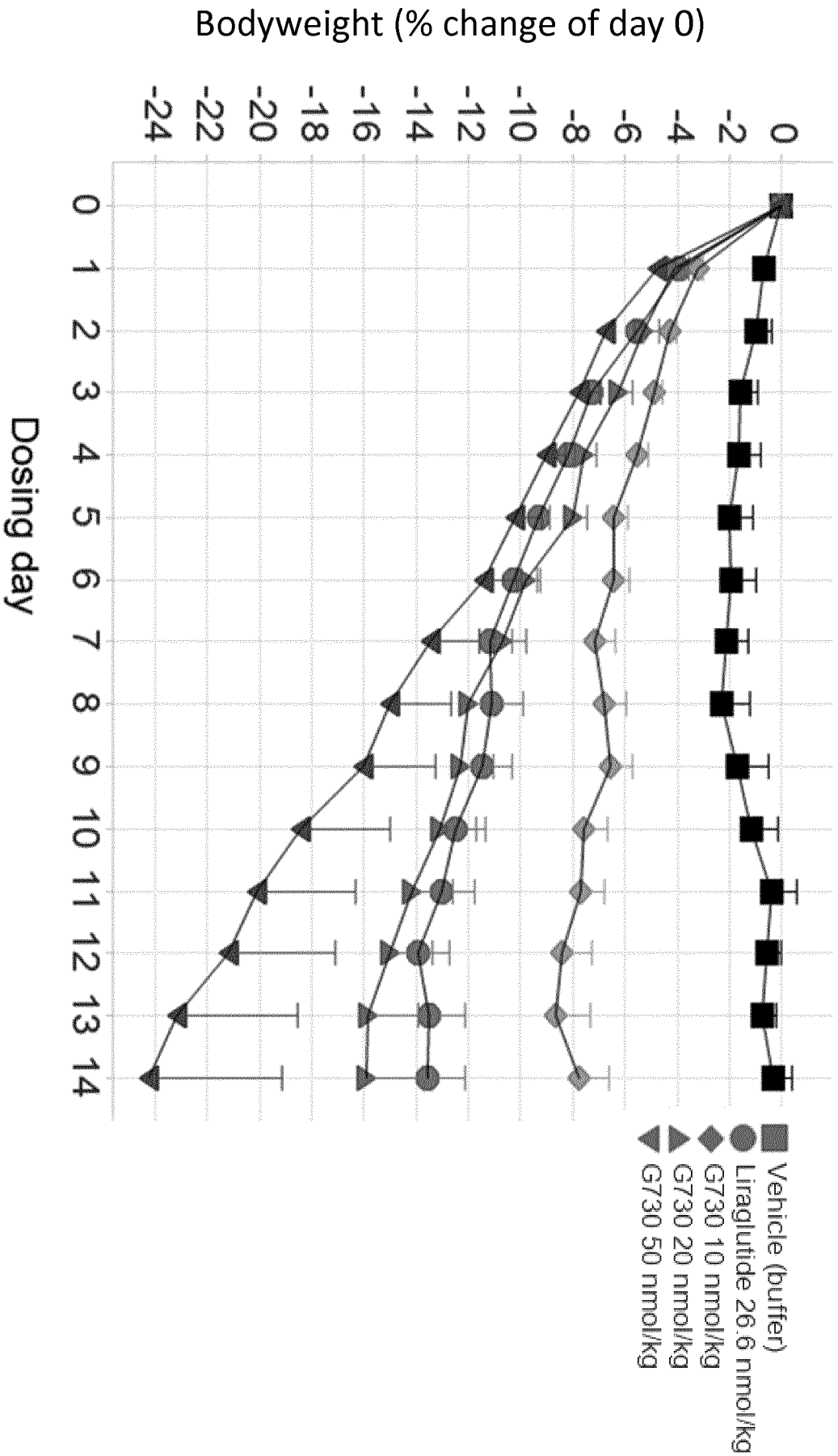

Bodyweight (% change of day 0)
0
-2
-4
-6
-8
-10
-12
-14
-16
-18
-20
-22
-24
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
Dosing day
Vehicle (buffer)
Liraglutide 26.6 nmol/kg
G730 10 nmol/kg
G730 20 nmol/kg
G730 50 nmol/kg

FIG. 1

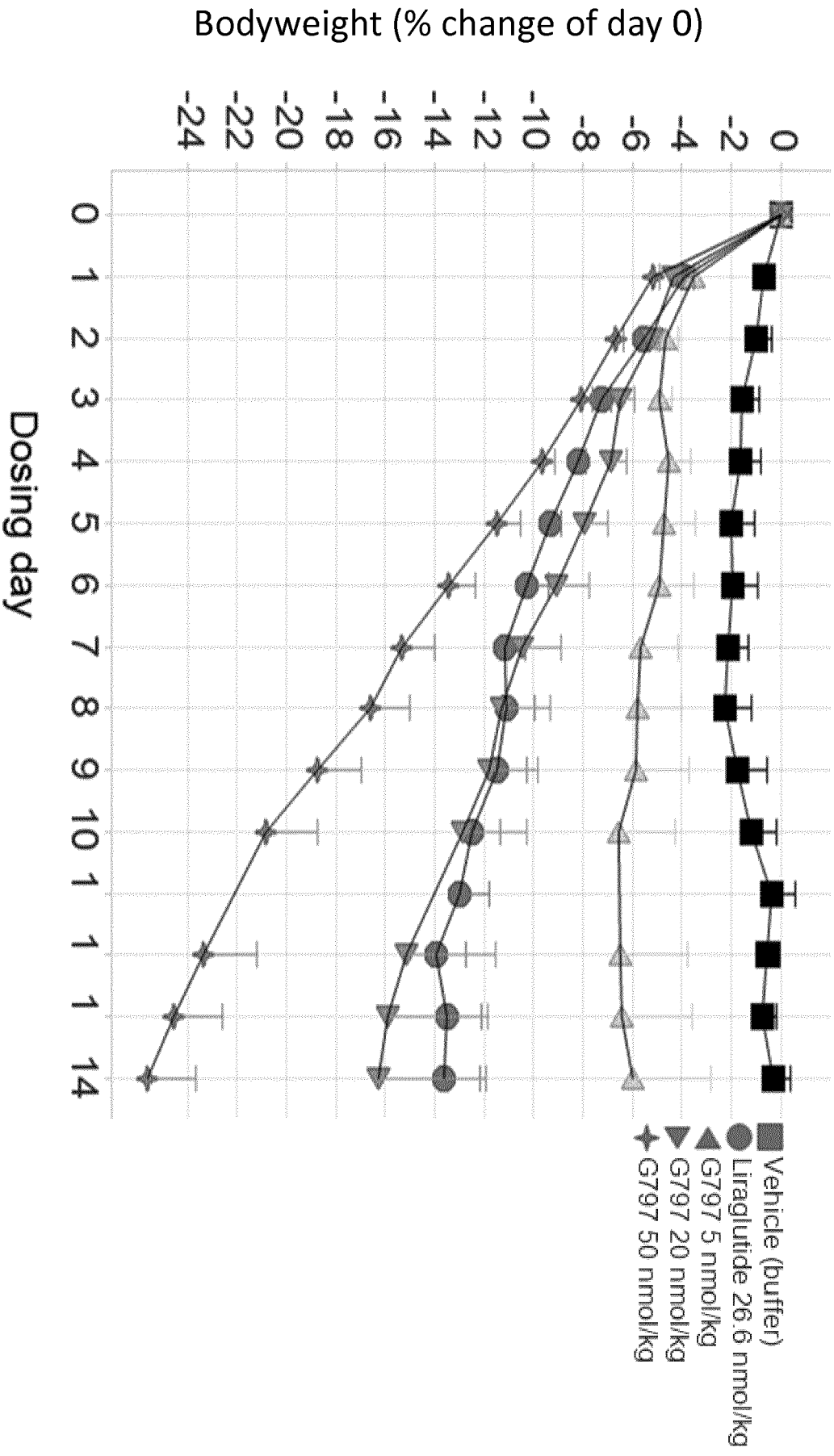

Bodyweight (% change of day 0)
0
-2
-4
-6
-8
-10
-12
-14
-16
-18
-20
-22
-24
Dosing day
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
Vehicle (buffer)
Liraglutide 26.6 nmol/kg
G797 5 nmol/kg
G797 20 nmol/kg
G797 50 nmol/kg

FIG. 2

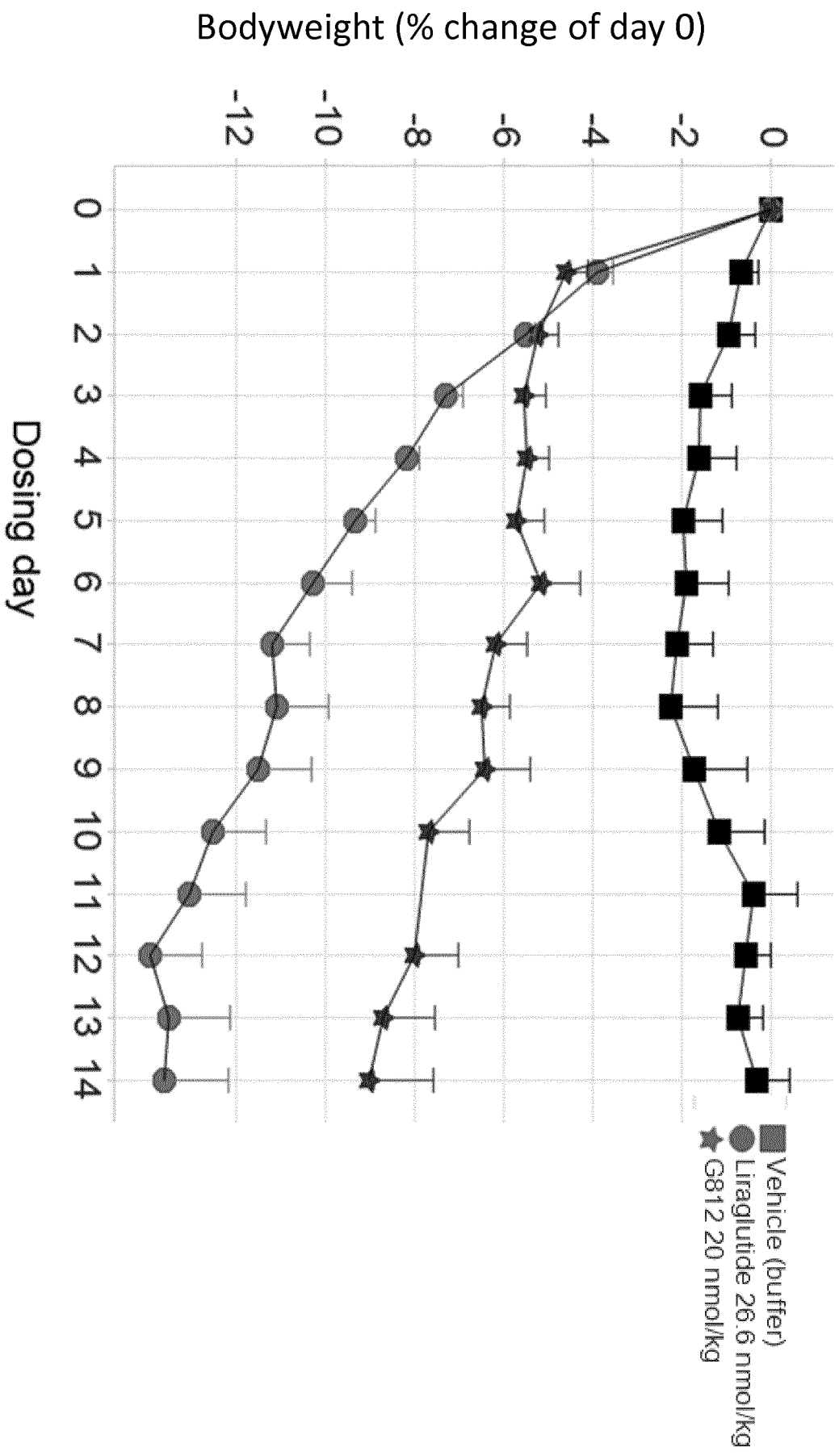

Bodyweight (% change of day 0)
0
-2
-4
-6
-8
-10
-12
Dosing day
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
Vehicle (buffer)
Liraglutide 26.6 nmol/kg
G812 20 nmol/kg

FIG. 3

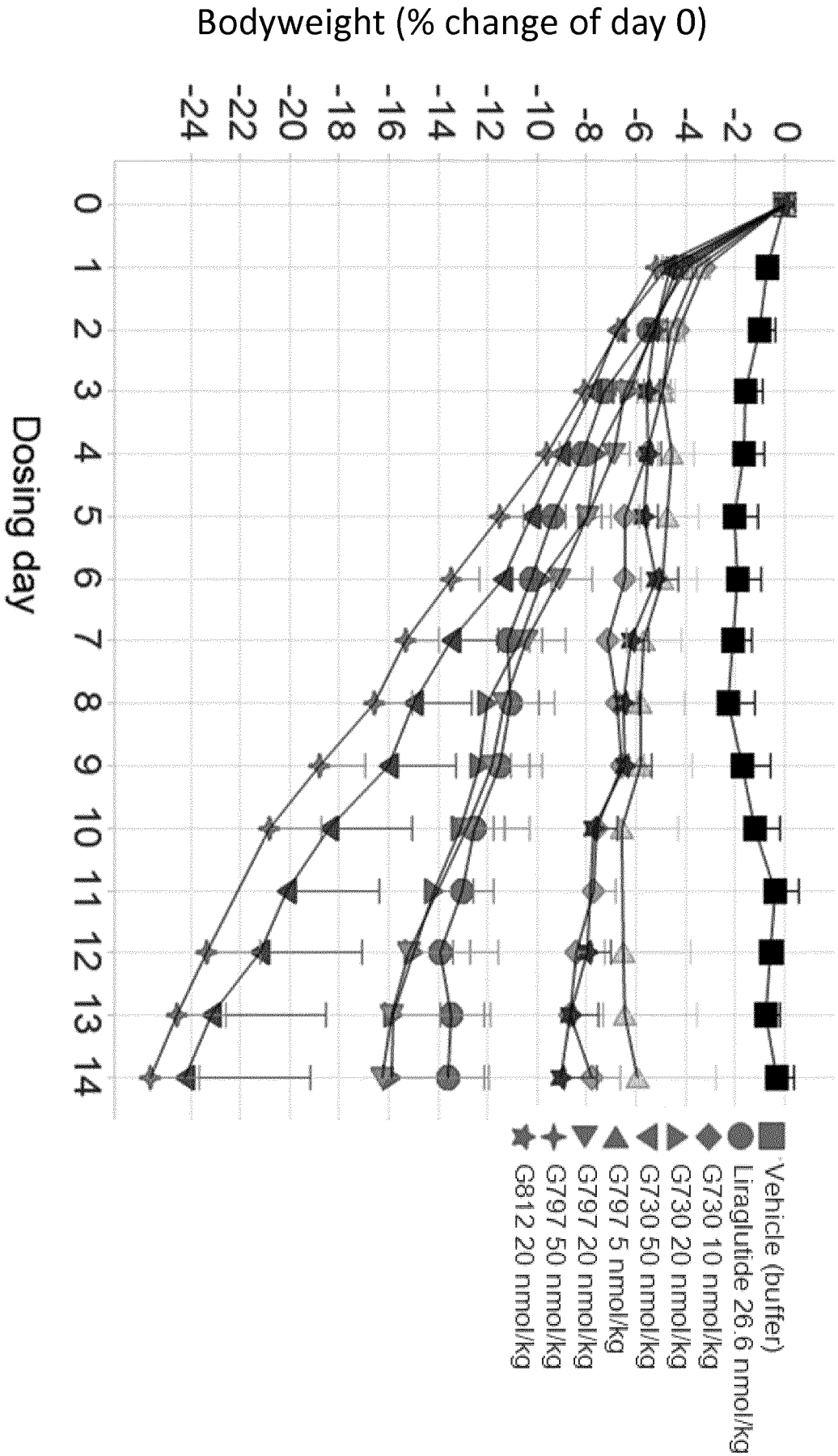

Bodyweight (% change of day 0)
0
-2
-4
-6
-8
-10
-12
-14
-16
-18
-20
-22
-24
Dosing day
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
Vehicle (buffer)
Liraglutide 26.6 nmol/kg
G730 10 nmol/kg
G730 20 nmol/kg
G730 50 nmol/kg
G797 5 nmol/kg
G797 20 nmol/kg
G797 50 nmol/kg
G812 20 nmol/kg

