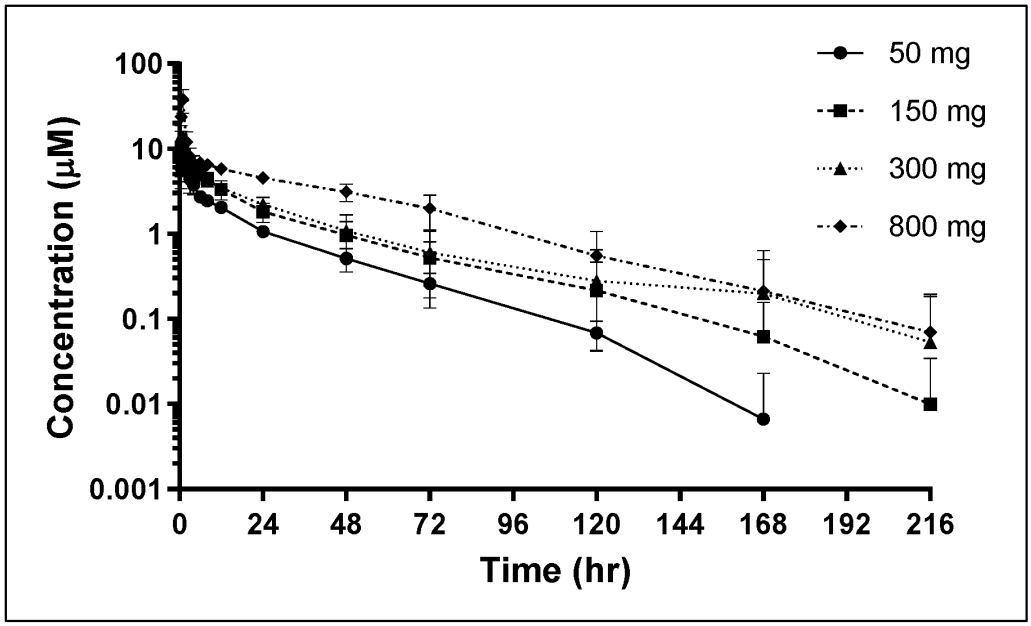

50 mg
150 mg
300 mg
800 mg
Concentration (μM)
100
10
1
0.1
0.01
0.001
0
24
48
72
96
120
144
168
192
216
Time (hr)

FIG. 1

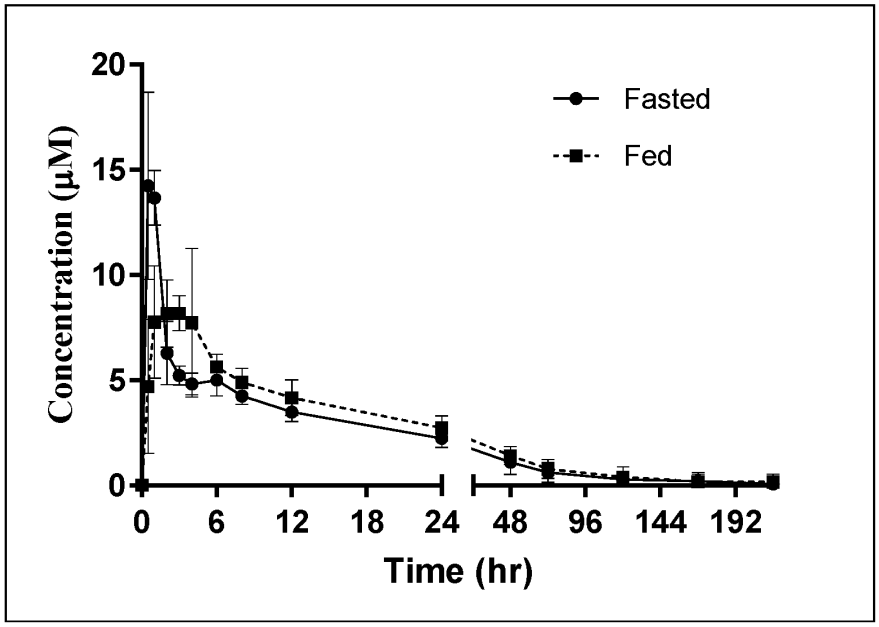

Fasted
Fed
Concentration (μM)
20
15
10
5
0
0
6
12
18
24
48
96
144
192
Time (hr)

FIG. 2

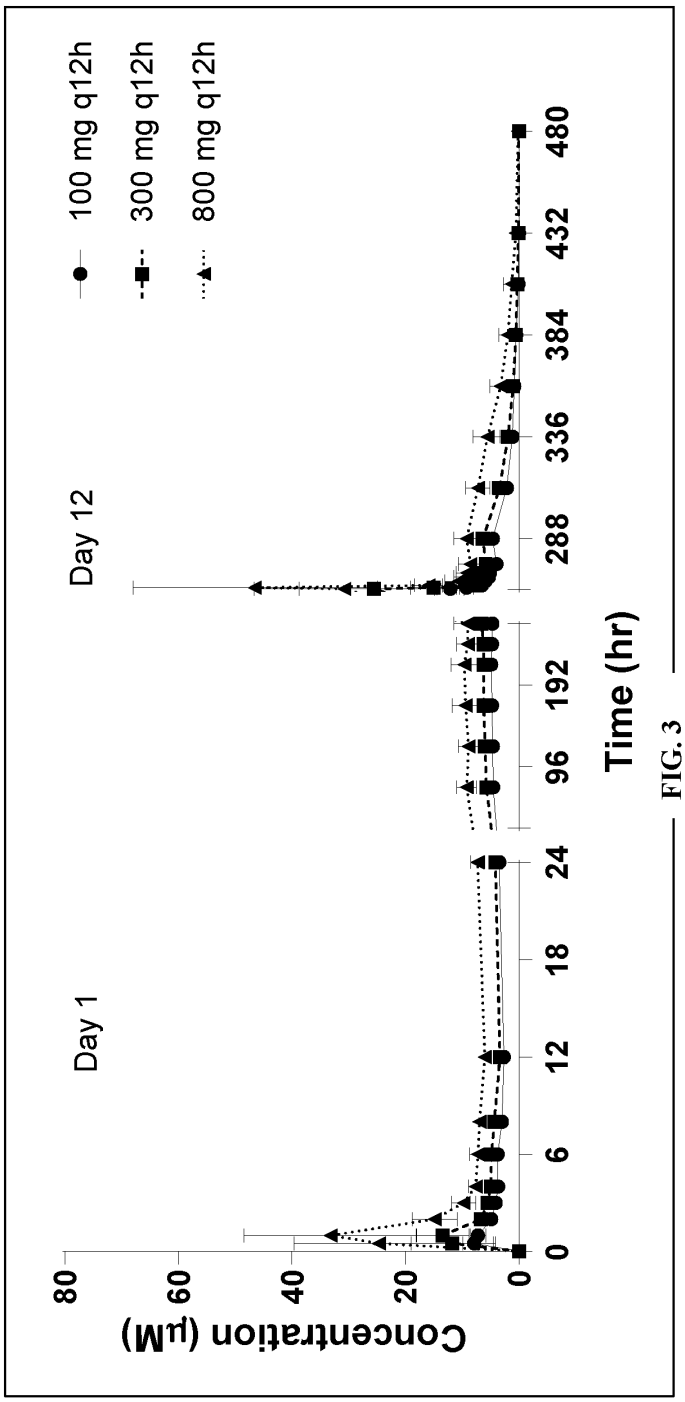

100 mg q12h
300 mg q12h
800 mg q12h
Day 1
Day 12
Concentration (μM)
0
20
40
60
80
0
6
12
18
24
96
192
288
336
384
432
480
Time (hr)

FIG. 3

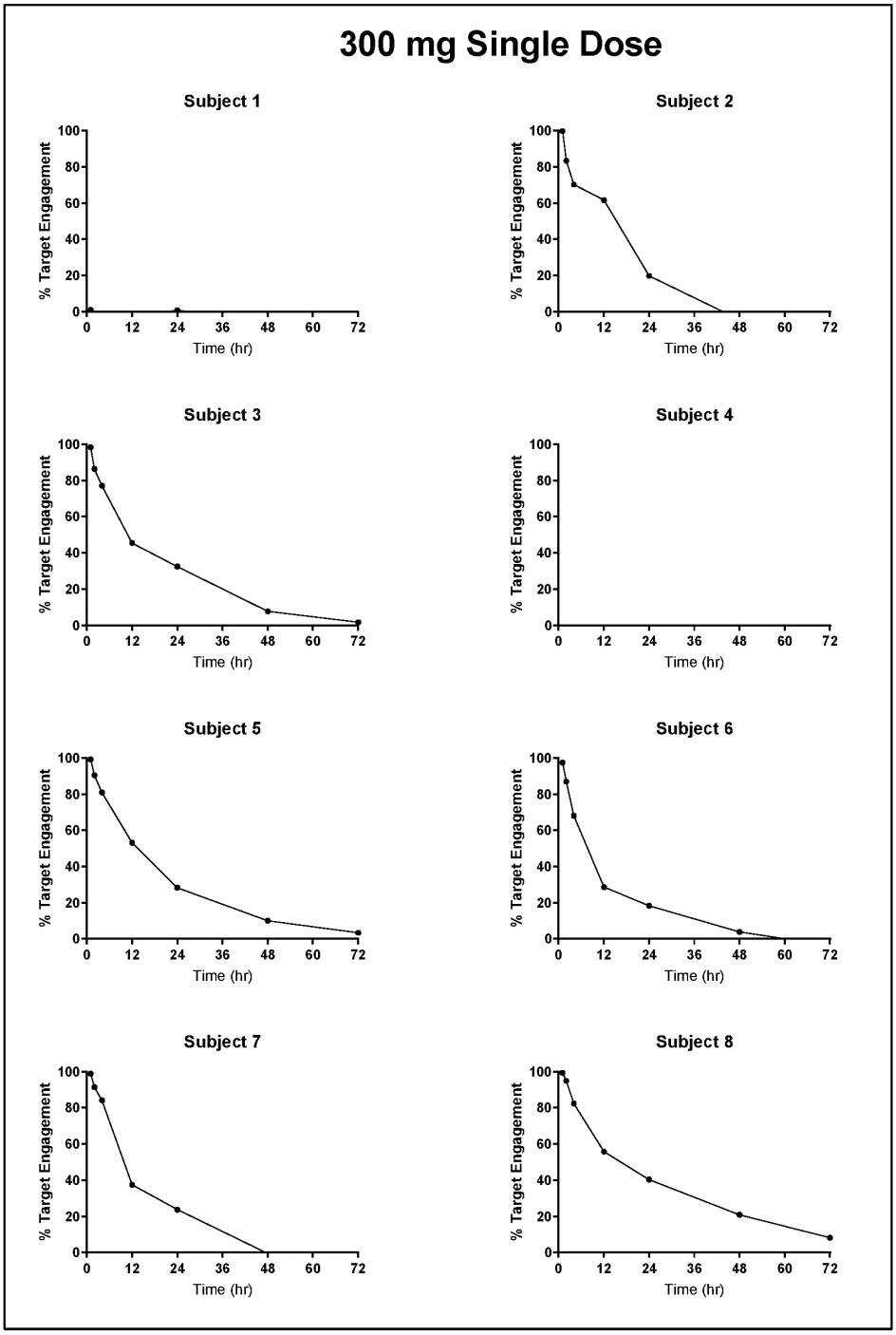

300 mg Single Dose
Subject 1
Subject 2
Subject 3
Subject 4
Subject 5
Subject 6
Subject 7
Subject 8
% Target Engagement
Time (hr)
0
12
24
36
48
60
72
20
40
60
80
100

FIG. 4

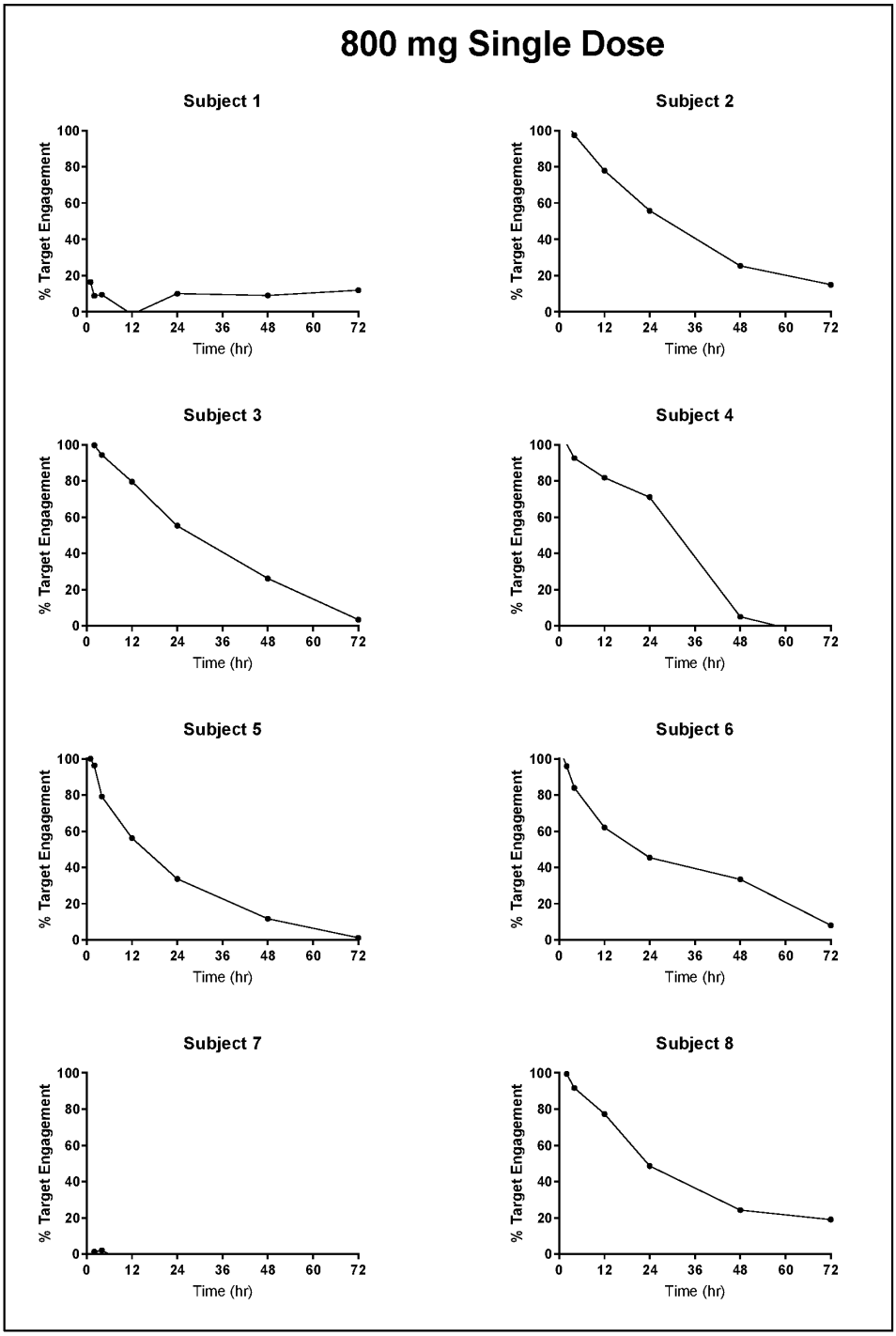

800 mg Single Dose
Subject 1
Subject 2
Subject 3
Subject 4
Subject 5
Subject 6
Subject 7
Subject 8
% Target Engagement
Time (hr)
0
20
40
60
80
100
0
12
24
36
48
60
72

