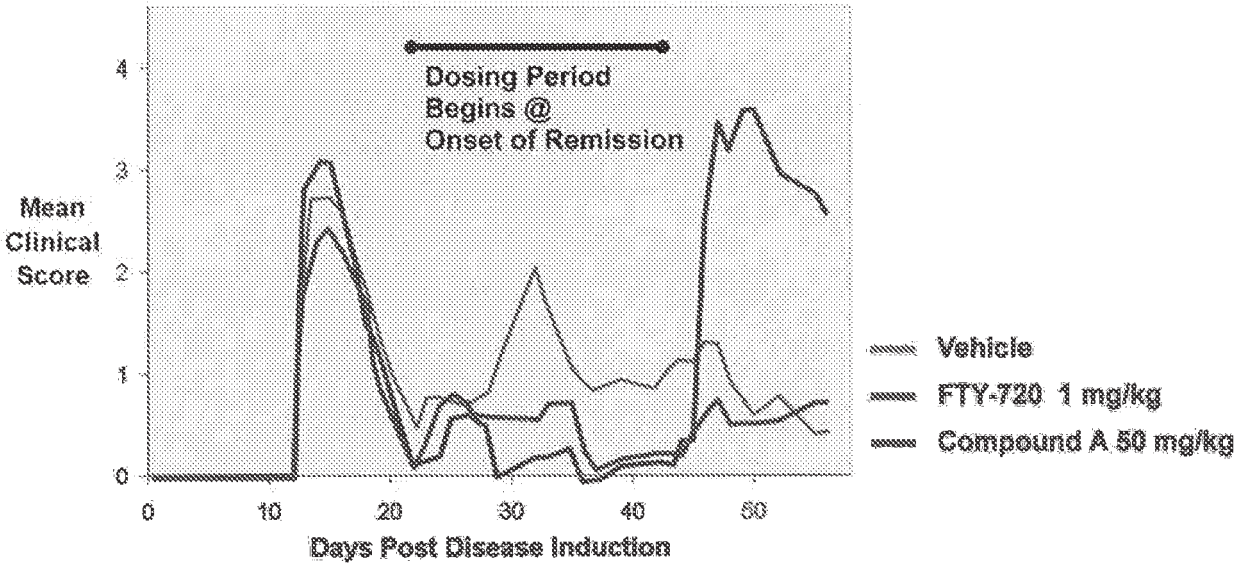

Dosing Period
Begins @
Onset of Remission
Mean
Clinical
Score
0
1
2
3
4
0
10
20
30
40
50
Days Post Disease Induction
Vehicle
FTY-720 1 mg/kg
Compound A 50 mg/kg

Figure 1.

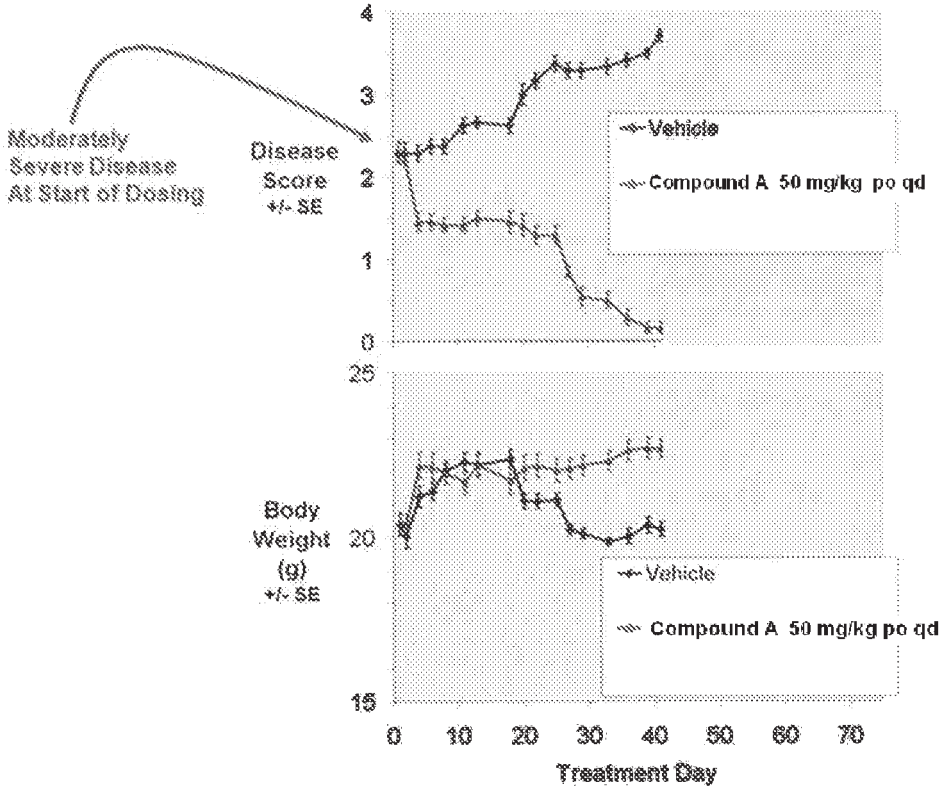

Moderately
Severe Disease
At Start of Dosing
Disease
Score
+/- SE
4
3
2
1
0
Vehicle
Compound A 50 mg/kg po qd
Body
Weight
(g)
+/- SE
25
20
15
Vehicle
Compound A 50 mg/kg po qd
0
10
20
30
40
50
60
70
Treatment Day

