Figure 1

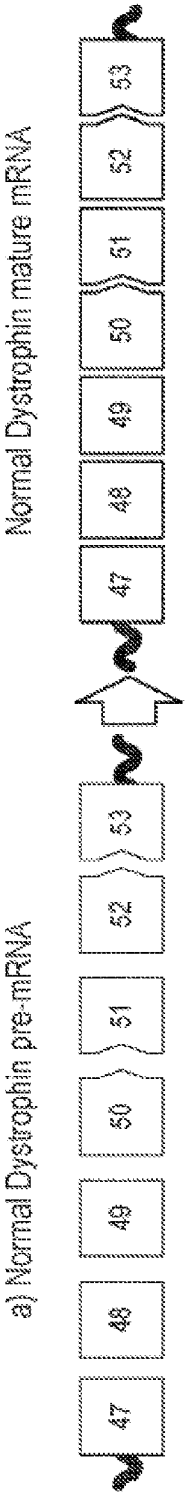

a) Normal Dystrophin pre-mRNA
47
48
49
50
51
52
53
Normal Dystrophin mature mRNA
47
48
49
50
51
52
53

Figure 2

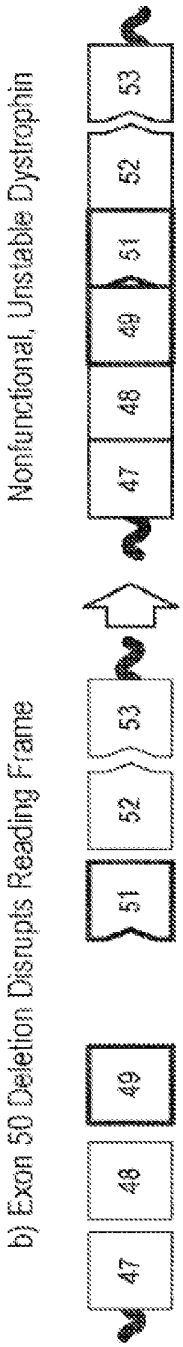

b) Exon 50 Deletion Disrupts Reading Frame
47
48
49
51
52
53
Nonfunctional, Unstable Dystrophin
47
48
49
51
52
53

Figure 3

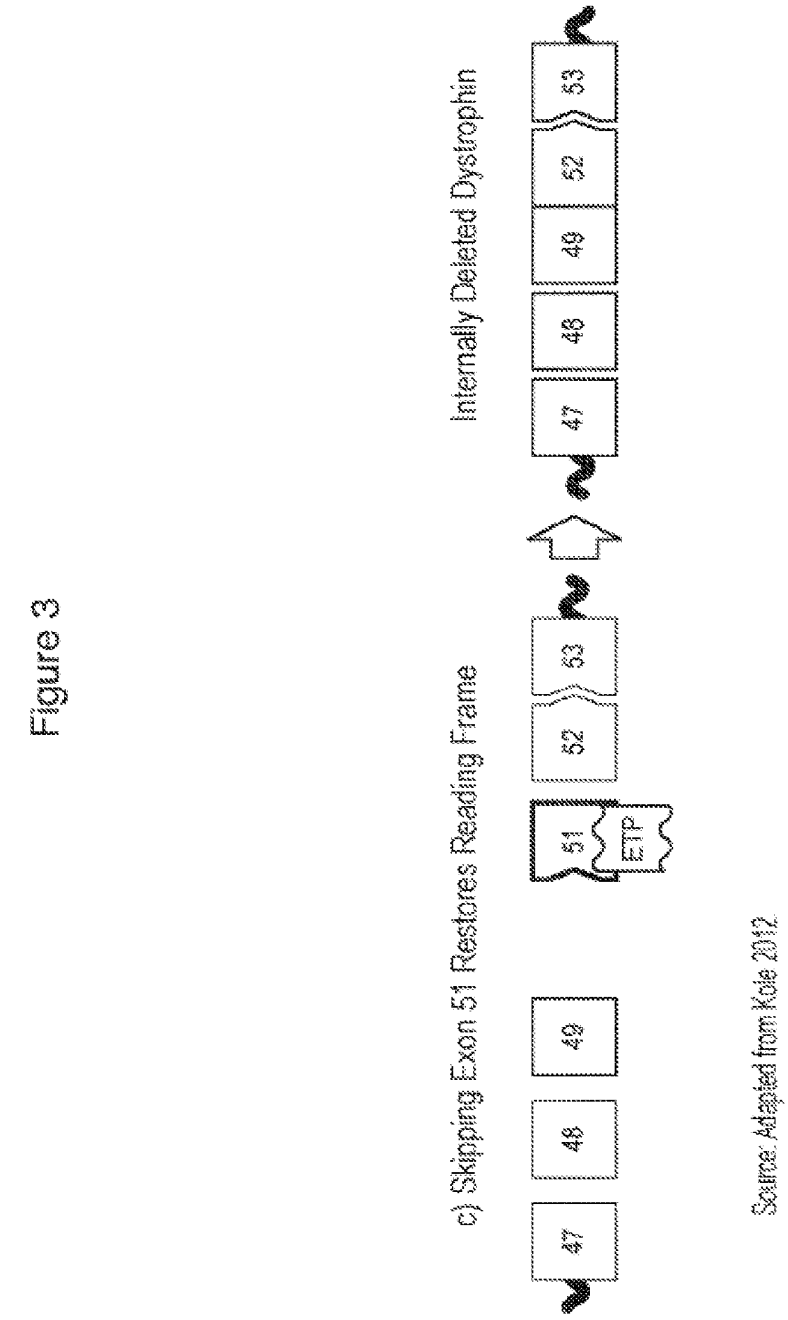

c) Skipping Exon 51 Restores Reading Frame
47
48
49
51
ETP
52
53
Internally Deleted Dystrophin
47
48
49
52
53
Source: Adapted from Kole 2012

Figure 4

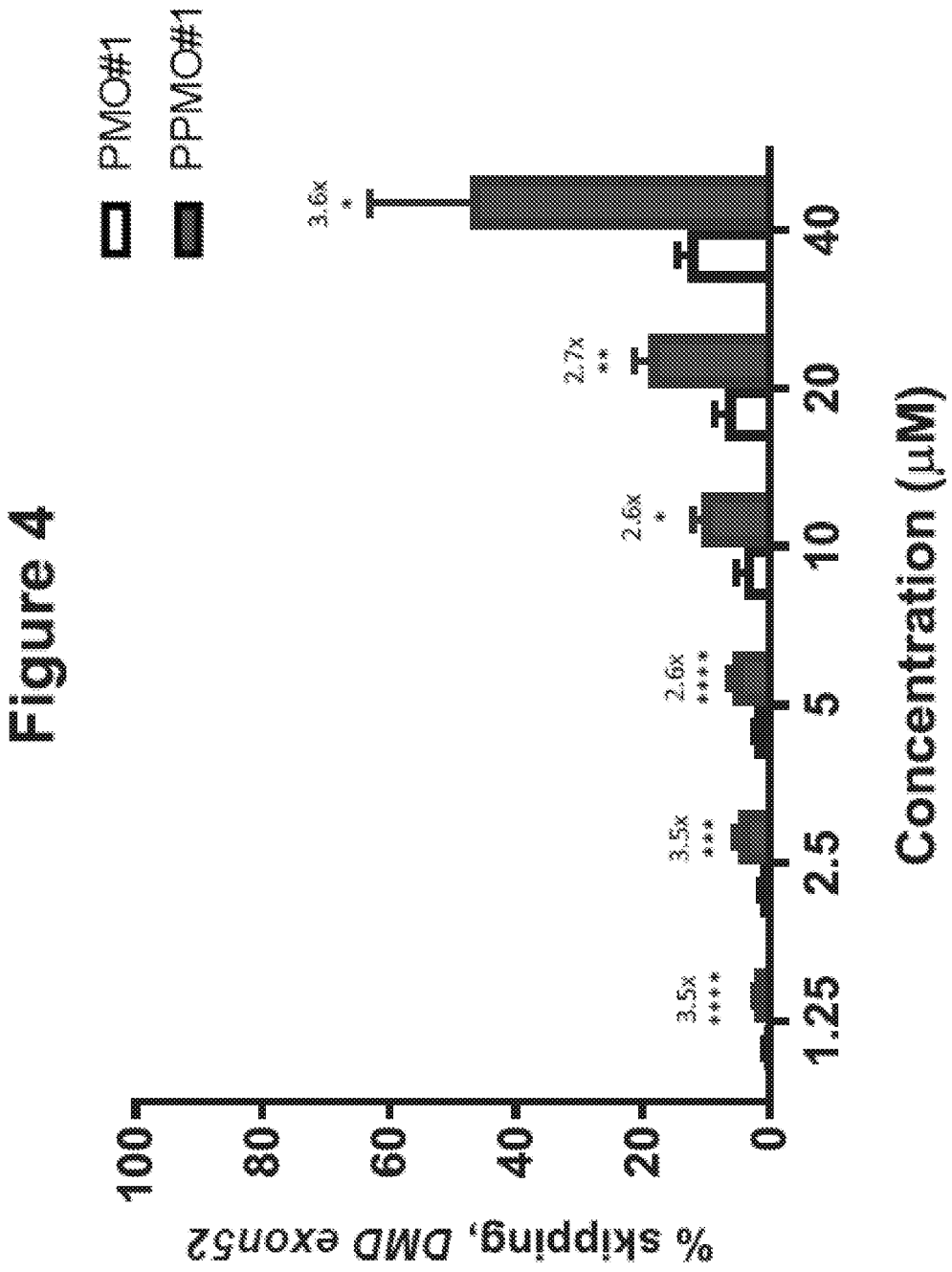

PMO#1
PPMO#1
% skipping, DMD exon52
100
80
60
40
20
0
1.25
2.5
5
10
20
40
Concentration (μM)
3.5x
****
3.5x
***
2.6x
****
2.6x
*
2.7x
**
3.6x
*

