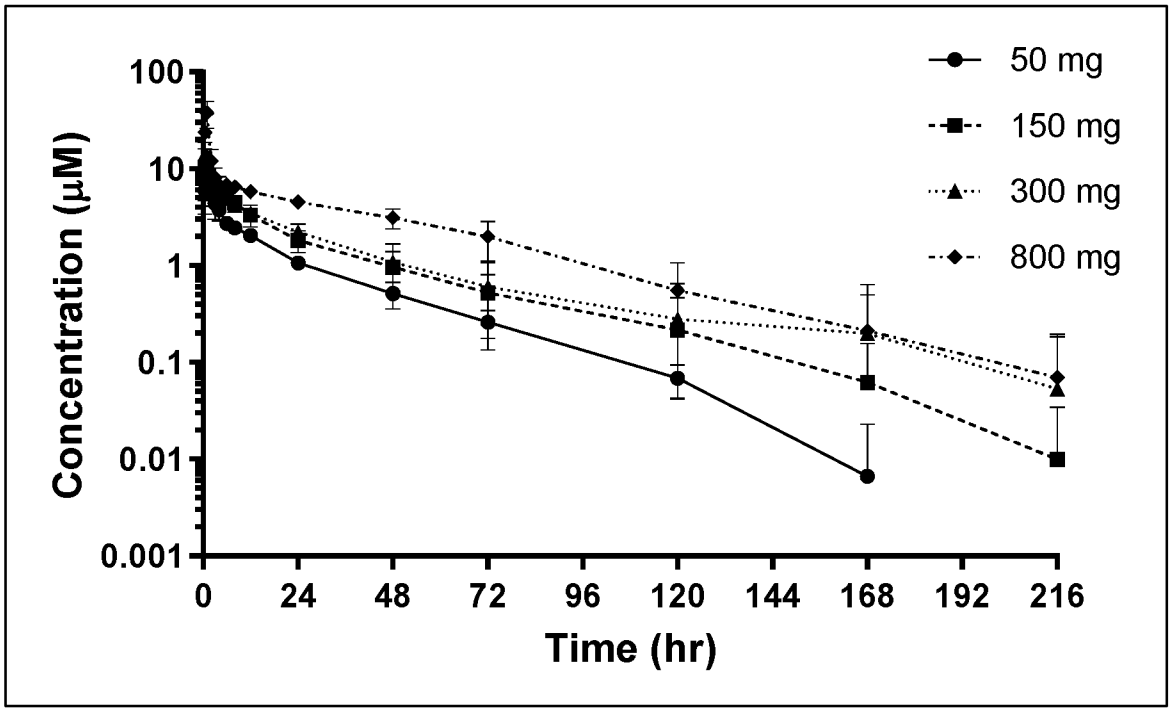

50 mg
150 mg
300 mg
800 mg
Concentration (μM)
100
10
1
0.1
0.01
0.001
0
24
48
72
96
120
144
168
192
216
Time (hr)

FIG. 1

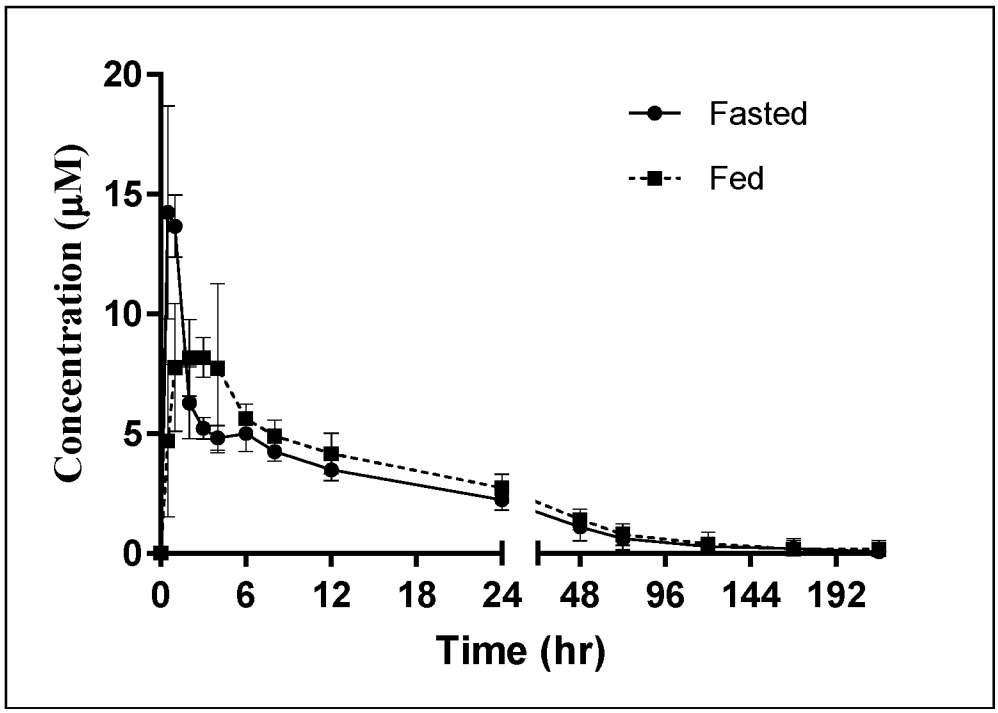

Fasted
Fed
Concentration (μM)
20
15
10
5
0
0
6
12
18
24
48
96
144
192
Time (hr)

FIG. 2

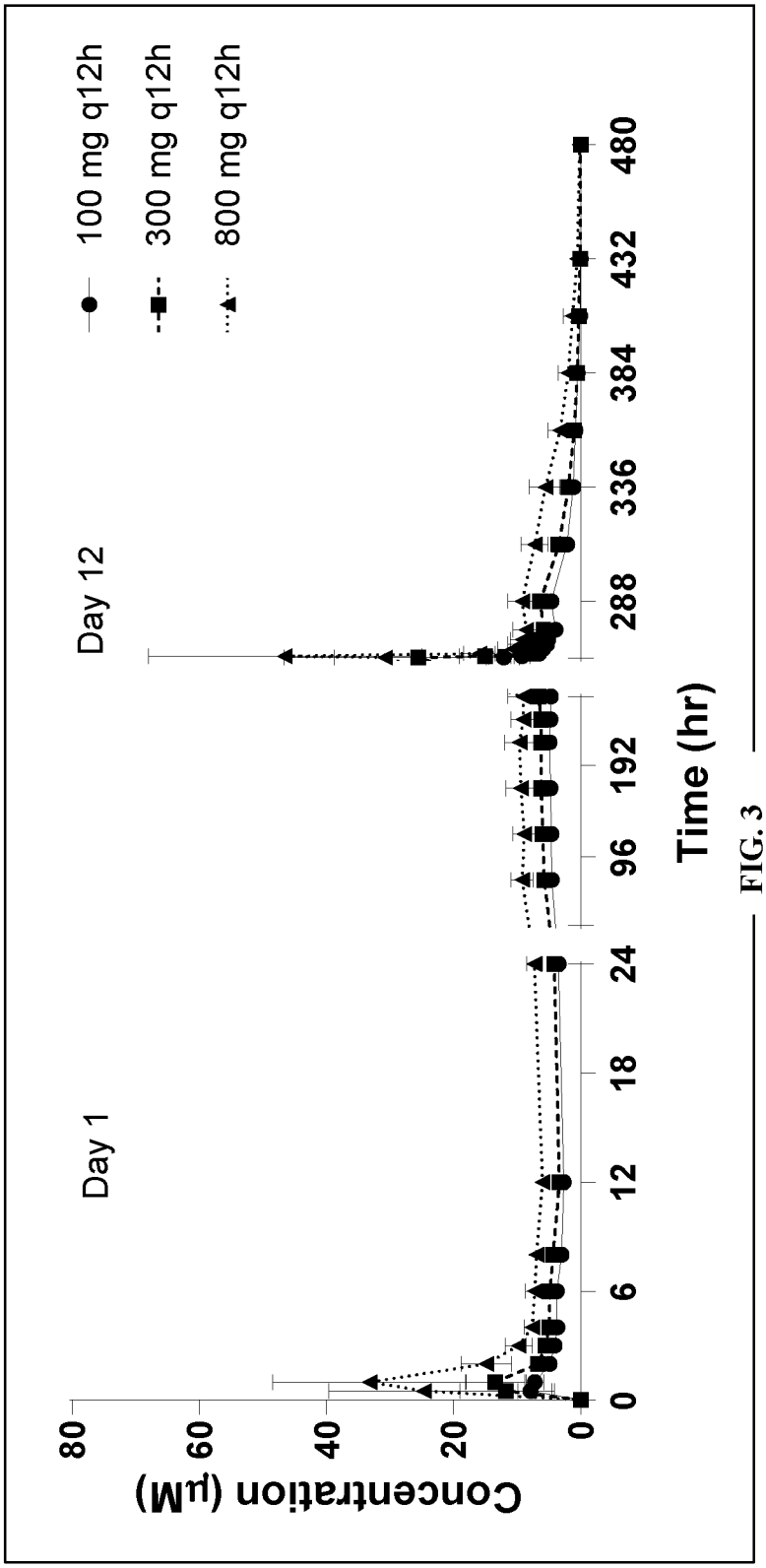

100 mg q12h
300 mg q12h
800 mg q12h
Day 1
Day 12
Concentration (μM)
0
20
40
60
80
0
6
12
18
24
96
192
288
336
384
432
480
Time (hr)

FIG. 3

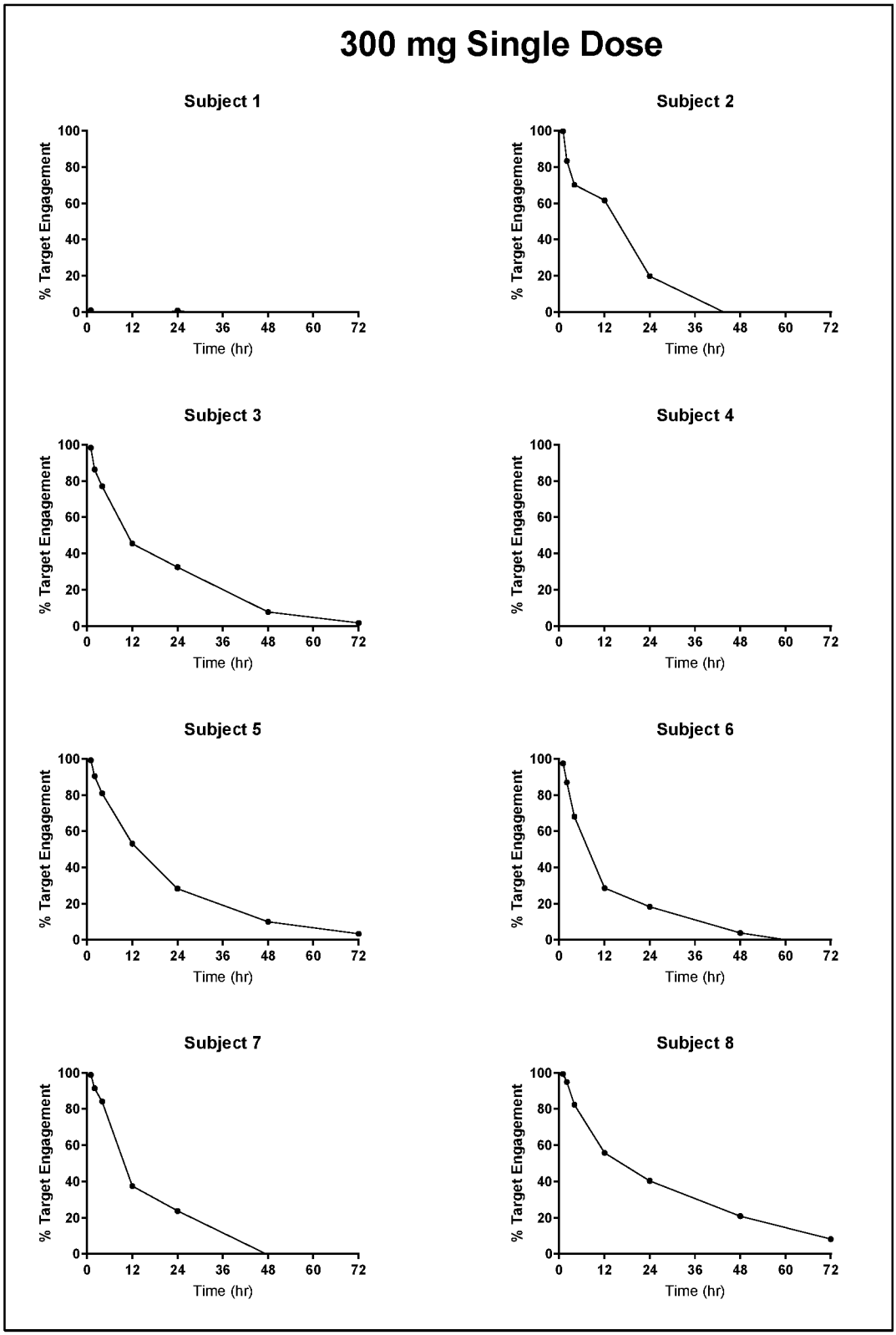

300 mg Single Dose
Subject 1
Subject 2
Subject 3
Subject 4
Subject 5
Subject 6
Subject 7
Subject 8
% Target Engagement
Time (hr)
0
12
24
36
48
60
72
20
40
80
100

FIG. 4

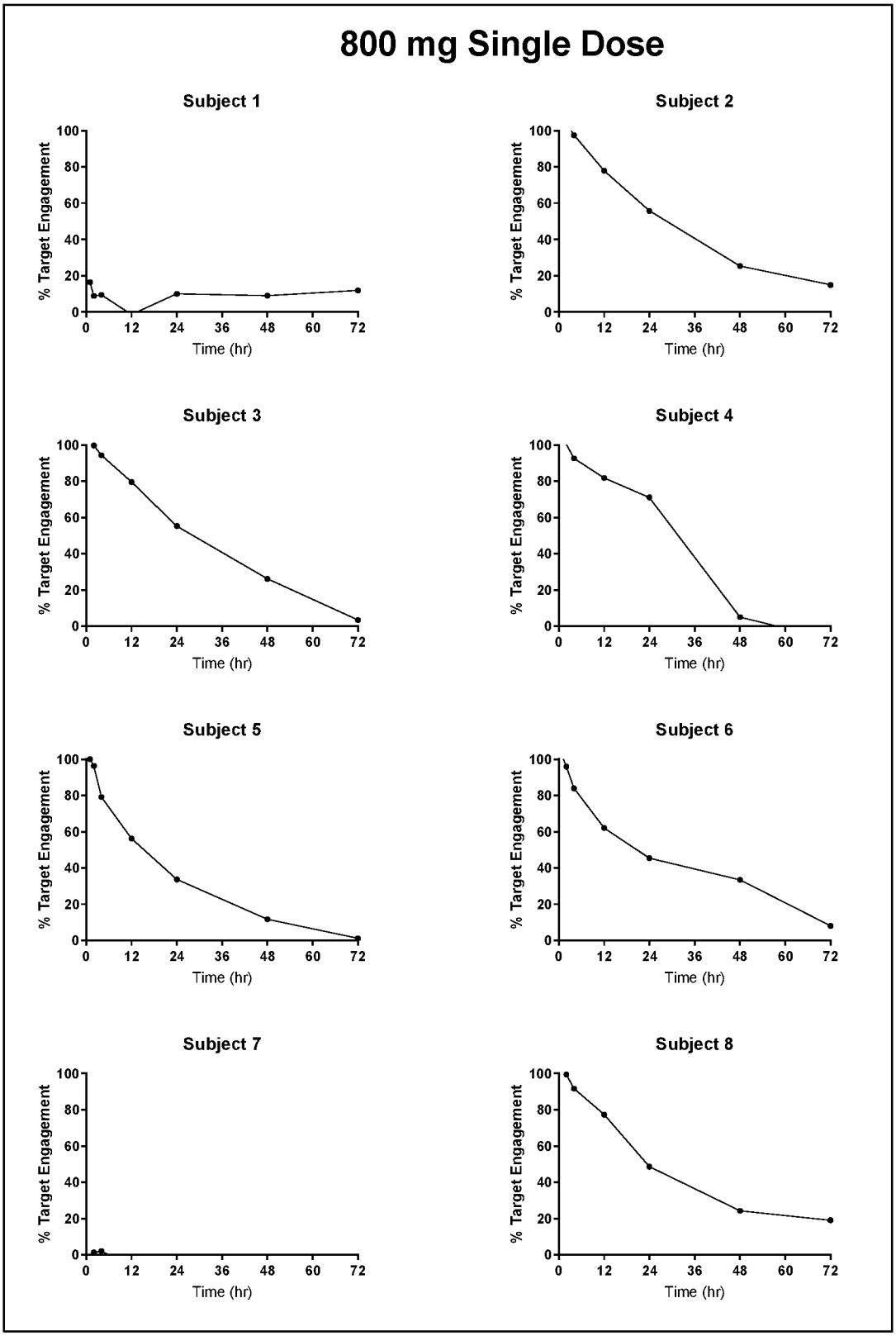

800 mg Single Dose
Subject 1
Subject 2
Subject 3
Subject 4
Subject 5
Subject 6
Subject 7
Subject 8
% Target Engagement
Time (hr)
0
12
24
36
48
60
72
20
40
80
100

