FIG. 1a

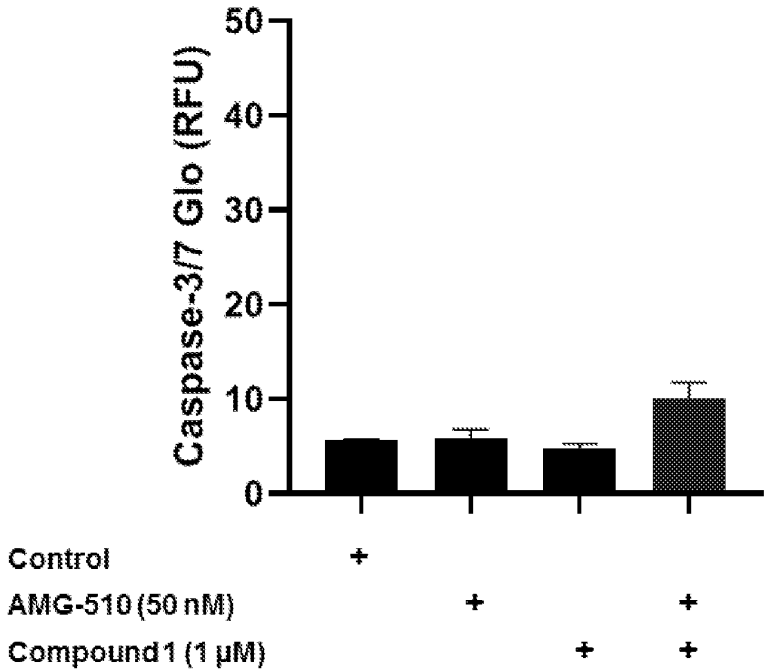

Caspase-3/7 Glo (RFU)
50
40
30
20
10
0
Control
AMG-510 (50 nM)
Compound 1 (1 μM)
+
+
+
+
+
+

FIG. 1b

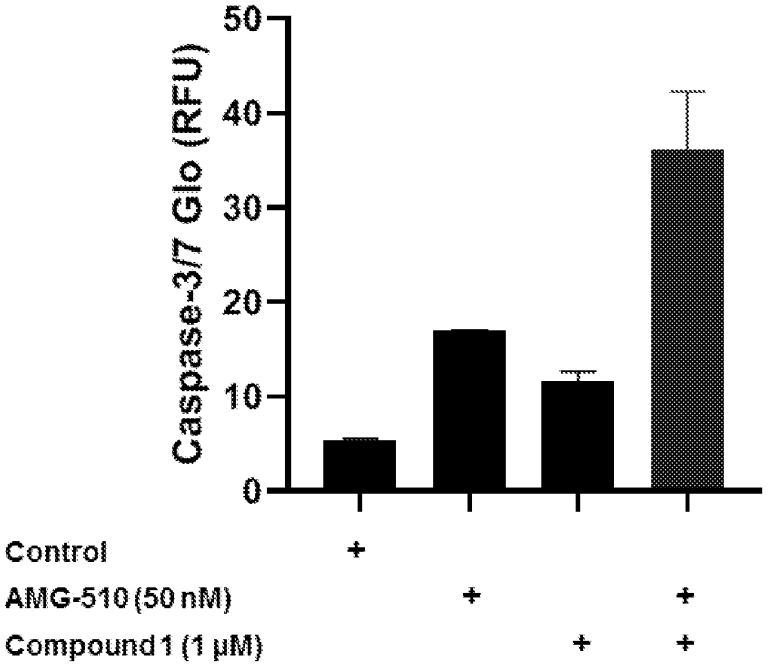

Caspase-3/7 Glo (RFU)
50
40
30
20
10
0
Control
AMG-510 (50 nM)
Compound 1 (1 μM)
+
+
+
+
+
+

FIG. 1c

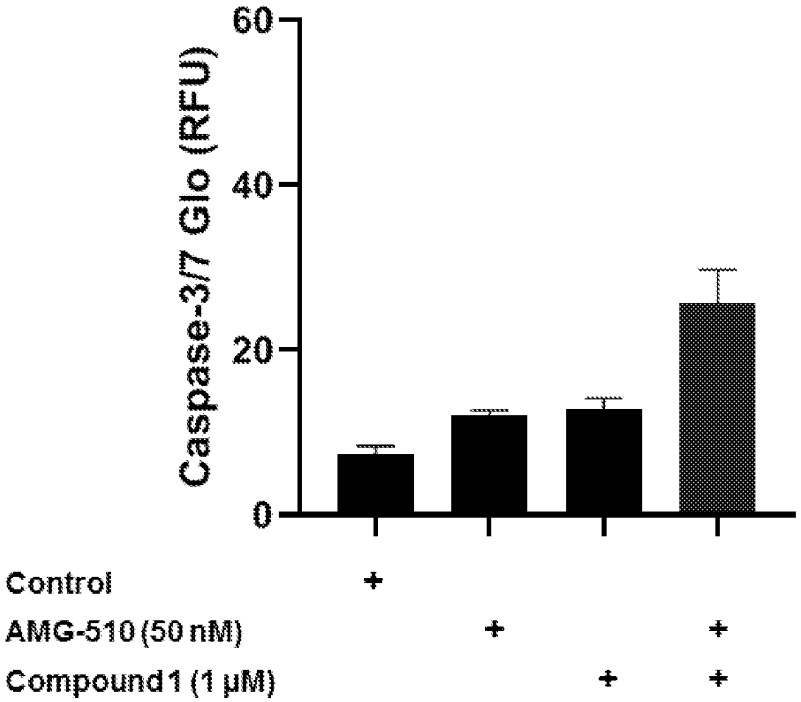

Caspase-3/7 Glo (RFU)
60
40
20
0
Control
AMG-510 (50 nM)
Compound 1 (1 µM)
+
+
+
+
+
+