Figure 5A

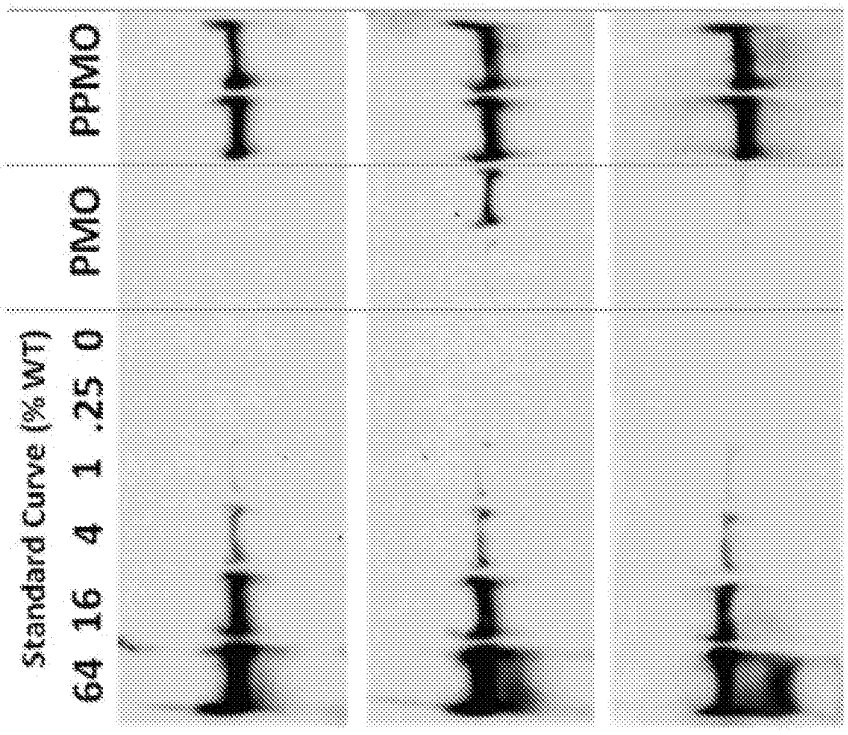


Figure 5B

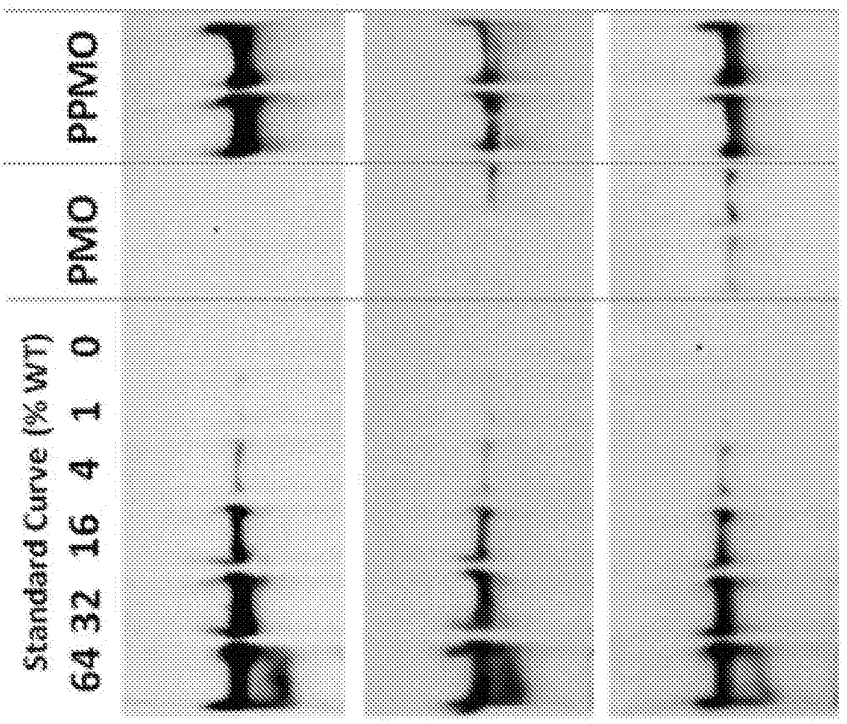


Figure 5C

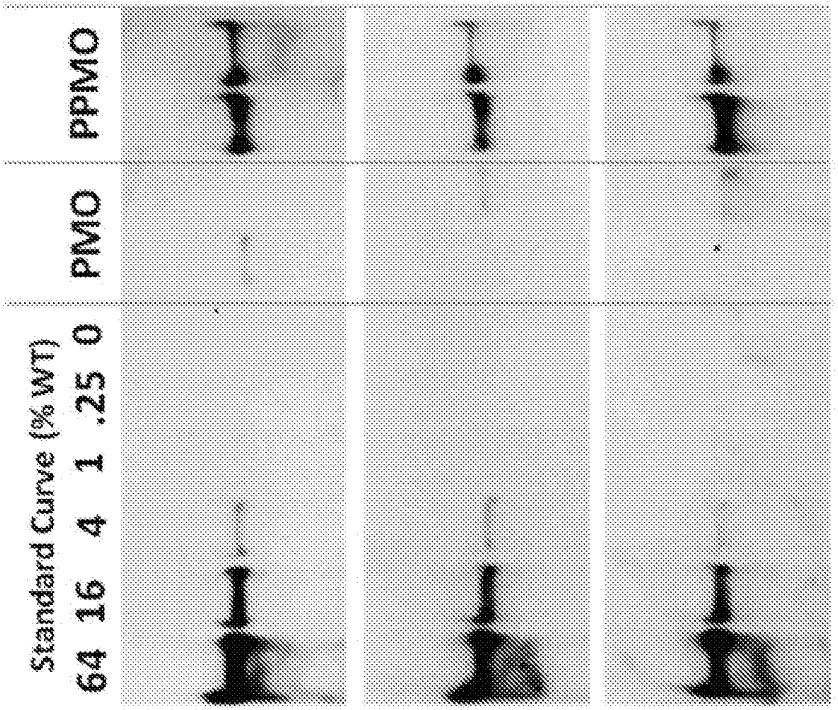
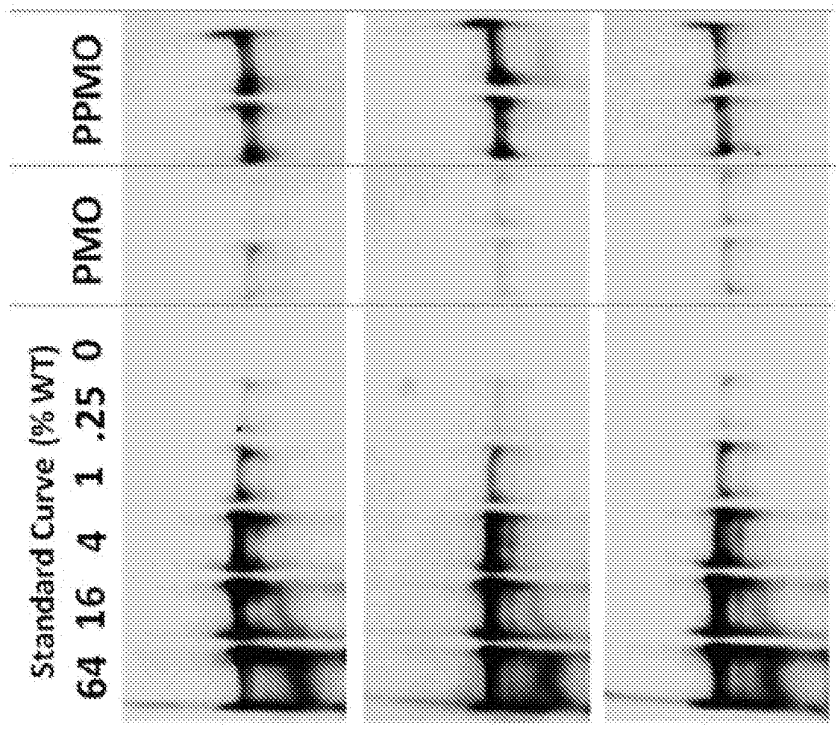


