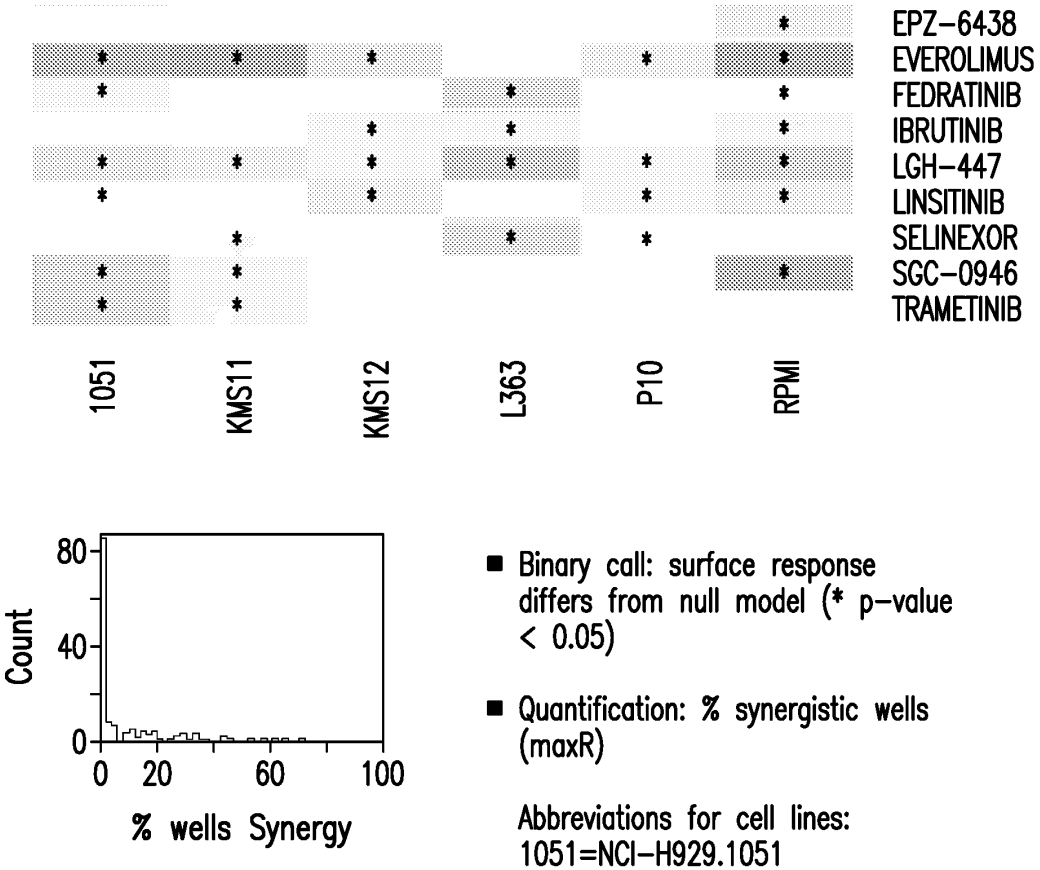

EPZ-6438
EVEROLIMUS
FEDRATINIB
IBRUTINIB
LGH-447
LINSITINIB
SELINEXOR
SGC-0946
TRAMETINIB
1051
KMS11
KMS12
L363
P10
RPMI
Count
80
40
0
0
20
60
100
% wells Synergy
Binary call: surface response differs from null model (* p-value < 0.05)
Quantification: % synergistic wells (maxR)
Abbreviations for cell lines:
1051=NCI-H929.1051
P10=OPM-2.P10
KMS12=KM5-12-PE
RPMI=RPMI-8226

FIG. 1

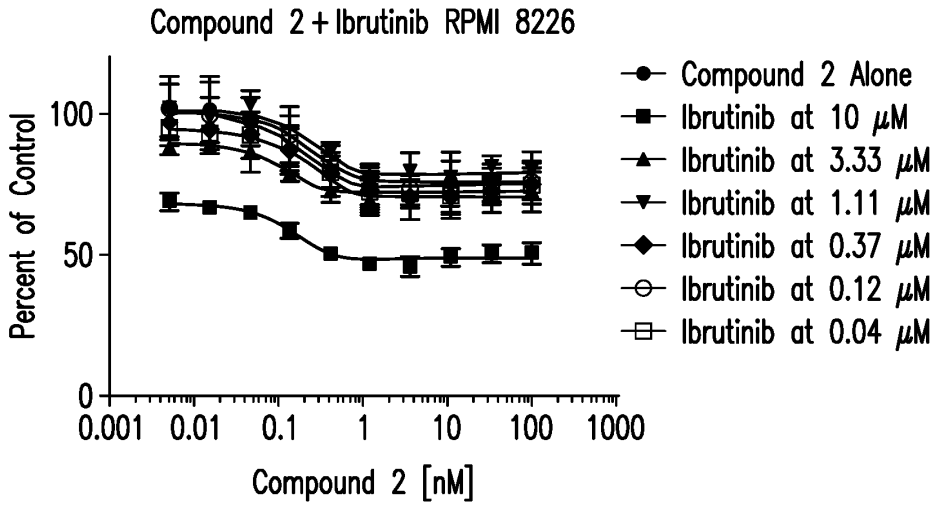

Compound 2 + Ibrutinib RPMI 8226
Percent of Control
100
50
0
0.001
0.01
0.1
1
10
100
1000
Compound 2 [nM]
Compound 2 Alone
Ibrutinib at 10 μM
Ibrutinib at 3.33 μM
Ibrutinib at 1.11 μM
Ibrutinib at 0.37 μM
Ibrutinib at 0.12 μM
Ibrutinib at 0.04 μM

FIG. 2A

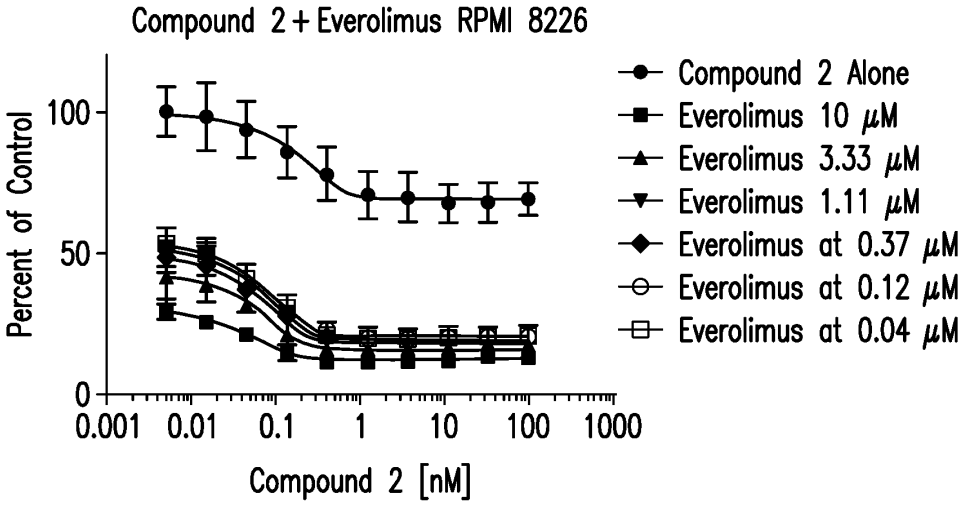

Compound 2 + Everolimus RPMI 8226
Percent of Control
100
50
0
0.001
0.01
0.1
1
10
100
1000
Compound 2 [nM]
Compound 2 Alone
Everolimus 10 μM
Everolimus 3.33 μM
Everolimus 1.11 μM
Everolimus at 0.37 μM
Everolimus at 0.12 μM
Everolimus at 0.04 μM

