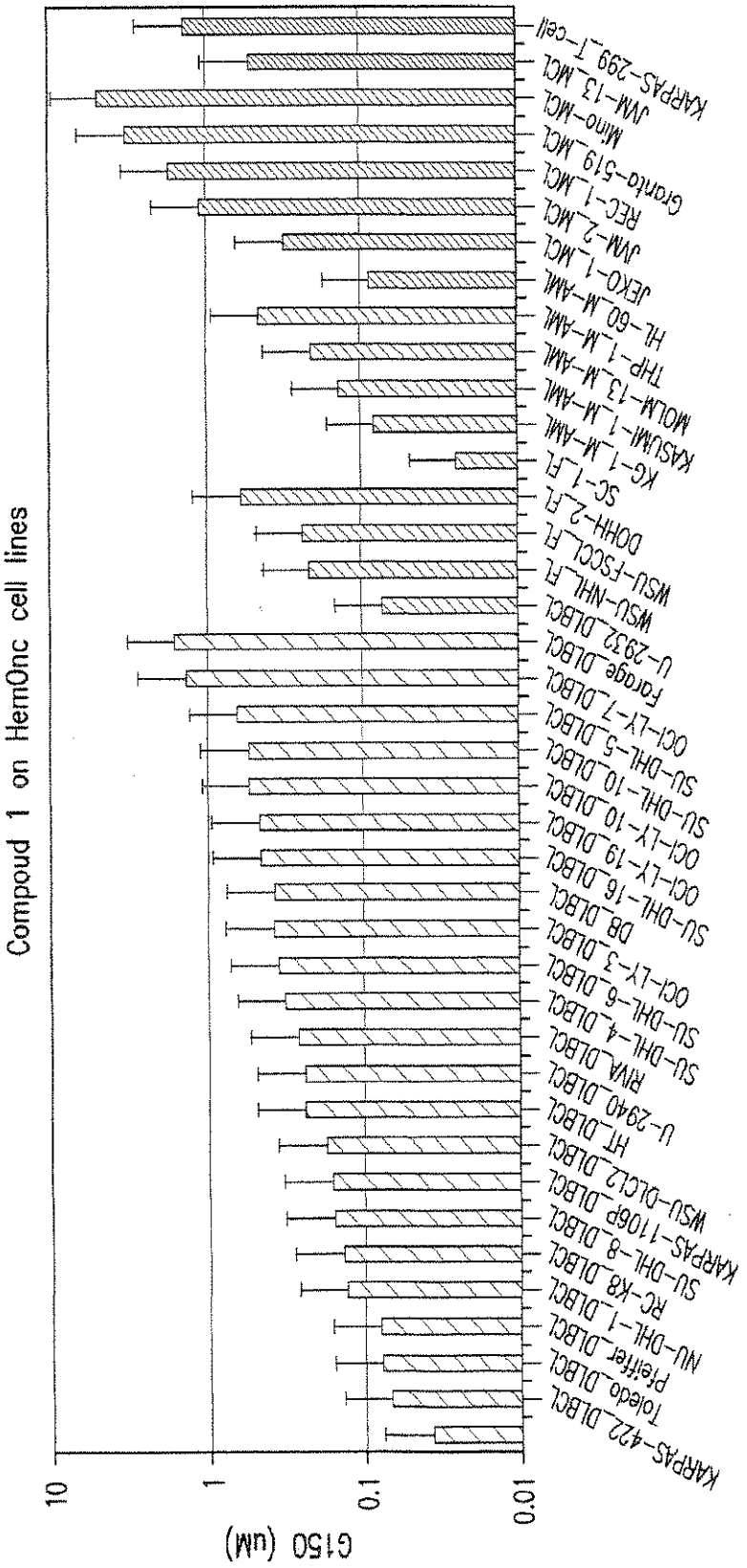

Compoud 1 on HemOnc cell lines
GI50 (uM)
10
1
0.1
0.01
KARPAS-422_DLBCL
Toledo_DLBCL
Pfeiffer_DLBCL
NU-DHL-1_DLBCL
RC-K8_DLBCL
SU-DHL-8_DLBCL
KARPAS-1106P_DLBCL
WSU-DLCL2_DLBCL
HT_DLBCL
U-2940_DLBCL
RIVA_DLBCL
SU-DHL-4_DLBCL
SU-DHL-6_DLBCL
OCI-LY-3_DLBCL
DB_DLBCL
SU-DHL-16_DLBCL
OCI-LY-19_DLBCL
OCI-LY-10_DLBCL
SU-DHL-10_DLBCL
SU-DHL-5_DLBCL
OCI-LY-7_DLBCL
Farage_DLBCL
U-2932_DLBCL
WSU-NHL_FL
WSU-FSCCL_FL
DOHH-2_FL
SC-1_FL
KG-1_M-AML
KASUMI-1_M-AML
MOLM-13_M-AML
THP-1_M-AML
HL-60_M-AML
JEKO-1_MCL
JVM-2_MCL
REC-1_MCL
Granta-519_MCL
Mino_MCL
JVM-13_MCL
KARPAS-299_T-cell

FIG. 1A

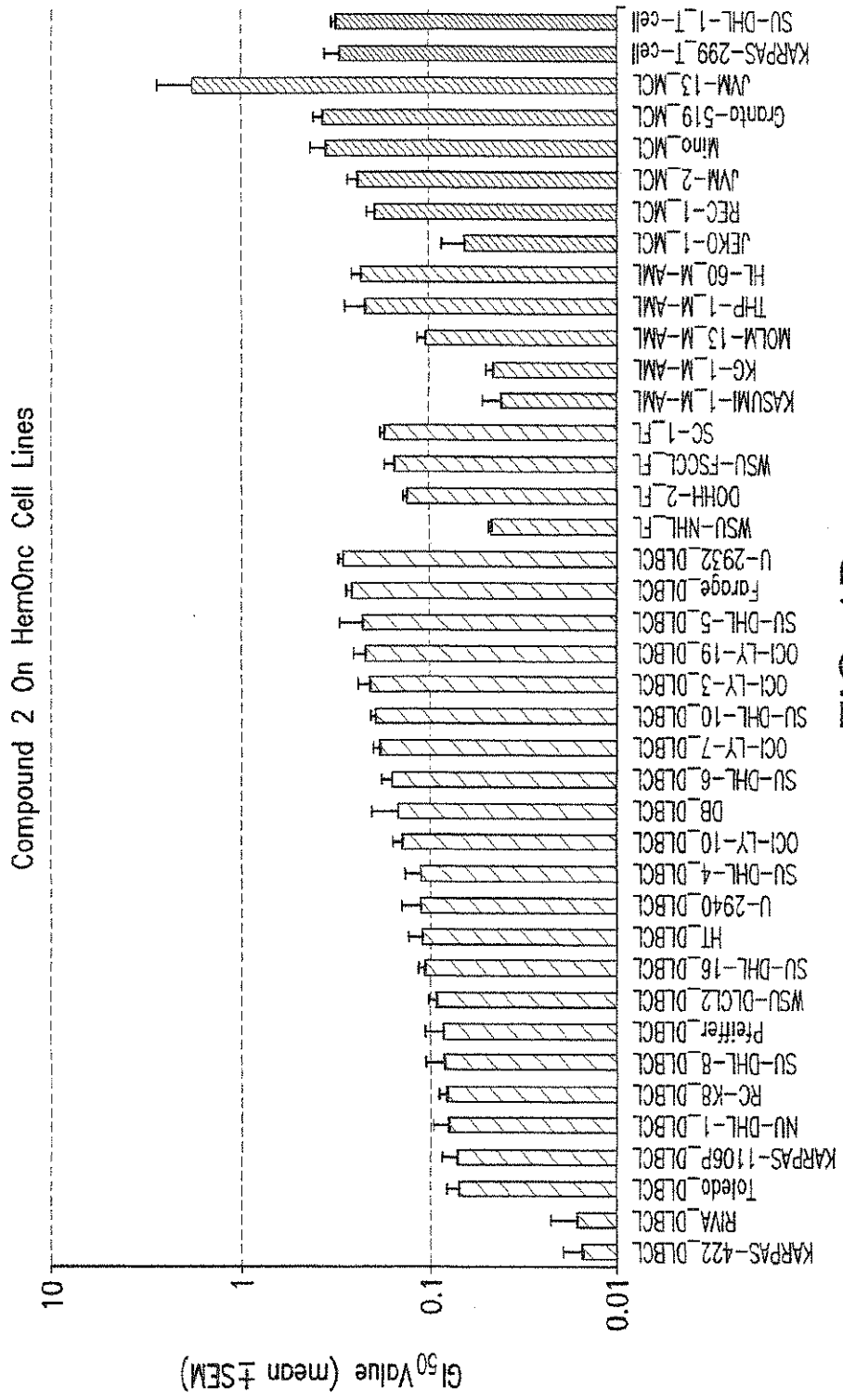

Compound 2 On HemOnc Cell Lines
GI50 Value (mean ±SEM)
10
1
0.1
0.01
KARPAS-422_DLBCL
RIVA_DLBCL
Toledo_DLBCL
KARPAS-1106P_DLBCL
NU-DHL-1_DLBCL
RC-K8_DLBCL
SU-DHL-8_DLBCL
Pfeiffer_DLBCL
WSU-DLCL2_DLBCL
SU-DHL-16_DLBCL
HT_DLBCL
U-2940_DLBCL
SU-DHL-4_DLBCL
OCI-LY-10_DLBCL
DB_DLBCL
SU-DHL-6_DLBCL
OCI-LY-7_DLBCL
SU-DHL-10_DLBCL
OCI-LY-3_DLBCL
OCI-LY-19_DLBCL
SU-DHL-5_DLBCL
Farage_DLBCL
U-2932_DLBCL
WSU-NHL_FL
DOHH-2_FL
WSU-FSCCL_FL
SC-1_FL
KASUMI-1_M-AML
KG-1_M-AML
MOLM-13_M-AML
THP-1_M-AML
HL-60_M-AML
JEKO-1_MCL
REC-1_MCL
JVM-2_MCL
Mino_MCL
Granta-519_MCL
JVM-13_MCL
KARPAS-299_T-cell
SU-DHL-1_T-cell

FIG. 1B

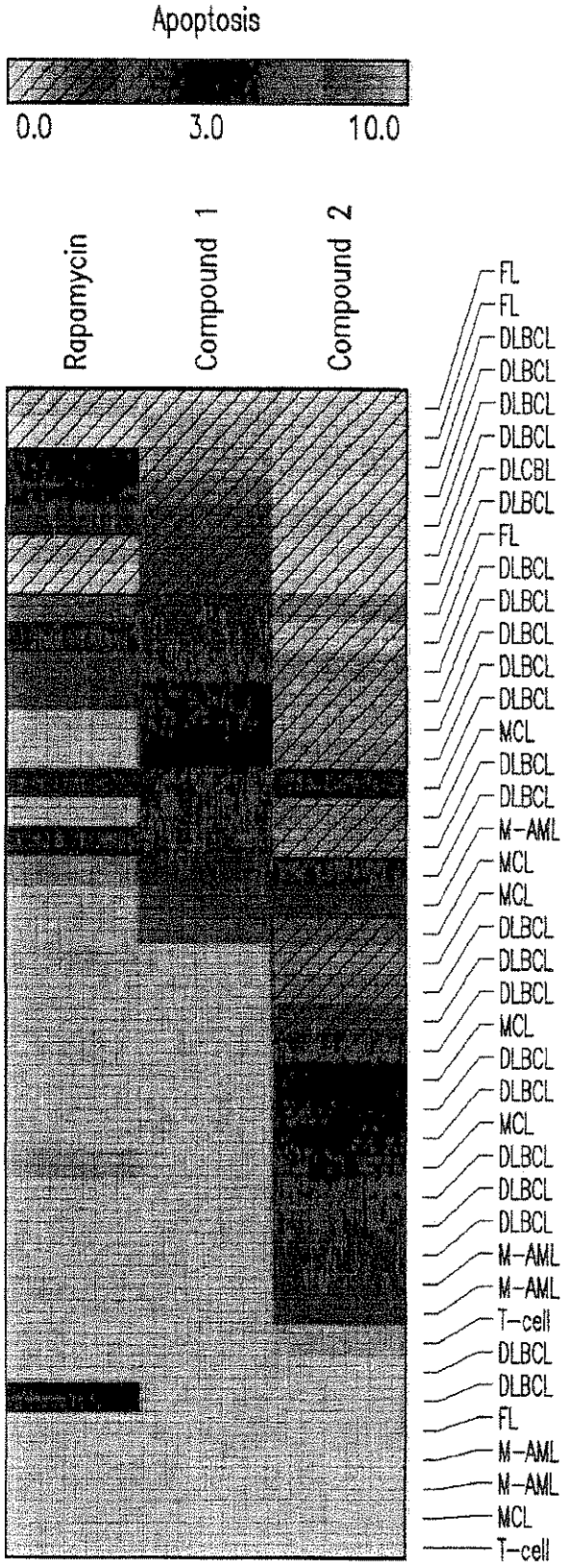

Apoptosis
0.0
3.0
10.0
Rapamycin
Compound 1
Compound 2
FL
FL
DLBCL
DLBCL
DLBCL
DLBCL
DLCBL
DLBCL
FL
DLBCL
DLBCL
DLBCL
DLBCL
DLBCL
MCL
DLBCL
DLBCL
M-AML
MCL
MCL
DLBCL
DLBCL
DLBCL
MCL
DLBCL
DLBCL
MCL
DLBCL
DLBCL
DLBCL
M-AML
M-AML
T-cell
DLBCL
DLBCL
FL
M-AML
M-AML
MCL
T-cell