FIG. 1d

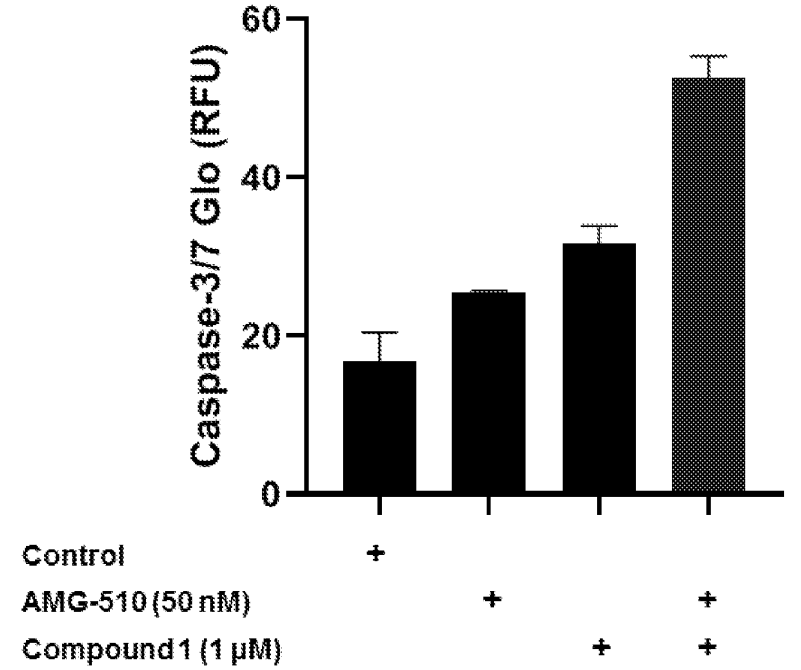

Caspase-3/7 Glo (RFU)
60
40
20
0
Control
AMG-510 (50 nM)
Compound 1 (1 µM)
+
+
+
+
+
+

FIG. 1e

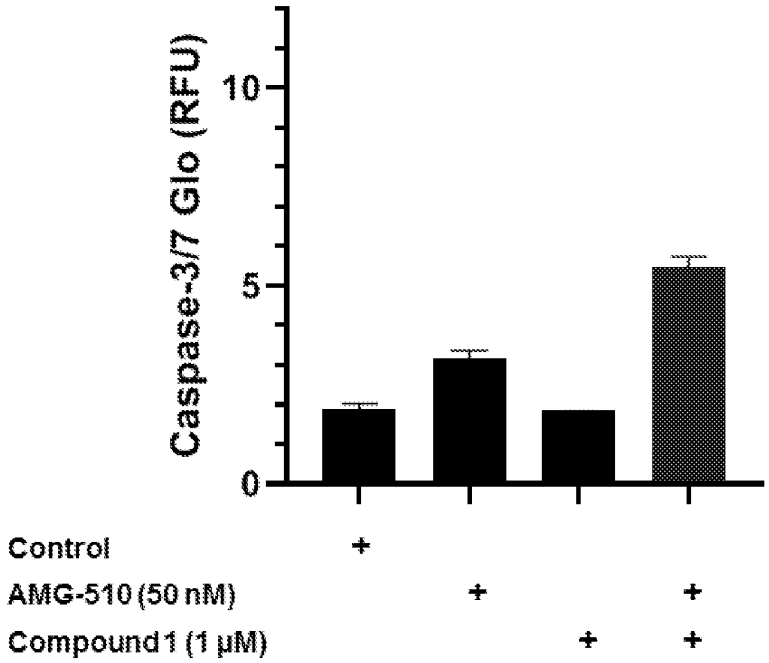

Caspase-3/7 Glo (RFU)
10
5
0
Control + + +
AMG-510 (50 nM) + +
Compound 1 (1 μM) + +

FIG. 1f

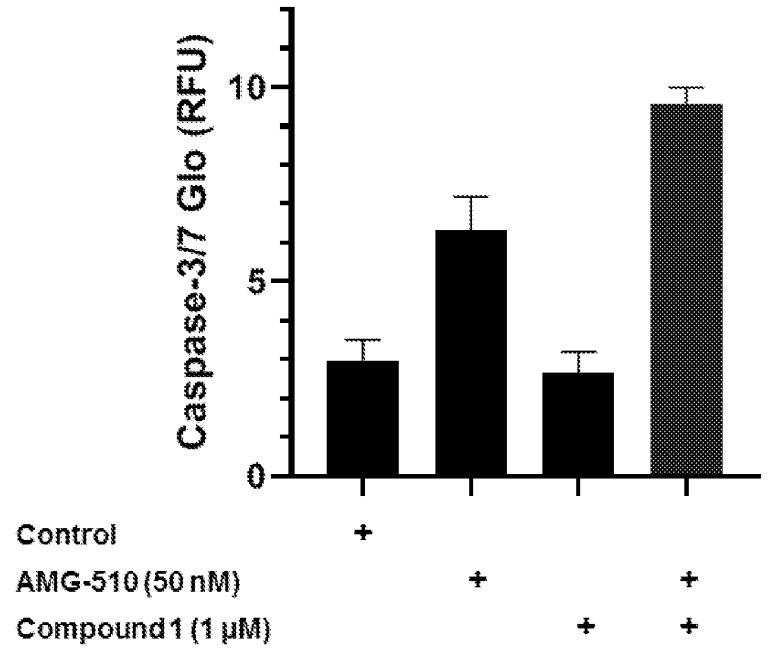

Caspase-3/7 Glo (RFU)
10
5
0
Control + + +
AMG-510 (50 nM) + +
Compound 1 (1 μM) + +

