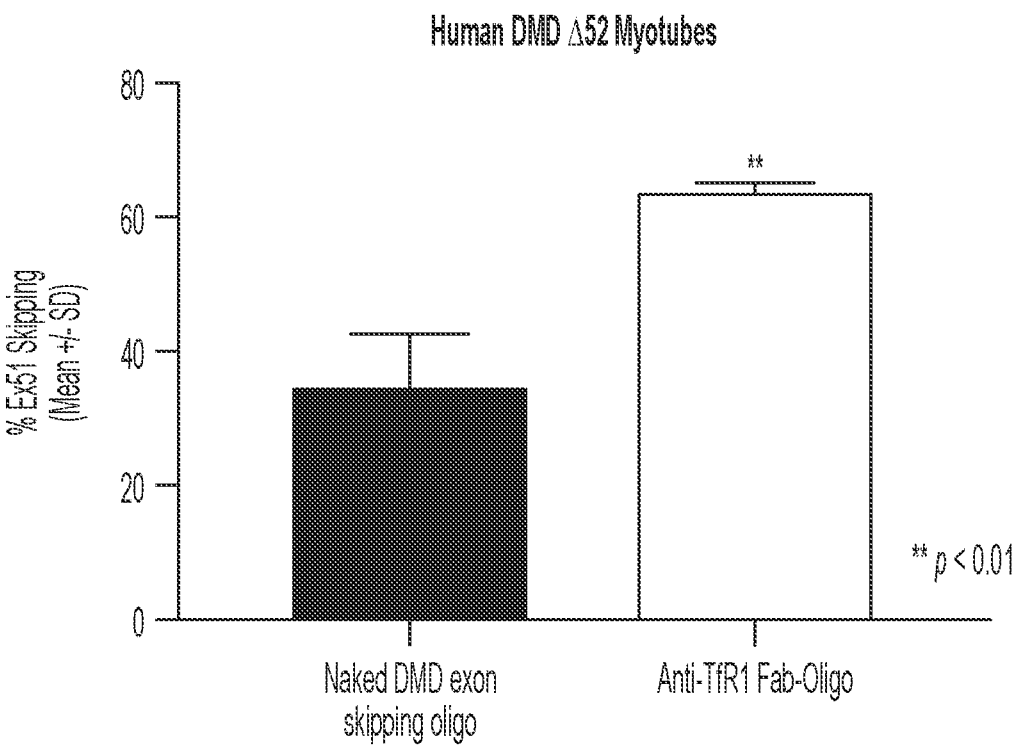

Human DMD Δ52 Myotubes
% Ex51 Skipping
(Mean +/- SD)
80
60
40
20
0
**
** p < 0.01
Naked DMD exon skipping oligo
Anti-TfR1 Fab-Oligo

FIG. 1A

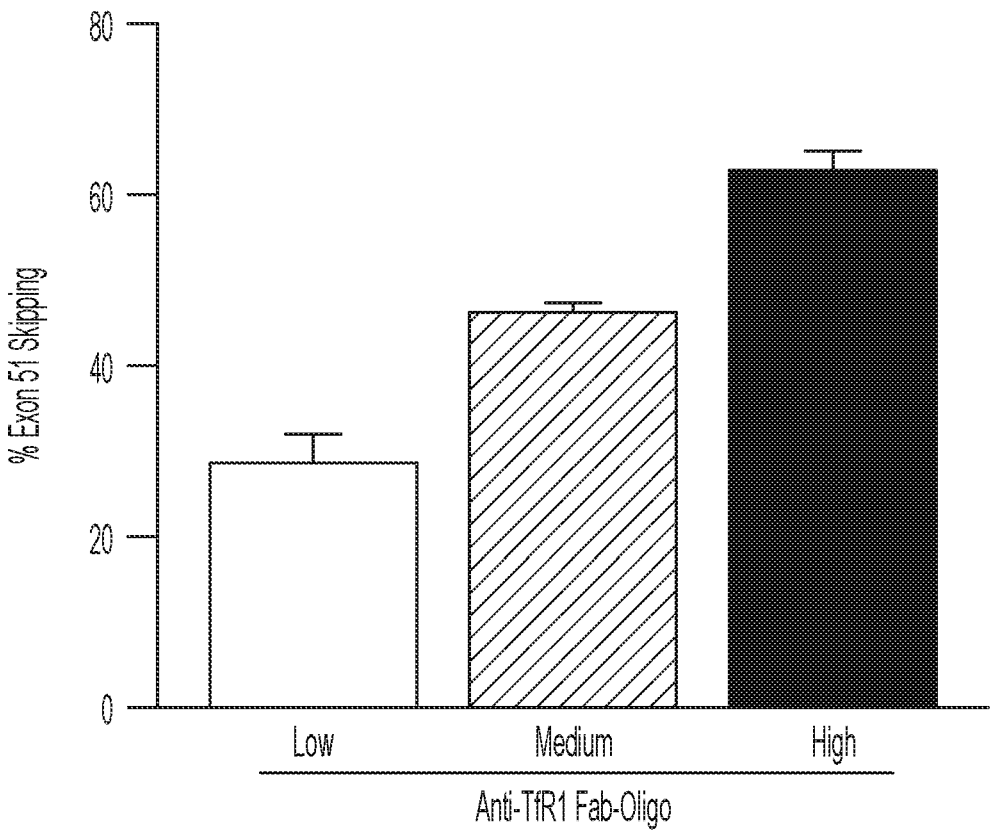

80
60
40
20
0
% Exon 51 Skipping
Low
Medium
High
Anti-TfR1 Fab-Oligo

FIG. 1B

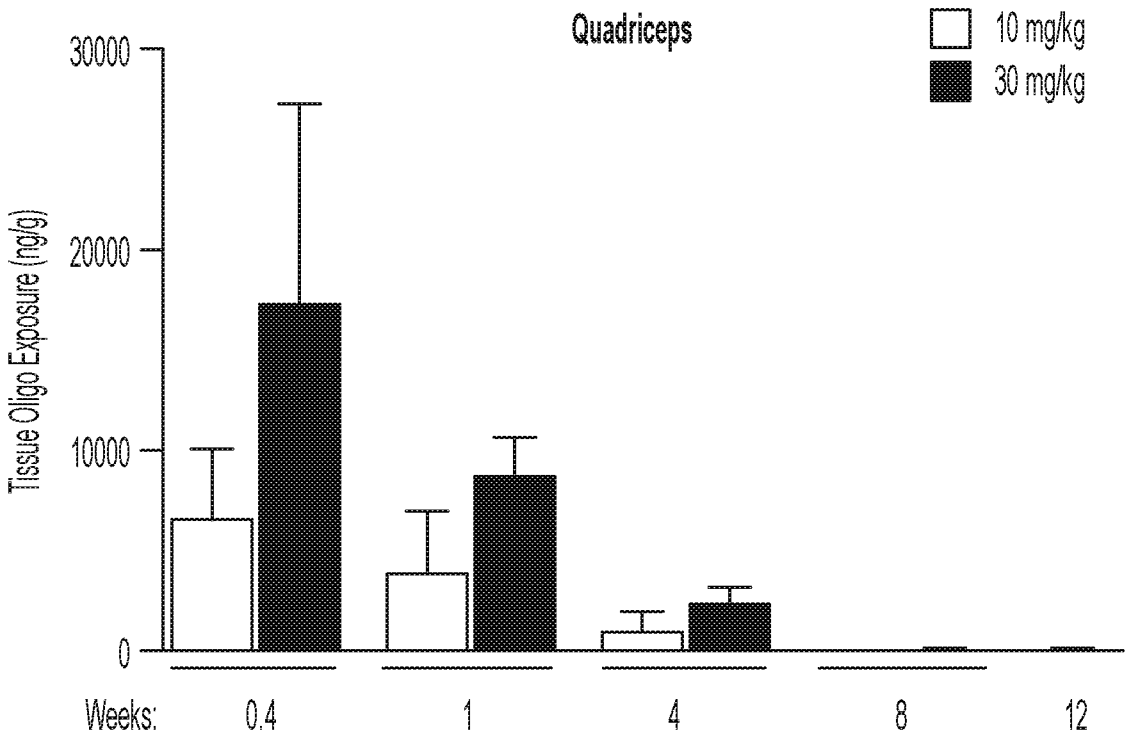

Quadriceps
10 mg/kg
30 mg/kg
Tissue Oligo Exposure (ng/g)
30000
20000
10000
0
Weeks:
0.4
1
4
8
12

FIG. 2A

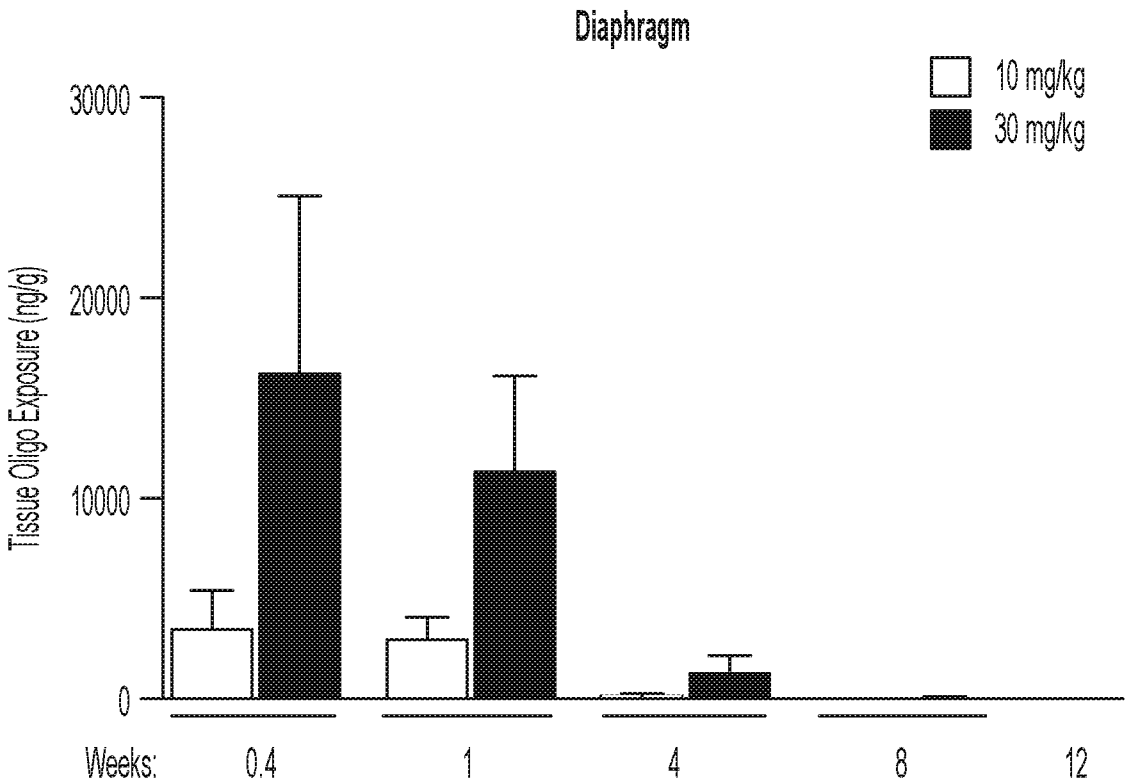

Diaphragm
10 mg/kg
30 mg/kg
Tissue Oligo Exposure (ng/g)
30000
20000
10000
0
Weeks:
0.4
1
4
8
12

FIG. 2B

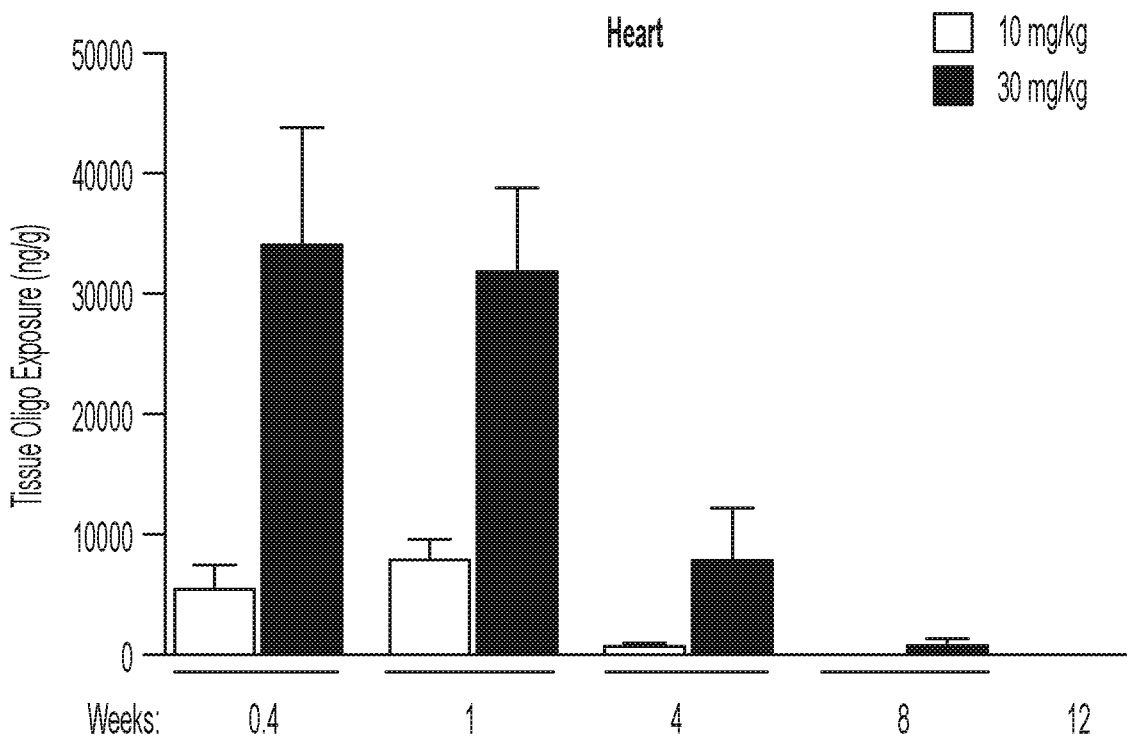

Heart
10 mg/kg
30 mg/kg
Tissue Oligo Exposure (ng/g)
50000
40000
30000
20000
10000
0
Weeks:
0.4
1
4
8
12

FIG. 2C

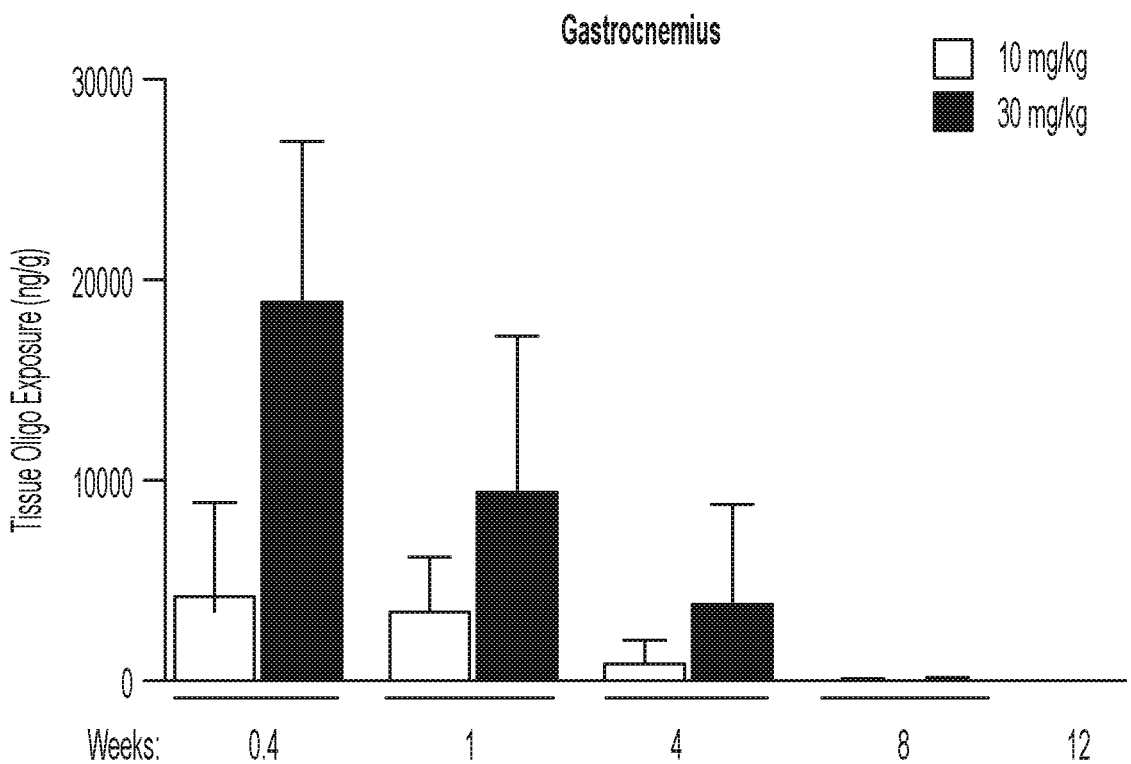

Gastrocnemius
10 mg/kg
30 mg/kg
Tissue Oligo Exposure (ng/g)
30000
20000
10000
0
Weeks:
0.4
1
4
8
12

FIG. 2D

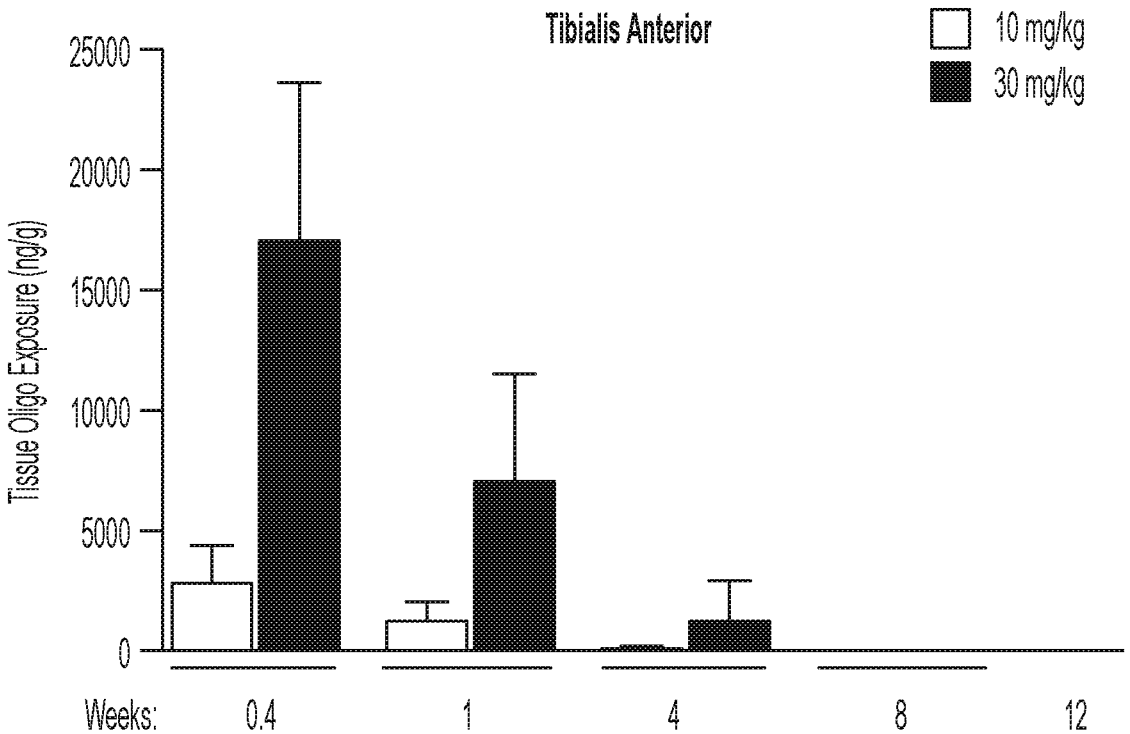

Tibialis Anterior
10 mg/kg
30 mg/kg
Tissue Oligo Exposure (ng/g)
25000
20000
15000
10000
5000
0
Weeks:
0.4
1
4
8
12