FIG. 2B

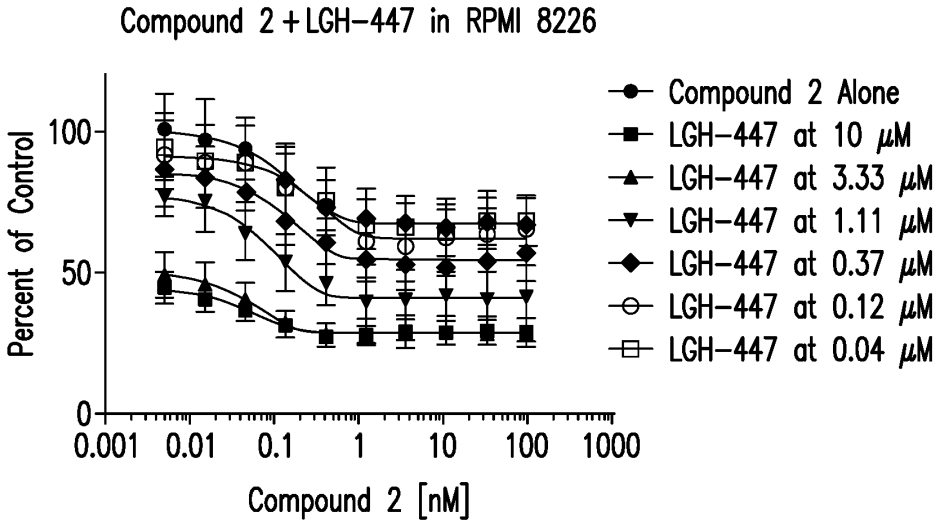

Compound 2 + LGH-447 in RPMI 8226
Percent of Control
100
50
0
0.001
0.01
0.1
1
10
100
1000
Compound 2 [nM]
Compound 2 Alone
LGH-447 at 10 μM
LGH-447 at 3.33 μM
LGH-447 at 1.11 μM
LGH-447 at 0.37 μM
LGH-447 at 0.12 μM
LGH-447 at 0.04 μM

FIG. 2C

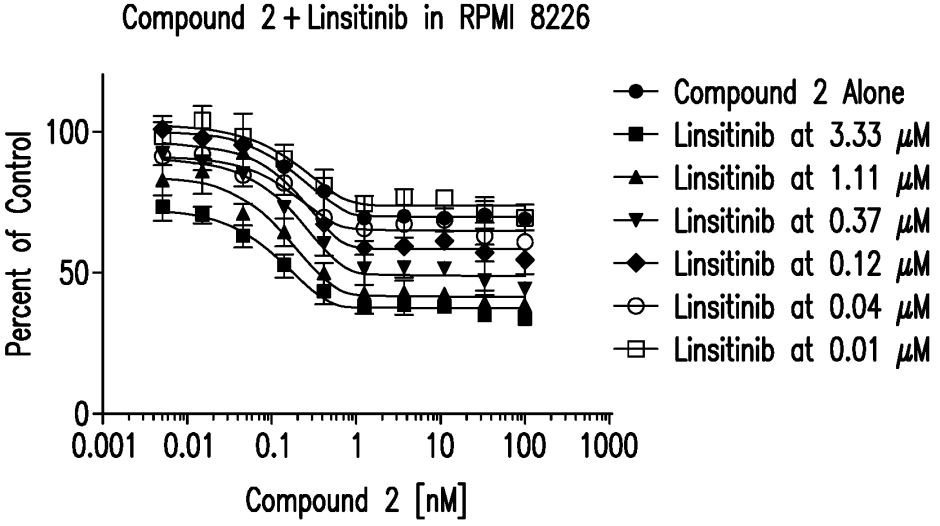

Compound 2 + Linsitinib in RPMI 8226
Percent of Control
100
50
0
0.001
0.01
0.1
1
10
100
1000
Compound 2 [nM]
Compound 2 Alone
Linsitinib at 3.33 μM
Linsitinib at 1.11 μM
Linsitinib at 0.37 μM
Linsitinib at 0.12 μM
Linsitinib at 0.04 μM
Linsitinib at 0.01 μM

FIG. 2D

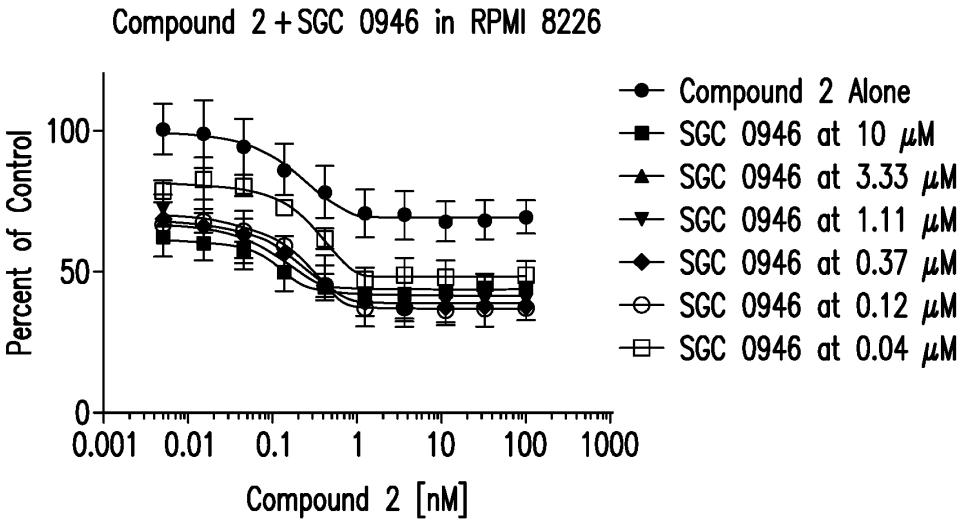

Compound 2 + SGC 0946 in RPMI 8226
Percent of Control
100
50
0
0.001
0.01
0.1
1
10
100
1000
Compound 2 [nM]
Compound 2 Alone
SGC 0946 at 10 μM
SGC 0946 at 3.33 μM
SGC 0946 at 1.11 μM
SGC 0946 at 0.37 μM
SGC 0946 at 0.12 μM
SGC 0946 at 0.04 μM