FIG. 5

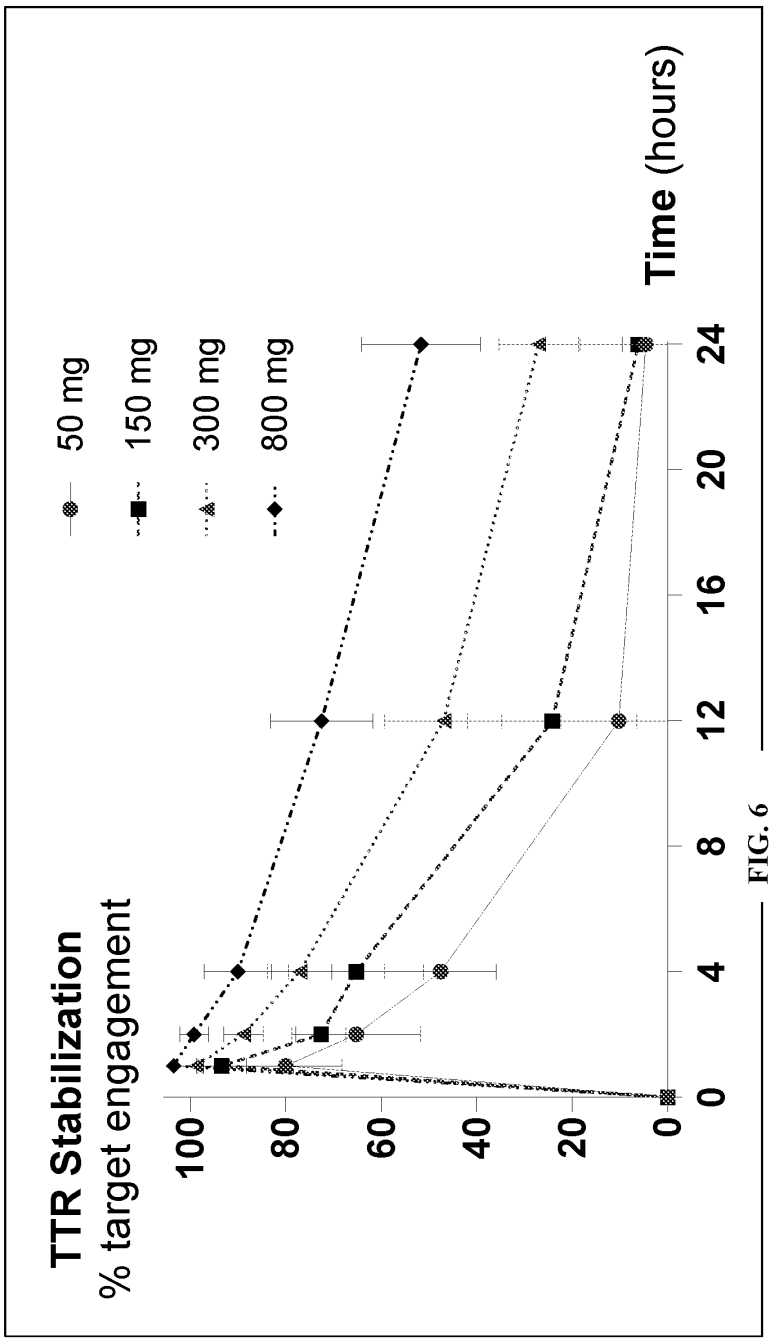

TTR Stabilization
% target engagement
100
80
60
40
20
0
0
4
8
12
16
20
24
Time (hours)
50 mg
150 mg
300 mg
800 mg

FIG. 6

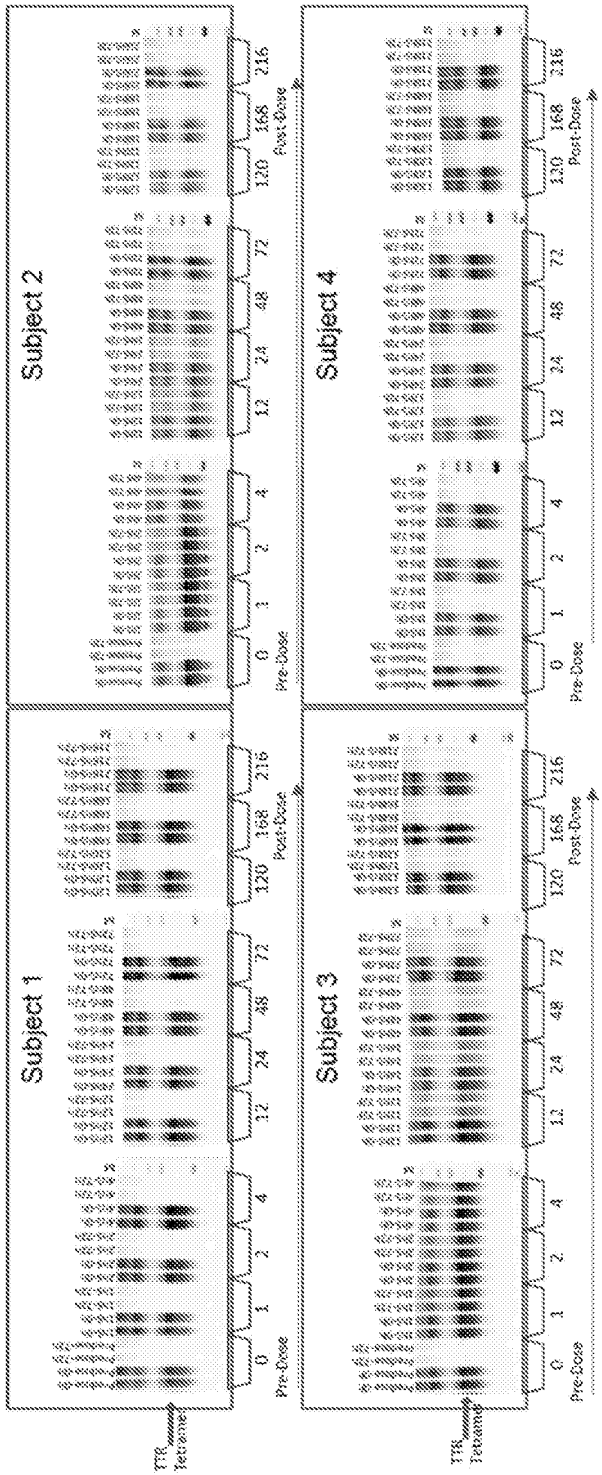

Subject 1
Subject 2
Subject 3
Subject 4
TTR Retainer
TTR Retainer
Pre-Dose
Post-Dose
0
1
2
4
12
24
48
72
120
168
216

FIG. 7A

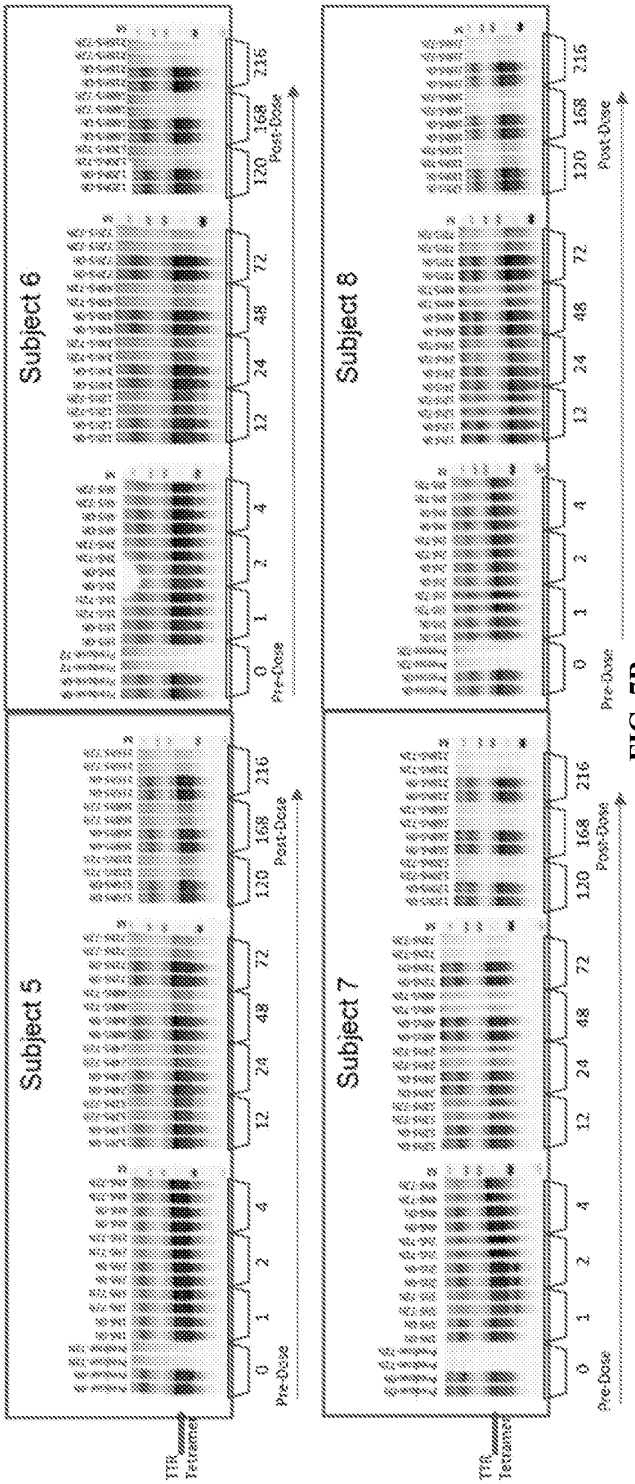

Subject 6
Subject 8
Subject 5
Subject 7
Pre-Dose
Post-Dose
0
1
2
4
12
24
48
72
120
168
216
TTR Tetramer

FIG. 7B

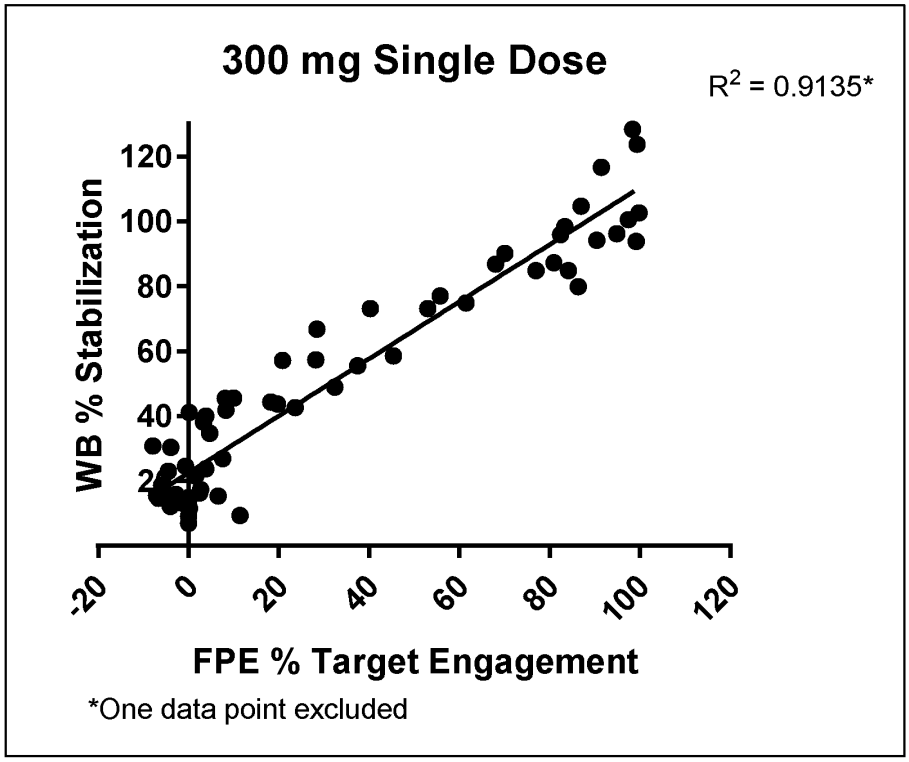

300 mg Single Dose
R^2 = 0.9135*
WB % Stabilization
120
100
80
60
40
20
-20
0
20
40
60
80
100
120
FPE % Target Engagement
*One data point excluded

FIG. 8

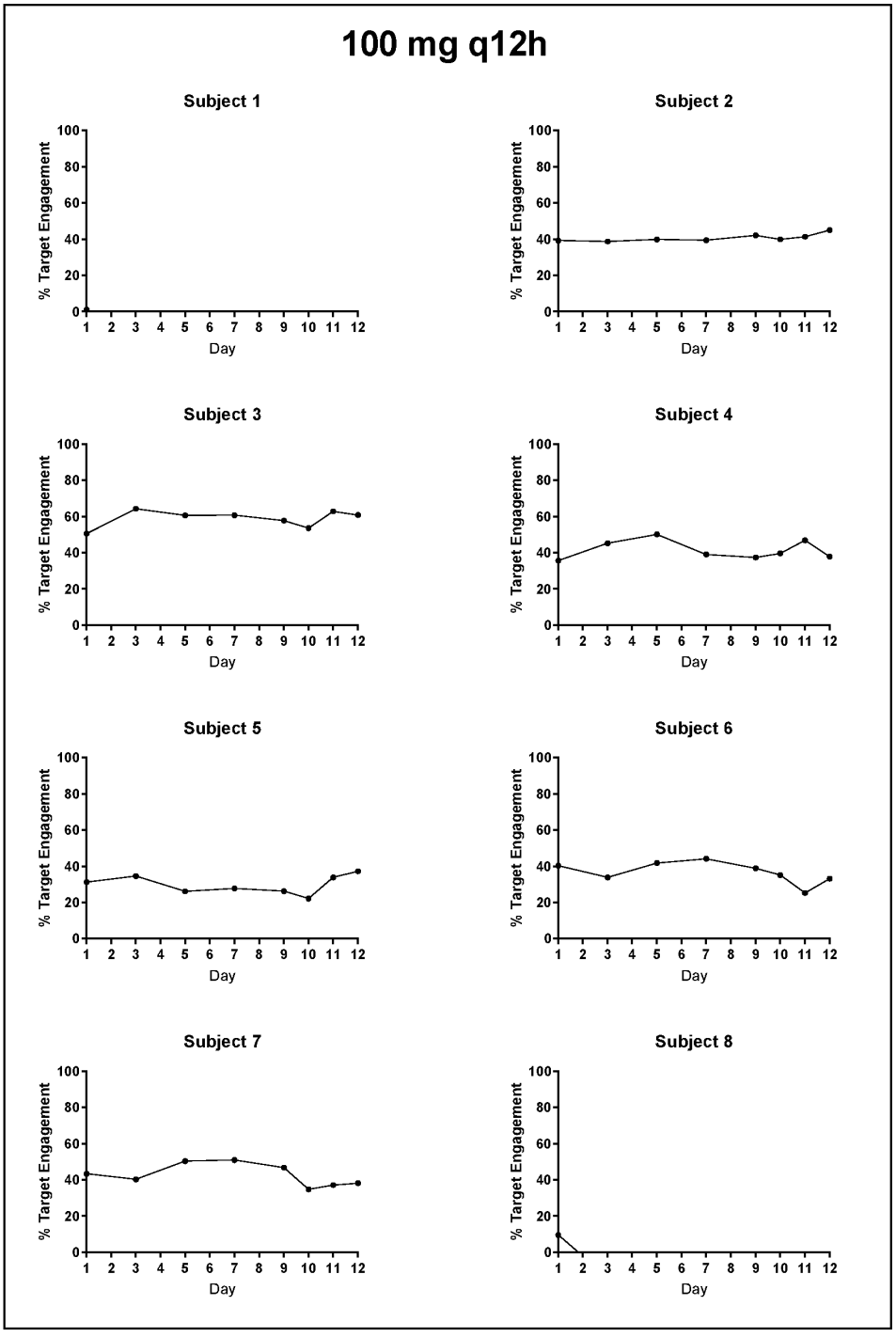

100 mg q12h
Subject 1
Subject 2
Subject 3
Subject 4
Subject 5
Subject 6
Subject 7
Subject 8
% Target Engagement
Day
0
20
40
60
80
100
1 2 3 4 5 6 7 8 9 10 11 12

