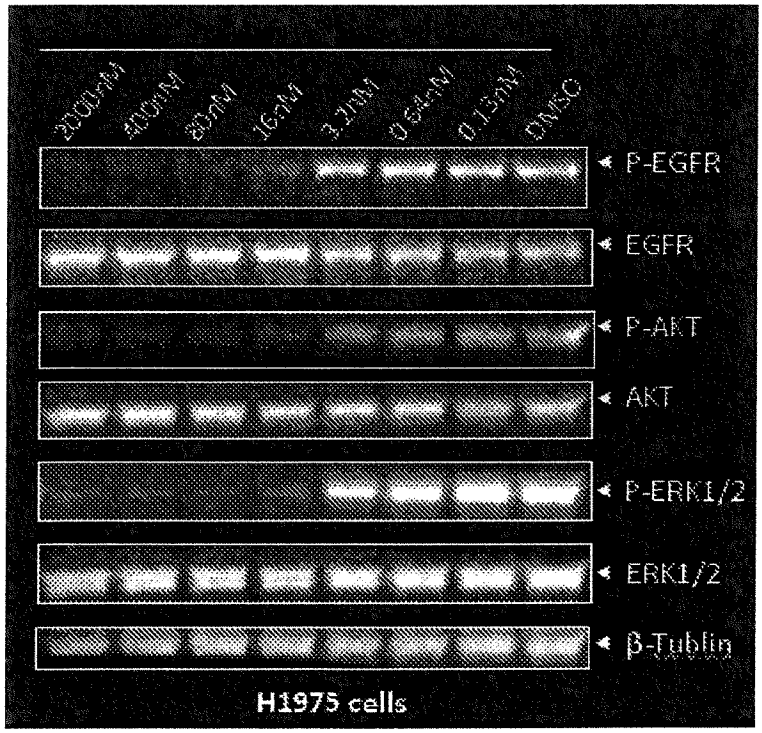

Figure 1

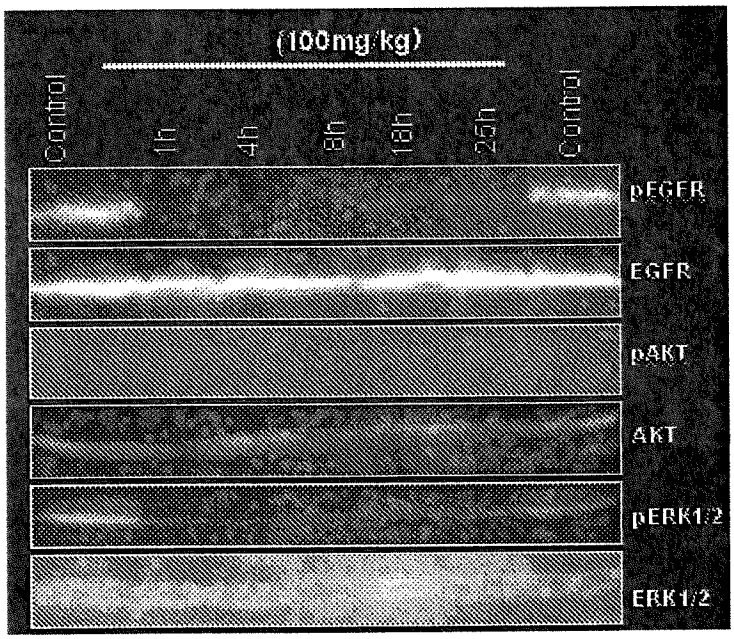
(100mg/kg)
Control
1h
4h
8h
18h
25h
Control
pEGFR
EGFR
pAKT
AKT
pERK1/2
ERK1/2

Figure 2

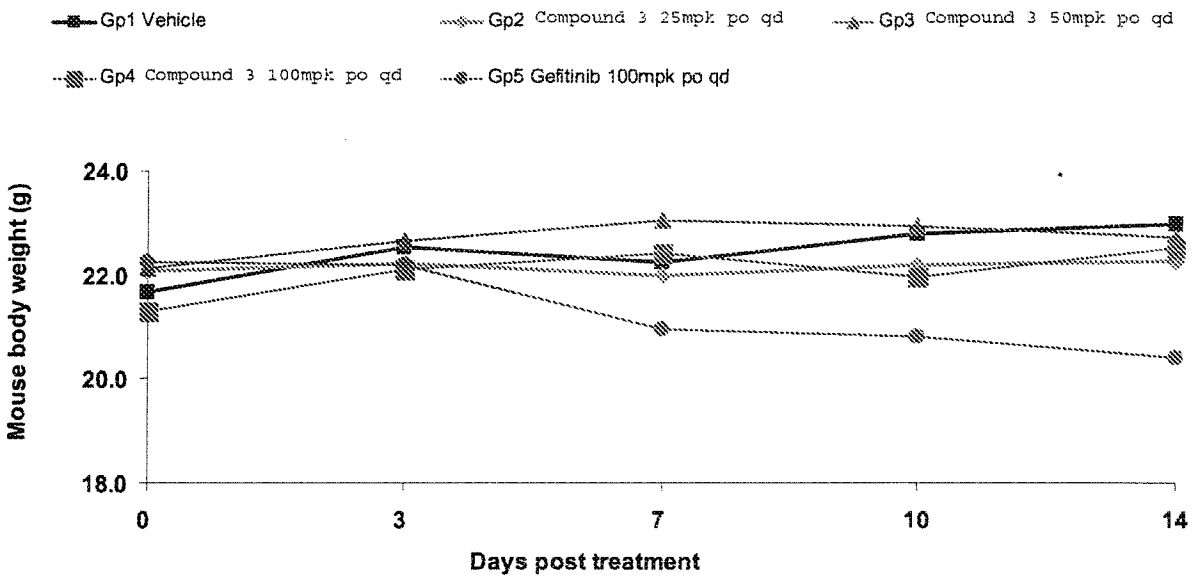
Gp1 Vehicle
Gp2 Compound 3 25mpk po qd
Gp3 Compound 3 50mpk po qd
Gp4 Compound 3 100mpk po qd
Gp5 Gefitinib 100mpk po qd
Mouse body weight (g)
24.0
22.0
20.0
18.0
0
3
7
10
14
Days post treatment

Figure 3

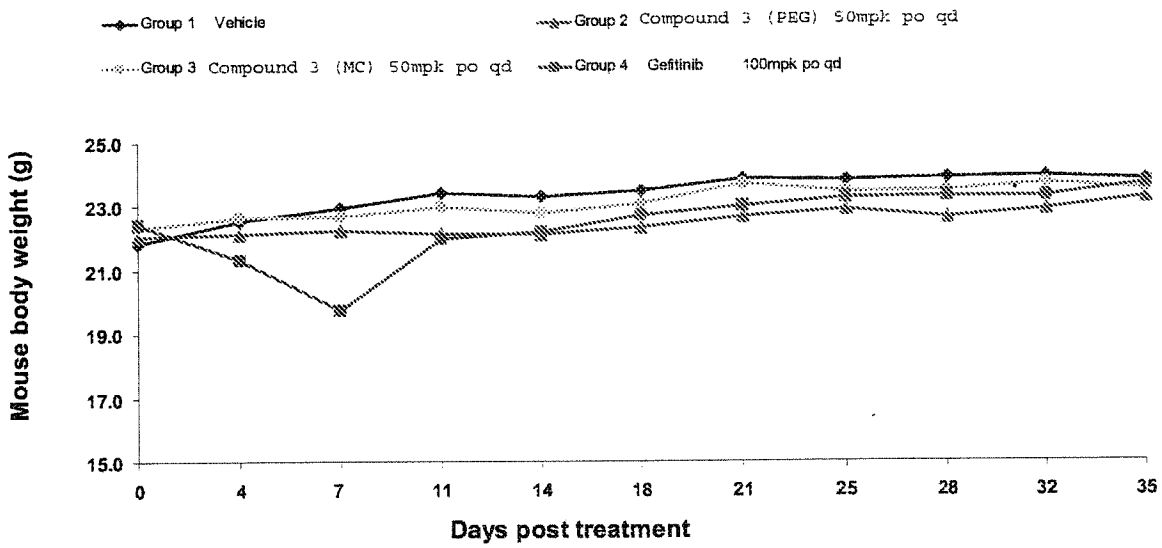
Group 1 Vehicle
Group 2 Compound 3 (PEG) 50mpk po qd
Group 3 Compound 3 (MC) 50mpk po qd
Group 4 Gefitinib 100mpk po qd
Mouse body weight (g)
25.0
23.0
21.0
19.0
17.0
15.0
0
4
7
11
14
18
21
25
28
32
35
Days post treatment

