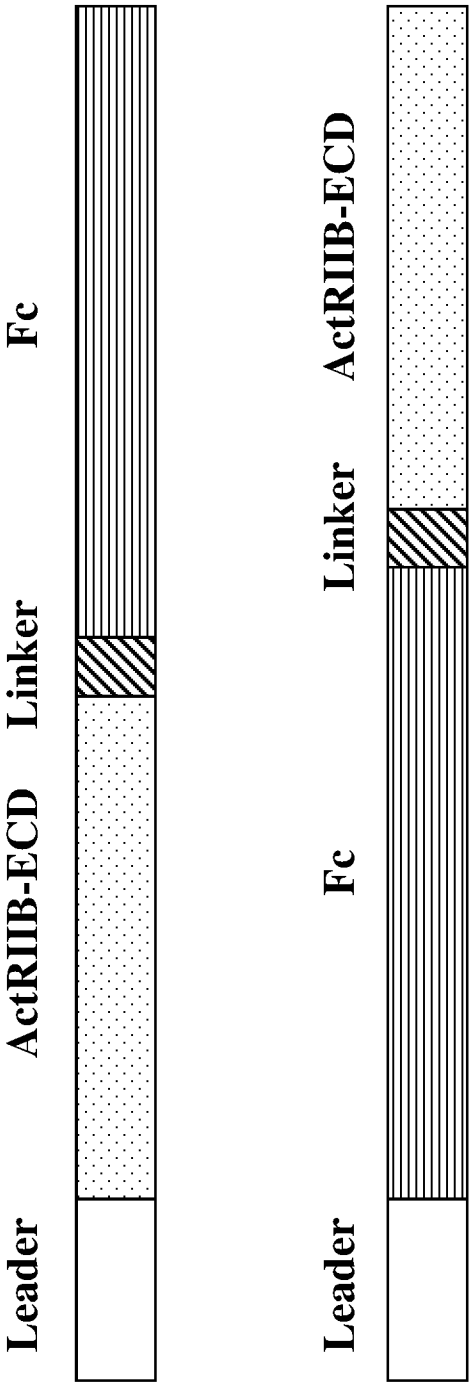


FIG 1

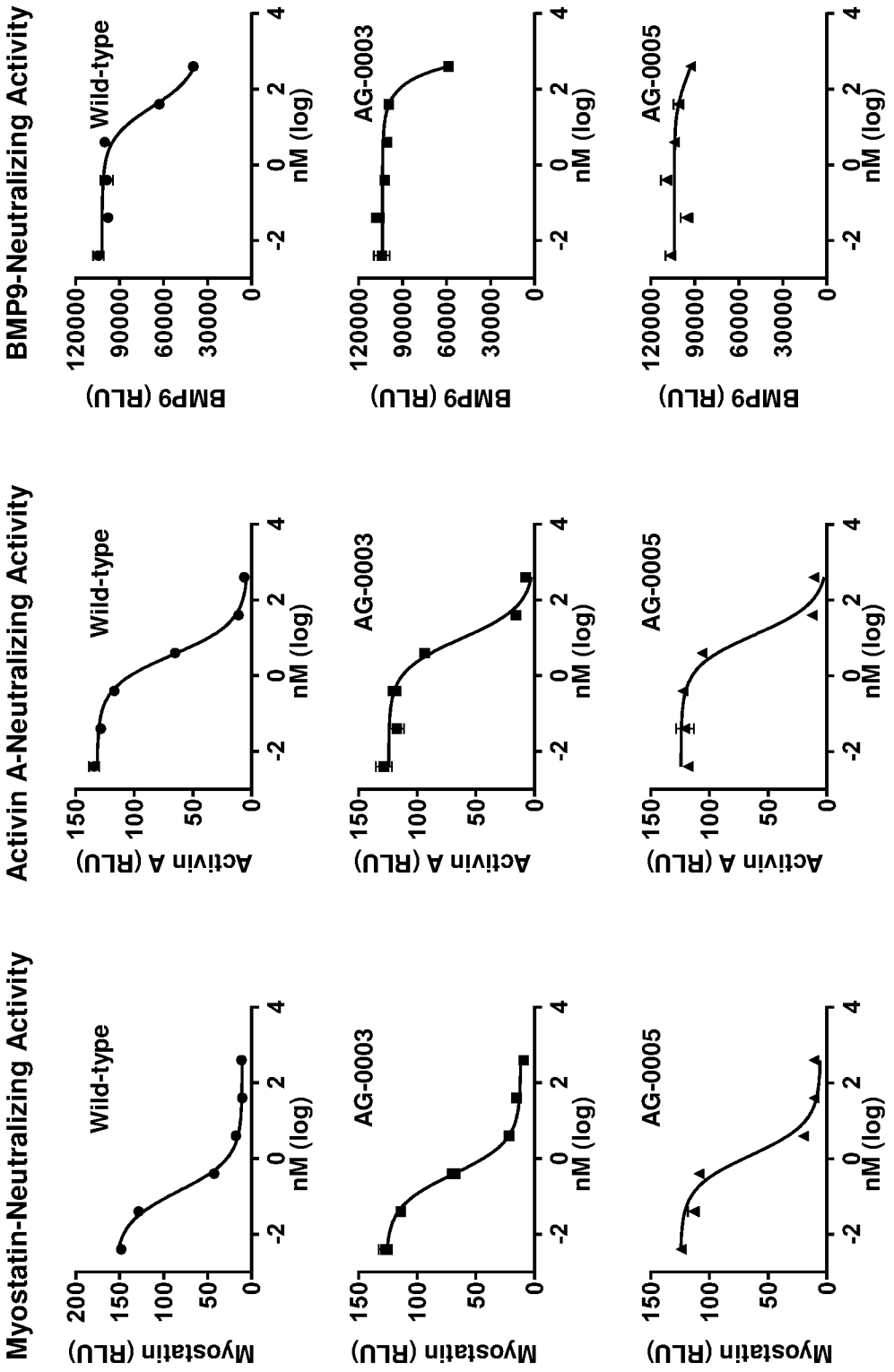

Myostatin-Neutralizing Activity
Activin A-Neutralizing Activity
BMP9-Neutralizing Activity
Wild-type
AG-0003
AG-0005
Myostatin (RLU)
Activin A (RLU)
BMP9 (RLU)
nM (log)

FIG 2

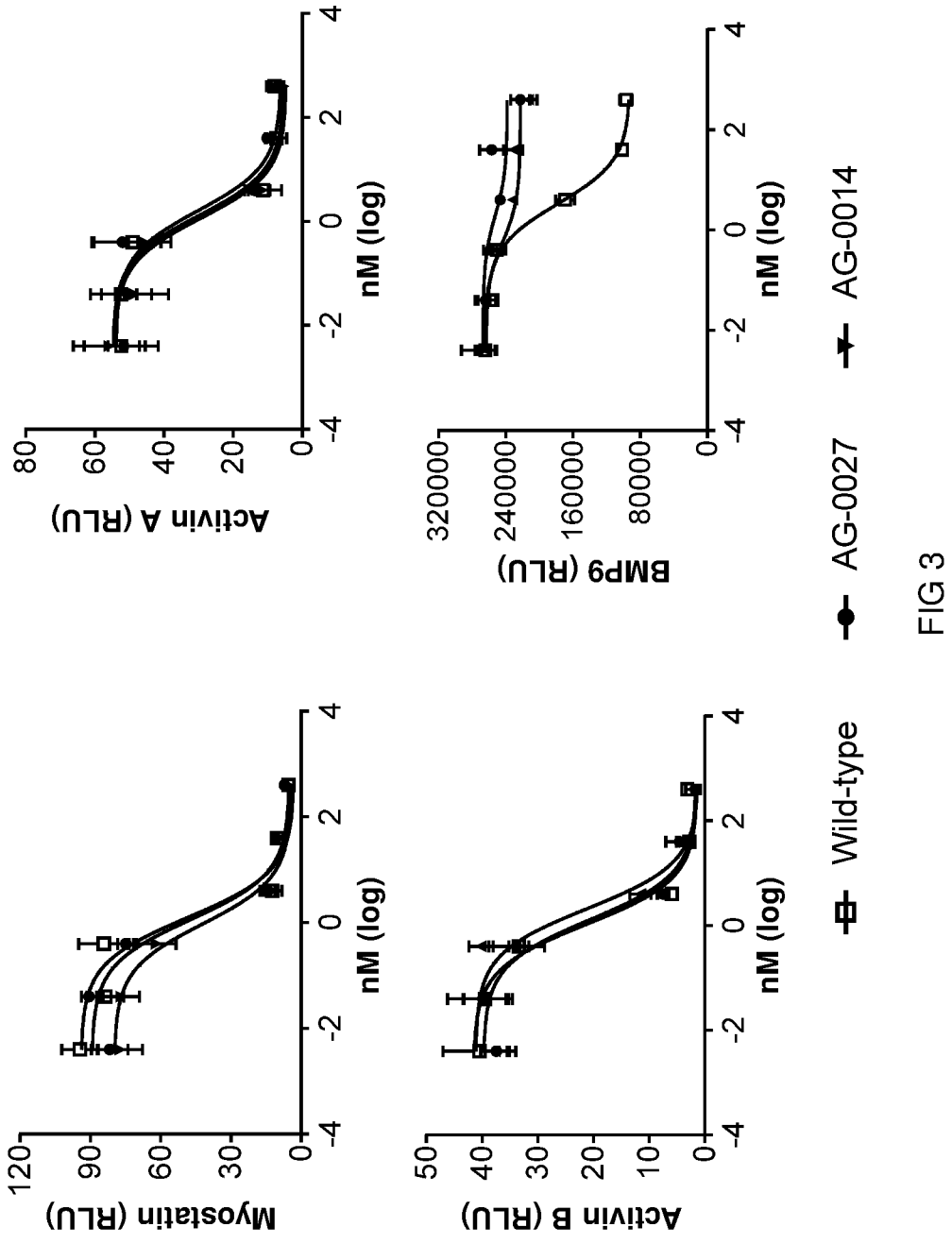

Activin A (RLU)
BMP9 (RLU)
Myostatin (RLU)
Activin B (RLU)
nM (log)
Wild-type
AG-0027
AG-0014

FIG 3

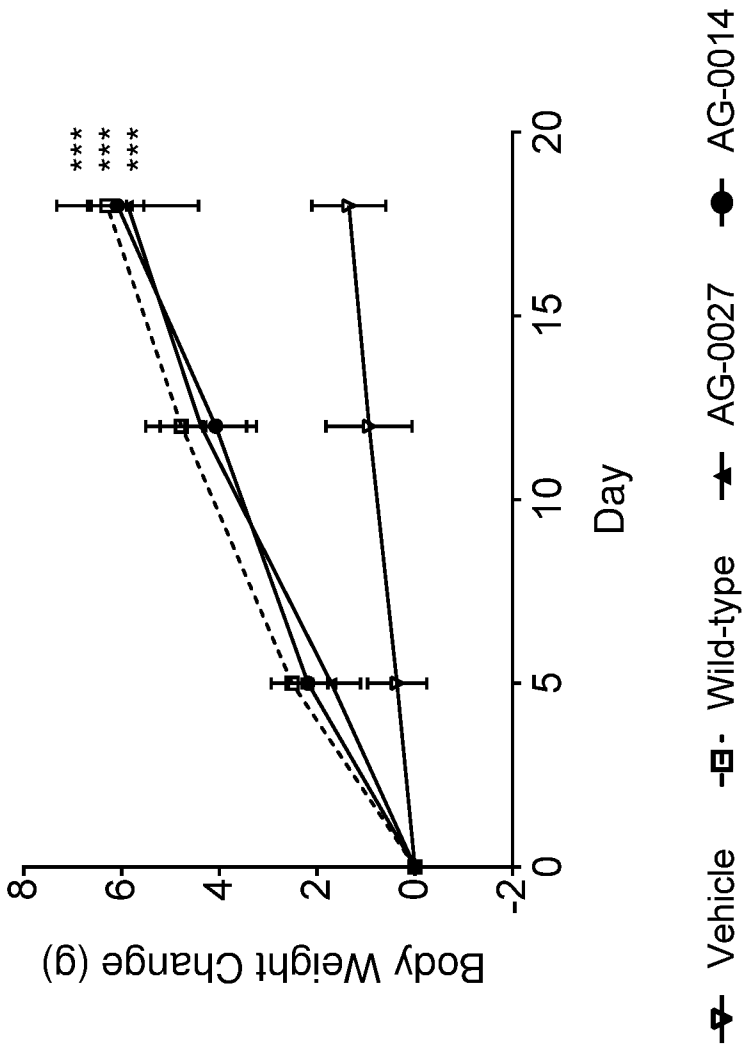

Body Weight Change (g)
8
6
4
2
0
-2
0
5
10
15
20
Day
***
***
***
Vehicle
Wild-type
AG-0027
AG-0014

