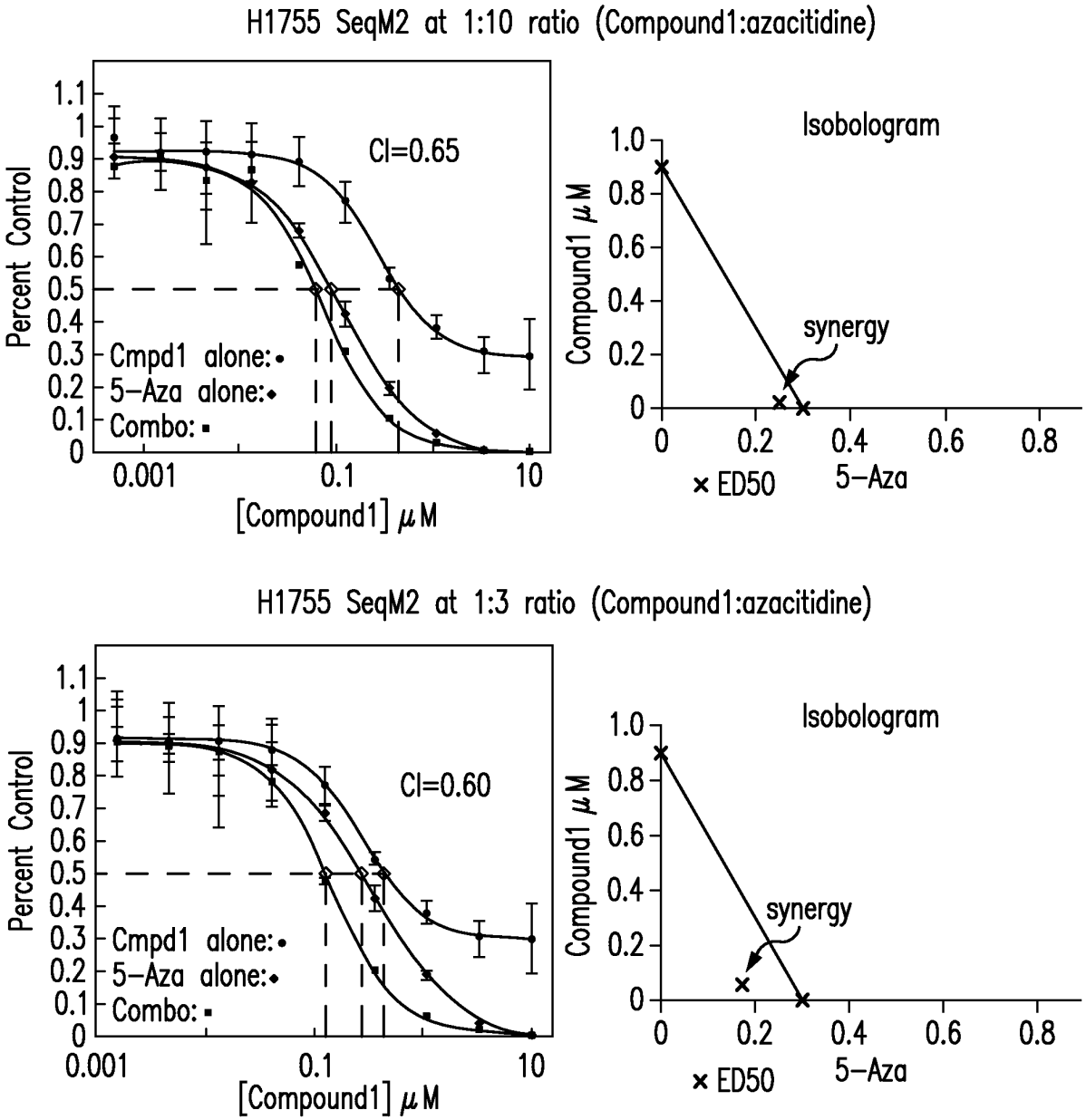

H1755 SeqM2 at 1:10 ratio (Compound1:azacitidine)
Percent Control
CI=0.65
Cmpd1 alone:
5-Aza alone:
Combo:
[Compound1] μM
Isobologram
Compound1 μM
synergy
× ED50
5-Aza
H1755 SeqM2 at 1:3 ratio (Compound1:azacitidine)
Percent Control
CI=0.60
Cmpd1 alone:
5-Aza alone:
Combo:
[Compound1] μM
Isobologram
Compound1 μM
synergy
× ED50
5-Aza