FIG. 2E

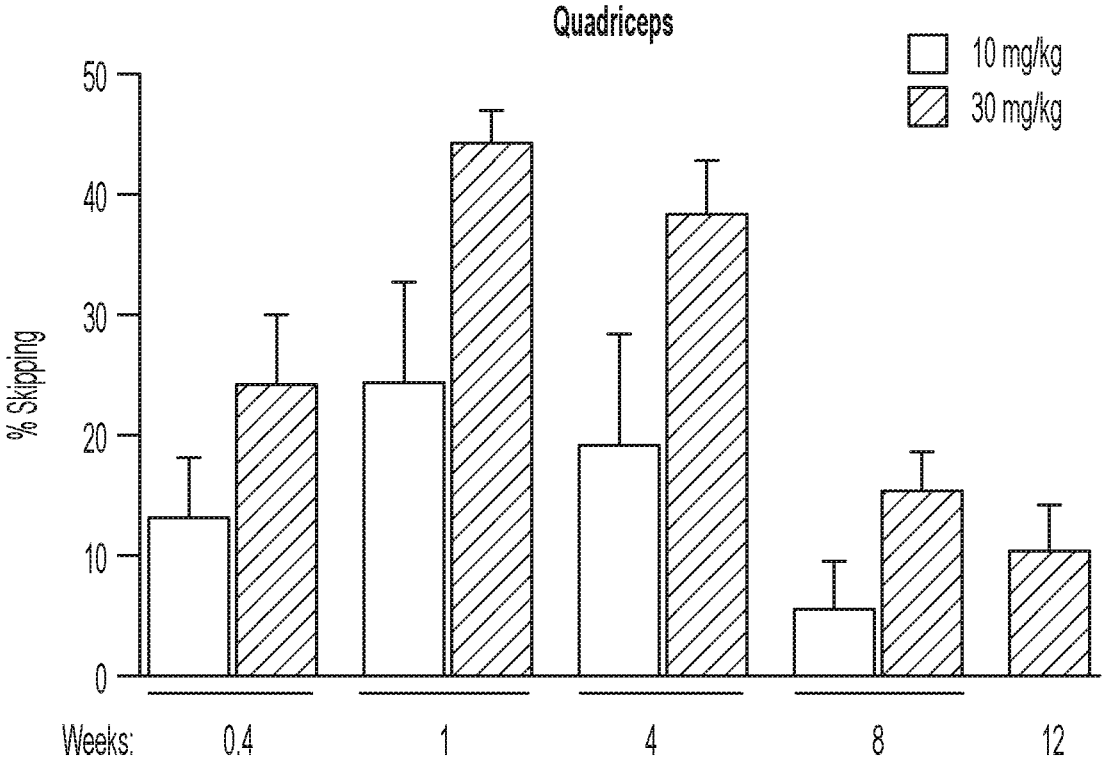

Quadriceps
10 mg/kg
30 mg/kg
% Skipping
50
40
30
20
10
0
Weeks:
0.4
1
4
8
12

FIG. 3A

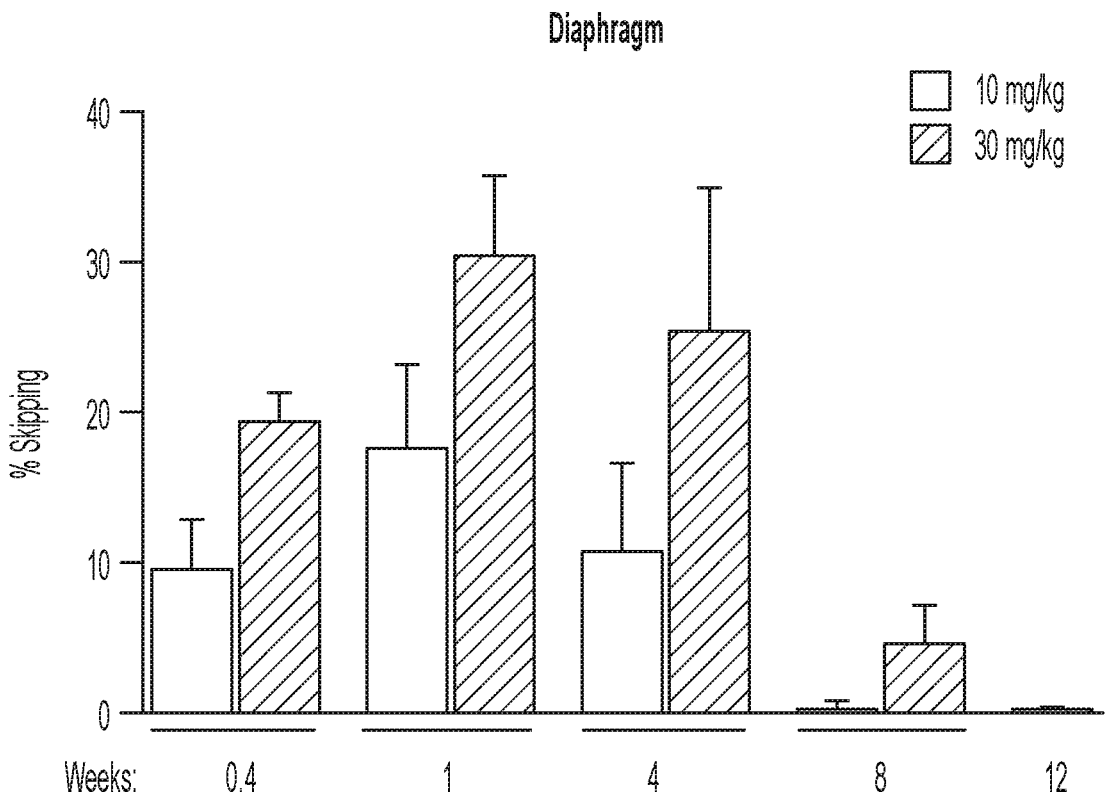

Diaphragm
10 mg/kg
30 mg/kg
% Skipping
40
30
20
10
0
Weeks:
0.4
1
4
8
12

FIG. 3B

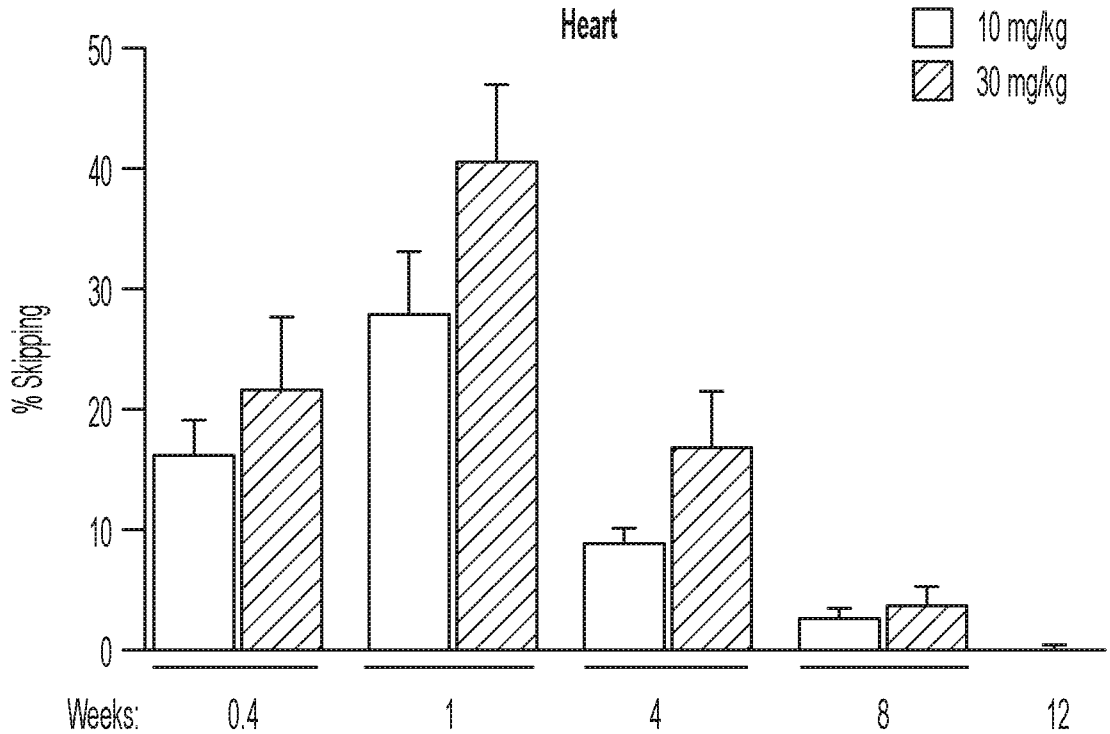

Heart
10 mg/kg
30 mg/kg
% Skipping
50
40
30
20
10
0
Weeks:
0.4
1
4
8
12

FIG. 3C

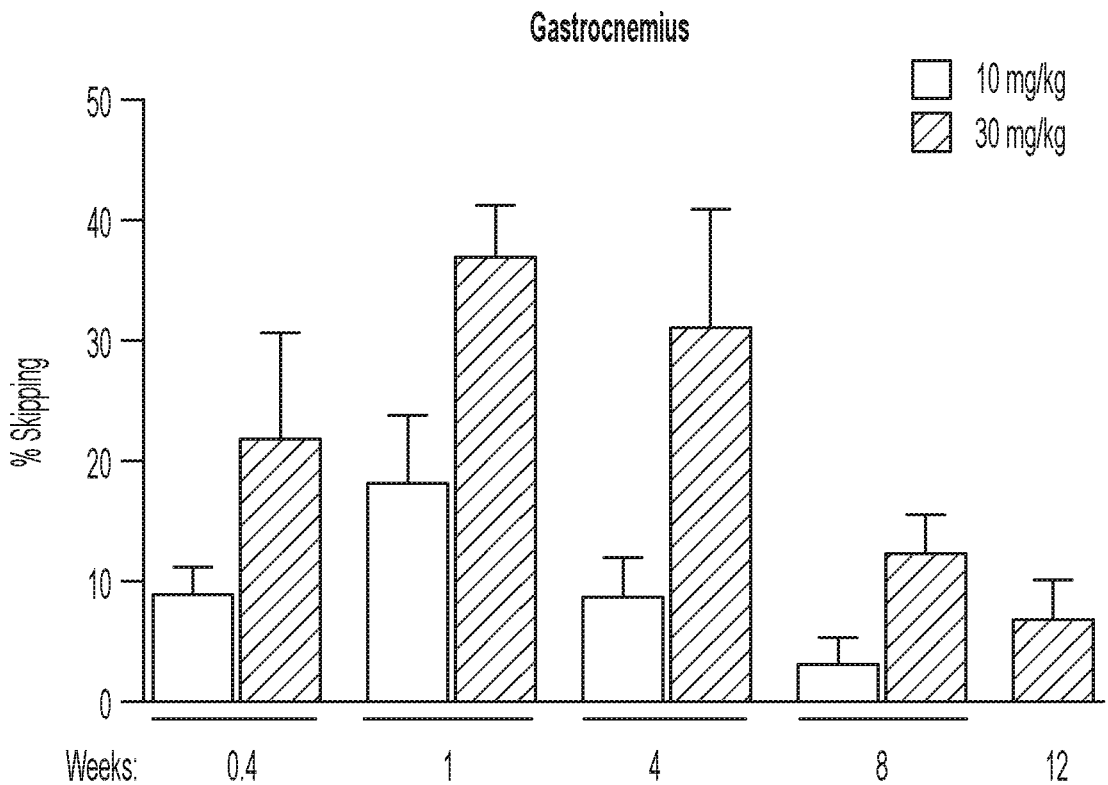

Gastrocnemius
10 mg/kg
30 mg/kg
% Skipping
50
40
30
20
10
0
Weeks:
0.4
1
4
8
12

FIG. 3D

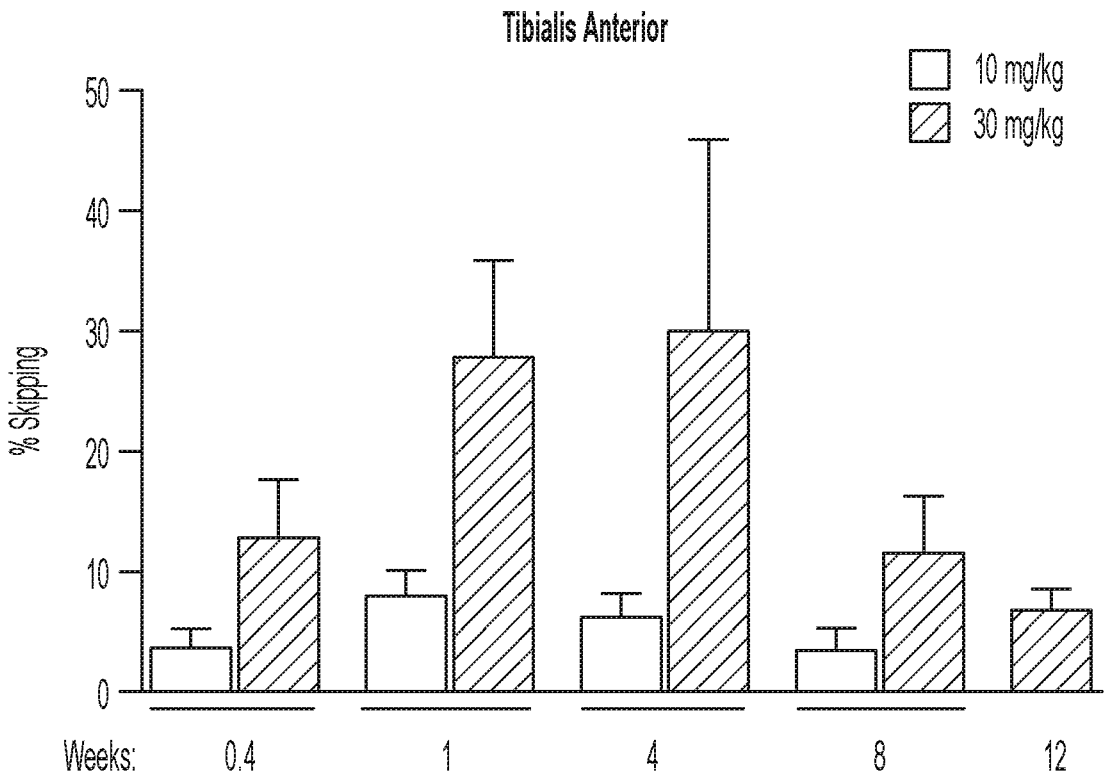

Tibialis Anterior
10 mg/kg
30 mg/kg
% Skipping
50
40
30
20
10
0
Weeks:
0.4
1
4
8
12

FIG. 3E

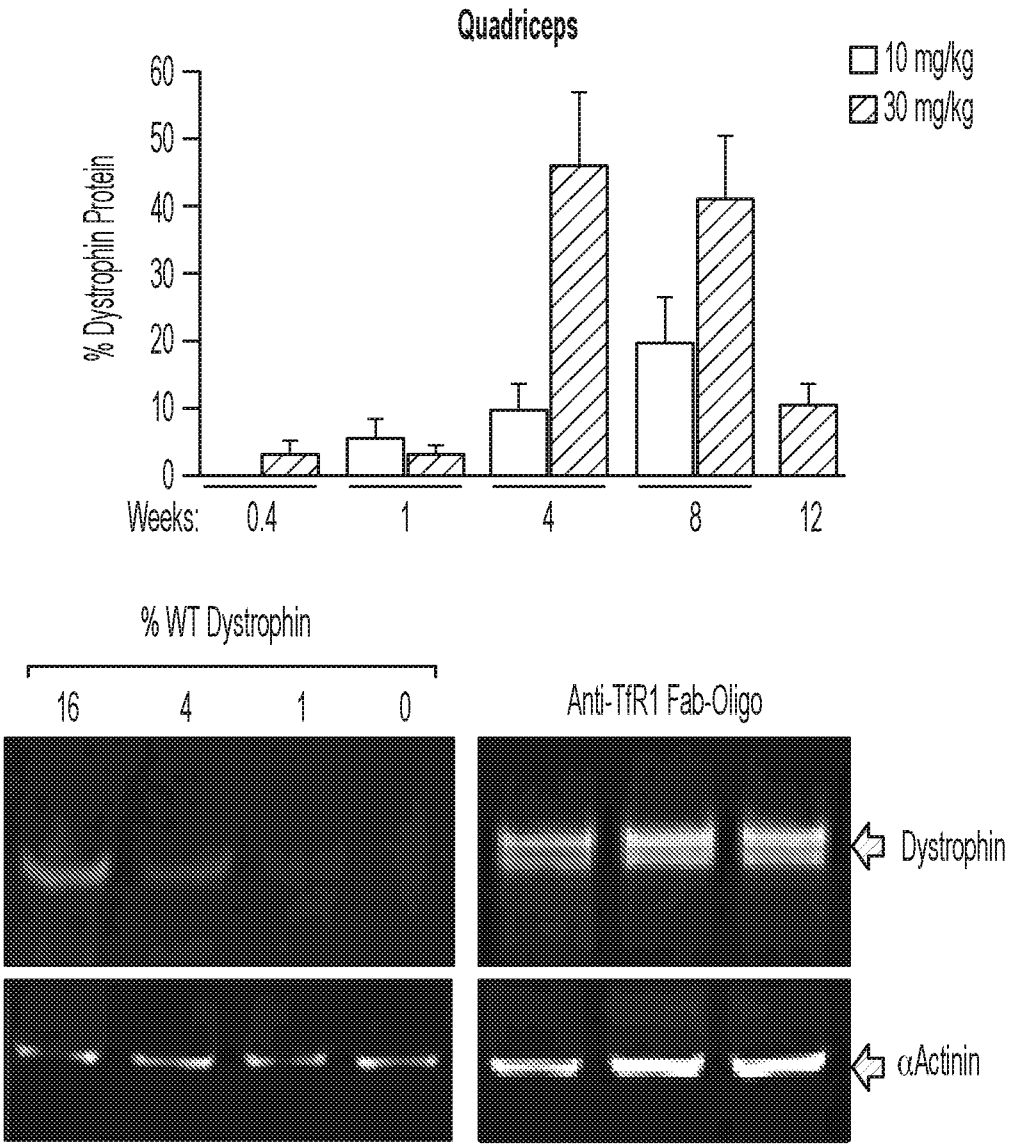

Quadriceps
10 mg/kg
30 mg/kg
% Dystrophin Protein
60
50
40
30
20
10
0
Weeks:
0.4
1
4
8
12
% WT Dystrophin
16
4
1
0
Anti-TfR1 Fab-Oligo
Dystrophin
αActinin

