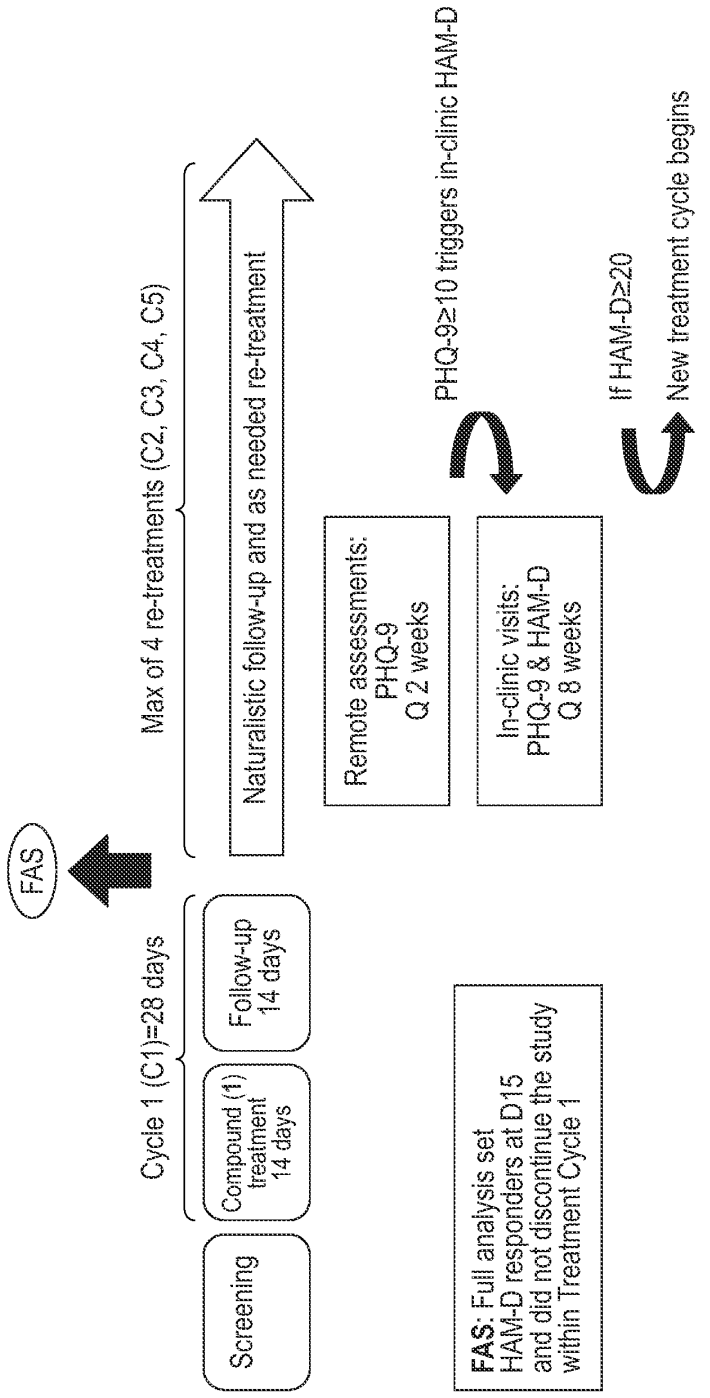

Screening
Cycle 1 (C1)=28 days
Compound (1) treatment 14 days
Follow-up 14 days
FAS
Max of 4 re-treatments (C2, C3, C4, C5)
Naturalistic follow-up and as needed re-treatment
Remote assessments: PHQ-9 Q 2 weeks
In-clinic visits: PHQ-9 & HAM-D Q 8 weeks
PHQ-9≥10 triggers in-clinic HAM-D
If HAM-D≥20
New treatment cycle begins
FAS: Full analysis set HAM-D responders at D15 and did not discontinue the study within Treatment Cycle 1

FIG. 1

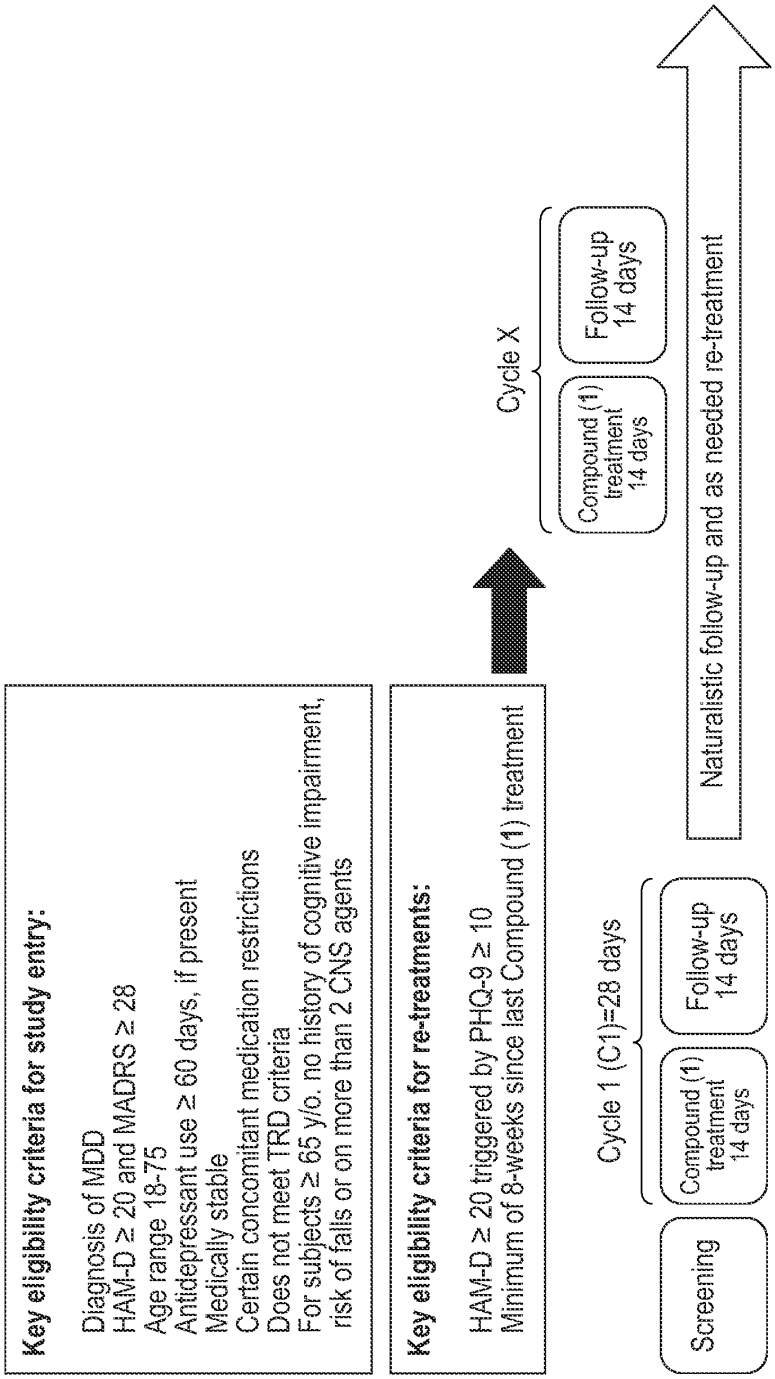

Key eligibility criteria for study entry:
Diagnosis of MDD
HAM-D ≥ 20 and MADRS ≥ 28
Age range 18-75
Antidepressant use ≥ 60 days, if present
Medically stable
Certain concomitant medication restrictions
Does not meet TRD criteria
For subjects ≥ 65 y/o. no history of cognitive impairment, risk of falls or on more than 2 CNS agents
Key eligibility criteria for re-treatments:
HAM-D ≥ 20 triggered by PHQ-9 ≥ 10
Minimum of 8-weeks since last Compound (1) treatment
Screening
Cycle 1 (C1)=28 days
Compound (1) treatment 14 days
Follow-up 14 days
Cycle X
Compound (1) treatment 14 days
Follow-up 14 days
Naturalistic follow-up and as needed re-treatment

FIG. 2

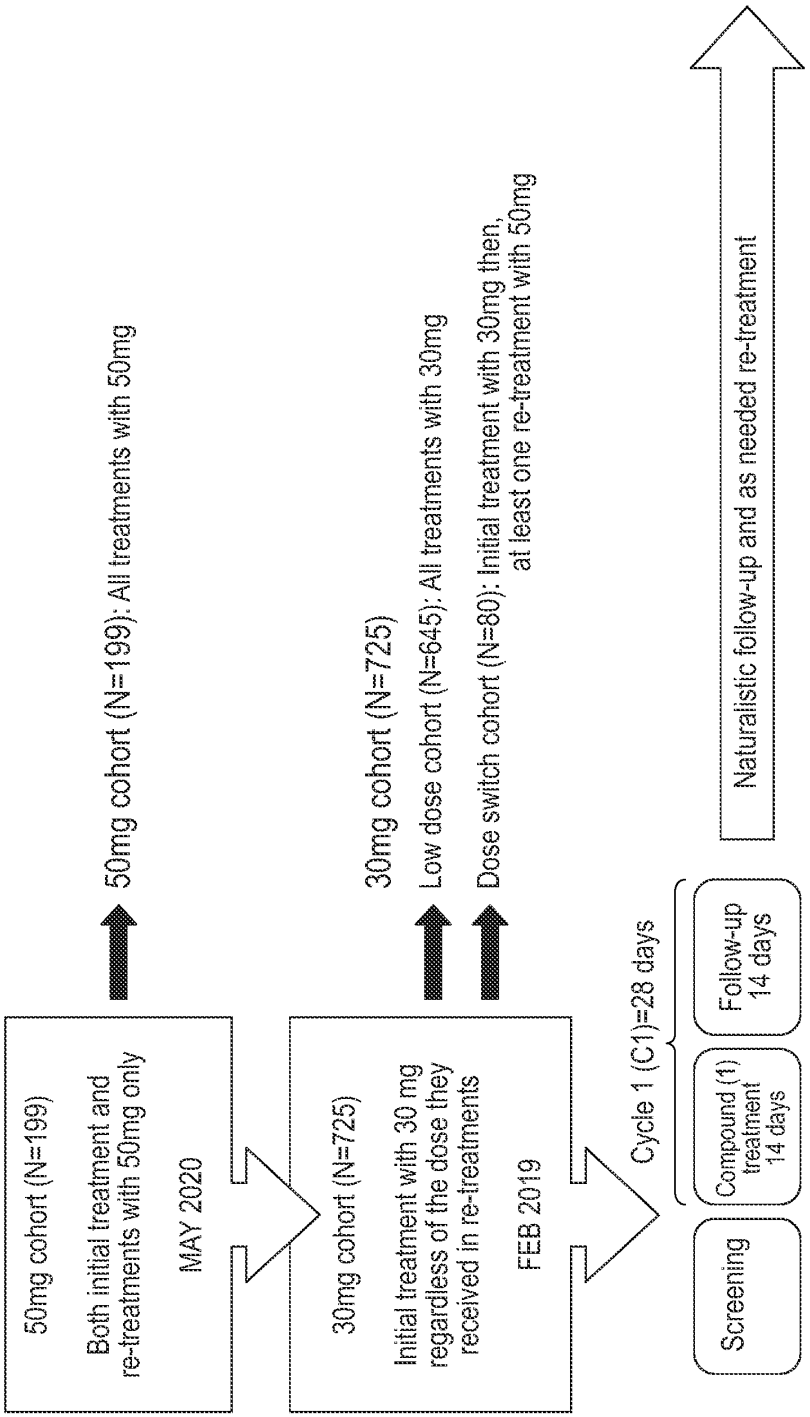
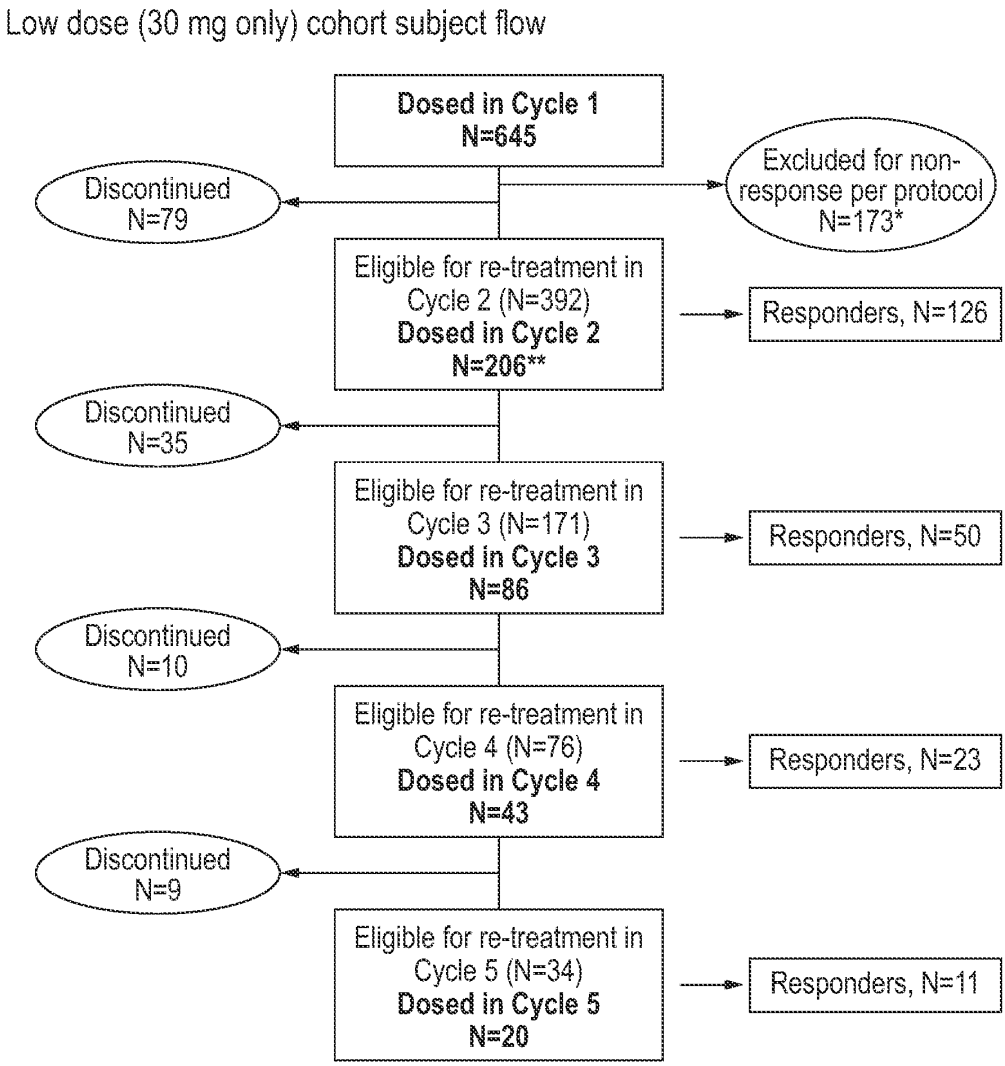

