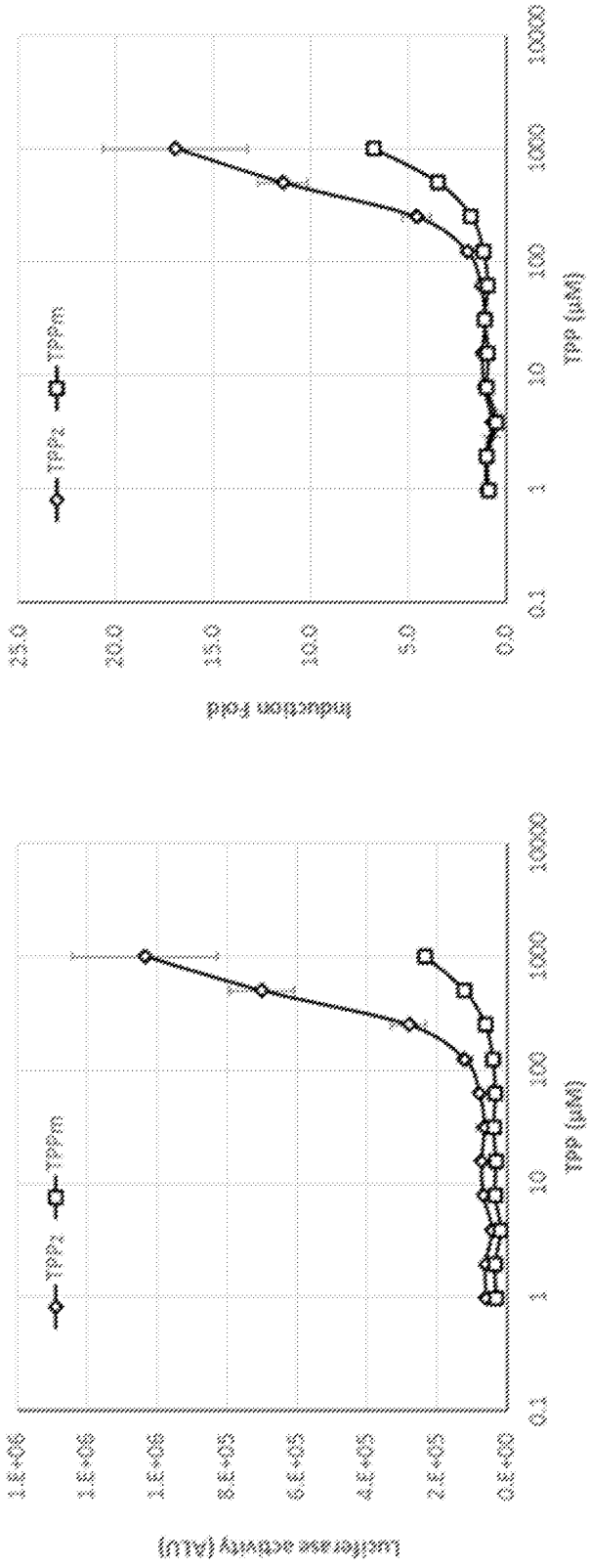

Induction fold
25.0
20.0
15.0
10.0
5.0
0.0
0.1
1
10
100
1000
10000
TPP (µM)
TPPz
TPPm
luciferase activity (RLU)
1.E+06
1.E+06
1.E+06
8.E+05
6.E+05
4.E+05
2.E+05
0.E+00
0.1
1
10
100
1000
10000
TPP (µM)
TPPz
TPPm

Fig. 1A

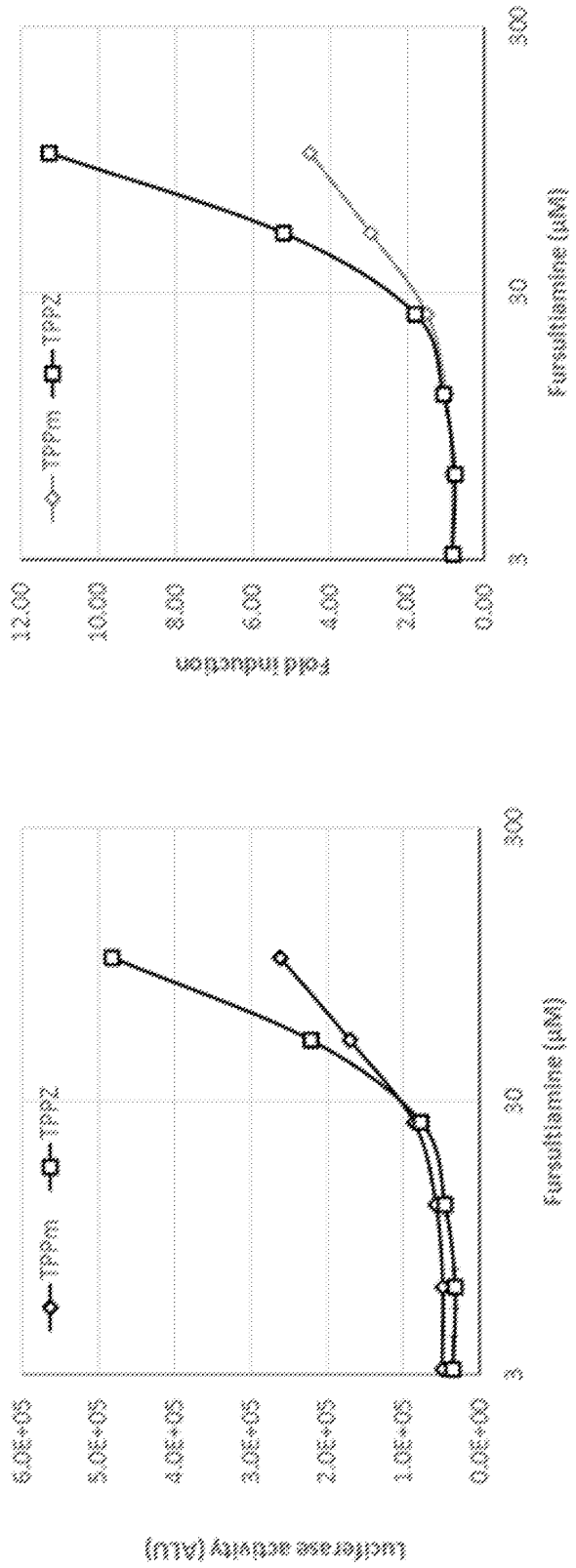

fold induction
12.00
10.00
8.00
6.00
4.00
2.00
0.00
TPPm
TPP2
3
30
300
Fursultiamine (uM)
luciferase activity (RLU)
6.0E+05
5.0E+05
4.0E+05
3.0E+05
2.0E+05
1.0E+05
0.0E+00
TPPm
TPP2
3
30
300
Fursultiamine (uM)

Fig. 1B

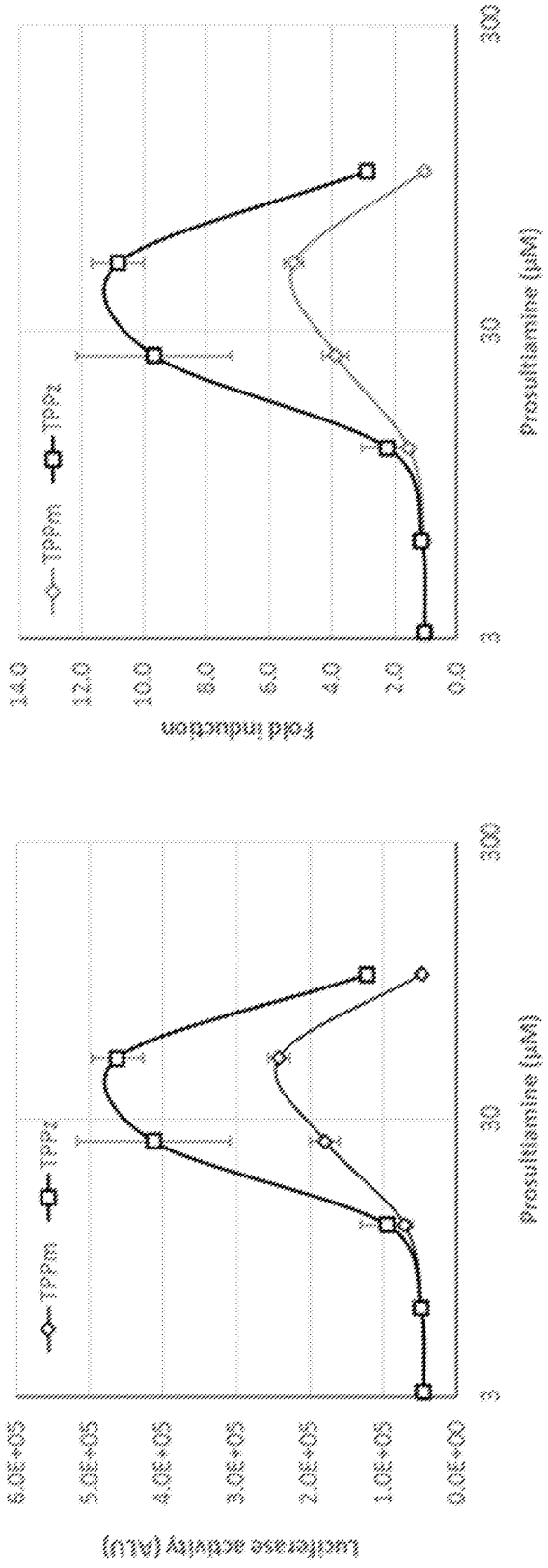

fold induction
14.0
12.0
10.0
8.0
6.0
4.0
2.0
0.0
3
30
300
Prosultiamine (μM)
TPPm
TPPx
luciferase activity (AUU)
6.0E+05
5.0E+05
4.0E+05
3.0E+05
2.0E+05
1.0E+05
0.0E+00

Fig. 1C

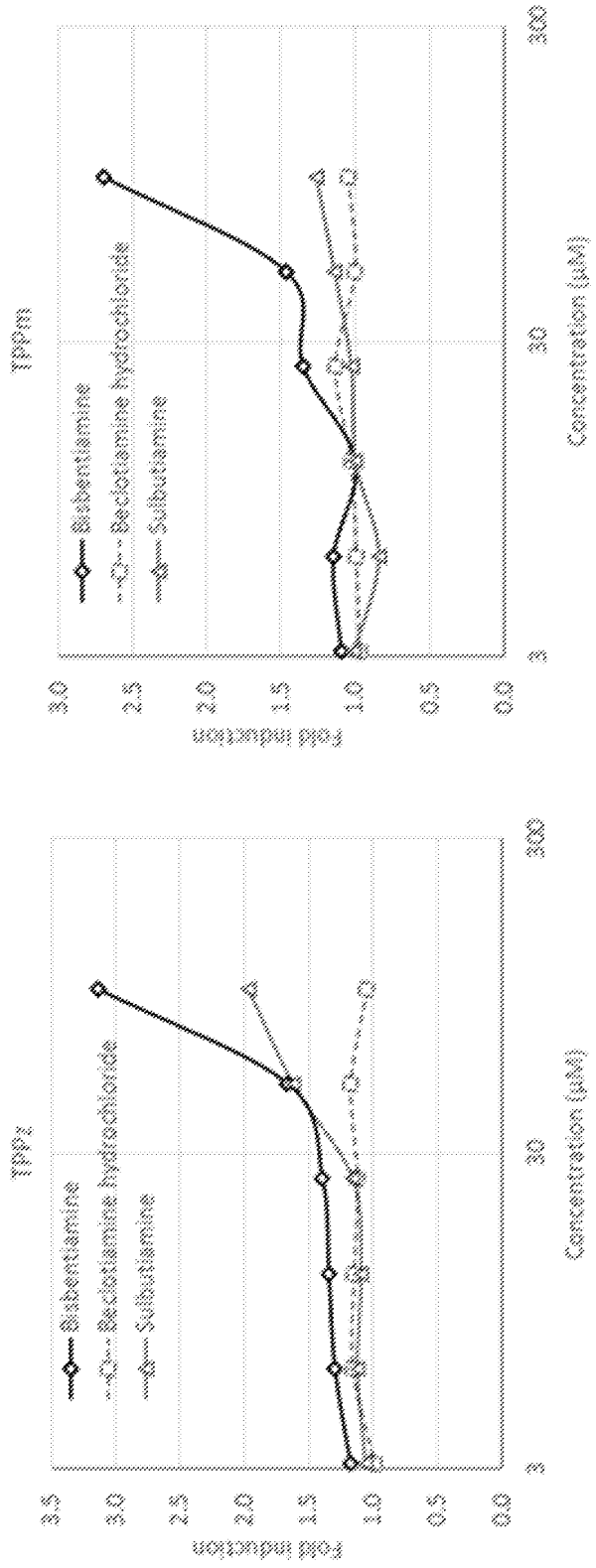

TPPm
Fold induction
Concentration (μM)
Benfotiamine
Benfotiamine hydrochloride
Sulbutiamine
TPPt
Fold induction
Concentration (μM)
Benfotiamine
Benfotiamine hydrochloride
Sulbutiamine