FIG. 2

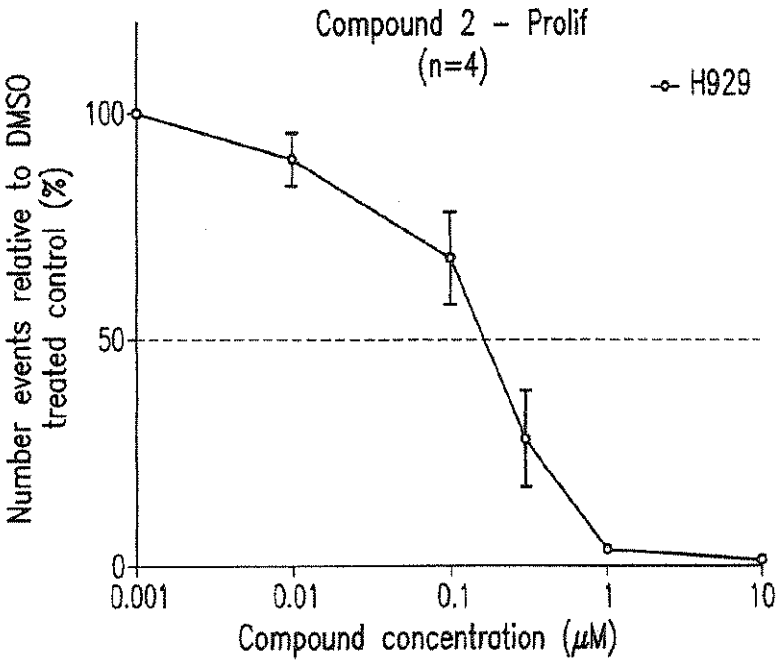

Compound 2 – Prolif
(n=4)
H929
Number events relative to DMSO treated control (%)
100
50
0
0.001
0.01
0.1
1
10
Compound concentration (μM)

FIG. 3A

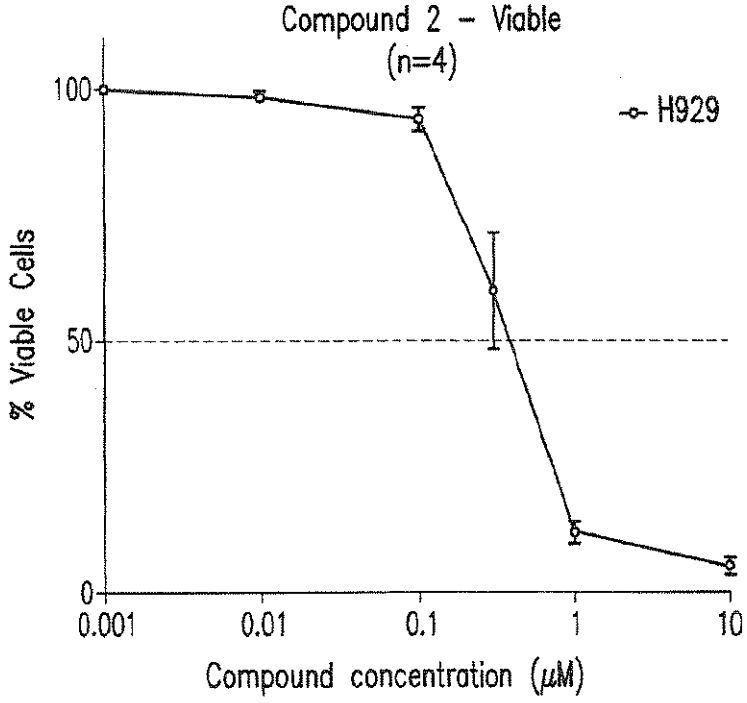

Compound 2 – Viable
(n=4)
H929
% Viable Cells
100
50
0
0.001
0.01
0.1
1
10
Compound concentration (μM)

FIG. 3B

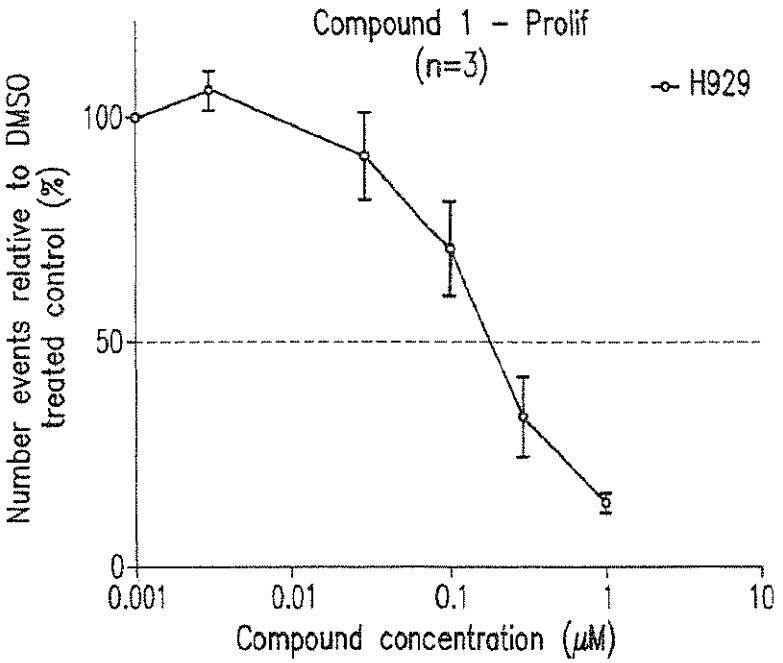

Compound 1 – Prolif
(n=3)
H929
Number events relative to DMSO treated control (%)
100
50
0
0.001
0.01
0.1
1
10
Compound concentration (μM)

FIG. 4A

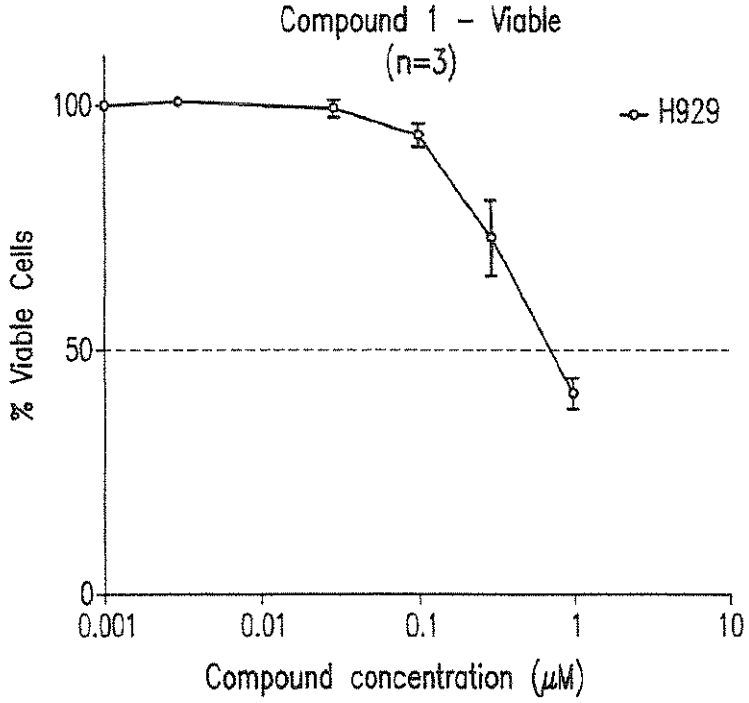

Compound 1 – Viable
(n=3)
H929
% Viable Cells
100
50
0
0.001
0.01
0.1
1
10
Compound concentration (μM)

FIG. 4B

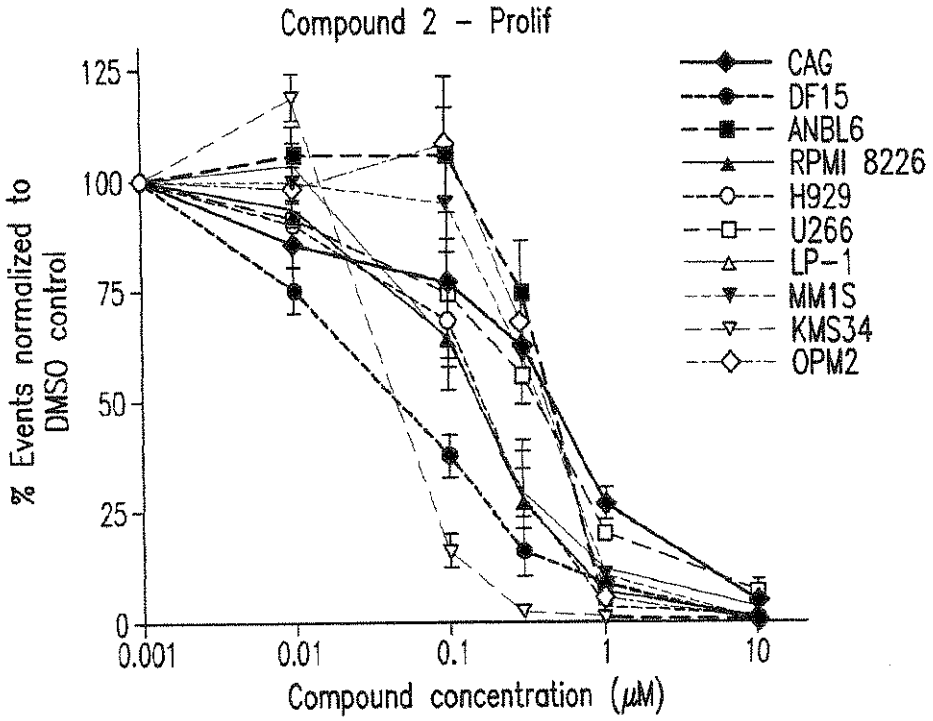

Compound 2 – Prolif
% Events normalized to DMSO control
125
100
75
50
25
0
0.001
0.01
0.1
1
10
Compound concentration (μM)
CAG
DF15
ANBL6
RPMI 8226
H929
U266
LP-1
MM1S
KMS34
OPM2

FIG. 5A

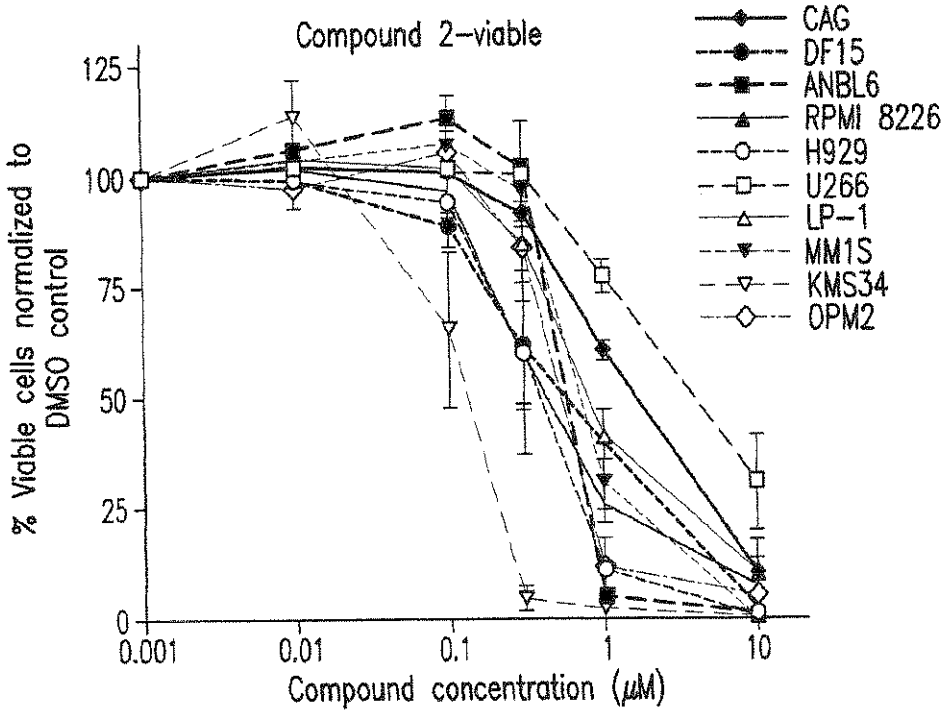

Compound 2–viable
% Viable cells normalized to DMSO control
125
100
75
50
25
0
0.001
0.01
0.1
1
10
Compound concentration (μM)
CAG
DF15
ANBL6
RPMI 8226
H929
U266
LP-1
MM1S
KMS34
OPM2

