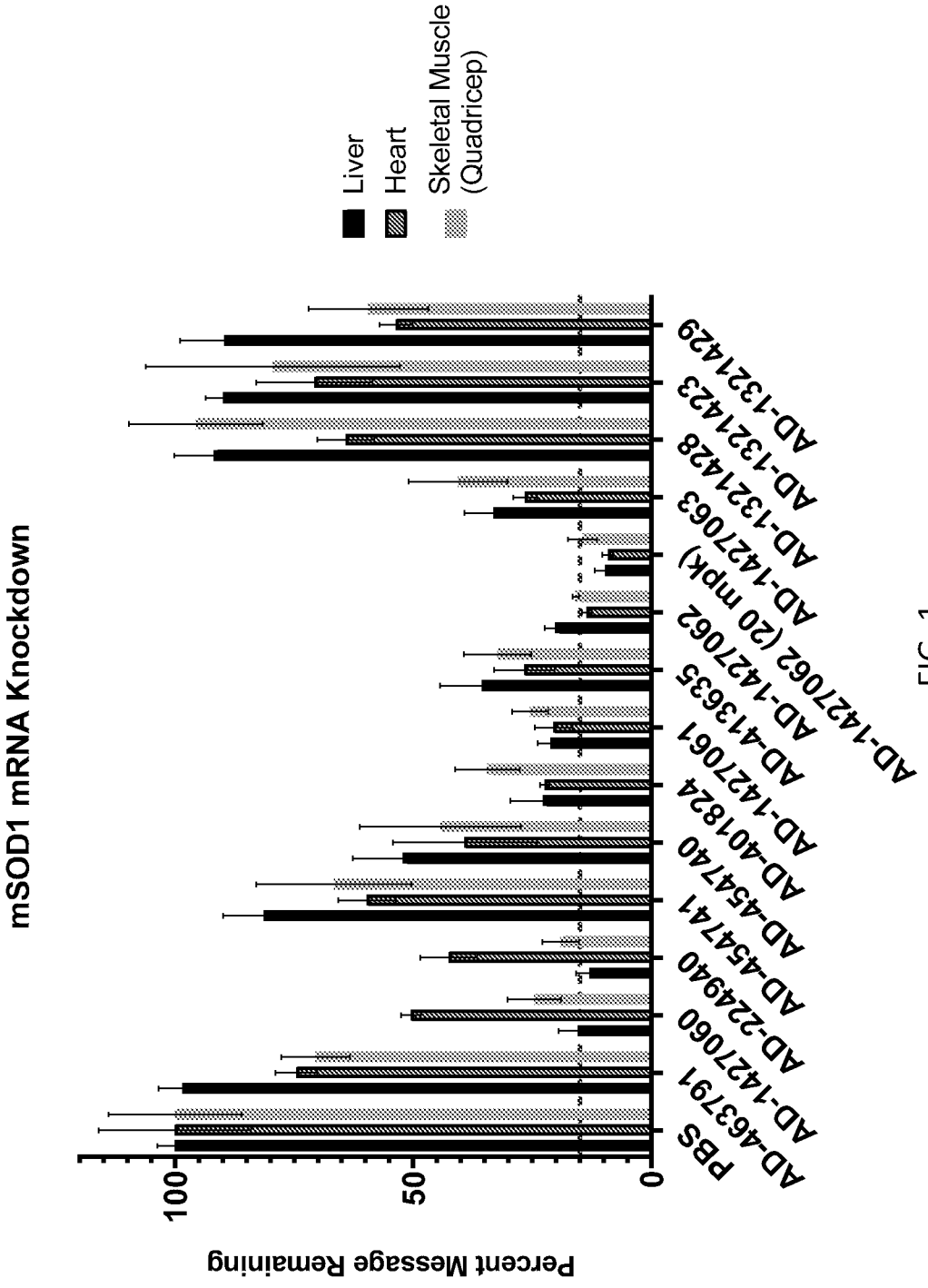

mSOD1 mRNA Knockdown
Liver
Heart
Skeletal Muscle (Quadricep)
Percent Message Remaining
100
50
0
PBS
AD-463791
AD-1427060
AD-2249040
AD-454741
AD-454740
AD-401824
AD-1427061
AD-413635
AD-1427062
AD-1427062 (20 mpk)
AD-1427063
AD-1321428
AD-1321423
AD-1321429

FIG. 1

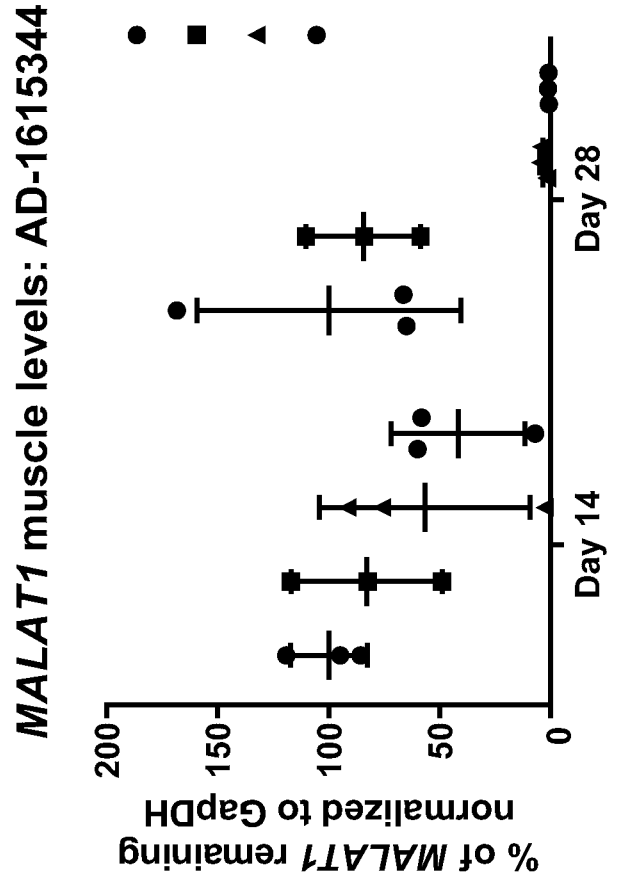

MALAT1 muscle levels: AD-1615344
PBS
1 mg/kg
5 mg/kg
20 mg/kg
% of MALAT1 remaining normalized to GapDH
200
150
100
50
0
Day 14
Day 28

