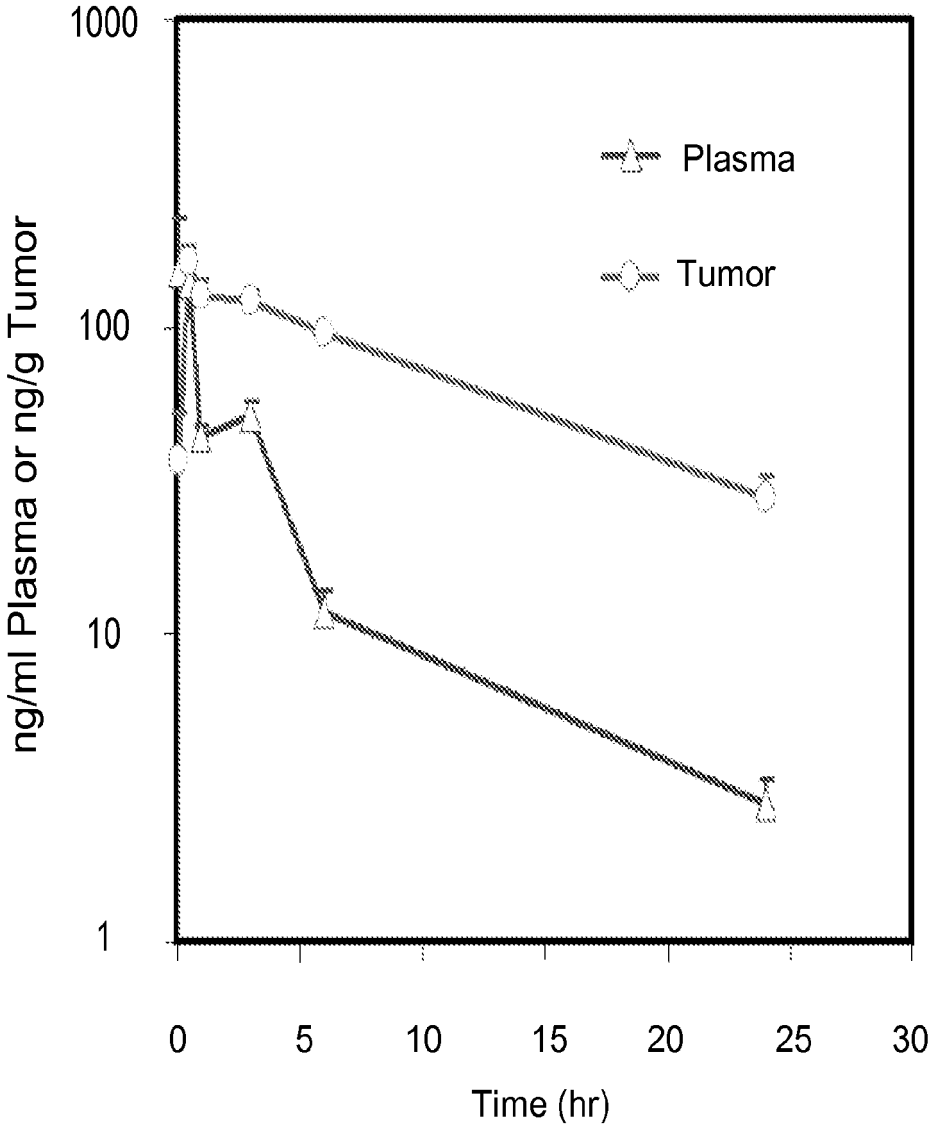

1000
100
10
1
ng/ml Plasma or ng/g Tumor
Plasma
Tumor
0
5
10
15
20
25
30
Time (hr)

FIG. 1

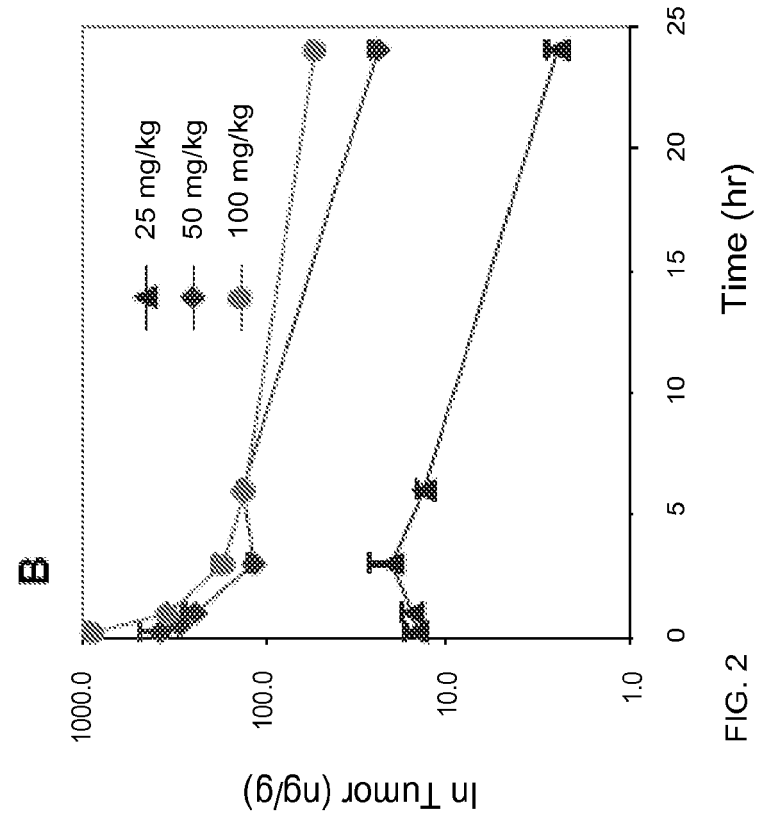
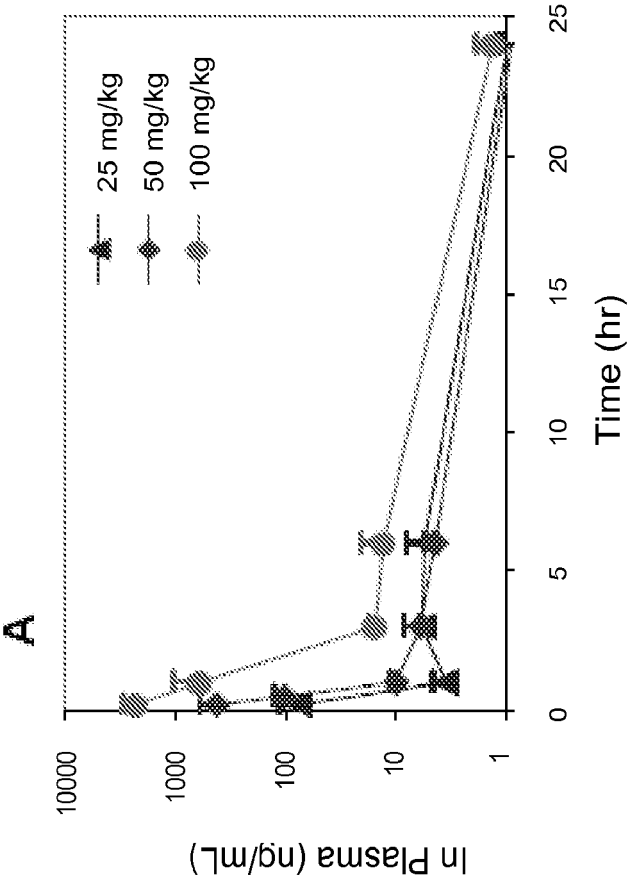

B
25 mg/kg
50 mg/kg
100 mg/kg
1000.0
100.0
10.0
1.0
0
5
10
15
20
25
Time (hr)
ln Tumor (ng/g)

FIG. 2


A
25 mg/kg
50 mg/kg
100 mg/kg
10000
1000
100
10
1
0
5
10
15
20
25
Time (hr)
ln Plasma (ng/mL)

C

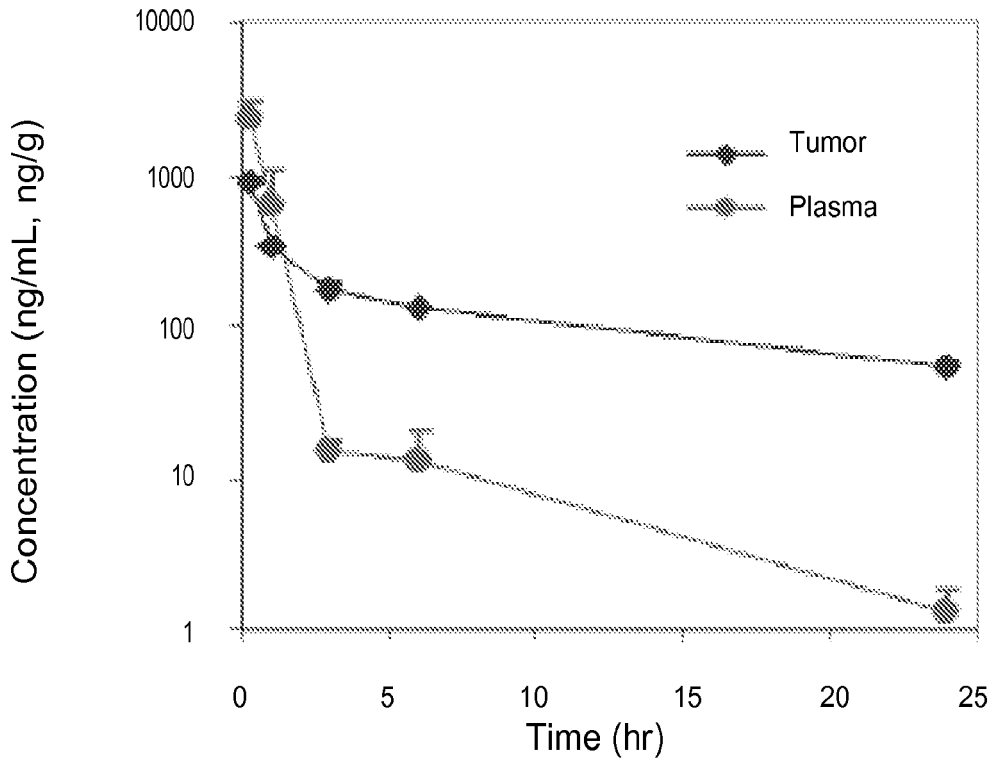

10000
1000
100
10
1
Concentration (ng/mL, ng/g)
Tumor
Plasma
0
5
10
15
20
25
Time (hr)

FIG. 2 cont...

