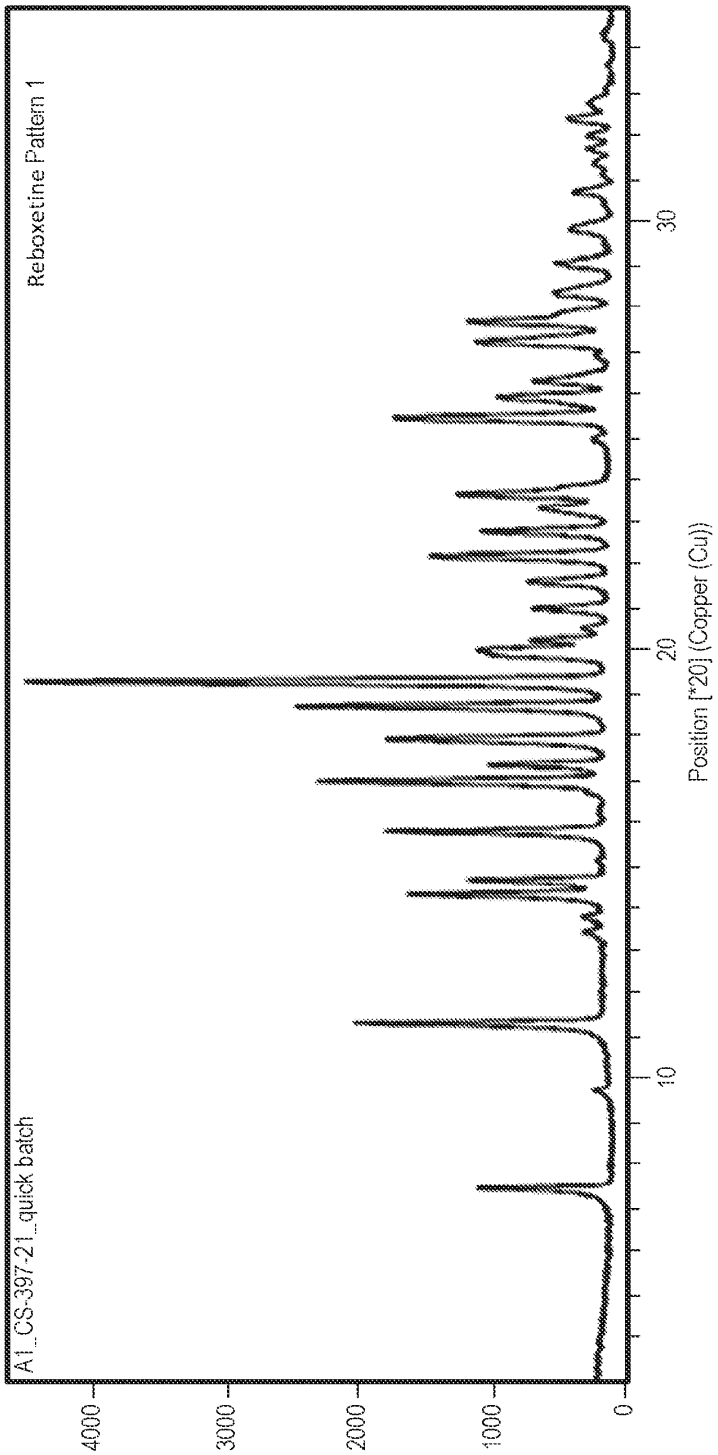

Reboxetine Pattern 1
A1_CS-397-21_quick batch
4000
3000
2000
1000
0
10
20
30
Position [°2θ] (Copper (Cu))

FIG. 1

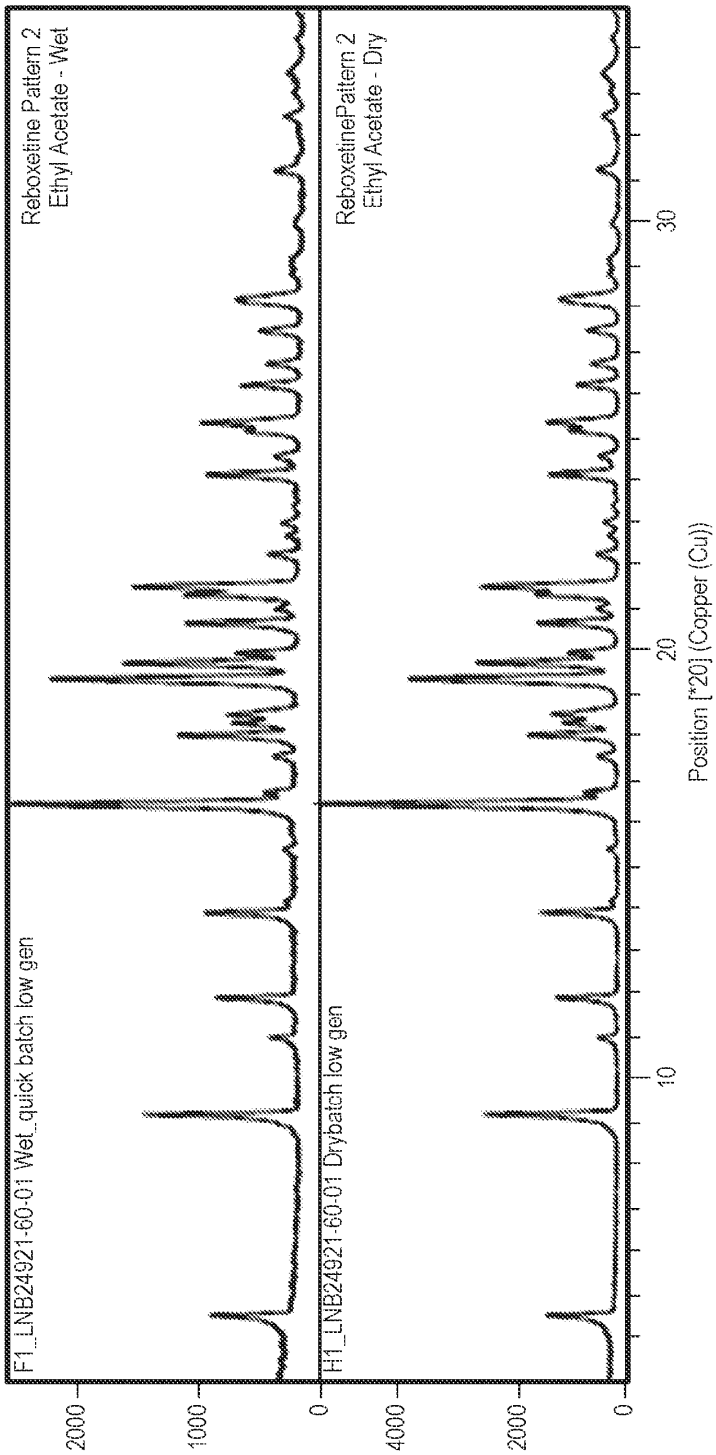

Reboxetine Pattern 2
Ethyl Acetate - Wet
F1_LNB24921-60-01 Wet_quick batch low gen
ReboxetinePattern 2
Ethyl Acetate - Dry
H1_LNB24921-60-01 Drybatch low gen
2000
1000
0
4000
2000
0
10
20
30
Position [°2θ] (Copper (Cu))