FIG. 5

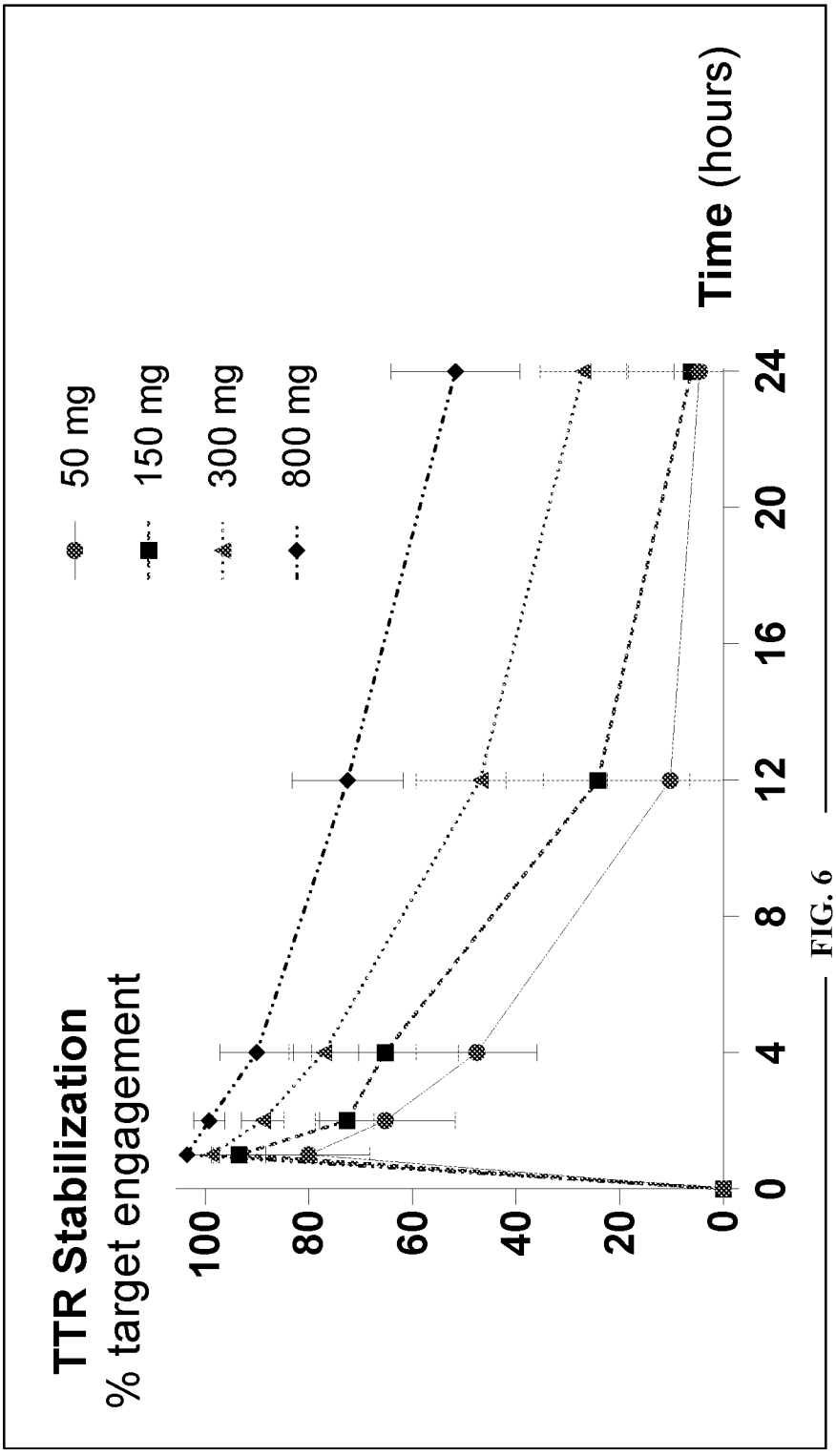

TTR Stabilization
% target engagement
100
80
60
40
20
0
0
4
8
12
16
20
24
Time (hours)
50 mg
150 mg
300 mg
800 mg

FIG. 6

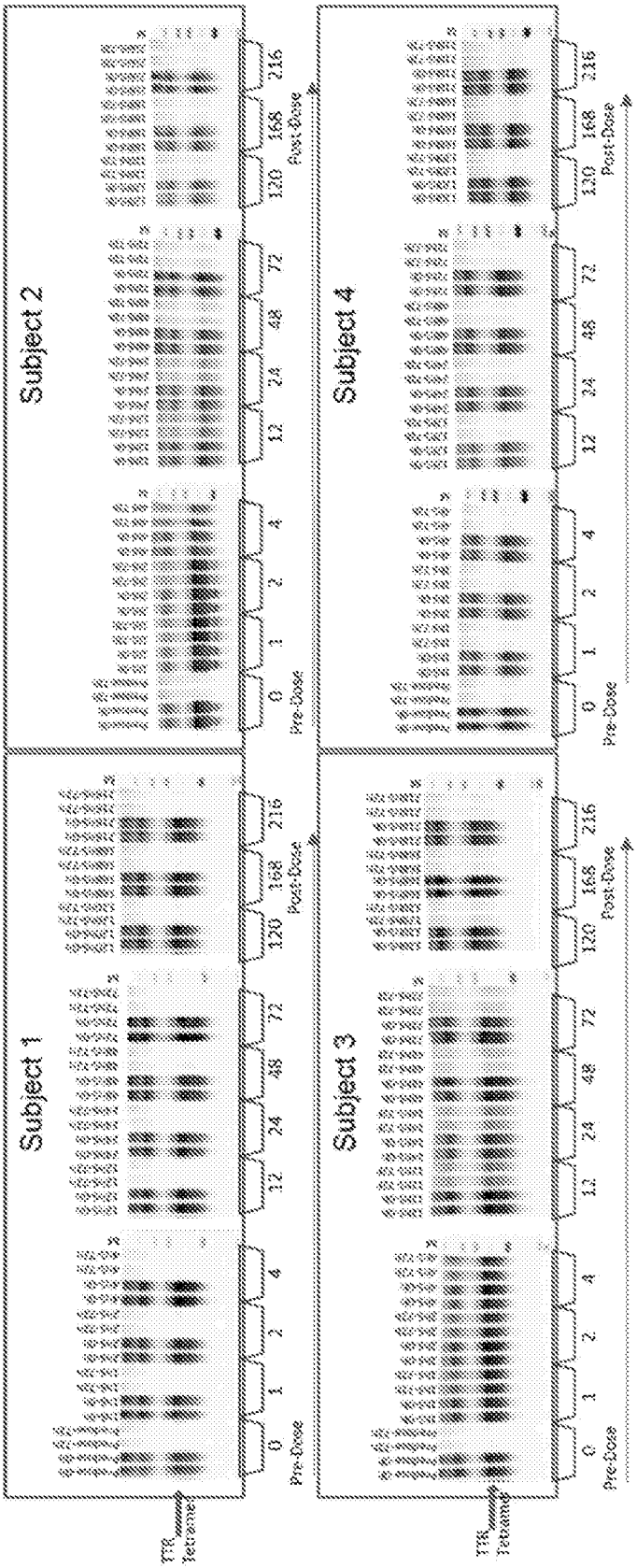

Subject 1
Subject 2
Subject 3
Subject 4
TTR Tetramer
0
1
2
4
12
24
48
72
120
168
216
Pre-Dose
Post-Dose

FIG. 7A

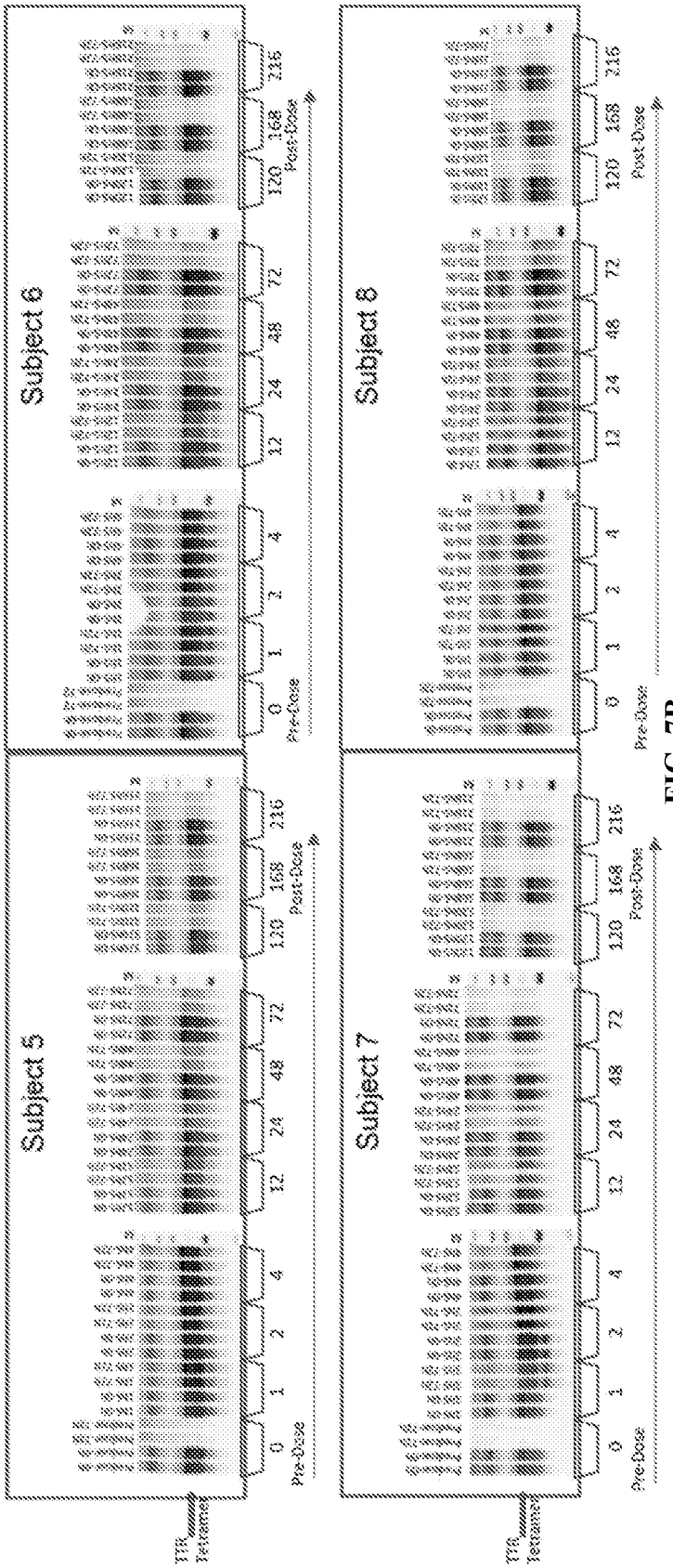

Subject 5
Subject 6
Subject 7
Subject 8
TTR Tetramer
Pre-Dose
Post-Dose
0
1
2
4
12
24
48
72
120
168
216

FIG. 7B

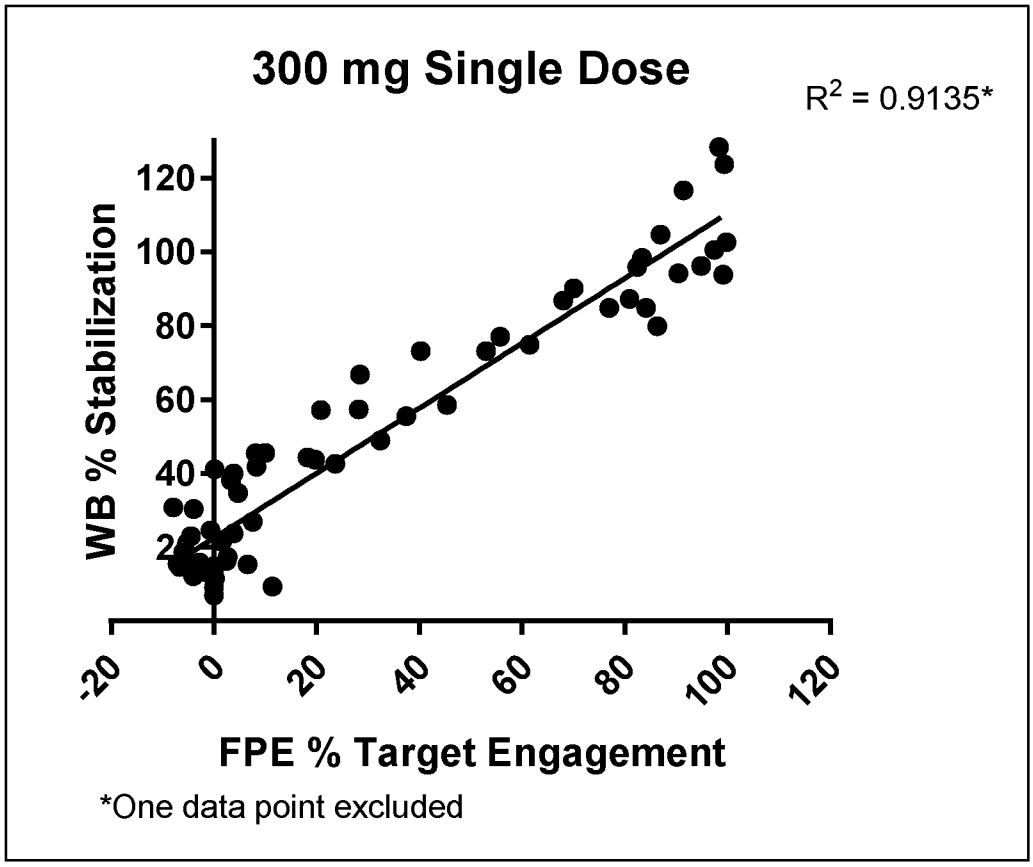

300 mg Single Dose
R2 = 0.9135*
WB % Stabilization
120
100
80
60
40
20
-20
0
20
40
60
80
100
120
FPE % Target Engagement
*One data point excluded

FIG. 8

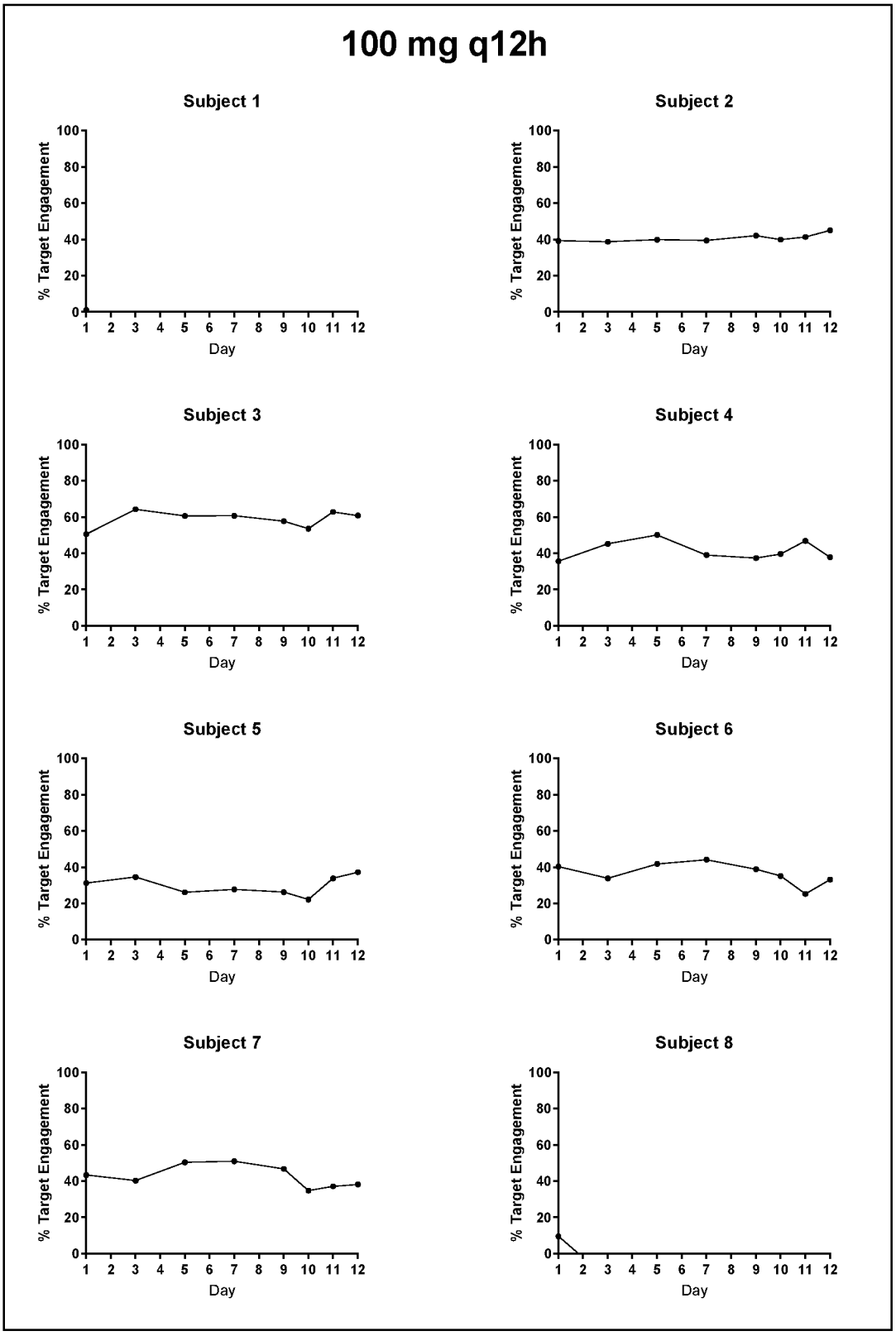

100 mg q12h
Subject 1
Subject 2
Subject 3
Subject 4
Subject 5
Subject 6
Subject 7
Subject 8
% Target Engagement
Day
0
20
40
60
80
100
1 2 3 4 5 6 7 8 9 10 11 12

