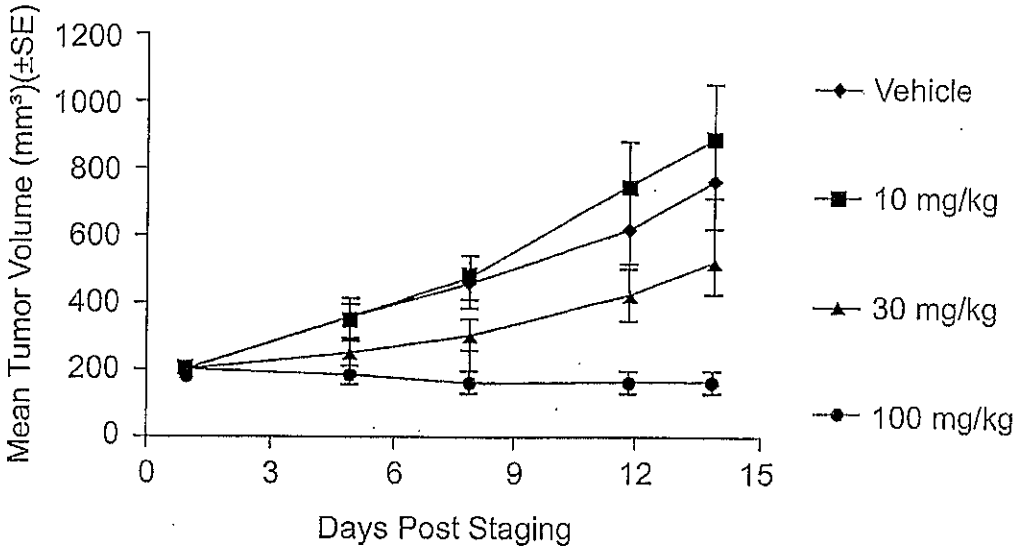


FIG. 1

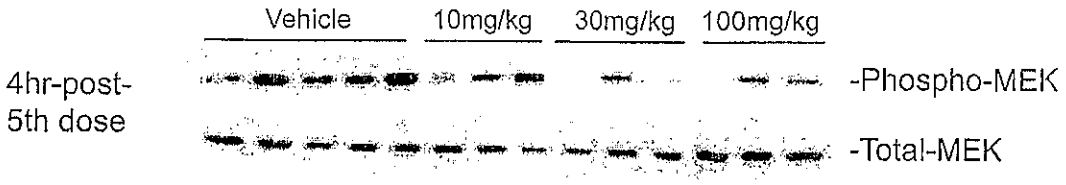


FIG. 2A

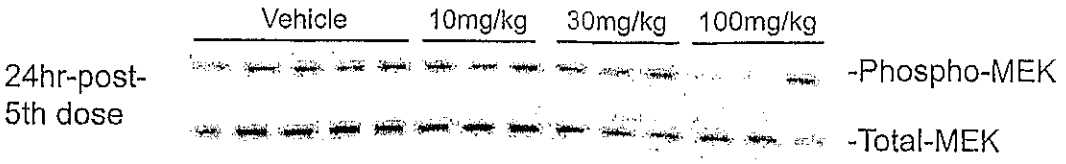


FIG. 2B

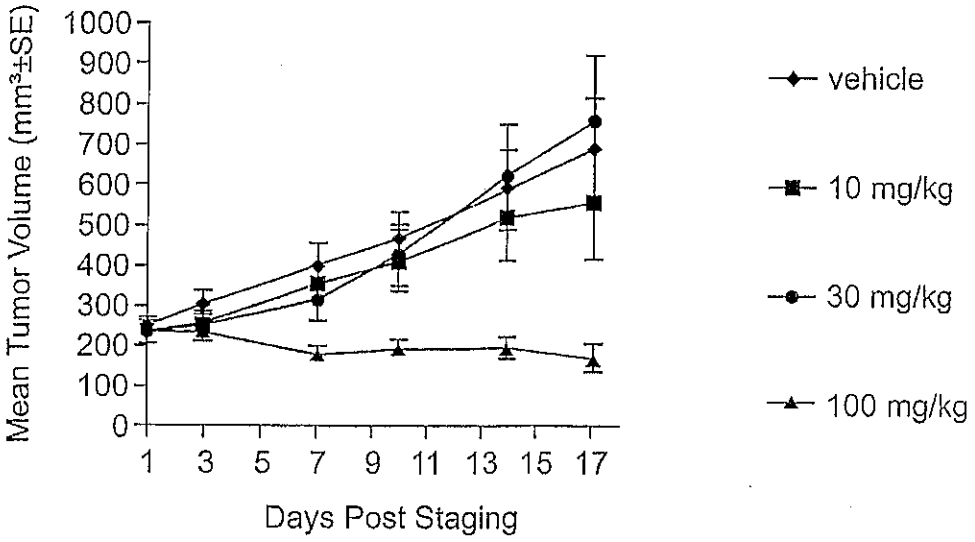


FIG. 3

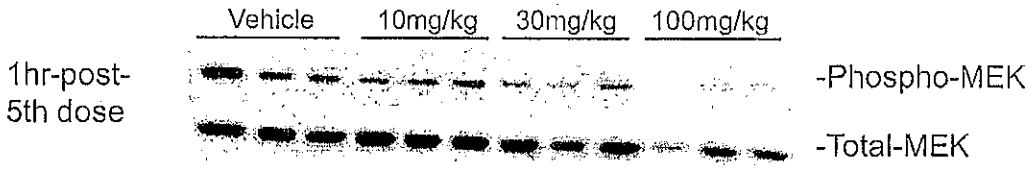


FIG. 4A