50mg cohort (N=199)
Both initial treatment and re-treatments with 50mg only
MAY 2020
30mg cohort (N=725)
Initial treatment with 30 mg regardless of the dose they received in re-treatments
FEB 2019
50mg cohort (N=199): All treatments with 50mg
30mg cohort (N=725)
Low dose cohort (N=645): All treatments with 30mg
Dose switch cohort (N=80): Initial treatment with 30mg then, at least one re-treatment with 50mg
Cycle 1 (C1)=28 days
Screening
Compound (1) treatment 14 days
Follow-up 14 days
Naturalistic follow-up and as needed re-treatment

FIG. 3



*One additional subject was a non-responder in C1 but completed the study.
**Includes 7 subjects who were non-responders but got dosed as part of PDs.
Note: A responder is defined as a subject with D15 HAM-D total score reduction >=50% since baseline. Non-responders in C1 are to be terminated from the study per protocol, but non-responders after C1 are not subject to termination from the study.

FIG. 4A

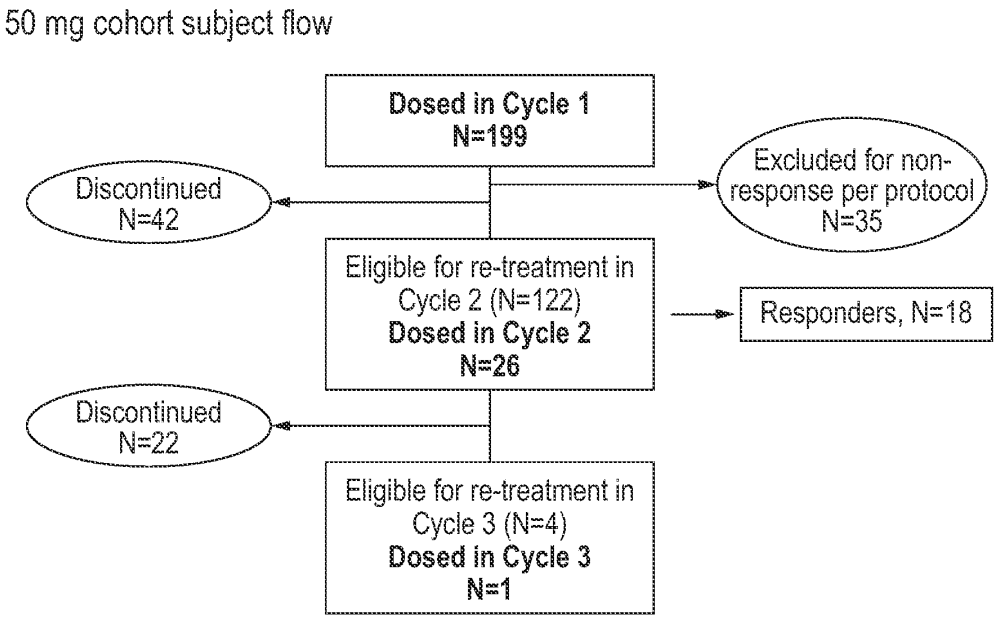

50 mg cohort subject flow
Dosed in Cycle 1
N=199
Discontinued
N=42
Excluded for non-response per protocol
N=35
Eligible for re-treatment in Cycle 2 (N=122)
Dosed in Cycle 2
N=26
Responders, N=18
Discontinued
N=22
Eligible for re-treatment in Cycle 3 (N=4)
Dosed in Cycle 3
N=1

FIG. 4B

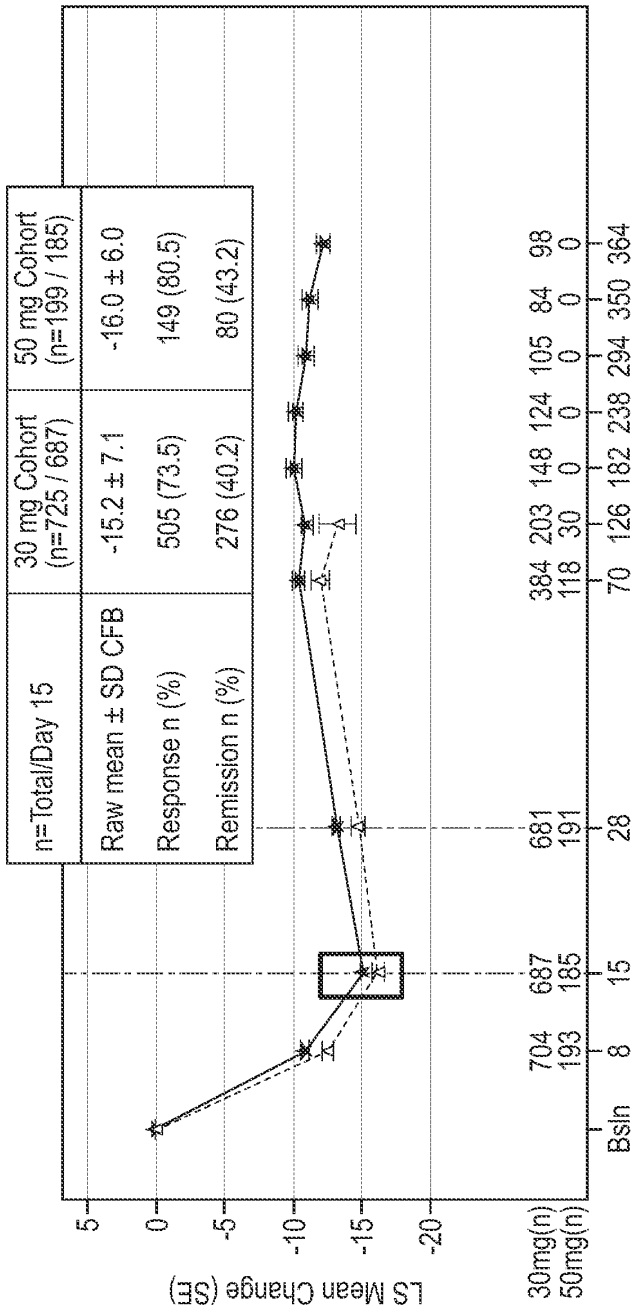

n=Total/Day 15
30 mg Cohort (n=725 / 687)
50 mg Cohort (n=199 / 185)
Raw mean ± SD CFB
-15.2 ± 7.1
-16.0 ± 6.0
Response n (%)
505 (73.5)
149 (80.5)
Remission n (%)
276 (40.2)
80 (43.2)
LS Mean Change (SE)
5
0
-5
-10
-15
-20
30mg(n)
50mg(n)
704 687 681
193 185 191
384 203 148 124 105 84 98
118 30 0 0 0 0 0
Bsln 8 15 28 70 126 182 238 294 350 364
Timepoint (Days)

FIG. 5

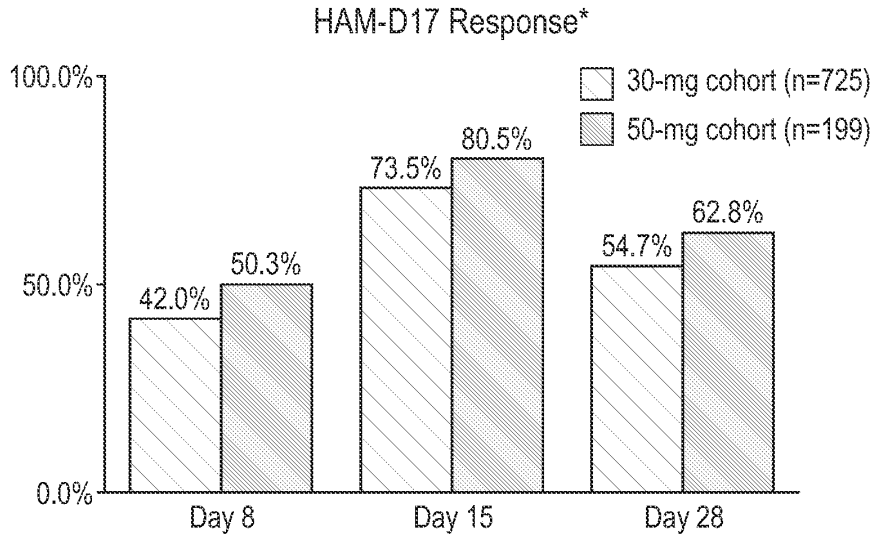

HAM-D17 Response*
100.0%
50.0%
0.0%
30-mg cohort (n=725)
50-mg cohort (n=199)
42.0%
50.3%
73.5%
80.5%
54.7%
62.8%
Day 8
Day 15
Day 28

FIG. 6A

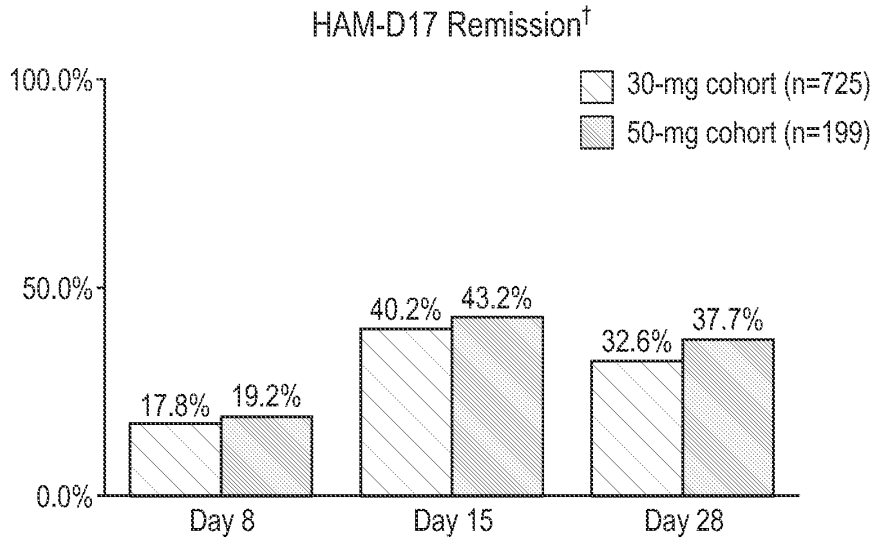

HAM-D17 Remission†
100.0%
50.0%
0.0%
30-mg cohort (n=725)
50-mg cohort (n=199)
17.8%
19.2%
40.2%
43.2%
32.6%
37.7%
Day 8
Day 15
Day 28