FIG. 4

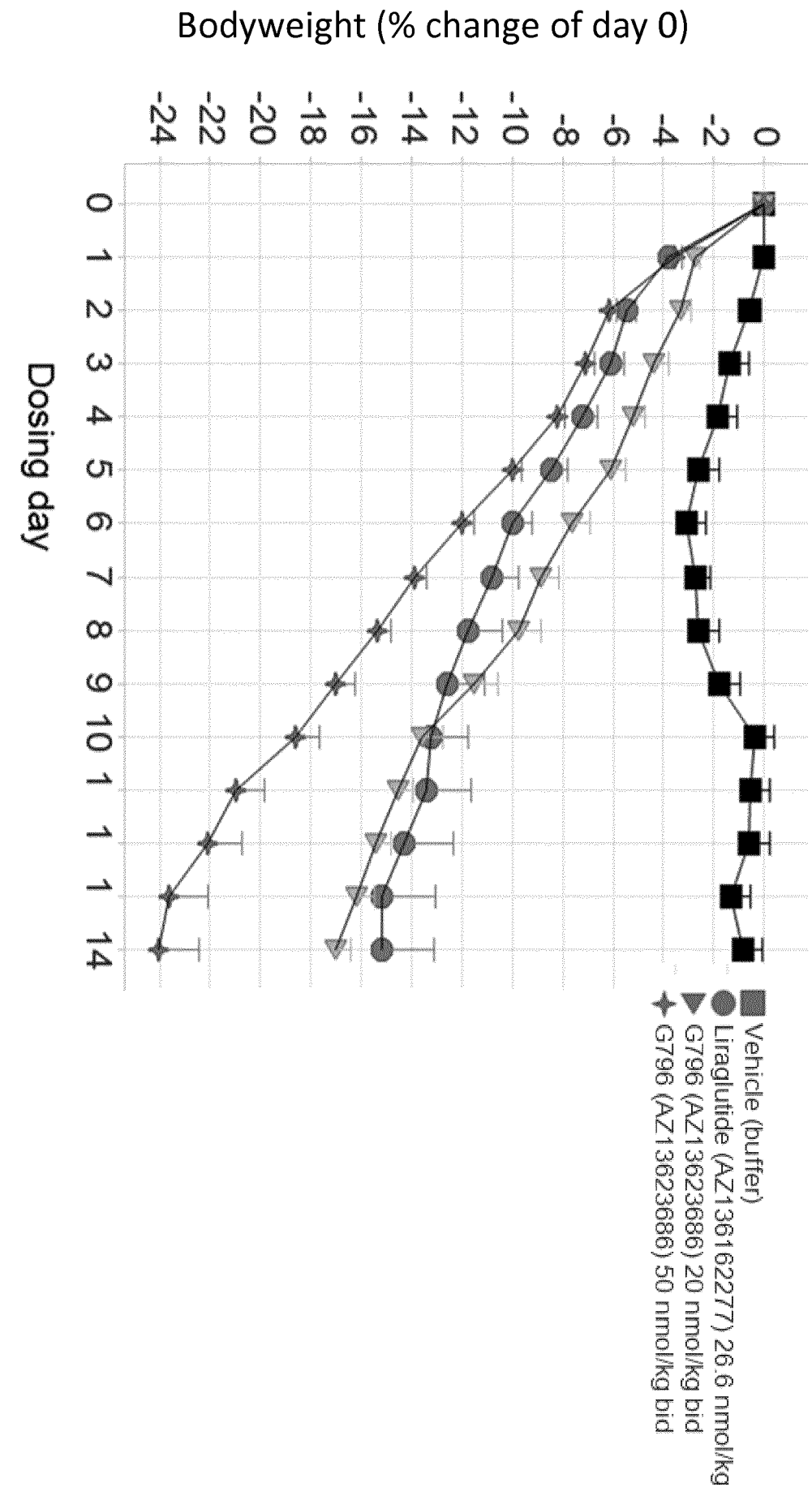

Bodyweight (% change of day 0)
0
-2
-4
-6
-8
-10
-12
-14
-16
-18
-20
-22
-24
0 1 2 3 4 5 6 7 8 9 10 1 1 1 1 14
Dosing day
Vehicle (buffer)
Liraglutide (AZ136162277) 26.6 nmol/kg
G796 (AZ13623686) 20 nmol/kg bid
G796 (AZ13623686) 50 nmol/kg bid

FIG. 5

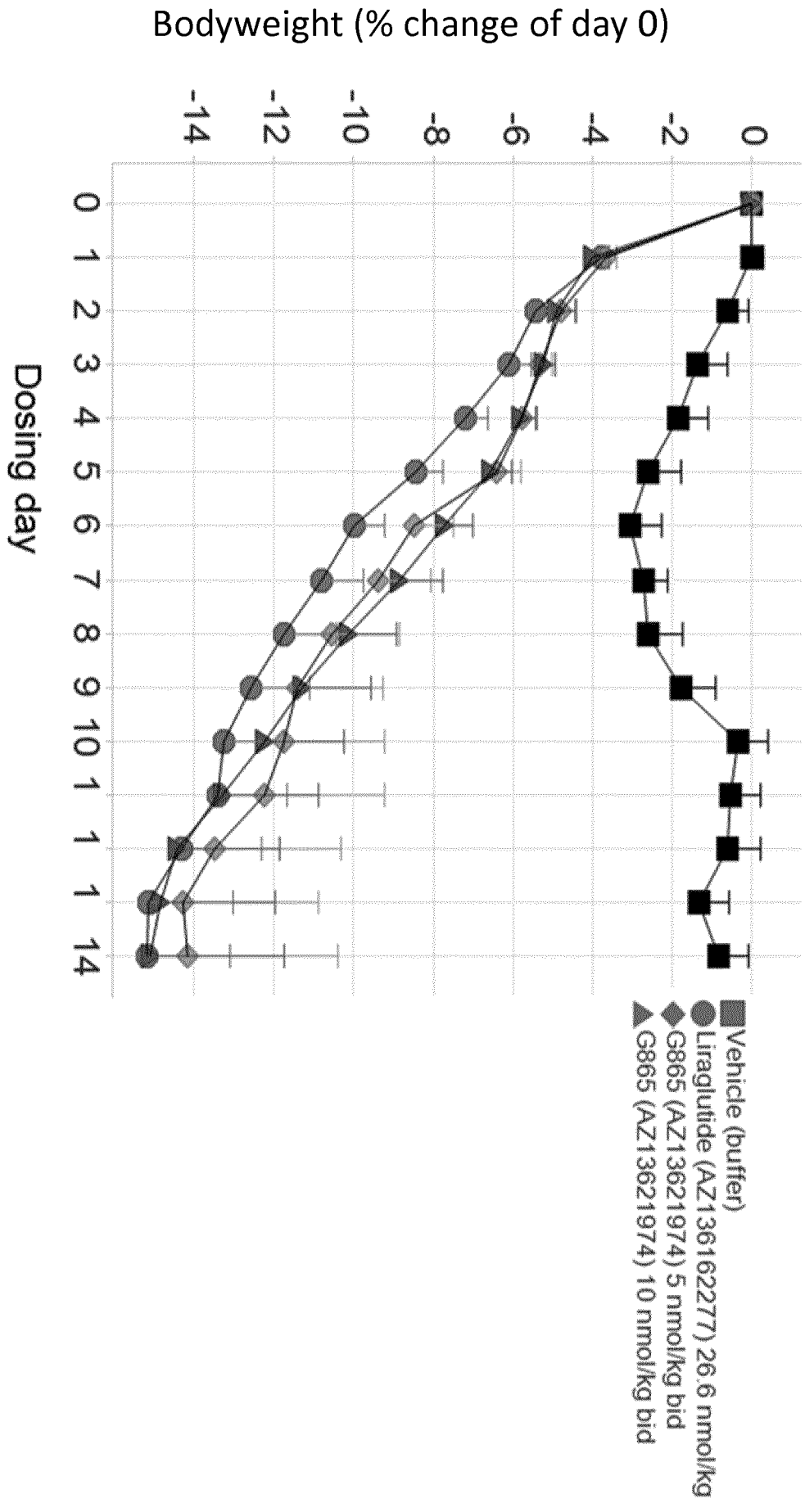

Bodyweight (% change of day 0)
0
-2
-4
-6
-8
-10
-12
-14
0 1 2 3 4 5 6 7 8 9 10 1 1 1 1 14
Dosing day
Vehicle (buffer)
Liraglutide (AZ136162277) 26.6 nmol/kg
G865 (AZ13621974) 5 nmol/kg bid
G865 (AZ13621974) 10 nmol/kg bid

FIG. 6

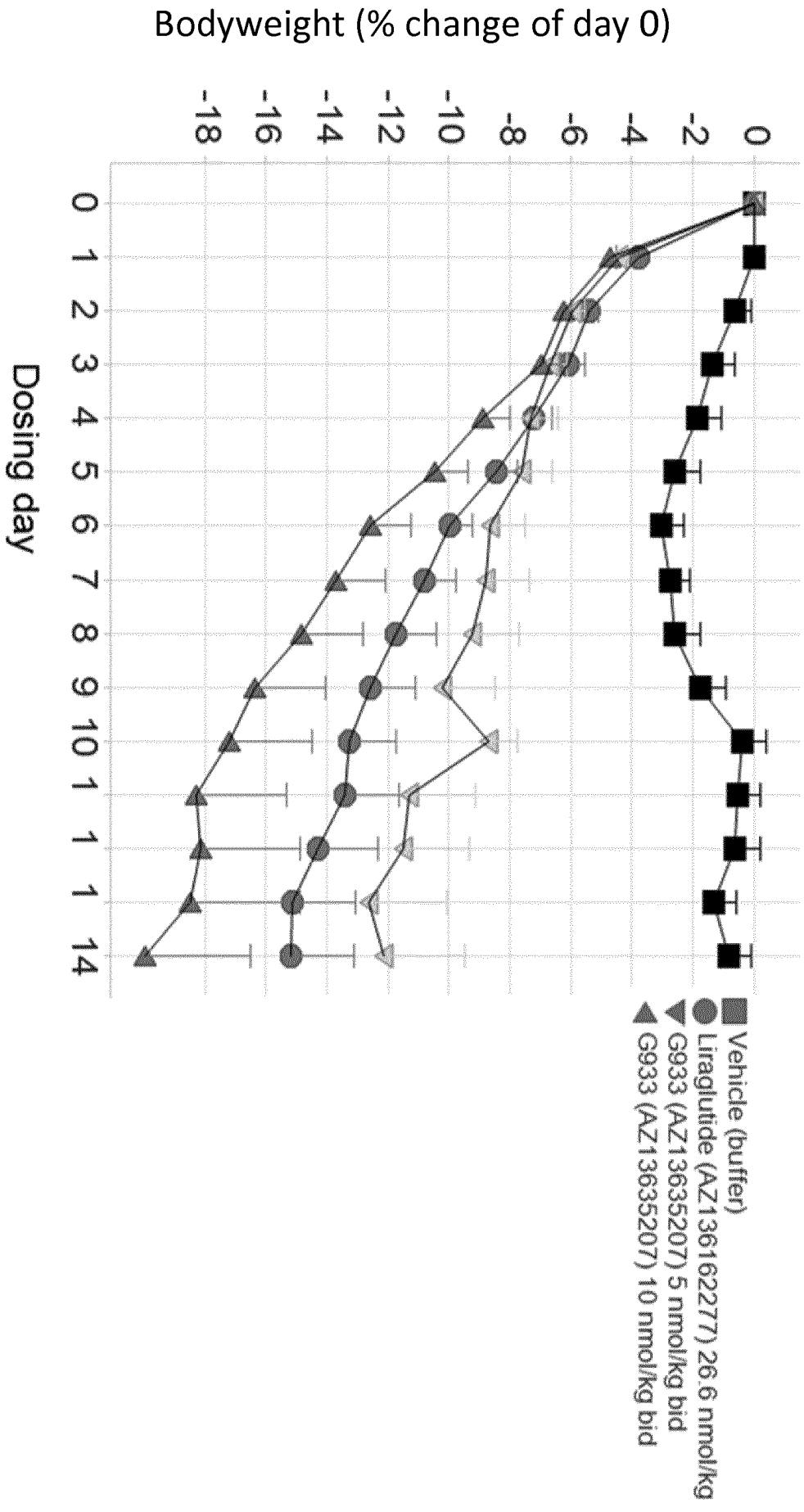

Bodyweight (% change of day 0)
0
-2
-4
-6
-8
-10
-12
-14
-16
-18
0 1 2 3 4 5 6 7 8 9 10 1 1 1 1 14
Dosing day
Vehicle (buffer)
Liraglutide (AZ136162277) 26.6 nmol/kg
G933 (AZ13635207) 5 nmol/kg bid
G933 (AZ13635207) 10 nmol/kg bid