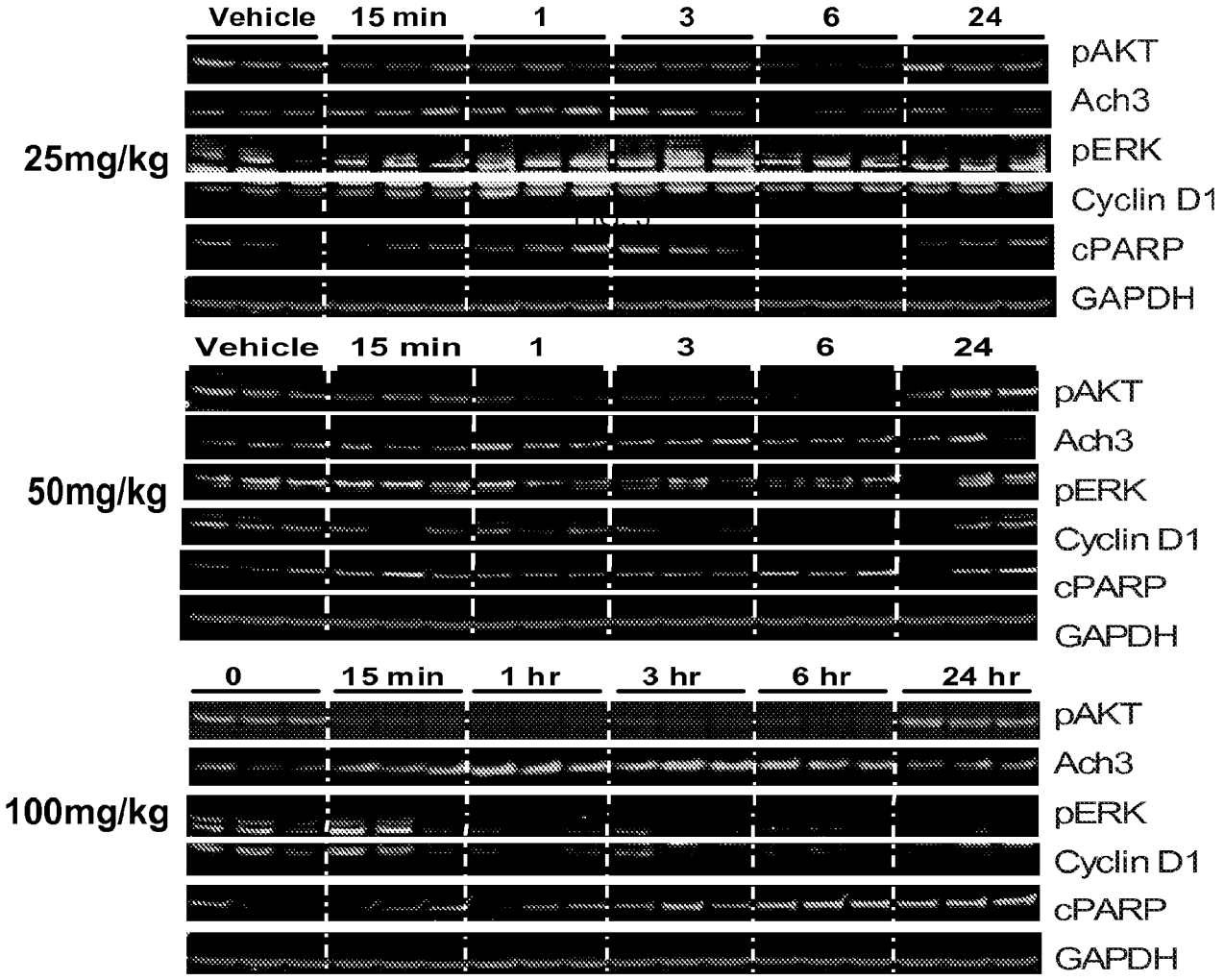

Vehicle
15 min
1
3
6
24
25mg/kg
pAKT
Ach3
pERK
Cyclin D1
cPARP
GAPDH
Vehicle
15 min
1
3
6
24
50mg/kg
pAKT
Ach3
pERK
Cyclin D1
cPARP
GAPDH
0
15 min
1 hr
3 hr
6 hr
24 hr
100mg/kg
pAKT
Ach3
pERK
Cyclin D1
cPARP
GAPDH

FIG. 3

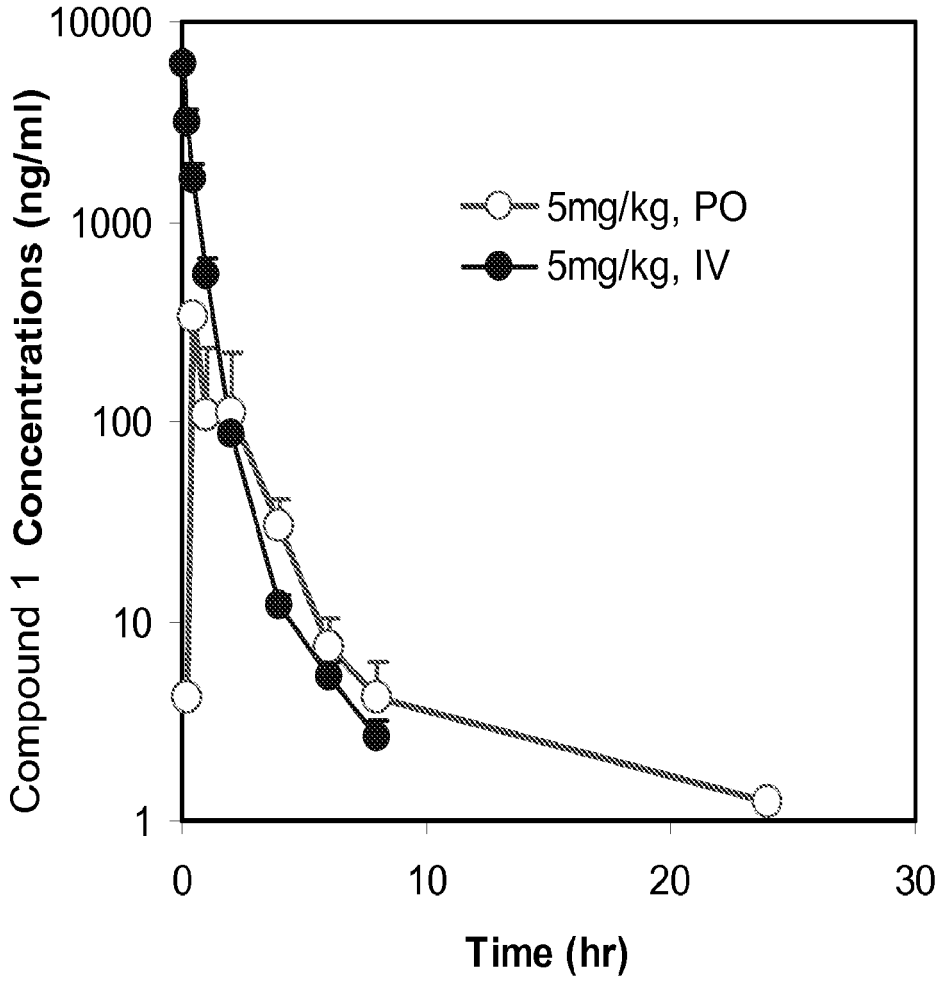

10000
1000
100
10
1
Compound 1 Concentrations (ng/ml)
5mg/kg, PO
5mg/kg, IV
0
10
20
30
Time (hr)