FIG. 1

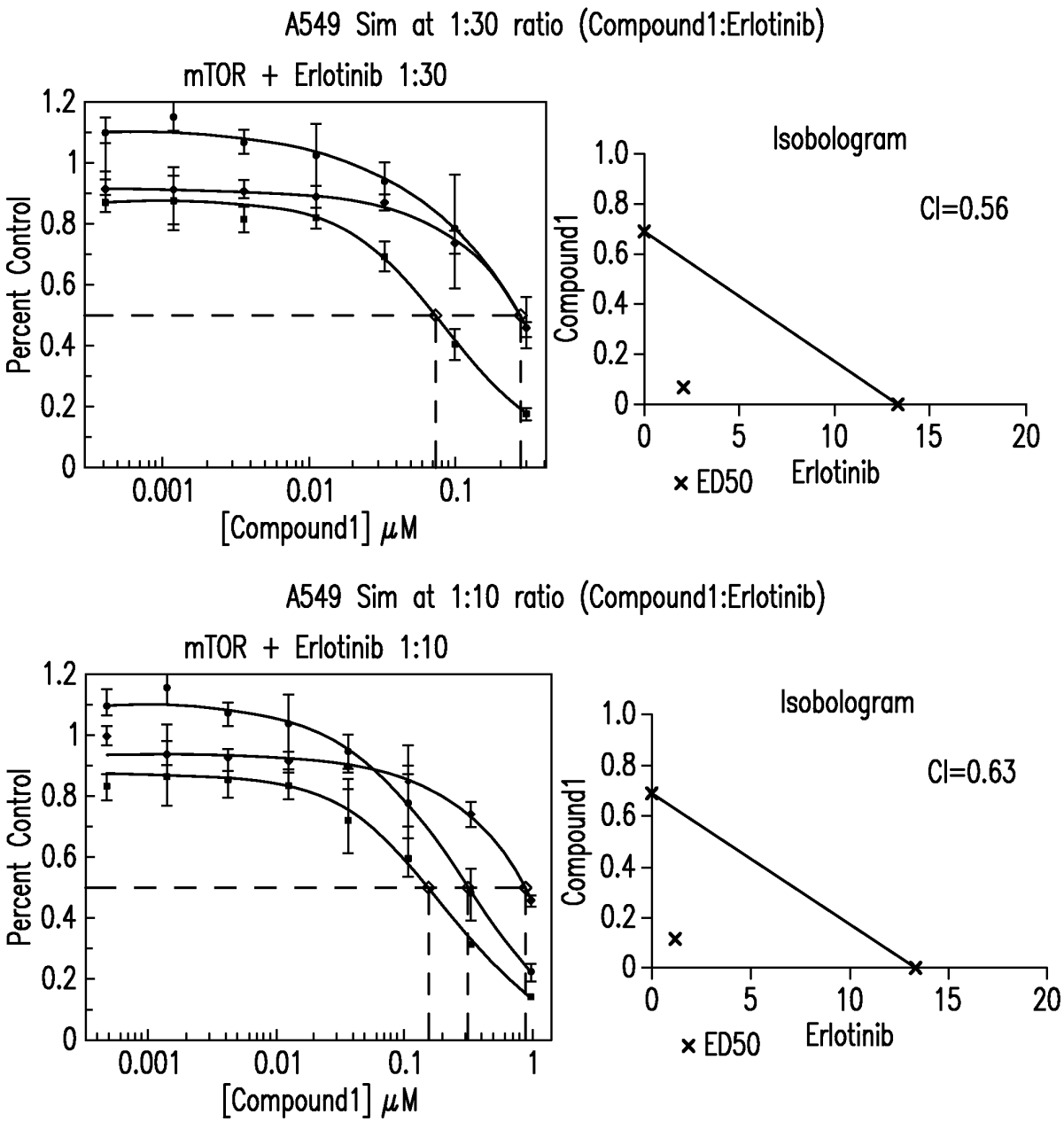

A549 Sim at 1:30 ratio (Compound1:Erlotinib)
mTOR + Erlotinib 1:30
Percent Control
[Compound1] μM
Isobologram
CI=0.56
Compound1
Erlotinib
ED50
A549 Sim at 1:10 ratio (Compound1:Erlotinib)
mTOR + Erlotinib 1:10
Percent Control
[Compound1] μM
Isobologram
CI=0.63
Compound1
Erlotinib
ED50

FIG. 2

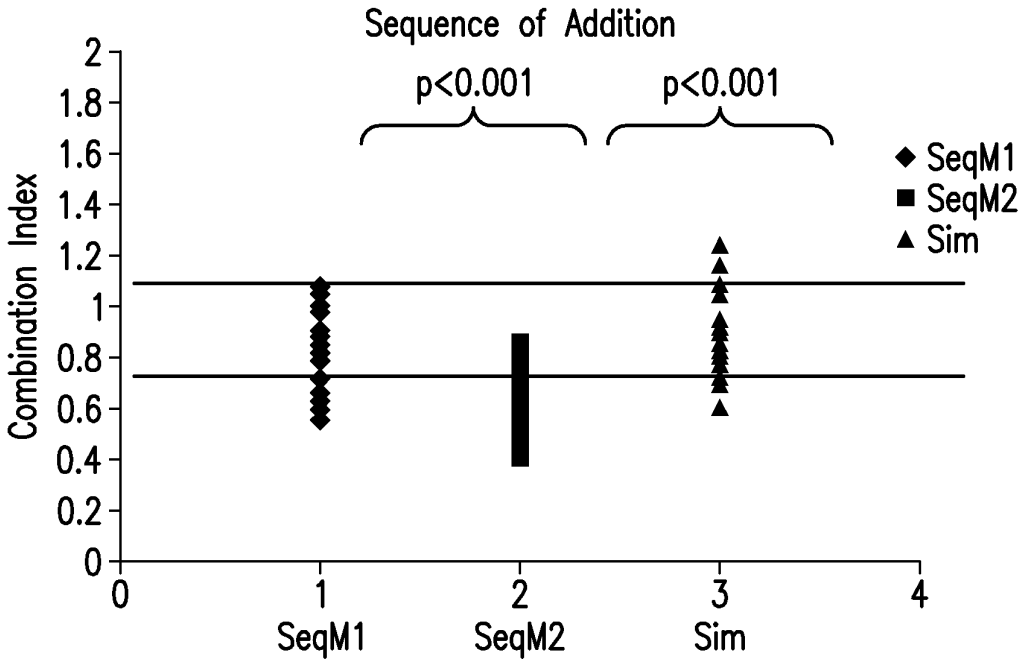

Sequence of Addition
p<0.001
p<0.001
Combination Index
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
SeqM1
SeqM2
Sim
0
1
2
3
4
SeqM1
SeqM2
Sim