Figure 2A

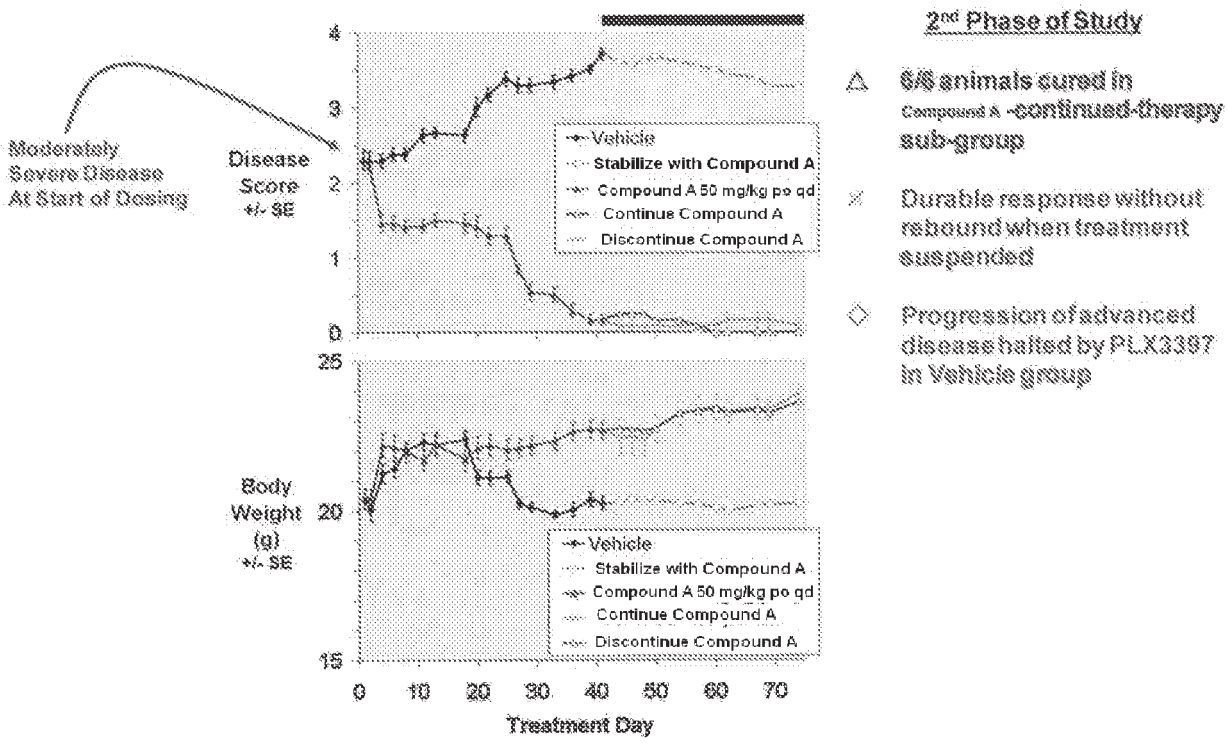

Moderately Severe Disease At Start of Dosing
Disease Score +/- SE
Vehicle
Stabilize with Compound A
Compound A 50 mg/kg po qd
Continue Compound A
Discontinue Compound A
Body Weight (g) +/- SE
Treatment Day
2nd Phase of Study
△ 6/6 animals cured in Compound A -continued-therapy sub-group
Durable response without rebound when treatment suspended
◇ Progression of advanced disease halted by PLX3397 in Vehicle group

Figure 2B

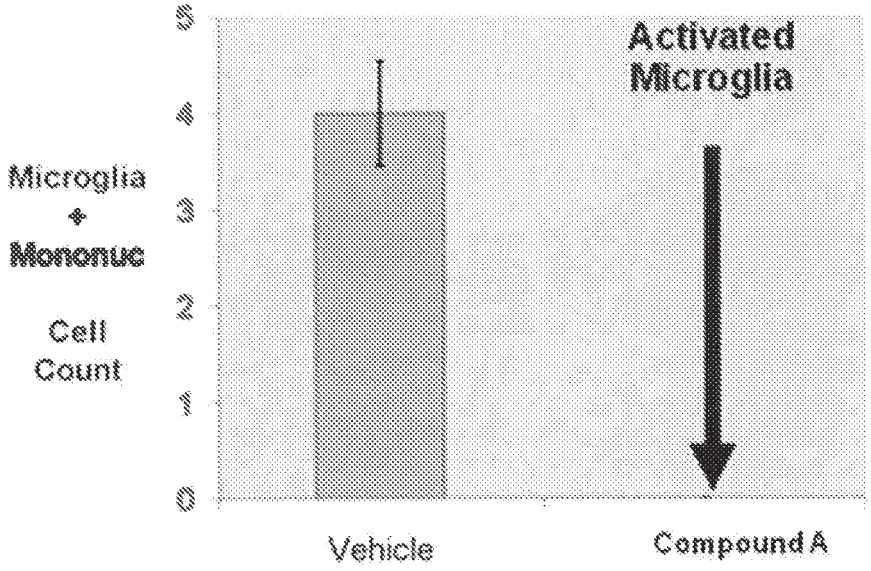

Activated Microglia
Microglia + Mononuc Cell Count
5
4
3
2
1
0
Vehicle
Compound A

