FIG. 1

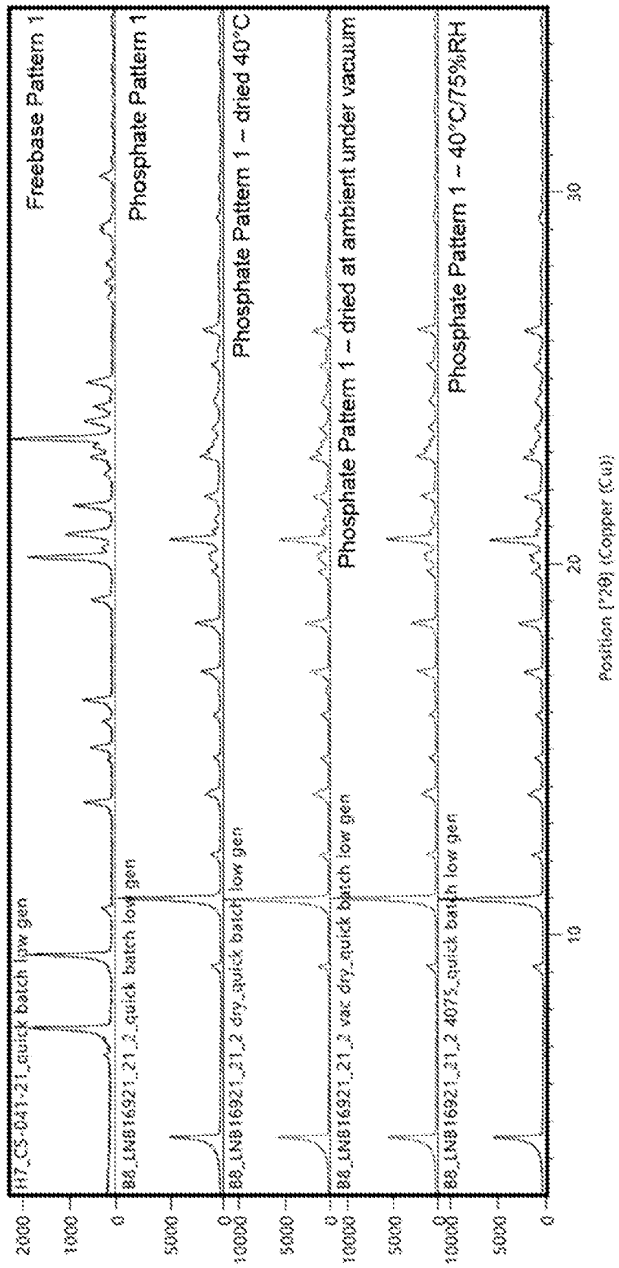

Freebase Pattern 1
Phosphate Pattern 1
Phosphate Pattern 1 – dried 40°C
Phosphate Pattern 1 – dried at ambient under vacuum
Phosphate Pattern 1 – 40°C/75%RH
Position [°2θ] (Copper (Cu))

FIG. 2

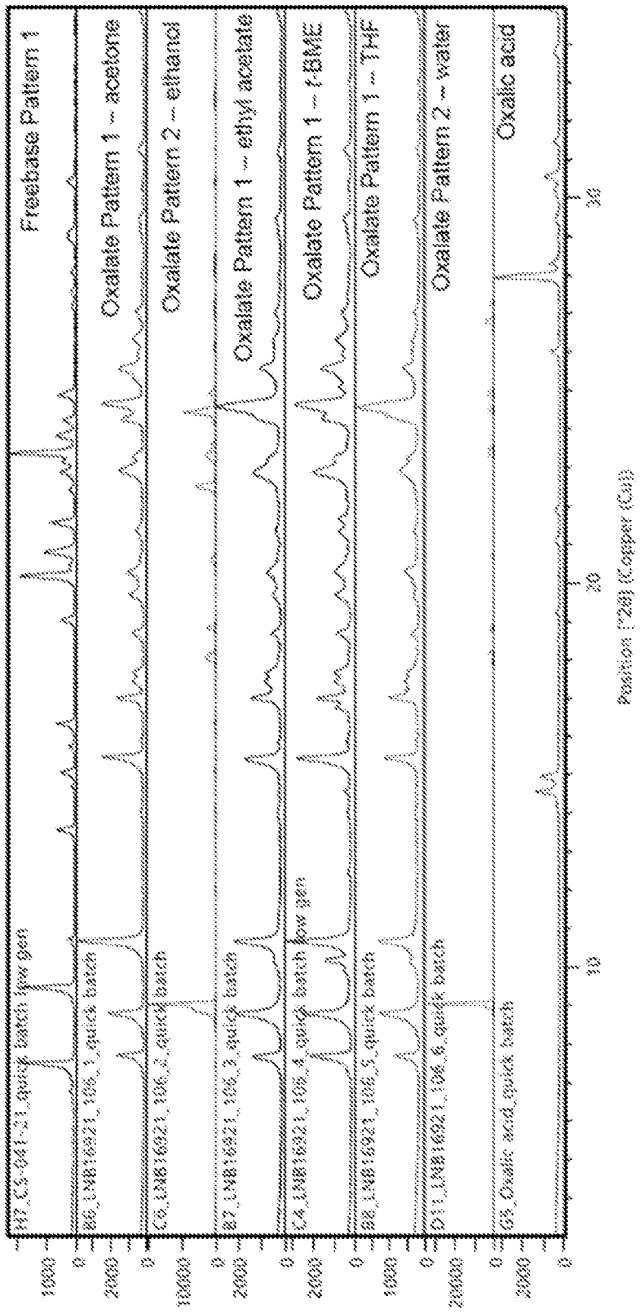

Freebase Pattern 1
Oxalate Pattern 1 -- acetone
Oxalate Pattern 2 -- ethanol
Oxalate Pattern 1 -- ethyl acetate
Oxalate Pattern 1 -- t-BME
Oxalate Pattern 1 -- THF
Oxalate Pattern 2 -- water
Oxalic acid
Position [°2θ] (Copper (Cu))

FIG. 3

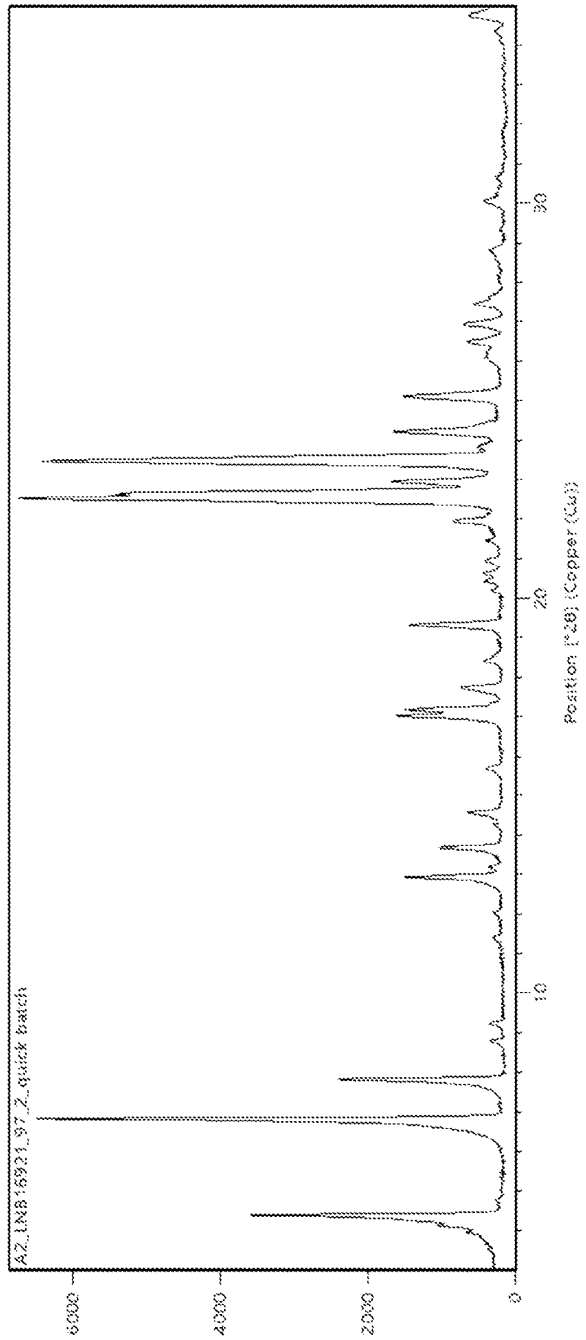

AZ_LNB16921_97_2_quick batch
6000
4000
2000
0
10
20
30
Position [°2θ] (Copper (Cu))

FIG. 4

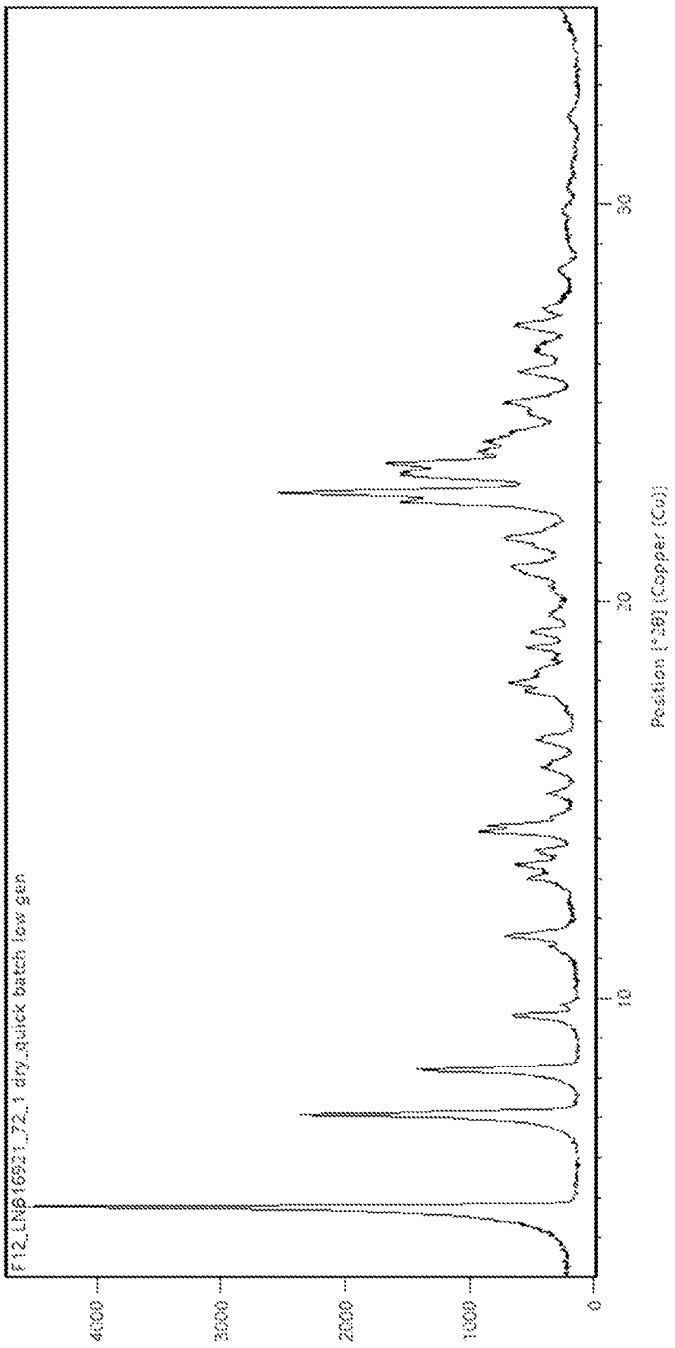

F12_LNP16921_72_1 dry_quick batch low gen
4000
3000
2000
1000
0
10
20
30
Position [°2θ] (Copper (Cu))

FIG. 5

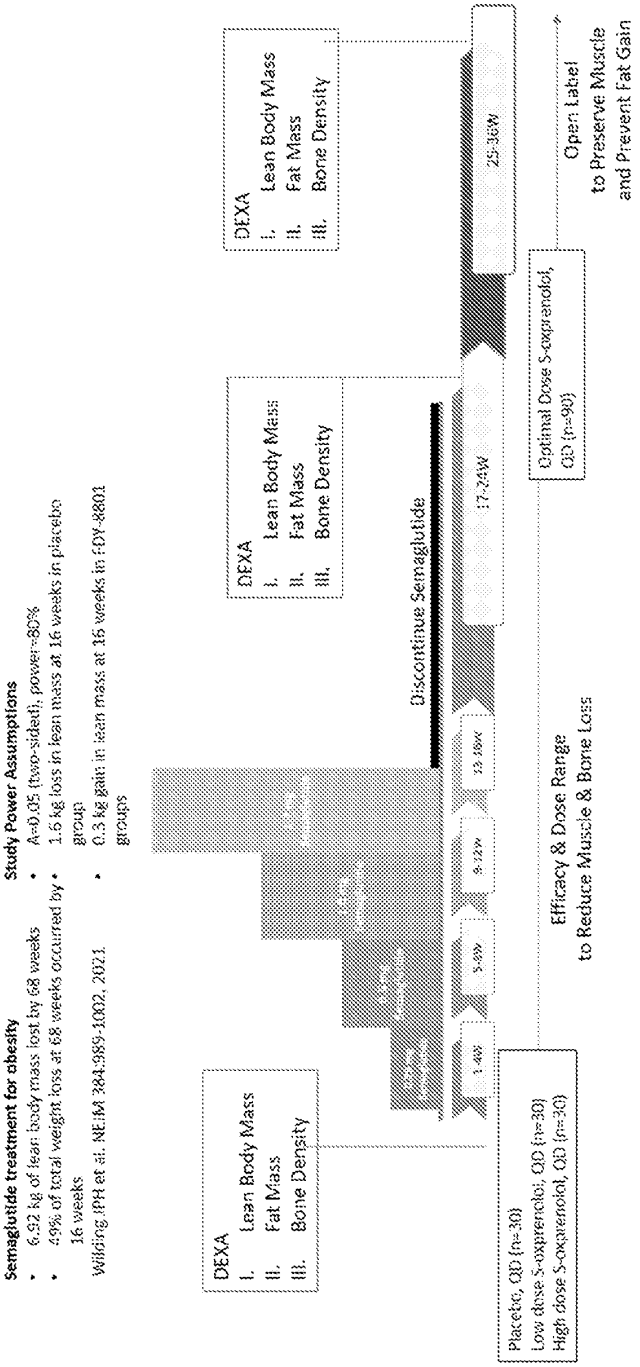

Semaglutide treatment for obesity
6.52 kg of lean body mass lost by 68 weeks
49% of total weight loss at 68 weeks occurred by 16 weeks
Wilding JPH et al. NEJM 384:989-1002, 2021.
Study Power Assumptions
A=0.05 (two-sided), power=80%
1.5 kg loss in lean mass at 16 weeks in placebo group
0.3 kg gain in lean mass at 16 weeks in f(X)-8803 groups
DEXA
I. Lean Body Mass
II. Fat Mass
III. Bone Density
Discontinue Semaglutide
DEXA
I. Lean Body Mass
II. Fat Mass
III. Bone Density
DEXA
I. Lean Body Mass
II. Fat Mass
III. Bone Density
1-4W
5-8W
9-12W
13-16W
17-24W
25-36W
Placebo, QD (n=30)
Low dose S-oxprenolol, QD (n=30)
High dose S-oxprenolol, QD (n=30)
Efficacy & Dose Range
to Reduce Muscle & Bone Loss
Optimal Dose S-oxprenolol, QD (n=90)
Open Label
to Preserve Muscle
and Prevent Fat Gain