FIG. 7

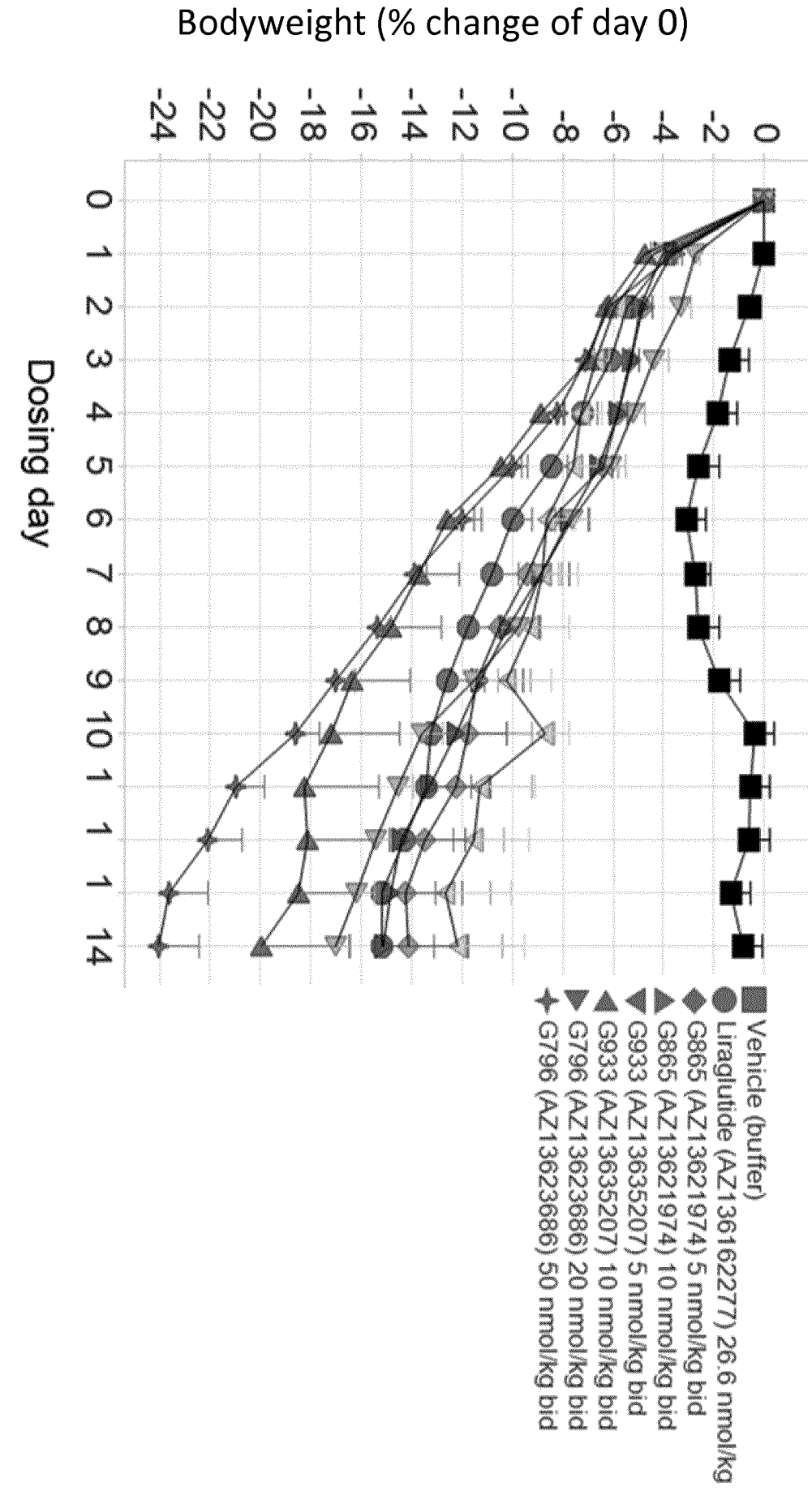

Bodyweight (% change of day 0)
0
-2
-4
-6
-8
-10
-12
-14
-16
-18
-20
-22
-24
0 1 2 3 4 5 6 7 8 9 10 1 1 1 1 14
Dosing day
Vehicle (buffer)
Liraglutide (AZ136162277) 26.6 nmol/kg
G865 (AZ13621974) 5 nmol/kg bid
G865 (AZ13621974) 10 nmol/kg bid
G933 (AZ13635207) 5 nmol/kg bid
G933 (AZ13635207) 10 nmol/kg bid
G796 (AZ13623686) 20 nmol/kg bid
G796 (AZ13623686) 50 nmol/kg bid

FIG. 8

FIG. 9

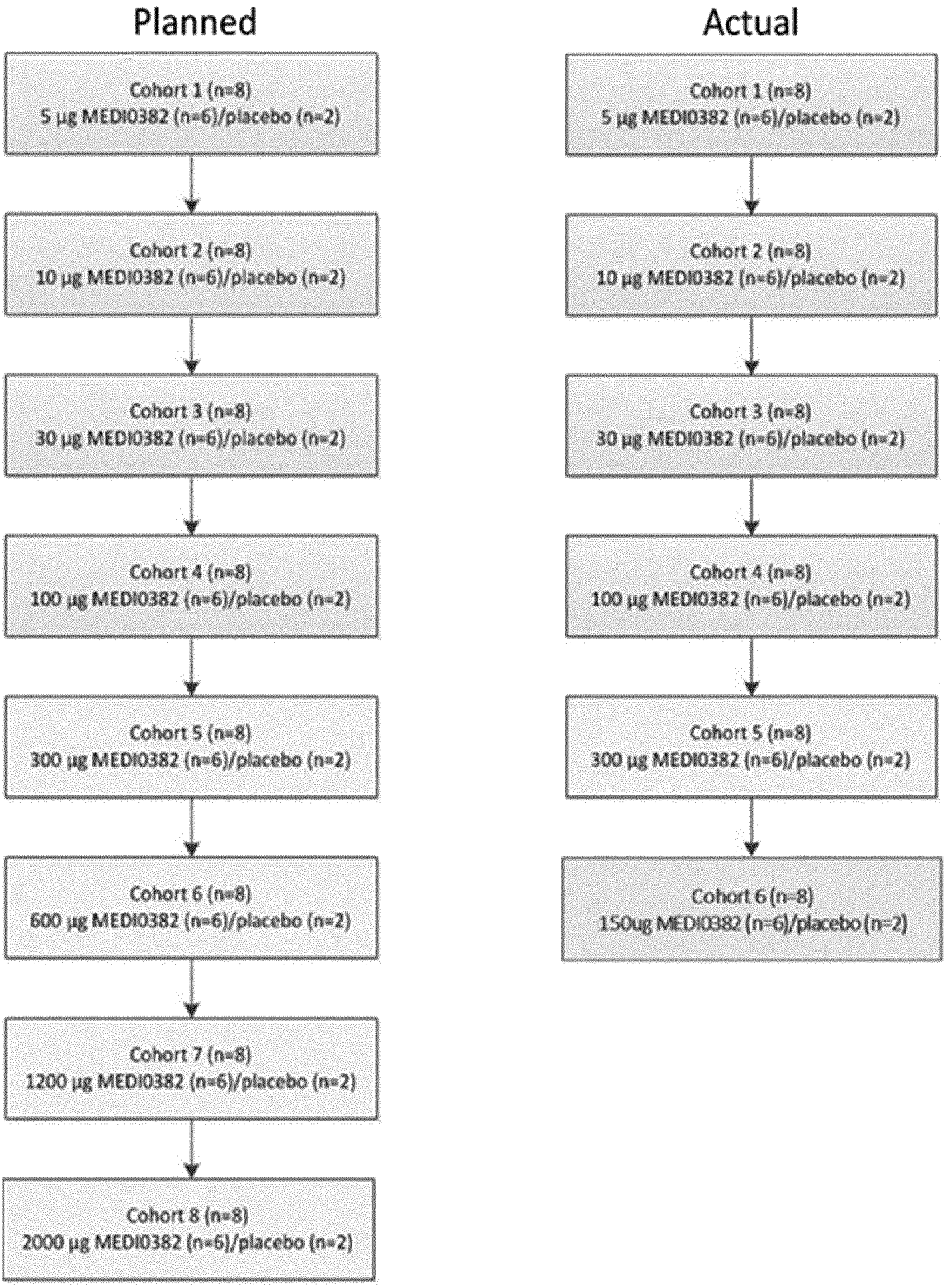

Planned
Cohort 1 (n=8)
5 µg MEDI0382 (n=6)/placebo (n=2)
Cohort 2 (n=8)
10 µg MEDI0382 (n=6)/placebo (n=2)
Cohort 3 (n=8)
30 µg MEDI0382 (n=6)/placebo (n=2)
Cohort 4 (n=8)
100 µg MEDI0382 (n=6)/placebo (n=2)
Cohort 5 (n=8)
300 µg MEDI0382 (n=6)/placebo (n=2)
Cohort 6 (n=8)
600 µg MEDI0382 (n=6)/placebo (n=2)
Cohort 7 (n=8)
1200 µg MEDI0382 (n=6)/placebo (n=2)
Cohort 8 (n=8)
2000 µg MEDI0382 (n=6)/placebo (n=2)
Actual
Cohort 1 (n=8)
5 µg MEDI0382 (n=6)/placebo (n=2)
Cohort 2 (n=8)
10 µg MEDI0382 (n=6)/placebo (n=2)
Cohort 3 (n=8)
30 µg MEDI0382 (n=6)/placebo (n=2)
Cohort 4 (n=8)
100 µg MEDI0382 (n=6)/placebo (n=2)
Cohort 5 (n=8)
300 µg MEDI0382 (n=6)/placebo (n=2)
Cohort 6 (n=8)
150ug MEDI0382 (n=6)/placebo (n=2)

FIG. 10

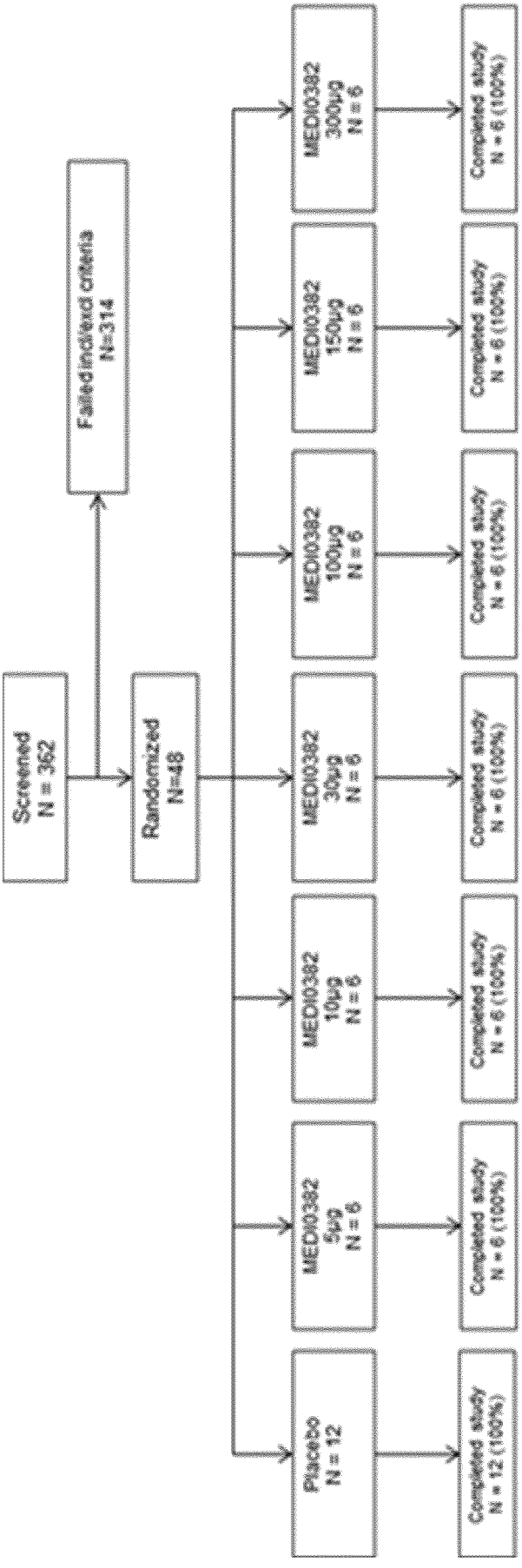

Screened
N = 362
Failed inclusion criteria
N=314
Randomized
N=48
Placebo
N = 12
MEDI0382
5µg
N = 6
MEDI0382
10µg
N = 6
MEDI0382
30µg
N = 6
MEDI0382
100µg
N = 6
MEDI0382
150µg
N = 6
MEDI0382
300µg
N = 6
Completed study
N = 12 (100%)
Completed study
N = 6 (100%)
Completed study
N = 6 (100%)
Completed study
N = 6 (100%)
Completed study
N = 6 (100%)
Completed study
N = 6 (100%)
Completed study
N = 6 (100%)

