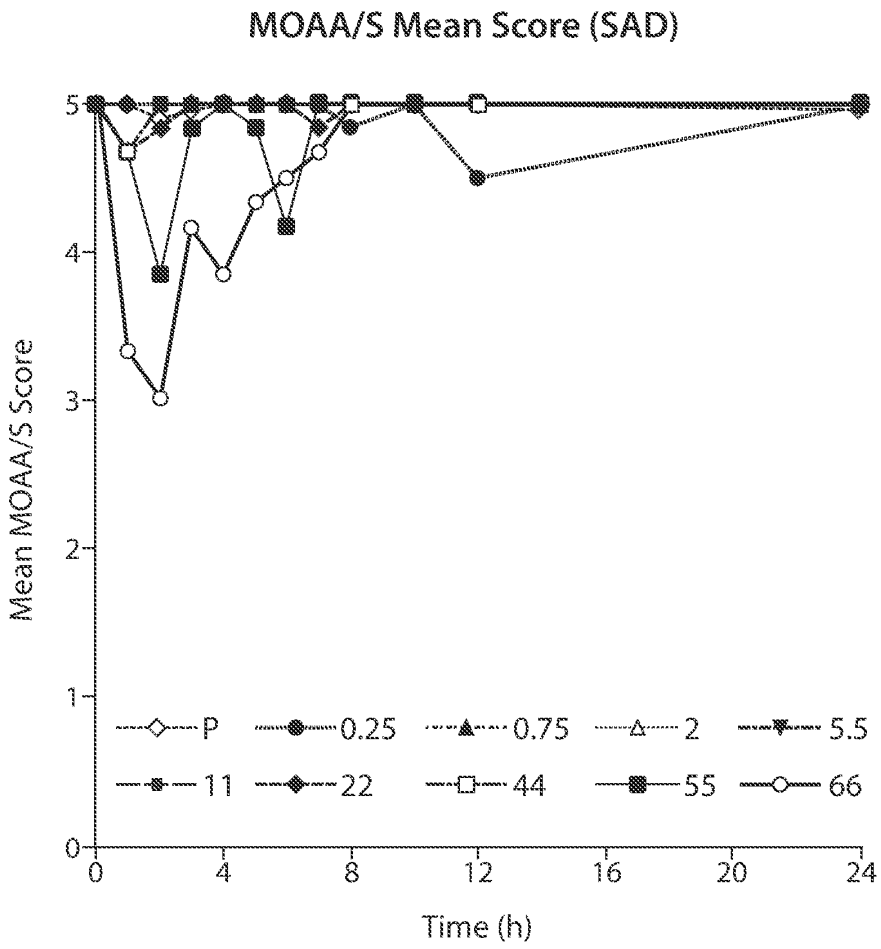

MOAA/S Mean Score (SAD)
Mean MOAA/S Score
0
1
2
3
4
5
0
4
8
12
16
20
24
Time (h)
P
0.25
0.75
2
5.5
11
22
44
55
66