FIG. 2a

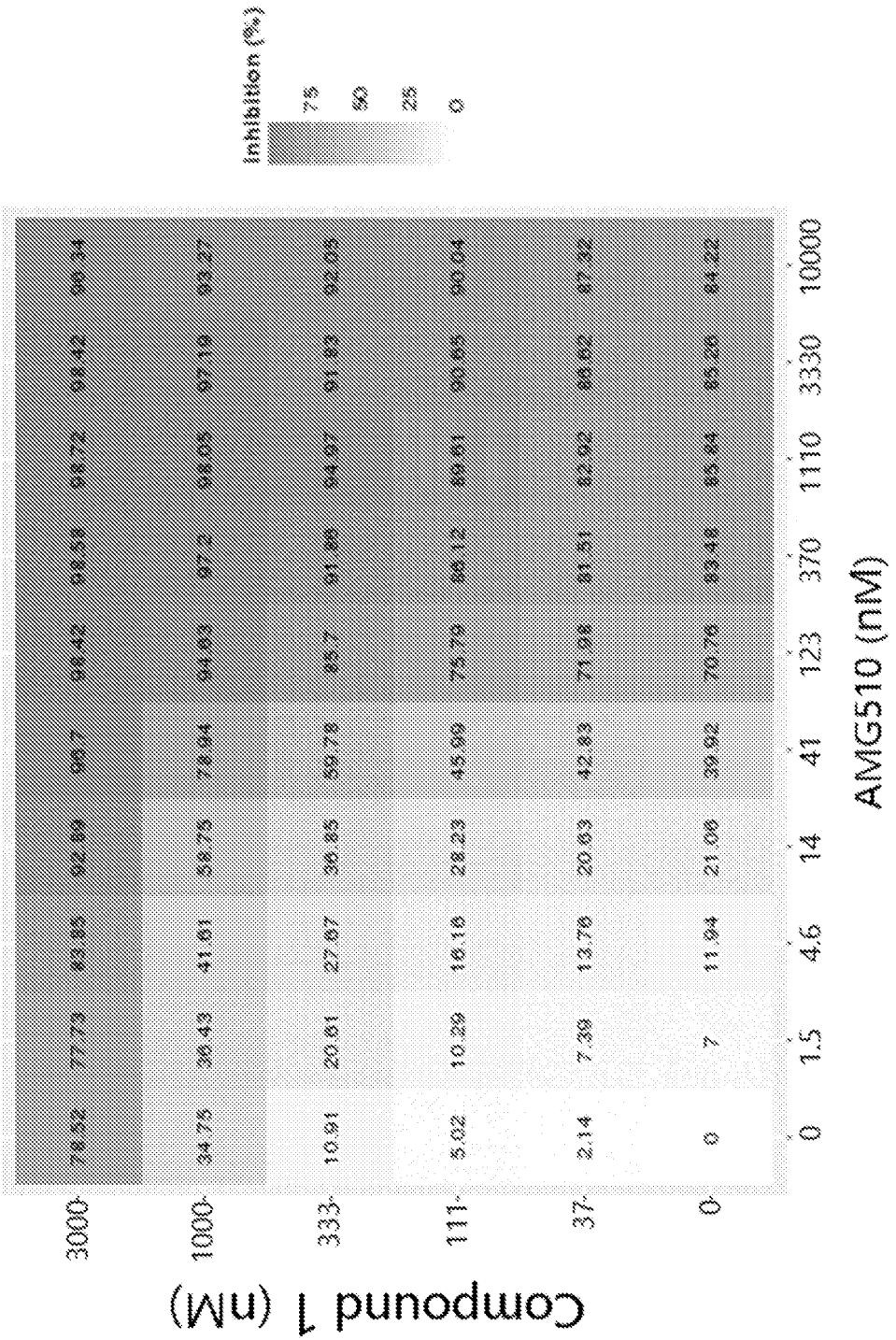

Inhibition (%)
75
50
25
0
Compound 1 (nM)
3000
1000
333
111
37
0
78.52 77.79 83.95 92.89 98.7 98.42 98.58 98.72 98.42 98.44
34.75 36.43 41.61 58.75 78.94 94.63 97.2 98.05 97.19 93.27
10.91 20.61 27.87 36.85 59.78 85.7 91.88 94.97 91.83 92.85
5.02 10.29 16.18 28.23 45.99 75.79 89.12 89.61 89.65 90.04
2.14 7.39 13.79 20.63 42.83 71.98 81.91 82.02 89.62 87.32
0 7 11.94 21.06 39.92 70.76 83.48 85.84 85.26 84.22
0 1.5 4.6 14 41 123 370 1110 3330 10000
AMG510 (nM)