Figure 2C

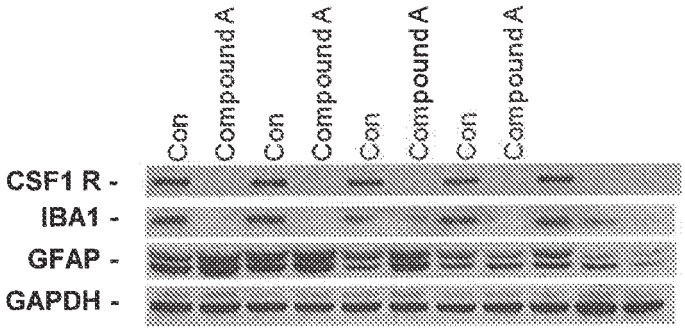


Figure 3A

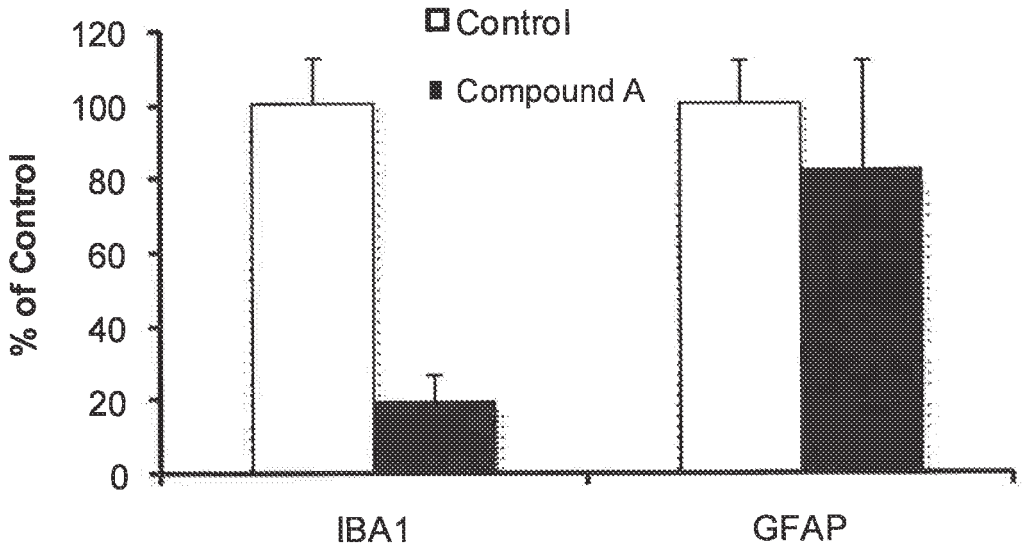


Figure 3B

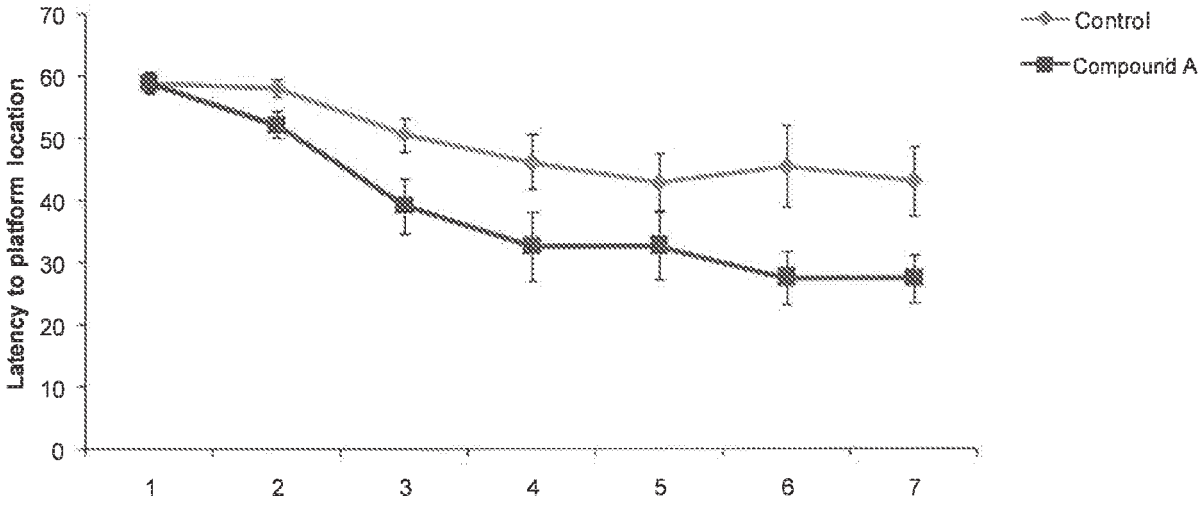


Figure 3C

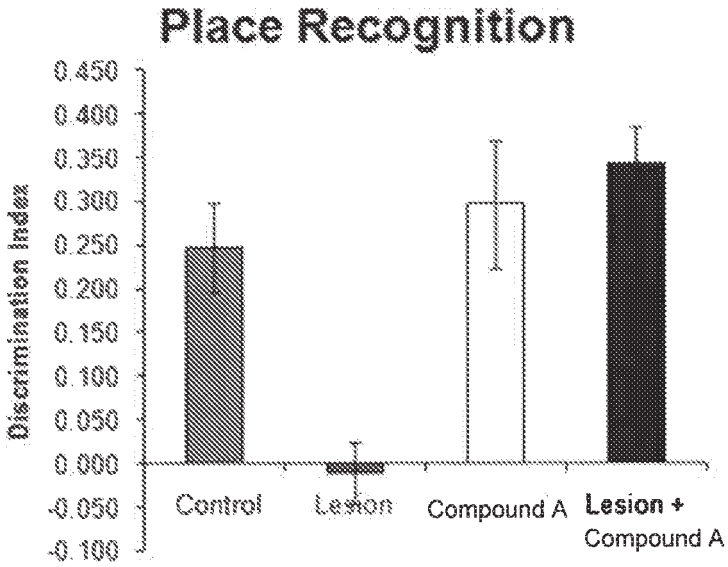


Figure 3D

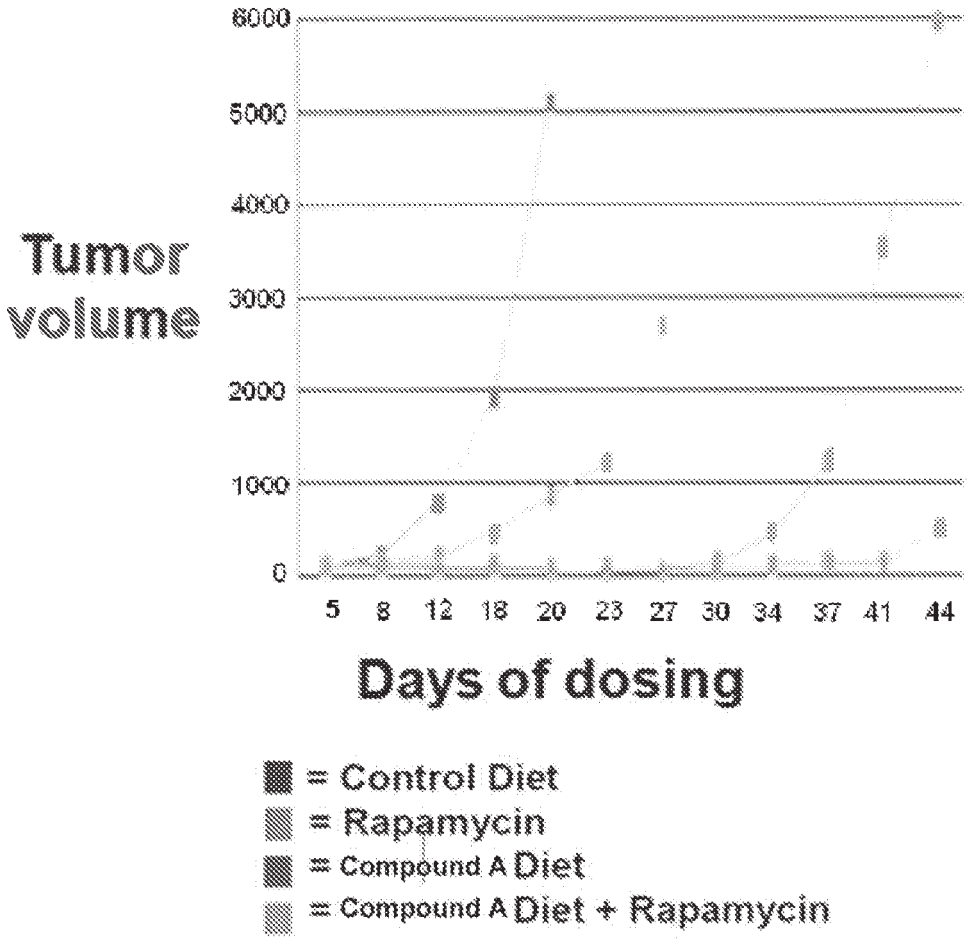

Tumor volume
6000
5000
4000
3000
2000
1000
0
5 8 12 18 20 23 27 30 34 37 41 44
Days of dosing
= Control Diet
= Rapamycin
= Compound A Diet
= Compound A Diet + Rapamycin

