FIG. 1

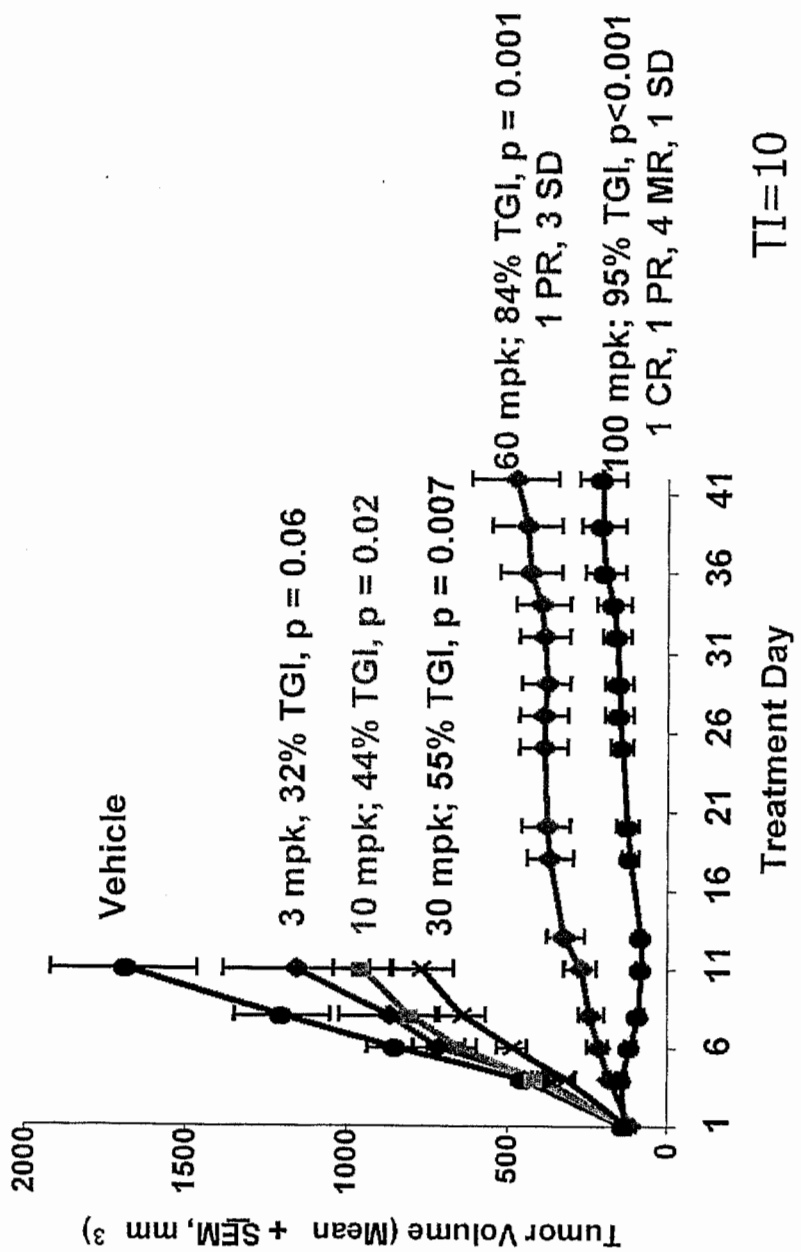

Vehicle
3 mpk, 32% TGI, p = 0.06
10 mpk; 44% TGI, p = 0.02
30 mpk; 55% TGI, p = 0.007
60 mpk; 84% TGI, p = 0.001
1 PR, 3 SD
100 mpk; 95% TGI, p<0.001
1 CR, 1 PR, 4 MR, 1 SD
Tumor Volume (Mean + SEM, mm 3)
2000
1500
1000
500
0
1
6
11
16
21
26
31
36
41
Treatment Day
TI=10

FIG. 2

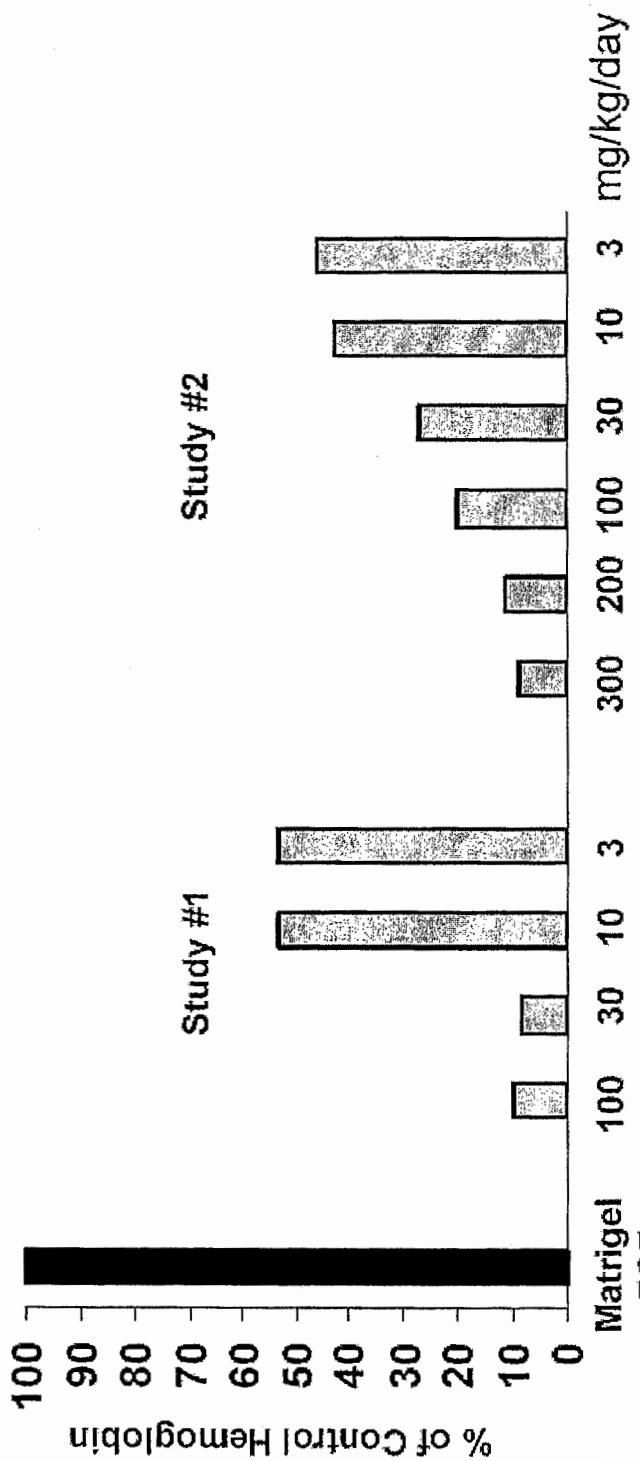

% of Control Hemoglobin
100
90
80
70
60
50
40
30
20
10
0
Matrigel
FGF
100
30
10
3
300
200
100
30
10
3
mg/kg/day
Study #1
Study #2

FIG. 3

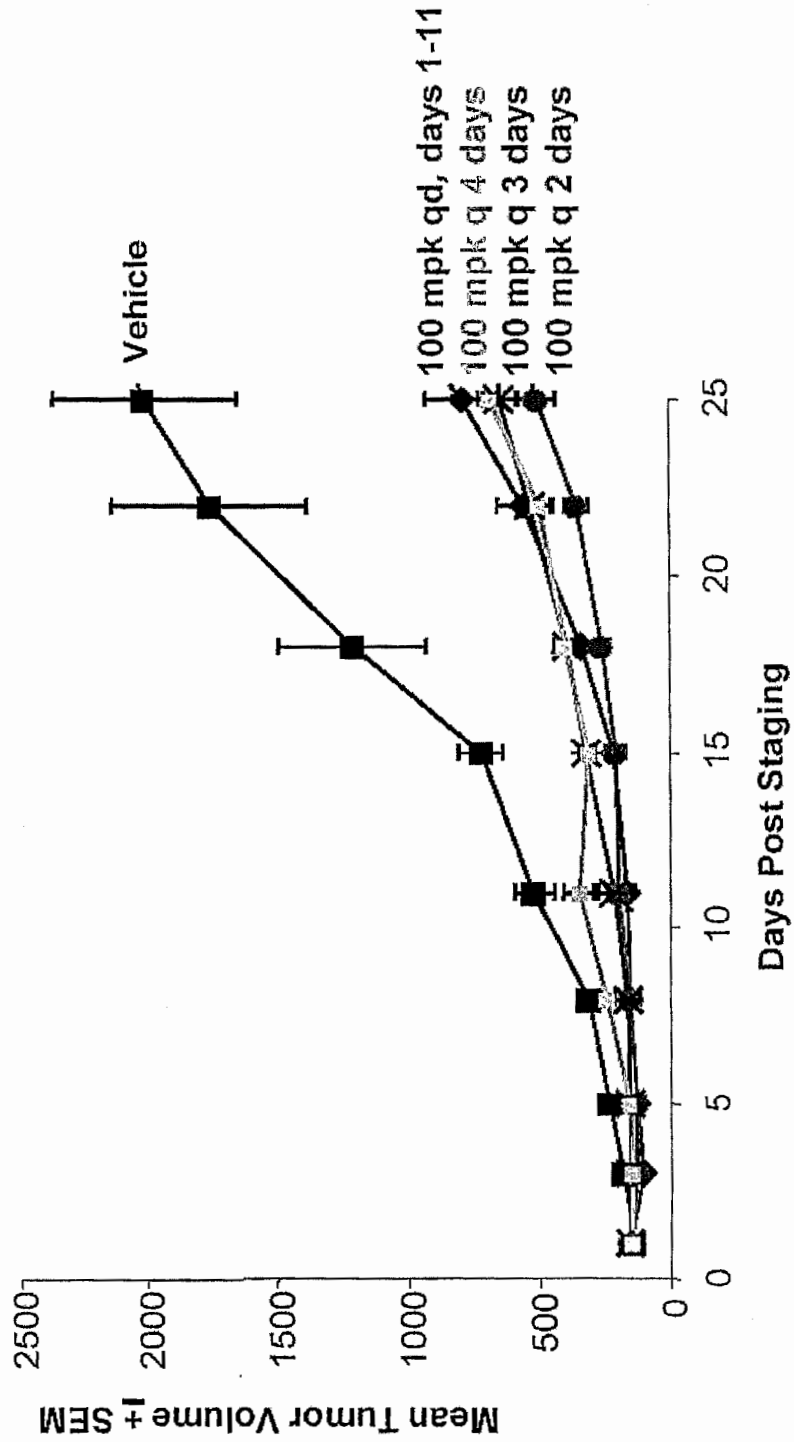
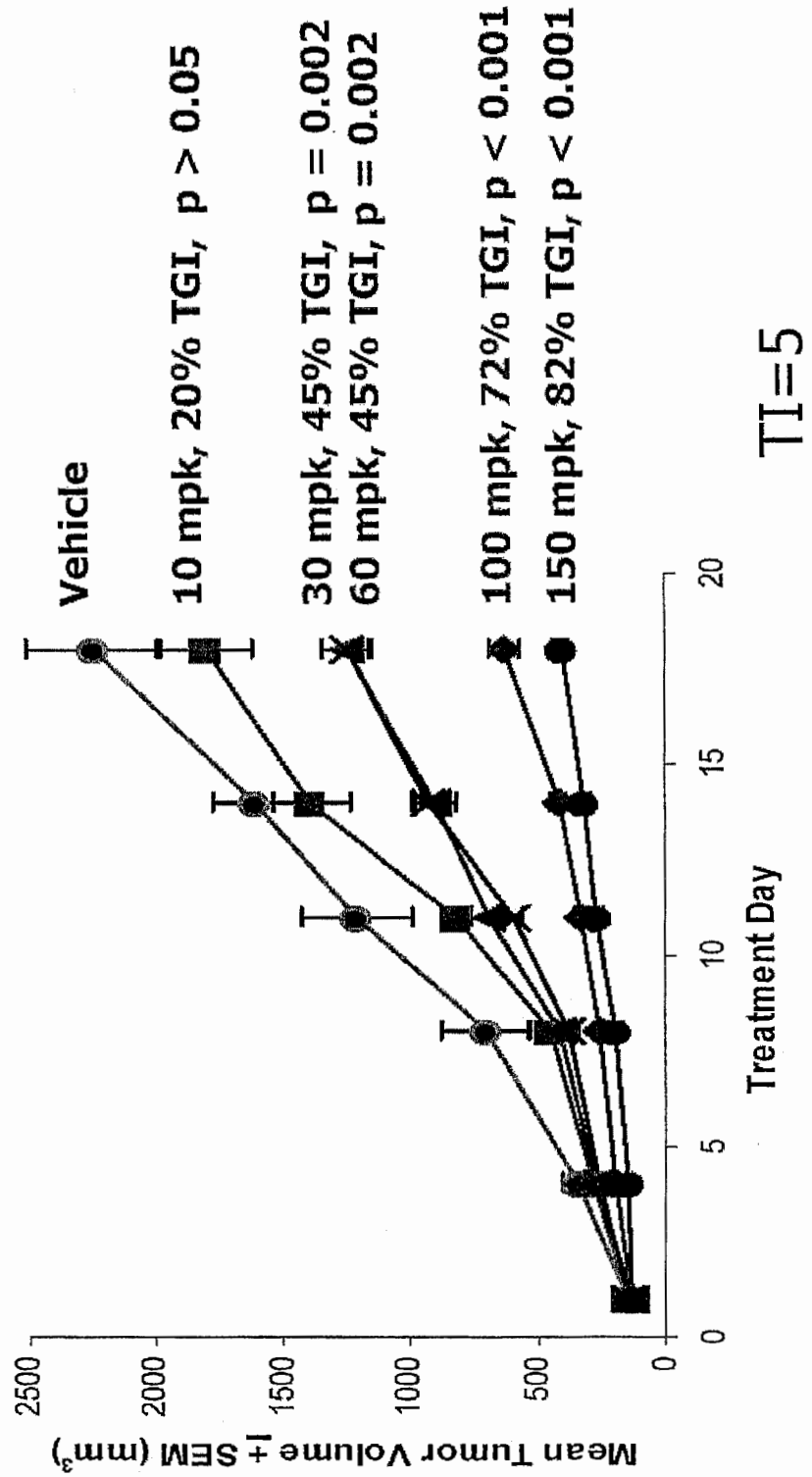