FIG. 2A

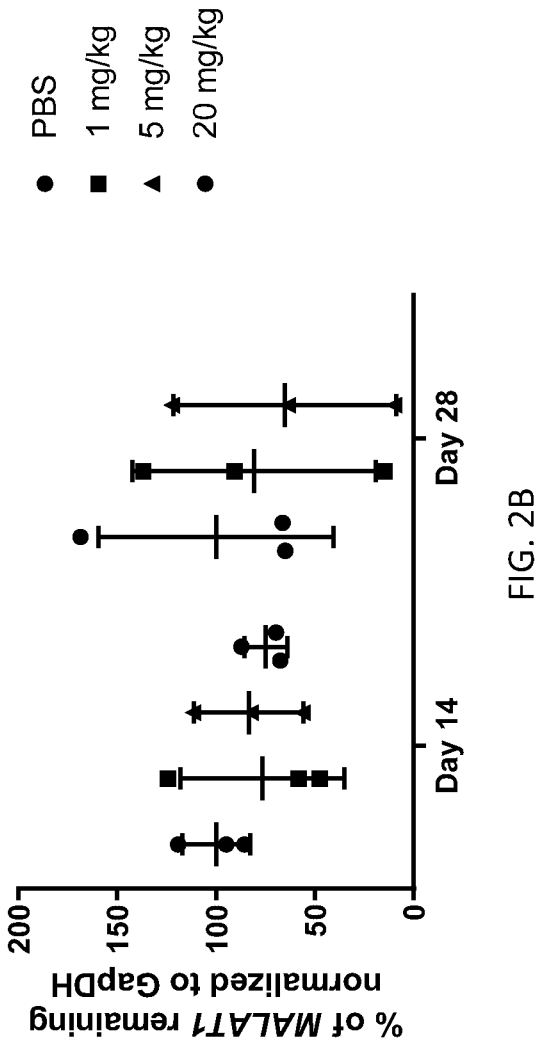

MALAT1 muscle levels: AD-1615345
PBS
1 mg/kg
5 mg/kg
20 mg/kg
% of MALAT1 remaining normalized to GapDH
200
150
100
50
0
Day 14
Day 28

FIG. 2B

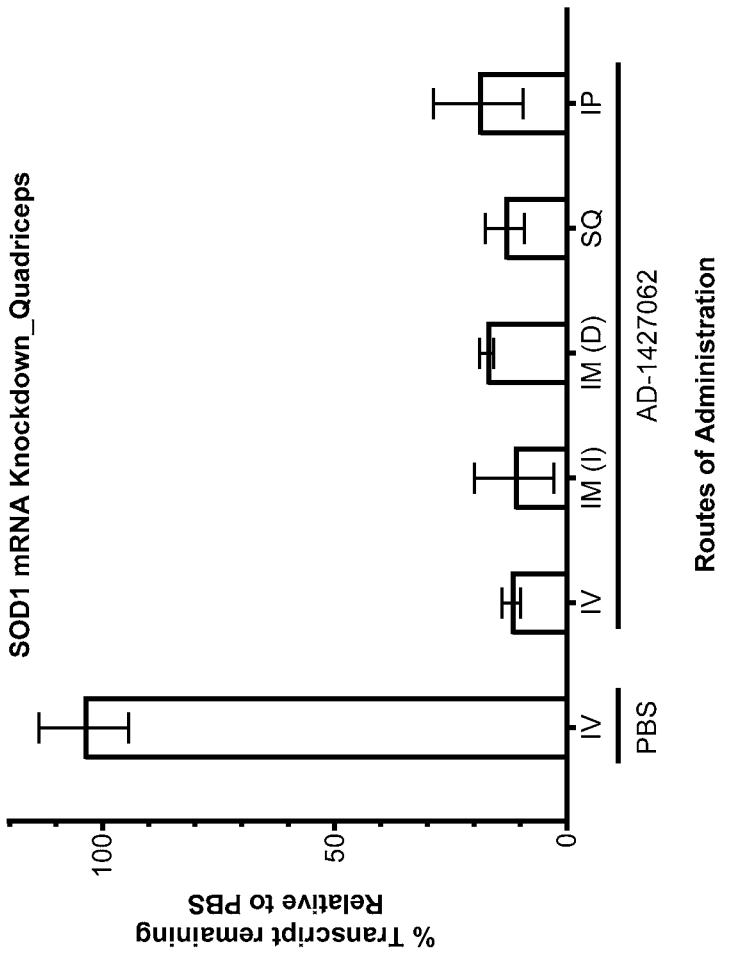

SOD1 mRNA Knockdown_Quadriceps
% Transcript remaining
Relative to PBS
100
50
0
PBS
IV
IV
IM (I)
IM (D)
SQ
IP
AD-1427062
Routes of Administration

FIG. 3A

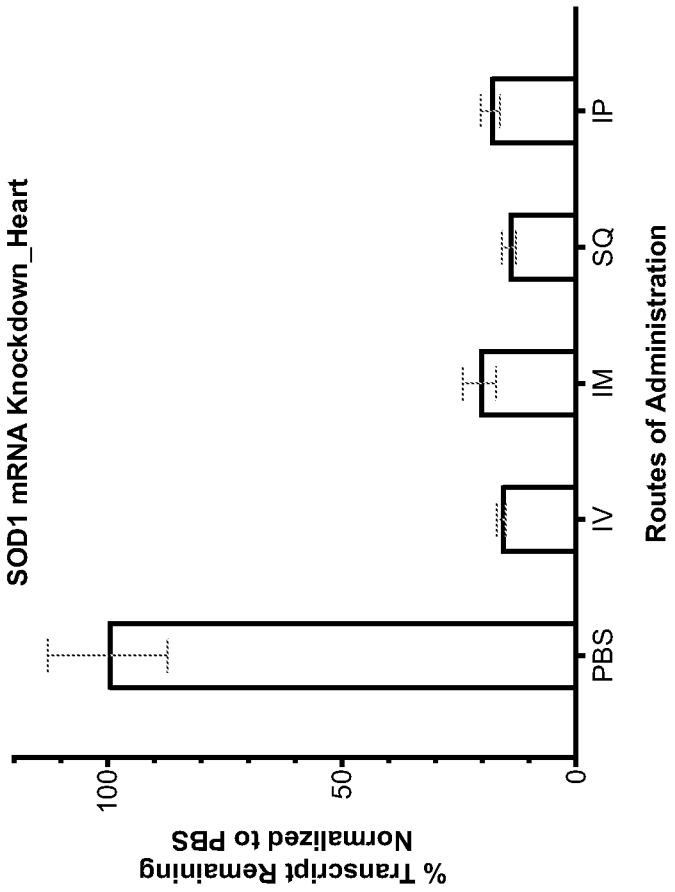

SOD1 mRNA Knockdown_Heart
% Transcript Remaining
Normalized to PBS
100
50
0
PBS
IV
IM
SQ
IP
Routes of Administration