Figure 4

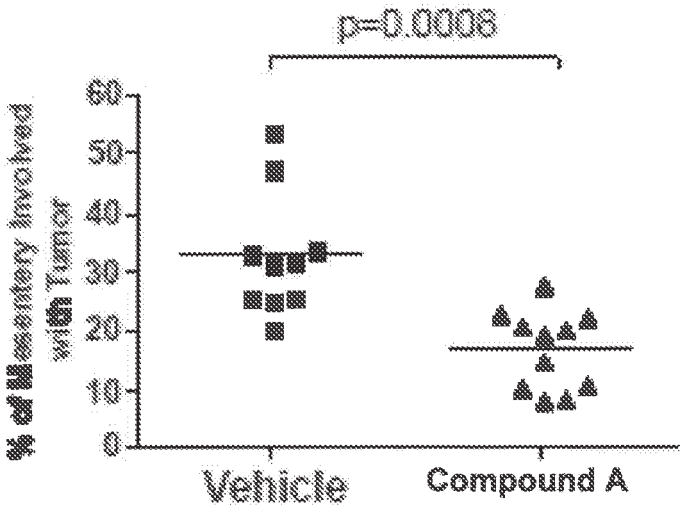

p=0.0008
% of Mesentery involved with Tumor
60
50
40
30
20
10
0
Vehicle
Compound A