FIG. 8

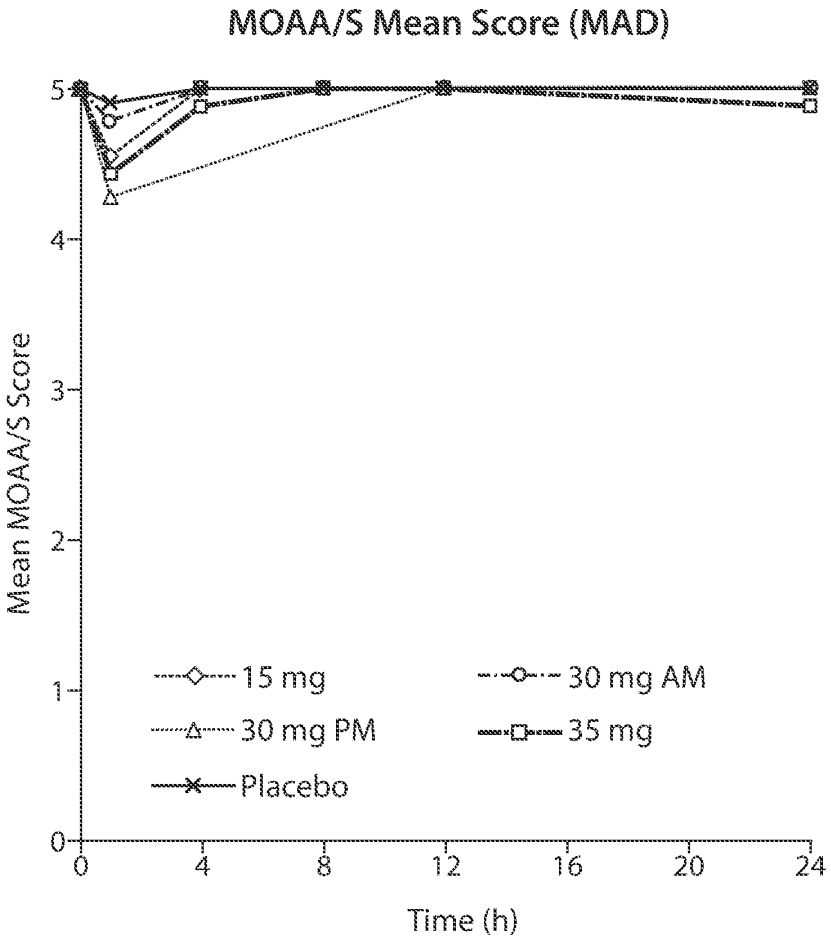

MOAA/S Mean Score (MAD)
Mean MOAA/S Score
0
1
2
3
4
5
0
4
8
12
16
20
24
Time (h)
15 mg
30 mg AM
30 mg PM
35 mg
Placebo

FIG. 9

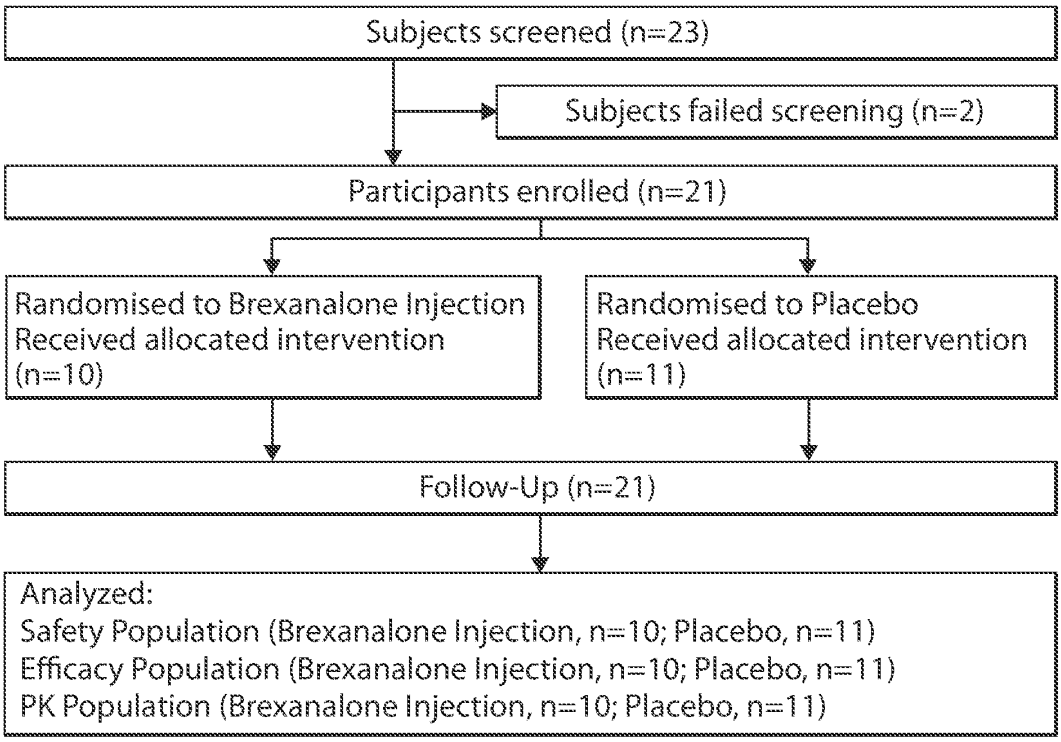

Subjects screened (n=23)
Subjects failed screening (n=2)
Participants enrolled (n=21)
Randomised to Brexanalone Injection
Received allocated intervention
(n=10)
Randomised to Placebo
Received allocated intervention
(n=11)
Follow-Up (n=21)
Analyzed:
Safety Population (Brexanalone Injection, n=10; Placebo, n=11)
Efficacy Population (Brexanalone Injection, n=10; Placebo, n=11)
PK Population (Brexanalone Injection, n=10; Placebo, n=11)