Figure 4

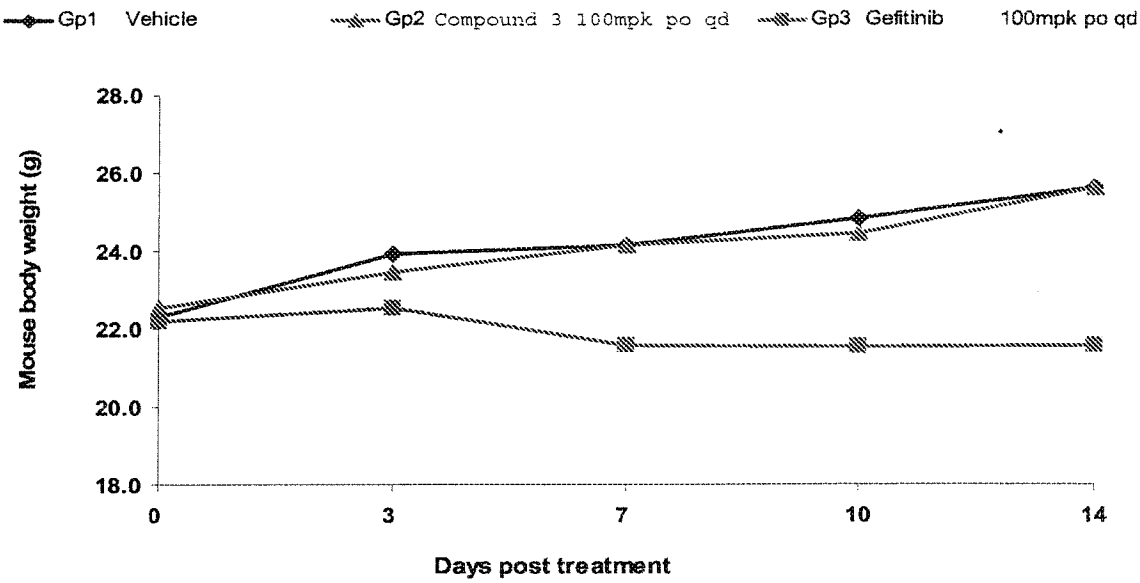
Gp1 Vehicle
Gp2 Compound 3 100mpk po qd
Gp3 Gefitinib 100mpk po qd
Mouse body weight (g)
28.0
26.0
24.0
22.0
20.0
18.0
0
3
7
10
14
Days post treatment

Figure 5

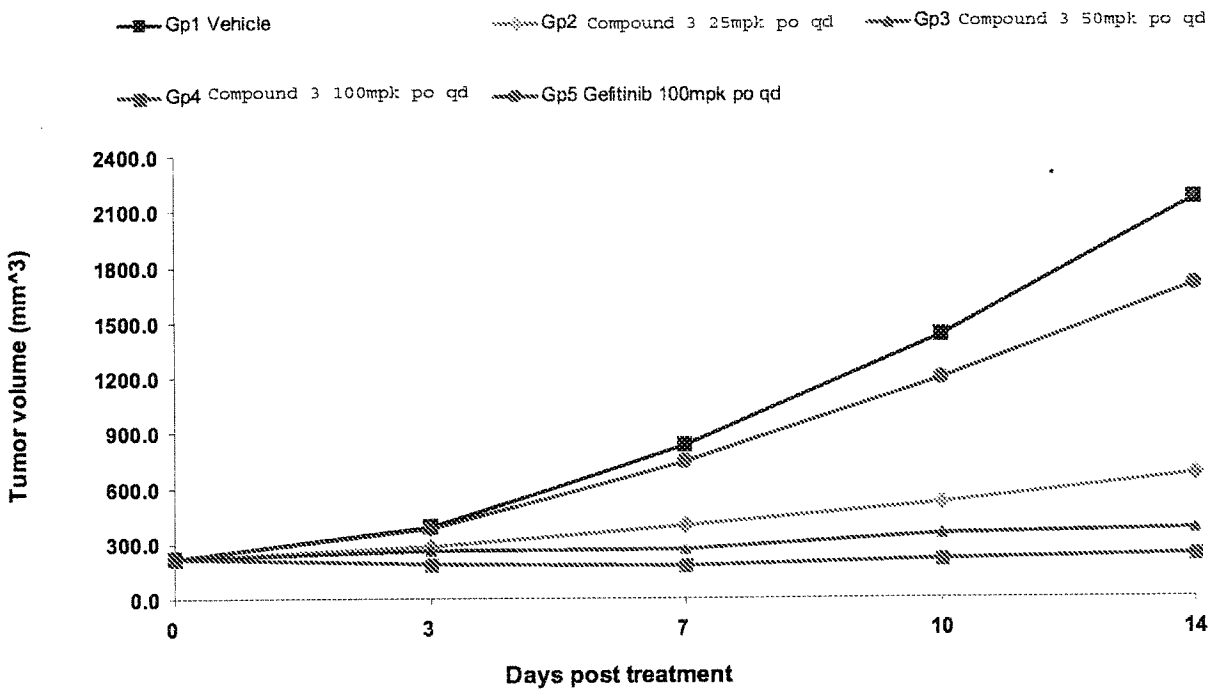
Gp1 Vehicle
Gp2 Compound 3 25mpk po qd
Gp3 Compound 3 50mpk po qd
Gp4 Compound 3 100mpk po qd
Gp5 Gefitinib 100mpk po qd
Tumor volume (mm^3)
2400.0
2100.0
1800.0
1500.0
1200.0
900.0
600.0
300.0
0.0
0
3
7
10
14
Days post treatment

Figure 6

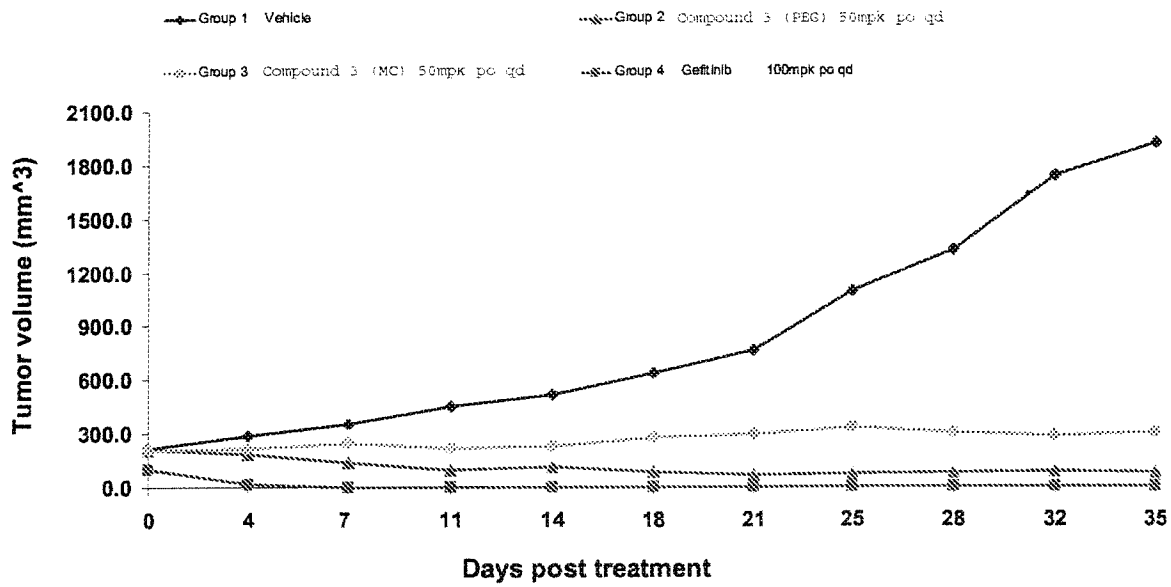
Group 1 Vehicle
Group 2 Compound 3 (PEG) 50mpk po qd
Group 3 Compound 3 (MC) 50mpk po qd
Group 4 Gefitinib 100mpk po qd
Tumor volume (mm^3)
2100.0
1800.0
1500.0
1200.0
900.0
600.0
300.0
0.0
0
4
7
11
14
18
21
25
28
32
35
Days post treatment