FIG. 3A

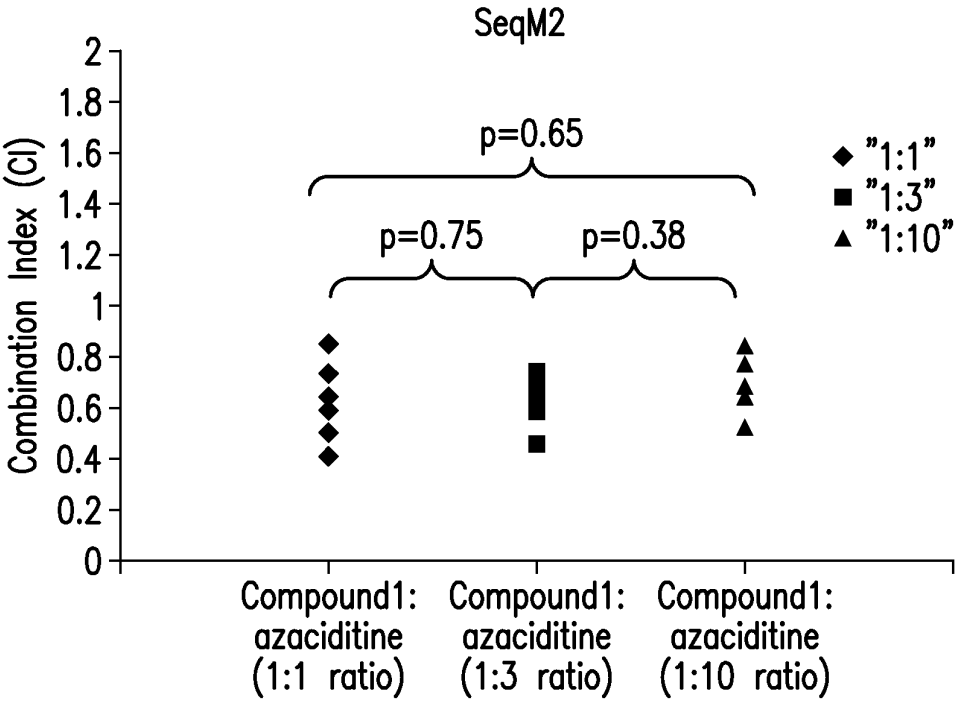

SeqM2
p=0.65
p=0.75
p=0.38
Combination Index (CI)
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
"1:1"
"1:3"
"1:10"
Compound1: azaciditine (1:1 ratio)
Compound1: azaciditine (1:3 ratio)
Compound1: azaciditine (1:10 ratio)

FIG. 3B

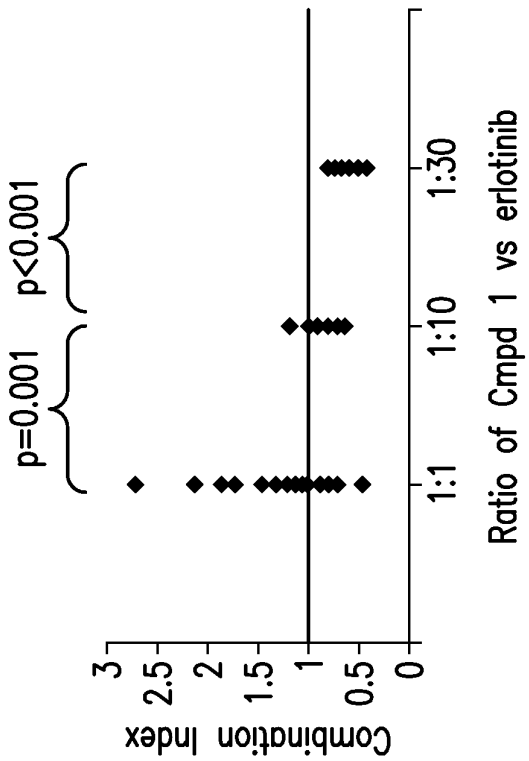

p=0.001
p<0.001
Combination Index
3
2.5
2
1.5
1
0.5
0
1:1
1:10
1:30
Ratio of Cmpd 1 vs erlotinib

FIG. 4B

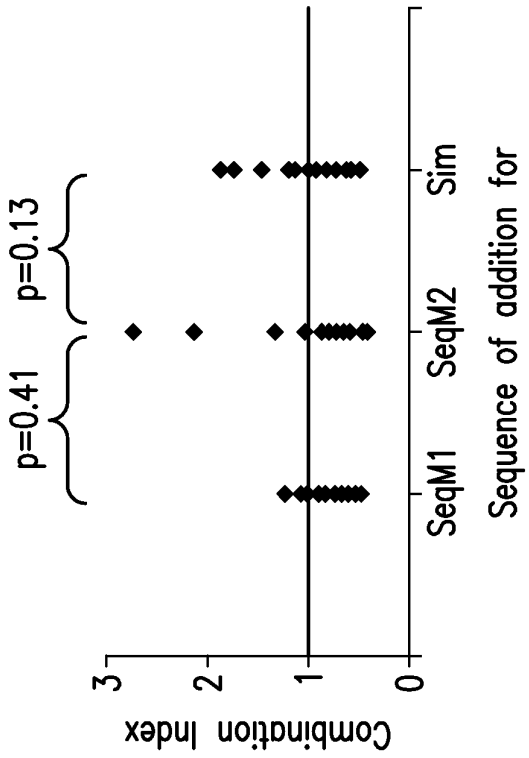

p=0.41
p=0.13
Combination Index
3
2
1
0
SeqM1
SeqM2
Sim
Sequence of addition for
Cmpd 1 + erlotinib