FIG. 9

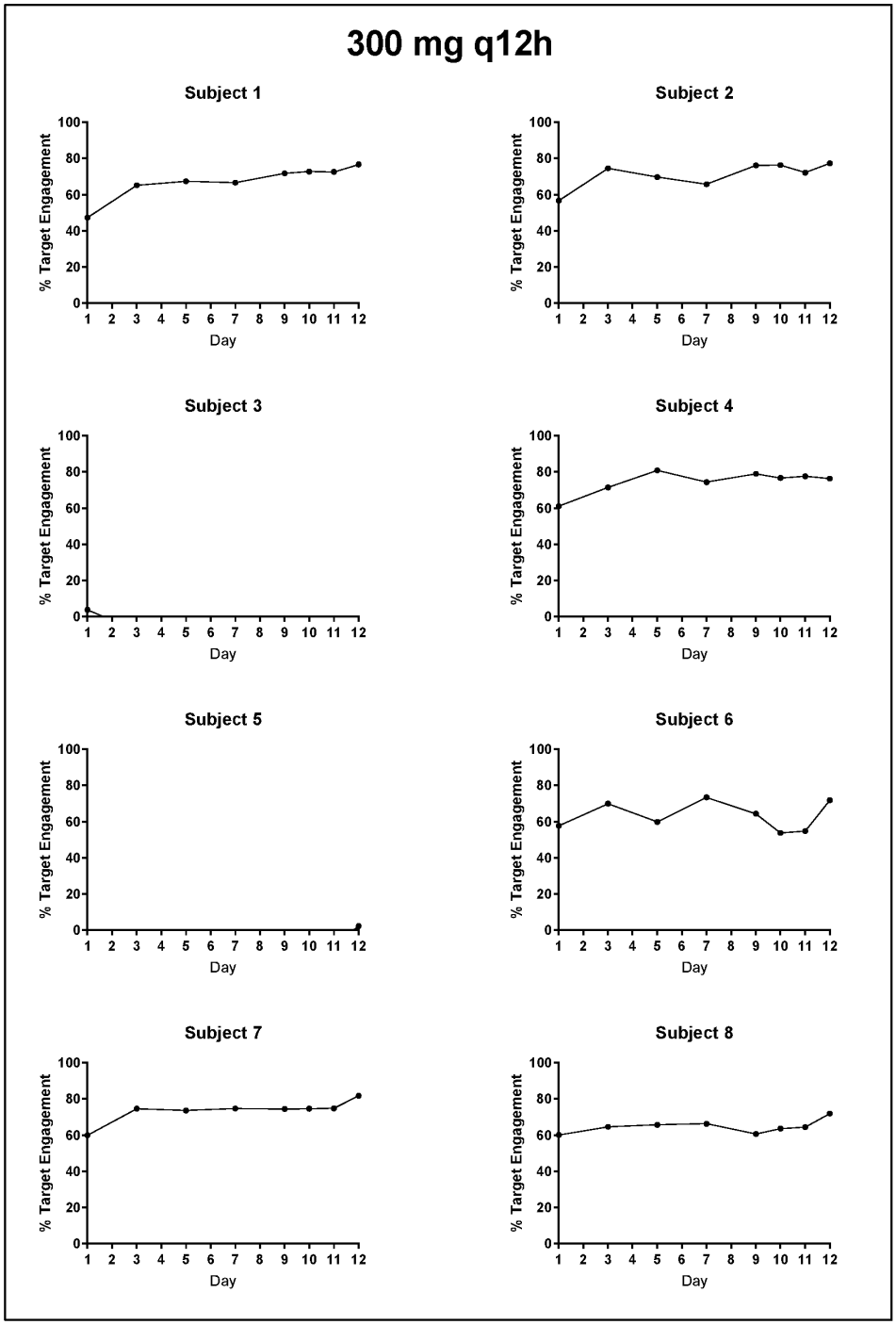

300 mg q12h
Subject 1
Subject 2
Subject 3
Subject 4
Subject 5
Subject 6
Subject 7
Subject 8
% Target Engagement
Day
0
20
40
60
80
100
1 2 3 4 5 6 7 8 9 10 11 12

FIG. 10

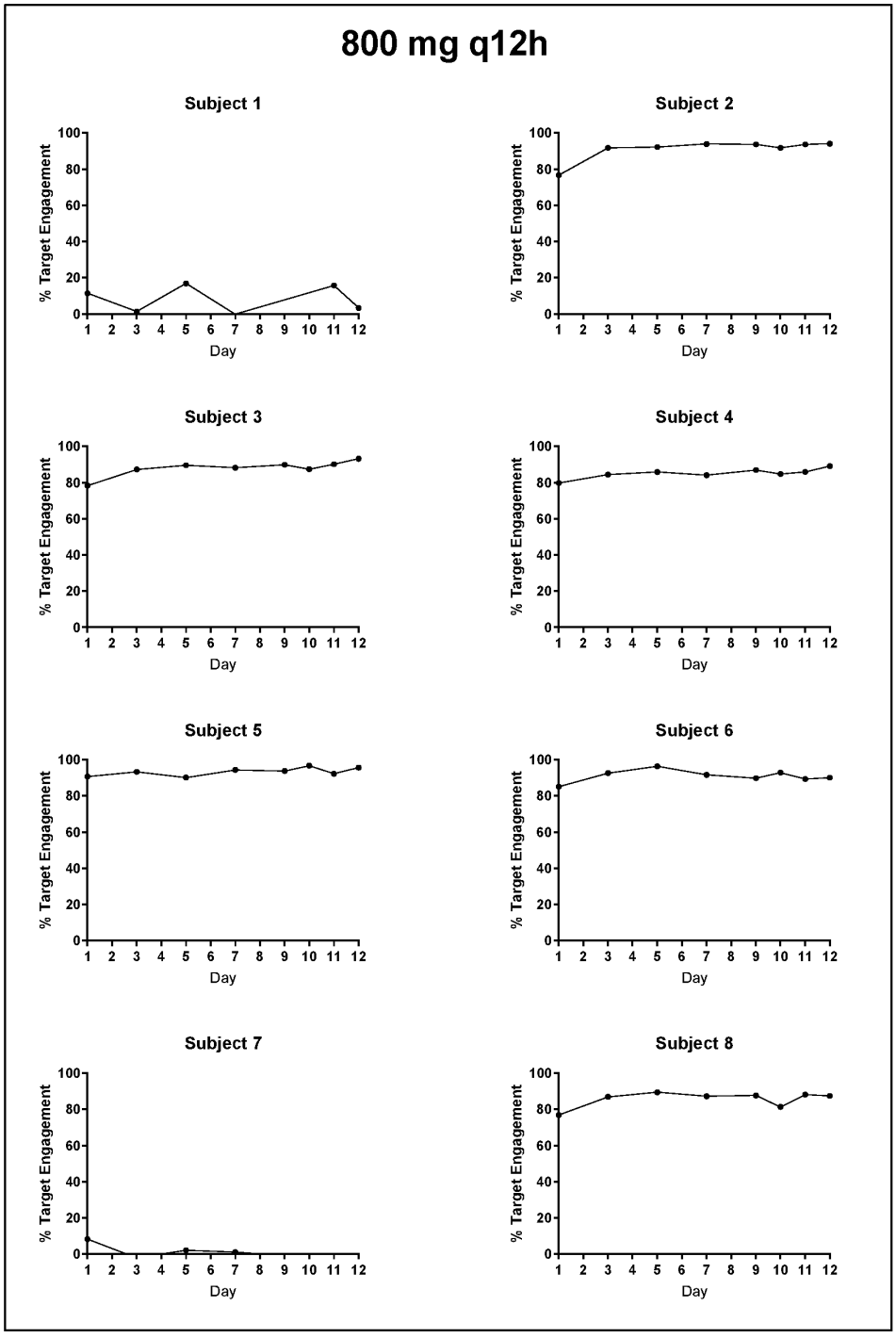
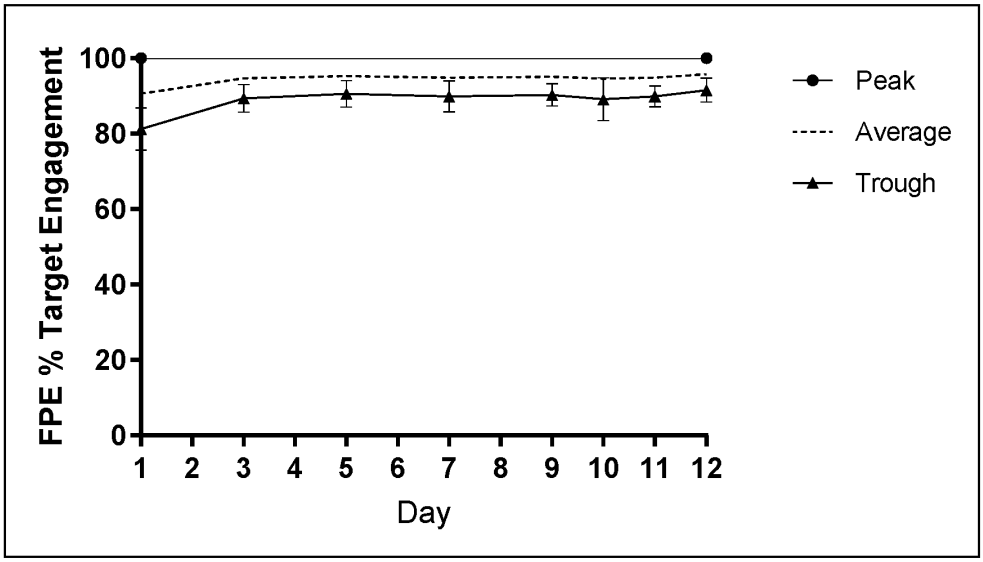

800 mg q12h
Subject 1
Subject 2
Subject 3
Subject 4
Subject 5
Subject 6
Subject 7
Subject 8
% Target Engagement
Day
0
20
40
60
80
100
1 2 3 4 5 6 7 8 9 10 11 12

FIG. 11



n = 6 subjects

FIG. 12

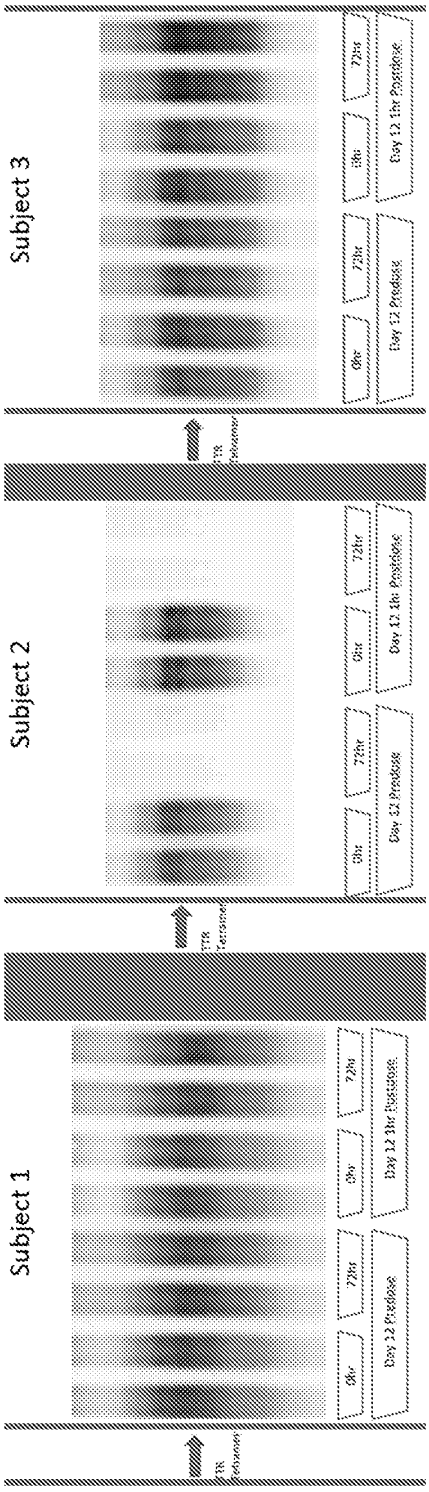

Subject 3
Subject 2
Subject 1
Day 12 Predose
0hr
72hr
Day 12 1hr Postdose
1hr
Day 12 Predose
0hr
72hr
Day 12 1hr Postdose
1hr
Day 12 Predose
0hr
72hr
Day 12 1hr Postdose
1hr

FIG. 13

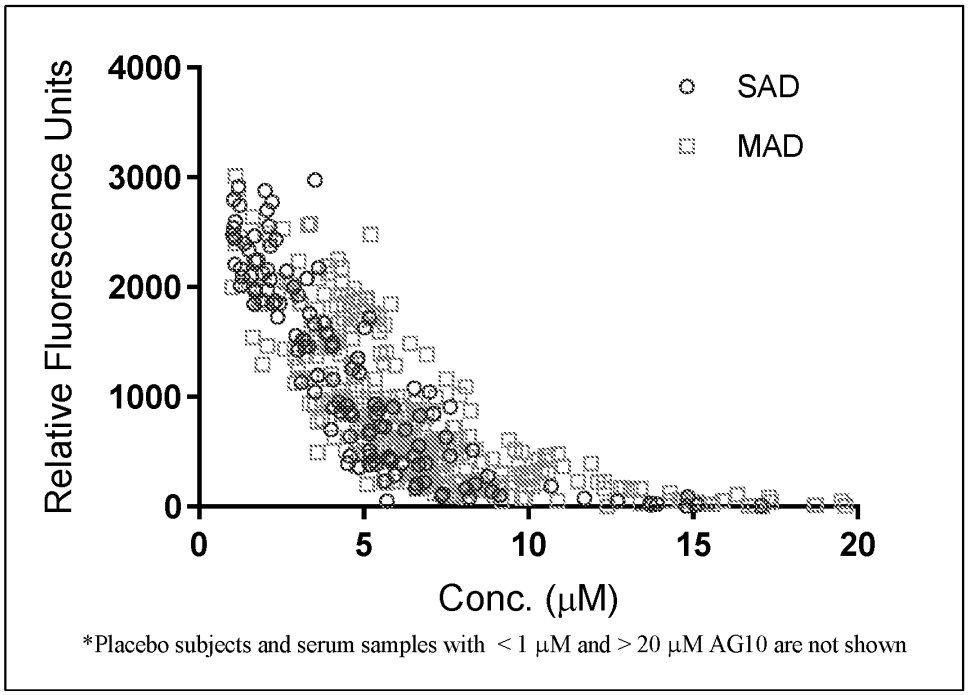

Relative Fluorescence Units
4000
3000
2000
1000
0
0
5
10
15
20
Conc. (μM)
SAD
MAD
*Placebo subjects and serum samples with < 1 μM and > 20 μM AG10 are not shown