FIG. 11

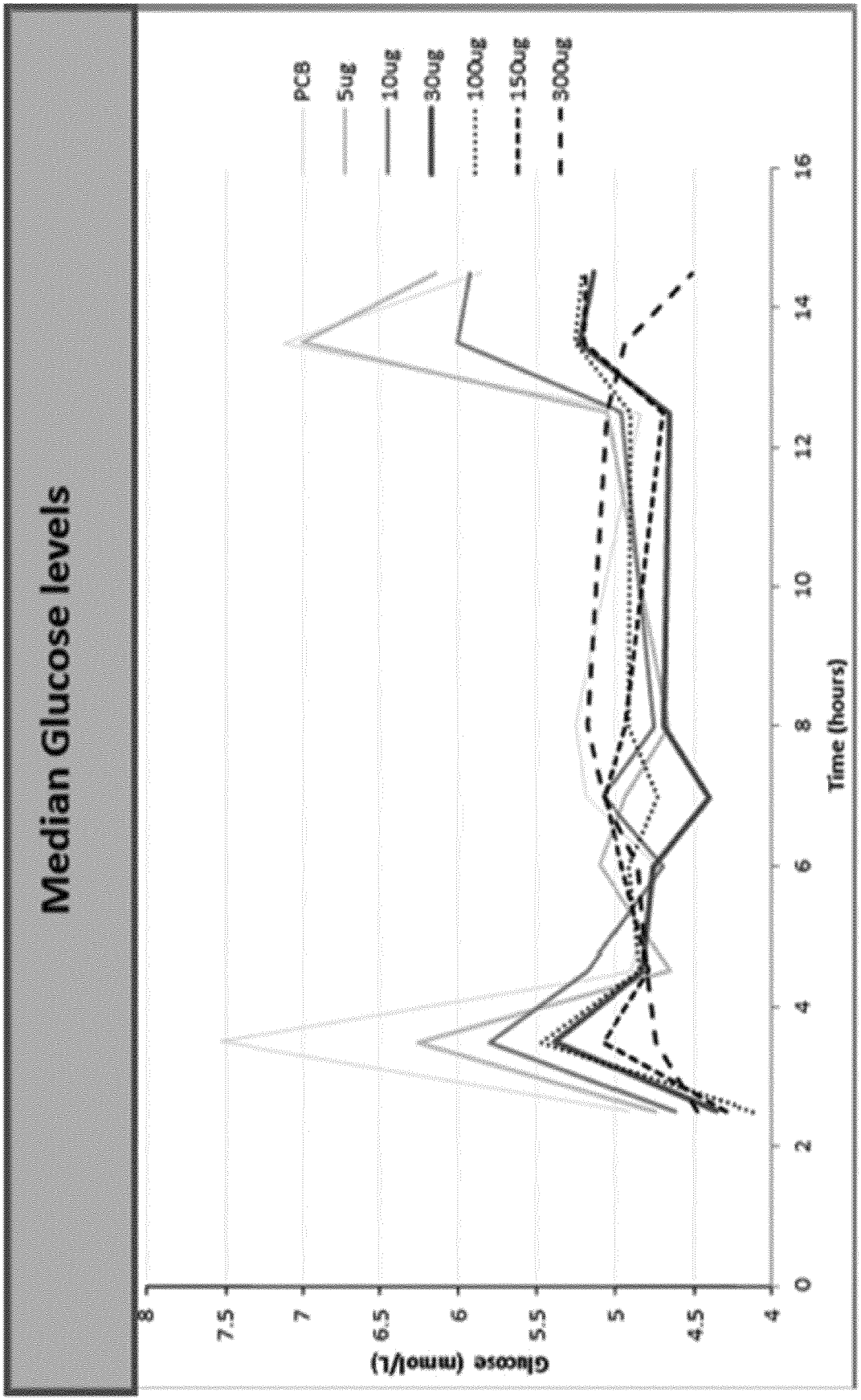

Median Glucose levels
PCB
5ug
10ug
30ug
100ug
150ug
300ug
Glucose (mmol/L)
8
7.5
7
6.5
6
5.5
5
4.5
4
Time (hours)
0
2
4
6
8
10
12
14
16

FIG. 12

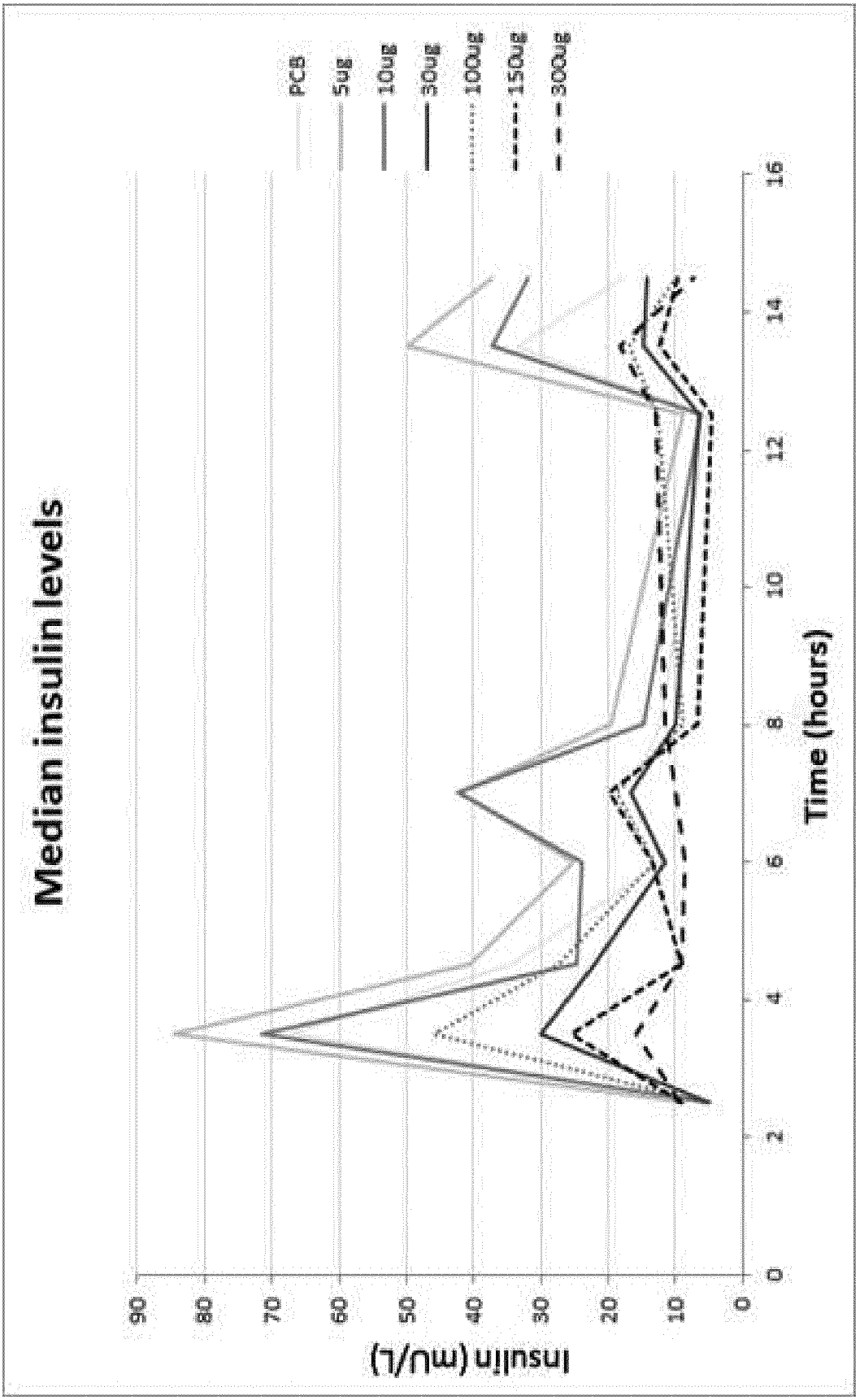

Median insulin levels
Insulin (mU/L)
Time (hours)
PCB
5ug
10ug
30ug
100ug
150ug
300ug
0
10
20
30
40
50
60
70
80
90
0
2
4
6
8
10
12
14
16

FIG. 13

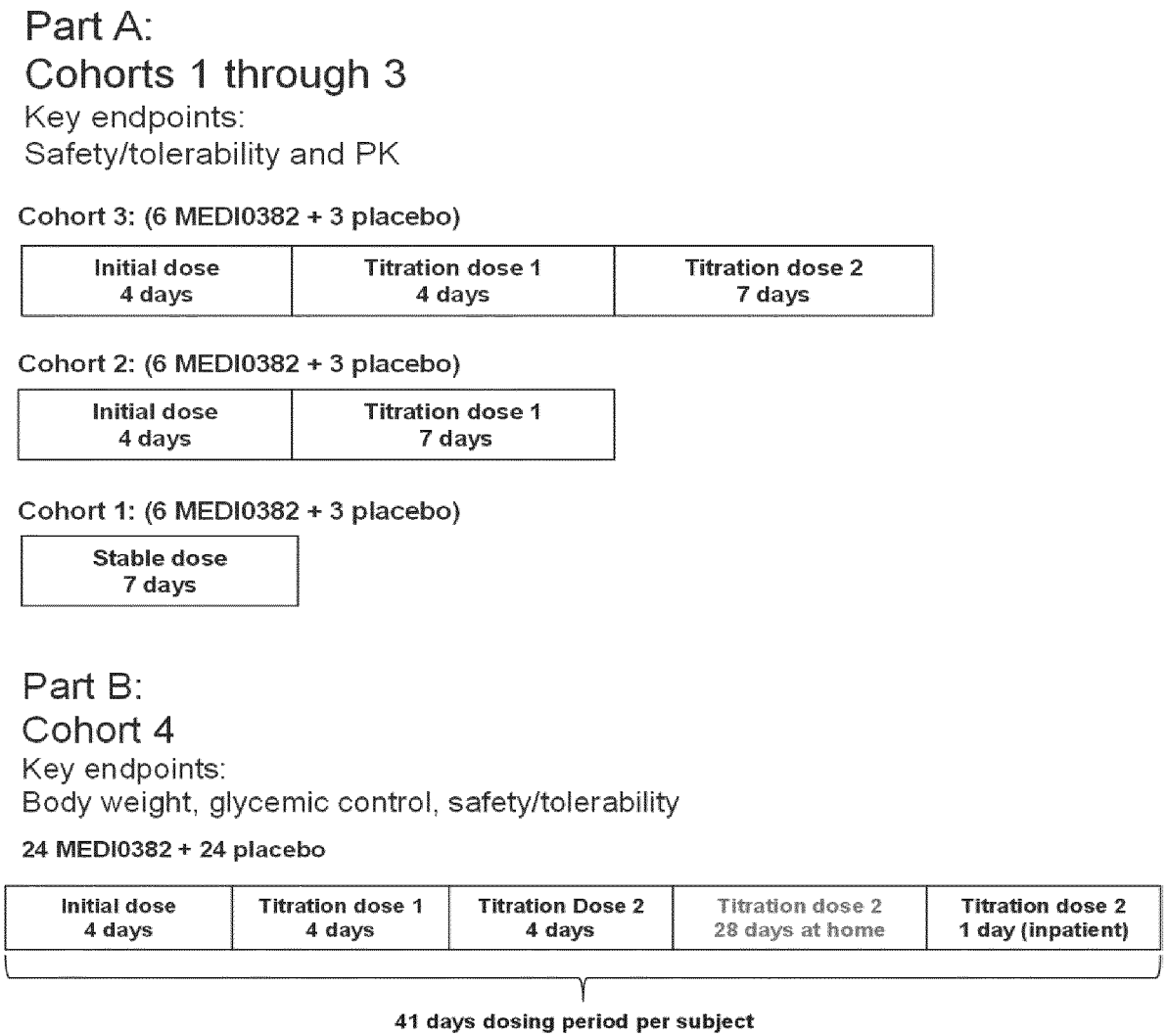

Part A:
Cohorts 1 through 3
Key endpoints:
Safety/tolerability and PK
Cohort 3: (6 MEDI0382 + 3 placebo)
Initial dose
4 days
Titration dose 1
4 days
Titration dose 2
7 days
Cohort 2: (6 MEDI0382 + 3 placebo)
Initial dose
4 days
Titration dose 1
7 days
Cohort 1: (6 MEDI0382 + 3 placebo)
Stable dose
7 days
Part B:
Cohort 4
Key endpoints:
Body weight, glycemic control, safety/tolerability
24 MEDI0382 + 24 placebo
Initial dose
4 days
Titration dose 1
4 days
Titration Dose 2
4 days
Titration dose 2
28 days at home
Titration dose 2
1 day (inpatient)
41 days dosing period per subject

FIG. 14

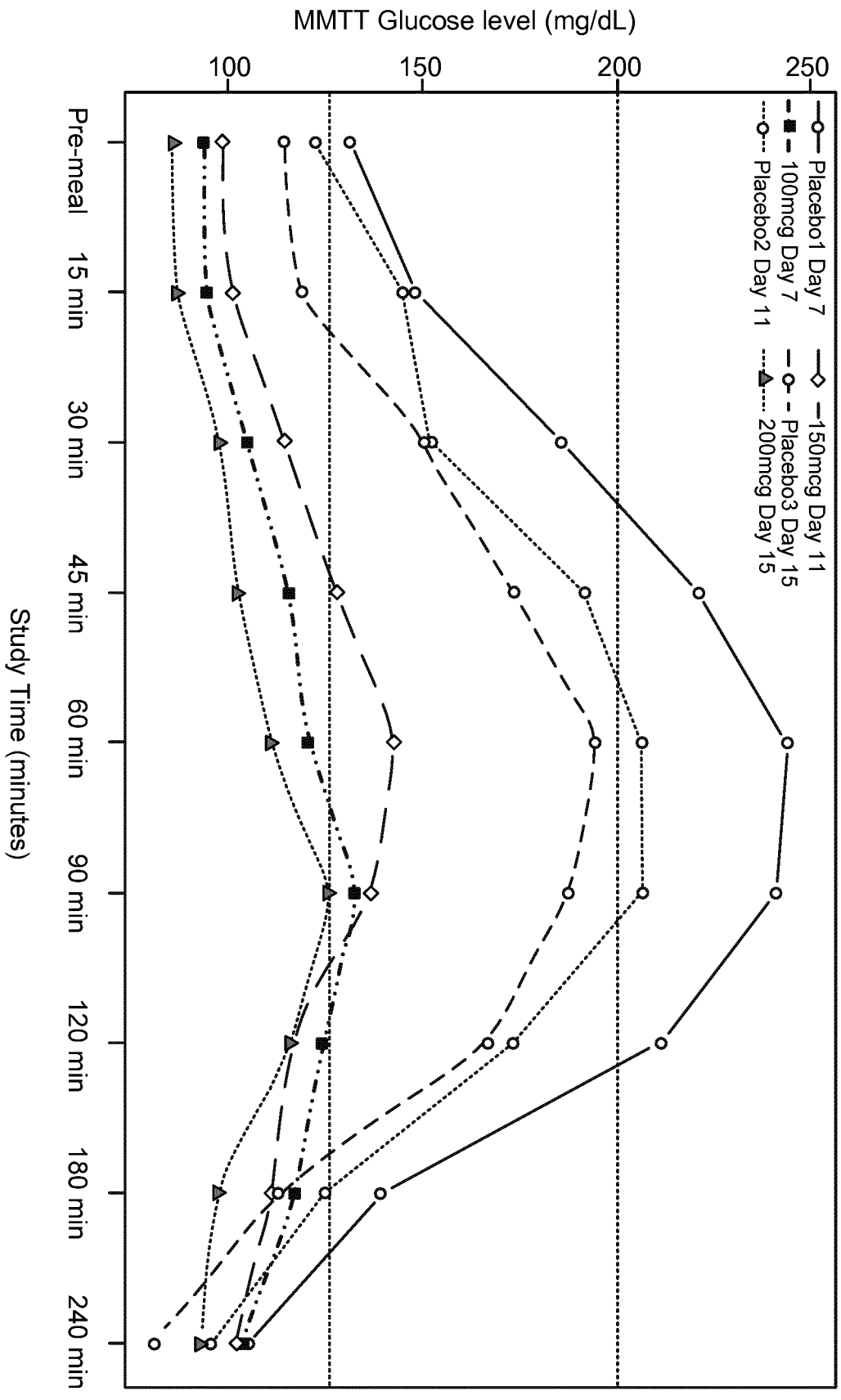

MMTT Glucose level (mg/dL)
100
150
200
250
Placebo1 Day 7
150mcg Day 11
100mcg Day 7
Placebo3 Day 15
Placebo2 Day 11
200mcg Day 15
Pre-meal
15 min
30 min
45 min
60 min
90 min
120 min
180 min
240 min
Study Time (minutes)