Fig. 1D

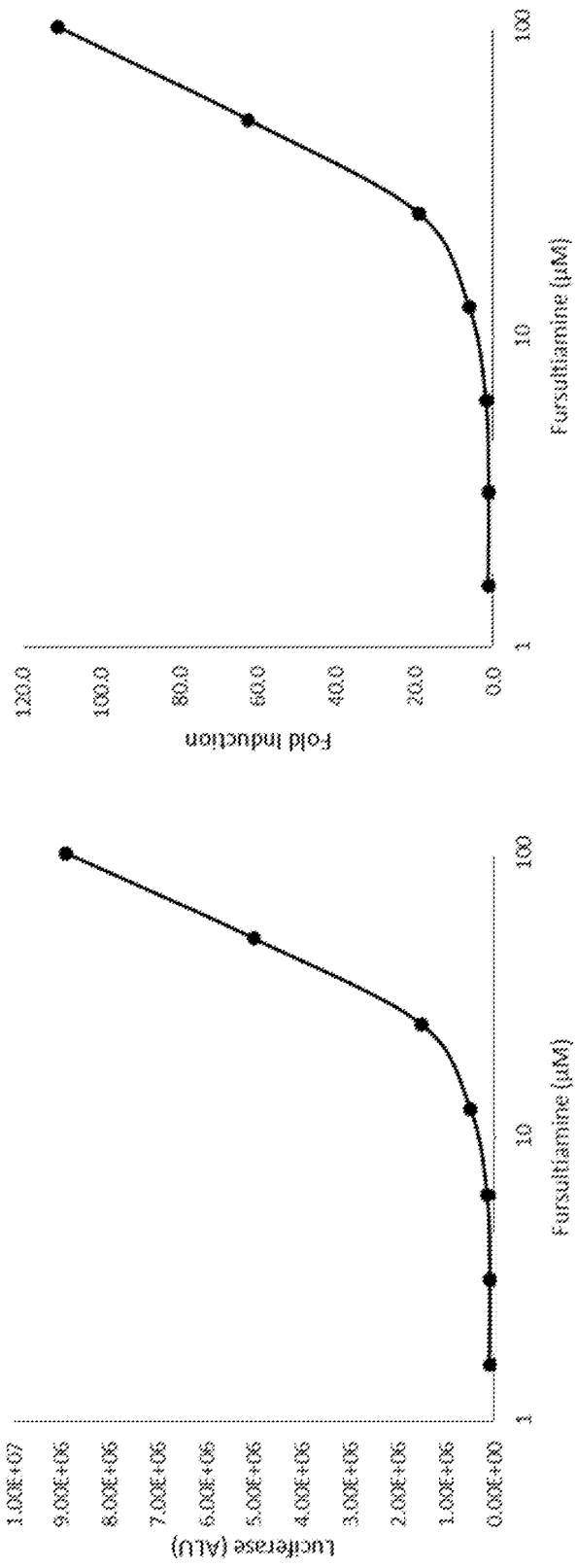

Fold Induction
120.0
100.0
80.0
60.0
40.0
20.0
0.0
1
10
100
Fursultiamine (µM)
Luciferase (ALU)
1.00E+07
9.00E+06
8.00E+06
7.00E+06
6.00E+06
5.00E+06
4.00E+06
3.00E+06
2.00E+06
1.00E+06
0.00E+00
1
10
100
Fursultiamine (µM)

Fig. 2A

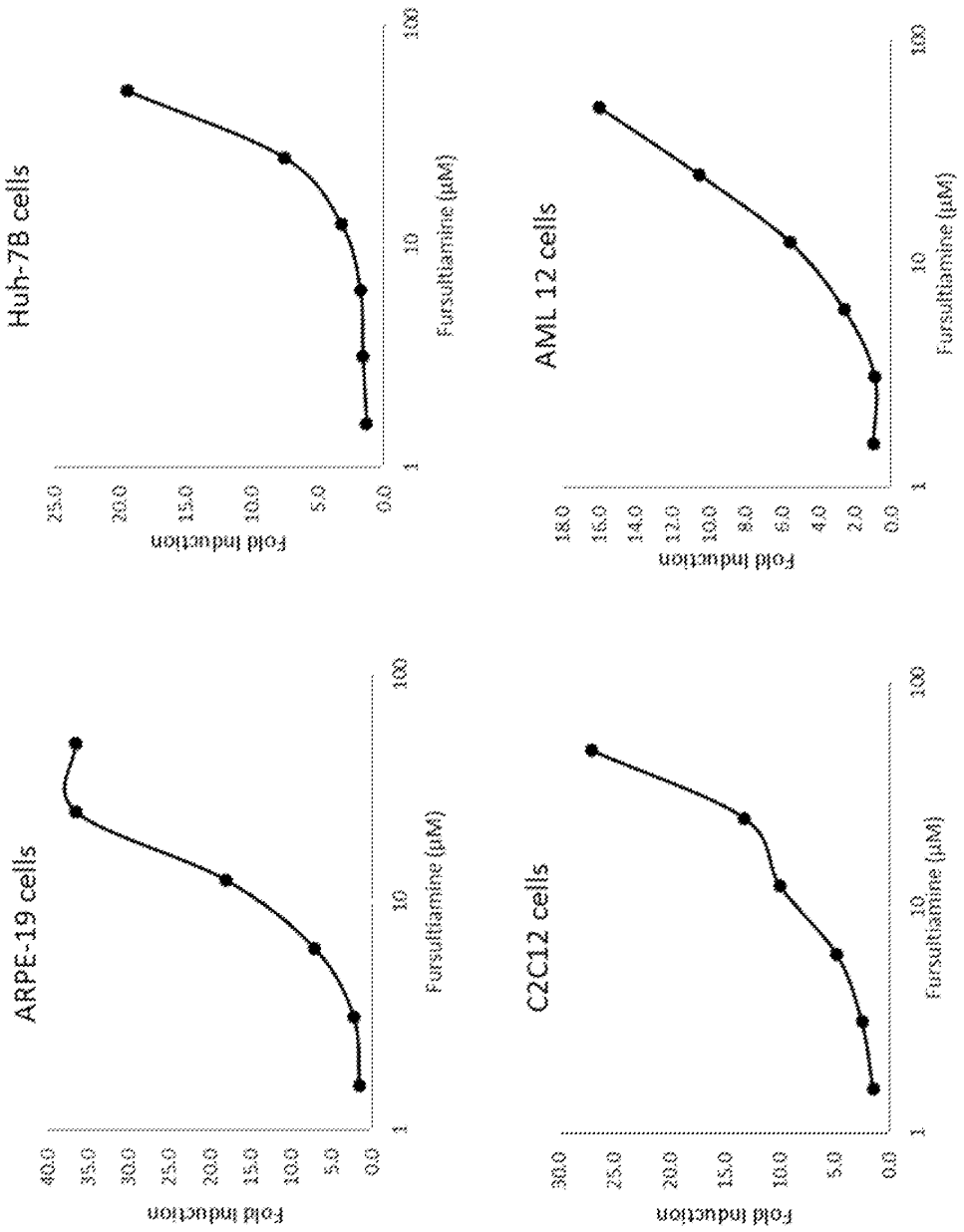

ARPE-19 cells
Huh-7B cells
C2C12 cells
AML 12 cells
Fold Induction
Fursultiamine (µM)
1
10
100

Fig. 2B

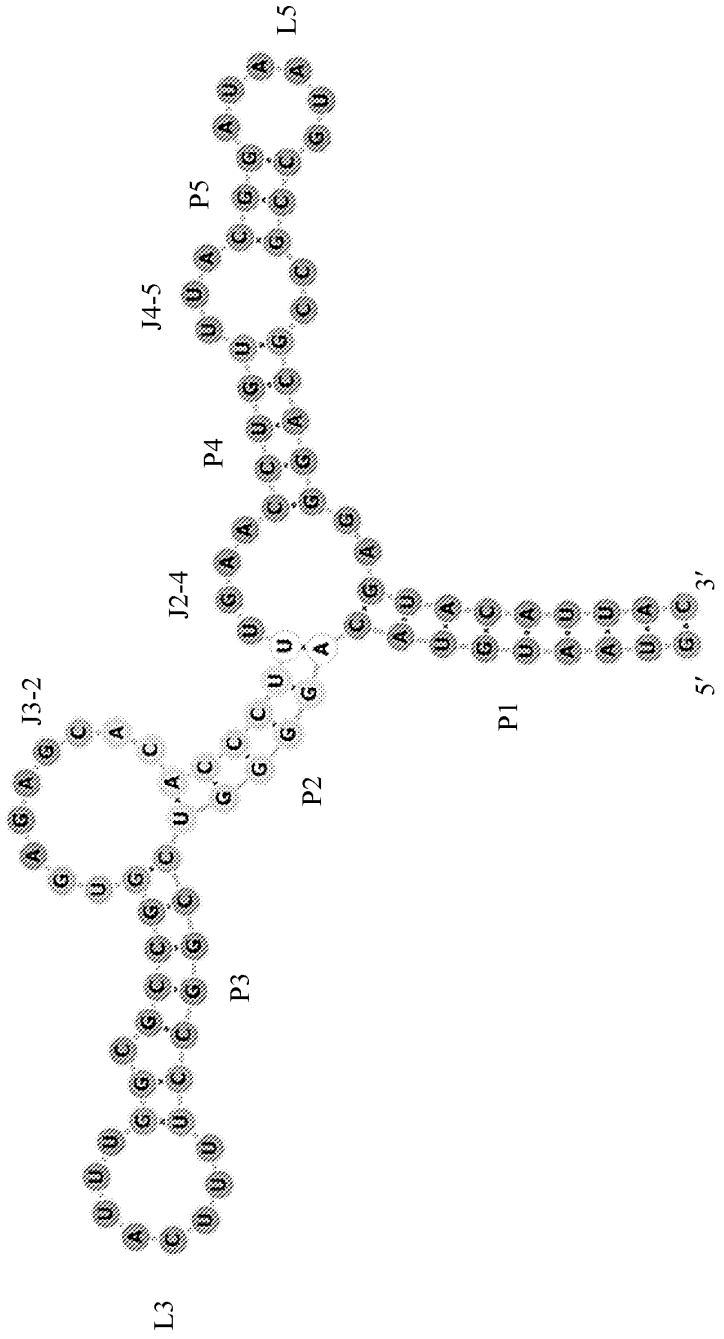


Fig. 3A

14G4 aptamer	ACAGGGGTCCGGCCTTTTCATTTGGCGCCGGTGAGAGCACACCCTTTGAACCTGTTTACGGATAATGCCGCCGCAGGGAGT
Library A1	ACAGGGGTCCGGCCTTTTCATTTGGCGCCGGTGAGAGCACACCCTTTGAACCTG**NNNNN**CGGATAATGCCG**NN**GCAGGGAGT
Library A2	AC**N**GGGGTCCGGCCTTTTCATTTGGCGCCGGTGAGAGCACACCCT**NNNNN**CCTGTTTACGGATAATGCCGCCGCAGGGAGT
Library A3	ACAGGGG**N**CCGGCCTTTTCATTTGGCGCCGGTGAGA**NNNNN**CCCTTTGAACCTGTTTACGGATAATGCCGCCGCAGGGAGT

Fig. 3B

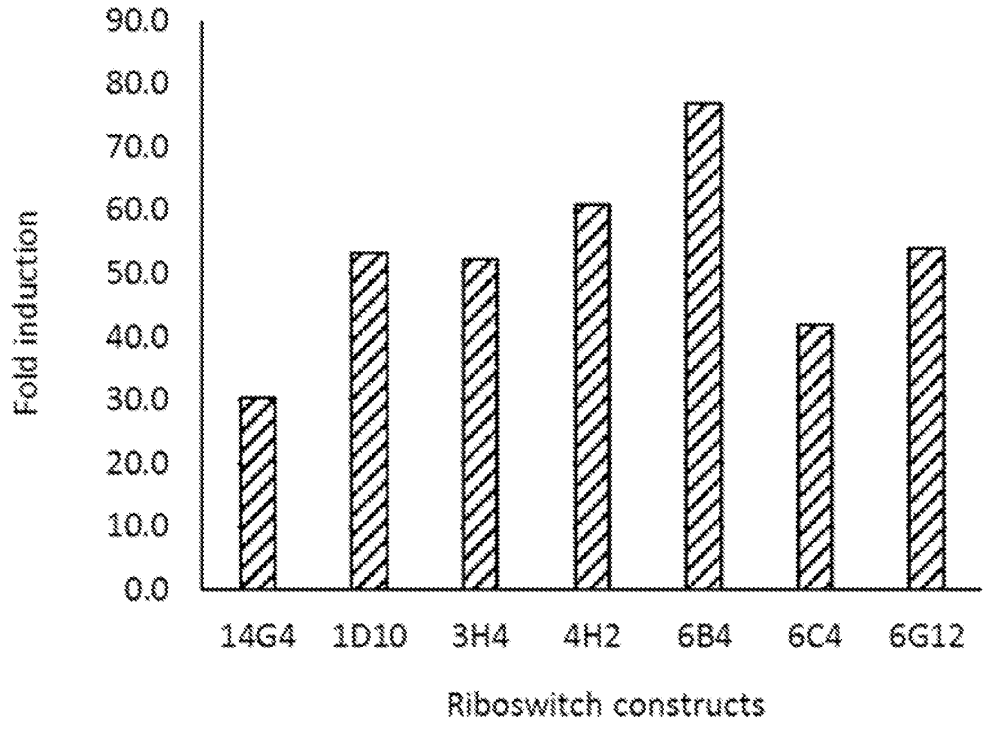

90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
Fold induction
14G4
1D10
3H4
4H2
6B4
6C4
6G12
Riboswitch constructs