FIG. 6

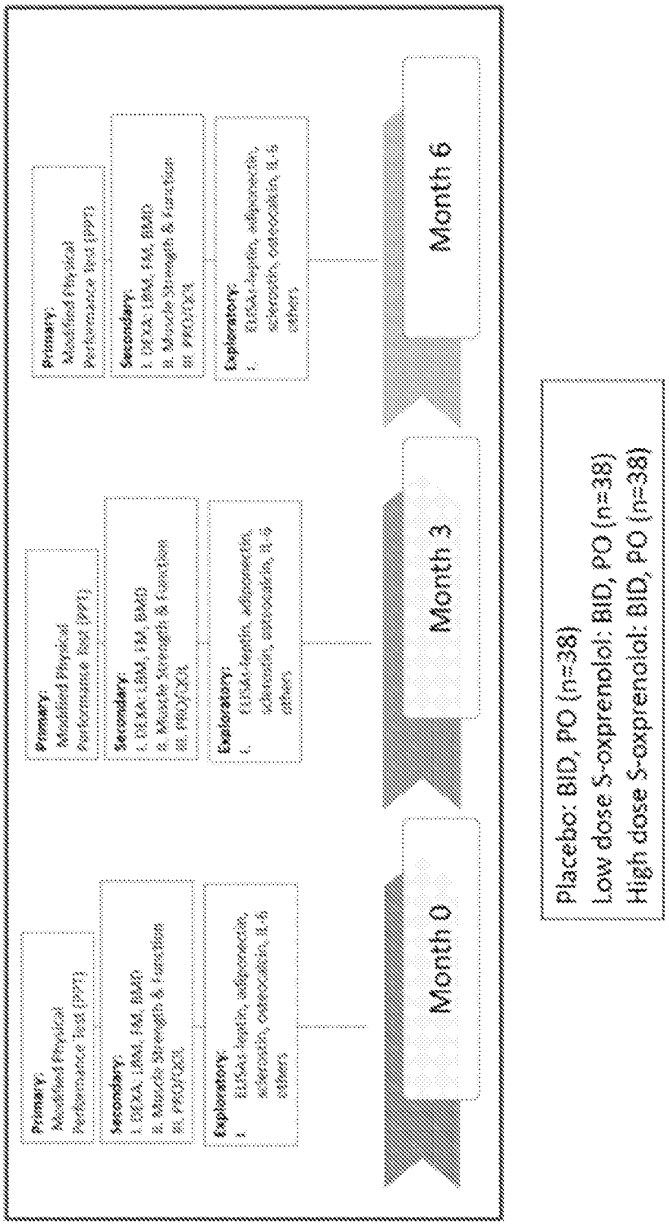

Primary:
Modified Physical Performance Test (PPT)
Secondary:
I. DEXA, BMI, HM, BMD
II. Muscle Strength & Function
III. PROMIS
Exploratory:
I. ELISA: leptin, adiponectin, sclerostin, osteocalcin, IL-6 others
Month 0
Month 3
Month 6
Placebo: BID, PO (n=38)
Low dose S-oxprenolol: BID, PO (n=38)
High dose S-oxprenaial: BID, PO (n=38)

FIG. 7

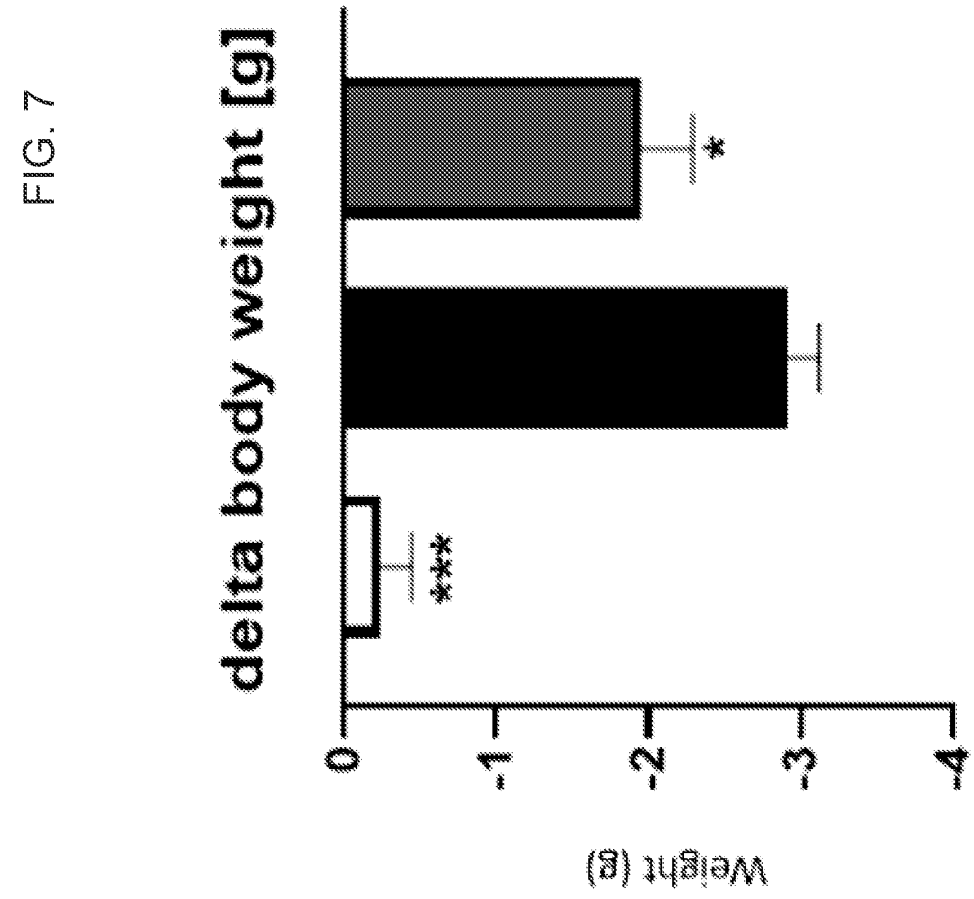

delta body weight [g]
sham (n=14)
placebo (n=13)
s-oxprenolol (n=8)
* p<0.05 vs. placebo
*** p<0.001 vs. placebo
***
*
0
-1
-2
-3
-4
Weight (g)

FIG. 8A

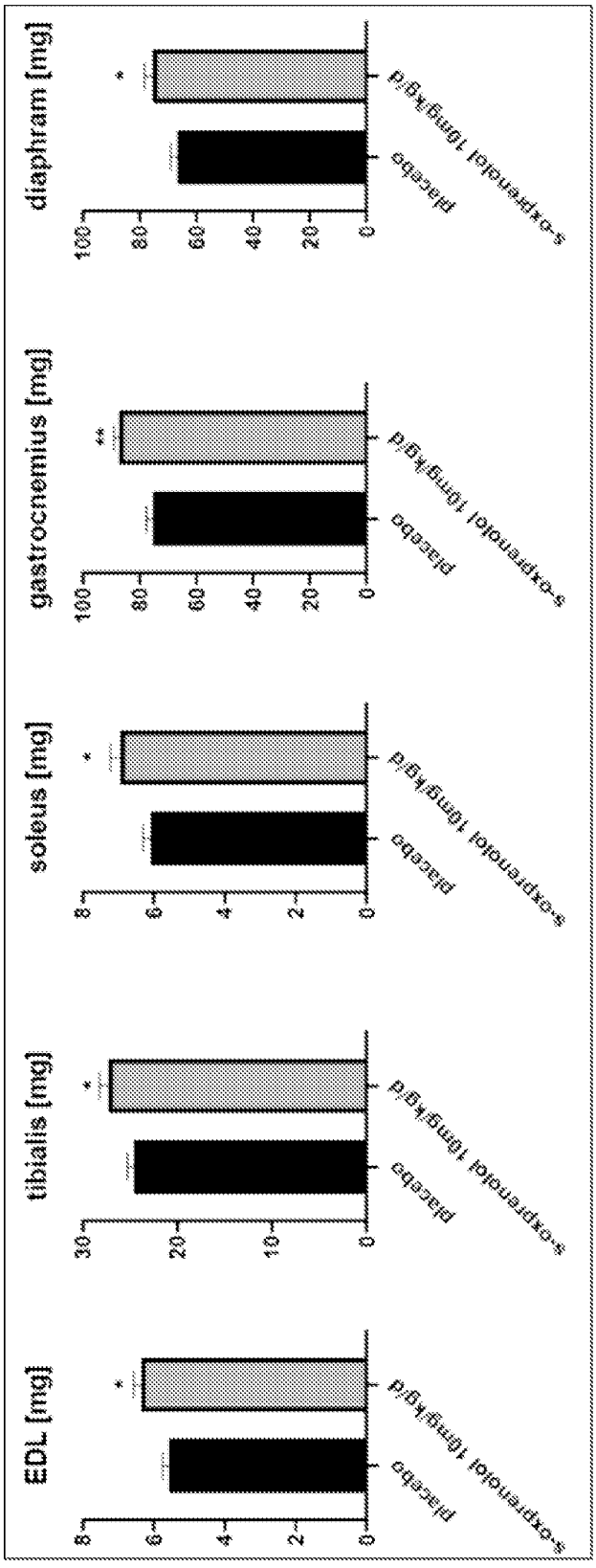

diaphragm [mg]
gastrocnemius [mg]
soleus [mg]
tibialis [mg]
EDL [mg]
placebo
s-expreniol 10mg/kg/d

FIG. 8B

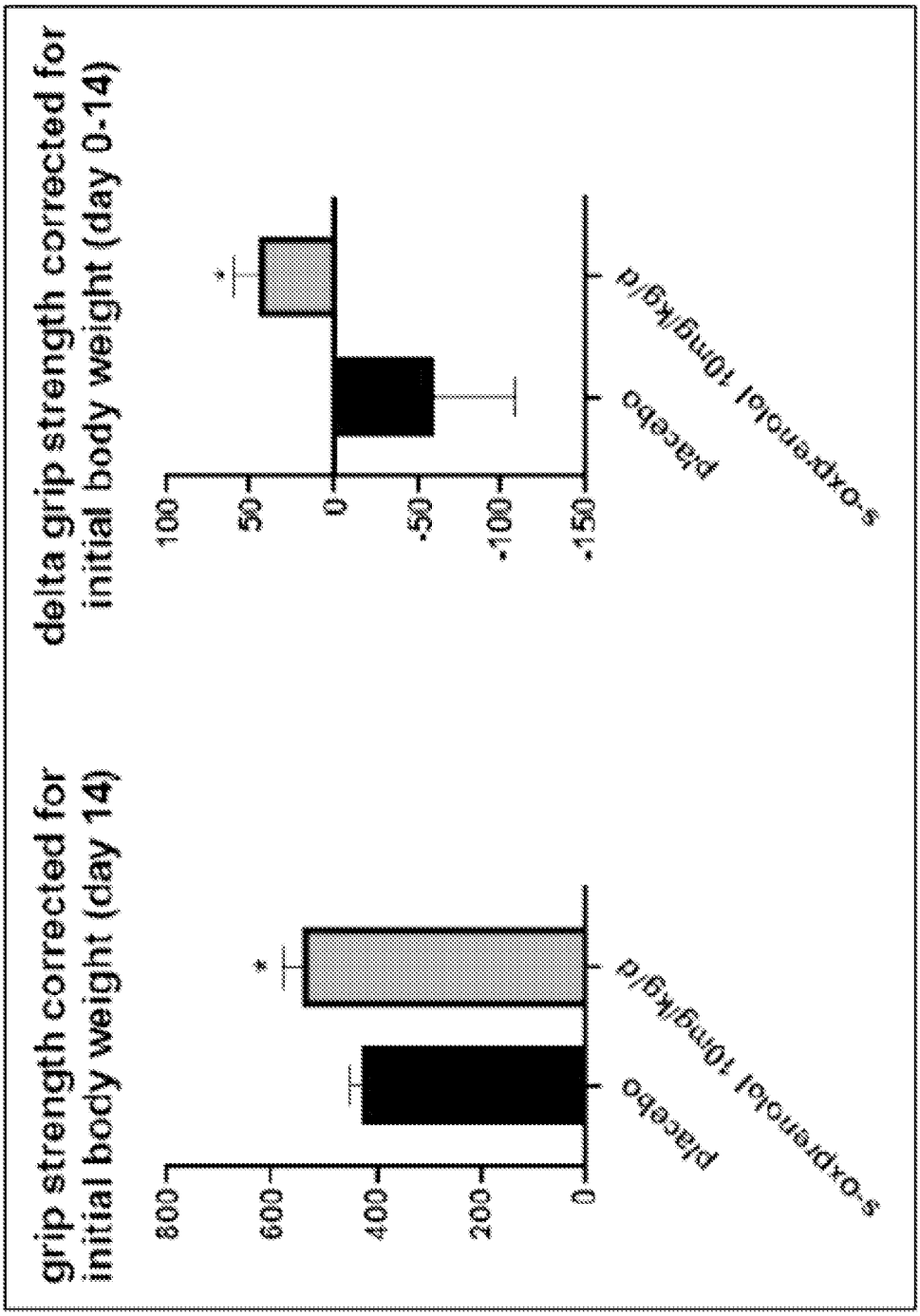

grip strength corrected for initial body weight (day 14)
800
600
400
200
0
*
placebo
s-oxprenolol 10mg/kg/d
delta grip strength corrected for initial body weight (day 0-14)
100
50
0
-50
-100
-150
*
placebo
s-oxprenolol 10mg/kg/d

FIG. 9

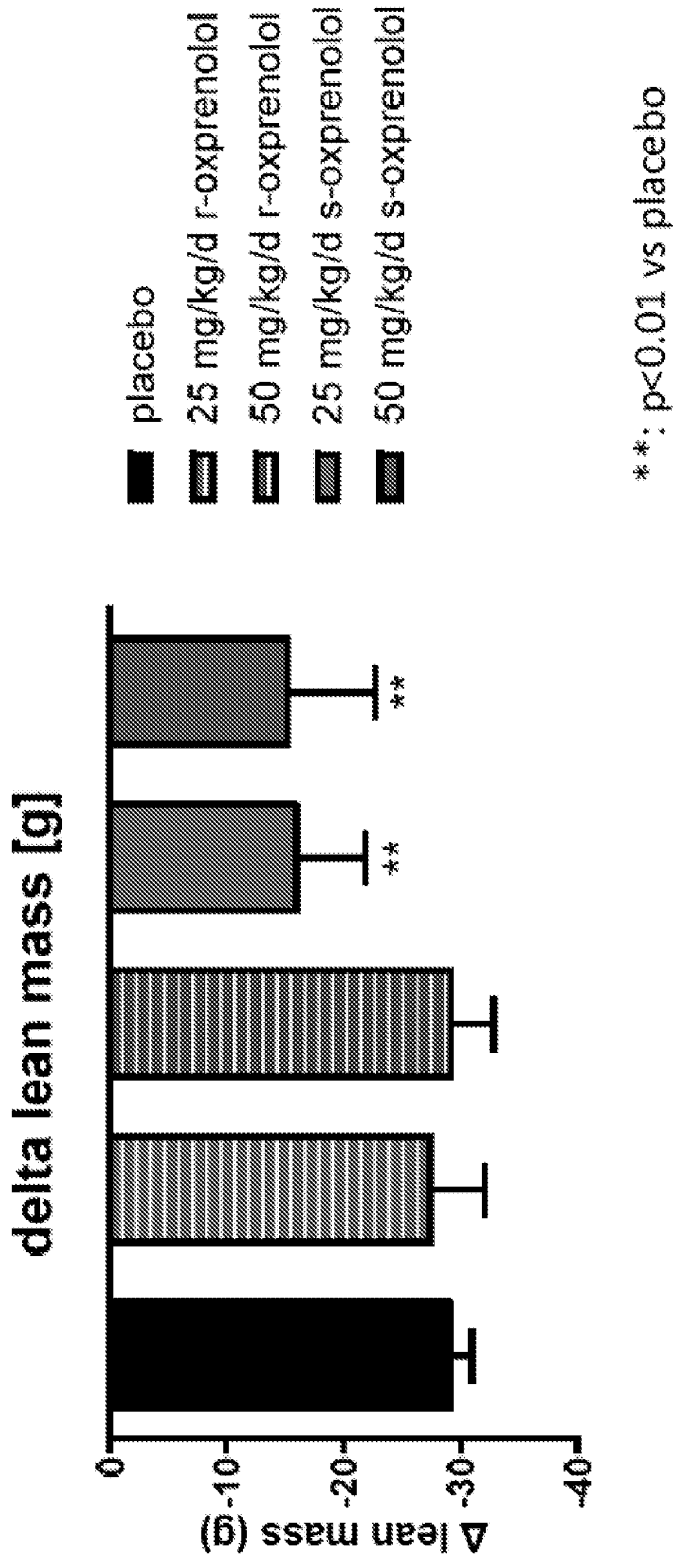

delta lean mass [g]
placebo
25 mg/kg/d r-oxprenolol
50 mg/kg/d r-oxprenolol
25 mg/kg/d s-oxprenolol
50 mg/kg/d s-oxprenolol
**: p<0.01 vs placebo
Δ lean mass (g)
0
-10
-20
-30
-40
**
**