FIG. 9

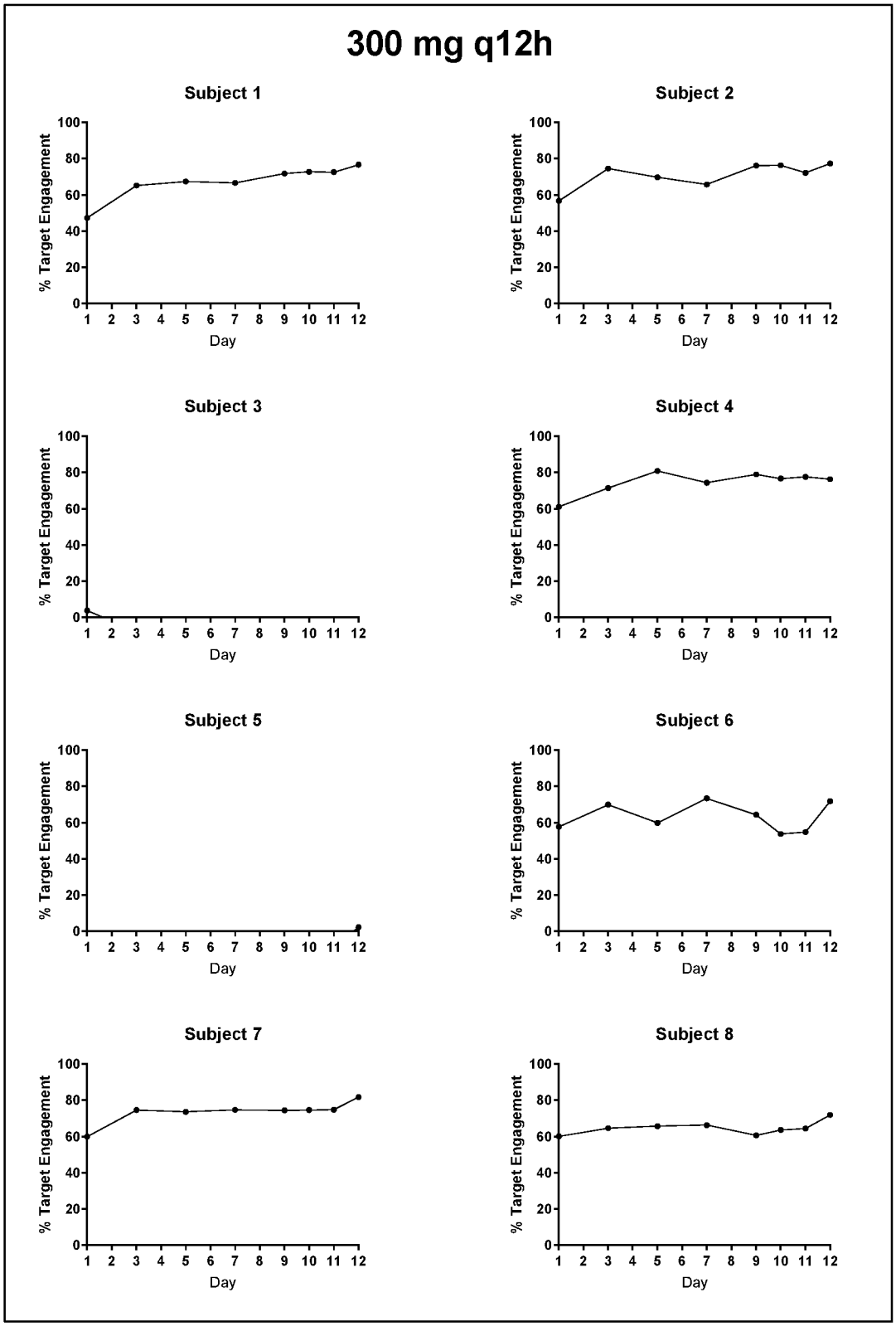

300 mg q12h
Subject 1
Subject 2
Subject 3
Subject 4
Subject 5
Subject 6
Subject 7
Subject 8
% Target Engagement
Day
0
20
40
60
80
100
1 2 3 4 5 6 7 8 9 10 11 12

FIG. 10

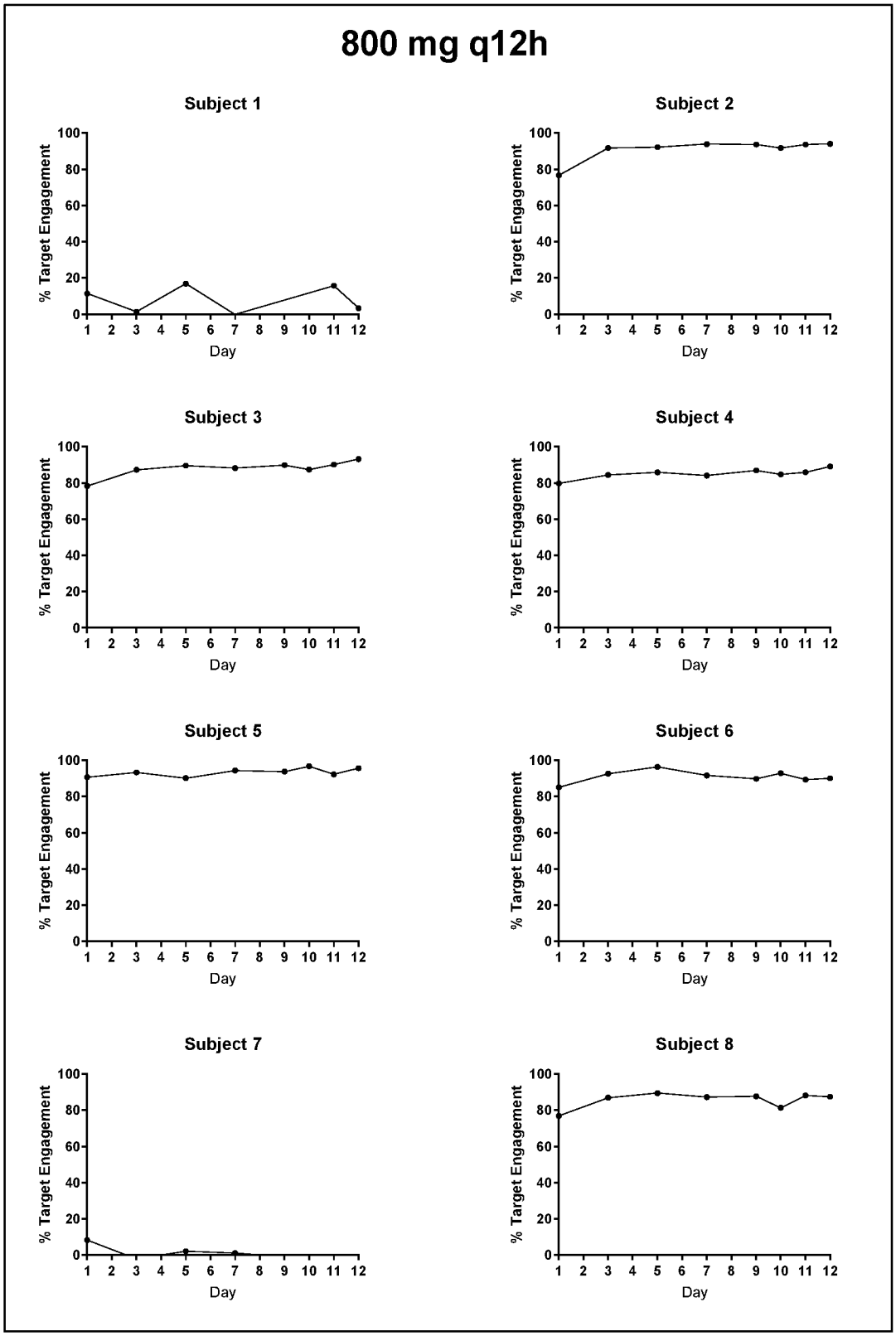
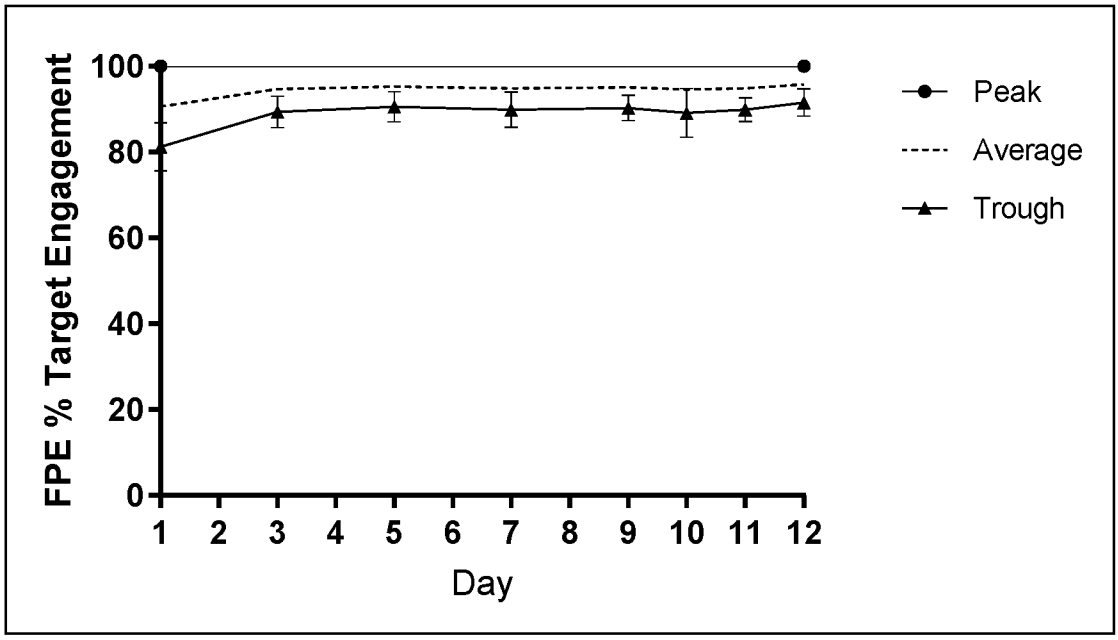

800 mg q12h
Subject 1
Subject 2
Subject 3
Subject 4
Subject 5
Subject 6
Subject 7
Subject 8
% Target Engagement
Day
0
20
40
60
80
100
1 2 3 4 5 6 7 8 9 10 11 12

FIG. 11



n = 6 subjects

FIG. 12

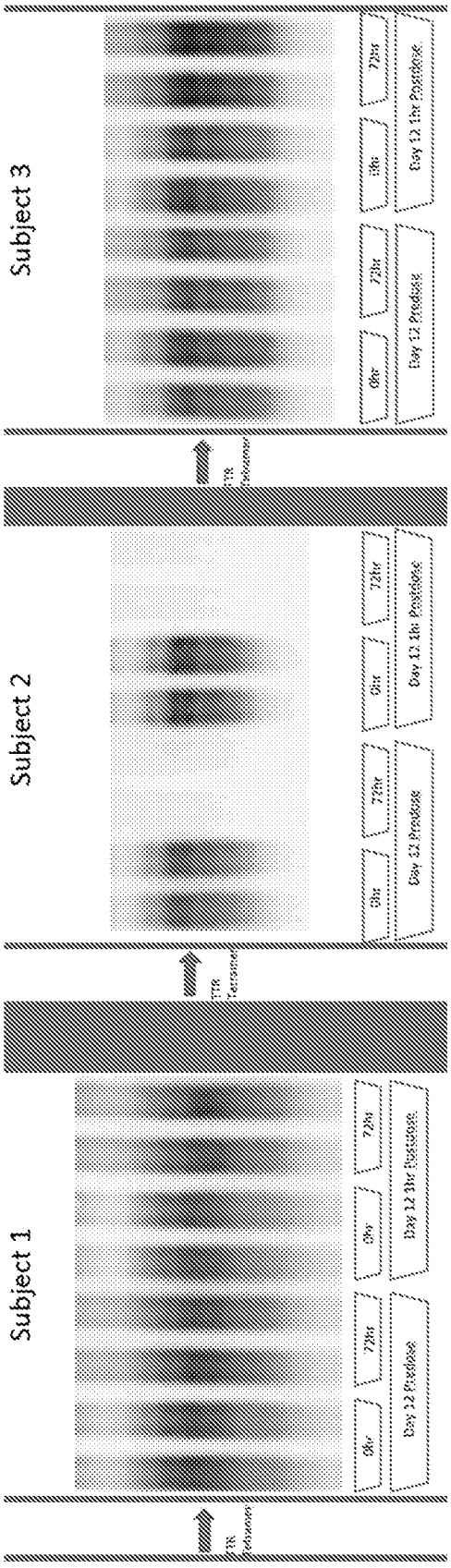

Subject 1
Subject 2
Subject 3
0hr
72hr
Day 12 Predose
Day 12 Hr Postdose
Day 13 Predose
Day 13 Hr Postdose

FIG. 13

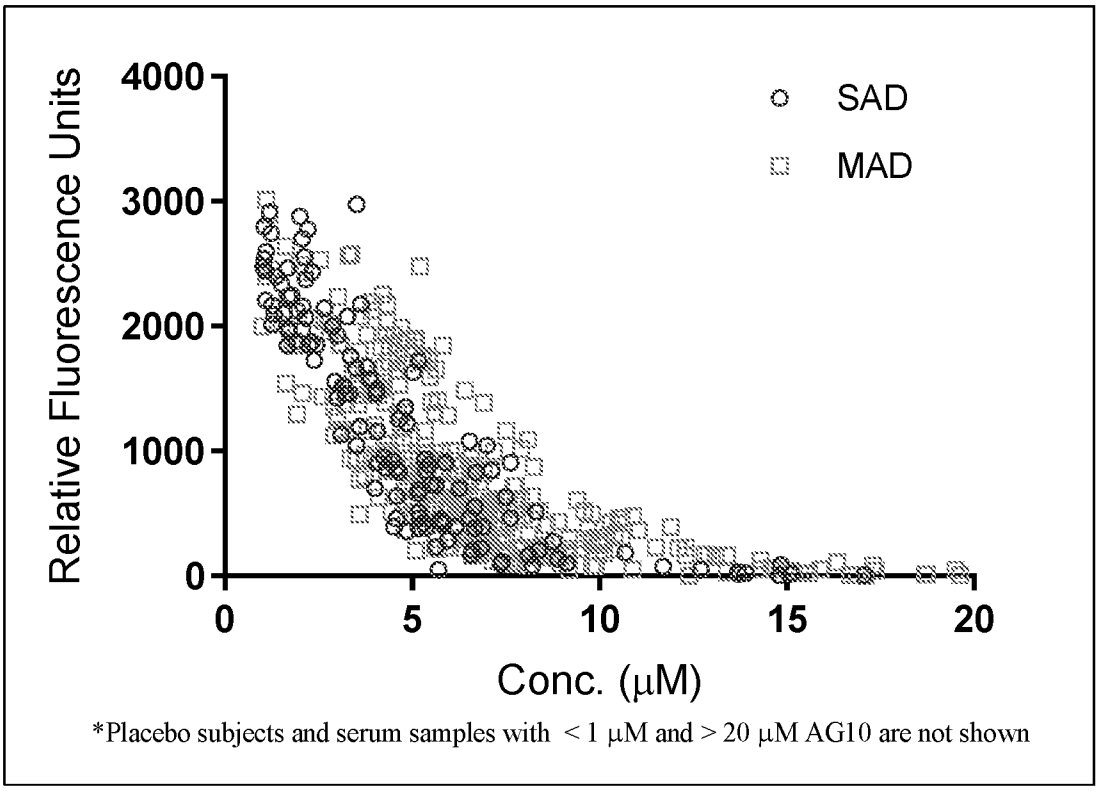

Relative Fluorescence Units
4000
3000
2000
1000
0
0
5
10
15
20
Conc. (μM)
SAD
MAD
*Placebo subjects and serum samples with < 1 μM and > 20 μM AG10 are not shown