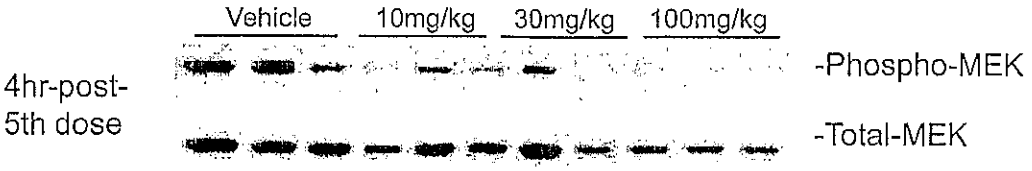


FIG. 4B

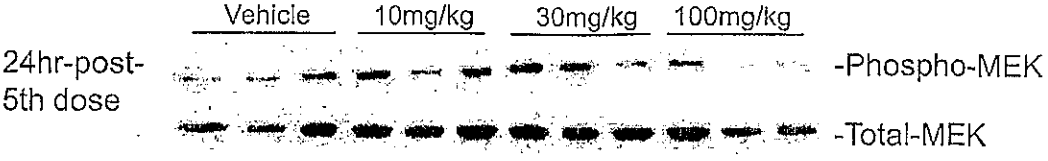


FIG. 4C

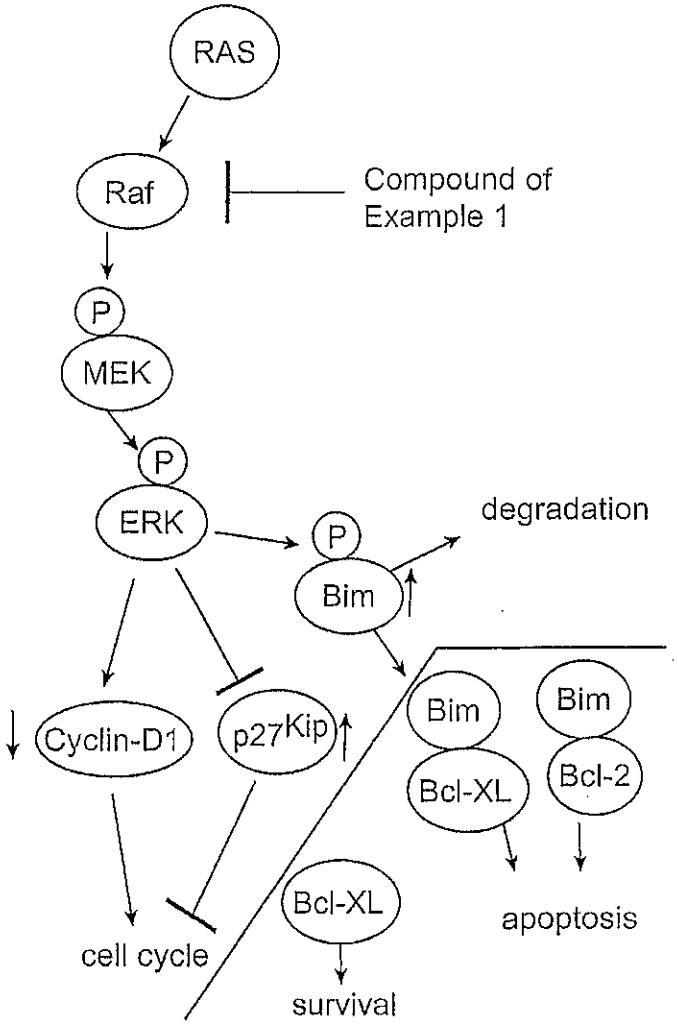

RAS
Raf
Compound of Example 1
P
MEK
P
ERK
P
Bim
degradation
Cyclin-D1
p27Kip
Bim
Bcl-XL
Bim
Bcl-2
Bcl-XL
cell cycle
survival
apoptosis