Figure 7

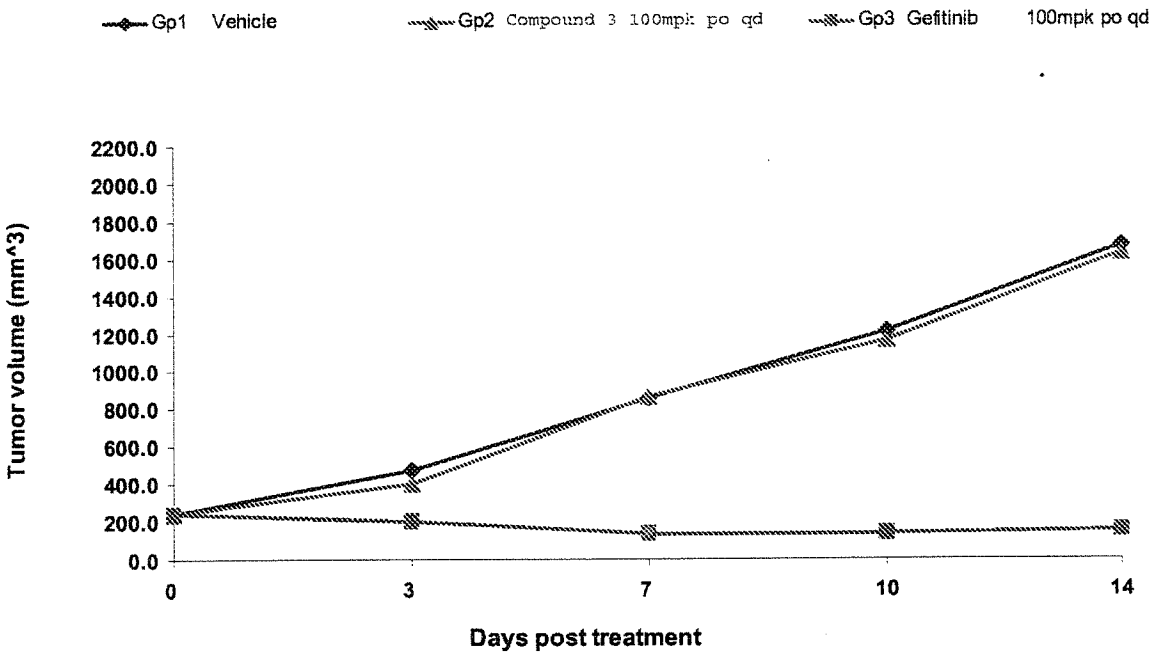
Gp1 Vehicle
Gp2 Compound 3 100mpk po qd
Gp3 Gefitinib 100mpk po qd
Tumor volume (mm^3)
2200.0
2000.0
1800.0
1600.0
1400.0
1200.0
1000.0
800.0
600.0
400.0
200.0
0.0
0
3
7
10
14
Days post treatment