FIG. 14

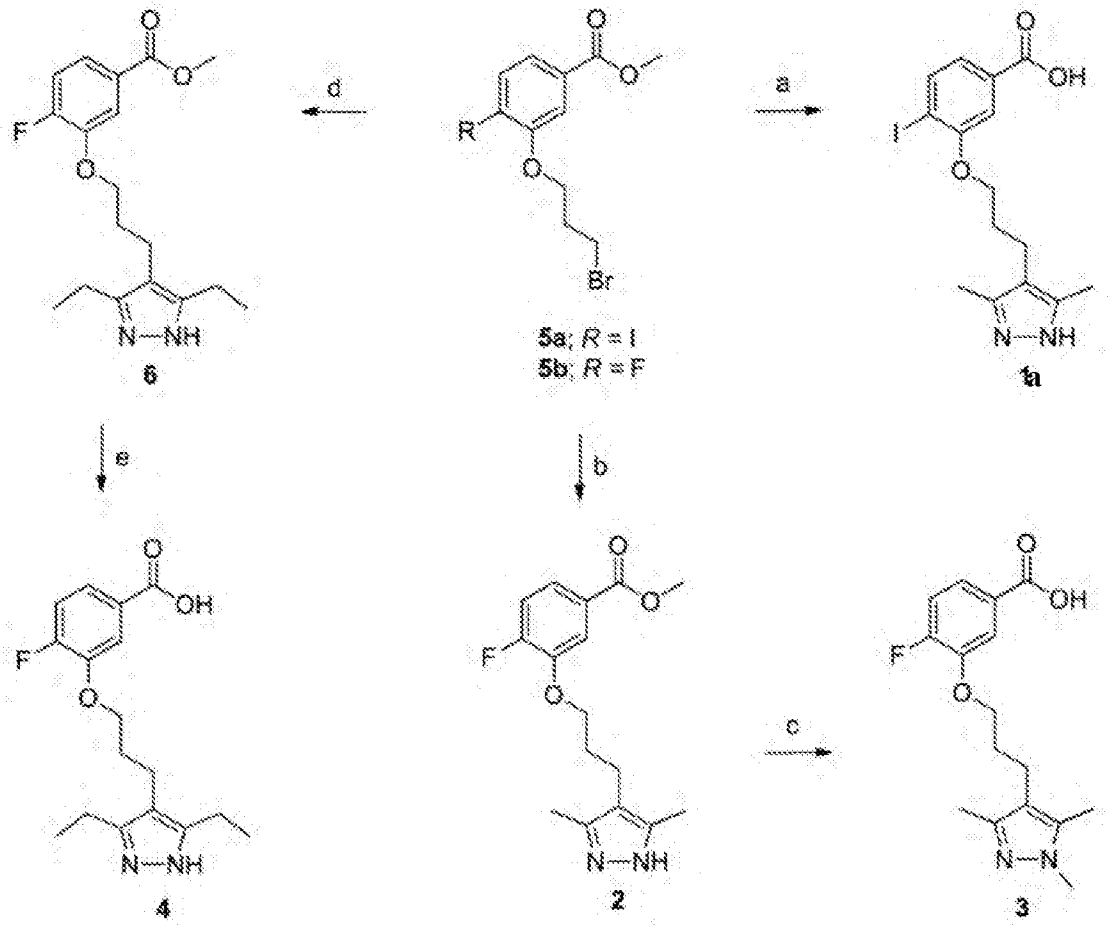


FIG. 15

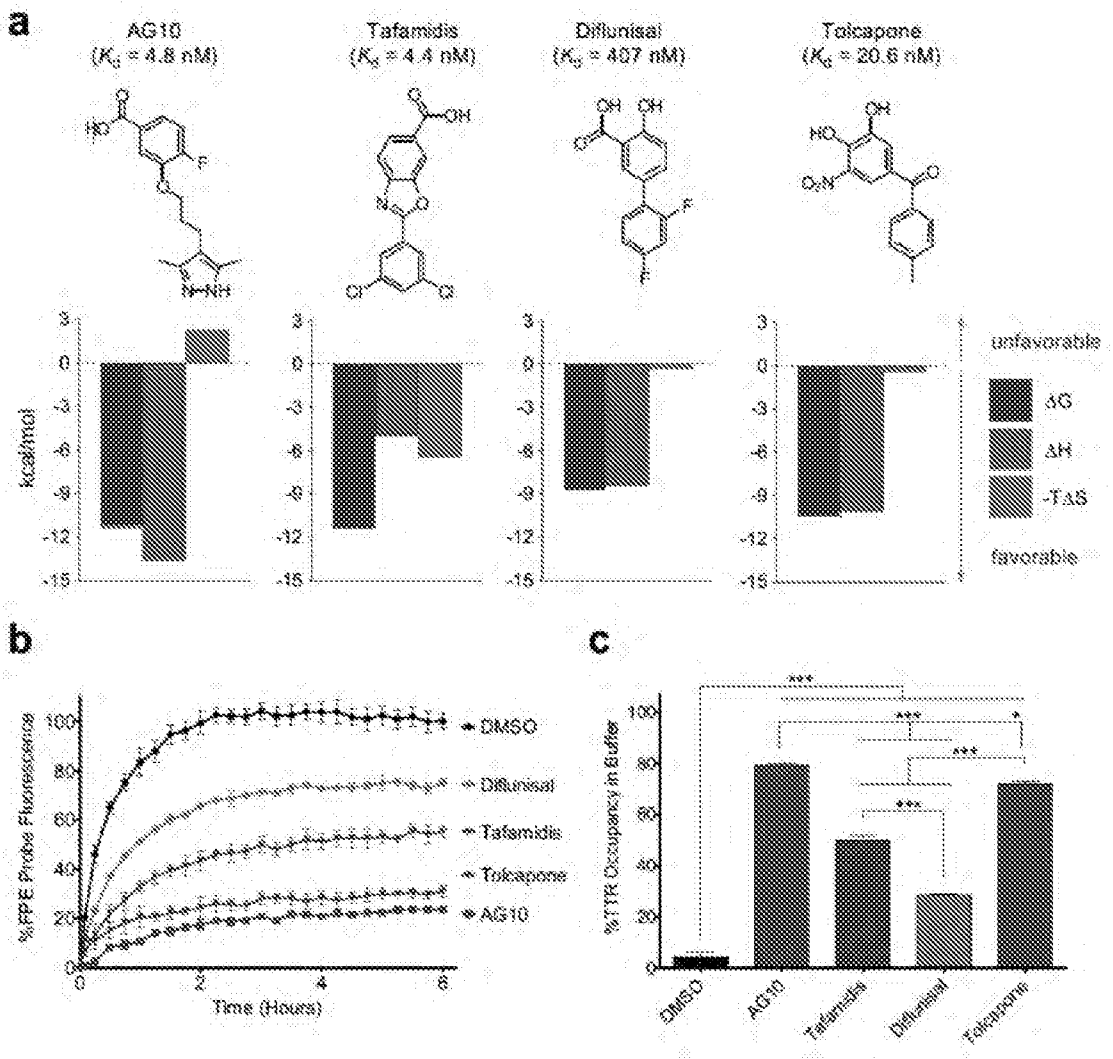

a
AG10
(K_i = 4.8 nM)
Tafamidis
(K_d = 4.4 nM)
Diflunisal
(K_d = 407 nM)
Tolcapone
(K_d = 20.6 nM)
kcal/mol
unfavorable
ΔG
ΔH
-TΔS
favorable
b
%FPE Probe Fluorescence
Time (Hours)
DMSO
Diflunisal
Tafamidis
Tolcapone
AG10
c
%TTR Occupancy in Buffer
DMSO
AG10
Tafamidis
Diflunisal
Tolcapone

FIG. 16

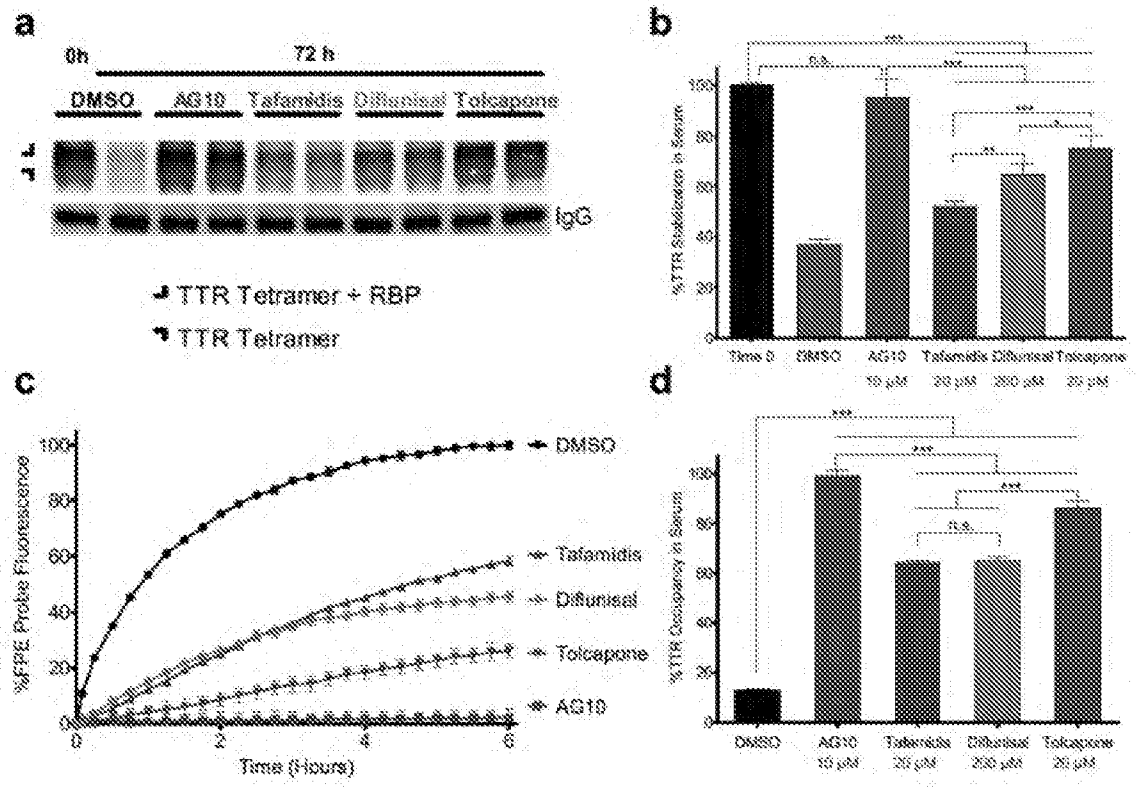

a
0h
72 h
DMSO
AG10
Tafamidis
Diflunisal
Tolcapone
WB: TTR
IgG
TTR Tetramer + RBP
TTR Tetramer
b
%TTR Stabilization in Serum
Time 0
DMSO
AG10
Tafamidis
Diflunisal
Tolcapone
c
% TTR Fluorescence Enhancement
DMSO
Tafamidis
Diflunisal
Tolcapone
AG10
Time (Hours)
d
%TTR Occupancy in Serum
DMSO
AG10
Tafamidis
Diflunisal
Tolcapone

FIG. 17

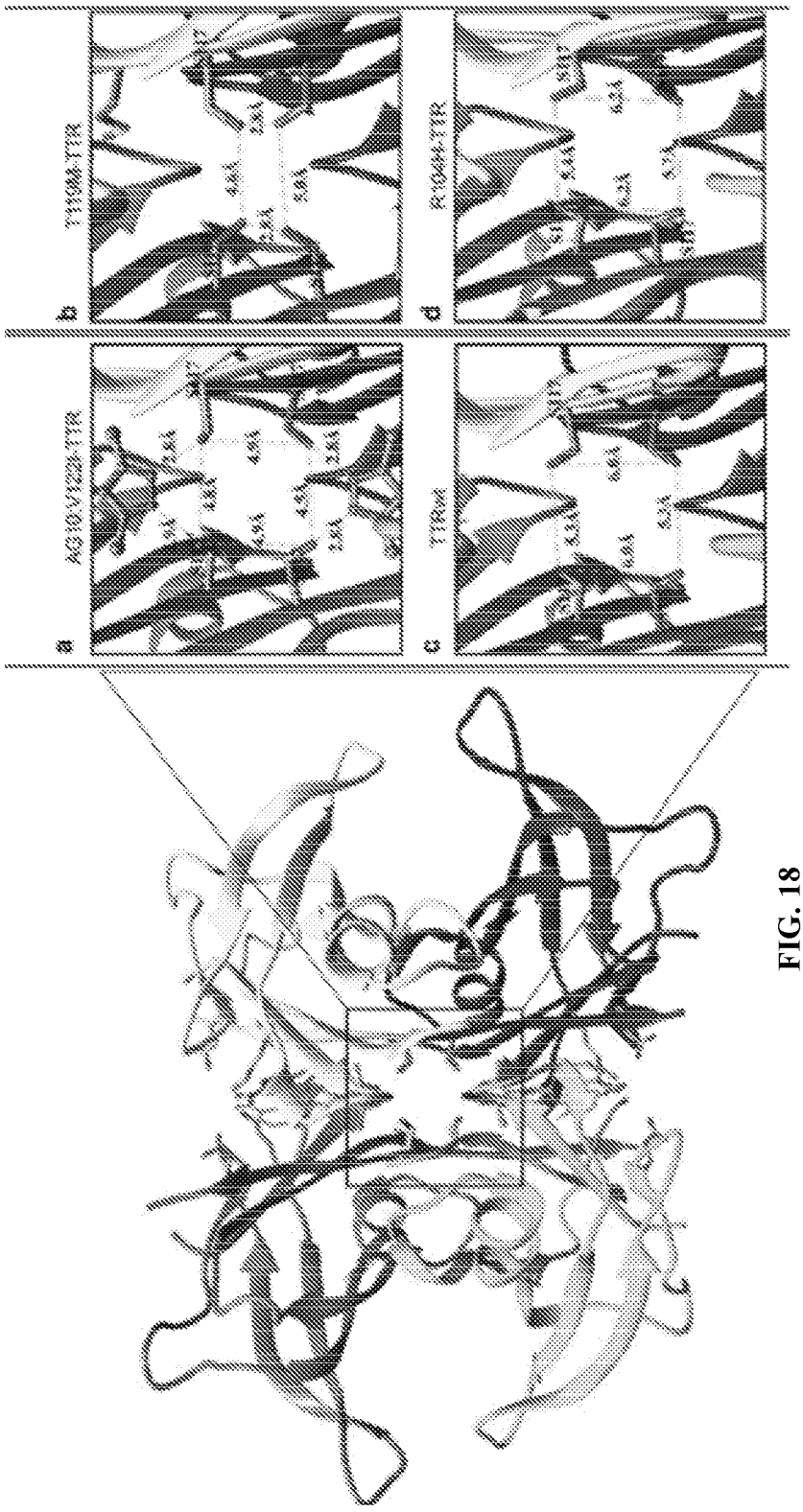


FIG. 18

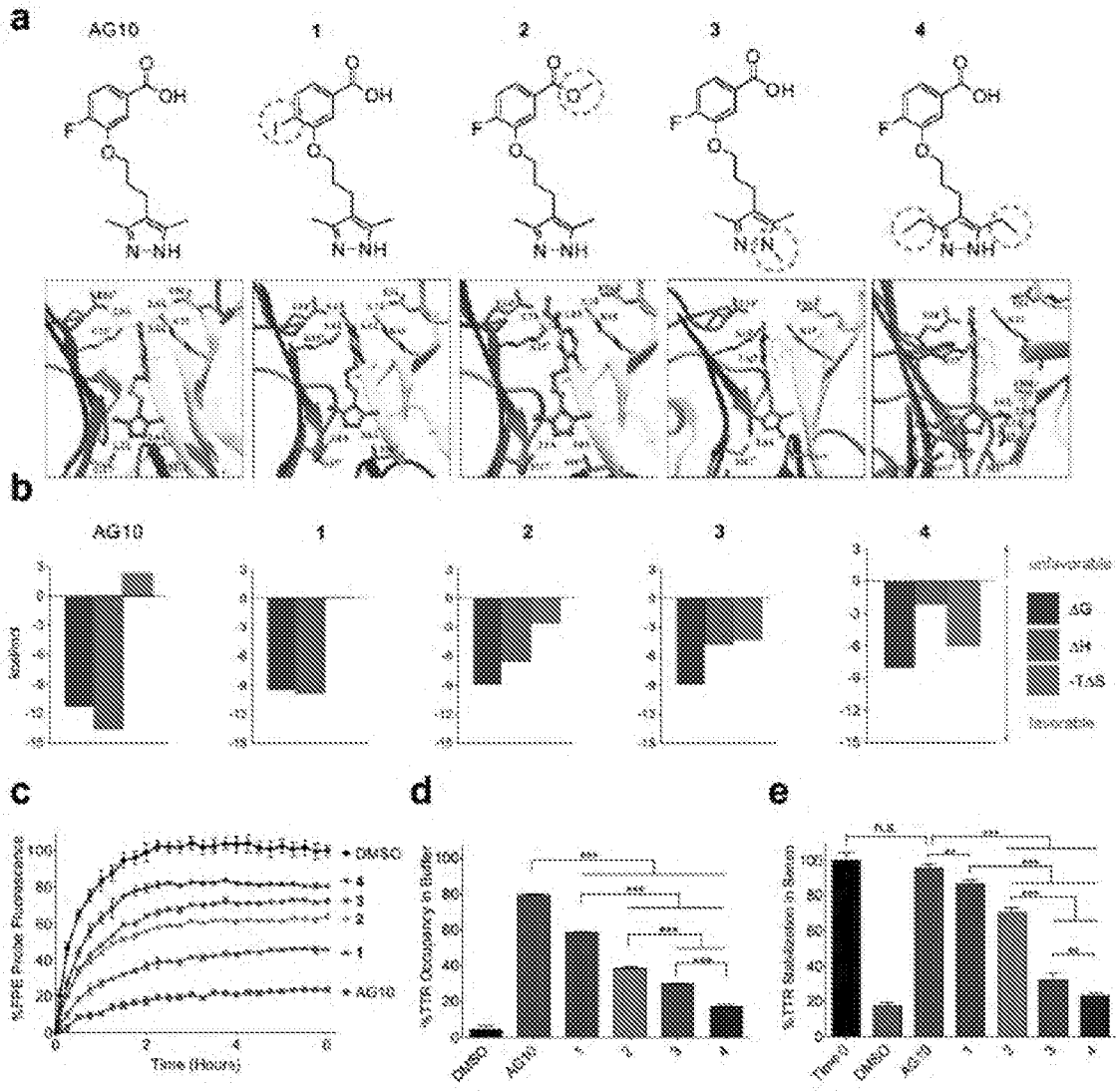

a
AG10
1
2
3
4
b
AG10
1
2
3
4
kcal/mol
ΔG
ΔH
-TΔS
c
%FPE Probe Fluorescence
Time (Hours)
DMSO
4
3
2
1
AG10
d
%TTR Occupancy in Buffer
DMSO
AG10
1
2
3
4
e
%TTR Stabilization in Serum
Time=0
DMSO
AG10
1
2
3
4

FIG. 19

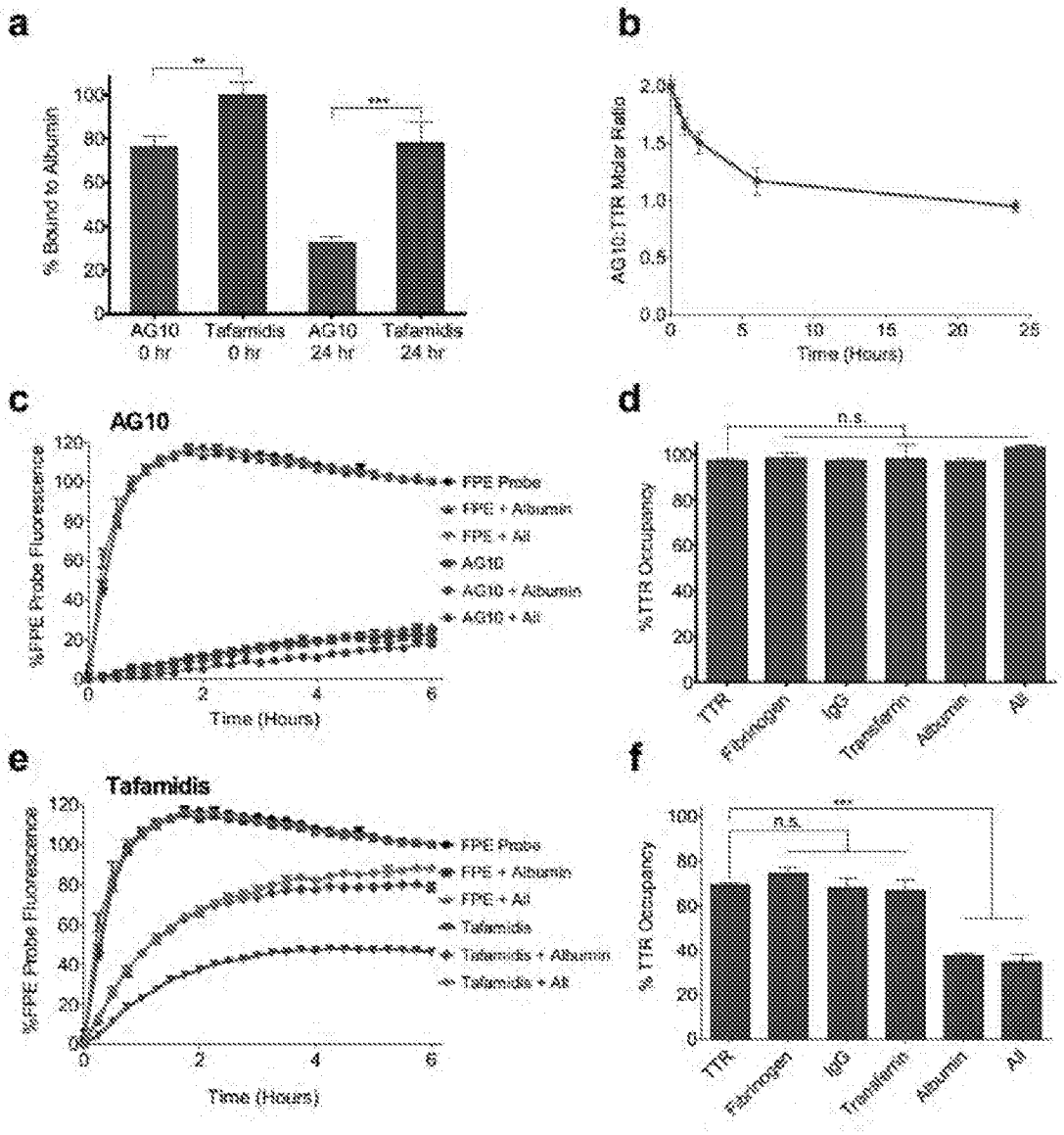

a
% Bound to Albumin
AG10 0 hr
Tafamidis 0 hr
AG10 24 hr
Tafamidis 24 hr
b
AG10:TTR Molar Ratio
Time (Hours)
c
AG10
%FPE Probe Fluorescence
FPE Probe
FPE + Albumin
FPE + Alt
AG10
AG10 + Albumin
AG10 + Alt
Time (Hours)
d
% TTR Occupancy
n.s.
TTR
Fibrinogen
IgG
Transferrin
Albumin
Alt
e
Tafamidis
%FPE Probe Fluorescence
FPE Probe
FPE + Albumin
FPE + Alt
Tafamidis
Tafamidis + Albumin
Tafamidis + Alt
Time (Hours)
f
% TTR Occupancy
***
n.s.
TTR
Fibrinogen
IgG
Transferrin
Albumin
Alt