FIG. 5

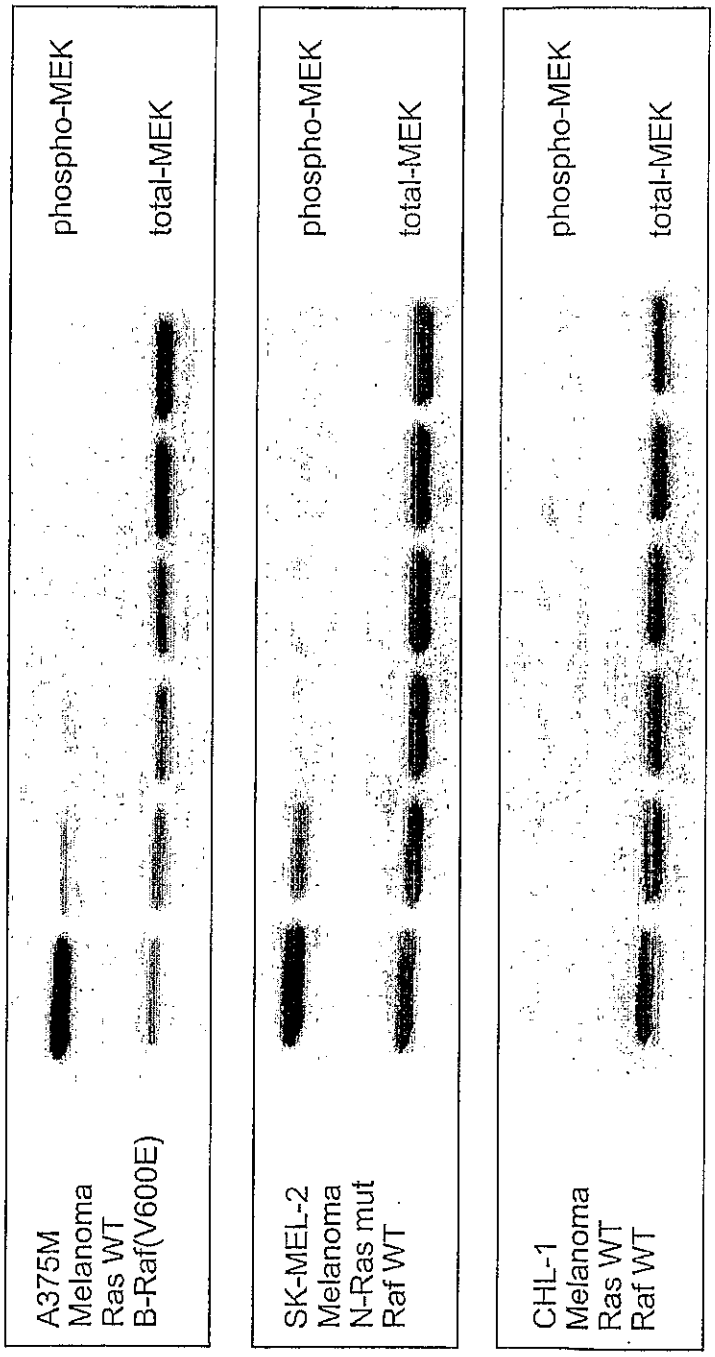


FIG. 6A

FIG. 6B

FIG. 6C

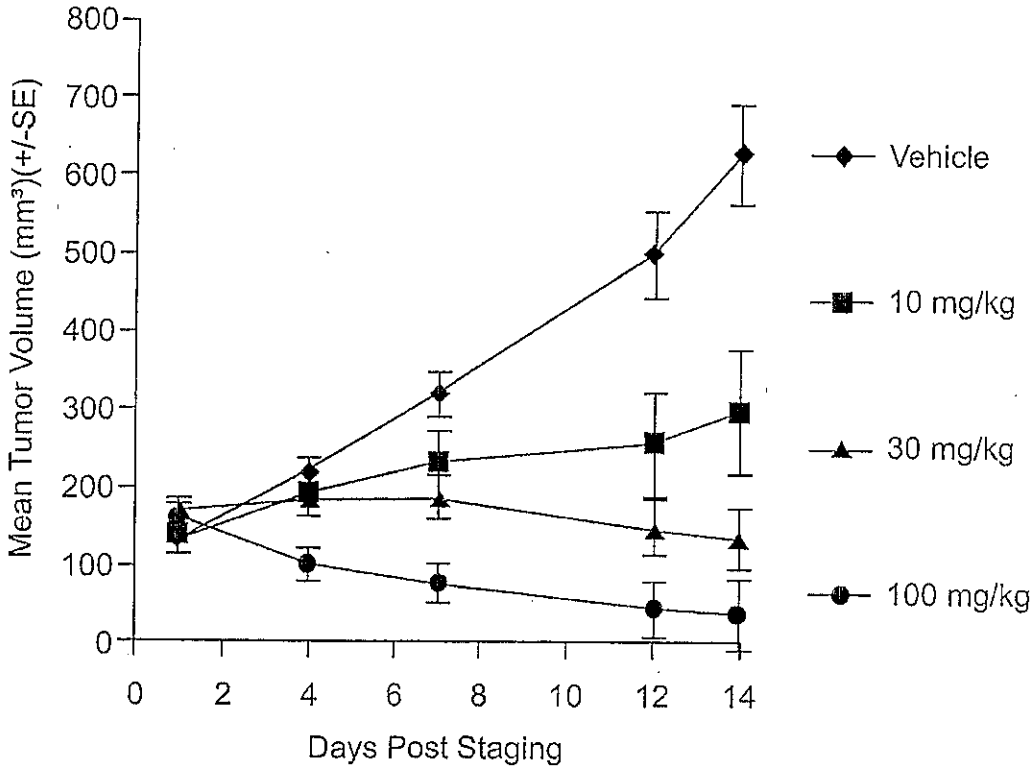

800
700
600
500
400
300
200
100
0
Mean Tumor Volume (mm³)(+/-SE)
0
2
4
6
8
10
12
14
Days Post Staging
Vehicle
10 mg/kg
30 mg/kg
100 mg/kg