Figure 8

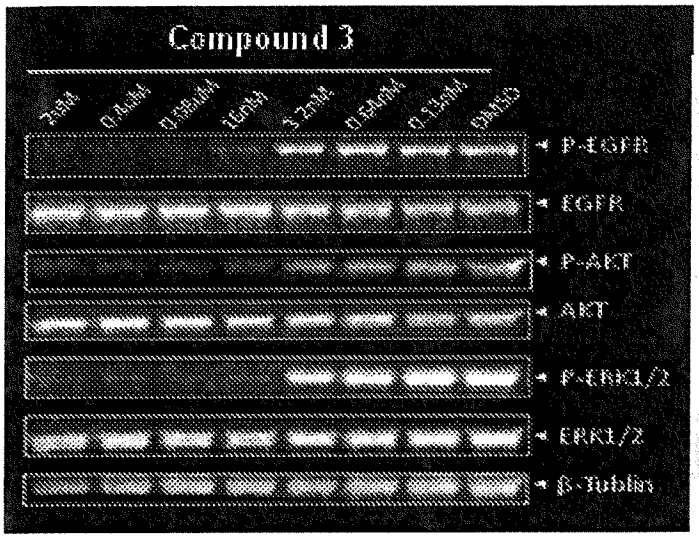

Figure 9A

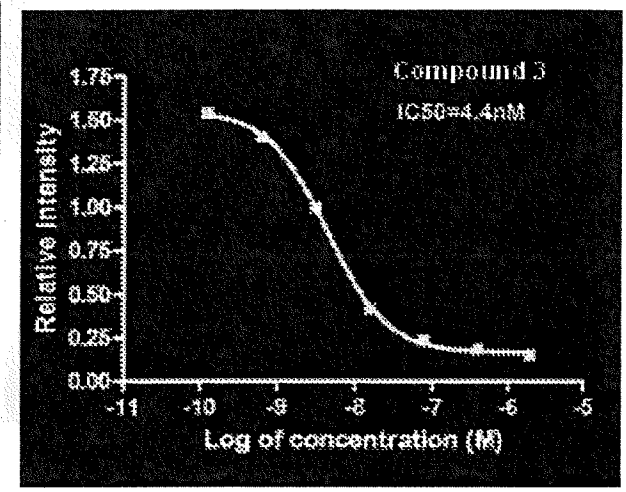

Figure 9B

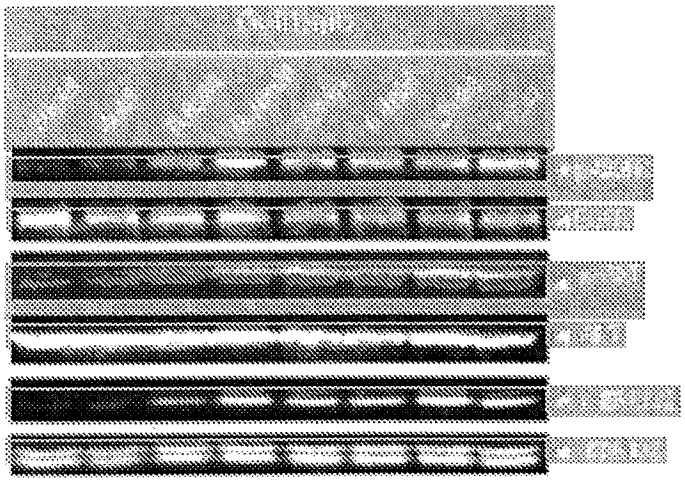

Figure 9C

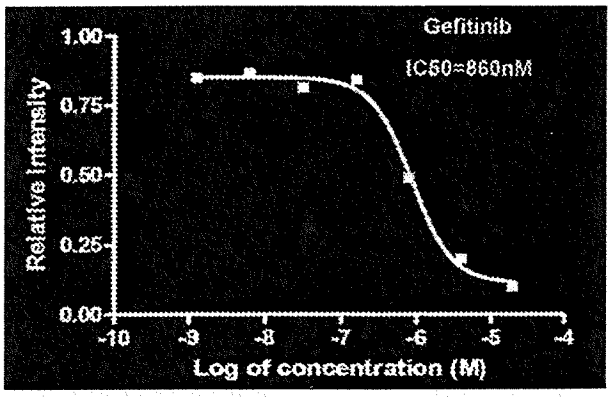

Figure 9D

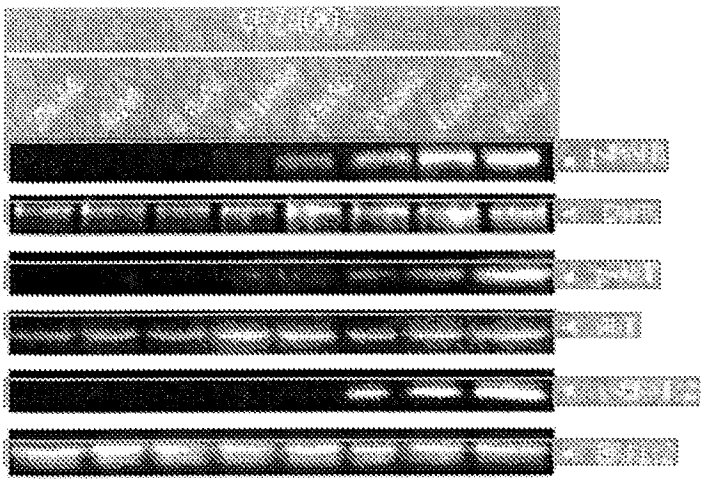

Figure 9E

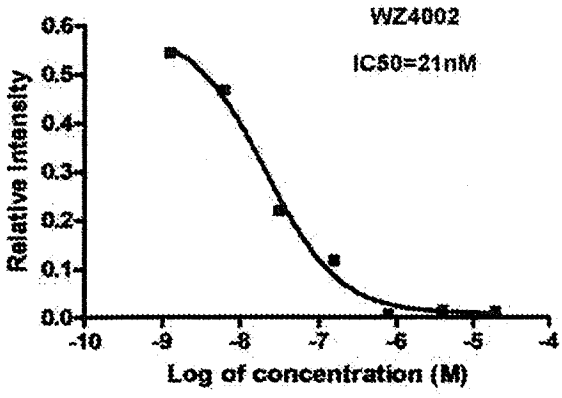

Figure 9F

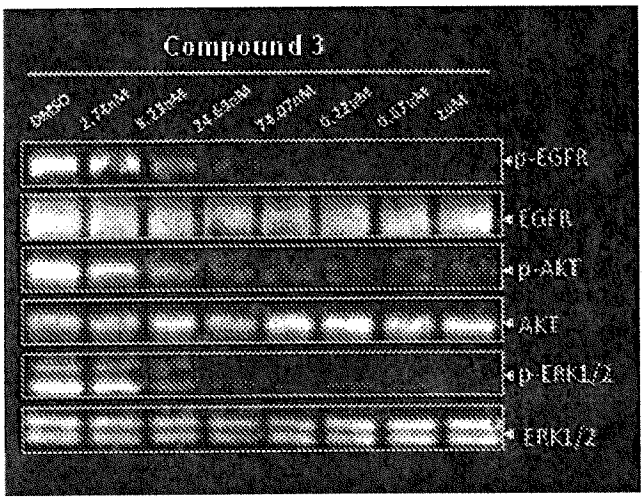

Figure 10A

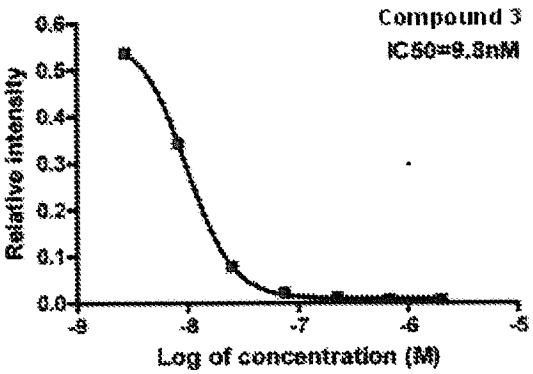

Figure 10B

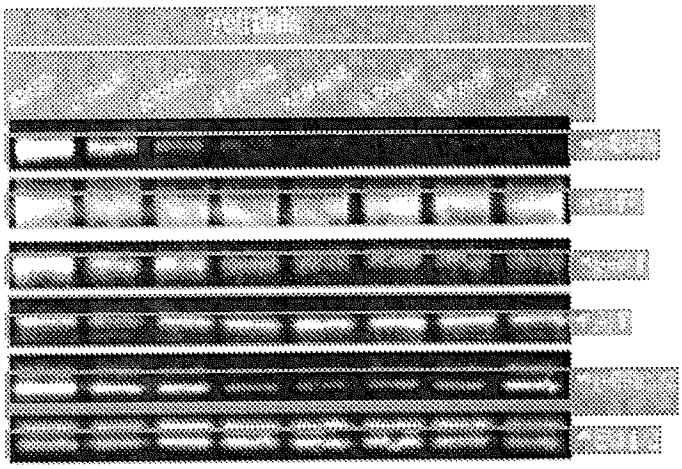

Figure 10C

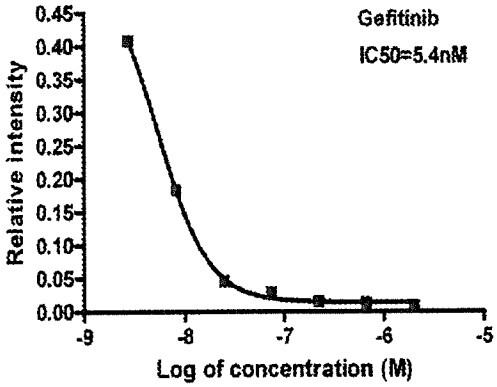

Figure 10D

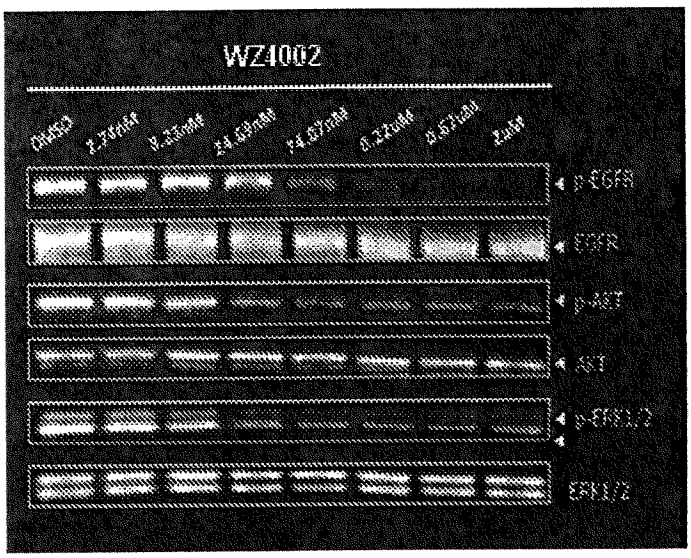

Figure 10E

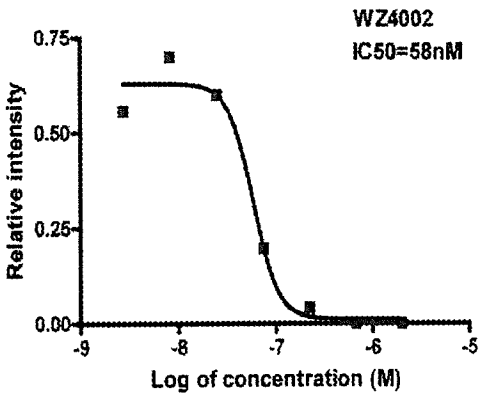

Figure 10F