FIG. 4A

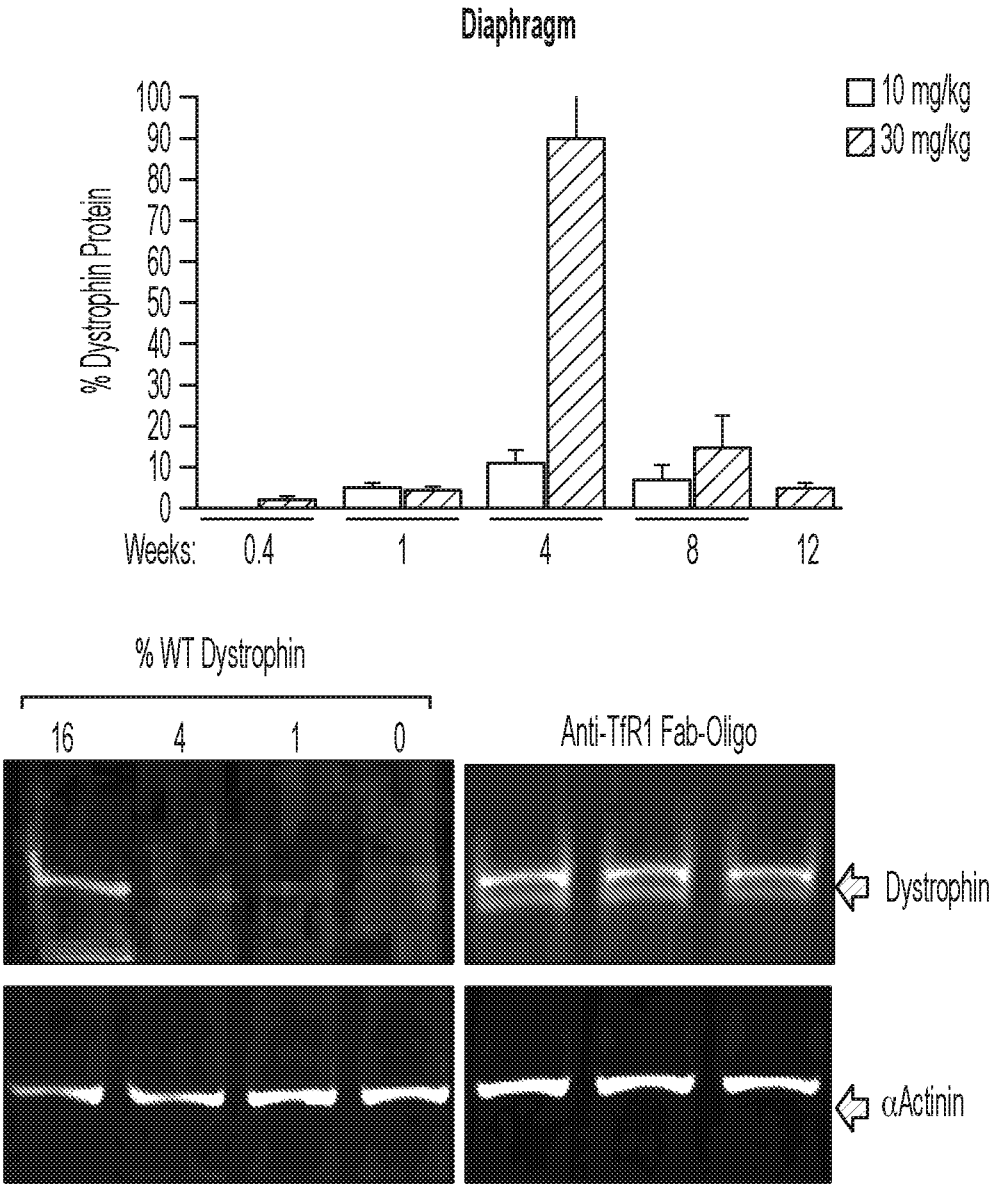

Diaphragm
10 mg/kg
30 mg/kg
% Dystrophin Protein
100
90
80
70
60
50
40
30
20
10
0
Weeks:
0.4
1
4
8
12
% WT Dystrophin
16
4
1
0
Anti-TfR1 Fab-Oligo
Dystrophin
αActinin

FIG. 4B

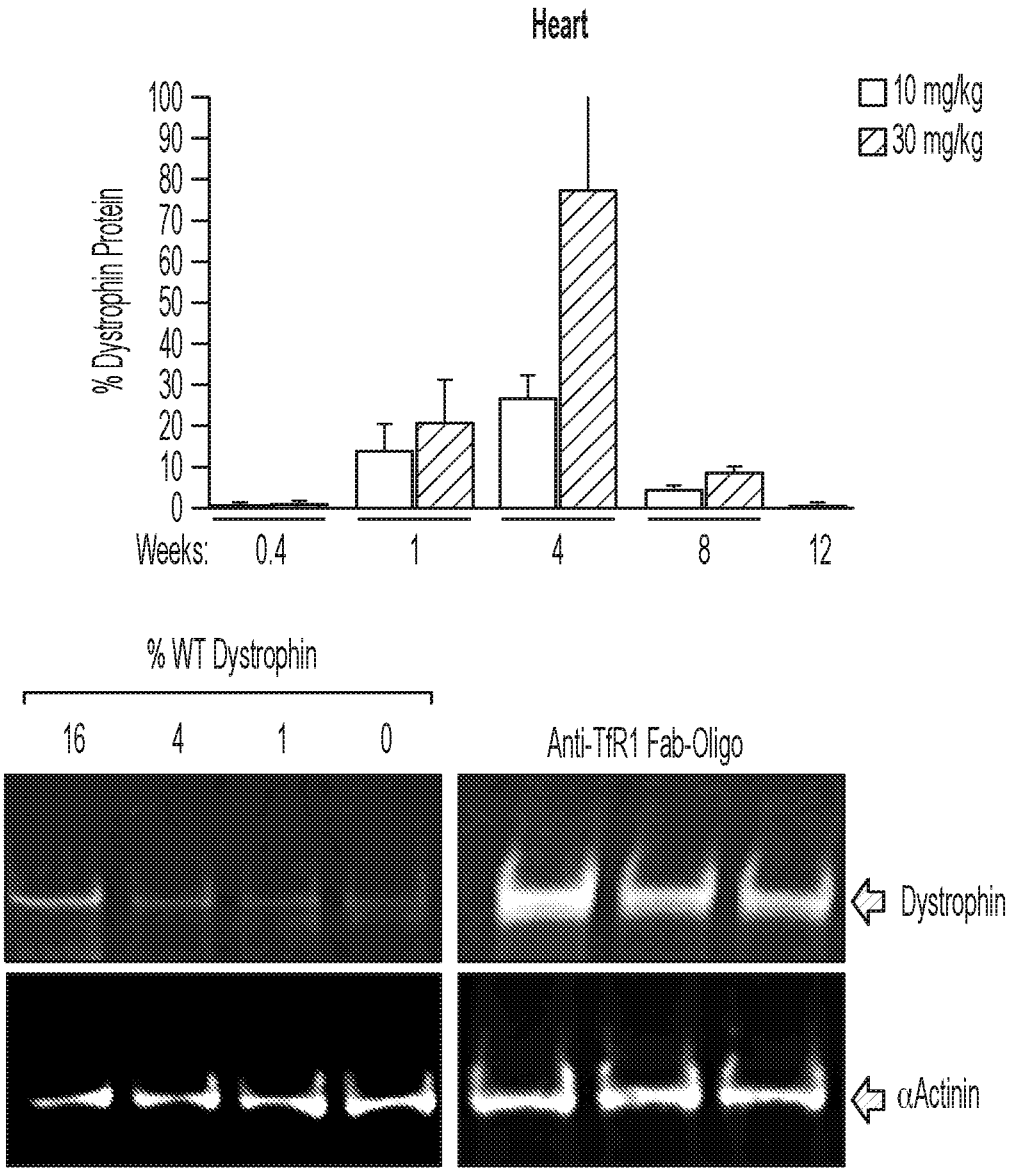

Heart
10 mg/kg
30 mg/kg
% Dystrophin Protein
100
90
80
70
60
50
40
30
20
10
0
Weeks:
0.4
1
4
8
12
% WT Dystrophin
16
4
1
0
Anti-TfR1 Fab-Oligo
Dystrophin
αActinin

FIG. 4C

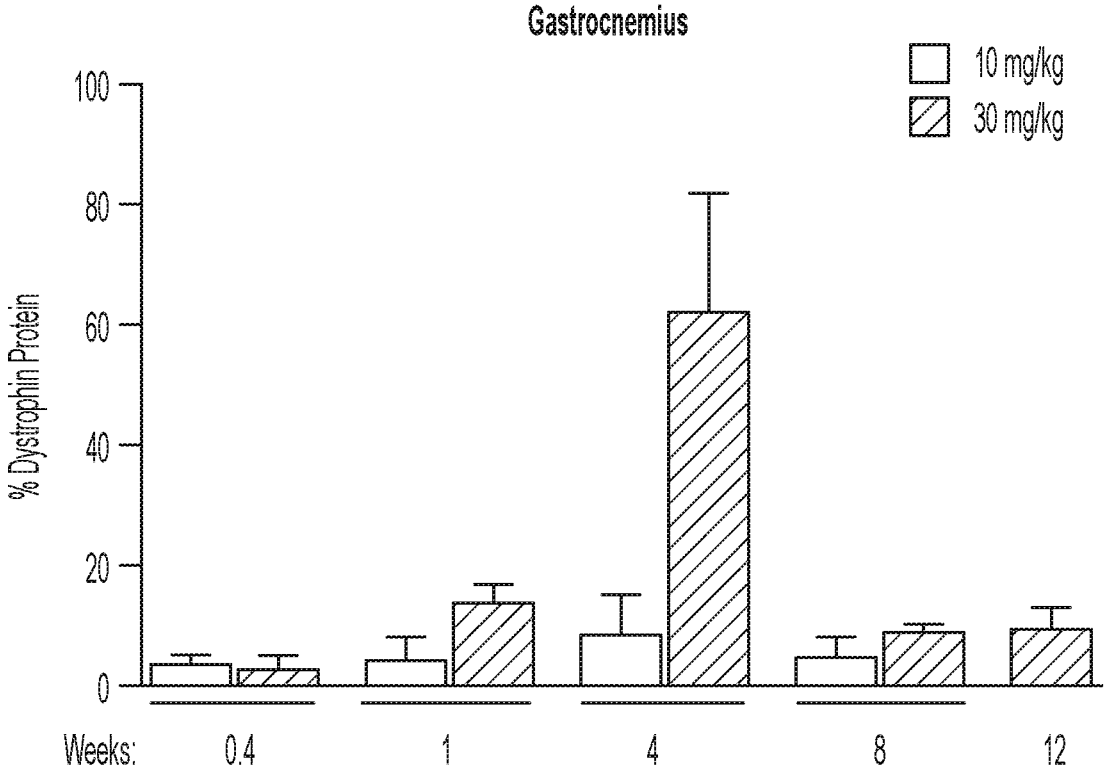

Gastrocnemius
10 mg/kg
30 mg/kg
% Dystrophin Protein
100
80
60
40
20
0
Weeks:
0.4
1
4
8
12

FIG. 4D

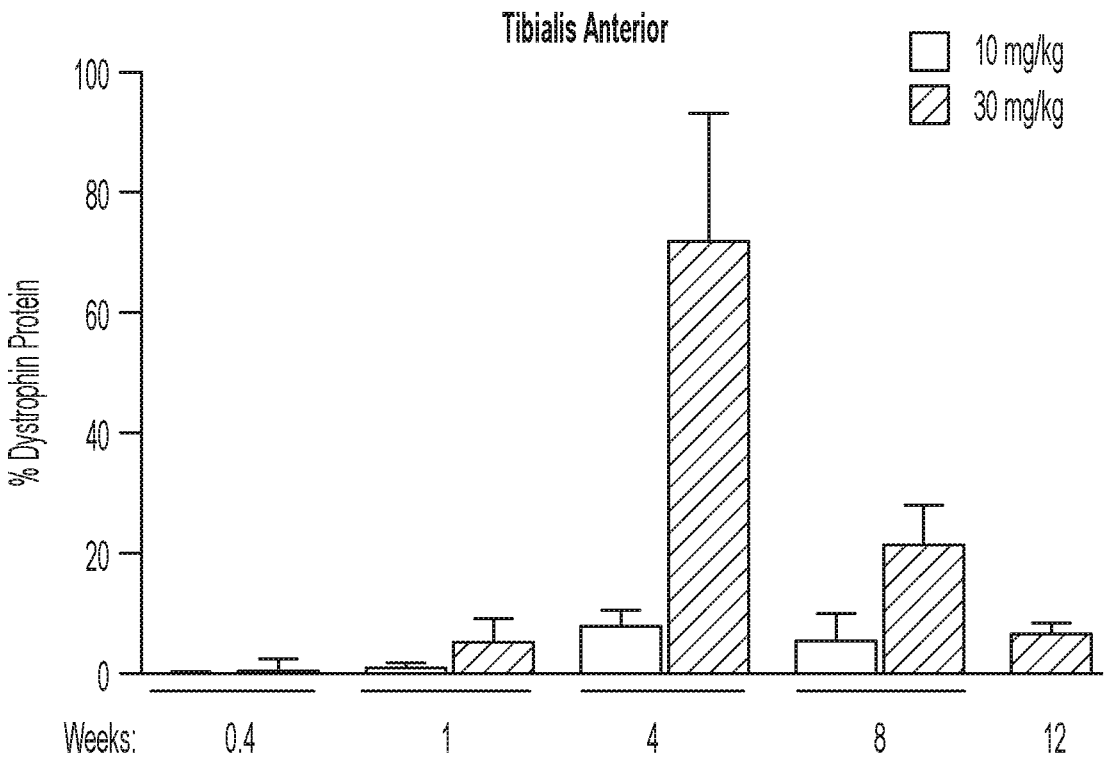
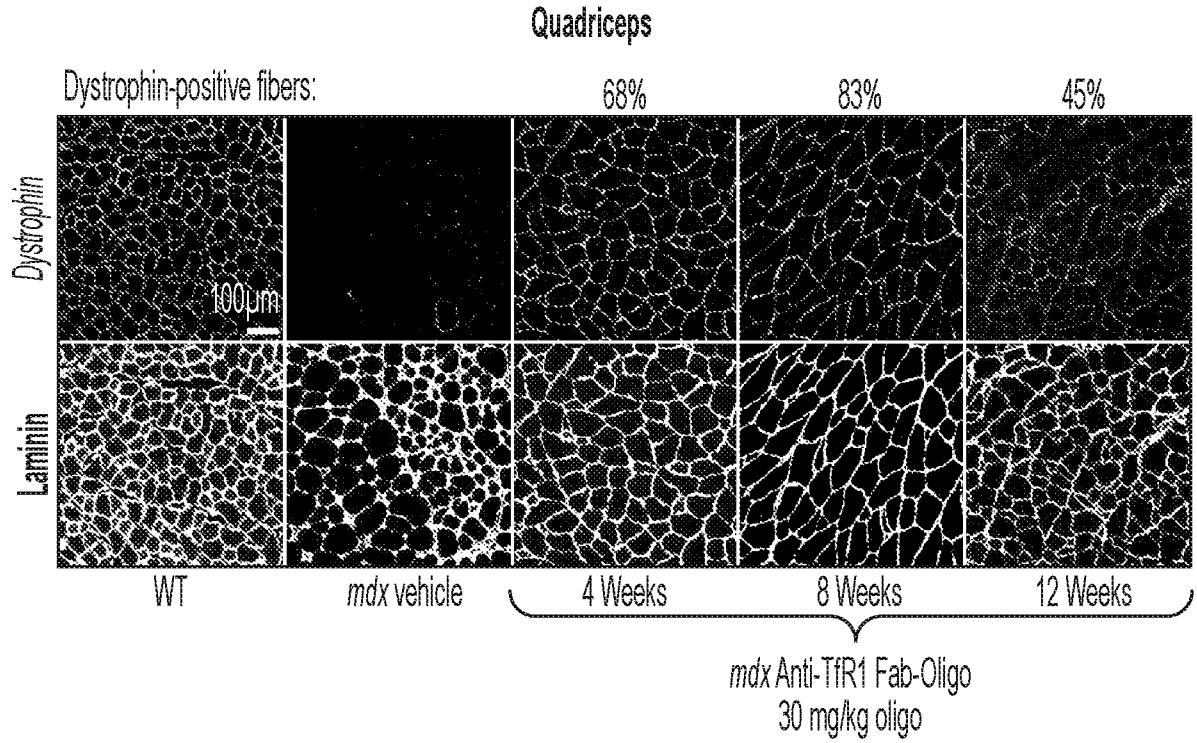

Tibialis Anterior
10 mg/kg
30 mg/kg
% Dystrophin Protein
100
80
60
40
20
0
Weeks:
0.4
1
4
8
12

FIG. 4E


Quadriceps
Dystrophin-positive fibers:
68%
83%
45%
Dystrophin
Laminin
100μm
WT
mdx vehicle
4 Weeks
8 Weeks
12 Weeks
mdx Anti-TfR1 Fab-Oligo
30 mg/kg oligo

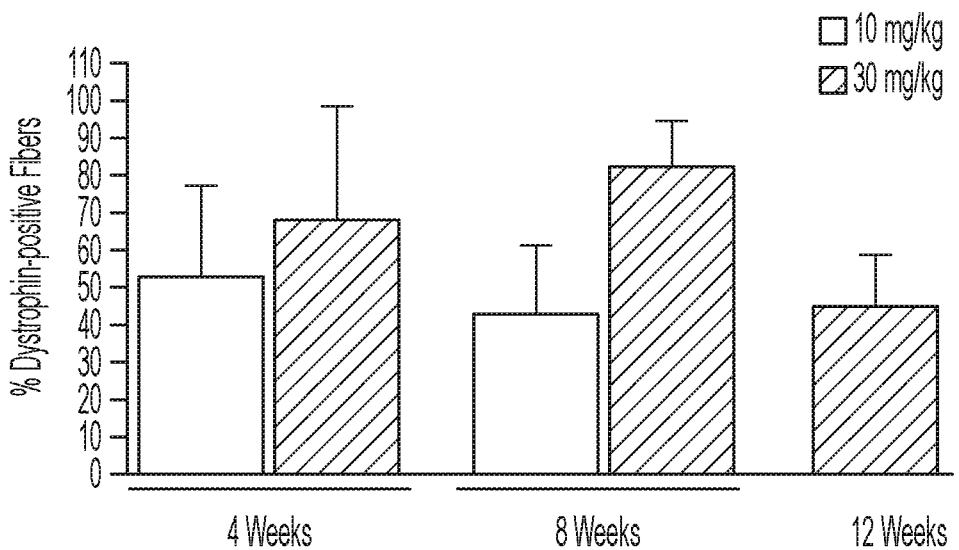

10 mg/kg
30 mg/kg
% Dystrophin-positive Fibers
0
10
20
30
40
50
60
70
80
90
100
110
4 Weeks
8 Weeks
12 Weeks