FIG. 6B

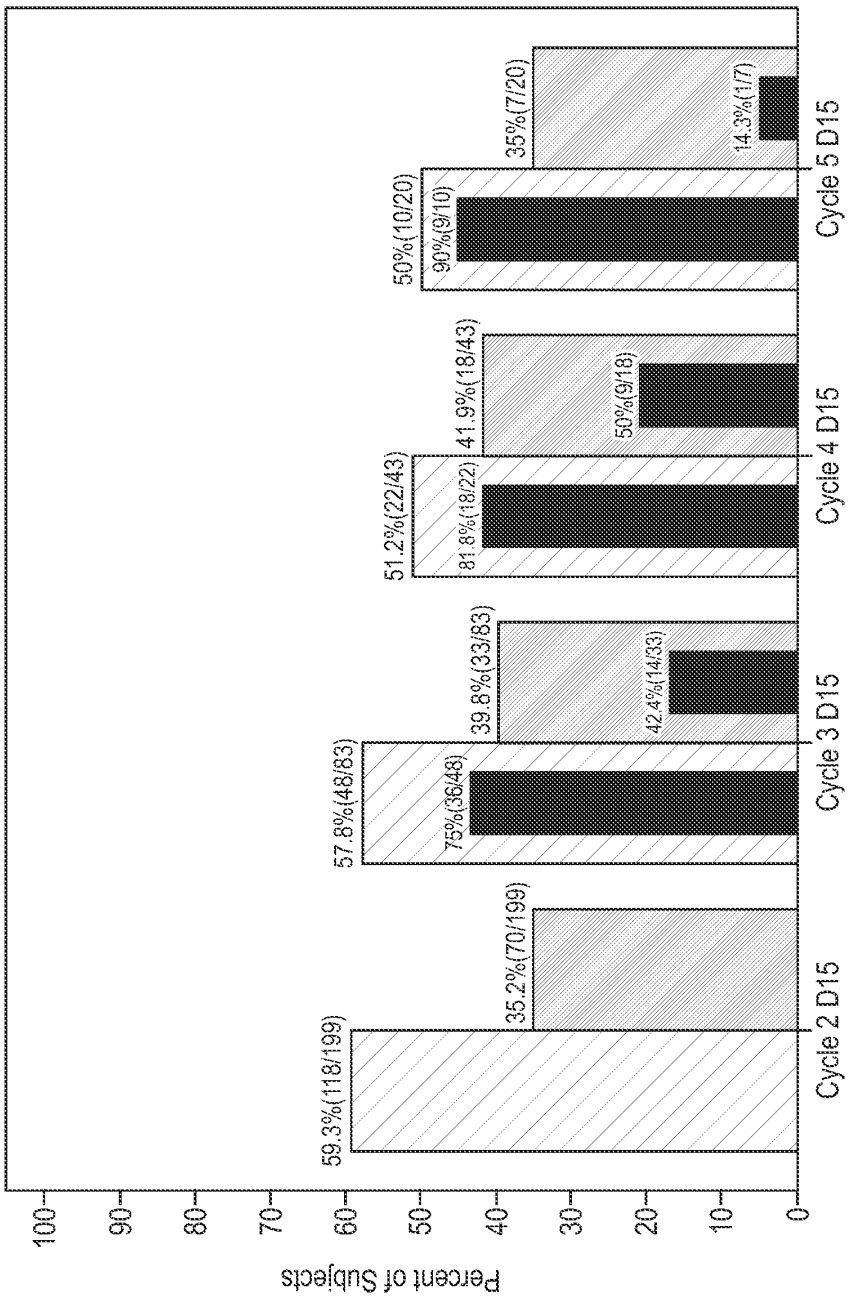

Percent of Subjects
100
90
80
70
60
50
40
30
20
10
0
59.3%(118/199)
35.2%(70/199)
57.8%(48/83)
75%(36/48)
39.8%(33/83)
42.4%(14/33)
51.2%(22/43)
81.8%(18/22)
41.9%(18/43)
50%(9/18)
50%(10/20)
90%(9/10)
35%(7/20)
14.3%(1/7)
Cycle 2 D15
Cycle 3 D15
Cycle 4 D15
Cycle 5 D15
Time point
Inside Bar represents % of Responders in Previous Cycle
Responder
Non Responder

FIG. 7

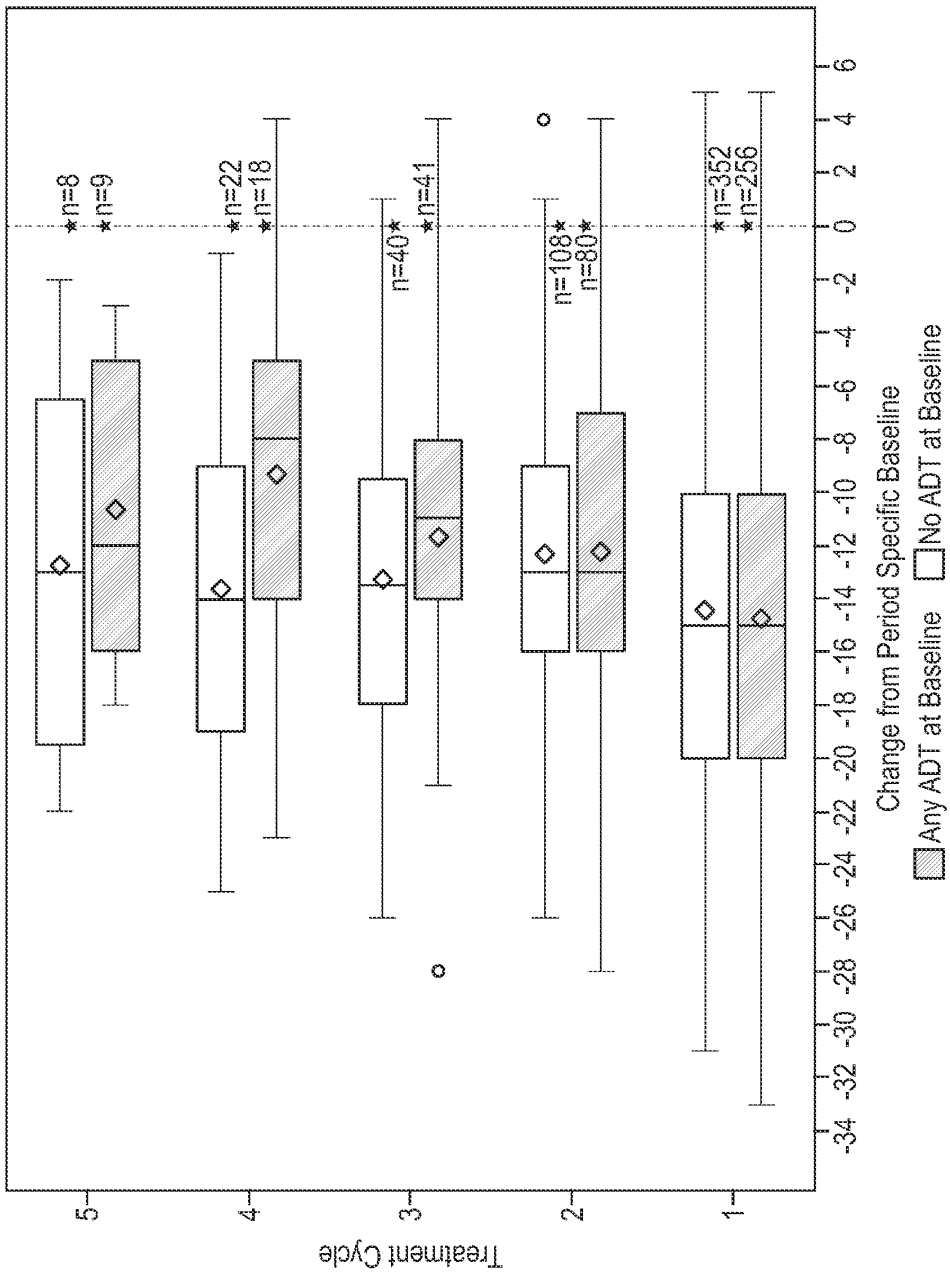

Treatment Cycle
5
4
3
2
1
n=8
n=9
n=22
n=18
n=40
n=41
n=108
n=80
n=352
n=256
-34 -32 -30 -28 -26 -24 -22 -20 -18 -16 -14 -12 -10 -8 -6 -4 -2 0 2 4 6
Change from Period Specific Baseline
Any ADT at Baseline
No ADT at Baseline

FIG. 8

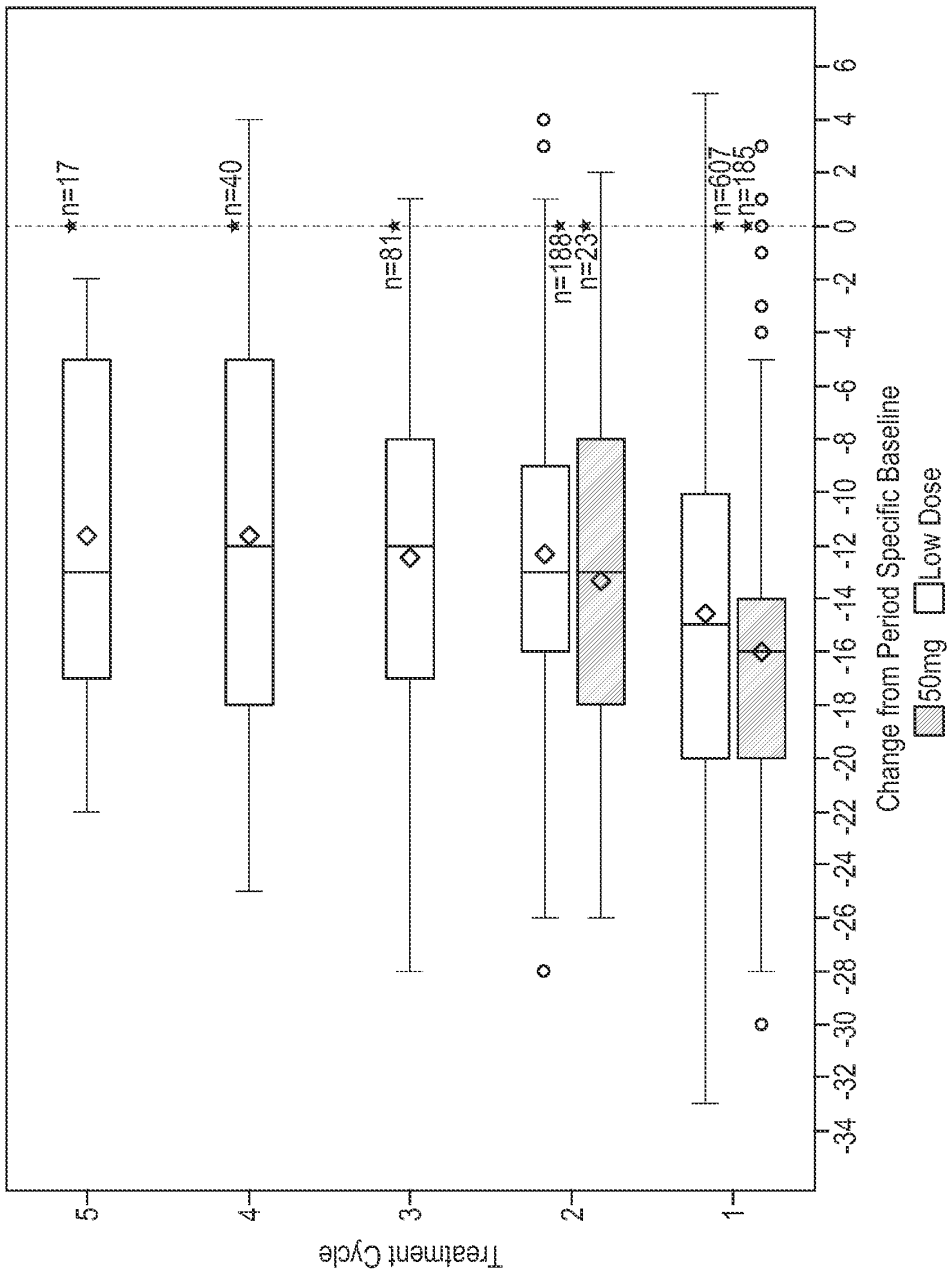

Treatment Cycle
5
4
3
2
1
n=17
n=40
n=81
n=188
n=23
n=607
n=185
6
4
2
0
-2
-4
-6
-8
-10
-12
-14
-16
-18
-20
-22
-24
-26
-28
-30
-32
-34
Change from Period Specific Baseline
50mg
Low Dose