FIG. 3B

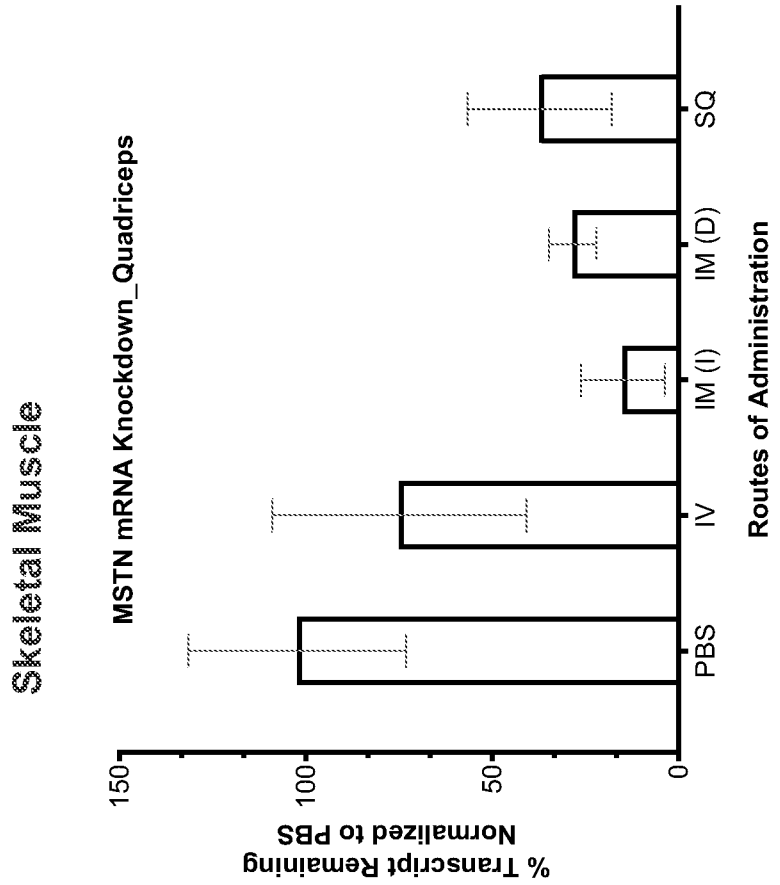


FIG. 3C

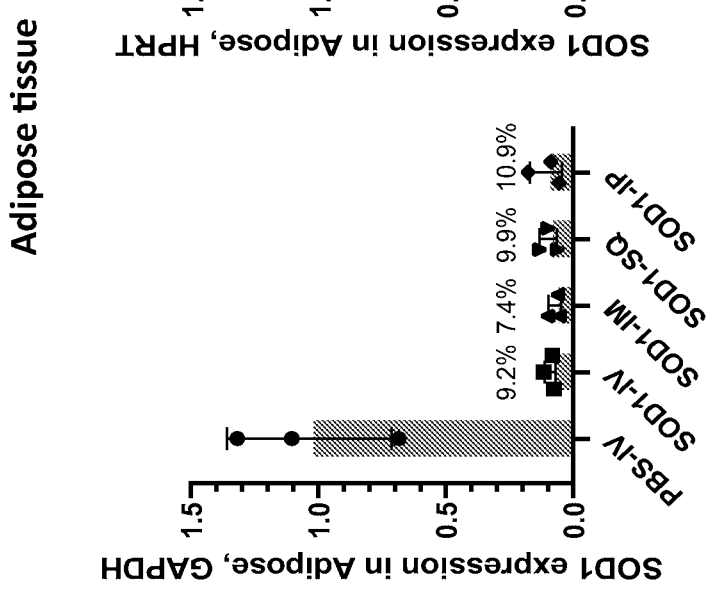


FIG. 3D

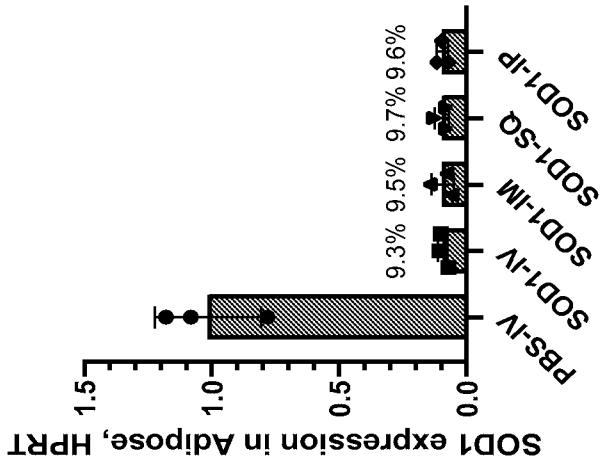


FIG. 3E

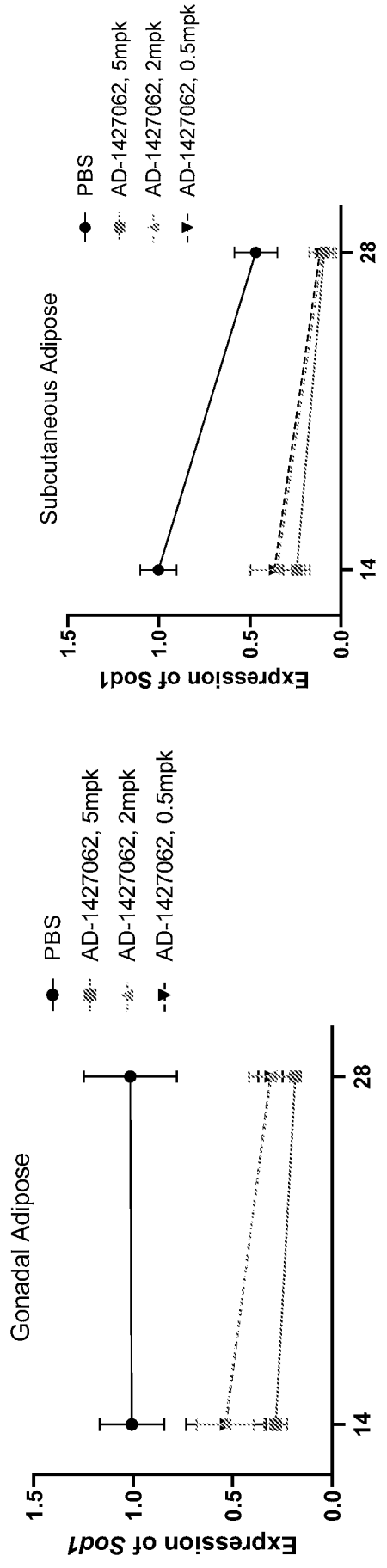


FIG. 4A