Figure 5

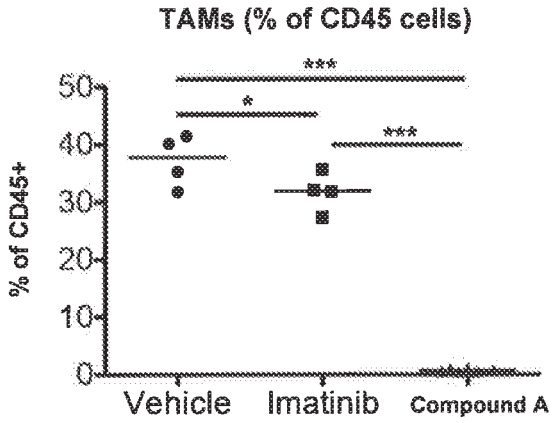


Figure 6A

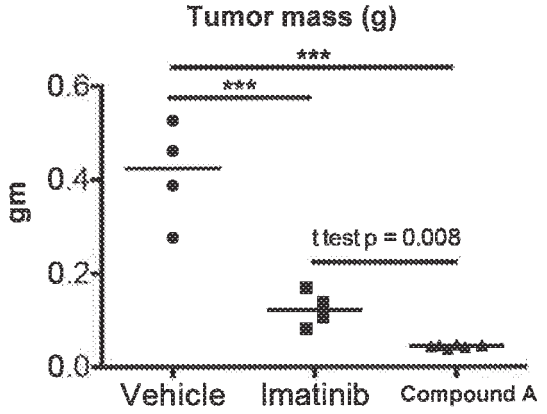


Figure 6B

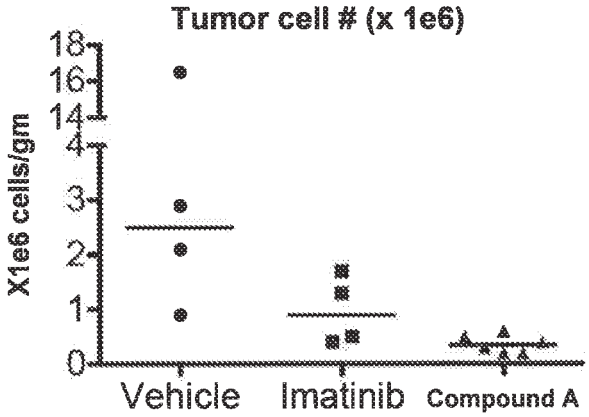


Figure 6C

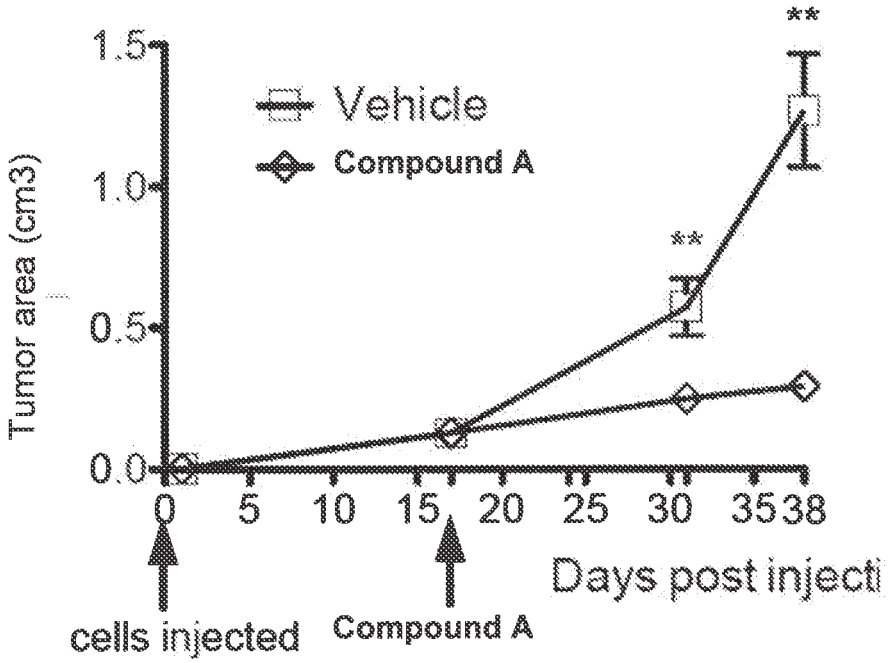


Figure 6D

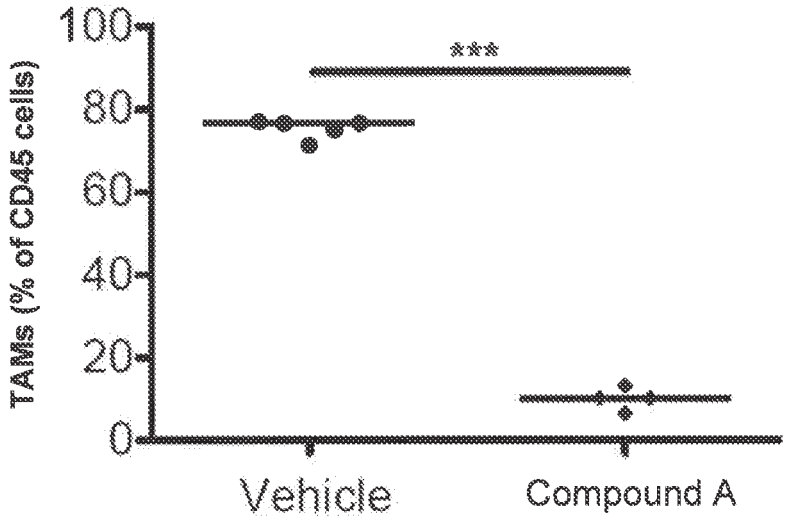


Figure 6E

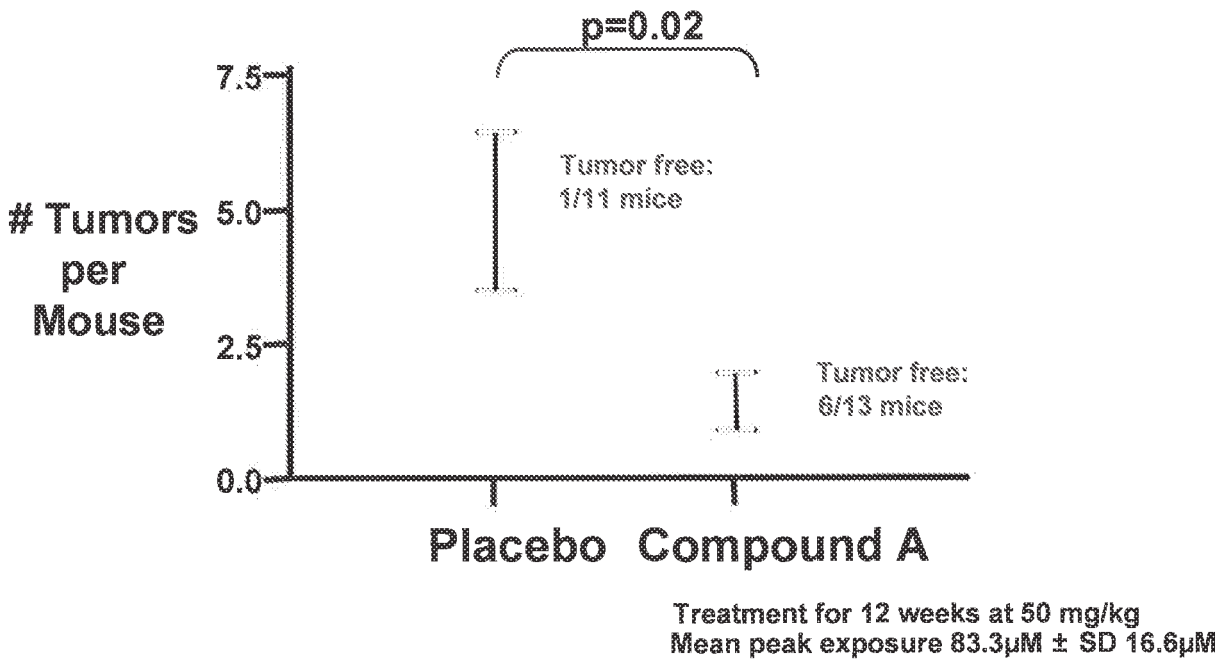


Figure 7A

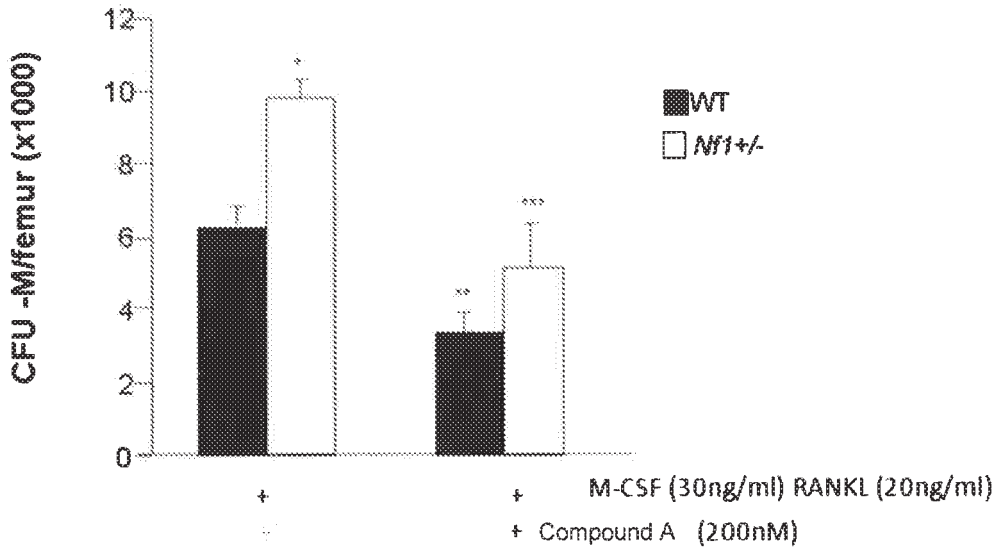


Figure 7B