FIG. 20

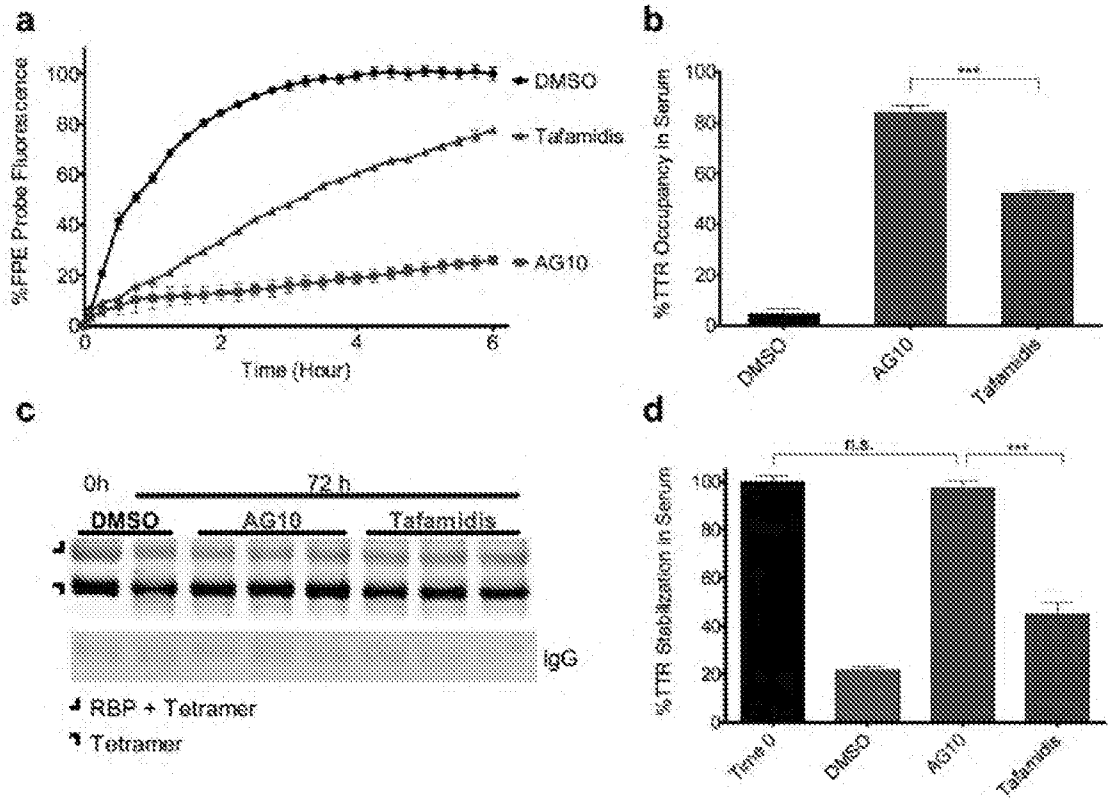

a
%FPE Probe Fluorescence
Time (Hour)
DMSO
Tafamidis
AG10
b
%TTR Occupancy in Serum
***
DMSO
AG10
Tafamidis
c
0h
72 h
DMSO
AG10
Tafamidis
IgG
RBP + Tetramer
Tetramer
d
%TTR Stabilization in Serum
n.s.
***
Time 0
DMSO
AG10
Tafamidis

FIG. 21

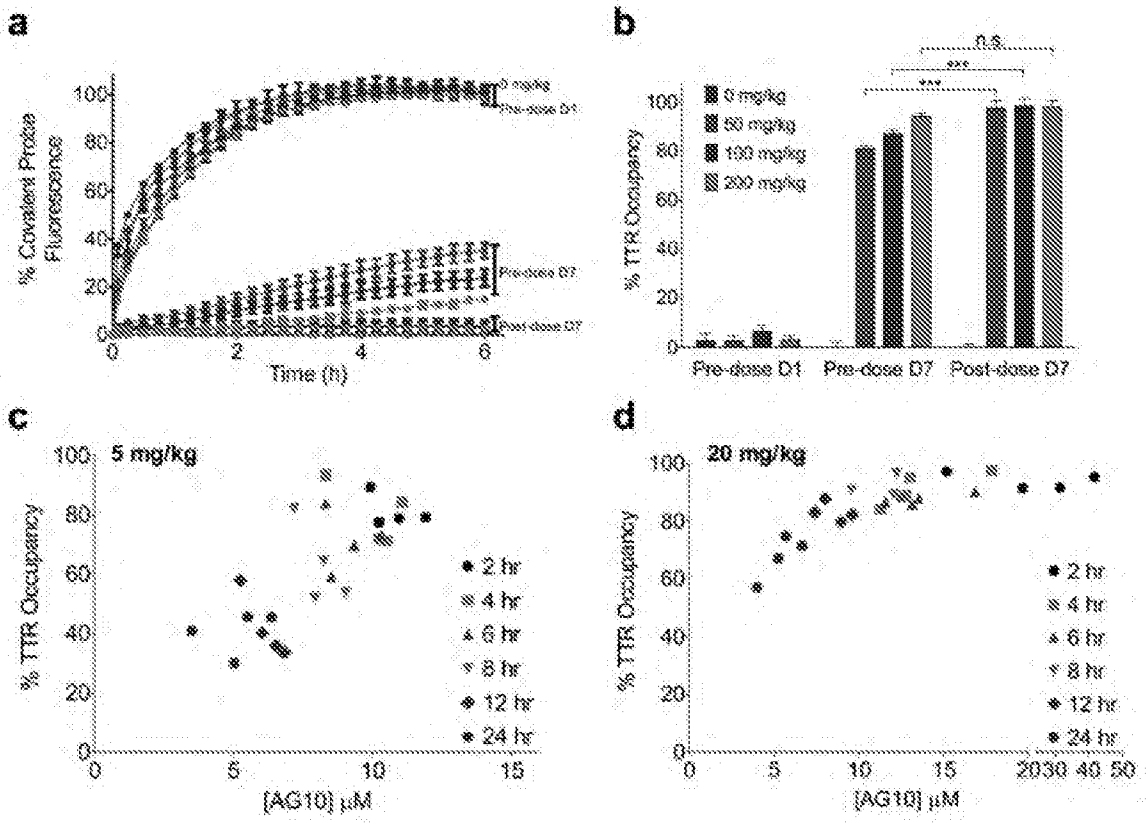

a
% Covalent Probe Fluorescence
Time (h)
b
% TTR Occupancy
0 mg/kg
50 mg/kg
100 mg/kg
200 mg/kg
n.s.
***
***
Pre-dose D1
Pre-dose D7
Post-dose D7
c
5 mg/kg
% TTR Occupancy
[AG10] µM
2 hr
4 hr
6 hr
8 hr
12 hr
24 hr
d
20 mg/kg
% TTR Occupancy
[AG10] µM
2 hr
4 hr
6 hr
8 hr
12 hr
24 hr

FIG. 22

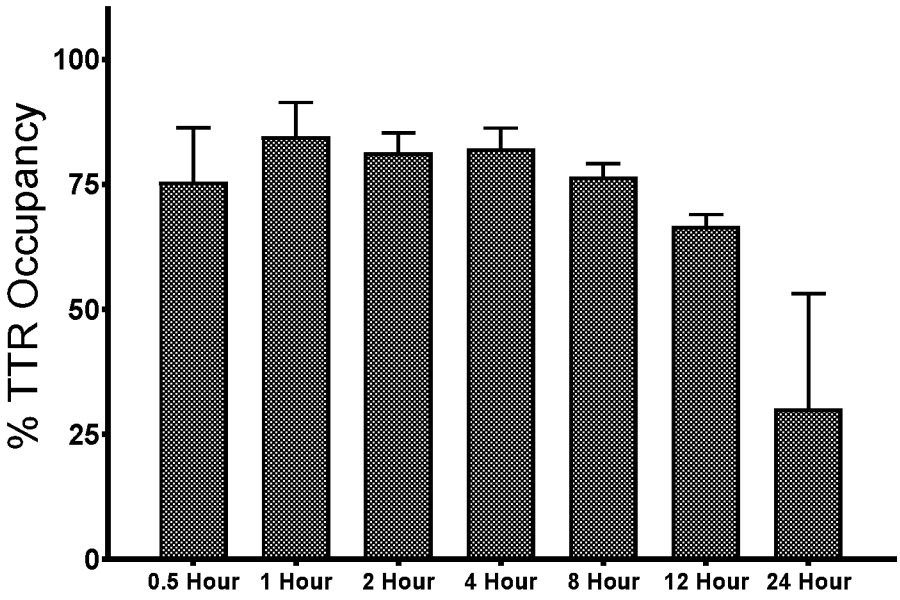

% TTR Occupancy
100
75
50
25
0
0.5 Hour
1 Hour
2 Hour
4 Hour
8 Hour
12 Hour
24 Hour

FIG. 23

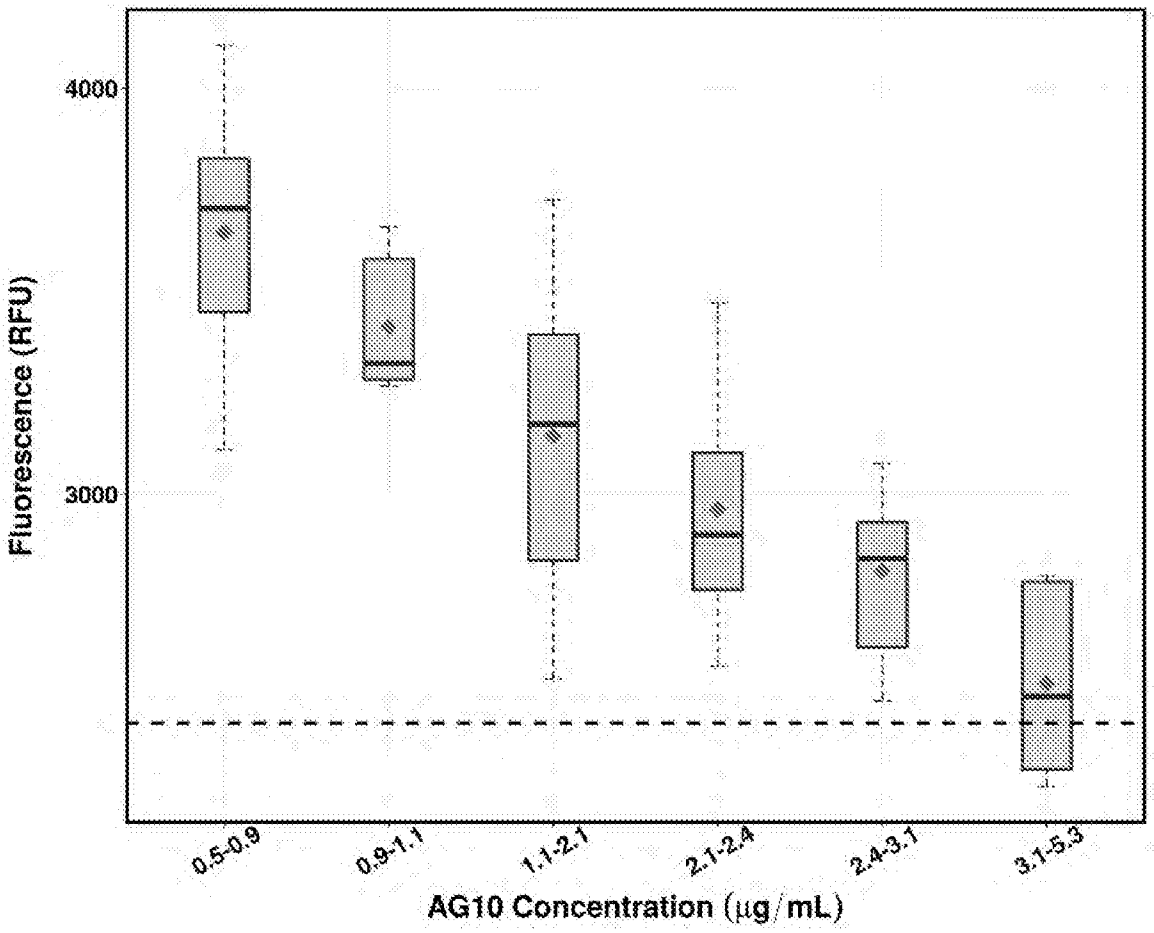

4000
3000
Fluorescence (RFU)
0.5-0.9
0.9-1.1
1.1-2.1
2.1-2.4
2.4-3.1
3.1-5.3
AG10 Concentration (µg/mL)

FIG. 24

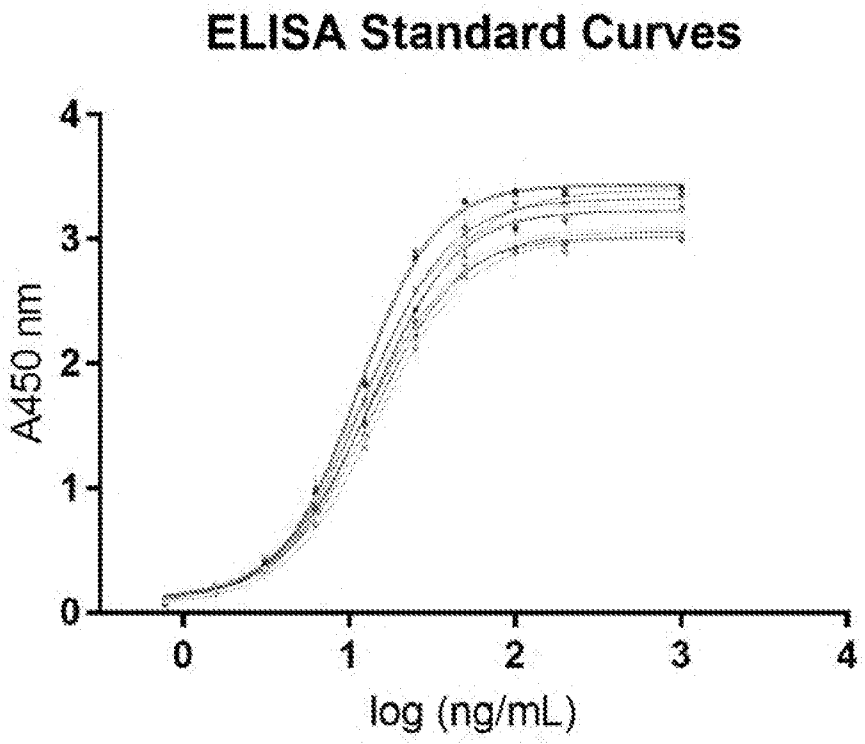

ELISA Standard Curves
A450 nm
0
1
2
3
4
log (ng/mL)

FIG. 25

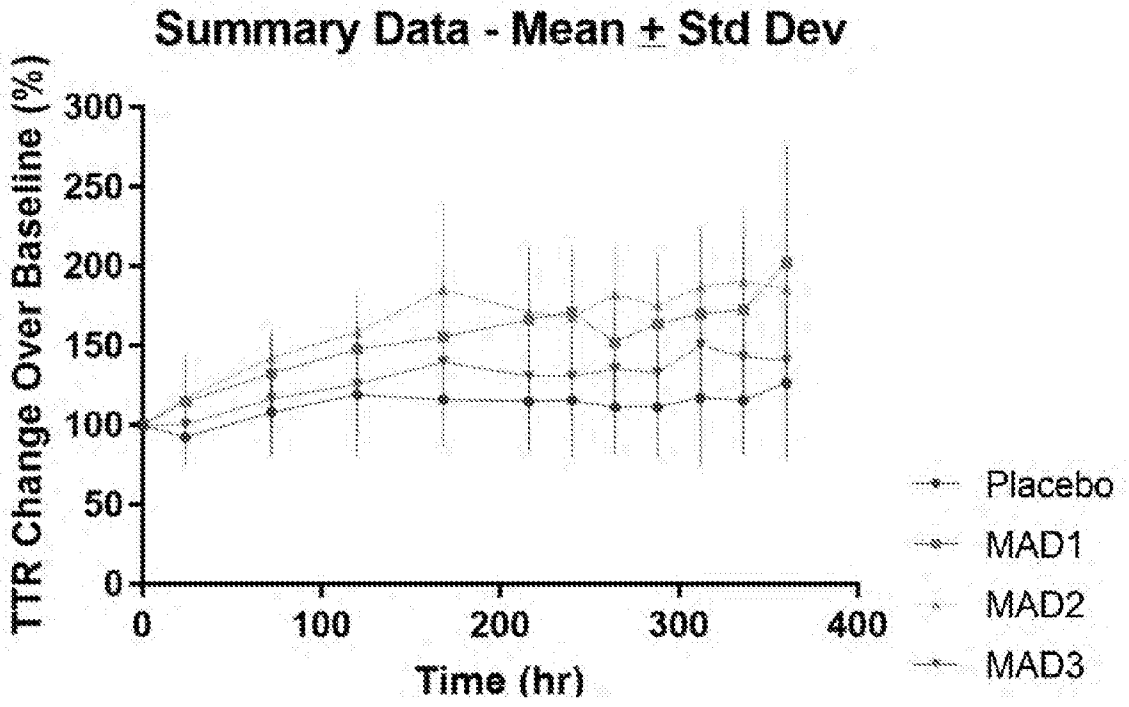

Summary Data - Mean ± Std Dev
TTR Change Over Baseline (%)
300
250
200
150
100
50
0
0
100
200
300
400
Time (hr)
Placebo
MAD1
MAD2
MAD3