FIG. 9

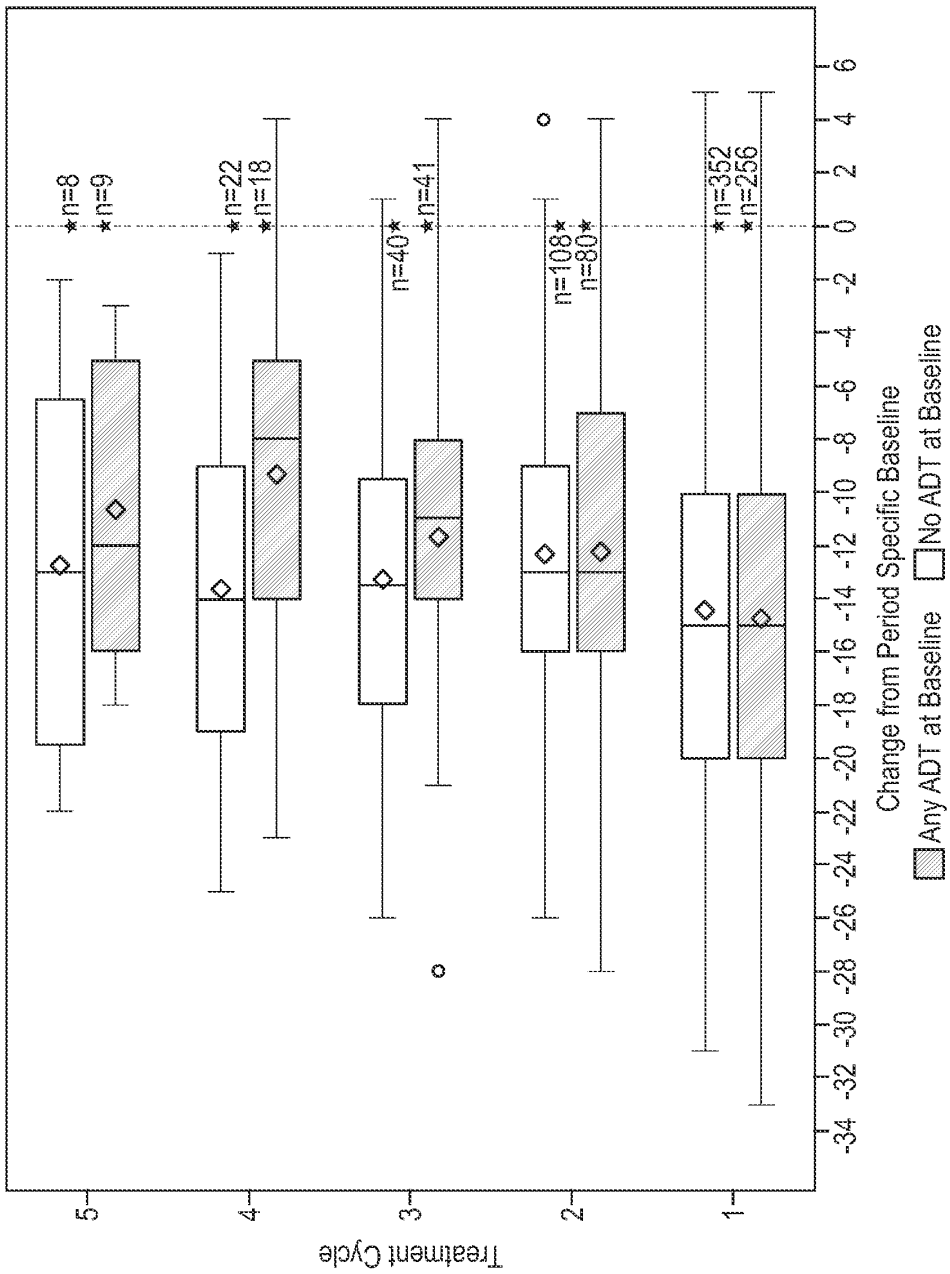

Treatment Cycle
5
4
3
2
1
n=8
n=9
n=22
n=18
n=40
n=41
n=108
n=80
n=352
n=256
-34 -32 -30 -28 -26 -24 -22 -20 -18 -16 -14 -12 -10 -8 -6 -4 -2 0 2 4 6
Change from Period Specific Baseline
Any ADT at Baseline
No ADT at Baseline

FIG. 10

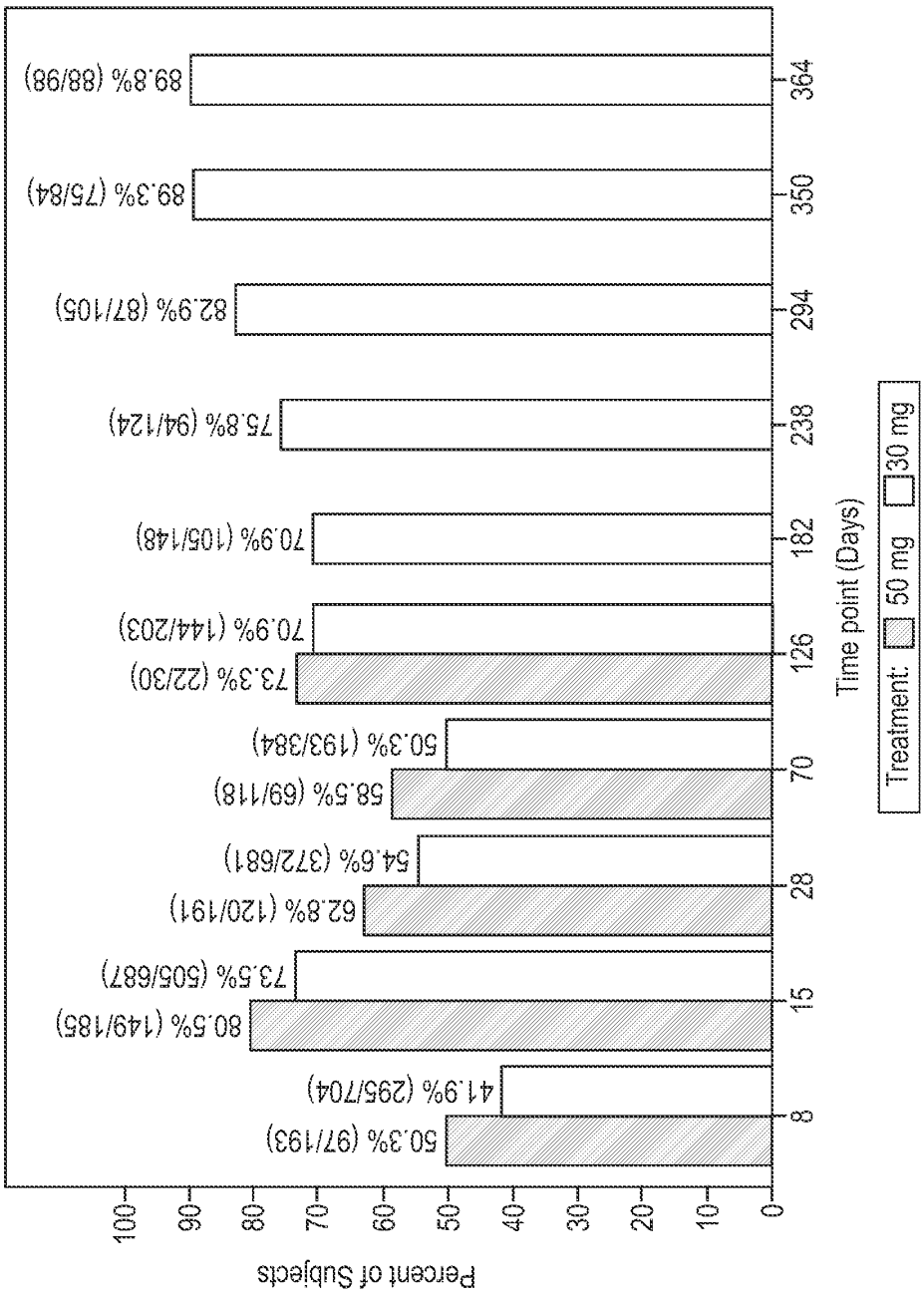

Percent of Subjects
0
10
20
30
40
50
60
70
80
90
100
50.3% (97/193)
41.9% (295/704)
80.5% (149/185)
73.5% (505/687)
62.8% (120/191)
54.6% (372/681)
58.5% (69/118)
50.3% (193/384)
73.3% (22/30)
70.9% (144/203)
70.9% (105/148)
75.8% (94/124)
82.9% (87/105)
89.3% (75/84)
89.8% (88/98)
8
15
28
70
126
182
238
294
350
364
Time point (Days)
Treatment: 50 mg 30 mg

FIG. 11

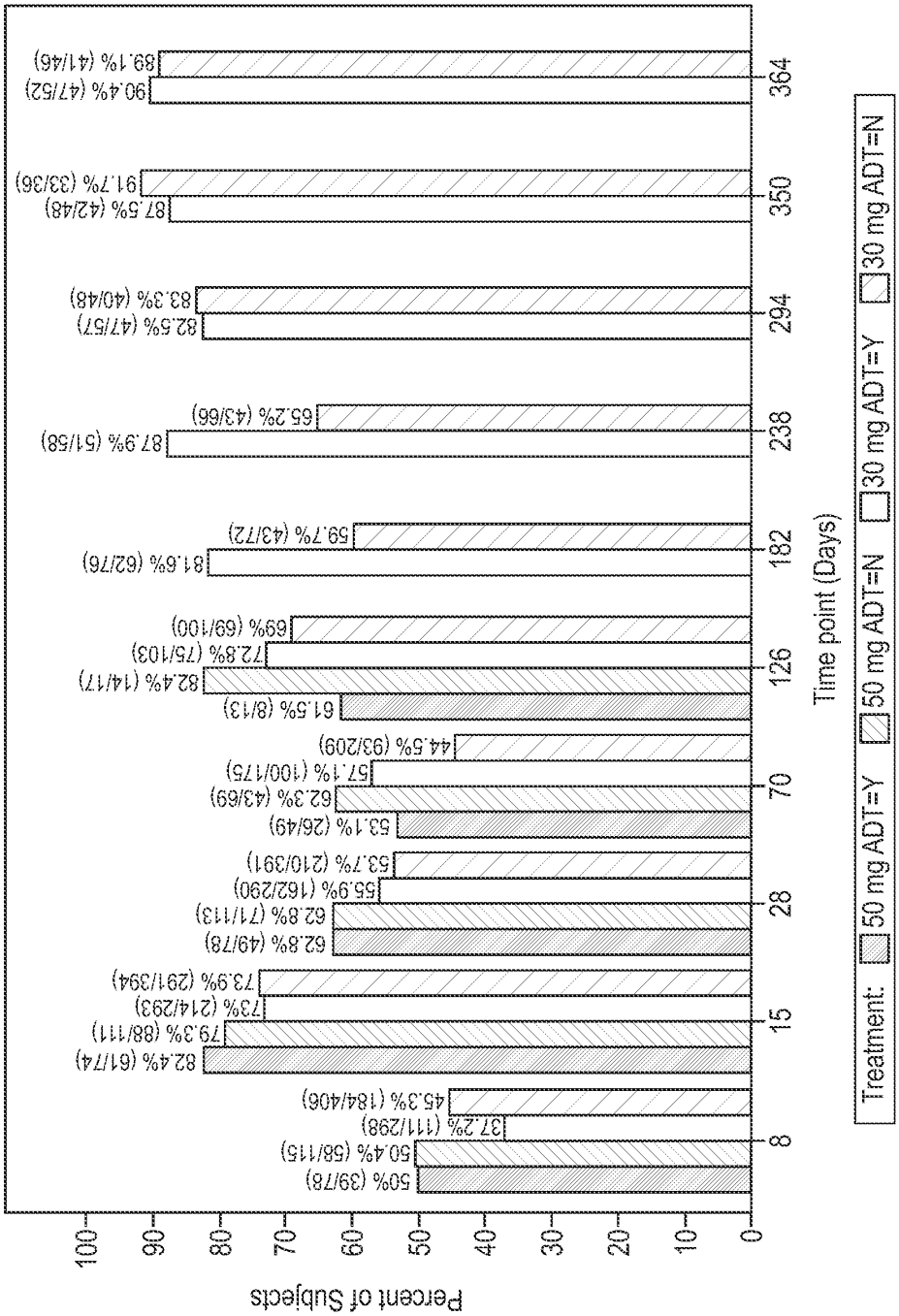

Percent of Subjects
0
10
20
30
40
50
60
70
80
90
100
Time point (Days)
8
15
28
70
126
182
238
294
350
364
50% (39/78)
50.4% (58/115)
37.2% (111/298)
45.3% (184/406)
82.4% (61/74)
79.3% (88/111)
73% (214/293)
73.9% (291/394)
62.8% (49/78)
62.8% (71/113)
55.9% (162/290)
53.7% (210/391)
53.1% (26/49)
62.3% (43/69)
57.1% (100/175)
44.5% (93/209)
61.5% (8/13)
82.4% (14/17)
72.8% (75/103)
69% (69/100)
81.6% (62/76)
59.7% (43/72)
87.9% (51/58)
65.2% (43/66)
82.5% (47/57)
83.3% (40/48)
87.5% (42/48)
91.7% (33/36)
90.4% (47/52)
89.1% (41/46)
Treatment:
50 mg ADT=Y
50 mg ADT=N
30 mg ADT=Y
30 mg ADT=N