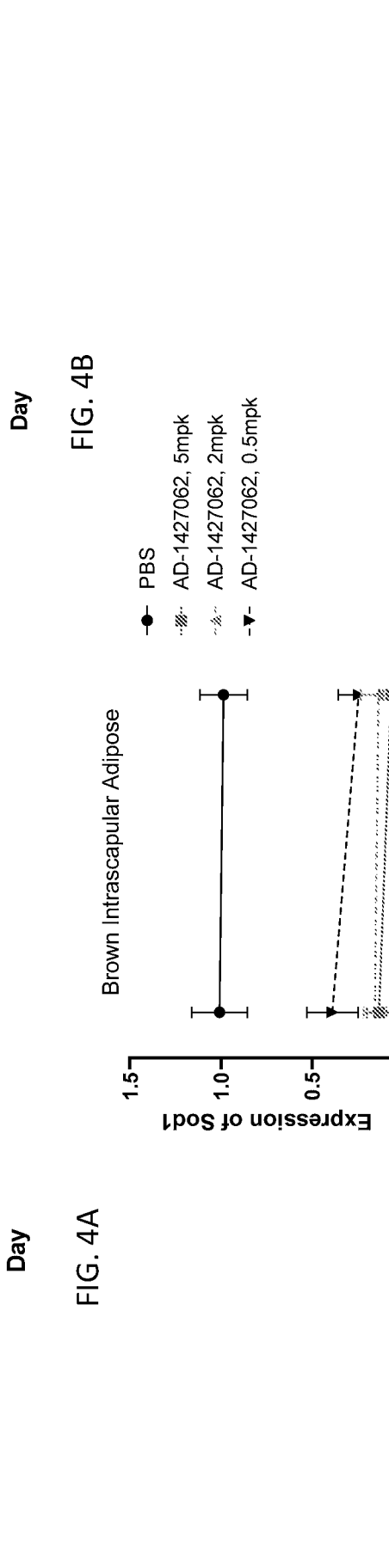


FIG. 4B

FIG. 4C

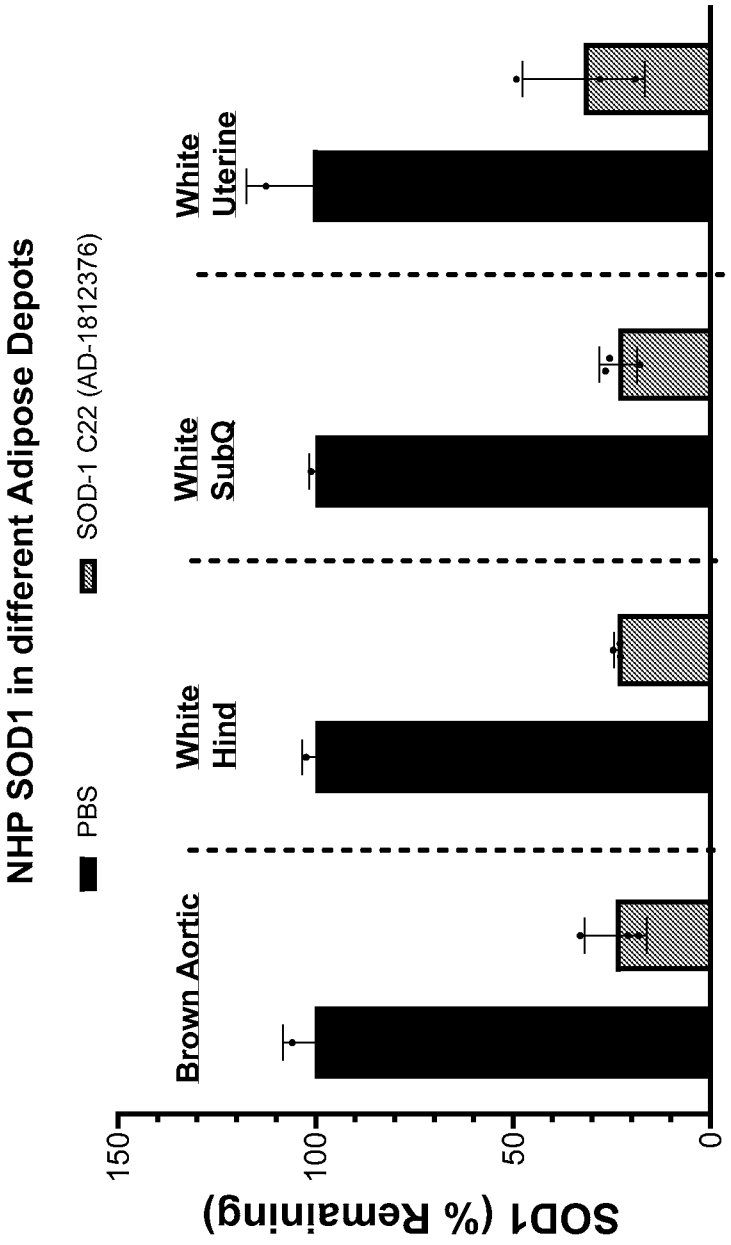

NHP SOD1 in different Adipose Depots
PBS
SOD-1 C22 (AD-1812376)
SOD1 (% Remaining)
150
100
50
0
Brown Aortic
White Hind
White SubQ
White Uterine