FIG. 4

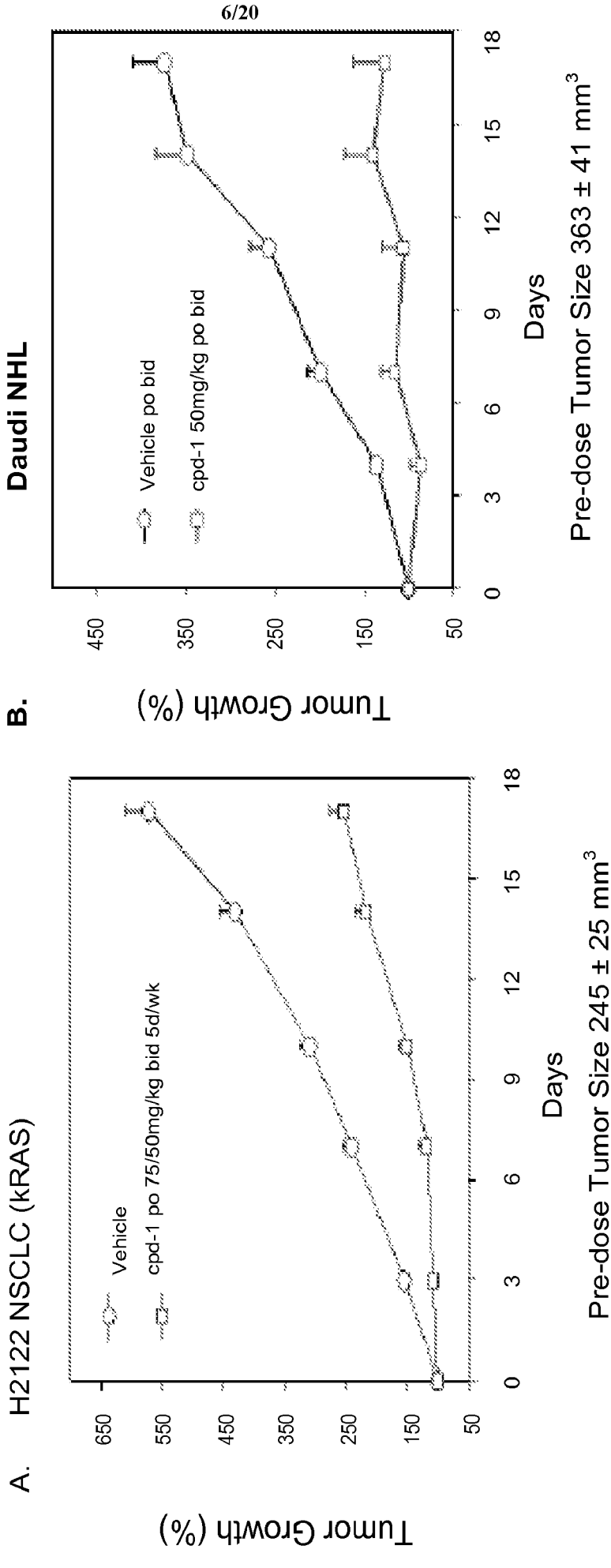

A.
H2122 NSCLC (kRAS)
Vehicle
cpd-1 po 75/50mg/kg bid 5d/wk
Tumor Growth (%)
650
550
450
350
250
150
50
0
3
6
9
12
15
18
Days
Pre-dose Tumor Size 245 ± 25 mm3
B.
Daudi NHL
Vehicle po bid
cpd-1 50mg/kg po bid
Tumor Growth (%)
450
350
250
150
50
0
3
6
9
12
15
18
Days
Pre-dose Tumor Size 363 ± 41 mm3

FIG. 5

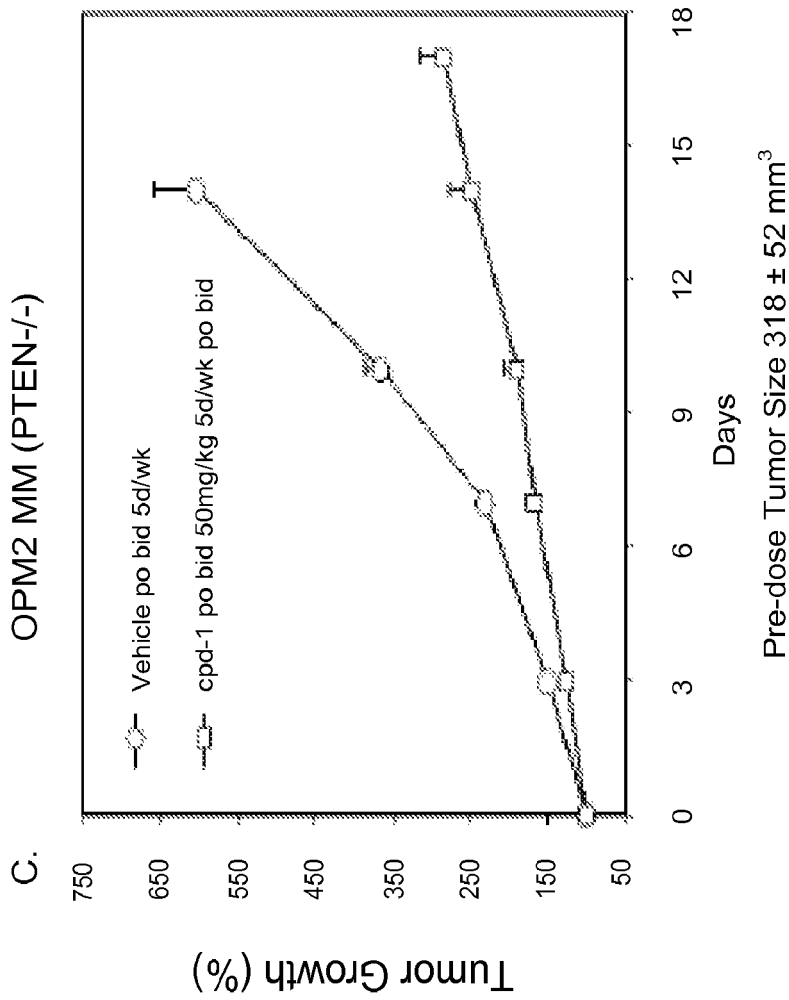

C.
OPM2 MM (PTEN-/-)
Vehicle po bid 5d/wk
cpd-1 po bid 50mg/kg 5d/wk po bid
Tumor Growth (%)
750
650
550
450
350
250
150
50
0
3
6
9
12
15
18
Days
Pre-dose Tumor Size 318 ± 52 mm3

FIG. 5 cont...

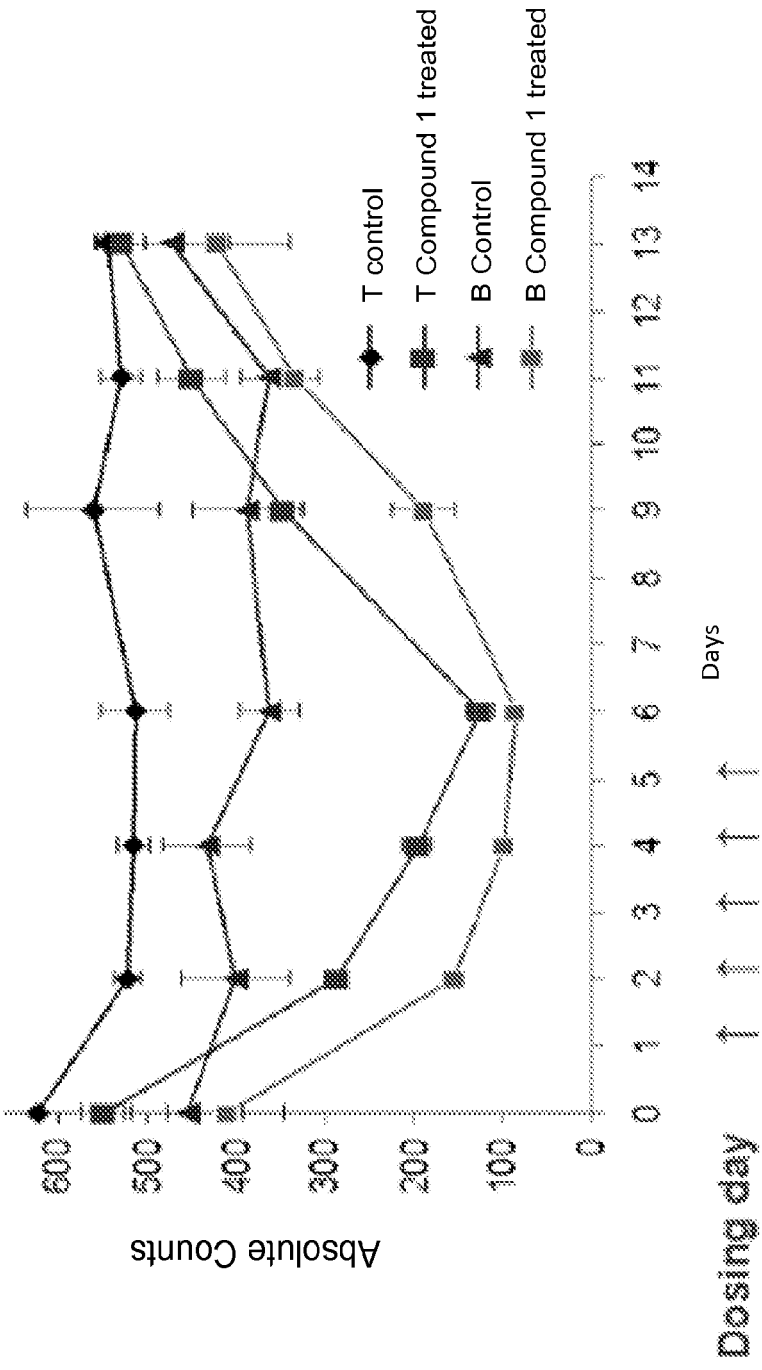

Absolute Counts
600
500
400
300
200
100
0
T control
T Compound 1 treated
B Control
B Compound 1 treated
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
Days
Dosing day