FIG. 5B

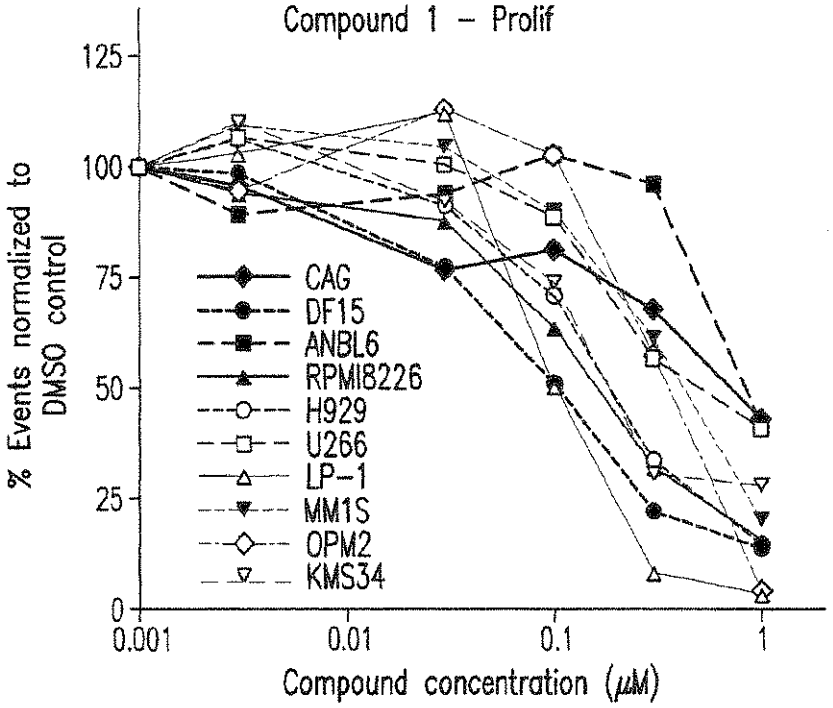

Compound 1 – Prolif
% Events normalized to DMSO control
125
100
75
50
25
0
0.001
0.01
0.1
1
Compound concentration (μM)
CAG
DF15
ANBL6
RPMI8226
H929
U266
LP-1
MM1S
OPM2
KMS34

FIG. 6A

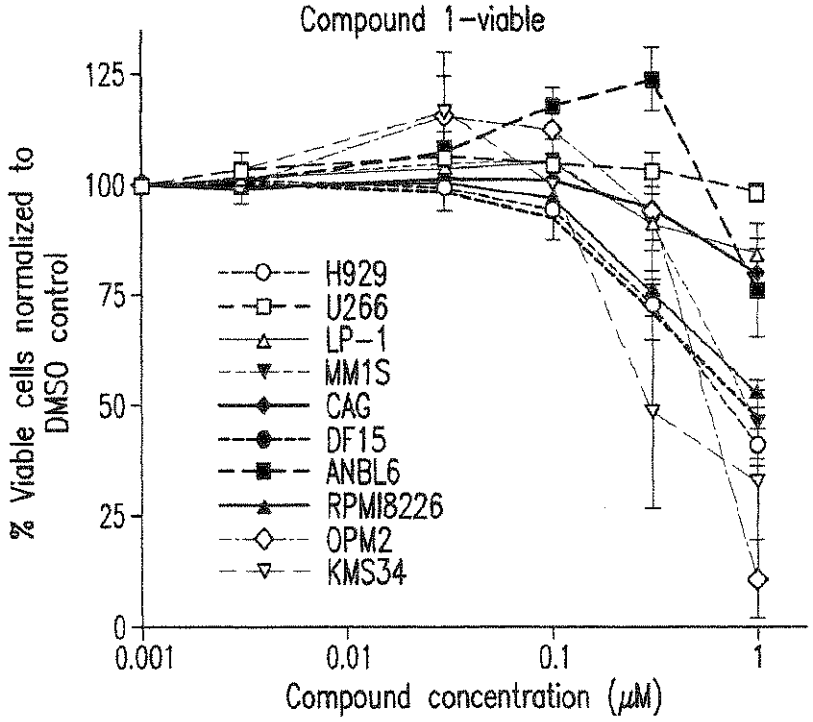

Compound 1–viable
% Viable cells normalized to DMSO control
125
100
75
50
25
0
0.001
0.01
0.1
1
Compound concentration (μM)
H929
U266
LP-1
MM1S
CAG
DF15
ANBL6
RPMI8226
OPM2
KMS34

FIG. 6B

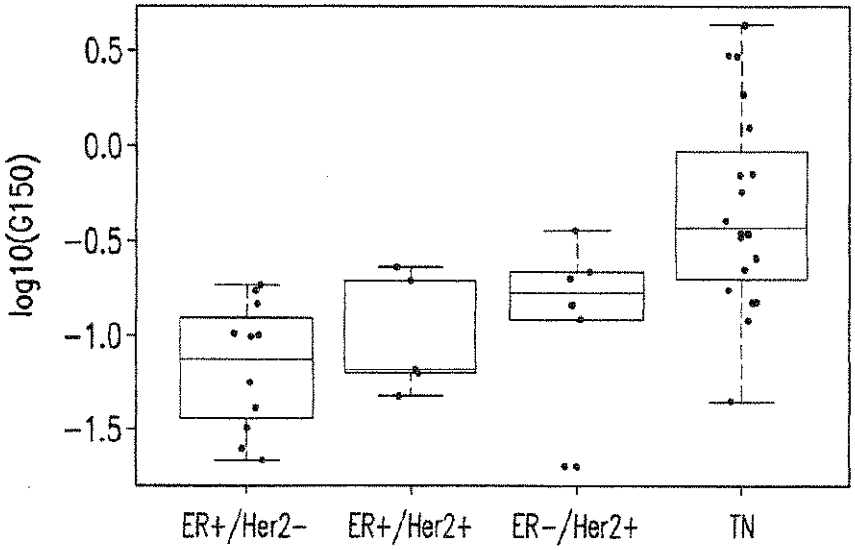

log10(G150)
0.5
0.0
−0.5
−1.0
−1.5
ER+/Her2−
ER+/Her2+
ER−/Her2+
TN

FIG. 7A

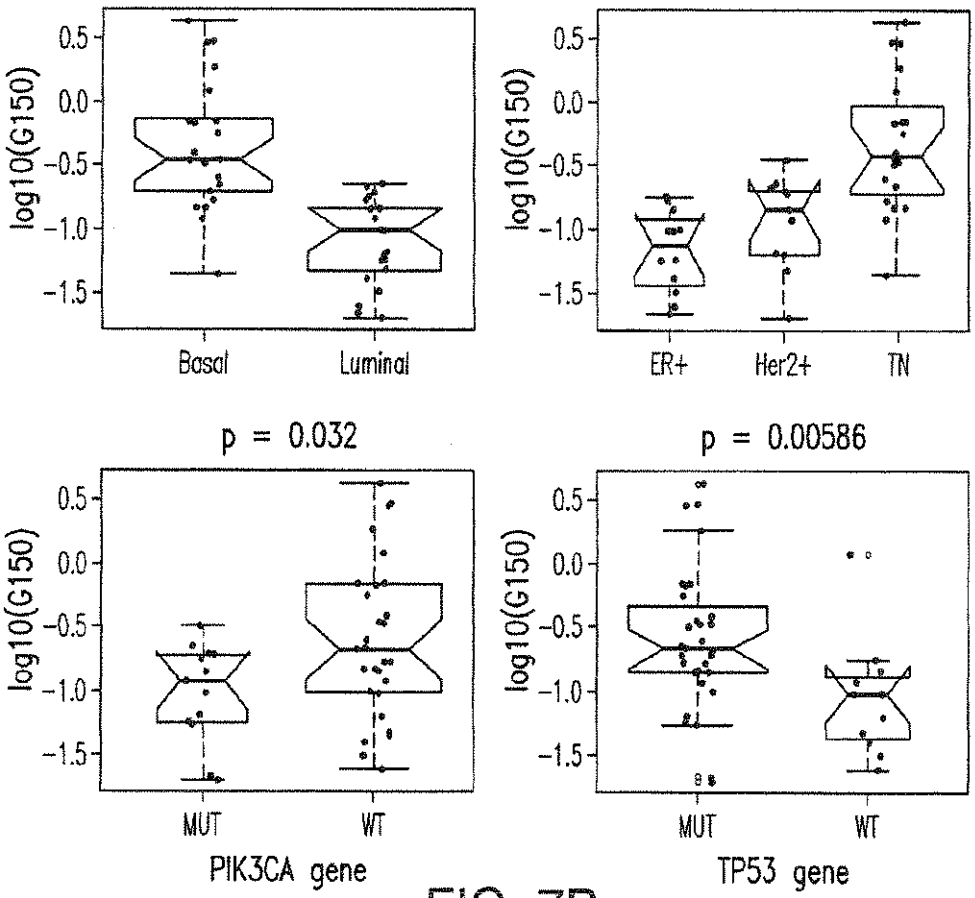

log10(G150)
Basal
Luminal
p = 0.032
ER+
Her2+
TN
p = 0.00586
MUT
WT
PIK3CA gene
TP53 gene

FIG. 7B

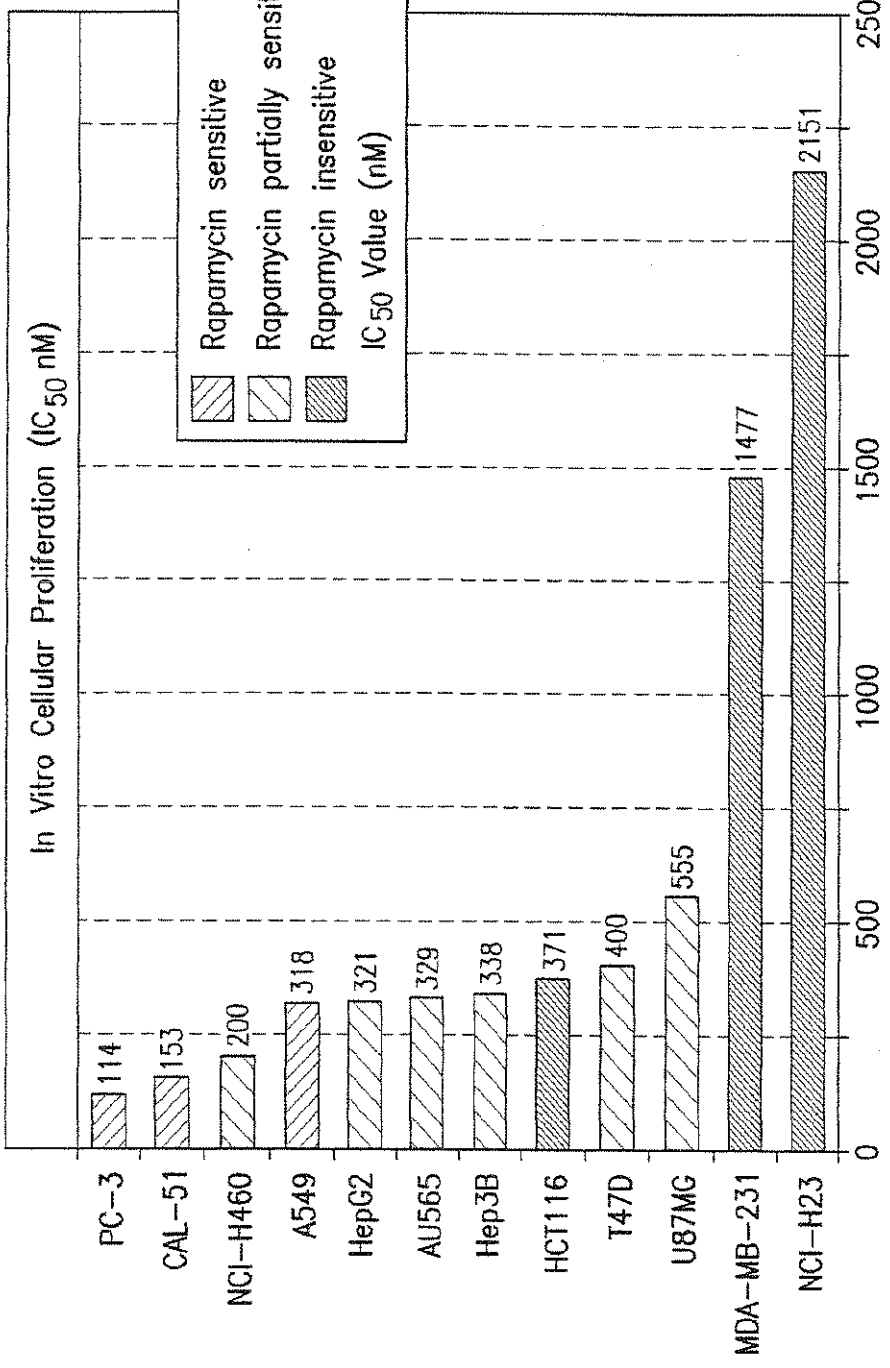

In Vitro Cellular Proliferation (IC50 nM)
Rapamycin sensitive
Rapamycin partially sensitive
Rapamycin insensitive
IC50 Value (nM)
PC-3
CAL-51
NCI-H460
A549
HepG2
AU565
Hep3B
HCT116
T47D
U87MG
MDA-MB-231
NCI-H23
114
153
200
318
321
329
338
371
400
555
1477
2151
0
500
1000
1500
2000
2500
Proliferation IC 50 (nM)