FIG. 10

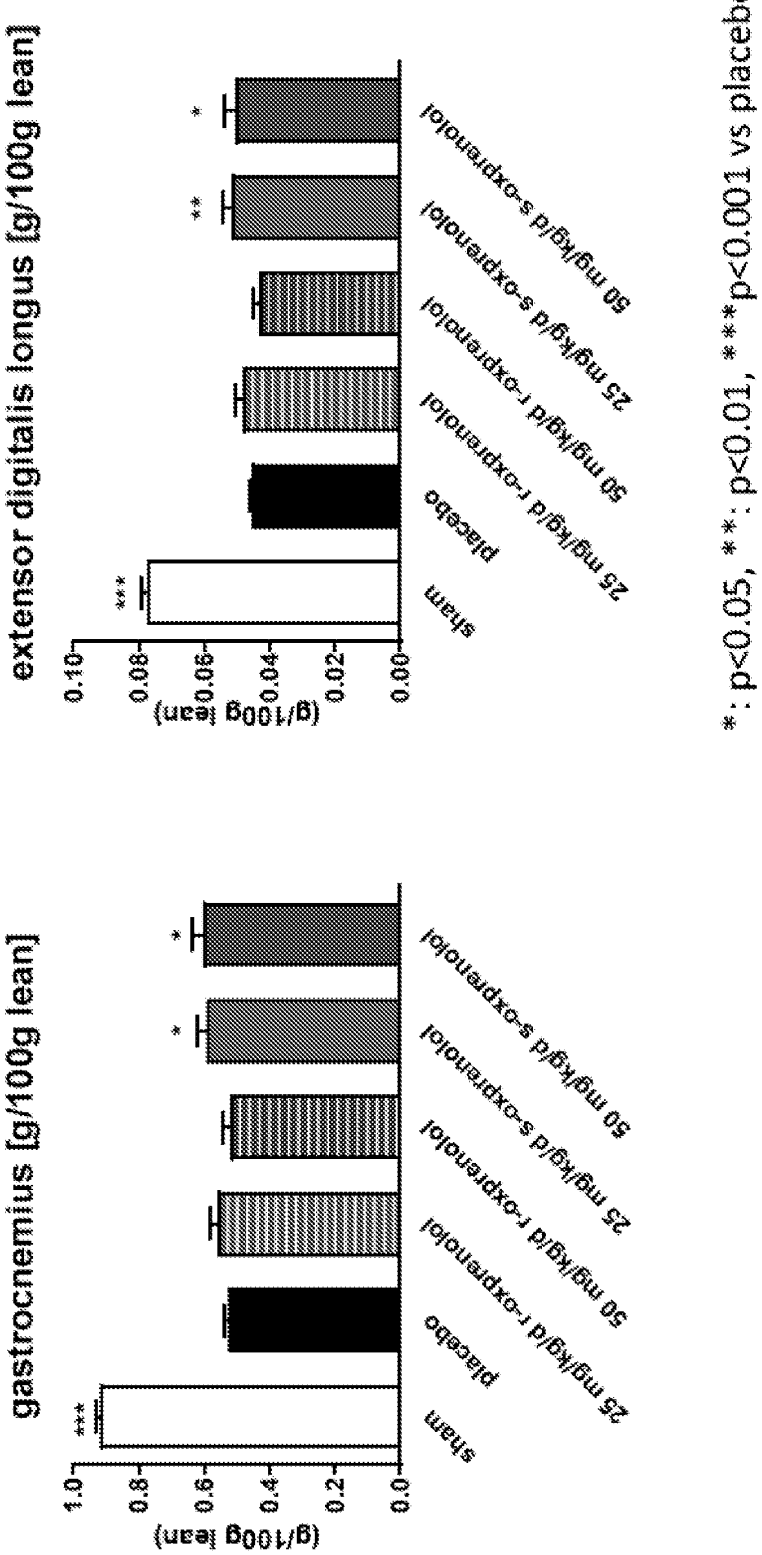

extensor digitalis longus [g/100g lean]
(g/100g lean)
0.10
0.08
0.06
0.04
0.02
0.00
***
*
**
sham
placebo
25 mg/kg/d r-oxprenolol
50 mg/kg/d r-oxprenolol
25 mg/kg/d s-oxprenolol
50 mg/kg/d s-oxprenolol
gastrocnemius [g/100g lean]
(g/100g lean)
1.0
0.8
0.6
0.4
0.2
0.0
***
*
*
sham
placebo
25 mg/kg/d r-oxprenolol
50 mg/kg/d r-oxprenolol
25 mg/kg/d s-oxprenolol
50 mg/kg/d s-oxprenolol
*: p<0.05, **: p<0.01, ***p<0.001 vs placebo

FIG. 11A

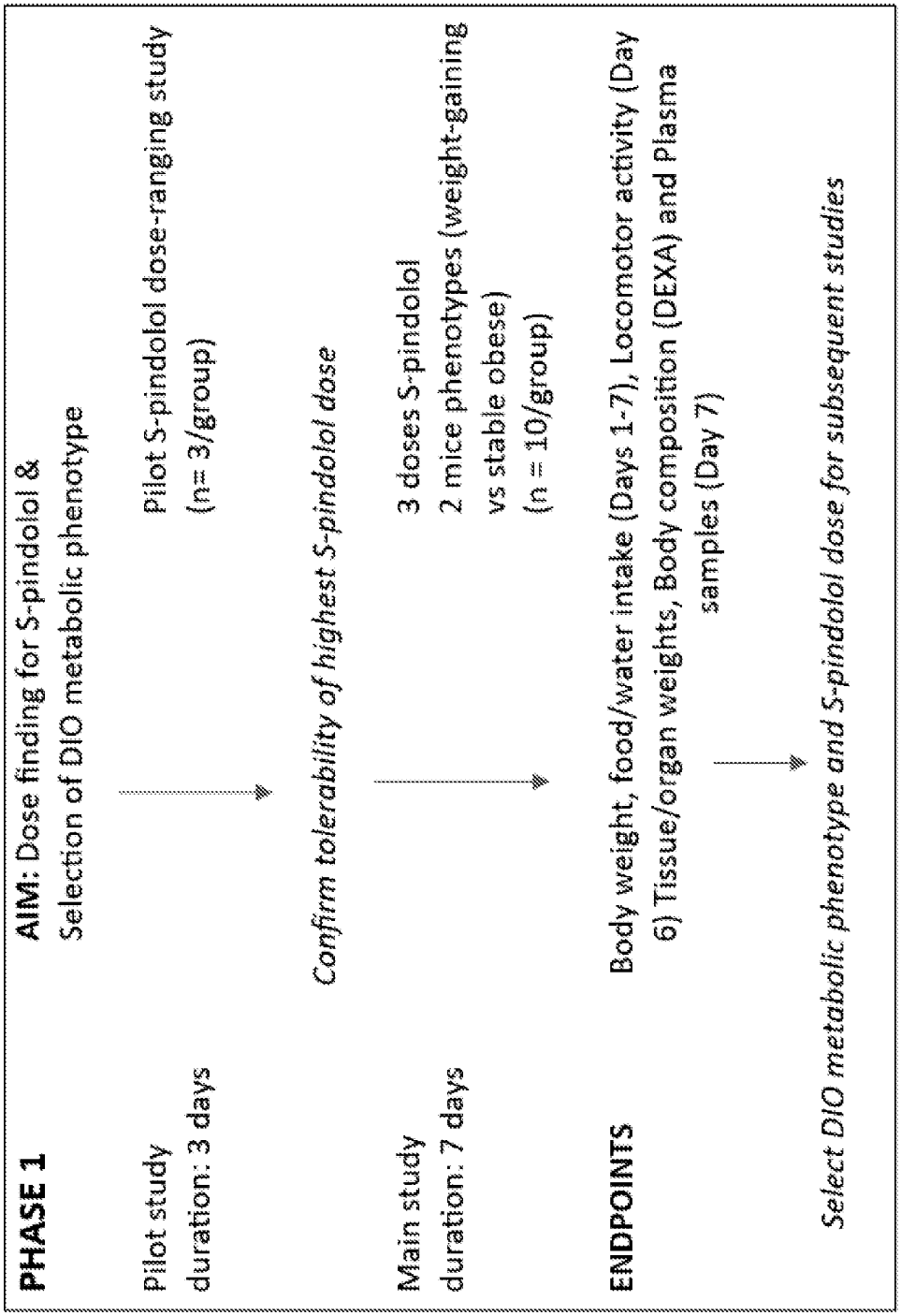

PHASE 1
AIM: Dose finding for S-pindolol &
Selection of DIO metabolic phenotype
Pilot study
duration: 3 days
Pilot S-pindolol dose-ranging study
(n= 3/group)
Confirm tolerability of highest S-pindolol dose
Main study
duration: 7 days
3 doses S-pindolol
2 mice phenotypes (weight-gaining
vs stable obese)
(n = 10/group)
ENDPOINTS
Body weight, food/water intake (Days 1-7), Locomotor activity (Day
6) Tissue/organ weights, Body composition (DEXA) and Plasma
samples (Day 7)
Select DIO metabolic phenotype and S-pindolol dose for subsequent studies

FIG. 11B

PHASE 2 **AIM:** Determine optimum anabolic agent to **preserve** muscle mass during GLP-1 agonist treatment

Pilot study duration:
3 days

Pilot 3 study; (S)-carvedilol & DHEA (n= 3/group)

Confirm tolerability of proposed dose

Main study duration:
28 days

Treatment arms (n= 10/group):
- GLP-1 agonist
- GLP-1 agonist + S-pindolol
- GLP-1 agonist + S-carvedilol
- GLP-1 agonist + DHEA
- Vehicle

ENDPOINTS

Body weight, food and water intake (Days 1-28), Grip strength (week 4), Body composition (DEXA), Tissue/organ weights, qPCR/genetic analysis (Day 28)

FIG. 11C

PHASE 3
AIM: Determine optimum anabolic agent to improve muscle:fat ratio of regained weight post-GLP-1 therapy
Duration of dosing: 28 days
GLP-1 agonist (5 groups n=10/group)
Stop GLP-1 agonist therapy
Allocate to one of the following treatments (n= 10/group):
- S-pindolol
- S-carvedilol
- DHEA
- Vehicle
- Control vehicle
Duration of dosing: 28 days
ENDPOINTS
Body weight, food and water intake (Days 1-56), Grip strength (week 8), Body composition (DEXA), Tissue/organ weights, qPCR/genetic analysis (Day 56)

FIG. 12

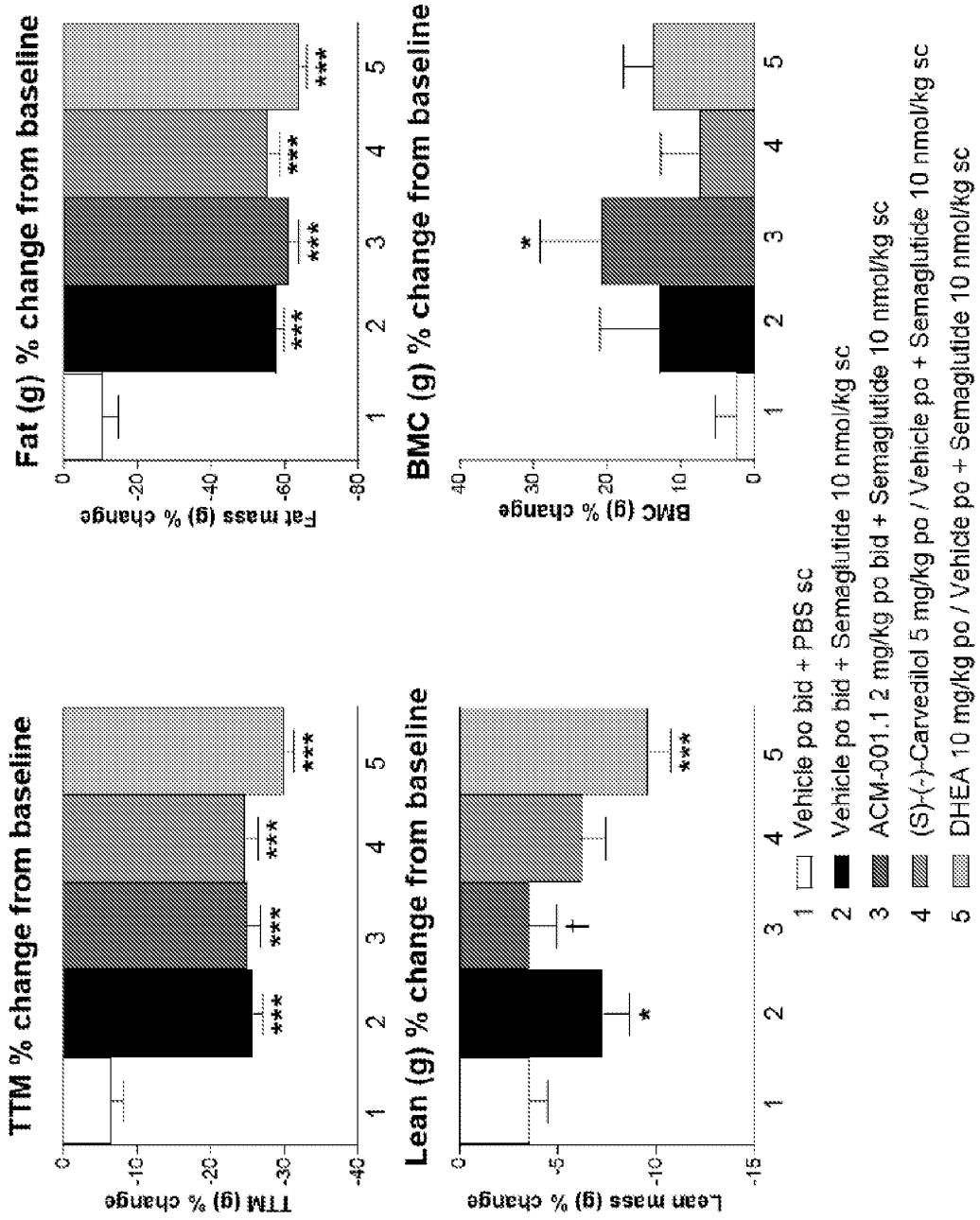

Fat (g) % change from baseline
Fat mass (g) % change
BMC (g) % change from baseline
BMC (g) % change
TTM % change from baseline
TTM (g) % change
Lean (g) % change from baseline
Lean mass (g) % change
1 Vehicle po bid + PBS sc
2 Vehicle po bid + Semaglutide 10 nmol/kg sc
3 ACM-001.1 2 mg/kg po bid + Semaglutide 10 nmol/kg sc
4 (S)-(-)-Carvedilol 5 mg/kg po / Vehicle po + Semaglutide 10 nmol/kg sc
5 DHEA 10 mg/kg po / Vehicle po + Semaglutide 10 nmol/kg sc

FIG. 13

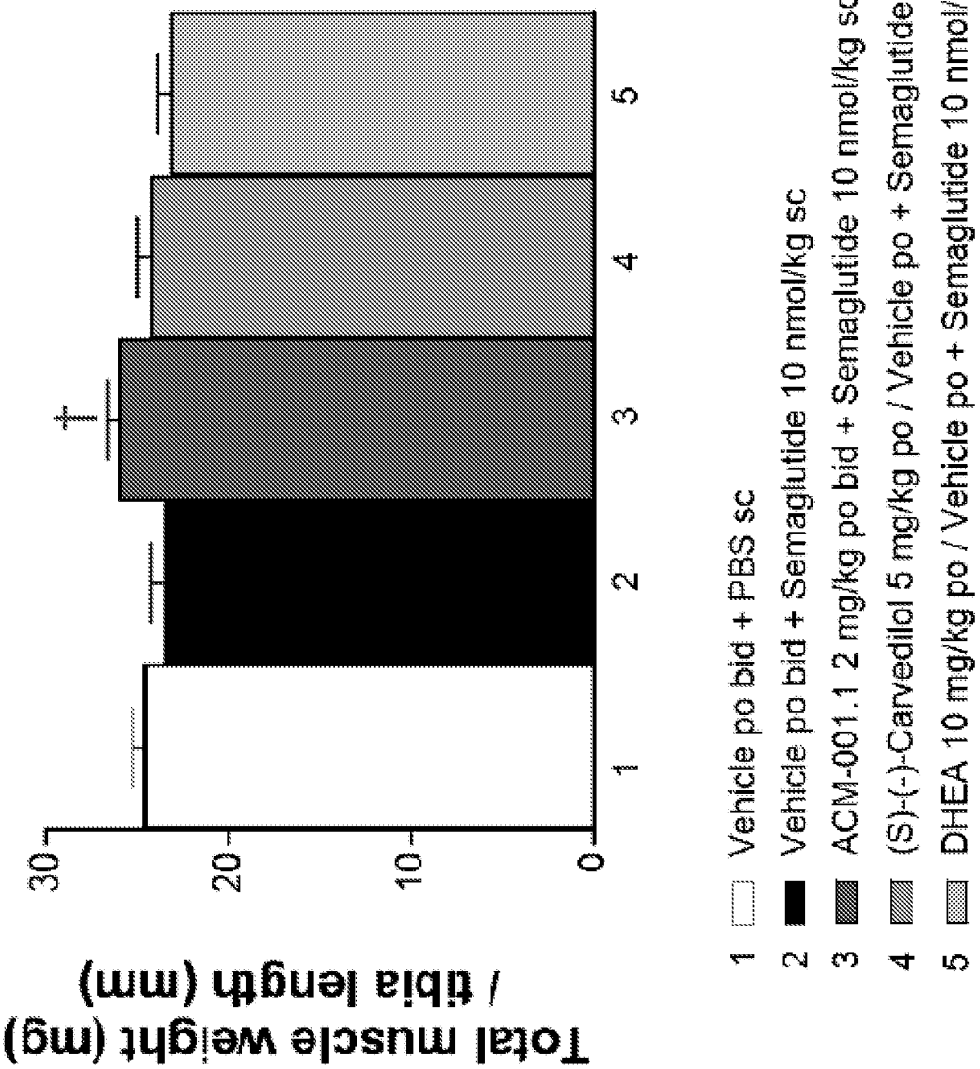

Total muscle
Total muscle weight (mg) / tibia length (mm)
30
20
10
0
1
2
3
4
5
1 Vehicle po bid + PBS sc
2 Vehicle po bid + Semaglutide 10 nmol/kg sc
3 ACM-001.1 2 mg/kg po bid + Semaglutide 10 nmol/kg sc
4 (S)-(-)-Carvedilol 5 mg/kg po / Vehicle po + Semaglutide 10 nmol/kg sc
5 DHEA 10 mg/kg po / Vehicle po + Semaglutide 10 nmol/kg sc