FIG. 4A

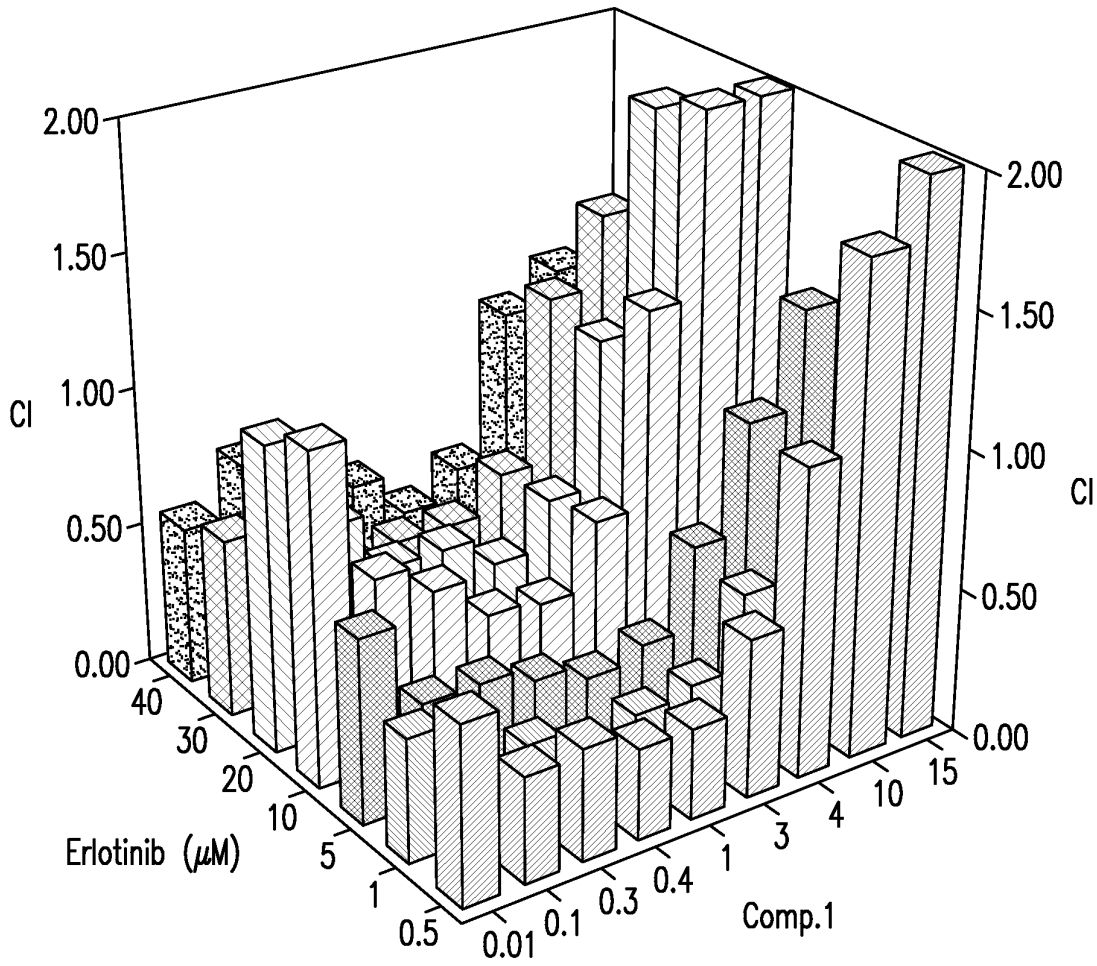

2.00
1.50
1.00
0.50
0.00
CI
40
30
20
10
5
1
0.5
Erlotinib (μM)
0.01
0.1
0.3
0.4
1
3
4
10
15
Comp.1
2.00
1.50
1.00
0.50
0.00
CI

FIG. 5A

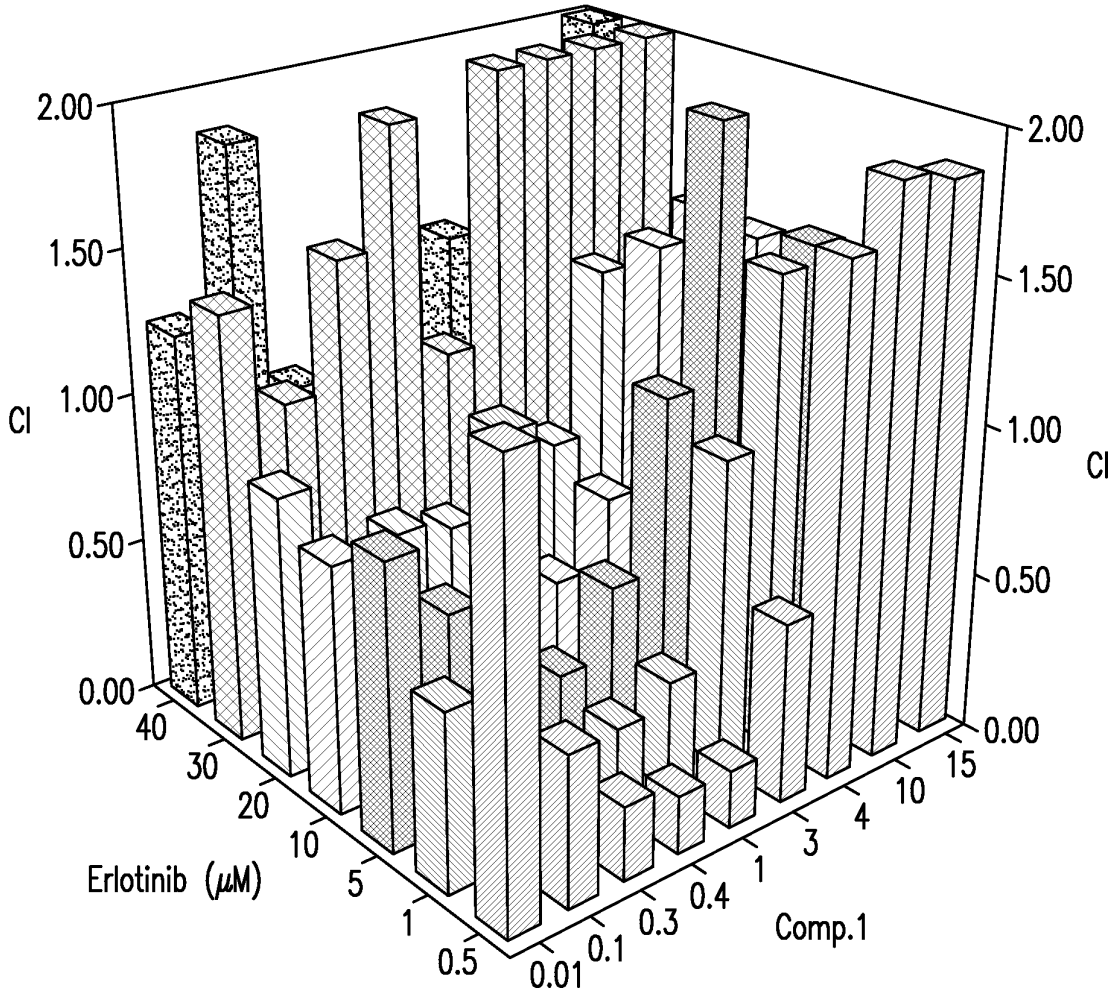

2.00
1.50
1.00
0.50
0.00
CI
40
30
20
10
5
1
0.5
Erlotinib (μM)
0.01
0.1
0.3
0.4
1
3
4
10
15
Comp.1
2.00
1.50
1.00
0.50
0.00
CI