FIG. 12

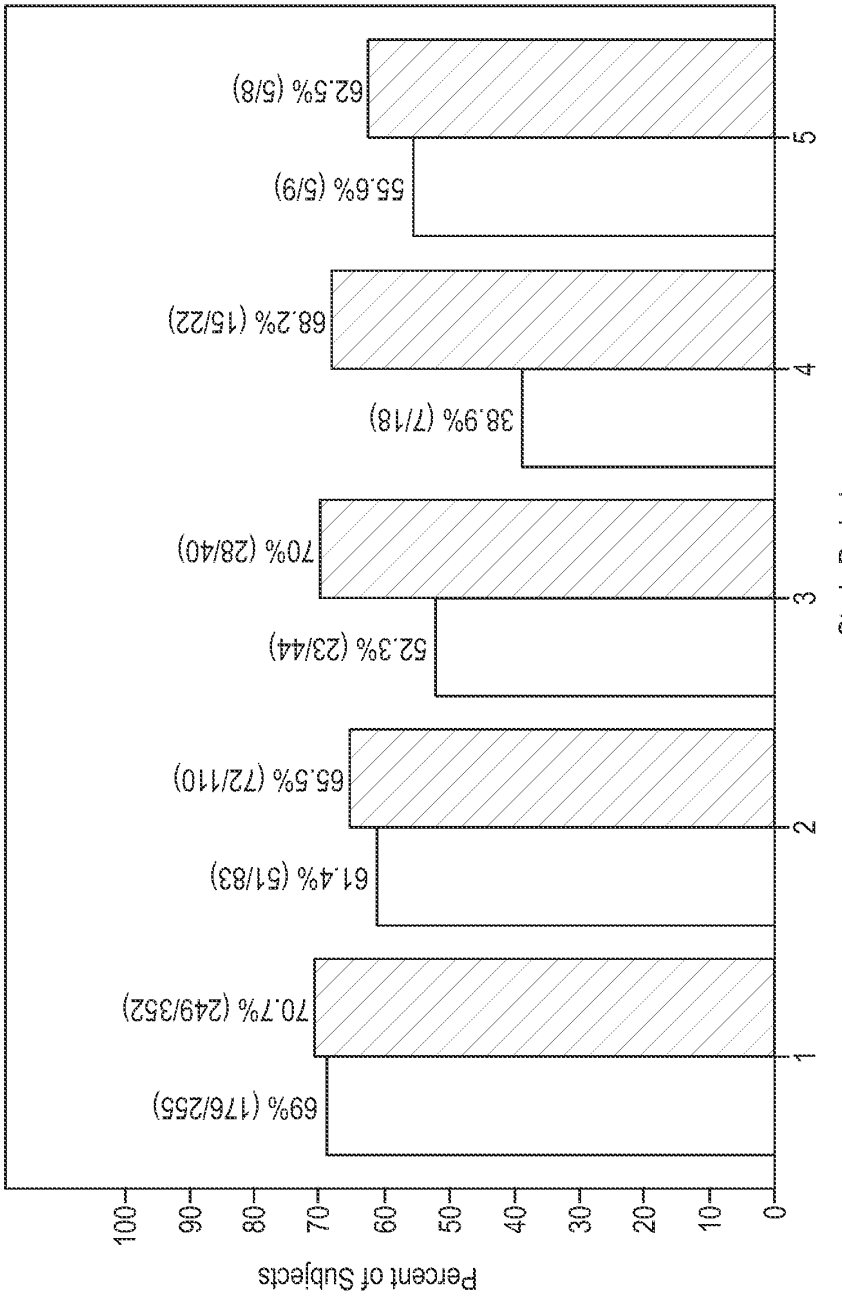

Percent of Subjects
0
10
20
30
40
50
60
70
80
90
100
69% (176/255)
70.7% (249/352)
61.4% (51/83)
65.5% (72/110)
52.3% (23/44)
70% (28/40)
38.9% (7/18)
68.2% (15/22)
55.6% (5/9)
62.5% (5/8)
1
2
3
4
5
Study Period
Treatment:
Low Dose ADT=Y
Low Dose ADT=N

FIG. 13

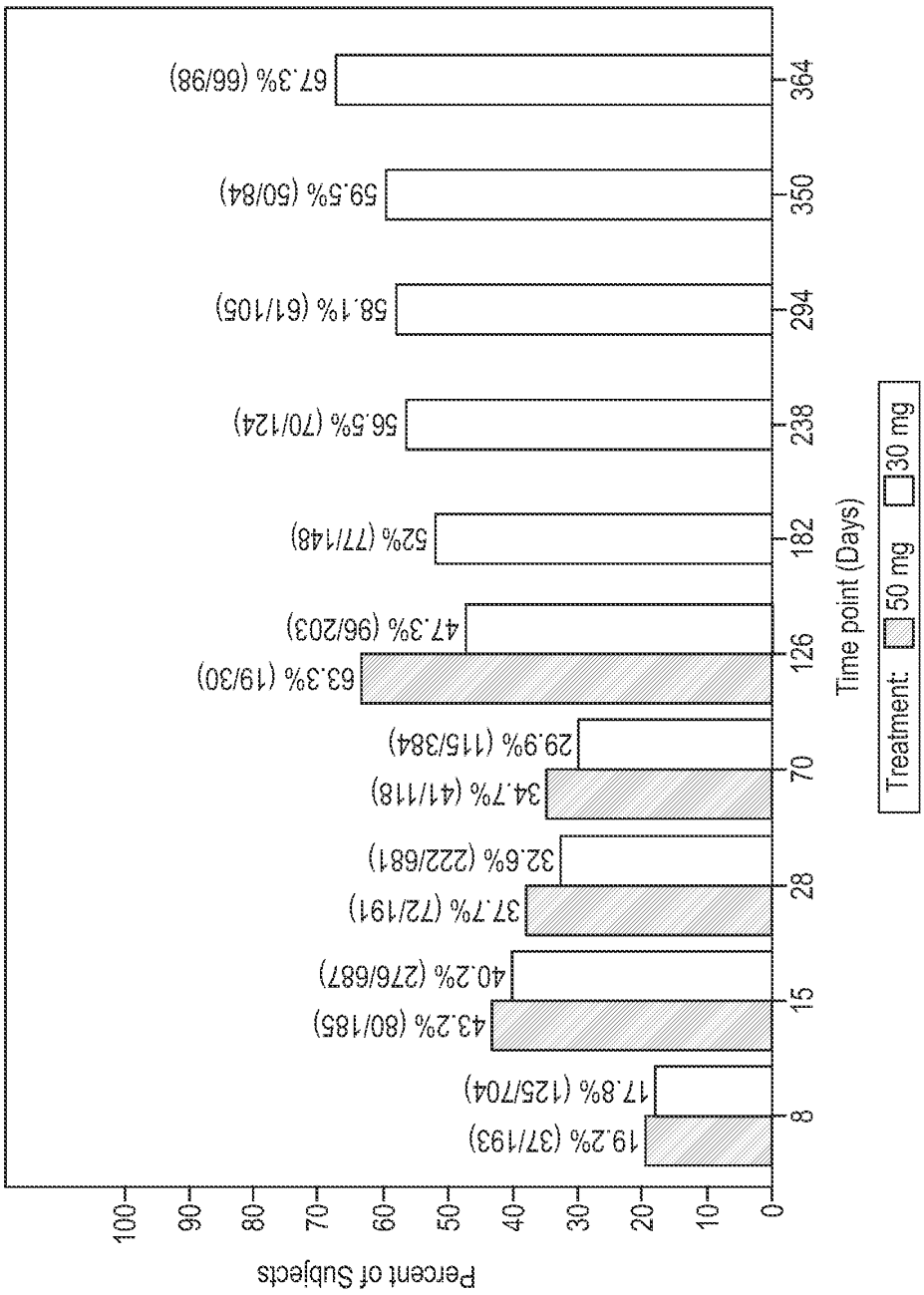

Percent of Subjects
0
10
20
30
40
50
60
70
80
90
100
Time point (Days)
8
15
28
70
126
182
238
294
350
364
Treatment: 50 mg 30 mg
19.2% (37/193)
17.8% (125/704)
43.2% (80/185)
40.2% (276/687)
37.7% (72/191)
32.6% (222/681)
34.7% (41/118)
29.9% (115/384)
63.3% (19/30)
47.3% (96/203)
52% (77/148)
56.5% (70/124)
58.1% (61/105)
59.5% (50/84)
67.3% (66/98)

FIG. 14

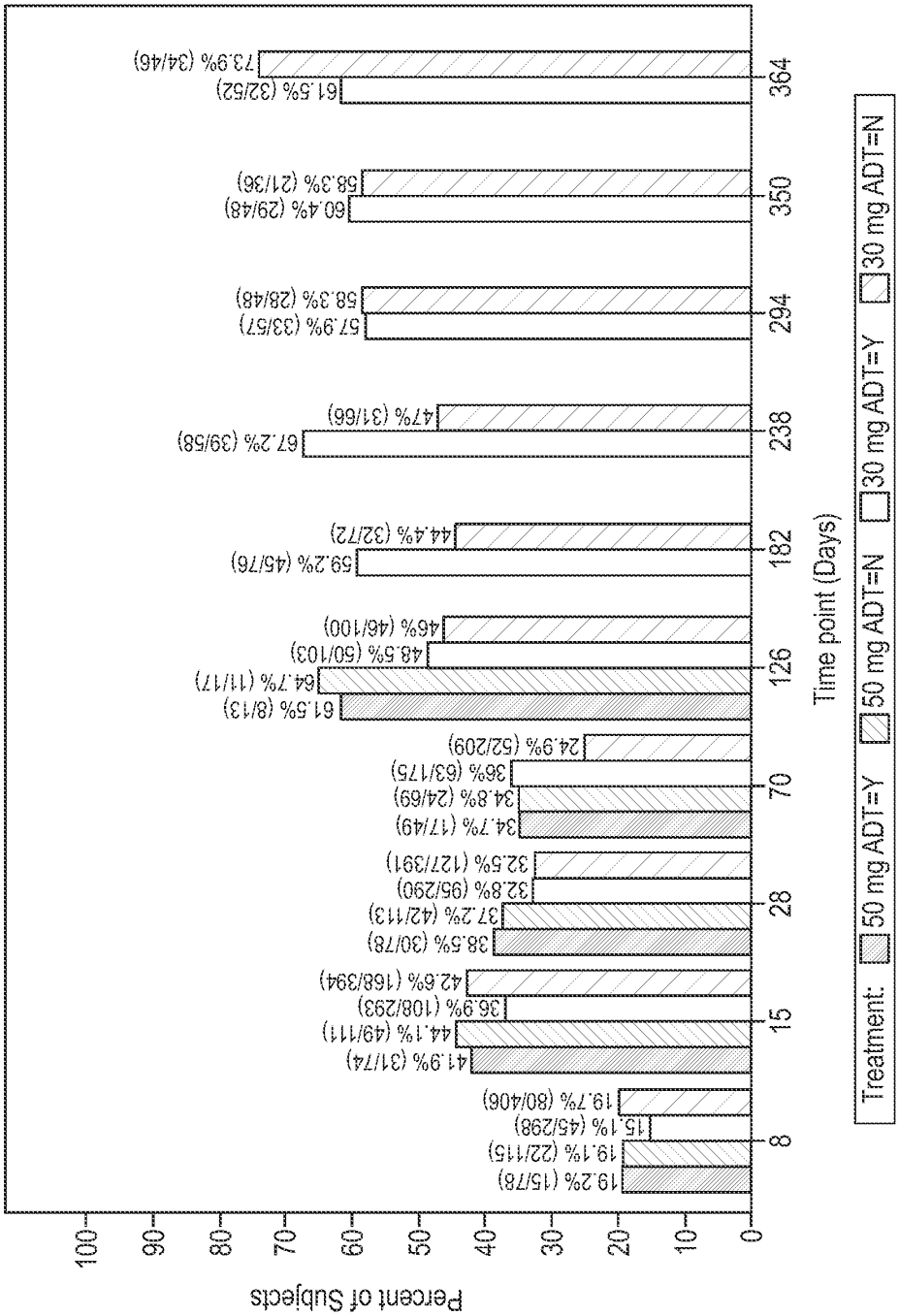

Percent of Subjects
0
10
20
30
40
50
60
70
80
90
100
Time point (Days)
8
15
28
70
126
182
238
294
350
364
19.2% (15/78)
19.1% (22/115)
15.1% (45/298)
19.7% (80/406)
41.9% (31/74)
44.1% (49/111)
36.9% (108/293)
42.6% (168/394)
38.5% (30/78)
37.2% (42/113)
32.8% (95/290)
32.5% (127/391)
34.7% (17/49)
34.8% (24/69)
36% (63/175)
24.9% (52/209)
61.5% (8/13)
64.7% (11/17)
48.5% (50/103)
46% (46/100)
44.4% (32/72)
59.2% (45/76)
47% (31/66)
67.2% (39/58)
57.9% (33/57)
58.3% (28/48)
60.4% (29/48)
58.3% (21/36)
61.5% (32/52)
73.9% (34/46)
Treatment:
50 mg ADT=Y
50 mg ADT=N
30 mg ADT=Y
30 mg ADT=N