Figure 5D



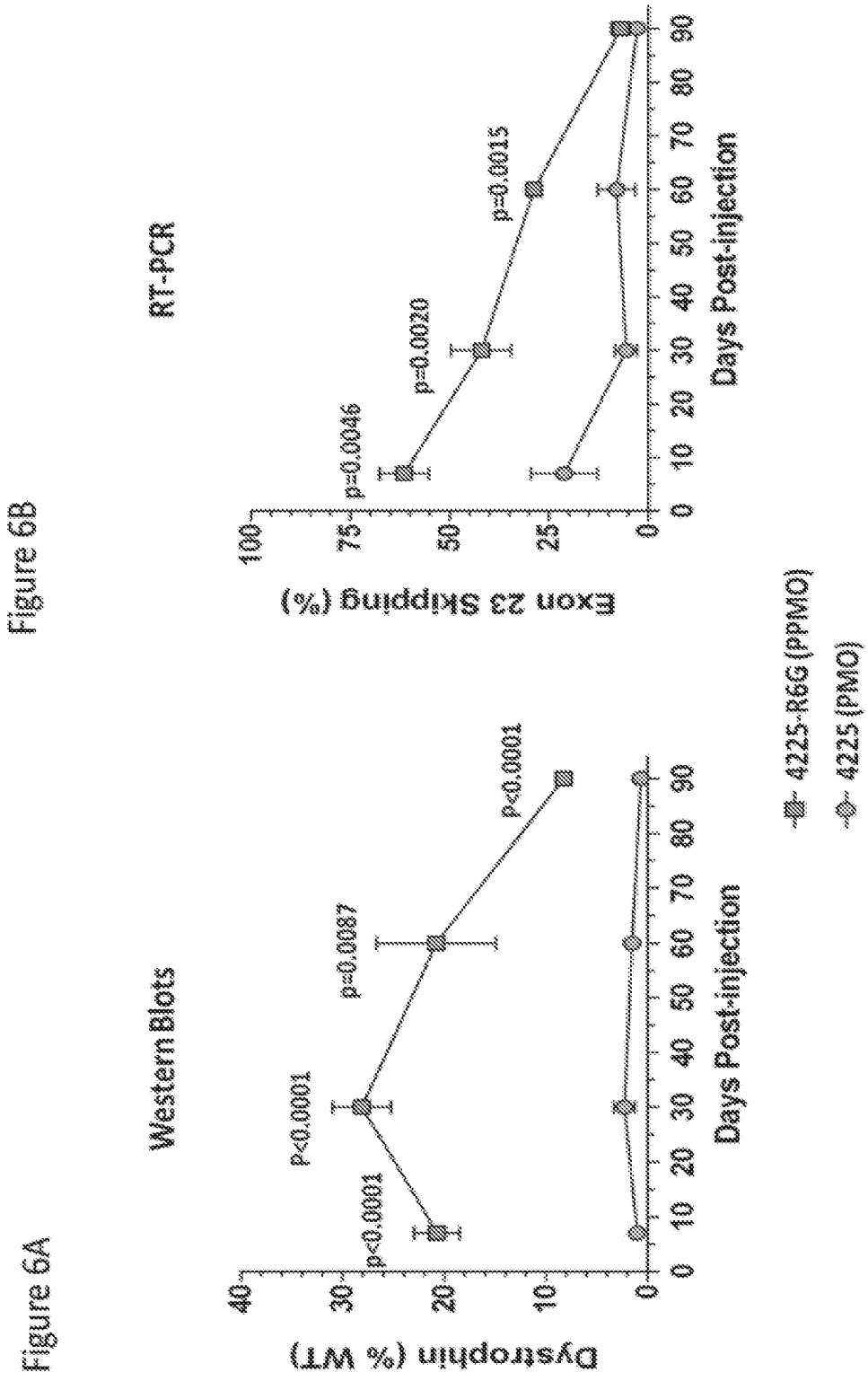

Figure 6A
Western Blots
Dystrophin (% WT)
40
30
20
10
0
p<0.0001
P<0.0001
p=0.0087
p<0.0001
0 10 20 30 40 50 60 70 80 90
Days Post-injection
Figure 6B
RT-PCR
Exon 23 Skipping (%)
100
75
50
25
0
p=0.0046
p=0.0020
p=0.0015
0 10 20 30 40 50 60 70 80 90
Days Post-injection
4225-R6G (PPMO)
4225 (PMO)