FIG 4

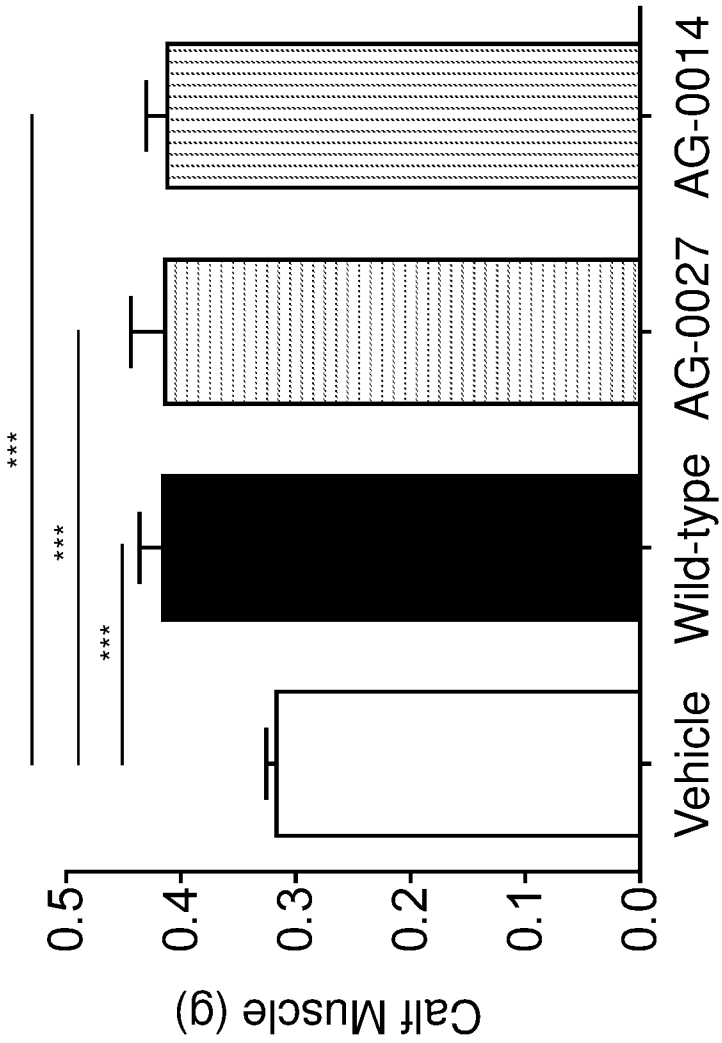

Calf Muscle (g)
0.0
0.1
0.2
0.3
0.4
0.5
***
***
***
Vehicle
Wild-type
AG-0027
AG-0014

FIG 5

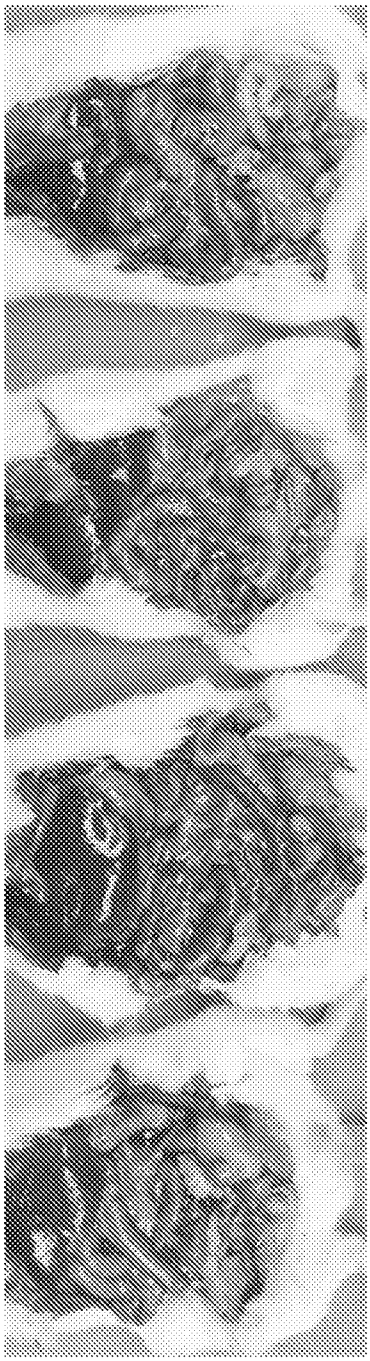


FIG 6

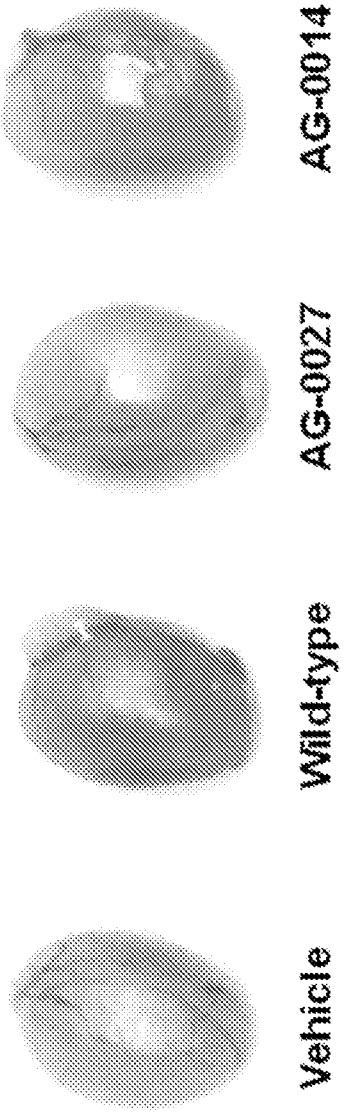


FIG 7

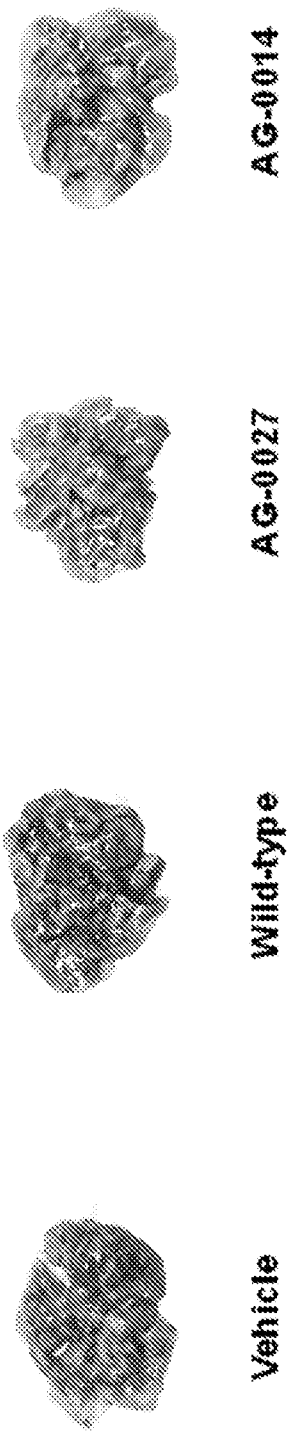
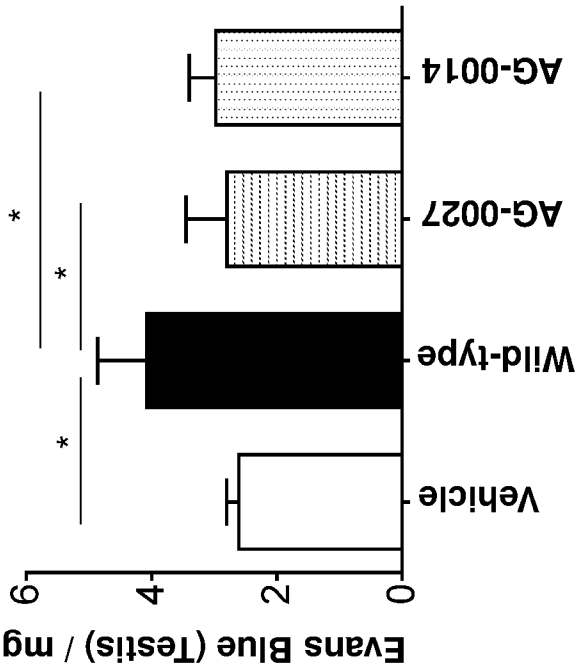


FIG 8


Evans Blue (Testis) / mg
0
2
4
6
*
*
*
Vehicle
Wild-type
AG-0027
AG-0014

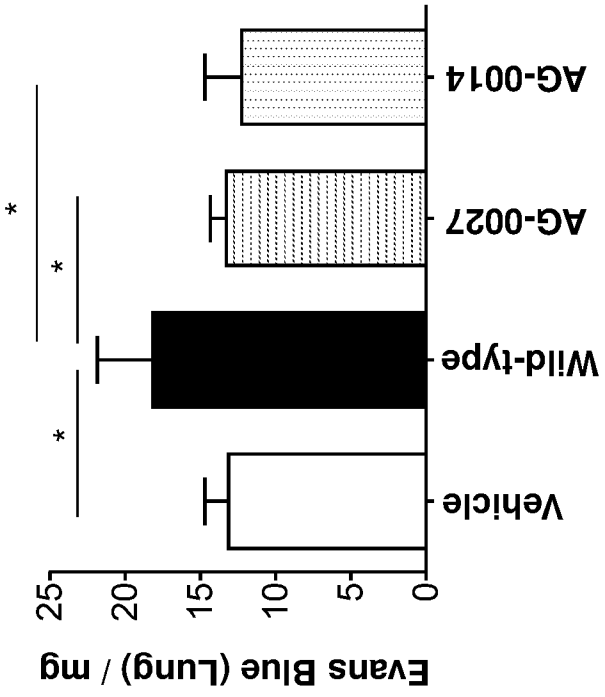

Evans Blue (Lung) / mg
0
5
10
15
20
25
*
*
*
Vehicle
Wild-type
AG-0027
AG-0014

FIG 9

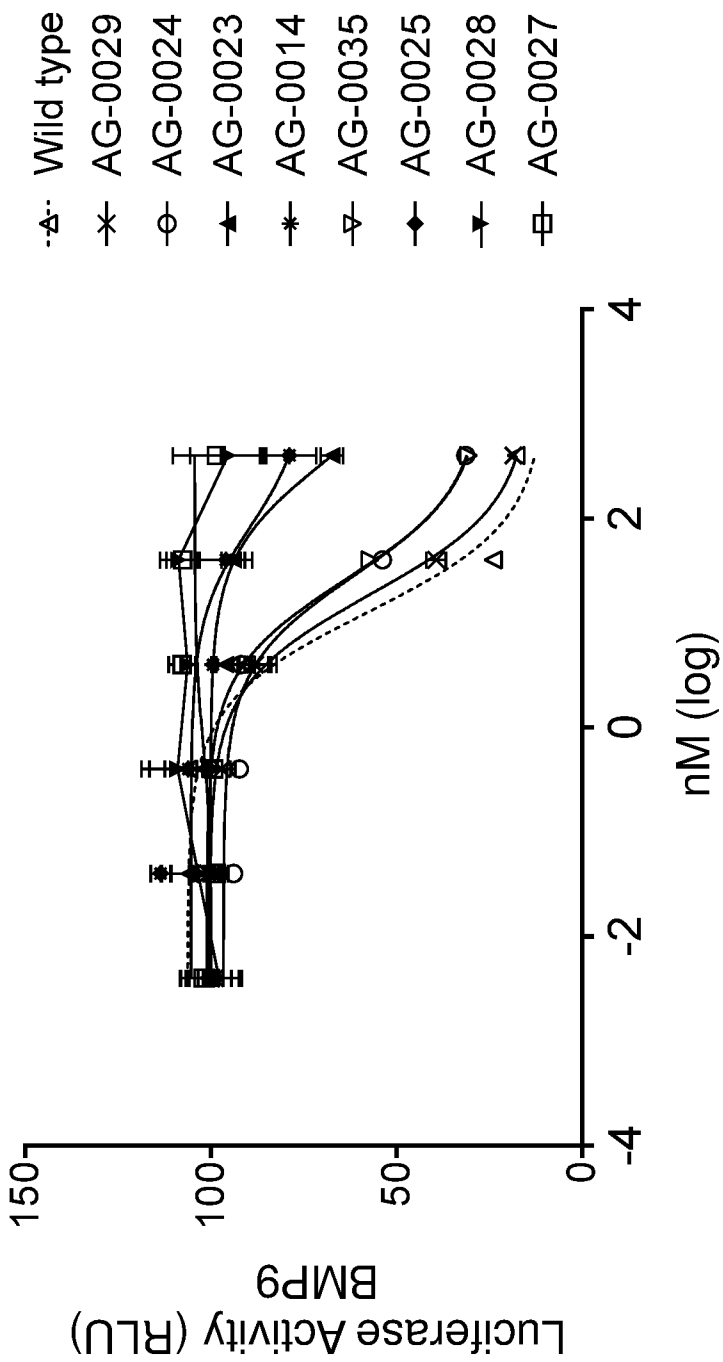

Wild type
AG-0029
AG-0024
AG-0023
AG-0014
AG-0035
AG-0025
AG-0028
AG-0027
Luciferase Activity (RLU)
BMP9
150
100
50
0
-4
-2
0
2
4
nM (log)