Mean Tumor Volume + SEM
2500
2000
1500
1000
500
0
0
5
10
15
20
25
Days Post Staging
Vehicle
100 mpk qd, days 1-11
100 mpk q 4 days
100 mpk q 3 days
100 mpk q 2 days

FIG. 4


Vehicle
10 mpk, 20% TGI, p > 0.05
30 mpk, 45% TGI, p = 0.002
60 mpk, 45% TGI, p = 0.002
100 mpk, 72% TGI, p < 0.001
150 mpk, 82% TGI, p < 0.001
Mean Tumor Volume ± SEM (mm³)
Treatment Day
0
500
1000
1500
2000
2500
5
10
15
20

TI=5

FIG. 5

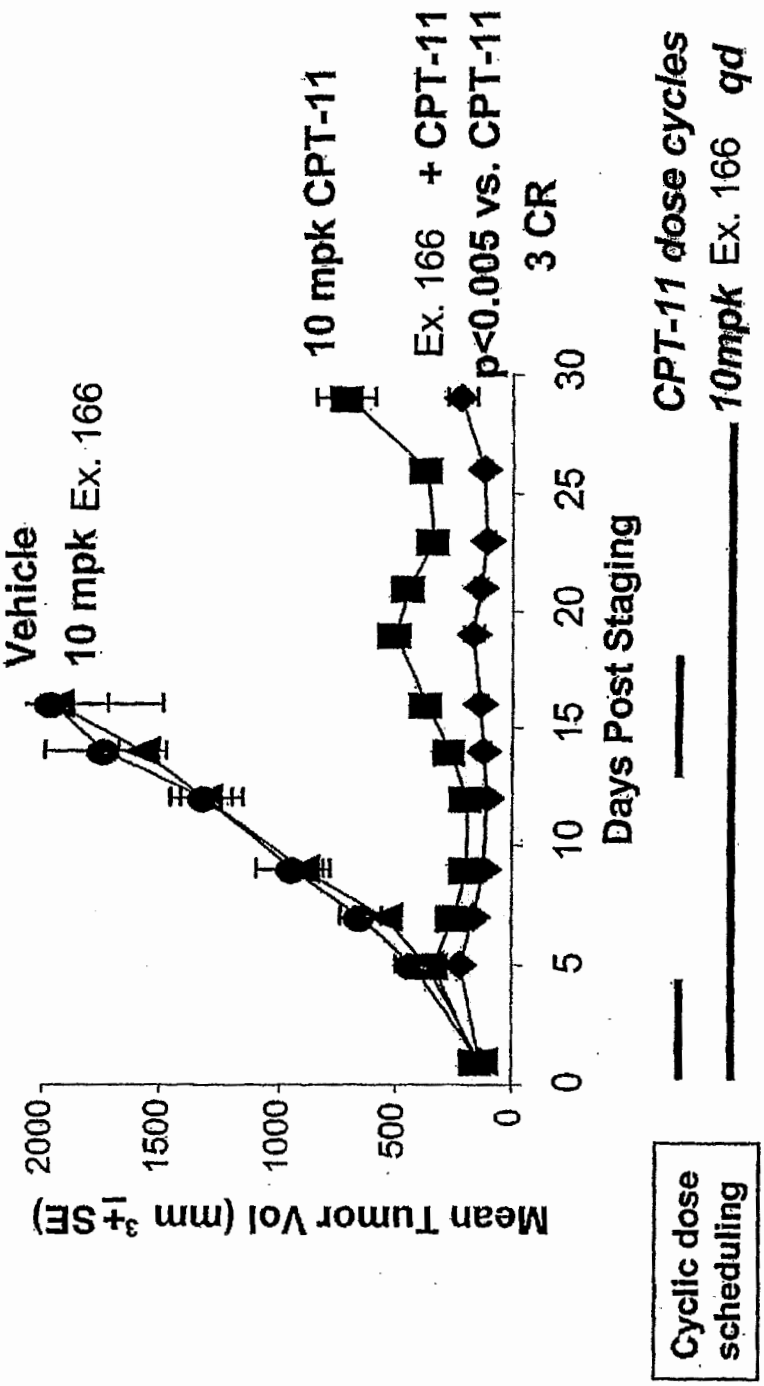

Vehicle
10 mpk Ex. 166
10 mpk CPT-11
Ex. 166 + CPT-11
p<0.005 vs. CPT-11
3 CR
Mean Tumor Vol (mm ³+ SE)
2000
1500
1000
500
0
0
5
10
15
20
25
30
Days Post Staging
Cyclic dose scheduling
CPT-11 dose cycles
10mpk Ex. 166 qd

FIG. 6

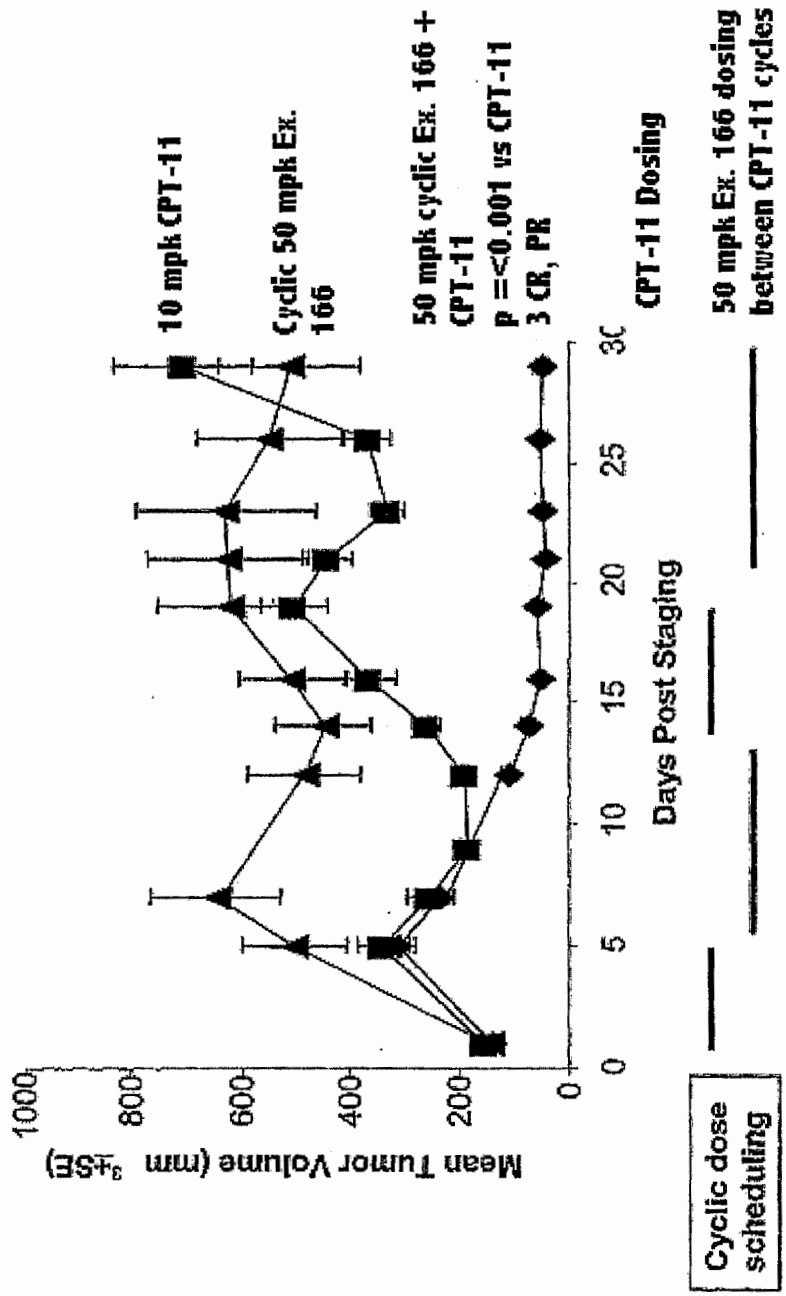

10 mpk CPT-11
Cyclic 50 mpk Ex. 166
50 mpk cyclic Ex. 166 + CPT-11
p =<0.001 vs CPT-11
3 CR, PR
Mean Tumor Volume (mm ³±SE)
1000
800
600
400
200
0
0
5
10
15
20
25
30
Days Post Staging
CPT-11 Dosing
Cyclic dose scheduling
50 mpk Ex. 166 dosing
between CPT-11 cycles

FIG. 7

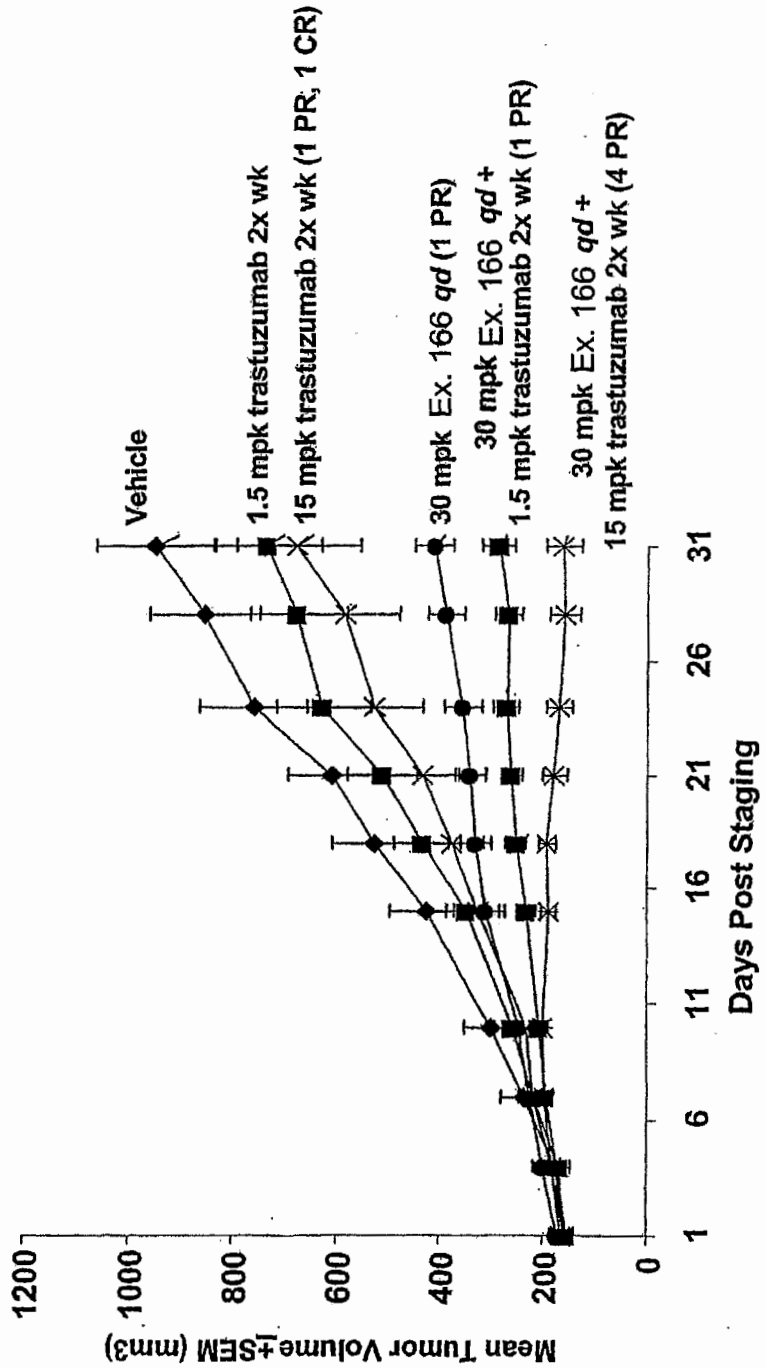

Vehicle
1.5 mpk trastuzumab 2x wk
15 mpk trastuzumab 2x wk (1 PR, 1 CR)
30 mpk Ex. 166 qd (1 PR)
30 mpk Ex. 166 qd + 1.5 mpk trastuzumab 2x wk (1 PR)
30 mpk Ex. 166 qd + 15 mpk trastuzumab 2x wk (4 PR)
Mean Tumor Volume+SEM (mm3)
1200
1000
800
600
400
200
0
1
6
11
16
21
26
31
Days Post Staging

FIG. 8

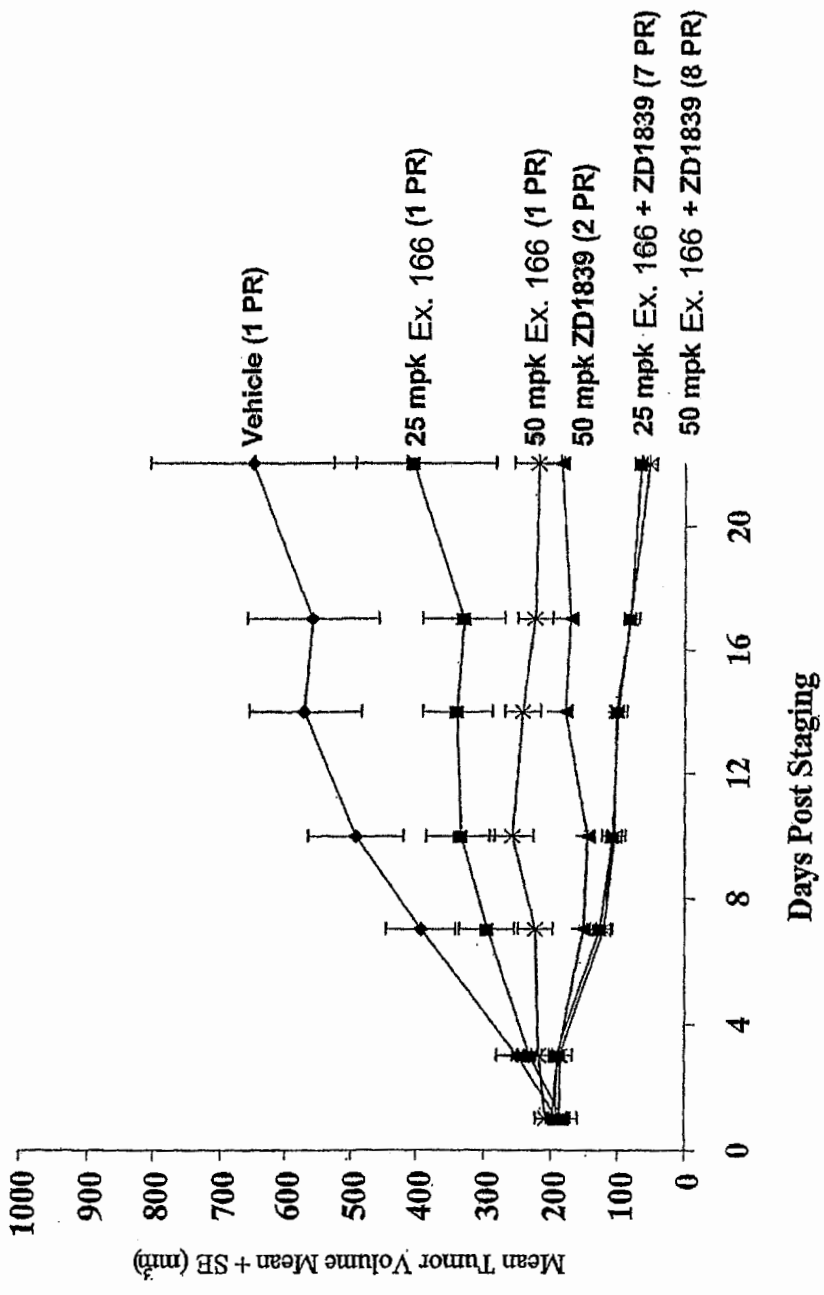

Mean Tumor Volume Mean + SE (mm3)
1000
900
800
700
600
500
400
300
200
100
0
0
4
8
12
16
20
Days Post Staging
Vehicle (1 PR)
25 mpk Ex. 166 (1 PR)
50 mpk Ex. 166 (1 PR)
50 mpk ZD1839 (2 PR)
25 mpk Ex. 166 + ZD1839 (7 PR)
50 mpk Ex. 166 + ZD1839 (8 PR)