Fig. 4A

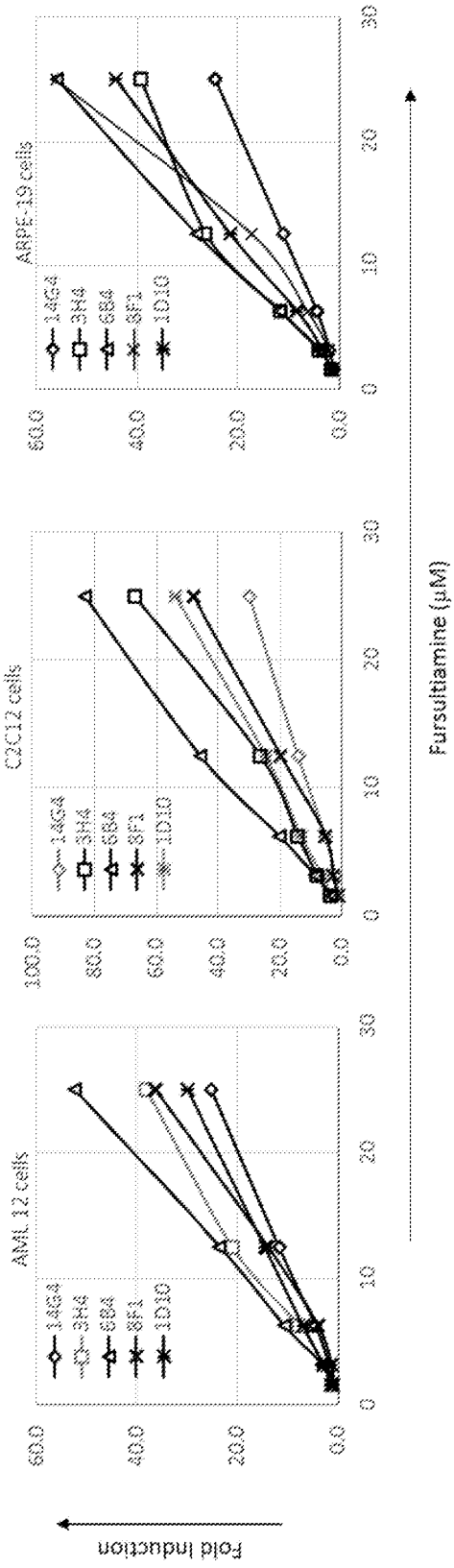

ARPE-19 cells
C2C12 cells
AML 12 cells
14G4
3H4
6B4
8F1
1D10
Fold Induction
Fursultiamine (μM)

Fig. 4B

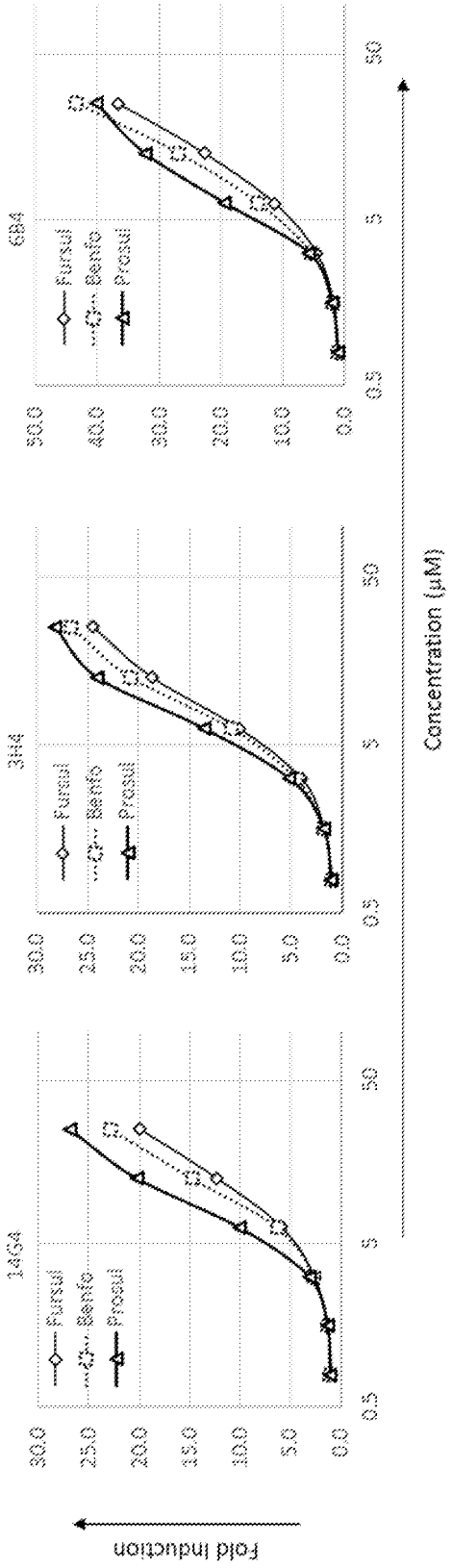

1464
3H4
6B4
Fursul
Benfo
Prosul
30.0
25.0
20.0
15.0
10.0
5.0
0.0
50.0
40.0
30.0
20.0
10.0
0.0
0.5
5
50
Concentration (µM)
Fold Induction

Fig. 4C

3H4 aptamer ACAGGGGTCCGGCCTTTTCATTTGGCGCCGGTGAGAGCACACCCTTTGAACCTGTTCACGGATAATGCCGCTGCAGGGAGT

Library A4 ACAGGGGTCCGGCCTTTTCATTTGGCGCCGGTGAGA**NNAN**ACCCTT**NNNN**ACCTGTTCACGGATAATGCCGCTGCAGGGAGT

Fig. 5

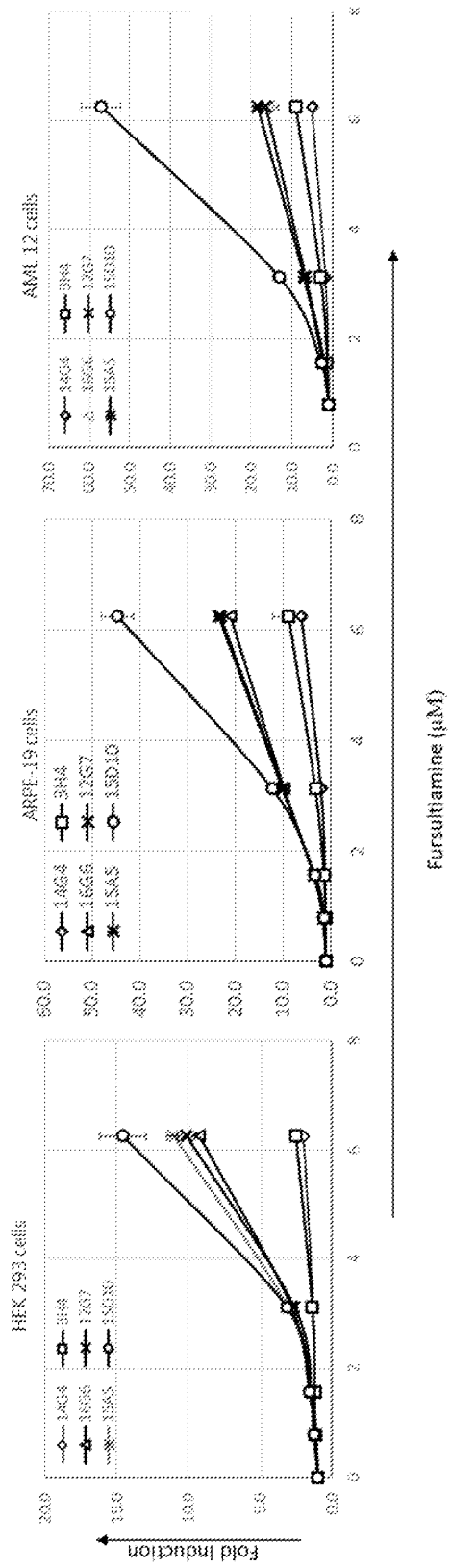

HEK 293 cells
ARPE-19 cells
AML 12 cells
Fold Induction
Fursultiamine (µM)

Fig. 6A

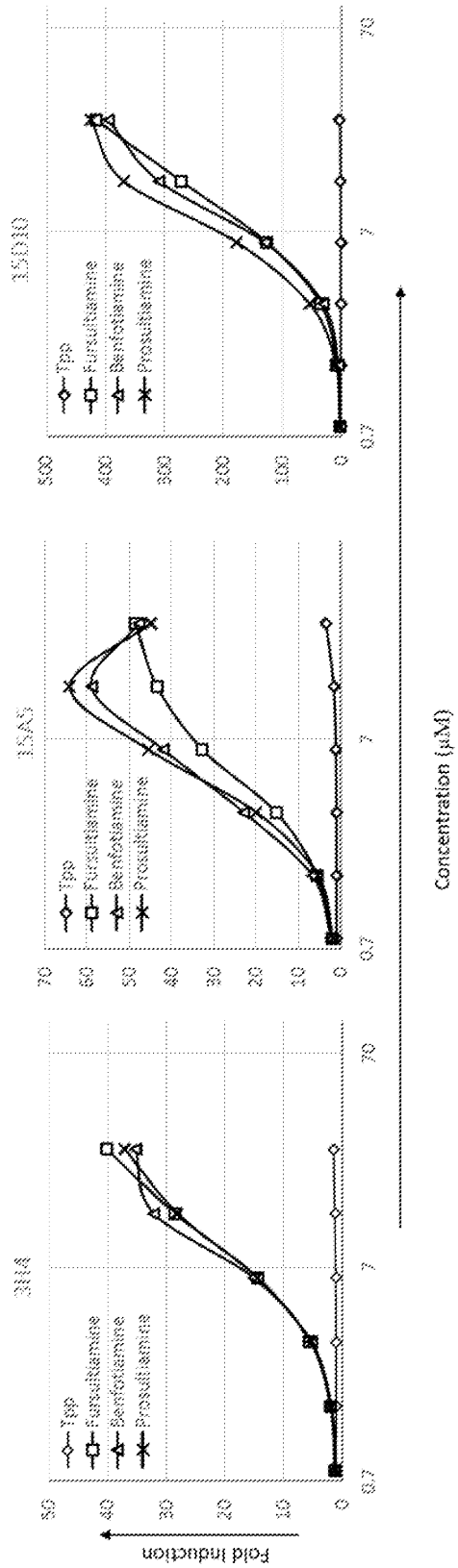

3H4
15A5
15D10
Tpp
Fursultiamine
Benfotiamine
Prosultiamine
Fold Induction
Concentration (μM)
0.7
7
70