FIG. 2E

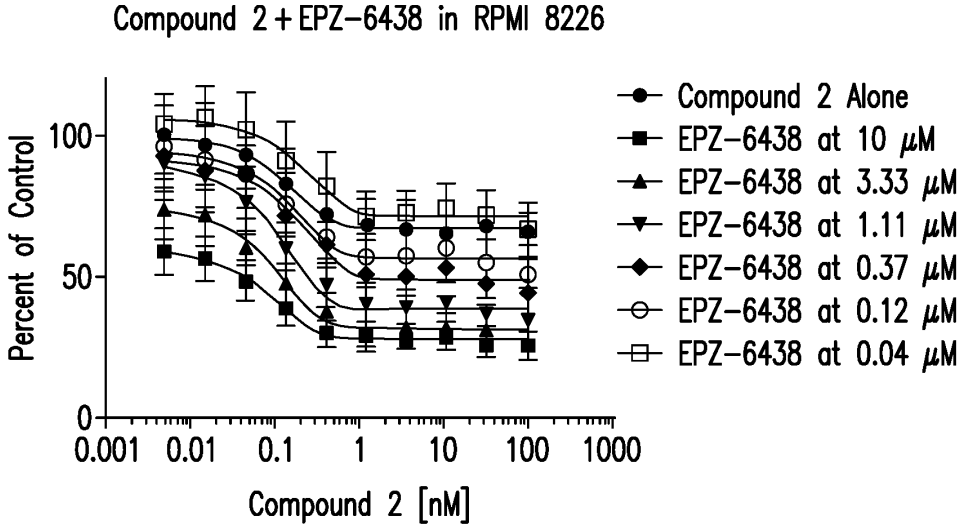

Compound 2 + EPZ-6438 in RPMI 8226
Percent of Control
100
50
0
0.001
0.01
0.1
1
10
100
1000
Compound 2 [nM]
Compound 2 Alone
EPZ-6438 at 10 μM
EPZ-6438 at 3.33 μM
EPZ-6438 at 1.11 μM
EPZ-6438 at 0.37 μM
EPZ-6438 at 0.12 μM
EPZ-6438 at 0.04 μM

FIG. 2F

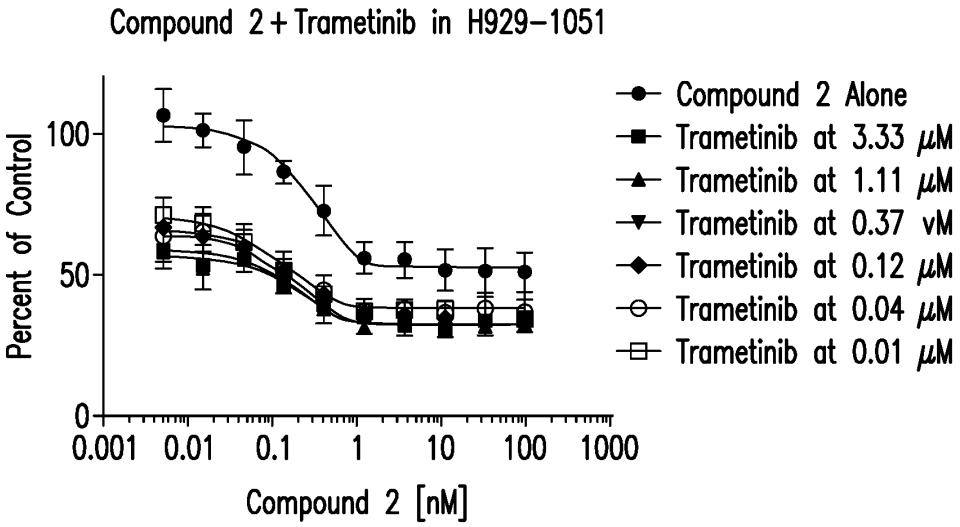

Compound 2 + Trametinib in H929-1051
Percent of Control
100
50
0
0.001
0.01
0.1
1
10
100
1000
Compound 2 [nM]
Compound 2 Alone
Trametinib at 3.33 μM
Trametinib at 1.11 μM
Trametinib at 0.37 vM
Trametinib at 0.12 μM
Trametinib at 0.04 μM
Trametinib at 0.01 μM

FIG. 2G

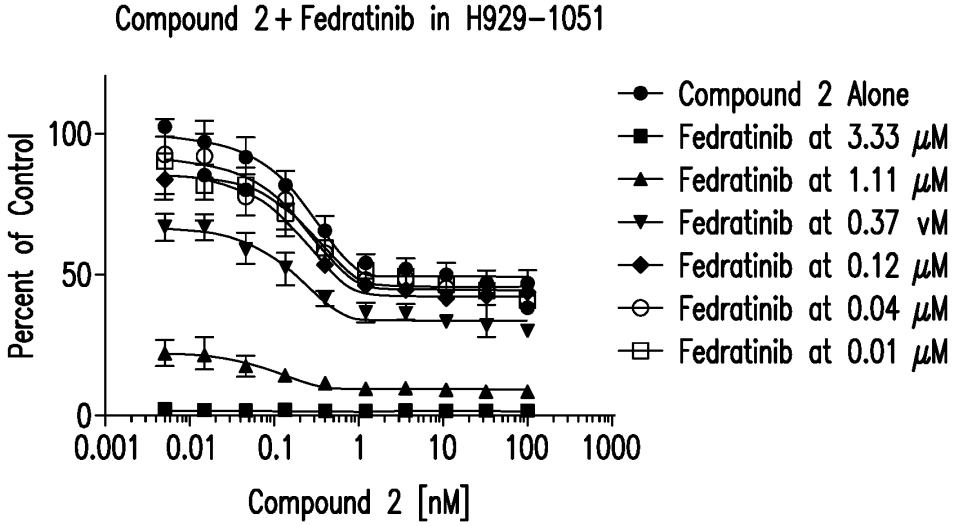

Compound 2 + Fedratinib in H929-1051
Percent of Control
100
50
0
0.001
0.01
0.1
1
10
100
1000
Compound 2 [nM]
Compound 2 Alone
Fedratinib at 3.33 μM
Fedratinib at 1.11 μM
Fedratinib at 0.37 vM
Fedratinib at 0.12 μM
Fedratinib at 0.04 μM
Fedratinib at 0.01 μM

FIG. 2H

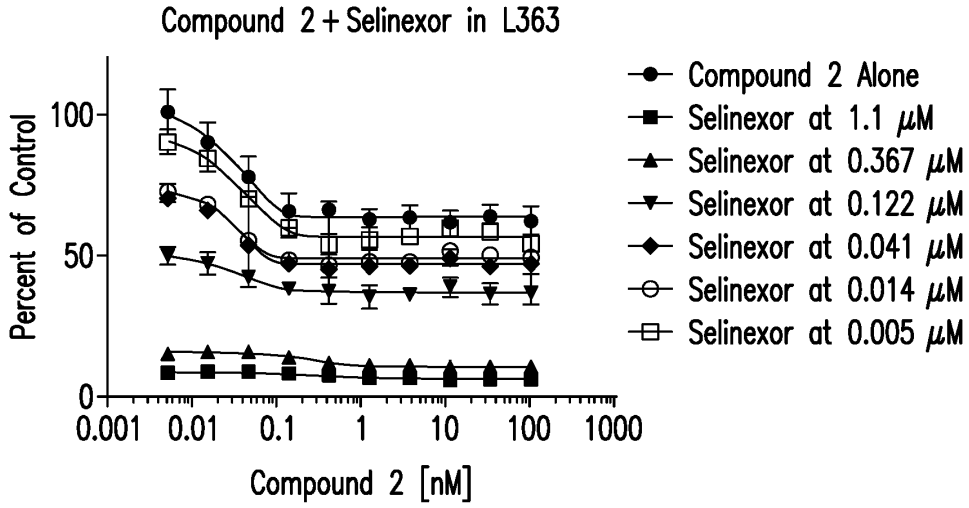

Compound 2 + Selinexor in L363
Percent of Control
100
50
0
0.001
0.01
0.1
1
10
100
1000
Compound 2 [nM]
Compound 2 Alone
Selinexor at 1.1 μM
Selinexor at 0.367 μM
Selinexor at 0.122 μM
Selinexor at 0.041 μM
Selinexor at 0.014 μM
Selinexor at 0.005 μM