FIG. 14

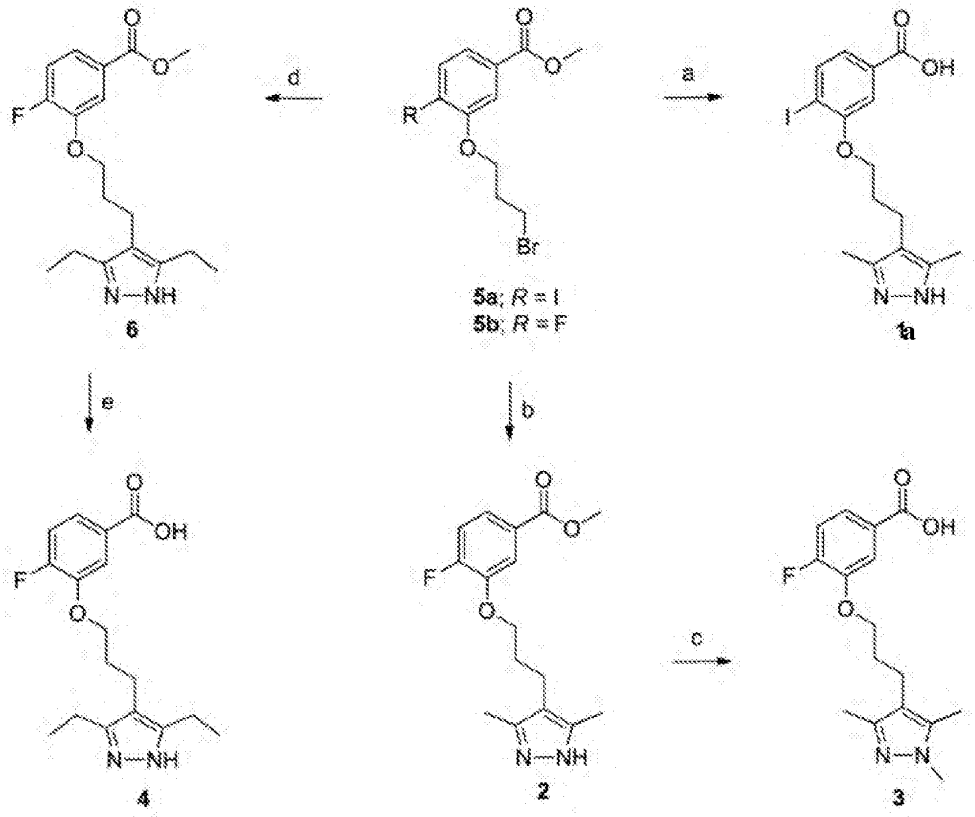


FIG. 15

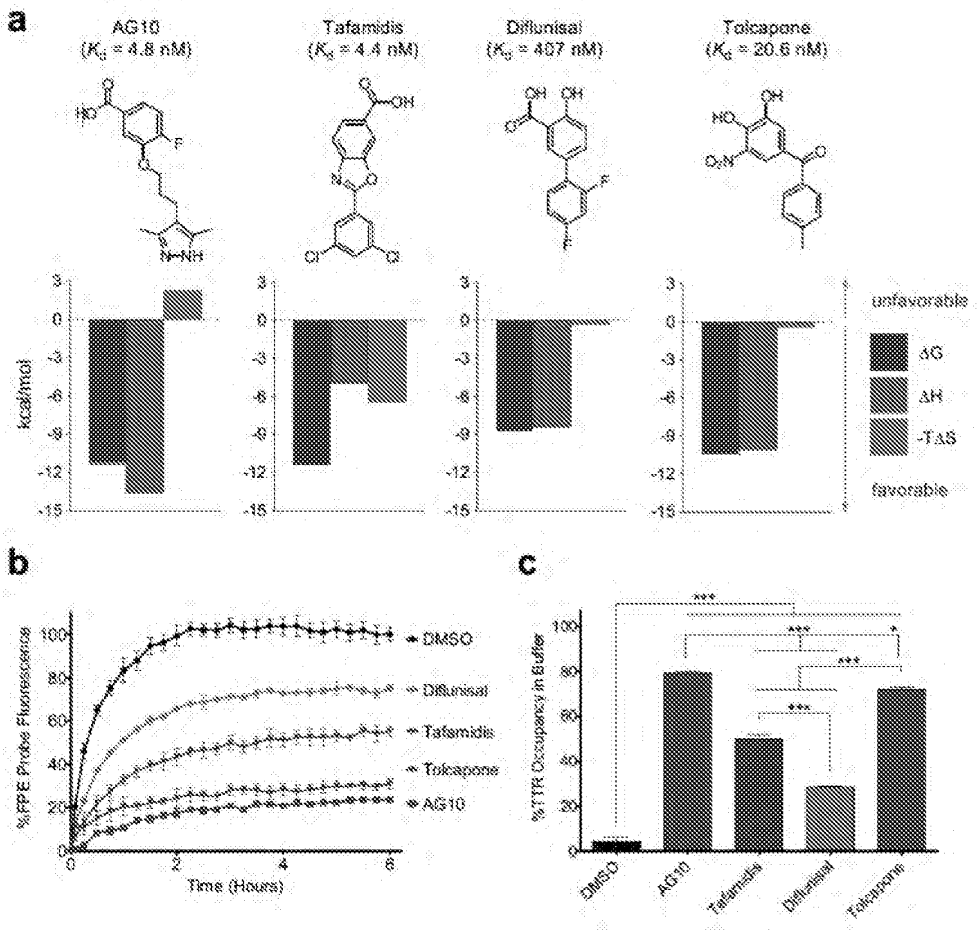

a
AG10
(K_i = 4.8 nM)
Tafamidis
(K_d = 4.4 nM)
Diflunisal
(K_d = 407 nM)
Tolcapone
(K_d = 20.6 nM)
kcal/mol
unfavorable
ΔG
ΔH
-TΔS
favorable
b
%FPE Probe Fluorescence
Time (Hours)
DMSO
Diflunisal
Tafamidis
Tolcapone
AG10
c
%TTR Occupancy in Buffer
DMSO
AG10
Tafamidis
Diflunisal
Tolcapone

FIG. 16

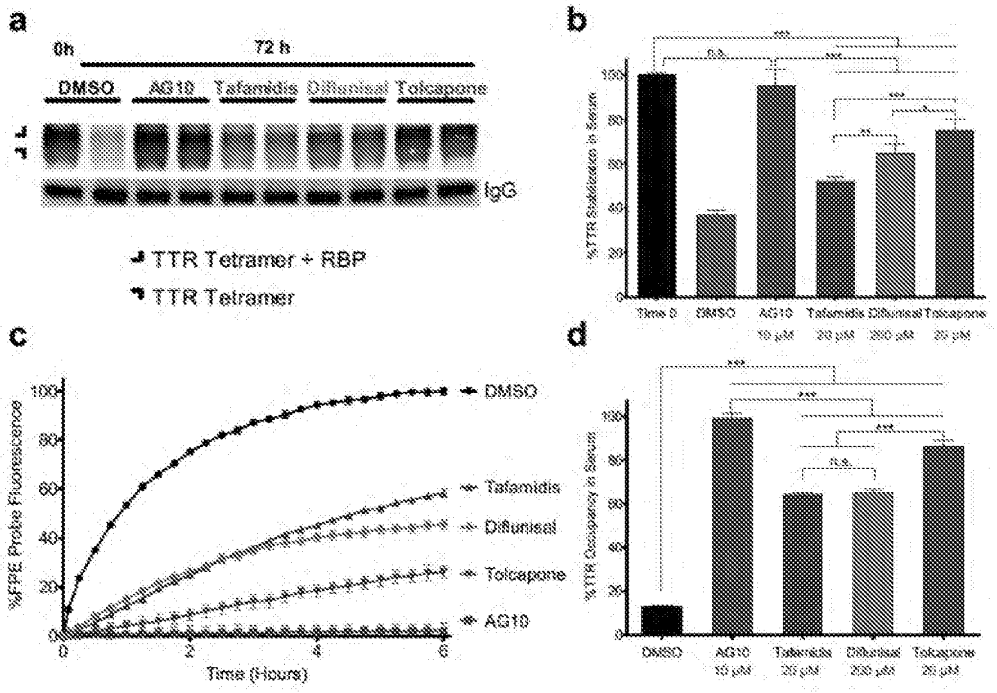

a
0h
72 h
DMSO
AG10
Tafamidis
Diflunisal
Tolcapone
TTR
IgG
TTR Tetramer + RBP
TTR Tetramer
b
%TTR Stabilization in Serum
Time 0
DMSO
AG10
Tafamidis
Diflunisal
Tolcapone
c
%FAP Probe Fluorescence
Time (Hours)
DMSO
Tafamidis
Diflunisal
Tolcapone
AG10
d
%TTR Occupancy in Serum
DMSO
AG10
Tafamidis
Diflunisal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

FIG. 17

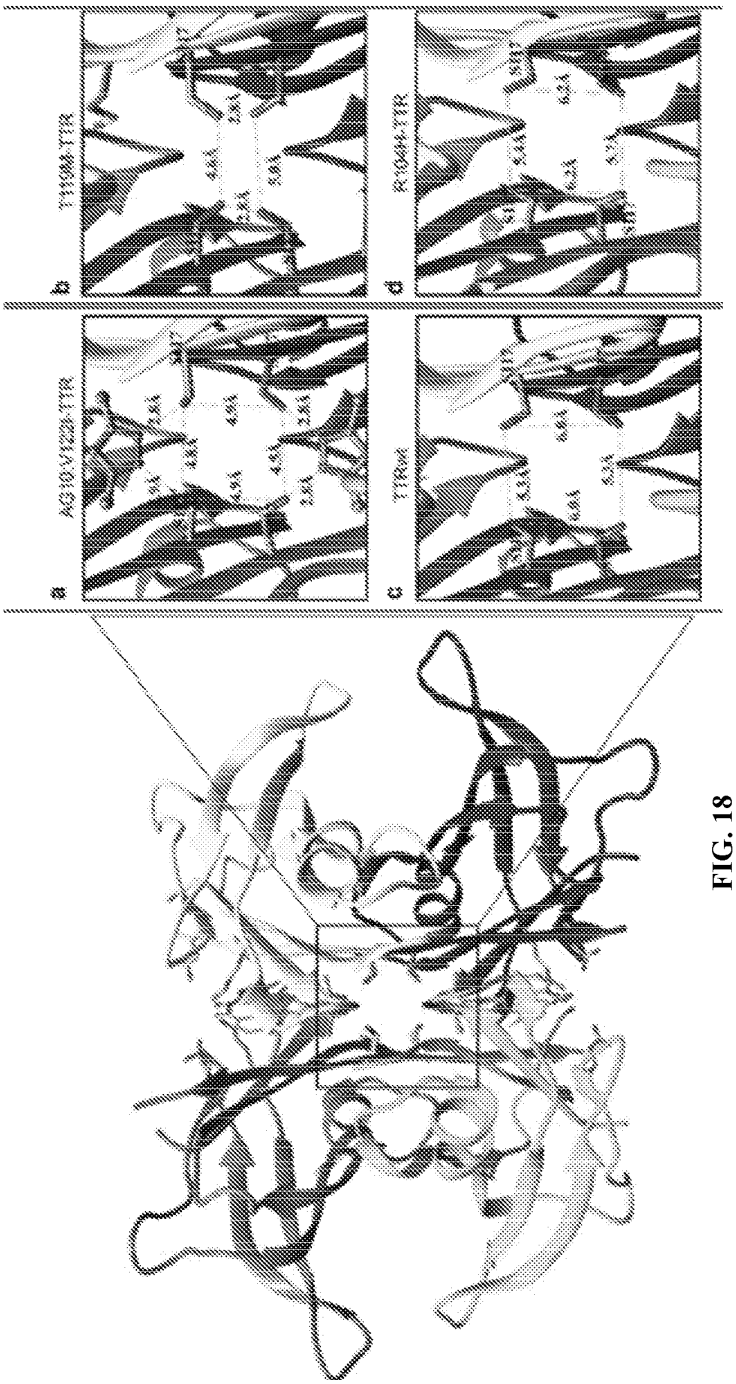


FIG. 18

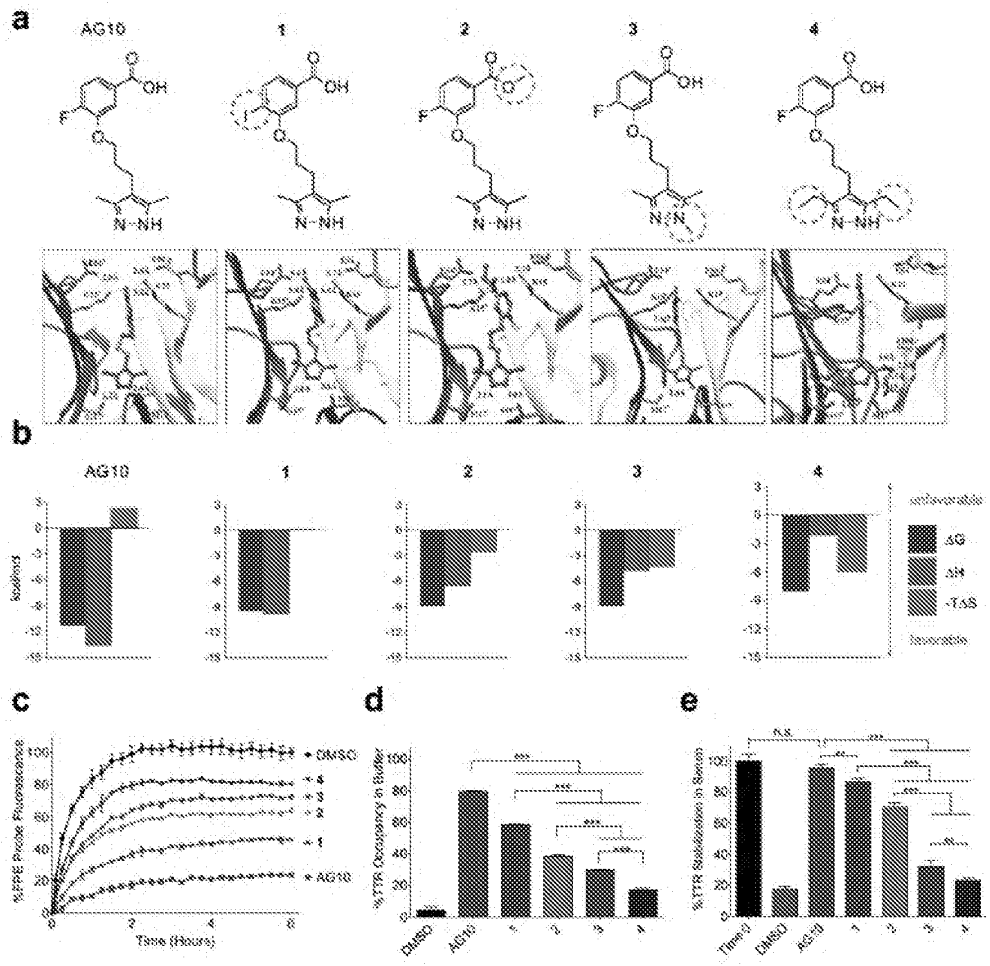

a
AG10
1
2
3
4
b
AG10
1
2
3
4
kcal/mole
ΔG
ΔH
-TΔS
c
%FPE Probe Fluorescence
Time (Hours)
DMSO
4
3
2
1
AG10
d
%TTR Occupancy in Buffer
DMSO
AG10
e
%TTR Stabilization in Serum
Time=0
DMSO
AG10