FIG. 8

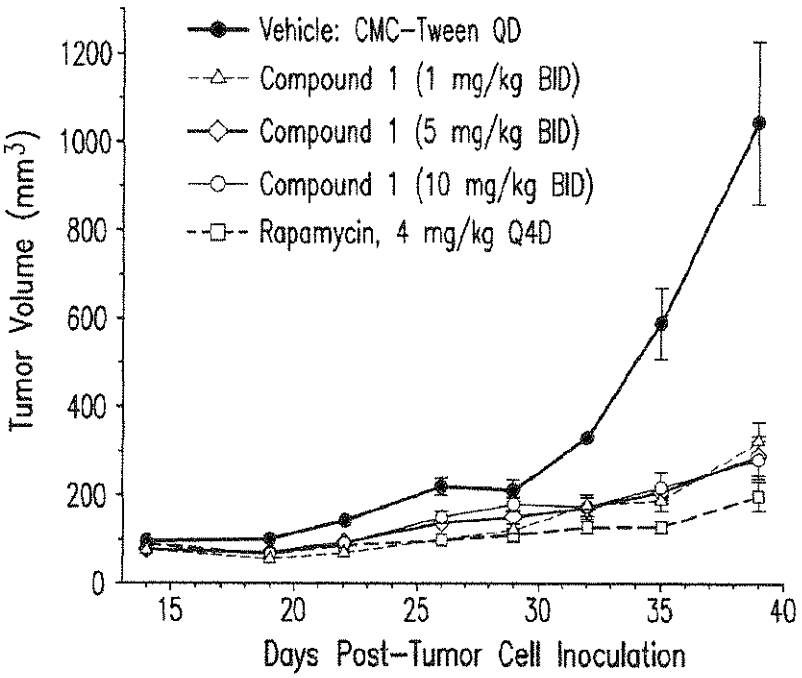

Vehicle: CMC-Tween QD
Compound 1 (1 mg/kg BID)
Compound 1 (5 mg/kg BID)
Compound 1 (10 mg/kg BID)
Rapamycin, 4 mg/kg Q4D
Tumor Volume (mm3)
0
200
400
600
800
1000
1200
15
20
25
30
35
40
Days Post-Tumor Cell Inoculation

FIG. 9

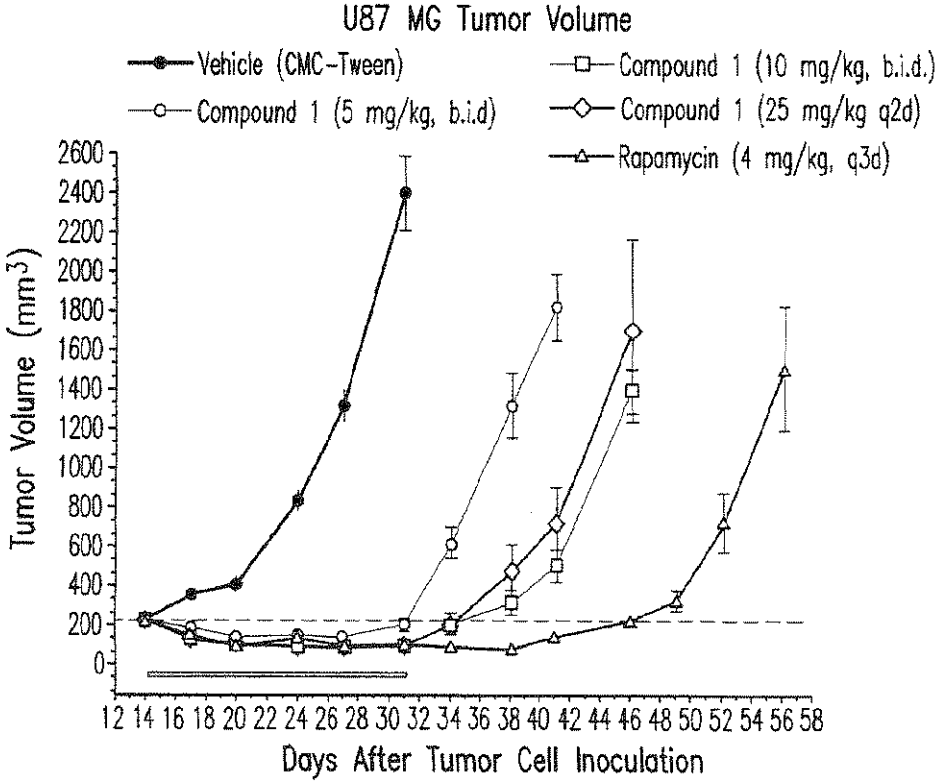

U87 MG Tumor Volume
Vehicle (CMC-Tween)
Compound 1 (5 mg/kg, b.i.d)
Compound 1 (10 mg/kg, b.i.d.)
Compound 1 (25 mg/kg q2d)
Rapamycin (4 mg/kg, q3d)
Tumor Volume (mm3)
0
200
400
600
800
1000
1200
1400
1600
1800
2000
2200
2400
2600
12 14 16 18 20 22 24 26 28 30 32 34 36 38 40 42 44 46 48 50 52 54 56 58
Days After Tumor Cell Inoculation

FIG. 10A

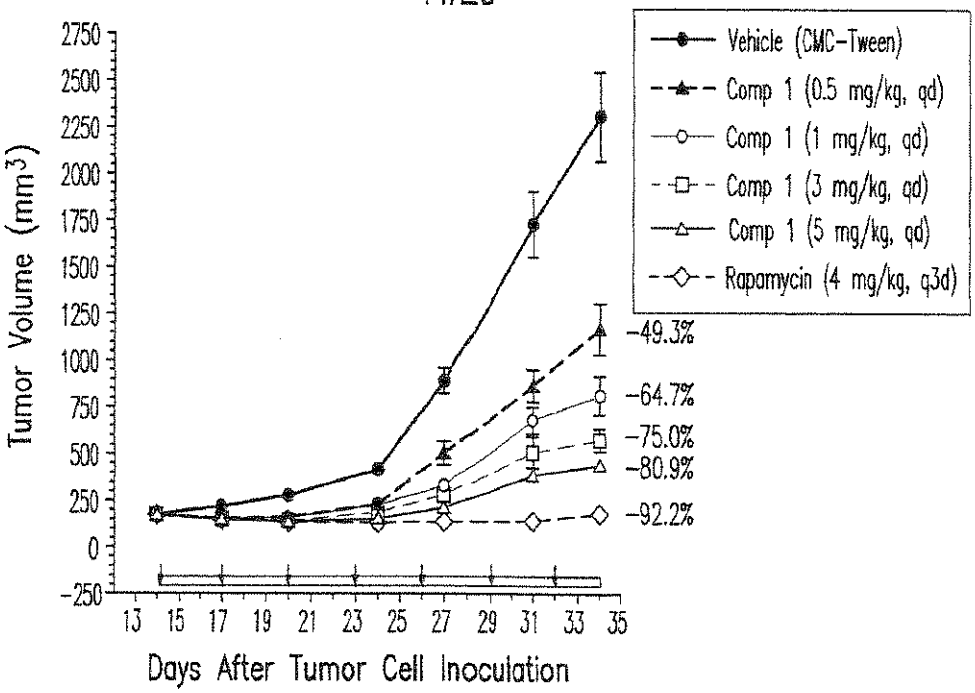


FIG. 10B

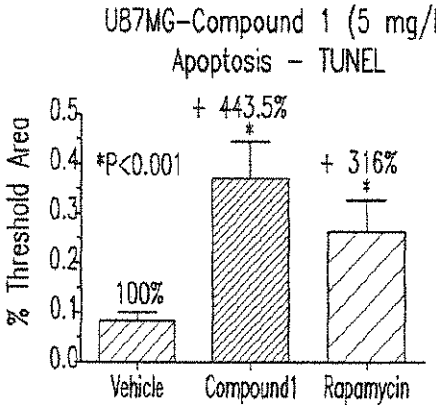


FIG. 10C

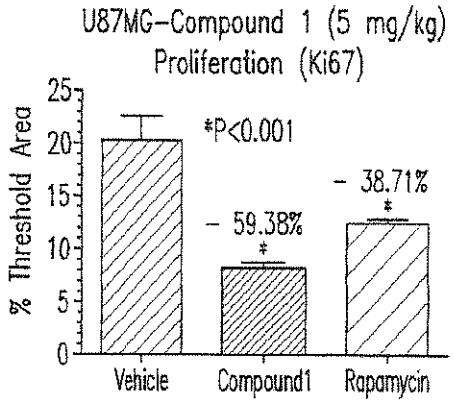


FIG. 10D

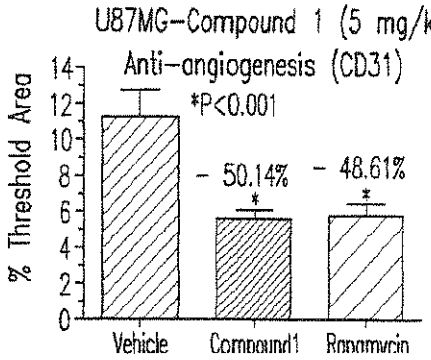


FIG. 10E

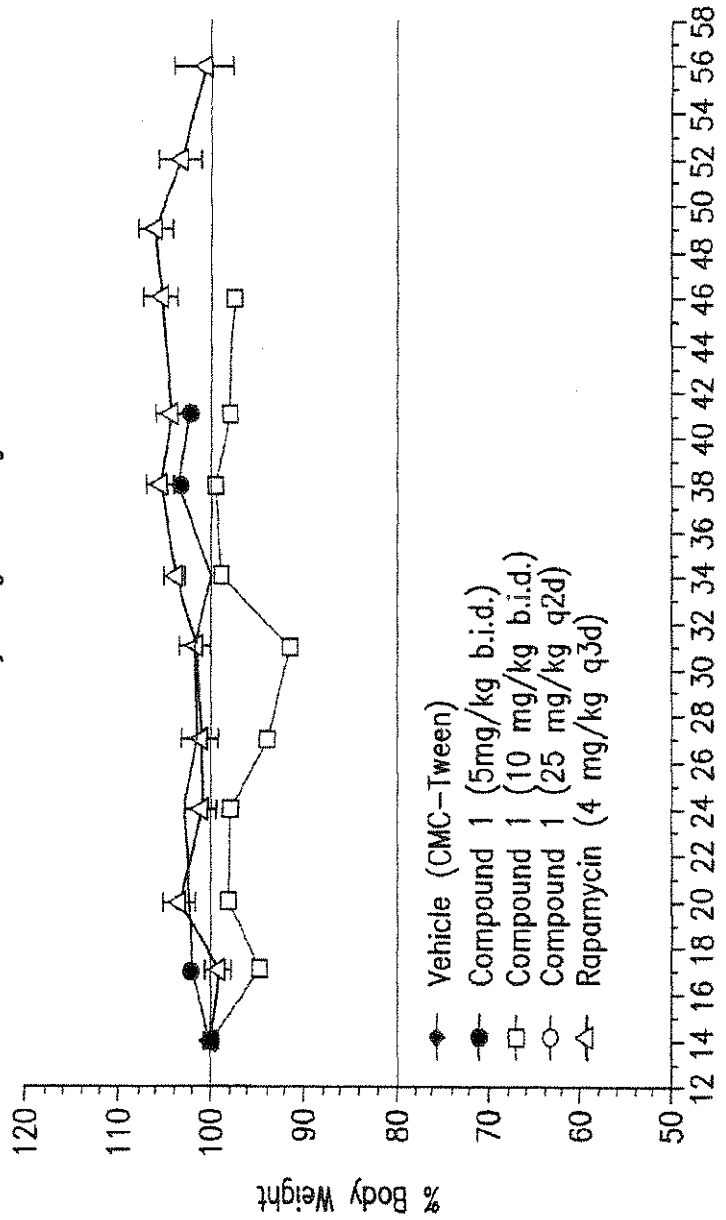

Body Weight Change
% Body Weight
120
110
100
90
80
70
60
50
12 14 16 18 20 22 24 26 28 30 32 34 36 38 40 42 44 46 48 50 52 54 56 58
Days After Tumor Cell Inoculation
Vehicle (CMC-Tween)
Compound 1 (5mg/kg b.i.d.)
Compound 1 (10 mg/kg b.i.d.)
Compound 1 (25 mg/kg q2d)
Rapamycin (4 mg/kg q3d)