FIG. 5A

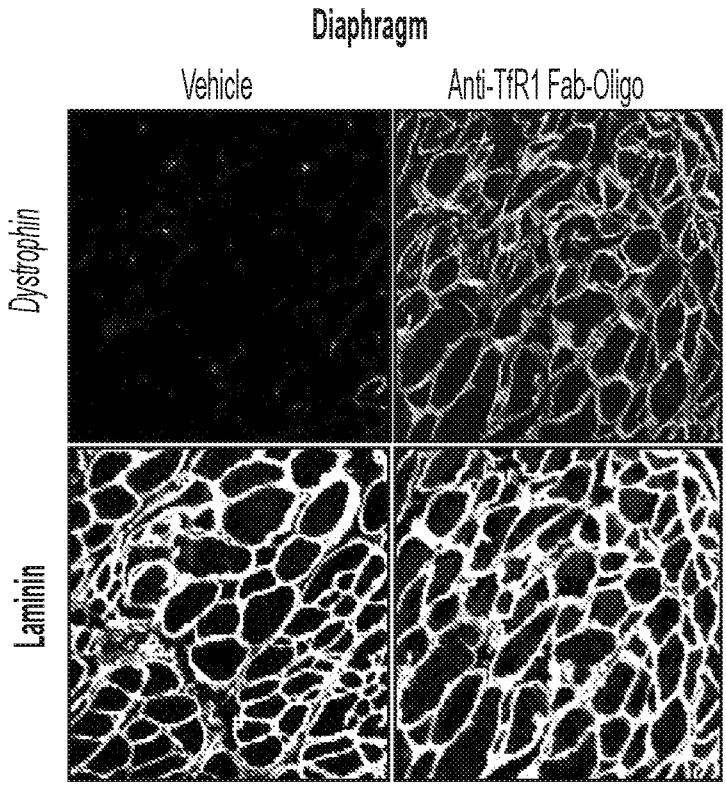


FIG. 5B

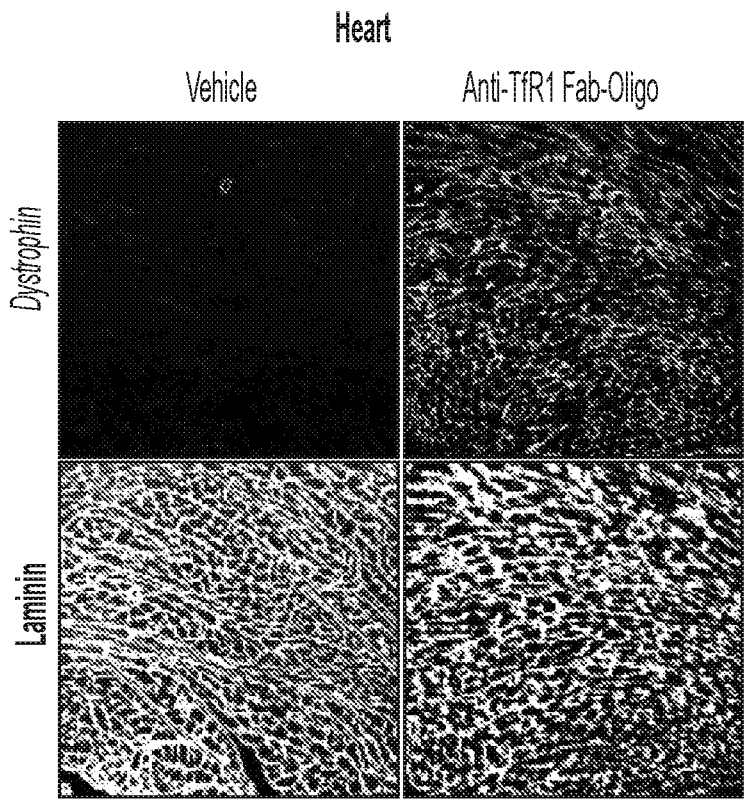


FIG. 5C

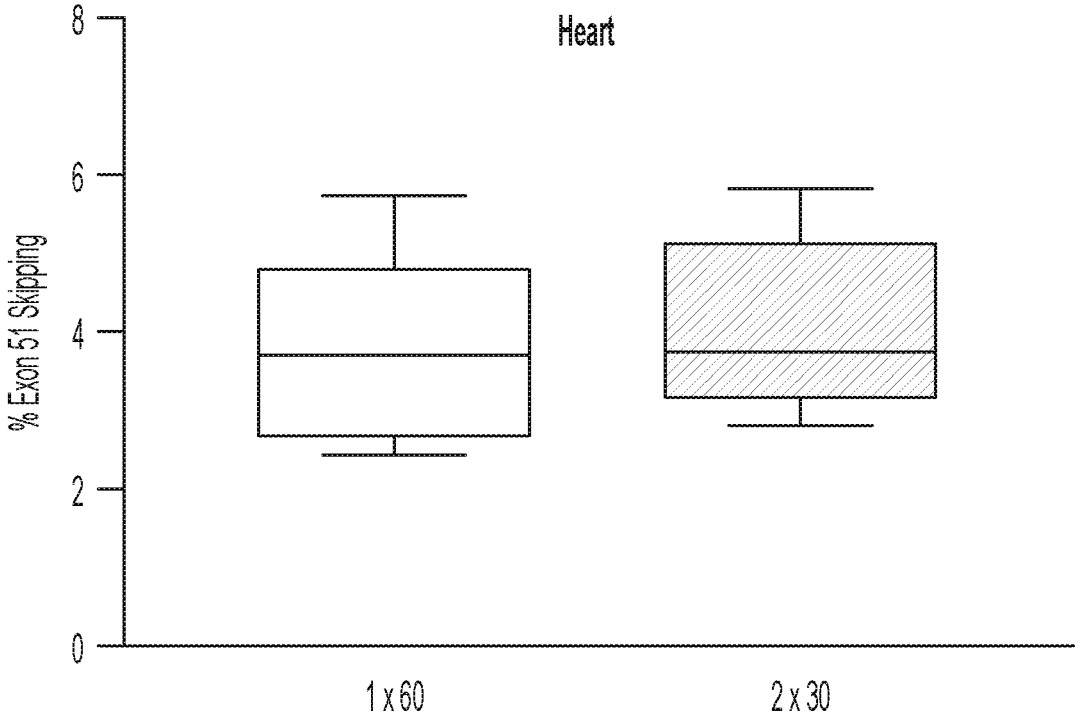

Heart
% Exon 51 Skipping
8
6
4
2
0
1 x 60
2 x 30

FIG. 6A

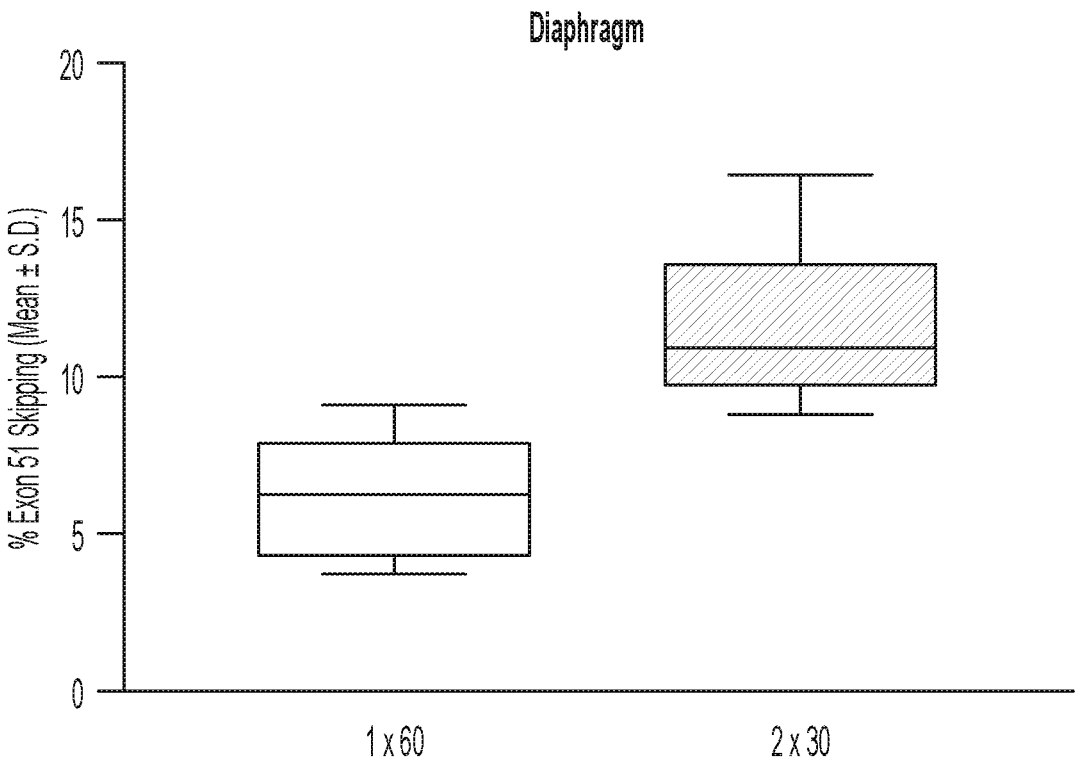

Diaphragm
% Exon 51 Skipping (Mean ± S.D.)
20
15
10
5
0
1 x 60
2 x 30

FIG. 6B

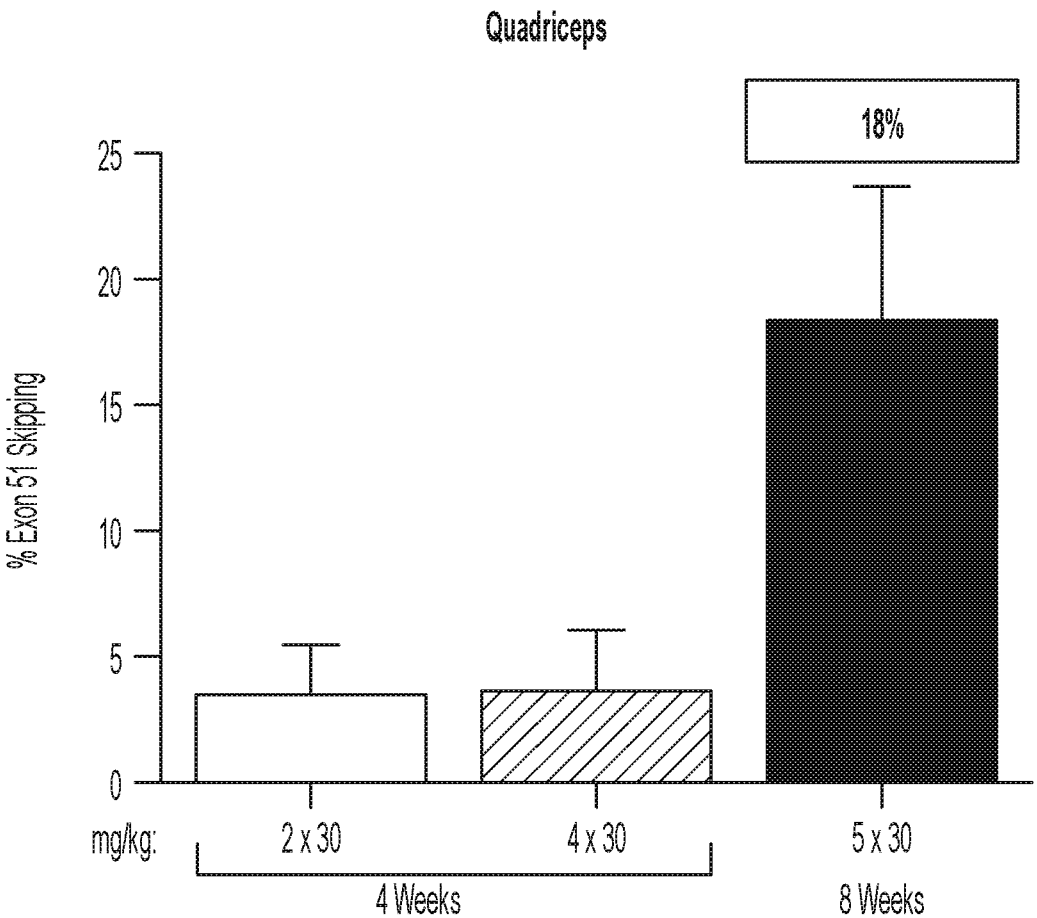

Quadriceps
18%
25
20
15
10
5
0
% Exon 51 Skipping
mg/kg:
2 x 30
4 x 30
5 x 30
4 Weeks
8 Weeks

FIG. 7A

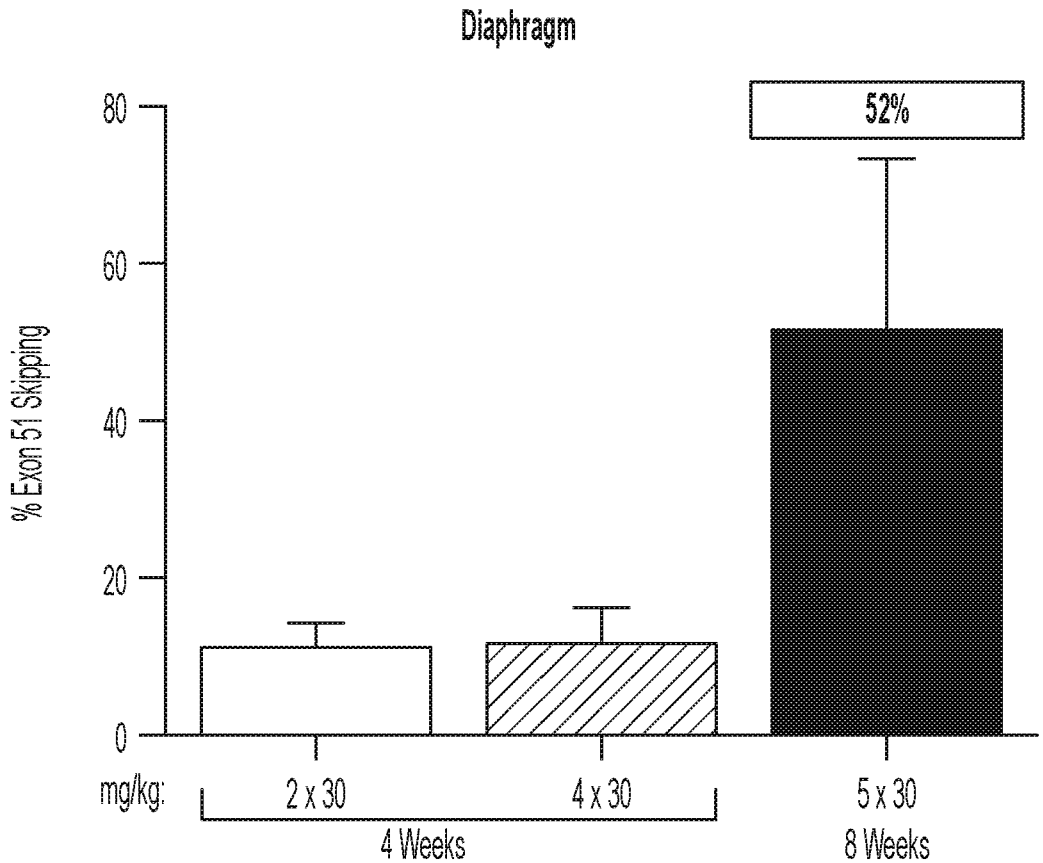

Diaphragm
% Exon 51 Skipping
80
60
40
20
0
52%
mg/kg:
2 x 30
4 x 30
5 x 30
4 Weeks
8 Weeks

FIG. 7B

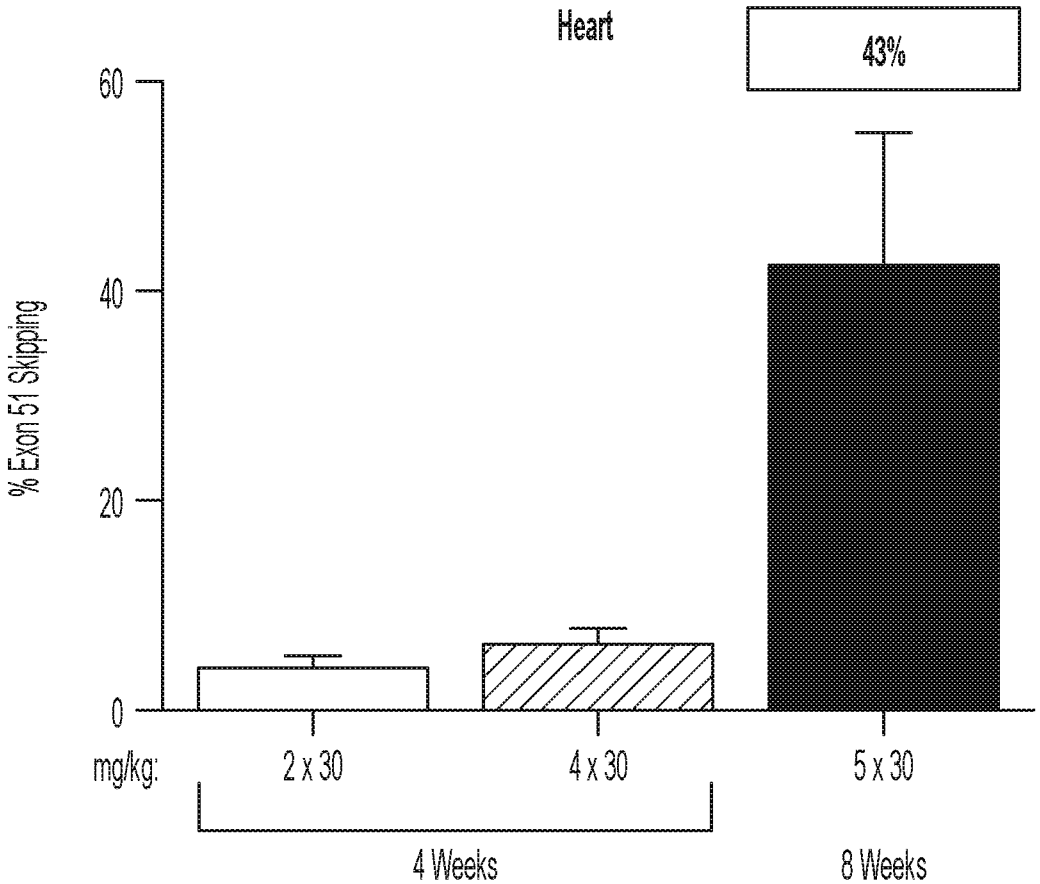

Heart
43%
60
40
20
0
% Exon 51 Skipping
mg/kg:
2 x 30
4 x 30
5 x 30
4 Weeks
8 Weeks

FIG. 7C

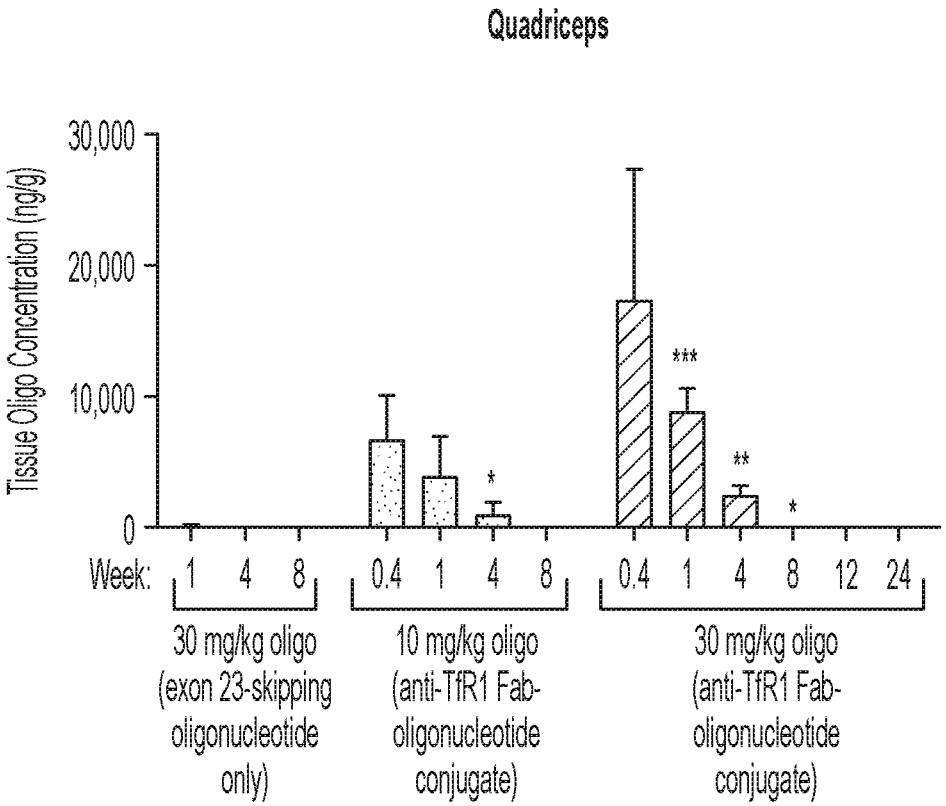

Quadriceps
Tissue Oligo Concentration (ng/g)
30,000
20,000
10,000
0
Week:
1
4
8
0.4
1
4
8
0.4
1
4
8
12
24
*
***
**
*
30 mg/kg oligo (exon 23-skipping oligonucleotide only)
10 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)
30 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)