FIG. 5B

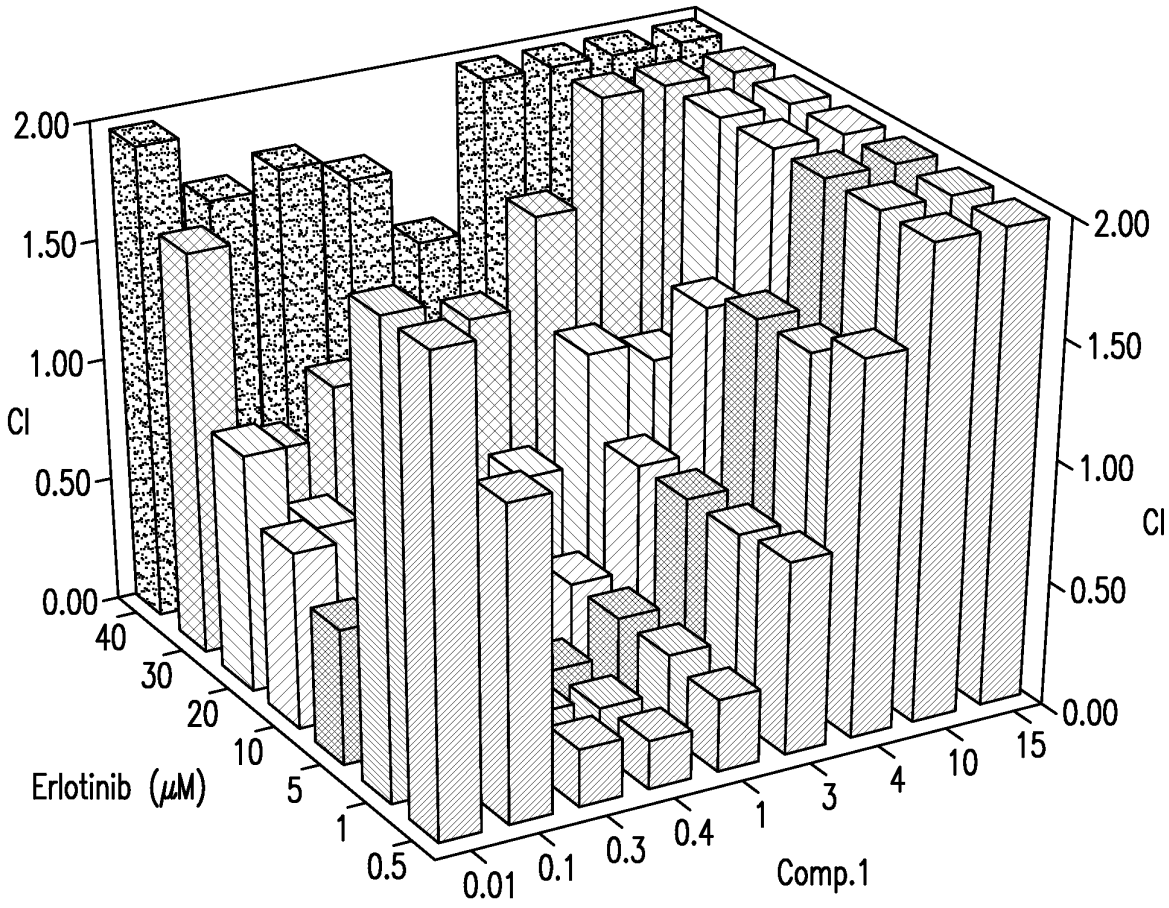

2.00
1.50
1.00
CI
0.50
0.00
40
30
20
10
5
1
0.5
Erlotinib (μM)
0.01
0.1
0.3
0.4
1
3
4
10
15
Comp.1
2.00
1.50
1.00
CI
0.50
0.00