FIG. 11

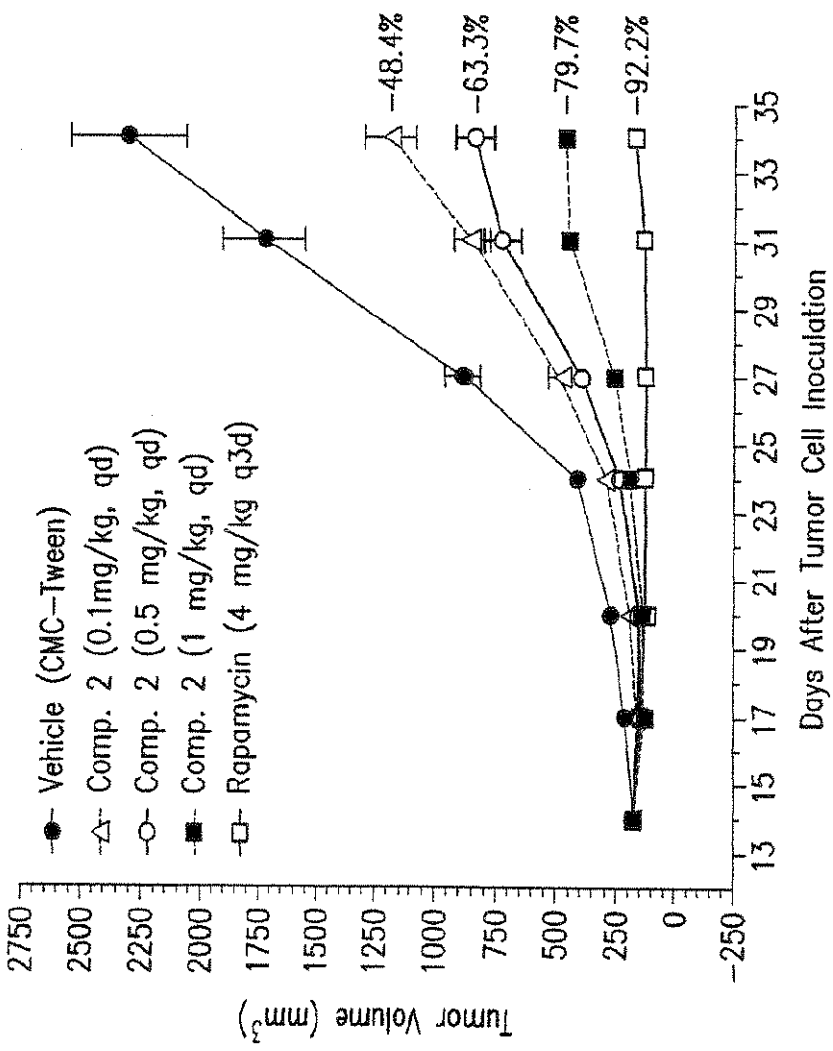

Vehicle (CMC–Tween)
Comp. 2 (0.1mg/kg, qd)
Comp. 2 (0.5 mg/kg, qd)
Comp. 2 (1 mg/kg, qd)
Rapamycin (4 mg/kg q3d)
-48.4%
-63.3%
-79.7%
-92.2%
Tumor Volume (mm³)
Days After Tumor Cell Inoculation
2750
2500
2250
2000
1750
1500
1250
1000
750
500
250
0
-250
13
15
17
19
21
23
25
27
29
31
33
35

FIG. 12

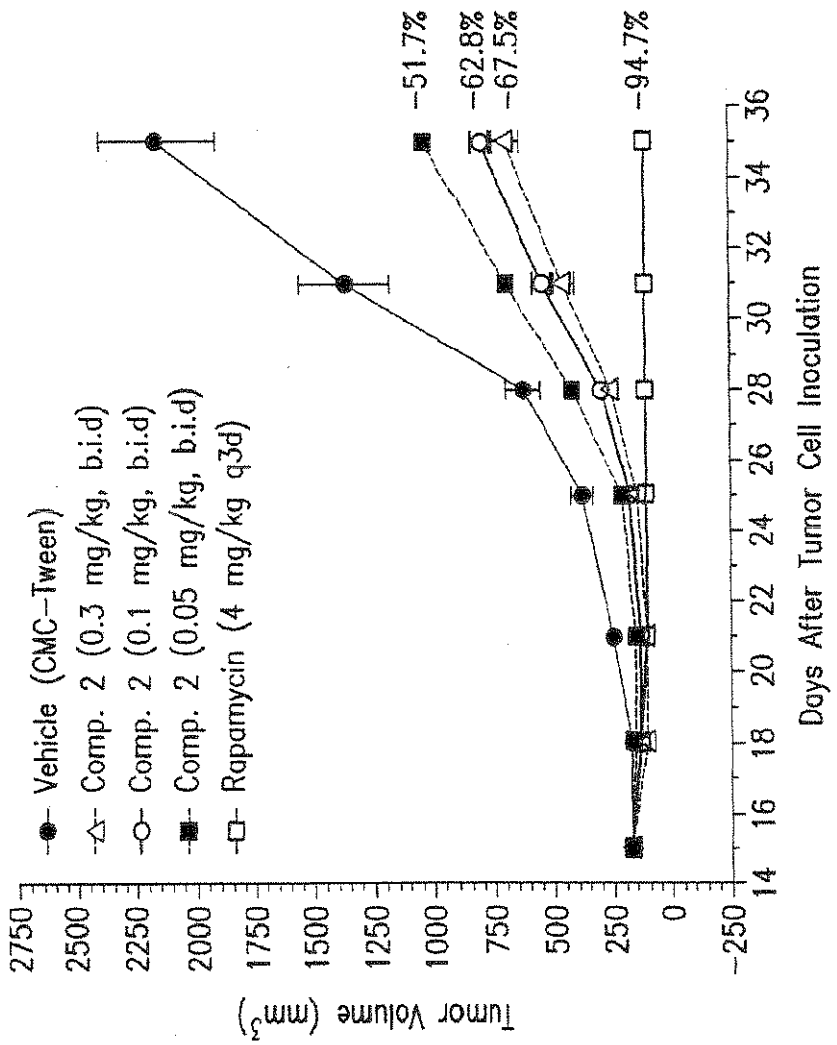
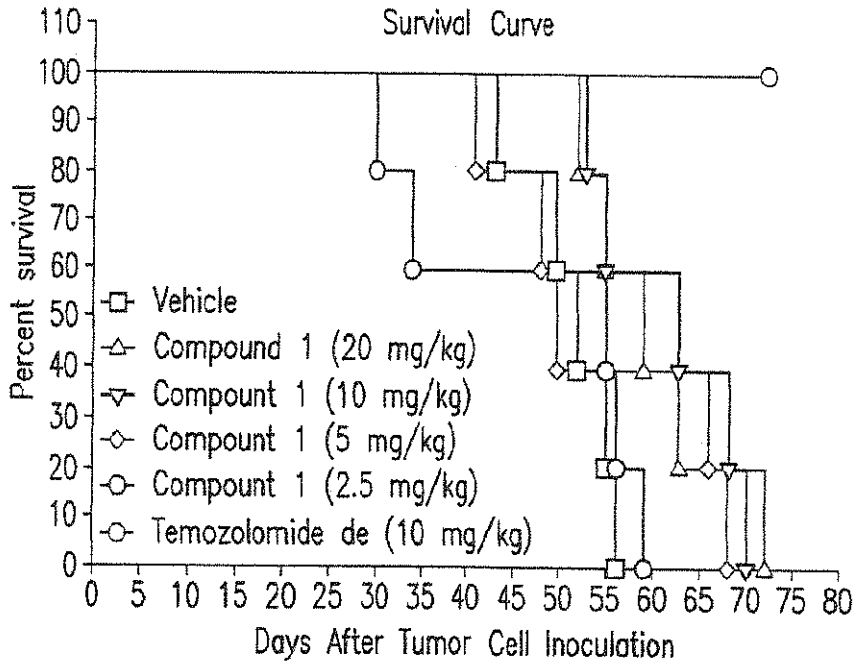

Vehicle (CMC–Tween)
Comp. 2 (0.3 mg/kg, b.i.d)
Comp. 2 (0.1 mg/kg, b.i.d)
Comp. 2 (0.05 mg/kg, b.i.d)
Rapamycin (4 mg/kg q3d)
-51.7%
-62.8%
-67.5%
-94.7%
Tumor Volume (mm³)
Days After Tumor Cell Inoculation
2750
2500
2250
2000
1750
1500
1250
1000
750
500
250
0
-250
14
16
18
20
22
24
26
28
30
32
34
36

FIG. 13



Group	Median Survival	P Value
Vehicle	52 days	
Cmpd 1 (20 mg/kg)	59 days	<0.05
Cmpd 1 (10 mg/kg)	63 days	<0.05
Cmpd 1 (5 mg/kg)	50 days	NS
Cmpd 1 (2.5 mg/kg)	55 days	NS
Temozolomide	>75 days	TBD

FIG. 14

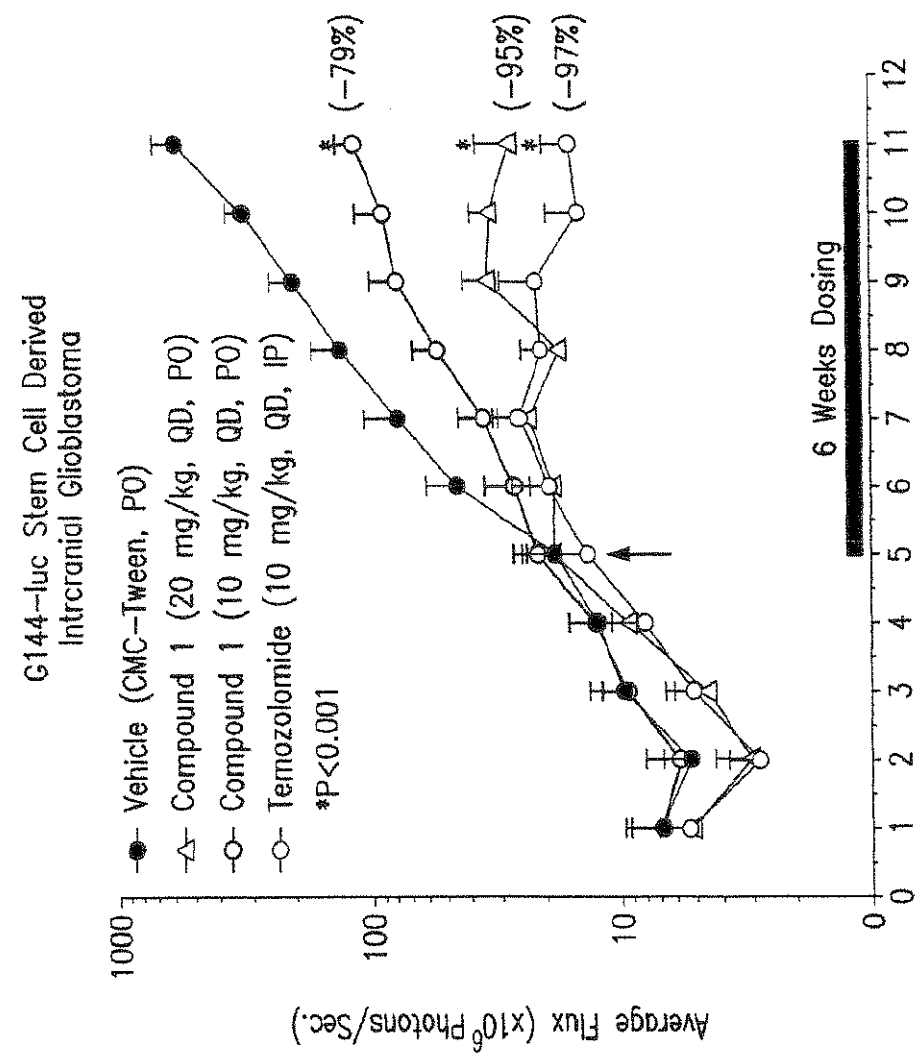
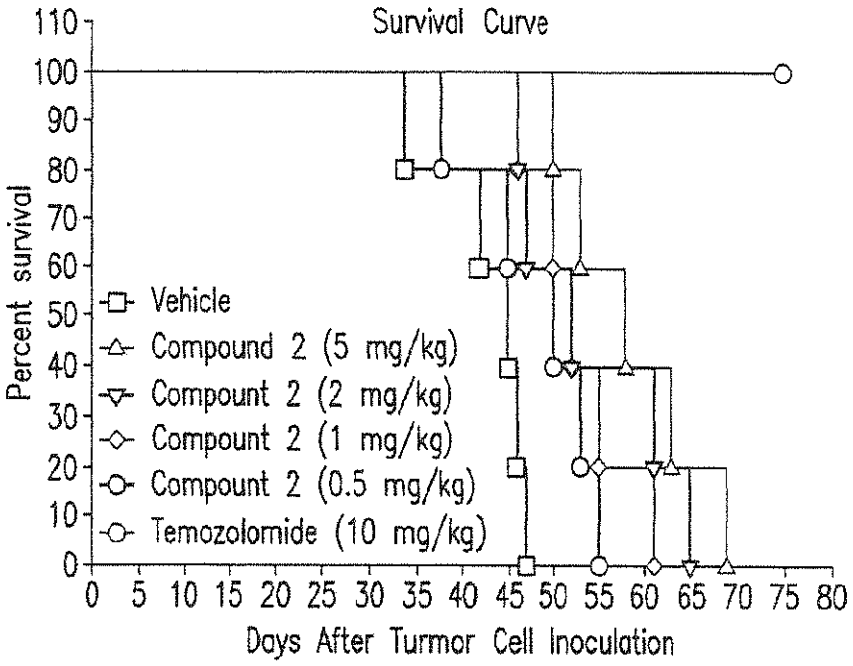