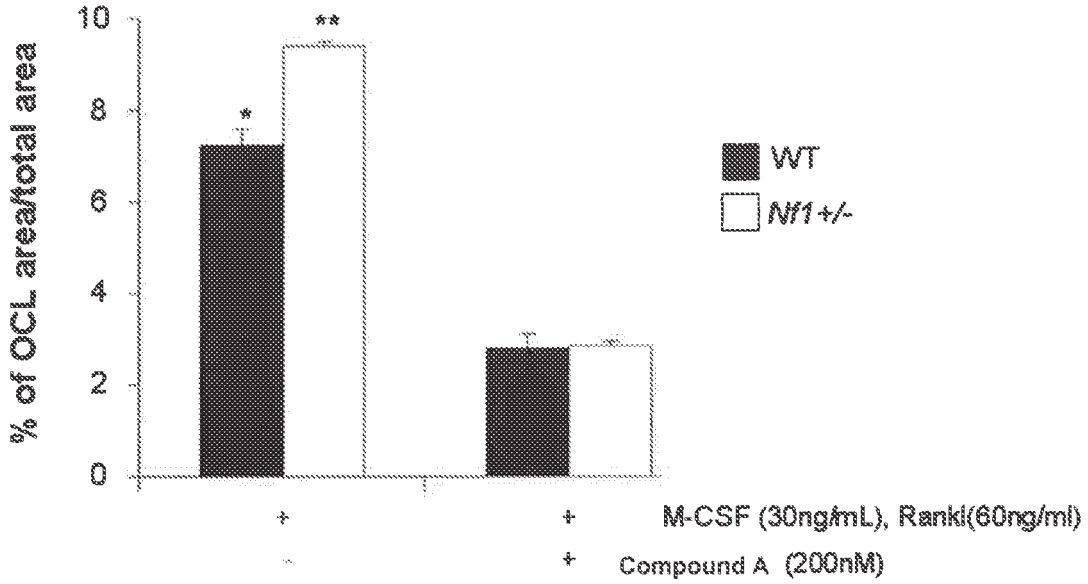


Figure 7C

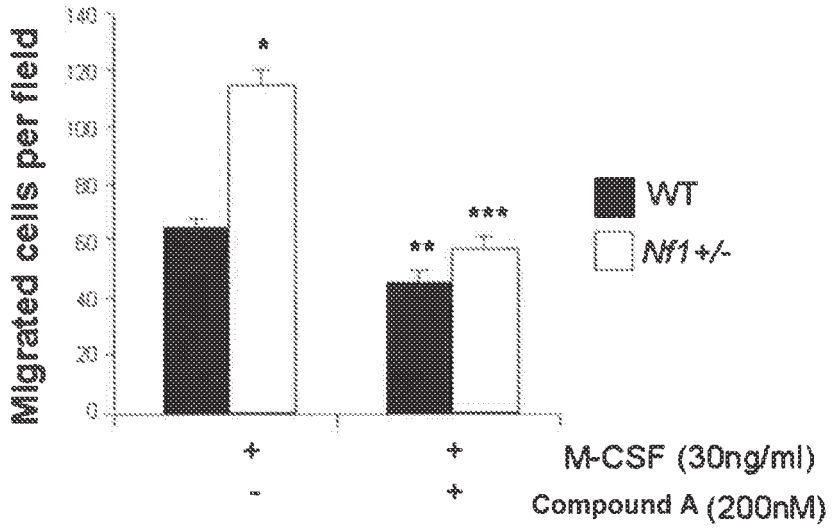


Figure 7D

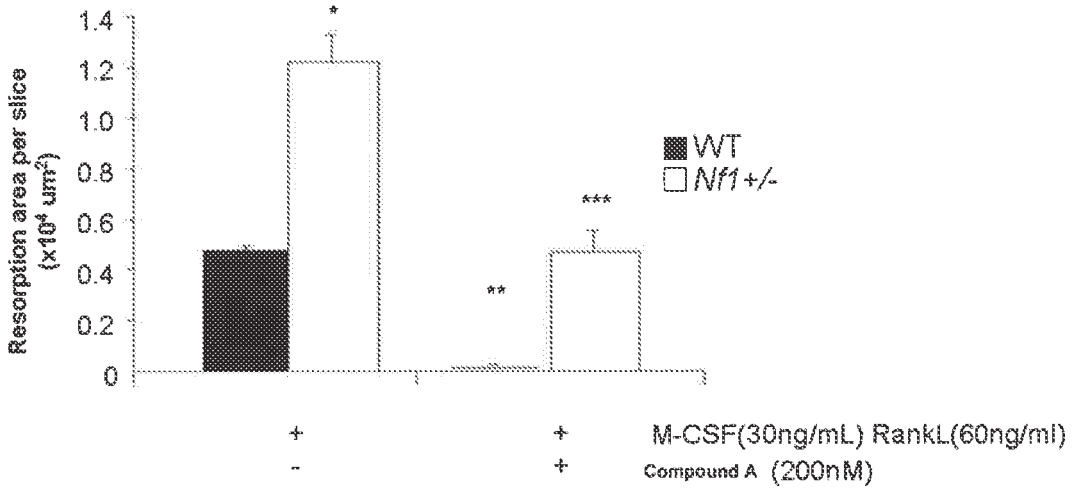


Figure 7E

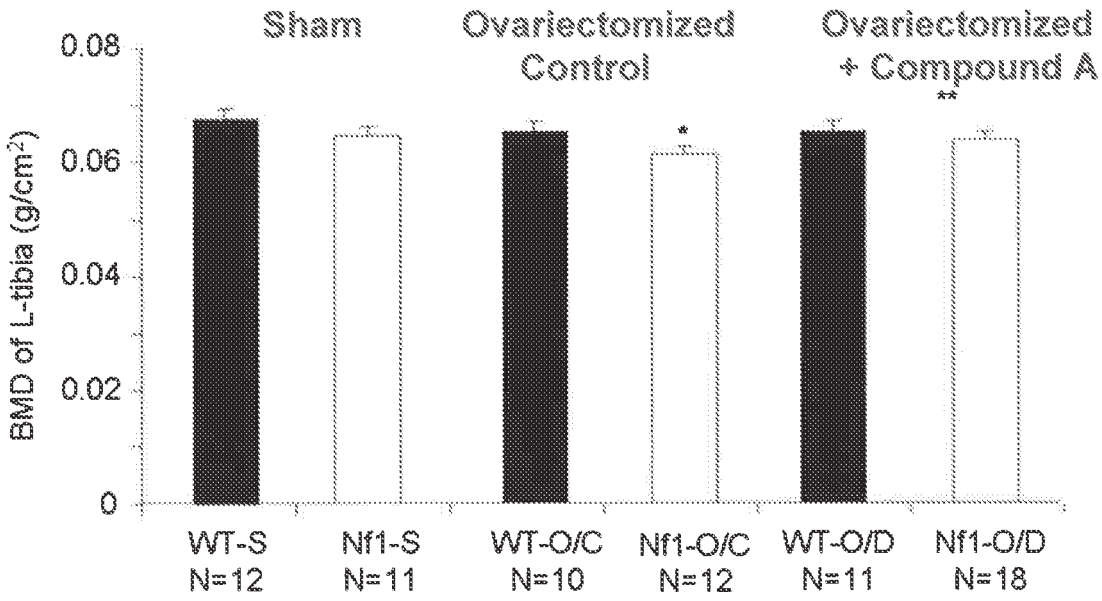


Figure 7F

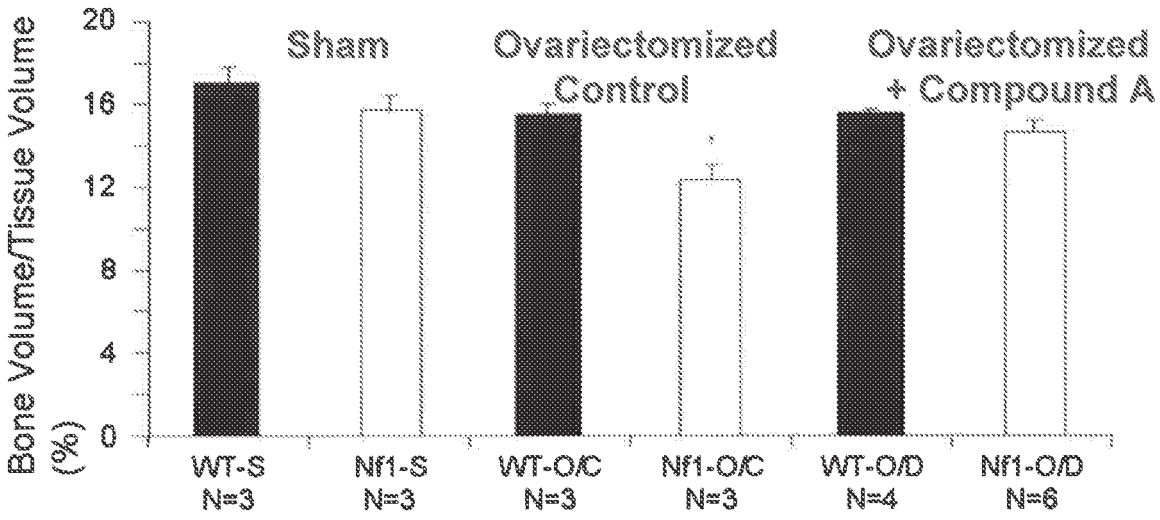

Bone Volume/Tissue Volume (%)
20
16
12
8
4
0
Sham
Ovariectomized Control
Ovariectomized + Compound A
WT-S N=3
Nf1-S N=3
WT-O/C N=3
Nf1-O/C N=3
WT-O/D N=4
Nf1-O/D N=6