Figure 7A

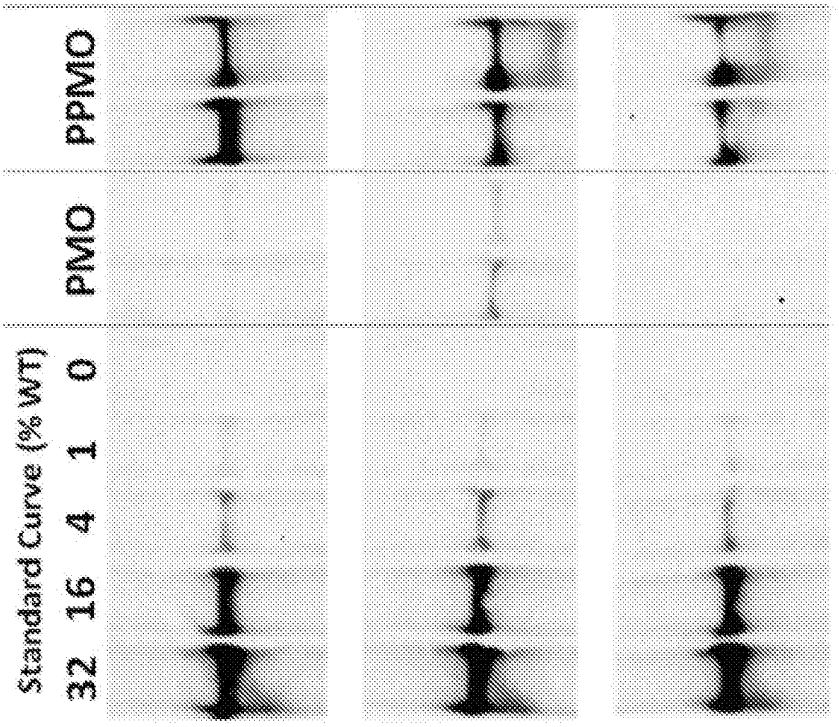


Figure 7B

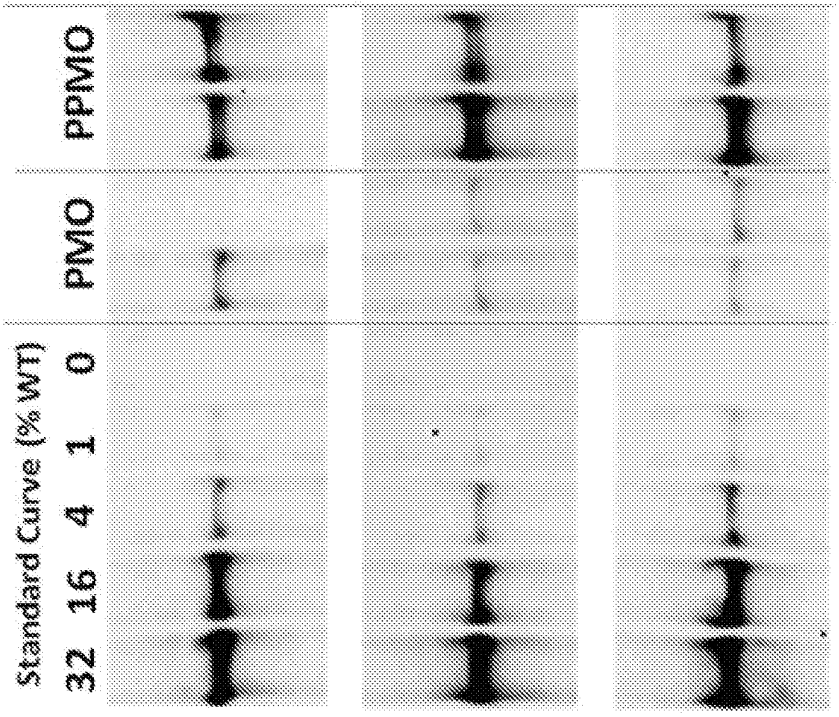


Figure 7C

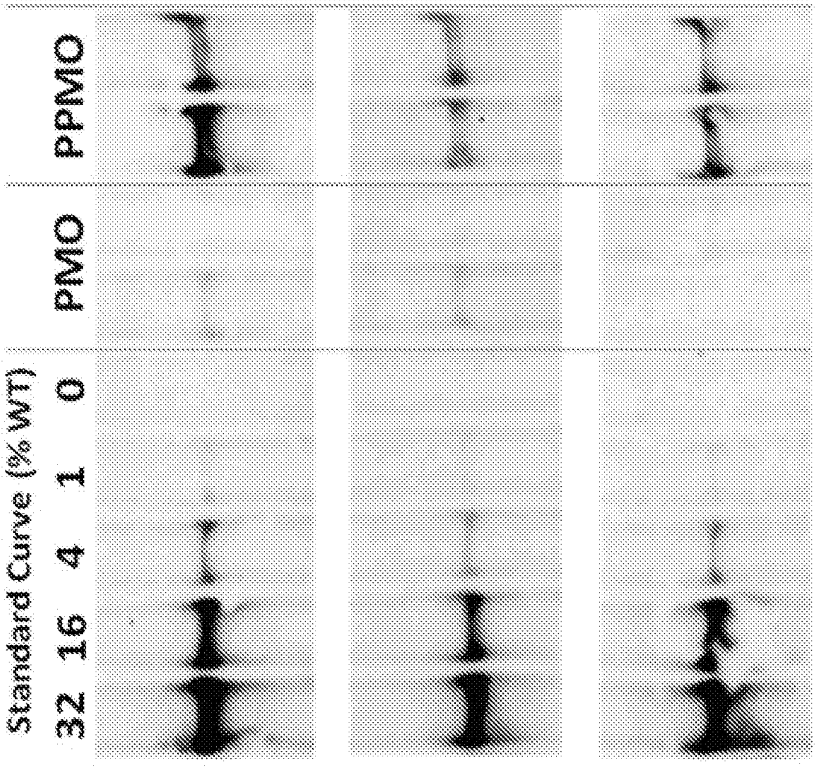


Figure 7D

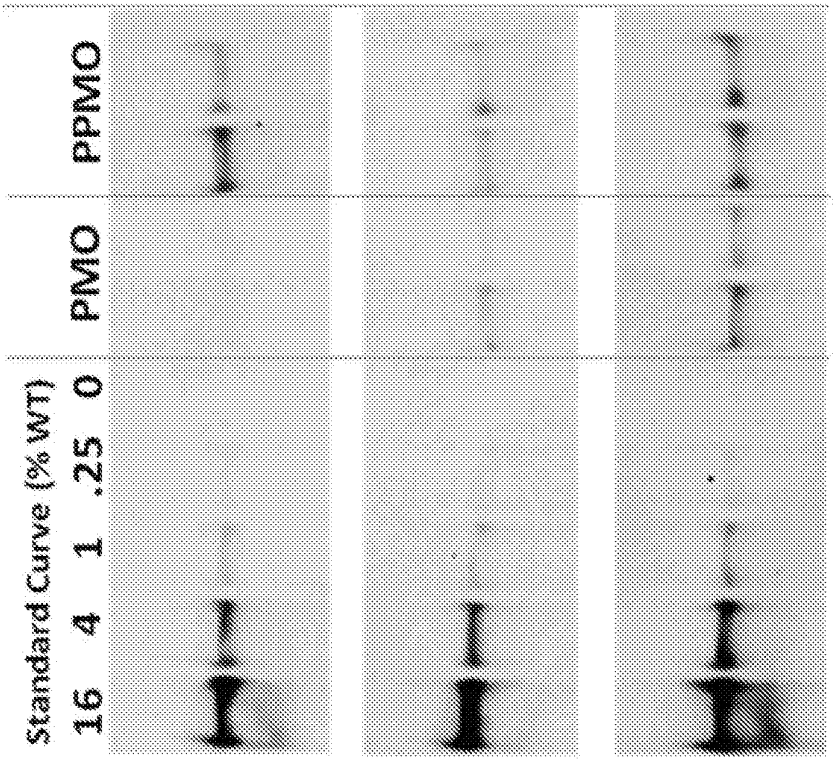


Figure 8A

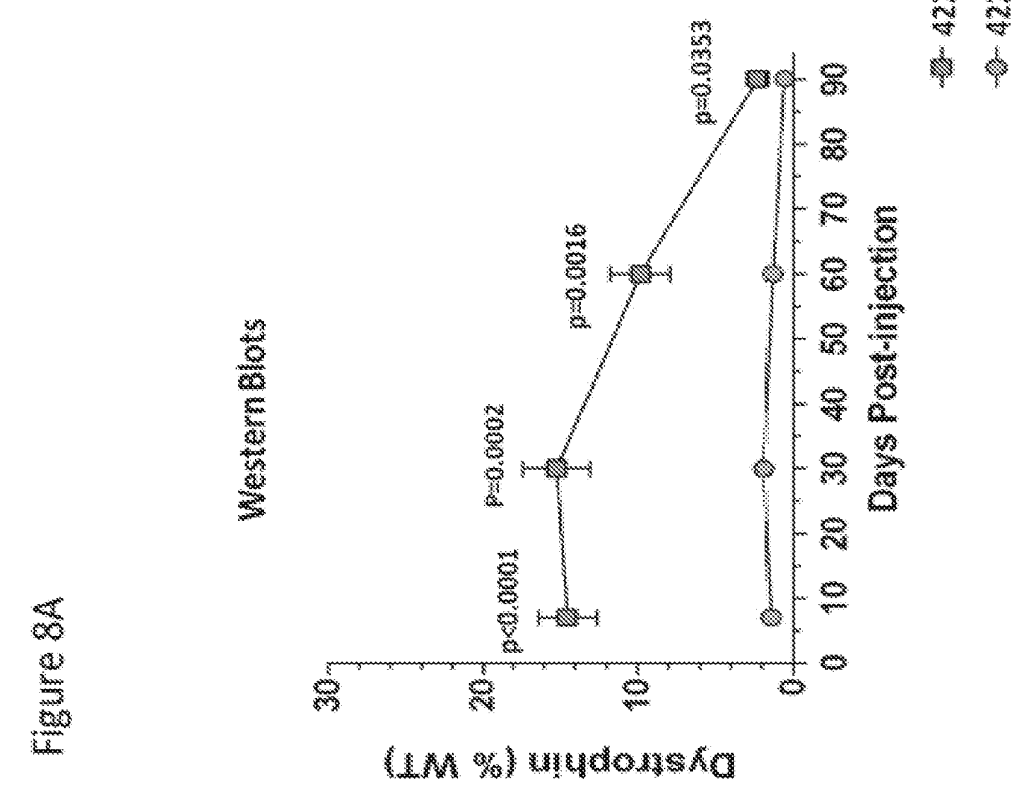


Figure 8B

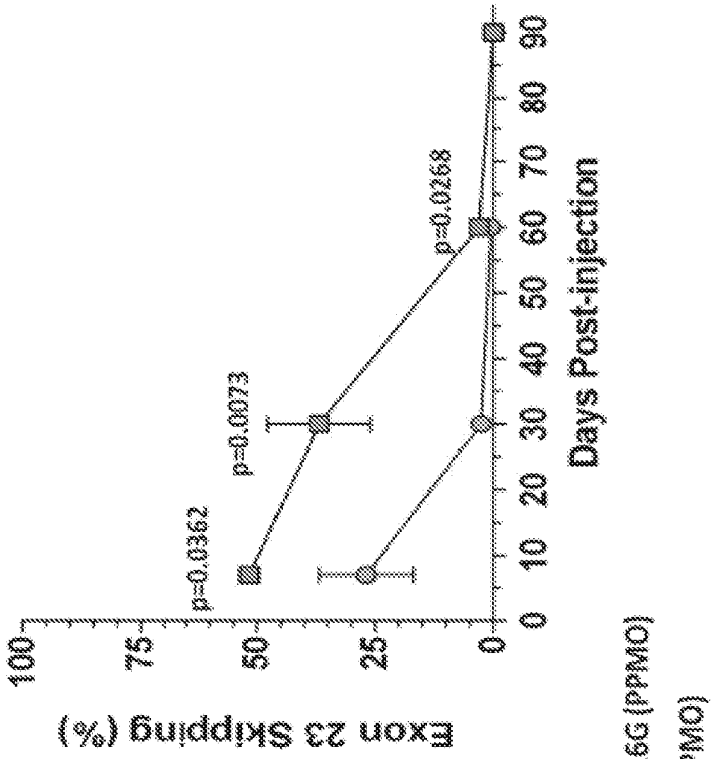


Figure 9A