FIG. 15

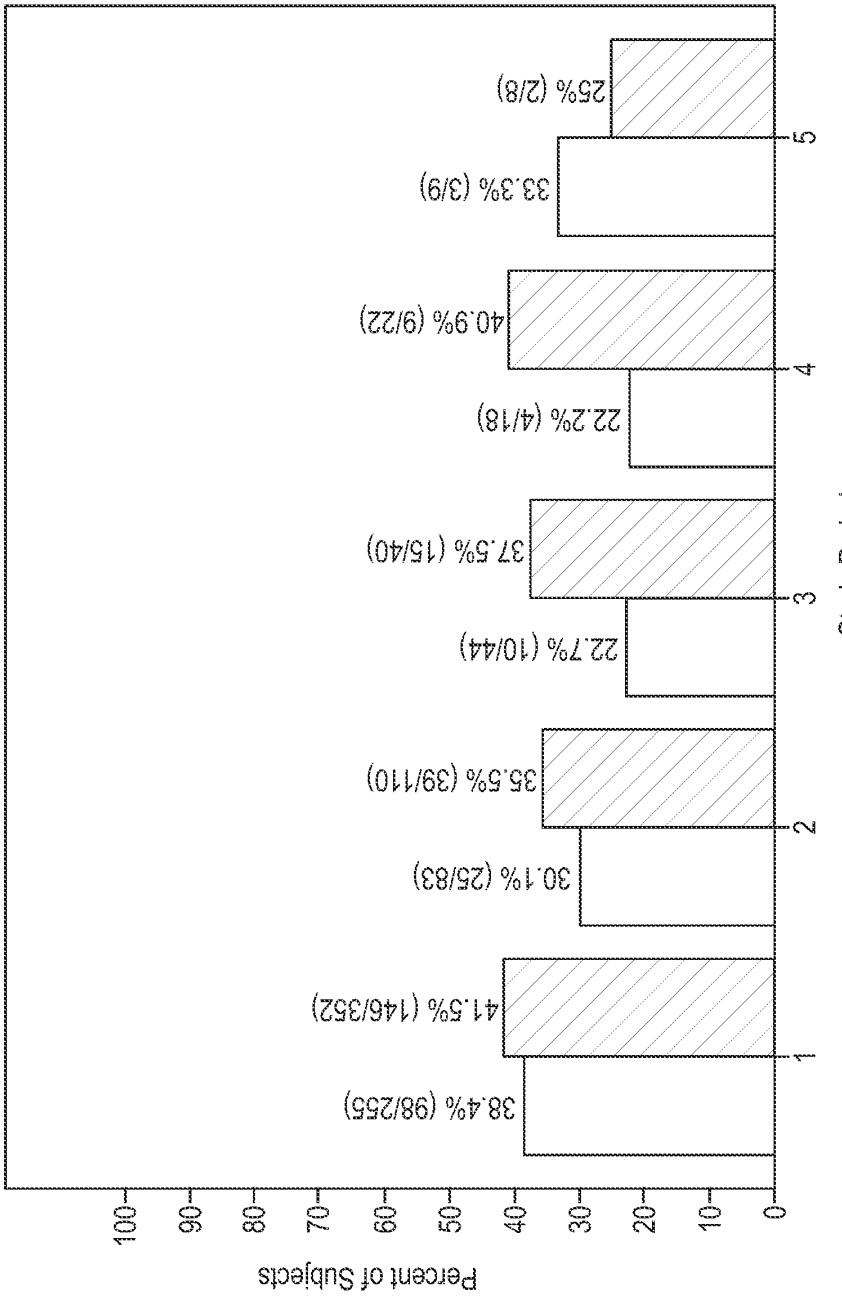

Percent of Subjects
0
10
20
30
40
50
60
70
80
90
100
38.4% (98/255)
41.5% (146/352)
30.1% (25/83)
35.5% (39/110)
22.7% (10/44)
37.5% (15/40)
22.2% (4/18)
40.9% (9/22)
33.3% (3/9)
25% (2/8)
1
2
3
4
5
Study Period
Treatment: Low Dose ADT=Y Low Dose ADT=N

FIG. 16

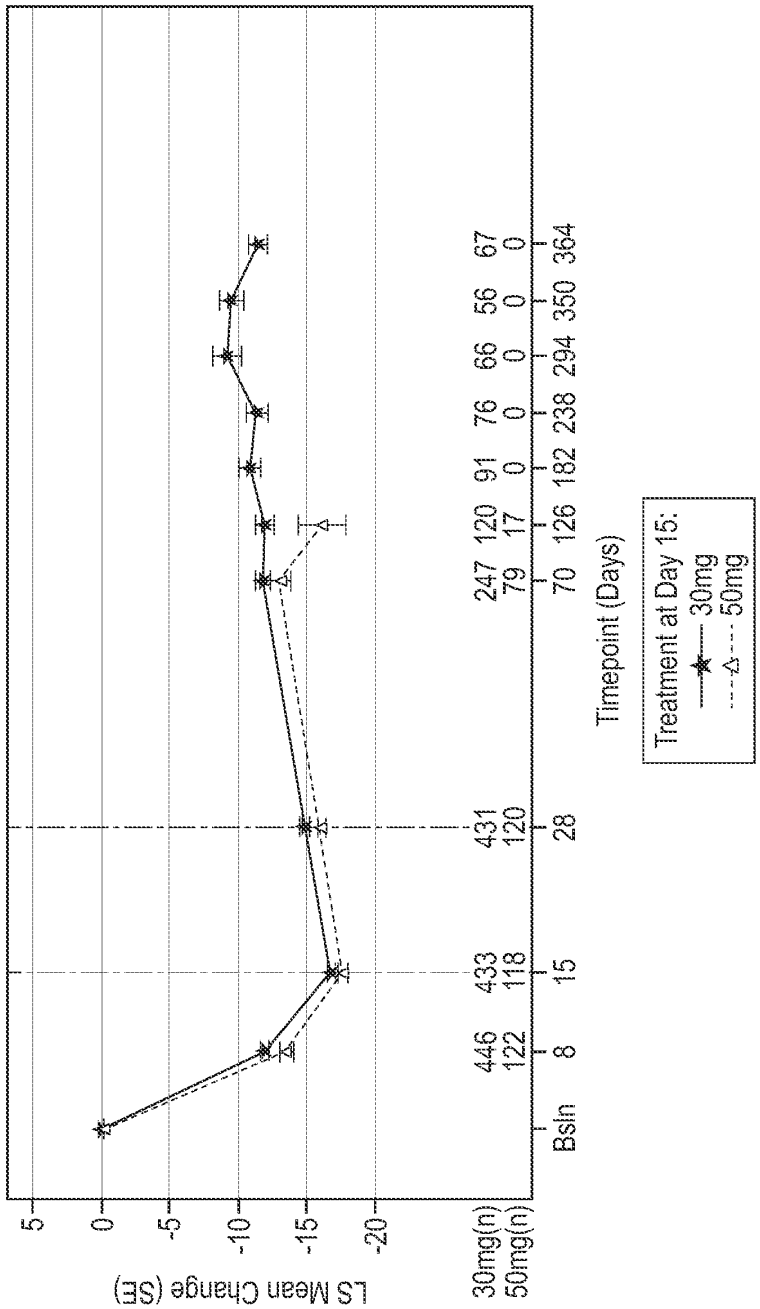

LS Mean Change (SE)
5
0
-5
-10
-15
-20
30mg(n)
50mg(n)
Bsln
8
15
28
Timepoint (Days)
446
122
433
118
431
120
247
79
120
17
91
0
76
0
66
0
56
0
67
0
70
126
182
238
294
350
364
Treatment at Day 15:
30mg
50mg

FIG. 17

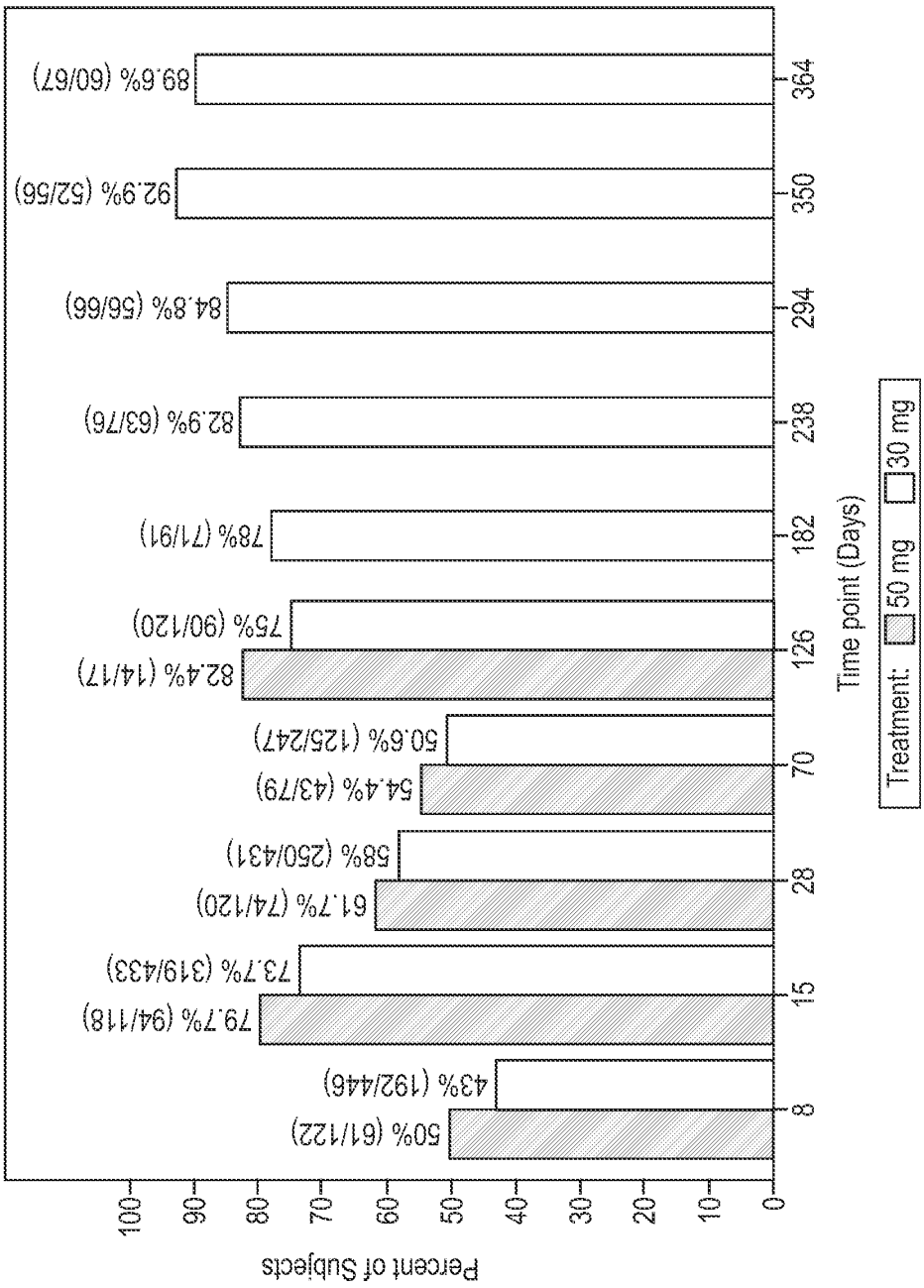

Percent of Subjects
0
10
20
30
40
50
60
70
80
90
100
8
15
28
70
126
182
238
294
350
364
Time point (Days)
Treatment: 50 mg 30 mg
50% (61/122)
43% (192/446)
79.7% (94/118)
73.7% (319/433)
61.7% (74/120)
58% (250/431)
54.4% (43/79)
50.6% (125/247)
82.4% (14/17)
75% (90/120)
78% (71/91)
82.9% (63/76)
84.8% (56/66)
92.9% (52/56)
89.6% (60/67)