FIG. 2

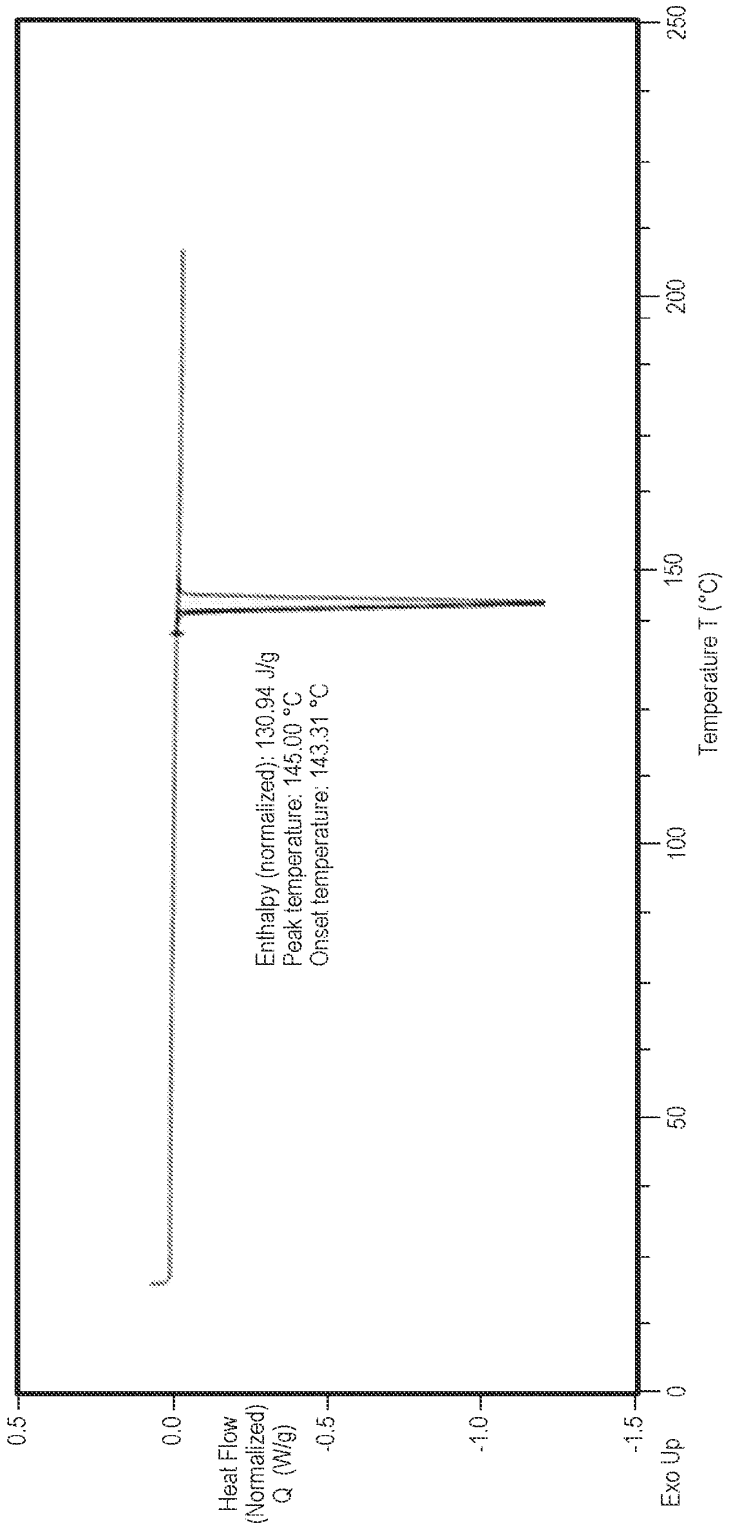

Enthalpy (normalized): 130.94 J/g
Peak temperature: 145.00 °C
Onset temperature: 143.31 °C
Heat Flow (Normalized) Q (W/g)
Exo Up
Temperature T (°C)
0.5
0.0
-0.5
-1.0
-1.5
0
50
100
150
200
250

FIG. 3

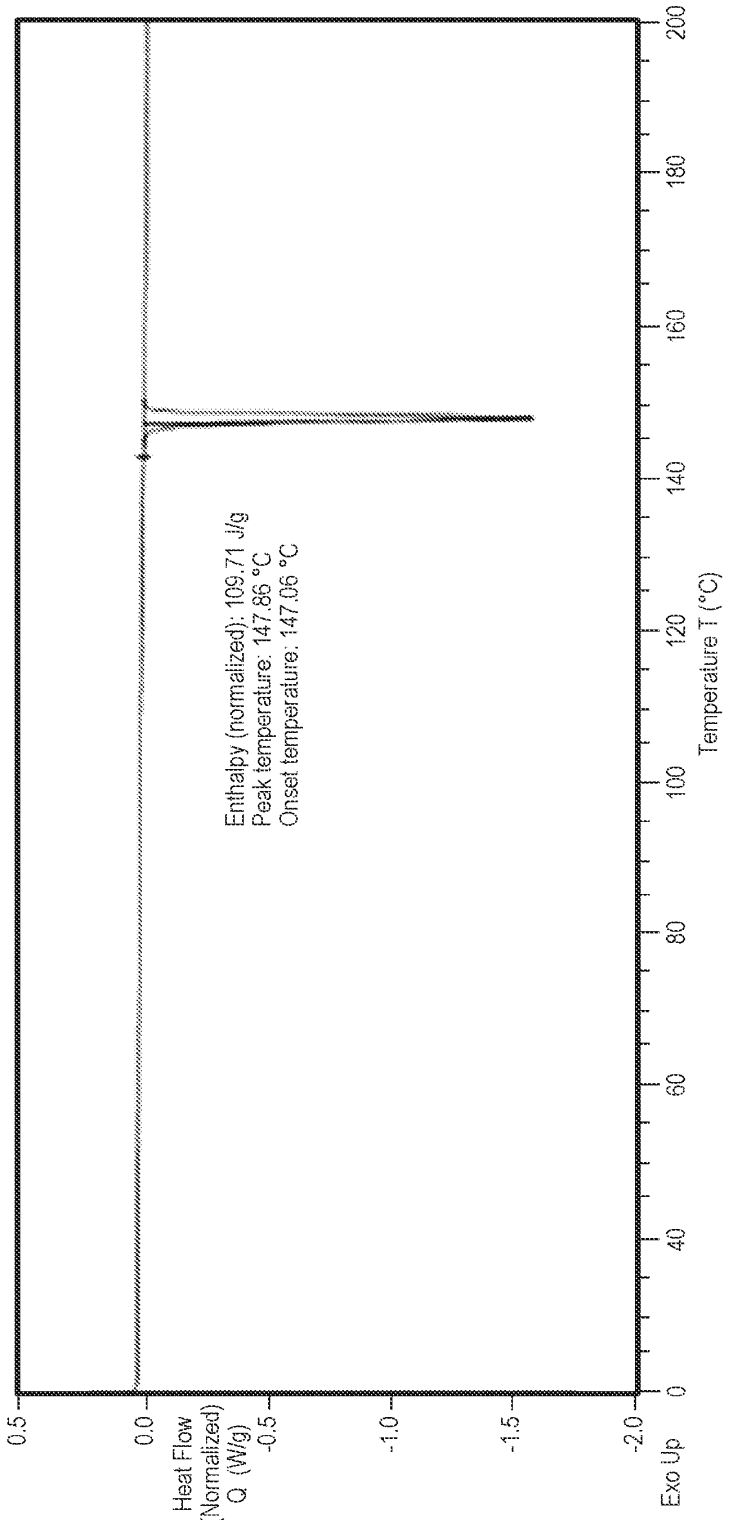
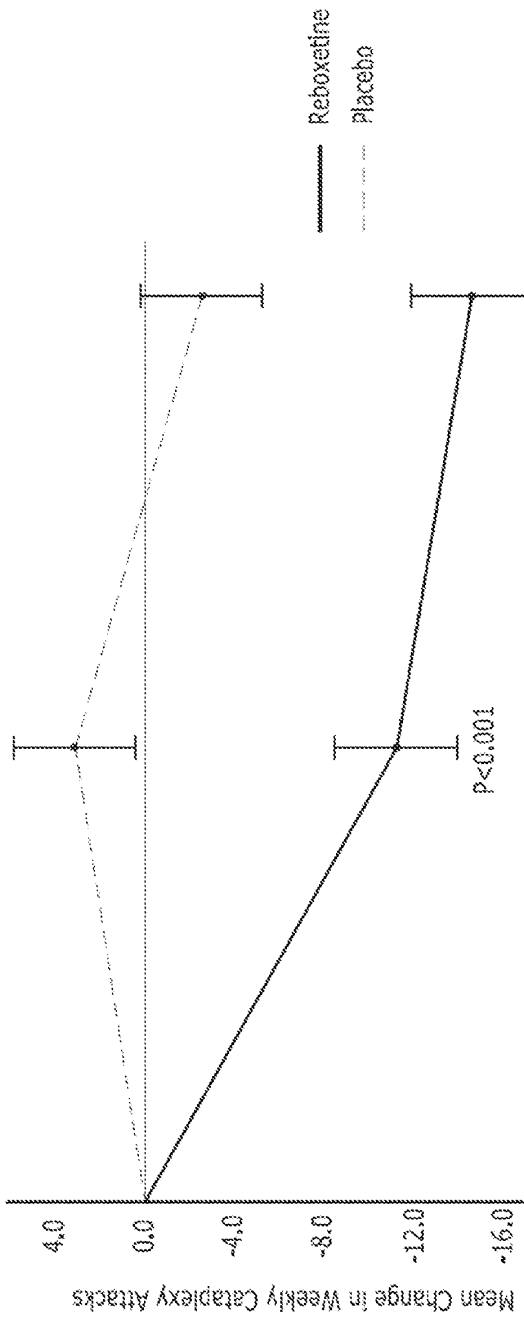

Enthalpy (normalized): 109.71 J/g
Peak temperature: 147.86 °C
Onset temperature: 147.06 °C
Heat Flow (Normalized) Q (W/g)
Exo Up
Temperature T (°C)
0.5
0.0
-0.5
-1.0
-1.5
-2.0
0
40
60
80
100
120
140
160
180
200

FIG. 4



Primary Endpoint	Reboxetine	Placebo	P-value
Overall Change in Average Weekly Cataplexy Attacks	-13.0	-0.3	<0.001
Week 2 Change in Average Weekly Cataplexy Attacks	-14.6	-2.6	0.002