Fig. 6B

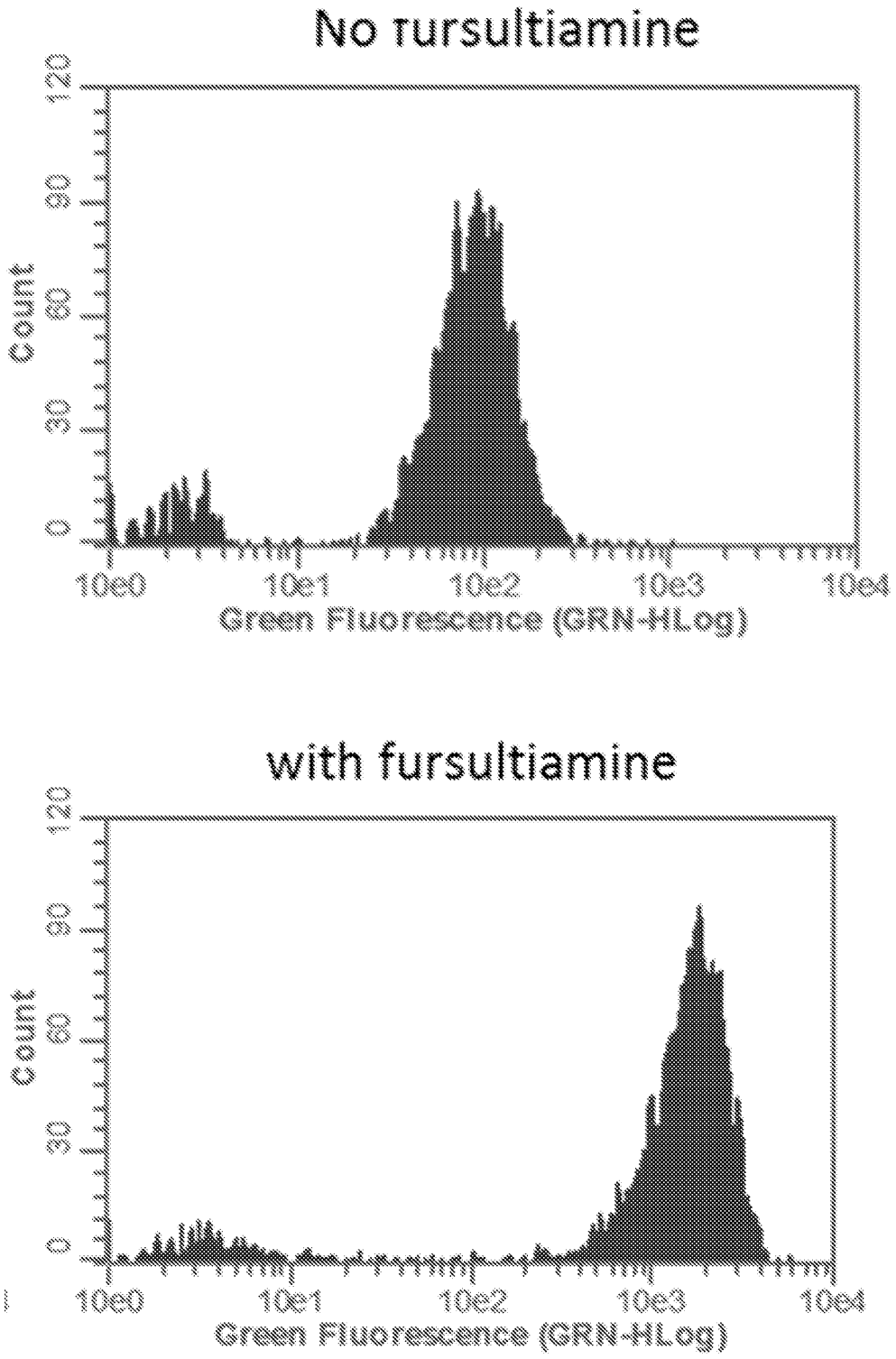

No tursultiamine
Count
0
30
60
90
120
10e0
10e1
10e2
10e3
10e4
Green Fluorescence (GRN-HLog)
with fursultiamine
Count
0
30
60
90
120
10e0
10e1
10e2
10e3
10e4
Green Fluorescence (GRN-HLog)

Fig. 7A

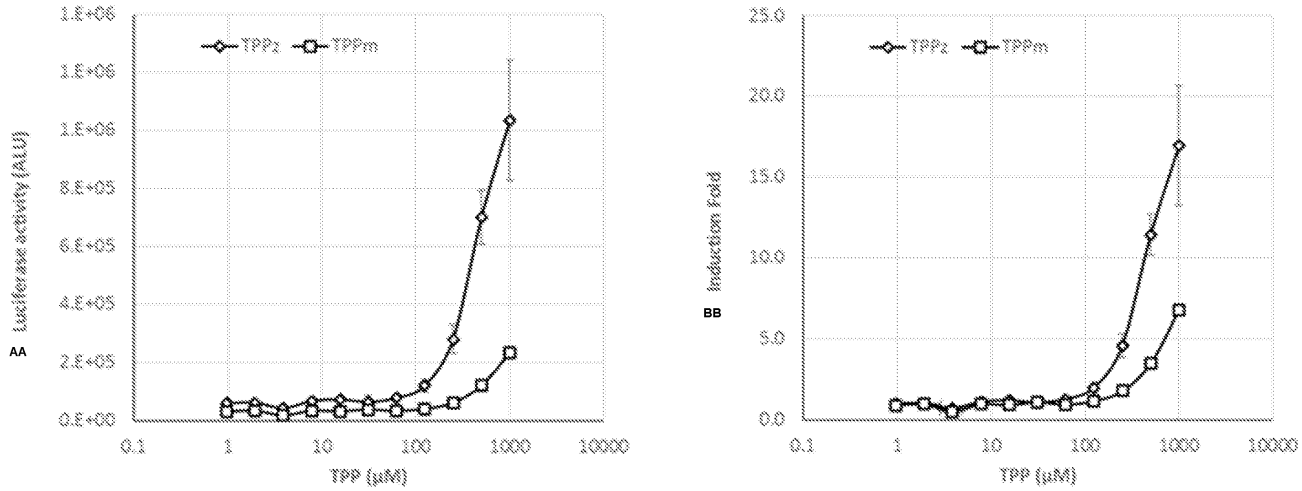


Fig. 1A

AA Activité de la luciférase (ALU)
BB Pli d'induction

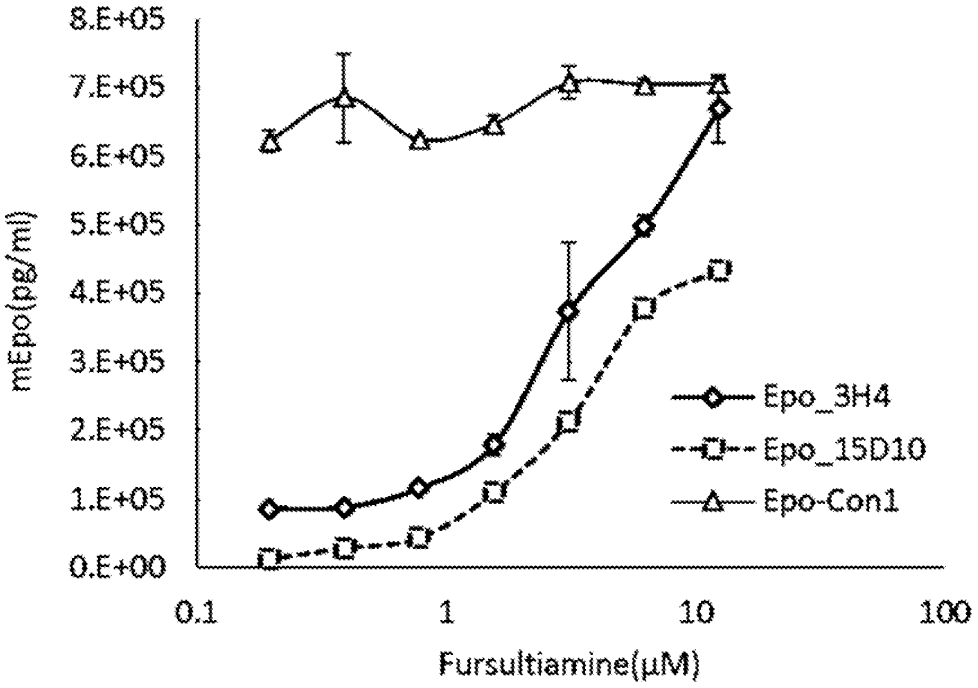

8.E+05
7.E+05
6.E+05
5.E+05
4.E+05
3.E+05
2.E+05
1.E+05
0.E+00
mEpo(pg/ml)
0.1
1
10
100
Fursultiamine(μM)
Epo_3H4
Epo_15D10
Epo-Con1

Fig. 7C

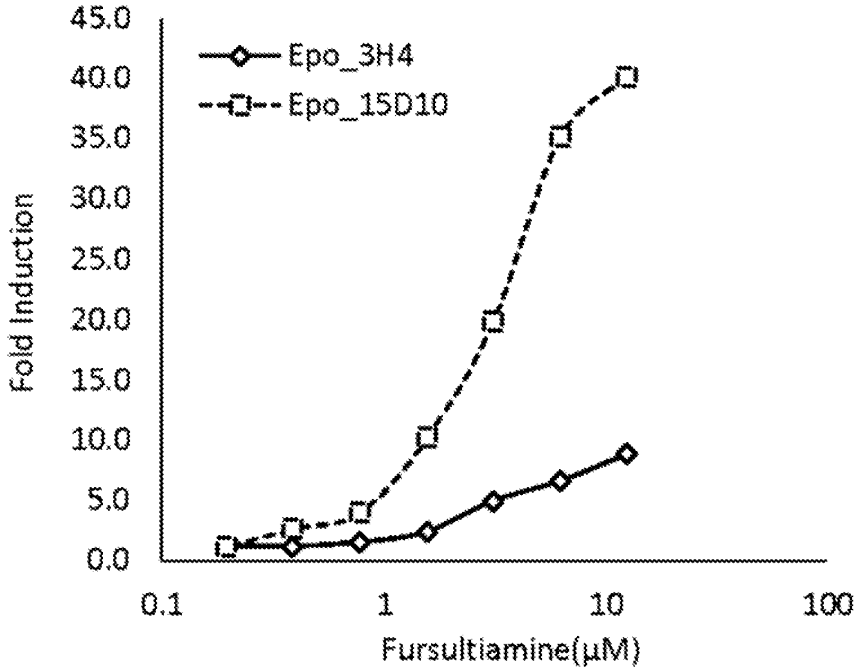

45.0
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
Fold Induction
0.1
1
10
100
Fursultiamine(μM)
Epo_3H4
Epo_15D10

Fig. 7D

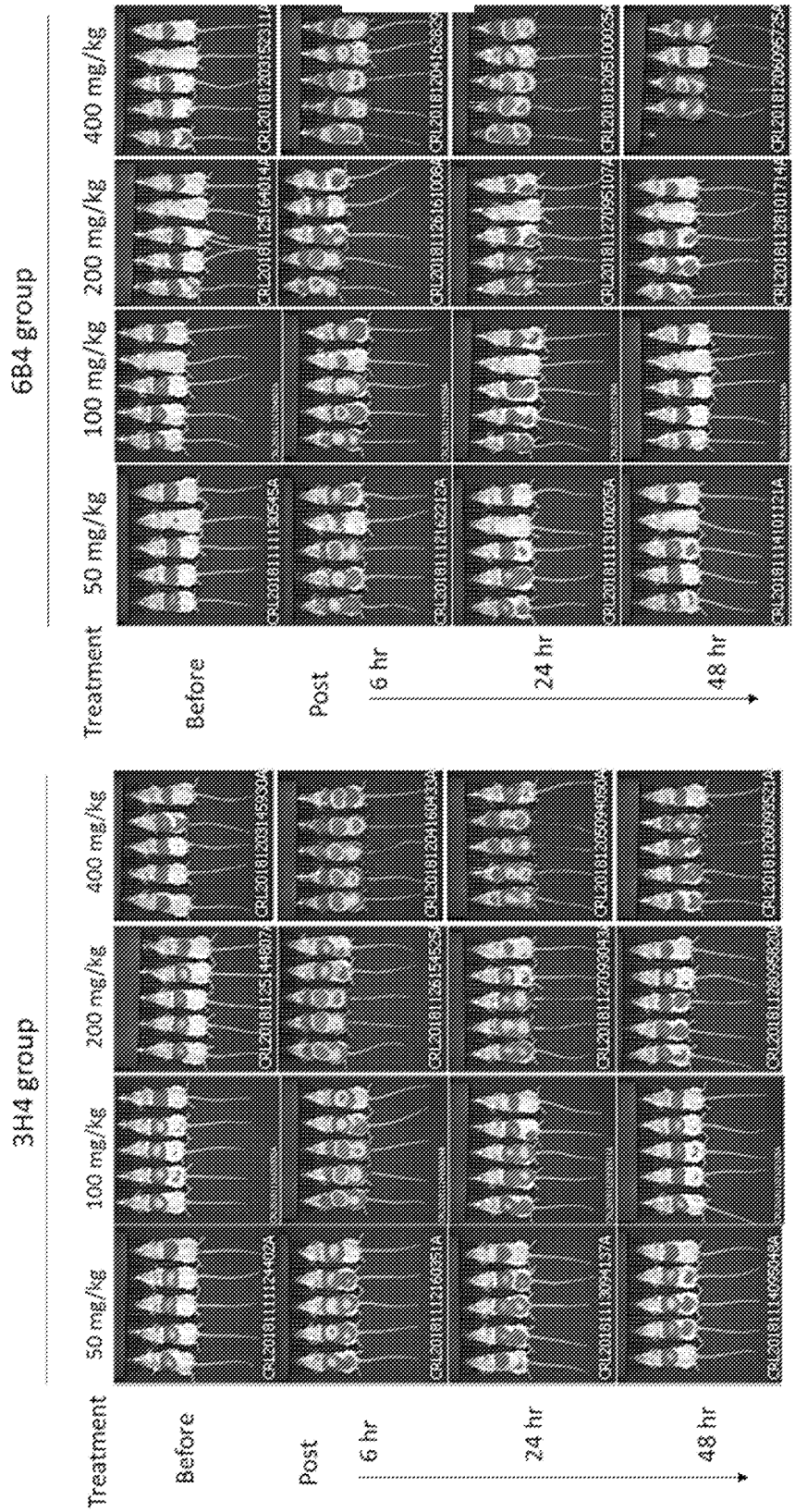

6B4 group
3H4 group
Treatment
50 mg/kg
100 mg/kg
200 mg/kg
400 mg/kg
Before
Post
6 hr
24 hr
48 hr