FIG. 5C

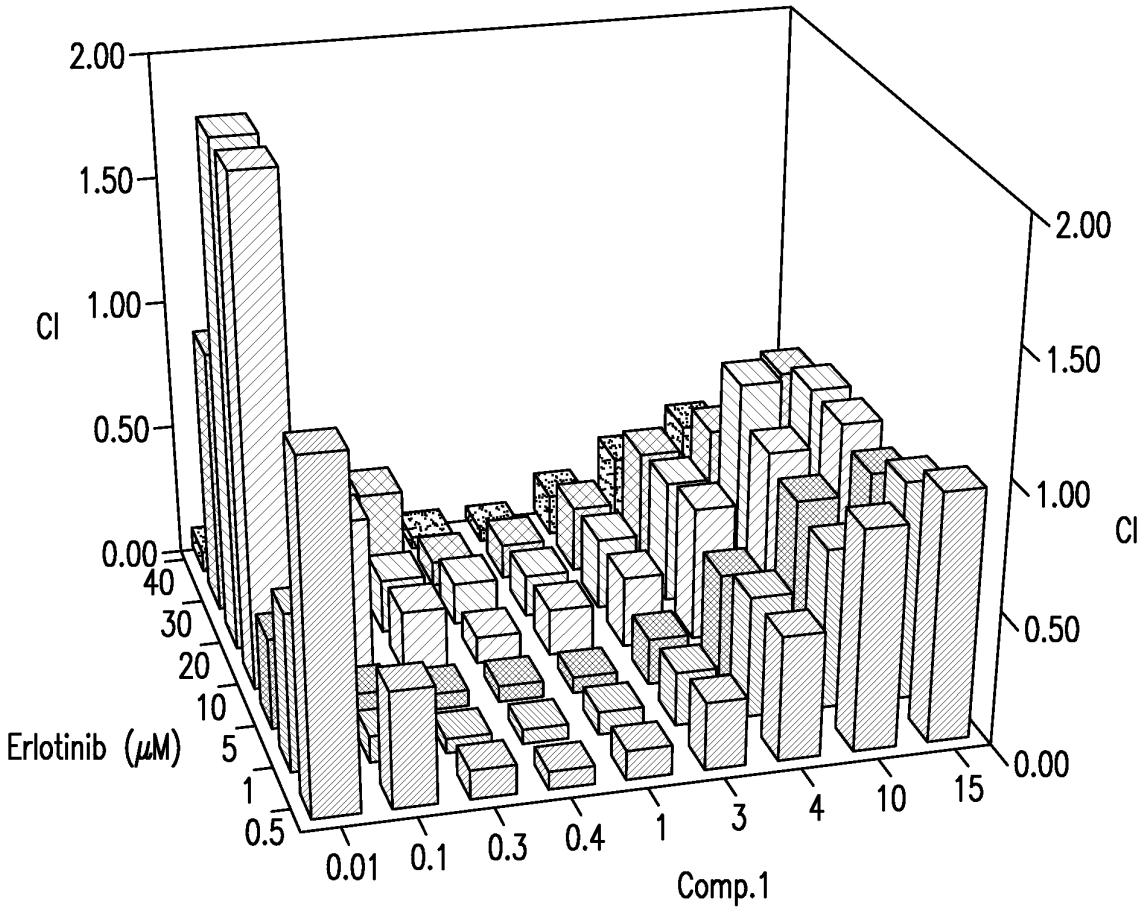

2.00
1.50
1.00
0.50
0.00
CI
40
30
20
10
5
1
0.5
Erlotinib (μM)
0.01
0.1
0.3
0.4
1
3
4
10
15
Comp.1
2.00
1.50
1.00
0.50
0.00
CI

FIG. 5D

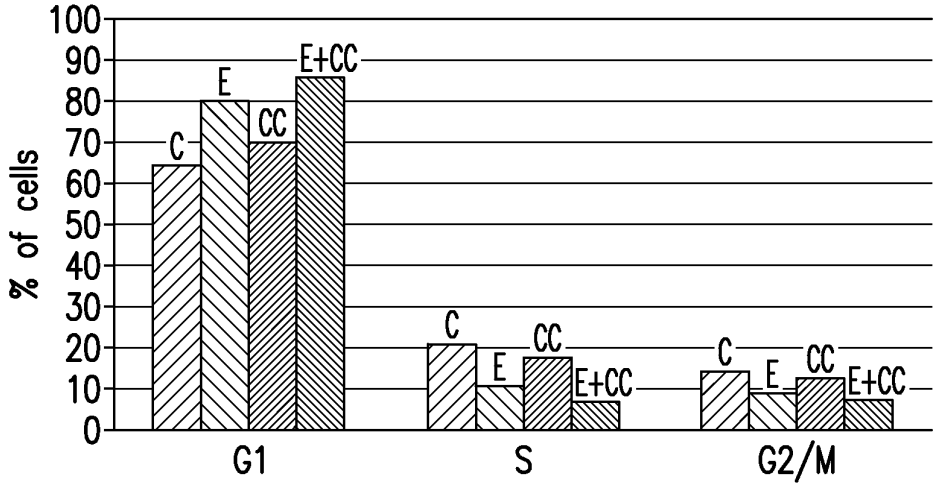

100
90
80
70
60
50
40
30
20
10
0
% of cells
C
E
CC
E+CC
C
E
CC
E+CC
C
E
CC
E+CC
G1
S
G2/M