FIG. 2b

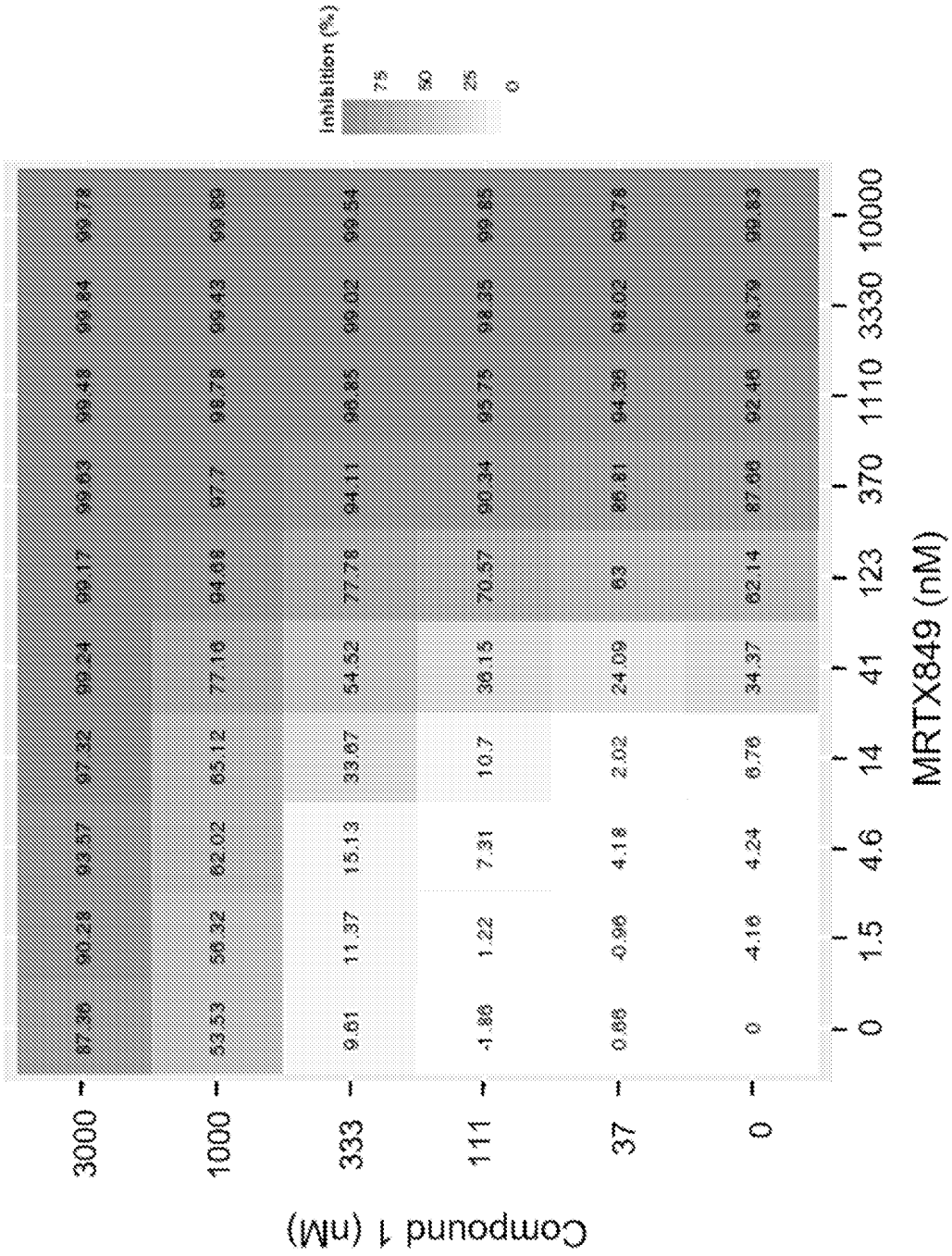

Inhibition (%)
75
50
25
0
Compound 1 (nM)
3000
1000
333
111
37
0
87.36 90.28 93.57 97.32 99.24 99.17 99.63 99.48 99.44 99.78
53.53 80.32 82.02 85.12 77.16 84.66 97.7 98.78 99.43 99.69
9.61 11.37 15.13 33.67 54.52 77.78 94.11 98.85 99.02 99.34
-1.86 1.22 7.31 10.7 36.15 70.57 90.34 95.75 98.35 99.85
0.66 0.96 4.18 2.02 24.09 63 85.81 94.36 98.02 99.78
0 4.16 4.24 8.76 34.37 62.14 87.69 92.48 98.79 99.83
0 1.5 4.6 14 41 123 370 1110 3330 10000
MRTX849 (nM)

FIG. 3a

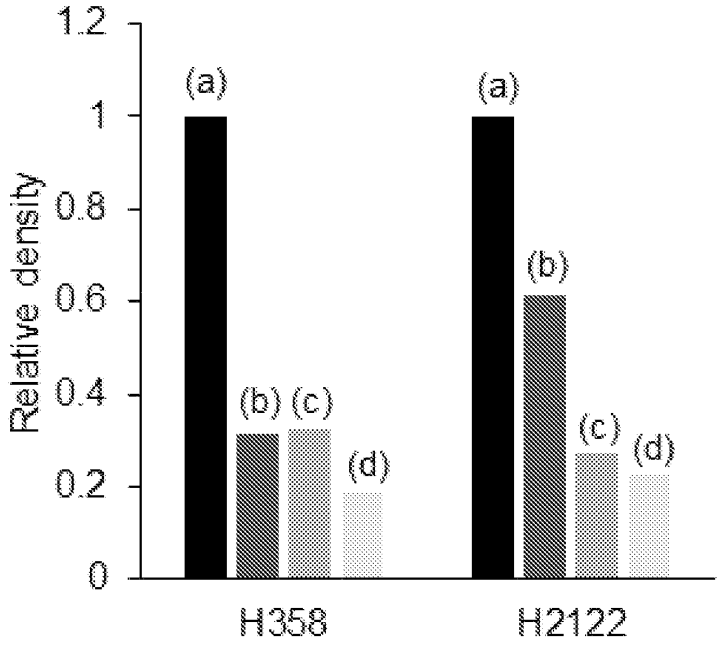

1.2
1
0.8
0.6
0.4
0.2
0
Relative density
(a)
(b) (c)
(d)
(a)
(b)
(c)
(d)
H358
H2122

FIG. 3b

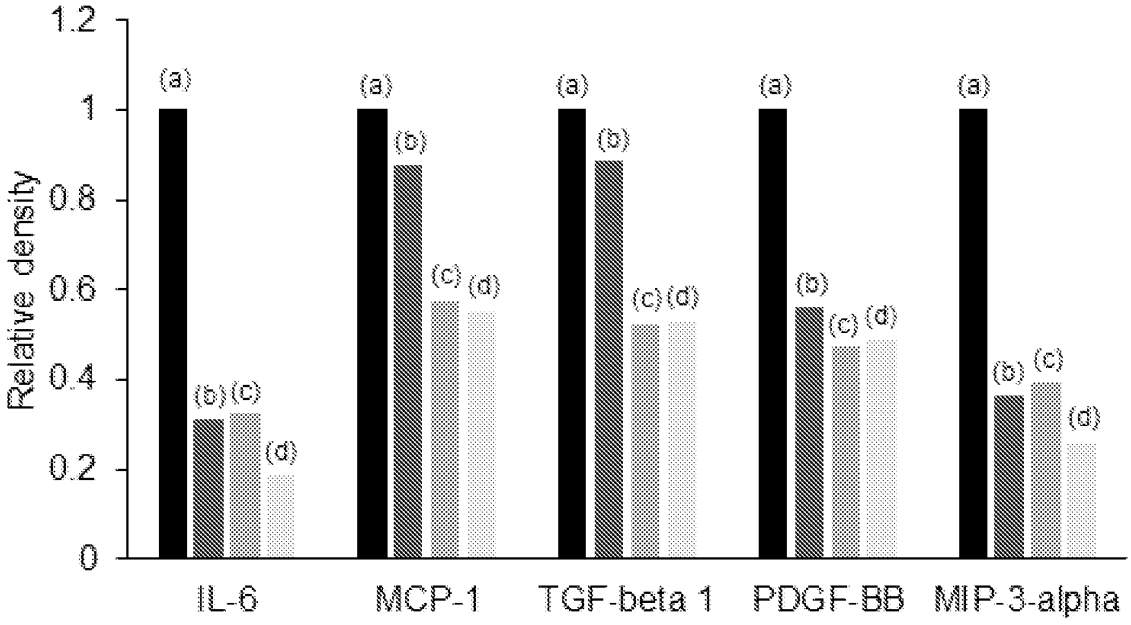

1.2
1
0.8
0.6
0.4
0.2
0
Relative density
IL-6
MCP-1
TGF-beta 1
PDGF-BB
MIP-3-alpha