Fig. 8A

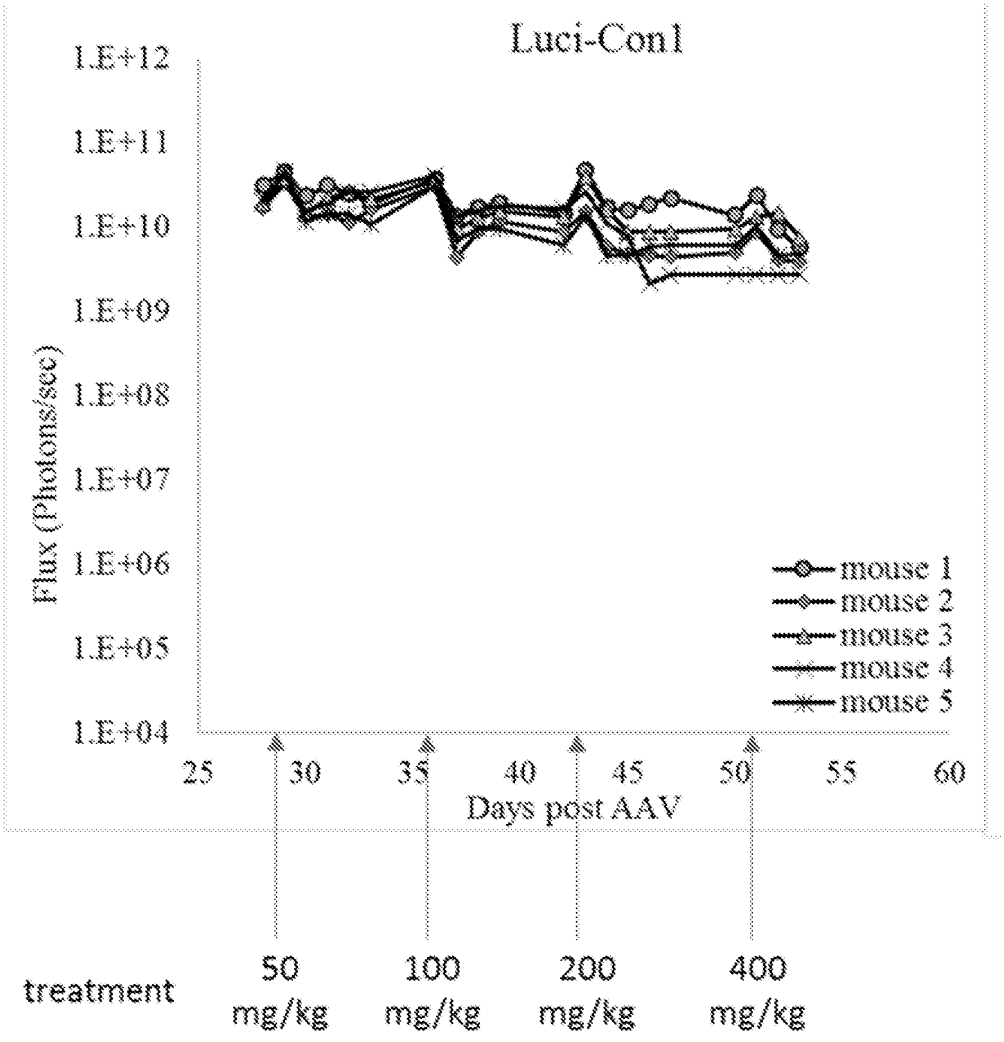

Luci-Con1
1.E+12
1.E+11
1.E+10
1.E+09
1.E+08
1.E+07
1.E+06
1.E+05
1.E+04
Flux (Photons/sec)
mouse 1
mouse 2
mouse 3
mouse 4
mouse 5
25
30
35
40
45
50
55
60
Days post AAV
treatment
50 mg/kg
100 mg/kg
200 mg/kg
400 mg/kg

Fig. 8B

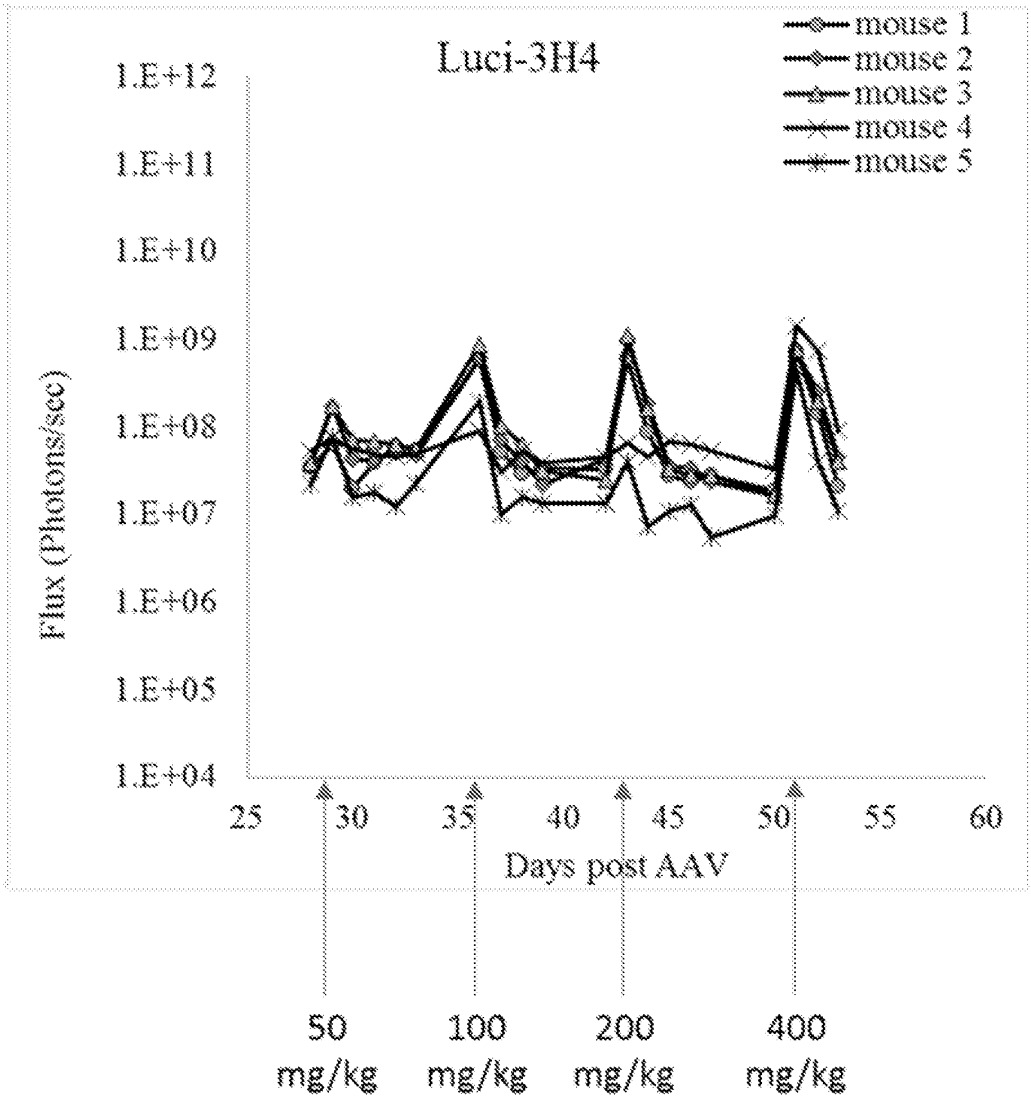

Luci-3H4
mouse 1
mouse 2
mouse 3
mouse 4
mouse 5
1.E+12
1.E+11
1.E+10
1.E+09
1.E+08
1.E+07
1.E+06
1.E+05
1.E+04
Flux (Photons/sec)
25
30
35
40
45
50
55
60
Days post AAV
50 mg/kg
100 mg/kg
200 mg/kg
400 mg/kg

Fig. 8B (cont.)

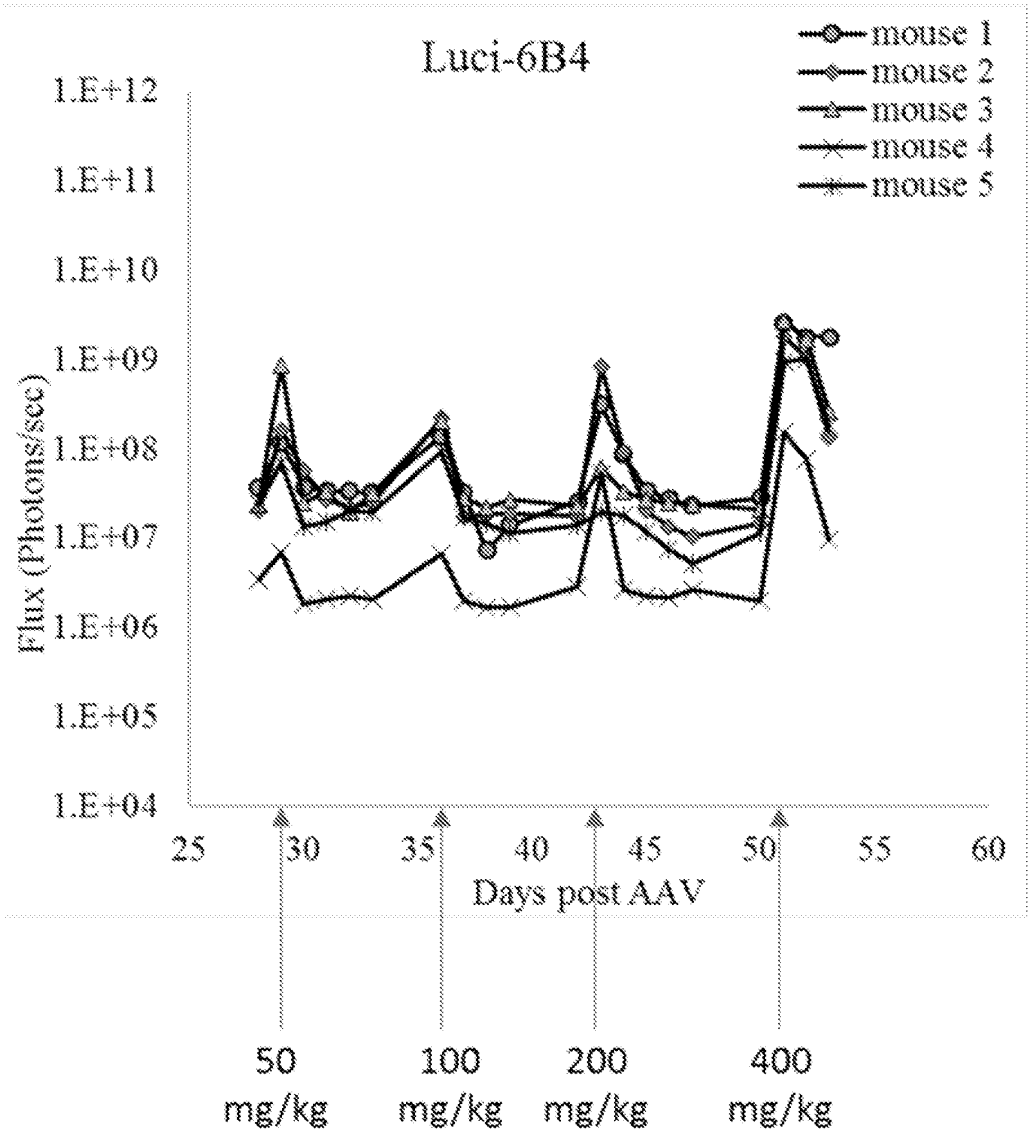

Luci-6B4
mouse 1
mouse 2
mouse 3
mouse 4
mouse 5
1.E+12
1.E+11
1.E+10
1.E+09
1.E+08
1.E+07
1.E+06
1.E+05
1.E+04
Flux (Photons/sec)
25
30
35
40
45
50
55
60
Days post AAV
50 mg/kg
100 mg/kg
200 mg/kg
400 mg/kg

Fig. 8B (cont.)