FIG. 26

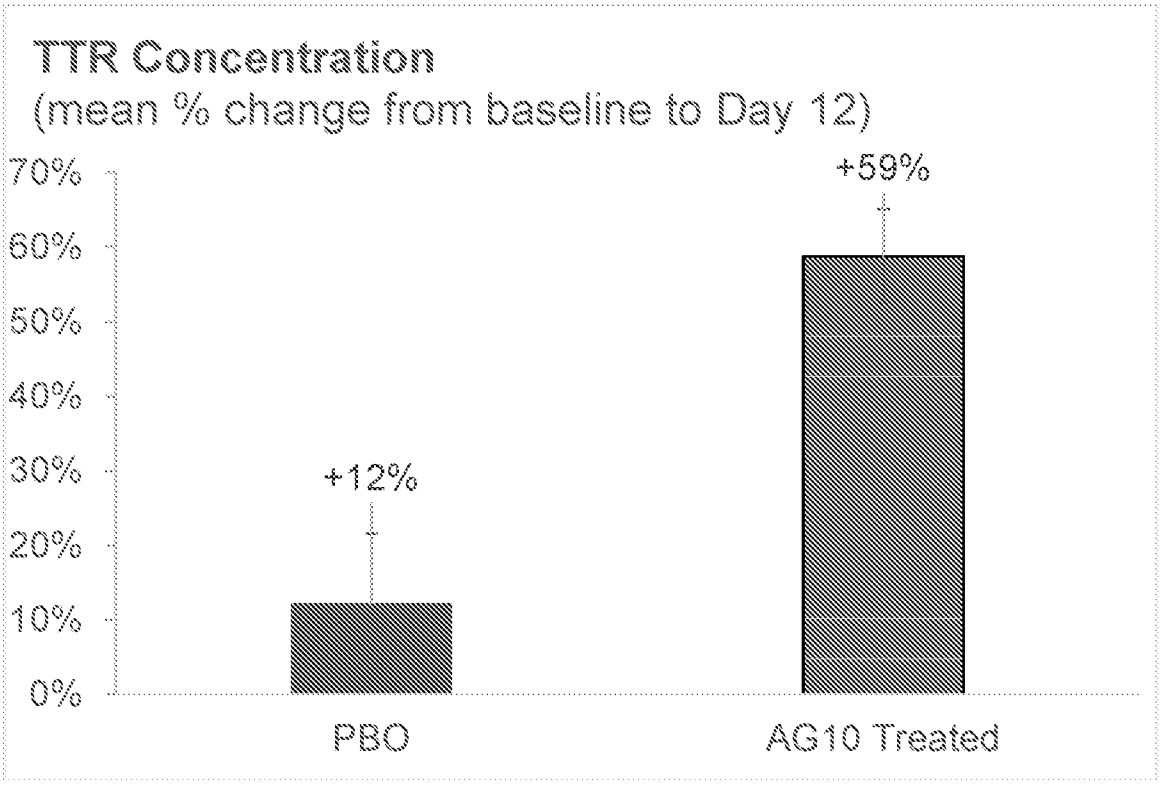

TTR Concentration
(mean % change from baseline to Day 12)
70%
60%
50%
40%
30%
20%
10%
0%
+12%
+59%
PBO
AG10 Treated

FIG. 27

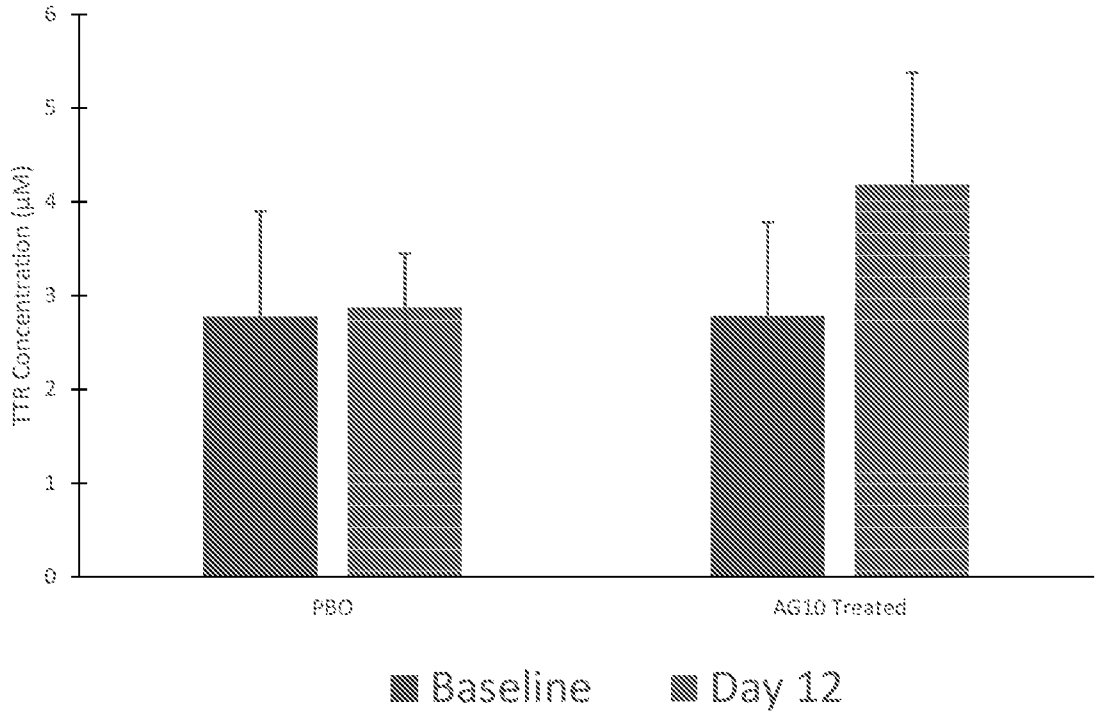

TTR Concentration (µM)
0
1
2
3
4
5
6
PBO
AG10 Treated
Baseline
Day 12

FIG. 28

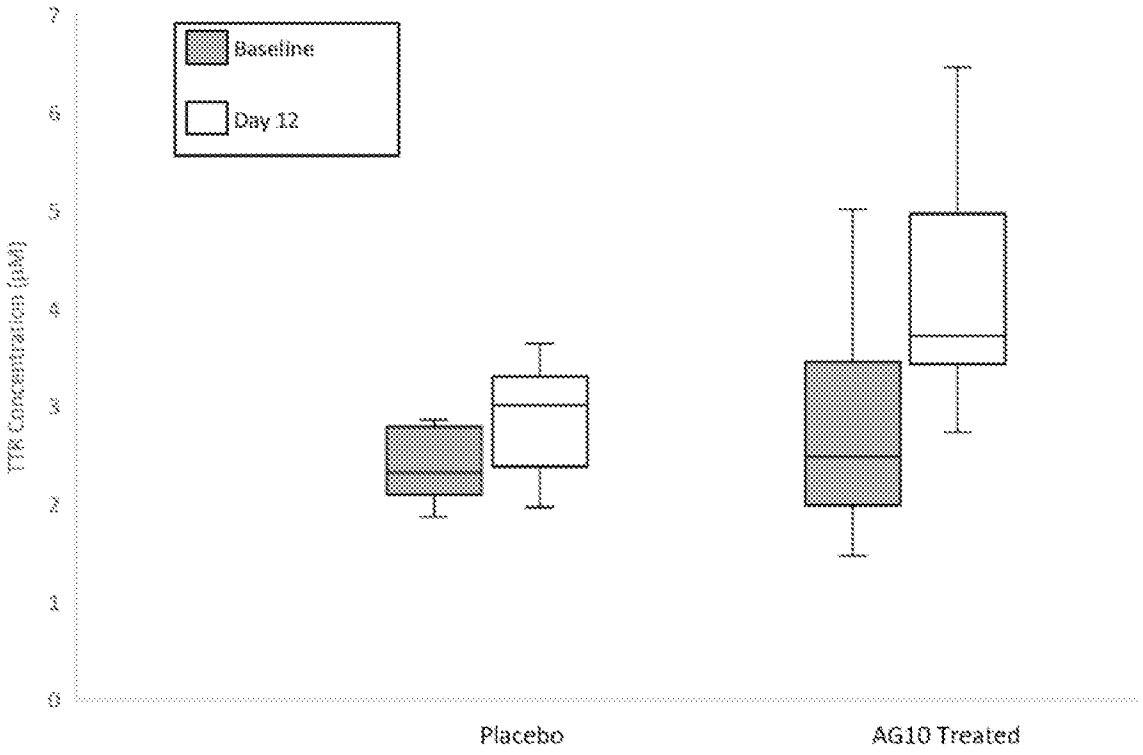

Baseline
Day 12
TTR Concentration (µg/dl)
0
1
2
3
4
5
6
7
Placebo
AG10 Treated

FIG. 29

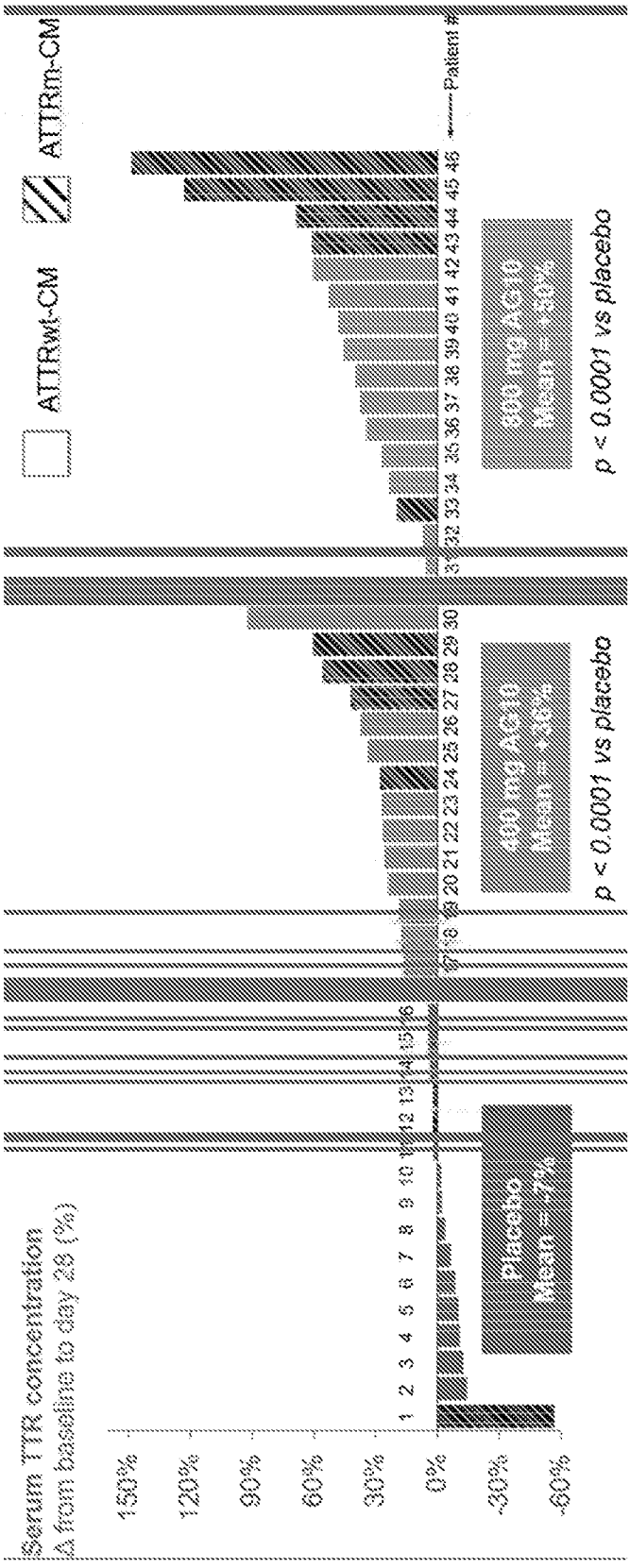

Serum TTR concentration
Δ from baseline to day 28 (%)
150%
120%
90%
60%
30%
0%
-30%
-60%
ATTRwt-CM
ATTRm-CM
Patient #
Placebo
Mean = -7%
400 mg ACH-0
Mean = -74%
p < 0.0001 vs placebo
400 mg ACH-0
Mean = -56%
p < 0.0001 vs placebo

FIG. 30

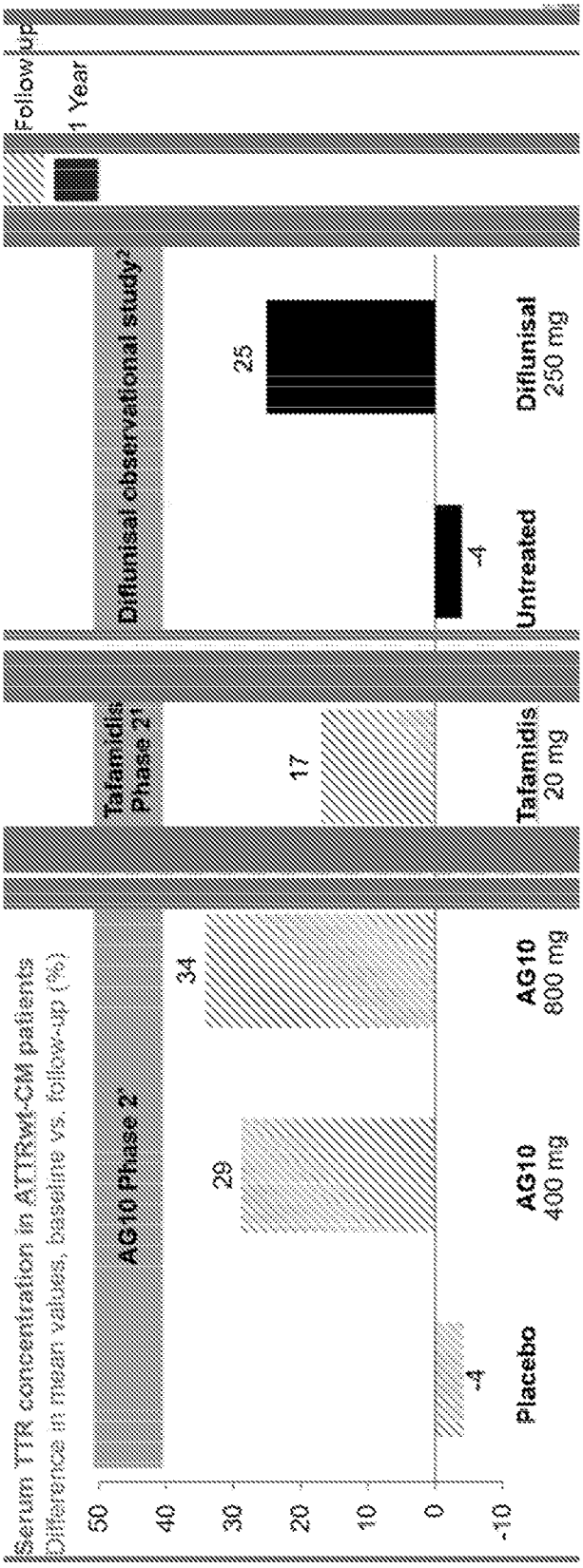

Serum TTR concentration in ATTRwt-CM patients
Difference in mean values, baseline vs. follow-up (%)
50
40
30
20
10
0
-10
AG10 Phase 2
Placebo
-4
29
AG10
400 mg
34
AG10
800 mg
Tafamidis
Phase 2¹
17
Tafamidis
20 mg
Diflunisal observational study²
-4
Untreated
25
Diflunisal
250 mg
Follow-up
1 Year

FIG. 31

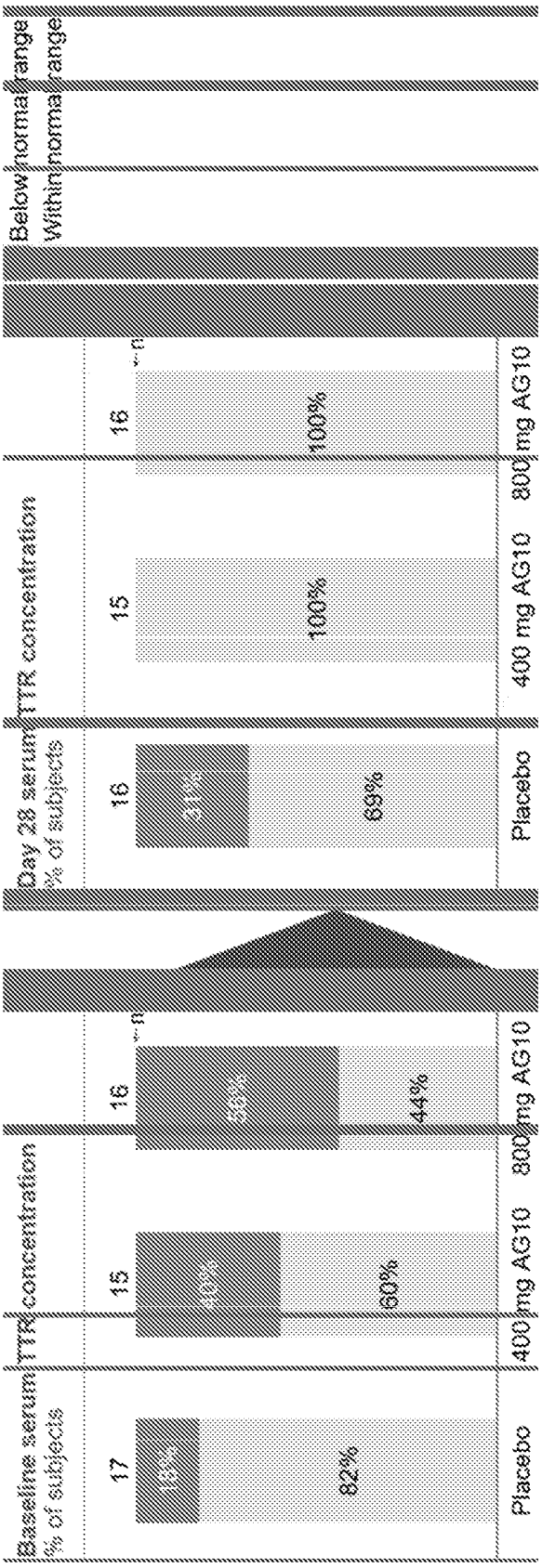

Baseline serum TTR concentration
% of subjects
Day 28 serum TTR concentration
% of subjects
Below normal range
Within normal range
n=
17
15
16
16
18%
82%
40%
60%
56%
44%
31%
69%
100%
100%
Placebo
400 mg AG10
800 mg AG10
Placebo
400 mg AG10
800 mg AG10