FIG. 5

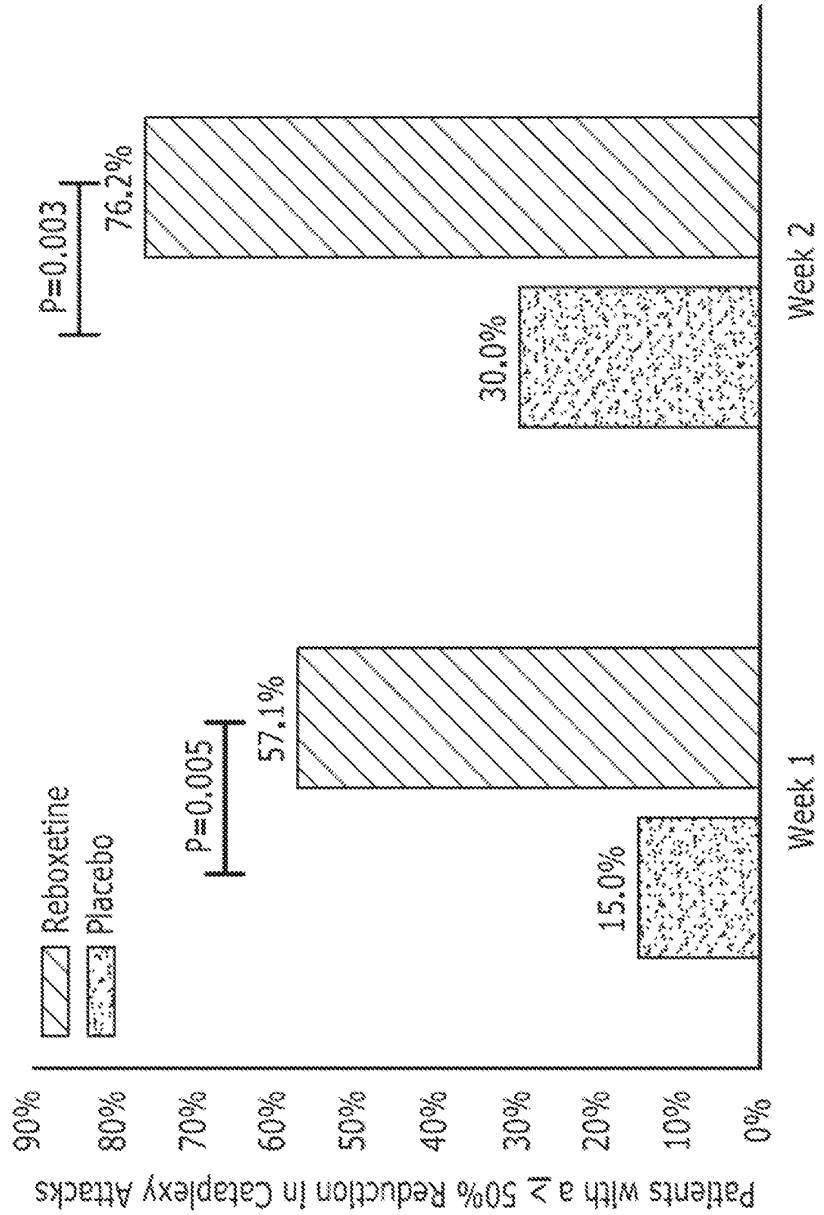

Patients with a ≥ 50% Reduction in Cataplexy Attacks
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Reboxetine
Placebo
P=0.005
57.1%
15.0%
P=0.003
76.2%
30.0%
Week 1
Week 2

FIG. 6

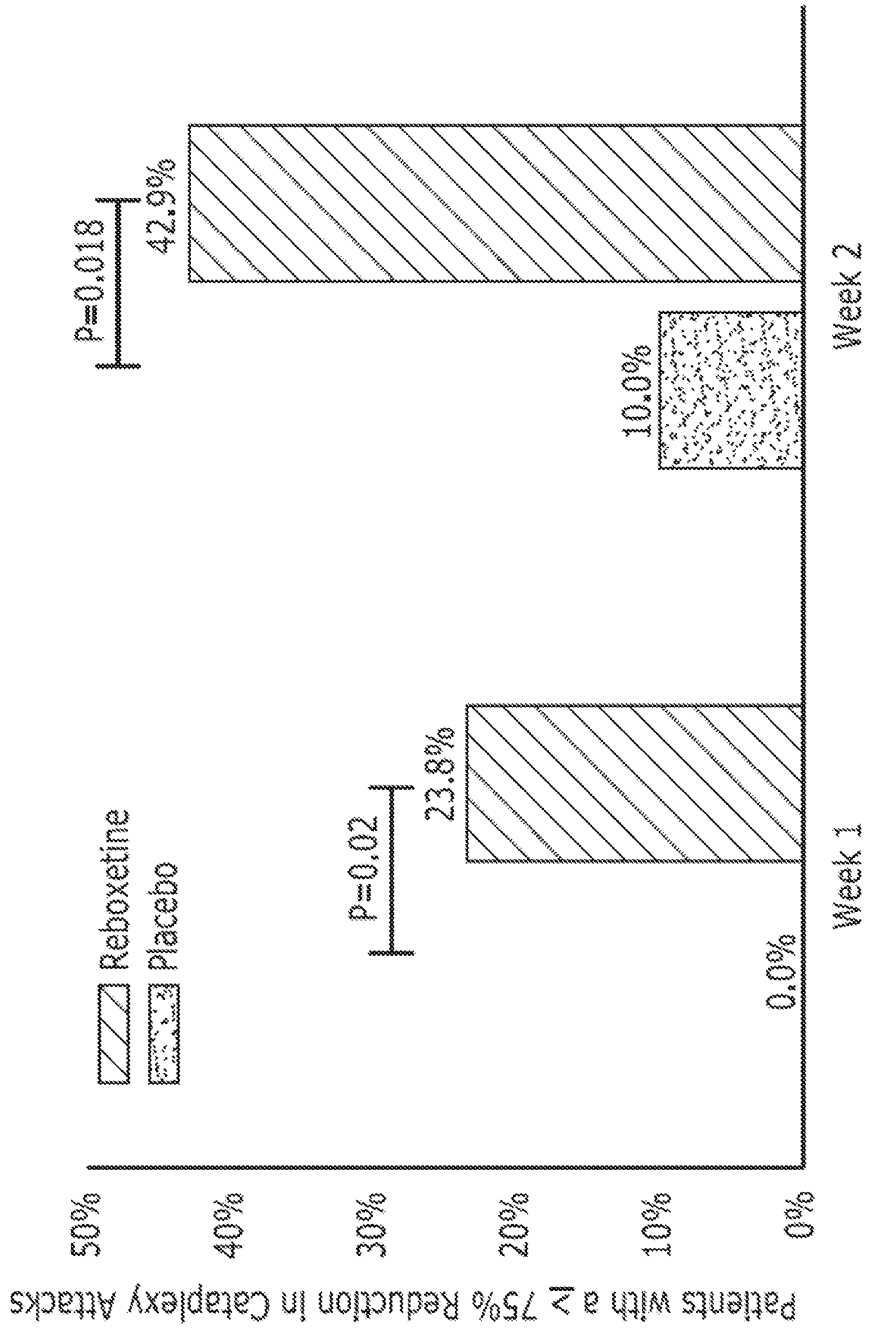

Patients with a ≥ 75% Reduction in Cataplexy Attacks
50%
40%
30%
20%
10%
0%
Reboxetine
Placebo
P=0.02
23.8%
0.0%
Week 1
P=0.018
42.9%
10.0%
Week 2