FIG. 7A

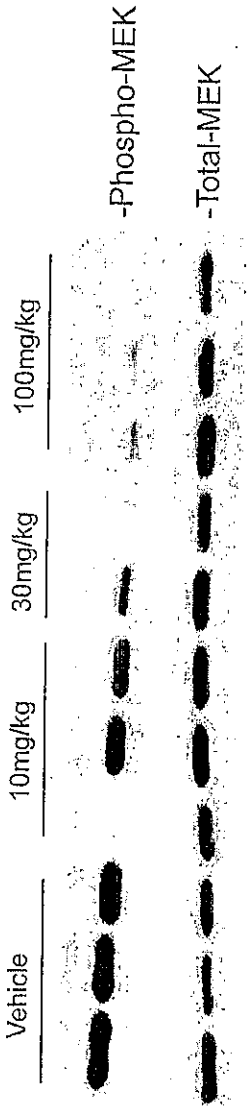

Vehicle
10mg/kg
30mg/kg
100mg/kg
-Phospho-MEK
-Total-MEK
8hr-post-14th dose

FIG. 7B

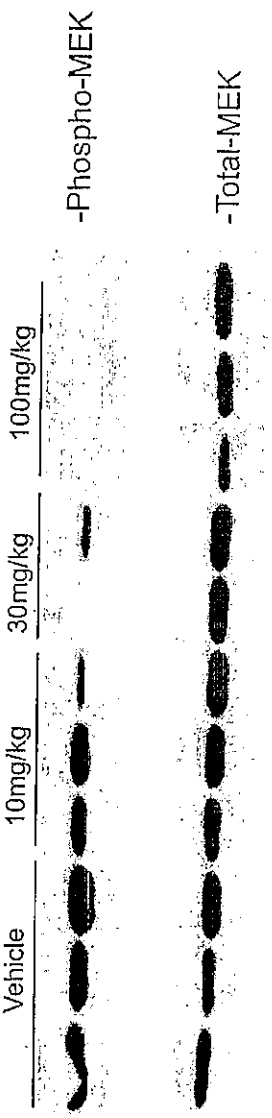

Vehicle
10mg/kg
30mg/kg
100mg/kg
-Phospho-MEK
-Total-MEK
24hr-post-14th dose

FIG. 7C

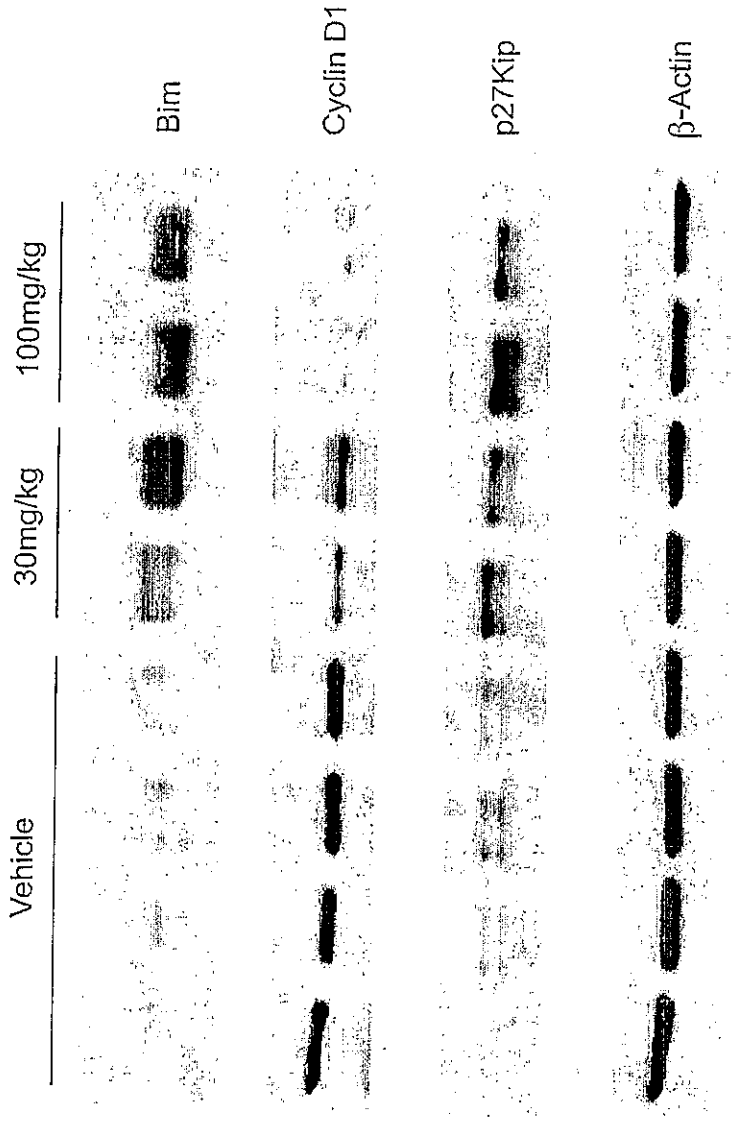


FIG. 7D