FIG. 32

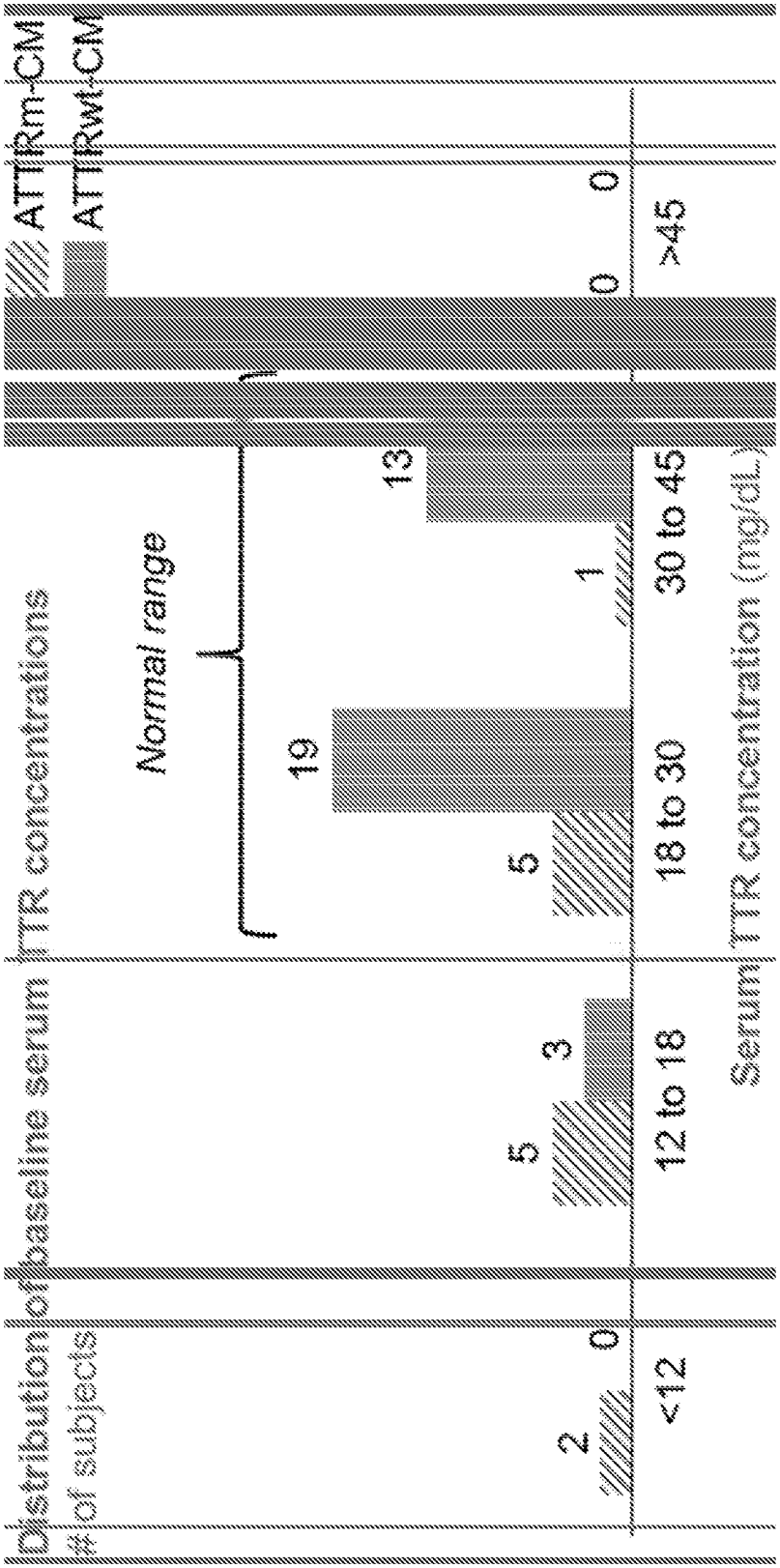

Distribution of baseline serum TTR concentrations
# of subjects
Serum TTR concentration (mg/dL)
<12
12 to 18
18 to 30
30 to 45
>45
Normal range
ATTRm-CM
ATTRwt-CM
2
0
5
3
5
19
1
13
1
0
0

FIG. 33

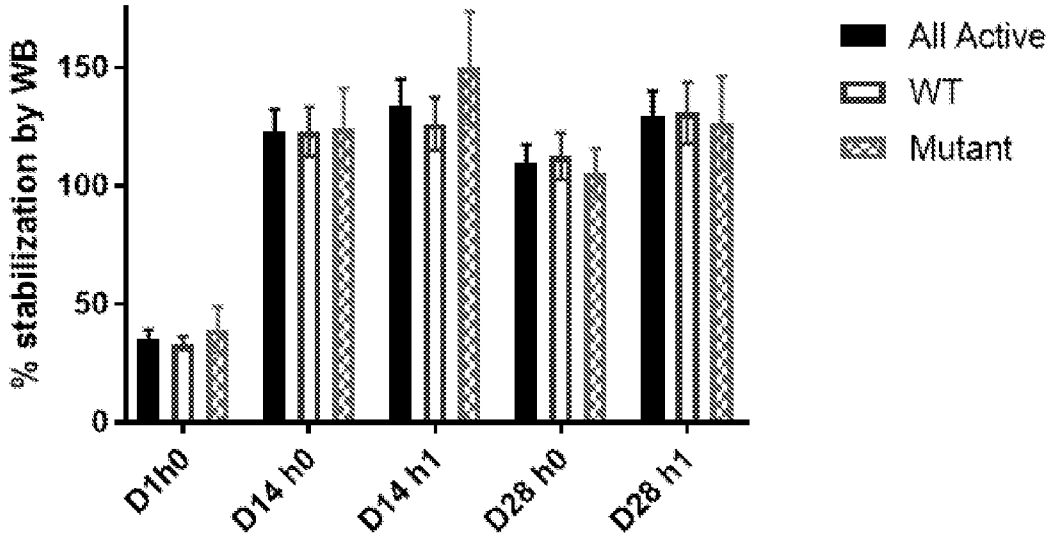

% stabilization by WB
150
100
50
0
D1h0
D14 h0
D14 h1
D28 h0
D28 h1
All Active
WT
Mutant

FIG. 34

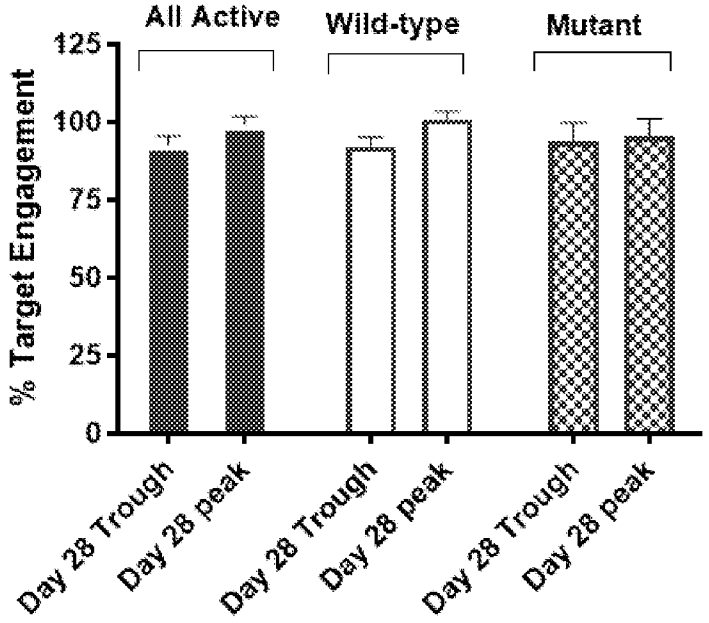

All Active
Wild-type
Mutant
% Target Engagement
125
100
75
50
25
0
Day 28 Trough
Day 28 peak
Day 28 Trough
Day 28 peak
Day 28 Trough
Day 28 peak

FIG. 35

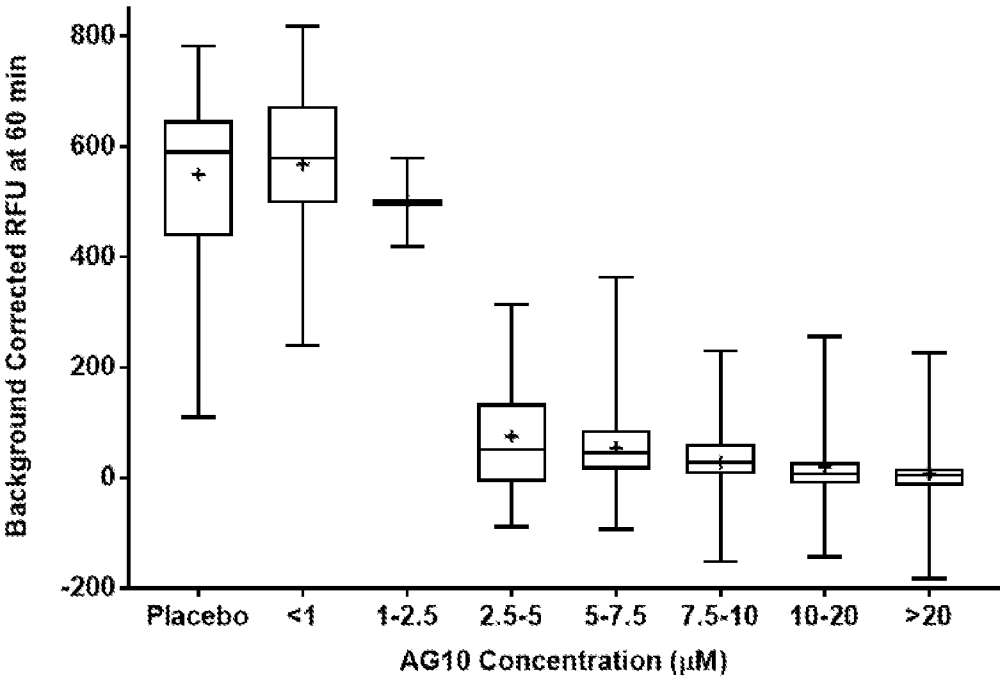

Background Corrected RFU at 60 min
800
600
400
200
0
-200
Placebo
<1
1-2.5
2.5-5
5-7.5
7.5-10
10-20
>20
AG10 Concentration (μM)

FIG. 36

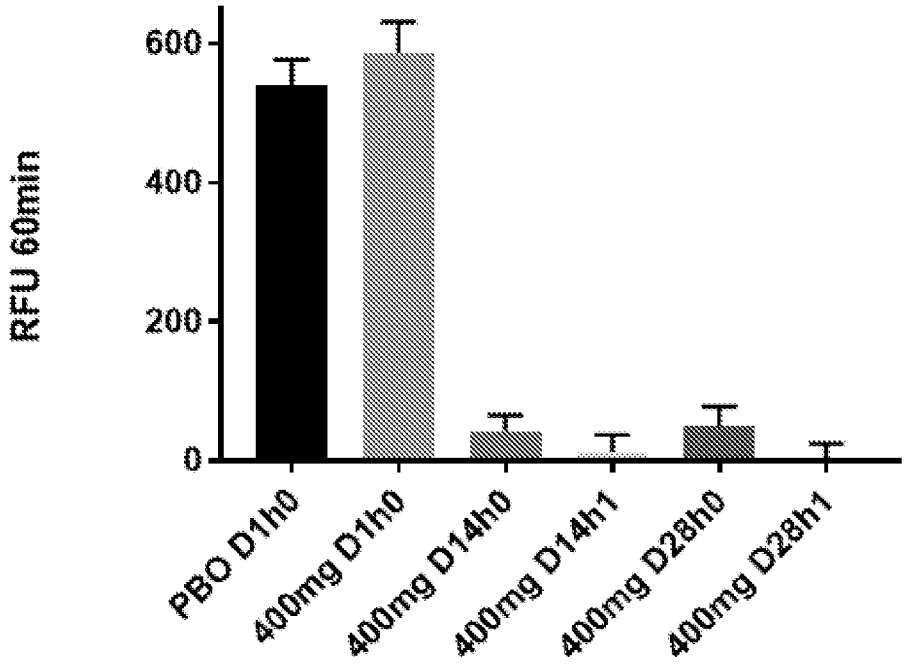

RFU 60min
600
400
200
0
PBO D1h0
400mg D1h0
400mg D14h0
400mg D14h1
400mg D28h0
400mg D28h1

FIG. 37

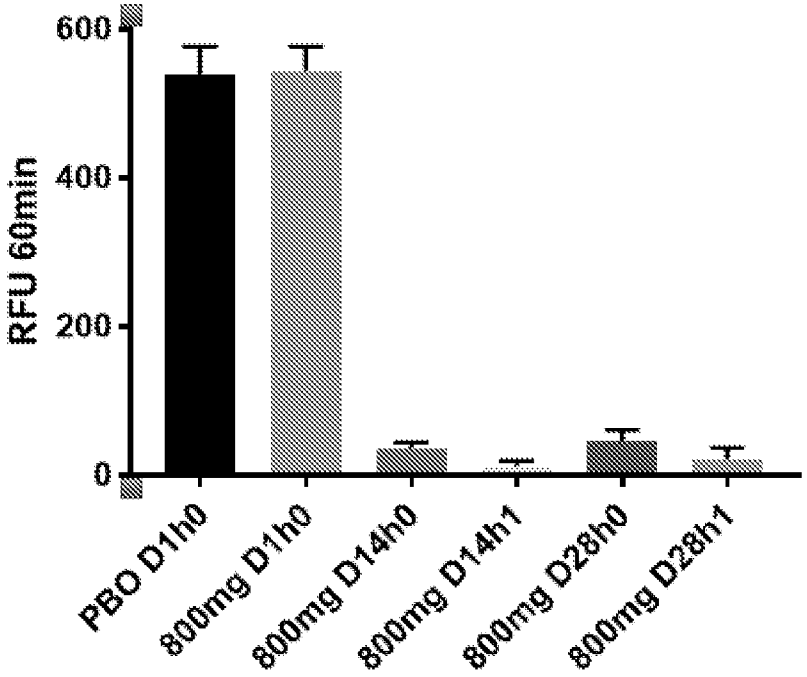

600
400
200
0
RFU 60min
PBO D1h0
800mg D1h0
800mg D14h0
800mg D14h1
800mg D28h0
800mg D28h1

FIG. 38

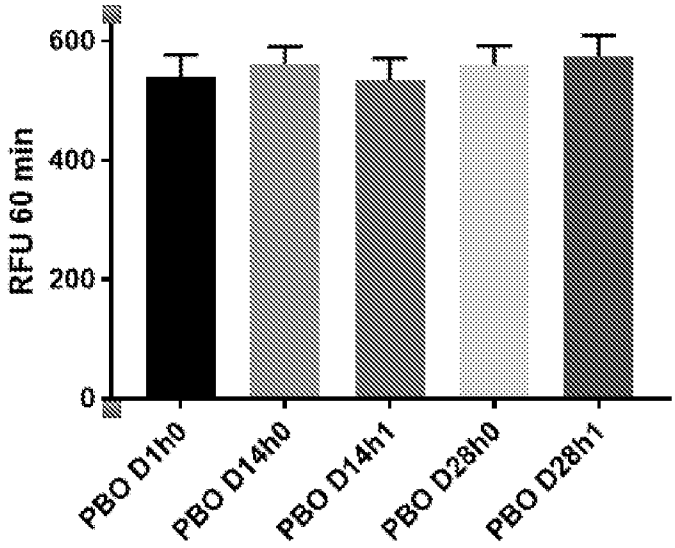

600
400
200
0
RFU 60 min
PBO D1h0
PBO D14h0
PBO D14h1
PBO D28h0
PBO D28h1

FIG. 39

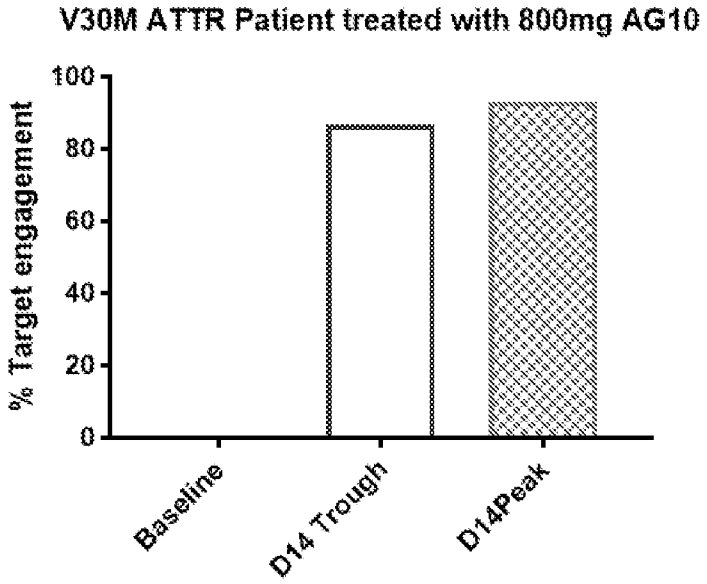

V30M ATTR Patient treated with 800mg AG10
% Target engagement
100
80
60
40
20
0
Baseline
D14 Trough
D14Peak