FIG 10

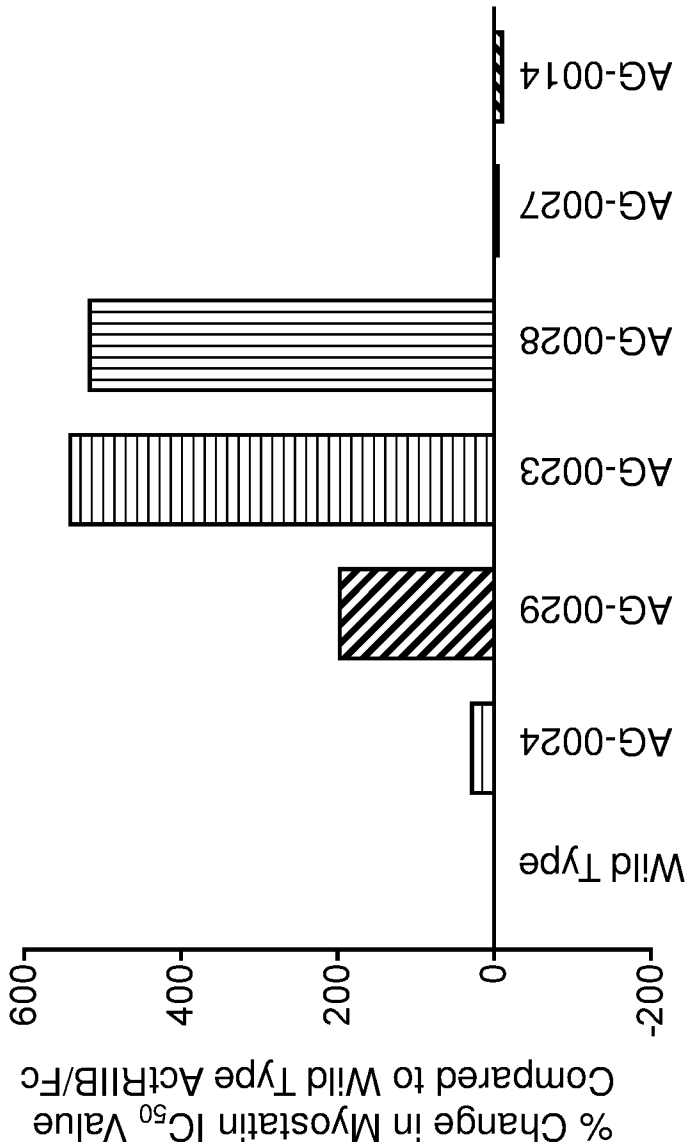

% Change in Myostatin IC_{50} Value
Compared to Wild Type ActRIIB/Fc
600
400
200
0
-200
Wild Type
AG-0024
AG-0029
AG-0023
AG-0028
AG-0027
AG-0014

FIG 11

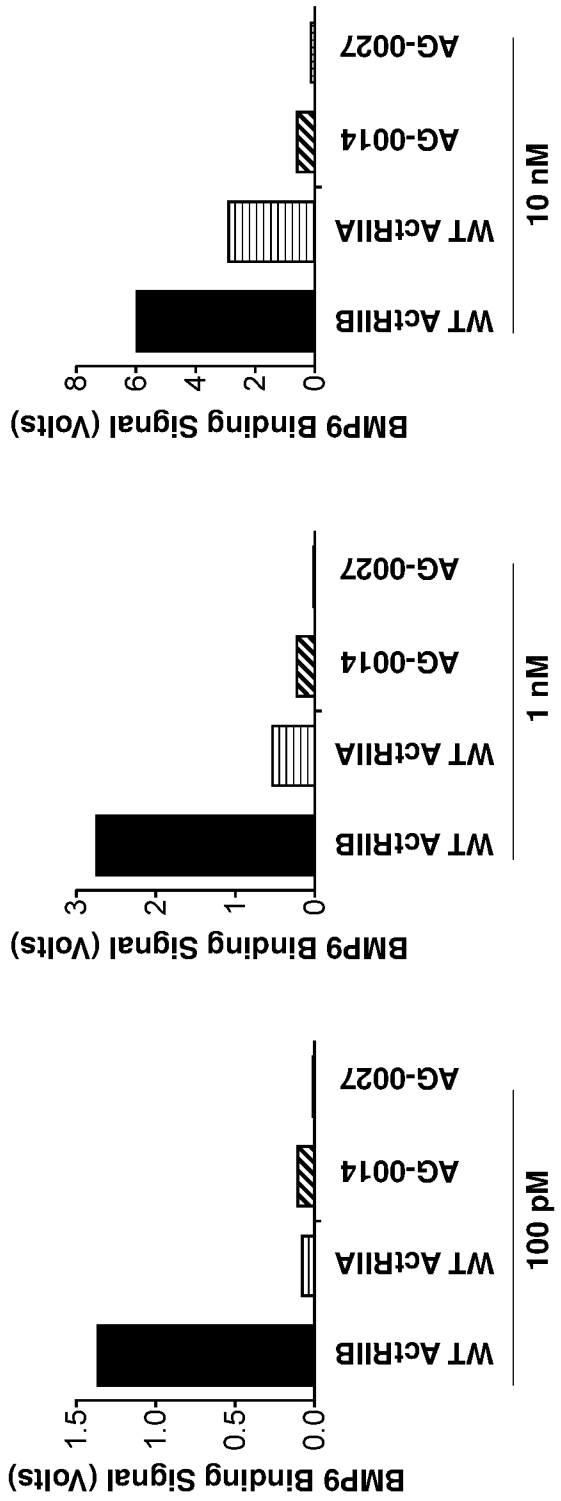

BMP9 Binding Signal (Volts)
0.0
0.5
1.0
1.5
100 pM
WT ActRIIB
WT ActRIIA
AG-0014
AG-0027
BMP9 Binding Signal (Volts)
0
1
2
3
1 nM
WT ActRIIB
WT ActRIIA
AG-0014
AG-0027
BMP9 Binding Signal (Volts)
0
2
4
6
8
10 nM
WT ActRIIB
WT ActRIIA
AG-0014
AG-0027

FIG 12

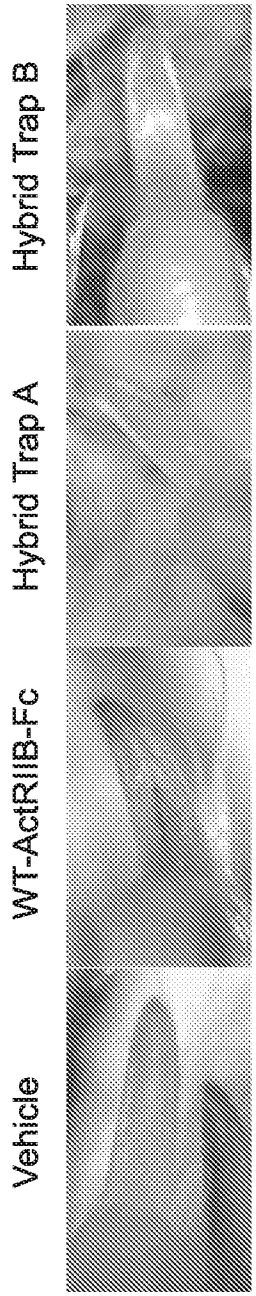


FIG 13

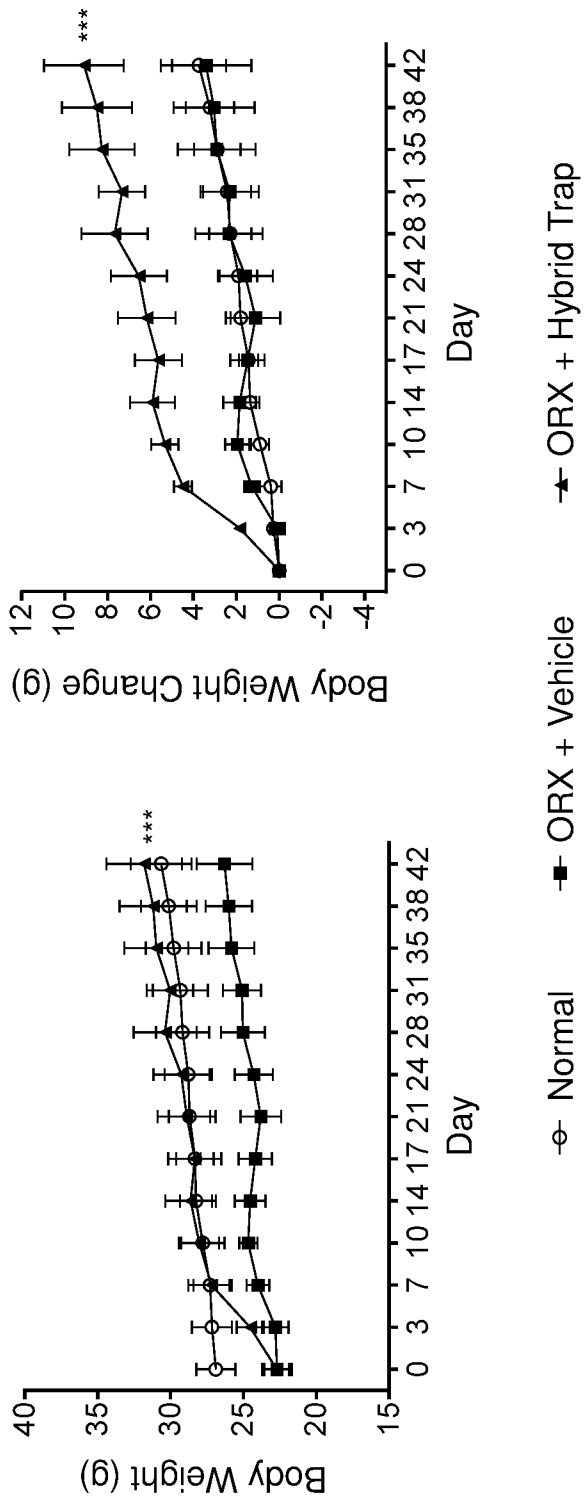

Body Weight (g)
40
35
30
25
20
15
0 3 7 10 14 17 21 24 28 31 35 38 42
Day
***
Body Weight Change (g)
12
10
8
6
4
2
0
-2
-4
0 3 7 10 14 17 21 24 28 31 35 38 42
Day
***
Normal
ORX + Vehicle
ORX + Hybrid Trap

FIG 14

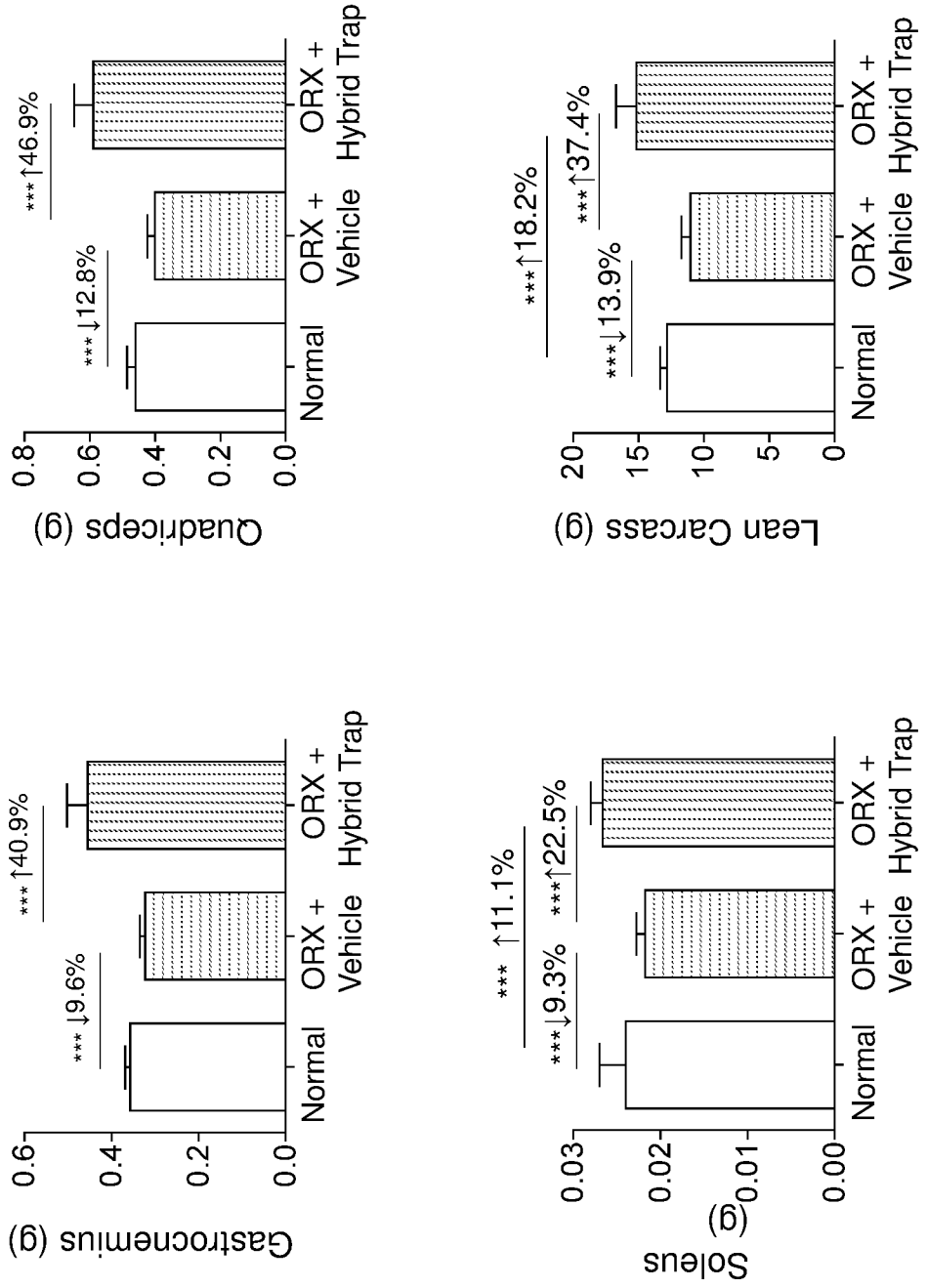

Quadriceps (g)
0.0
0.2
0.4
0.6
0.8
***↓12.8%
***↑46.9%
*** ↑28%
Normal
ORX + Vehicle
ORX + Hybrid Trap
Lean Carcass (g)
0
5
10
15
20
***↓13.9%
***↑37.4%
***↑18.2%
Normal
ORX + Vehicle
ORX + Hybrid Trap
Soleus (g)
0.00
0.01
0.02
0.03
***↓9.3%
***↑22.5%
*** ↑11.1%
Normal
ORX + Vehicle
ORX + Hybrid Trap
Gastrocnemius (g)
0.0
0.2
0.4
0.6
***↓9.6%
***↑40.9%
*** ↑27.4%
Normal
ORX + Vehicle
ORX + Hybrid Trap