FIG. 8A

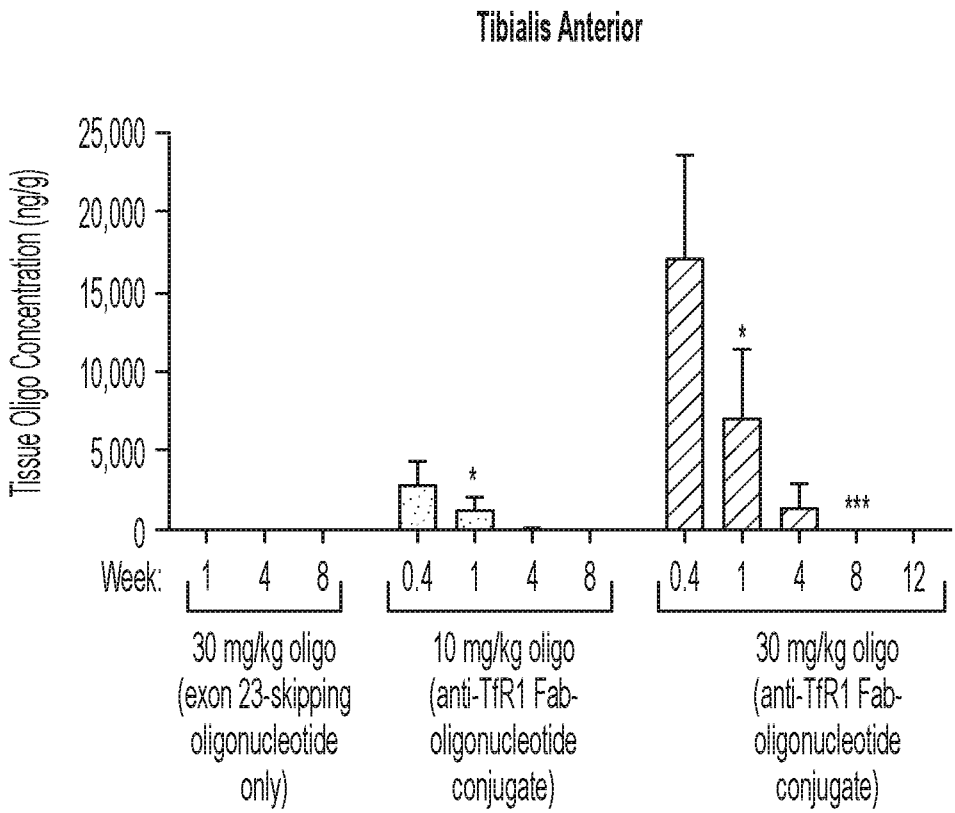

Tibialis Anterior
Tissue Oligo Concentration (ng/g)
25,000
20,000
15,000
10,000
5,000
0
Week:
1
4
8
0.4
1
4
8
0.4
1
4
8
12
*
*
***
30 mg/kg oligo (exon 23-skipping oligonucleotide only)
10 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)
30 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)

FIG. 8B

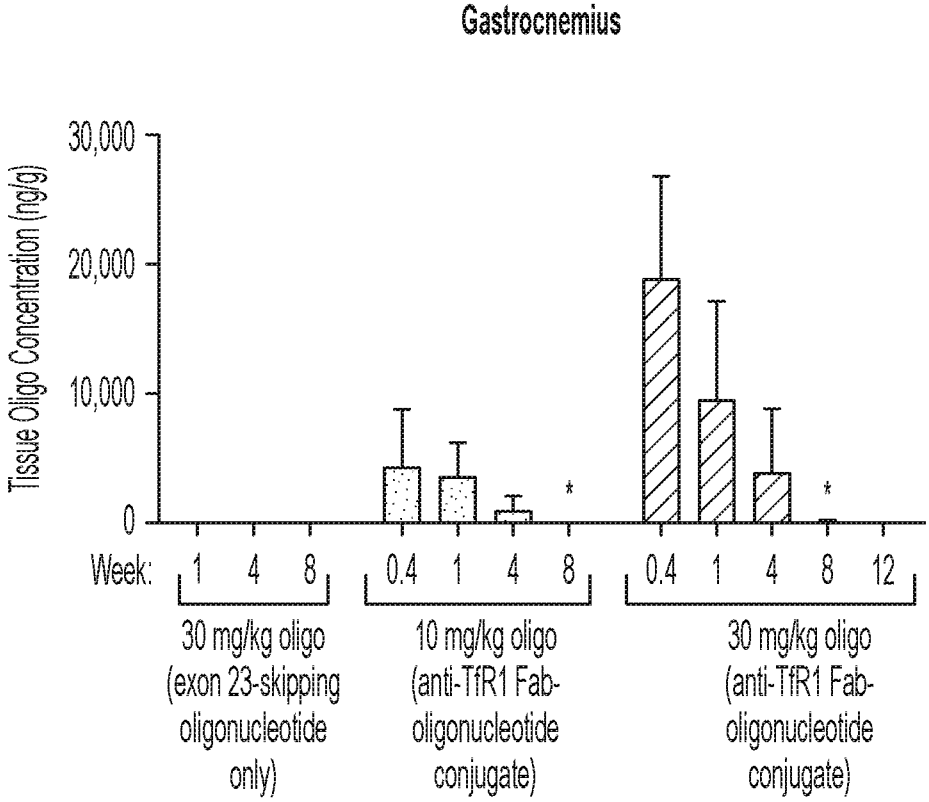

Gastrocnemius
Tissue Oligo Concentration (ng/g)
30,000
20,000
10,000
0
Week:
1
4
8
0.4
1
4
8
0.4
1
4
8
12
*
*
30 mg/kg oligo (exon 23-skipping oligonucleotide only)
10 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)
30 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)

FIG. 8C

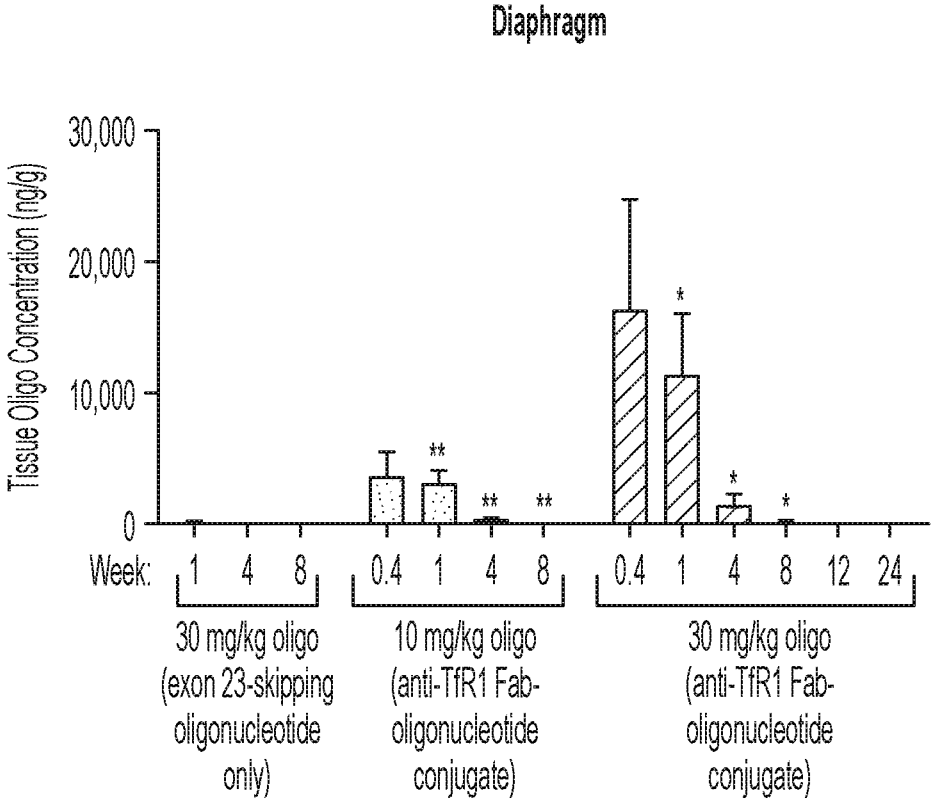

Diaphragm
Tissue Oligo Concentration (ng/g)
30,000
20,000
10,000
0
Week:
1
4
8
0.4
1
4
8
0.4
1
4
8
12
24
**
**
**
*
*
*
30 mg/kg oligo (exon 23-skipping oligonucleotide only)
10 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)
30 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)

FIG. 8D

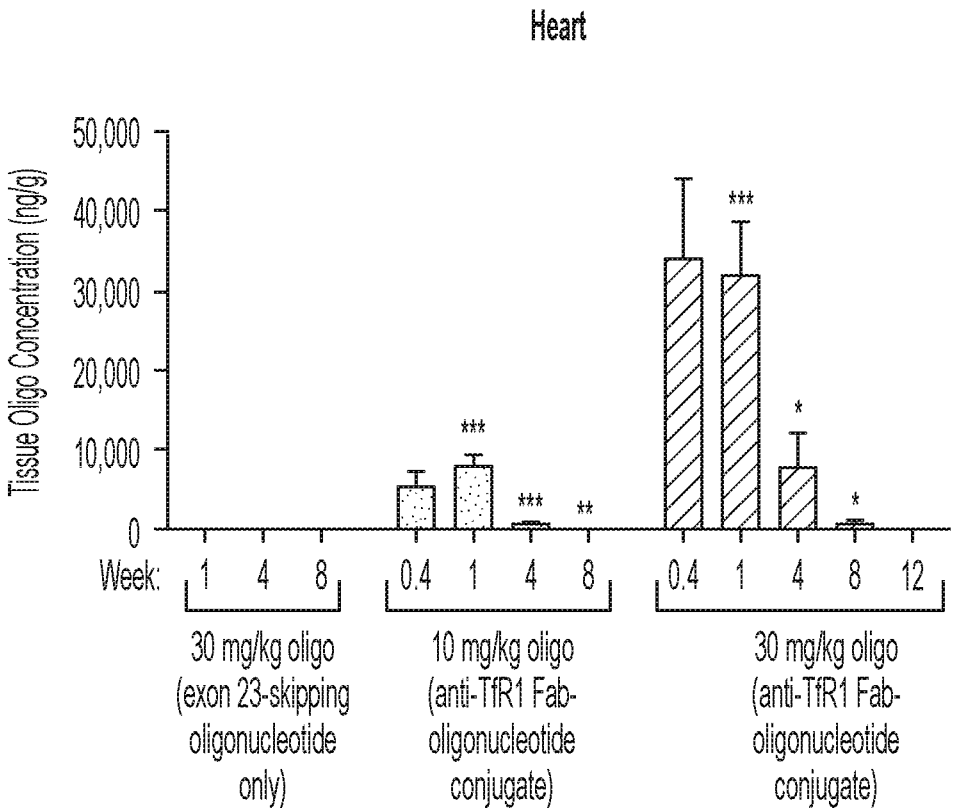

Heart
Tissue Oligo Concentration (ng/g)
50,000
40,000
30,000
20,000
10,000
0
***
***
**
***
*
*
Week:
1
4
8
0.4
1
4
8
0.4
1
4
8
12
30 mg/kg oligo (exon 23-skipping oligonucleotide only)
10 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)
30 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)

FIG. 8E

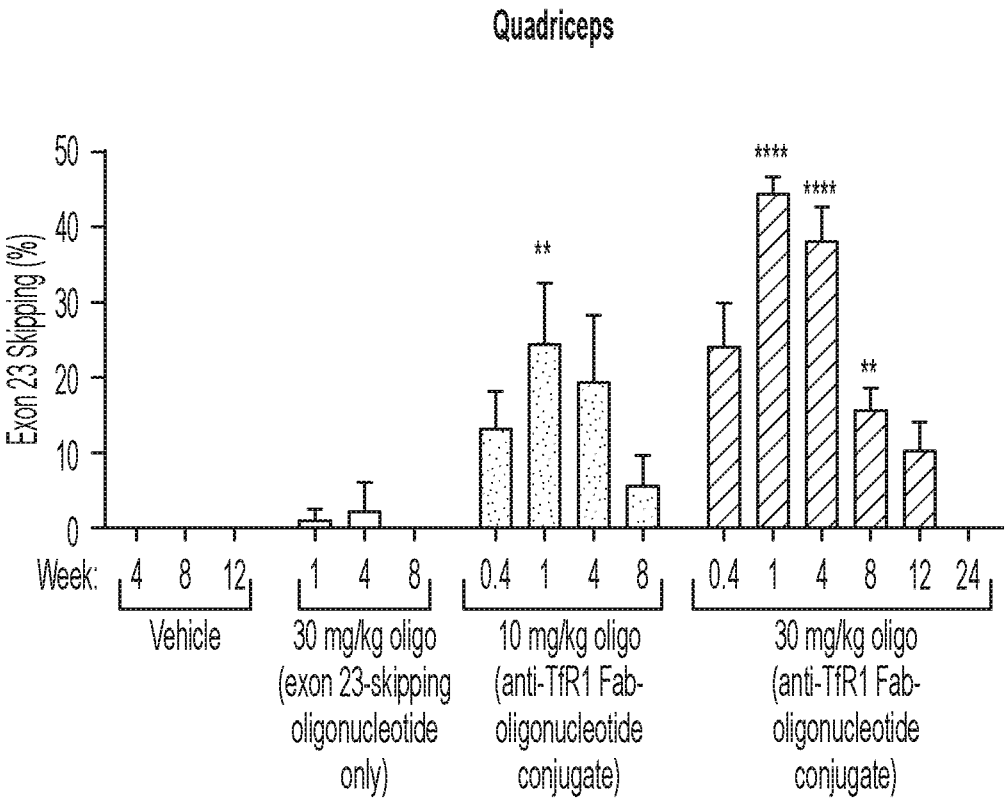

Quadriceps
Exon 23 Skipping (%)
50
40
30
20
10
0
**
****
****
**
Week:
4 8 12
1 4 8
0.4 1 4 8
0.4 1 4 8 12 24
Vehicle
30 mg/kg oligo (exon 23-skipping oligonucleotide only)
10 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)
30 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)

FIG. 9A

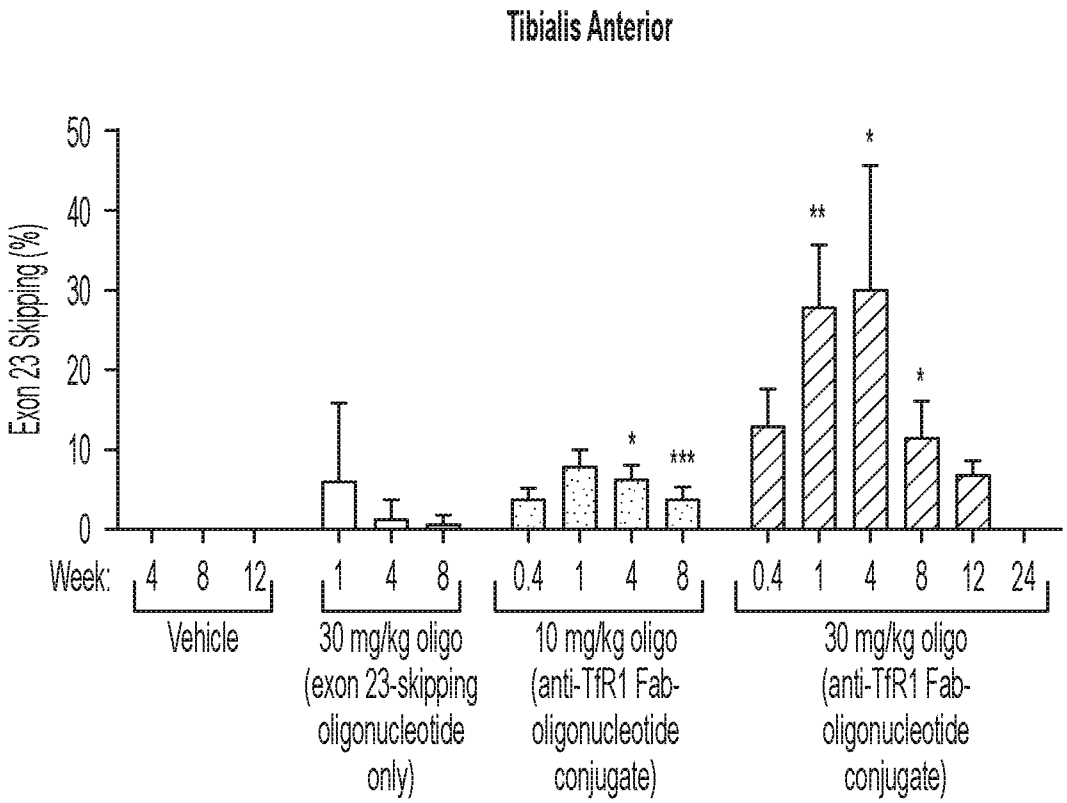

Tibialis Anterior
Exon 23 Skipping (%)
50
40
30
20
10
0
Week:
4 8 12
1 4 8
0.4 1 4 8
0.4 1 4 8 12 24
*
***
**
*
*
Vehicle
30 mg/kg oligo (exon 23-skipping oligonucleotide only)
10 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)
30 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)

FIG. 9B

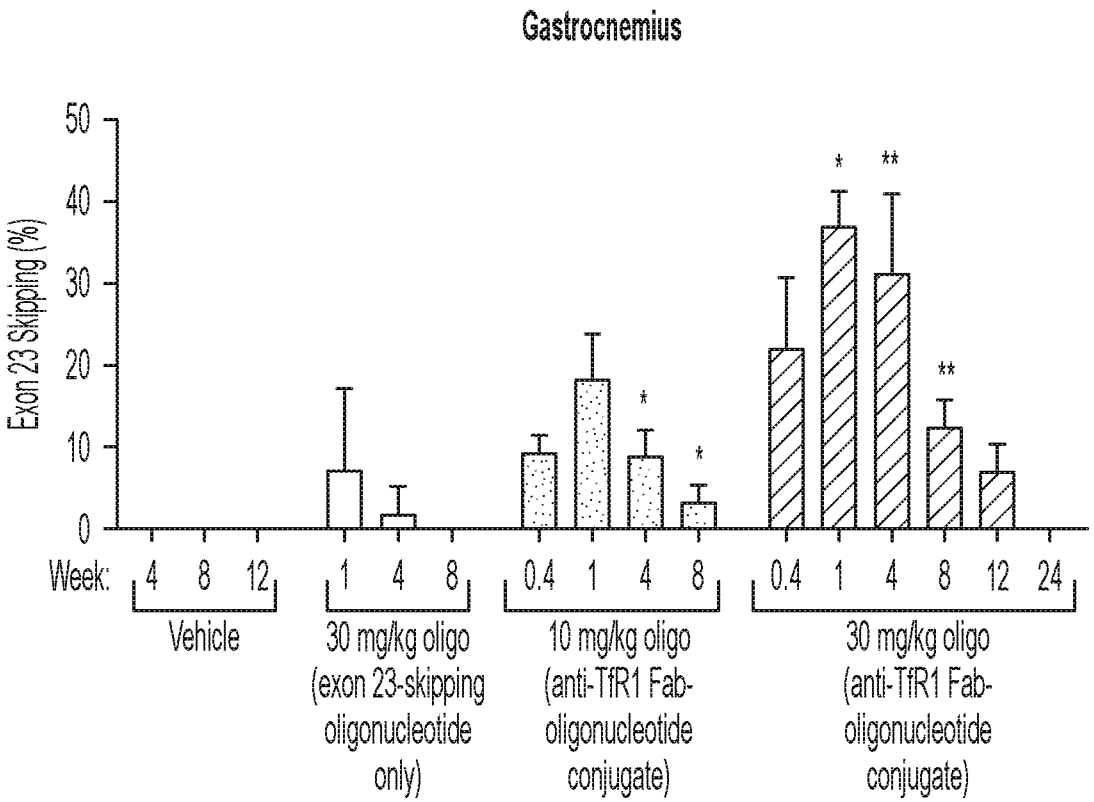

Gastrocnemius
Exon 23 Skipping (%)
50
40
30
20
10
0
Week:
4 8 12
1 4 8
0.4 1 4 8
0.4 1 4 8 12 24
Vehicle
30 mg/kg oligo (exon 23-skipping oligonucleotide only)
10 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)
30 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)