FIG. 7

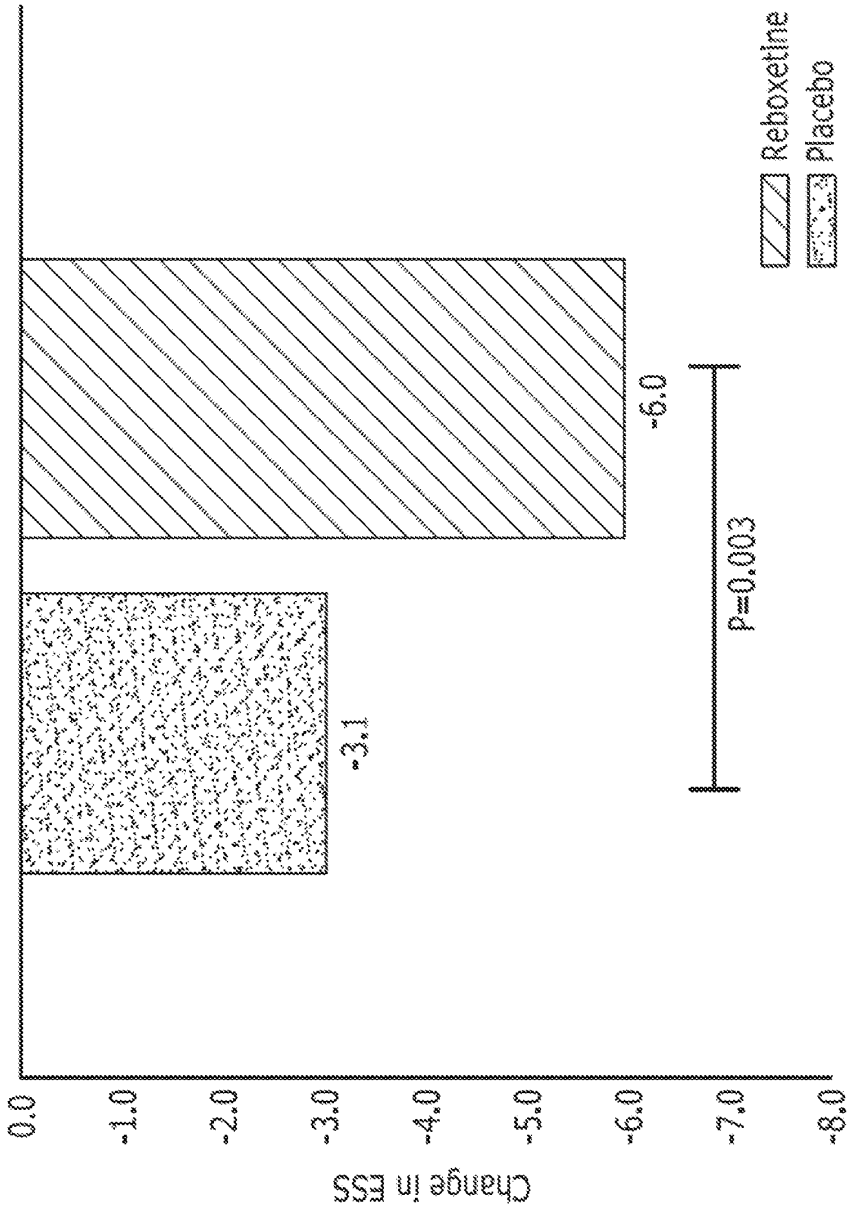
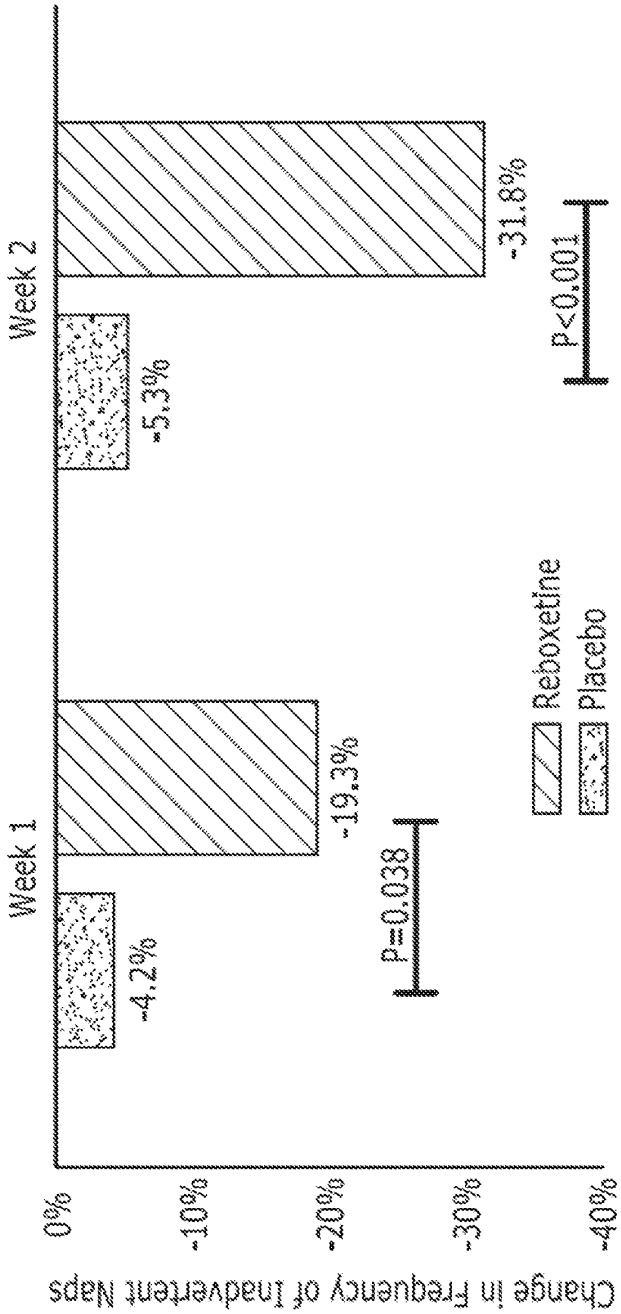

Change in ESS
0.0
-1.0
-2.0
-3.0
-4.0
-5.0
-6.0
-7.0
-8.0
-3.1
-6.0
P=0.003
Placebo
Reboxetine

FIG. 8



Change in Weekly Mean Number of Inadvertent Naps	Reboxetine	Placebo	P-value
Week 1	-3.57	-0.77	0.038
Week 2	-5.88	-0.98	<0.001

FIG. 9

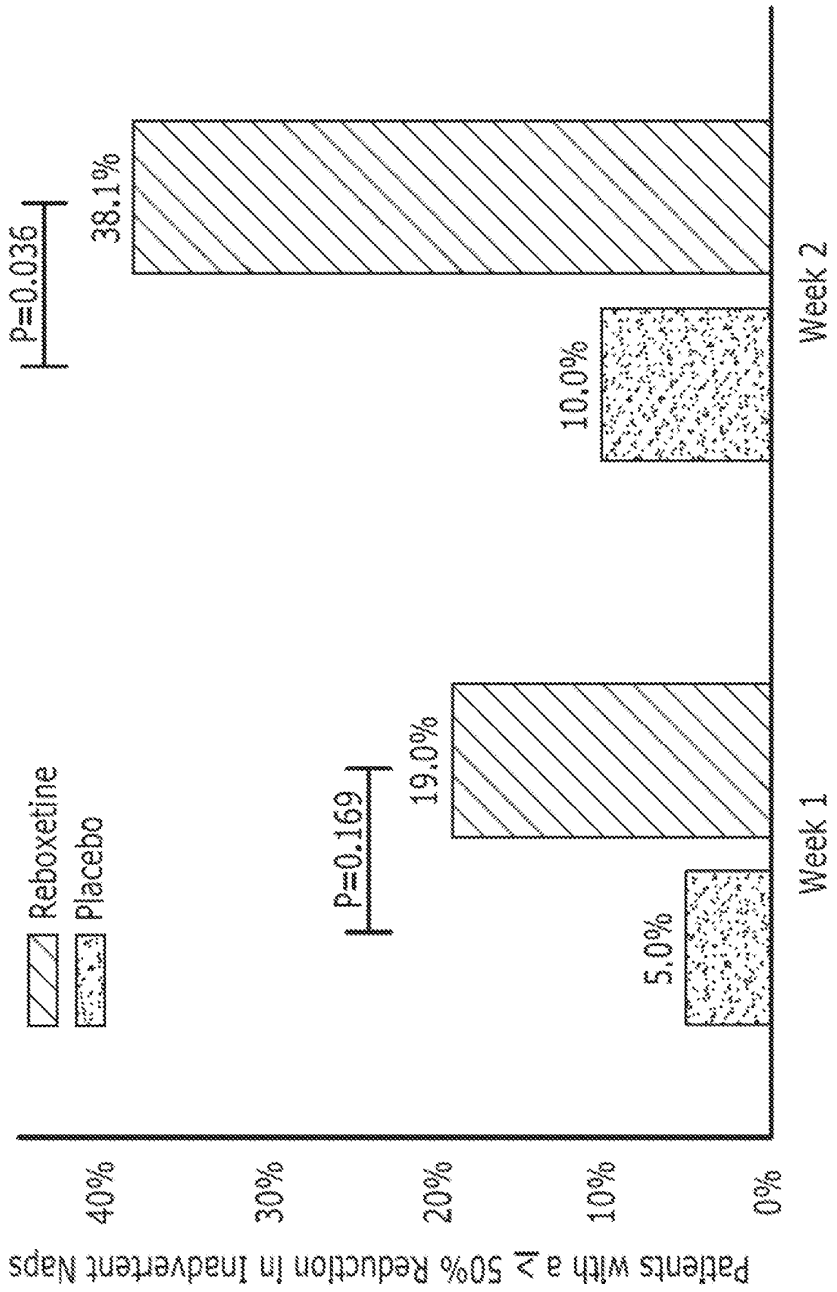

Patients with a ≥ 50% Reduction in Inadvertent Naps
40%
30%
20%
10%
0%
Reboxetine
Placebo
P=0.036
38.1%
10.0%
P=0.169
19.0%
5.0%
Week 1
Week 2