FIG 15

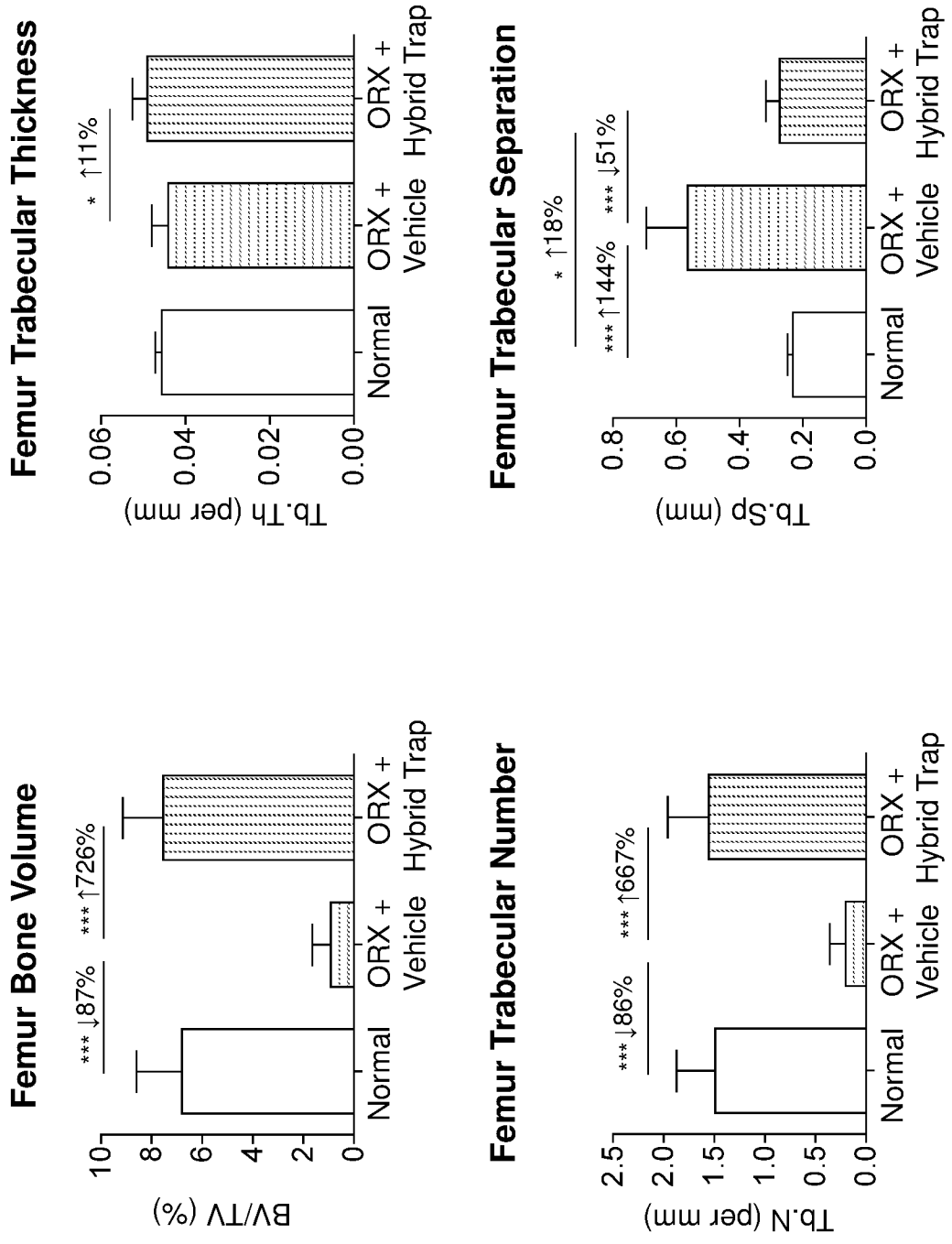

Femur Bone Volume
BV/TV (%)
*** ↓87%
*** ↑726%
Normal
ORX + Vehicle
ORX + Hybrid Trap
Femur Trabecular Thickness
Tb.Th (per mm)
* ↑11%
Femur Trabecular Number
Tb.N (per mm)
*** ↓86%
*** ↑667%
Femur Trabecular Separation
Tb.Sp (mm)
* ↑18%
*** ↑144%
*** ↓51%

FIG 16

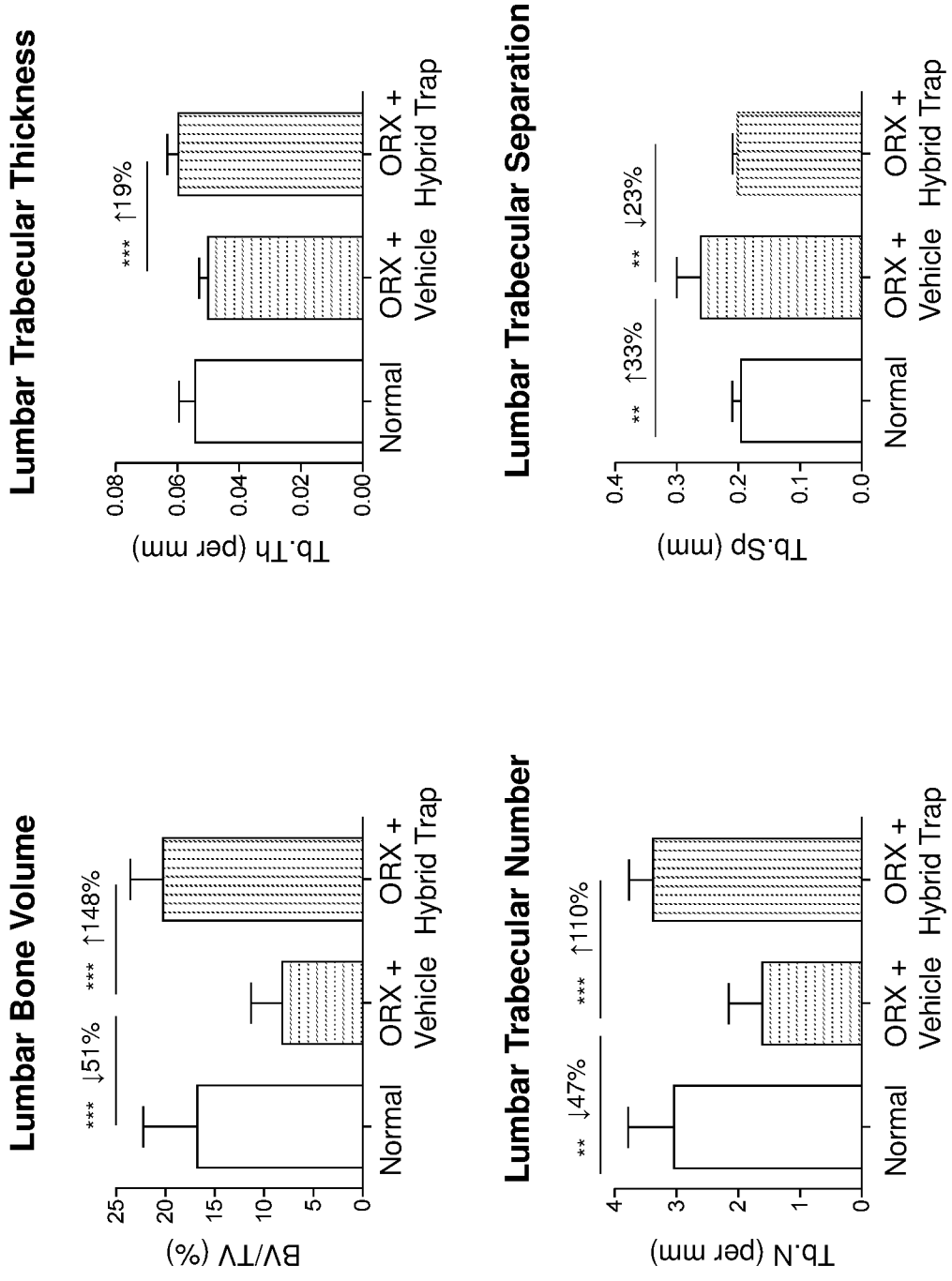

Lumbar Bone Volume
*** ↓51%
*** ↑148%
BV/TV (%)
0
5
10
15
20
25
Normal
ORX + Vehicle
ORX + Hybrid Trap
Lumbar Trabecular Thickness
*** ↑19%
Tb.Th (per mm)
0.00
0.02
0.04
0.06
0.08
Normal
ORX + Vehicle
ORX + Hybrid Trap
Lumbar Trabecular Number
** ↓47%
*** ↑110%
Tb.N (per mm)
0
1
2
3
4
Normal
ORX + Vehicle
ORX + Hybrid Trap
Lumbar Trabecular Separation
** ↑33%
** ↓23%
Tb.Sp (mm)
0.0
0.1
0.2
0.3
0.4
Normal
ORX + Vehicle
ORX + Hybrid Trap

FIG 17

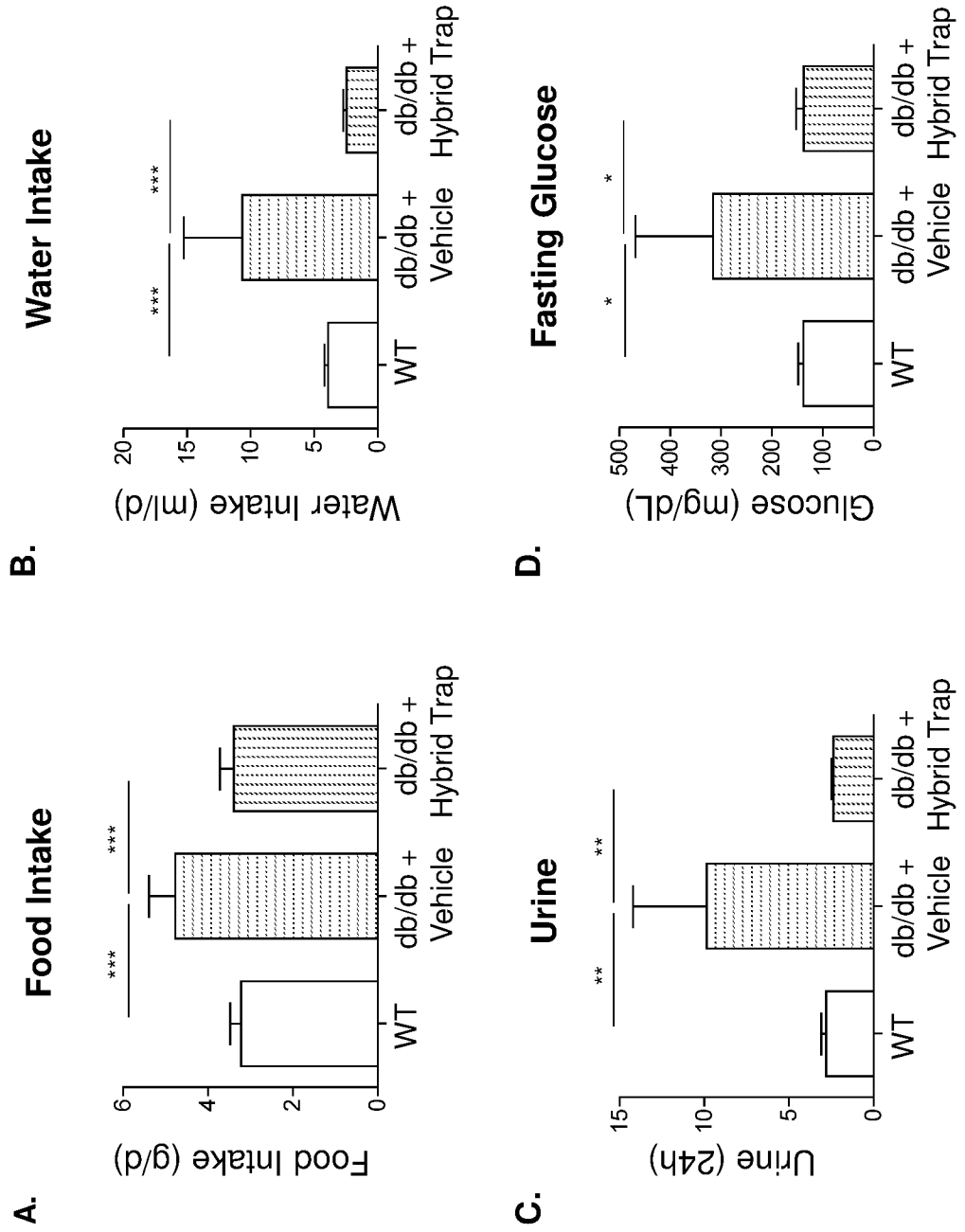

A.
Food Intake
Food Intake (g/d)
0
2
4
6
***
***
WT
db/db + Vehicle
db/db + Hybrid Trap
B.
Water Intake
Water Intake (ml/d)
0
5
10
15
20
***
***
WT
db/db + Vehicle
db/db + Hybrid Trap
C.
Urine
Urine (24h)
0
5
10
15
**
**
WT
db/db + Vehicle
db/db + Hybrid Trap
D.
Fasting Glucose
Glucose (mg/dL)
0
100
200
300
400
500
*
*
WT
db/db + Vehicle
db/db + Hybrid Trap