FIG. 6

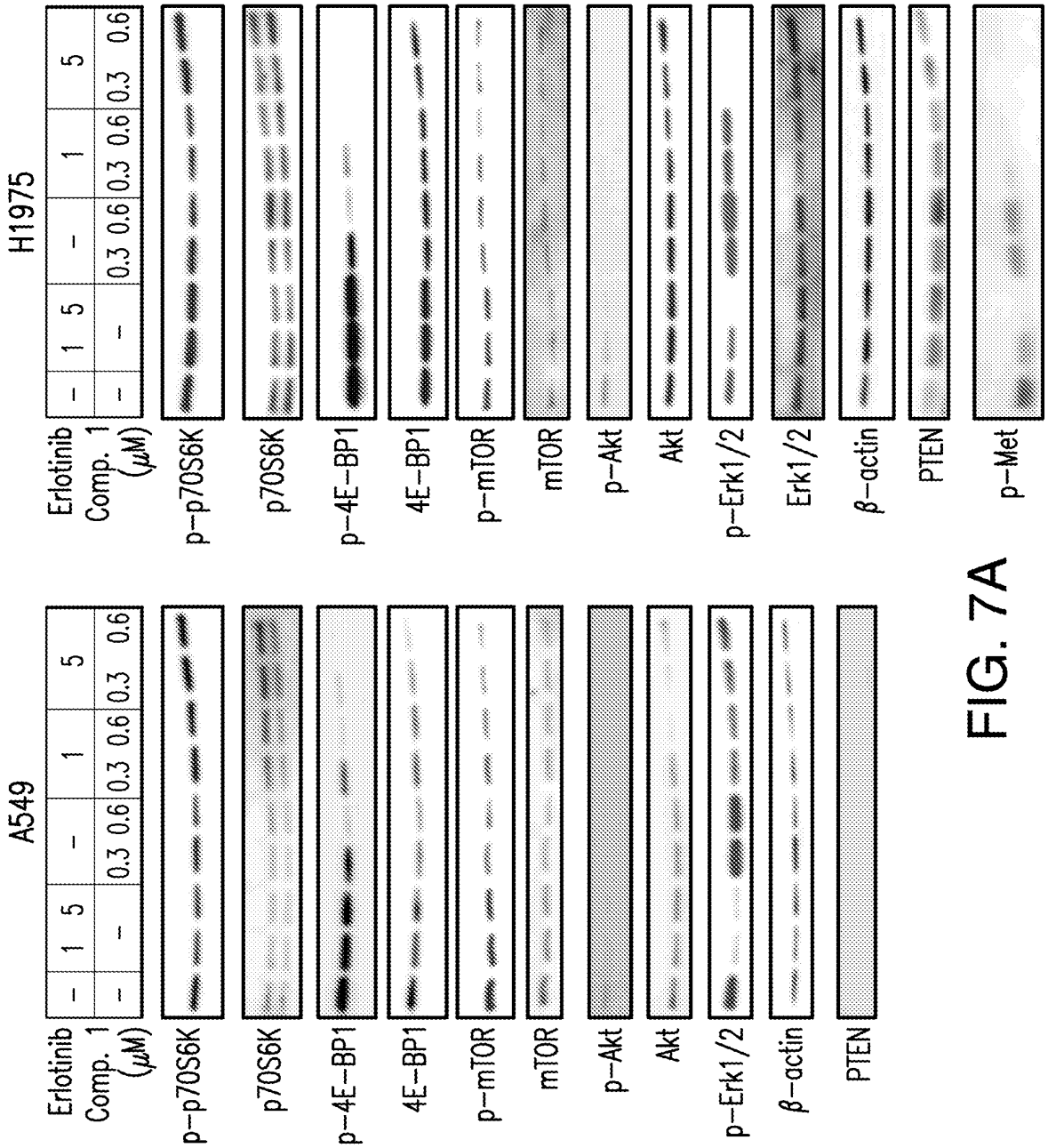

A549
Erlotinib – 1 5 – 1 5
Comp. 1 (μM) – – 0.3 0.6 0.3 0.6 0.3 0.6
p-p70S6K
p70S6K
p-4E-BP1
4E-BP1
p-mTOR
mTOR
p-Akt
Akt
p-Erk1/2
β-actin
PTEN
H1975
Erlotinib – 1 5 – 1 5
Comp. 1 (μM) – – 0.3 0.6 0.3 0.6 0.3 0.6
p-p70S6K
p70S6K
p-4E-BP1
4E-BP1
p-mTOR
mTOR
p-Akt
Akt
p-Erk1/2
Erk1/2
β-actin
PTEN
p-Met

FIG. 7A

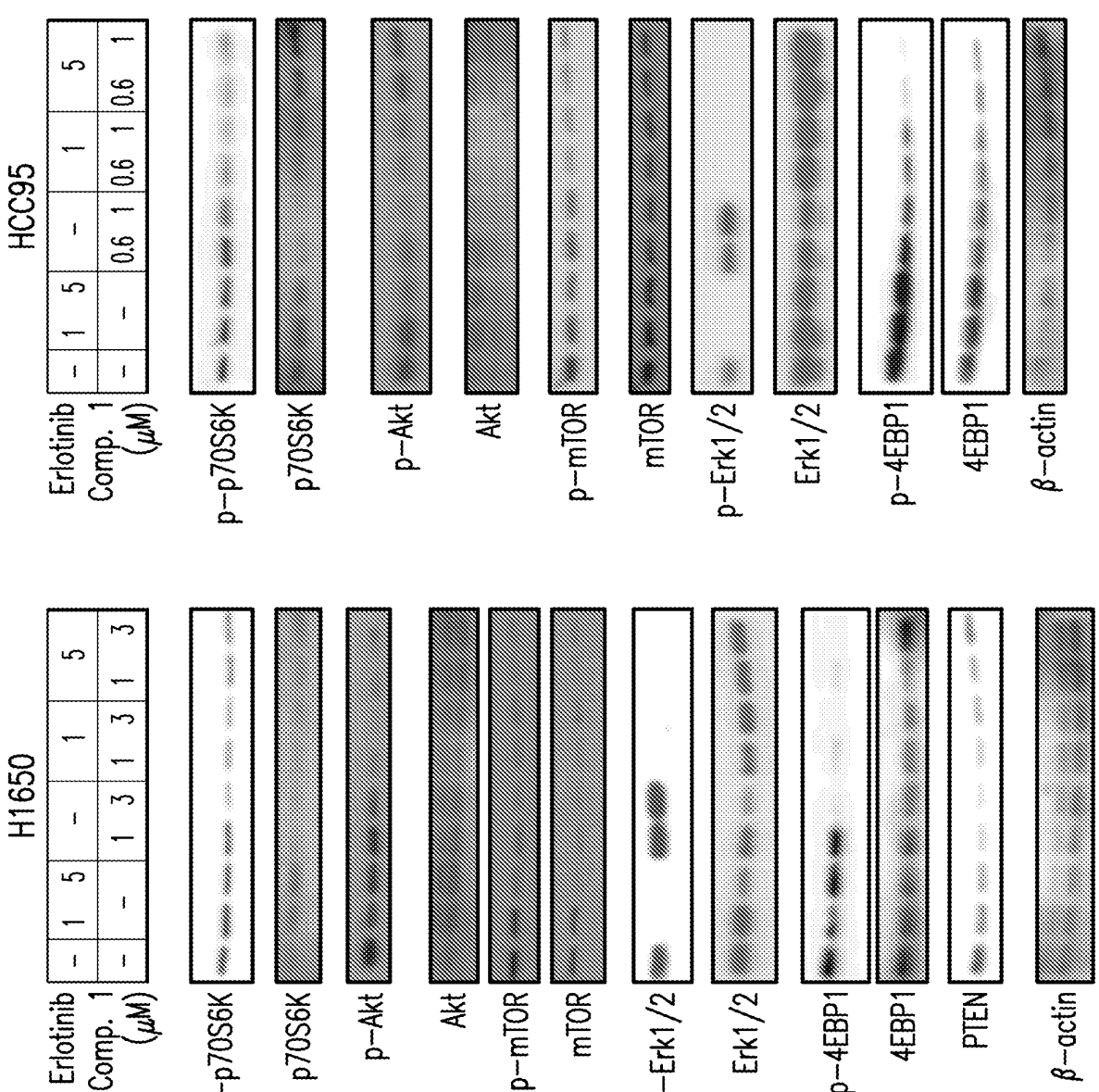

H1650
Erlotinib (μM)
Comp. 1 (μM)
– 1 5 – 1 5
– – 1 3 1 3 1 3
p–p70S6K
p70S6K
p–Akt
Akt
p–mTOR
mTOR
p–Erk1/2
Erk1/2
p–4EBP1
4EBP1
PTEN
β–actin
HCC95
Erlotinib (μM)
Comp. 1 (μM)
– 1 5 – 1 5
– – 0.6 1 0.6 1 0.6 1
p–p70S6K
p70S6K
p–Akt
Akt
p–mTOR
mTOR
p–Erk1/2
Erk1/2
p–4EBP1
4EBP1
β–actin