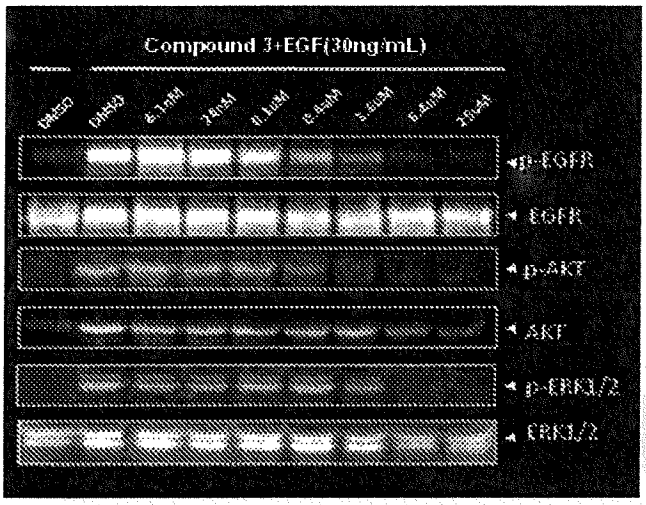

Figure 11A

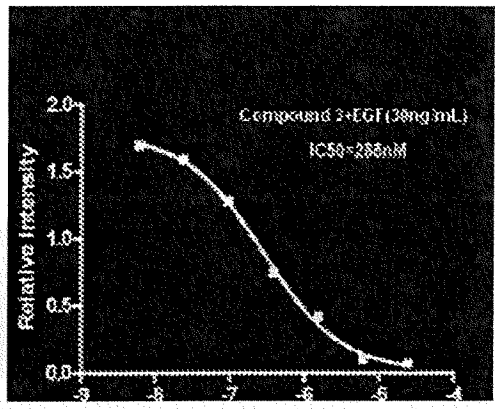

Figure 11B

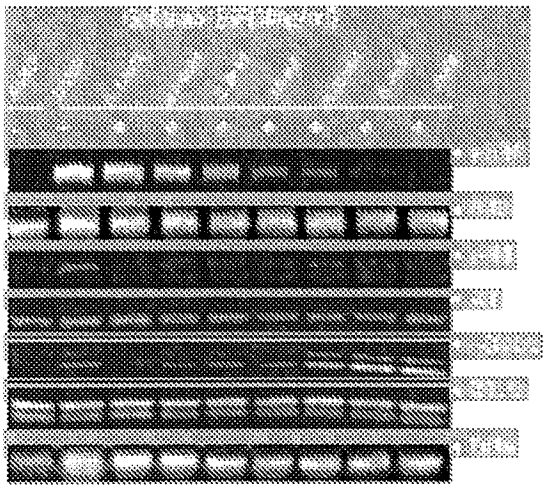

Figure 11C

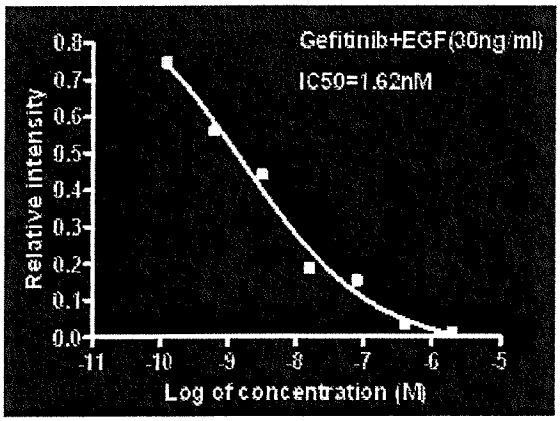

Figure 11D

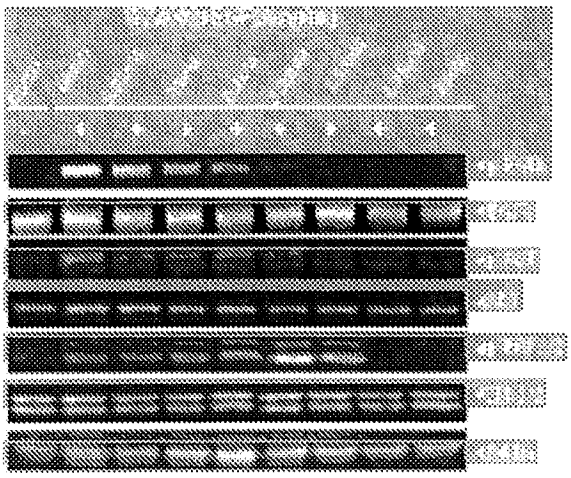

Figure 11E

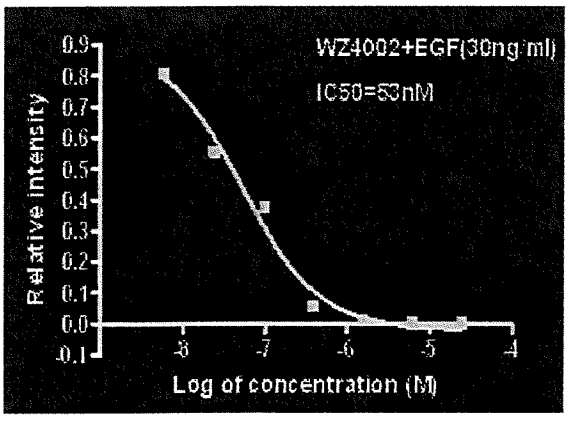

Figure 11F

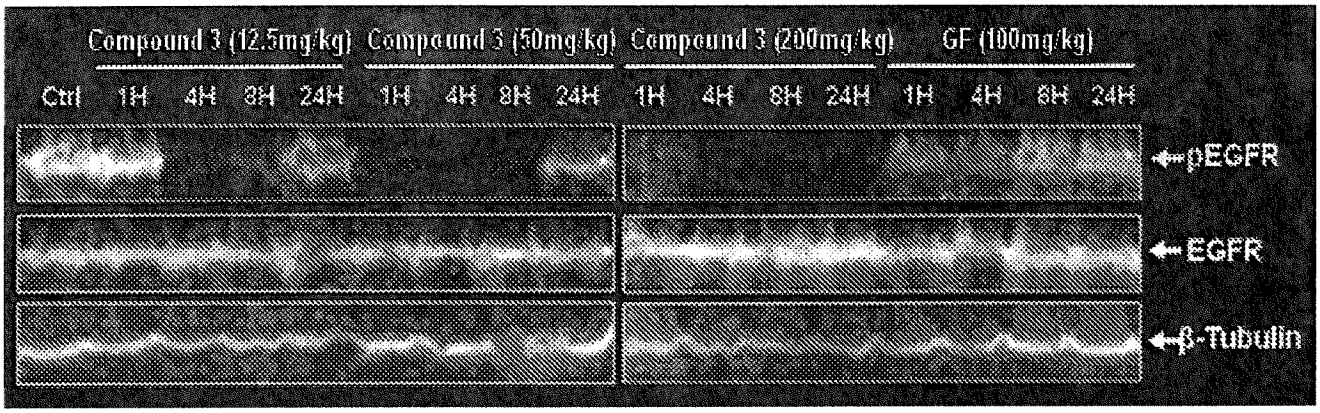
Compound 3 (12.5mg/kg)
Compound 3 (50mg/kg)
Compound 3 (200mg/kg)
GF (100mg/kg)
Ctrl
1H
4H
8H
24H
pEGFR
EGFR
β-Tubulin

Figure 12

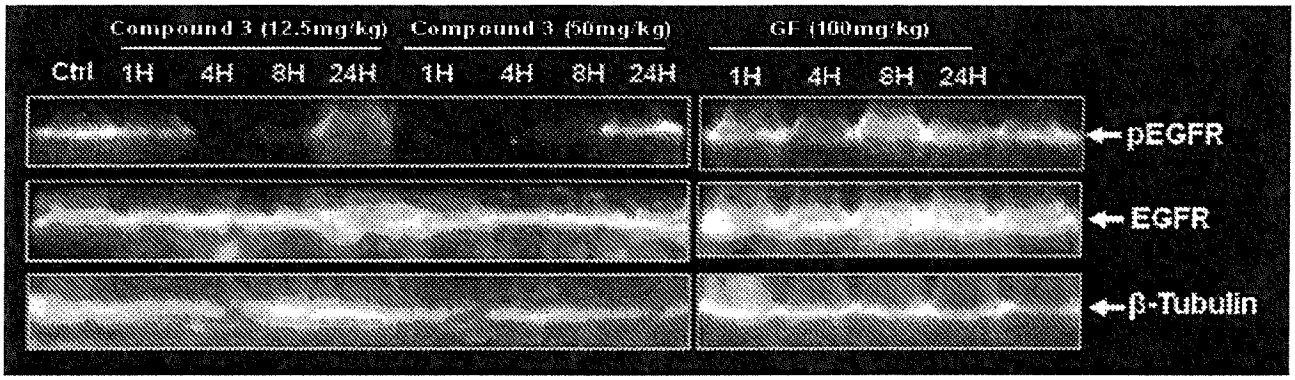
Compound 3 (12.5mg/kg)
Compound 3 (50mg/kg)
GF (100mg/kg)
Ctrl
1H
4H
8H
24H
1H
4H
8H
24H
1H
4H
8H
24H
pEGFR
EGFR
β-Tubulin