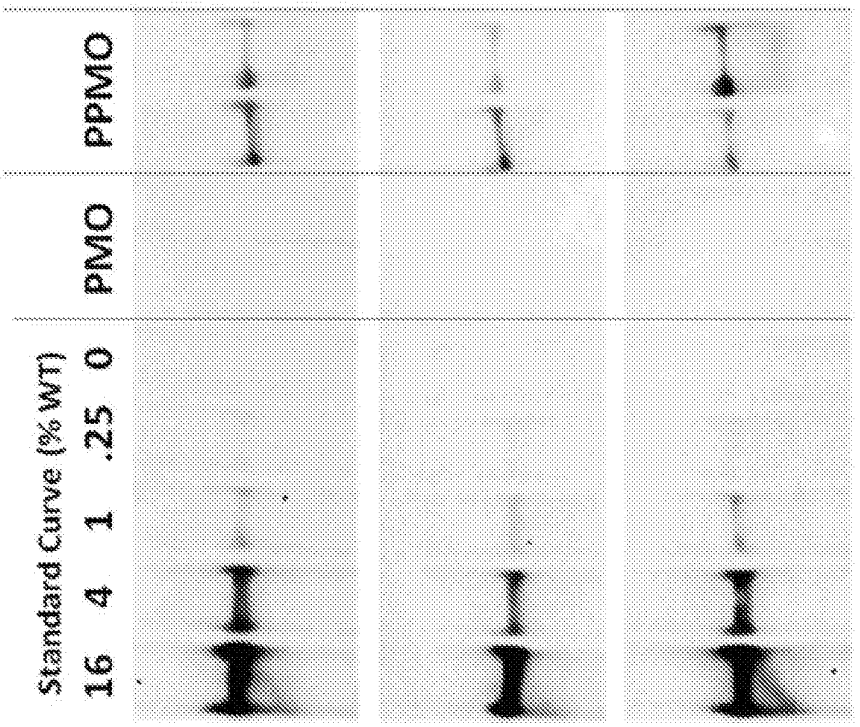


Figure 9B

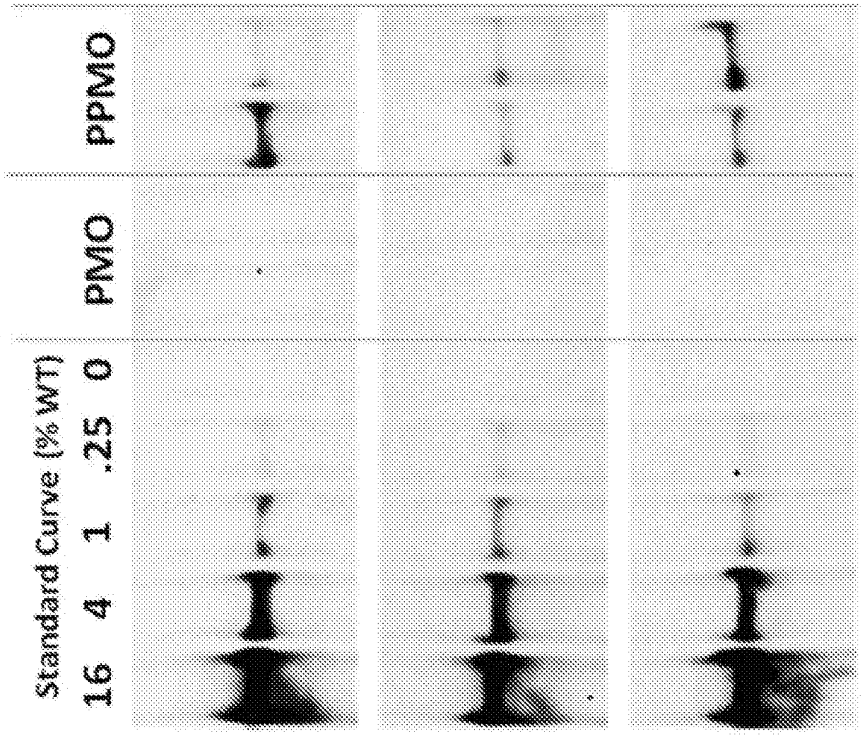


Figure 9C

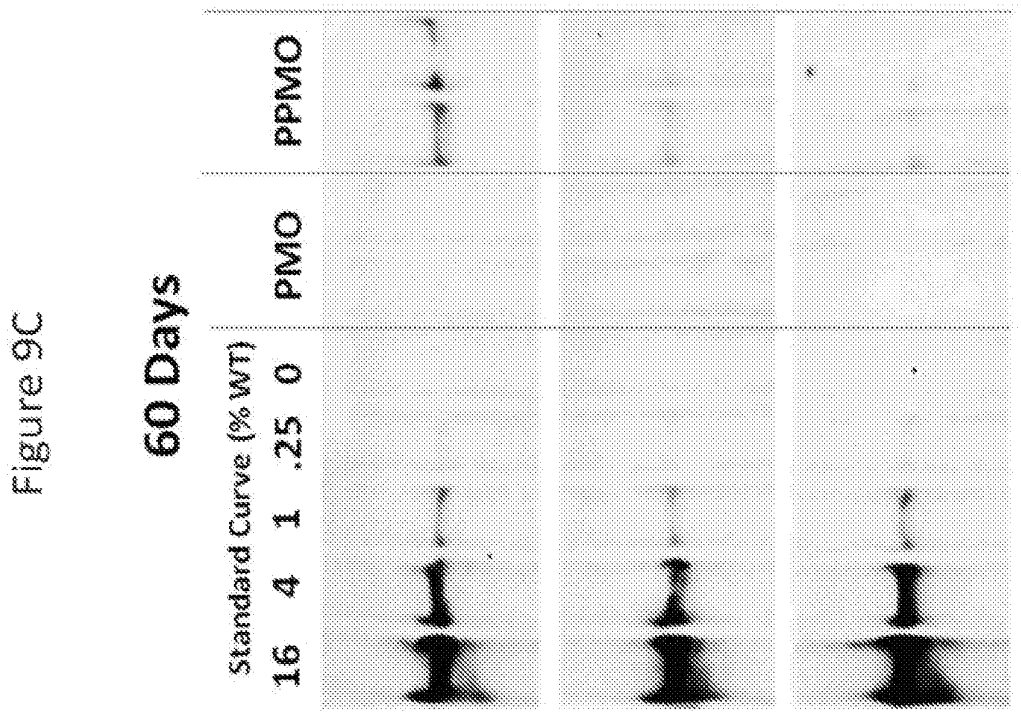


Figure 9D

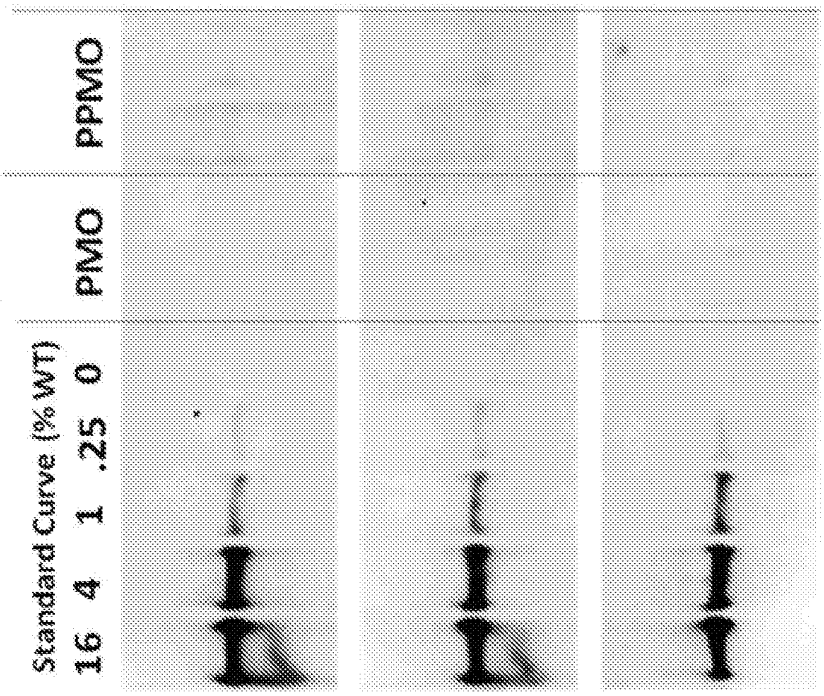


Figure 10A

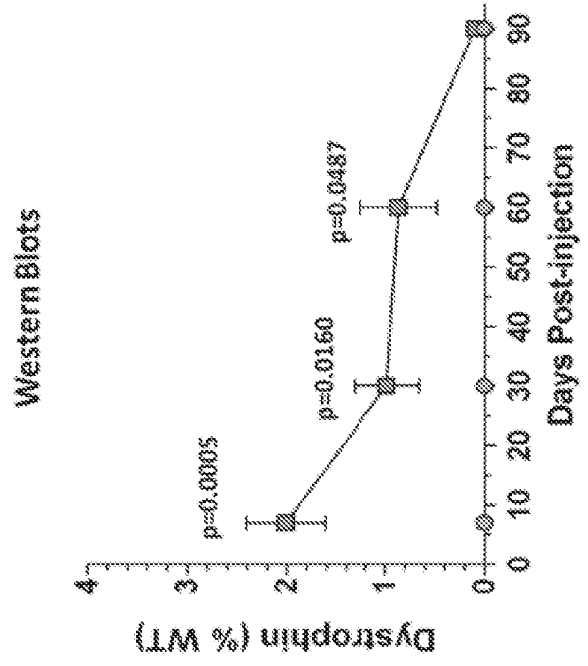


Figure 10B

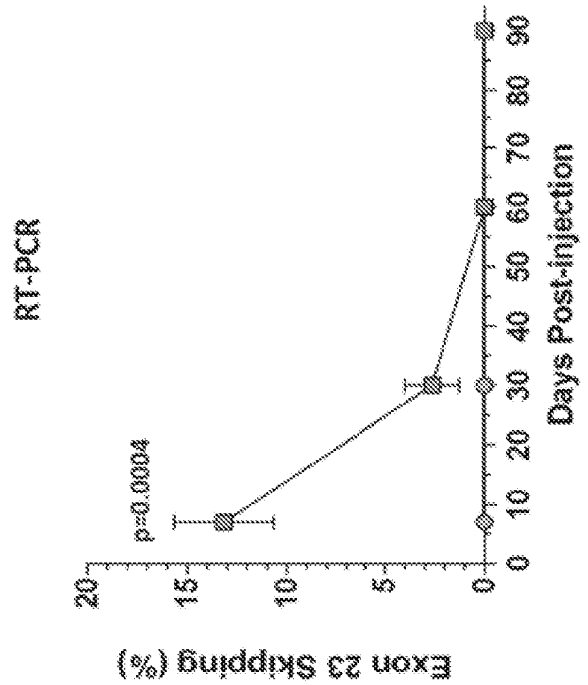


Figure 11

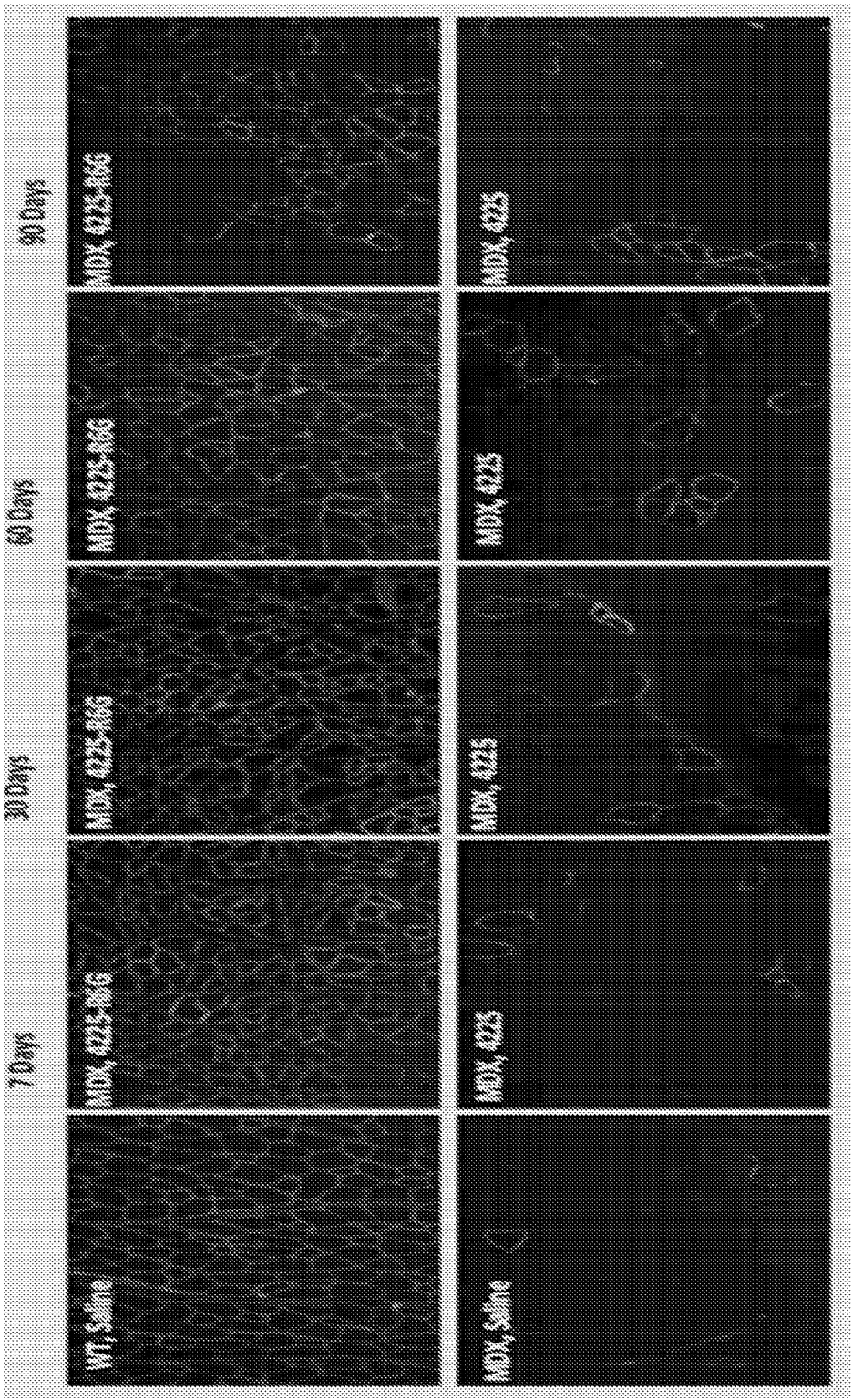