FIG. 7B

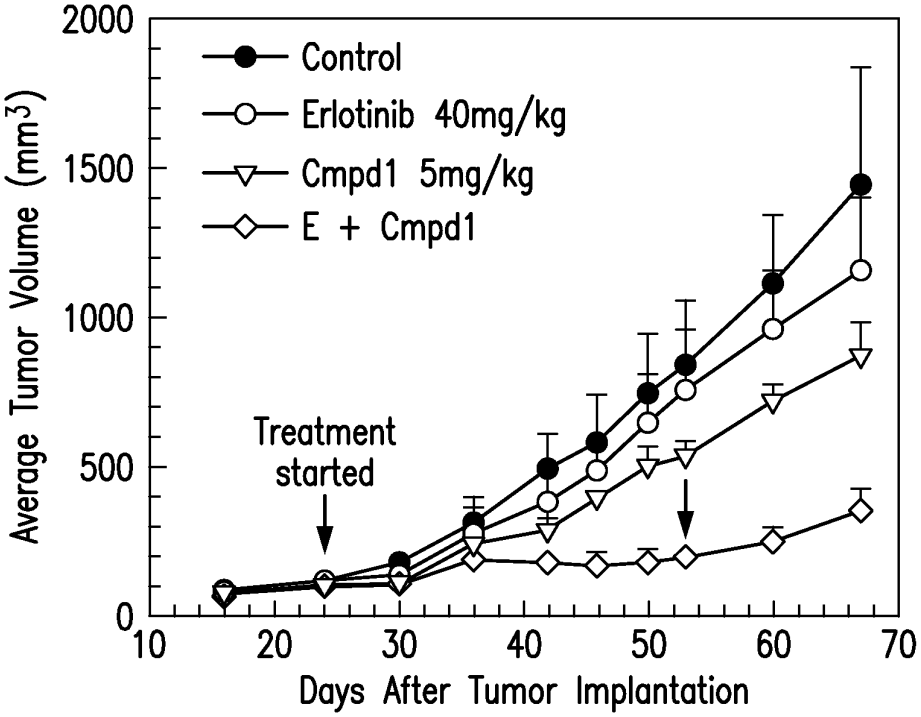

2000
1500
1000
500
0
Average Tumor Volume (mm3)
Control
Erlotinib 40mg/kg
Cmpd1 5mg/kg
E + Cmpd1
Treatment started
10
20
30
40
50
60
70
Days After Tumor Implantation

FIG. 8

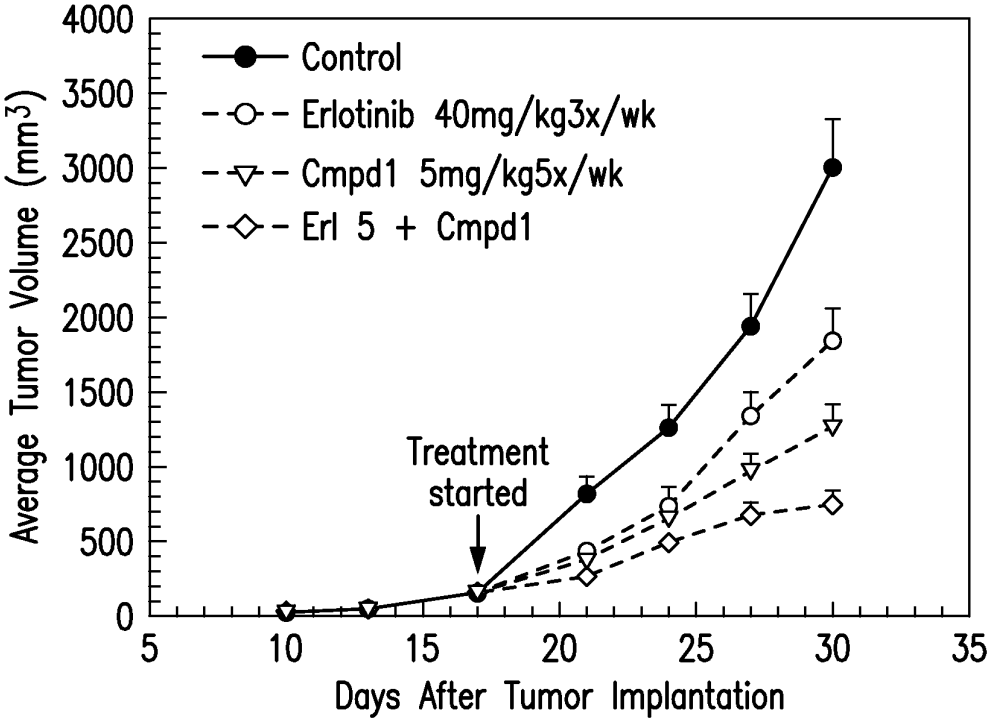

Control
Erlotinib 40mg/kg3x/wk
Cmpd1 5mg/kg5x/wk
Erl 5 + Cmpd1
Treatment started
Average Tumor Volume (mm3)
Days After Tumor Implantation
0
500
1000
1500
2000
2500
3000
3500
4000
5
10
15
20
25
30
35

FIG. 9