G144-luc Stem Cell Derived
Intrcranial Glioblastoma
Vehicle (CMC-Tween, PO)
Compound 1 (20 mg/kg, QD, PO)
Compound 1 (10 mg/kg, QD, PO)
Temozolomide (10 mg/kg, QD, IP)
*P<0.001
(-79%)
(-95%)
(-97%)
6 Weeks Dosing
Average Flux (x10^6 Photons/Sec.)
Weeks After Tumor Cell Inoculation
1000
100
10
0
0
1
2
3
4
5
6
7
8
9
10
11
12

FIG. 15



Group	Median Survival	P Value (Log-rank test)
Vehicle	45 days	
Compound 2 (5 mg/kg)	58 days	0.0018
Compound 2 (2 mg/kg)	52 days	0.018
Compound 2 (1 mg/kg)	52 days	0.0088
Compound 2 (0.5 mg/kg)	50 days	NS
Temozolomide	TBD	TBD

FIG. 16

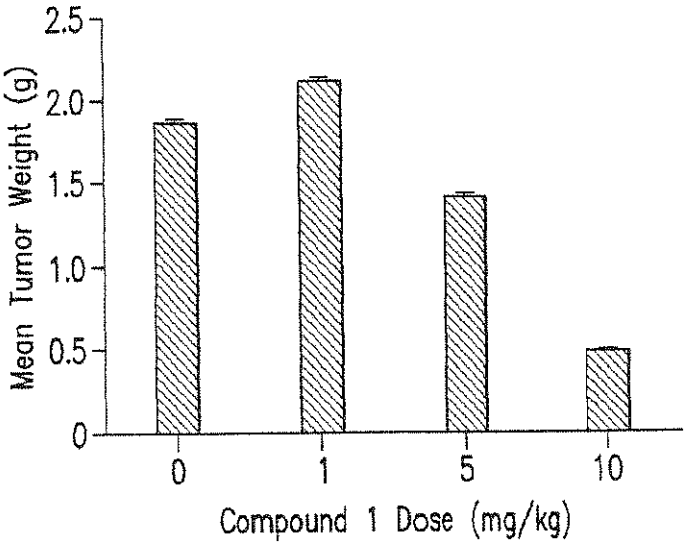

Mean Tumor Weight (g)
2.5
2.0
1.5
1.0
0.5
0
0
1
5
10
Compound 1 Dose (mg/kg)

FIG. 17

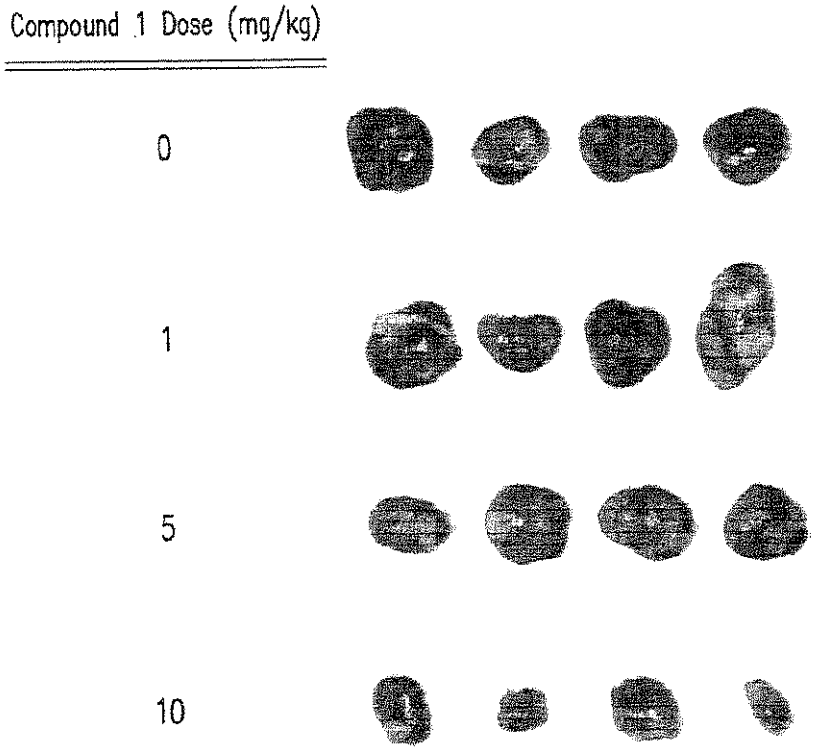

Compound 1 Dose (mg/kg)
0
1
5
10

FIG. 18

Tumor Growth Delay (Median time to endpoint versus control group)

Compound1 Dose (mg/kg)	% Tumor Growth Inhibition (Day 12)		% Tumor Growth Delay	
0	–		–	
0.3	–8	*	4	*
3	44		25	
10	73		76	

* statistically significant

FIG. 19

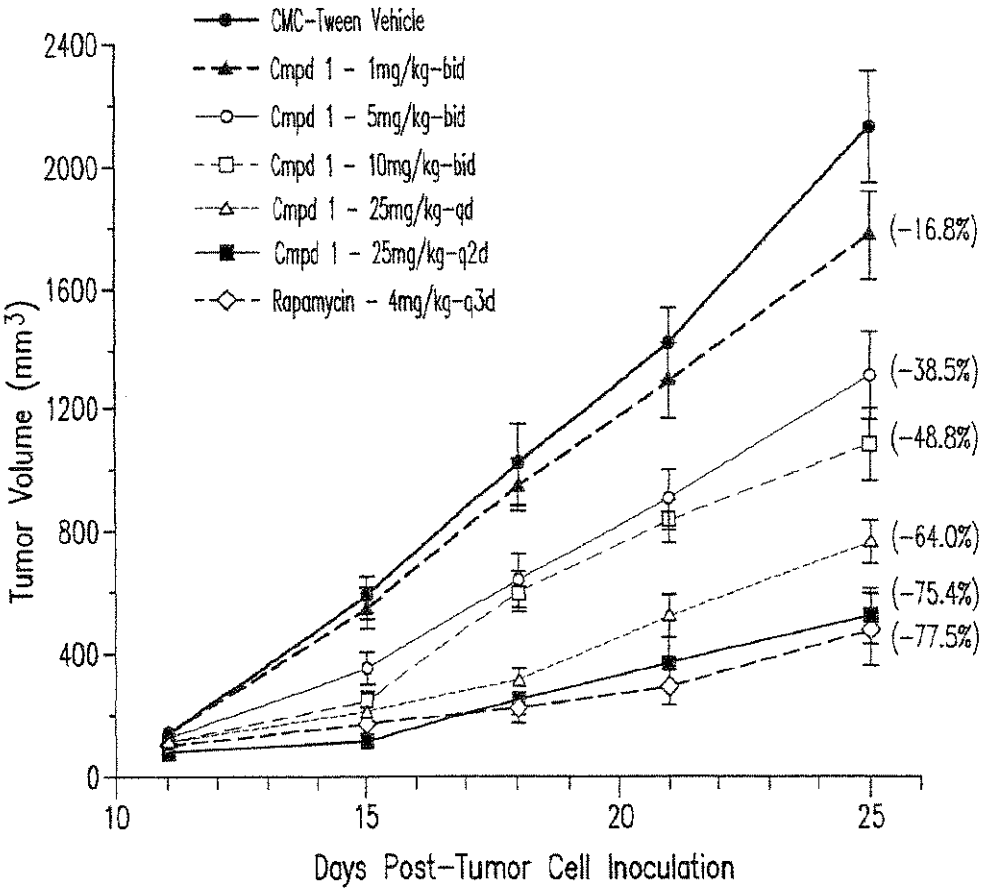
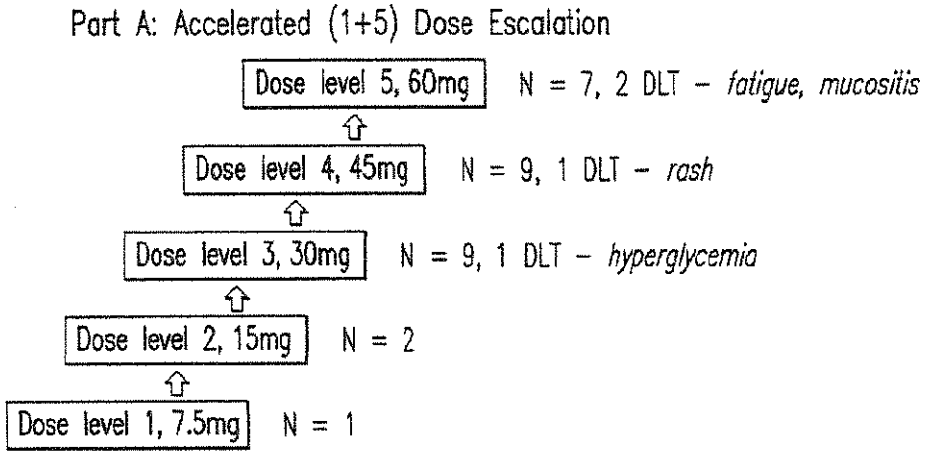


FIG. 20

Age Mean (Range)	50	25–80
Gender (n,%) M F	 9 19	 32 68
ECOG (n, %) 0 1 2	 16 11 1	 57 39 4
Tumor Type (n, %) CRC Breast Pancreas NSCLC GBM HCC Salivary Other* (1 each)	 6 3 3 2 2 2 2 8	 21 11 11 7 7 7 7 29
No. Prior Therapis (n, %) 1–3 >3	 14 14	 50 50

FIG. 21



DLT Definition:

grade ≥ 3 Comp. 1 related AE, except rash ≤ 4 days, diarrhea/vomiting < 3 days
fasting hyperglycemia: grade 2 > 14 days, grade 3 > 4 days
heme: F&N, grade 4 ANC or platelets > 7 days, grade 3/4 platelets with bleeding
liver: grade 3 not associated with PD in liver, and grade 4

FIG. 22

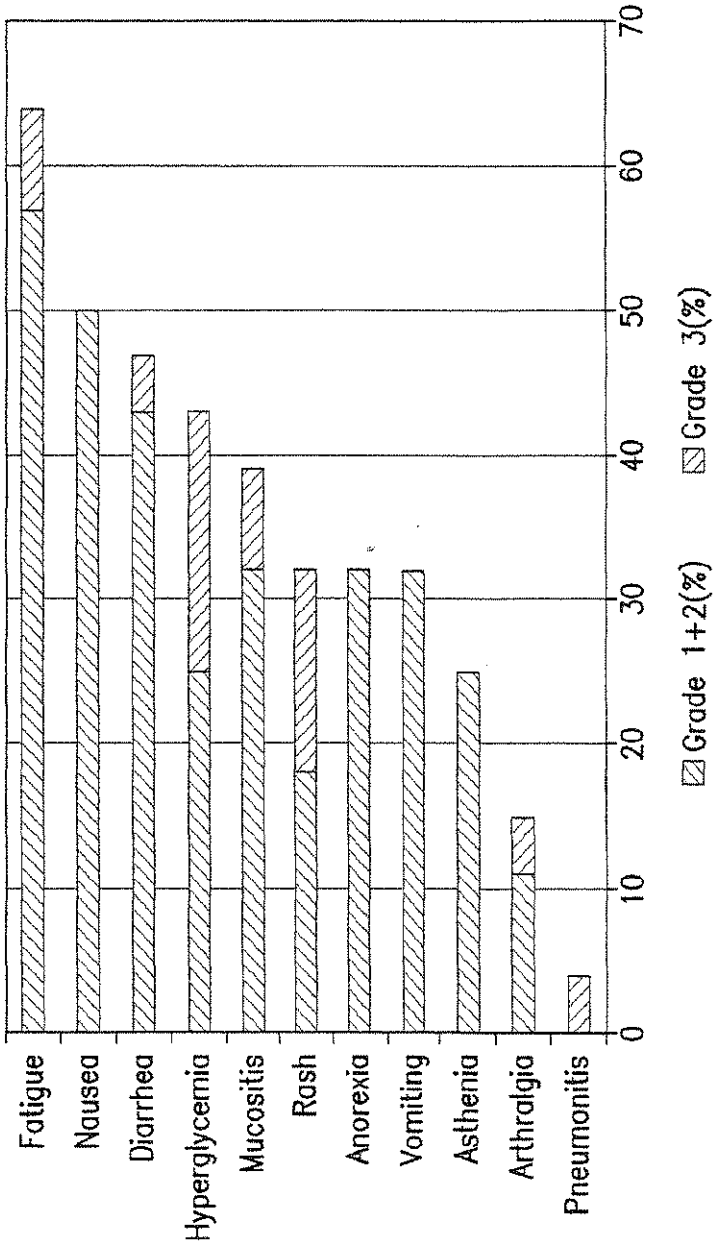

Fatigue
Nausea
Diarrhea
Hyperglycemia
Mucositis
Rash
Anorexia
Vomiting
Asthenia
Arthralgia
Pneumonitis
0
10
20
30
40
50
60
70
Grade 1+2(%)
Grade 3(%)