FIG. 14

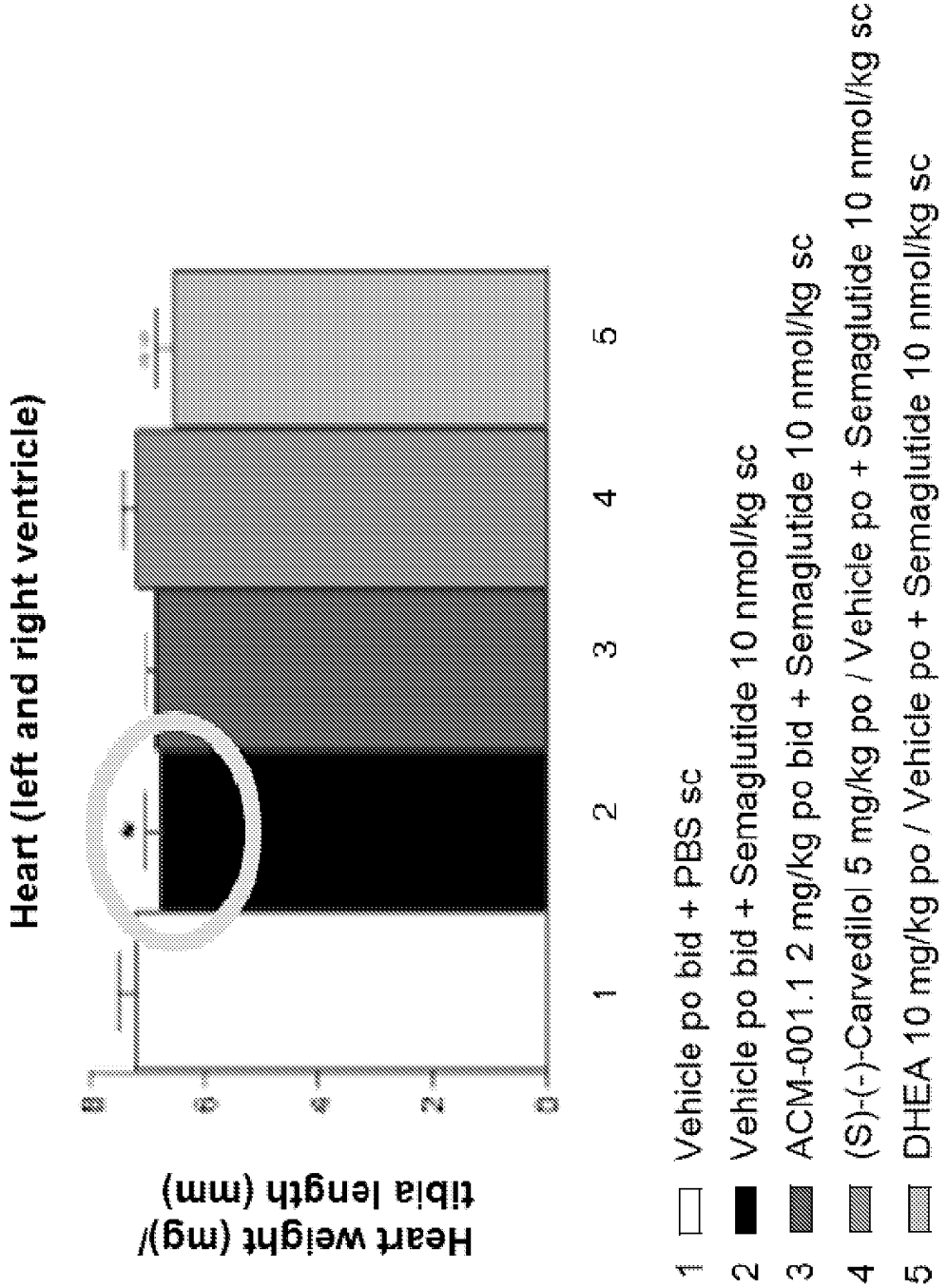

Heart (left and right ventricle)
Heart weight (mg)/
tibia length (mm)
0
2
4
6
8
1
2
3
4
5
1 Vehicle po bid + PBS sc
2 Vehicle po bid + Semaglutide 10 nmol/kg sc
3 ACM-001.1 2 mg/kg po bid + Semaglutide 10 nmol/kg sc
4 (S)-(-)-Carvedilol 5 mg/kg po / Vehicle po + Semaglutide 10 nmol/kg sc
5 DHEA 10 mg/kg po / Vehicle po + Semaglutide 10 nmol/kg sc

FIG. 15

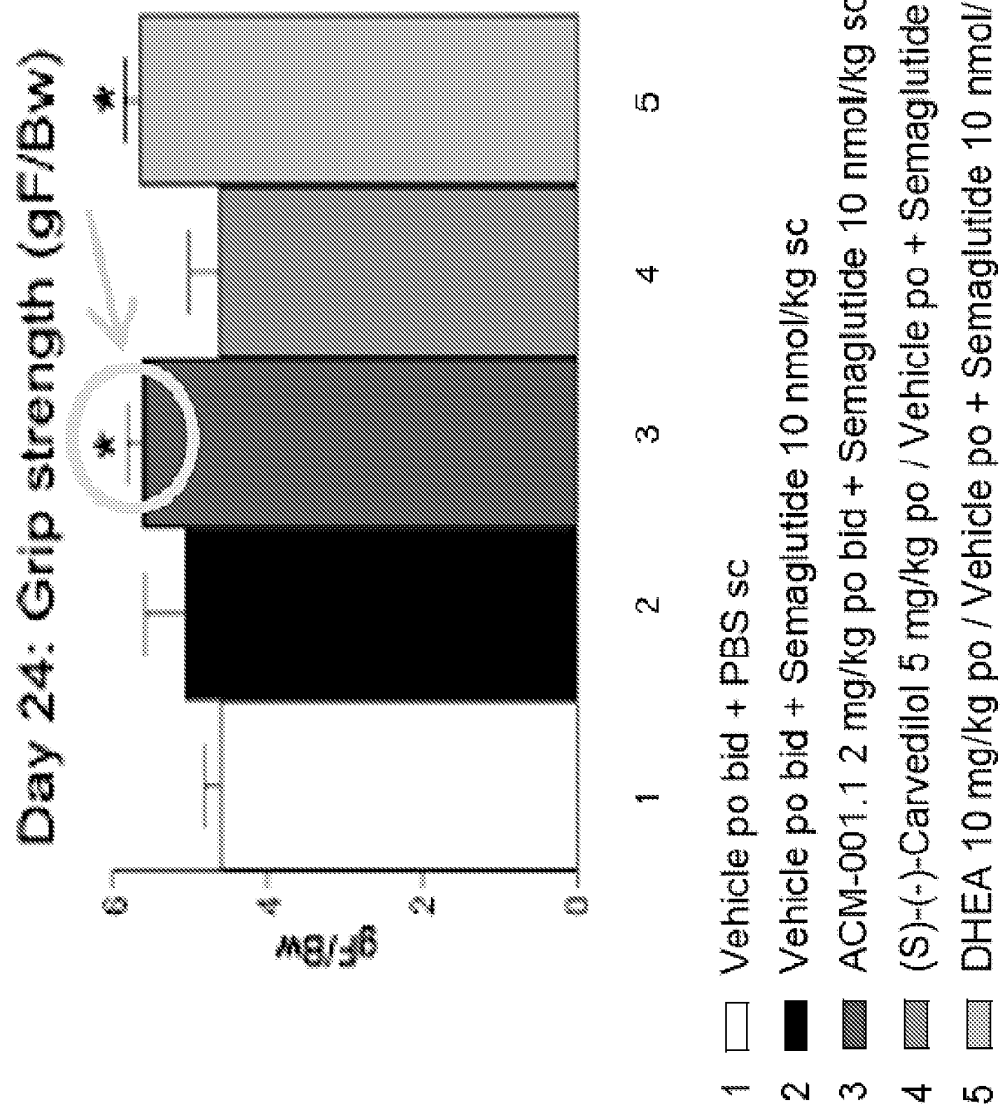

Day 24: Grip strength (gF/Bw)
gF/Bw
0
2
4
6
1
2
3
4
5
1 Vehicle po bid + PBS sc
2 Vehicle po bid + Semaglutide 10 nmol/kg sc
3 ACM-001.1 2 mg/kg po bid + Semaglutide 10 nmol/kg sc
4 (S)-(-)-Carvedilol 5 mg/kg po / Vehicle po + Semaglutide 10 nmol/kg sc
5 DHEA 10 mg/kg po / Vehicle po + Semaglutide 10 nmol/kg sc

FIG. 16

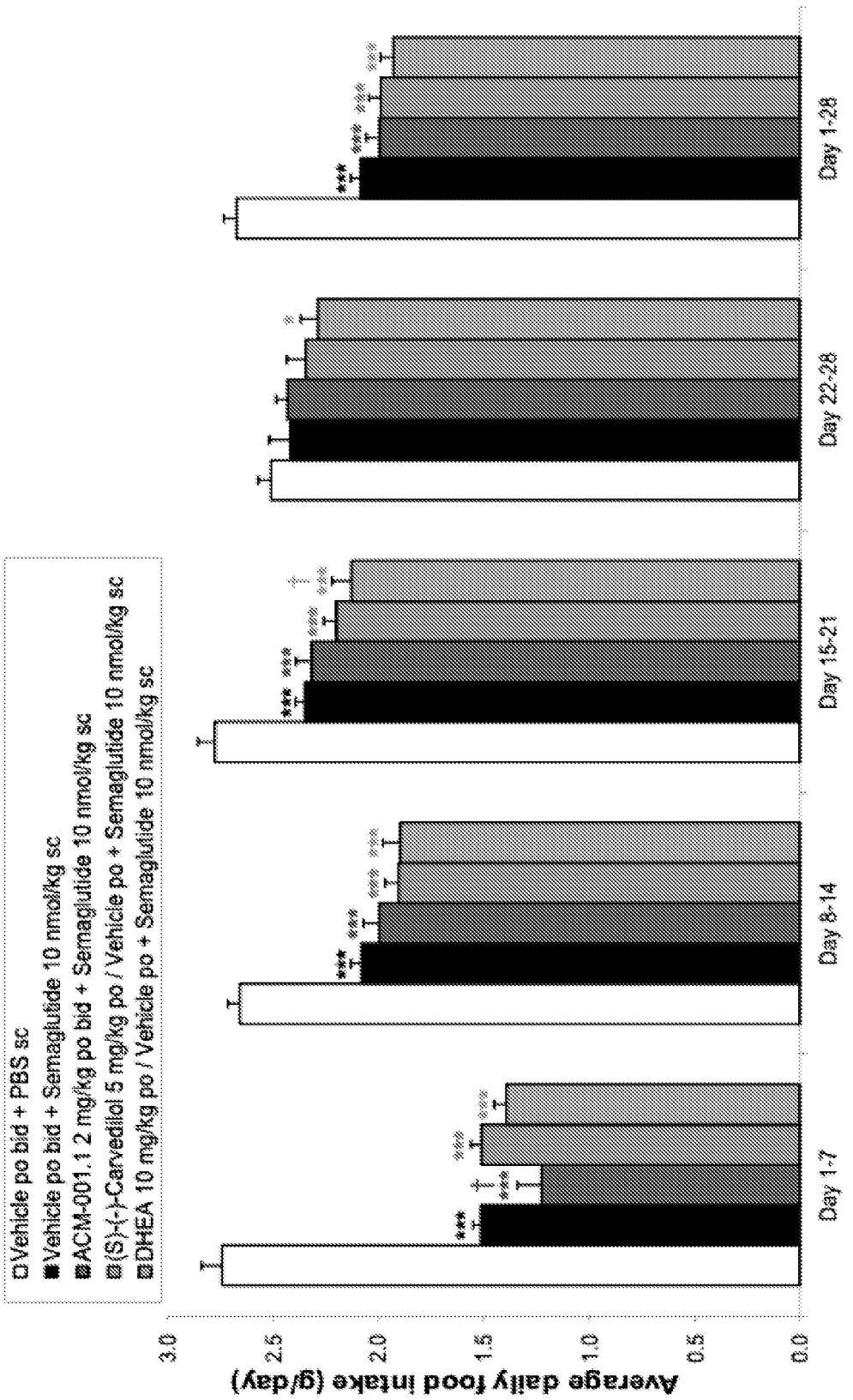

Vehicle po bid + PBS sc
Vehicle po bid + Semaglutide 10 nmol/kg sc
ACM-001.1 2 mg/kg po bid + Semaglutide 10 nmol/kg sc
(S)-(-)-Carvedilol 5 mg/kg po / Vehicle po + Semaglutide 10 nmol/kg sc
DHEA 10 mg/kg po / Vehicle po + Semaglutide 10 nmol/kg sc
Average daily food intake (g/day)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Day 1-7
Day 8-14
Day 15-21
Day 22-28
Day 1-28

FIG. 17

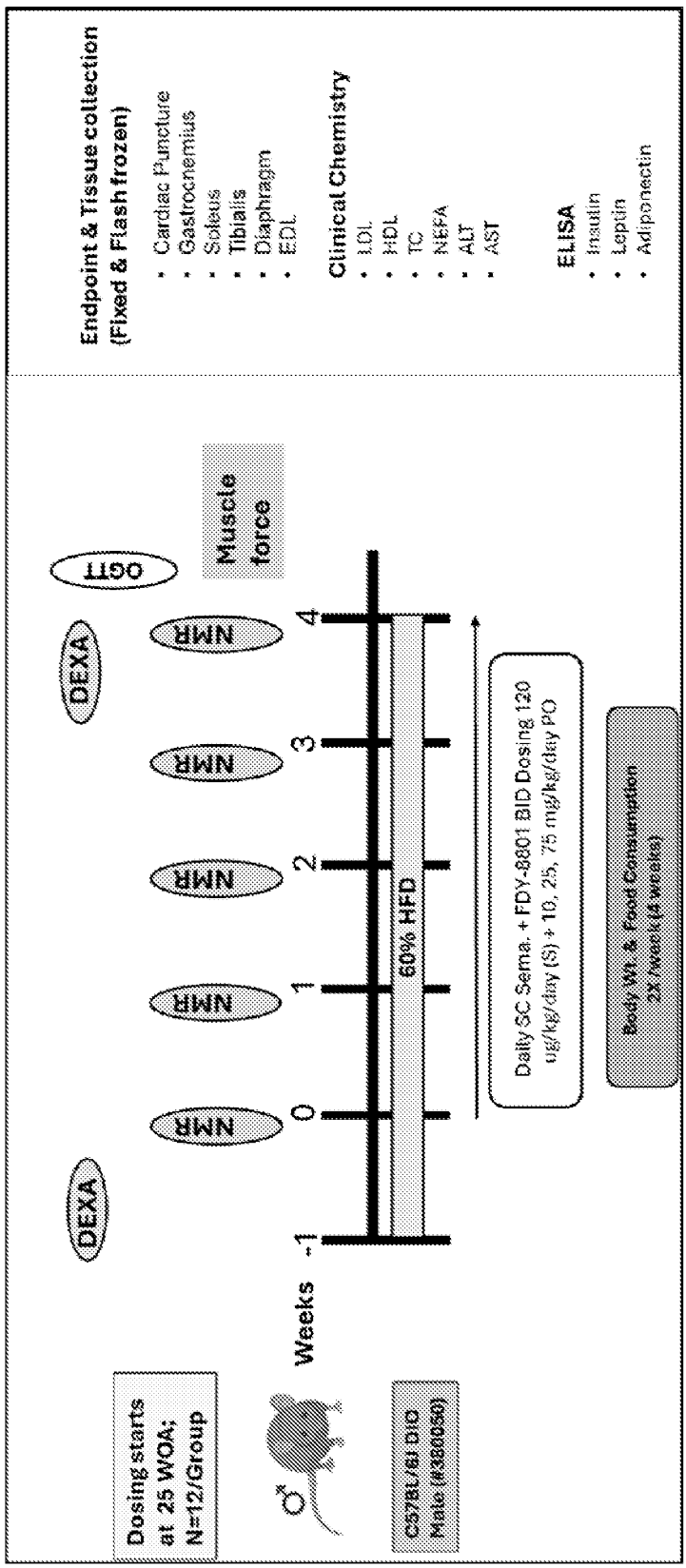

Endpoint & Tissue collection
(Fixed & Flash frozen)
Cardiac Puncture
Gastrocnemius
Soleus
Tibialis
Diaphragm
EDL
Clinical Chemistry
LDL
HDL
TC
NEFA
ALT
AST
ELISA
Insulin
Leptin
Adiponectin
Muscle force
OGTT
DEXA
NMR
NMR
NMR
NMR
DEXA
-1
0
1
2
3
4
Weeks
60% HFD
Daily SC Sema. + FDY-8801 BID Dosing 120 ug/kg/day (S) + 10, 25, 75 mg/kg/day PO
Body Wt. & Food Consumption 2X /week (4 weeks)
Dosing starts at 25 WOA; N=12/Group
C57BL/6J DIO Male (#380050)