FIG. 2I

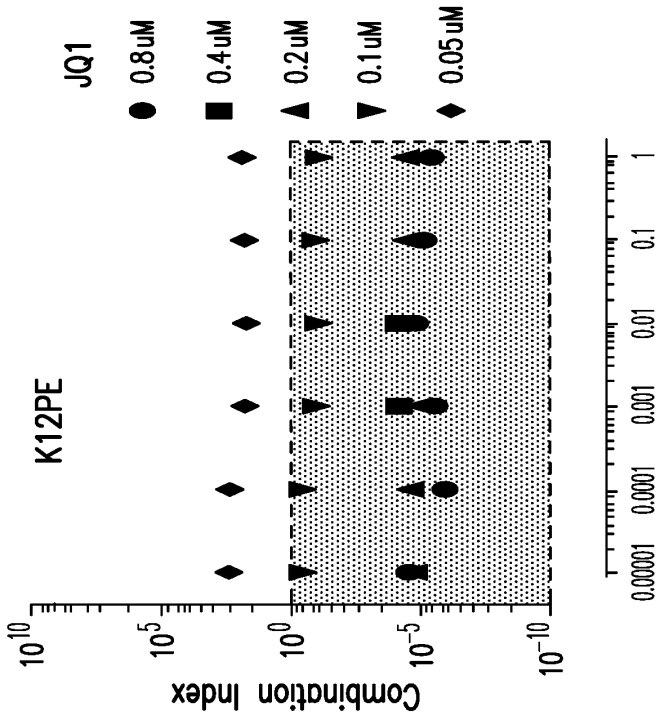

JQ1
0.8uM
0.4uM
0.2uM
0.1uM
0.05uM
K12PE
Combination Index
Compound 2 (μM)

FIG. 3B

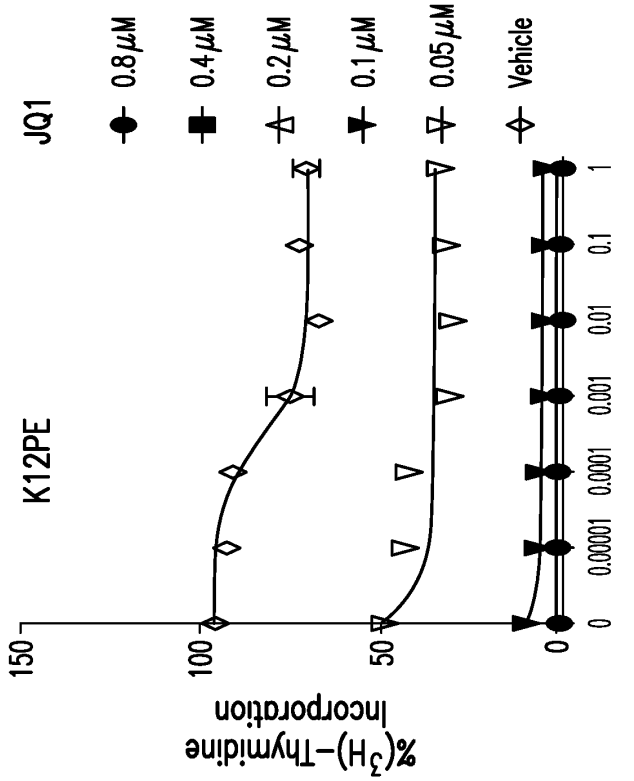

JQ1
0.8μM
0.4μM
0.2μM
0.1μM
0.05μM
Vehicle
K12PE
%(3H)-Thymidine Incorporation
Compound 2 (μM)

FIG. 3A

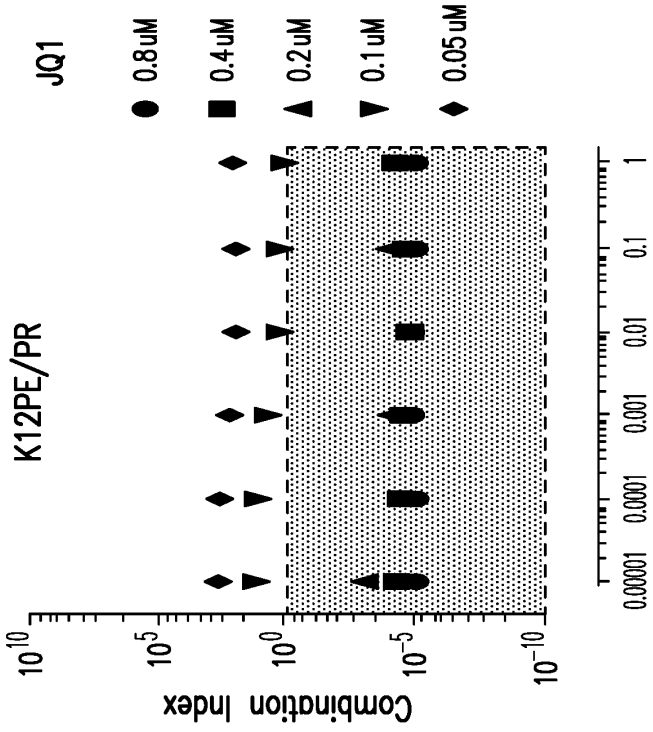

JQ1
0.8uM
0.4uM
0.2uM
0.1uM
0.05uM
K12PE/PR
Combination Index
10^{10}
10^{5}
10^{0}
10^{-5}
10^{-10}
0.00001 0.0001 0.001 0.01 0.1 1
Compound 2 (μM)