FIG. 15

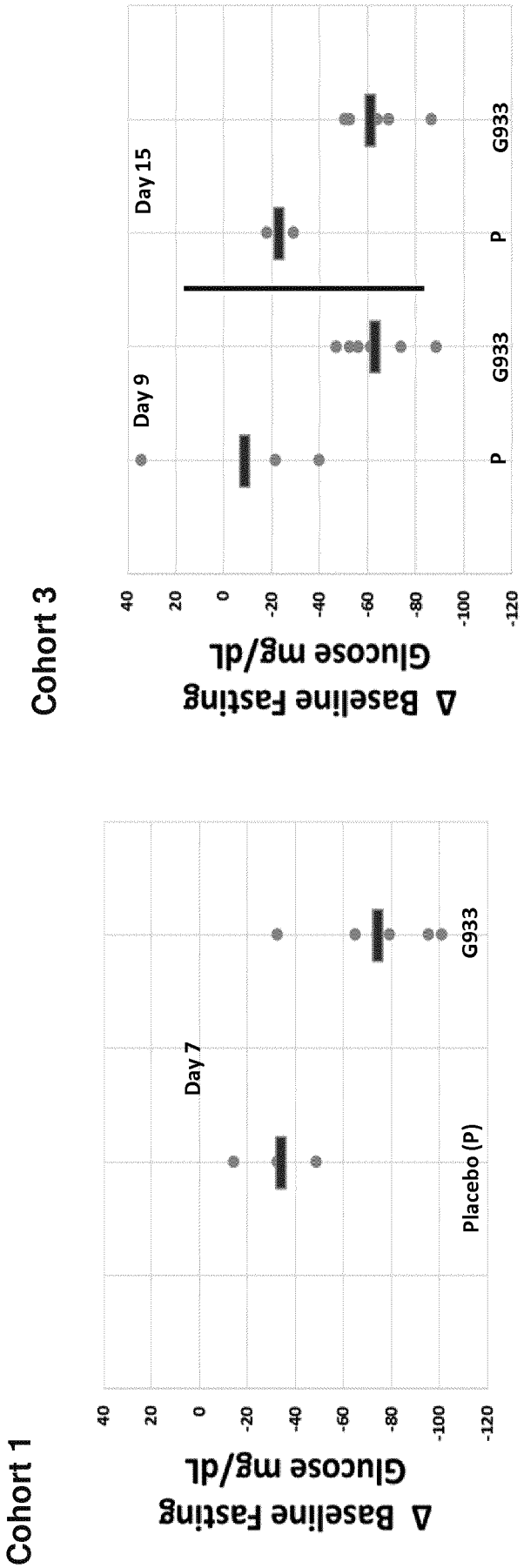

Cohort 1
Δ Baseline Fasting Glucose mg/dL
40
20
0
-20
-40
-60
-80
-100
-120
Day 7
Placebo (P)
G933
Cohort 3
Δ Baseline Fasting Glucose mg/dL
Day 9
Day 15
P
G933
P
G933

FIG. 16

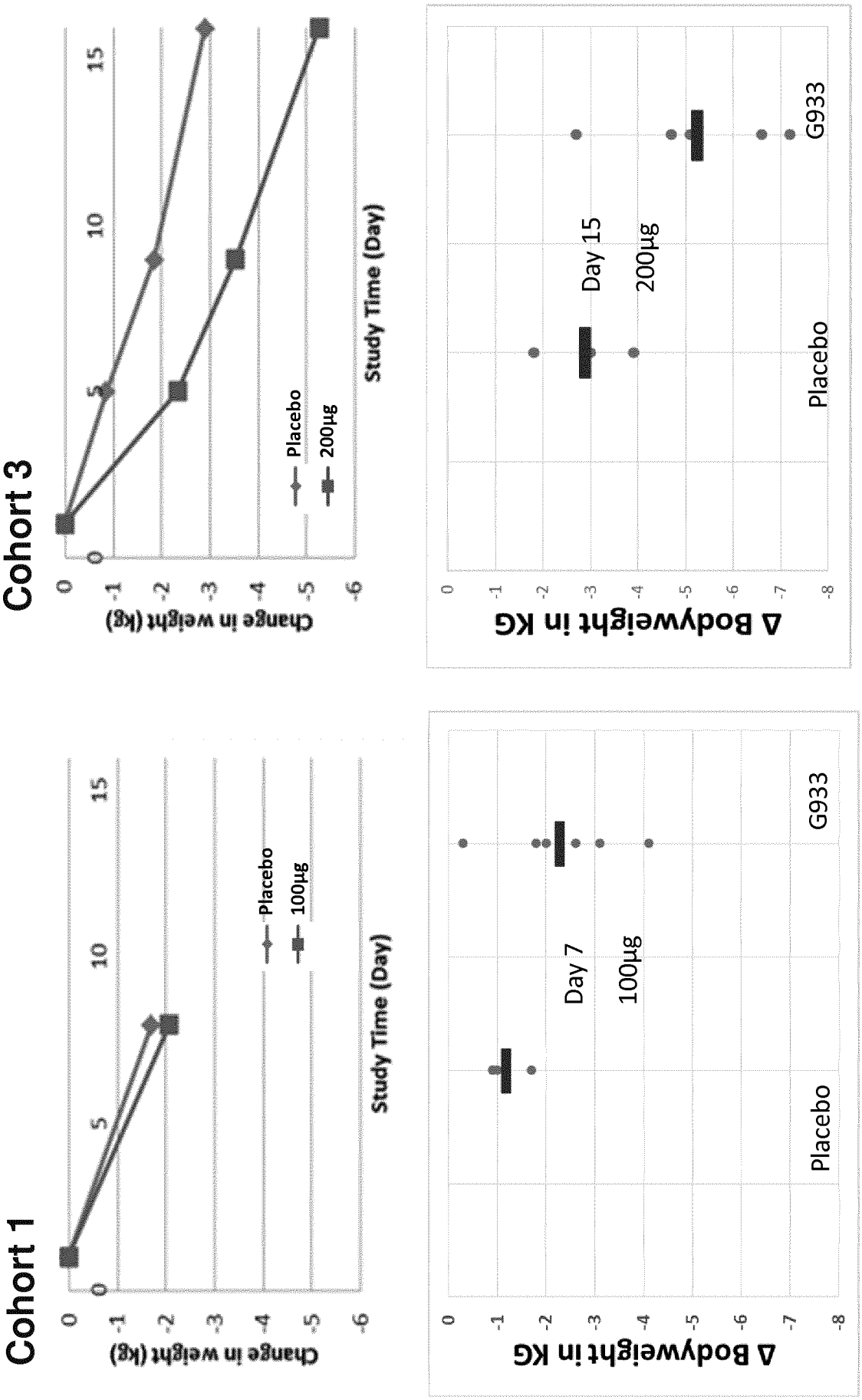

Cohort 1
Change in weight (kg)
Study Time (Day)
Placebo
100µg
Δ Bodyweight in KG
Day 7
Placebo
100µg
G933
Cohort 3
Change in weight (kg)
Study Time (Day)
Placebo
200µg
Δ Bodyweight in KG
Day 15
Placebo
200µg
G933

FIG. 17

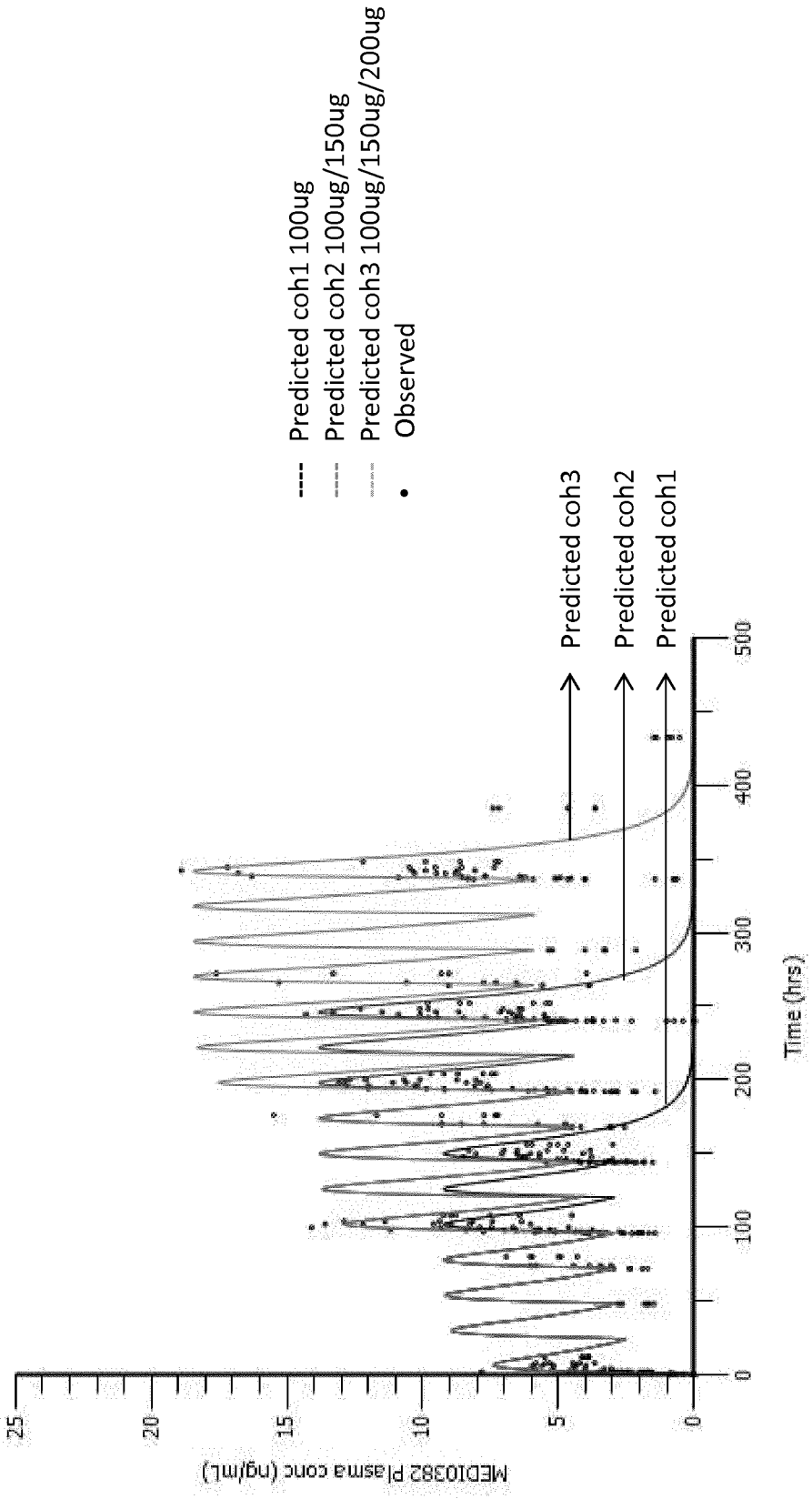

Predicted coh1 100ug
Predicted coh2 100ug/150ug
Predicted coh3 100ug/150ug/200ug
Observed
Predicted coh3
Predicted coh2
Predicted coh1
MED10382 Plasma conc (ng/mL)
Time (hrs)
0
5
10
15
20
25
0
100
200
300
400
500

FIG. 18

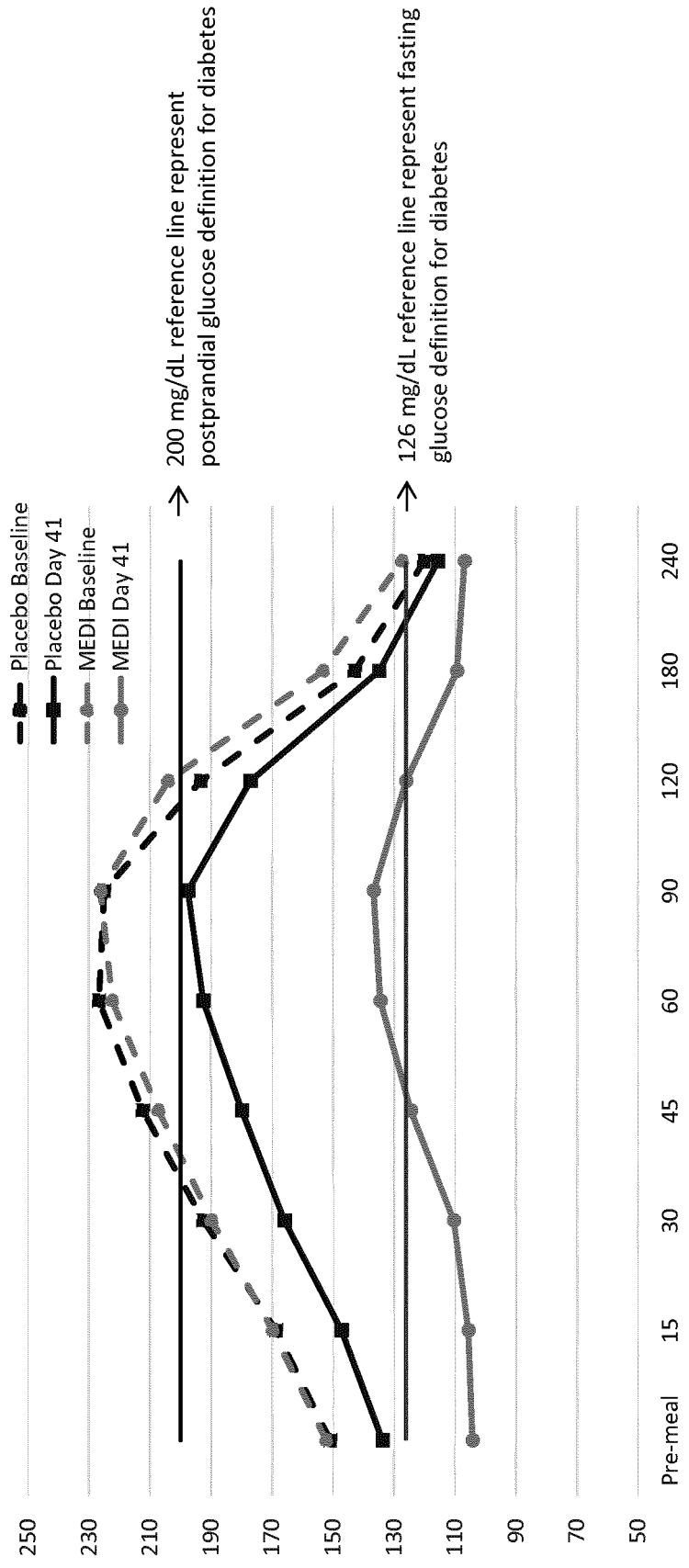

MMT Glucose level (mg/dL)
250
230
210
190
170
150
130
110
90
70
50
Pre-meal
15
30
45
60
90
120
180
240
Study Time
Placebo Baseline
Placebo Day 41
MEDI Baseline
MEDI Day 41
200 mg/dL reference line represent postprandial glucose definition for diabetes
126 mg/dL reference line represent fasting glucose definition for diabetes