FIG. 9A

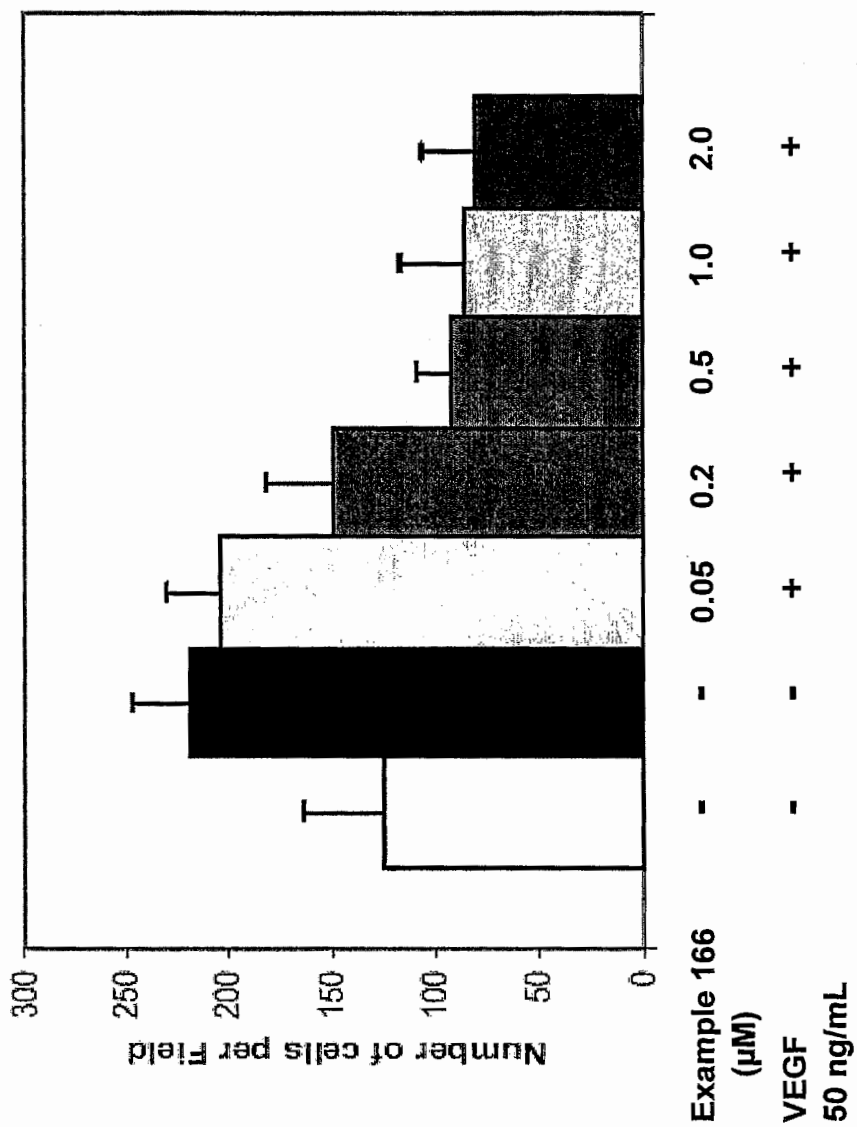

Number of cells per Field
300
250
200
150
100
50
0
Example 166 (μM)
- - 0.05 0.2 0.5 1.0 2.0
VEGF 50 ng/mL
- - + + + + +

FIG. 9B

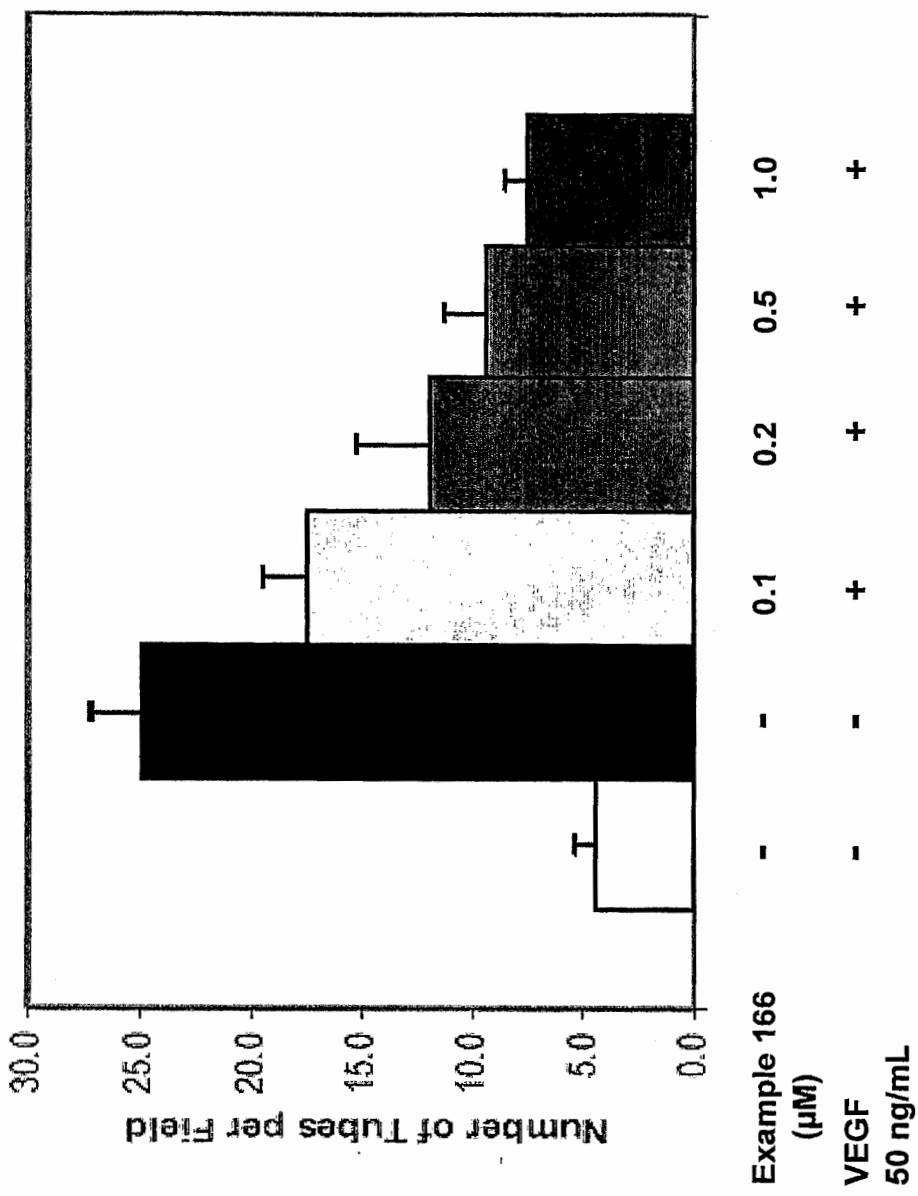

Number of Tubes per Field
30.0
25.0
20.0
15.0
10.0
5.0
0.0
Example 166 (μM)
- - 0.1 0.2 0.5 1.0
VEGF 50 ng/mL
- - + + + +

FIG. 10

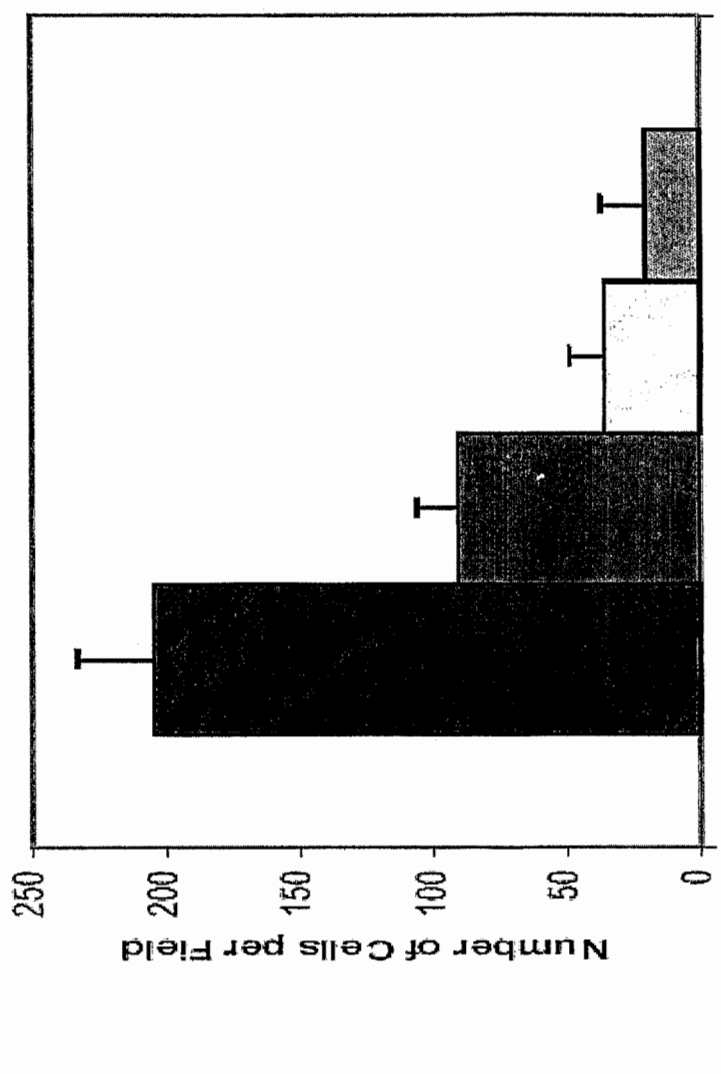

Number of Cells per Field
250
200
150
100
50
0
-
0.1
0.5
1.0
Example 166
(μM)

FIG. 11

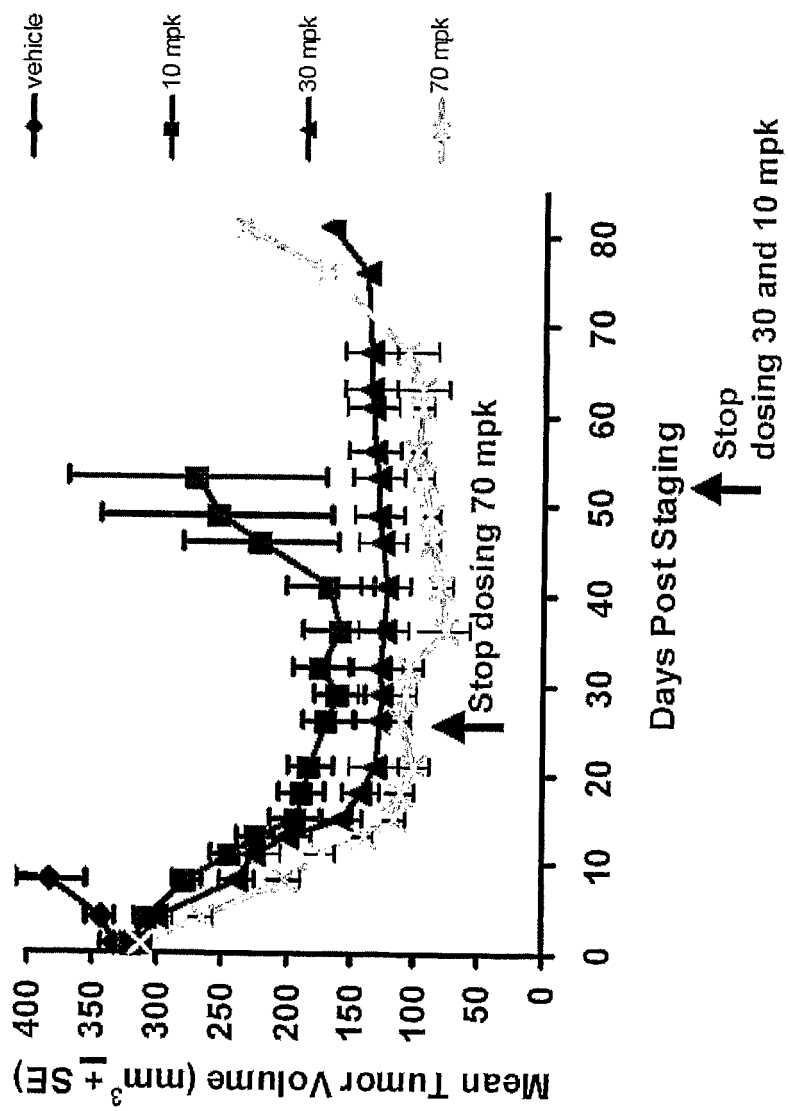

vehicle
10 mpk Ex. 166
30 mpk Ex. 166
70 mpk Ex. 166
>92% TGI, (1CR, 6 PR)
>94% TGI (1 CR; 7 PR)
>96% TGI (1CR; 9PR)
Mean Tumor Volume (mm3 + SE)
400
350
300
250
200
150
100
50
0
0
10
20
30
40
50
60
70
80
Days Post Staging
Stop dosing 70 mpk
Stop dosing 30 and 10 mpk