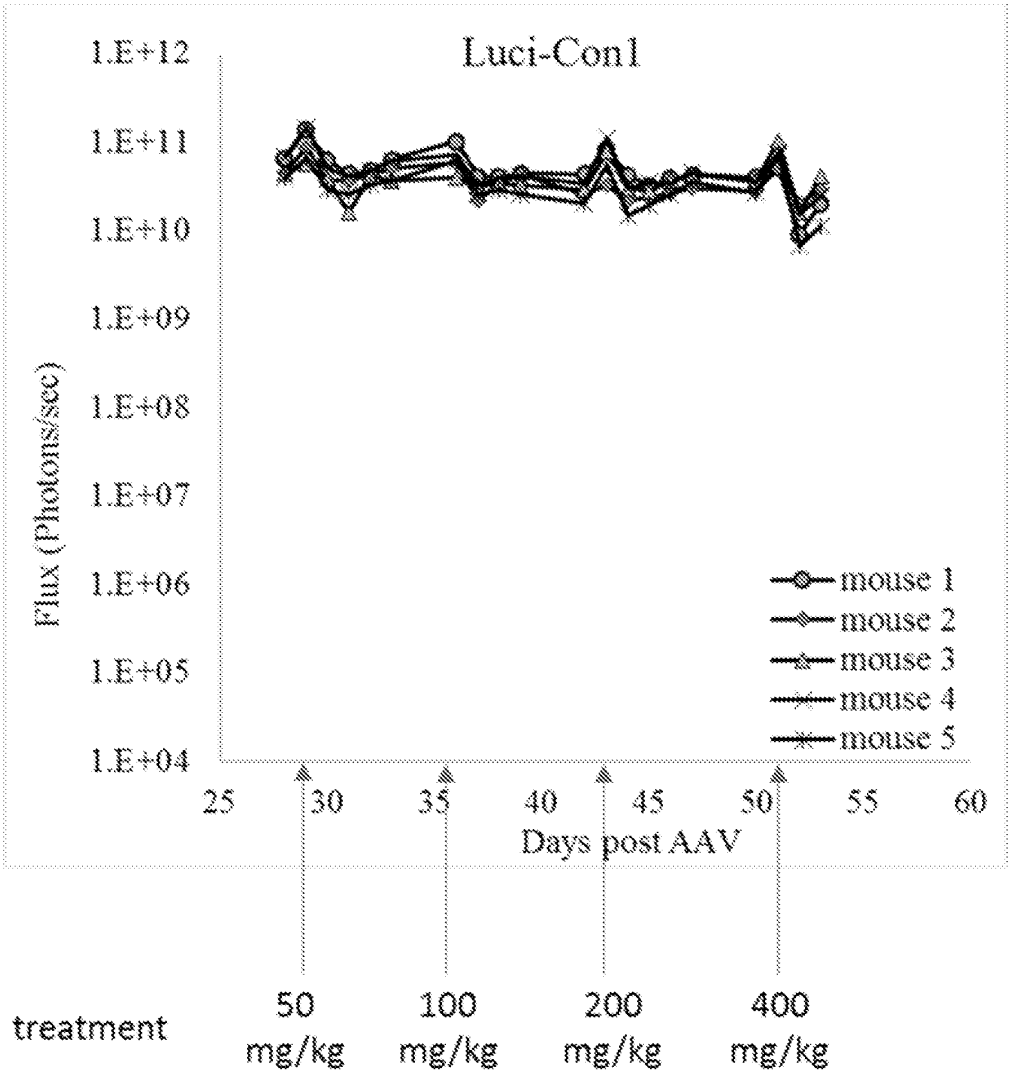

Luci-Con1
1.E+12
1.E+11
1.E+10
1.E+09
1.E+08
1.E+07
1.E+06
1.E+05
1.E+04
Flux (Photons/sec)
mouse 1
mouse 2
mouse 3
mouse 4
mouse 5
25
30
35
40
45
50
55
60
Days post AAV
treatment
50 mg/kg
100 mg/kg
200 mg/kg
400 mg/kg

Fig. 8C

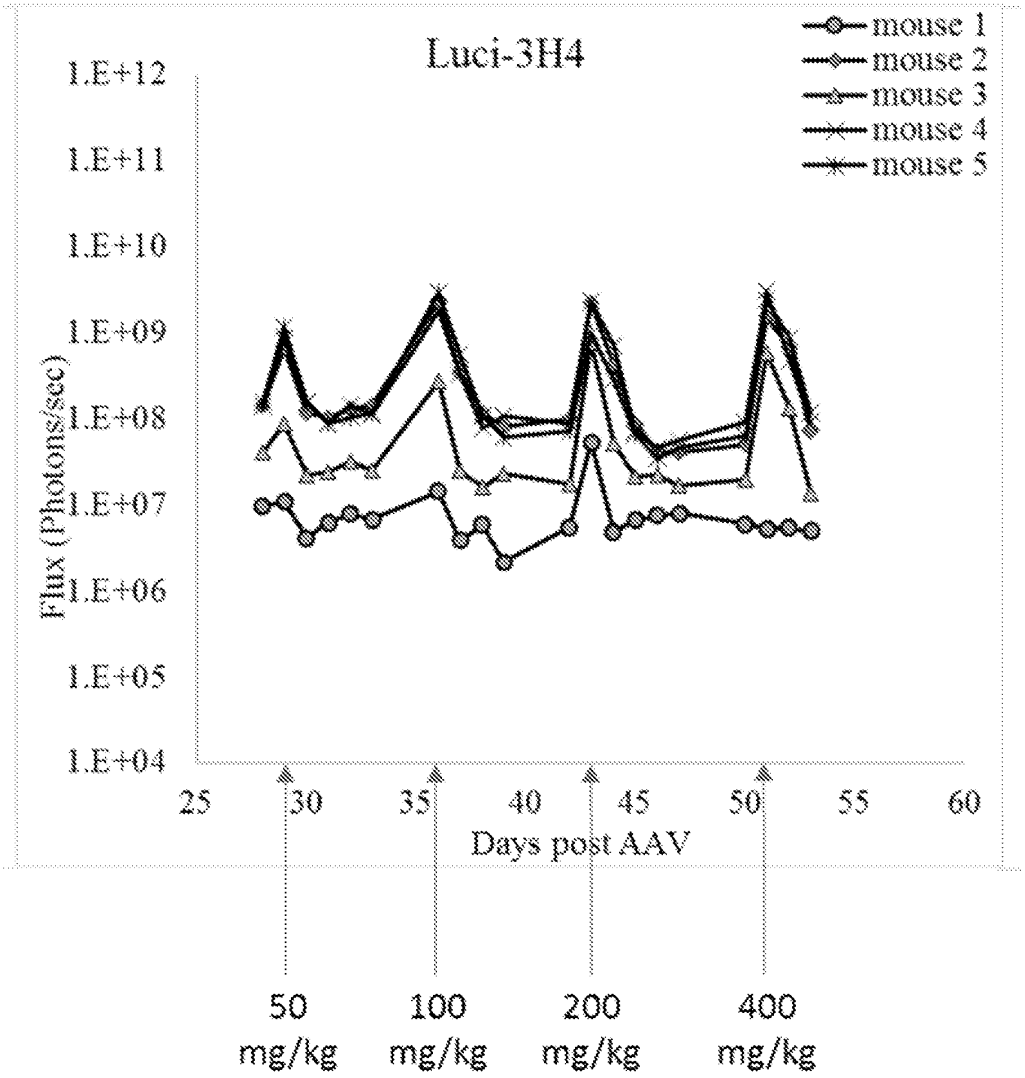

Luci-3H4
mouse 1
mouse 2
mouse 3
mouse 4
mouse 5
1.E+12
1.E+11
1.E+10
1.E+09
1.E+08
1.E+07
1.E+06
1.E+05
1.E+04
Flux (Photons/sec)
25
30
35
40
45
50
55
60
Days post AAV
50 mg/kg
100 mg/kg
200 mg/kg
400 mg/kg

Fig. 8C (cont.)

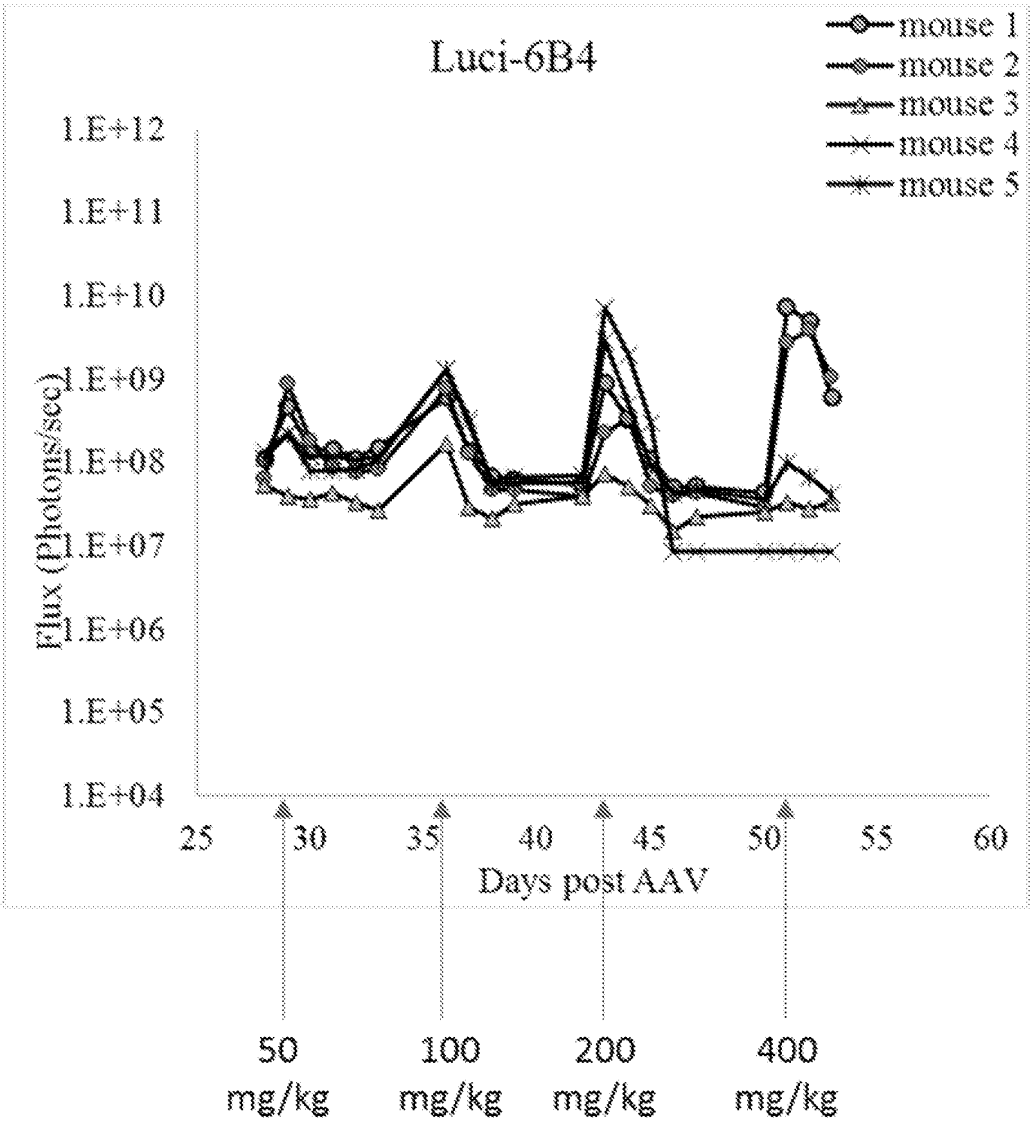

Luci-6B4
mouse 1
mouse 2
mouse 3
mouse 4
mouse 5
1.E+12
1.E+11
1.E+10
1.E+09
1.E+08
1.E+07
1.E+06
1.E+05
1.E+04
Flux (Photons/sec)
25
30
35
40
45
50
55
60
Days post AAV
50 mg/kg
100 mg/kg
200 mg/kg
400 mg/kg

Fig. 8C (cont.)