FIG. 19

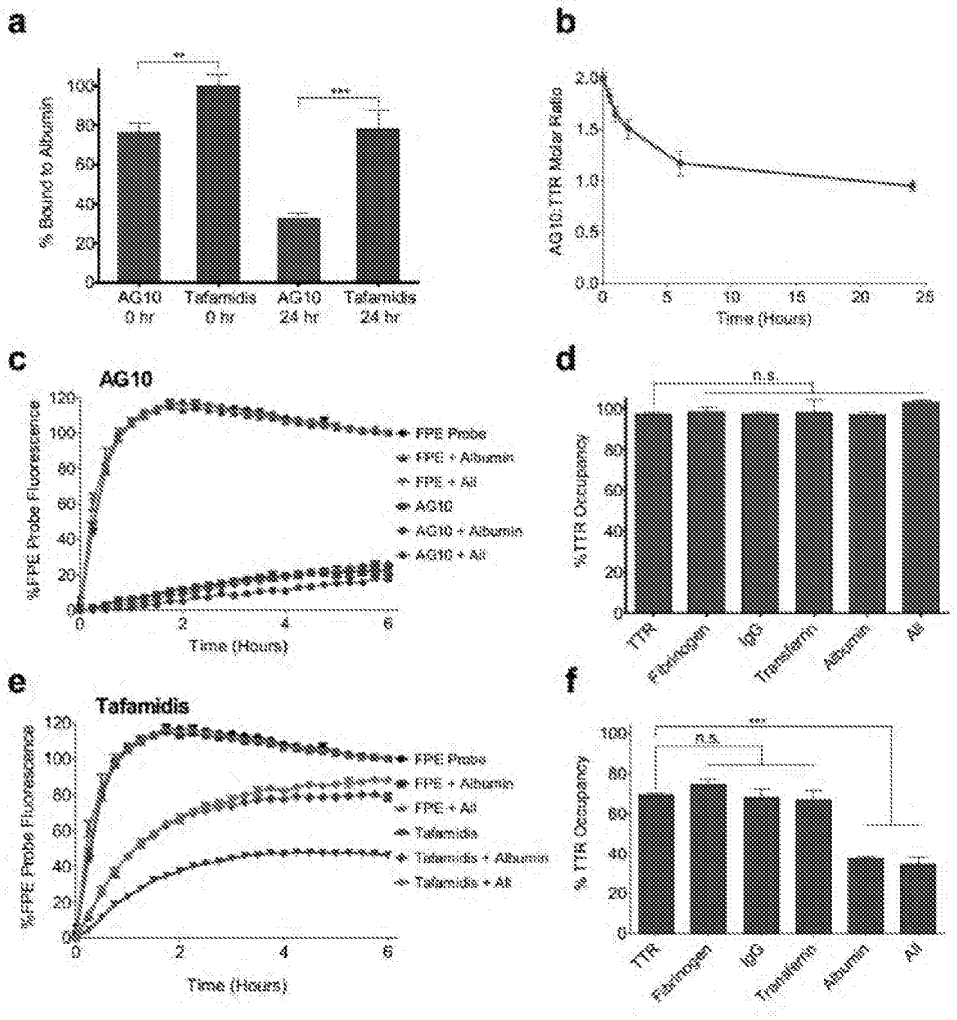

a
% Bound to Albumin
AG10 0 hr
Tafamidis 0 hr
AG10 24 hr
Tafamidis 24 hr
b
AG10:TTR Molar Ratio
Time (Hours)
c
AG10
%FPE Probe Fluorescence
FPE Probe
FPE + Albumin
FPE + All
AG10
AG10 + Albumin
AG10 + All
Time (Hours)
d
% TTR Occupancy
n.s.
TTR
Fibrinogen
IgG
Transferrin
Albumin
All
e
Tafamidis
%FPE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

FIG. 20

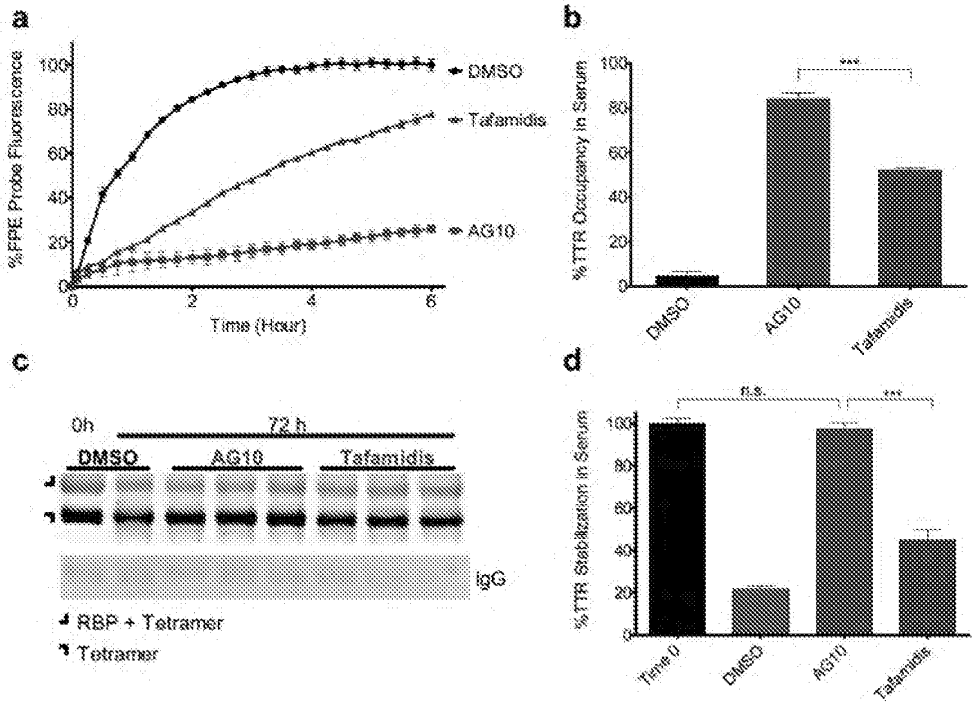

a
%FPE Probe Fluorescence
Time (Hour)
DMSO
Tafamidis
AG10
b
%TTR Occupancy in Serum
***
DMSO
AG10
Tafamidis
c
0h
72 h
DMSO
AG10
Tafamidis
IgG
RBP + Tetramer
Tetramer
d
%TTR Stabilization in Serum
n.s.
***
Time 0
DMSO
AG10
Tafamidis

FIG. 21

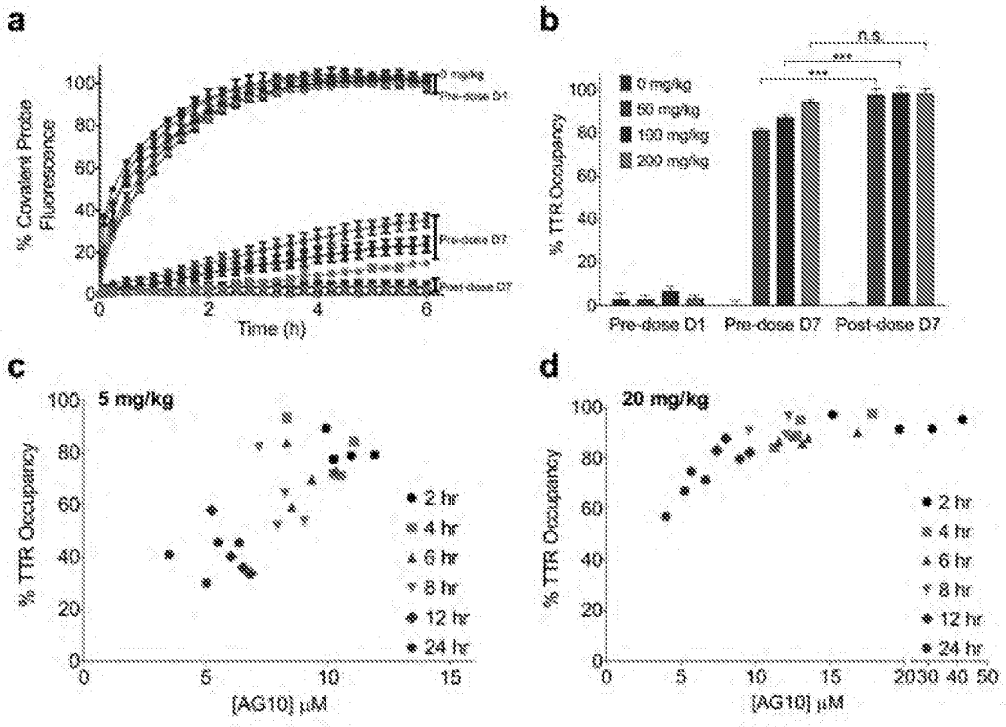

a
% Covalent Probe Fluorescence
Time (h)
b
% TTR Occupancy
0 mg/kg
50 mg/kg
100 mg/kg
200 mg/kg
n.s.
***
***
Pre-dose D1
Pre-dose D7
Post-dose D7
c
5 mg/kg
% TTR Occupancy
[AG10] µM
2 hr
4 hr
6 hr
8 hr
12 hr
24 hr
d
20 mg/kg
% TTR Occupancy
[AG10] µM
2 hr
4 hr
6 hr
8 hr
12 hr
24 hr

FIG. 22

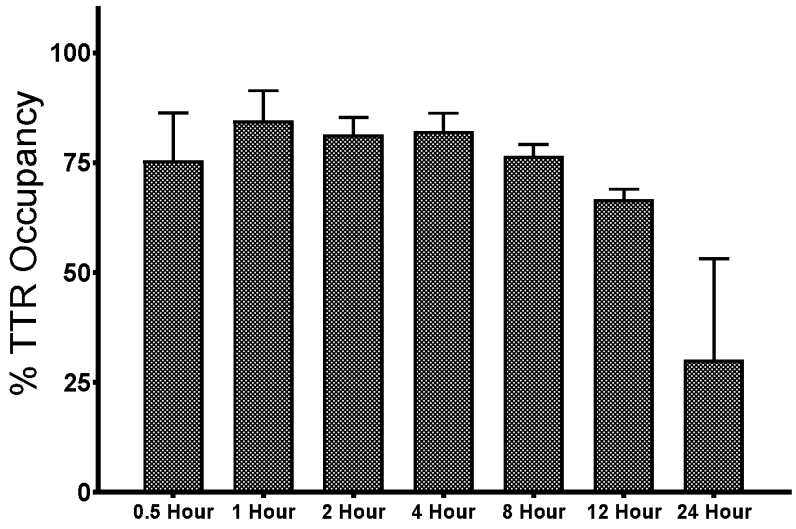

% TTR Occupancy
100
75
50
25
0
0.5 Hour
1 Hour
2 Hour
4 Hour
8 Hour
12 Hour
24 Hour

FIG. 23

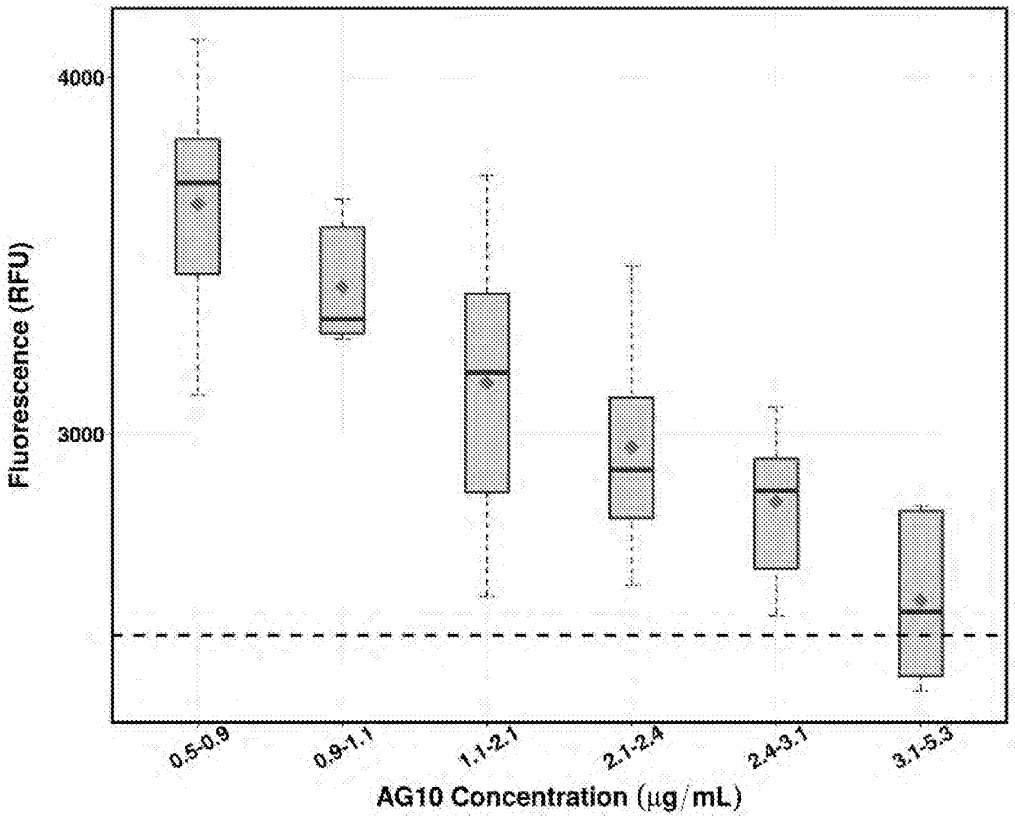

4000
3000
Fluorescence (RFU)
0.5-0.9
0.9-1.1
1.1-2.1
2.1-2.4
2.4-3.1
3.1-5.3
AG10 Concentration (µg/mL)

FIG. 24

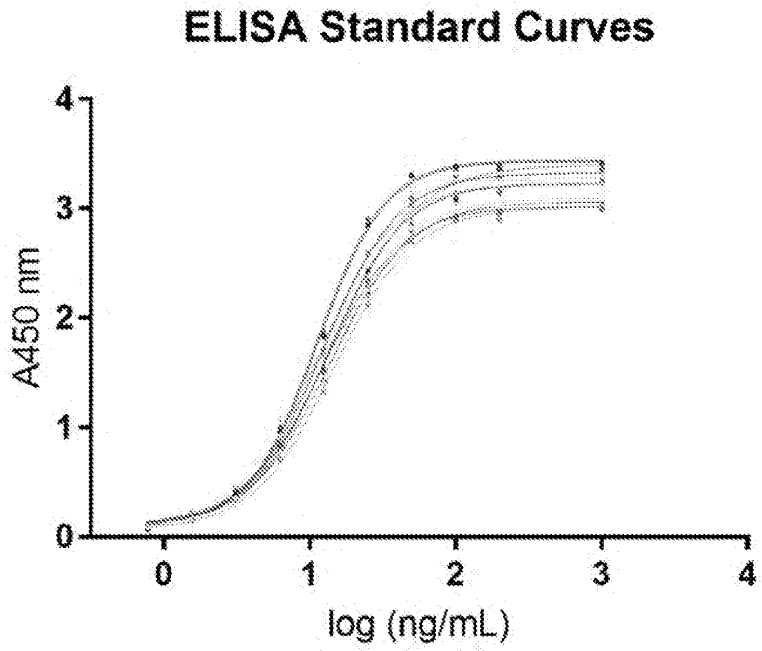

ELISA Standard Curves
A450 nm
0
1
2
3
4
log (ng/mL)

FIG. 25

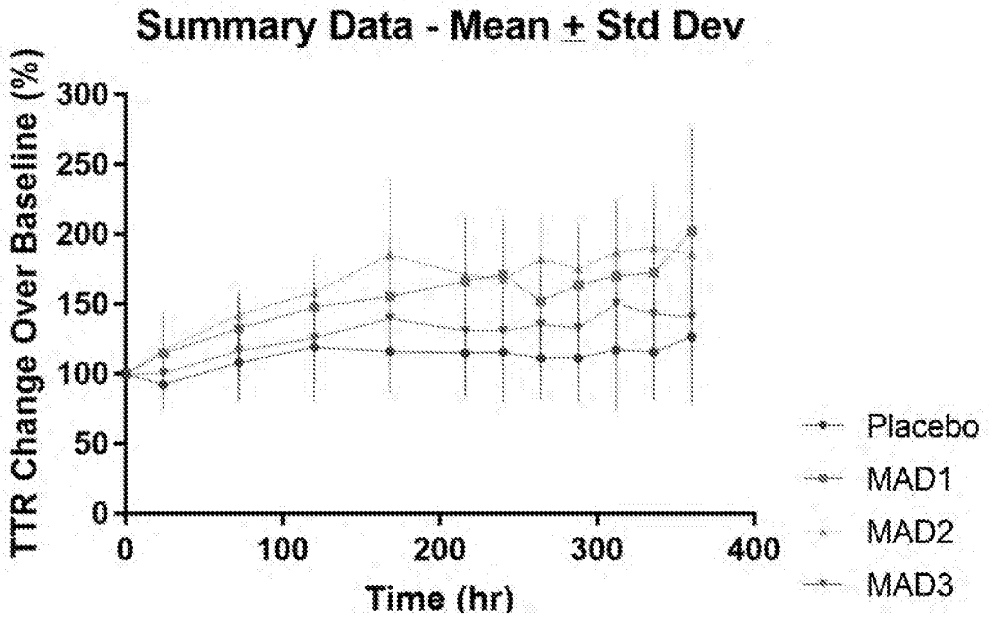

Summary Data - Mean ± Std Dev
TTR Change Over Baseline (%)
300
250
200
150
100
50
0
0
100
200
300
400
Time (hr)
Placebo
MAD1
MAD2
MAD3