FIG. 12

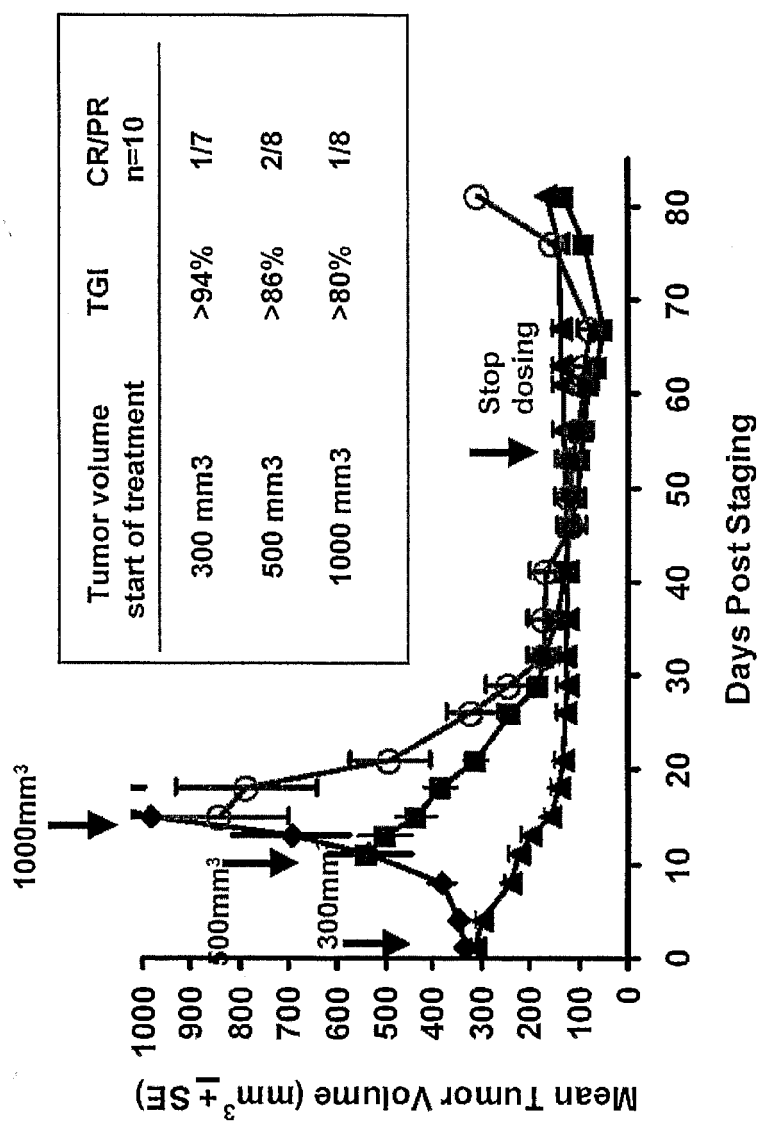

Tumor volume start of treatment
TGI
CR/PR n=10
300 mm3
>94%
1/7
500 mm3
>86%
2/8
1000 mm3
>80%
1/8
1000mm3
500mm3
300mm3
Stop dosing
Mean Tumor Volume (mm3 ± SE)
Days Post Staging
0
100
200
300
400
500
600
700
800
900
1000
0
10
20
30
40
50
60
70
80

FIG. 13

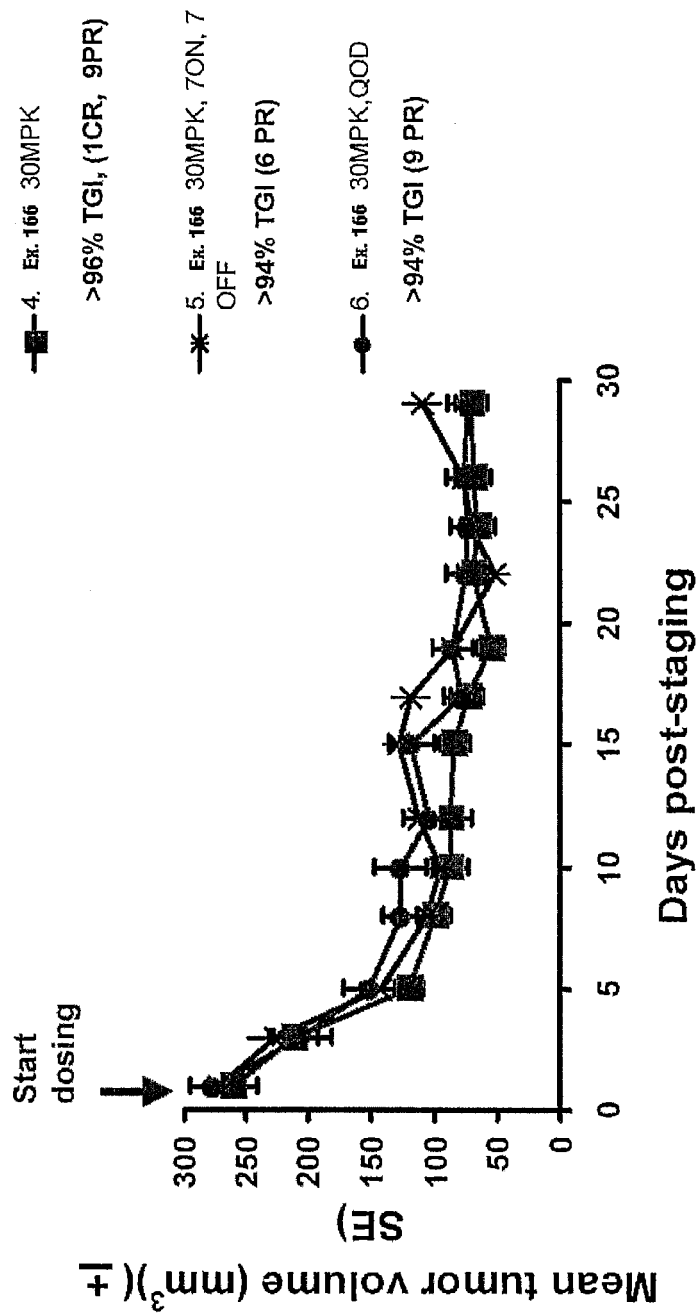
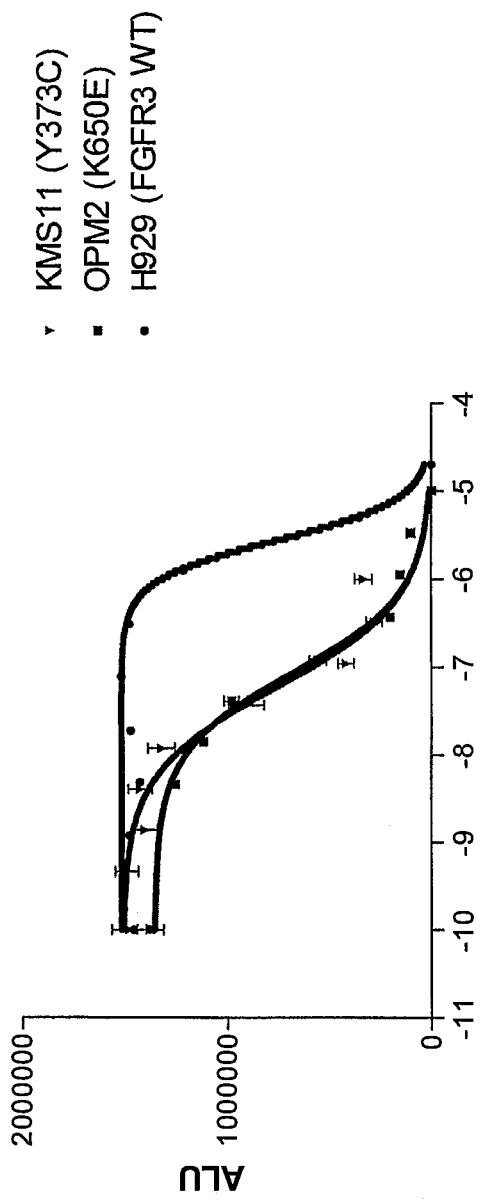

4. Ex. 166 30MPK
>96% TGI, (1CR, 9PR)
5. Ex. 166 30MPK, 7ON, 7 OFF
>94% TGI (6 PR)
6. Ex. 166 30MPK,QOD
>94% TGI (9 PR)
Start dosing
Mean tumor volume (mm3)(± SE)
Days post-staging
0
50
100
150
200
250
300
0
5
10
15
20
25
30

FIG. 14



	KMS11	OPM2	H929
BOTTOM (Constant)	0.0	0.0	0.0
TOP	1.5180e+006	1.3600e+006	1.5220e+006
LOGEC50	-7.225	-7.063	-5.583
HILLSLOPE	-0.8926	-0.9733	-1.890
EC50	5.9570e-008	8.6500e-008	2.6150e-006