FIG 18

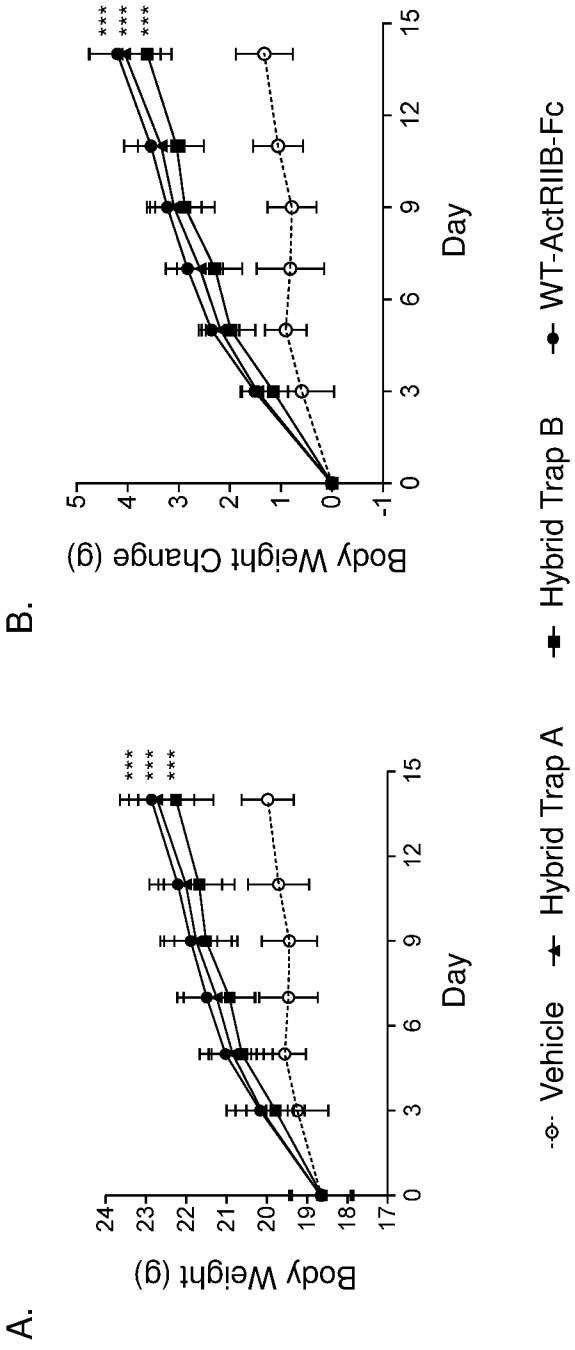

A.
Body Weight (g)
24
23
22
21
20
19
18
17
0
3
6
9
12
15
Day
***
***
***
B.
Body Weight Change (g)
5
4
3
2
1
0
-1
0
3
6
9
12
15
Day
***
***
***
Vehicle
Hybrid Trap A
Hybrid Trap B
WT-ActRIIB-Fc

FIG 19

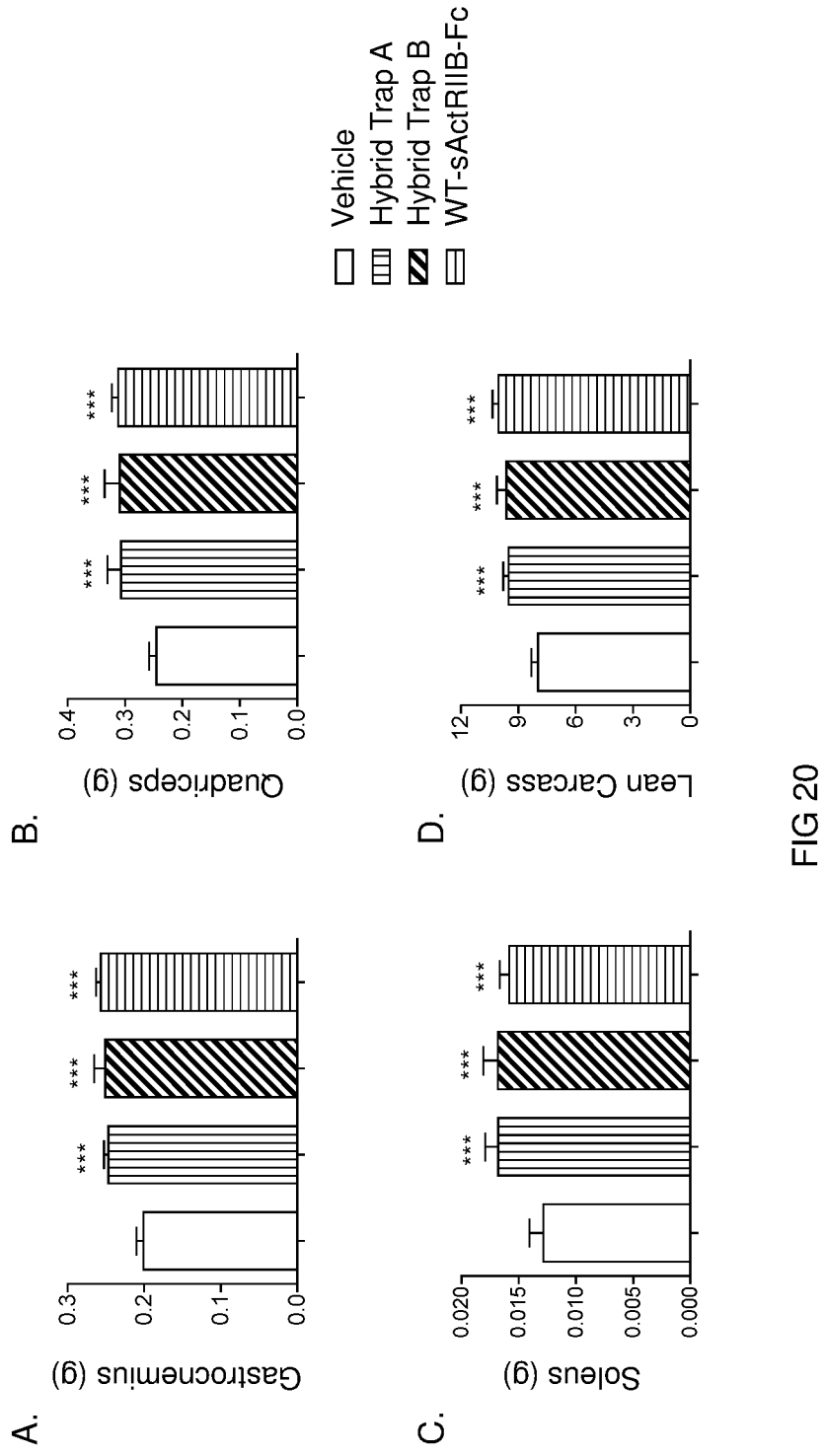

Vehicle
Hybrid Trap A
Hybrid Trap B
WT-sActRIIB-Fc
A.
Gastrocnemius (g)
0.3
0.2
0.1
0.0
***
B.
Quadriceps (g)
0.4
0.3
0.2
0.1
0.0
C.
Soleus (g)
0.020
0.015
0.010
0.005
0.000
D.
Lean Carcass (g)
12
9
6
3
0

FIG 20

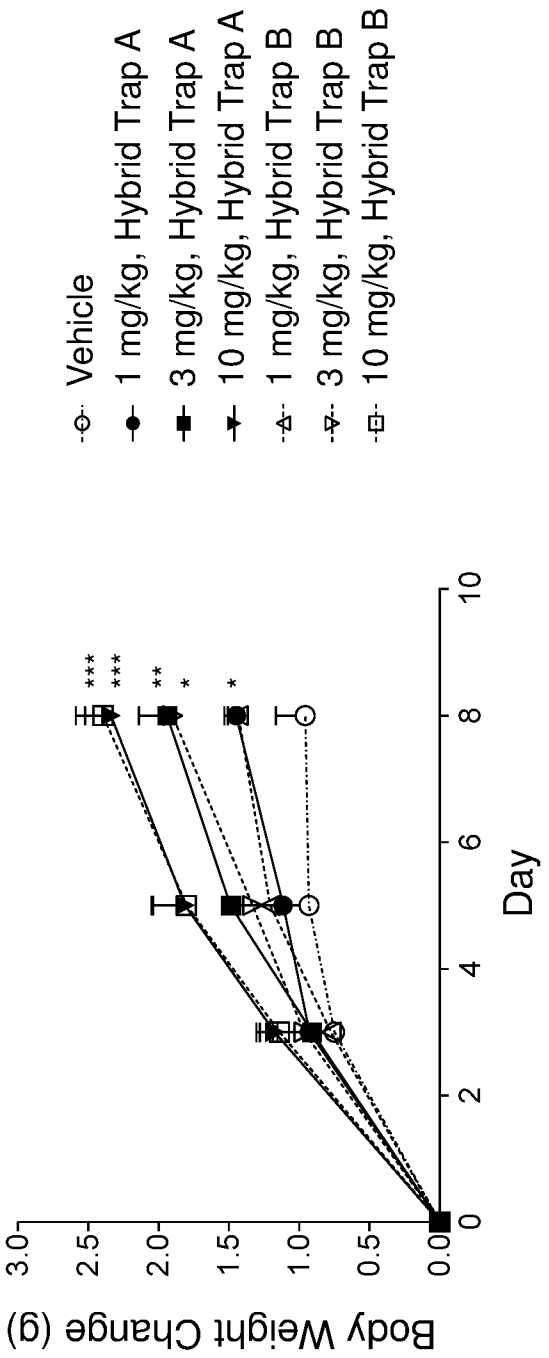

Vehicle
1 mg/kg, Hybrid Trap A
3 mg/kg, Hybrid Trap A
10 mg/kg, Hybrid Trap A
1 mg/kg, Hybrid Trap B
3 mg/kg, Hybrid Trap B
10 mg/kg, Hybrid Trap B
Body Weight Change (g)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
2
4
6
8
10
Day
***
***
**
*
*
*

FIG 21

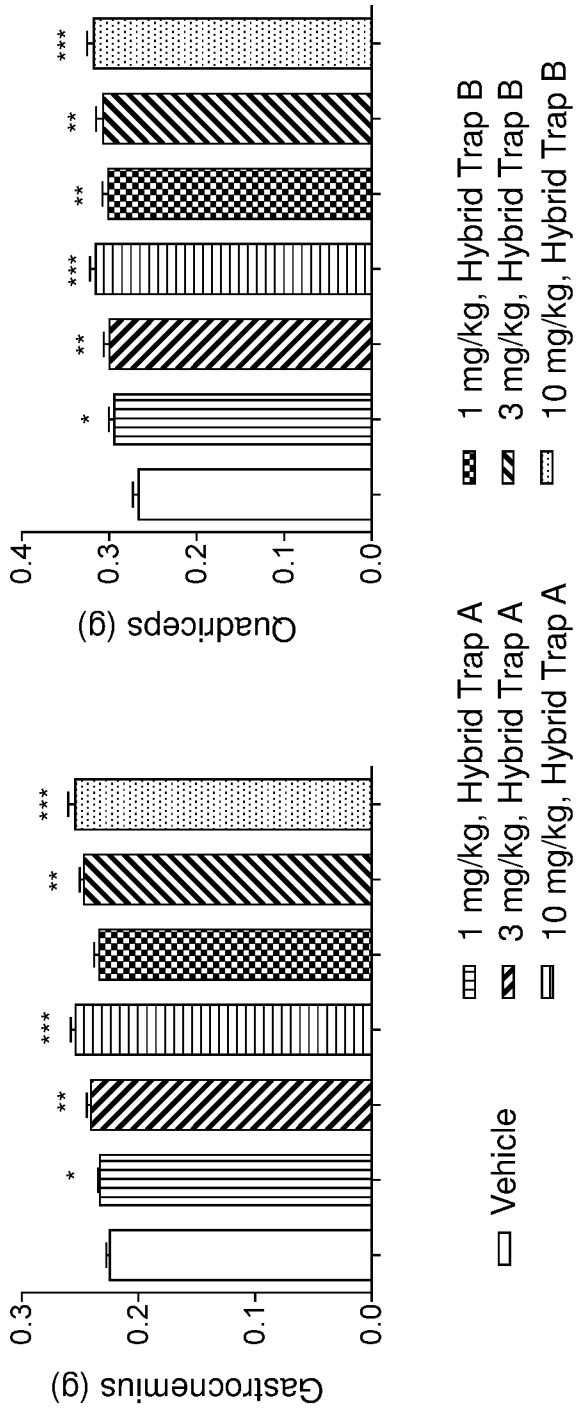

Gastrocnemius (g)
0.0
0.1
0.2
0.3
*
**
***
Quadriceps (g)
0.0
0.1
0.2
0.3
0.4
Vehicle
1 mg/kg, Hybrid Trap A
3 mg/kg, Hybrid Trap A
10 mg/kg, Hybrid Trap A
1 mg/kg, Hybrid Trap B
3 mg/kg, Hybrid Trap B
10 mg/kg, Hybrid Trap B