FIG. 10

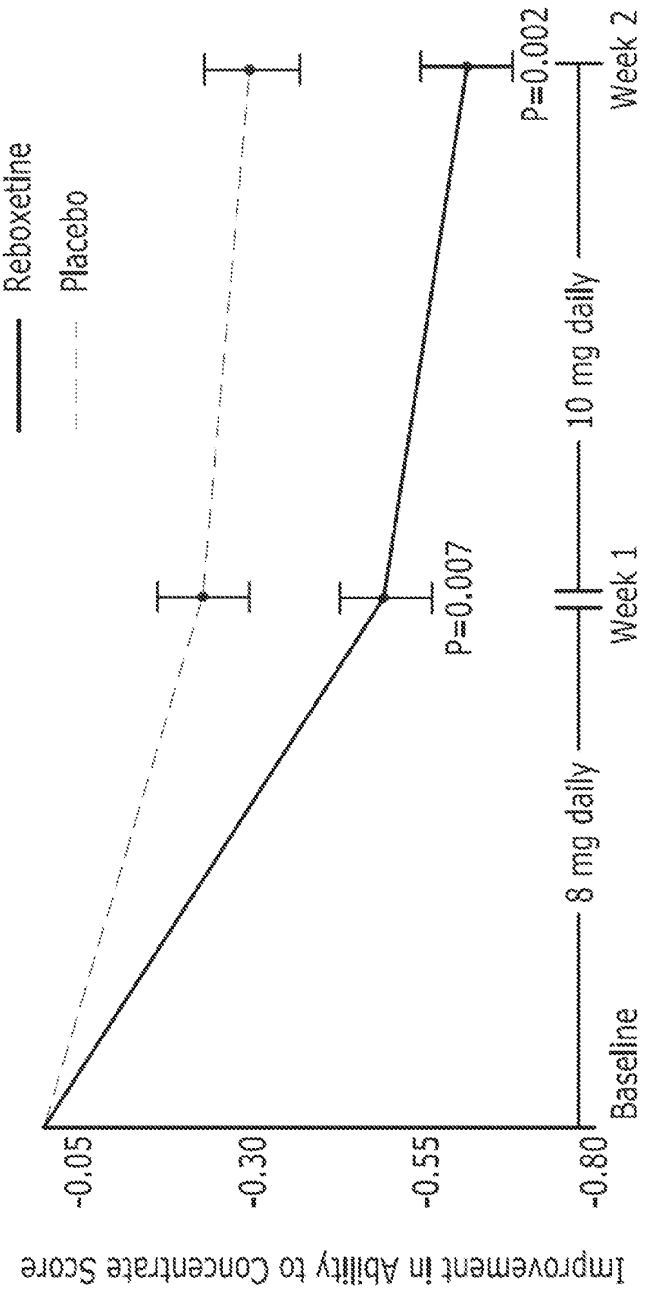

Reboxetine
Placebo
Improvement in Ability to Concentrate Score
-0.05
-0.30
-0.55
-0.80
Baseline
8 mg daily
Week 1
10 mg daily
Week 2
P=0.007
P=0.002
Ability to concentrate was collected daily on a 5-point scale where
1=very good, 2=good, 3=average, 4=poor, 5=very poor

FIG. 11

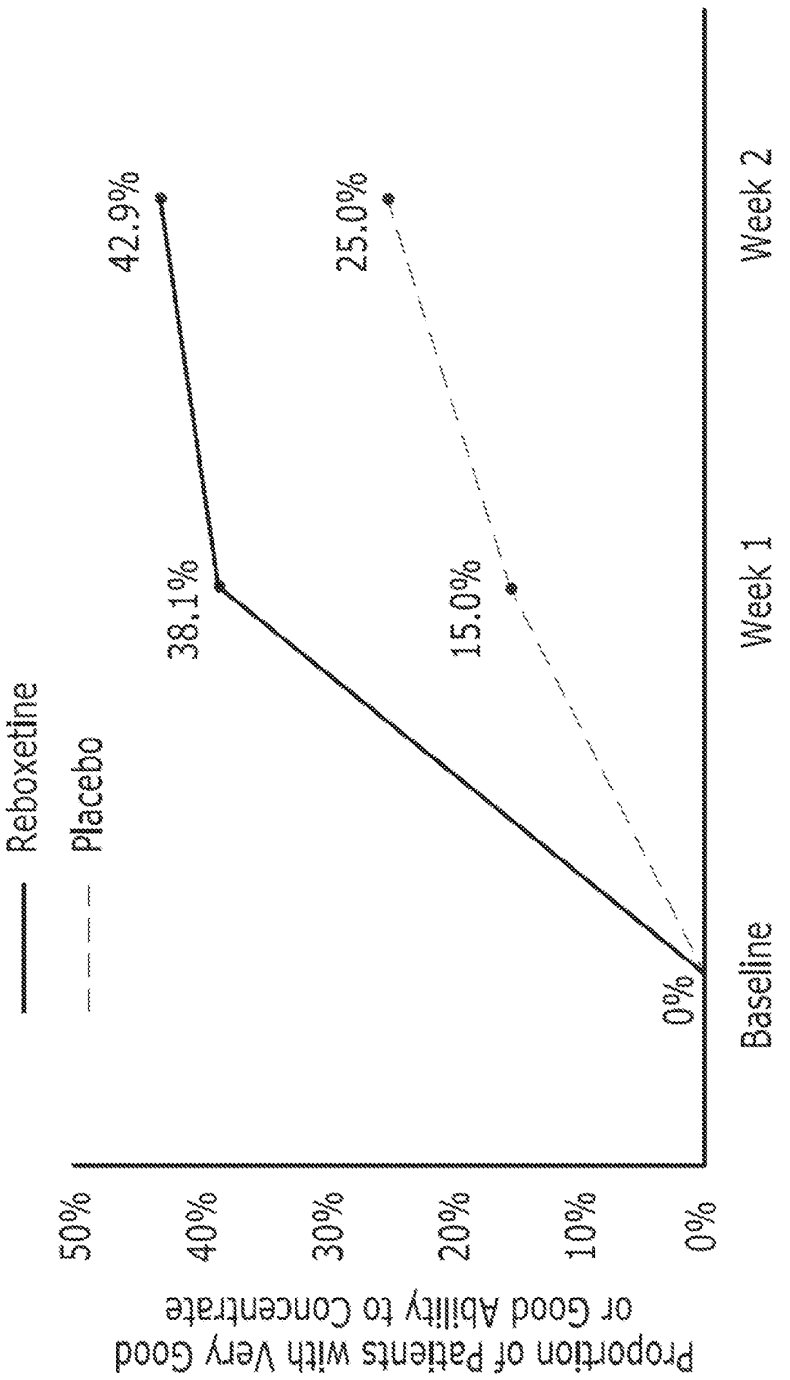

Proportion of Patients with Very Good
or Good Ability to Concentrate
50%
40%
30%
20%
10%
0%
Baseline
Week 1
Week 2
0%
38.1%
42.9%
15.0%
25.0%
Reboxetine
Placebo