FIG. 18A

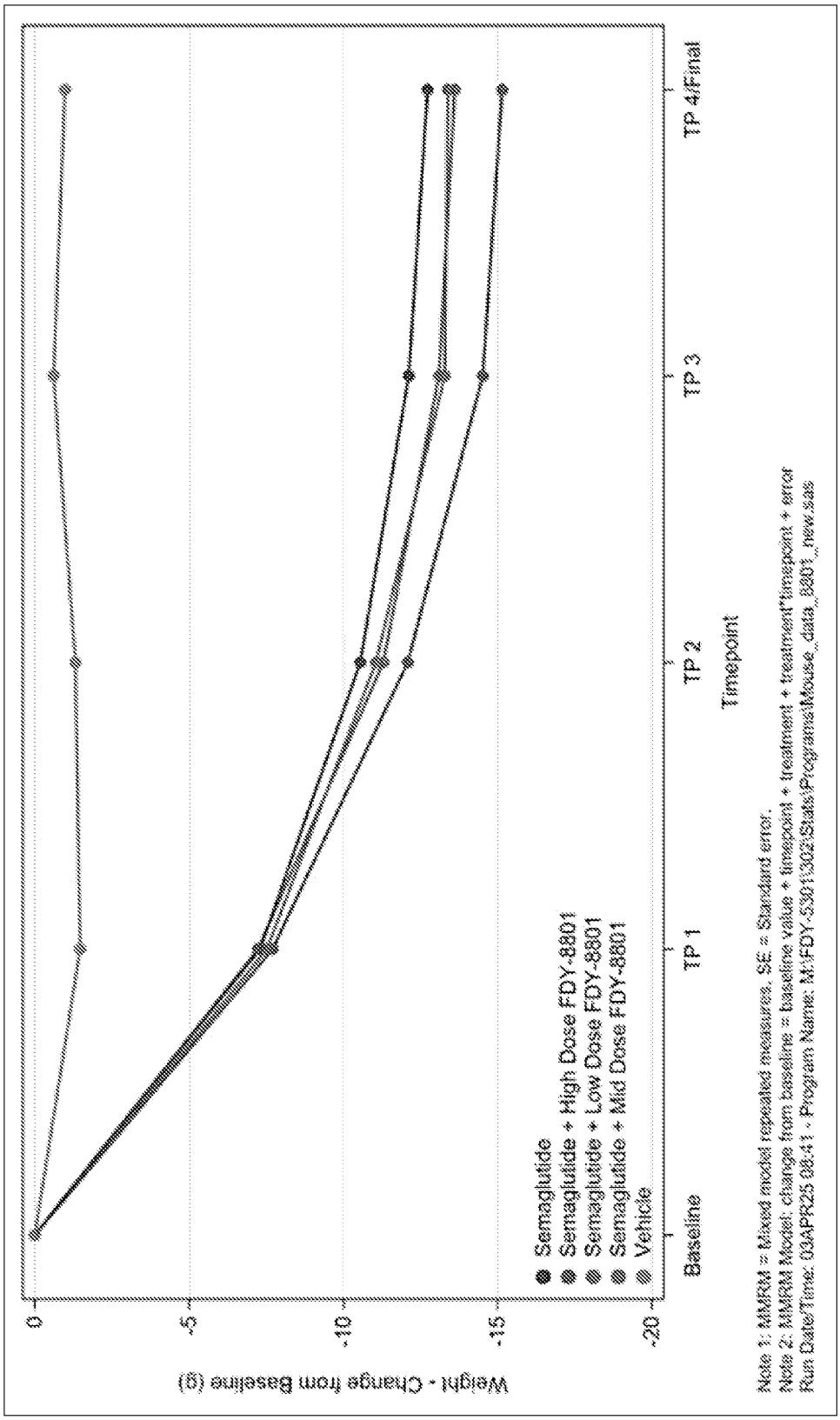

Weight - Change from Baseline (g)
0
-5
-10
-15
-20
Baseline
TP 1
TP 2
TP 3
TP 4/Final
Timepoint
Semaglutide
Semaglutide + High Dose FDY-8801
Semaglutide + Low Dose FDY-8801
Semaglutide + Mid Dose FDY-8801
Vehicle
Note 1: MMRM = Mixed model repeated measures, SE = Standard error.
Note 2: MMRM Model: change from baseline value + timepoint + treatment + treatment*timepoint + error
Run Date/Time: 03APR25 08:41 - Program Name: M:\FDY-5301\3023\Stats\Programs\Mouse_data_8801_new.sas

FIG. 18B

Change from Baseline in Body Weight, Fat, and Lean Mass at Timepoint 4 (Final)
Mixed Model Repeated Measures Analysis

Endpoint	Treatment Arm / Comparison	LSMean (SE)	95% CI	P-Value
Weight (g)	Semaglutide + High Dose FDY-8801	-15.138 (0.503)	(-16.141, -14.136)	
	Semaglutide + Mid Dose FDY-8801	-13.601 (0.503)	(-14.603, -12.599)	
	Semaglutide + Low Dose FDY-8801	-13.394 (0.505)	(-14.399, -12.388)	
	Semaglutide	-12.730 (0.525)	(-13.782, -11.678)	
	Vehicle	-9.977 (0.564)	(-11.980, -8.025)	
	Semaglutide + High Dose FDY-8801 vs. Vehicle	-14.161 (0.712)	(-15.578, -12.743)	<.0001
	Semaglutide + Mid Dose FDY-8801 vs. Vehicle	-12.624 (0.712)	(-14.041, -11.206)	<.0001
	Semaglutide + Low Dose FDY-8801 vs. Vehicle	-12.416 (0.714)	(-13.837, -10.996)	<.0001
	Semaglutide vs. Vehicle	-11.752 (0.729)	(-13.204, -10.301)	<.0001
	Semaglutide + High Dose FDY-8801 vs. Semaglutide	-2.409 (0.731)	(-3.865, -0.954)	0.0013
	Semaglutide + Mid Dose FDY-8801 vs. Semaglutide	-0.871 (0.730)	(-2.324, 0.582)	0.2362
	Semaglutide + Low Dose FDY-8801 vs. Semaglutide	-0.664 (0.734)	(-2.125, 0.797)	0.3685

MMRM = Mixed model repeated measures, SE = Standard error.
MMRM Model: change from baseline = baseline value + timepoint + treatment + treatment*timepoint + error
Run Date/Time: 03APR25 08:41 - Program Name: M:\FDY-3801\302 Stats\Programs\Mouse_data_8801_new.sas

FIG. 19A

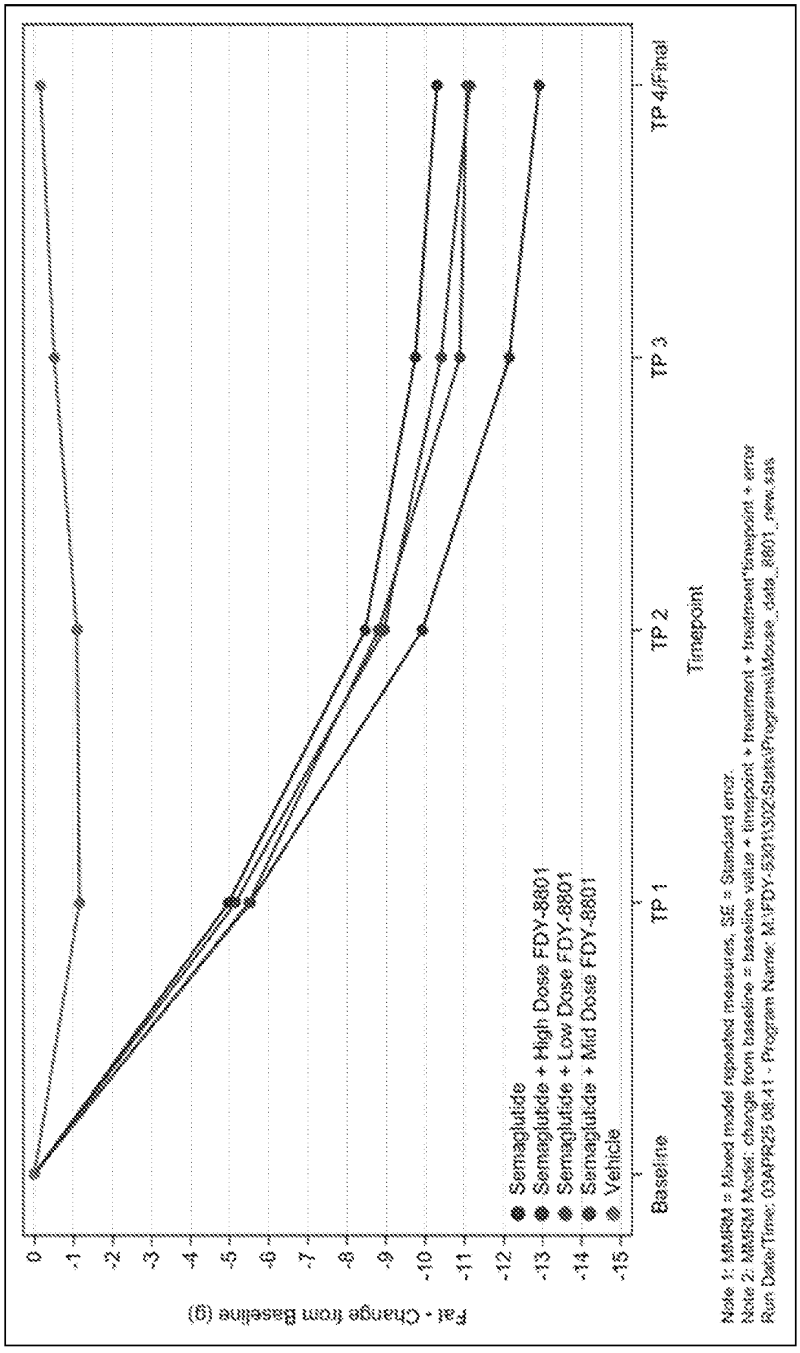
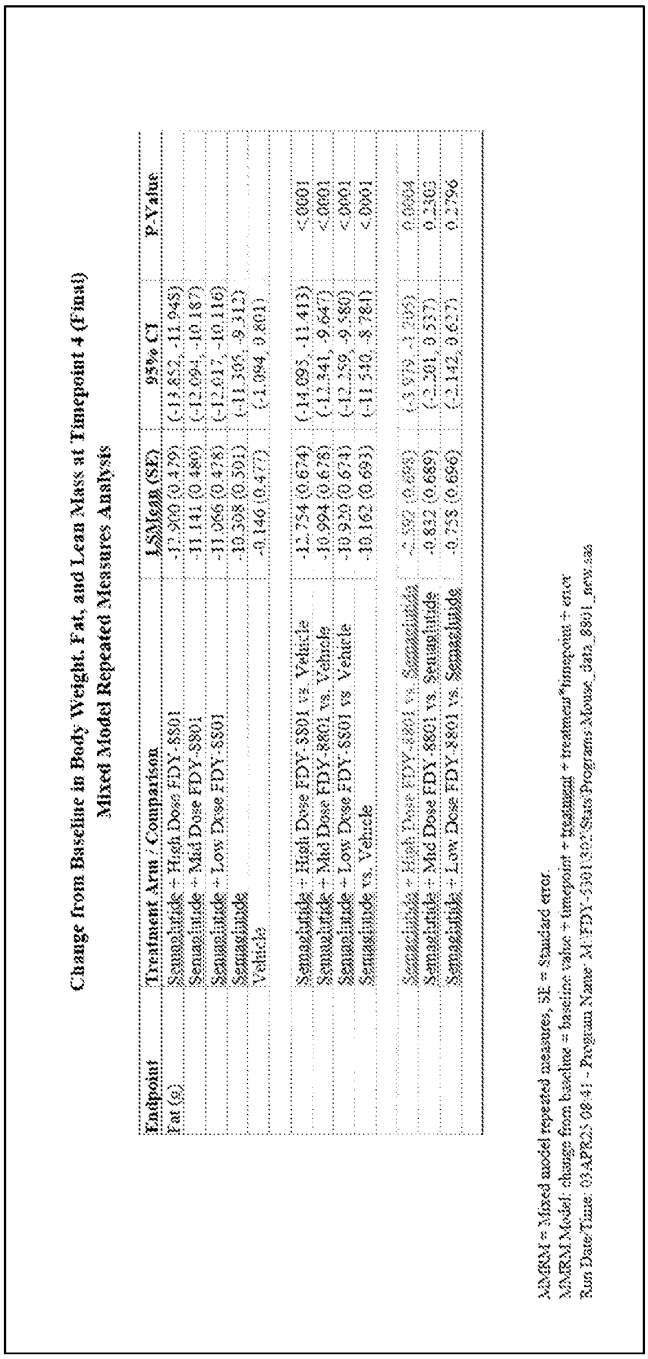

Fat - Change from Baseline (g)
0
-1
-2
-3
-4
-5
-6
-7
-8
-9
-10
-11
-12
-13
-14
-15
Baseline
TP 1
TP 2
TP 3
TP 4/Final
Timepoint
Semaglutide
Semaglutide + High Dose FDY-8801
Semaglutide + Low Dose FDY-8801
Semaglutide + Mid Dose FDY-8801
Vehicle
Note 1: MMRM = Mixed model repeated measures, SE = Standard error.
Note 2: MMRM Model: change from baseline = baseline value + timepoint + treatment + treatment*timepoint + error
Run Date/Time: 03APR25 08:41 - Program Name: M:\FDY-5201\302\Stats\Programs\Mouse_data_8801_new.sas

FIG. 19B



Change from Baseline in Body Weight, Fat, and Lean Mass at Timepoint 4 (Final)
Mixed Model Repeated Measures Analysis

Endpoint	Treatment Arm / Comparison	LSMean (SE)	95% CI	P Value
Fat (g)	Semaglutide + High Dose FDY-8801	-12.909 (0.479)	(-13.852, -11.965)	
	Semaglutide + Mid Dose FDY-8801	-11.141 (0.480)	(-12.094, -10.187)	
	Semaglutide + Low Dose FDY-8801	-11.066 (0.478)	(-12.017, -10.116)	
	Semaglutide	-10.308 (0.501)	(-11.305, -9.312)	
	Vehicle	-9.146 (0.477)	(-10.094, -8.201)	
	Semaglutide + High Dose FDY-8801 vs. Vehicle	-12.754 (0.674)	(-14.095, -11.413)	<.0001
	Semaglutide + Mid Dose FDY-8801 vs. Vehicle	-10.994 (0.678)	(-12.341, -9.647)	<.0001
	Semaglutide + Low Dose FDY-8801 vs. Vehicle	-10.920 (0.674)	(-12.259, -9.580)	<.0001
	Semaglutide vs. Vehicle	-10.162 (0.693)	(-11.540, -8.784)	<.0001
	Semaglutide + High Dose FDY-8801 vs. Semaglutide	-2.592 (0.698)	(-3.979, -1.205)	0.0004
	Semaglutide + Mid Dose FDY-8801 vs. Semaglutide	-0.832 (0.689)	(-2.201, 0.537)	0.2303
	Semaglutide + Low Dose FDY-8801 vs. Semaglutide	-0.758 (0.696)	(-2.142, 0.627)	0.2796