Figure 13

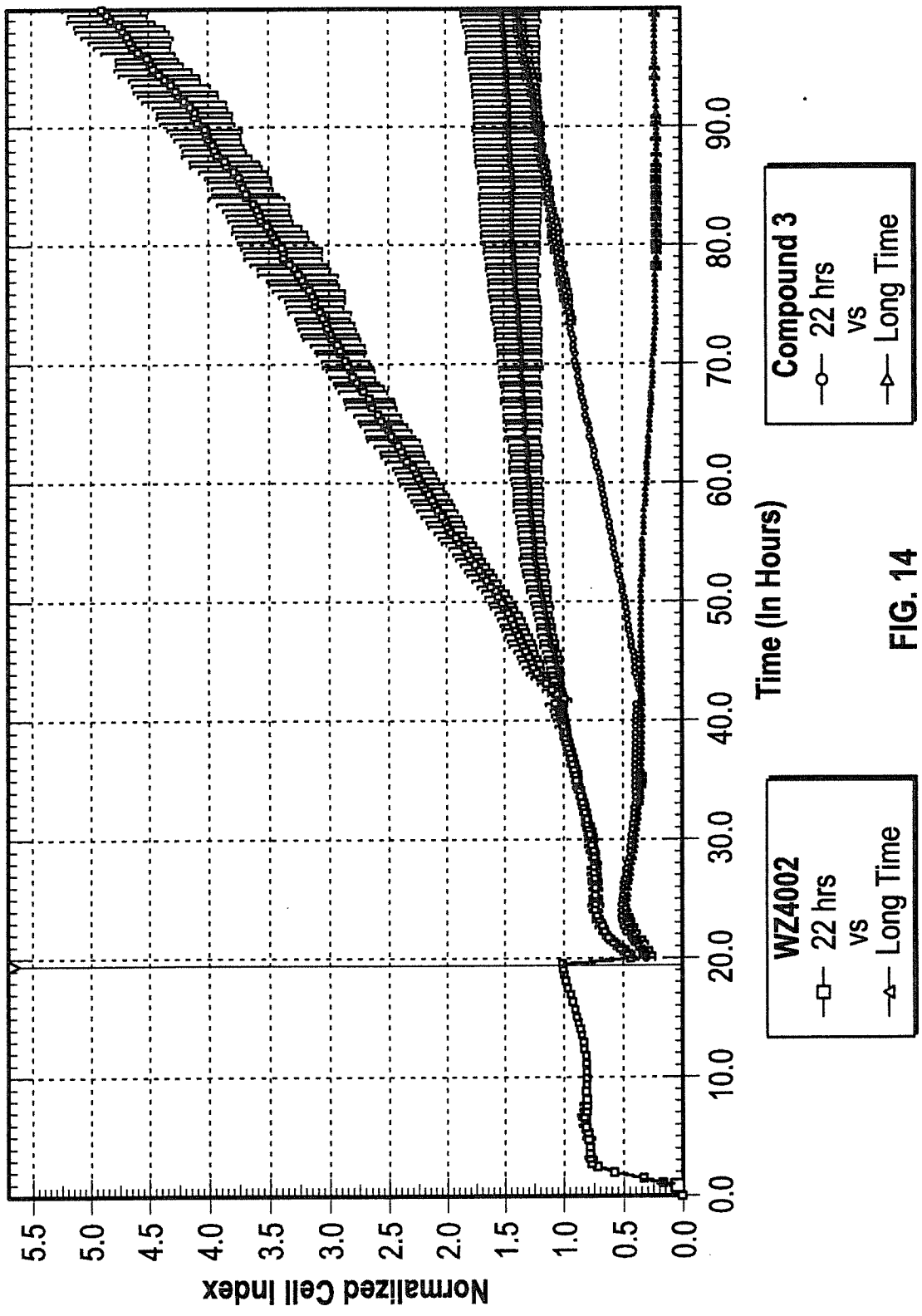
Normalized Cell Index
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
Time (In Hours)
WZ4002
22 hrs
vs
Long Time
Compound 3
22 hrs
vs
Long Time

FIG. 14

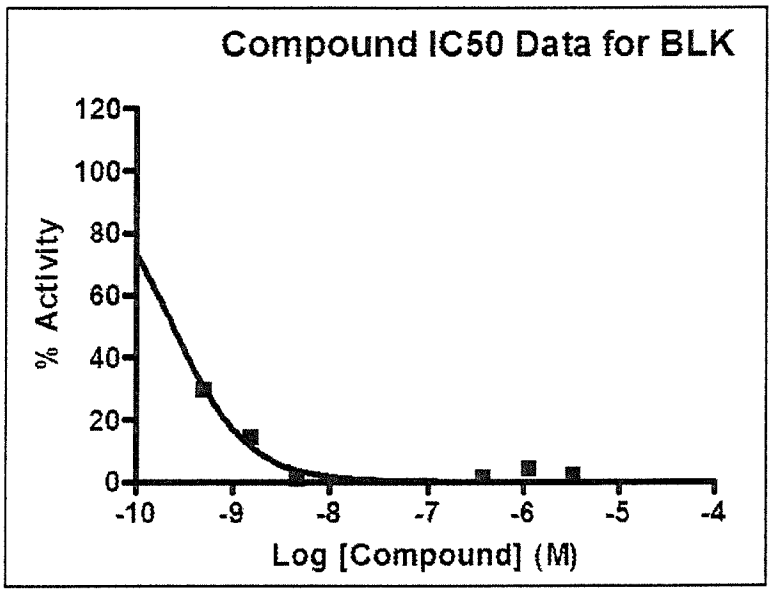

Figure 15A

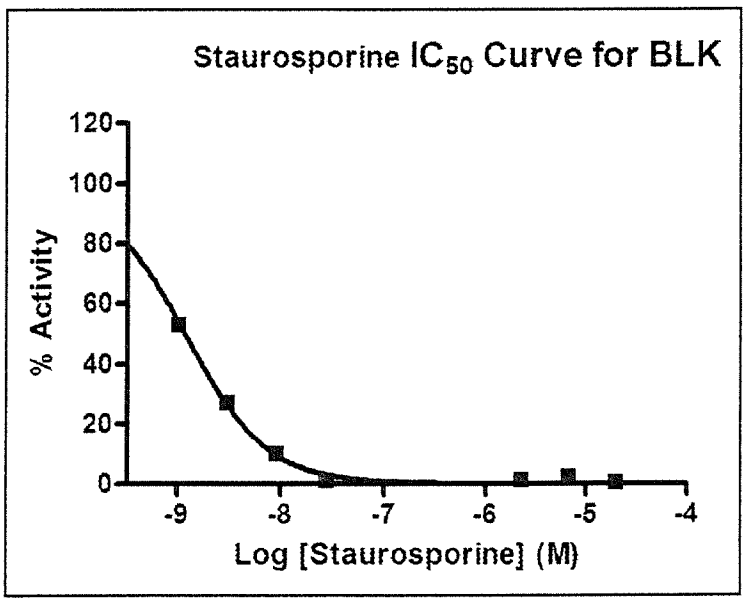

Figure 15B

Figure 15

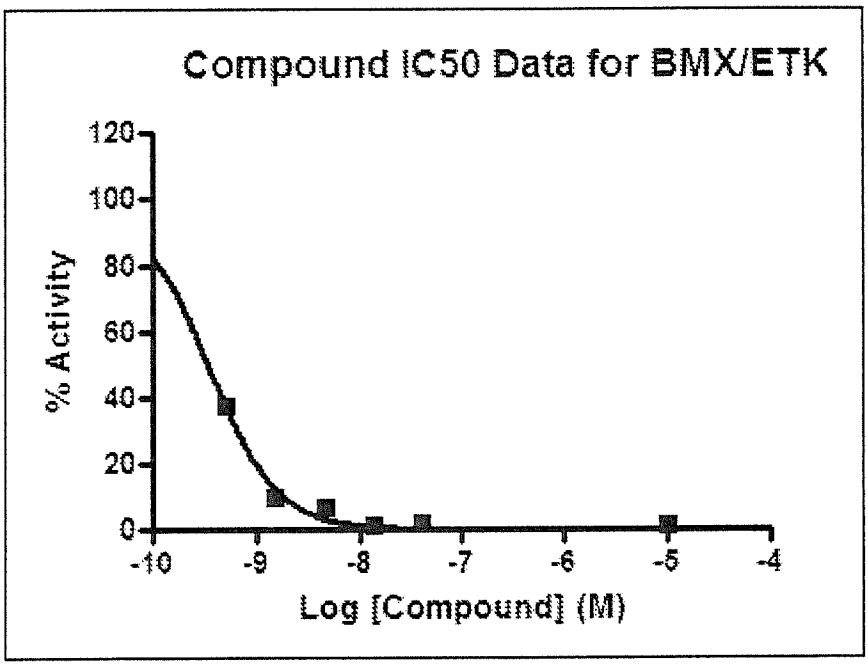
Compound IC50 Data for BMX/ETK
% Activity
120
100
80
60
40
20
0
-10
-9
-8
-7
-6
-5
-4
Log [Compound] (M)