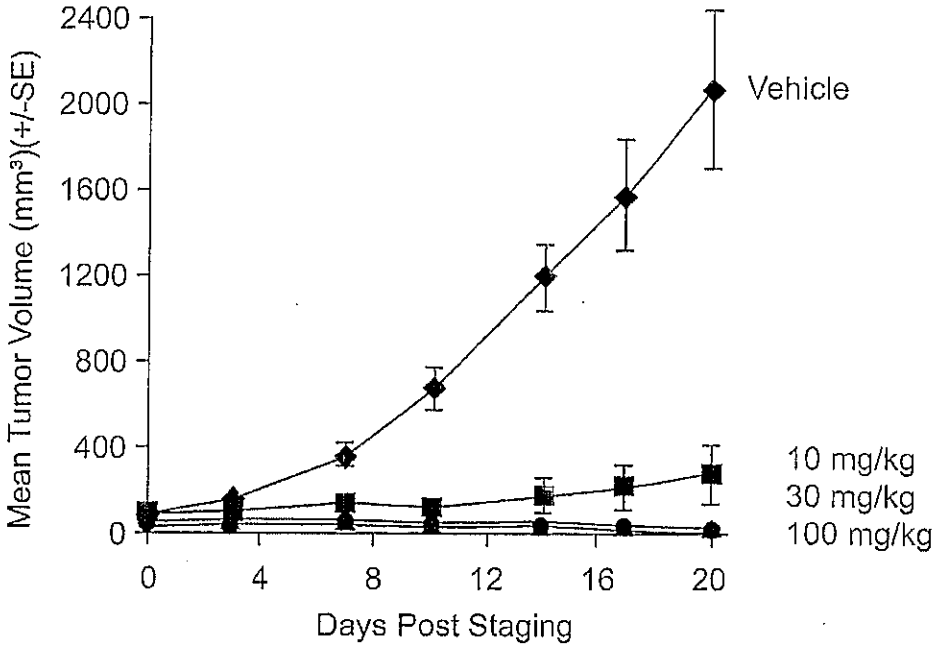


FIG. 8A

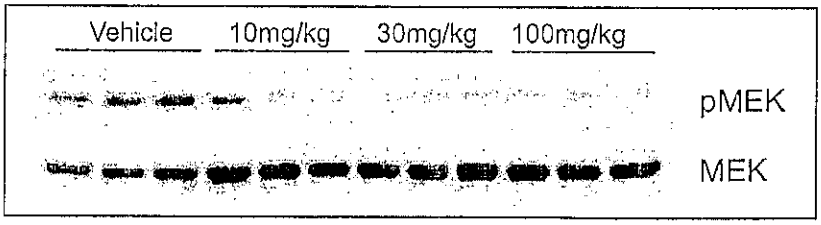


FIG. 8B

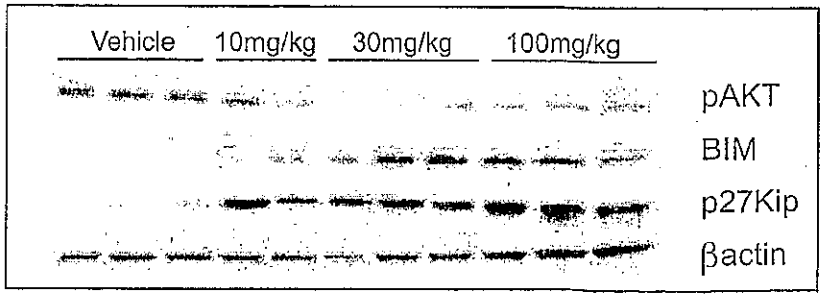


FIG. 8C

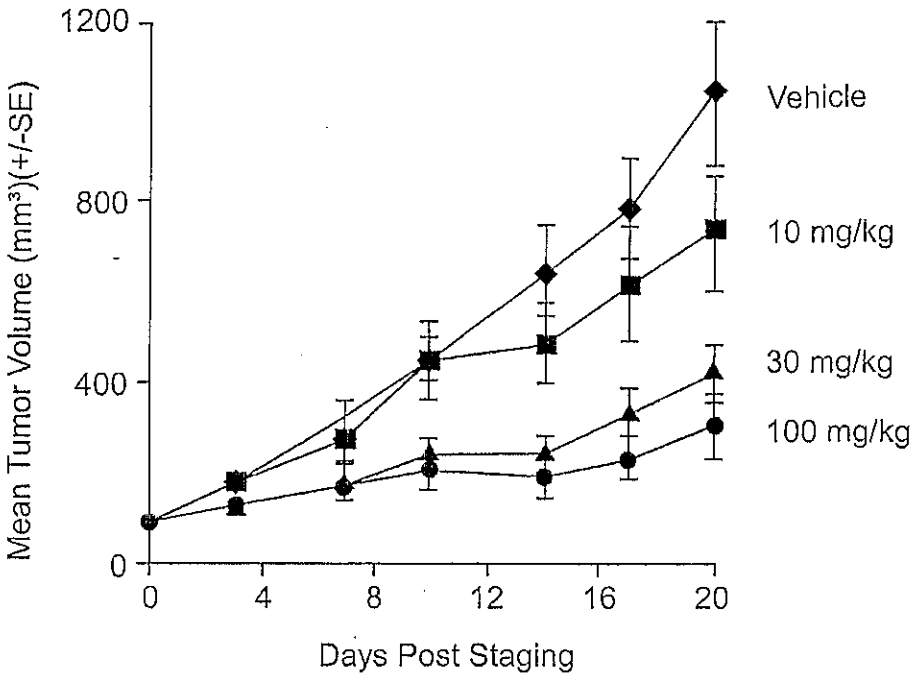


FIG. 9A

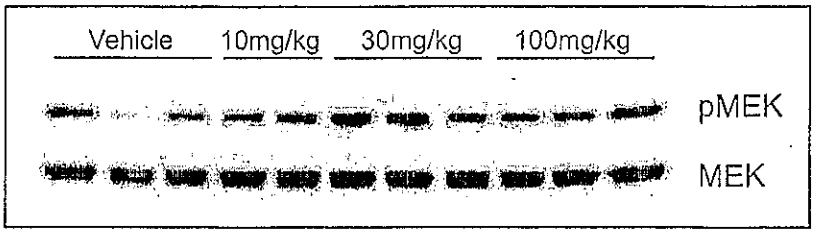


FIG. 9B

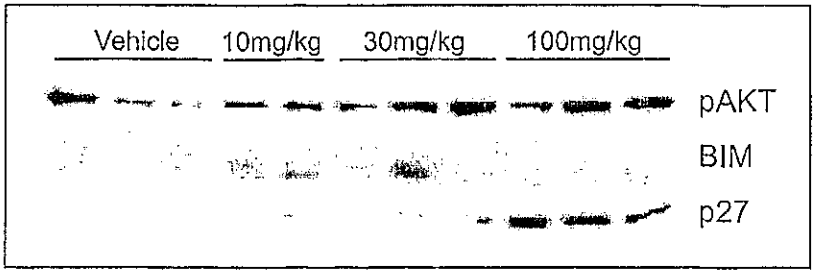


FIG. 9C

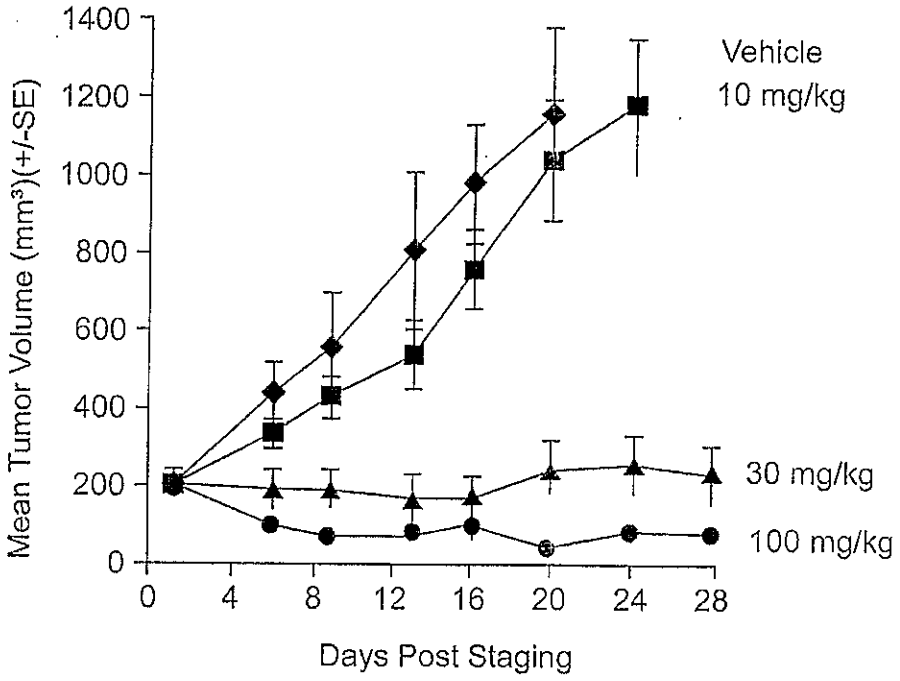