FIG. 3c

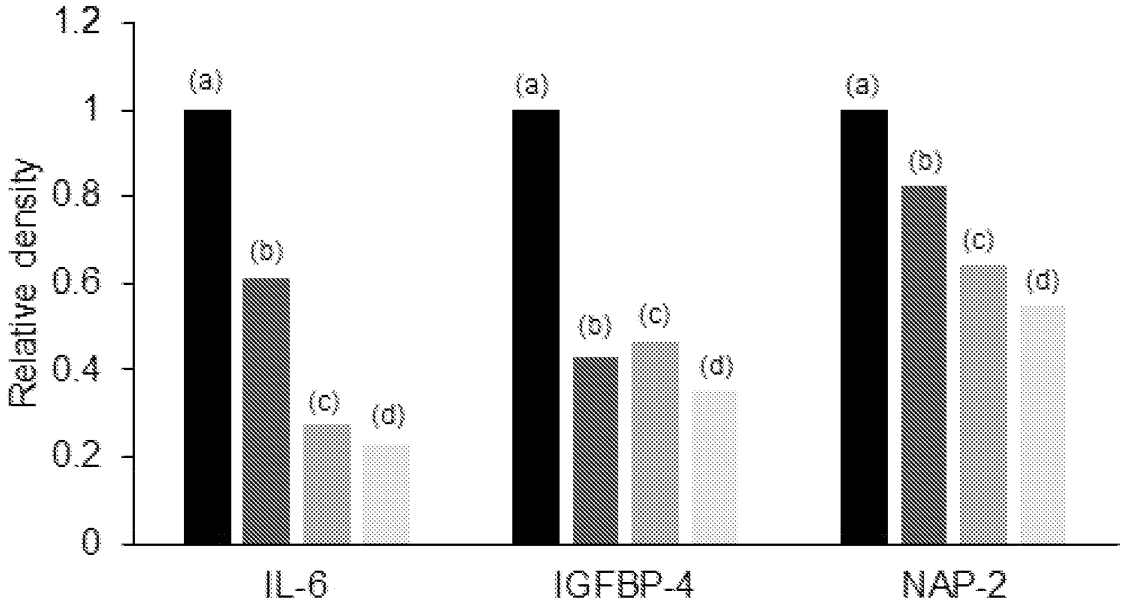

1.2
1
0.8
0.6
0.4
0.2
0
Relative density
(a)
(b)
(c)
(d)
IL-6
IGFBP-4
NAP-2

FIG. 3d

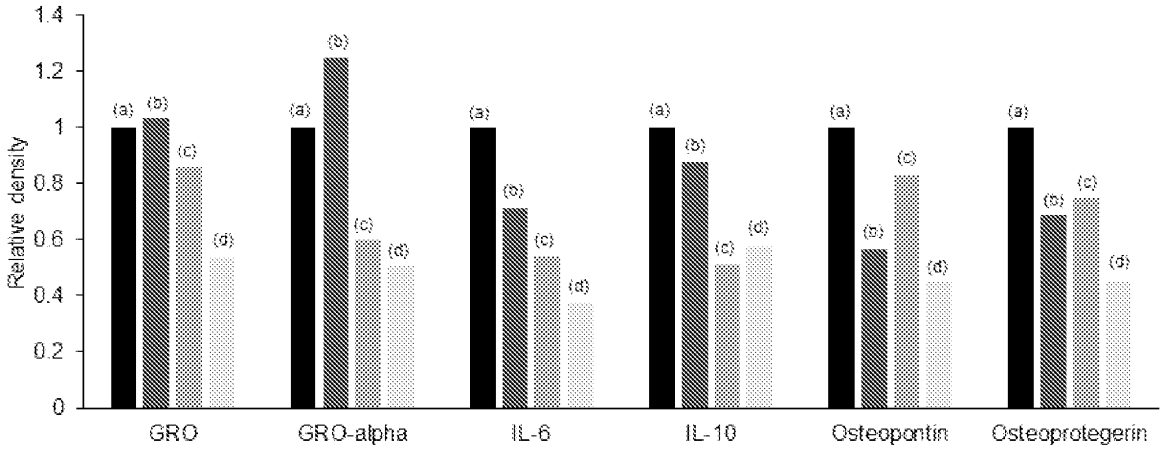

1.4
1.2
1
0.8
0.6
0.4
0.2
0
Relative density
GRO
GRO-alpha
IL-6
IL-10
Osteopontin
Osteoprotegerin

FIG. 3e

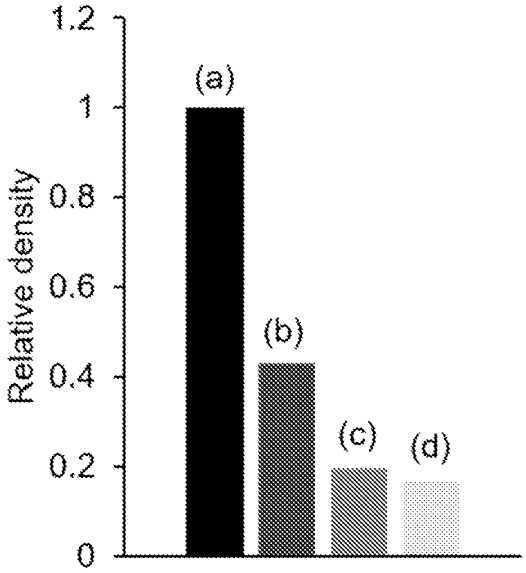

1.2
1
0.8
0.6
0.4
0.2
0
Relative density
(a)
(b)
(c)
(d)