FIG. 18

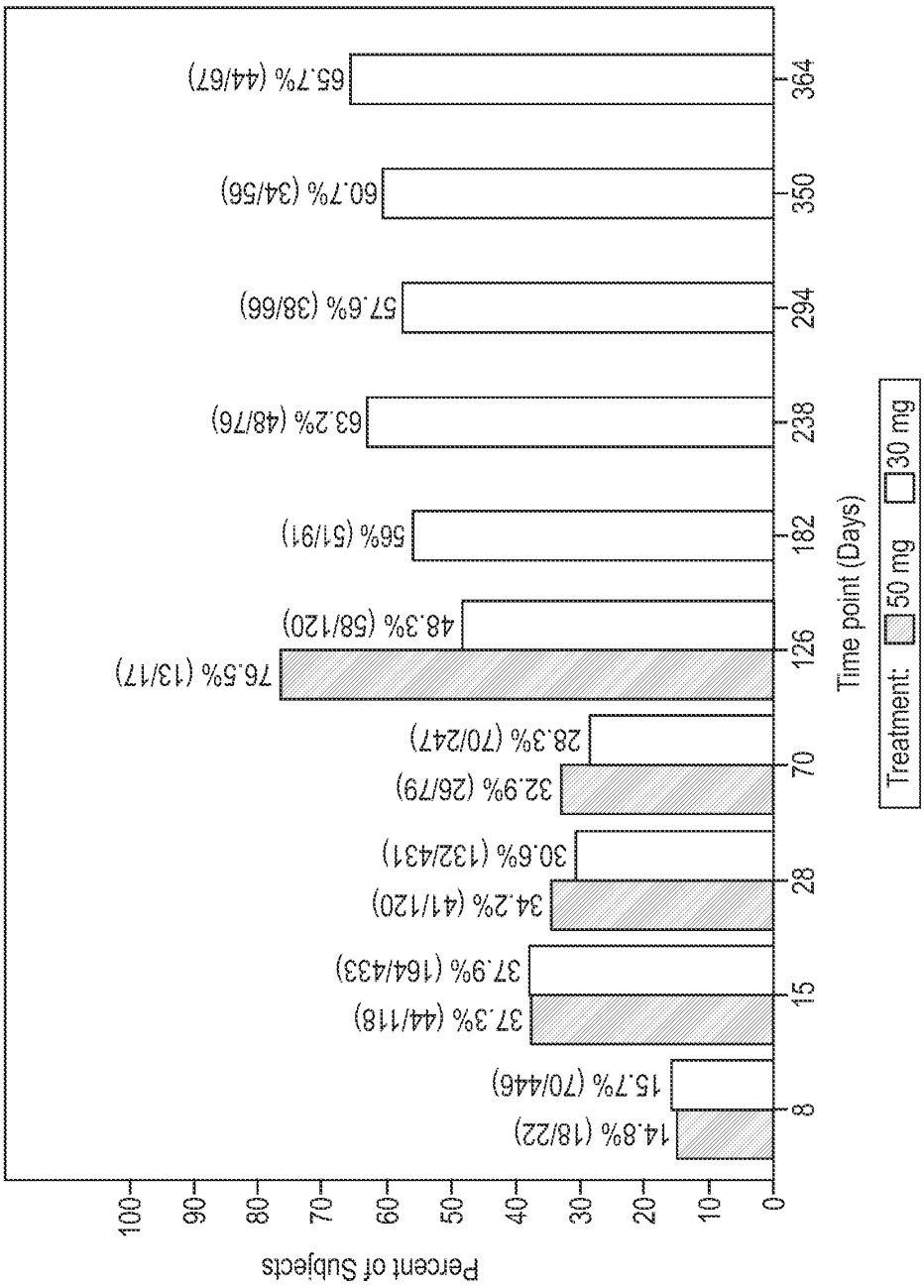

Percent of Subjects
0
10
20
30
40
50
60
70
80
90
100
Time point (Days)
8
15
28
70
126
182
238
294
350
364
Treatment: 50 mg 30 mg
14.8% (18/22)
15.7% (70/446)
37.3% (44/118)
37.9% (164/433)
34.2% (41/120)
30.6% (132/431)
32.9% (26/79)
28.3% (70/247)
76.5% (13/17)
48.3% (58/120)
56% (51/91)
63.2% (48/76)
57.6% (38/66)
60.7% (34/56)
65.7% (44/67)

FIG. 19

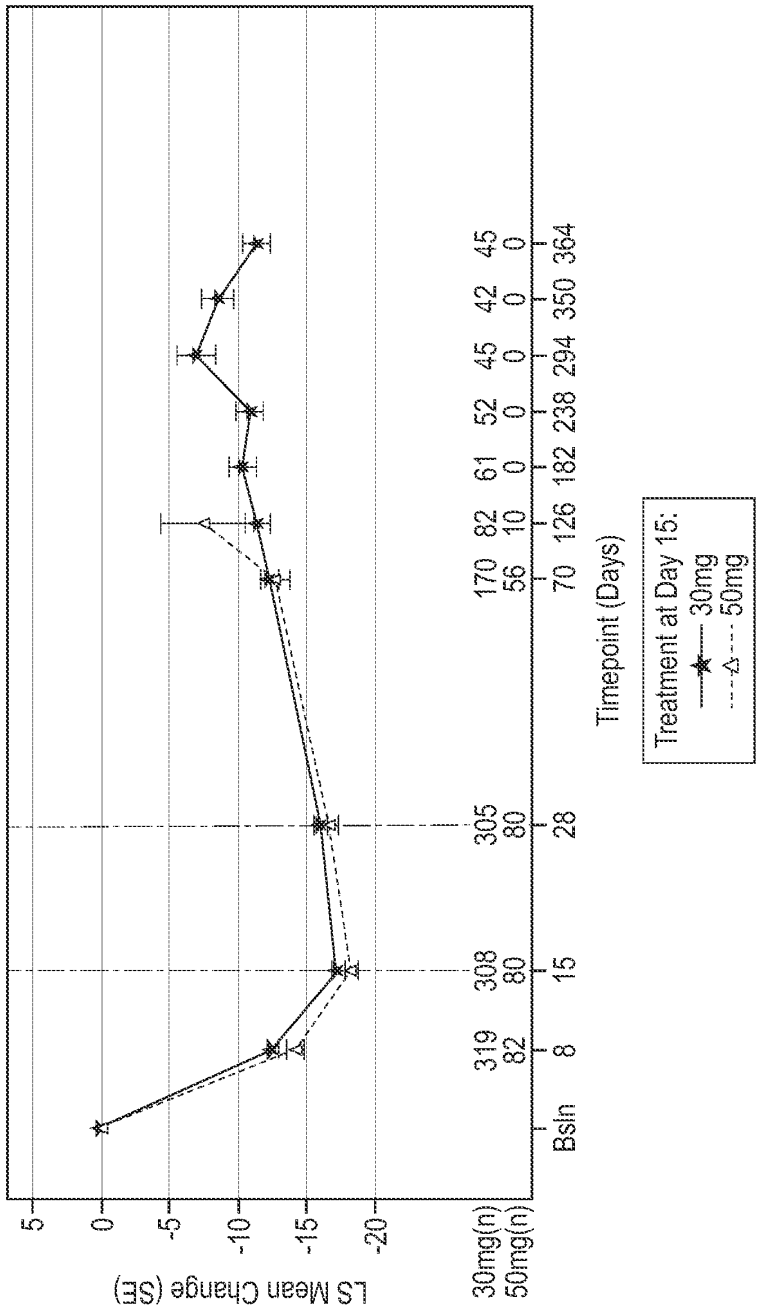

LS Mean Change (SE)
5
0
-5
-10
-15
-20
30mg(n)
50mg(n)
Bsln
319
82
8
308
80
15
305
80
28
170
56
70
82
10
126
61
0
182
52
0
238
45
0
294
42
0
350
45
0
364
Timepoint (Days)
Treatment at Day 15:
30mg
50mg

FIG. 20

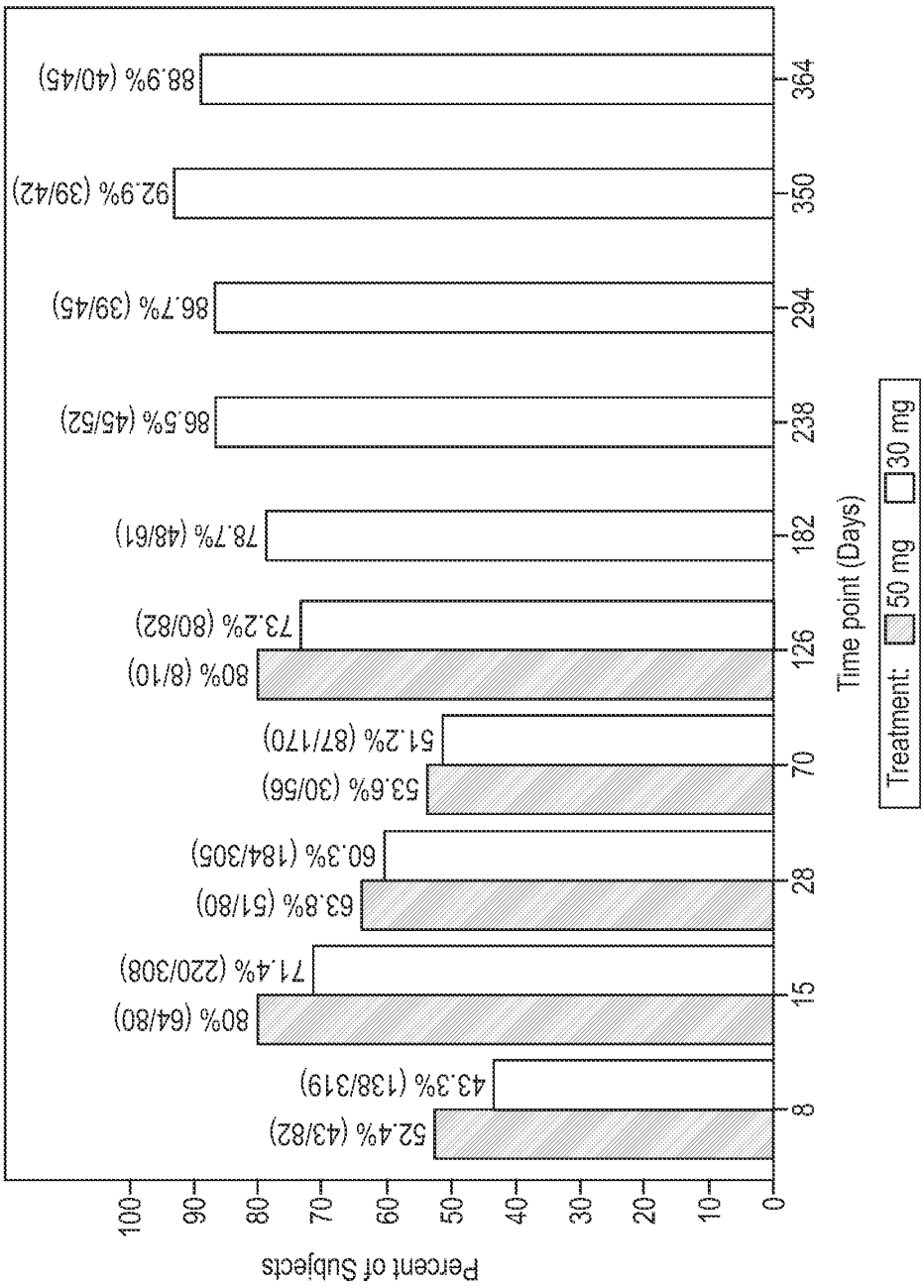

Percent of Subjects
0
10
20
30
40
50
60
70
80
90
100
52.4% (43/82)
43.3% (138/319)
80% (64/80)
71.4% (220/308)
63.8% (51/80)
60.3% (184/305)
53.6% (30/56)
51.2% (87/170)
80% (8/10)
73.2% (80/82)
78.7% (48/61)
86.5% (45/52)
86.7% (39/45)
92.9% (39/42)
88.9% (40/45)
8
15
28
70
126
182
238
294
350
364
Time point (Days)
Treatment: 50 mg 30 mg

FIG. 21

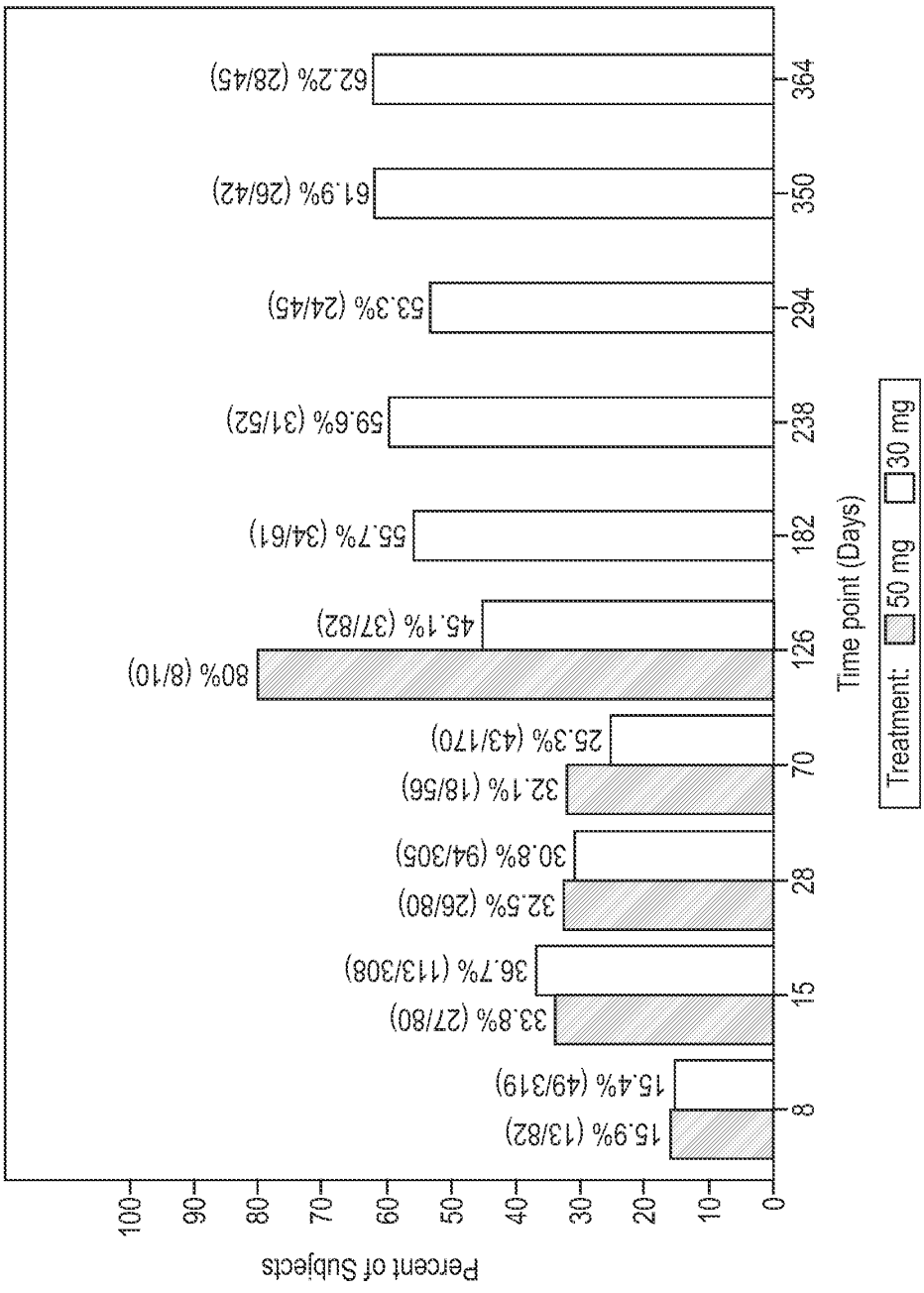

Percent of Subjects
0
10
20
30
40
50
60
70
80
90
100
Time point (Days)
8
15
28
70
126
182
238
294
350
364
Treatment: 50 mg 30 mg
15.9% (13/82)
15.4% (49/319)
33.8% (27/80)
36.7% (113/308)
32.5% (26/80)
30.8% (94/305)
32.1% (18/56)
25.3% (43/170)
80% (8/10)
45.1% (37/82)
55.7% (34/61)
59.6% (31/52)
53.3% (24/45)
61.9% (26/42)
62.2% (28/45)