FIG. 15

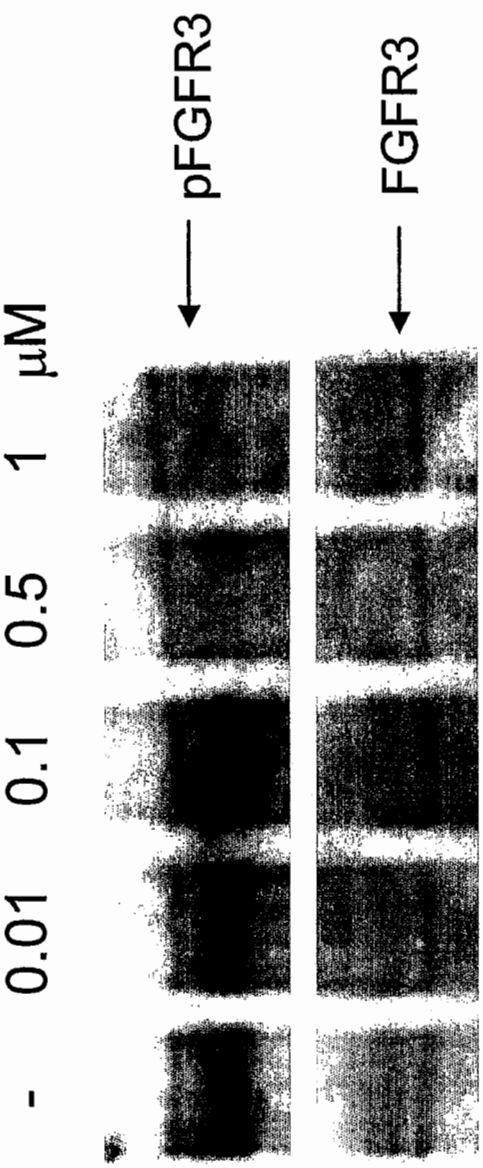


FIG. 16A

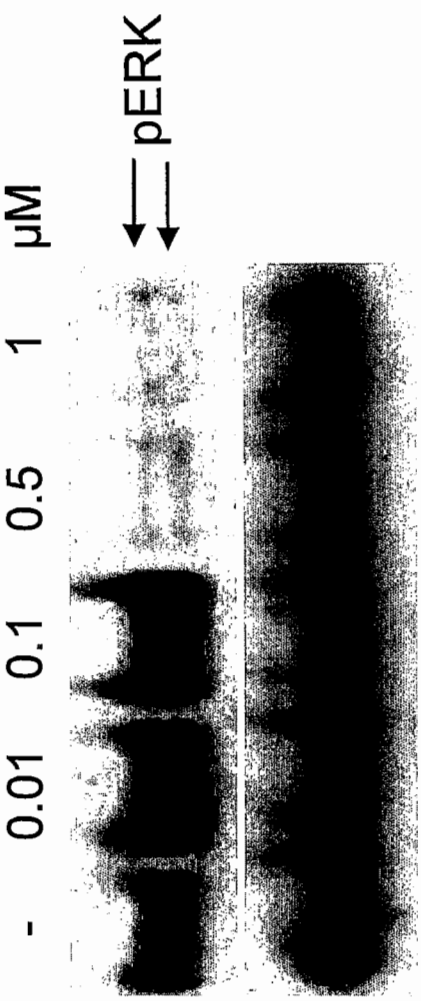


FIG. 16B

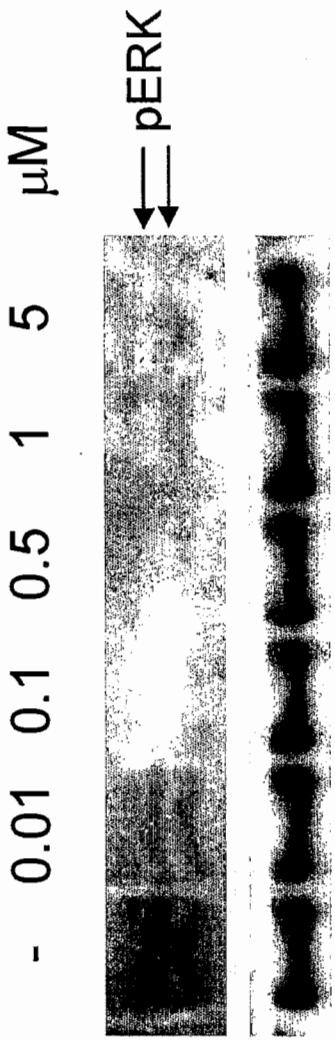


FIG. 16C

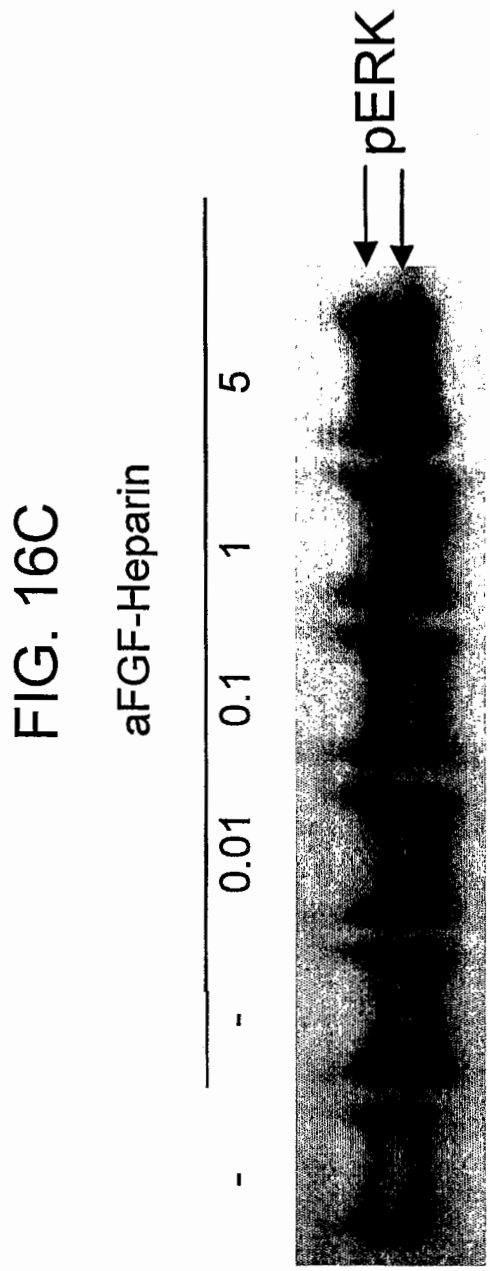


FIG. 17

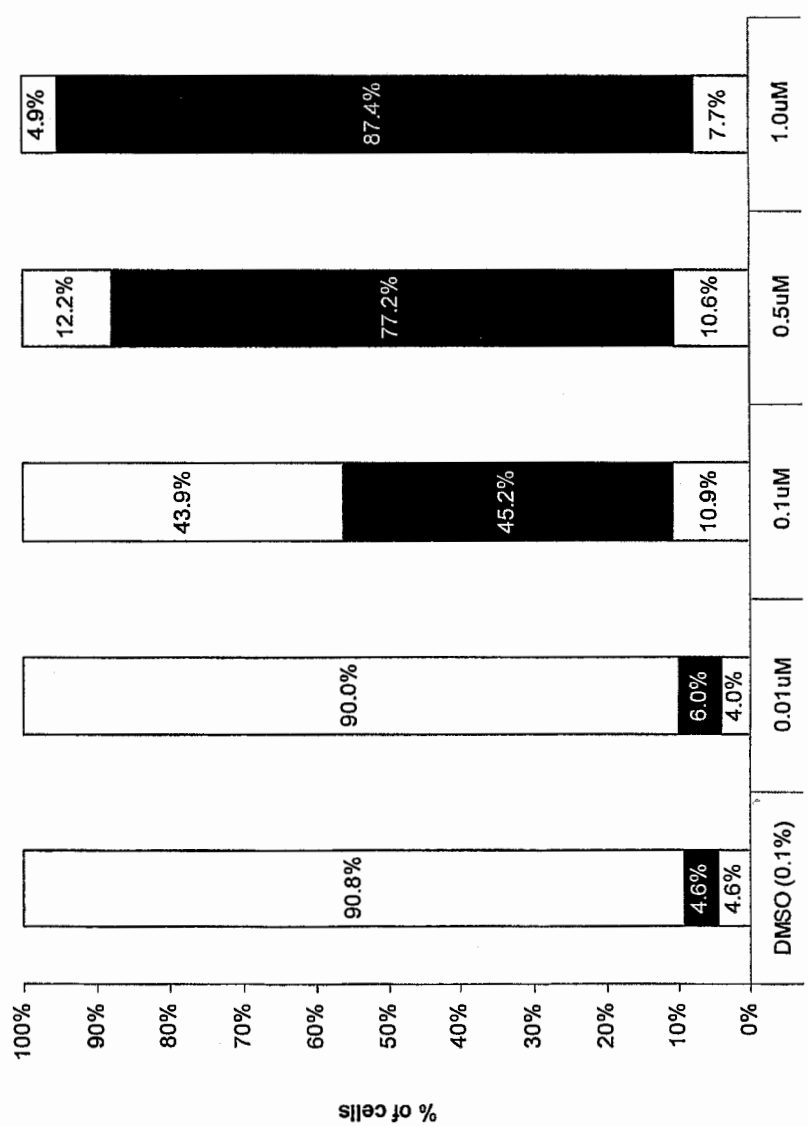

Annexin(-) 7-AAD(-) Non-Apoptotic
Annexin(-) 7-AAD(+) Incompletely stained cells, free nuclei, cell debris
Annexin(+) 7-AAD(+) Late Stage Apoptotic, Necrotic, Dead
Annexin(+) 7-AAD(-) Early Stage Apoptotic
% of cells
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
DMSO (0.1%)
0.01uM
0.1uM
0.5uM
1.0uM
90.8%
4.6%
4.6%
90.0%
6.0%
4.0%
43.9%
45.2%
10.9%
12.2%
77.2%
10.6%
4.9%
87.4%
7.7%

FIG. 18

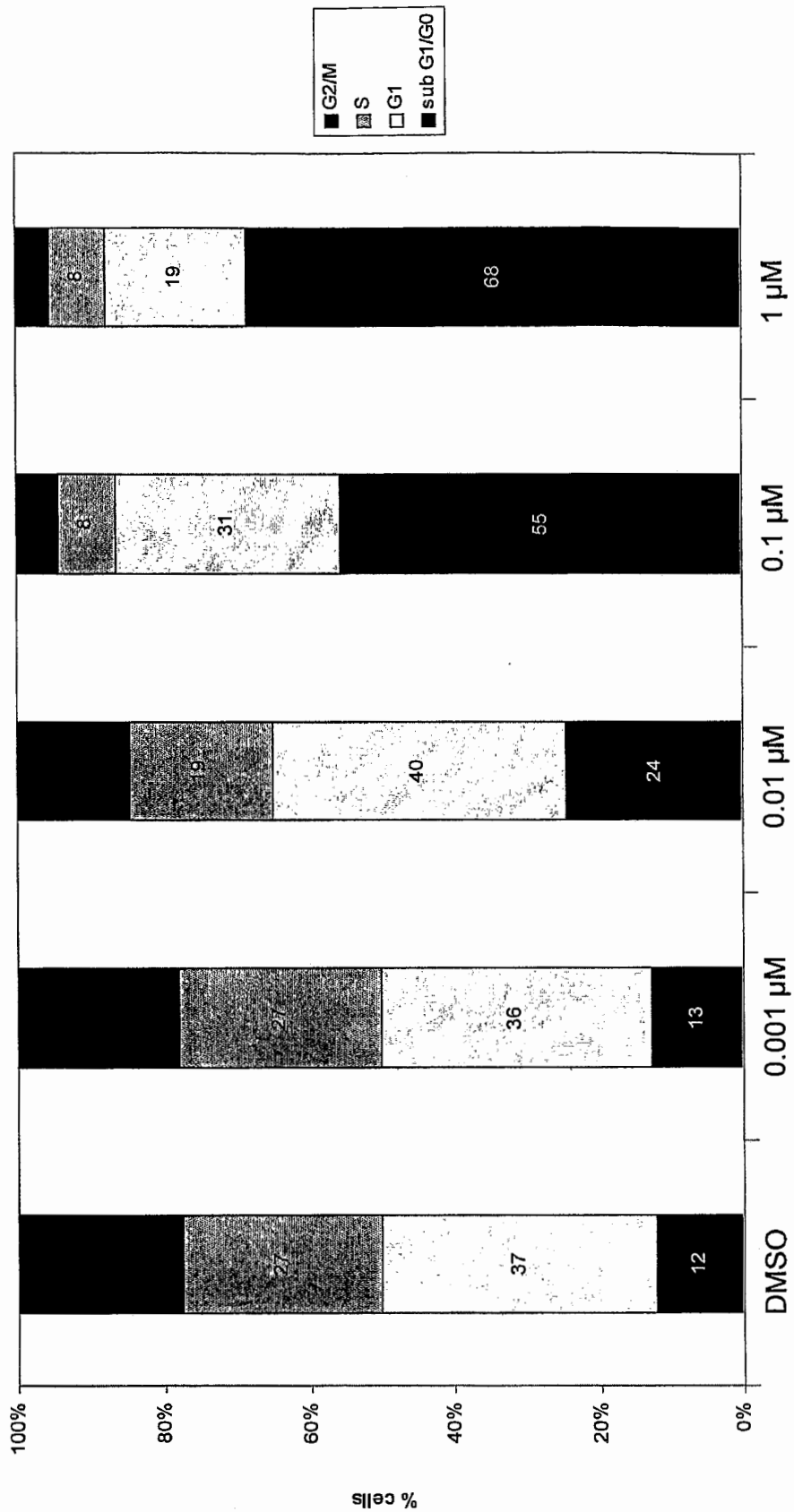

G2/M
S
G1
sub G1/G0
% cells
100%
80%
60%
40%
20%
0%
DMSO
0.001 µM
0.01 µM
0.1 µM
1 µM
12
37
27
13
36
40
19
24
8
31
55
8
19
68

FIG. 19

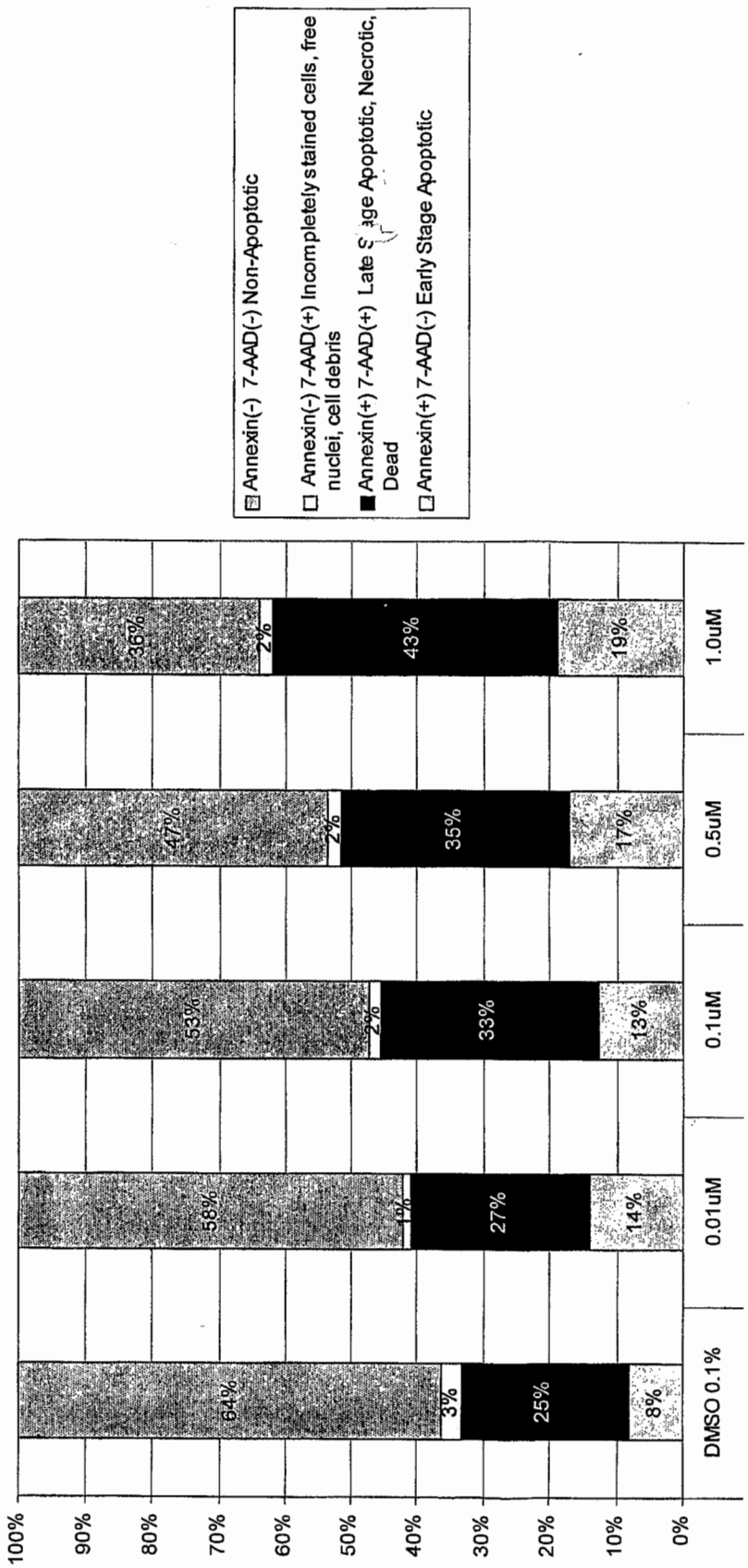

Annexin(-) 7-AAD(-) Non-Apoptotic
Annexin(-) 7-AAD(+) Incompletely stained cells, free nuclei, cell debris
Annexin(+) 7-AAD(+) Late Stage Apoptotic, Necrotic, Dead
Annexin(+) 7-AAD(-) Early Stage Apoptotic
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
DMSO 0.1%
0.01uM
0.1uM
0.5uM
1.0uM
64%
3%
25%
8%
58%
1%
27%
14%
53%
2%
33%
13%
47%
2%
35%
17%
36%
2%
43%
19%