FIG. 5

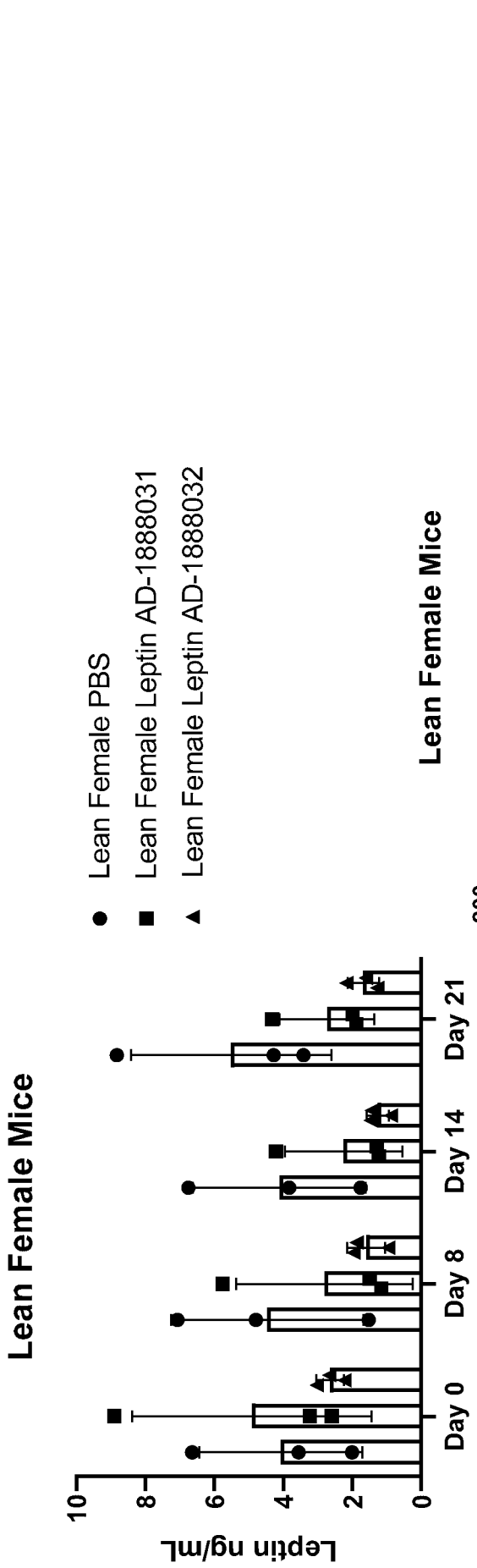

Lean Female Mice
Leptin ng/mL
0
2
4
6
8
10
Day 0
Day 8
Day 14
Day 21
Lean Female PBS
Lean Female Leptin AD-1888031
Lean Female Leptin AD-1888032

FIG. 6A

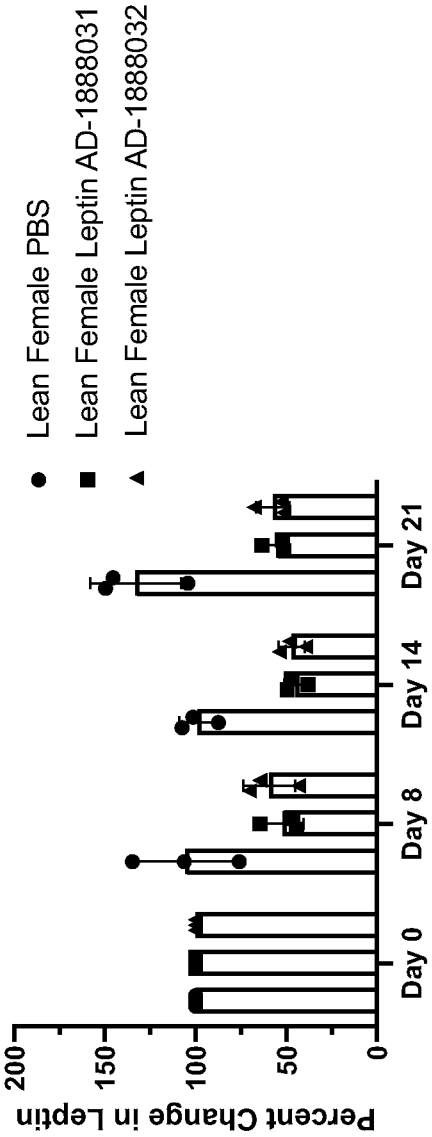

Lean Female Mice
Percent Change in Leptin
0
50
100
150
200
Day 0
Day 8
Day 14
Day 21
Lean Female PBS
Lean Female Leptin AD-1888031
Lean Female Leptin AD-1888032

FIG. 6B

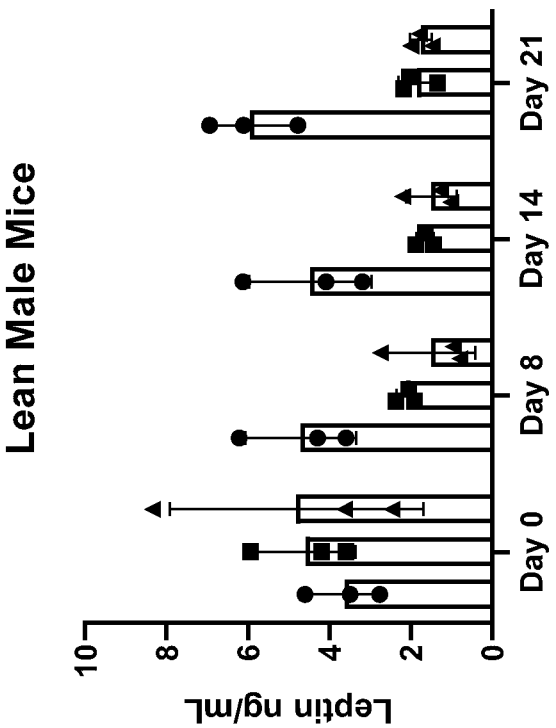

Lean Male Mice
Leptin ng/mL
0
2
4
6
8
10
Day 0
Day 8
Day 14
Day 21
Lean Male Leptin PBS
Lean Male Leptin AD-1888031
Lean Male Leptin AD-1888032

FIG. 7A

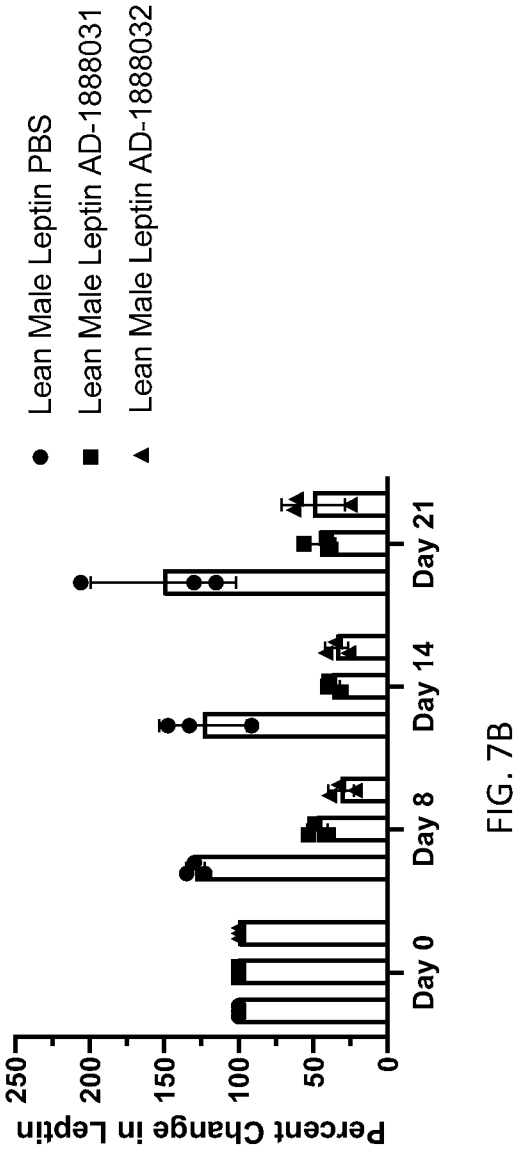

Lean Male Mice
Percent Change in Leptin
0
50
100
150
200
250
Day 0
Day 8
Day 14
Day 21
Lean Male Leptin PBS
Lean Male Leptin AD-1888031
Lean Male Leptin AD-1888032