Figure 7G

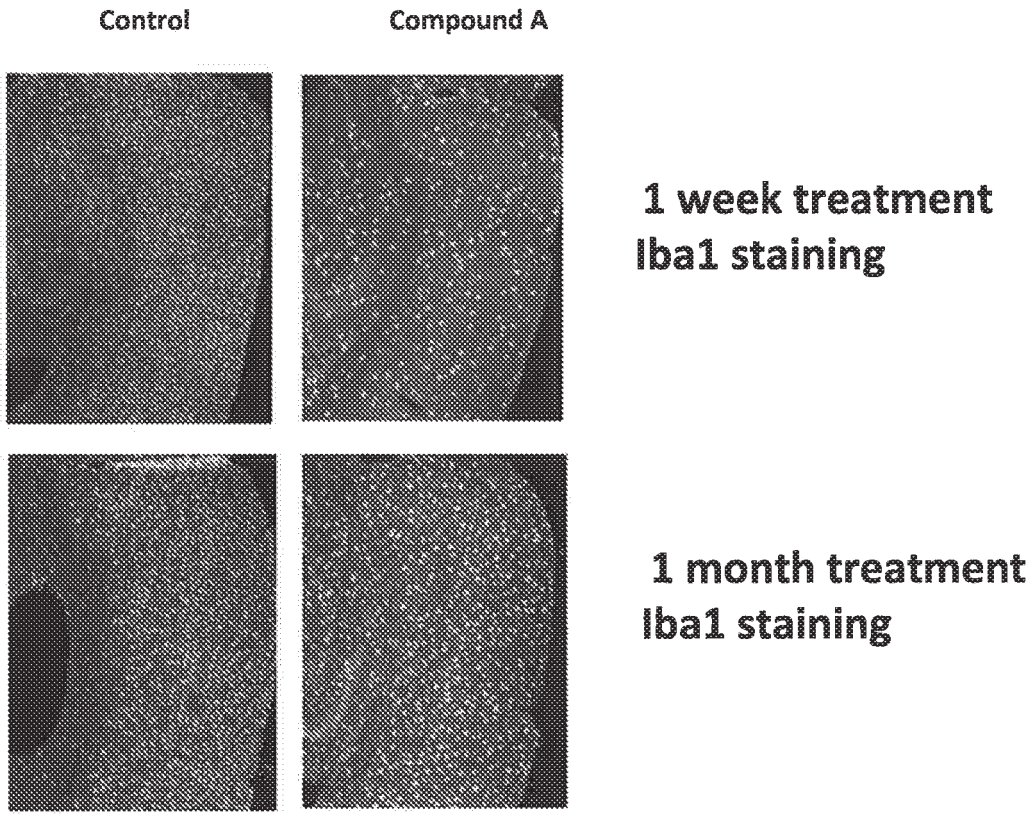

Control
Compound A
1 week treatment
Iba1 staining
1 month treatment
Iba1 staining