FIG. 22

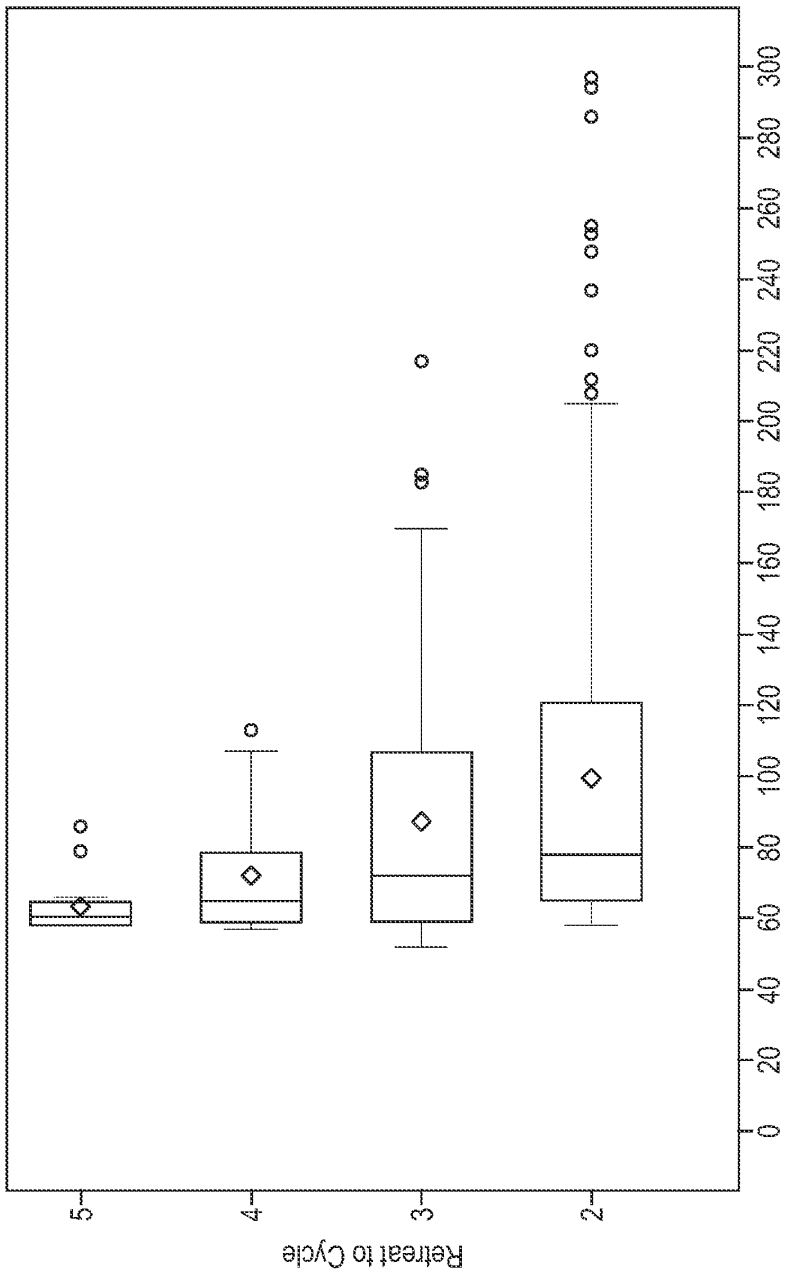

Retreat to Cycle
5
4
3
2
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
Days to Retreat
Low Dose

FIG. 23

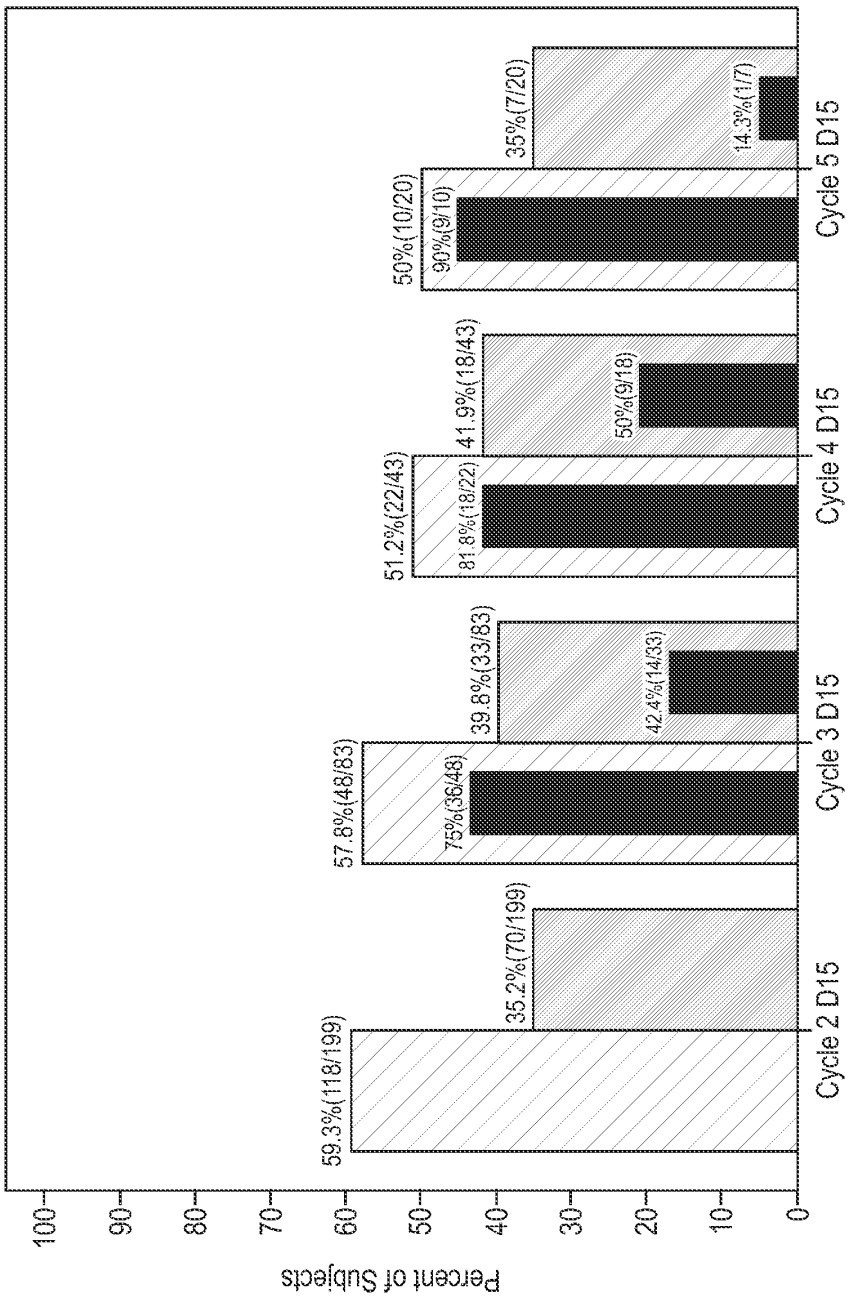

Percent of Subjects
100
90
80
70
60
50
40
30
20
10
0
59.3%(118/199)
35.2%(70/199)
57.8%(48/83)
75%(36/48)
39.8%(33/83)
42.4%(14/33)
51.2%(22/43)
81.8%(18/22)
41.9%(18/43)
50%(9/18)
50%(10/20)
90%(9/10)
35%(7/20)
14.3%(1/7)
Cycle 2 D15
Cycle 3 D15
Cycle 4 D15
Cycle 5 D15
Time point
Inside Bar represents % of Responders in Previous Cycle
Responder
Non Responder

FIG. 24

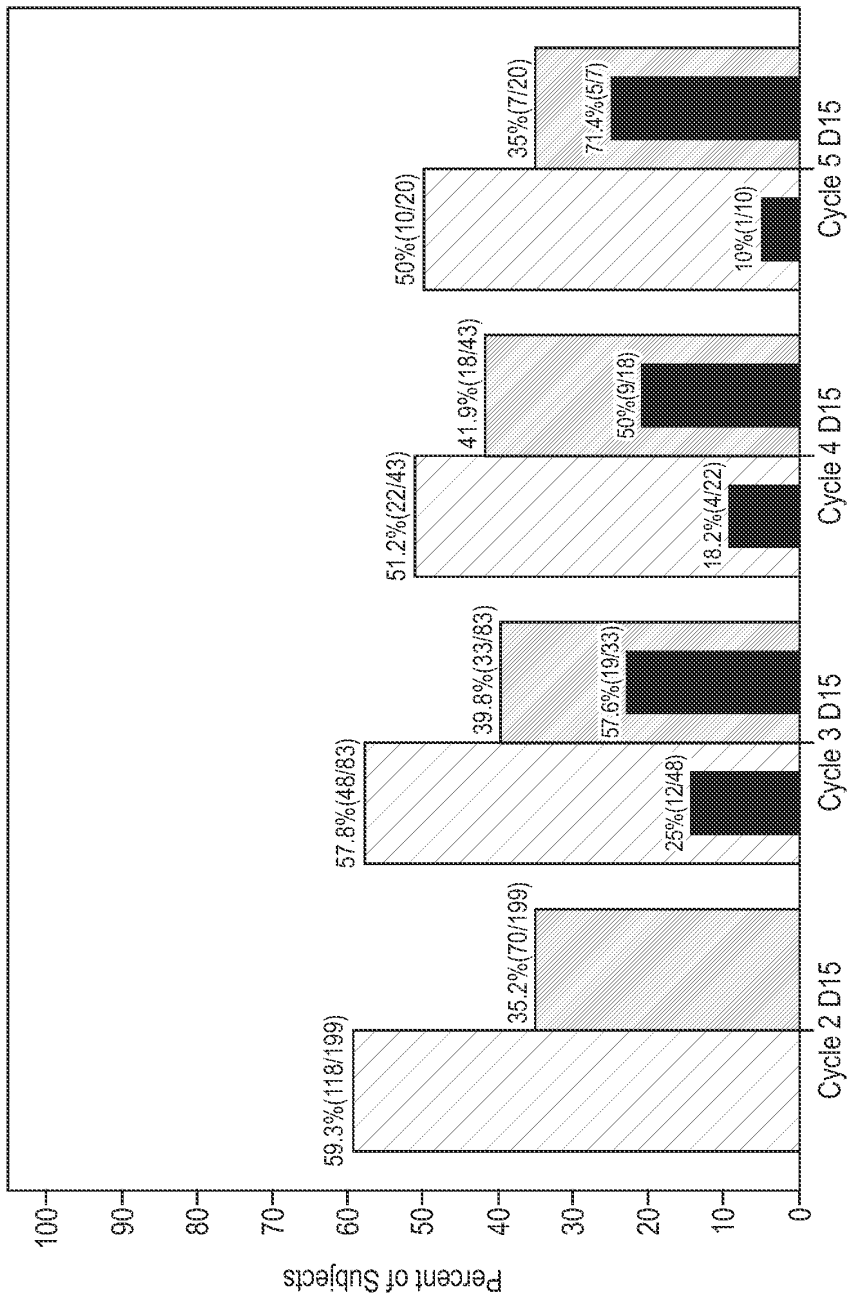

Percent of Subjects
100
90
80
70
60
50
40
30
20
10
0
59.3%(118/199)
35.2%(70/199)
57.8%(48/83)
25%(12/48)
39.8%(33/83)
57.6%(19/33)
51.2%(22/43)
18.2%(4/22)
41.9%(18/43)
50%(9/18)
50%(10/20)
10%(1/10)
35%(7/20)
71.4%(5/7)
Cycle 2 D15
Cycle 3 D15
Cycle 4 D15
Cycle 5 D15
Time point
Inside Bar represents % of Responders in Previous Cycle
Responder
Non Responder

FIG. 25