7 Days
30 Days
60 Days
90 Days
VH, Saline
MDX, Saline
MDX, 025-366
MDX, 025
MDX, 025-366
MDX, 025
MDX, 025-366
MDX, 025

FIG. 12B

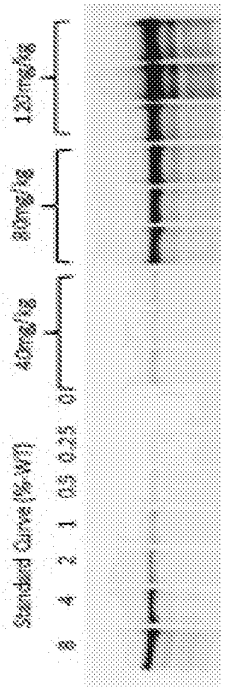


FIG. 12A

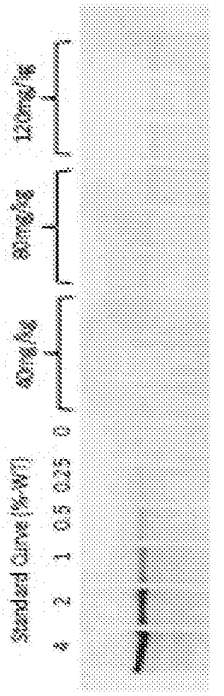


FIG. 13

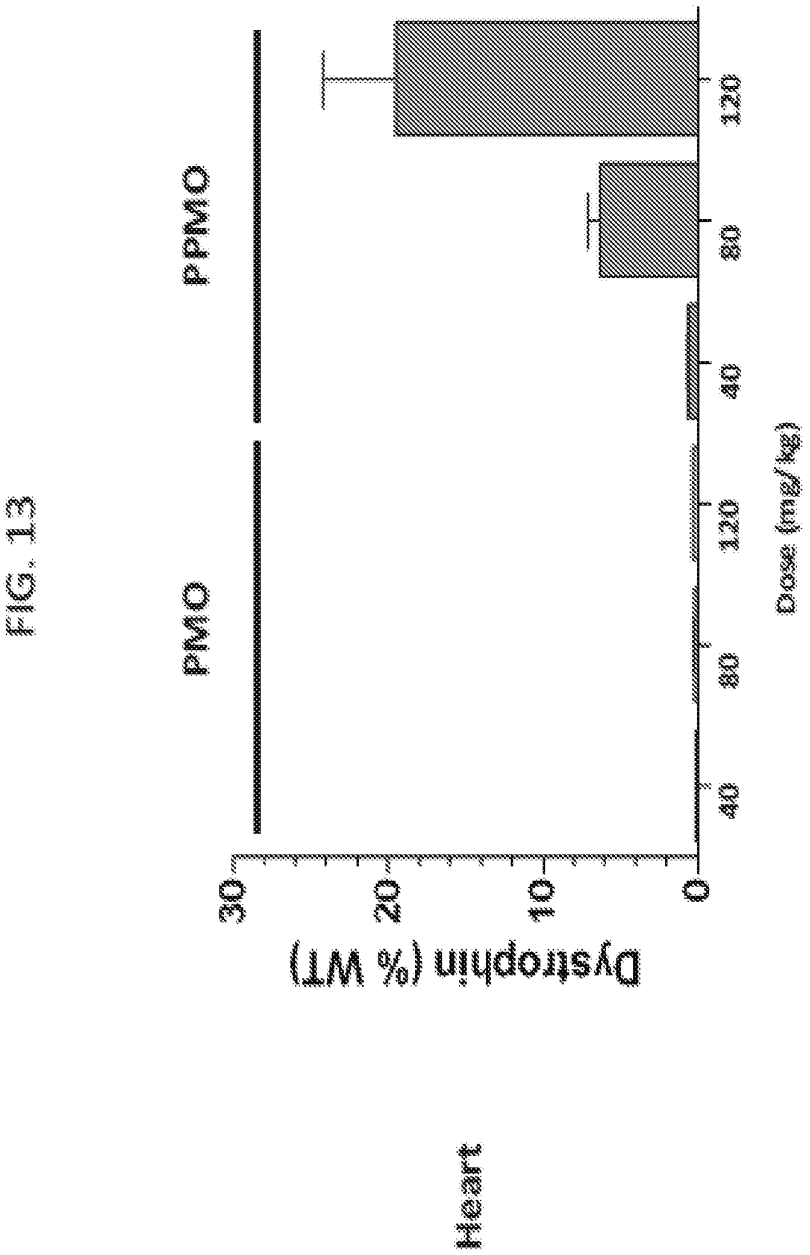

Heart
Dystrophin (% WT)
0
10
20
30
PMO
PPMO
40
80
120
40
80
120
Dose (mg/kg)