Figure 16

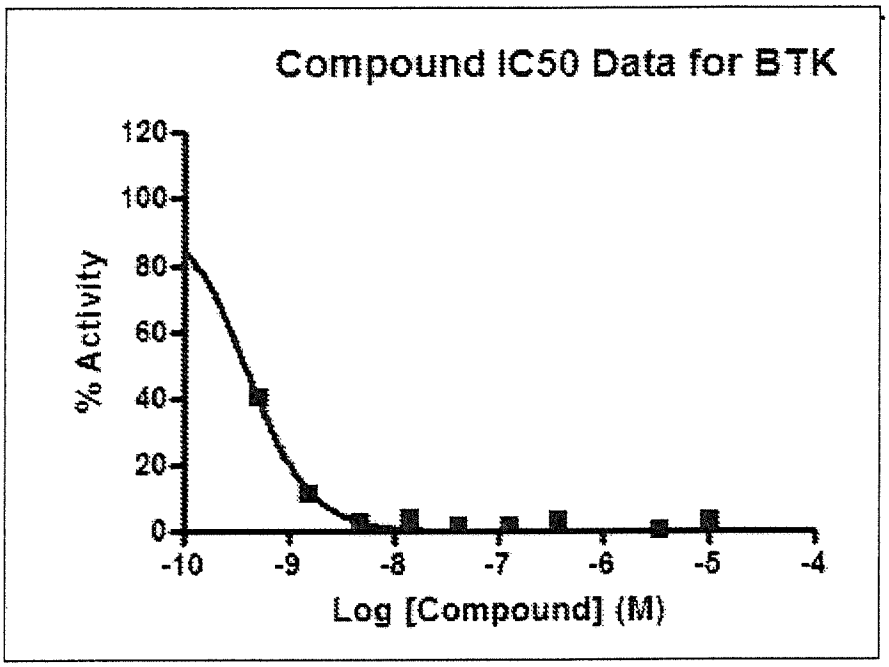
Compound IC50 Data for BTK
% Activity
120
100
80
60
40
20
0
-10
-9
-8
-7
-6
-5
-4
Log [Compound] (M)

Figure 17

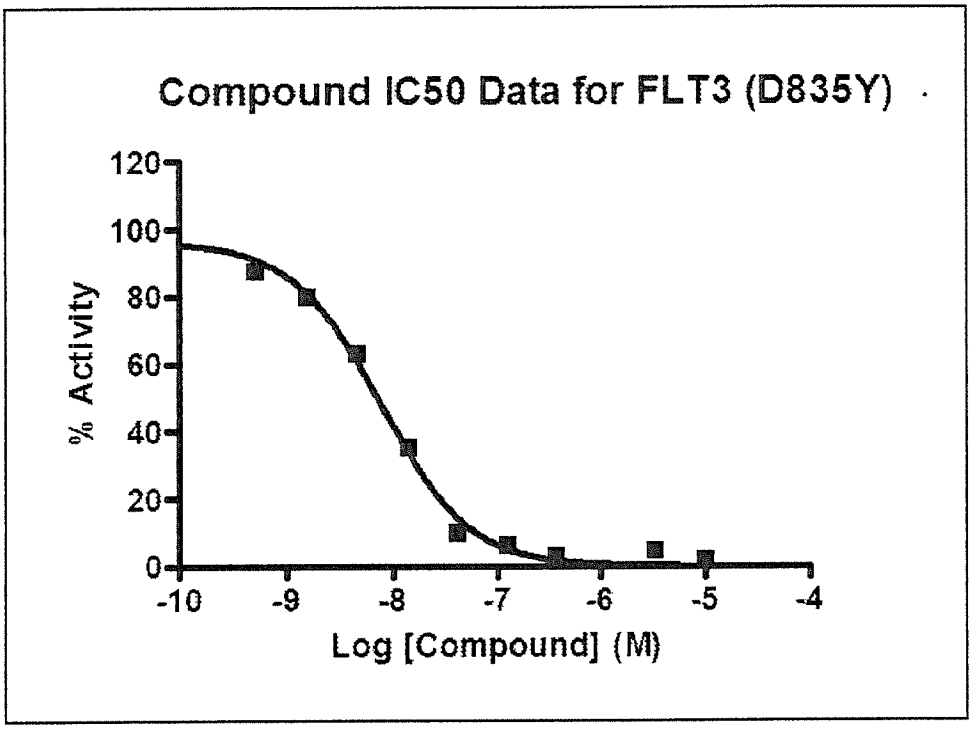
Compound IC50 Data for FLT3 (D835Y)
% Activity
120
100
80
60
40
20
0
-10
-9
-8
-7
-6
-5
-4
Log [Compound] (M)

Figure 18

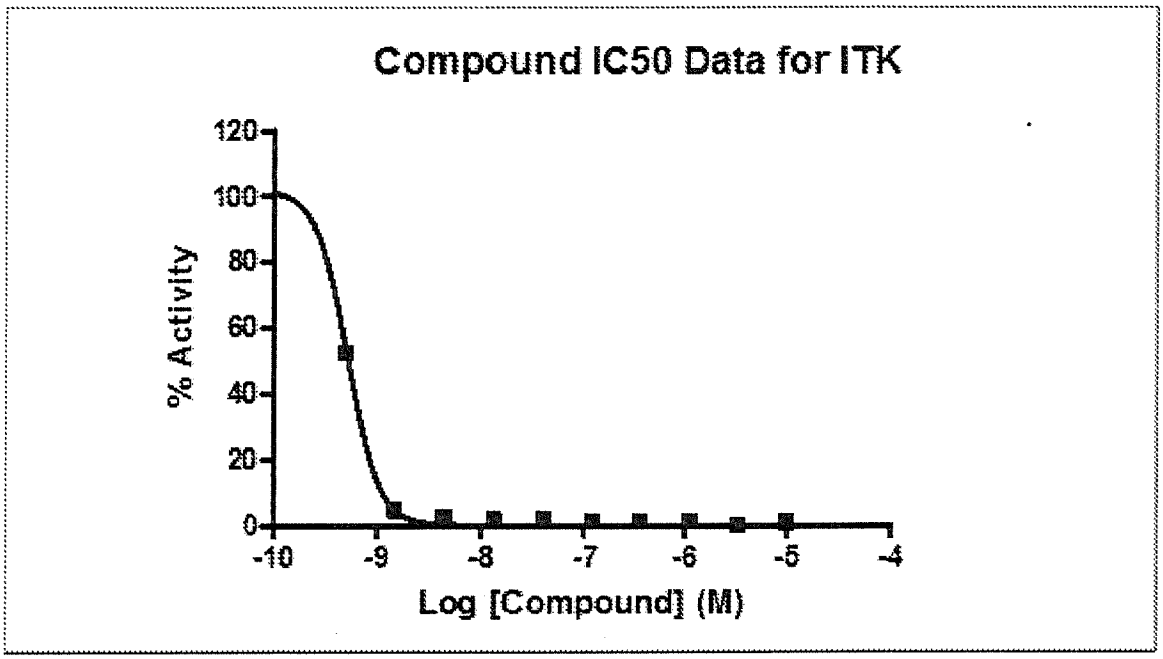
Compound IC50 Data for ITK
% Activity
120
100
80
60
40
20
0
-10
-9
-8
-7
-6
-5
-4
Log [Compound] (M)