FIG. 40

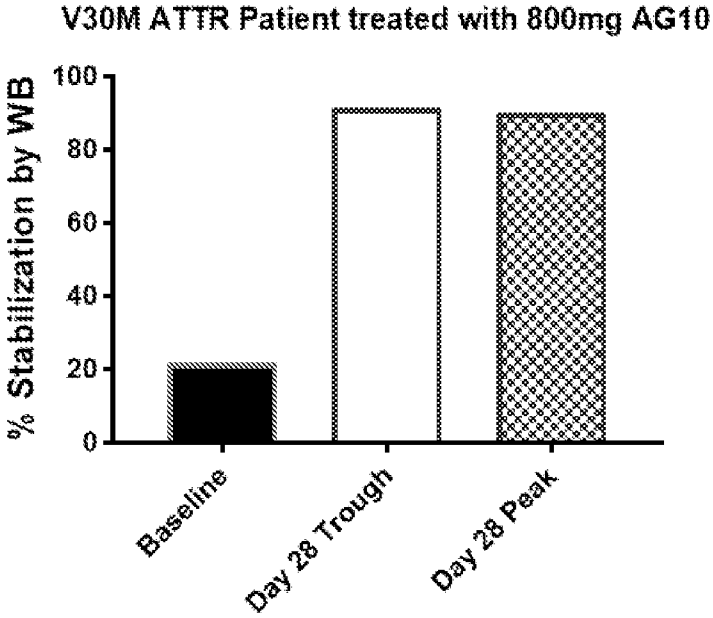

V30M ATTR Patient treated with 800mg AG10
% Stabilization by WB
100
80
60
40
20
0
Baseline
Day 28 Trough
Day 28 Peak

FIG. 41

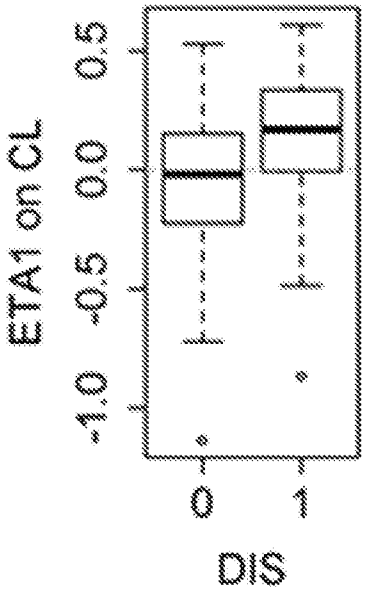


FIG. 42A

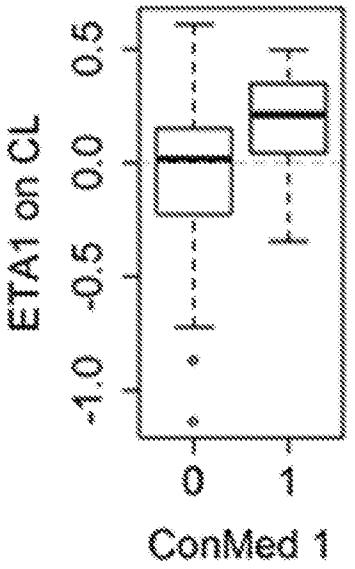


FIG. 42B

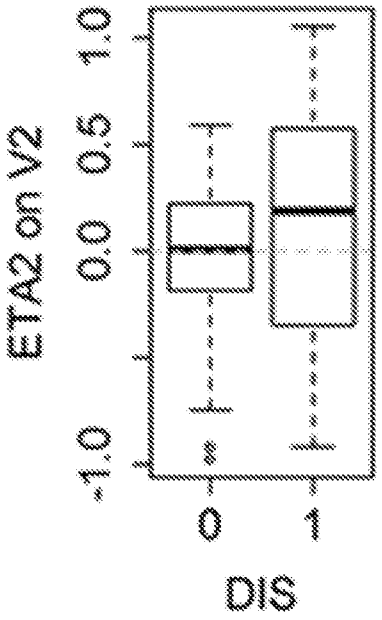


FIG. 42C

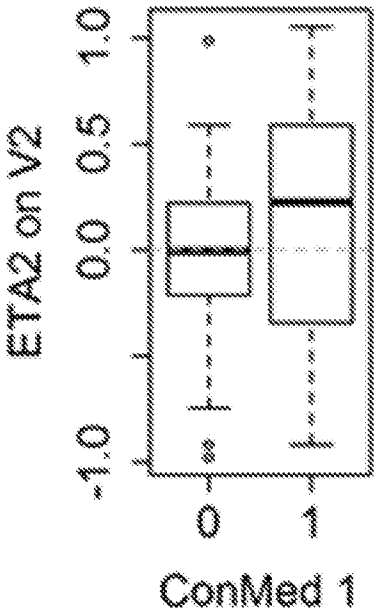


FIG. 42D

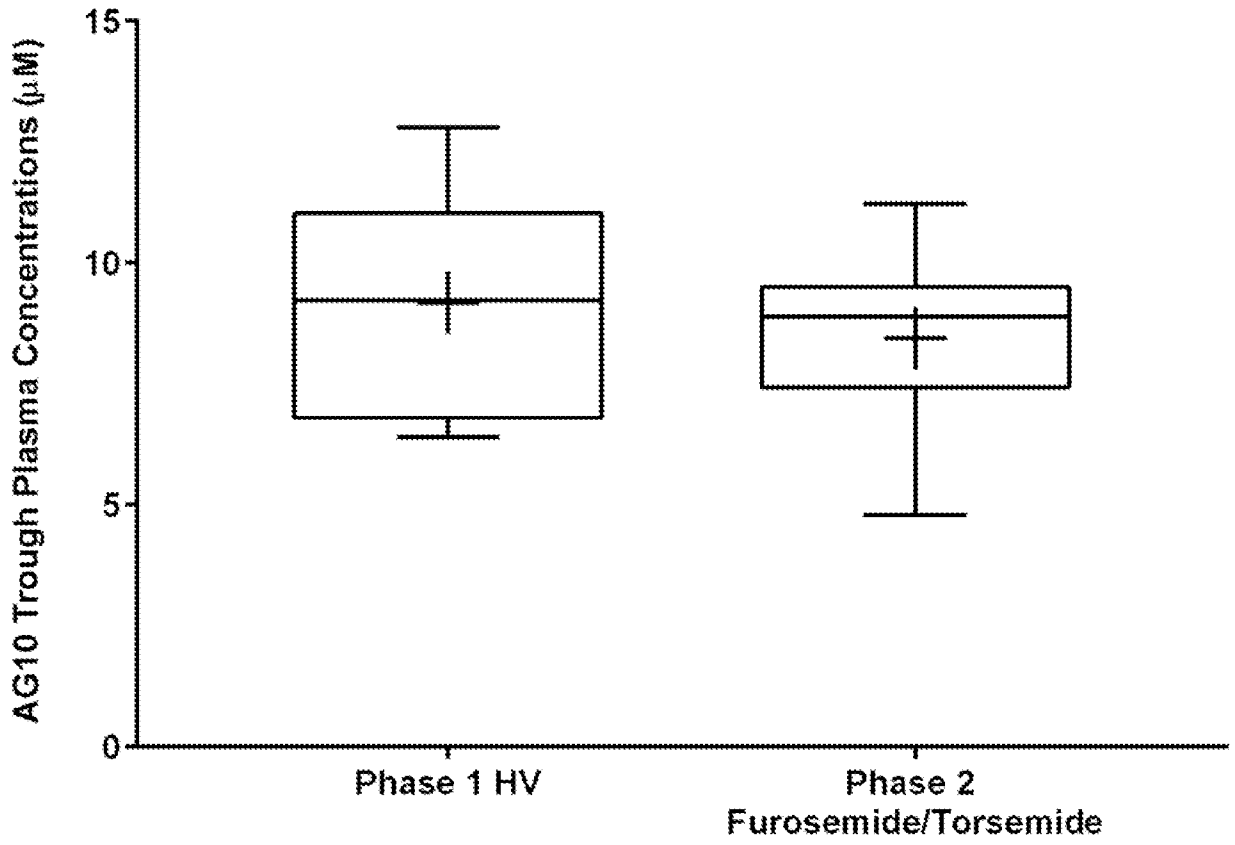

AG10 Trough Plasma Concentrations (μM)
15
10
5
0
Phase 1 HV
Phase 2
Furosemide/Torsemide

FIG. 43

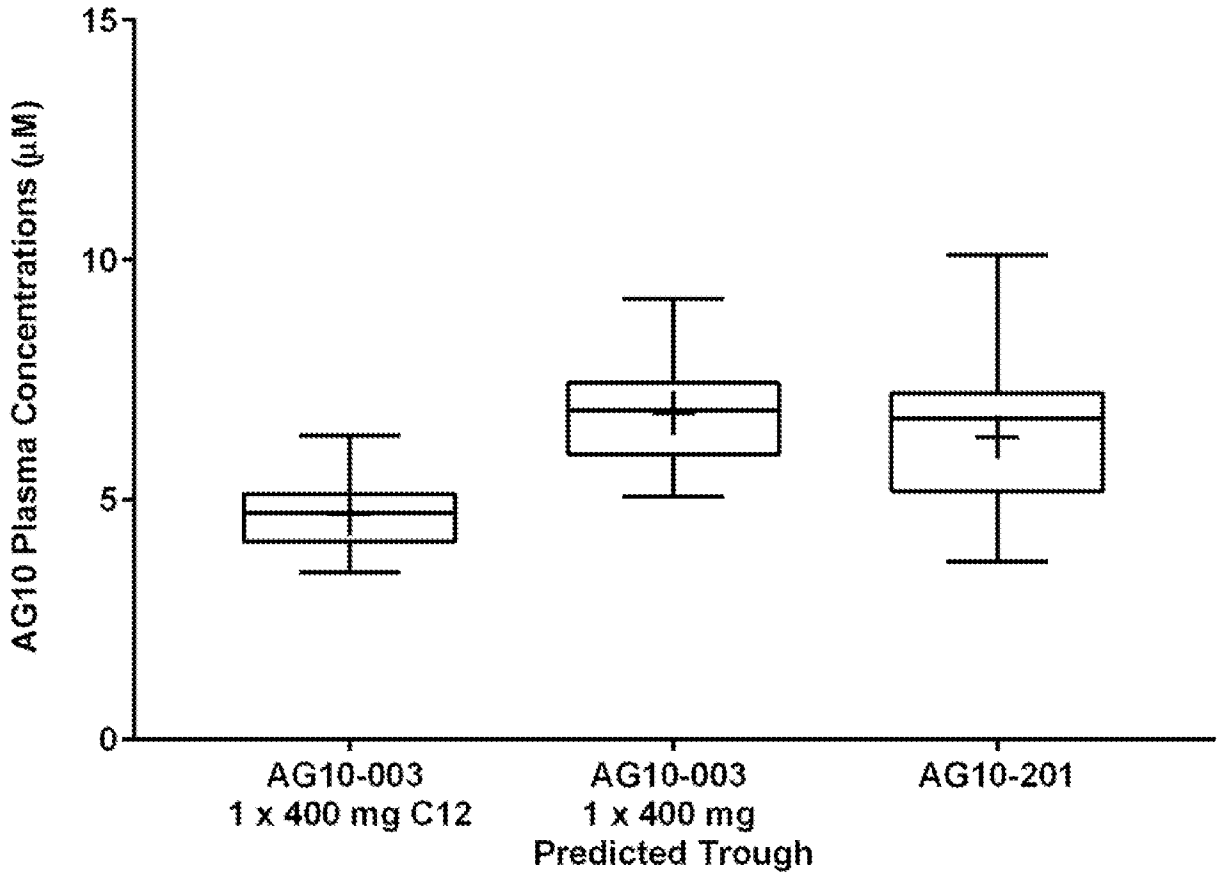

15
10
5
0
AG10 Plasma Concentrations (µM)
AG10-003
1 x 400 mg C12
AG10-003
1 x 400 mg
Predicted Trough
AG10-201

FIG. 44

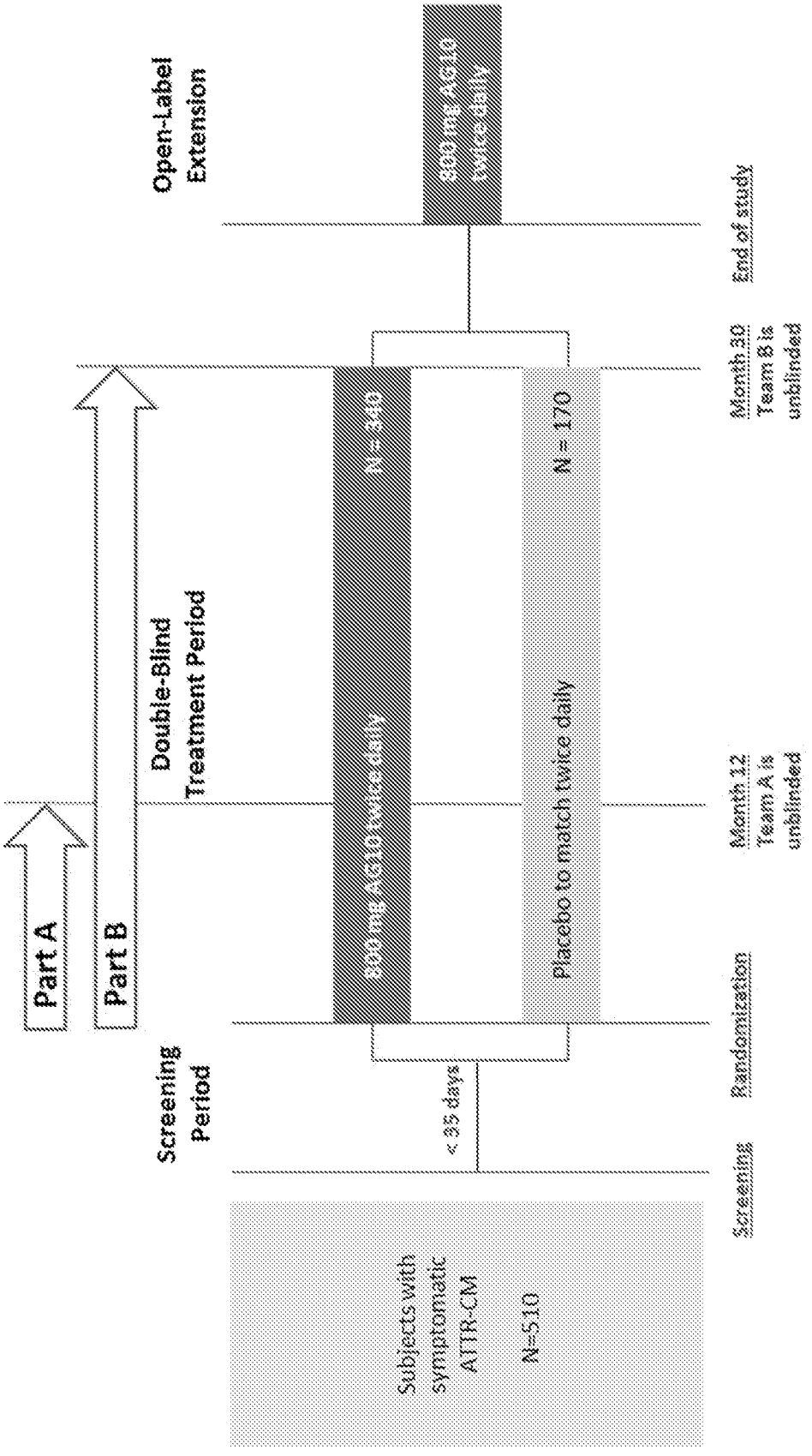

Subjects with symptomatic ATTR-CM
N=510
Screening
< 35 days
Randomization
Screening Period
Part A
Part B
Double-Blind Treatment Period
300 mg AG10 twice daily
N = 340
Placebo to match twice daily
N = 170
Month 12
Team A is unblinded
Month 30
Team B is unblinded
End of study
Open-Label Extension
300 mg AG10 twice daily

FIG. 45

85746598v.1

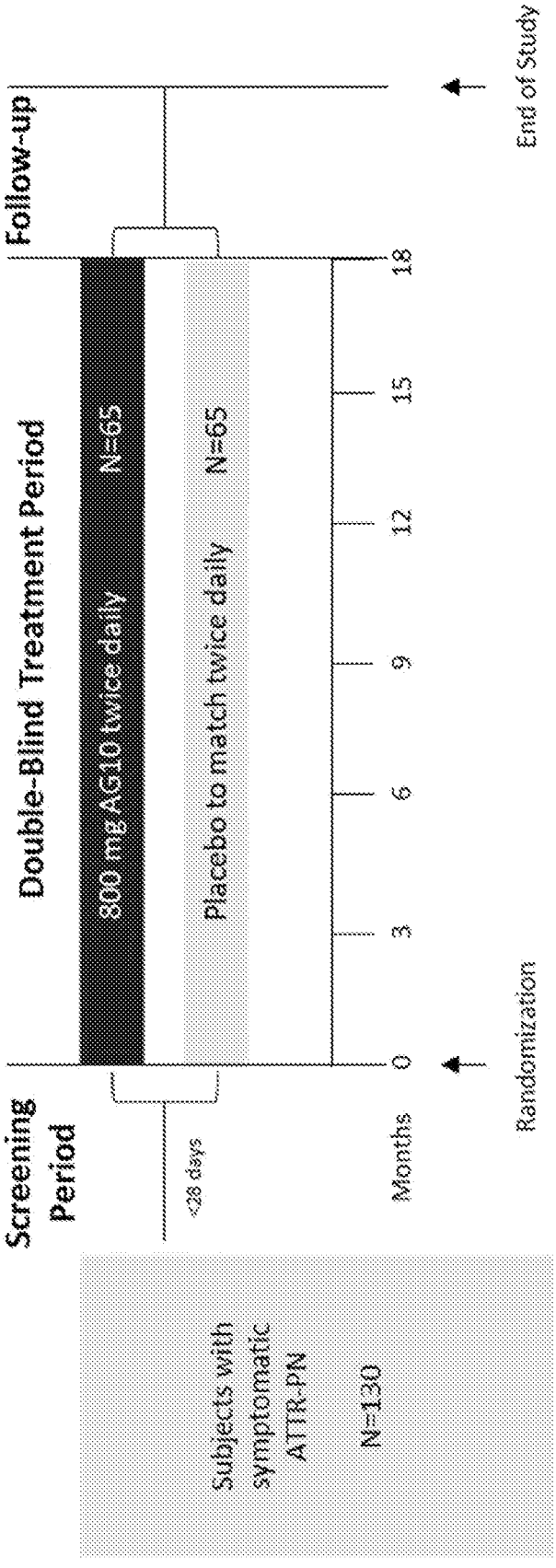


FIG. 46