FIG. 3f

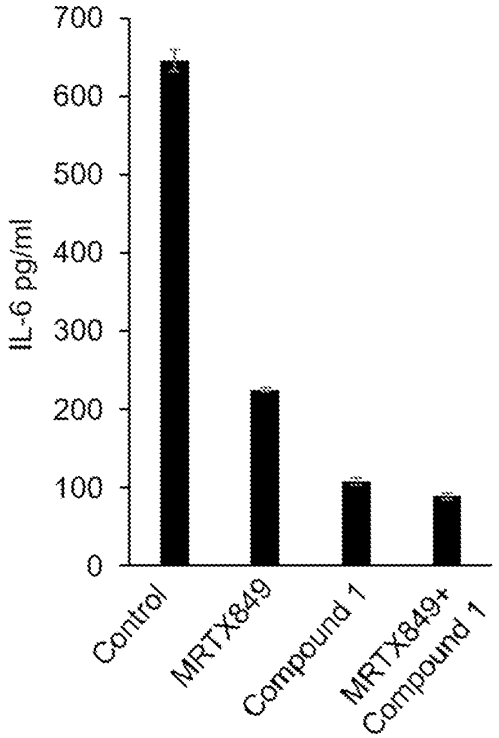

700
600
500
400
300
200
100
0
IL-6 pg/ml
Control
MRTX849
Compound 1
MRTX849+ Compound 1

FIG. 3g

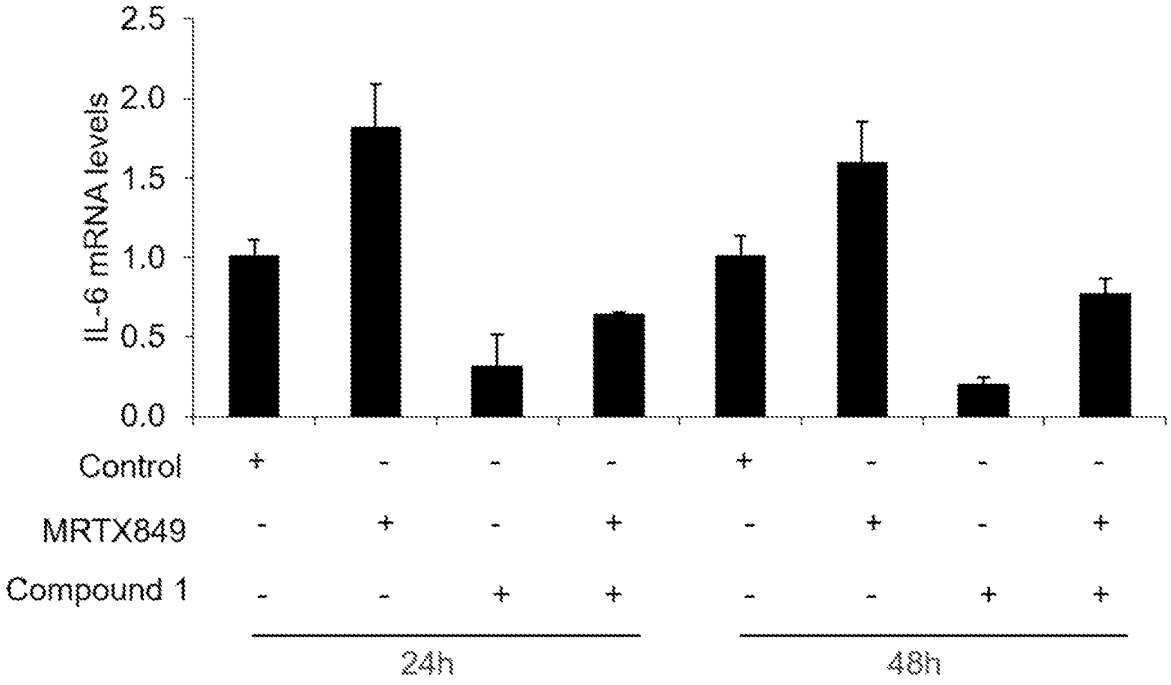

IL-6 mRNA levels
2.5
2.0
1.5
1.0
0.5
0.0
Control
MRTX849
Compound 1
24h
48h

FIG. 4a

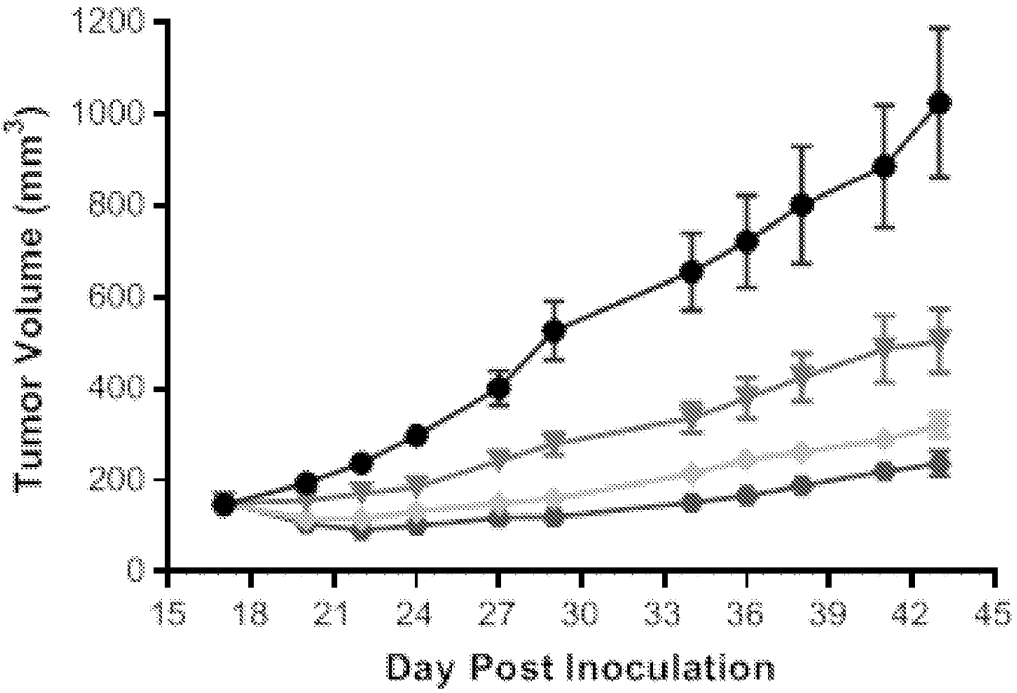

Tumor Volume (mm3)
1200
1000
800
600
400
200
0
15
18
21
24
27
30
33
36
39
42
45
Day Post Inoculation