FIG. 9C

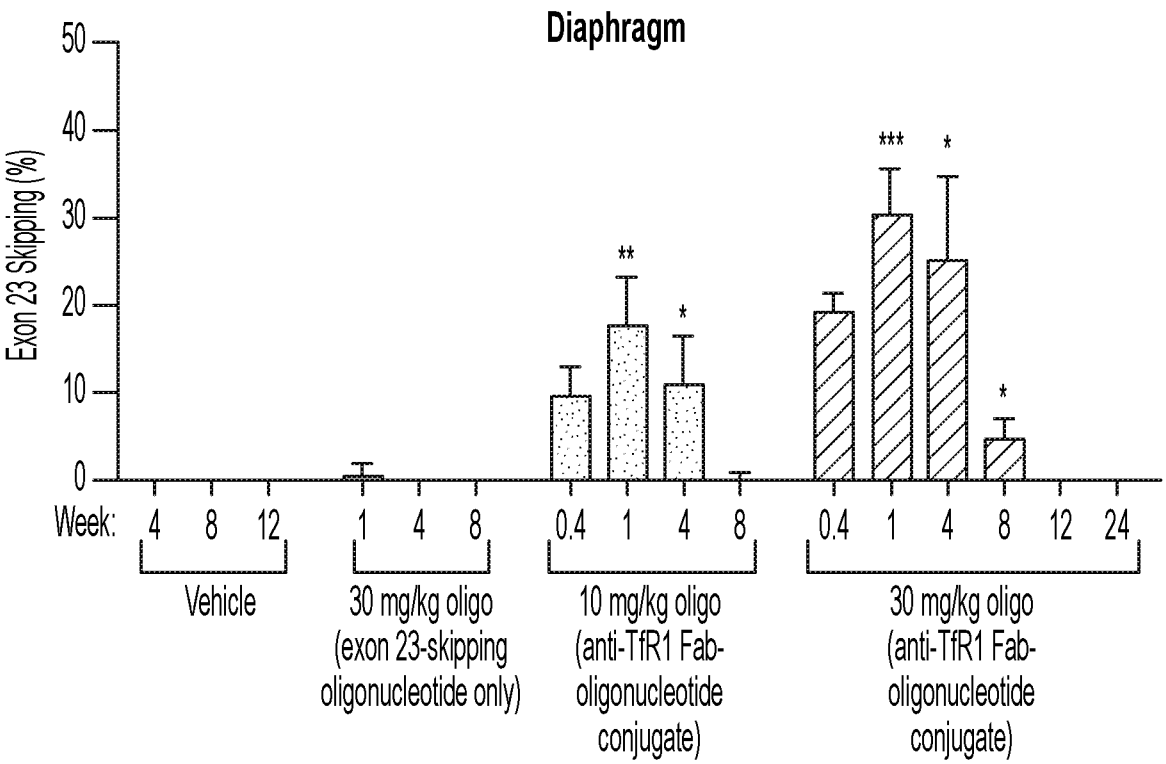

Diaphragm
Exon 23 Skipping (%)
50
40
30
20
10
0
Week:
4 8 12 1 4 8 0.4 1 4 8 0.4 1 4 8 12 24
**
*
***
*
*
Vehicle
30 mg/kg oligo (exon 23-skipping oligonucleotide only)
10 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)
30 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)

FIG. 9D

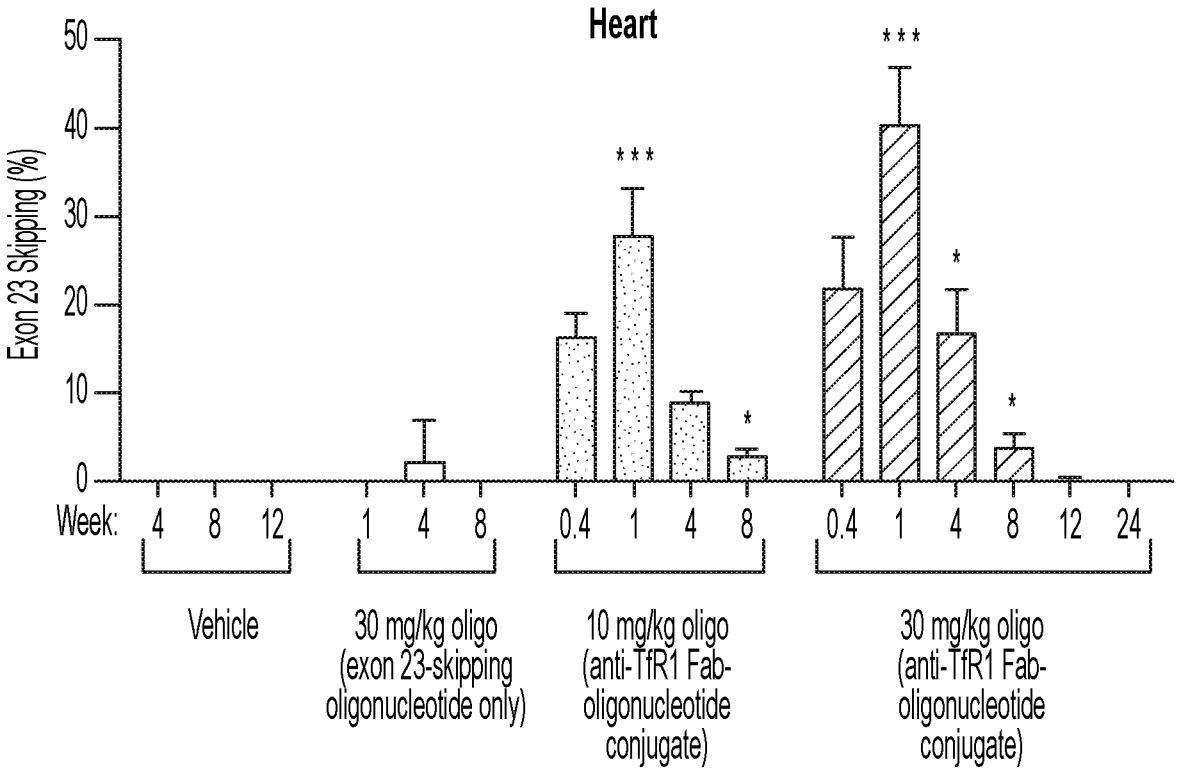

Heart
Exon 23 Skipping (%)
50
40
30
20
10
0
Week:
4 8 12
1 4 8
0.4 1 4 8
0.4 1 4 8 12 24
***
***
*
*
*
Vehicle
30 mg/kg oligo (exon 23-skipping oligonucleotide only)
10 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)
30 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)

FIG. 9E

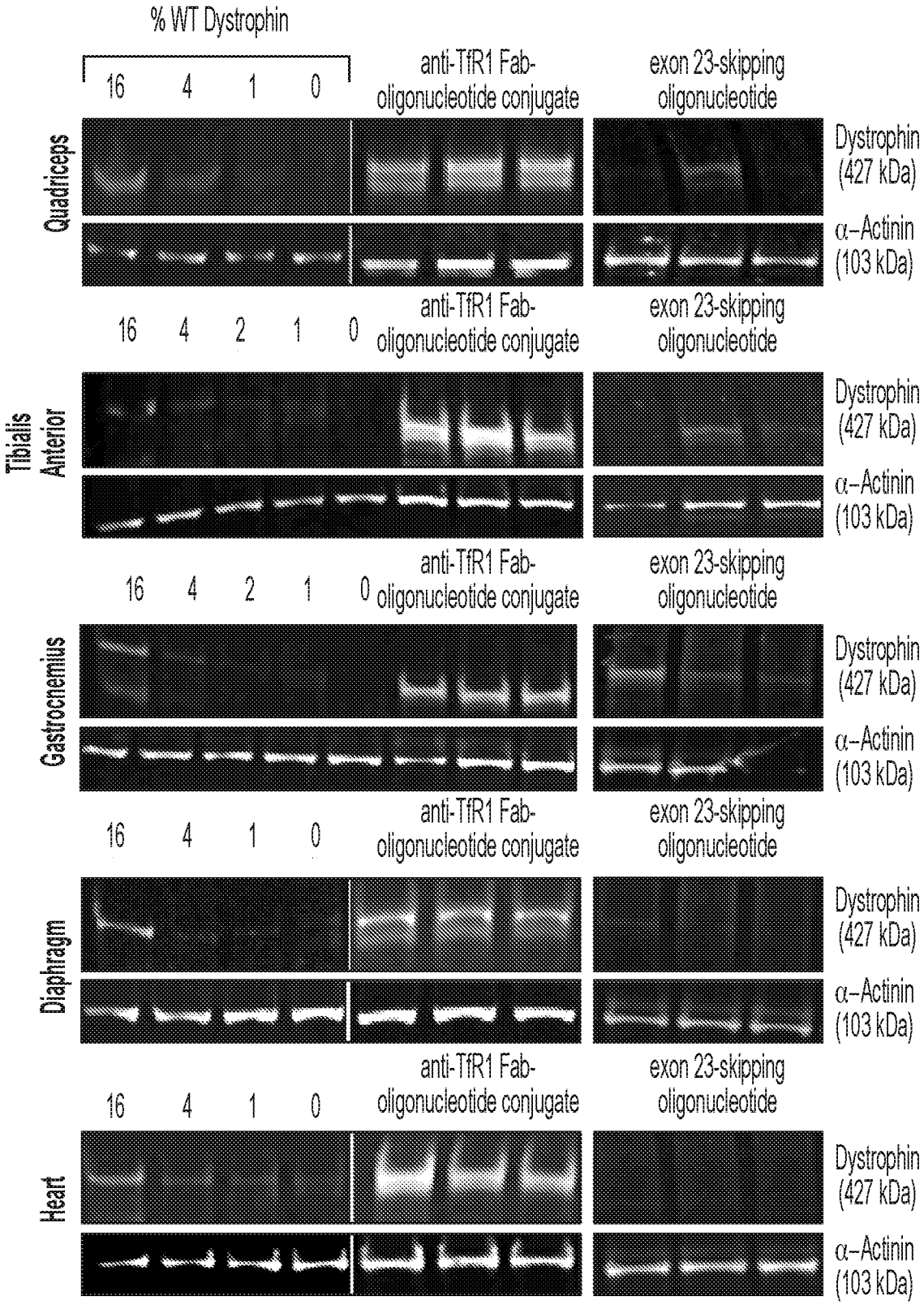

% WT Dystrophin
16
4
1
0
anti-TfR1 Fab-oligonucleotide conjugate
exon 23-skipping oligonucleotide
Quadriceps
Dystrophin (427 kDa)
α-Actinin (103 kDa)
16
4
2
1
0
anti-TfR1 Fab-oligonucleotide conjugate
exon 23-skipping oligonucleotide
Tibialis Anterior
Dystrophin (427 kDa)
α-Actinin (103 kDa)
16
4
2
1
0
anti-TfR1 Fab-oligonucleotide conjugate
exon 23-skipping oligonucleotide
Gastrocnemius
Dystrophin (427 kDa)
α-Actinin (103 kDa)
16
4
1
0
anti-TfR1 Fab-oligonucleotide conjugate
exon 23-skipping oligonucleotide
Diaphragm
Dystrophin (427 kDa)
α-Actinin (103 kDa)
16
4
1
0
anti-TfR1 Fab-oligonucleotide conjugate
exon 23-skipping oligonucleotide
Heart
Dystrophin (427 kDa)
α-Actinin (103 kDa)

FIG. 10A

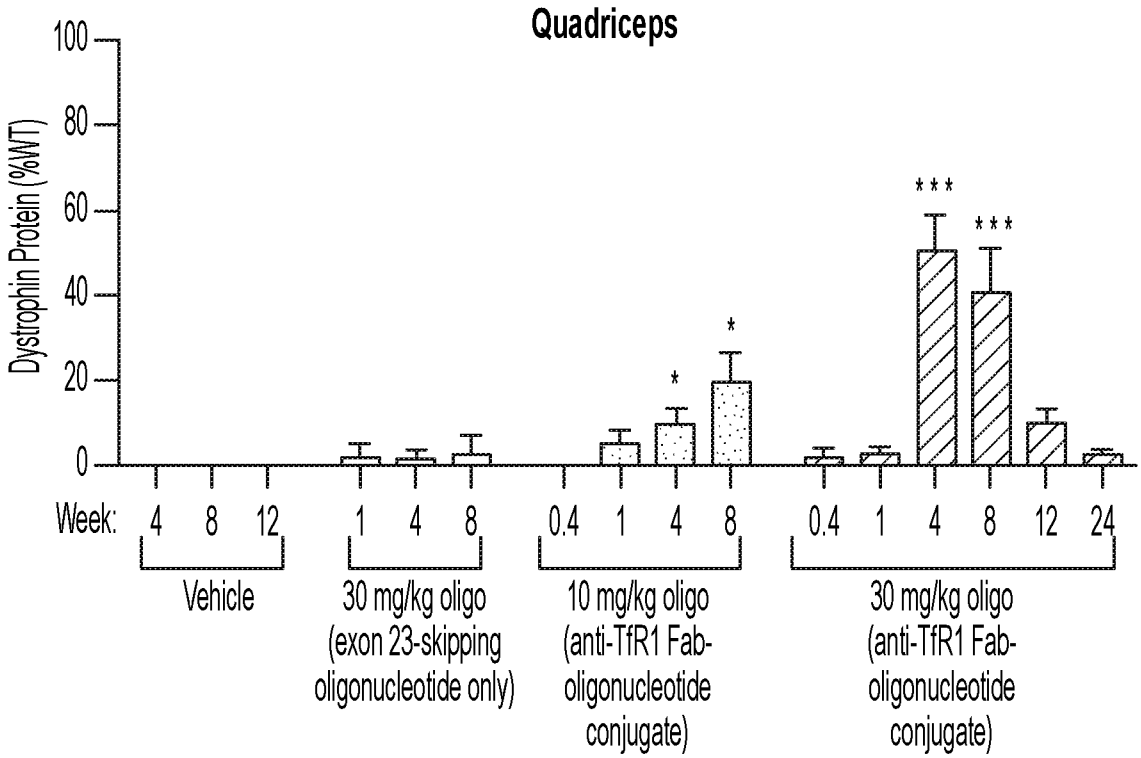

Quadriceps
Dystrophin Protein (%WT)
100
80
60
40
20
0
Week:
4
8
12
1
4
8
0.4
1
4
8
0.4
1
4
8
12
24
*
*
***
***
Vehicle
30 mg/kg oligo (exon 23-skipping oligonucleotide only)
10 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)
30 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)

FIG. 10B

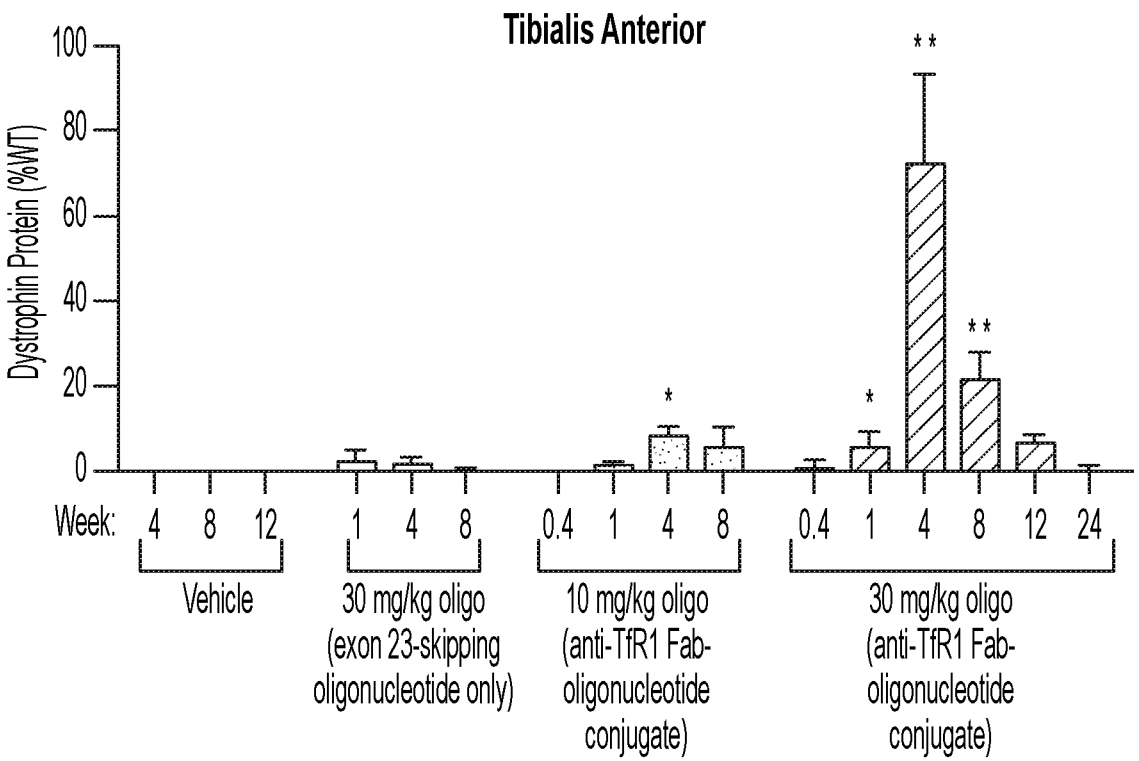

Tibialis Anterior
Dystrophin Protein (%WT)
100
80
60
40
20
0
Week:
4 8 12
1 4 8
0.4 1 4 8
0.4 1 4 8 12 24
*
*
**
**
Vehicle
30 mg/kg oligo (exon 23-skipping oligonucleotide only)
10 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)
30 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)