FIG. 19

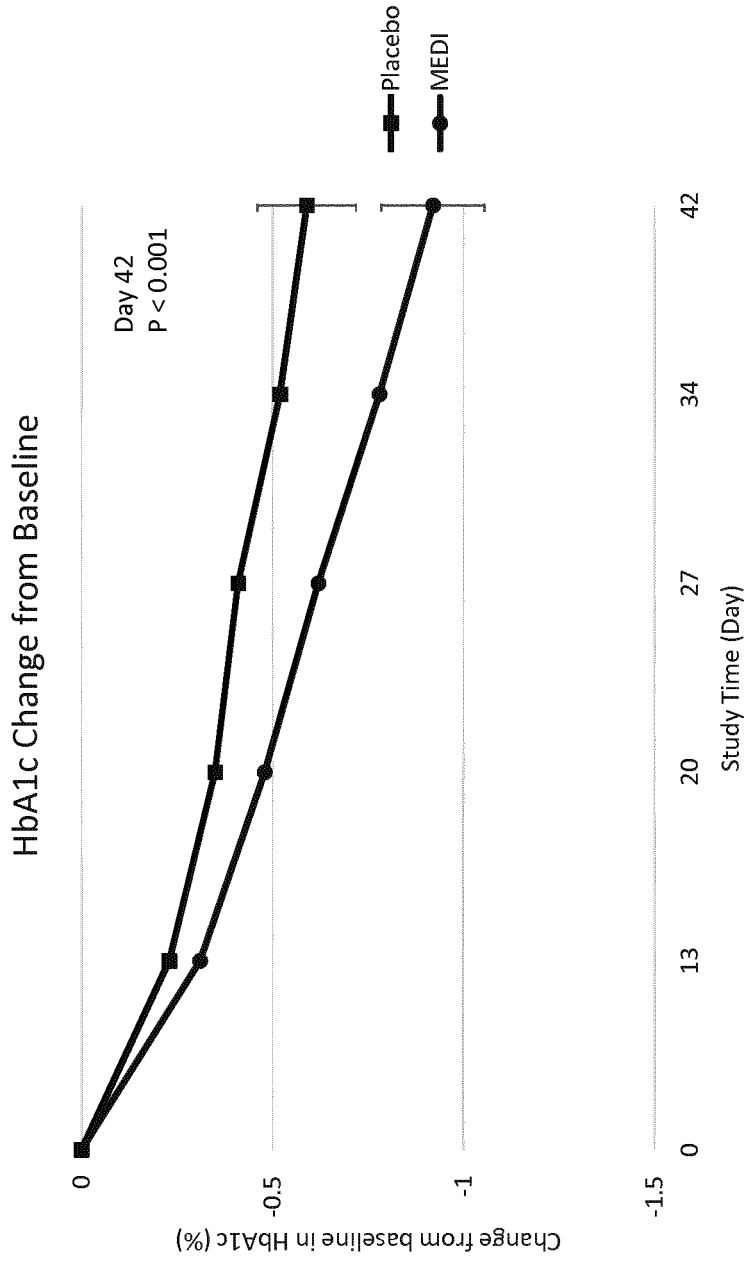
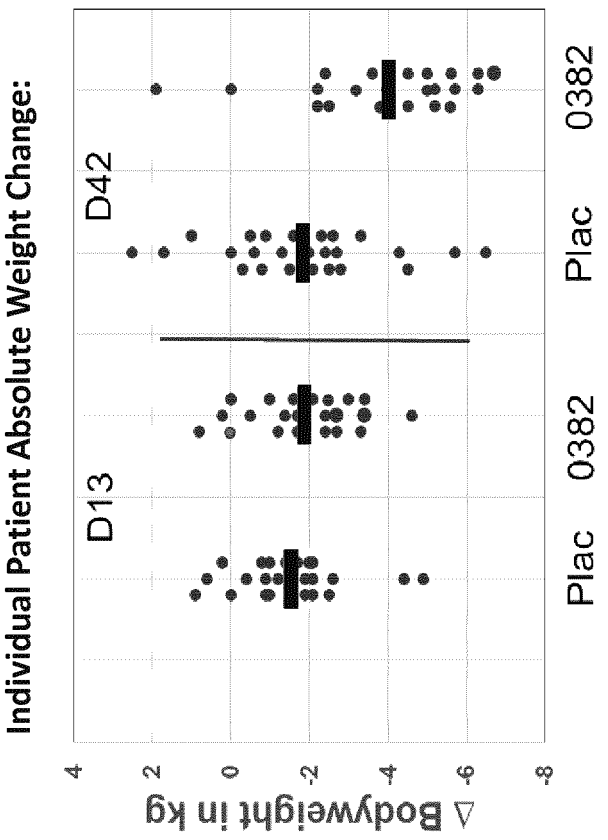

HbA1c Change from Baseline
Day 42
P < 0.001
Placebo
MEDI
0
-0.5
-1
-1.5
Change from baseline in HbA1c (%)
0
13
20
27
34
42
Study Time (Day)

FIG. 20


Individual Patient Absolute Weight Change:
D13
D42
Plac
0382
Plac
0382
Δ Bodyweight in kg
4
2
0
-2
-4
-6
-8

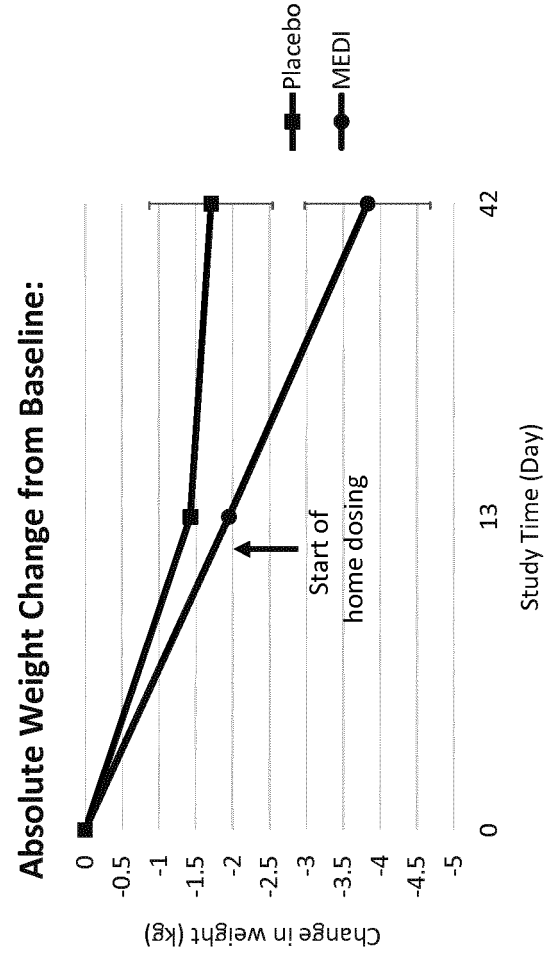

Absolute Weight Change from Baseline:
Placebo
MEDI
Start of
home dosing
Change in weight (kg)
0
-0.5
-1
-1.5
-2
-2.5
-3
-3.5
-4
-4.5
-5
0
13
42
Study Time (Day)

FIG. 21

Subjects with ≥ 5% Weight Loss from Baseline

Treatment	n/N (%)	Odds Ratio (90% CI)
MEDI0382	10/25 (40.0%)	12.9 (2.0, 81.0)
Placebo	1/26 (3.9%)	

% Weight Change from Baseline:

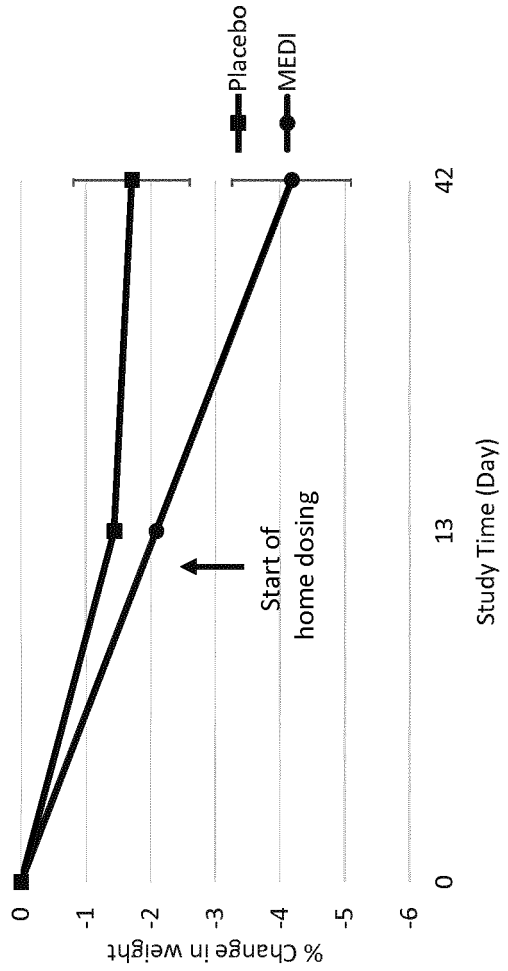


FIG. 22

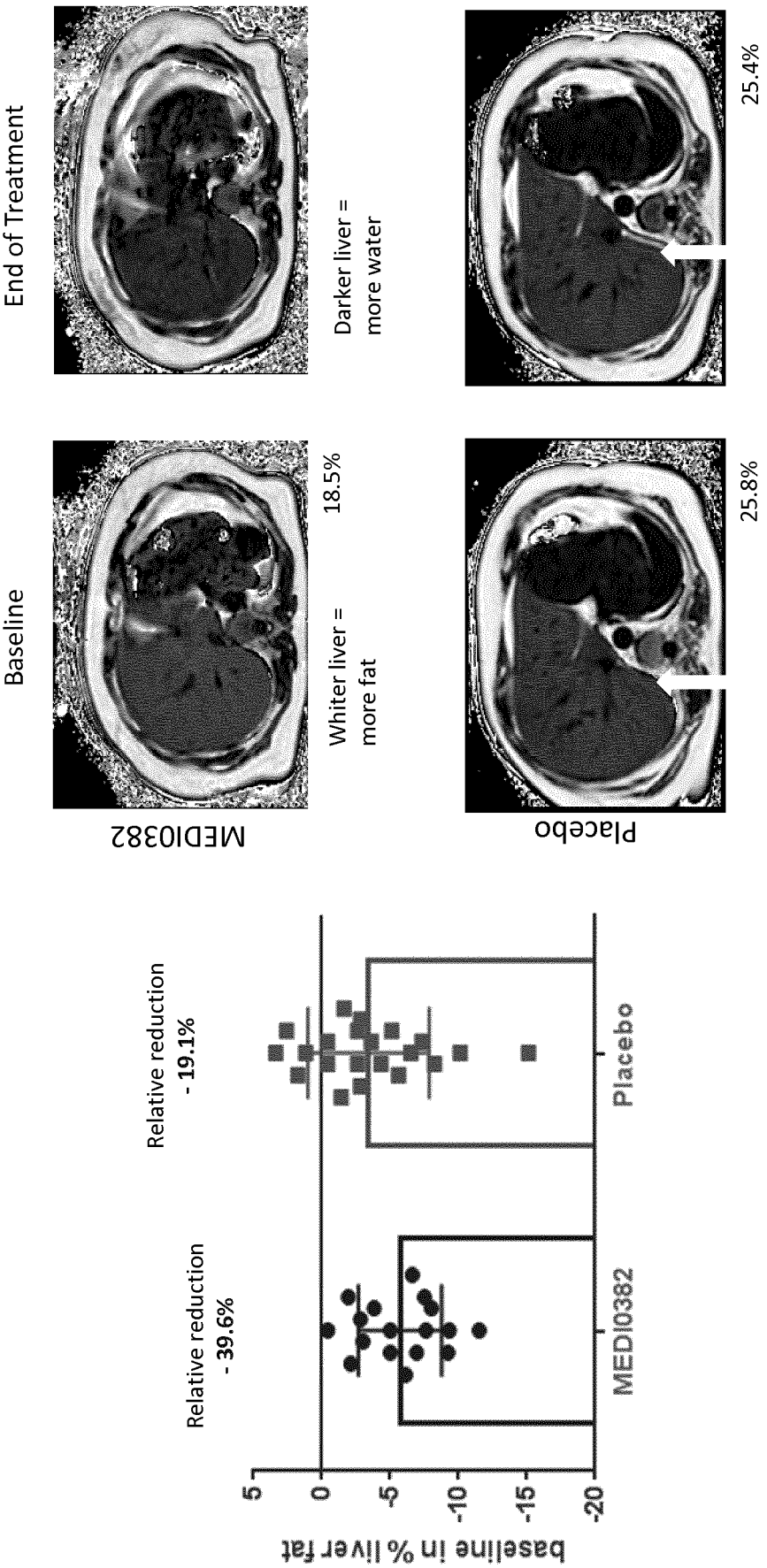
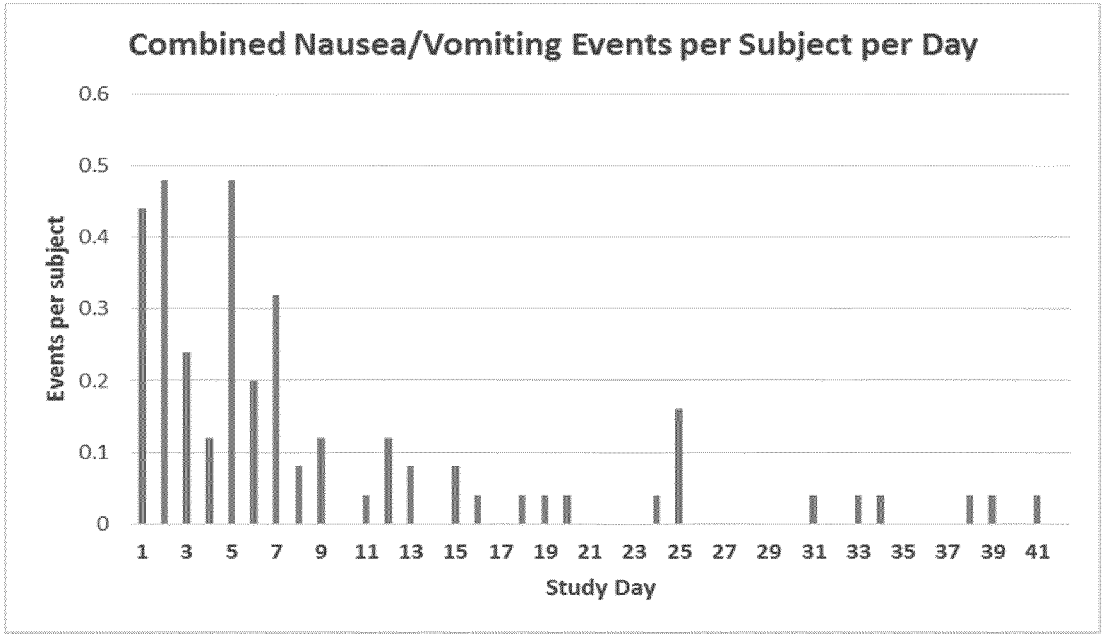