FIG. 6

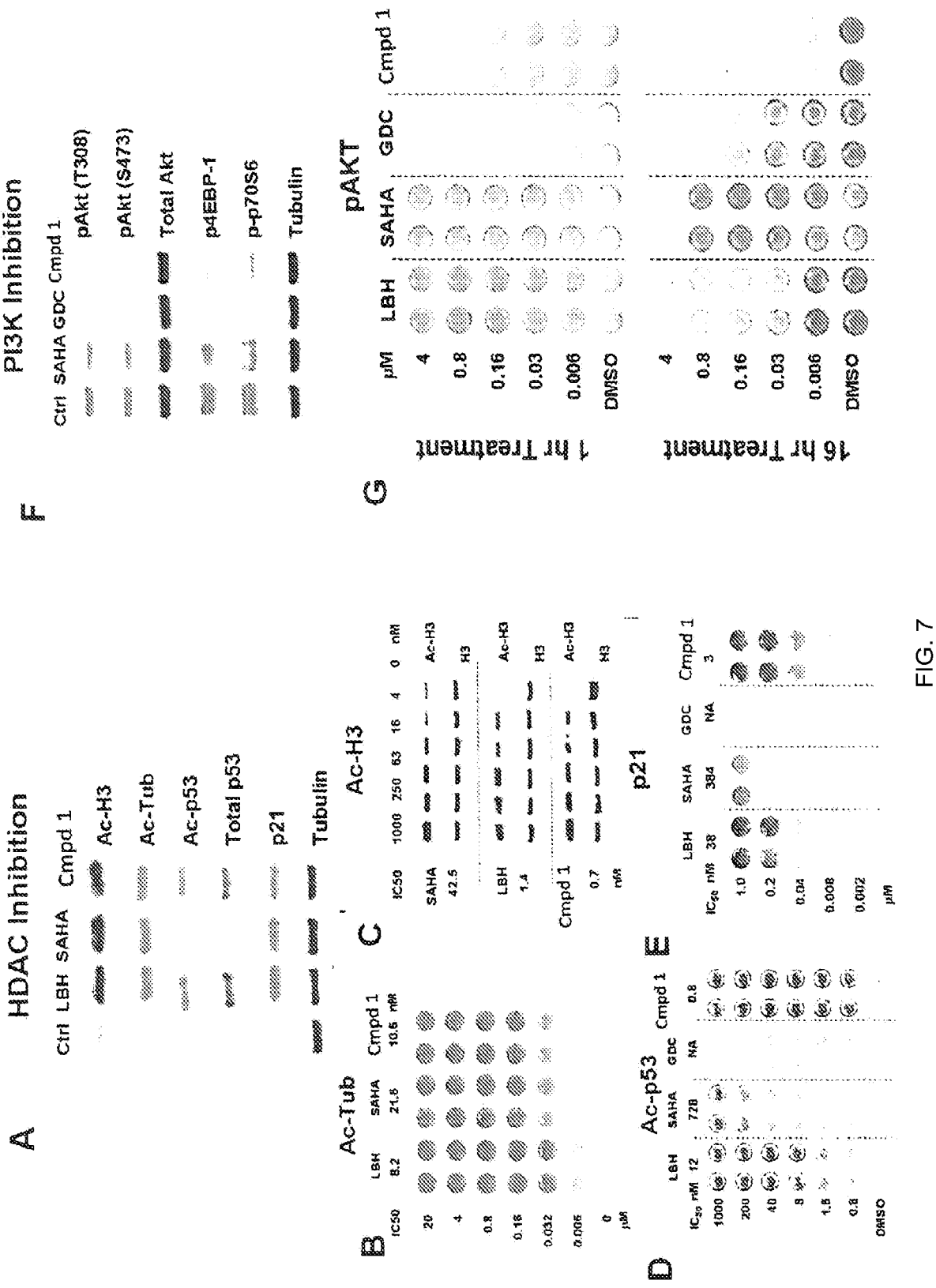

A
HDAC Inhibition
Ctrl LBH SAHA Cmpd 1
Ac-H3
Ac-Tub
Ac-p53
Total p53
p21
Tubulin
B
Ac-Tub
C
Ac-H3
D
Ac-p53
E
p21
F
PI3K Inhibition
Ctrl SAHA GDC Cmpd 1
pAkt (T308)
pAkt (S473)
Total Akt
p4EBP-1
p-p70S6
Tubulin
G
pAKT
1 hr Treatment
16 hr Treatment

FIG. 7

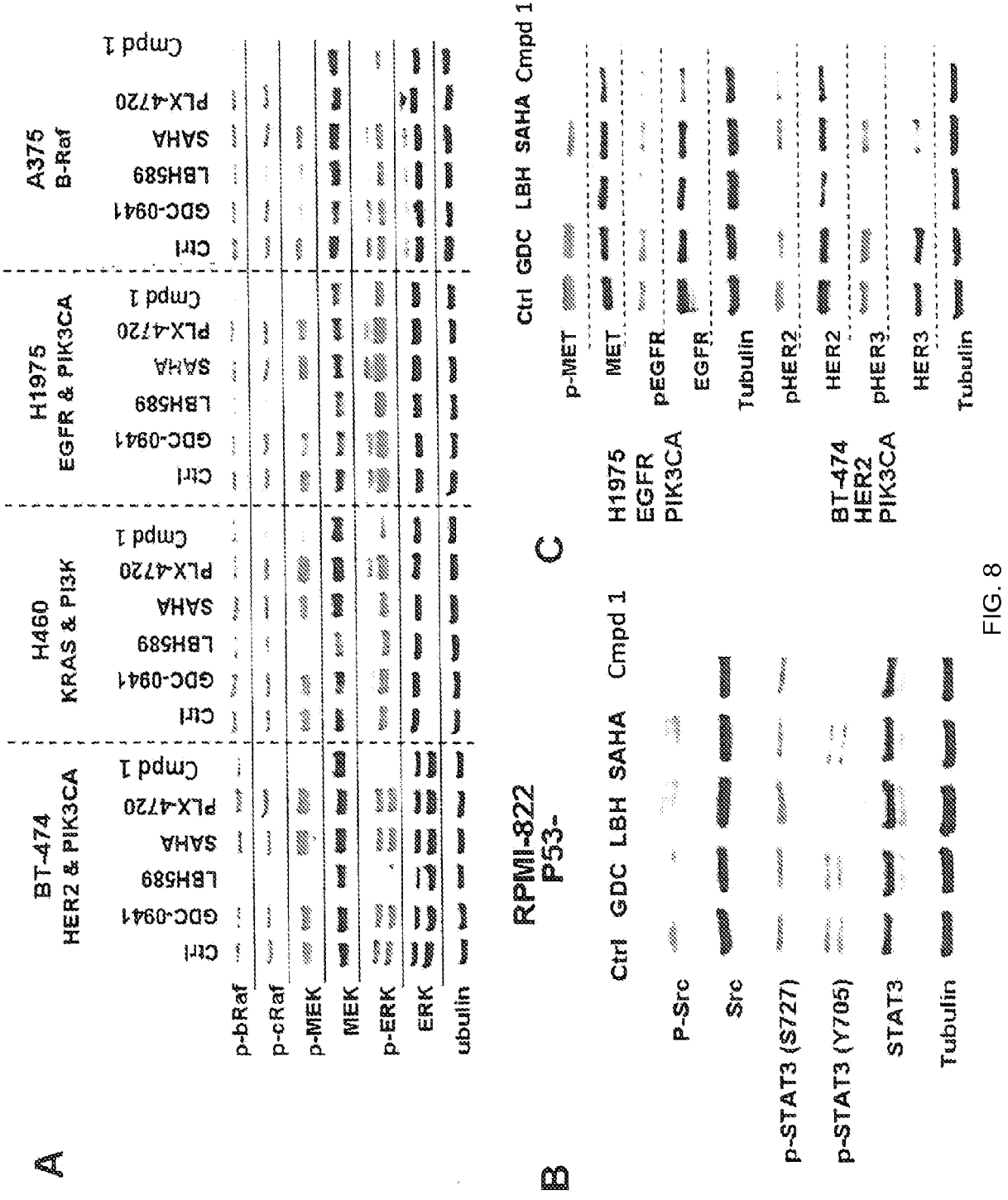

A
BT-474
HER2 & PIK3CA
H460
KRAS & PI3K
H1975
EGFR & PIK3CA
A375
B-Raf
Ctrl
GDC-0941
LBH589
SAHA
PLX-4720
Cmpd 1
p-bRaf
p-cRaf
p-MEK
MEK
p-ERK
ERK
ubulin
B
RPMI-822
P53-
Ctrl GDC LBH SAHA Cmpd 1
P-Src
Src
p-STAT3 (S727)
p-STAT3 (Y705)
STAT3
Tubulin
C
H1975
EGFR
PIK3CA
Ctrl GDC LBH SAHA Cmpd 1
p-MET
MET
pEGFR
EGFR
Tubulin
pHER2
HER2
BT-474
HER2
PIK3CA
pHER3
HER3
Tubulin