MMRM = Mixed model repeated measures, SE = Standard error.
MMRM Model: change from baseline = baseline value + timepoint + treatment + treatment*timepoint + error
Run Date/Time: 03APR25 08:41 - Program Name: M:\FDY-5301302\Stats Programs\Mouse_data_8801_new.sas

FIG. 20

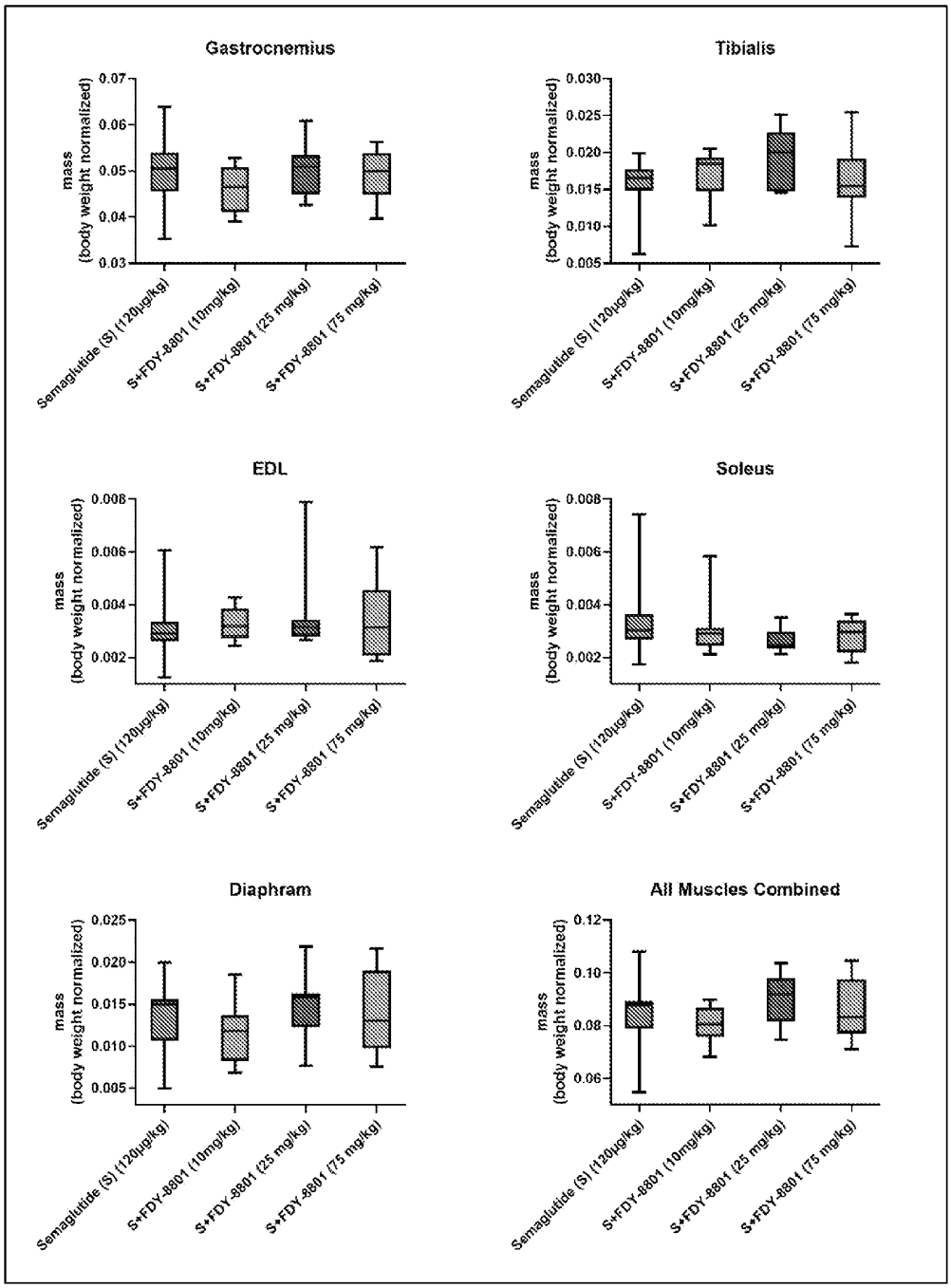

Gastrocnemius
mass (body weight normalized)
0.07
0.06
0.05
0.04
0.03
Semaglutide (S) (120µg/kg)
S+FDY-8801 (10mg/kg)
S+FDY-8801 (25 mg/kg)
S+FDY-8801 (75 mg/kg)
Tibialis
mass (body weight normalized)
0.030
0.025
0.020
0.015
0.010
0.005
Semaglutide (S) (120µg/kg)
S+FDY-8801 (10mg/kg)
S+FDY-8801 (25 mg/kg)
S+FDY-8801 (75 mg/kg)
EDL
mass (body weight normalized)
0.008
0.006
0.004
0.002
Semaglutide (S) (120µg/kg)
S+FDY-8801 (10mg/kg)
S+FDY-8801 (25 mg/kg)
S+FDY-8801 (75 mg/kg)
Soleus
mass (body weight normalized)
0.008
0.006
0.004
0.002
Semaglutide (S) (120µg/kg)
S+FDY-8801 (10mg/kg)
S+FDY-8801 (25 mg/kg)
S+FDY-8801 (75 mg/kg)
Diaphram
mass (body weight normalized)
0.025
0.020
0.015
0.010
0.005
Semaglutide (S) (120µg/kg)
S+FDY-8801 (10mg/kg)
S+FDY-8801 (25 mg/kg)
S+FDY-8801 (75 mg/kg)
All Muscles Combined
mass (body weight normalized)
0.12
0.10
0.08
0.06
Semaglutide (S) (120µg/kg)
S+FDY-8801 (10mg/kg)
S+FDY-8801 (25 mg/kg)
S+FDY-8801 (75 mg/kg)

FIG. 21A

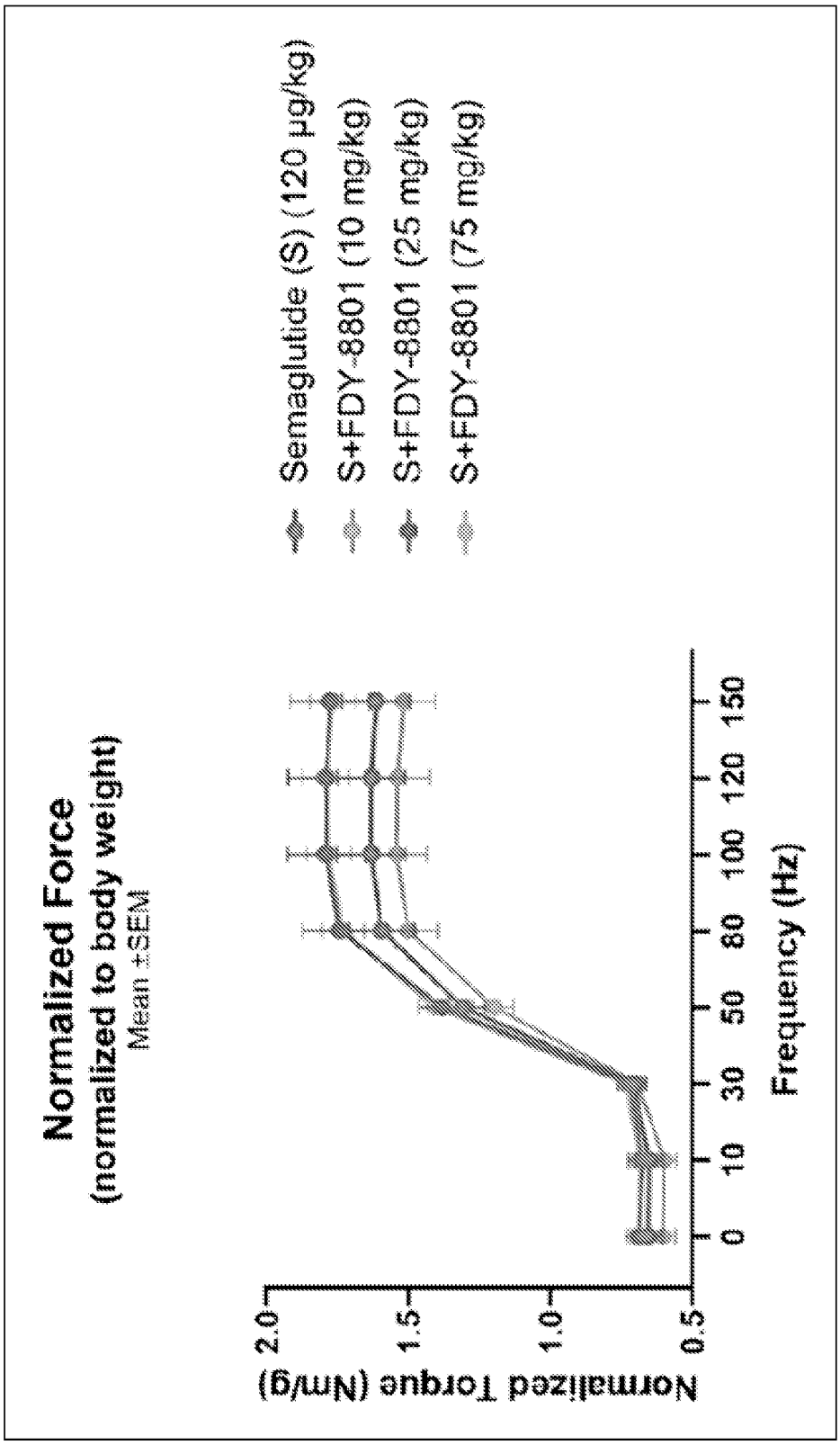

Normalized Force
(normalized to body weight)
Mean ±SEM
Semaglutide (S) (120 µg/kg)
S+FDY-8801 (10 mg/kg)
S+FDY-8801 (25 mg/kg)
S+FDY-8801 (75 mg/kg)
Normalized Torque (Nm/g)
2.0
1.5
1.0
0.5
0
10
30
50
80
100
120
150
Frequency (Hz)

FIG. 21B

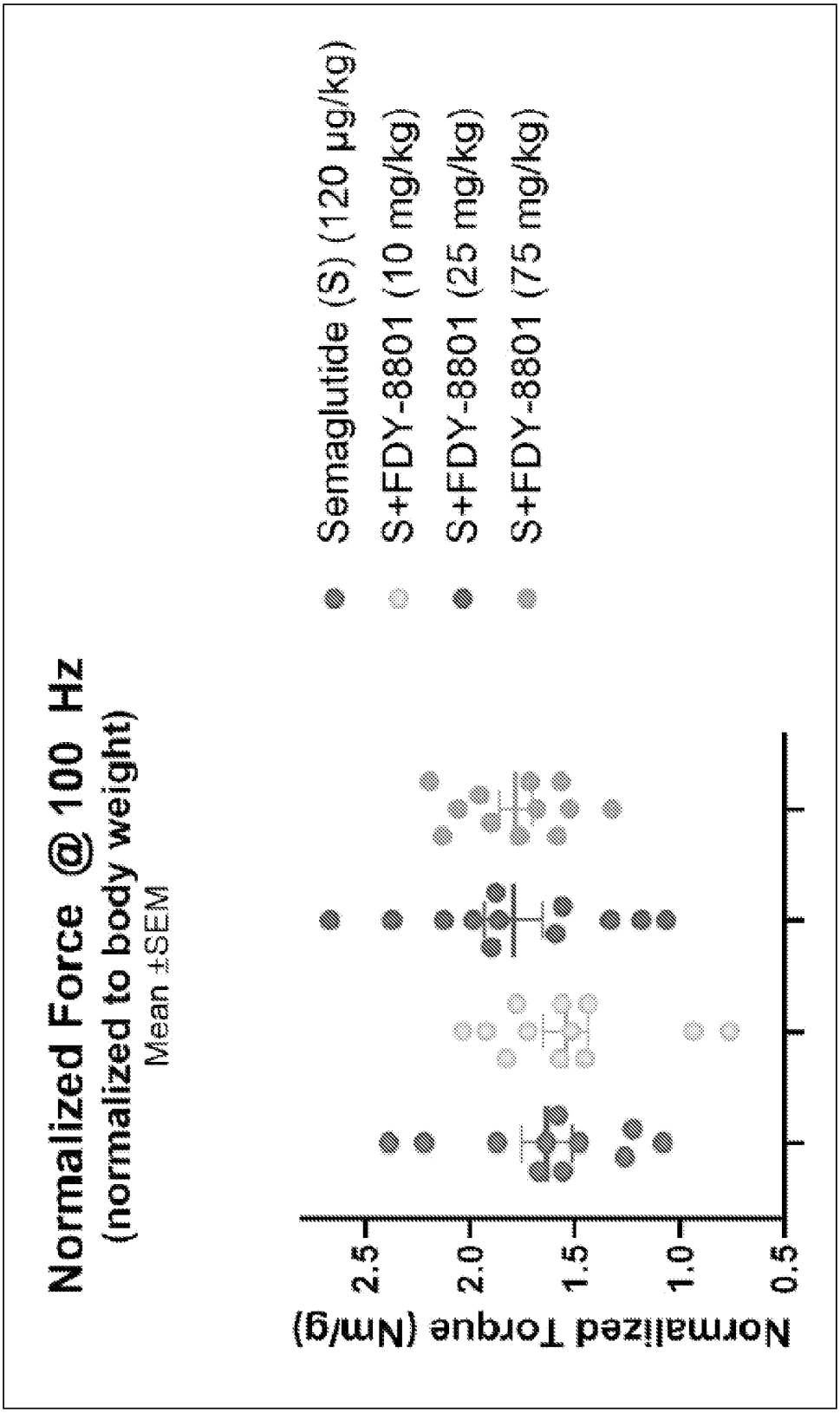

Normalized Force @ 100 Hz
(normalized to body weight)
Mean ±SEM
Semaglutide (S) (120 µg/kg)
S+FDY-8801 (10 mg/kg)
S+FDY-8801 (25 mg/kg)
S+FDY-8801 (75 mg/kg)
Normalized Torque (Nm/g)
2.5
2.0
1.5
1.0
0.5

FIG. 22

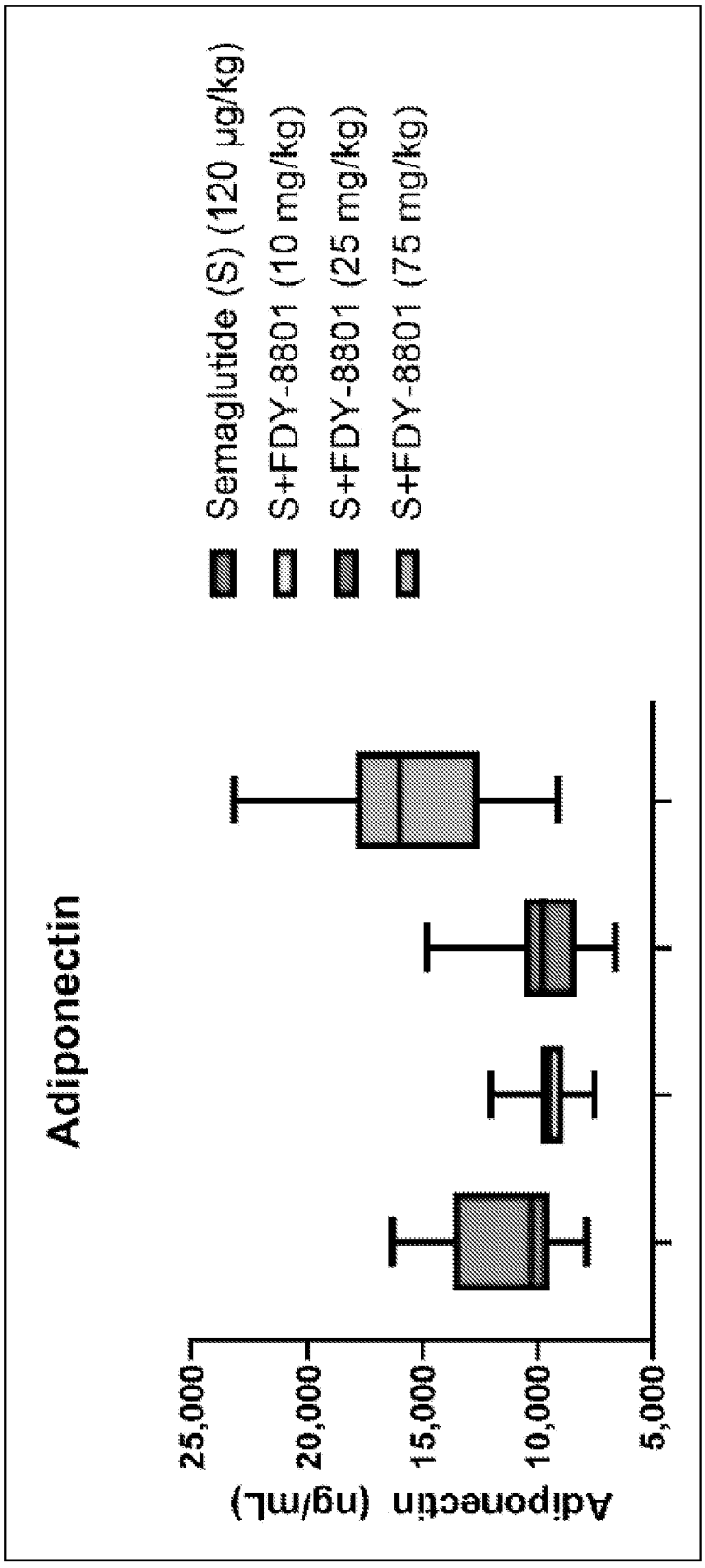

Adiponectin
Semaglutide (S) (120 µg/kg)
S+FDY-8801 (10 mg/kg)
S+FDY-8801 (25 mg/kg)
S+FDY-8801 (75 mg/kg)
Adiponectin (ng/mL)
25,000
20,000
15,000
10,000
5,000