FIG. 23

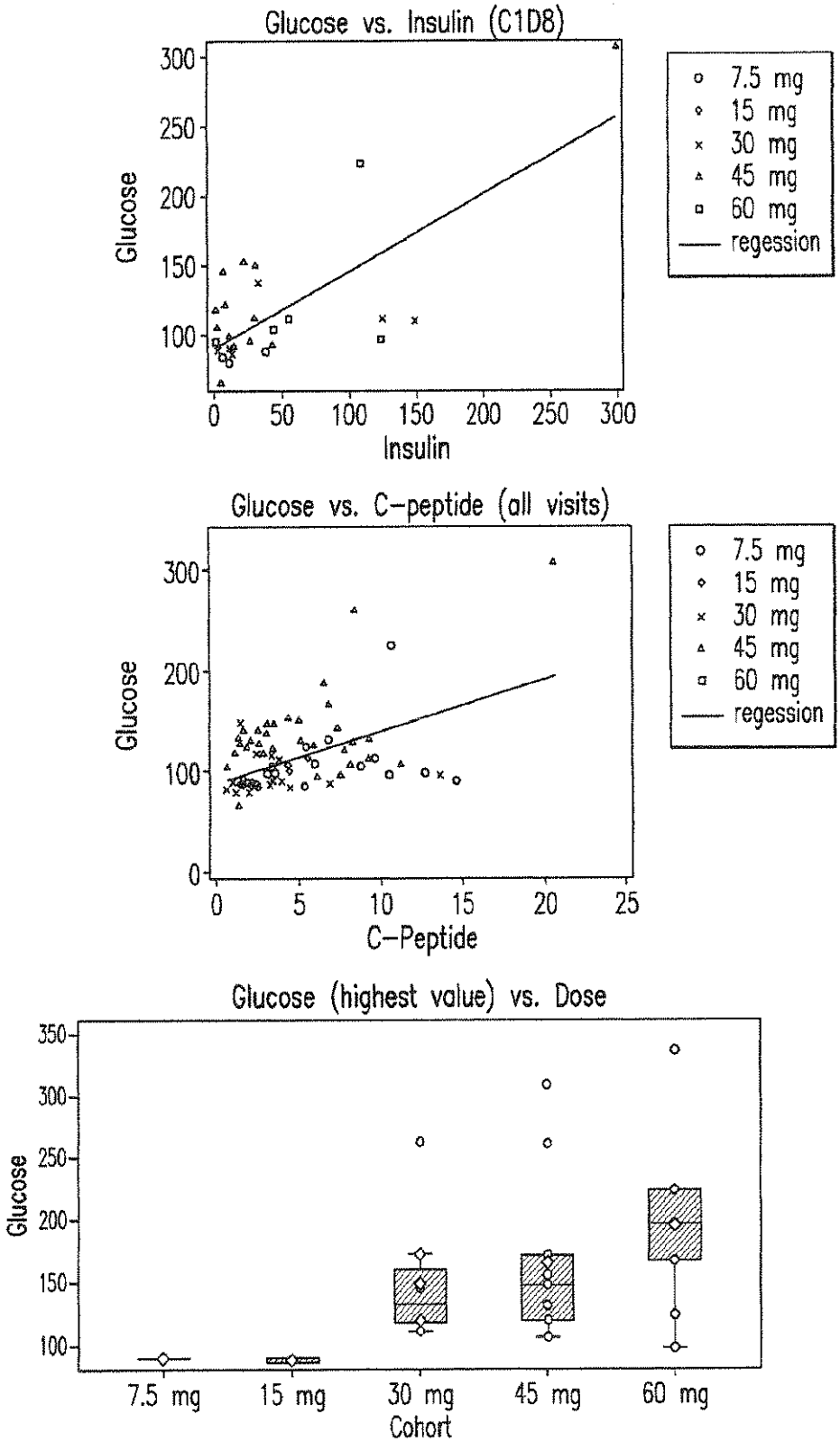

Glucose vs. Insulin (C1D8)
Glucose
Insulin
7.5 mg
15 mg
30 mg
45 mg
60 mg
regession
Glucose vs. C-peptide (all visits)
Glucose
C-Peptide
7.5 mg
15 mg
30 mg
45 mg
60 mg
regession
Glucose (highest value) vs. Dose
Glucose
7.5 mg
15 mg
30 mg
45 mg
60 mg
Cohort

FIG. 24

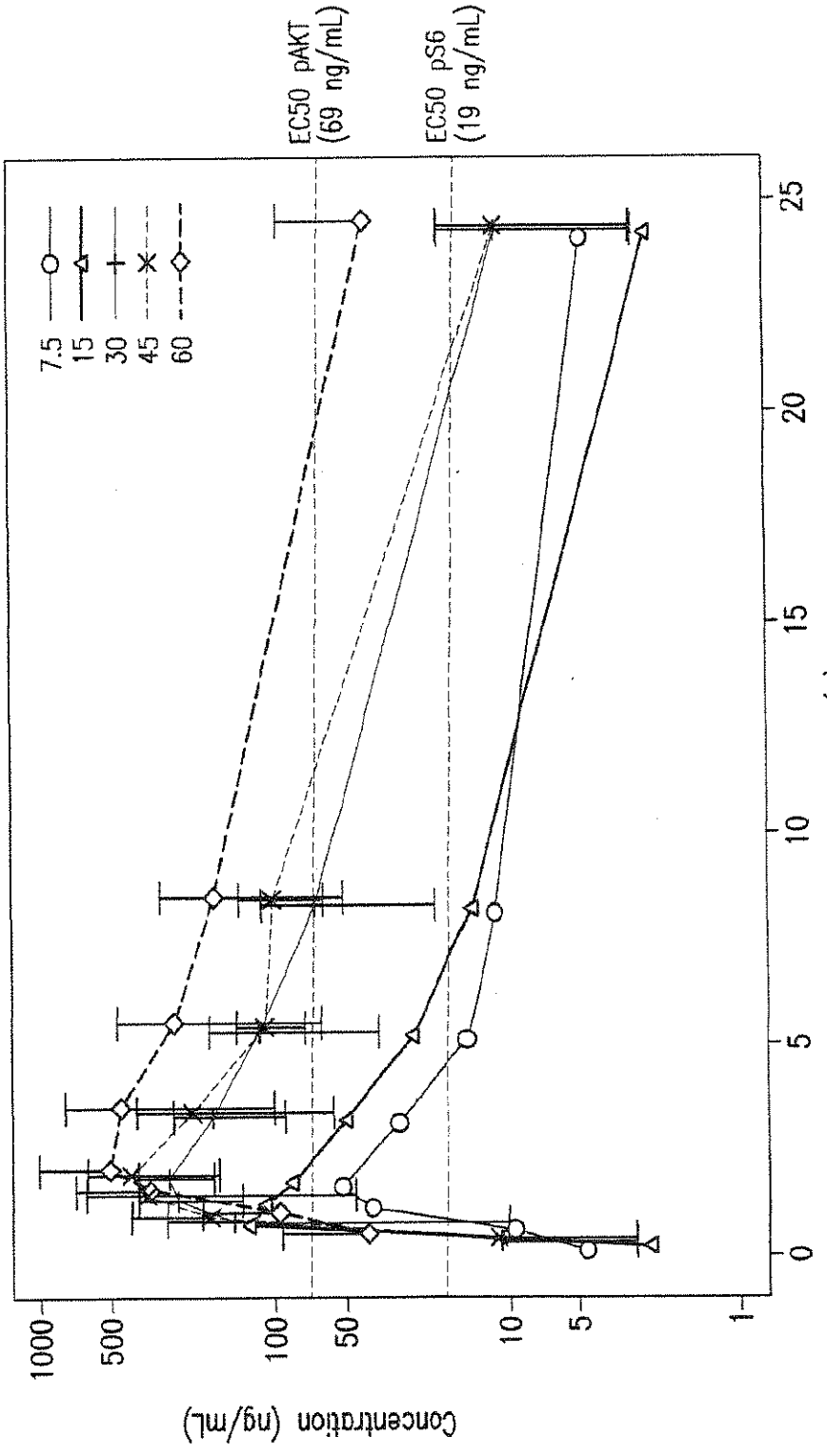

EC50 pAKT
(69 ng/mL)
EC50 pS6
(19 ng/mL)
7.5
15
30
45
60
Concentration (ng/mL)
1000
500
100
50
10
5
1
0
5
10
15
20
25
Time (h)

FIG. 25

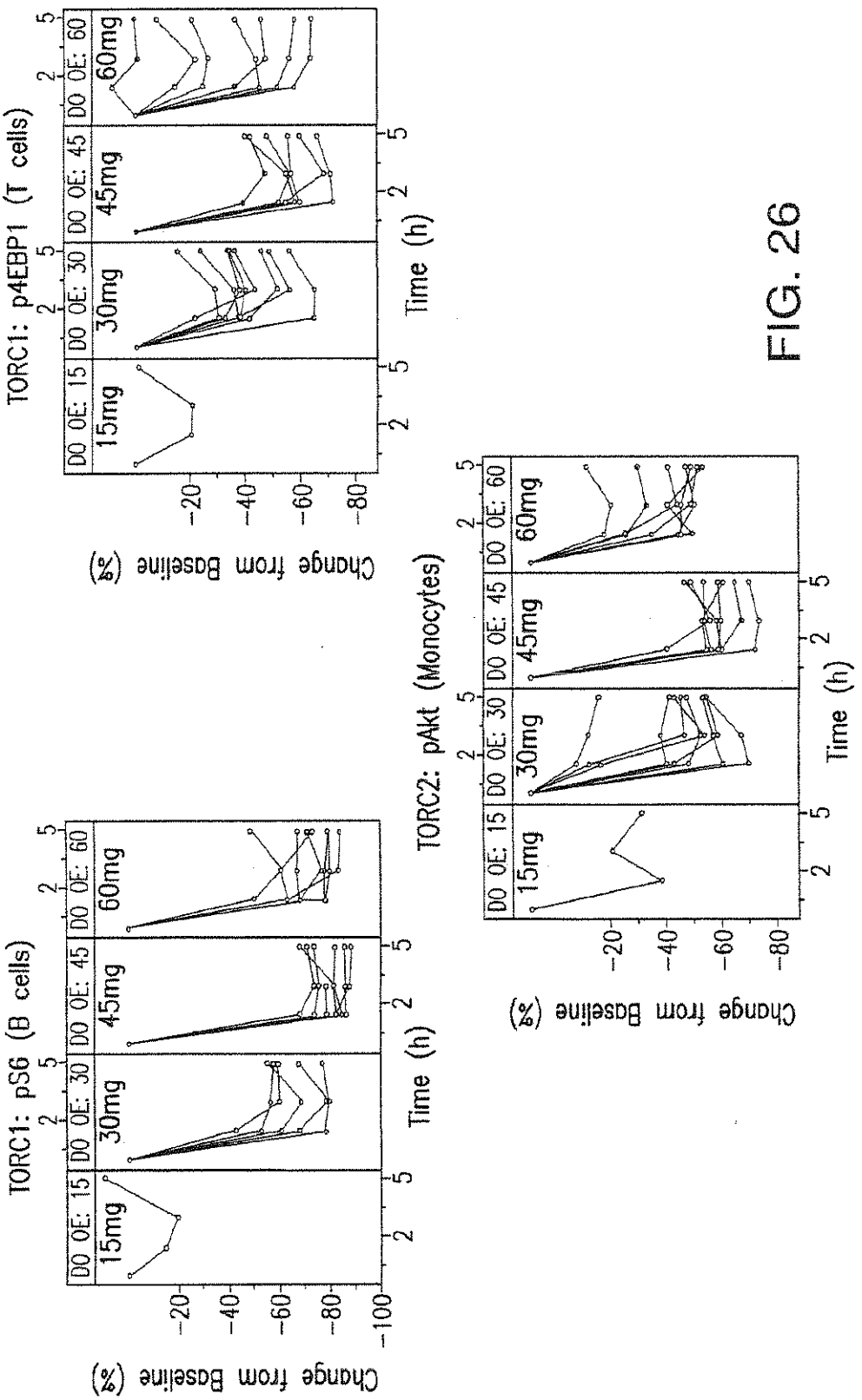

TORC1: pS6 (B cells)
TORC1: p4EBP1 (T cells)
TORC2: pAkt (Monocytes)
DO OE: 15
DO OE: 30
DO OE: 45
DO OE: 60
15mg
30mg
45mg
60mg
Change from Baseline (%)
Time (h)