FIG. 26

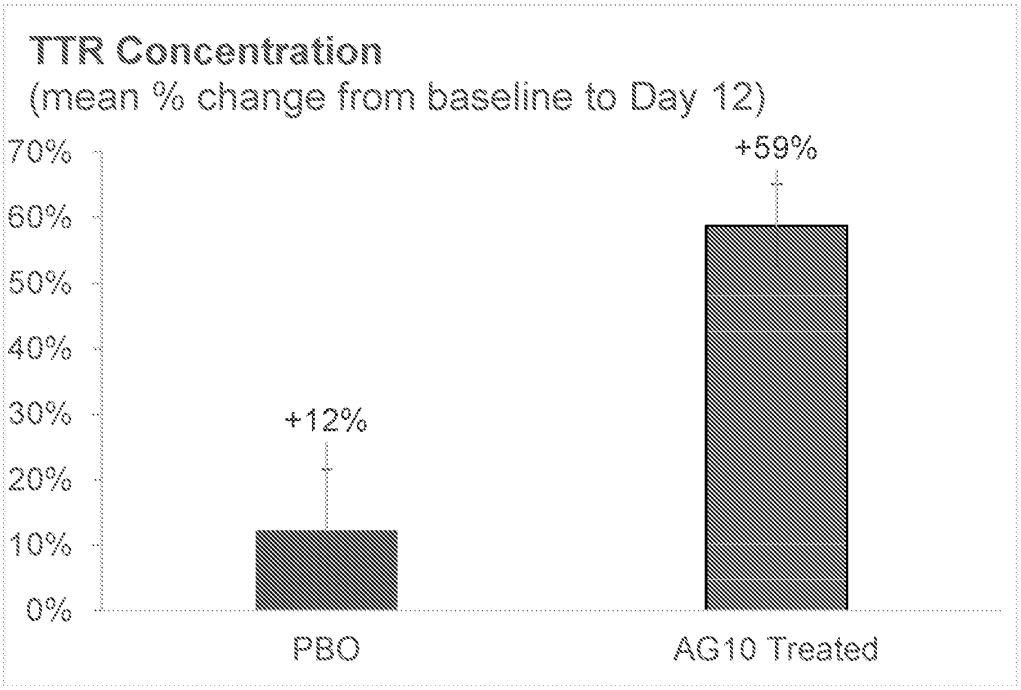

TTR Concentration
(mean % change from baseline to Day 12)
70%
60%
50%
40%
30%
20%
10%
0%
+12%
+59%
PBO
AG10 Treated

FIG. 27

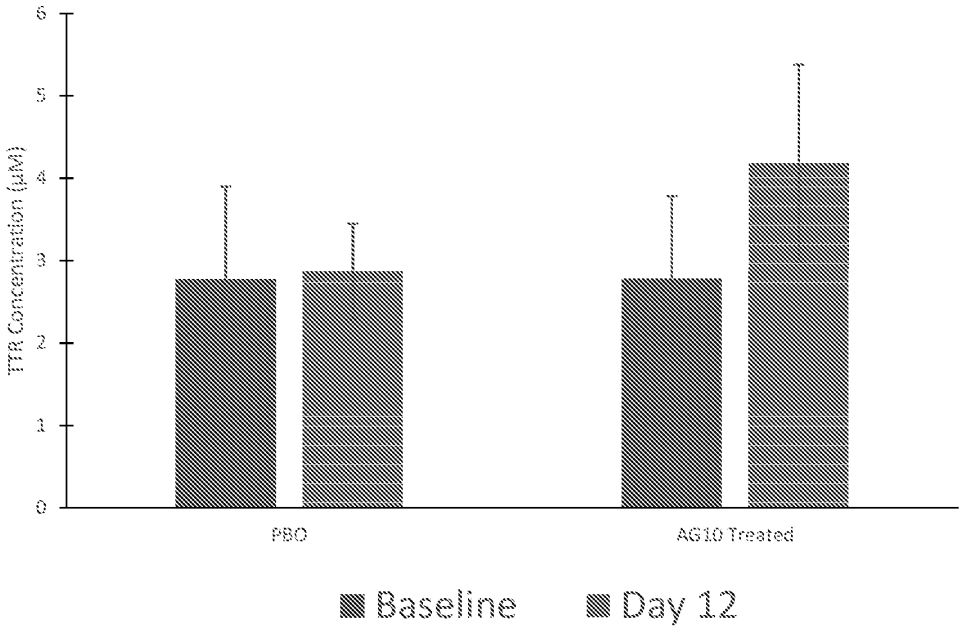

TTR Concentration (µM)
0
1
2
3
4
5
6
PBO
AG10 Treated
Baseline
Day 12

FIG. 28

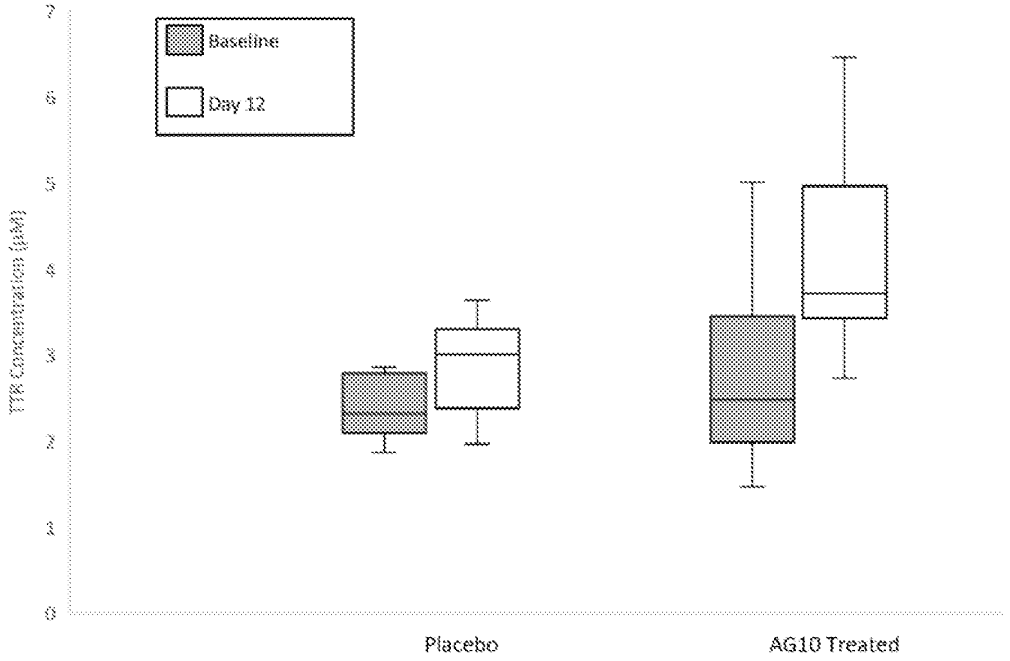


FIG. 29

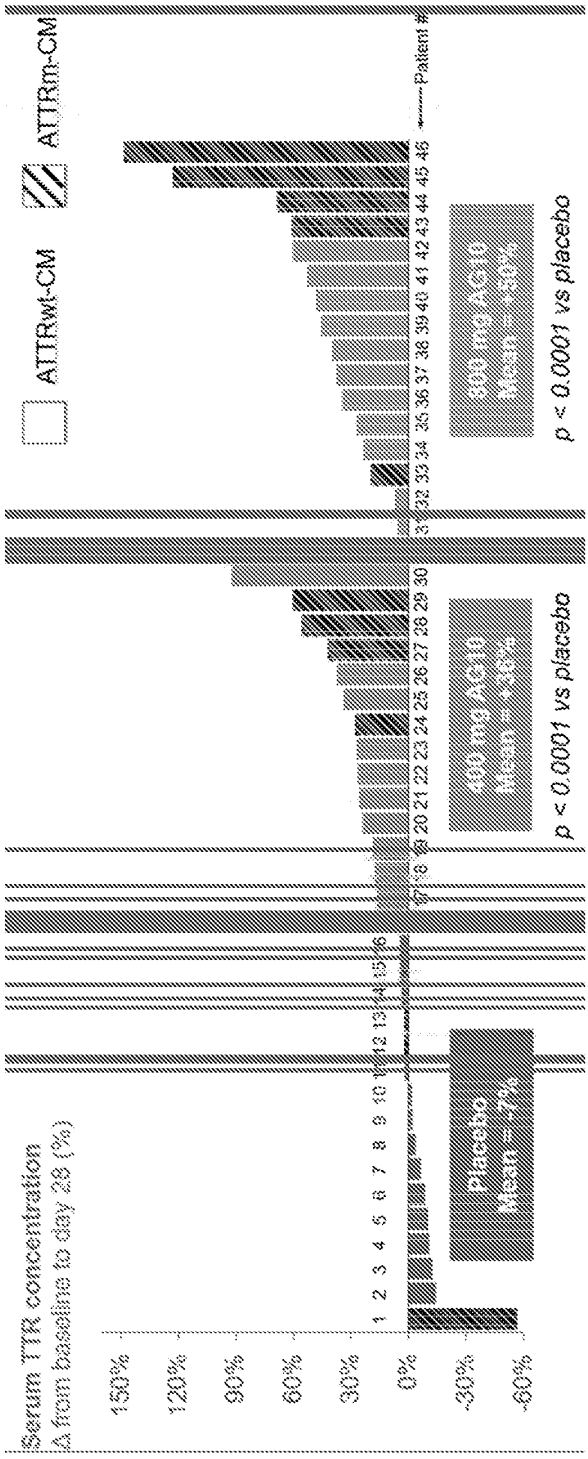

Serum TTR concentration
Δ from baseline to day 28 (%)
150%
120%
90%
60%
30%
0%
-30%
-60%
ATTRwt-CM
ATTRm-CM
Patient #
Placebo
Mean -7%
400 mg AG10
Mean -74%
p < 0.0001 vs placebo
800 mg AG10
Mean -84%
p < 0.0001 vs placebo

FIG. 30

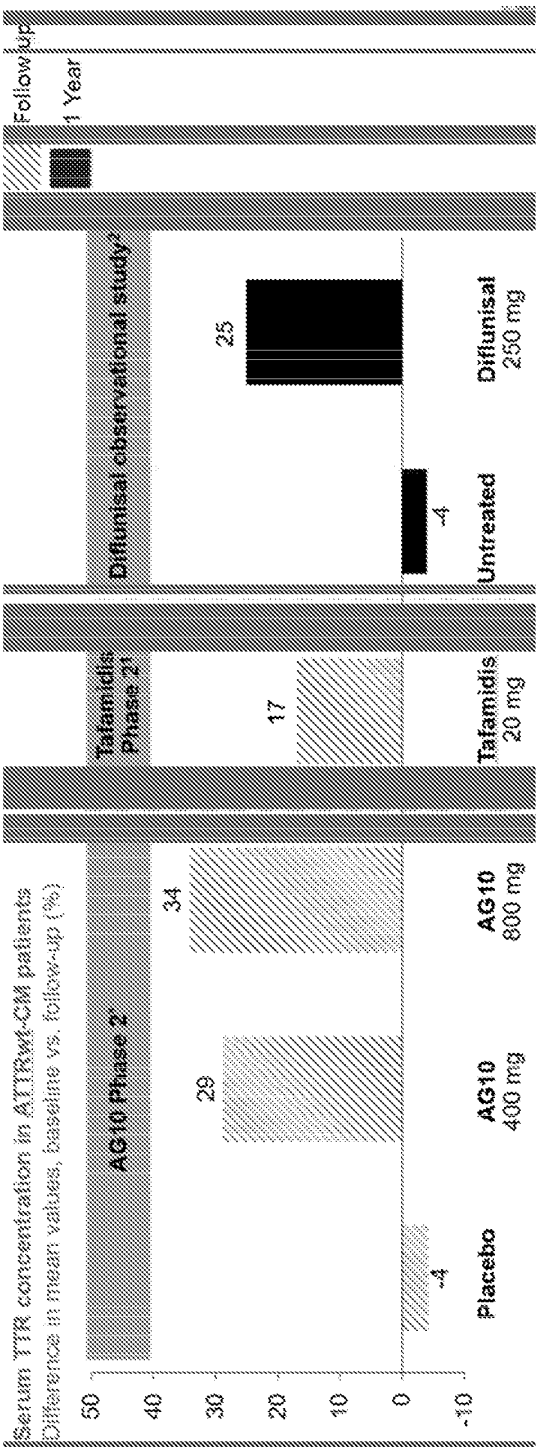

Serum TTR concentration in ATTRwt-CM patients
Difference in mean values, baseline vs. follow-up (%)
60
40
30
20
10
0
-10
AG10 Phase 2¹
Placebo
-4
AG10
400 mg
29
AG10
800 mg
34
Tafamidis
Phase 2¹
Tafamidis
20 mg
17
Diflunisal observational study²
Untreated
-4
Diflunisal
250 mg
25
Follow-up
1 Year

FIG. 31

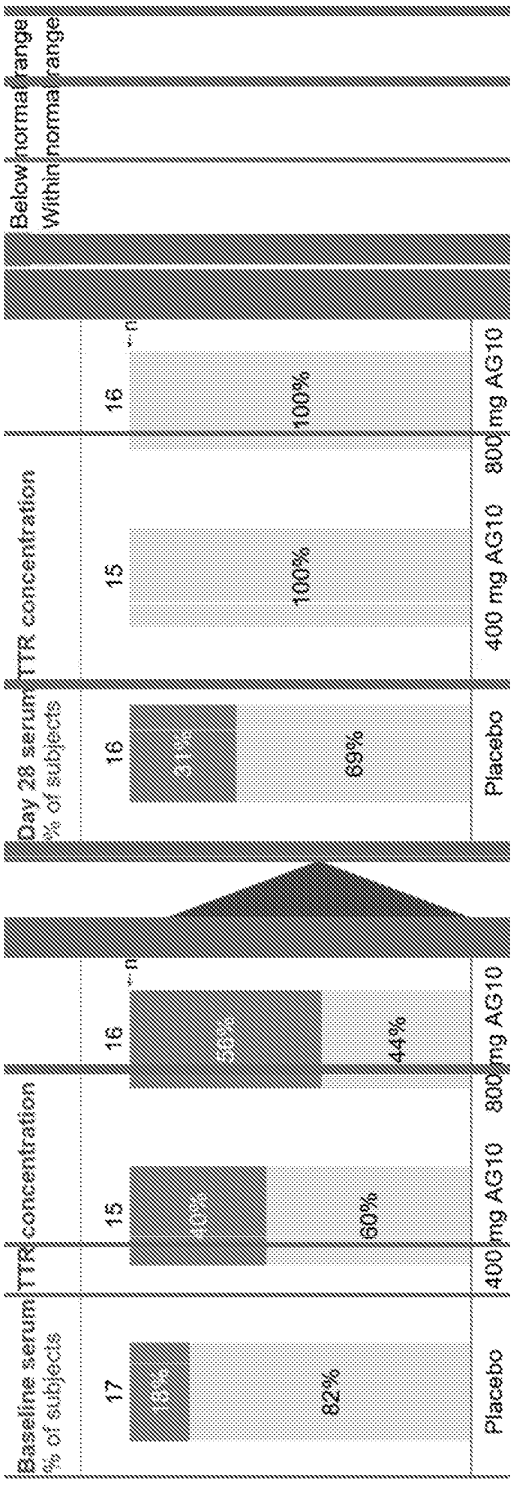

Baseline serum TTR concentration
% of subjects
Placebo
400 mg AG10
800 mg AG10
17
15
16
18%
82%
40%
60%
56%
44%
Day 28 serum TTR concentration
% of subjects
Placebo
400 mg AG10
800 mg AG10
16
15
16
31%
69%
100%
100%
100%
Below normal range
Within normal range