FIG 22

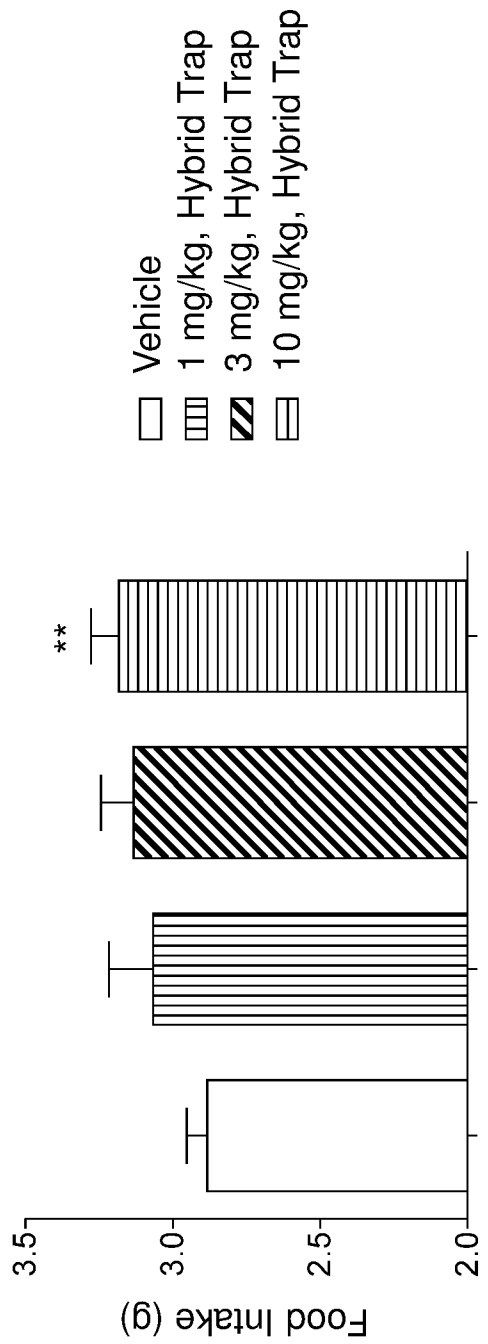

Vehicle
1 mg/kg, Hybrid Trap
3 mg/kg, Hybrid Trap
10 mg/kg, Hybrid Trap
**
Food Intake (g)
3.5
3.0
2.5
2.0

FIG 23

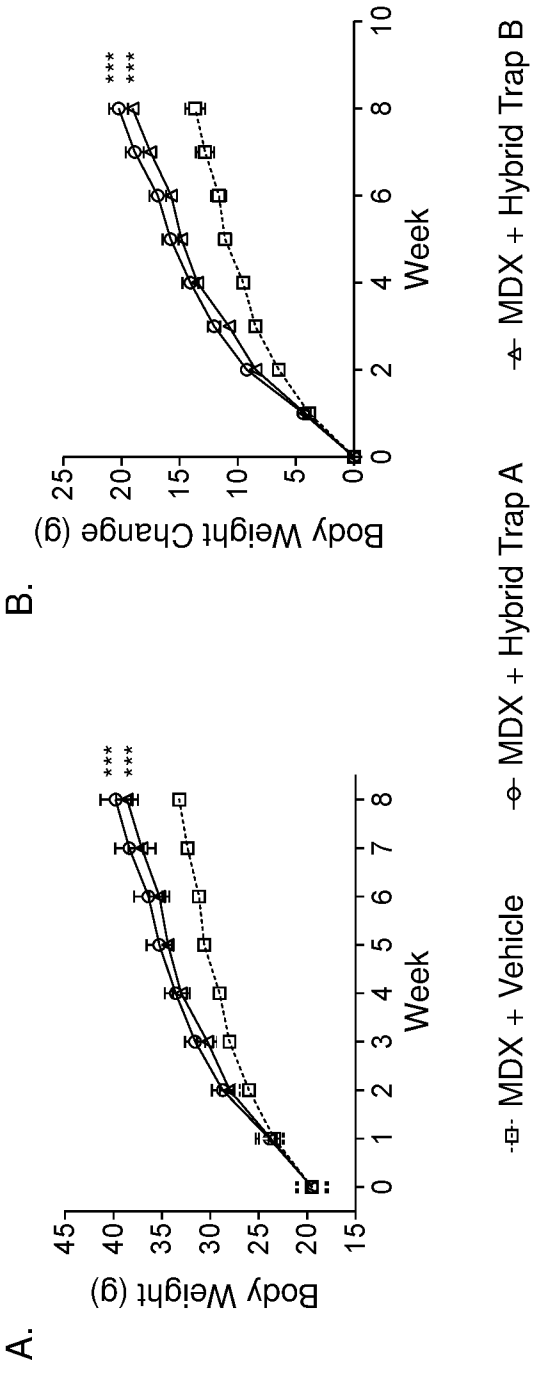

A.
Body Weight (g)
45
40
35
30
25
20
15
0 1 2 3 4 5 6 7 8
Week
***
***
B.
Body Weight Change (g)
25
20
15
10
5
0
0 2 4 6 8 10
Week
***
***
MDX + Vehicle
MDX + Hybrid Trap A
MDX + Hybrid Trap B

FIG 24

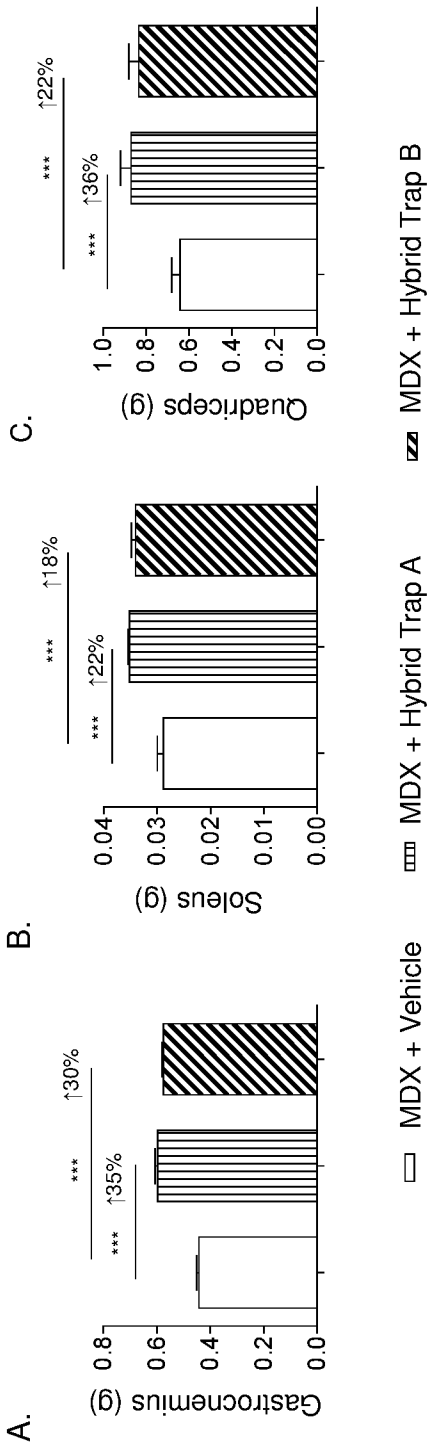

A.
Gastrocnemius (g)
0.0
0.2
0.4
0.6
0.8
***
↑35%
***
↑30%
B.
Soleus (g)
0.00
0.01
0.02
0.03
0.04
***
↑22%
***
↑18%
C.
Quadriceps (g)
0.0
0.2
0.4
0.6
0.8
1.0
***
↑36%
***
↑22%
MDX + Vehicle
MDX + Hybrid Trap A
MDX + Hybrid Trap B

FIG 25

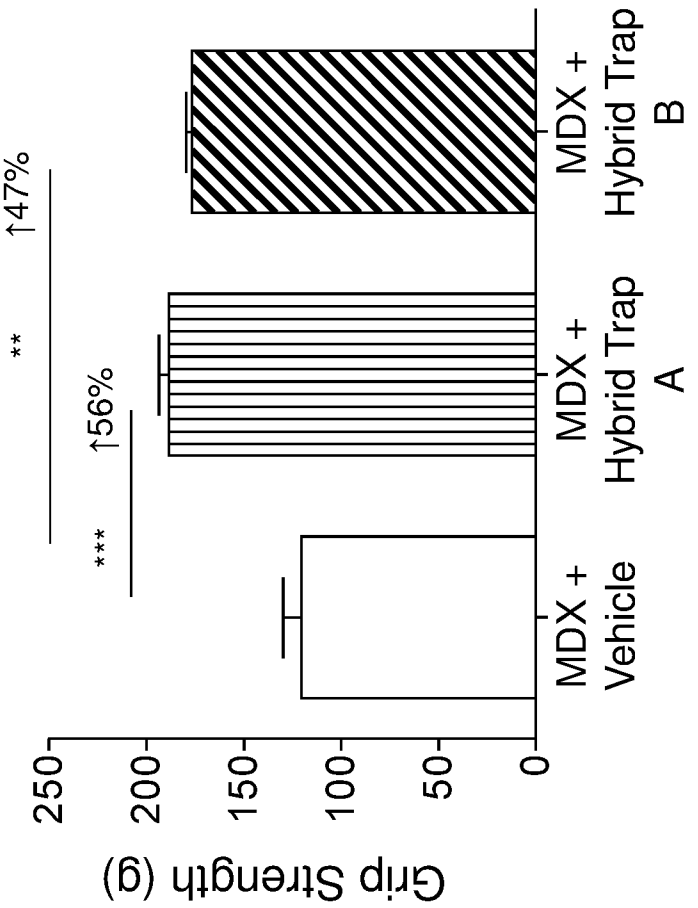

Grip Strength (g)
250
200
150
100
50
0
***
↑56%
**
↑47%
MDX + Vehicle
MDX + Hybrid Trap A
MDX + Hybrid Trap B

FIG 26

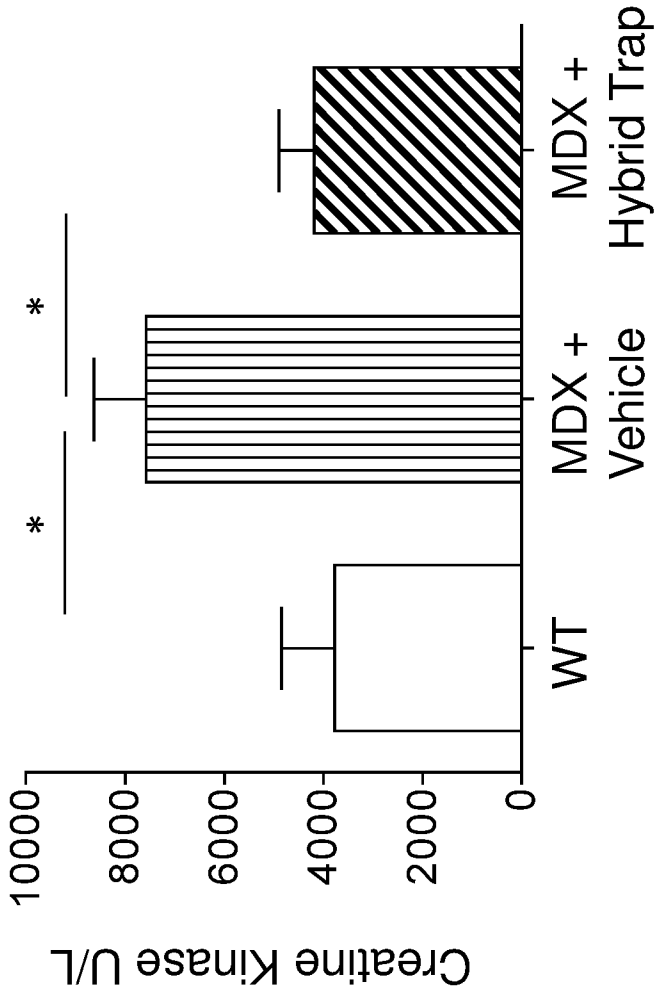

Creatine Kinase U/L
10000
8000
6000
4000
2000
0
*
*
WT
MDX + Vehicle
MDX + Hybrid Trap