FIG. 8

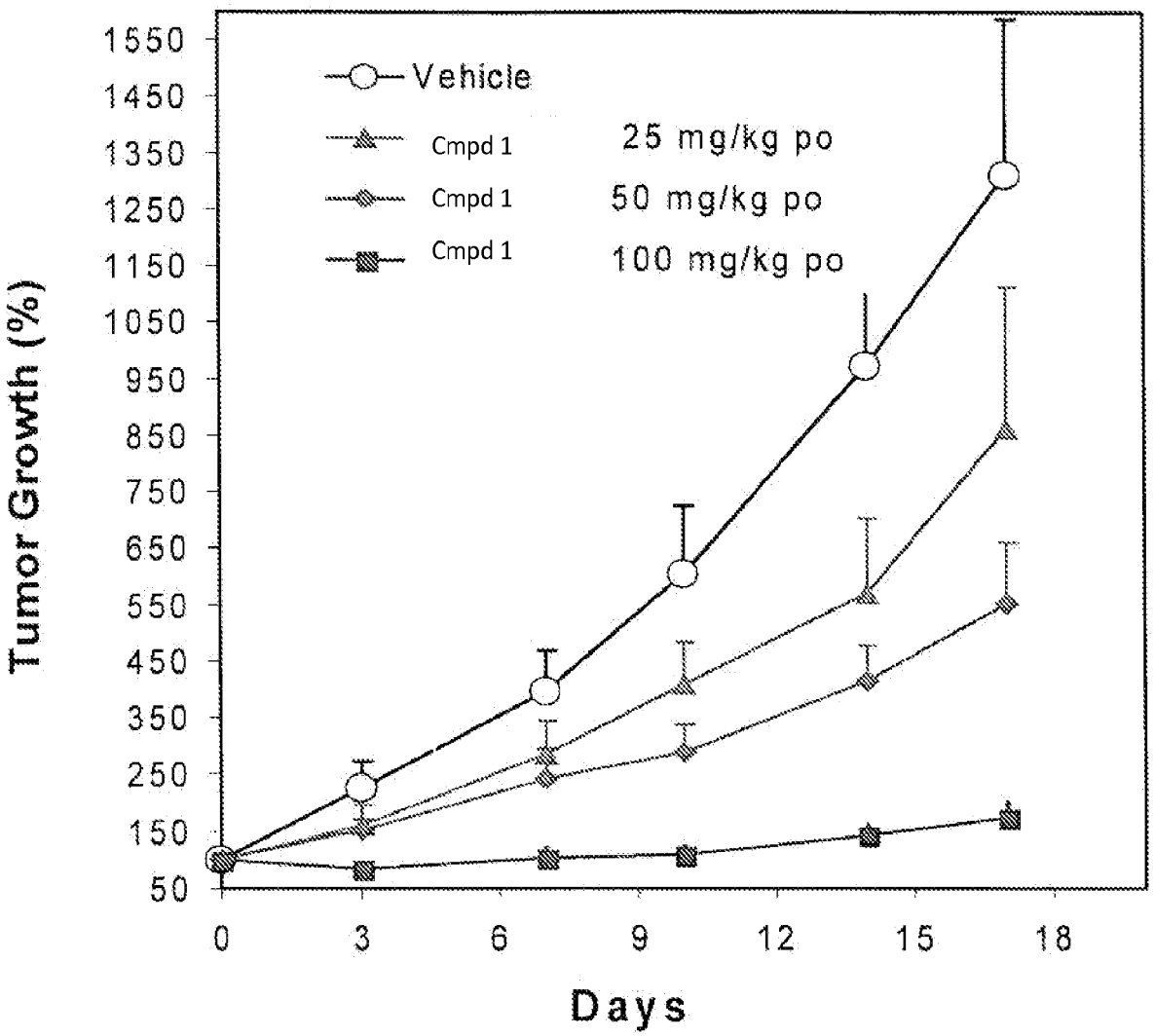

Tumor Growth (%)
1550
1450
1350
1250
1150
1050
950
850
750
650
550
450
350
250
150
50
Vehicle
Cmpd 1
25 mg/kg po
Cmpd 1
50 mg/kg po
Cmpd 1
100 mg/kg po
0
3
6
9
12
15
18
Days

FIG. 9

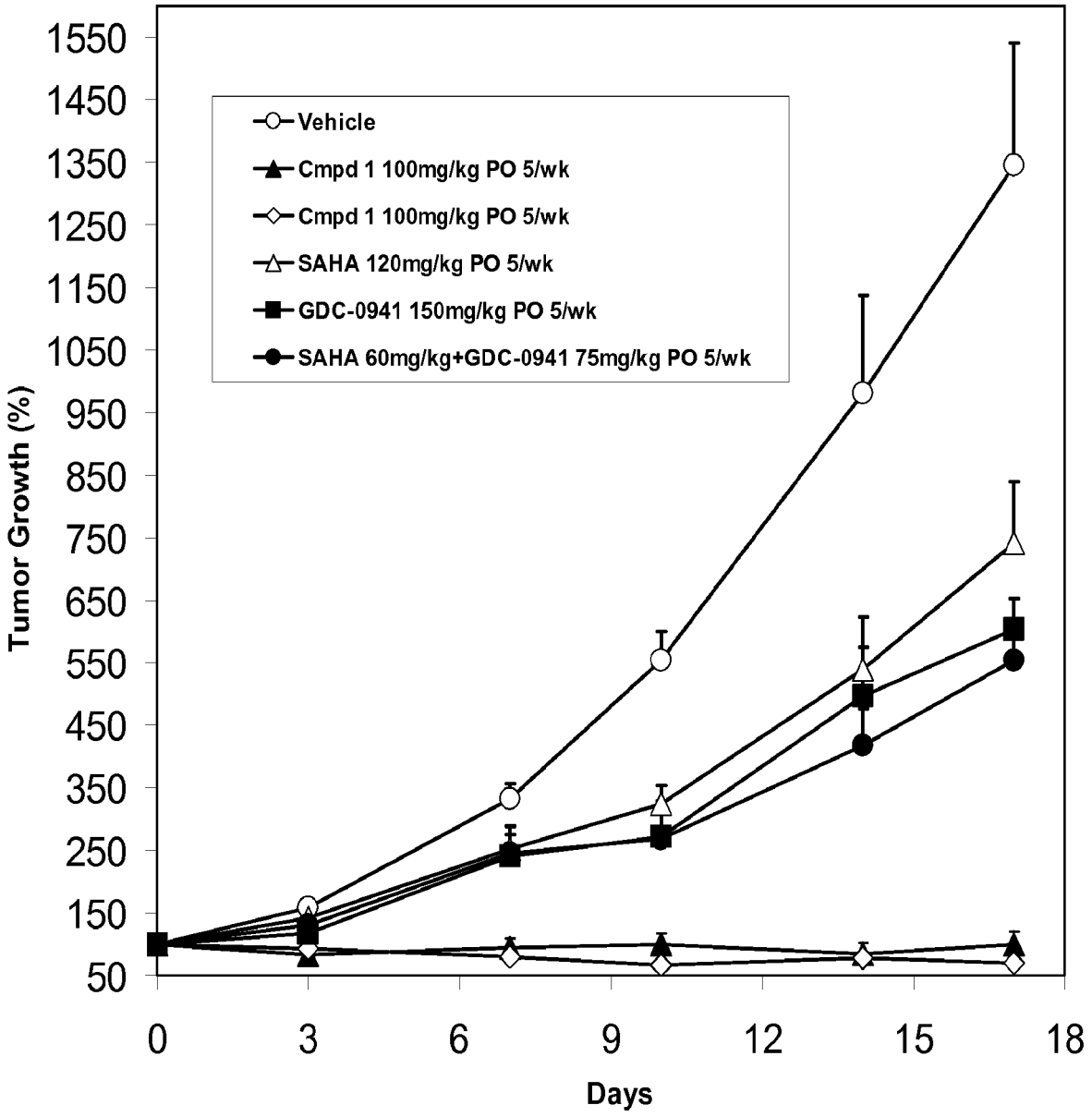

Vehicle
Cmpd 1 100mg/kg PO 5/wk
Cmpd 1 100mg/kg PO 5/wk
SAHA 120mg/kg PO 5/wk
GDC-0941 150mg/kg PO 5/wk
SAHA 60mg/kg+GDC-0941 75mg/kg PO 5/wk
Tumor Growth (%)
1550
1450
1350
1250
1150
1050
950
850
750
650
550
450
350
250
150
50
0
3
6
9
12
15
18
Days