Figure 19

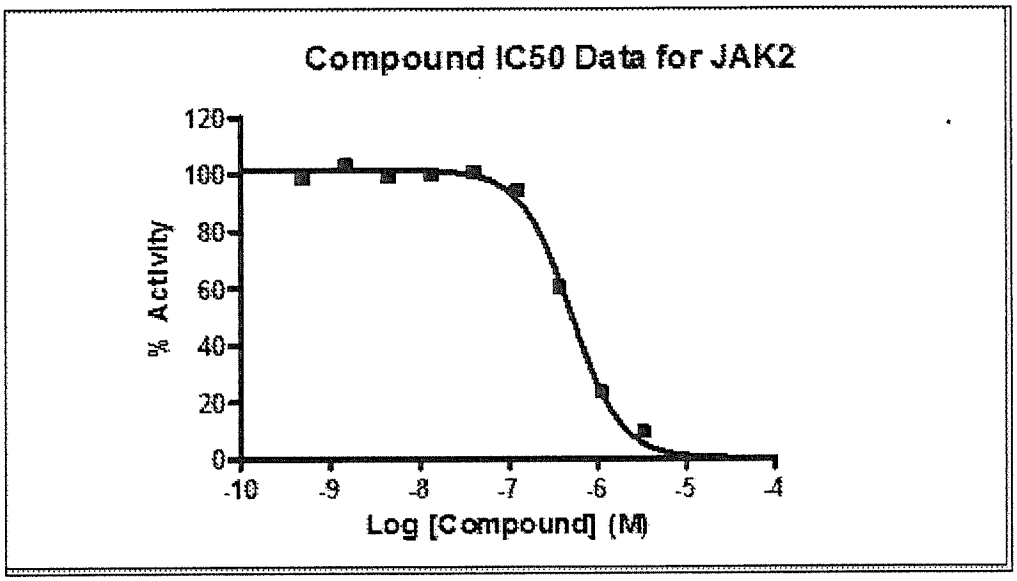
Compound IC50 Data for JAK2
% Activity
120
100
80
60
40
20
0
-10
-9
-8
-7
-6
-5
-4
Log [Compound] (M)

Figure 20

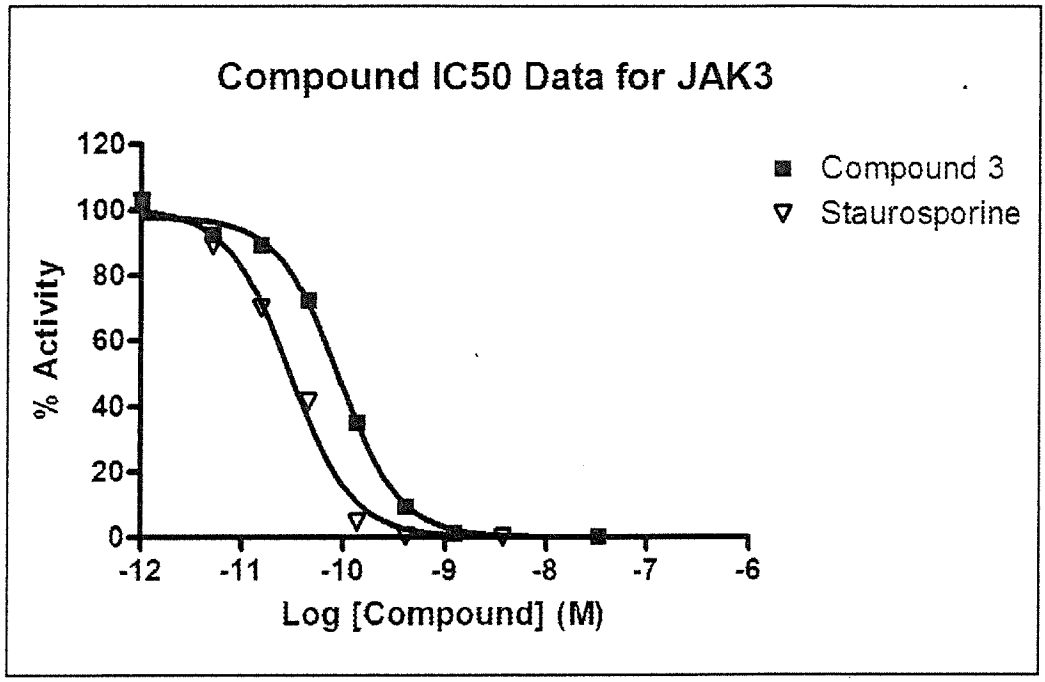
Compound IC50 Data for JAK3
Compound 3
Staurosporine
% Activity
120
100
80
60
40
20
0
-12
-11
-10
-9
-8
-7
-6
Log [Compound] (M)

Figure 21

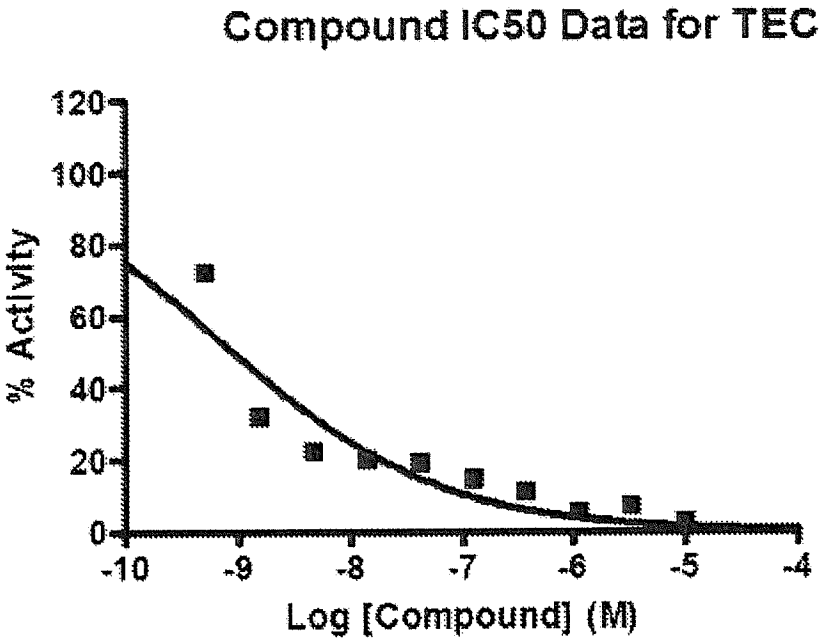
Compound IC50 Data for TEC
% Activity
120
100
80
60
40
20
0
-10
-9
-8
-7
-6
-5
-4
Log [Compound] (M)

Figure 22

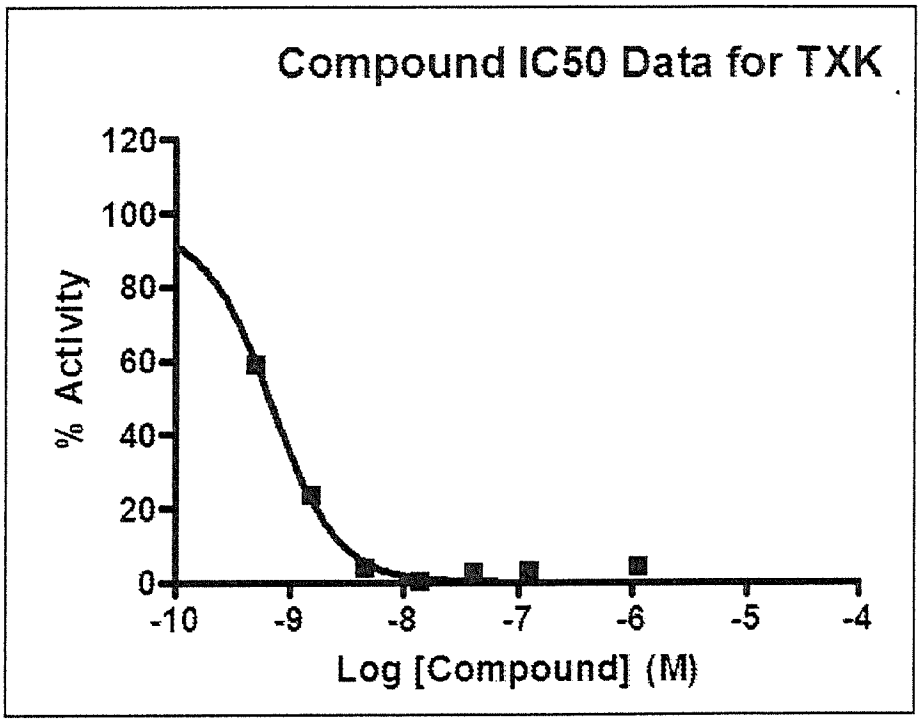
Compound IC50 Data for TXK
% Activity
120
100
80
60
40
20
0
-10
-9
-8
-7
-6
-5
-4
Log [Compound] (M)

Figure 23