Figure 8

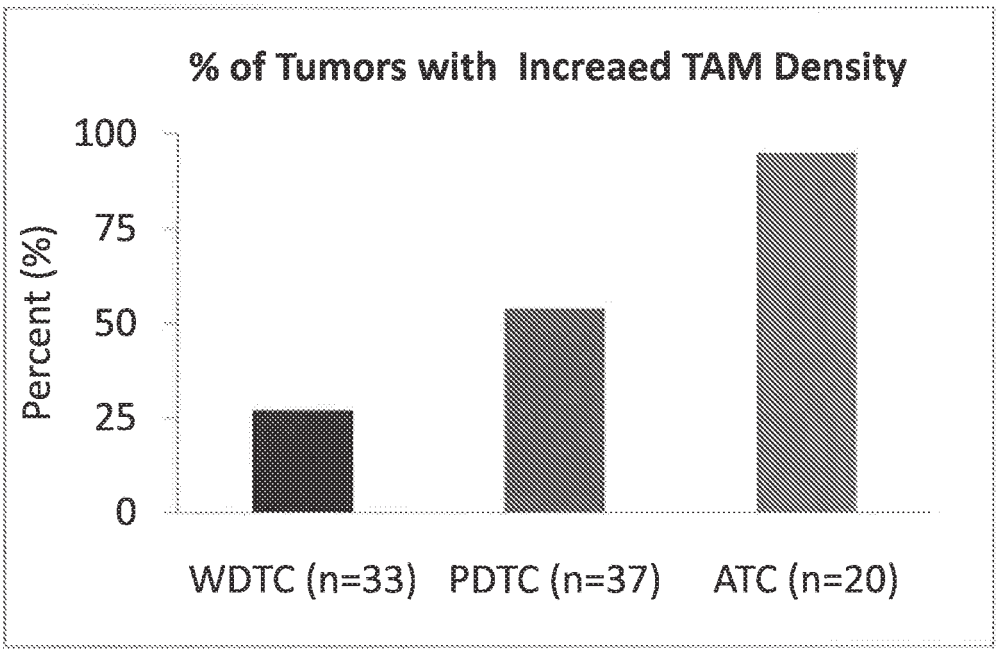


Figure 9A

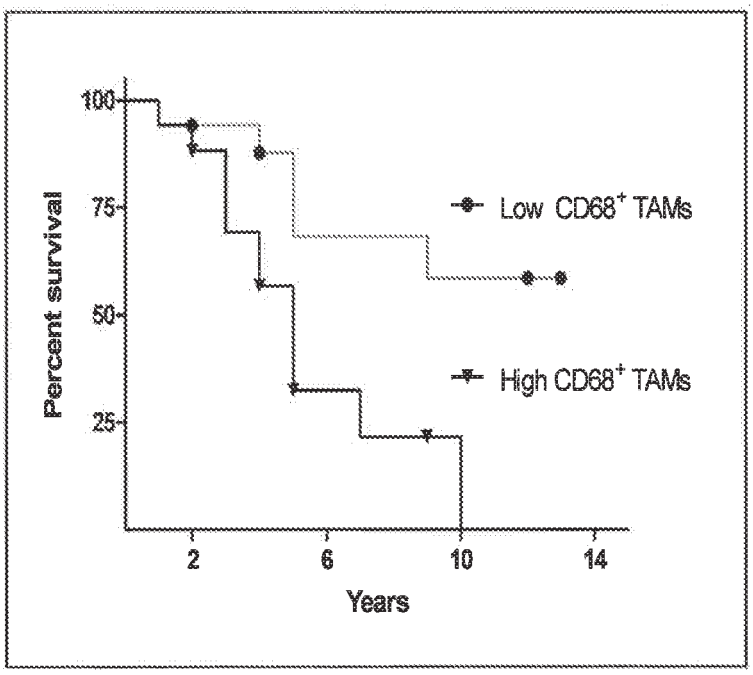


Figure 9B

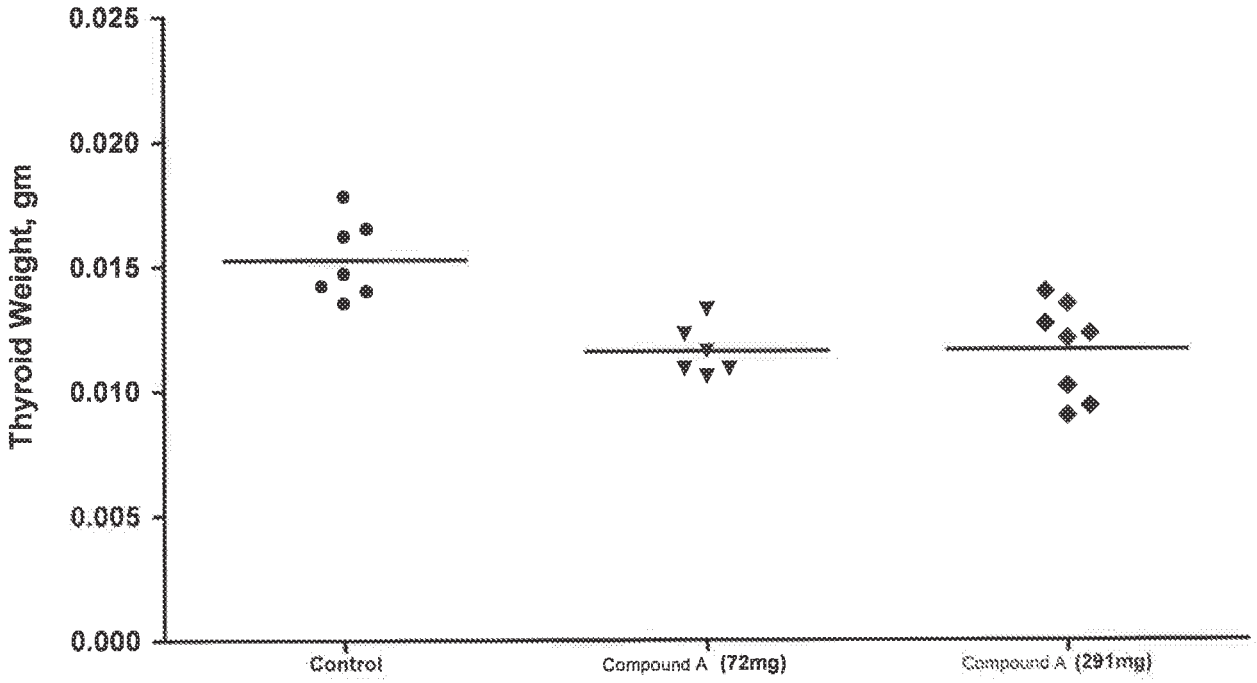

Thyroid Weight, gm
0.025
0.020
0.015
0.010
0.005
0.000
Control
Compound A (72mg)
Compound A (291mg)

Figure 9C

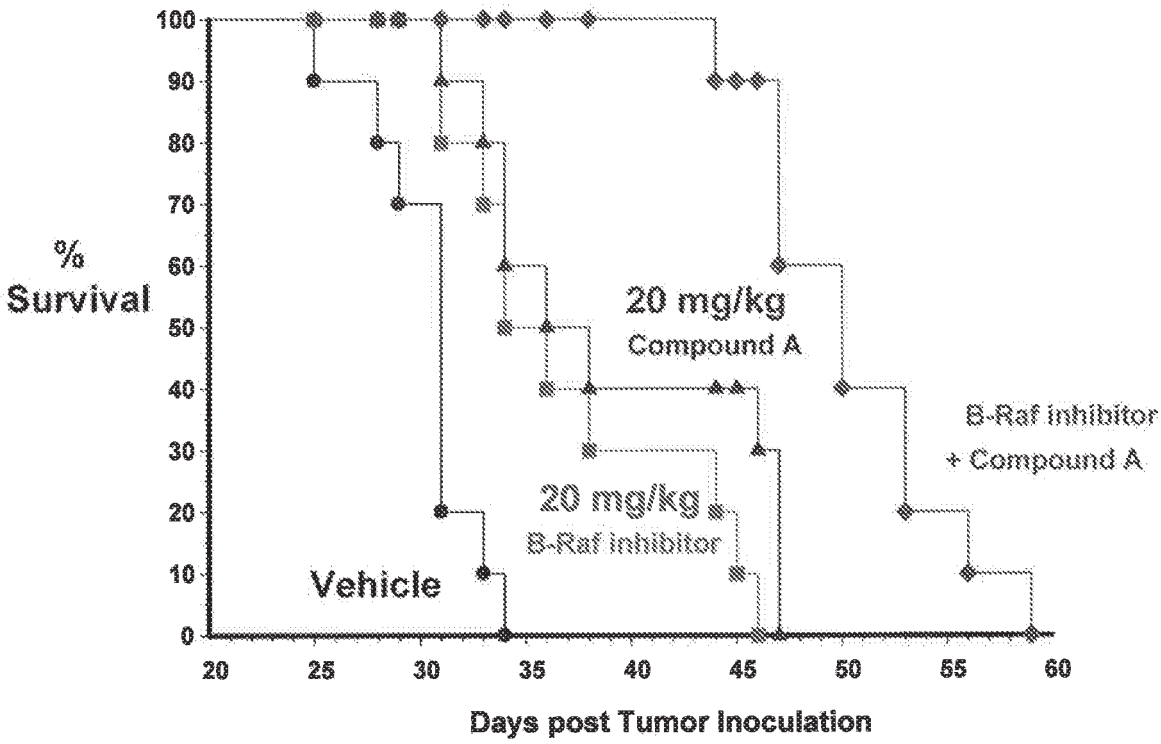

100
90
80
70
60
50
40
30
20
10
0
%
Survival
20 mg/kg
Compound A
B-Raf inhibitor
+ Compound A
20 mg/kg
B-Raf inhibitor
Vehicle
20
25
30
35
40
45
50
55
60
Days post Tumor Inoculation

Figure 10