FIG. 10C

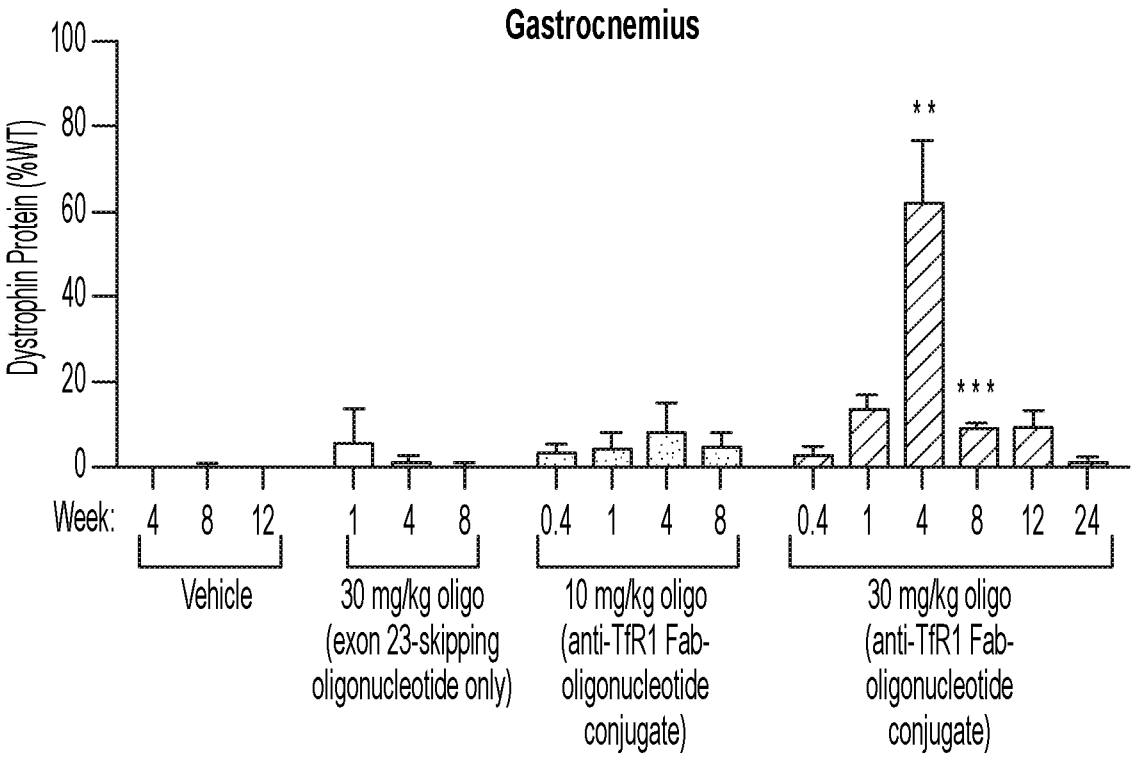

Gastrocnemius
Dystrophin Protein (%WT)
100
80
60
40
20
0
**
***
Week:
4
8
12
1
4
8
0.4
1
4
8
0.4
1
4
8
12
24
Vehicle
30 mg/kg oligo (exon 23-skipping oligonucleotide only)
10 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)
30 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)

FIG. 10D

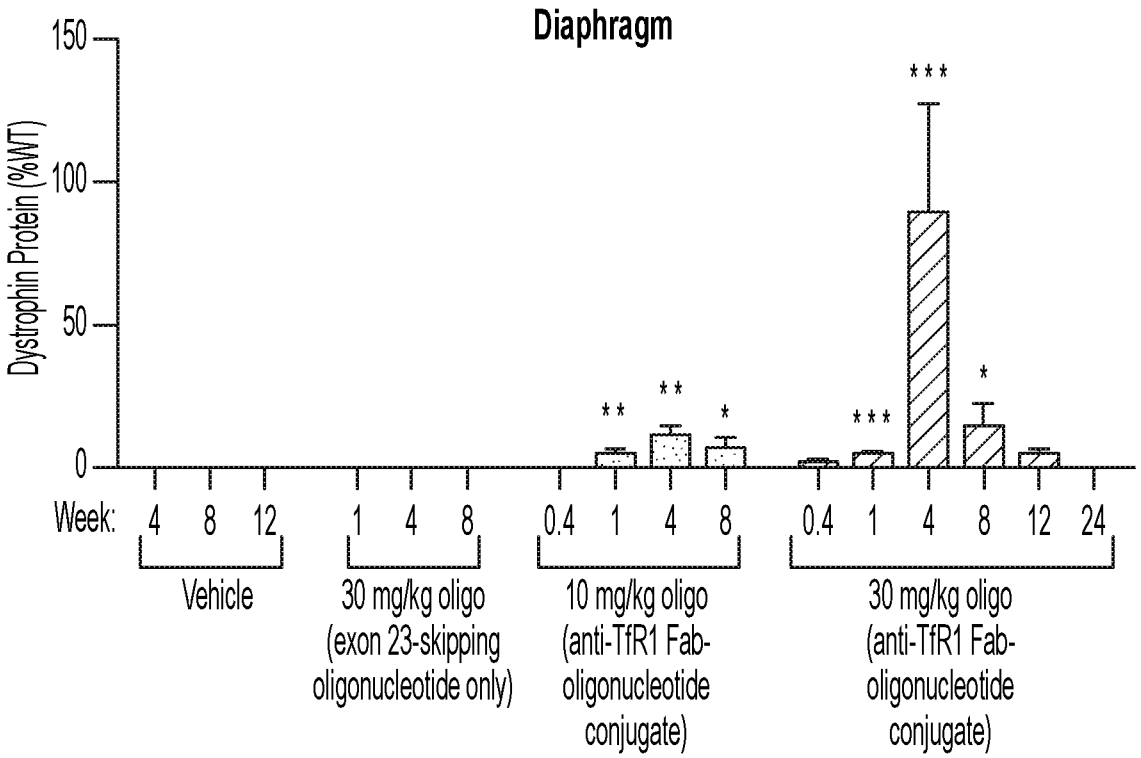

Diaphragm
Dystrophin Protein (%WT)
150
100
50
0
Week:
4 8 12
1 4 8
0.4 1 4 8
0.4 1 4 8 12 24
Vehicle
30 mg/kg oligo (exon 23-skipping oligonucleotide only)
10 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)
30 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)

FIG. 10E

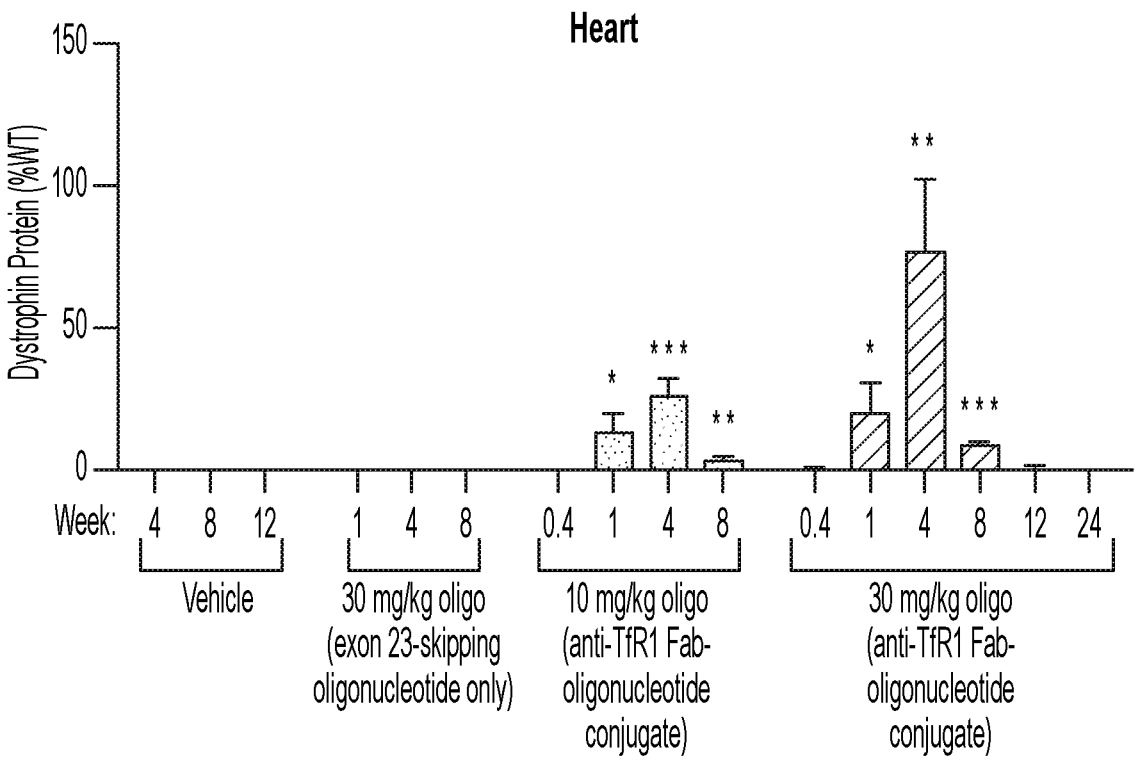

Heart
Dystrophin Protein (%WT)
150
100
50
0
Week:
4 8 12
1 4 8
0.4 1 4 8
0.4 1 4 8 12 24
Vehicle
30 mg/kg oligo (exon 23-skipping oligonucleotide only)
10 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)
30 mg/kg oligo (anti-TfR1 Fab-oligonucleotide conjugate)