FIG. 4b

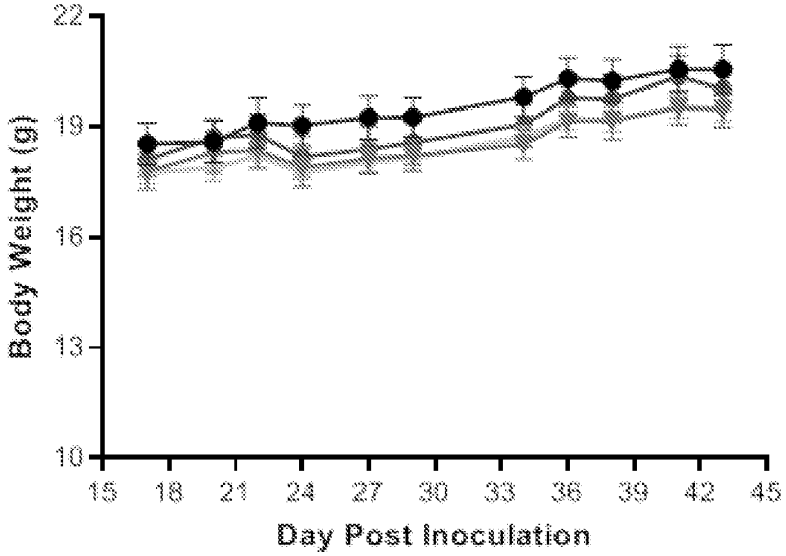

Body Weight (g)
22
19
16
13
10
15
18
21
24
27
30
33
36
39
42
45
Day Post Inoculation

FIG. 5a

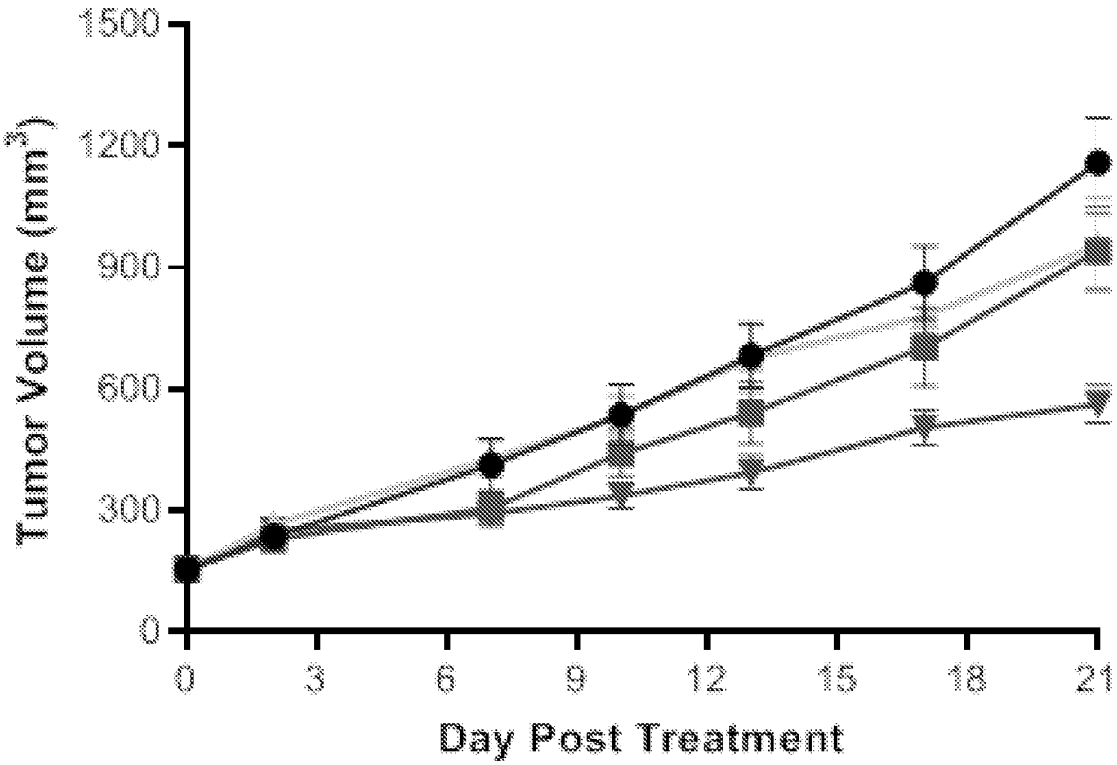

1500
1200
900
600
300
0
Tumor Volume (mm3)
0
3
6
9
12
15
18
21
Day Post Treatment