FIG. 10A

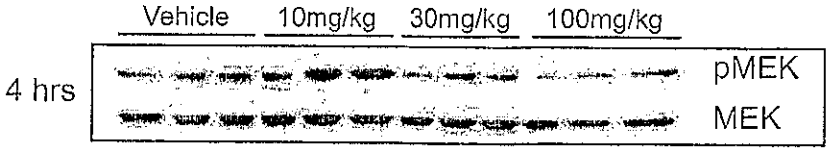


FIG. 10B

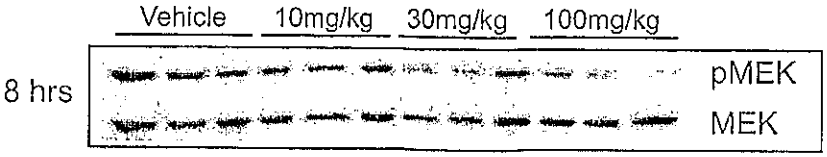


FIG. 10C

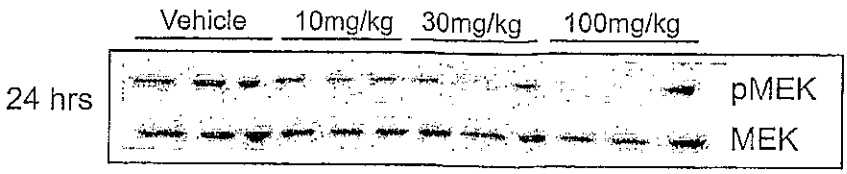


FIG. 10D

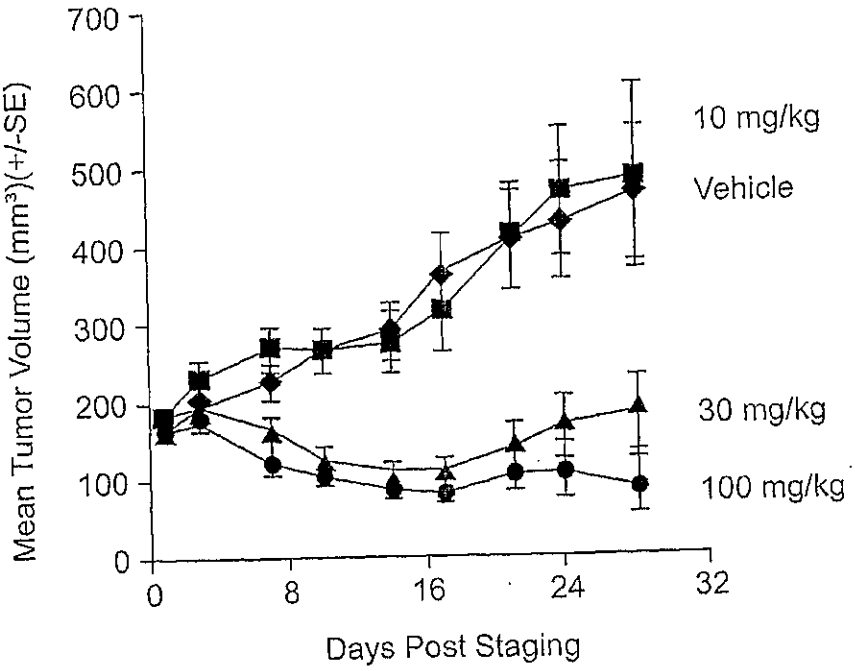

700
600
500
400
300
200
100
0
Mean Tumor Volume (mm³)(+/-SE)
0
8
16
24
32
Days Post Staging
10 mg/kg
Vehicle
30 mg/kg
100 mg/kg