FIG. 20

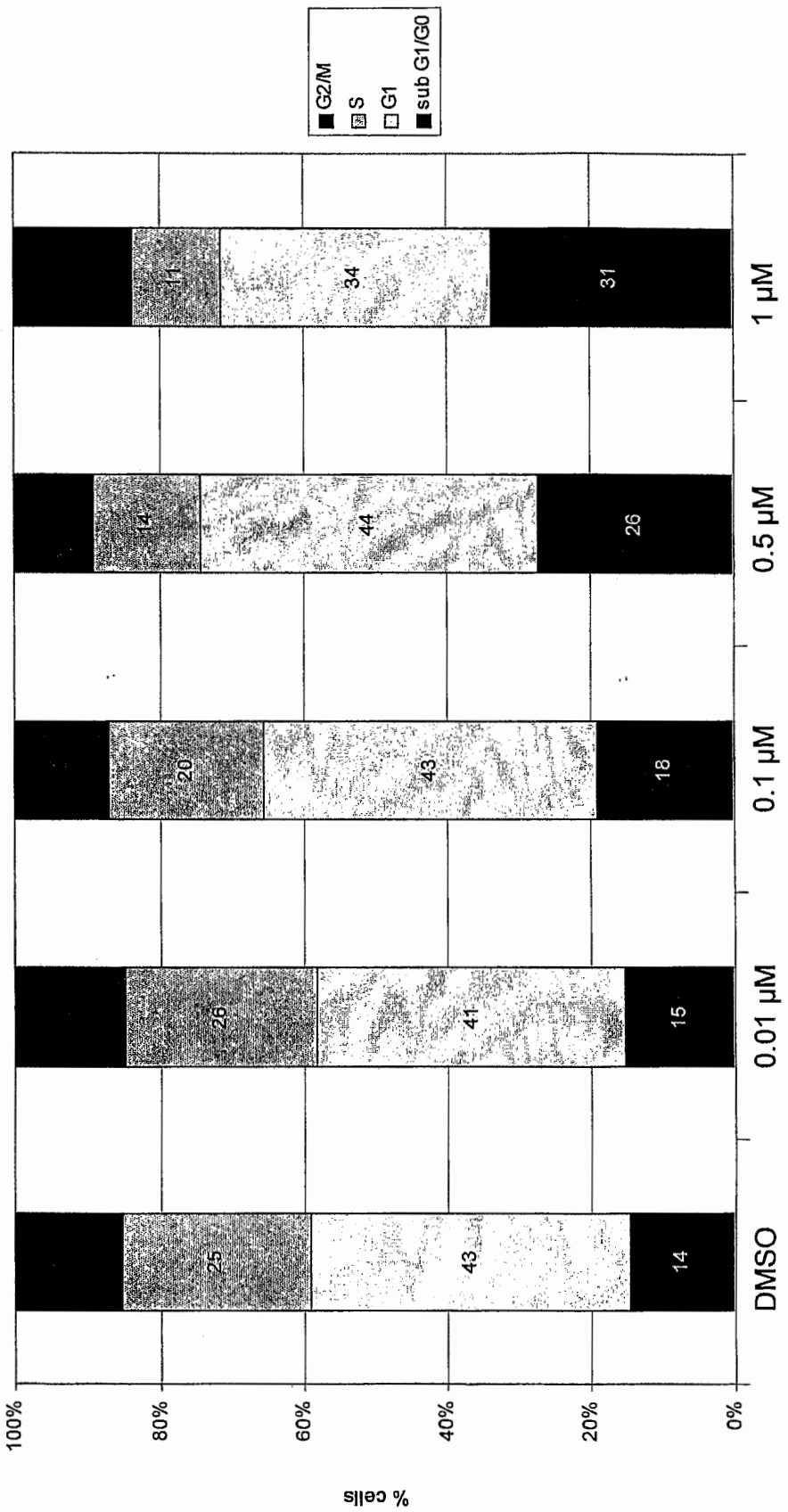

G2/M
S
G1
sub G1/G0
100%
80%
60%
40%
20%
0%
% cells
DMSO
0.01 µM
0.1 µM
0.5 µM
1 µM
14
25
43
15
26
41
18
20
43
26
14
44
31
11
34

FIG. 21

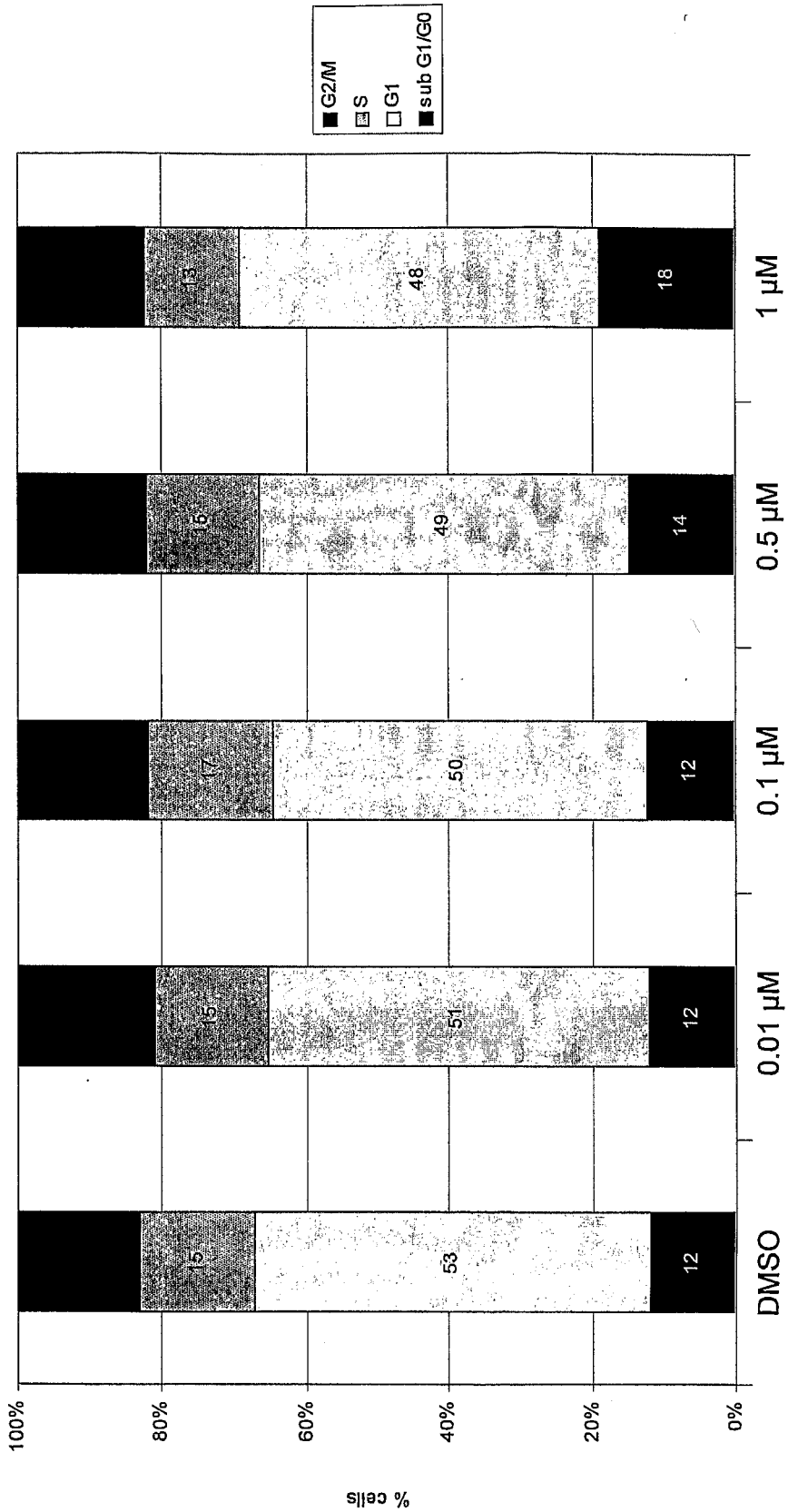
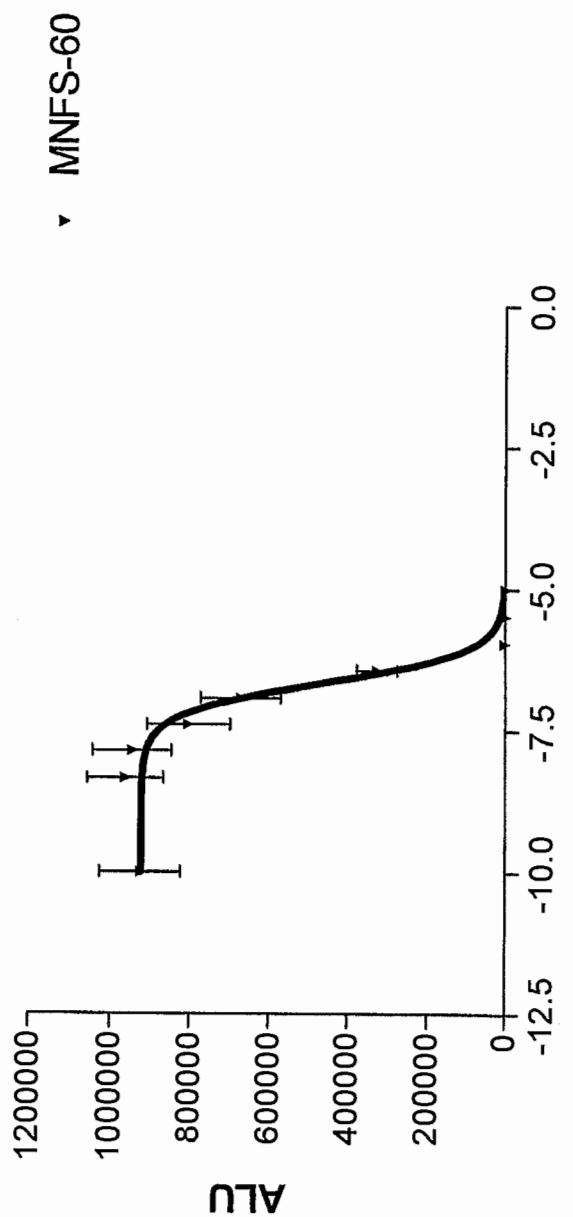

G2/M
S
G1
sub G1/G0
% cells
100%
80%
60%
40%
20%
0%
DMSO
0.01 µM
0.1 µM
0.5 µM
1 µM
12
15
53
12
12
15
51
12
12
17
50
12
14
15
49
14
18
13
48
18

FIG. 22



BOTTOM (CONSTANT)	992.0
TOP (Constant)	924783
LOG EC_{50}	-6.651
HILLSLOPE	-1.561
EC_{50}	2.2350e-007

FIG. 23

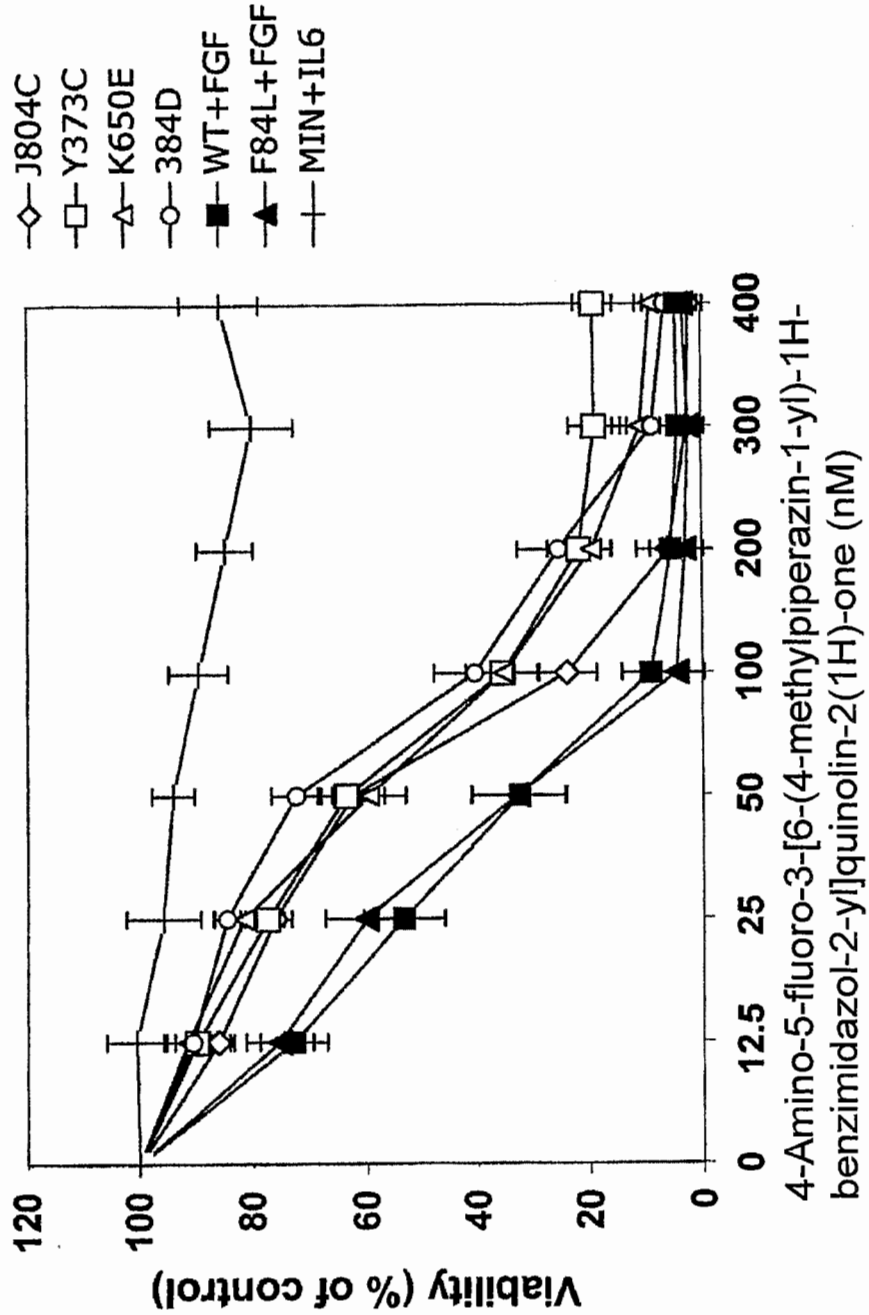

J804C
Y373C
K650E
384D
WT+FGF
F84L+FGF
MIN+IL6
Viability (% of control)
120
100
80
60
40
20
0
0
12.5
25
50
100
200
300
400
4-Amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one (nM)