FIG 27

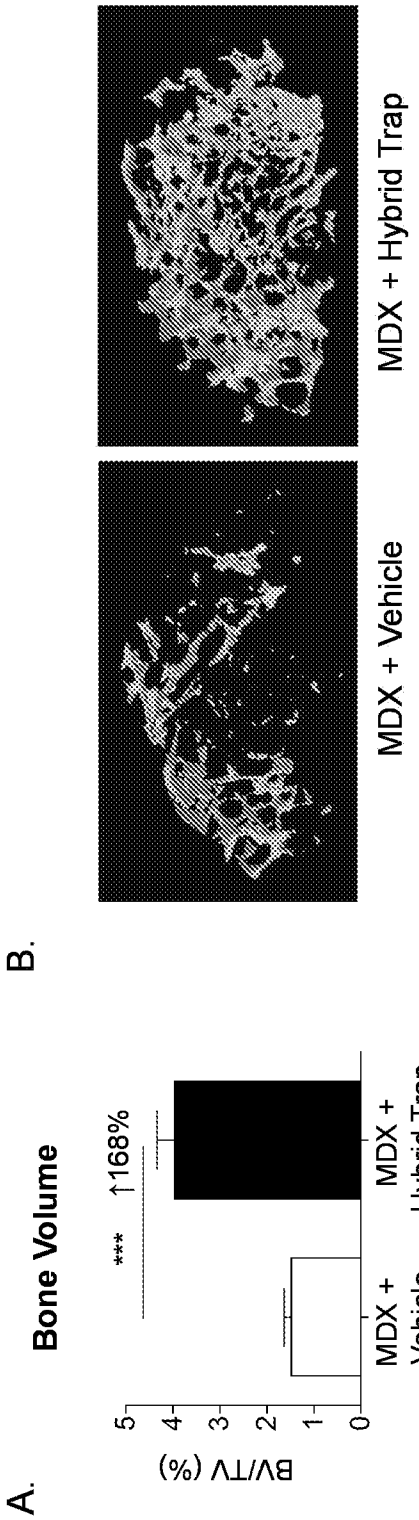

A.
Bone Volume
BV/TV (%)
0
1
2
3
4
5
***
↑168%
MDX + Vehicle
MDX + Hybrid Trap
B.
MDX + Vehicle
MDX + Hybrid Trap

FIG 28

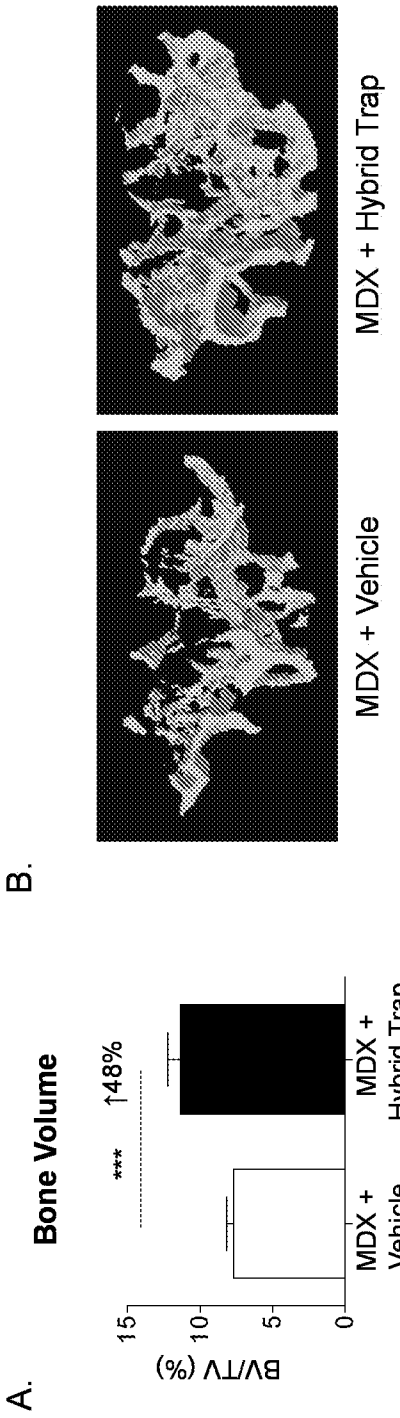

A.
Bone Volume
***
↑48%
BV/TV (%)
15
10
5
0
MDX + Vehicle
MDX + Hybrid Trap
B.
MDX + Vehicle
MDX + Hybrid Trap

FIG 29

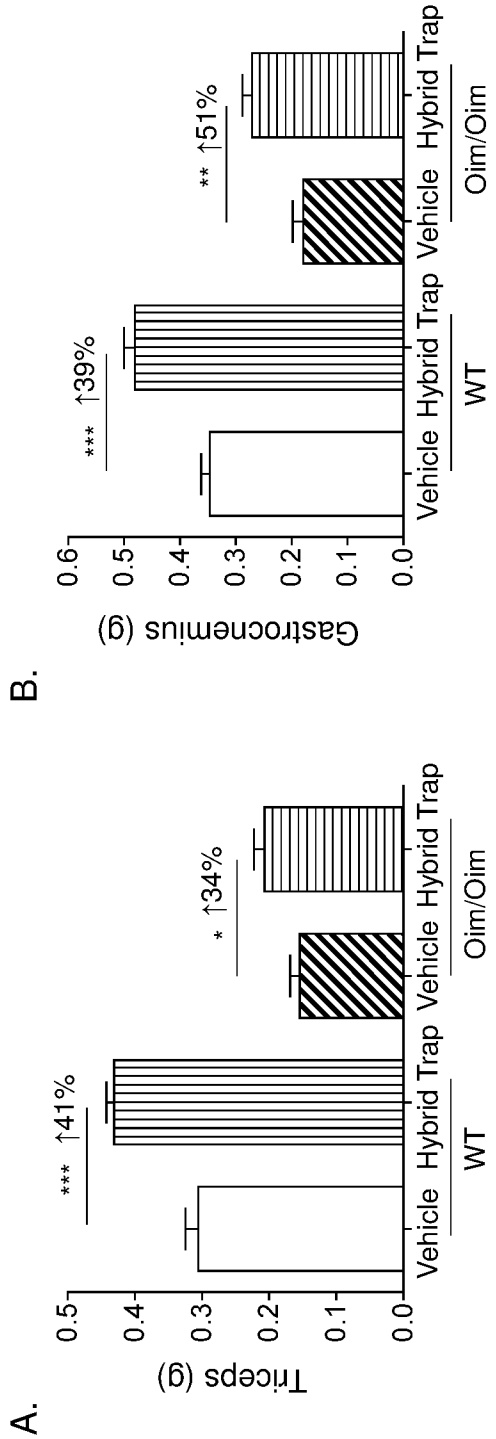

A.
Triceps (g)
0.0
0.1
0.2
0.3
0.4
0.5
*** ↑41%
* ↑34%
Vehicle
Hybrid Trap
Vehicle
Hybrid Trap
WT
Oim/Oim
B.
Gastrocnemius (g)
0.0
0.1
0.2
0.3
0.4
0.5
0.6
*** ↑39%
** ↑51%
Vehicle
Hybrid Trap
Vehicle
Hybrid Trap
WT
Oim/Oim

FIG 30

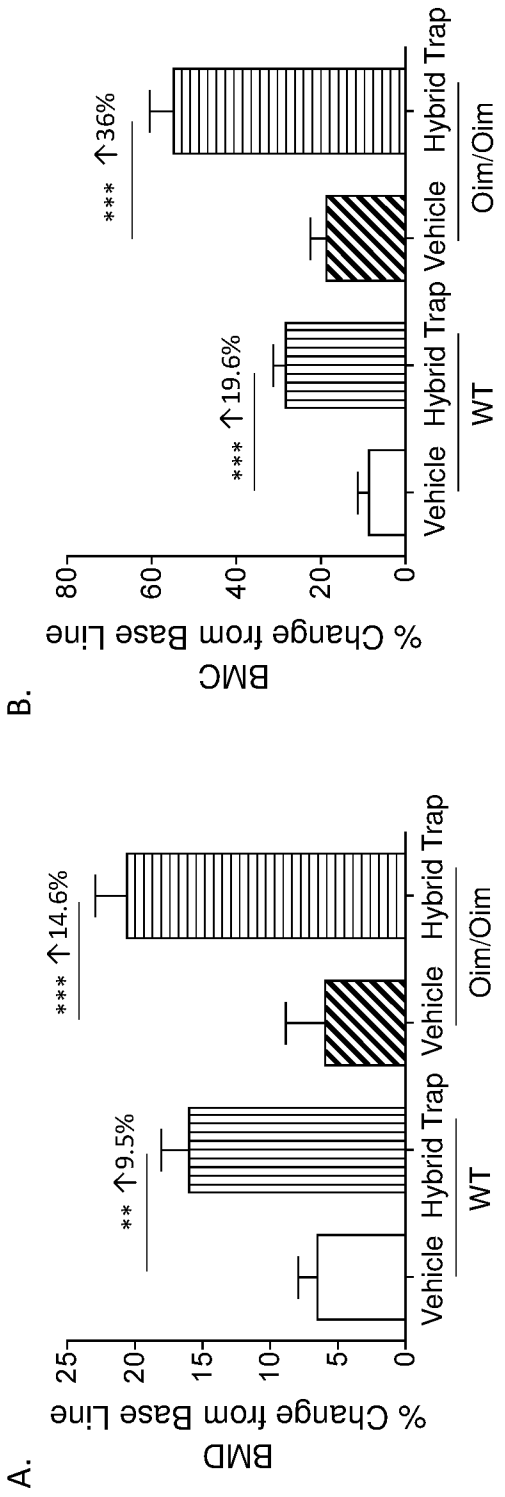

A.
BMD
% Change from Base Line
25
20
15
10
5
0
** ↑9.5%
*** ↑14.6%
Vehicle
Hybrid Trap
Vehicle
Hybrid Trap
WT
Oim/Oim
B.
BMC
% Change from Base Line
80
60
40
20
0
*** ↑19.6%
*** ↑36%
Vehicle
Hybrid Trap
Vehicle
Hybrid Trap
WT
Oim/Oim

FIG 31

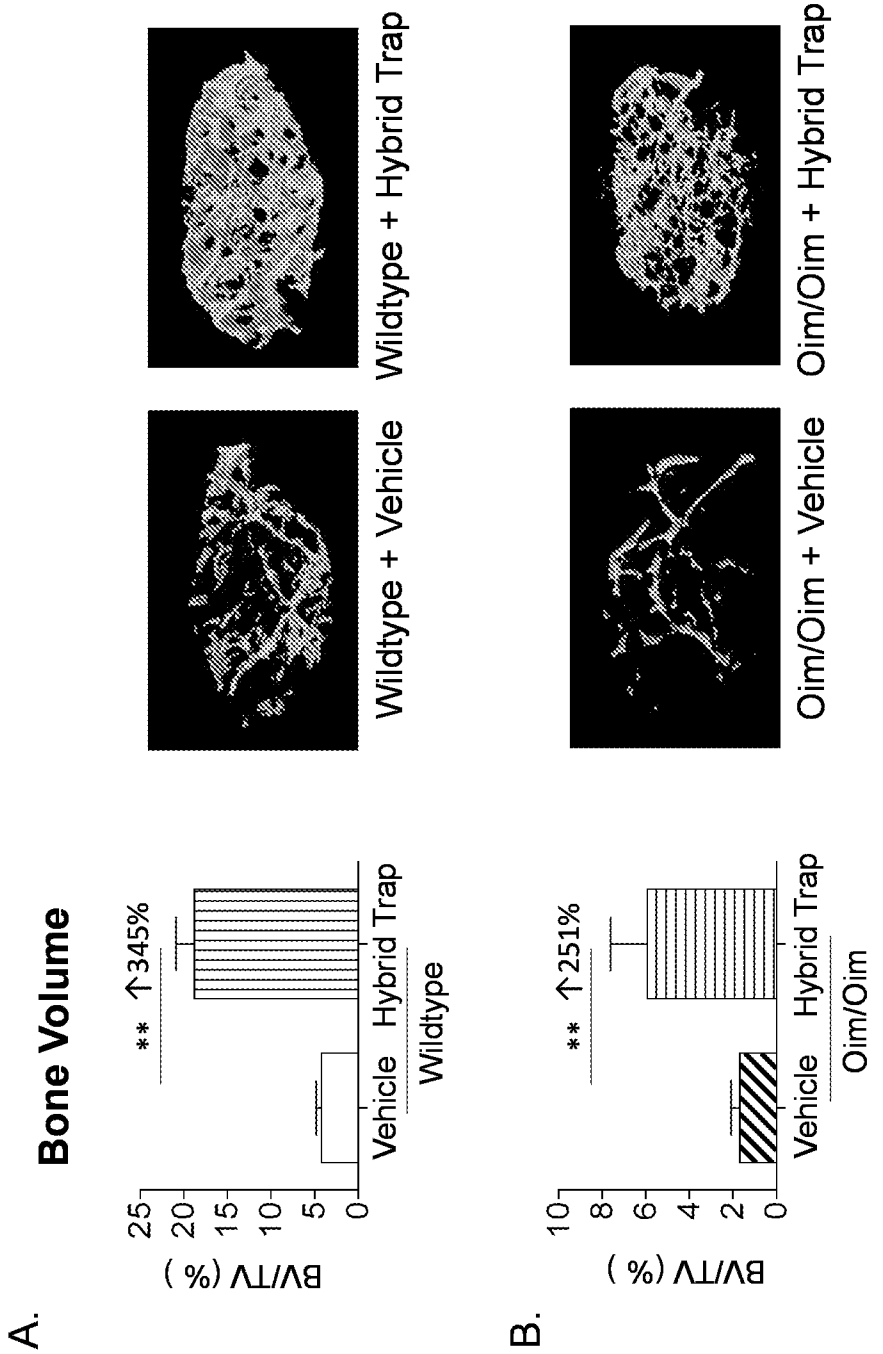

A.
Bone Volume
** ↑345%
BV/TV (%)
25
20
15
10
5
0
Vehicle
Hybrid Trap
Wildtype
Wildtype + Vehicle
Wildtype + Hybrid Trap
B.
** ↑251%
BV/TV (%)
10
8
6
4
2
0
Vehicle
Hybrid Trap
Oim/Oim
Oim/Oim + Vehicle
Oim/Oim + Hybrid Trap