FIG. 11

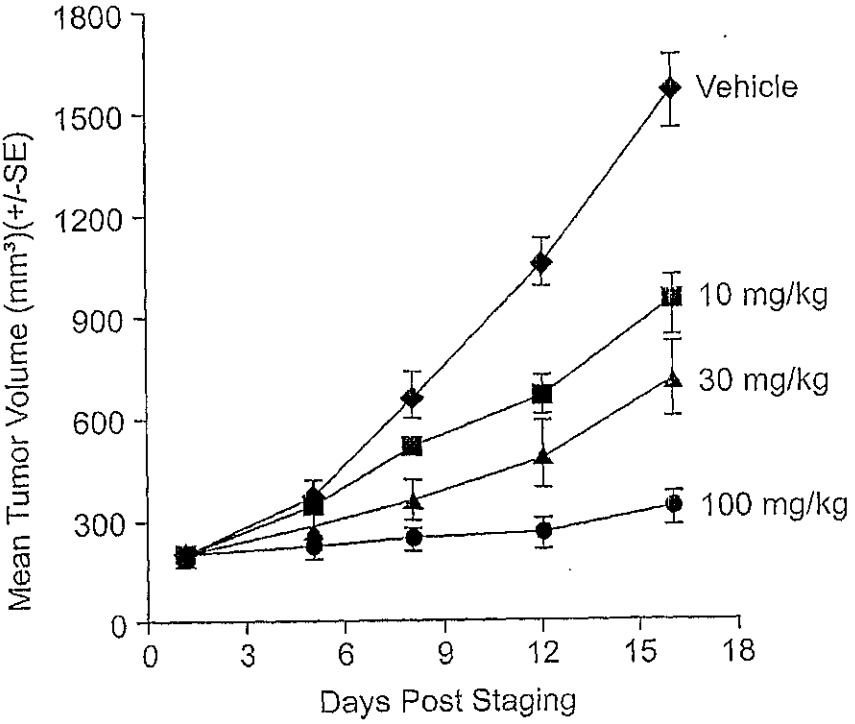


FIG. 12A

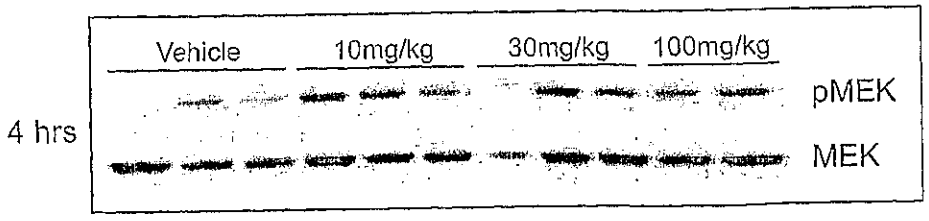


FIG. 12B

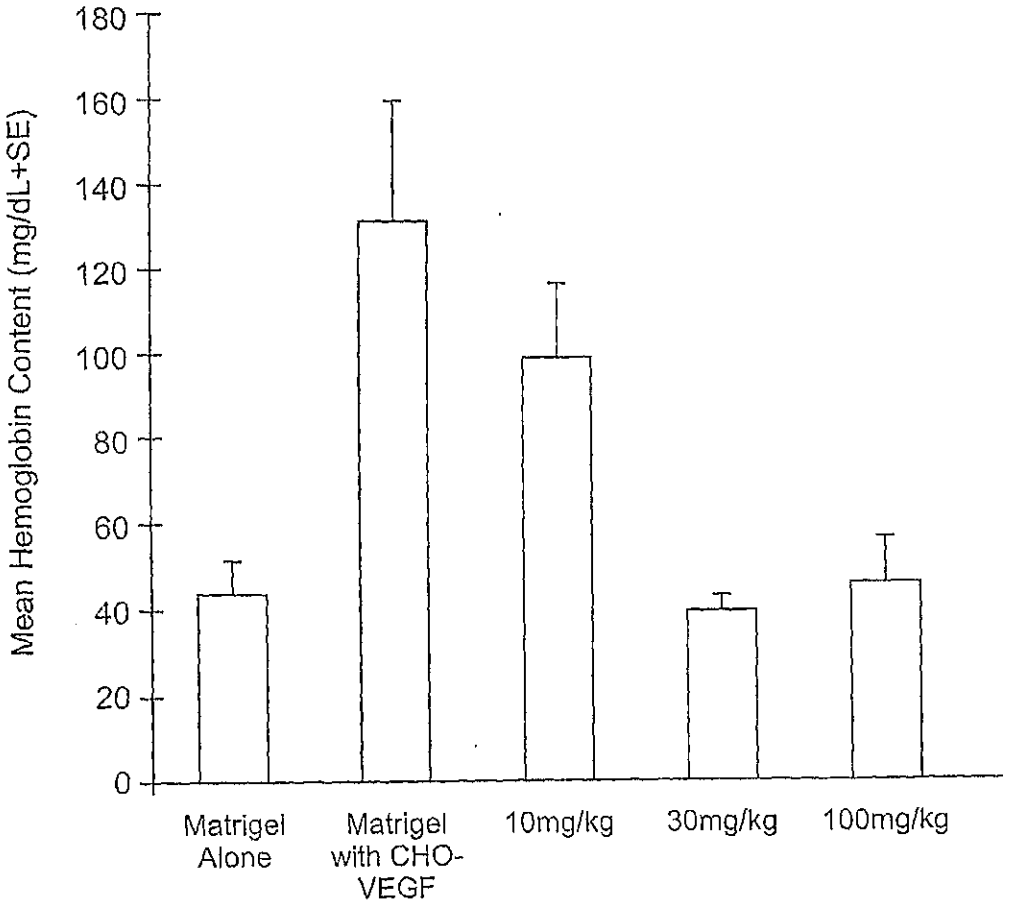

Mean Hemoglobin Content (mg/dL+SE)
180
160
140
120
100
80
60
40
20
0
Matrigel Alone
Matrigel with CHO-VEGF
10mg/kg
30mg/kg
100mg/kg