Baseline
End of Treatment
MEDI0382
Placebo
18.5%
25.8%
25.4%
Whiter liver = more fat
Darker liver = more water
Relative reduction - 39.6%
Relative reduction - 19.1%
Absolute change from baseline in % liver fat
5
0
-5
-10
-15
-20
MEDI0382
Placebo

FIG. 23

	Dose level of MEDI0382 Up titration			
No. of Events	100µg	150µg	200µg	Placebo
Nausea	22	14	15	7
Vomiting	23	18	14	0



Data includes total number of vomiting events and incidences where nausea was first reported per day

FIG. 24

Cohort 5 - 12 active + 4 placebo

100µg 5 days 3 inpatient	150µg 5 days outpatient	200µg 5 days outpatient	300µg 7 days 3+1 inpatient

Cohort 6 - 12 active + 4 placebo

100µg 5 days 3 inpatient	200µg 5 days outpatient	300µg 7 days 3+1 inpatient

FIG. 25

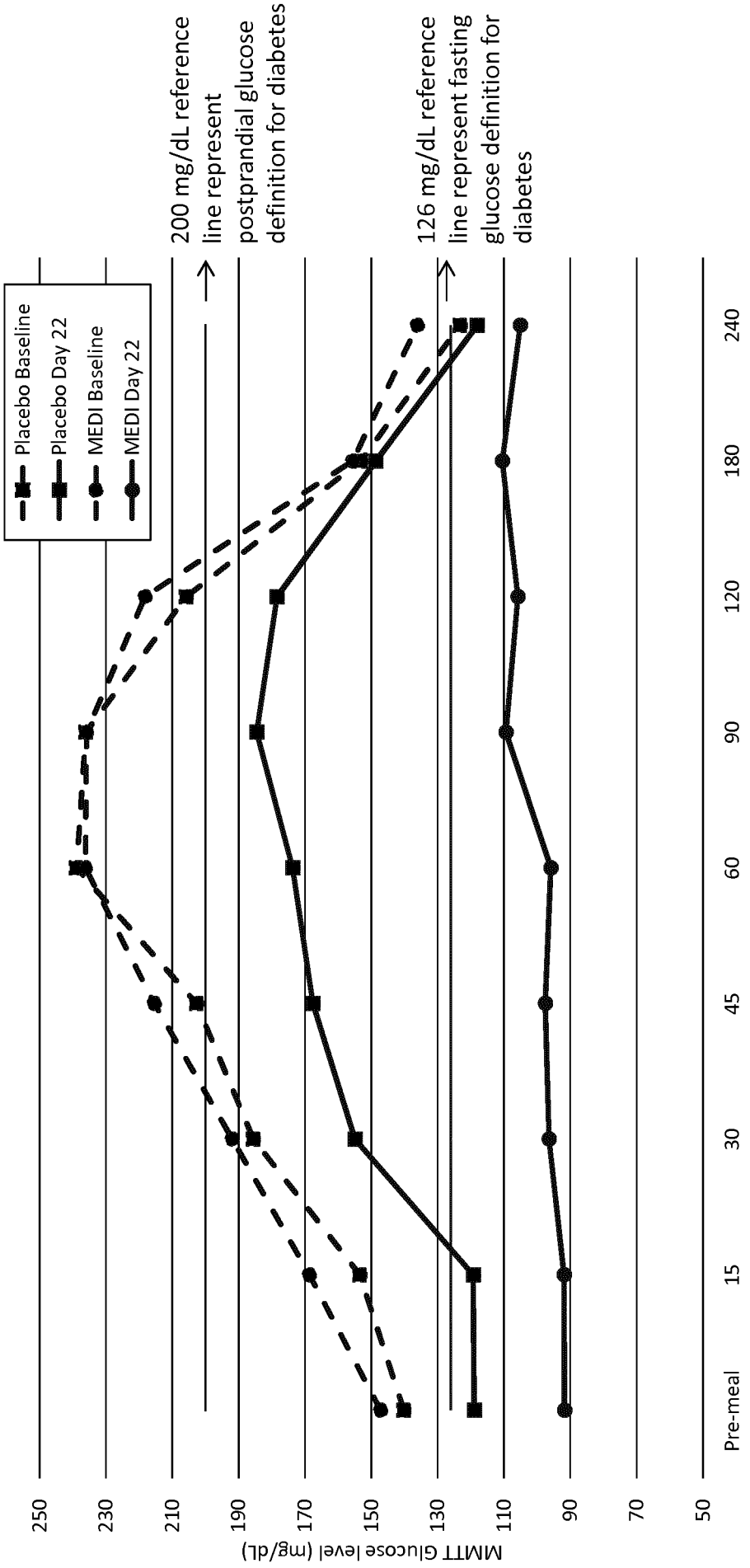

Placebo Baseline
Placebo Day 22
MEDI Baseline
MEDI Day 22
200 mg/dL reference line represent postprandial glucose definition for diabetes
126 mg/dL reference line represent fasting glucose definition for diabetes
MMTT Glucose level (mg/dL)
250
230
210
190
170
150
130
110
90
70
50
Pre-meal
15
30
45
60
90
120
180
240
Study Time (minutes)

FIG. 26

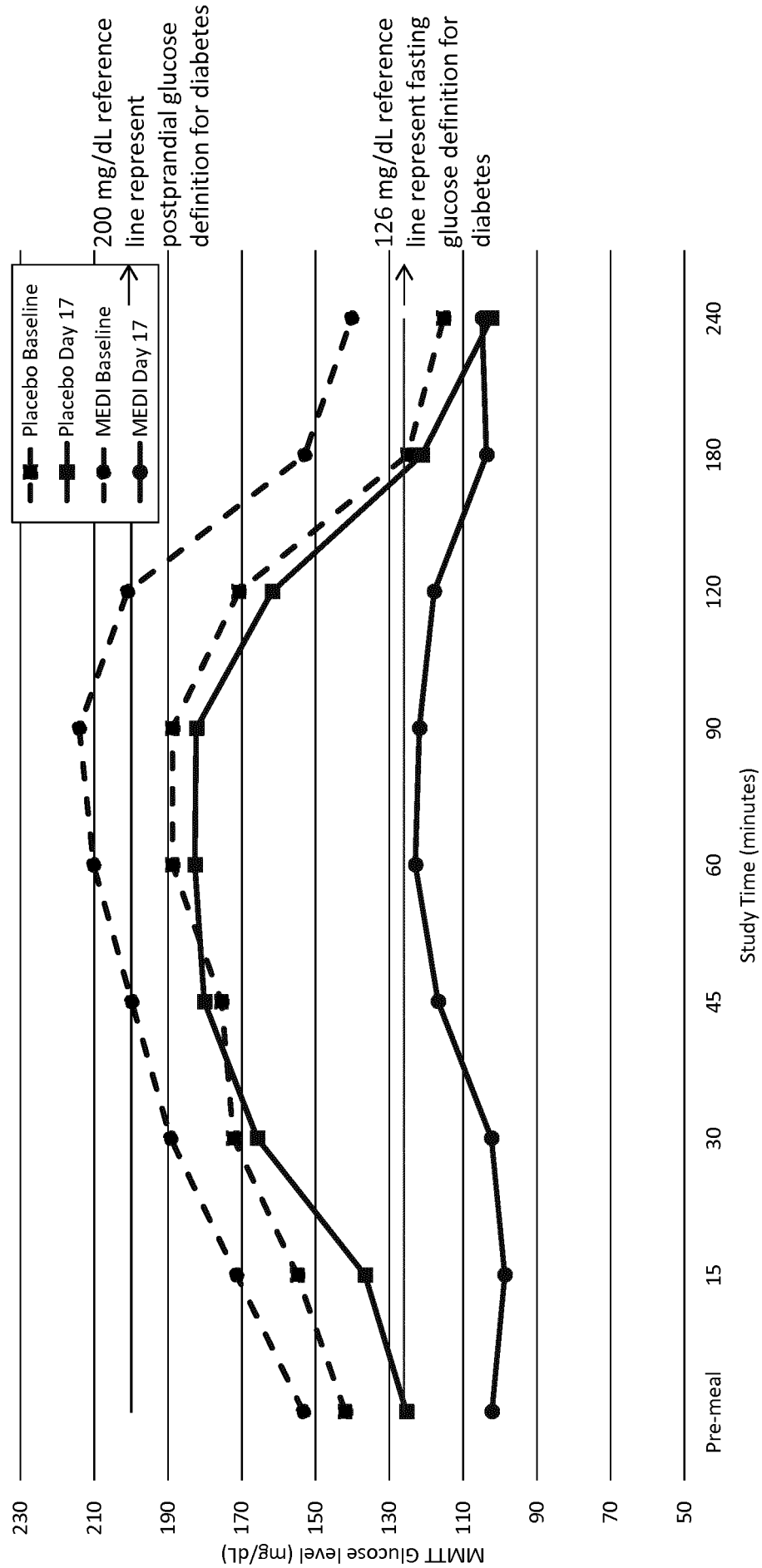

Placebo Baseline
Placebo Day 17
MEDI Baseline
MEDI Day 17
200 mg/dL reference line represent postprandial glucose definition for diabetes
126 mg/dL reference line represent fasting glucose definition for diabetes
MMTT Glucose level (mg/dL)
230
210
190
170
150
130
110
90
70
50
Pre-meal
15
30
45
60
90
120
180
240
Study Time (minutes)

FIG. 27

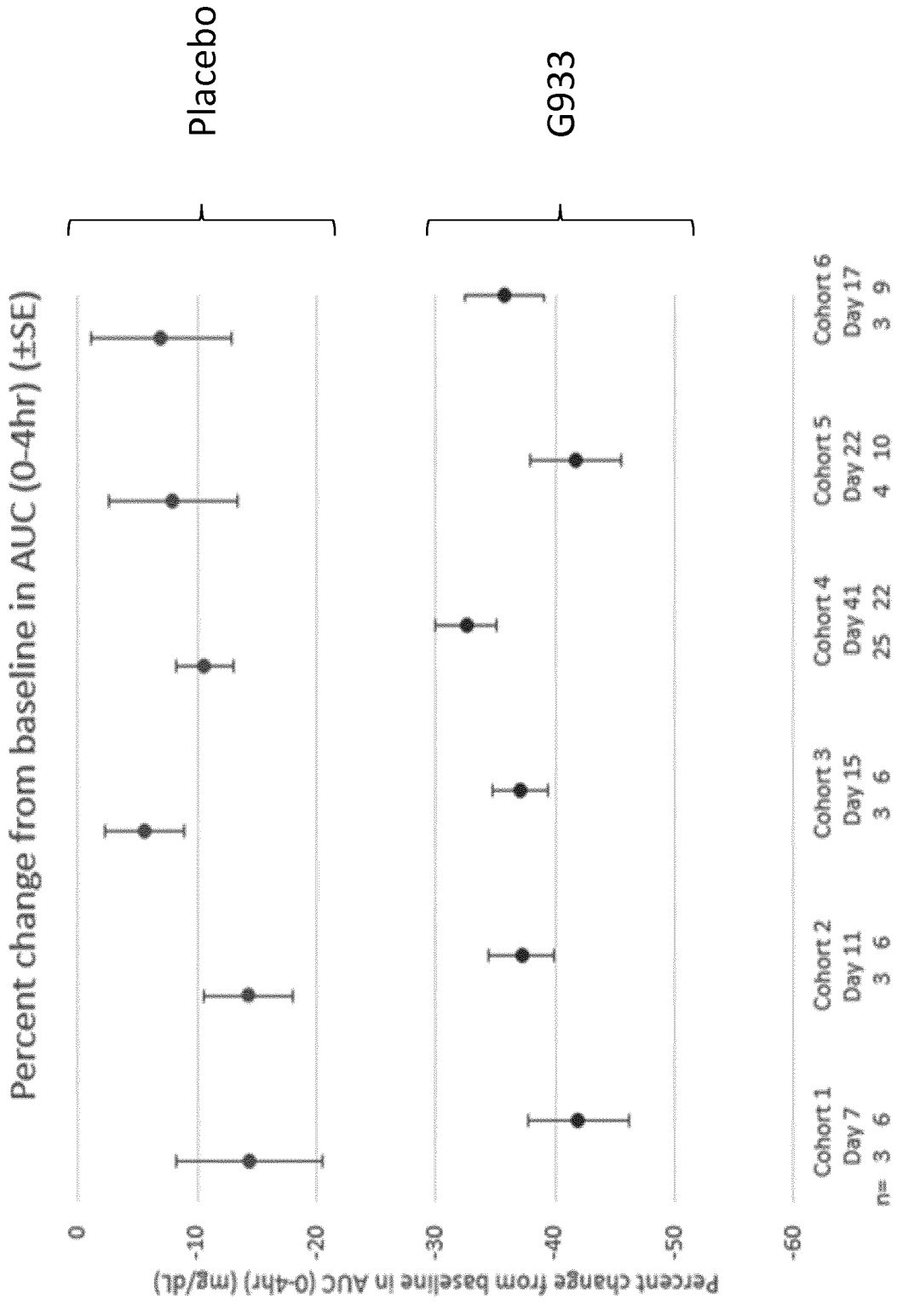

Placebo
G933
Percent change from baseline in AUC (0-4hr) (±SE)
Percent change from baseline in AUC (0-4hr) (mg/dL)
0
-10
-20
-30
-40
-50
-60
Cohort 1 Cohort 2 Cohort 3 Cohort 4 Cohort 5 Cohort 6
Day 7 Day 11 Day 15 Day 41 Day 22 Day 17
n= 3 6 3 6 3 6 25 22 4 10 3 9