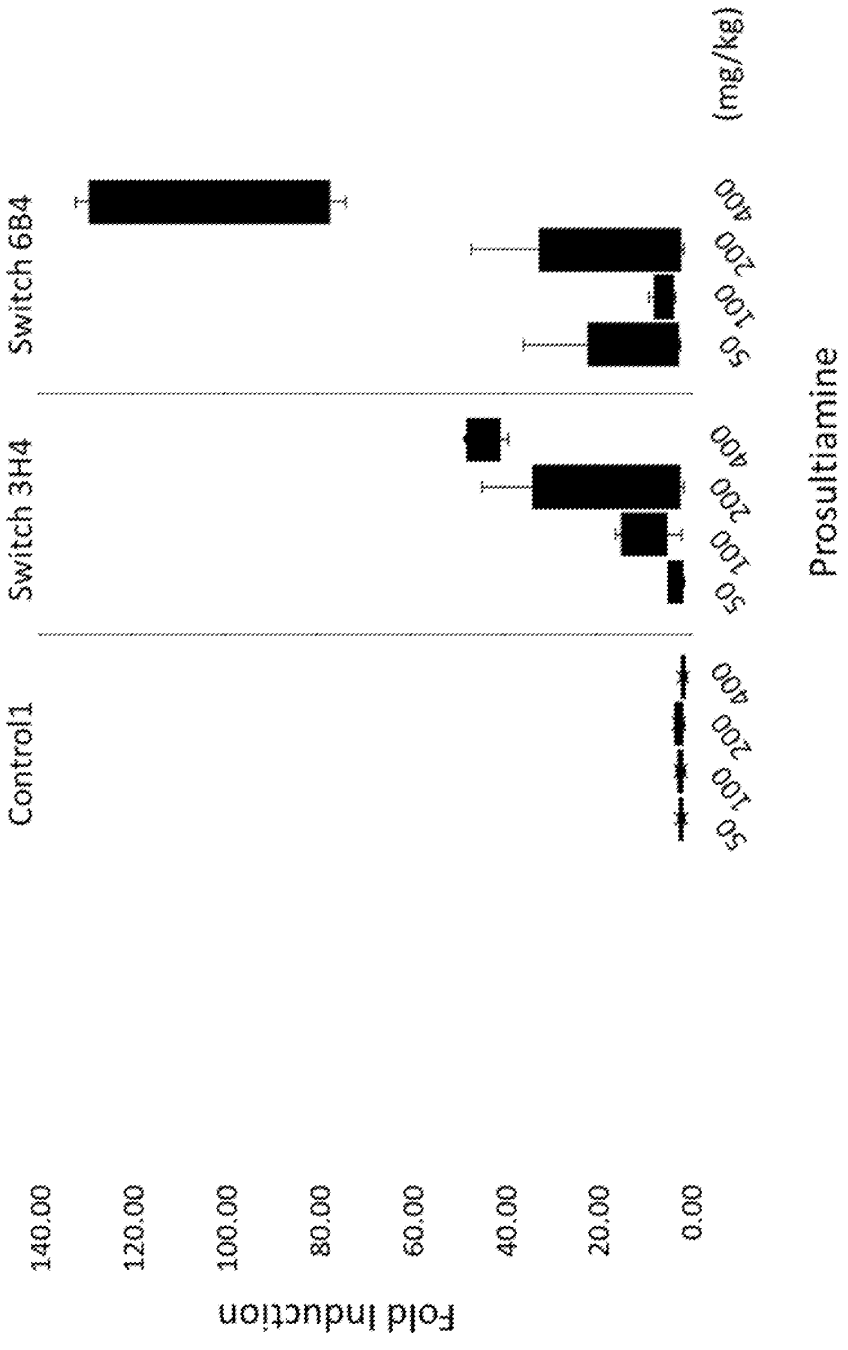

Fold Induction
140.00
120.00
100.00
80.00
60.00
40.00
20.00
0.00
Control1
Switch 3H4
Switch 6B4
50
100
200
400
(mg/kg)
Prosultiamine

Fig. 8D

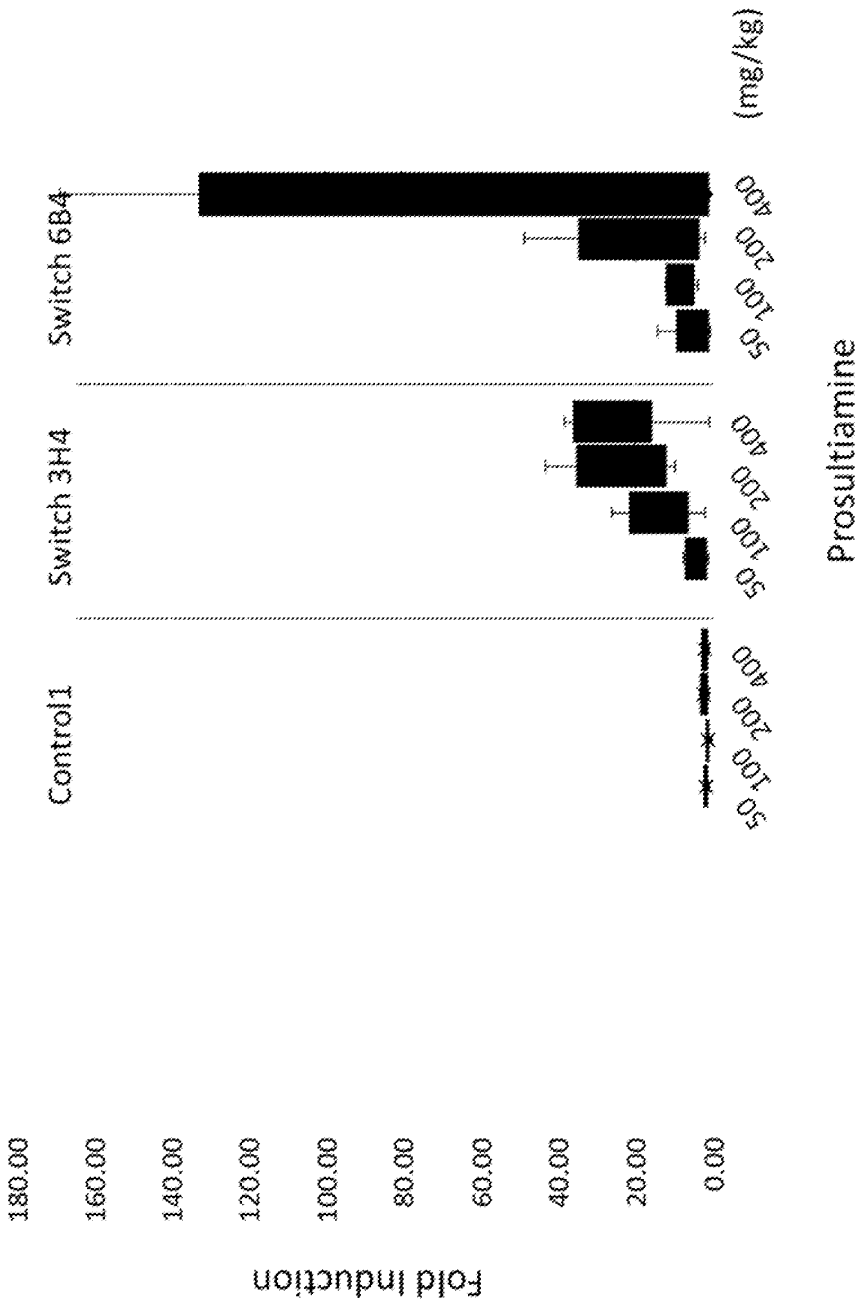

Fold Induction
180.00
160.00
140.00
120.00
100.00
80.00
60.00
40.00
20.00
0.00
Control1
Switch 3H4
Switch 6B4
50
100
200
400
(mg/kg)
Prosultiamine

Fig. 8E

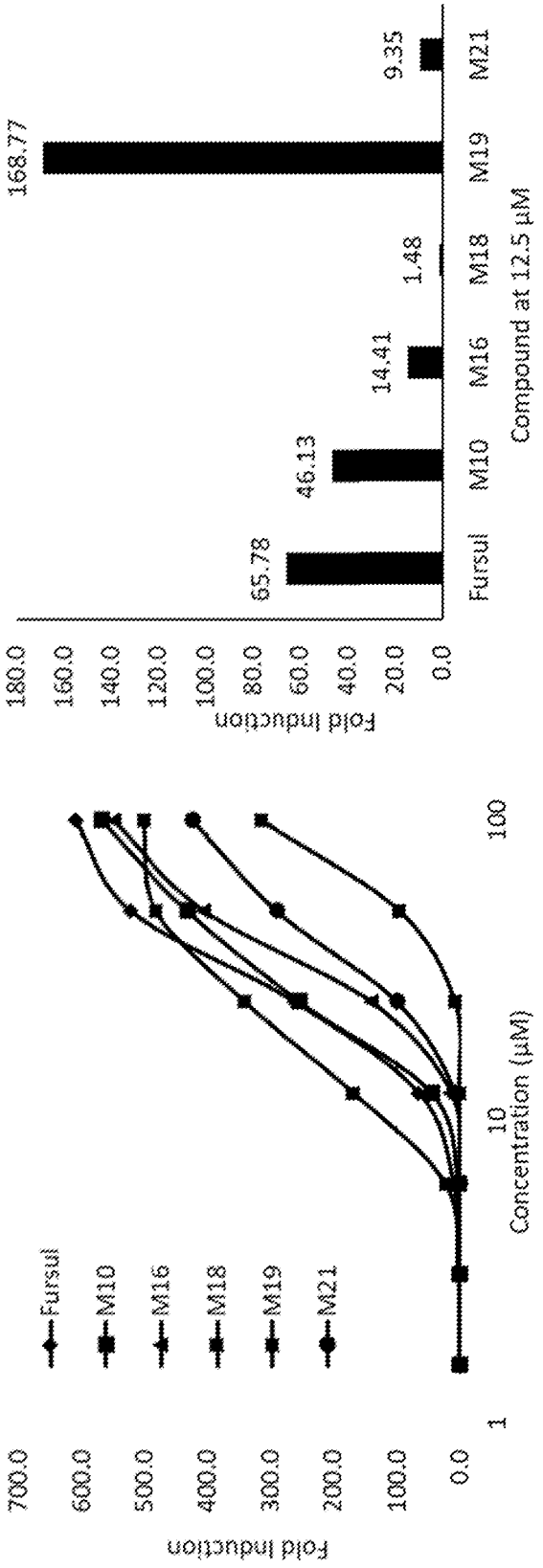

Fold Induction
Concentration (µM)
Fursul
M10
M16
M18
M19
M21
Fold Induction
Compound at 12.5 µM
65.78
46.13
14.41
1.48
168.77
9.35

Fig. 9A

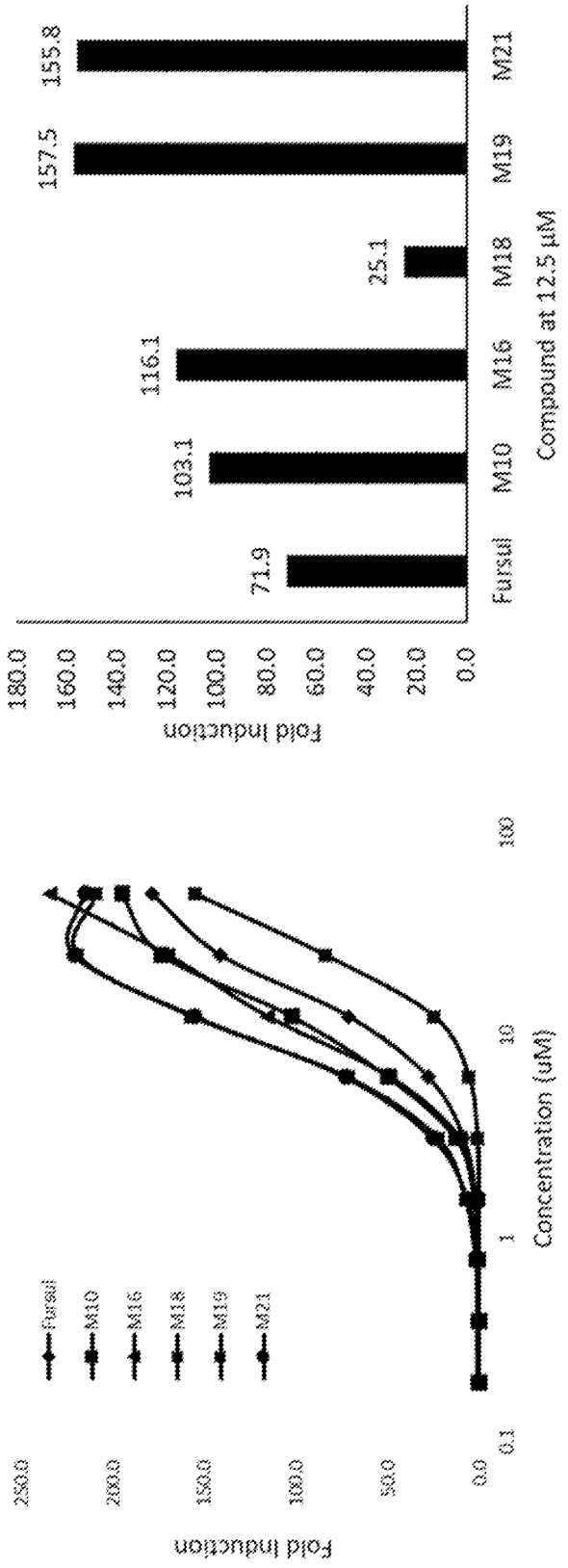

Fold Induction
180.0
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
71.9
103.1
116.1
25.1
157.5
155.8
Fursul
M10
M16
M18
M19
M21
Compound at 12.5 µM
Fold Induction
250.0
200.0
150.0
100.0
50.0
0.0
0.1
1
10
100
Concentration (uM)
Fursul
M10
M16
M18
M19
M21