FIG. 7B

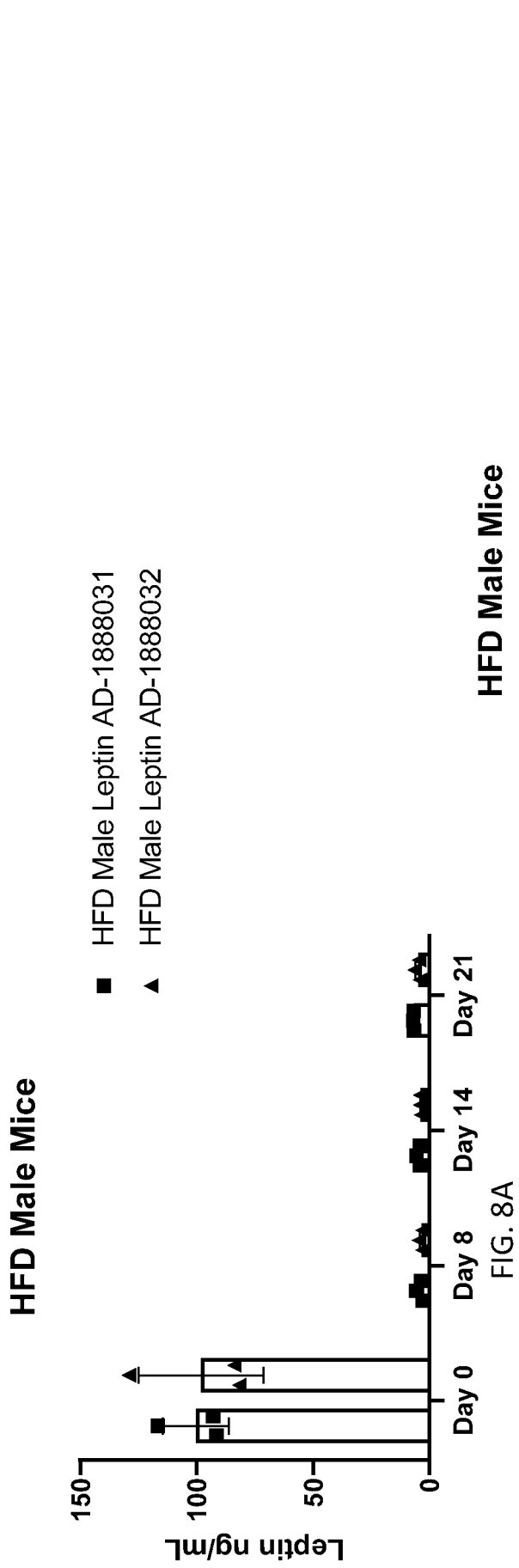

HFD Male Mice
HFD Male Leptin AD-1888031
HFD Male Leptin AD-1888032
Leptin ng/mL
150
100
50
0
Day 0
Day 8
Day 14
Day 21

FIG. 8A

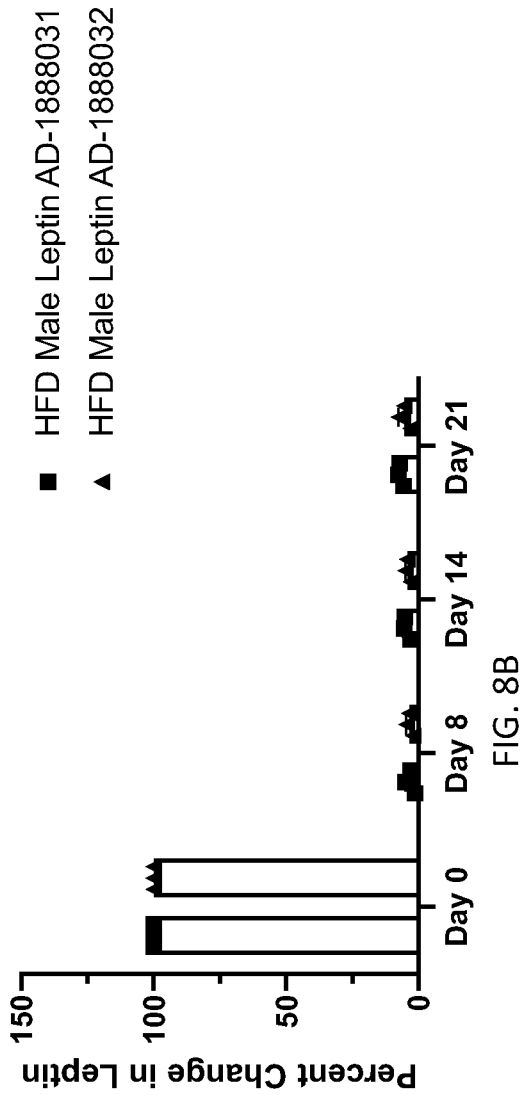

HFD Male Mice
HFD Male Leptin AD-1888031
HFD Male Leptin AD-1888032
Percent Change in Leptin
150
100
50
0
Day 0
Day 8
Day 14
Day 21

FIG. 8B

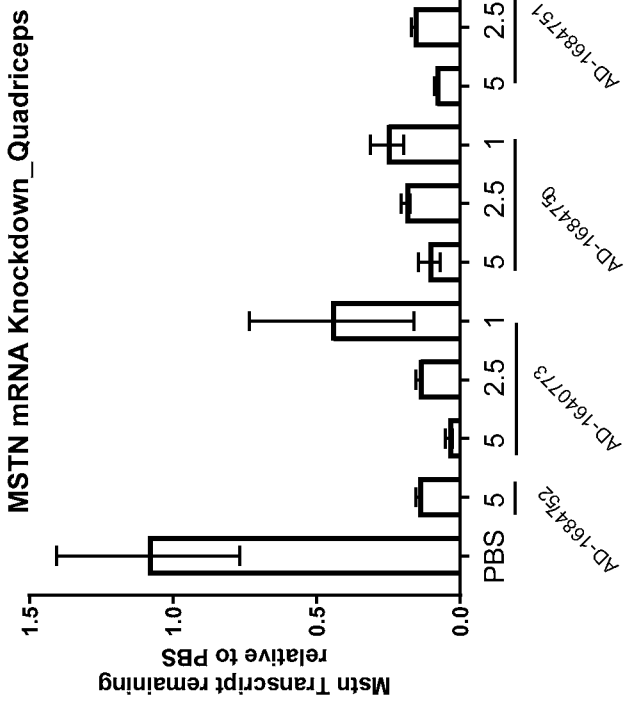

MSTN mRNA Knockdown_Quadriceps
Mstn Transcript remaining relative to PBS
1.5
1.0
0.5
0.0
PBS
5
5
2.5
1
5
2.5
1
5
2.5
1 mg/kg
AD-1684752
AD-1640773
AD-1684750
AD-1684751
Groups