FIG. 13

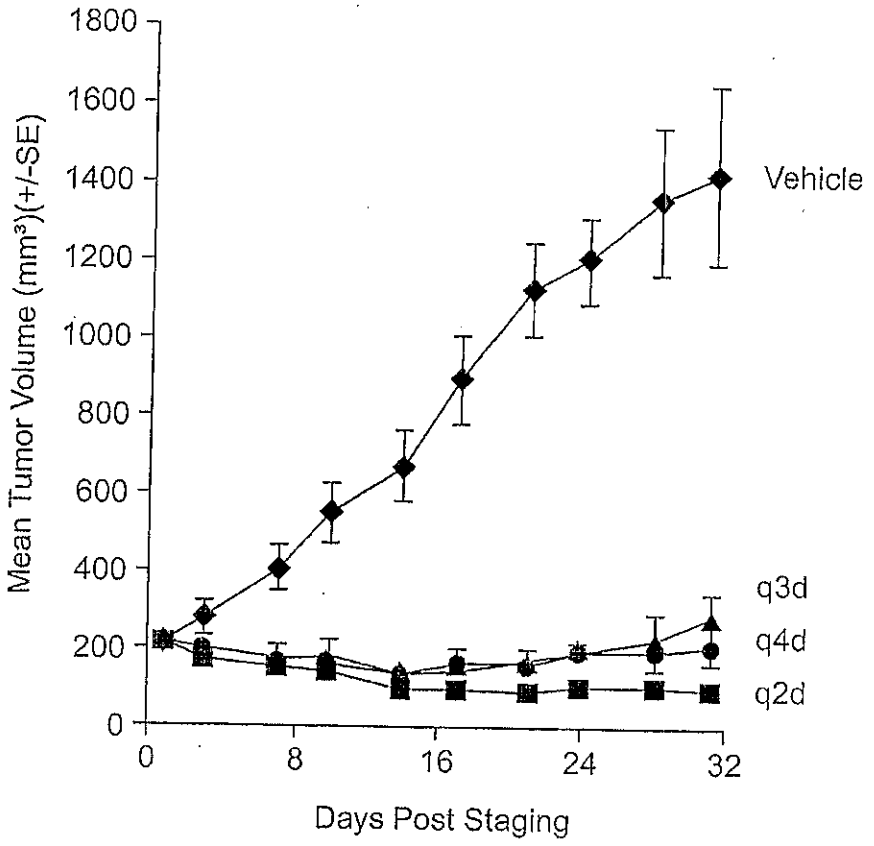


FIG. 14A

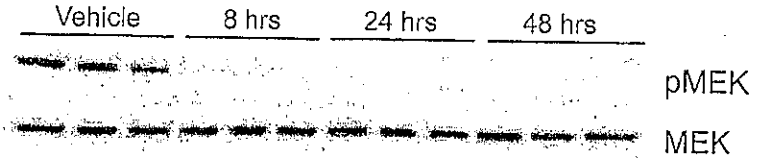


FIG. 14B

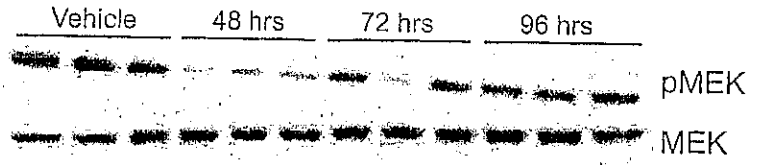


FIG. 14C

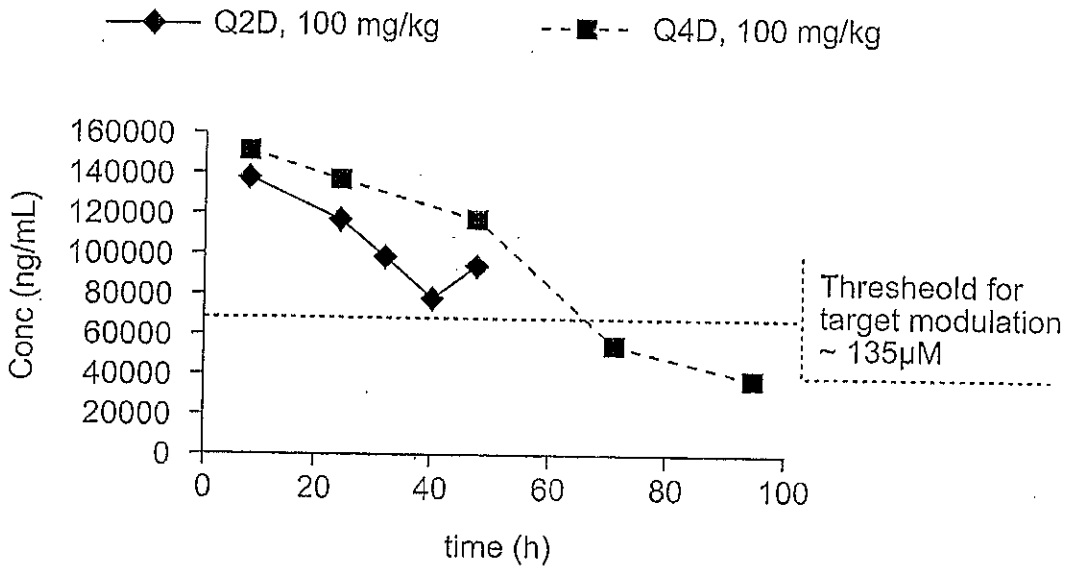

Q2D, 100 mg/kg
Q4D, 100 mg/kg
Conc (ng/mL)
160000
140000
120000
100000
80000
60000
40000
20000
0
0
20
40
60
80
100
time (h)
Thresheold for
target modulation
~ 135μM

FIG. 15