Fig. 9B

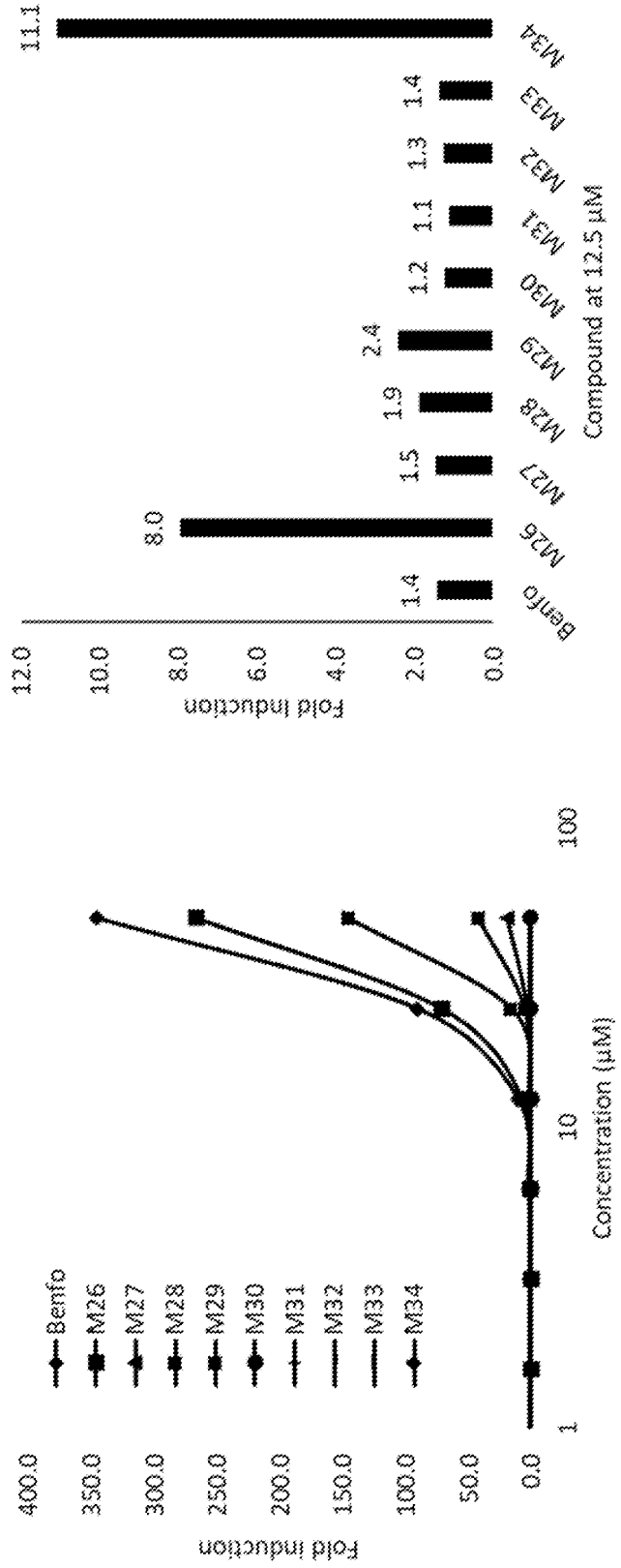
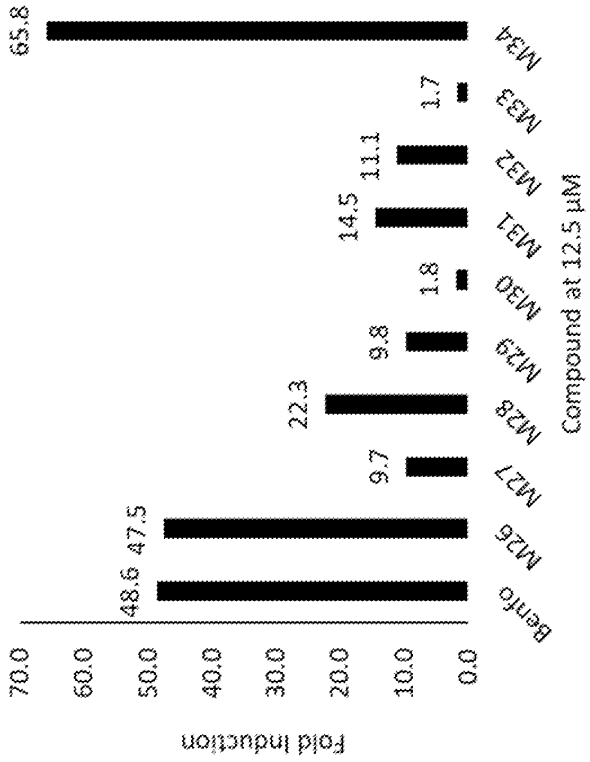

Fold induction
12.0
10.0
8.0
6.0
4.0
2.0
0.0
Benfo
M26
M27
M28
M29
M30
M31
M32
M33
M34
1.4
8.0
1.5
1.9
2.4
1.2
1.1
1.3
1.4
11.1
Compound at 12.5 µM
Fold induction
400.0
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0.0
1
10
100
Concentration (µM)
Benfo
M26
M27
M28
M29
M30
M31
M32
M33
M34

Fig. 9C


Fold Induction
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
Benfo
M26
M27
M28
M29
M30
M31
M32
M33
M34
48.6
47.5
9.7
22.3
9.8
1.8
14.5
11.1
1.7
65.8
Compound at 12.5 µM

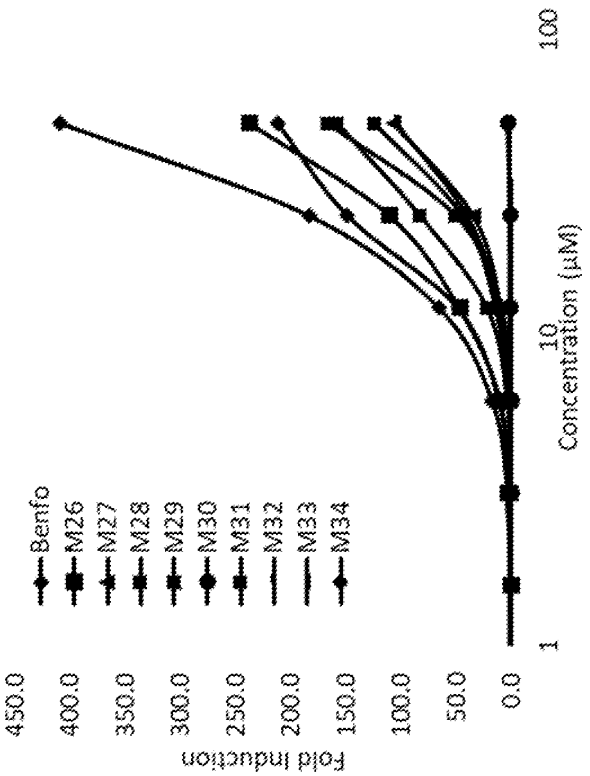

Fold Induction
450.0
400.0
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0.0
Benfo
M26
M27
M28
M29
M30
M31
M32
M33
M34
1
10
100
Concentration (µM)

Fig. 9D

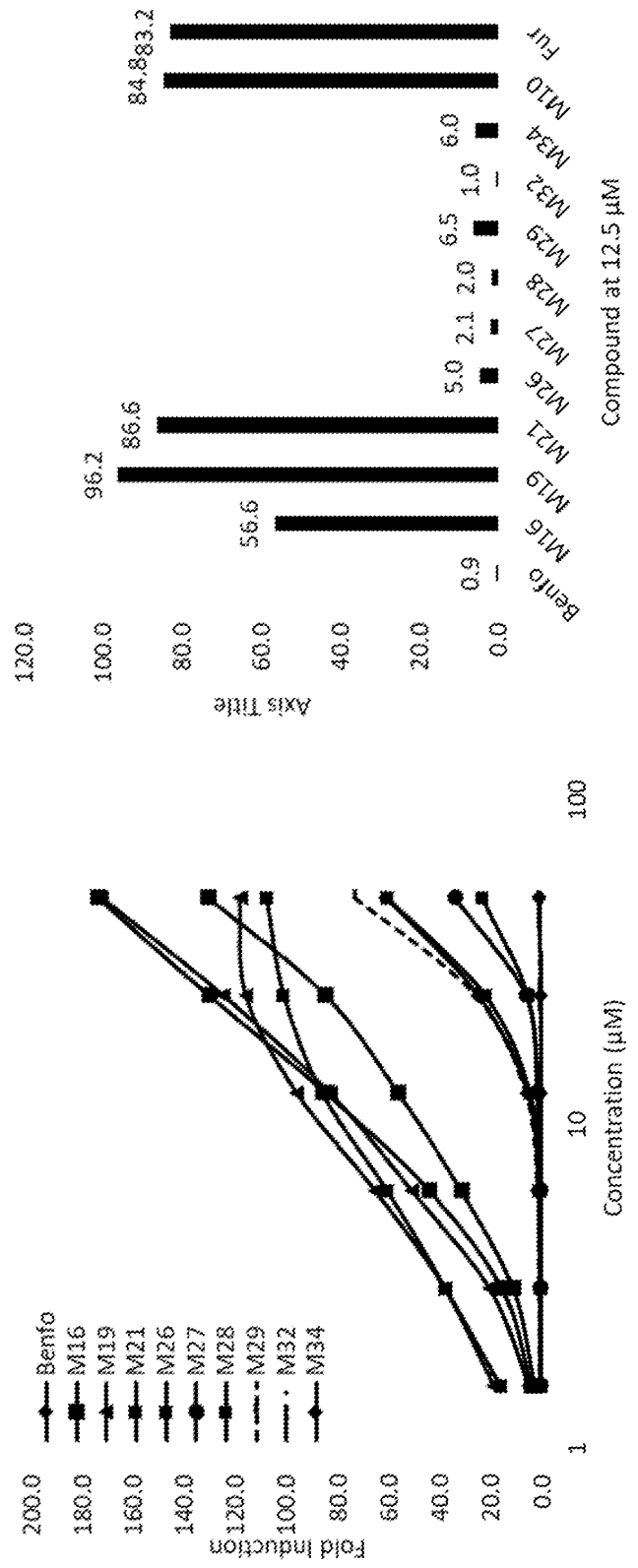

Benfo
M16
M19
M21
M26
M27
M28
M29
M32
M34
Fold Induction
Concentration (µM)
Axis Title
Compound at 12.5 µM
Fur
M10
M34
M32
M29
M28
M27
M26
M21
M19
M16
Benfo
84.8
83.2
96.2
86.6
56.6
5.0
2.1
2.0
6.5
1.0
6.0
0.9

Fig. 9E

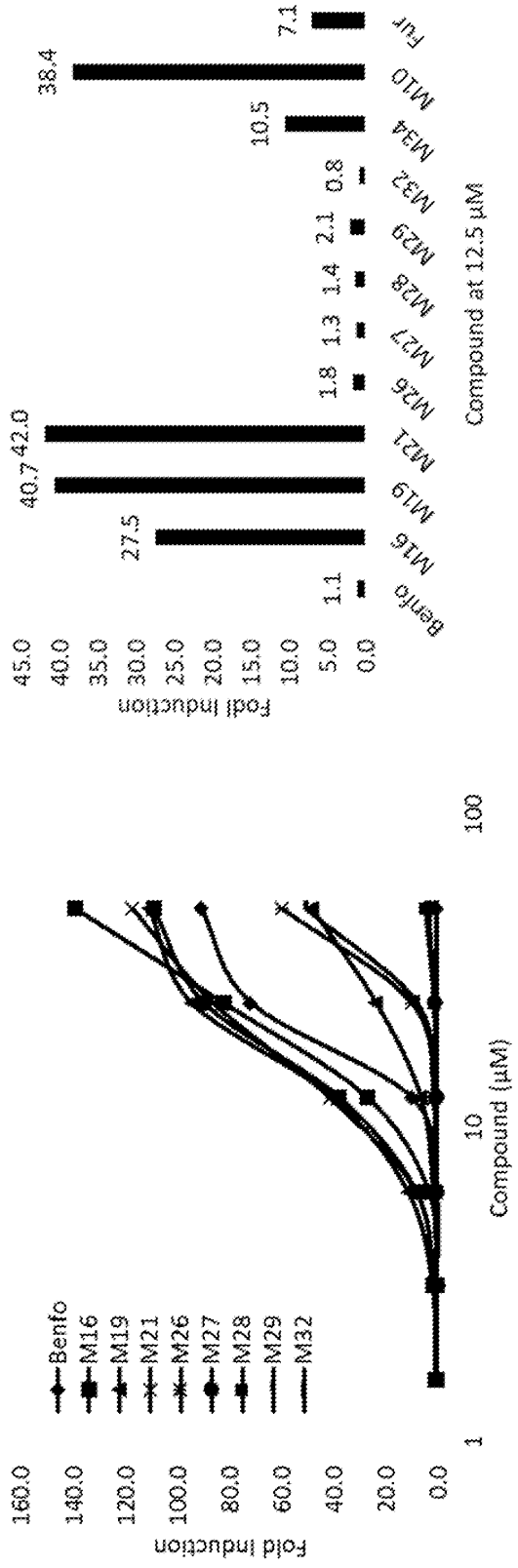

Fold Induction
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
1
10
100
Compound (µM)
Benfo
M16
M19
M21
M26
M27
M28
M29
M32
Fold Induction
45.0
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
Benfo
M16
M19
M21
M26
M27
M28
M29
M32
M34
M10
Fur
1.1
27.5
40.7
42.0
1.8
1.3
1.4
2.1
0.8
10.5
38.4
7.1
Compound at 12.5 µM

Fig. 9F