FIG. 12

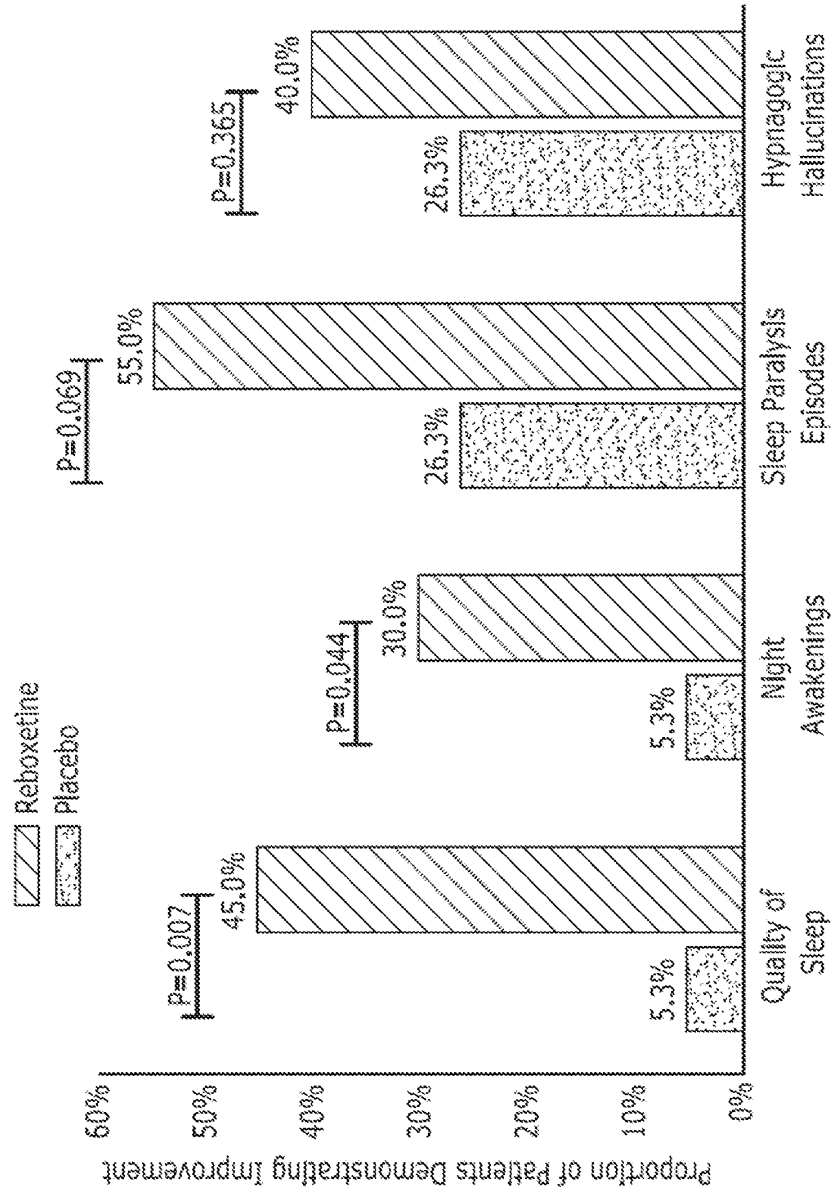

Reboxetine
Placebo
Proportion of Patients Demonstrating Improvement
60%
50%
40%
30%
20%
10%
0%
P=0.007
45.0%
5.3%
Quality of Sleep
P=0.044
30.0%
5.3%
Night Awakenings
P=0.069
55.0%
26.3%
Sleep Paralysis Episodes
P=0.365
40.0%
26.3%
Hypnagogic Hallucinations

FIG. 13

Characteristic	Reboxetine (n=46)	Placebo (n=44)
Age (years)	36	34.2
Sex (% male)	45.7%	34.1%
Time since diagnosis (years, mean)	7.9	6.3
Weekly frequency of cataplexy attacks (median)	19.3	21.6
CGI-S for EDS (mean)	5.3	5.1
ESS total score (mean)	18.3	17.3
CGI-S for narcolepsy (mean)	5.2	4.9
Use of modafinil or armodafinil (%)	32.6%	29.5%
Anxiety/depression, EQ-5D-5L scale (%)	45.5%	45.0%

FIG. 14

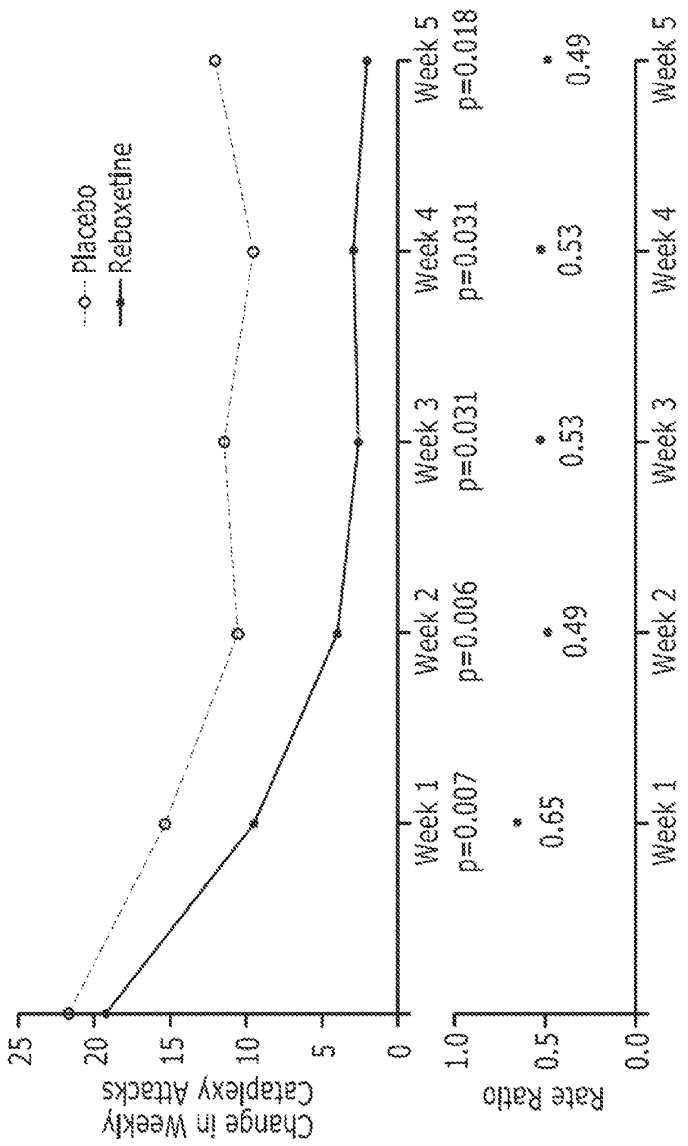

Placebo
Reboxetine
Change in Weekly Cataplexy Attacks
25
20
15
10
5
0
Rate Ratio
1.0
0.5
0.0
Week 1
p=0.007
0.65
Week 2
p=0.006
0.49
Week 3
p=0.031
0.53
Week 4
p=0.031
0.53
Week 5
p=0.018
0.49

FIG. 15

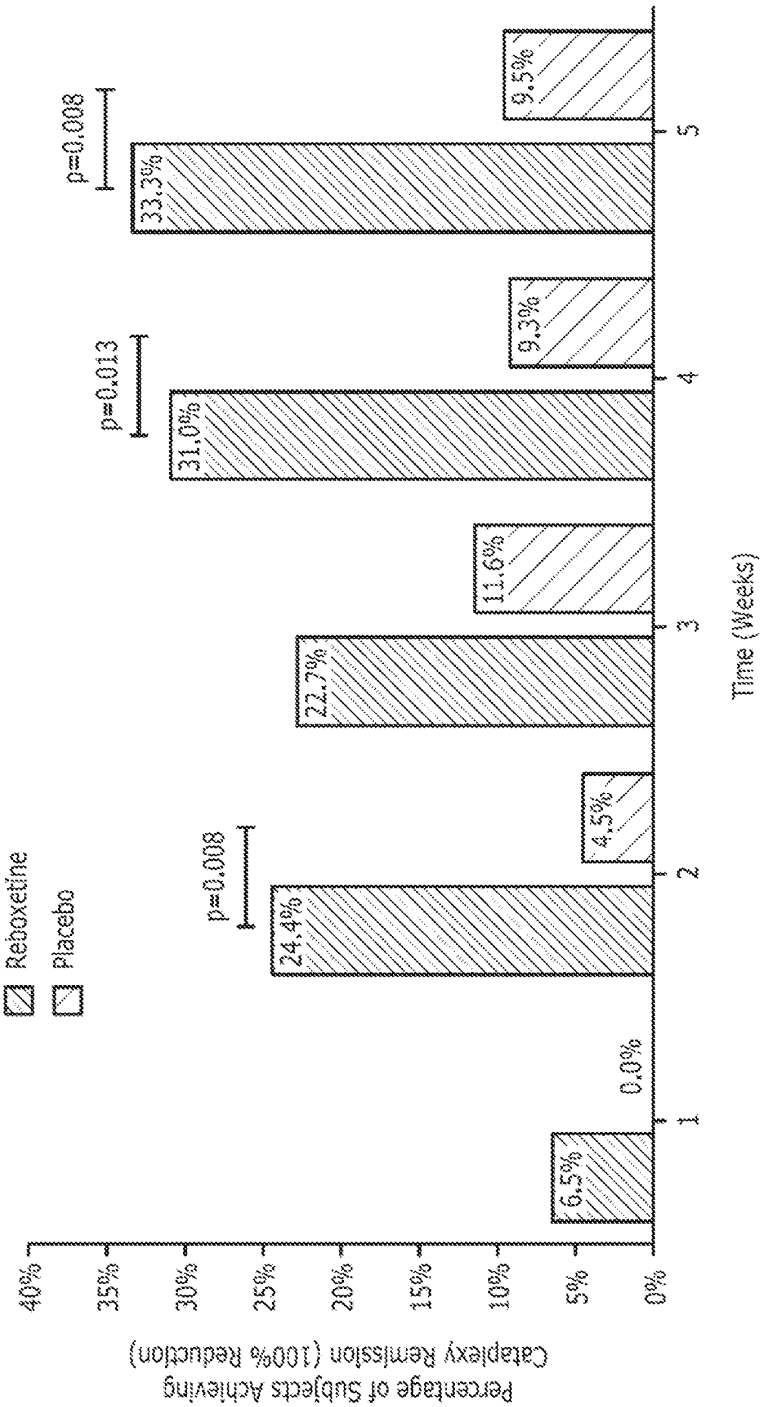

Percentage of Subjects Achieving
Cataplexy Remission (100% Reduction)
40%
35%
30%
25%
20%
15%
10%
5%
0%
Reboxetine
Placebo
p=0.008
p=0.013
p=0.008
6.5%
0.0%
24.4%
4.5%
22.7%
11.6%
31.0%
9.3%
33.3%
9.5%
1
2
3
4
5
Time (Weeks)