FIG. 3D

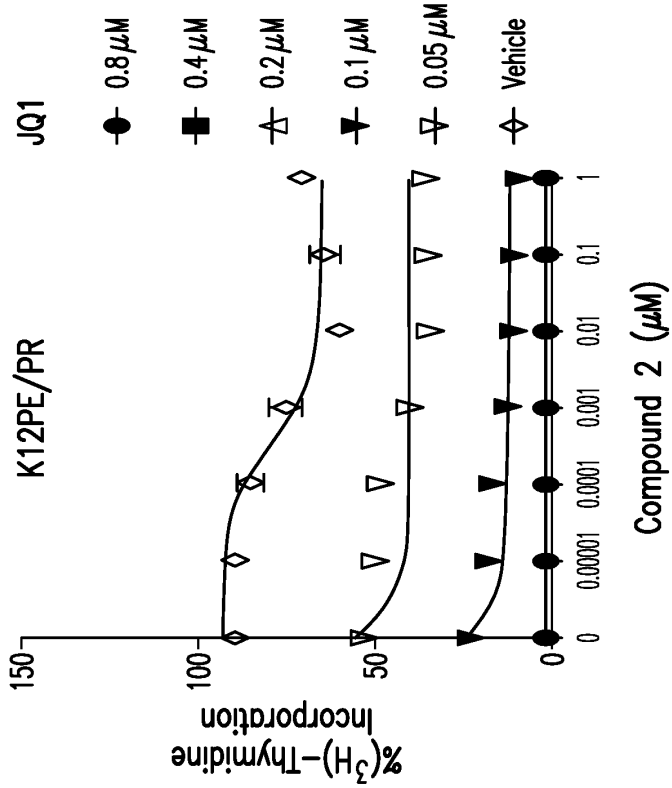

JQ1
0.8μM
0.4μM
0.2μM
0.1μM
0.05μM
Vehicle
K12PE/PR
%(^{3}H)-Thymidine Incorporation
150
100
50
0
0 0.00001 0.0001 0.001 0.01 0.1 1
Compound 2 (μM)

FIG. 3C

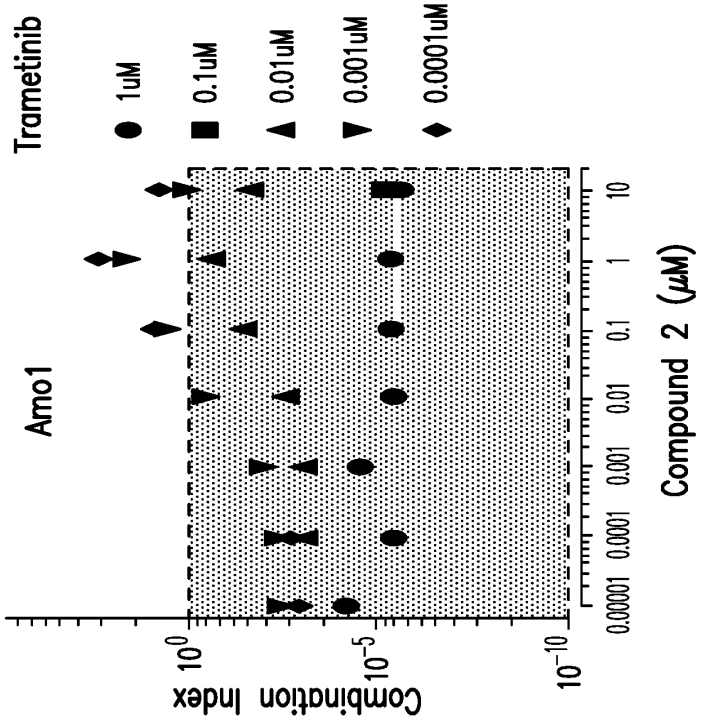

Trametinib
1uM
0.1uM
0.01uM
0.001uM
0.0001uM
Amo1
Combination Index
10^{0}
10^{-5}
10^{-10}
0.00001 0.0001 0.001 0.01 0.1 1 10
Compound 2 (μM)

FIG. 4B

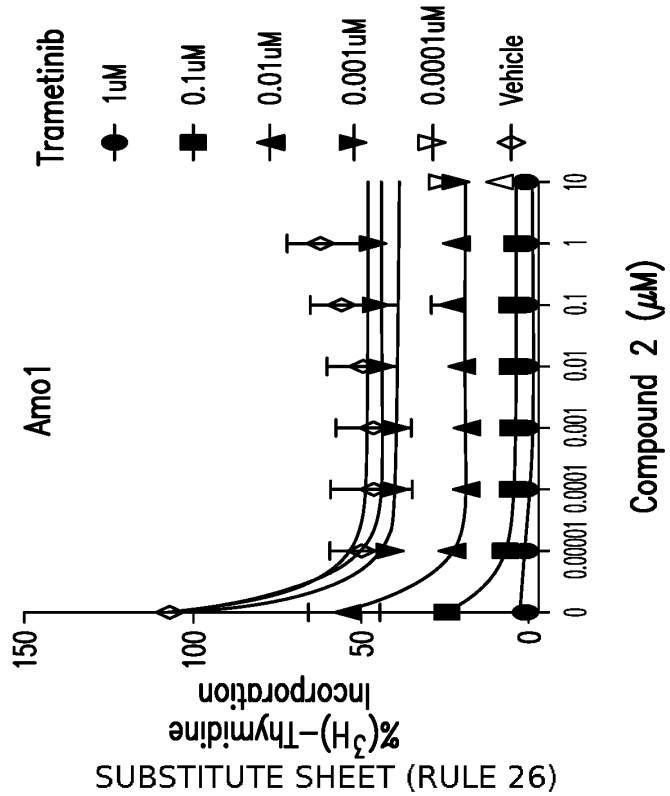

Trametinib
1uM
0.1uM
0.01uM
0.001uM
0.0001uM
Vehicle
Amo1
%(^{3}H)–Thymidine Incorporation
150
100
50
0
0 0.00001 0.0001 0.001 0.01 0.1 1 10
Compound 2 (μM)

FIG. 4A

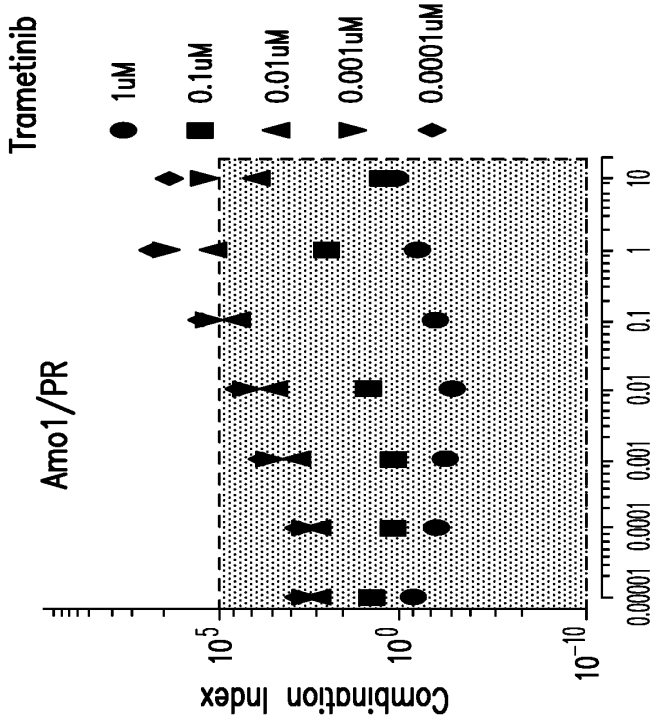

Trametinib
1uM
0.1uM
0.01uM
0.001uM
0.0001uM
Amo1/PR
Combination Index
10^{5}
10^{0}
10^{-10}
0.00001 0.0001 0.001 0.01 0.1 1 10
Compound 2 (μM)