Figure 14B

Diaphragm -
PPMO

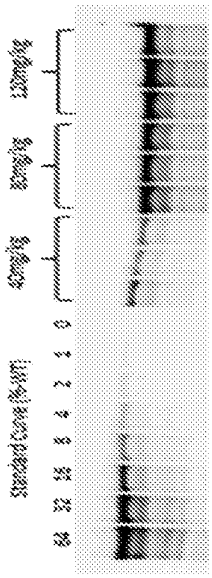


Figure 14A

Diaphragm -
PMO

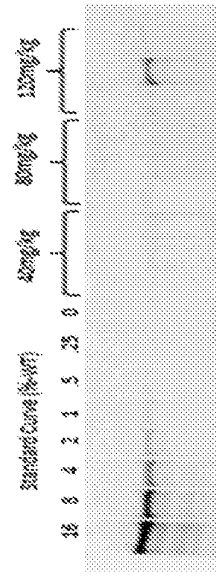


FIG. 15

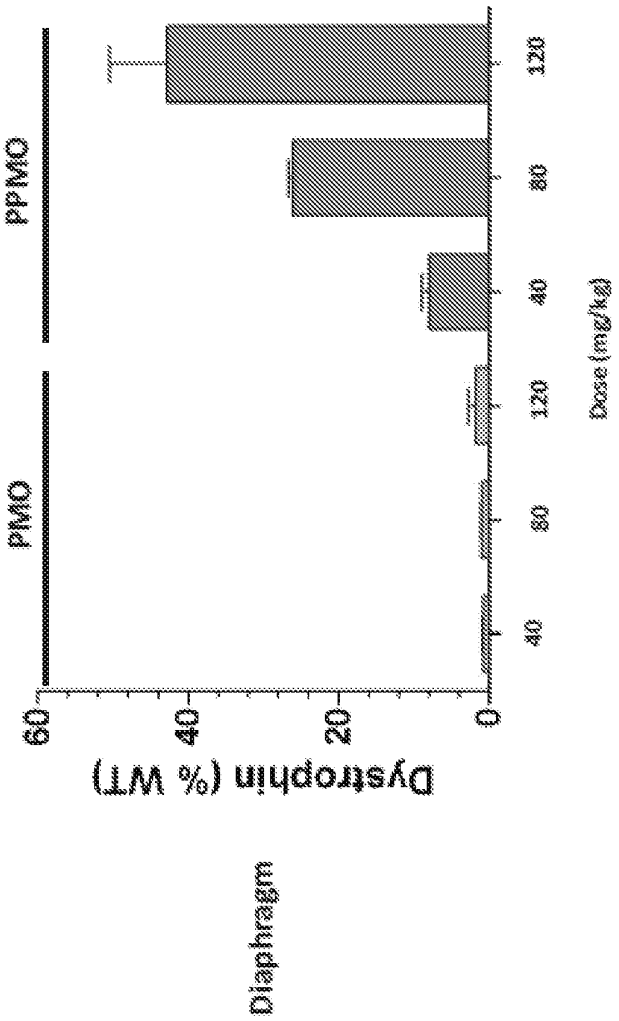

Diaphragm
Dystrophin (% WT)
0
20
40
60
PMO
PPMO
40
80
120
40
80
120
Dose (mg/kg)

FIG. 16A

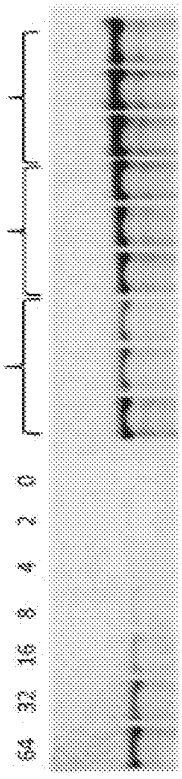


FIG. 16B

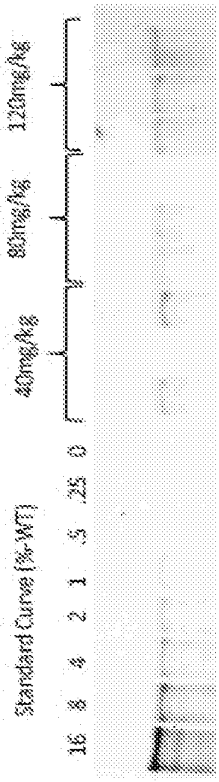
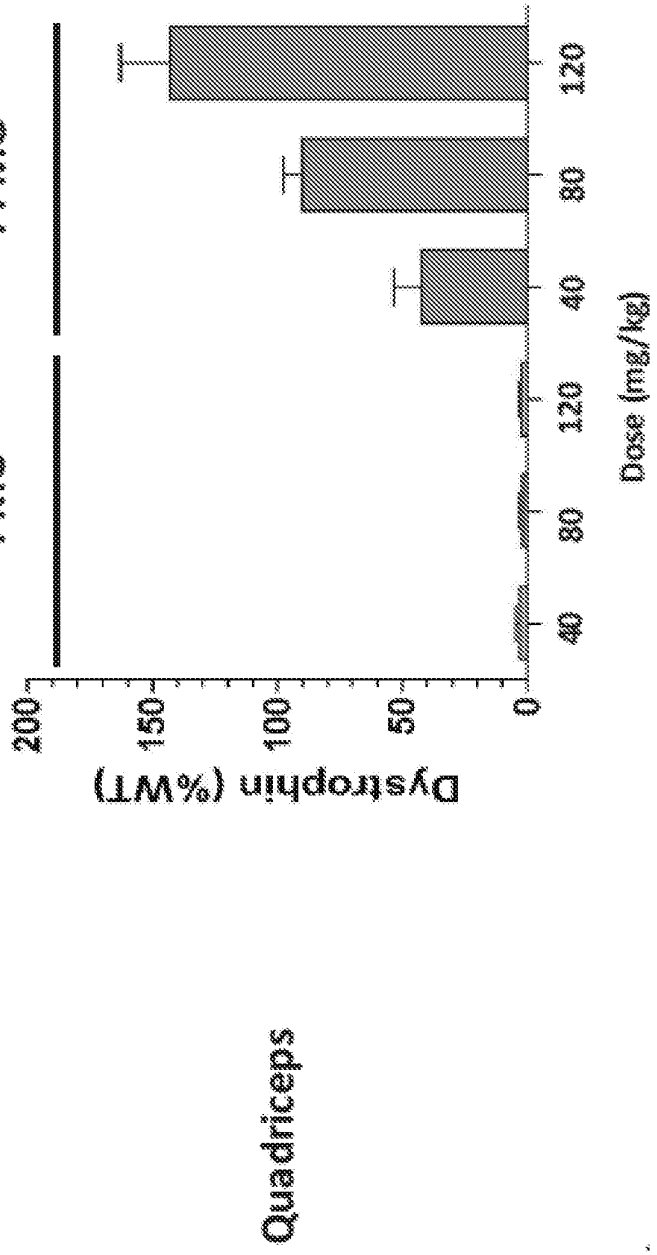


FIG. 17


PMO
PPMO
Dystrophin (%WT)
200
150
100
50
0
40
80
120
40
80
120
Dose (mg/kg)
Quadriceps

Cycle No.: Subunit (SU)	Pre-coupling Treatment				Coupling Cycle		Post-Coupling Treatment	
	1	2	3	4			1	2
	30% TFE/DCM Wash	CYTFA Solution[1]	Neutralization Solution	DCM Wash	Quantity SU (g) NEM (L) DMI (L)	RT Coupling Time (Hrs.)	DCM Wash	30% TFE/DCM Wash
1:DPG	5.5L	a) 5.5L b) 5.5L, 122ml	3x5.5L	5.5L	536.7g; 195 ml NEM; 3.2L DMI	5	5.5L	2x5.5L
2:T	7.0L	a) 7L b) 7L, 158ml	3x7L	2x7L	468.2g and 195ml NEM 3.2L DMI	4.25	7L	2x7L
3:T	8L	a) 8L b) 8L, 182ml	3x8L	2x8L	536.7g; 195ml NEM; 3.4L DMI	4.25	8L	2x8L
4:DPG	9L	a) 9L b) 9L, 206ml	3x9L	2x9L	536.7g; 195ml NEM; 3.6L DMI	4.25	9L	2x9L
5:C	9.5L	a) 9.5L b) 9.5L, 220ml	3x9.5L	2x9.5L	555.2g; 195ml NEM; 3.4L DMI	4.25	9.5L	2x9.5L
6:C	10L	a) 10L b) 10L, 232ml	3x10L	2x10L	555.2g; 195ml NEM; 3.45L DMI	4.25	10L	2x10L
7:T	11L	a) 11L b) 11L, 256ml	3x11L	2x11L	536.7g; 195ml NEM;	4.25	11L	2x11L