FIG. 10

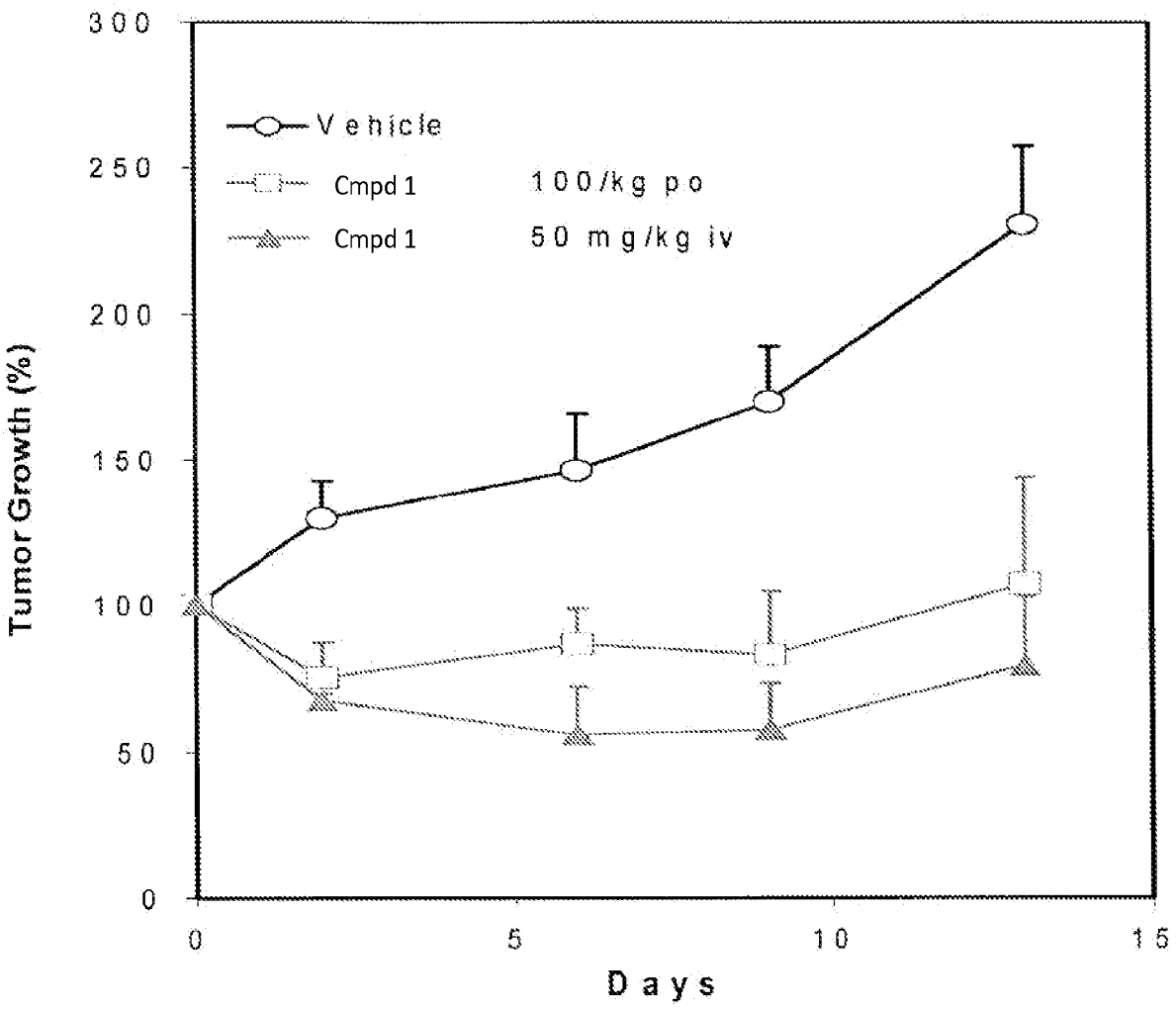

300
250
200
150
100
50
0
Tumor Growth (%)
Vehicle
Cmpd 1 100/kg po
Cmpd 1 50 mg/kg iv
0
5
10
15
Days

FIG. 11

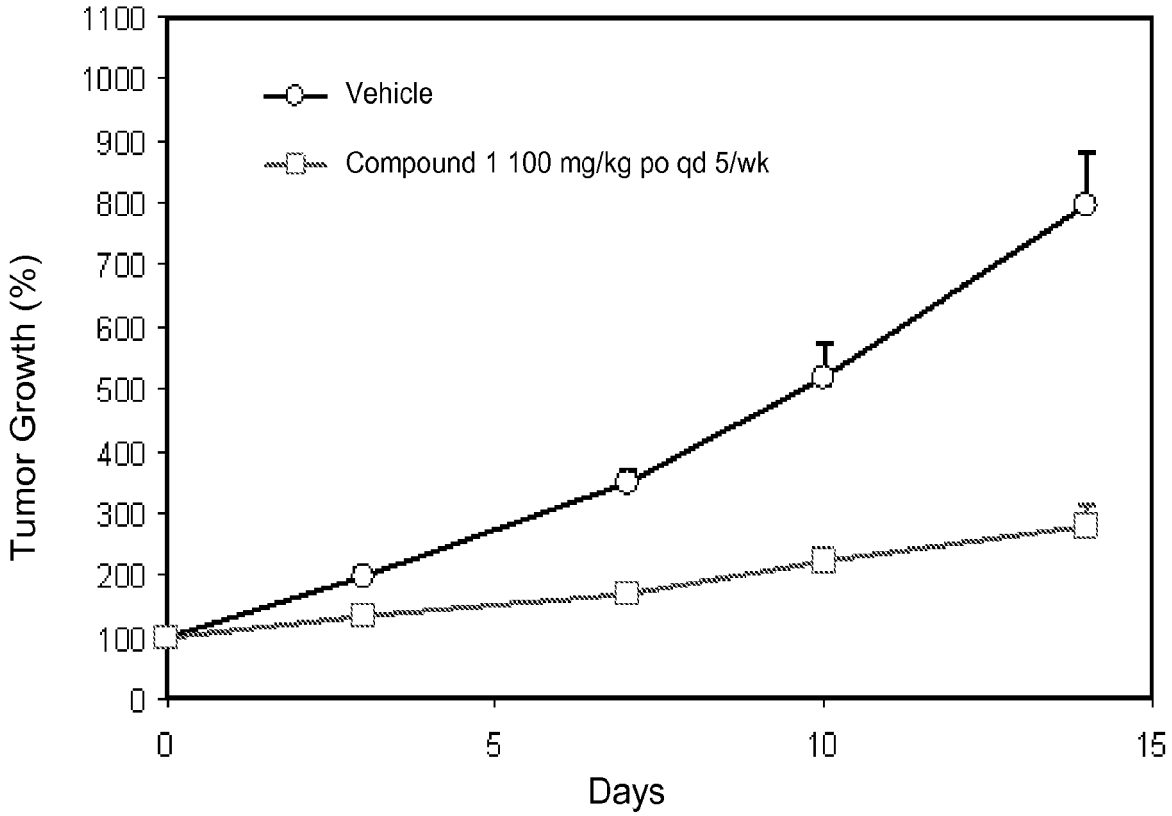

1100
1000
900
800
700
600
500
400
300
200
100
0
Tumor Growth (%)
Vehicle
Compound 1 100 mg/kg po qd 5/wk
0
5
10
15
Days

FIG. 12

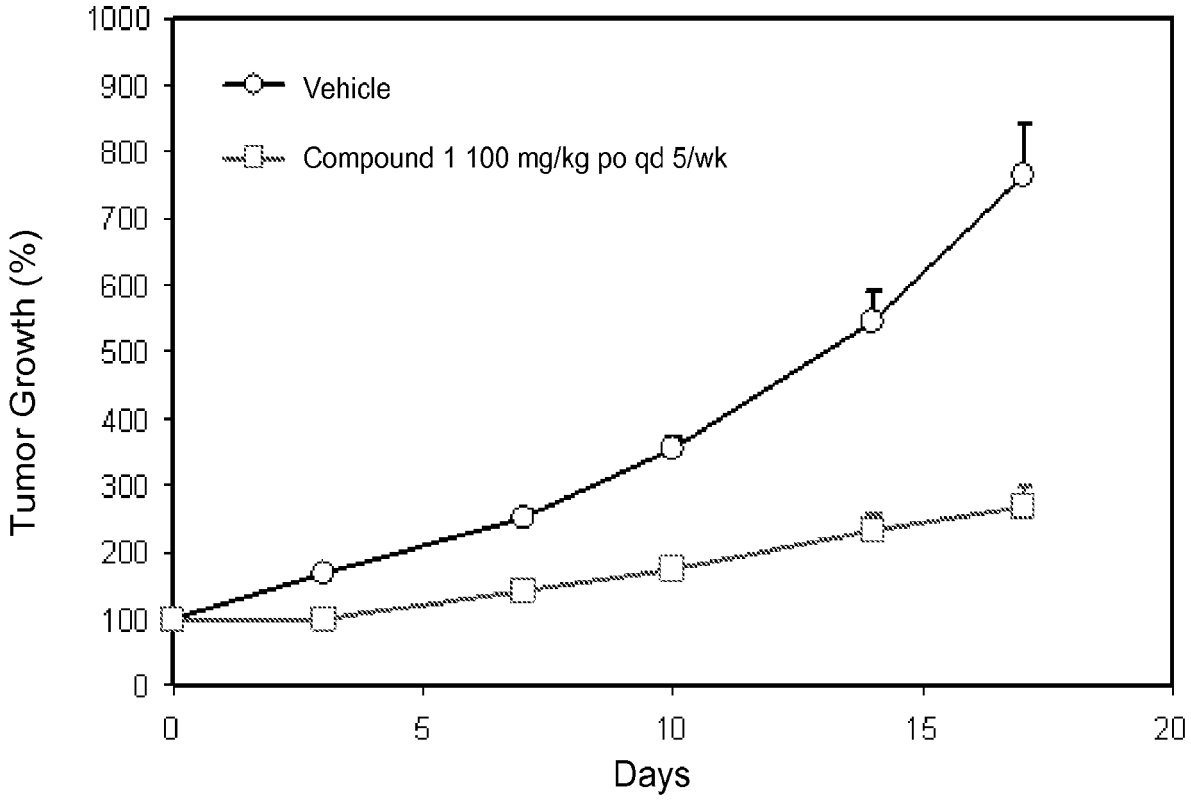

1000
900
800
700
600
500
400
300
200
100
0
Tumor Growth (%)
Vehicle
Compound 1 100 mg/kg po qd 5/wk
0
5
10
15
20
Days