FIG. 4D

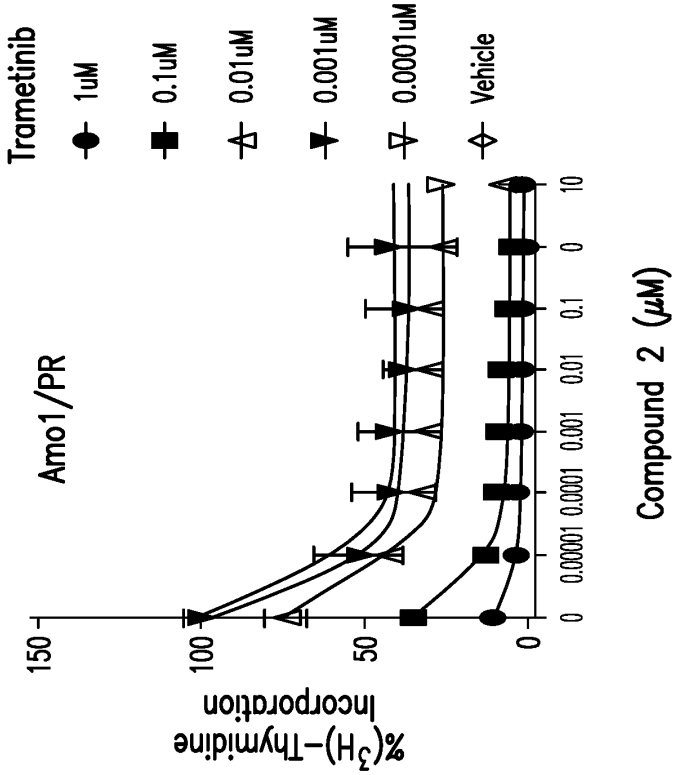

Trametinib
1uM
0.1uM
0.01uM
0.001uM
0.0001uM
Vehicle
Amo1/PR
%(^{3}H)–Thymidine Incorporation
150
100
50
0
0 0.00001 0.0001 0.001 0.01 0.1 0 10
Compound 2 (μM)

FIG. 4C

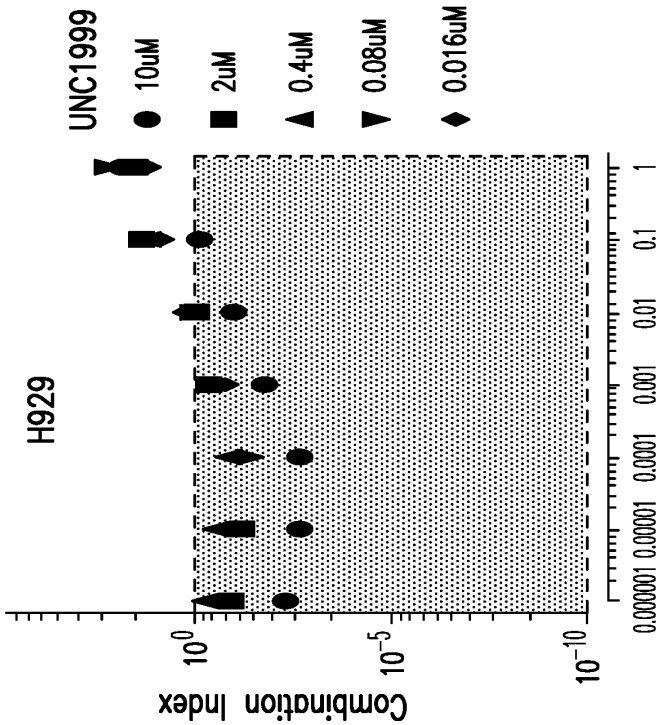

H929
UNC1999
10uM
2uM
0.4uM
0.08uM
0.016uM
Combination Index
10^{0}
10^{-5}
10^{-10}
0.000001 0.00001 0.0001 0.001 0.01 0.1 1
Compound 2 (μM)

FIG. 5B

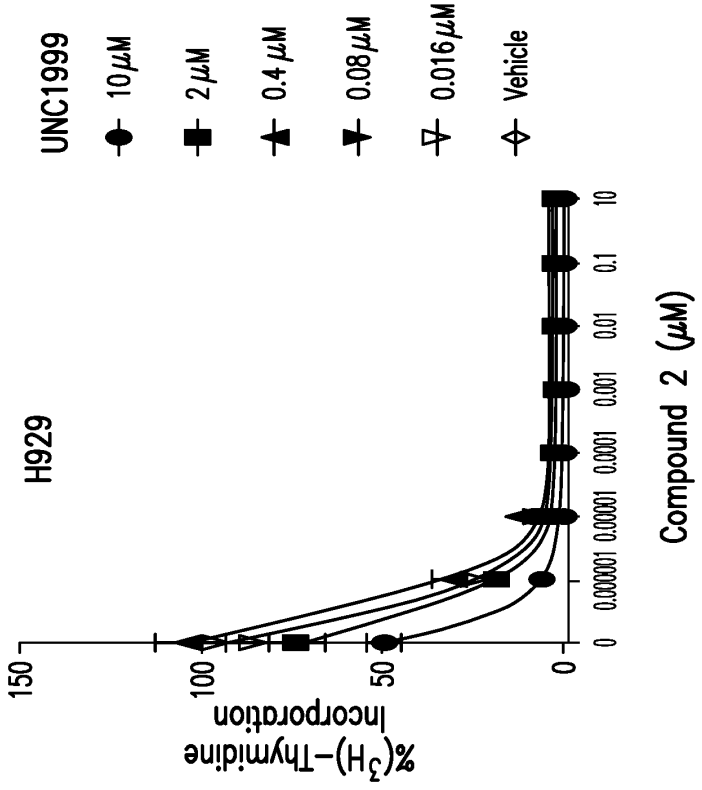

H929
UNC1999
10μM
2μM
0.4μM
0.08μM
0.016μM
Vehicle
%(^{3}H)–Thymidine Incorporation
150
100
50
0
0 0.000001 0.00001 0.0001 0.001 0.01 0.1 1 10
Compound 2 (μM)

FIG. 5A

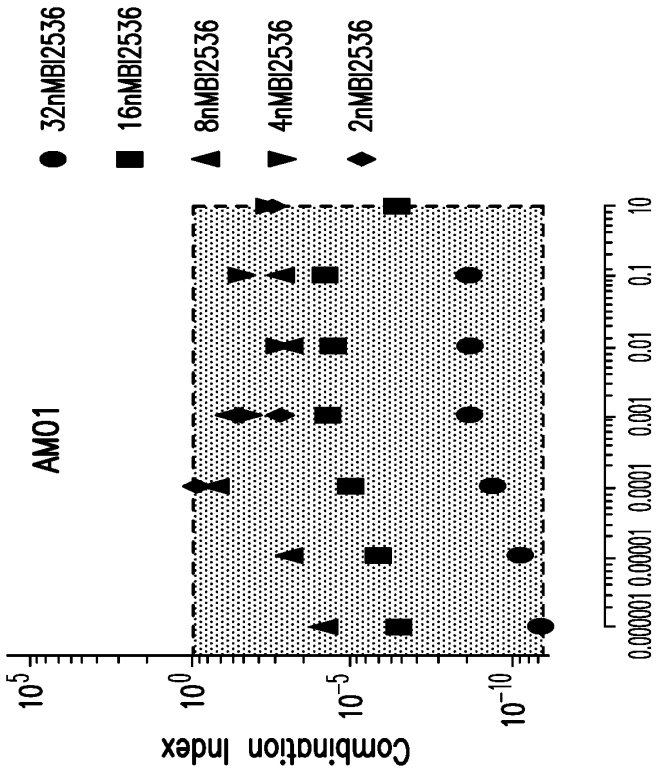

32nMBI2536
16nMBI2536
8nMBI2536
4nMBI2536
2nMBI2536
AM01
Combination Index
10^{5}
10^{0}
10^{-5}
10^{-10}
0.000001 0.00001 0.0001 0.001 0.01 0.1 10
Compound 2 (μM)