FIG. 9A

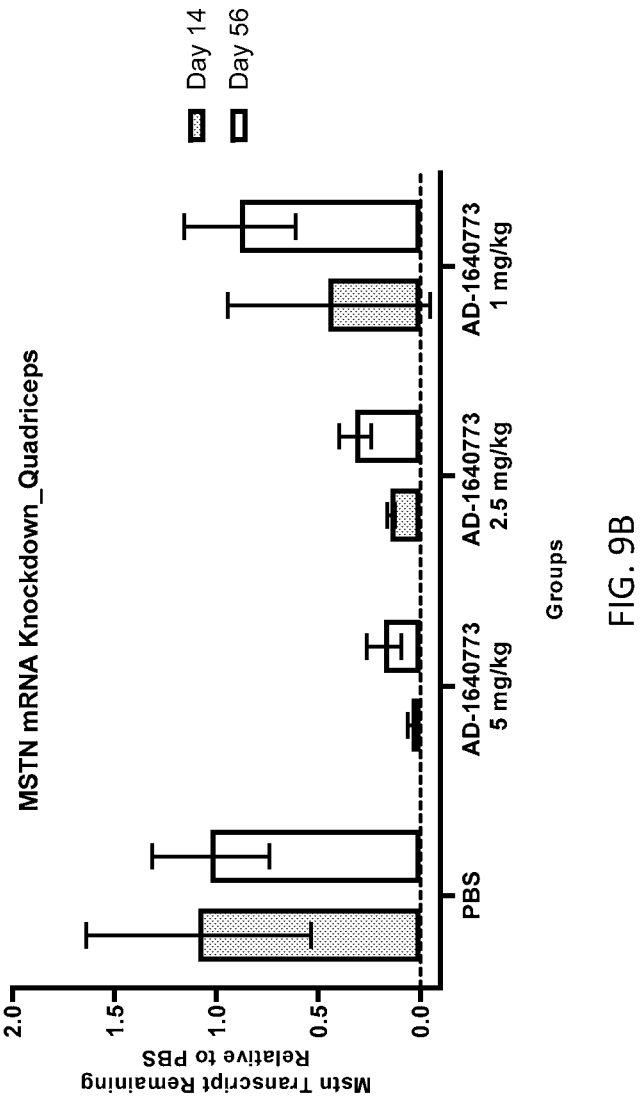

MSTN mRNA Knockdown_Quadriceps
Day 14
Day 56
Mstn Transcript Remaining Relative to PBS
2.0
1.5
1.0
0.5
0.0
PBS
AD-1640773 5 mg/kg
AD-1640773 2.5 mg/kg
AD-1640773 1 mg/kg
Groups

FIG. 9B

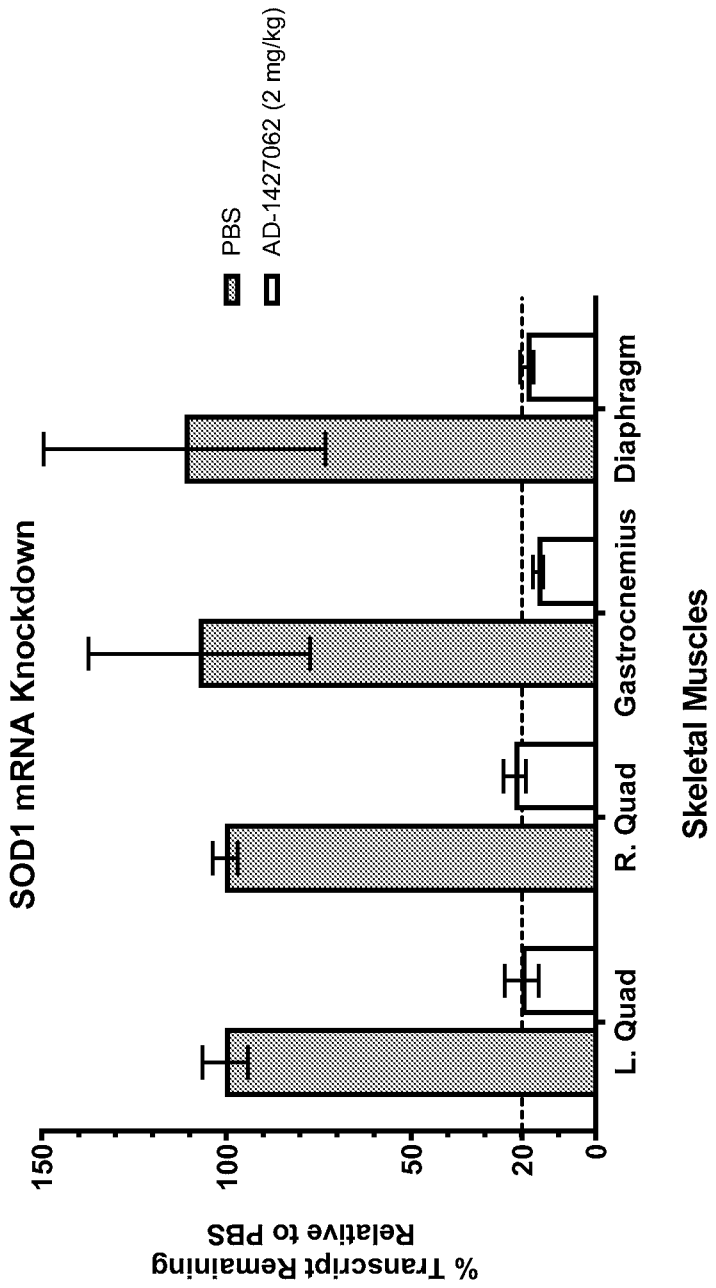

SOD1 mRNA Knockdown
PBS
AD-1427062 (2 mg/kg)
% Transcript Remaining
Relative to PBS
150
100
50
20
0
L. Quad
R. Quad
Gastrocnemius
Diaphragm
Skeletal Muscles