FIG. 13

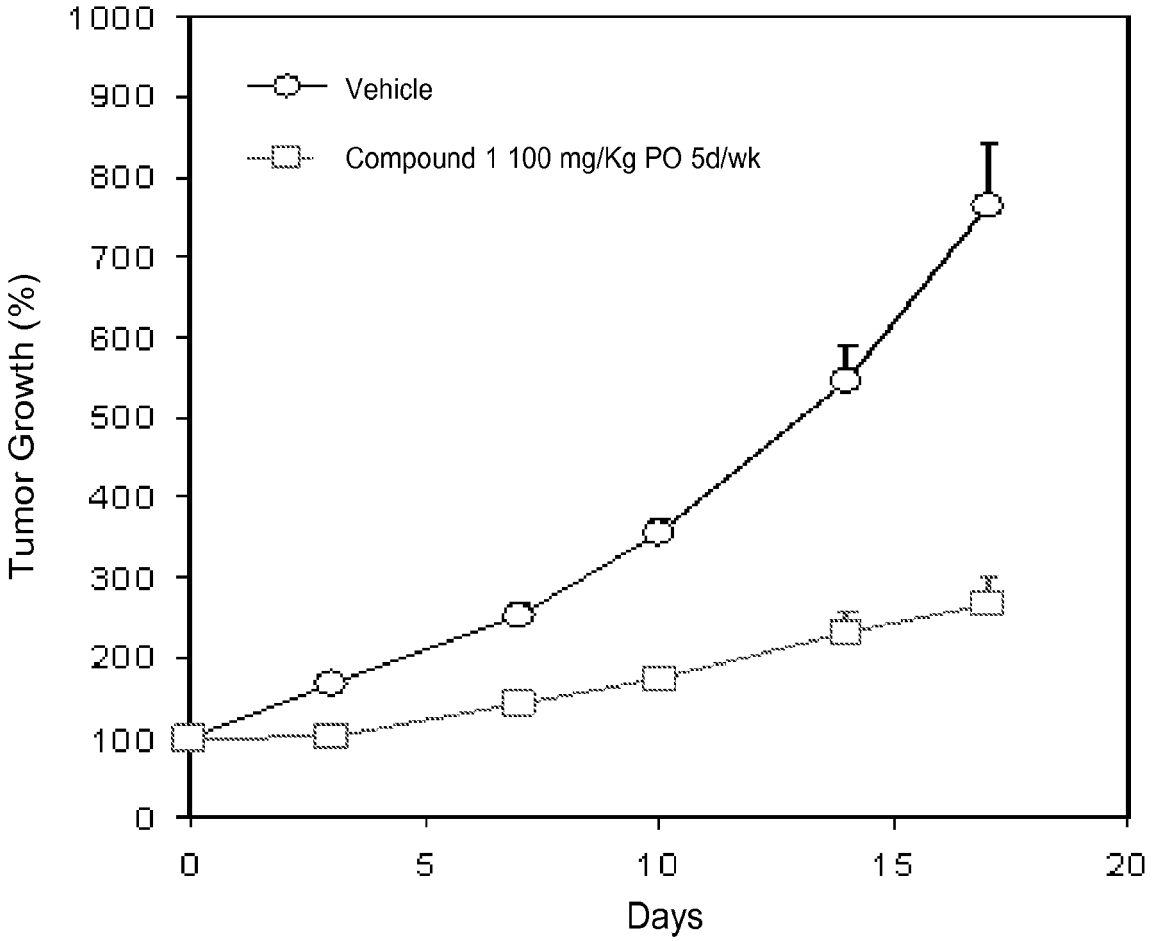

1000
900
800
700
600
500
400
300
200
100
0
Tumor Growth (%)
Vehicle
Compound 1 100 mg/Kg PO 5d/wk
0
5
10
15
20
Days

FIG. 14

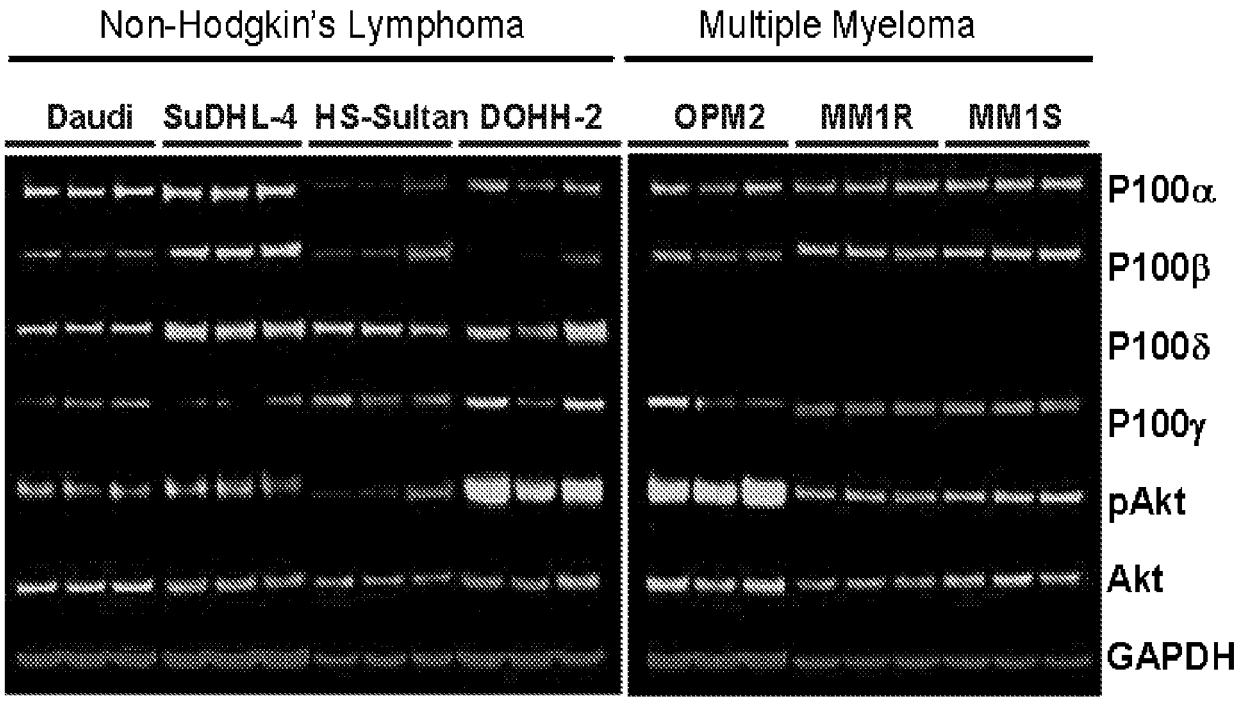

Non-Hodgkin's Lymphoma
Multiple Myeloma
Daudi
SuDHL-4
HS-Sultan
DOHH-2
OPM2
MM1R
MM1S
P100α
P100β
P100δ
P100γ
pAkt
Akt
GAPDH