FIG. 6B

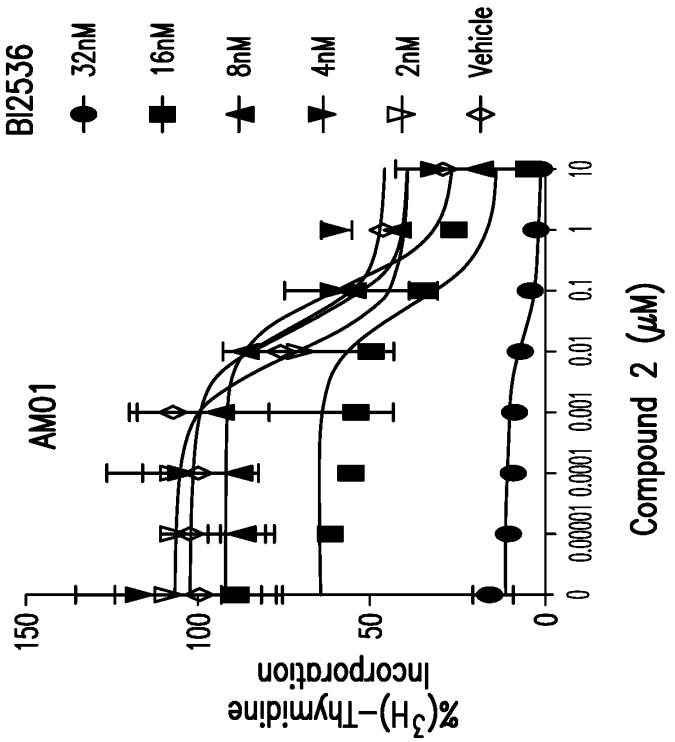

BI2536
32nM
16nM
8nM
4nM
2nM
Vehicle
AM01
%(^{3}H)–Thymidine Incorporation
150
100
50
0
0 0.00001 0.0001 0.001 0.01 0.1 1 10
Compound 2 (μM)

FIG. 6A

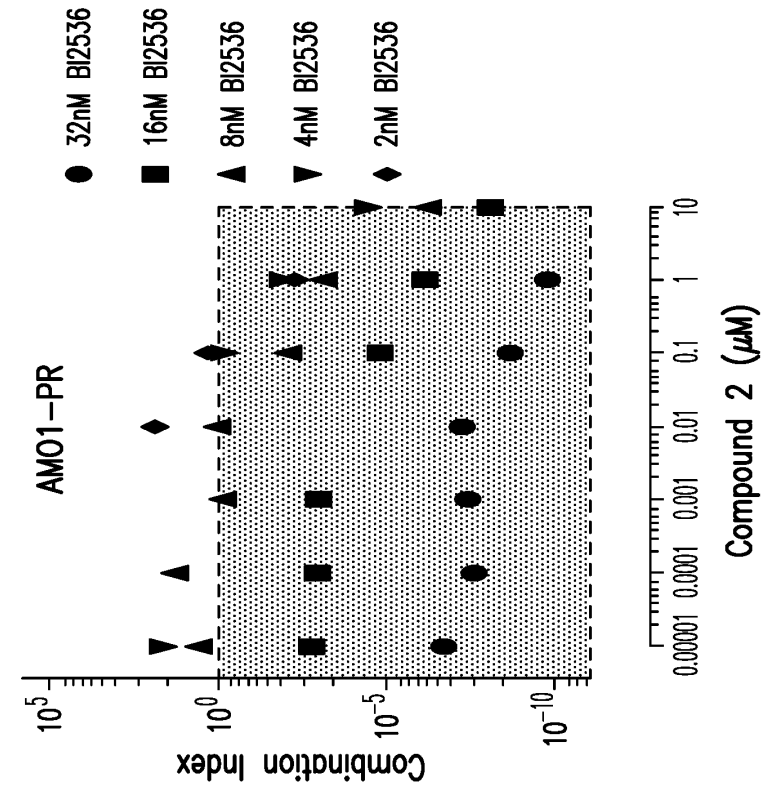

32nM BI2536
16nM BI2536
8nM BI2536
4nM BI2536
2nM BI2536
AMO1–PR
Combination Index
10^{5}
10^{0}
10^{-5}
10^{-10}
0.00001 0.0001 0.001 0.01 0.1 1 10
Compound 2 (μM)

FIG. 6D

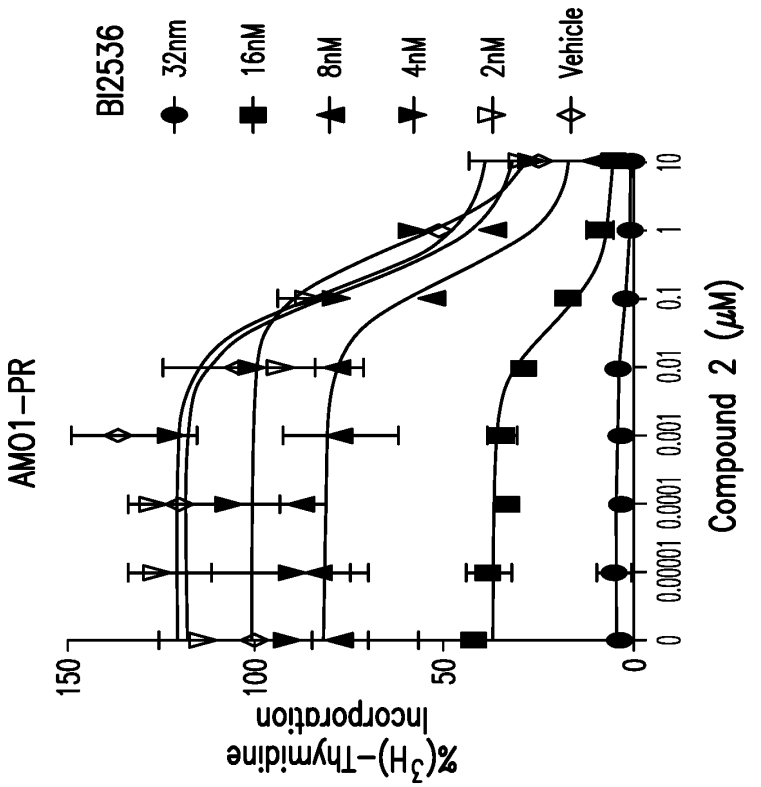

BI2536
32nm
16nM
8nM
4nM
2nM
Vehicle
AMO1–PR
%(^{3}H)–Thymidine Incorporation
150
100
50
0
0 0.00001 0.0001 0.001 0.01 0.1 1 10
Compound 2 (μM)