FIG. 10F

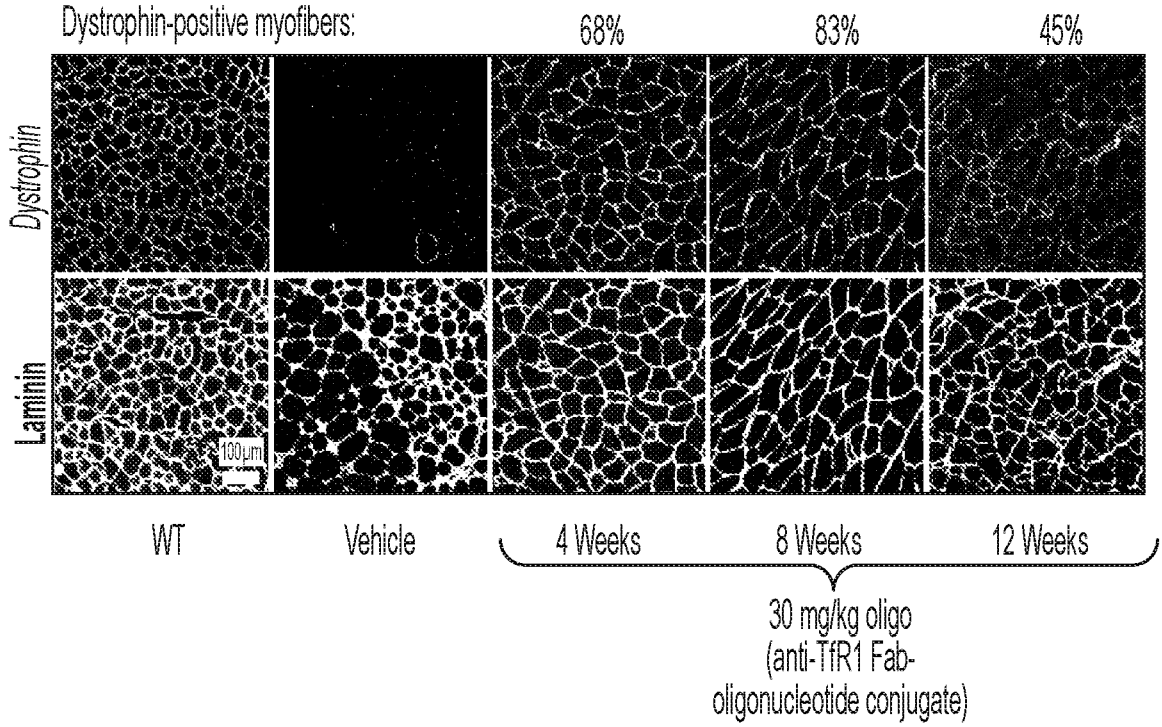


FIG. 11A

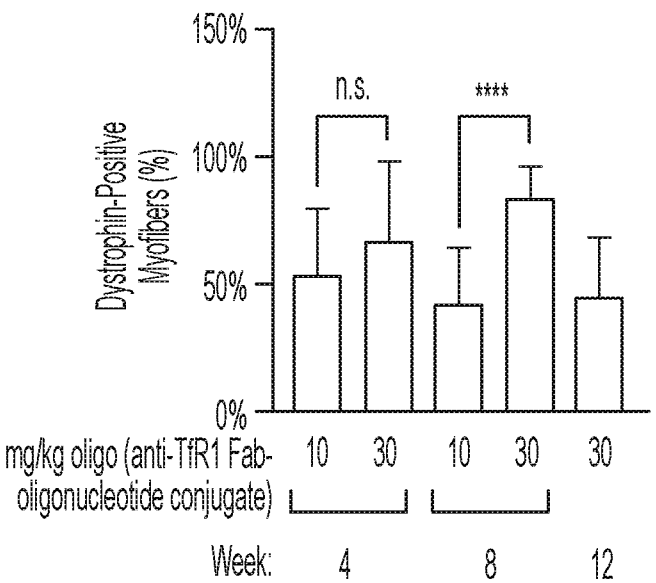


FIG. 11B

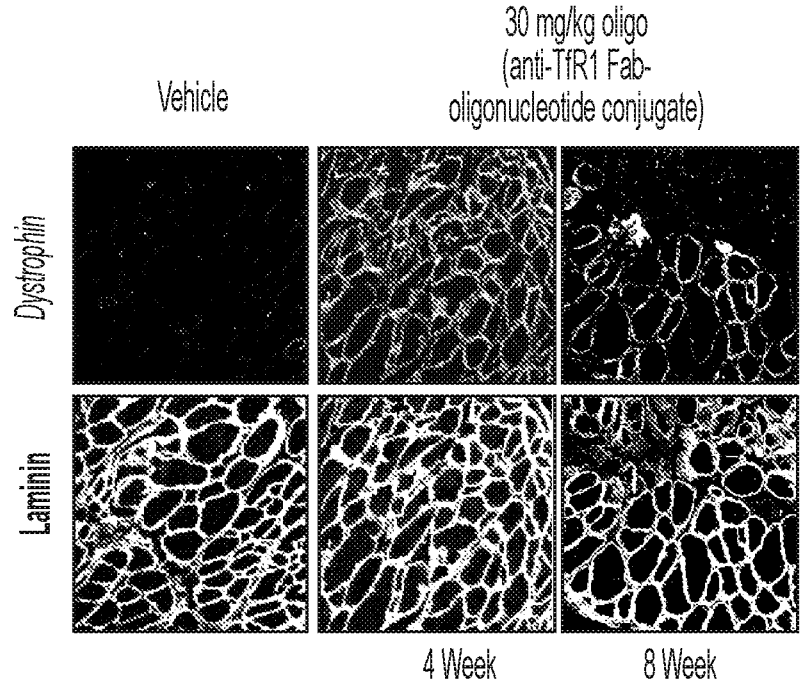


FIG. 11C

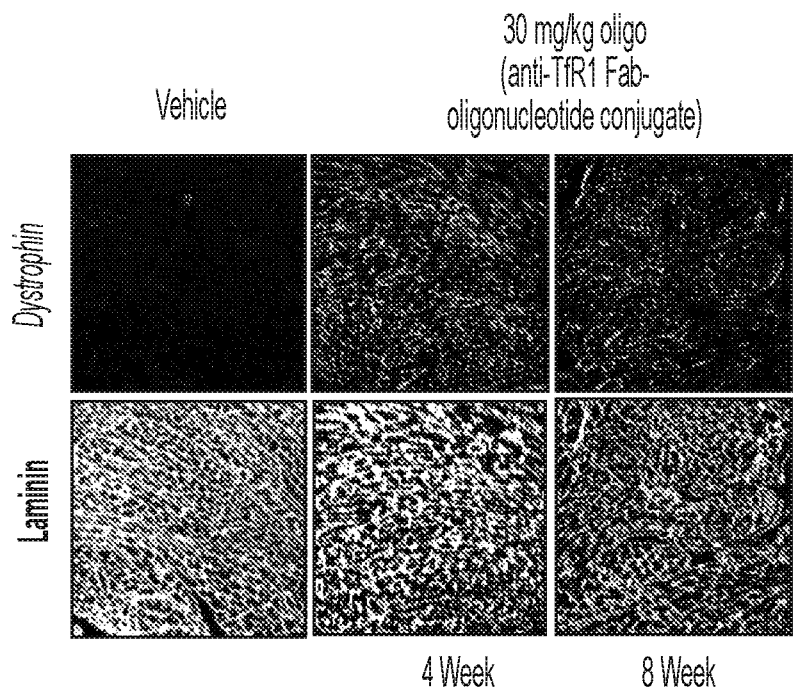


FIG. 11D

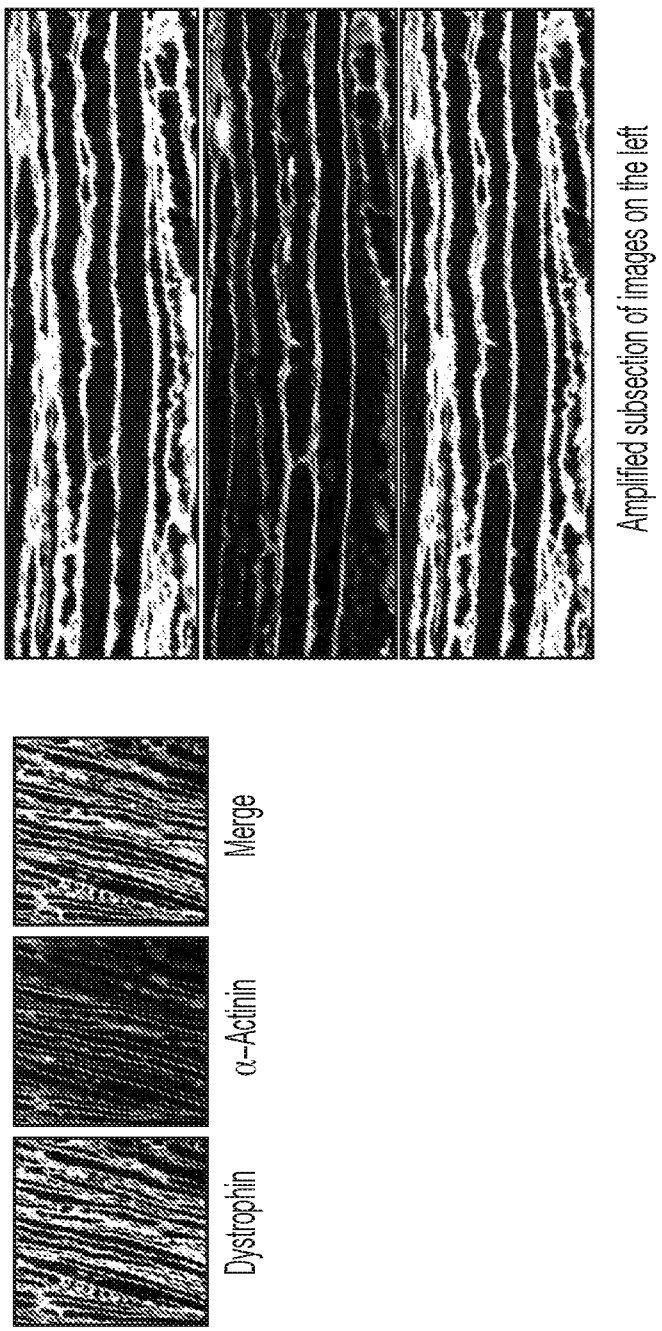

Dystrophin
α-Actinin
Merge
Amplified subsection of images on the left

FIG. 12

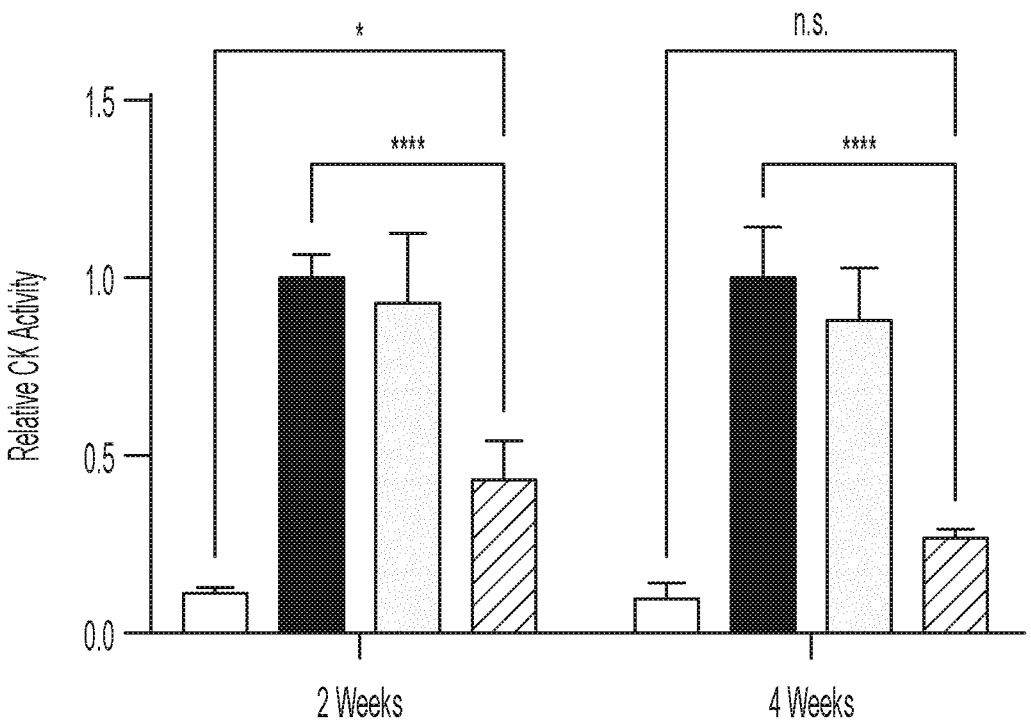


FIG. 13A

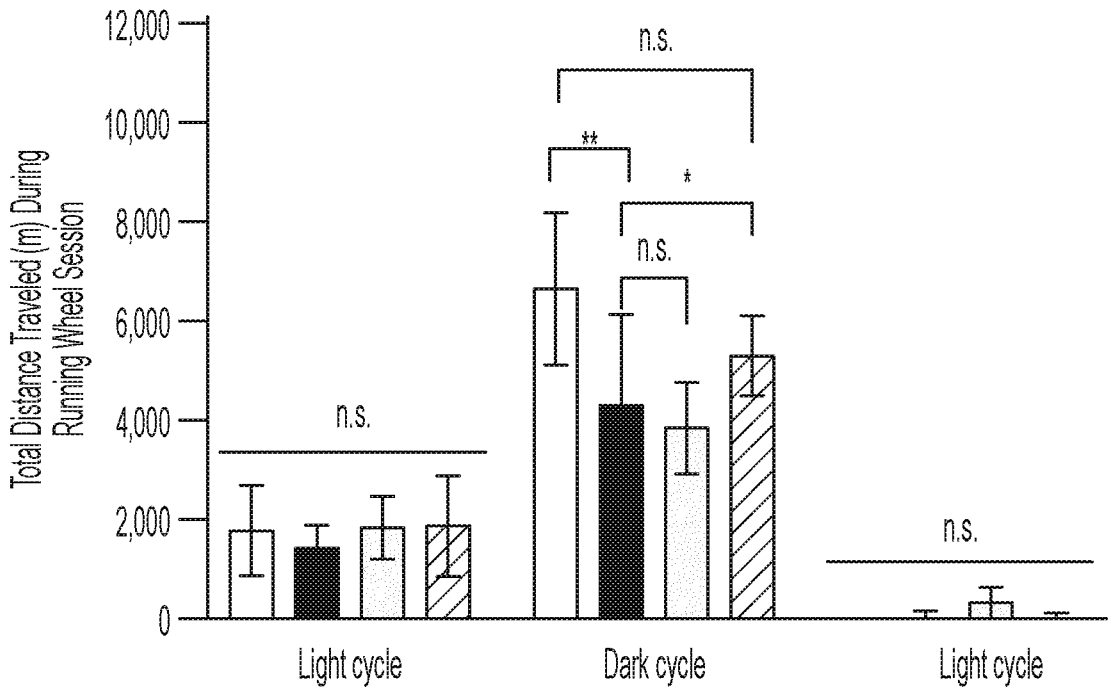

Total Distance Traveled (m) During Running Wheel Session
12,000
10,000
8,000
6,000
4,000
2,000
0
n.s.
**
*
n.s.
n.s.
n.s.
Light cycle
Dark cycle
Light cycle

FIG. 13B

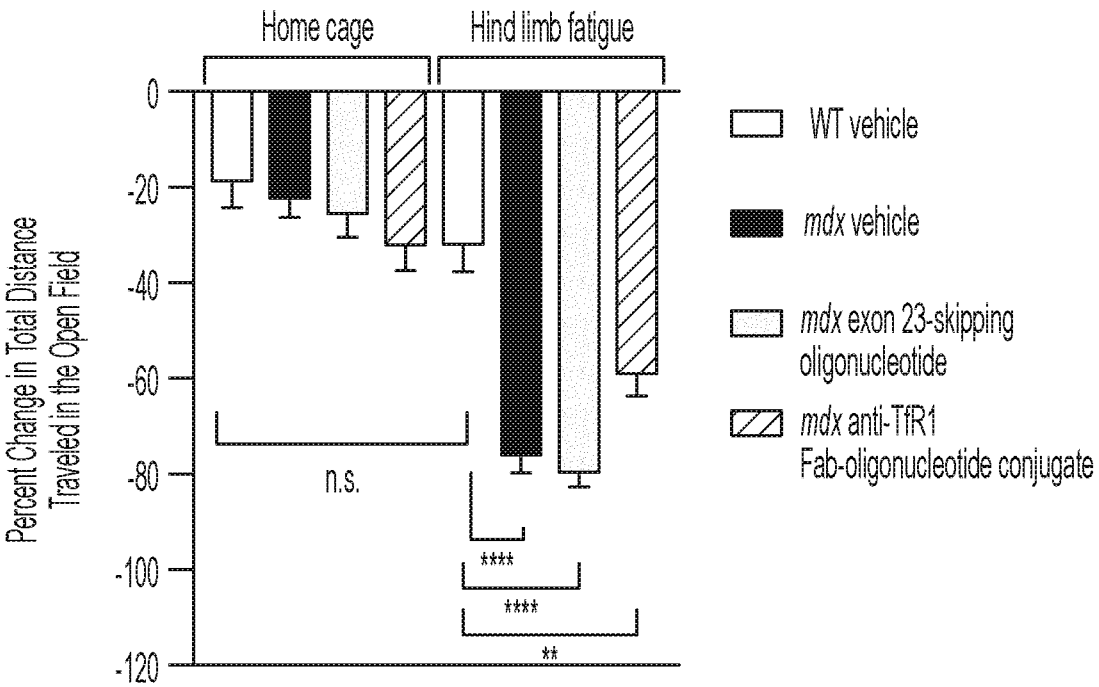

Home cage
Hind limb fatigue
0
-20
-40
-60
-80
-100
-120
Percent Change in Total Distance Traveled in the Open Field
n.s.
****
****
**
WT vehicle
mdx vehicle
mdx exon 23-skipping oligonucleotide
mdx anti-TfR1 Fab-oligonucleotide conjugate

FIG. 13C

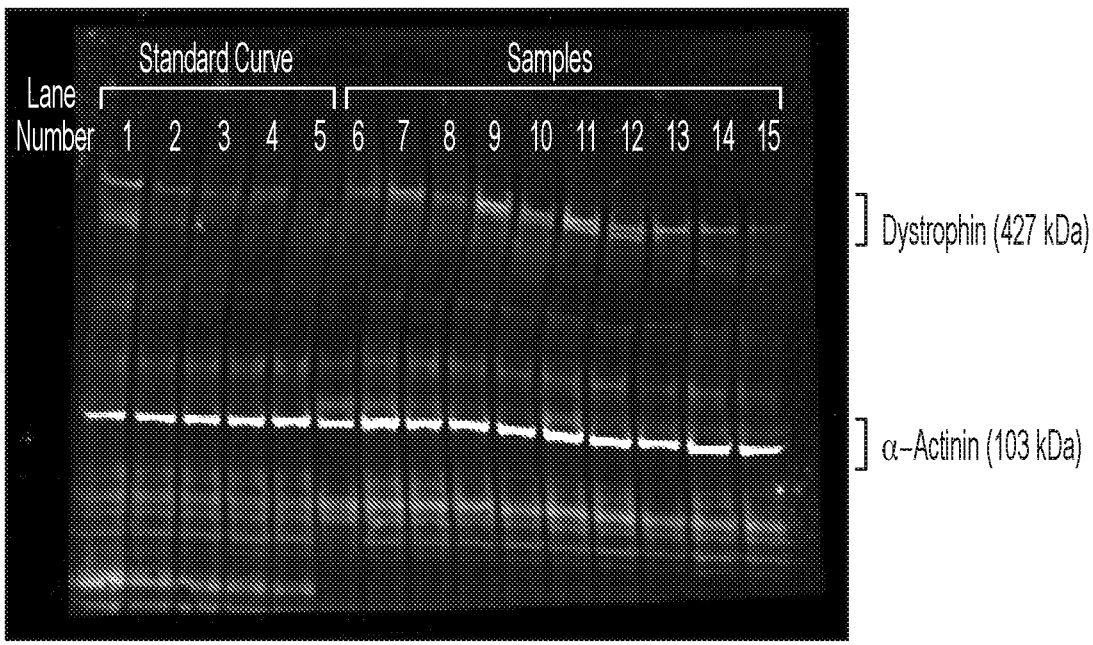


FIG. 14A

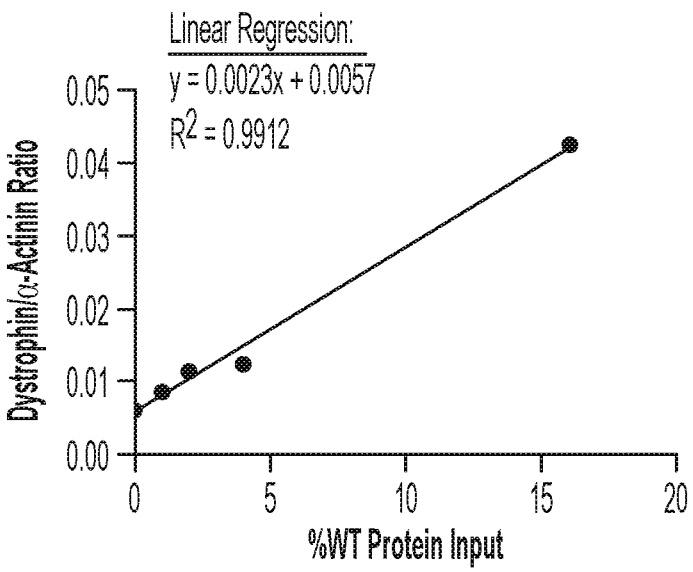


FIG. 14B

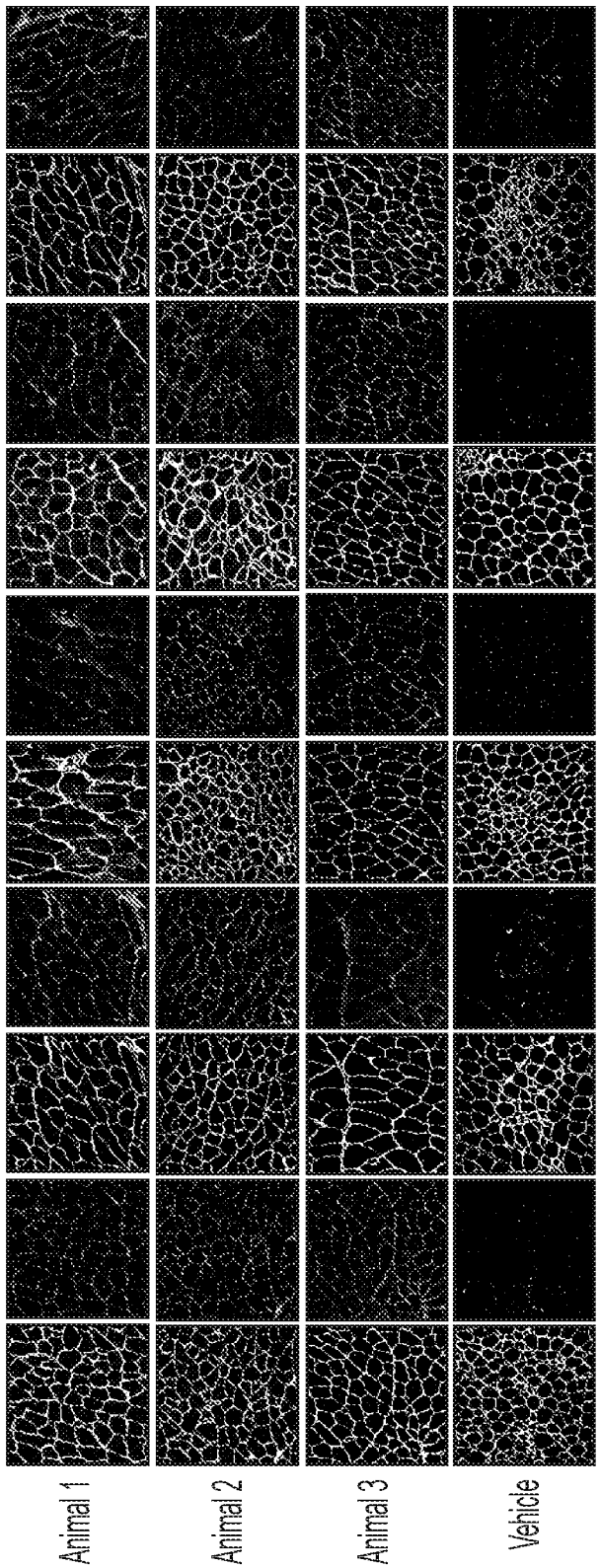

Field 1
Field 2
Field 3
Field 4
Field 5
Animal 1
Animal 2
Animal 3
Vehicle
Laminin
Dystrophin

FIG. 15

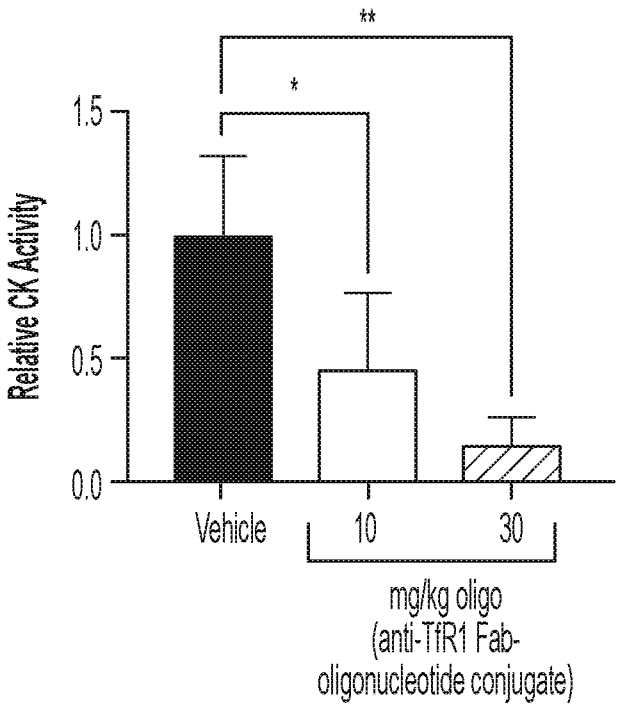


FIG. 16A

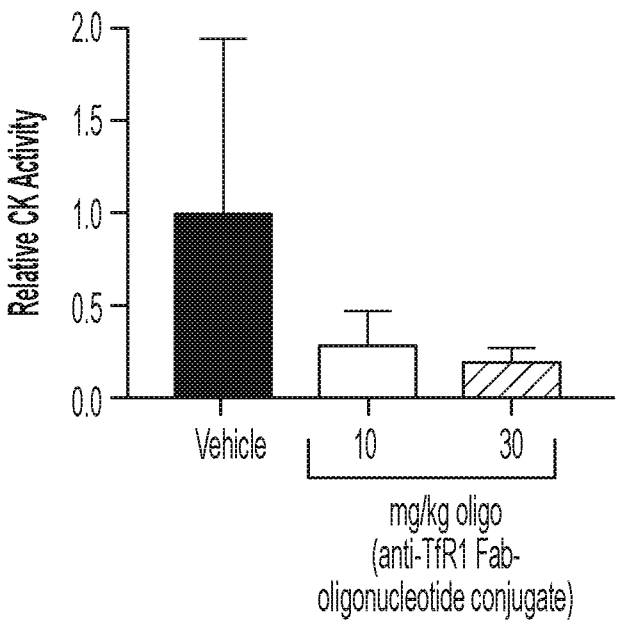


FIG. 16B

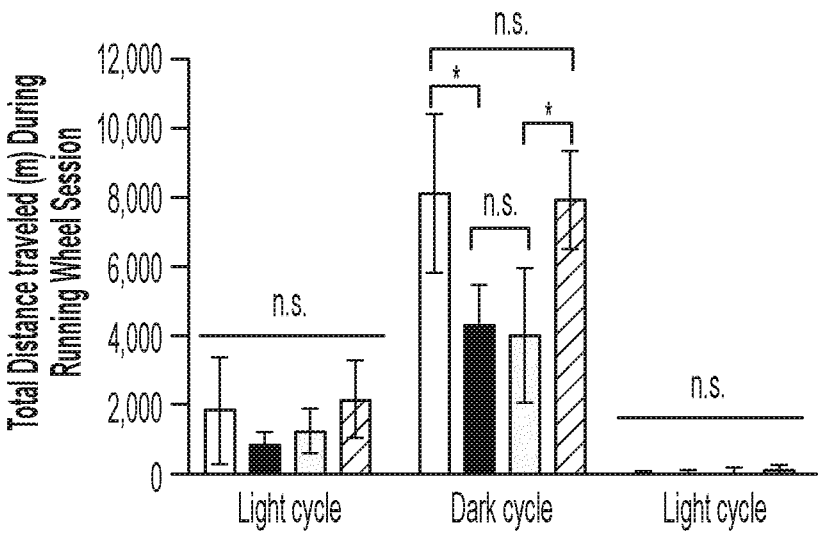


FIG. 17A

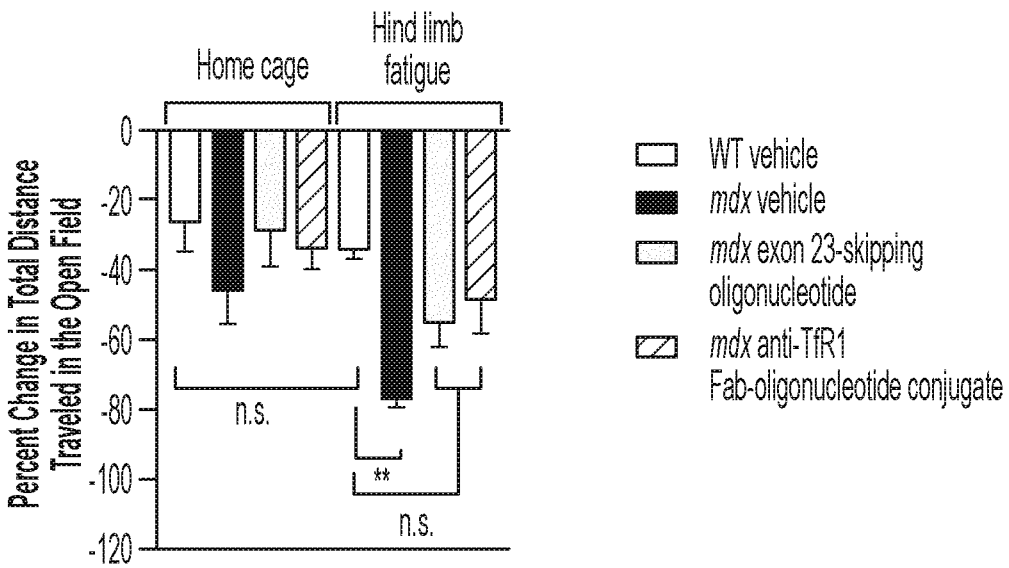


FIG. 17B