FIG. 32

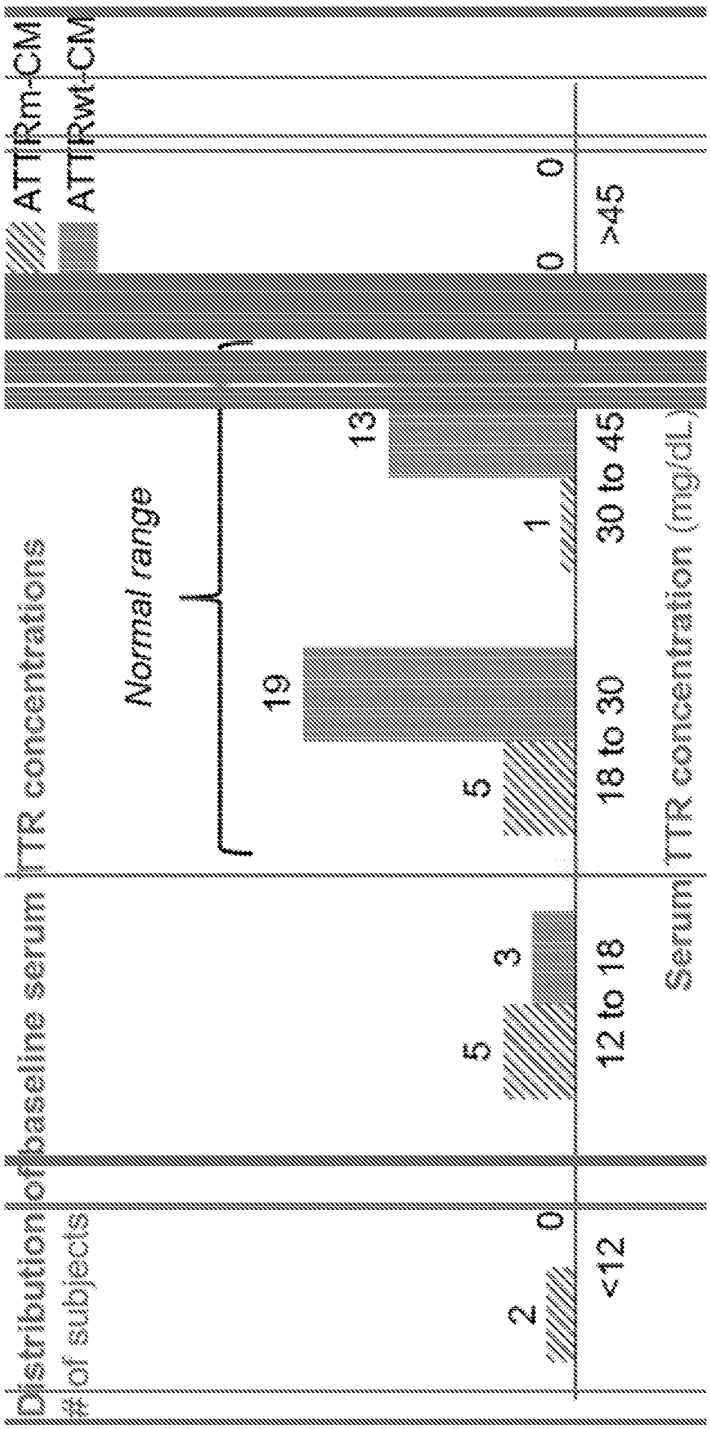

Distribution of baseline serum TTR concentrations
# of subjects
ATTRm-CM
ATTRwt-CM
Normal range
2
0
5
3
19
5
13
1
0
0
<12
12 to 18
18 to 30
30 to 45
>45
Serum TTR concentration (mg/dL)

FIG. 33

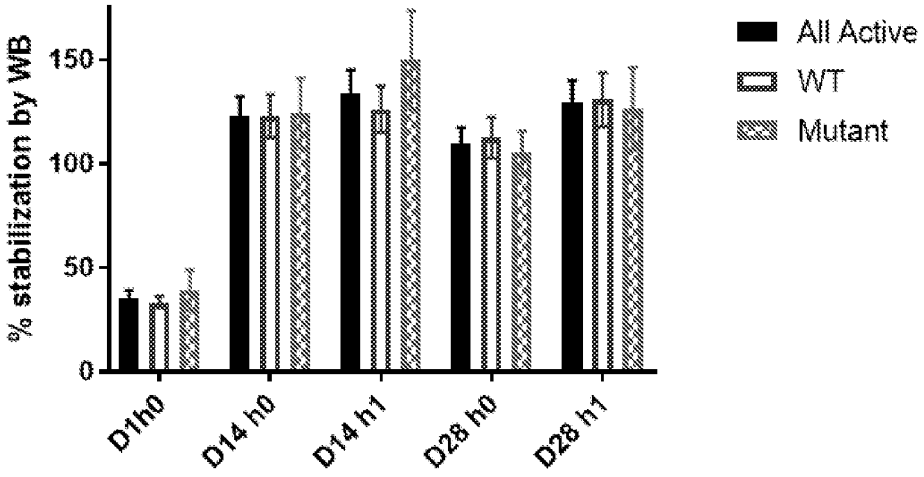

% stabilization by WB
150
100
50
0
D1h0
D14 h0
D14 h1
D28 h0
D28 h1
All Active
WT
Mutant

FIG. 34

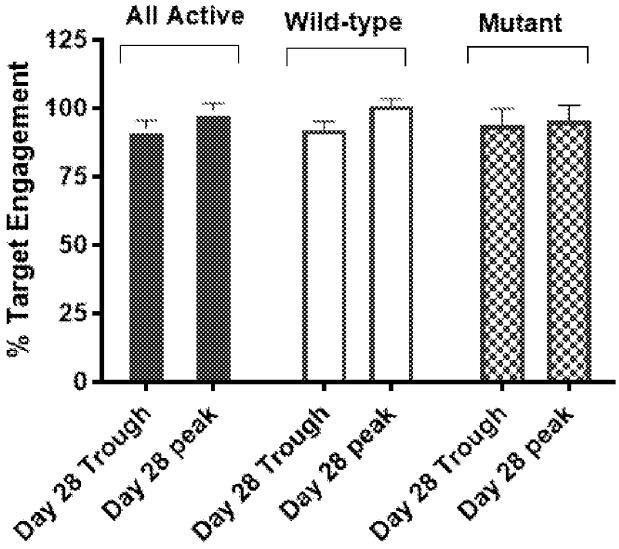

All Active
Wild-type
Mutant
% Target Engagement
125
100
75
50
25
0
Day 28 Trough
Day 28 peak
Day 28 Trough
Day 28 peak
Day 28 Trough
Day 28 peak

FIG. 35

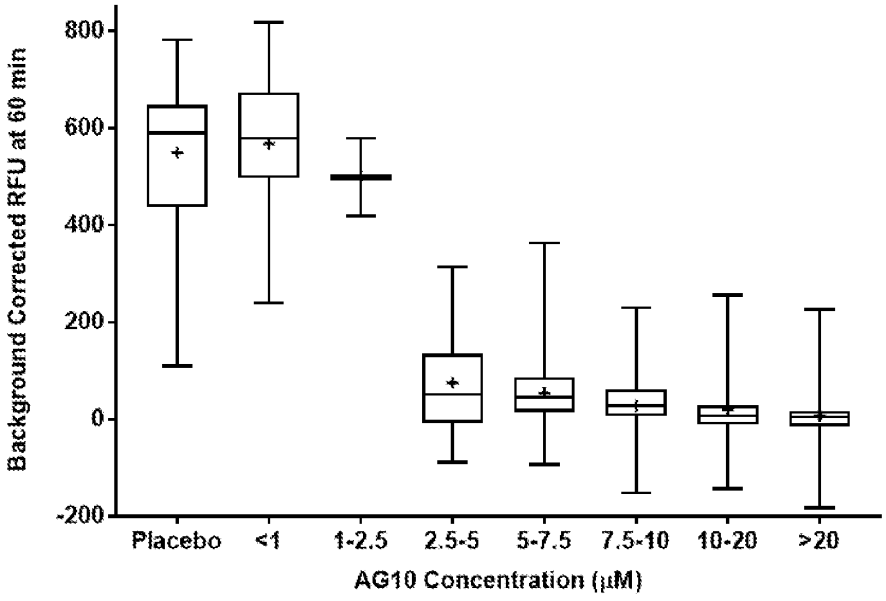

Background Corrected RFU at 60 min
800
600
400
200
0
-200
Placebo
<1
1-2.5
2.5-5
5-7.5
7.5-10
10-20
>20
AG10 Concentration (μM)

FIG. 36

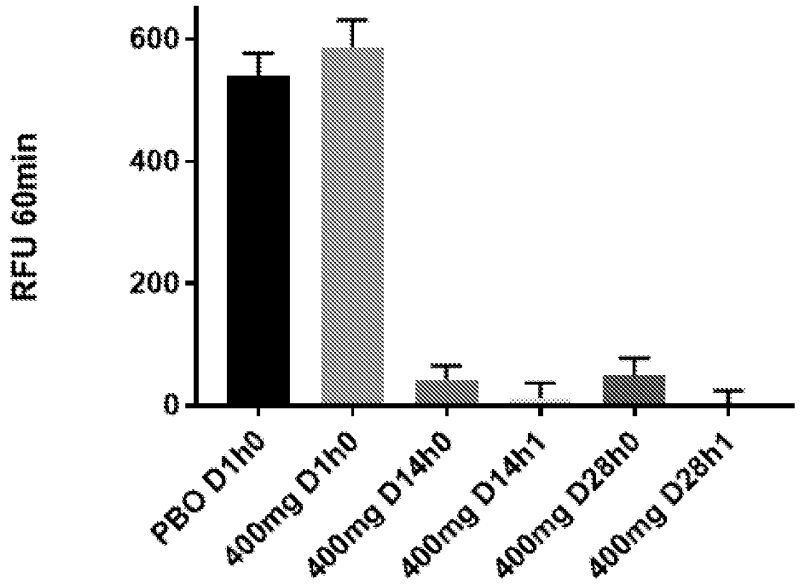

RFU 60min
600
400
200
0
PBO D1h0
400mg D1h0
400mg D14h0
400mg D14h1
400mg D28h0
400mg D28h1

FIG. 37

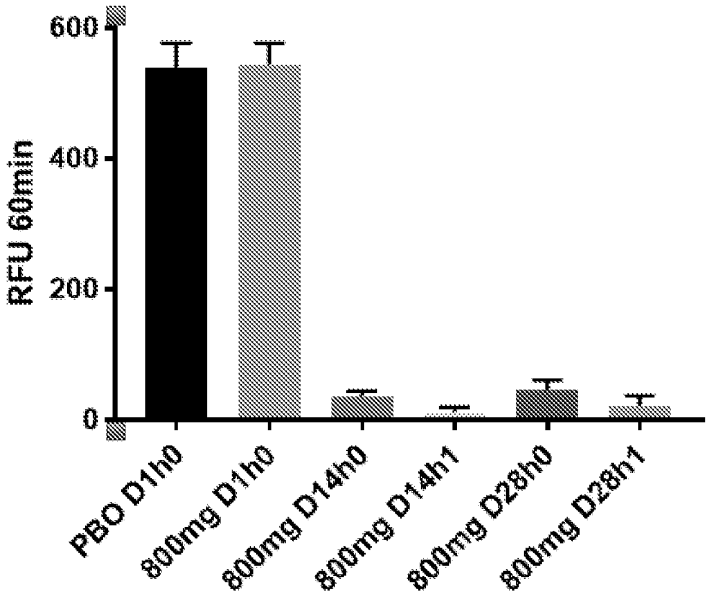

600
400
200
0
RFU 60min
PBO D1h0
800mg D1h0
800mg D14h0
800mg D14h1
800mg D28h0
800mg D28h1

FIG. 38

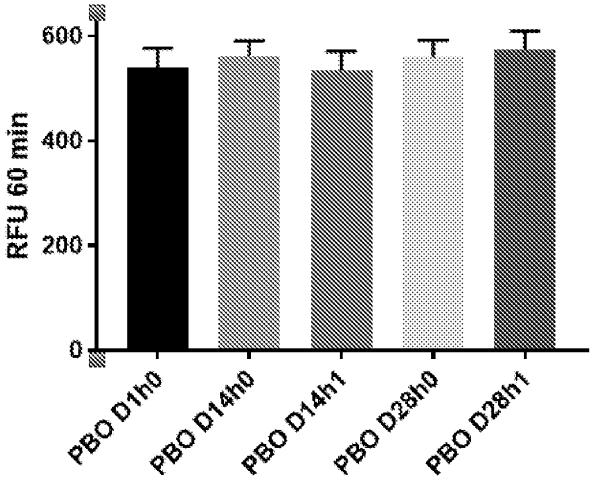

600
400
200
0
RFU 60 min
PBO D1h0
PBO D14h0
PBO D14h1
PBO D28h0
PBO D28h1

FIG. 39

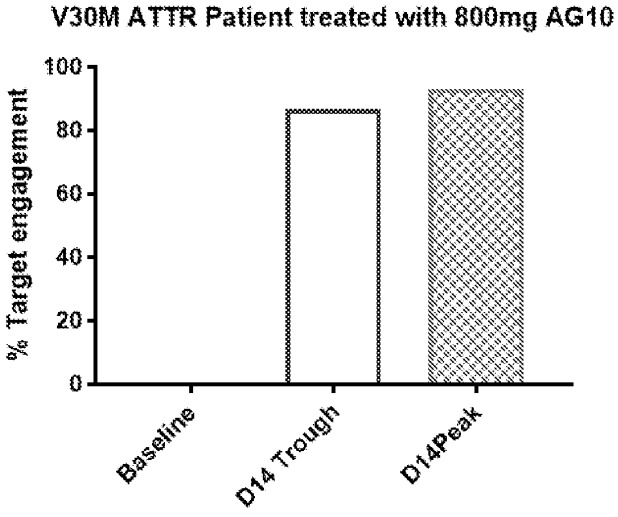

V30M ATTR Patient treated with 800mg AG10
% Target engagement
100
80
60
40
20
0
Baseline
D14 Trough
D14Peak