FIG. 24

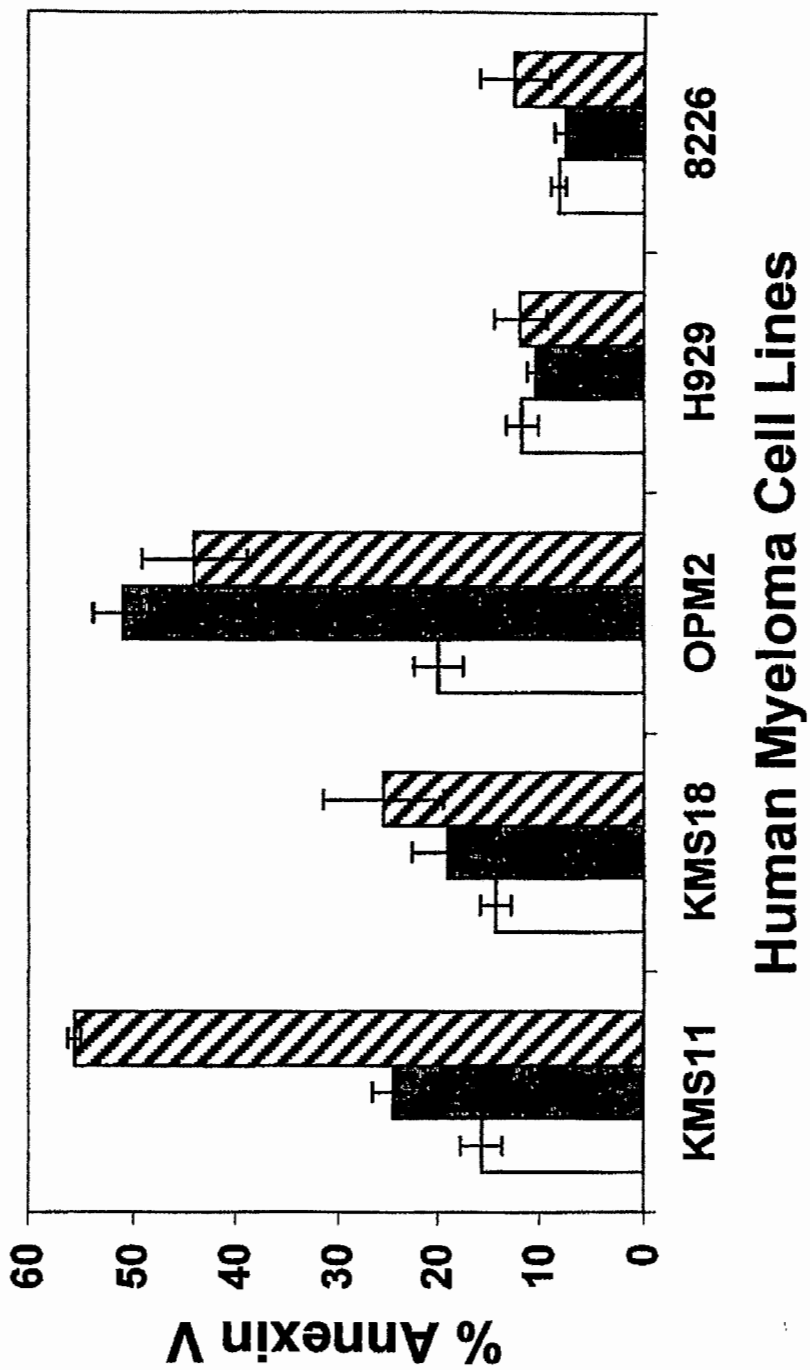
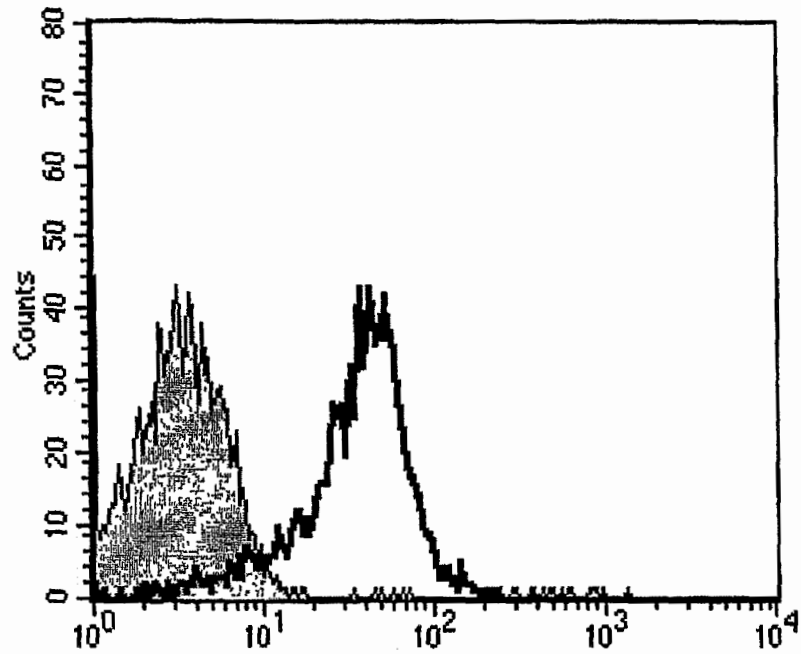
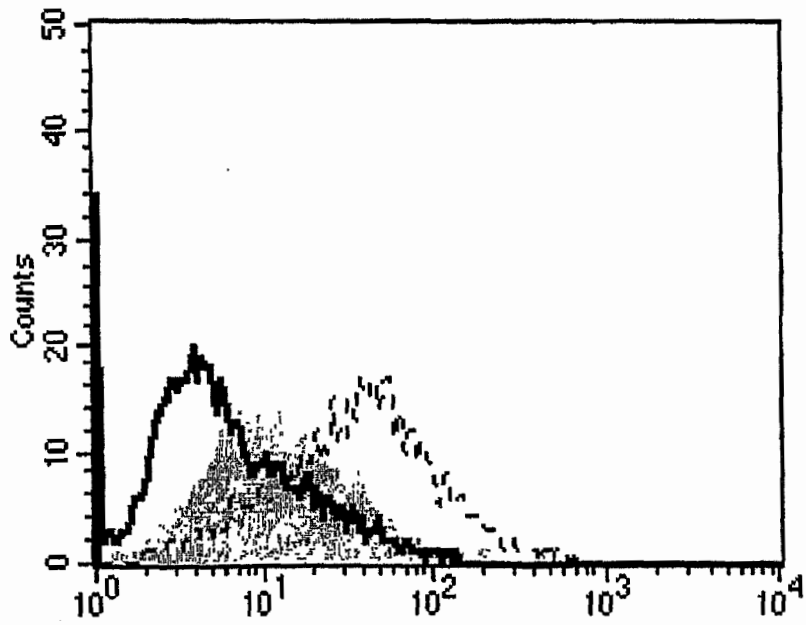

% Annexin V
60
50
40
30
20
10
0
KMS11
KMS18
OPM2
H929
8226
Human Myeloma Cell Lines