FIG. 26

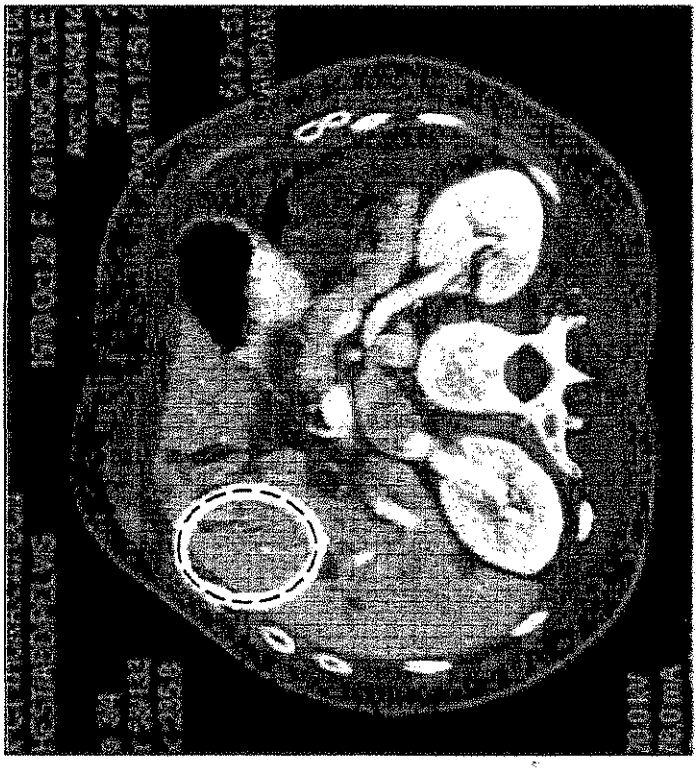


FIG. 27B

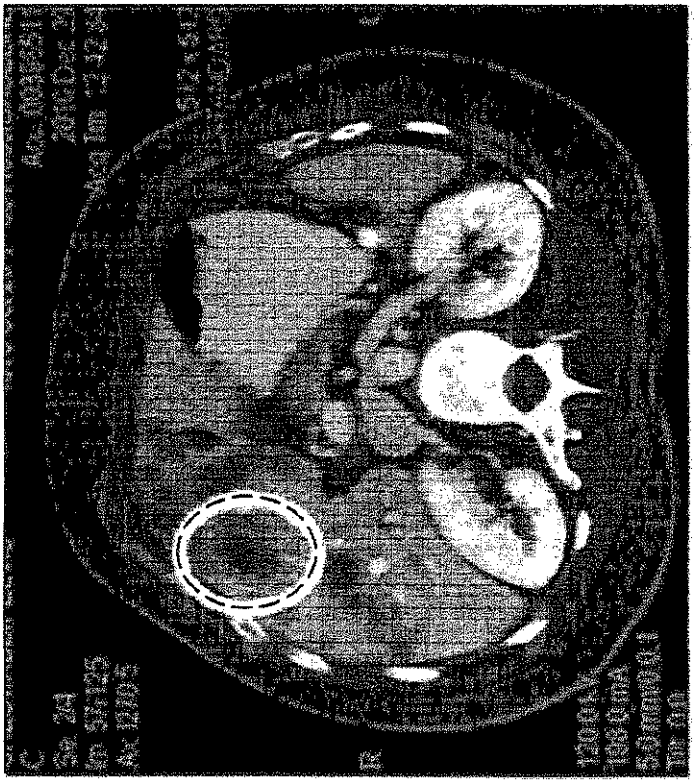


FIG. 27A

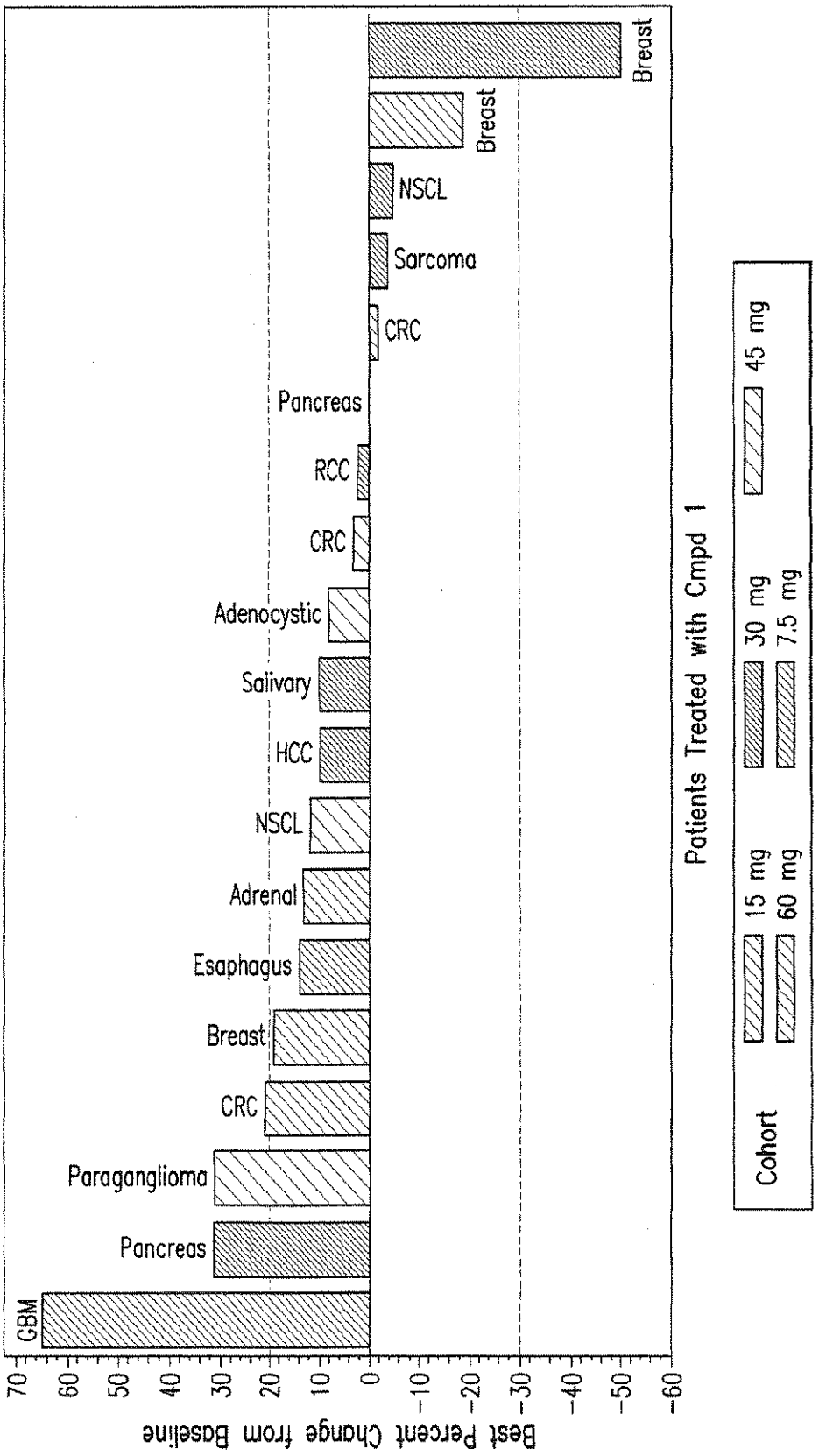

Best Percent Change from Baseline
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
GBM
Pancreas
Paraganglioma
CRC
Breast
Esaphagus
Adrenal
NSCL
HCC
Salivary
Adenocystic
CRC
RCC
Pancreas
CRC
Sarcoma
NSCL
Breast
Breast
Patients Treated with Cmpd 1
Cohort
15 mg
60 mg
30 mg
7.5 mg
45 mg

FIG. 28

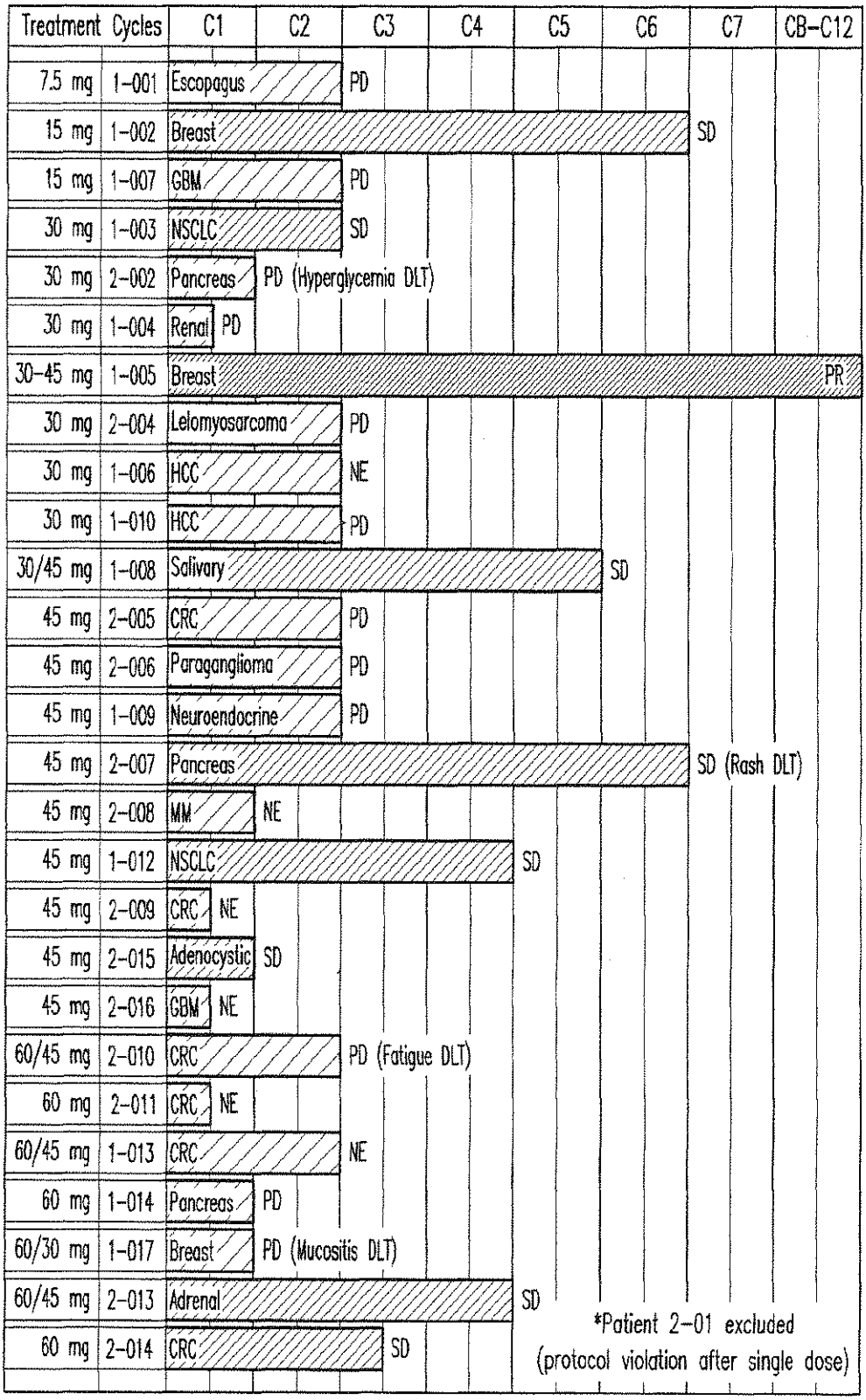

Treatment Cycles
C1
C2
C3
C4
C5
C6
C7
CB-C12
7.5 mg 1-001 Escopagus PD
15 mg 1-002 Breast SD
15 mg 1-007 GBM PD
30 mg 1-003 NSCLC SD
30 mg 2-002 Pancreas PD (Hyperglycemia DLT)
30 mg 1-004 Renal PD
30-45 mg 1-005 Breast PR
30 mg 2-004 Leiomyosarcoma PD
30 mg 1-006 HCC NE
30 mg 1-010 HCC PD
30/45 mg 1-008 Salivary SD
45 mg 2-005 CRC PD
45 mg 2-006 Paraganglioma PD
45 mg 1-009 Neuroendocrine PD
45 mg 2-007 Pancreas SD (Rash DLT)
45 mg 2-008 MM NE
45 mg 1-012 NSCLC SD
45 mg 2-009 CRC NE
45 mg 2-015 Adenocystic SD
45 mg 2-016 GBM NE
60/45 mg 2-010 CRC PD (Fatigue DLT)
60 mg 2-011 CRC NE
60/45 mg 1-013 CRC NE
60 mg 1-014 Pancreas PD
60/30 mg 1-017 Breast PD (Mucositis DLT)
60/45 mg 2-013 Adrenal SD
60 mg 2-014 CRC SD
*Patient 2-01 excluded
(protocol violation after single dose)

FIG. 29