FIG. 16

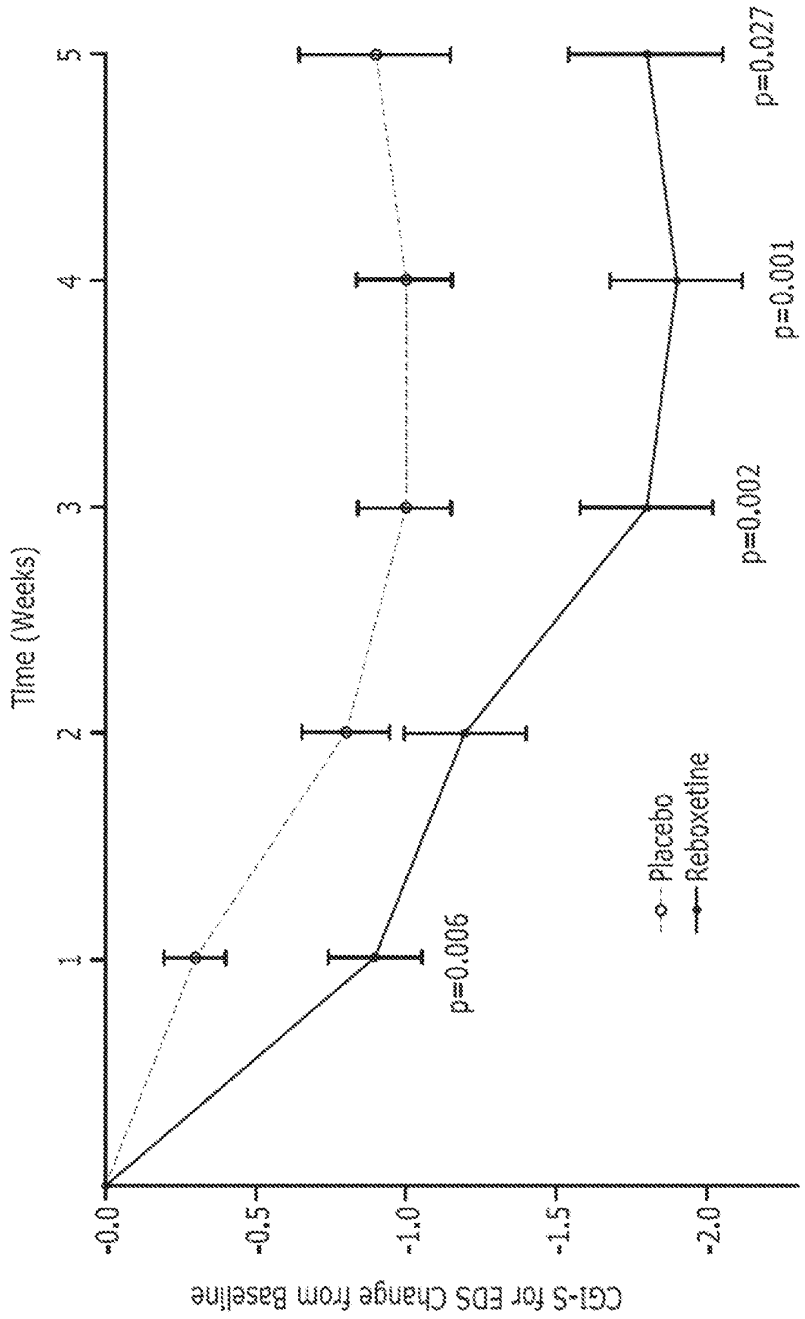

CGI-S for EDS Change from Baseline
-0.0
-0.5
-1.0
-1.5
-2.0
Time (Weeks)
1
2
3
4
5
Placebo
Reboxetine
p=0.006
p=0.002
p=0.001
p=0.027

FIG. 17

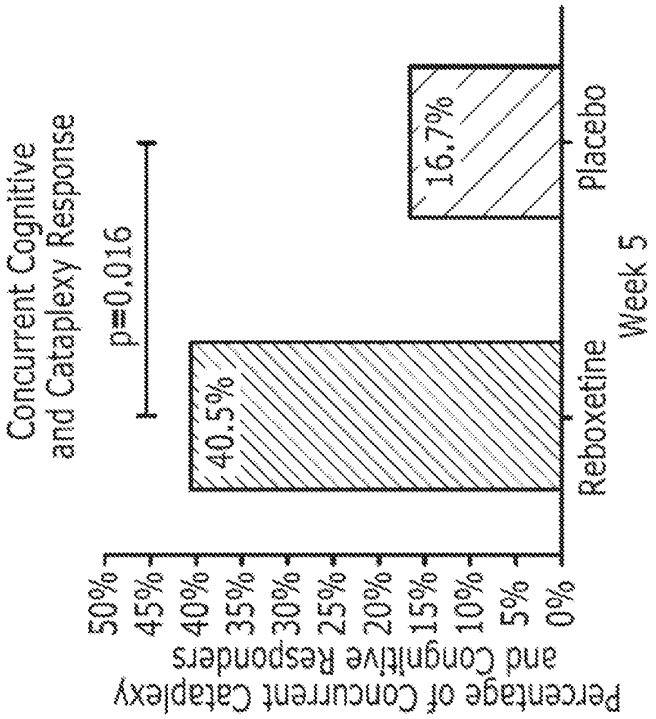


FIG. 18B

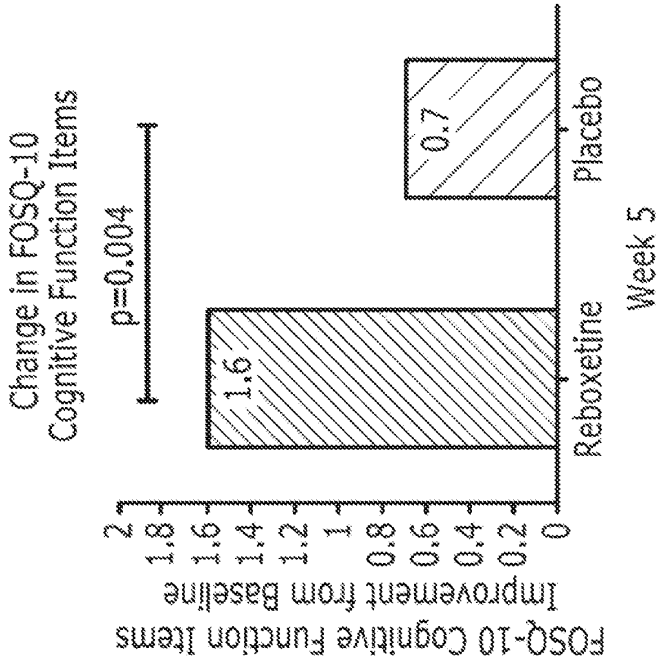


FIG. 18A

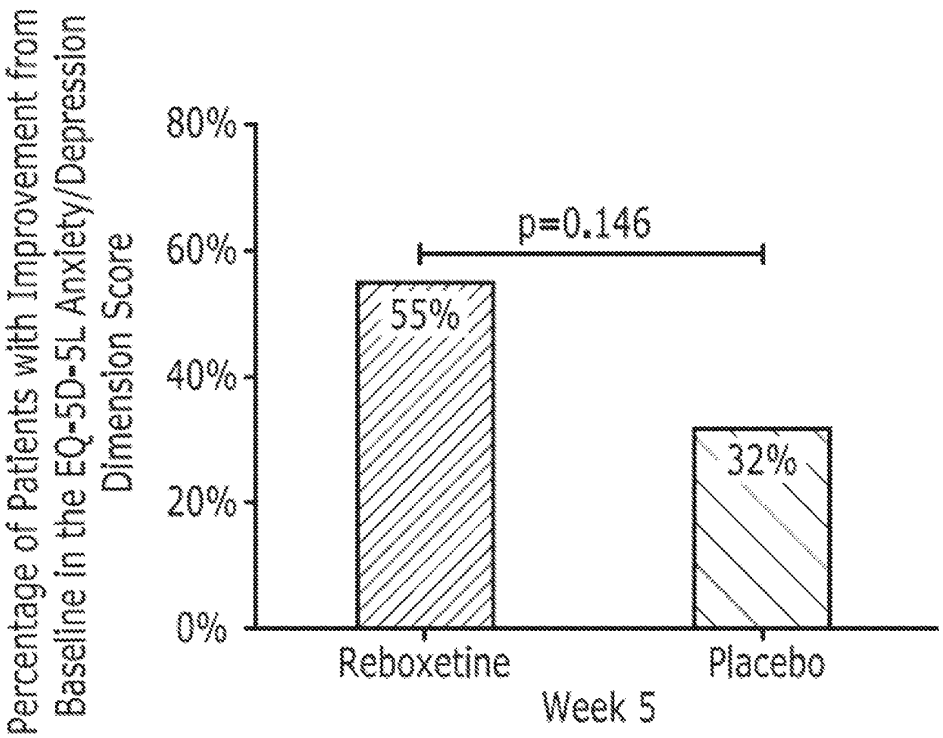

Percentage of Patients with Improvement from Baseline in the EQ-5D-5L Anxiety/Depression Dimension Score
80%
60%
40%
20%
0%
p=0.146
55%
32%
Reboxetine
Placebo
Week 5

FIG. 19

Current Treatment Types Used by NT1 Patients (n=203)

	Currently Take
Wake Promoting Agents	53%
Oxybates	47%
Stimulants	42%
Antidepressants (for narcolepsy)	38%
Other (nighttime medication)	10%
Other (daytime medication)	7%

37% of respondents diagnosed with depression, of whom 80% take medication to manage it.