FIG. 15

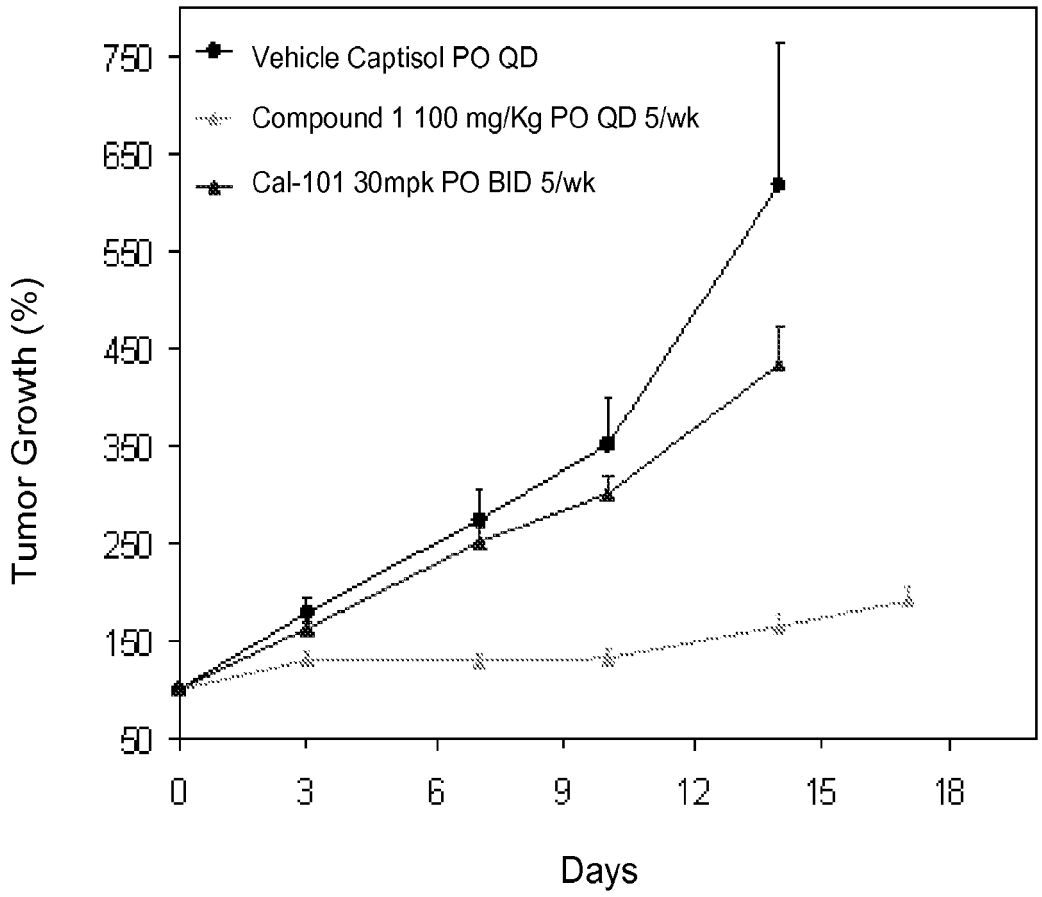

Vehicle Captisol PO QD
Compound 1 100 mg/Kg PO QD 5/wk
Cal-101 30mpk PO BID 5/wk
Tumor Growth (%)
750
650
550
450
350
250
150
50
0
3
6
9
12
15
18
Days

FIG. 16

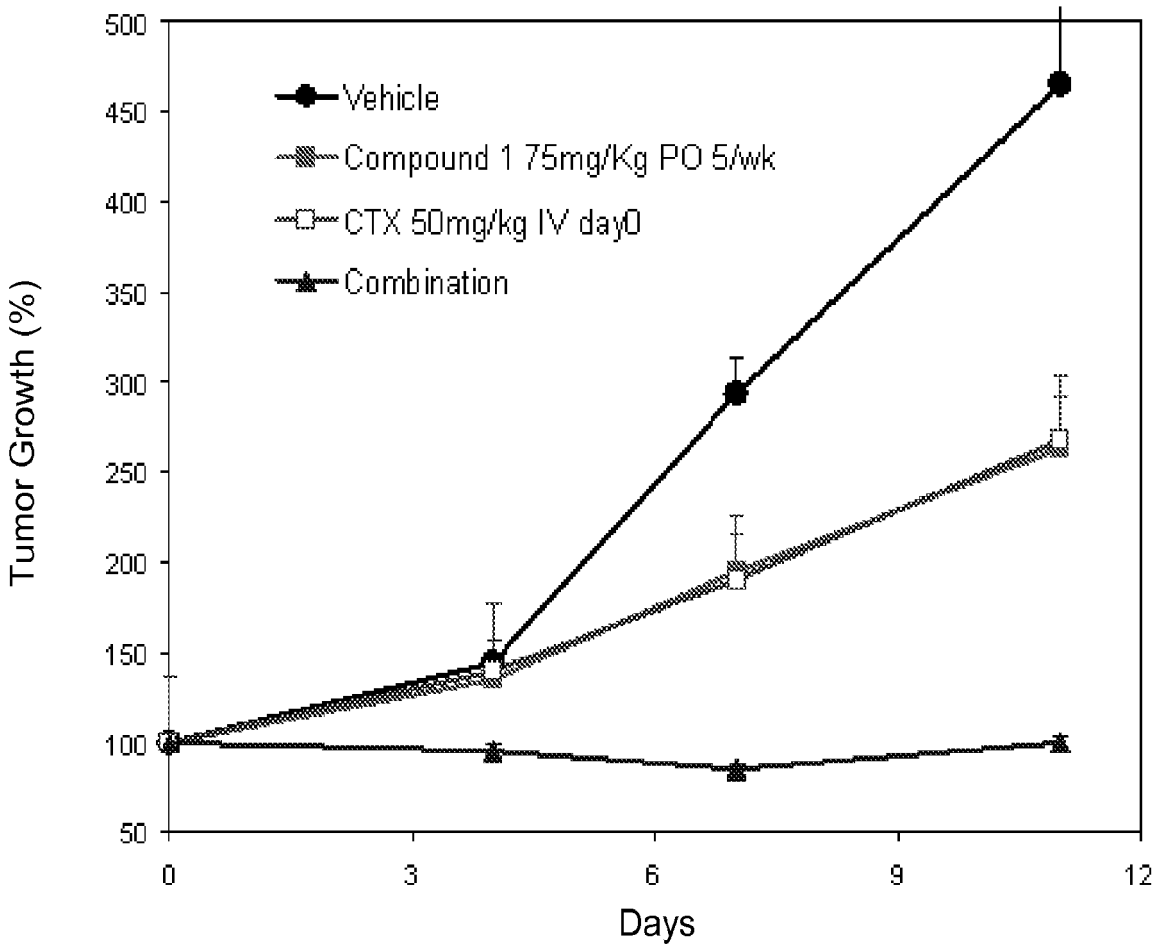

Tumor Growth (%)
500
450
400
350
300
250
200
150
100
50
0
3
6
9
12
Days
Vehicle
Compound 1 75mg/Kg PO 5/wk
CTX 50mg/kg IV day0
Combination

FIG. 17

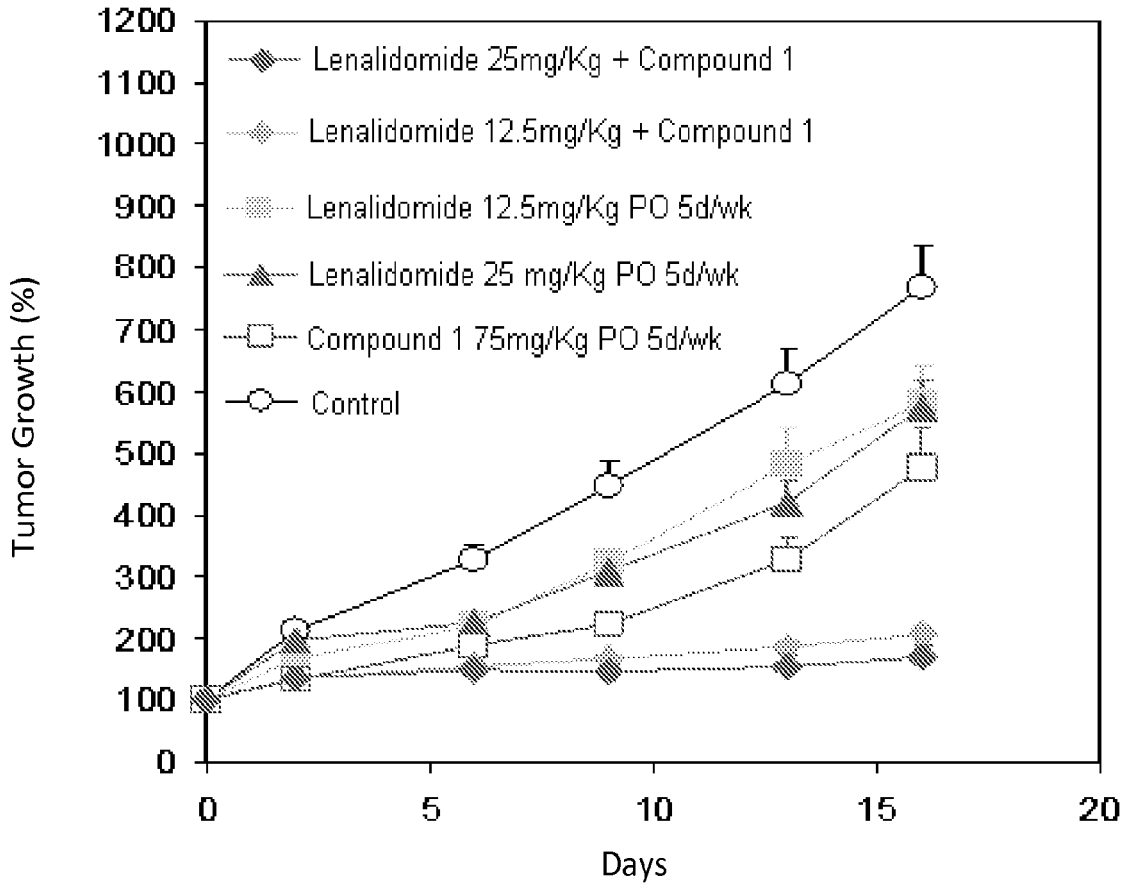

1200
1100
1000
900
800
700
600
500
400
300
200
100
0
Tumor Growth (%)
0
5
10
15
20
Days
Lenalidomide 25mg/Kg + Compound 1
Lenalidomide 12.5mg/Kg + Compound 1
Lenalidomide 12.5mg/Kg PO 5d/wk
Lenalidomide 25 mg/Kg PO 5d/wk
Compound 1 75mg/Kg PO 5d/wk
Control

FIG. 18