FIG 32

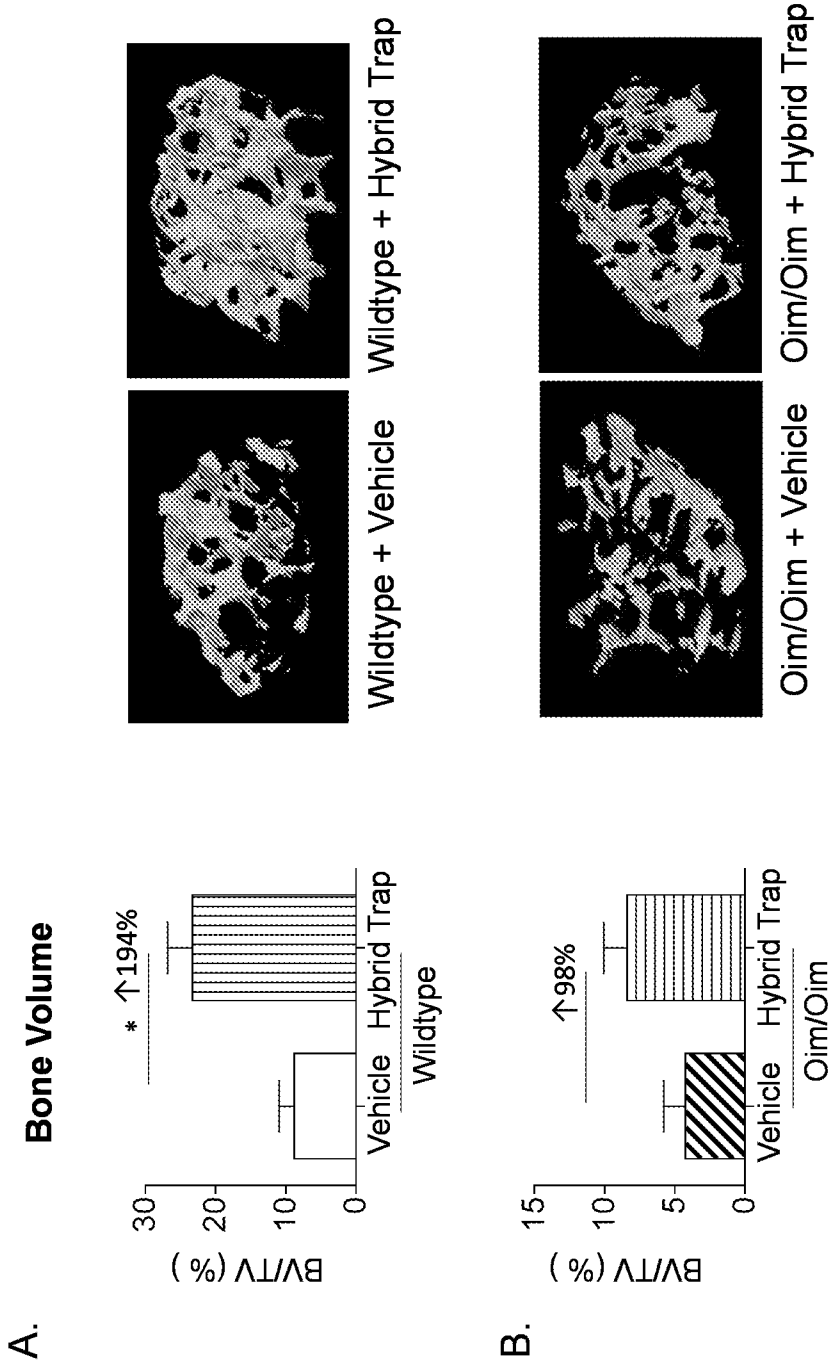
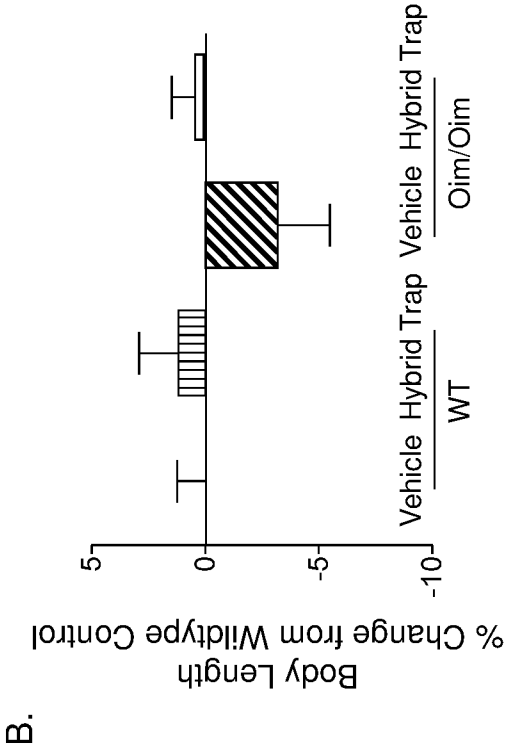

A.
Bone Volume
* ↑194%
BV/TV (%)
30
20
10
0
Vehicle
Hybrid Trap
Wildtype
B.
↑98%
BV/TV (%)
15
10
5
0
Vehicle
Hybrid Trap
Oim/Oim
Wildtype + Vehicle
Wildtype + Hybrid Trap
Oim/Oim + Vehicle
Oim/Oim + Hybrid Trap

FIG 33


B.
Body Length
% Change from Wildtype Control
5
0
-5
-10
Vehicle
Hybrid Trap
WT
Vehicle
Hybrid Trap
Oim/Oim

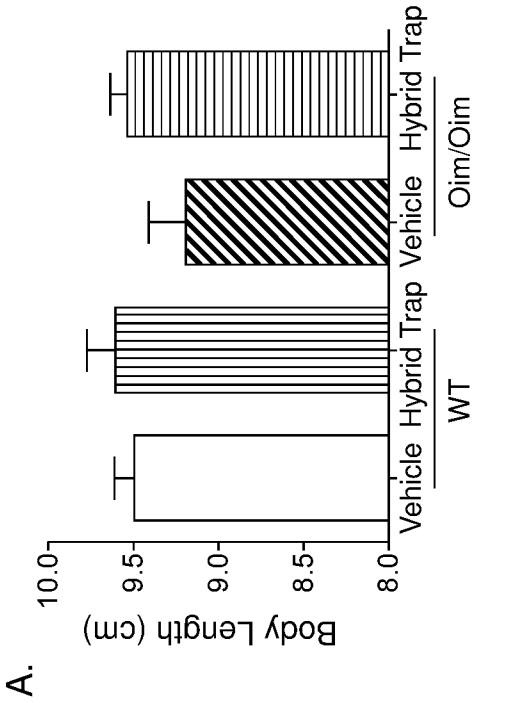

A.
Body Length (cm)
10.0
9.5
9.0
8.5
8.0
Vehicle
Hybrid Trap
WT
Vehicle
Hybrid Trap
Oim/Oim

FIG 34

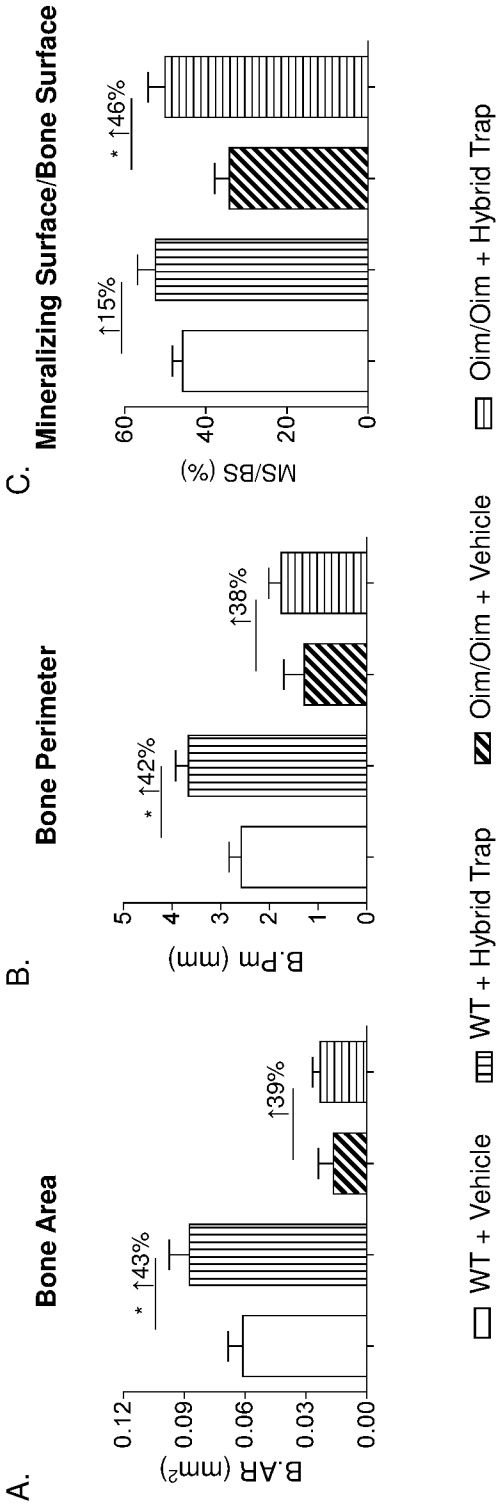

A.
Bone Area
B.Ar (mm²)
0.12
0.09
0.06
0.03
0.00
* ↑43%
↑39%
B.
Bone Perimeter
B.Pm (mm)
5
4
3
2
1
0
* ↑42%
↑38%
C.
Mineralizing Surface/Bone Surface
MS/BS (%)
60
40
20
0
↑15%
* ↑46%
WT + Vehicle
WT + Hybrid Trap
Oim/Oim + Vehicle
Oim/Oim + Hybrid Trap

FIG 35

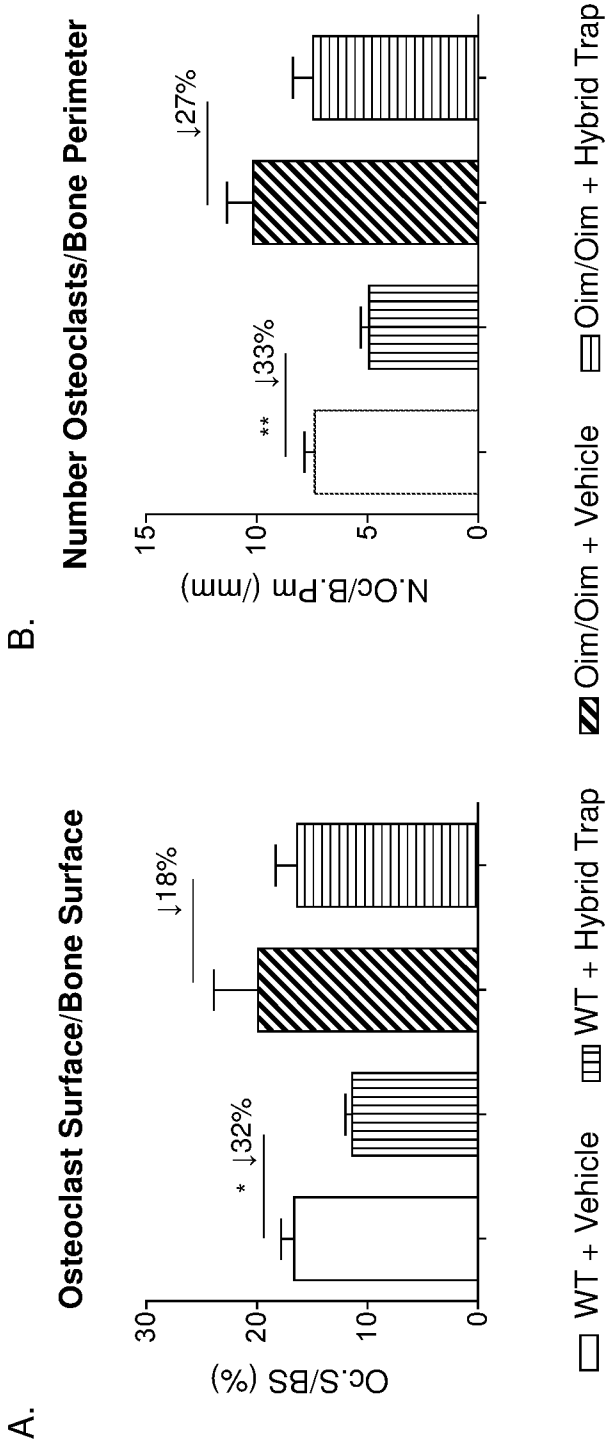

A.
Osteoclast Surface/Bone Surface
Oc.S/BS (%)
30
20
10
0
* ↓32%
↓18%
B.
Number Osteoclasts/Bone Perimeter
N.Oc/B.Pm (/mm)
15
10
5
0
** ↓33%
↓27%
WT + Vehicle
WT + Hybrid Trap
Oim/Oim + Vehicle
Oim/Oim + Hybrid Trap

FIG 36