FIG. 10

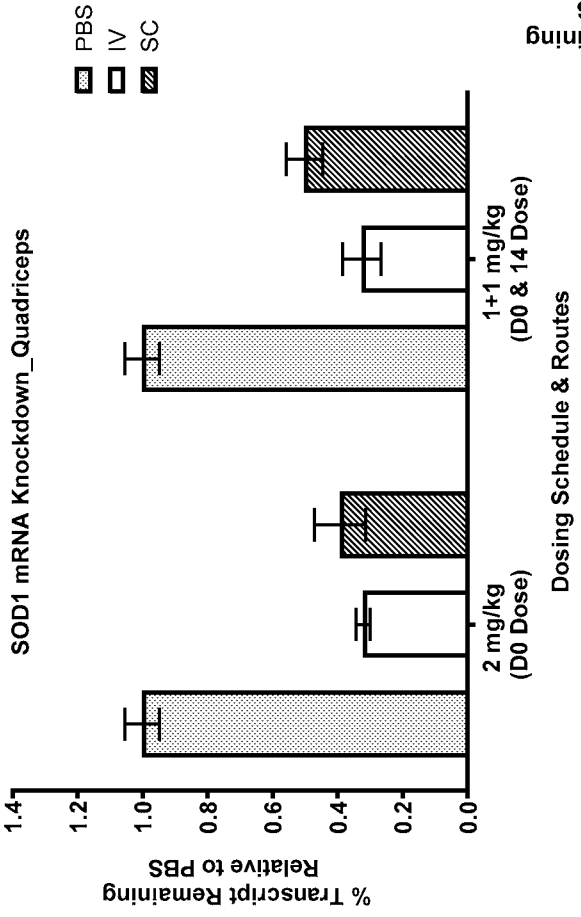

SOD1 mRNA Knockdown_Quadriceps
PBS
IV
SC
% Transcript Remaining Relative to PBS
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
2 mg/kg (D0 Dose)
1+1 mg/kg (D0 & 14 Dose)
Dosing Schedule & Routes

FIG. 11

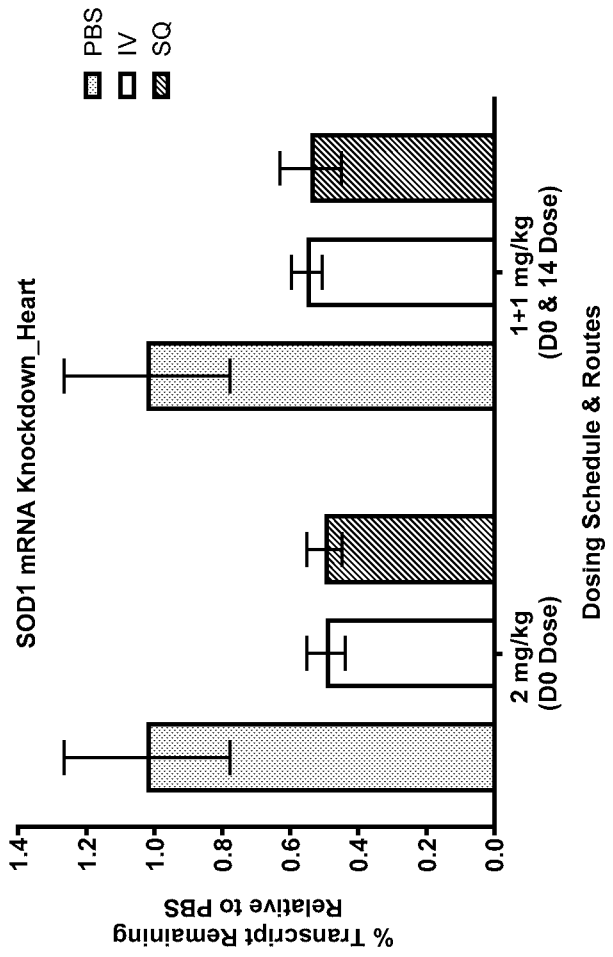

SOD1 mRNA Knockdown_Heart
PBS
IV
SQ
% Transcript Remaining Relative to PBS
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
2 mg/kg (D0 Dose)
1+1 mg/kg (D0 & 14 Dose)
Dosing Schedule & Routes

FIG. 12

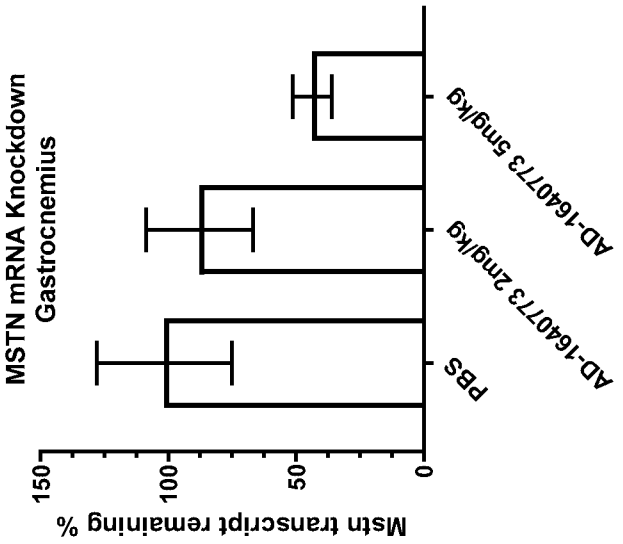


FIG. 13B

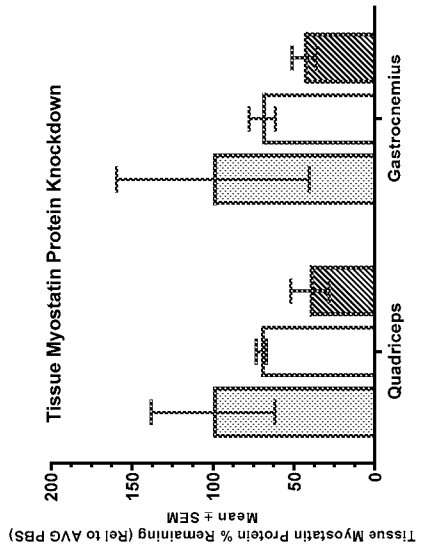


FIG. 13C

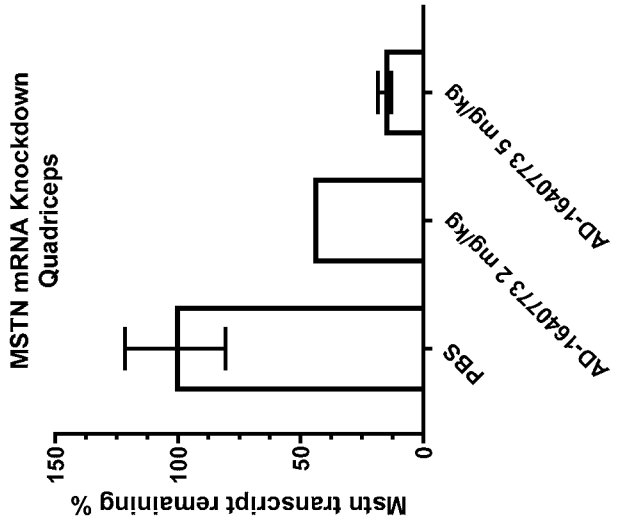


FIG. 13A