FIG. 23

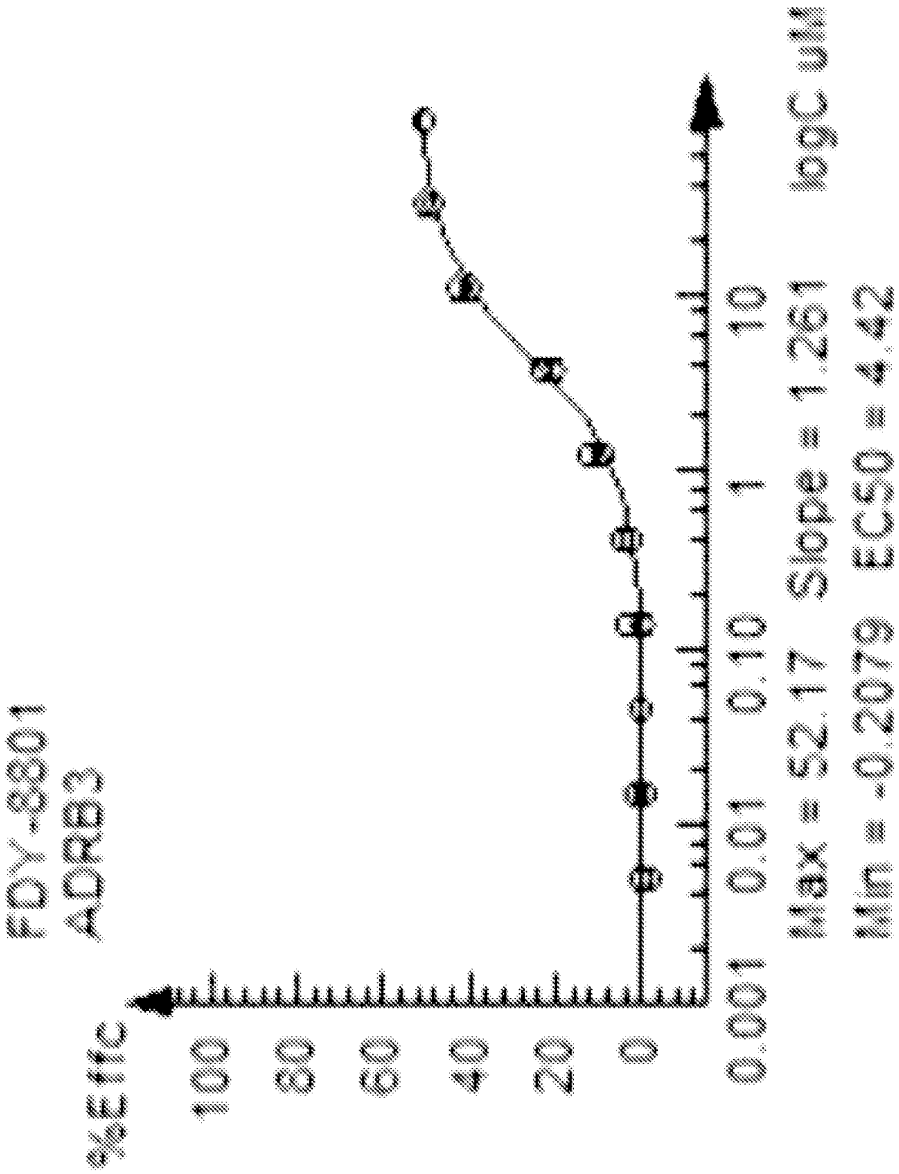

FOY-8801
ADR3
%Effc
100
80
60
40
20
0
0.001
0.01
0.10
1
10
logC uM
Max = 52.17 Slope = 1.261
Min = -0.2079 EC50 = 4.42

FIG. 24

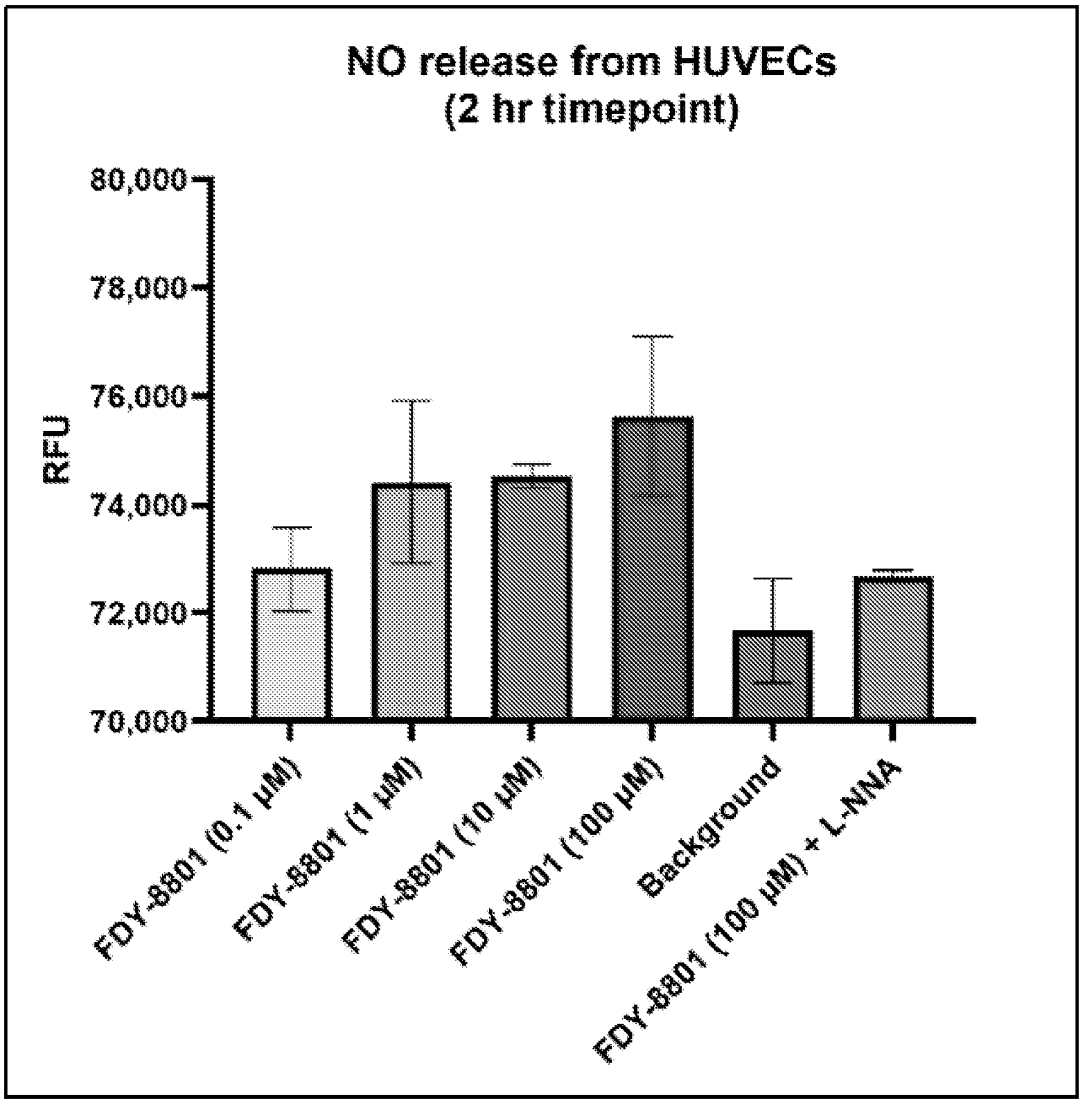

NO release from HUVECs
(2 hr timepoint)
RFU
80,000
78,000
76,000
74,000
72,000
70,000
FDY-8801 (0.1 µM)
FDY-8801 (1 µM)
FDY-8801 (10 µM)
FDY-8801 (100 µM)
Background
FDY-8801 (100 µM) + L-NNA

FIG. 25

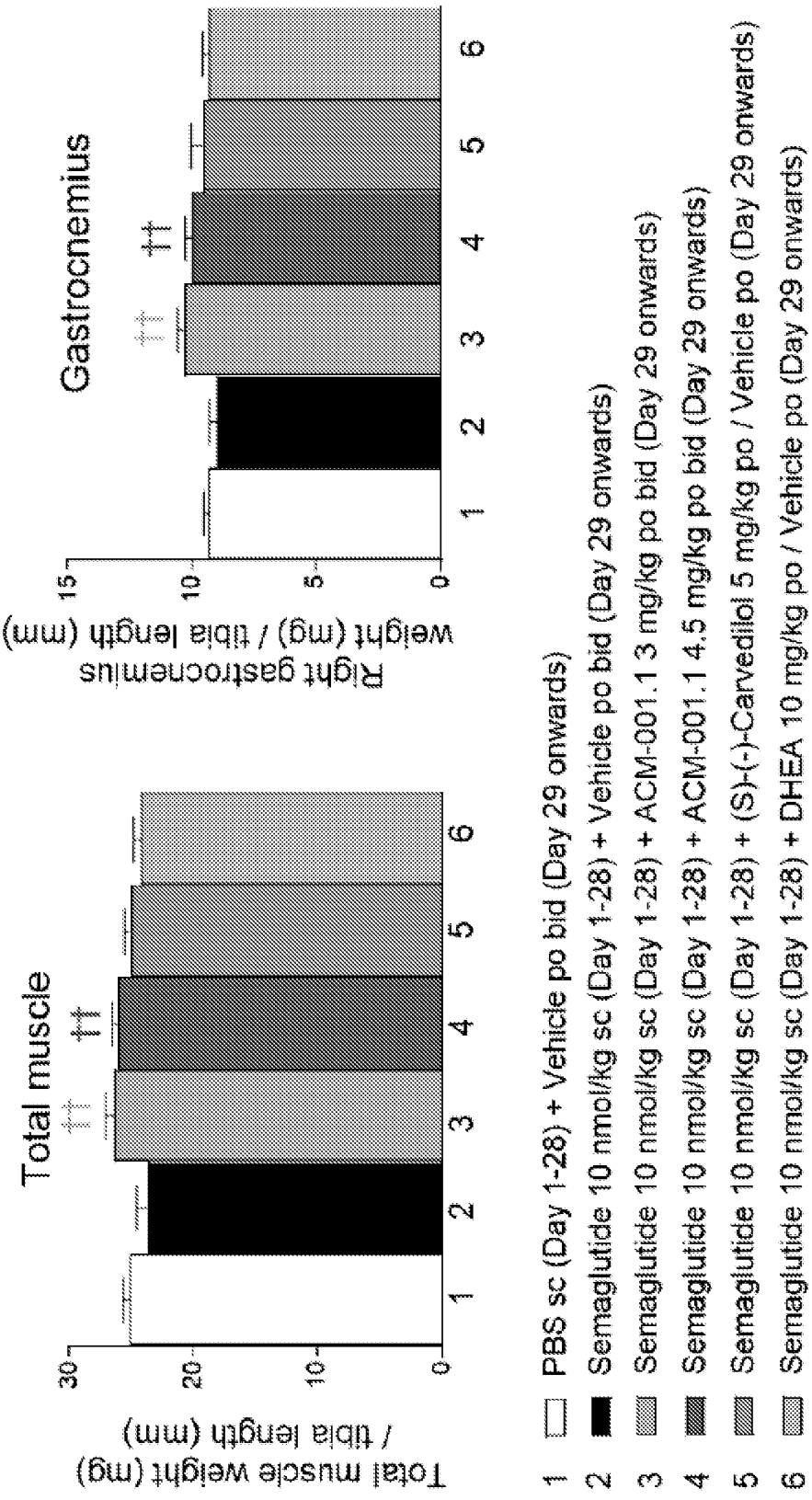

Gastrocnemius
Right gastrocnemius weight (mg) / tibia length (mm)
Total muscle
Total muscle weight (mg) / tibia length (mm)
1 PBS sc (Day 1-28) + Vehicle po bid (Day 29 onwards)
2 Semaglutide 10 nmol/kg sc (Day 1-28) + Vehicle po bid (Day 29 onwards)
3 Semaglutide 10 nmol/kg sc (Day 1-28) + ACM-001.1 3 mg/kg po bid (Day 29 onwards)
4 Semaglutide 10 nmol/kg sc (Day 1-28) + ACM-001.1 4.5 mg/kg po bid (Day 29 onwards)
5 Semaglutide 10 nmol/kg sc (Day 1-28) + (S)-(-)-Carvedilol 5 mg/kg po / Vehicle po (Day 29 onwards)
6 Semaglutide 10 nmol/kg sc (Day 1-28) + DHEA 10 mg/kg po / Vehicle po (Day 29 onwards)