Figure 18

[1] ml indicates the amount of 1:1 NEM/DCM

Cycle No.: Subunit (SU)	Pre-coupling Treatment				Coupling Cycle		Post-Coupling Treatment	
	1	2	3	4			1	2
	30% TFE/DCM Wash	CYTFA Solution[1]	Neutralization Solution	DCM Wash	Quantity SU (g) NEM (L) DMI (L)	RT Coupling Time (Hrs.)	DCM Wash	30% TFE/DCM Wash
					3.57L DMI			
8:C	11L	a) 11L b) 11L, 256ml	3x11L	2x11L	555.2g; 195ml NEM; 3.64L DMI	4.25	11L	2x11L
9:C	11.5L	a) 11.5L b) 11.5L, 268ml	3x11.5L	2x 11.5L	468.2g; 195ml NEM; 3.72L DMI	4.25	11.5L	2x11.5L
10:DPG	12L	a) 12L b) 12L, 280ml	3x12L	2x12L	536.7g; 195ml NEM; 3.96L DMI	4.25	12L	2x12L
11:DPG	13.5L	a) 13.5L b) 13.5L, 204ml	3x13.5L	2x 13.5L	721.7g; 253ml NEM; 4.02L DMI	4.25	13.5L	2x13.5L
12:T	13.5L	a) 13.5L b) 13.5L, 204ml	3x13.5L	2x 13.5L	721.7g; 253ml NEM; 4.02L DMI	4.25	13.5L	2x13.5L
13:T	14L	a) 14L b) 14L, 216ml	3x14L	2x14L	941.9g; 253ml NEM; 4.02L DMI	4.25	14L	2x14L
14:C	14.5L	a) 14.5L b) 14.5L, 228ml	3x14.5L	2x 14.5L	941.9g; 253ml NEM; 4.1L DMI	4.25	14.5L	2x14.5L

Figure 18 (continued)

Cycle No.: Subunit (SU)	Pre-coupling Treatment				Coupling Cycle		Post-Coupling Treatment	
	1	2	3	4			1	2
	30% TFE/DCM Wash	CYTFA Solution[1]	Neutralization Solution	DCM Wash	Quantity SU (g) NEM (L) DMI (L)	RT Coupling Time (Hrs.)	DCM Wash	30% TFE/DCM Wash
15:T	15.5L	a) 15.5L b) 15.5L, 254ml	3x15.5L	2x 15.5L	721.7g; 253ml NEM; 4.26L DMI	4.25	15.5L	2x15.5L
16:DPG	15.5L	a) 15.5L b) 15.5L, 254ml	3x15.5L	2x 15.5L	721.7g; 253ml NEM; 4.26L DMI	4.25	15.5L	2x15.5L
17:A	16L	a) 16L b) 16L, 366ml	3x16L	2x16L	941.9g; 253ml NEM; 4.4L DMI	4.75	16L	2x16L
18:A	16.5L	a) 16.5L b) 16.5L, 378ml	3x16.5L	2x 16.5L	721.7g; 253ml NEM; 4.4L DMI	4.25	16.5L	2x16.5L
19: DPG	16.5L	a) 16.5L b) 16.5L, 378ml	3x16.5L	2x 16.5L	608.7g; 253ml NEM; 4.57L DMI	4.25	16.5L	2x16.5L
20:DPG	17L	a) 17L b) 17L, 390ml	3x17L	2x17L	941.9g; 253ml NEM; 4.57L DMI	4.75	17L	2x17L
21:T	17L	a) 17L b) 17L, 390ml	3x17L	2x17L	1159.2g; 311ml NEM; 4.72L DMI	4.25	17L	2x17L
22: DPG	17.5L	a) 17.5L b) 17.5L, 402ml	3x17.5L	2x 17.5L	858.7g; 311ml NEM;	4.75	17.5L	2x17.5L

Figure 18 (continued)

Cycle No.: Subunit (SU)	Pre-coupling Treatment				Coupling Cycle		Post-Coupling Treatment	
	1	2	3	4			1	2
	30% TFE/DCM Wash	CYTFA Solution[1]	Neutralization Solution	DCM Wash	Quantity SU (g) NEM (L) DMI (L)	RT Coupling Time (Hrs.)	DCM Wash	30% TFE/DCM Wash
					4.72L DMI			
23:T	17.5L	a) 17.5L b) 17.5L, 402ml	3x17.5L	2x 17.5L	888.3g; 311ml NEM; 4.88L DMI	4.25	17.5L	2x17.5L
24:T	18L	a) 18L b) 18L, 414ml	3x18L	2x18L	749.1g; 311ml NEM; 4.95L DMI	4.25	18L	2x18L
25:C	18L	a) 18L b) 18L, 414ml	3x18L	2x18L	749.1g; 311ml NEM; 5.1L DMI	4.25	18L	2x18L

Figure 18 (continued)

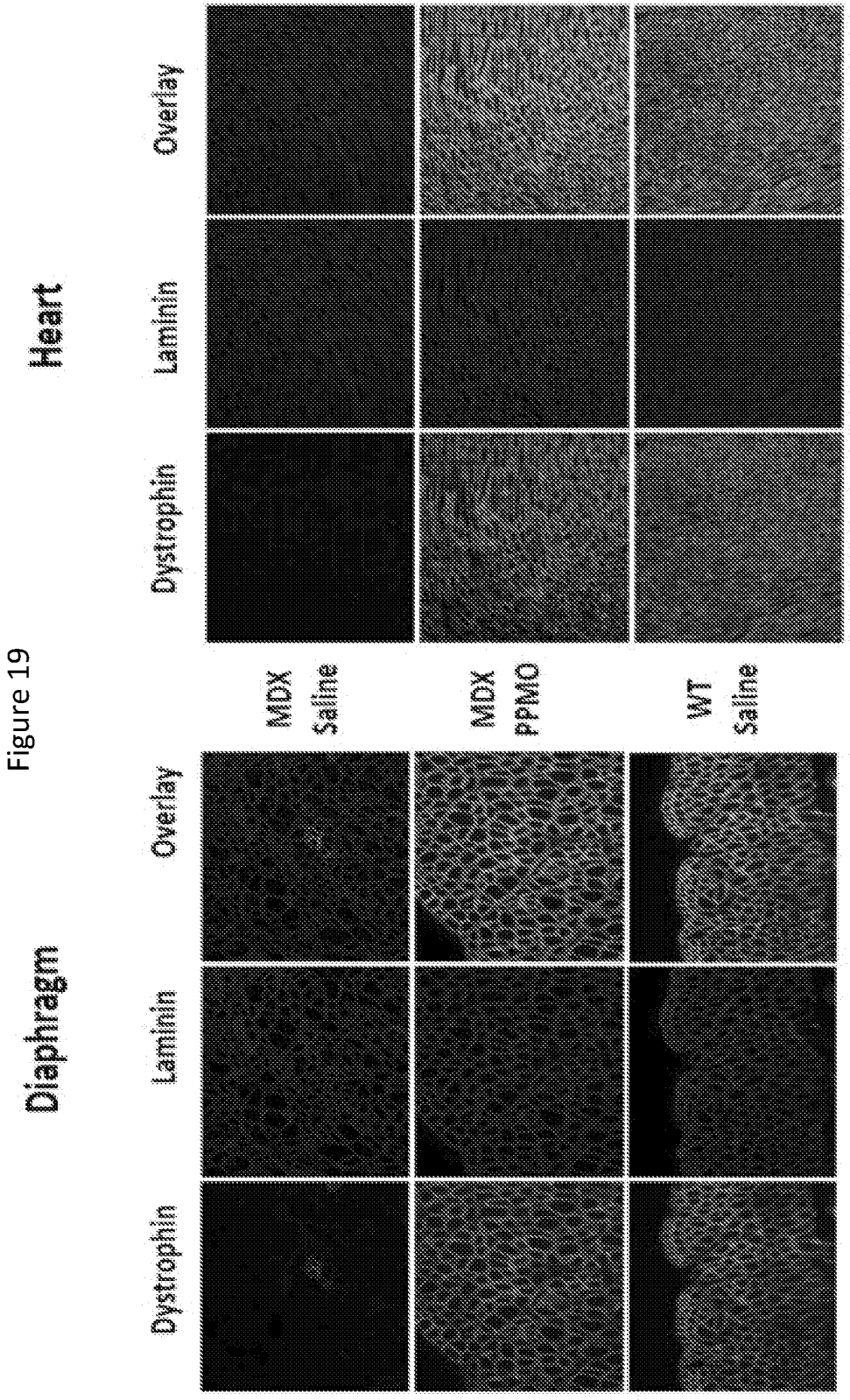

Heart
Diaphragm
Dystrophin
Laminin
Overlay
MDX Saline
MDX PPMO
WT Saline

Figure 19