FIG. 28

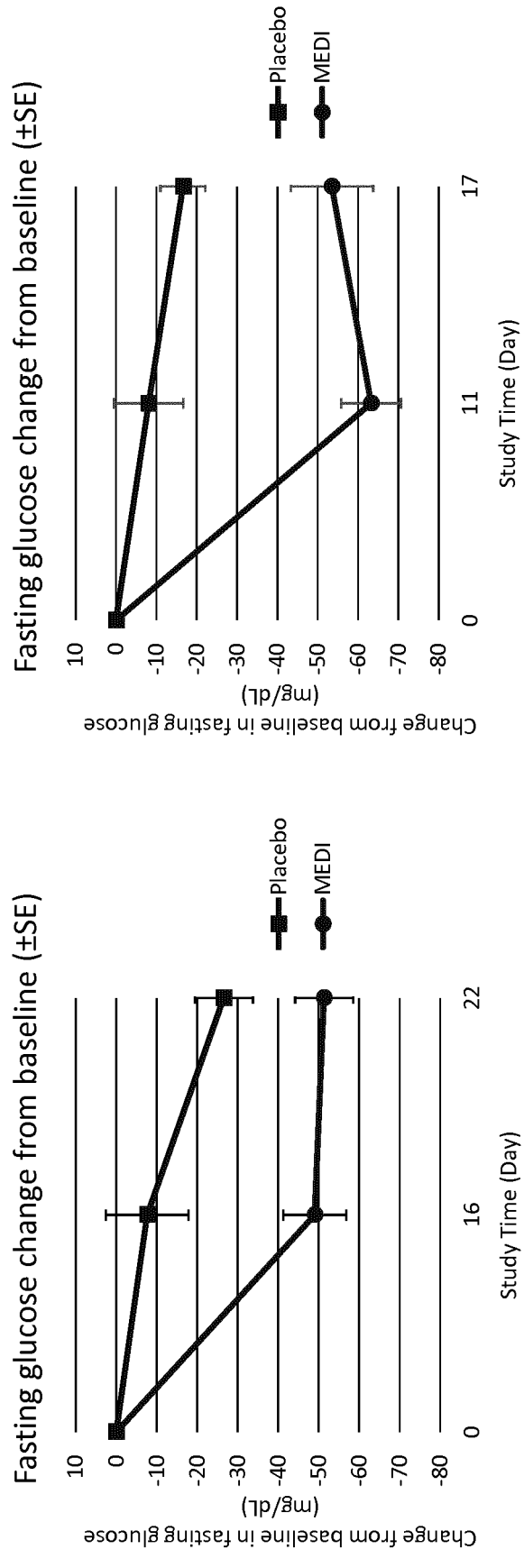

Cohort 5
Fasting glucose change from baseline (±SE)
Change from baseline in fasting glucose (mg/dL)
10
0
-10
-20
-30
-40
-50
-60
-70
-80
0
16
22
Study Time (Day)
Placebo
MEDI
Cohort 6
Fasting glucose change from baseline (±SE)
Change from baseline in fasting glucose (mg/dL)
10
0
-10
-20
-30
-40
-50
-60
-70
-80
0
11
17
Study Time (Day)
Placebo
MEDI

FIG. 29

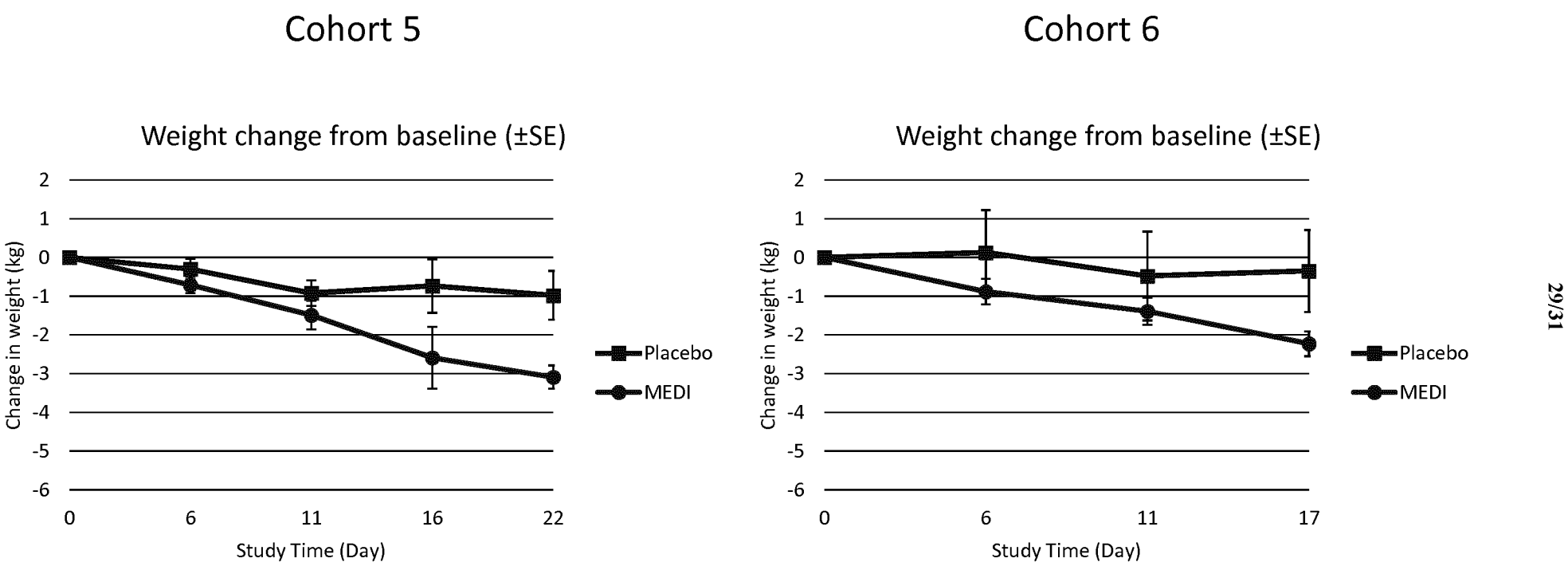
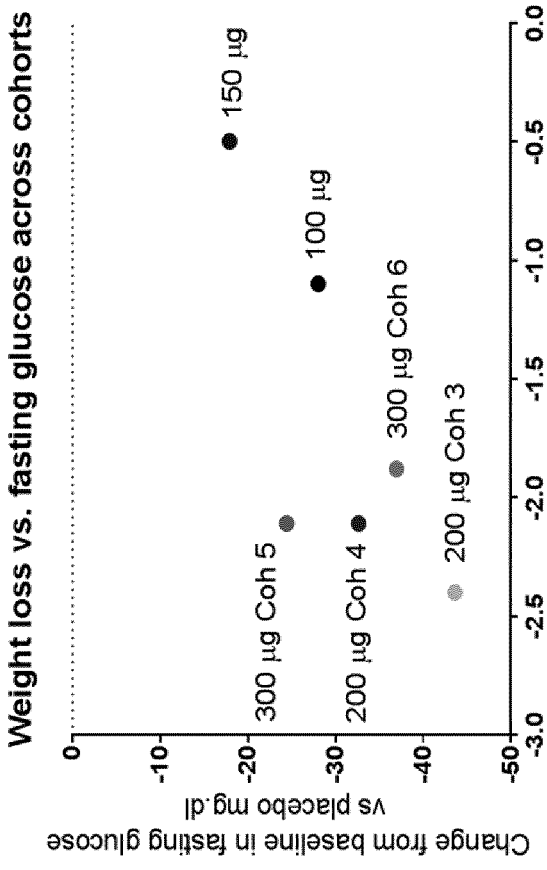

Cohort 5
Weight change from baseline (±SE)
Change in weight (kg)
2
1
0
-1
-2
-3
-4
-5
-6
0
6
11
16
22
Study Time (Day)
Placebo
MEDI
Cohort 6
Weight change from baseline (±SE)
Change in weight (kg)
2
1
0
-1
-2
-3
-4
-5
-6
0
6
11
17
Study Time (Day)
Placebo
MEDI

FIG. 30


Weight loss vs. fasting glucose across cohorts
Change from baseline in fasting glucose vs placebo mg.dl
0
-10
-20
-30
-40
-50
-3.0
-2.5
-2.0
-1.5
-1.0
-0.5
0.0
Weight change from baseline vs placebo kg
300 µg Coh 5
200 µg Coh 4
150 µg
100 µg
300 µg Coh 6
200 µg Coh 3

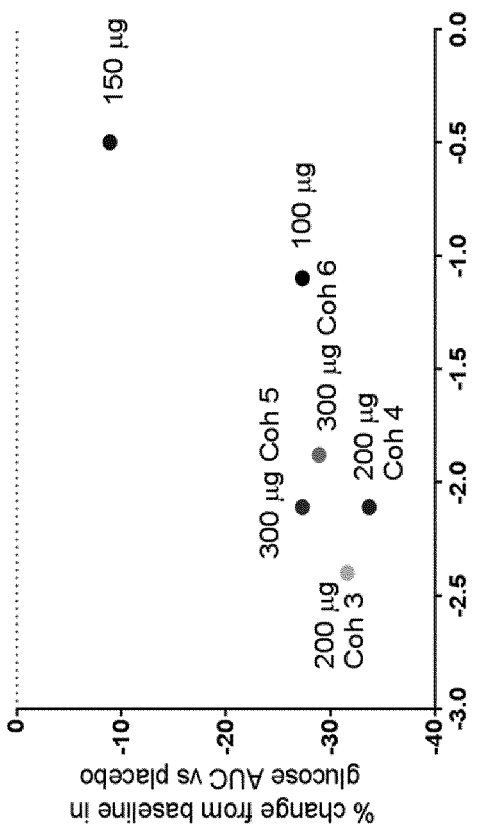
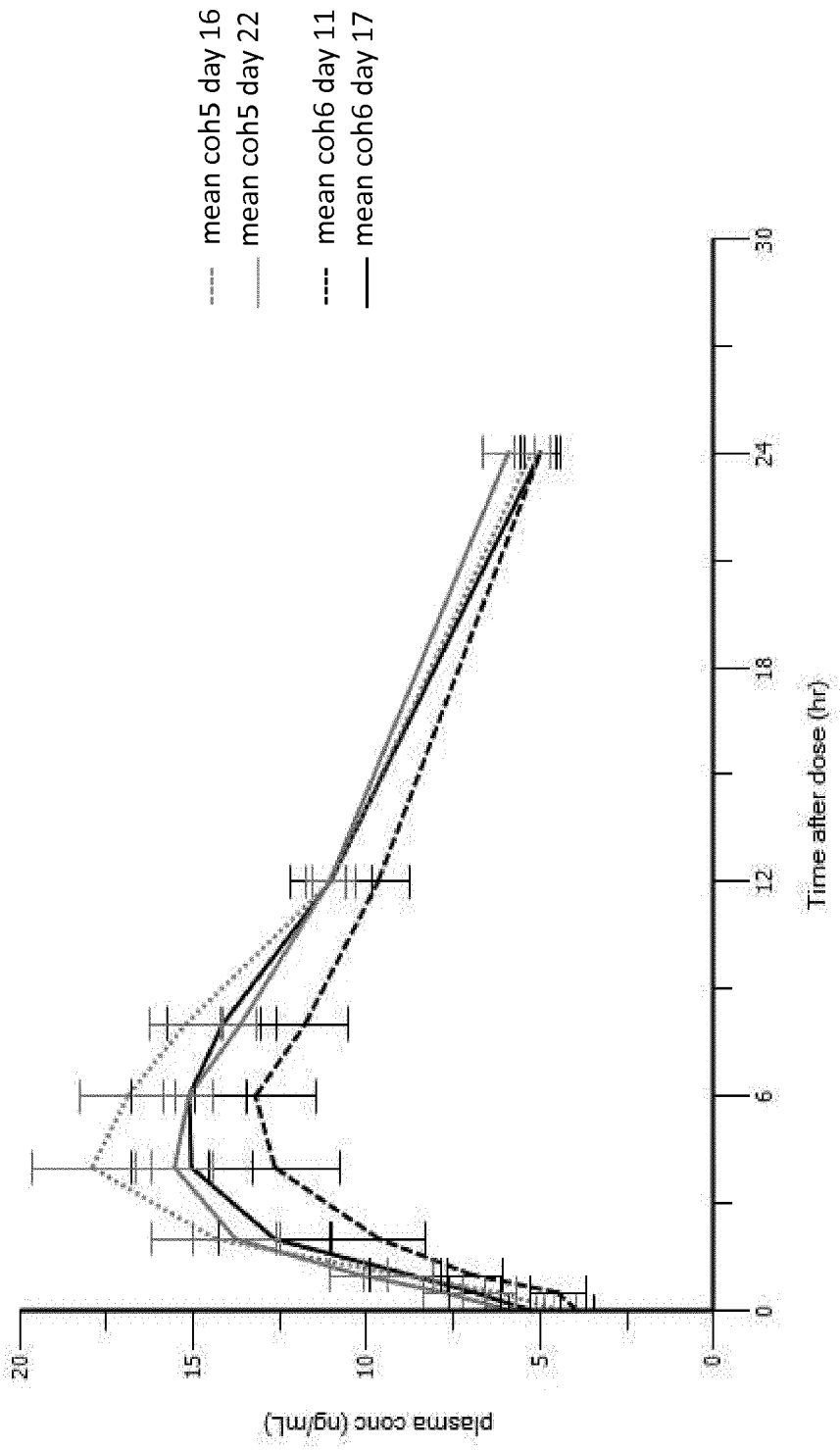

Weight loss vs. glucose AUC MMTT
% change from baseline in glucose AUC vs placebo
0
-10
-20
-30
-40
-3.0
-2.5
-2.0
-1.5
-1.0
-0.5
0.0
Weight change from baseline vs placebo
150 µg
300 µg Coh 5
100 µg
300 µg Coh 6
200 µg Coh 4
200 µg Coh 3

FIG. 31


mean coh5 day 16
mean coh5 day 22
mean coh6 day 11
mean coh6 day 17
plasma conc (ng/mL)
Time after dose (hr)
0
5
10
15
20
0
6
12
18
24
30