FIG. 10

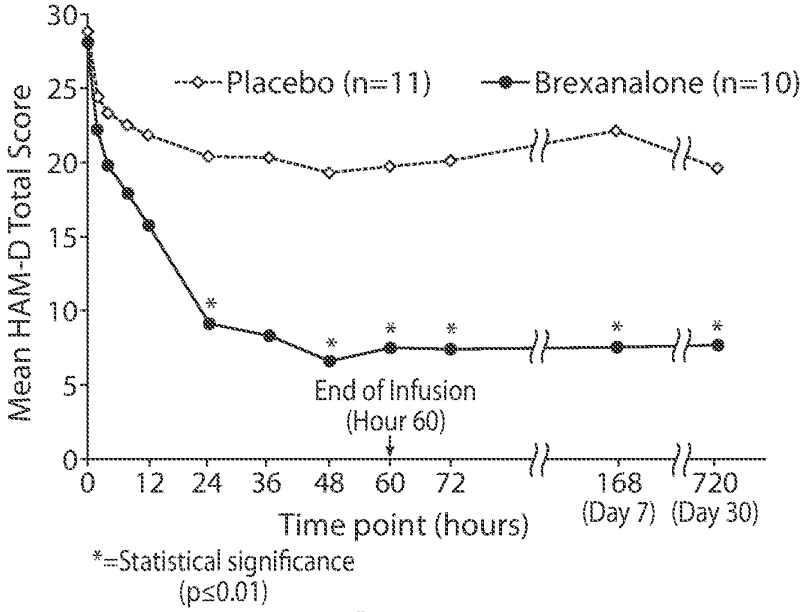


FIG. 11A

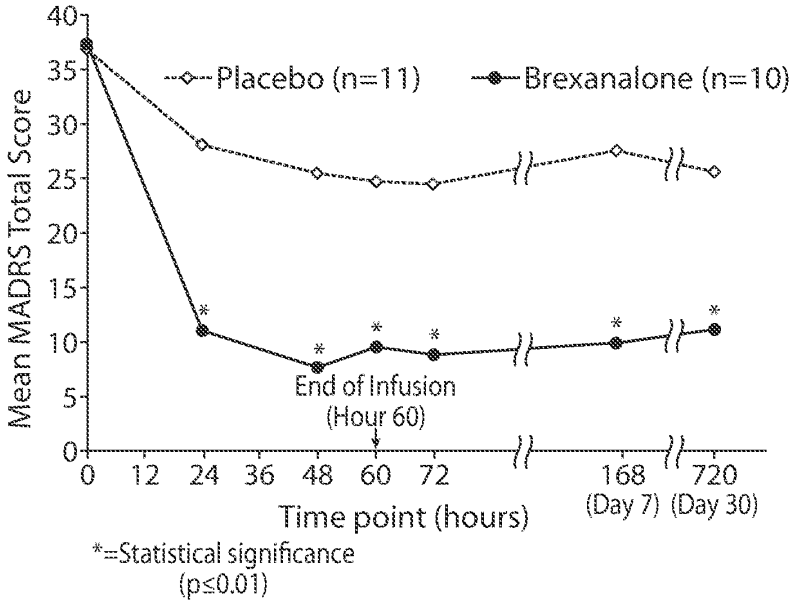


FIG. 11B

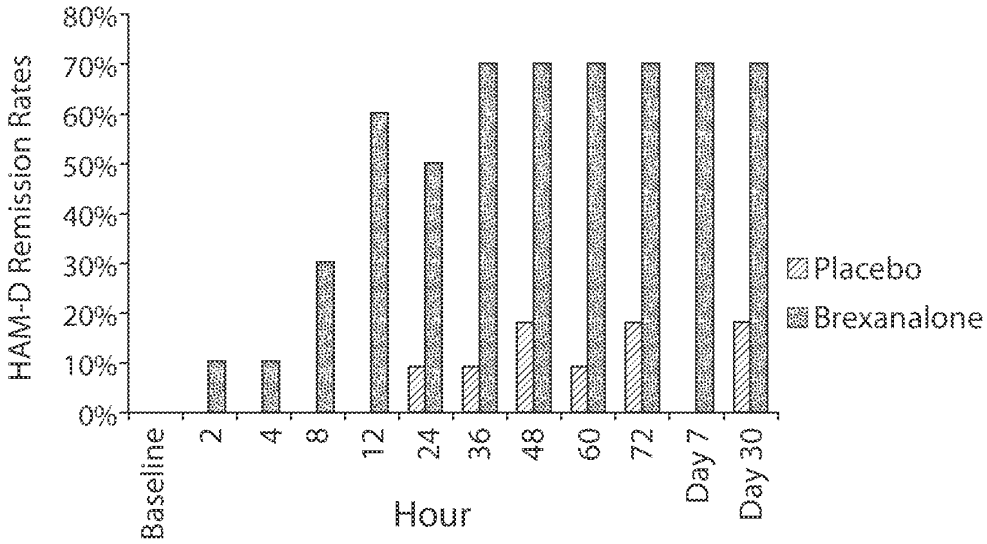

HAM-D Remission Rates
80%
70%
60%
50%
40%
30%
20%
10%
0%
Baseline
2
4
8
12
24
36
48
60
72
Day 7
Day 30
Hour
Placebo
Brexanalone

FIG. 12