FIG. 26

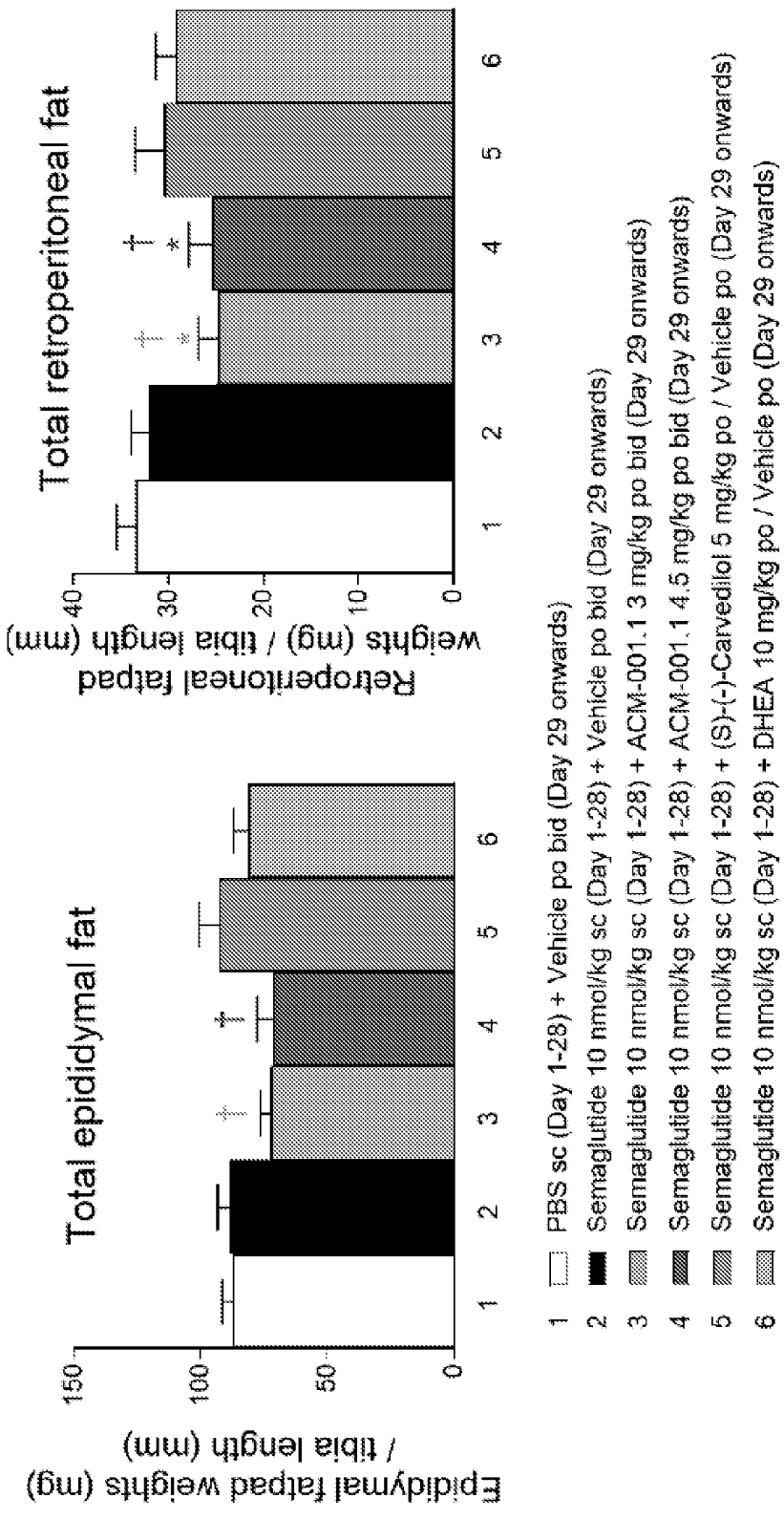

Total epididymal fat
Epididymal fatpad weights (mg) / tibia length (mm)
150
100
50
0
1 2 3 4 5 6
Total retroperitoneal fat
Retroperitoneal fatpad weights (mg) / tibia length (mm)
40
30
20
10
0
1 2 3 4 5 6
1 PBS sc (Day 1-28) + Vehicle po bid (Day 29 onwards)
2 Semaglutide 10 nmol/kg sc (Day 1-28) + Vehicle po bid (Day 29 onwards)
3 Semaglutide 10 nmol/kg sc (Day 1-28) + ACM-001.1 3 mg/kg po bid (Day 29 onwards)
4 Semaglutide 10 nmol/kg sc (Day 1-28) + ACM-001.1 4.5 mg/kg po bid (Day 29 onwards)
5 Semaglutide 10 nmol/kg sc (Day 1-28) + (S)-(-)-Carvedilol 5 mg/kg po / Vehicle po (Day 29 onwards)
6 Semaglutide 10 nmol/kg sc (Day 1-28) + DHEA 10 mg/kg po / Vehicle po (Day 29 onwards)

FIG. 27

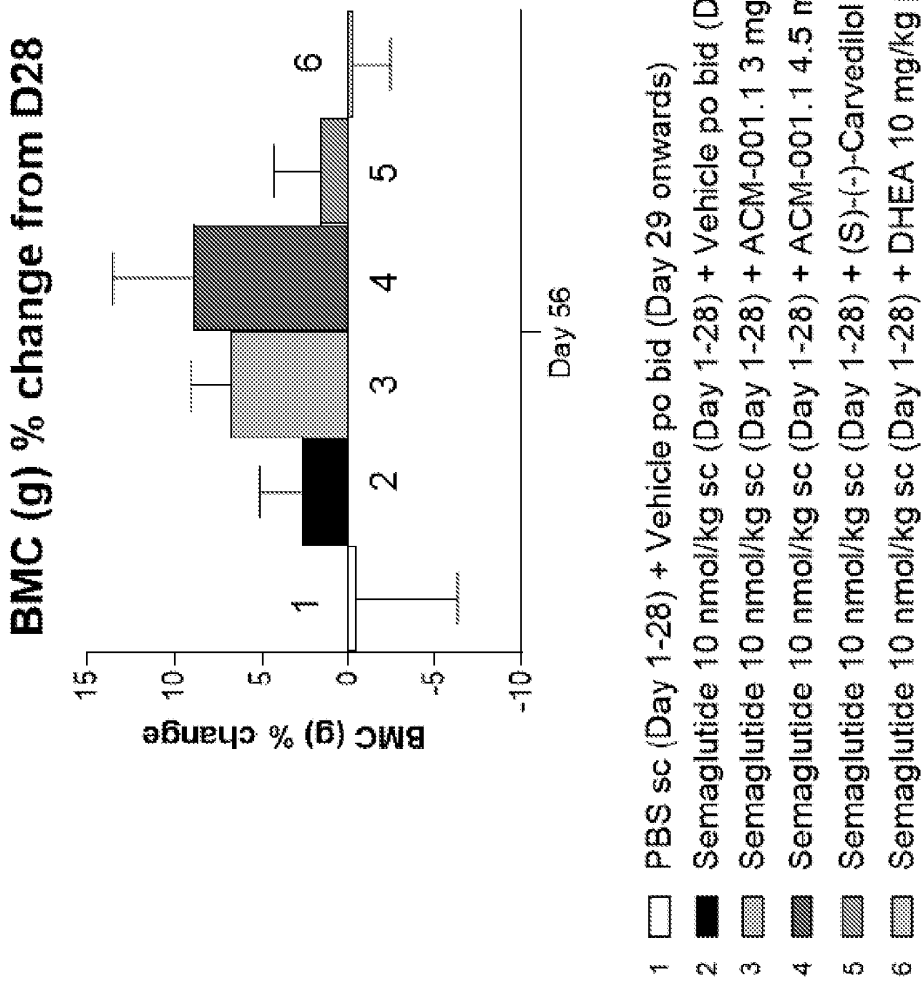
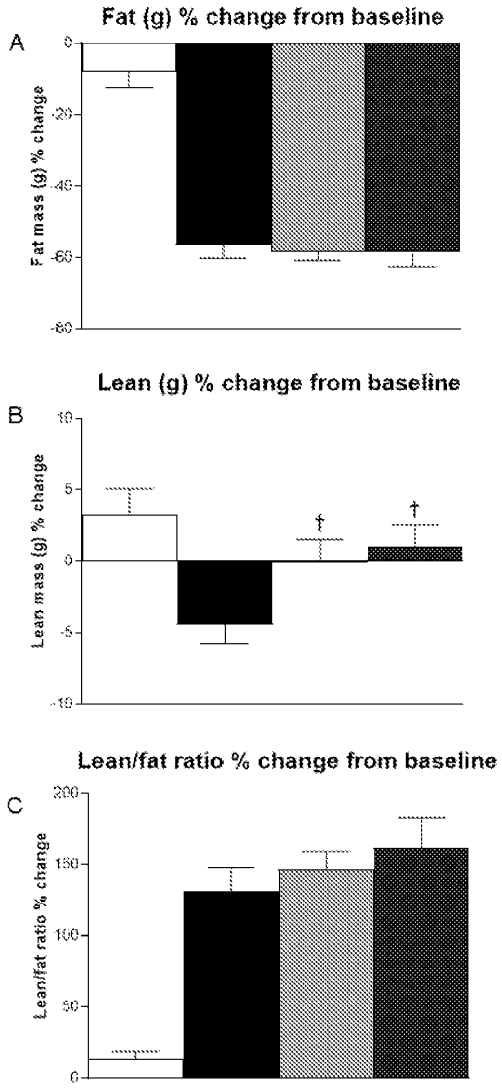

BMC (g) % change from D28
BMC (g) % change
15
10
5
0
-5
-10
1
2
3
4
5
6
Day 56
1 PBS sc (Day 1-28) + Vehicle po bid (Day 29 onwards)
2 Semaglutide 10 nmol/kg sc (Day 1-28) + Vehicle po bid (Day 29 onwards)
3 Semaglutide 10 nmol/kg sc (Day 1-28) + ACM-001.1 3 mg/kg po bid (Day 29 onwards)
4 Semaglutide 10 nmol/kg sc (Day 1-28) + ACM-001.1 4.5 mg/kg po bid (Day 29 onwards)
5 Semaglutide 10 nmol/kg sc (Day 1-28) + (S)-(-)-Carvedilol 5 mg/kg po / Vehicle po (Day 29 onwards)
6 Semaglutide 10 nmol/kg sc (Day 1-28) + DHEA 10 mg/kg po / Vehicle po (Day 29 onwards)

FIG. 28



1 Vehicle sc + Vehicle po bid (Day 1 onwards)
2 Semaglutide 10 nmol/kg sc + Vehicle po bid (Day 1 onwards)
3 Semaglutide 10 nmol/kg sc + ACM-001.1 3 mg/kg po bid (Day 1 onwards)
4 Semaglutide 10 nmol/kg sc + ACM-001.1 4.5 mg/kg po bid (Day 1 onwards)

FIG. 29

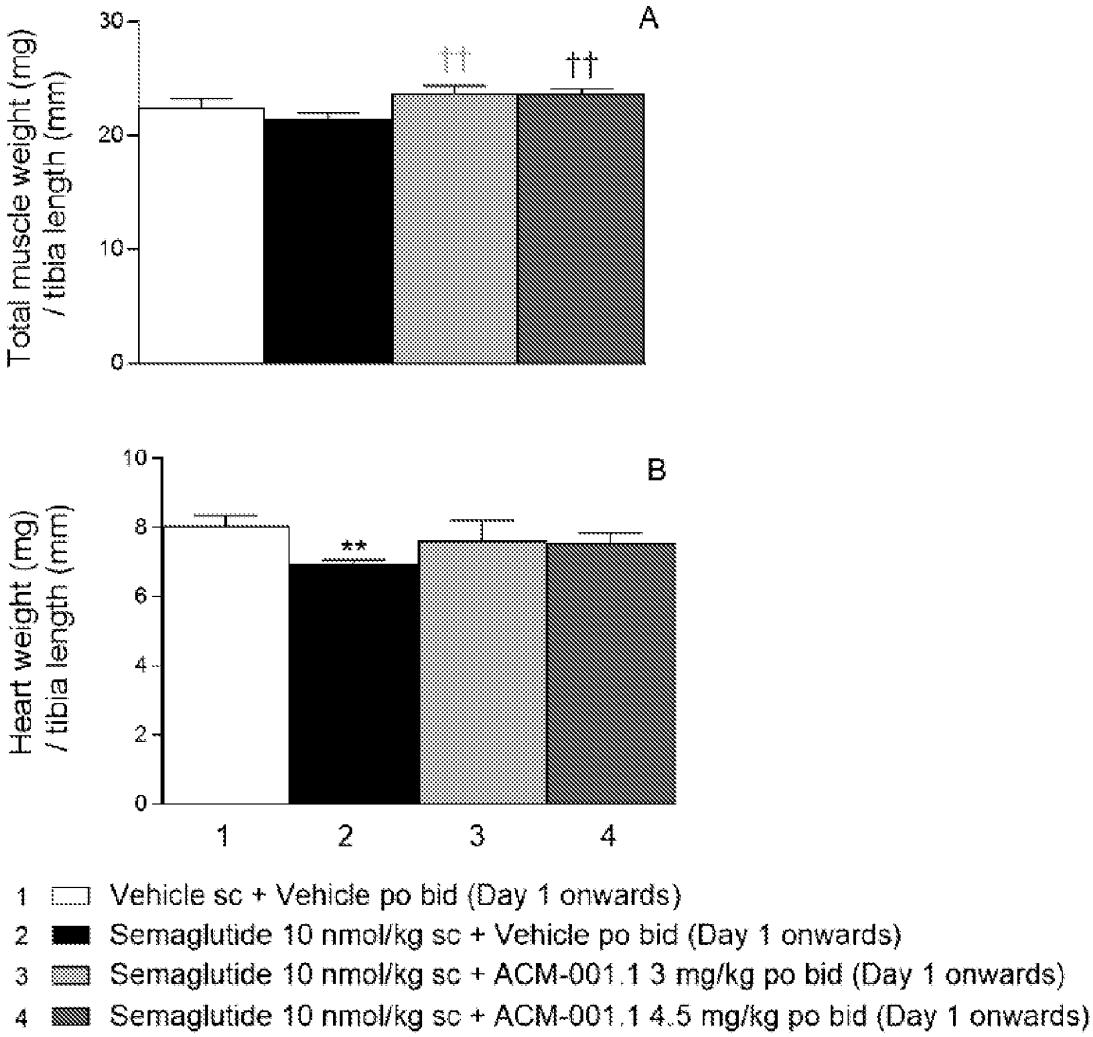
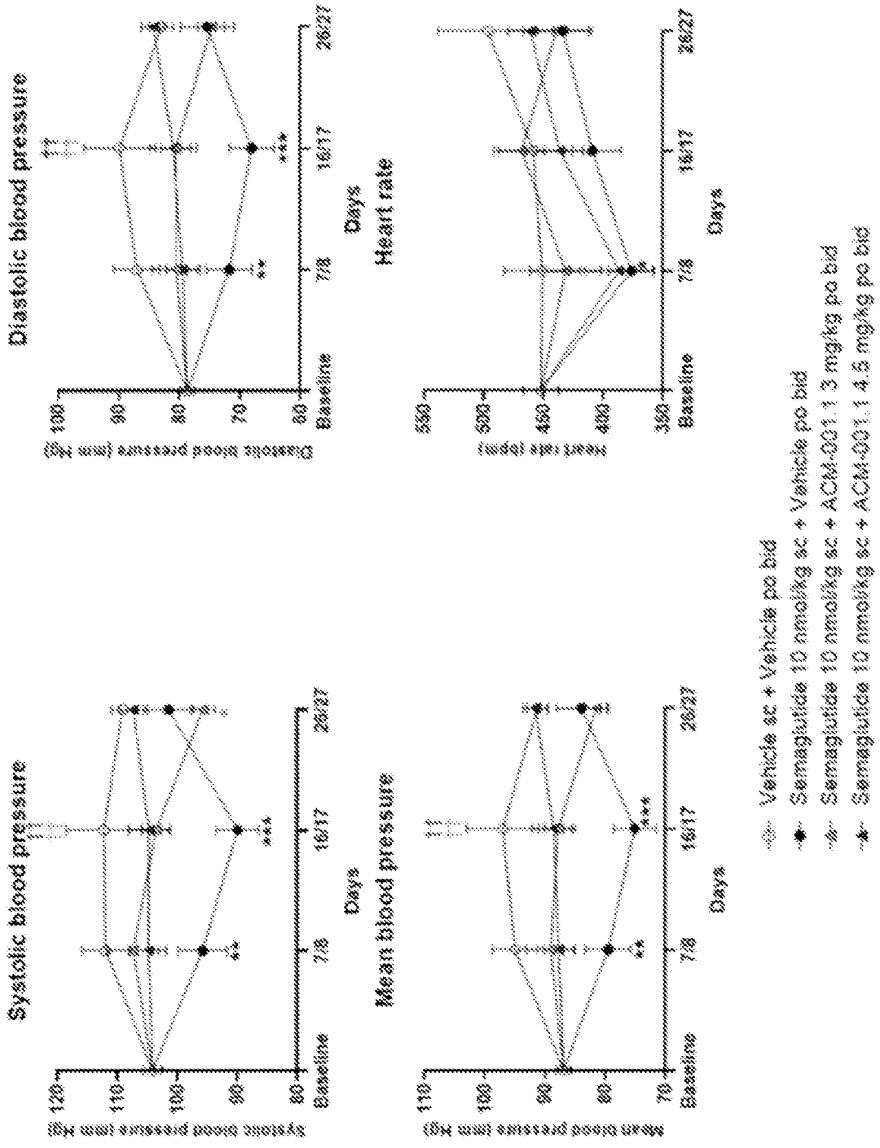

A
Total muscle weight (mg) / tibia length (mm)
30
20
10
0
††
††
B
Heart weight (mg) / tibia length (mm)
10
8
6
4
2
0
**
1
2
3
4
1 Vehicle sc + Vehicle po bid (Day 1 onwards)
2 Semaglutide 10 nmol/kg sc + Vehicle po bid (Day 1 onwards)
3 Semaglutide 10 nmol/kg sc + ACM-001.1 3 mg/kg po bid (Day 1 onwards)
4 Semaglutide 10 nmol/kg sc + ACM-001.1 4.5 mg/kg po bid (Day 1 onwards)

FIG. 30


Systolic blood pressure
Diastolic blood pressure
Mean blood pressure
Heart rate
Days
Baseline
7/8
16/17
26/27
Vehicle sc + Vehicle po bid
Semaglutide 10 nmol/kg sc + Vehicle po bid
Semaglutide 10 nmol/kg sc + ACM-001 1.3 mg/kg po bid
Semaglutide 10 nmol/kg sc + ACM-001 4.6 mg/kg po bid