FIG. 20

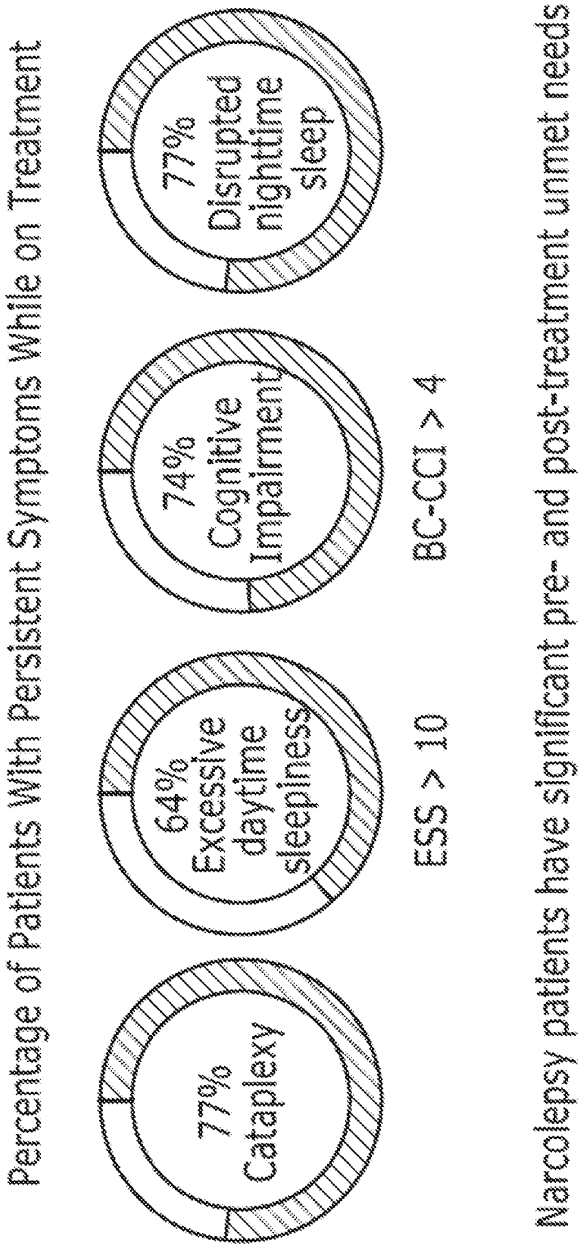

Percentage of Patients With Persistent Symptoms While on Treatment
77% Cataplexy
64% Excessive daytime sleepiness
74% Cognitive Impairment
77% Disrupted nighttime sleep
ESS > 10
BC-CCI > 4
Narcolepsy patients have significant pre- and post-treatment unmet needs

FIG. 21

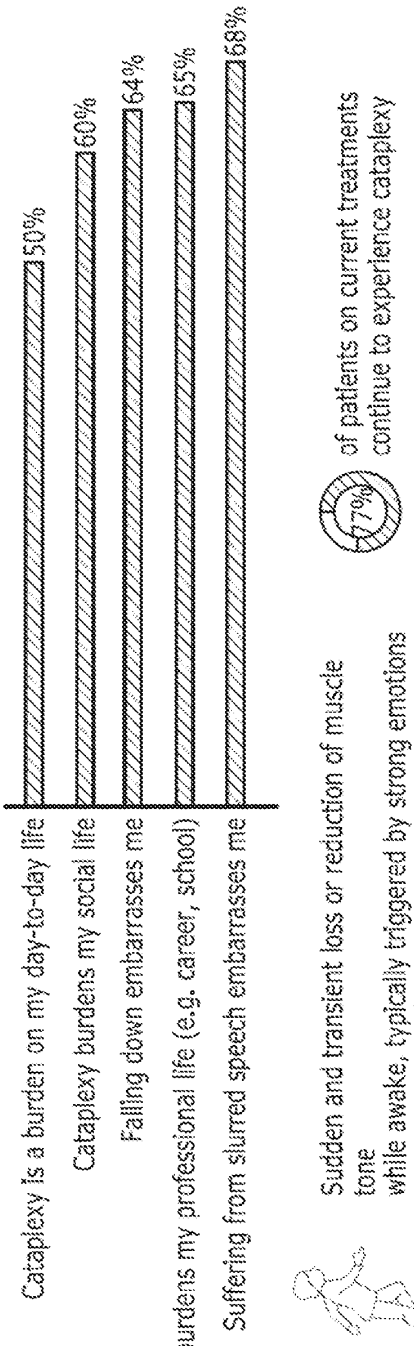

Cataplexy is a burden on my day-to-day life
50%
Cataplexy burdens my social life
60%
Falling down embarrasses me
64%
Cataplexy burdens my professional life (e.g. career, school)
65%
Suffering from slurred speech embarrasses me
68%
Sudden and transient loss or reduction of muscle tone
while awake, typically triggered by strong emotions
(e.g., laughter, elation, surprise, anger)
17%
of patients on current treatments continue to experience cataplexy

FIG. 22

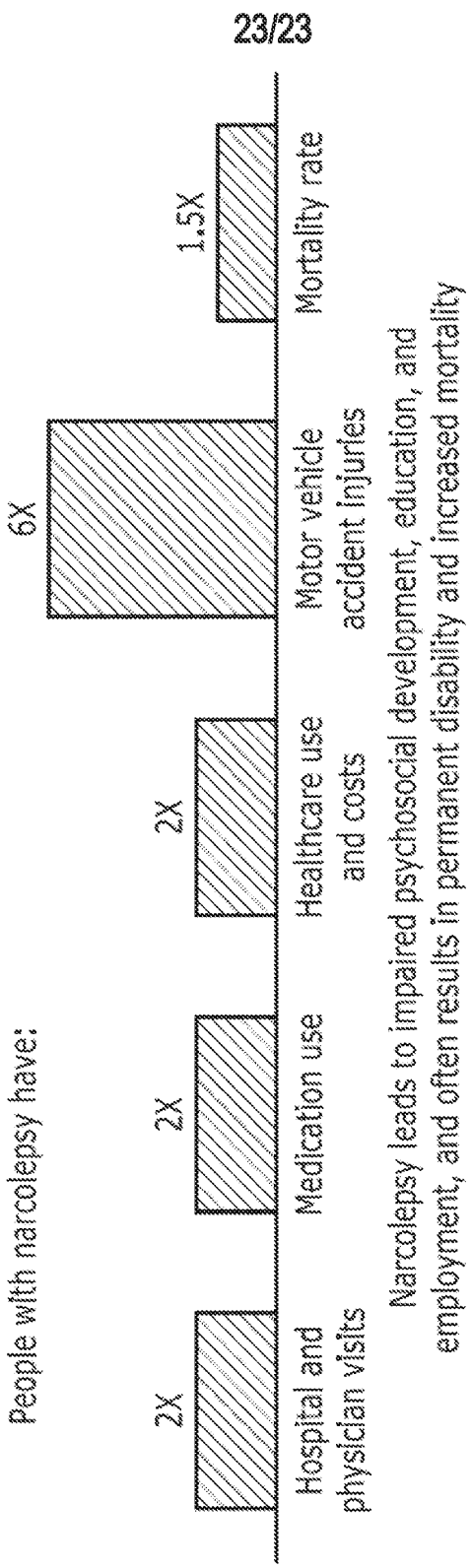

People with narcolepsy have:
2X
Hospital and physician visits
2X
Medication use
2X
Healthcare use and costs
6X
Motor vehicle accident injuries
1.5X
Mortality rate
Narcolepsy leads to impaired psychosocial development, education, and employment, and often results in permanent disability and increased mortality

FIG. 23