FIG. 5b

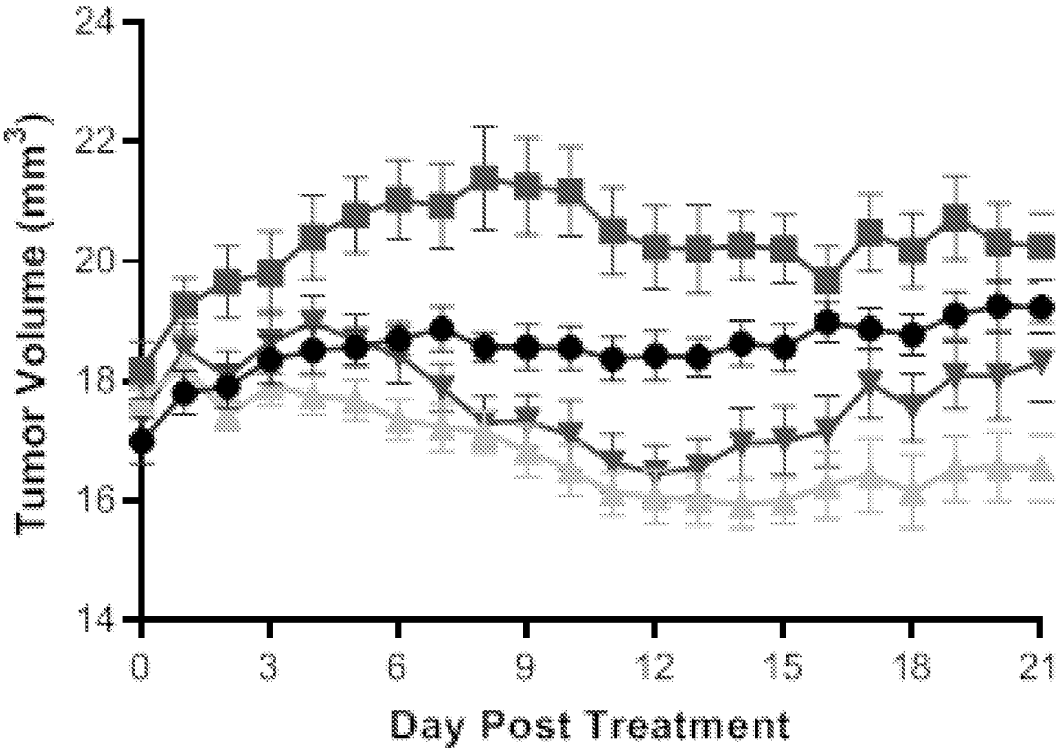

Tumor Volume (mm3)
24
22
20
18
16
14
0
3
6
9
12
15
18
21
Day Post Treatment

FIG. 6a

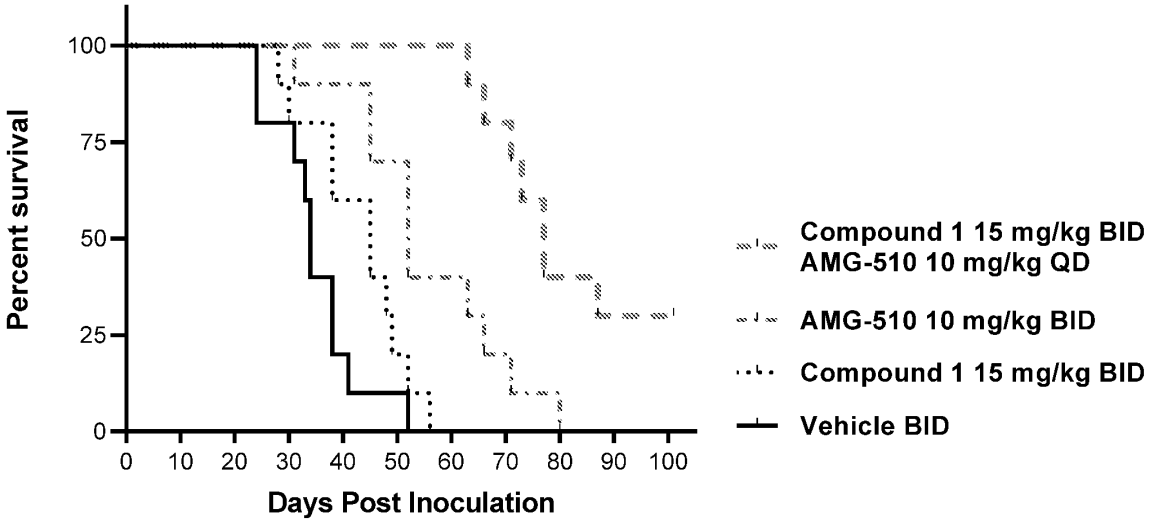
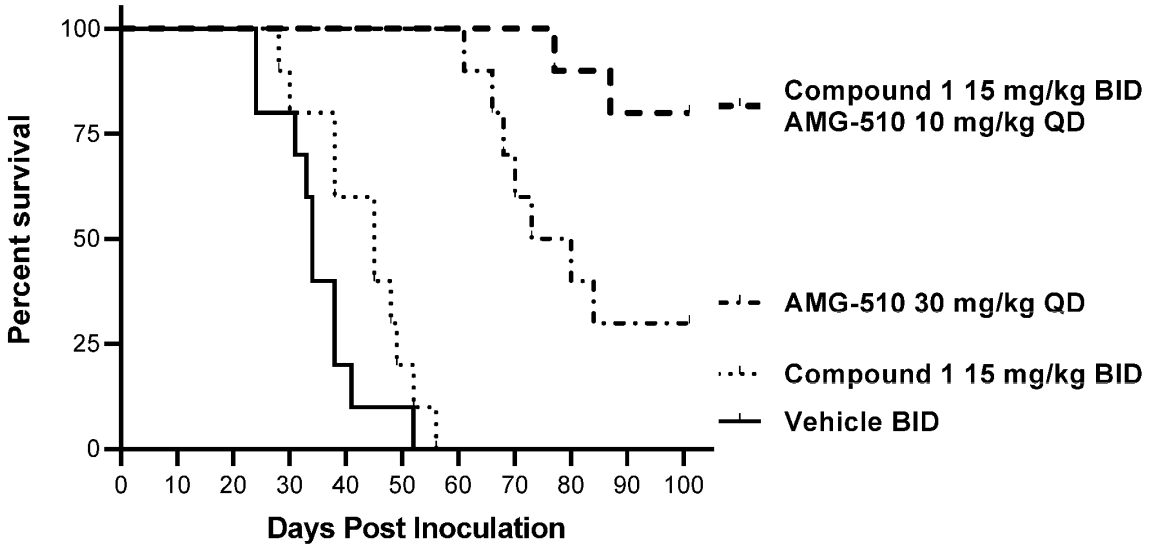

Percent survival
100
75
50
25
0
0 10 20 30 40 50 60 70 80 90 100
Days Post Inoculation
Compound 1 15 mg/kg BID
AMG-510 10 mg/kg QD
AMG-510 10 mg/kg BID
Compound 1 15 mg/kg BID
Vehicle BID

FIG. 6b


Percent survival
100
75
50
25
0
0 10 20 30 40 50 60 70 80 90 100
Days Post Inoculation
Compound 1 15 mg/kg BID
AMG-510 10 mg/kg QD
AMG-510 30 mg/kg QD
Compound 1 15 mg/kg BID
Vehicle BID