FIG. 40

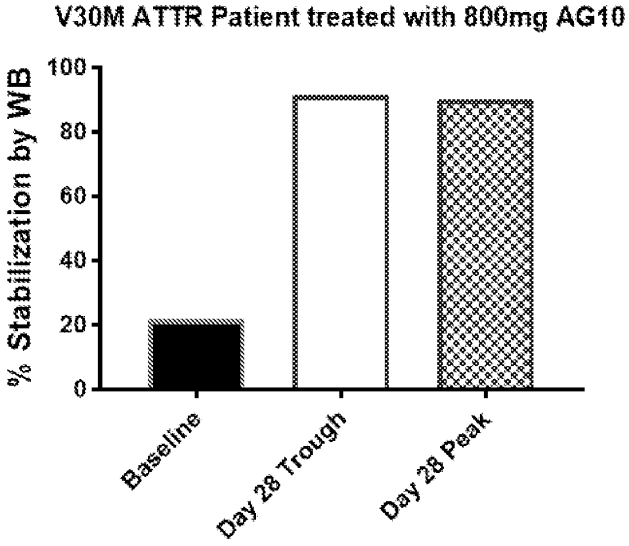

V30M ATTR Patient treated with 800mg AG10
% Stabilization by WB
100
80
60
40
20
0
Baseline
Day 28 Trough
Day 28 Peak

FIG. 41

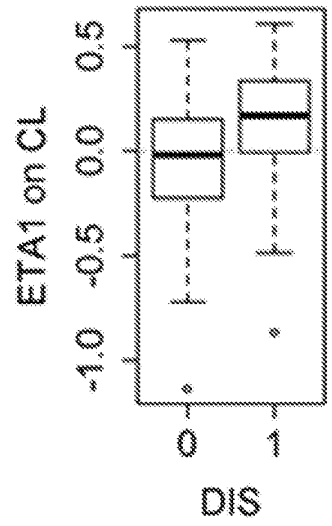


FIG. 42A

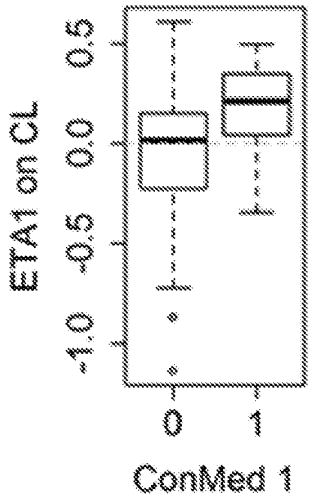


FIG. 42B

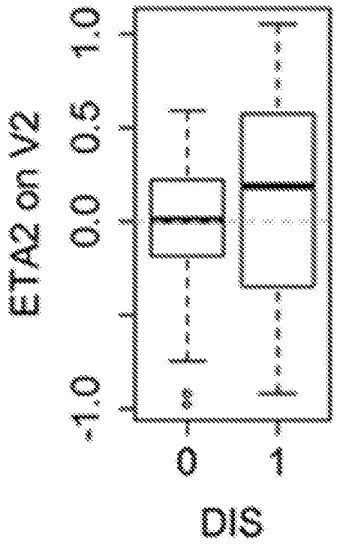


FIG. 42C

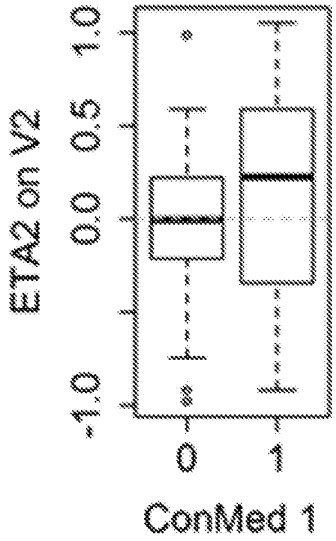


FIG. 42D

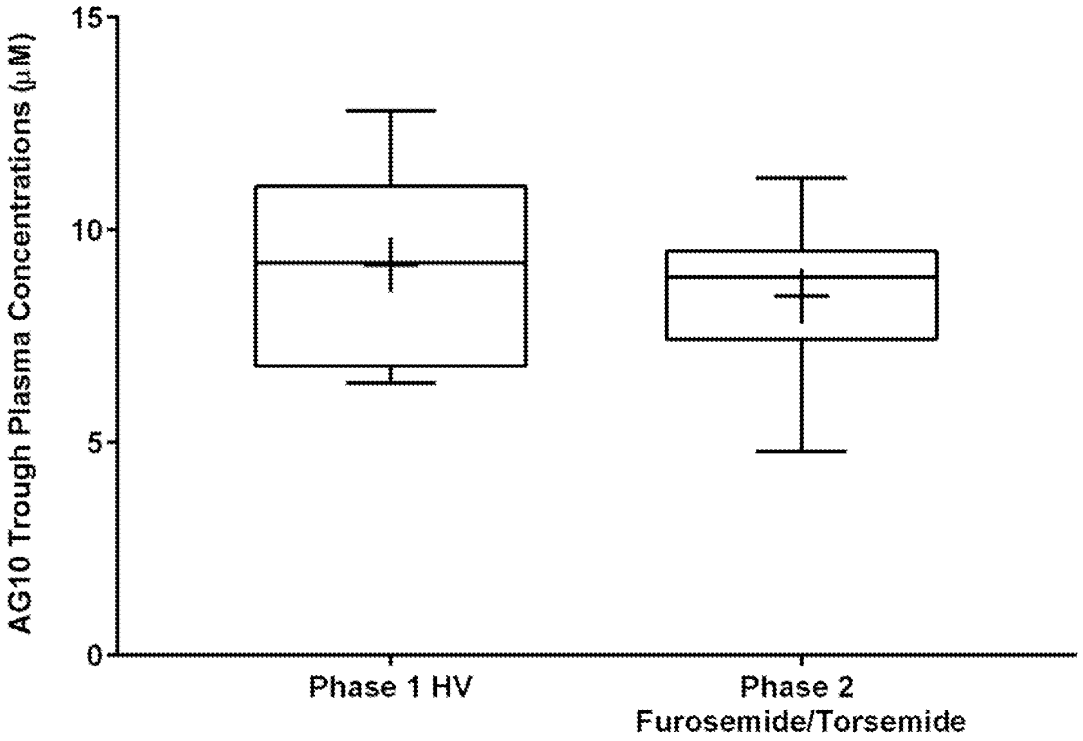

AG10 Trough Plasma Concentrations (μM)
15
10
5
0
Phase 1 HV
Phase 2
Furosemide/Torsemide

FIG. 43

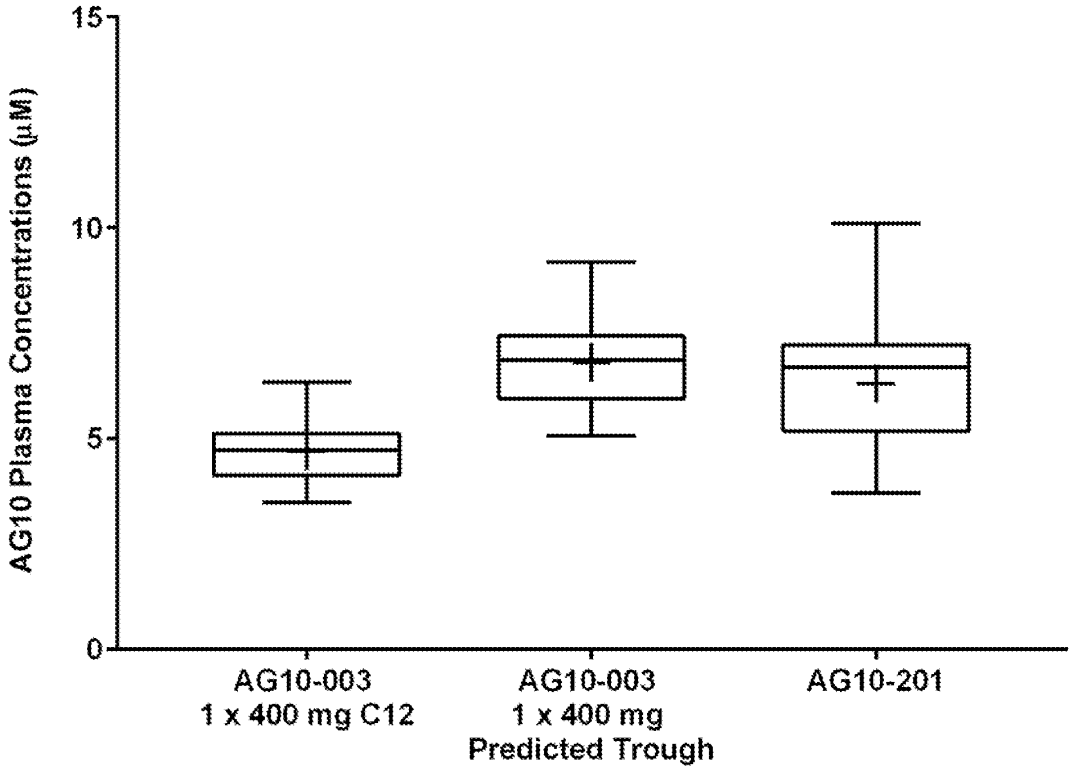

15
10
5
0
AG10 Plasma Concentrations (µM)
AG10-003
1 x 400 mg C12
AG10-003
1 x 400 mg
Predicted Trough
AG10-201

FIG. 44

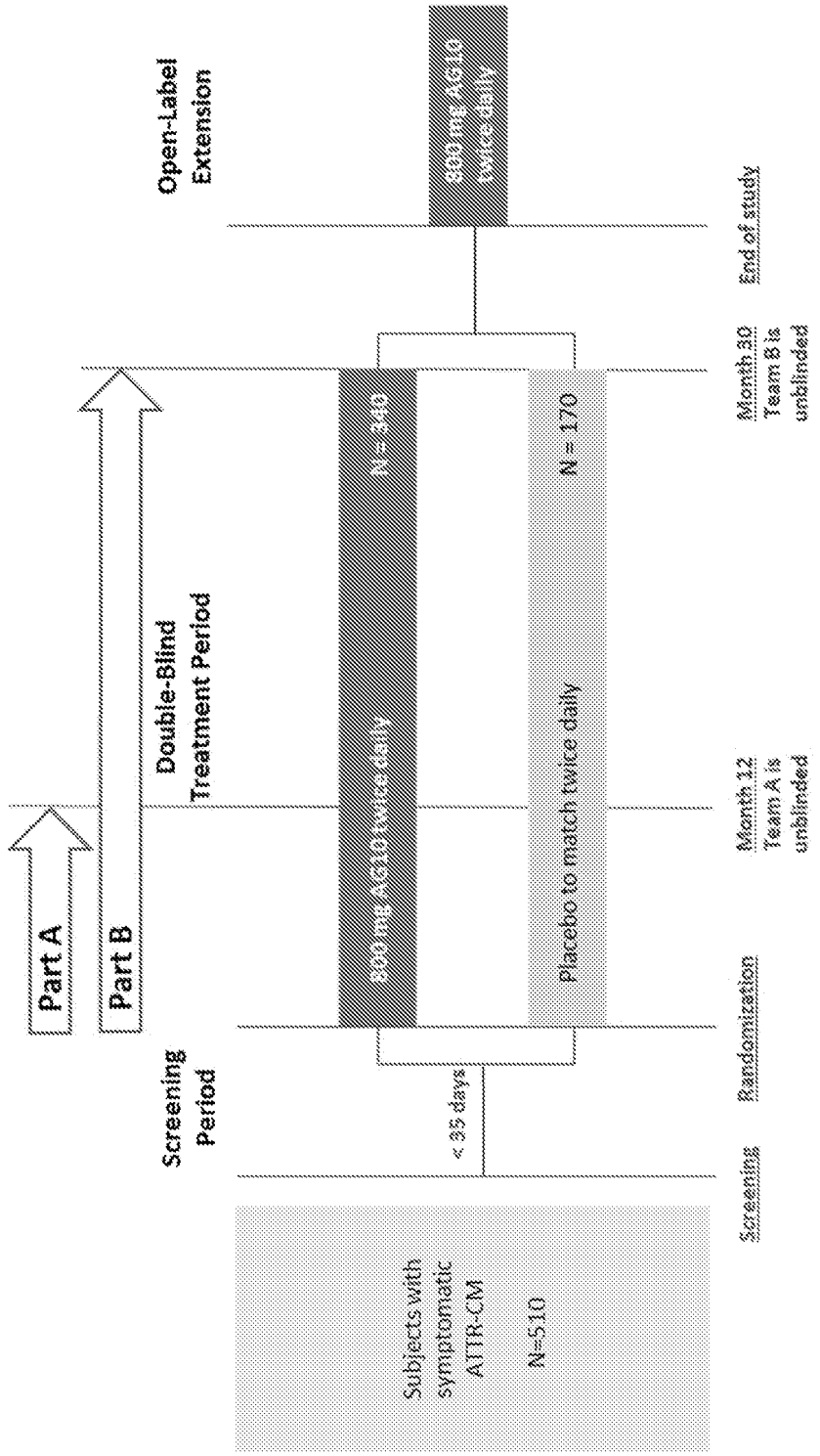

Subjects with symptomatic ATTR-CM
N=510
Screening
< 35 days
Randomization
Month 12
Team A is unblinded
Month 30
Team B is unblinded
End of study
Screening Period
Double-Blind Treatment Period
Open-Label Extension
Part A
Part B
300 mg AG10 twice daily
Placebo to match twice daily
N = 340
N = 170
300 mg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

FIG. 45

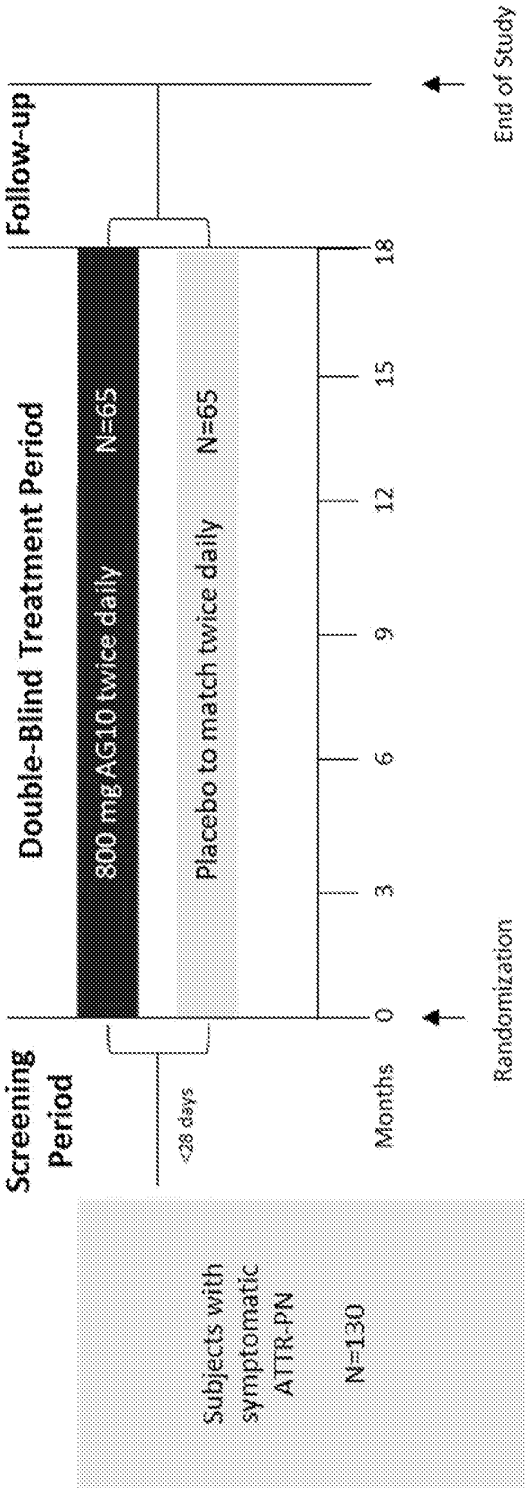

Subjects with symptomatic ATTR-PN
N=130
Screening Period
<28 days
Double-Blind Treatment Period
800 mg AG10 twice daily N=65
Placebo to match twice daily N=65
Follow-up
Months
0
3
6
9
12
15
18
Randomization
End of Study

FIG. 46