FIG. 25A



FGFR3

FIG. 25B



p-ERK1/2

FIG. 25C

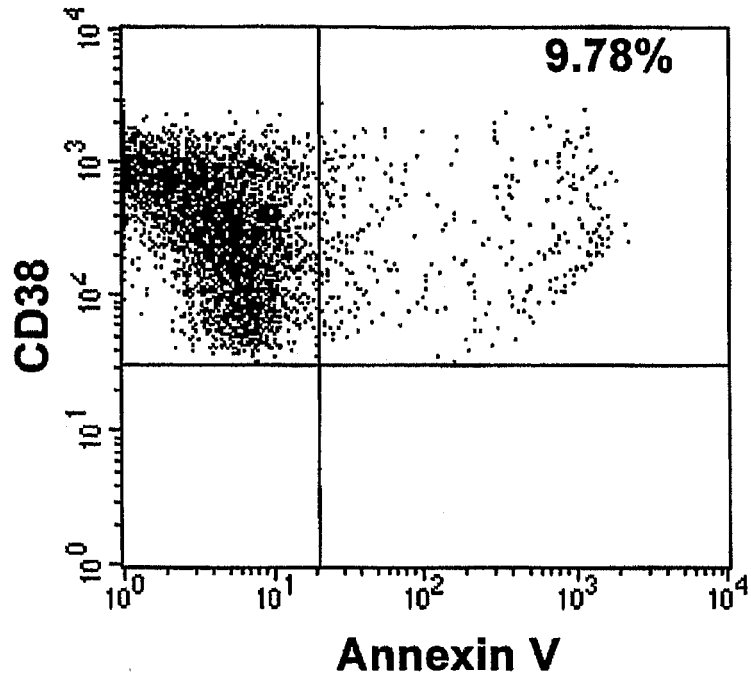


FIG. 25D

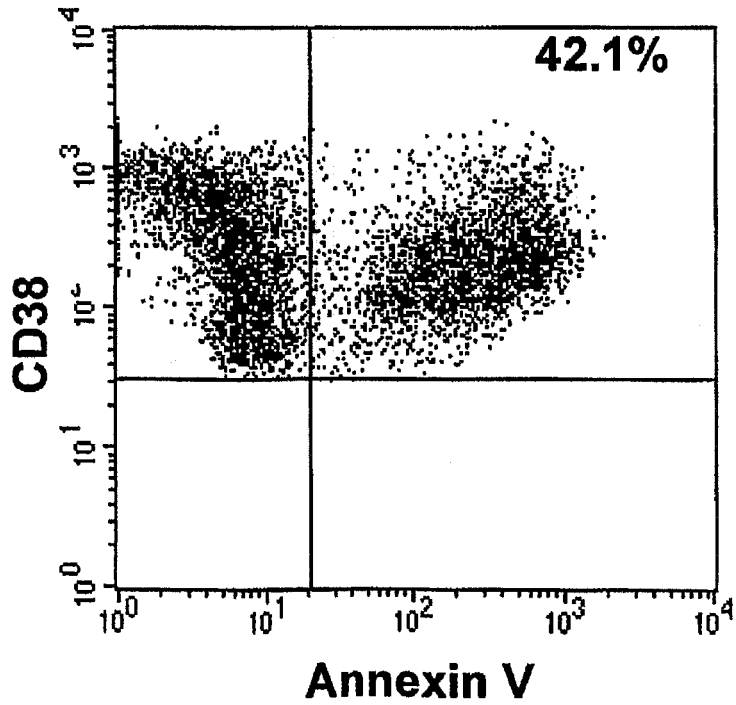


FIG. 26A

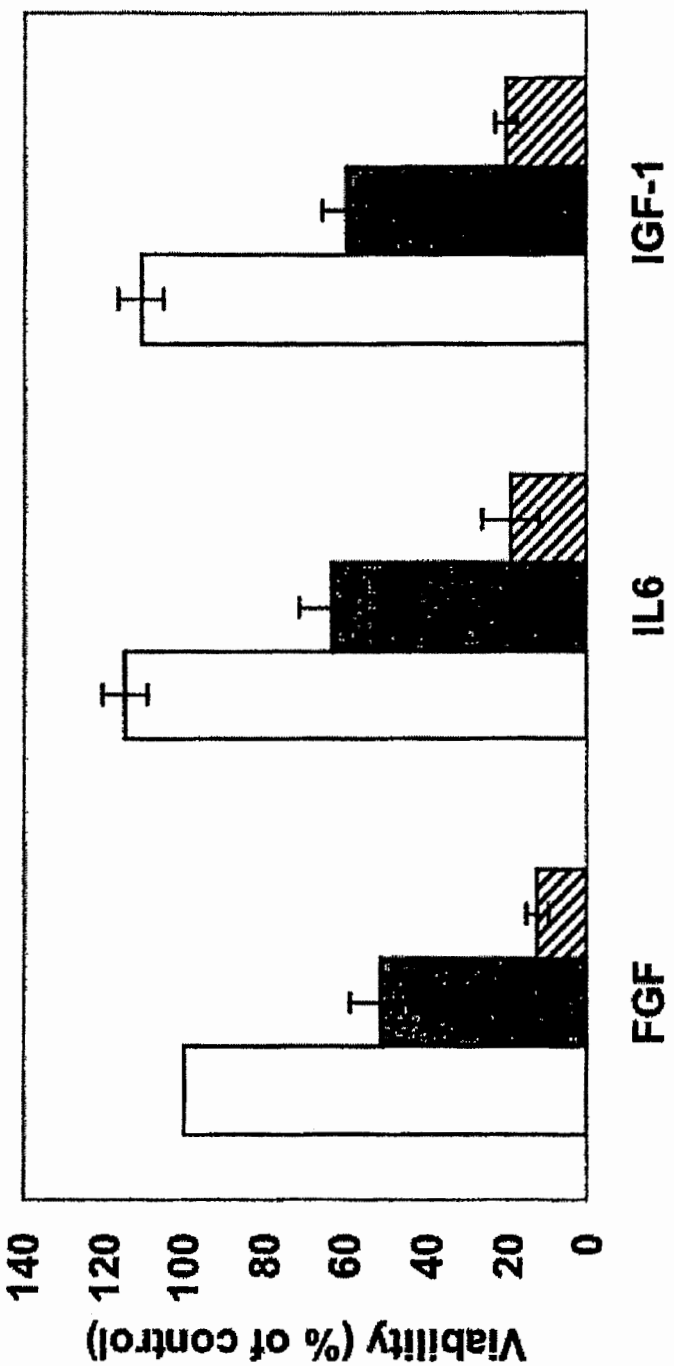


FIG. 26B

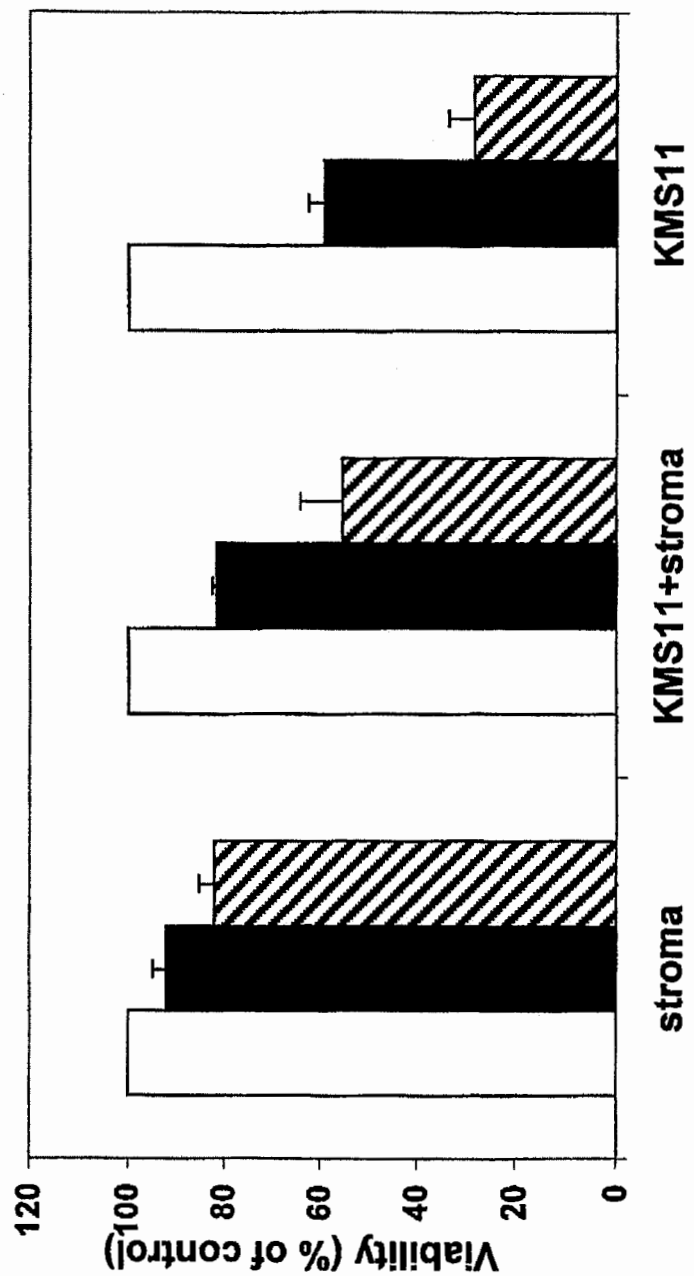

Viability (% of control)
120
100
80
60
40
20
0
stroma
KMS11+stroma
KMS11

FIG. 27

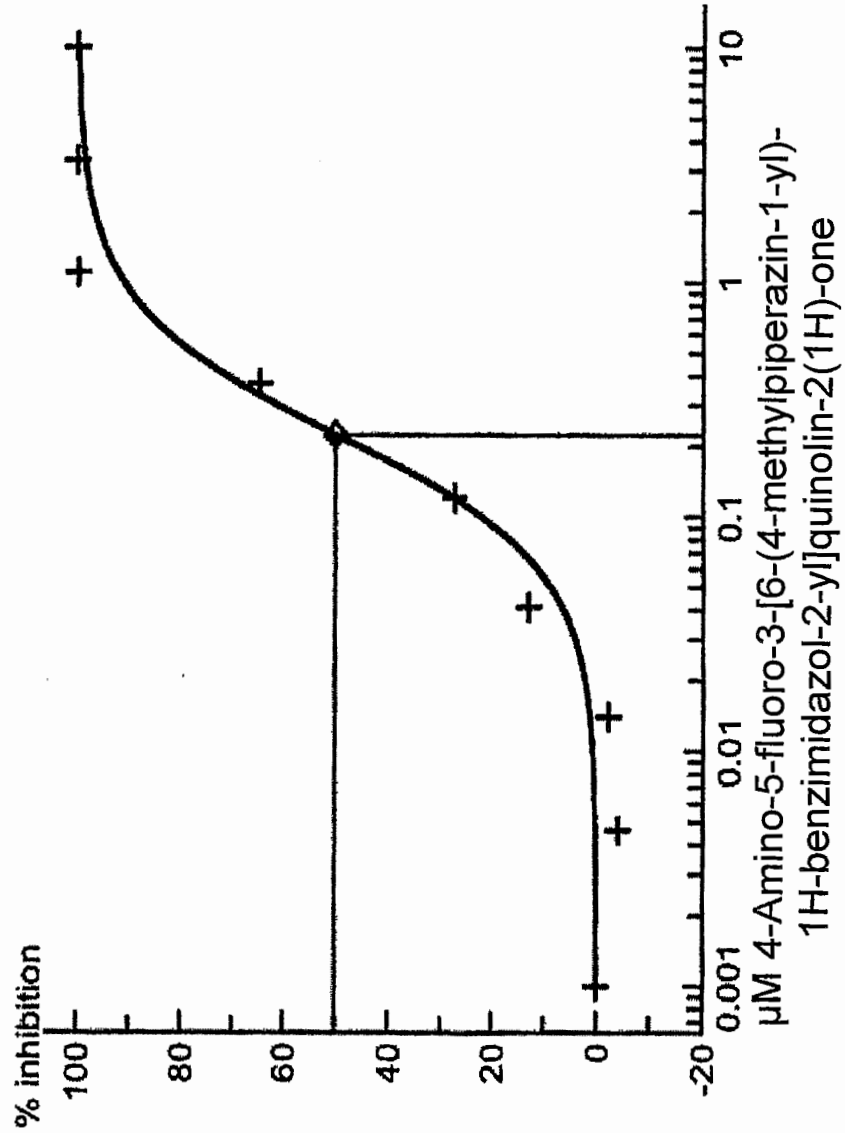

% inhibition
100
80
60
40
20
0
-20
0.001
0.01
0.1
1
10
μM 4-Amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one

FIG. 28

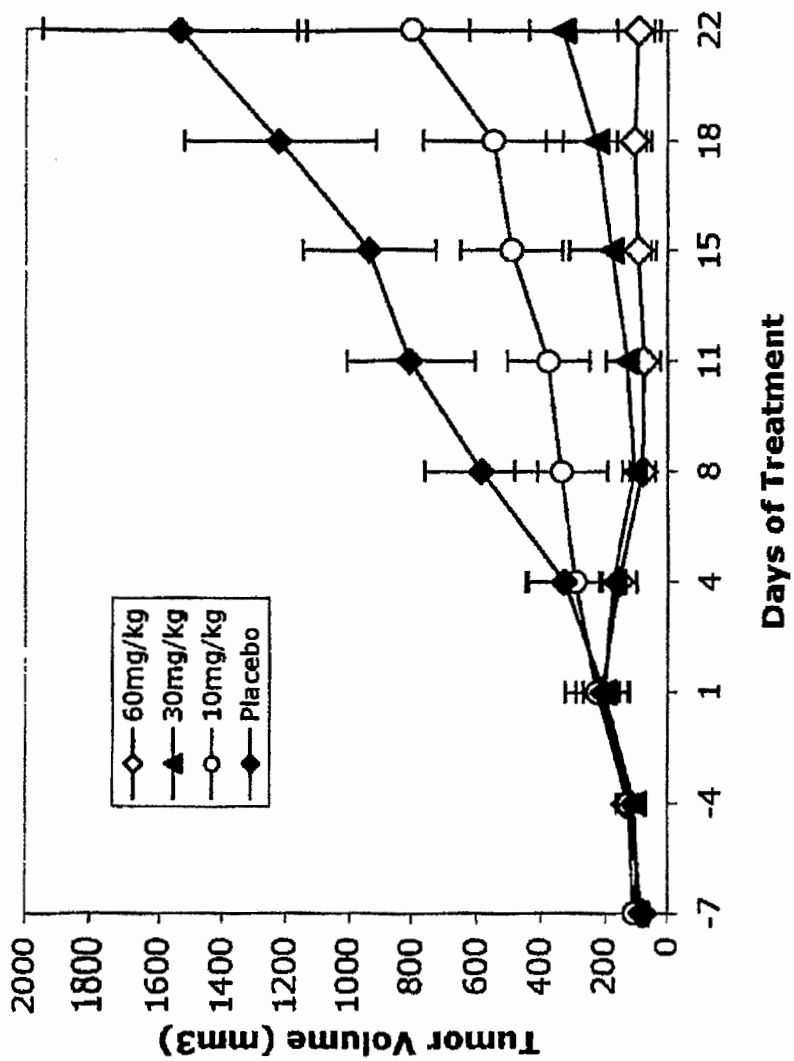

Tumor Volume (mm3)
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-7
-4
1
4
8
11
15
18
22
Days of Treatment
60mg/kg
30mg/kg
10mg/kg
Placebo

FIG. 29

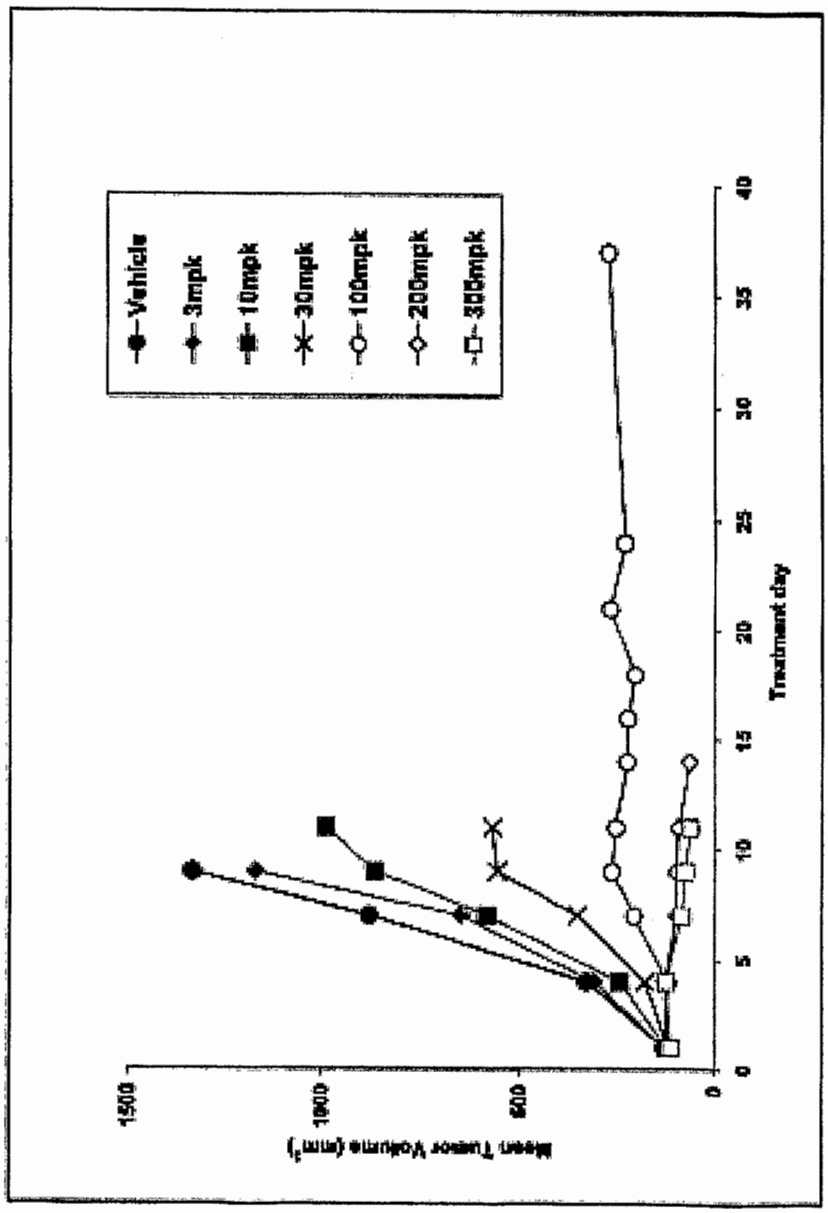
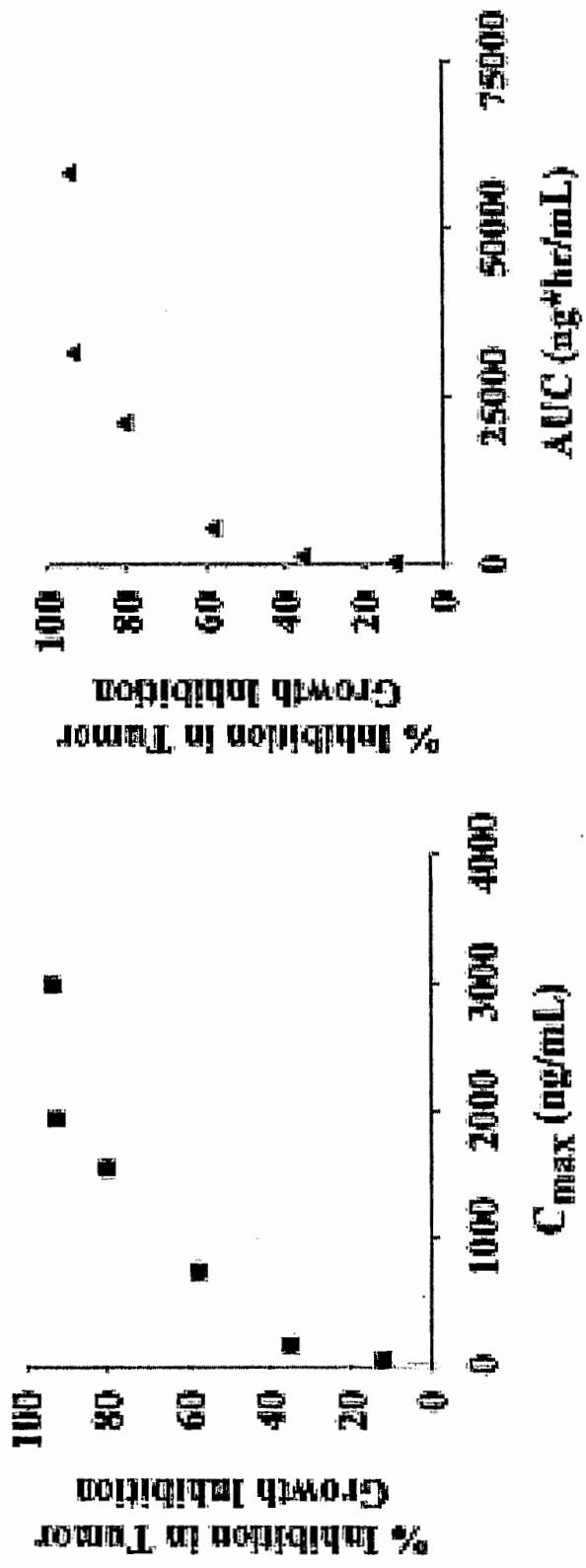

Vehicle
3mpk
10mpk
30mpk
100mpk
200mpk
300mpk
Mean Tumor Volume (mm³)
1500
1000
500
0
0
5
10
15
20
25
30
35
40
Treatment day

FIG. 30


% Inhibition in Tumor Growth Inhibition
100
80
60
40
20
0
0
1000
2000
3000
4000
C_{max} (ng/mL)
% Inhibition in Tumor Growth Inhibition
100
80
60
40
20
0
0
25000
50000
75000
AUC (ng*hr/mL)