FIG. 6C

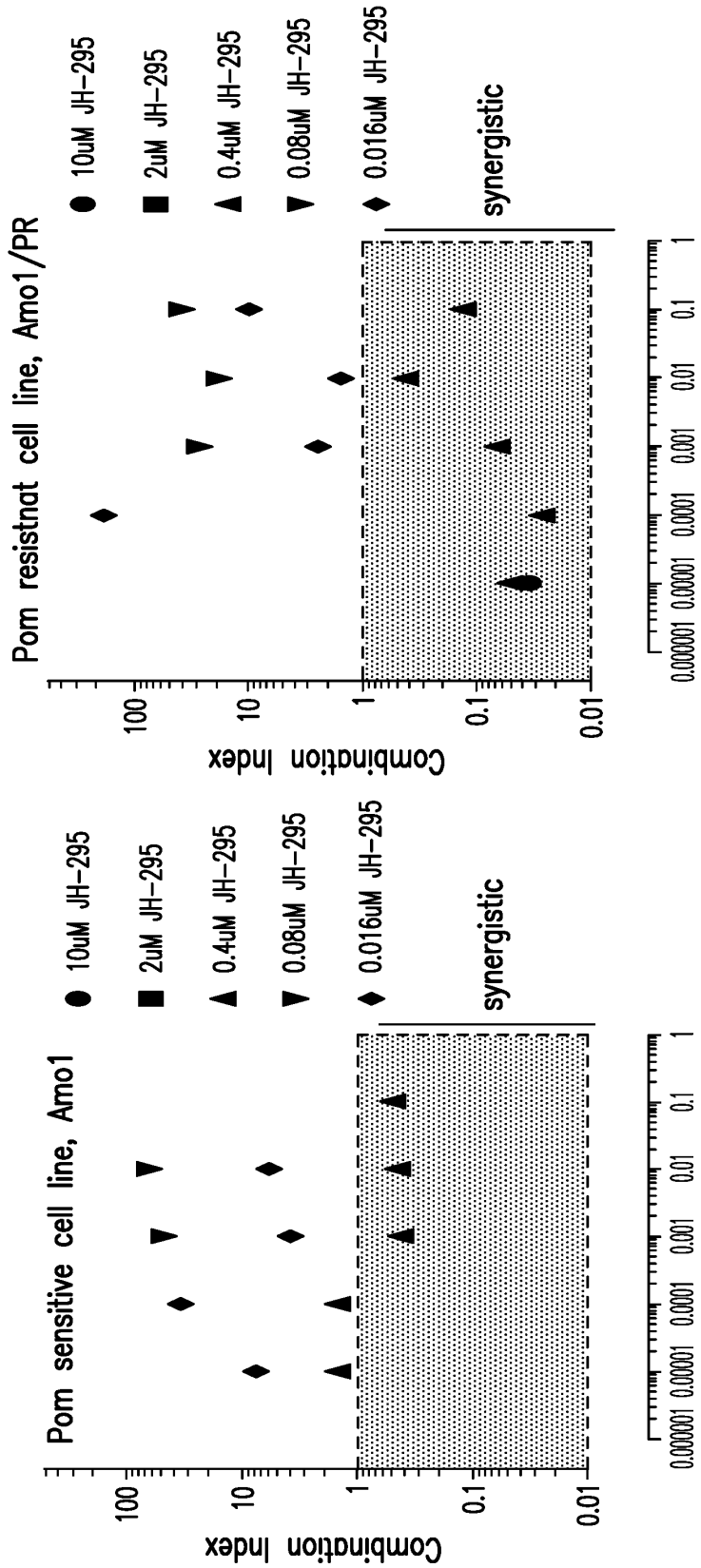

Pom sensitive cell line, Amo1
10uM JH-295
2uM JH-295
0.4uM JH-295
0.08uM JH-295
0.016uM JH-295
synergistic
Combination Index
100
10
1
0.1
0.01
0.000001 0.00001 0.0001 0.001 0.01 0.1 1
Compound 2 (μM)

FIG. 7A

Pom resistnat cell line, Amo1/PR
10uM JH-295
2uM JH-295
0.4uM JH-295
0.08uM JH-295
0.016uM JH-295
synergistic
Combination Index
100
10
1
0.1
0.01
0.000001 0.00001 0.0001 0.001 0.01 0.1 1
Compound 2 (μM)

FIG. 7B

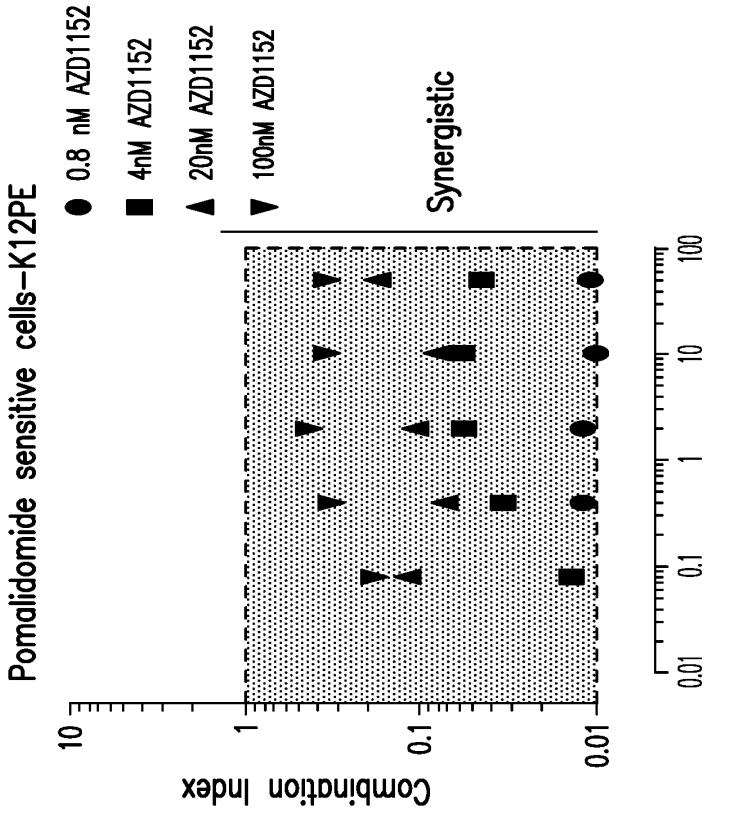

Pomalidomide sensitive cells–K12PE
0.8 nM AZD1152
4nM AZD1152
20nM AZD1152
100nM AZD1152
Synergistic
Combination Index
10
1
0.1
0.01
0.01
0.1
1
10
100
Compound 2 (μM)

FIG. 8B

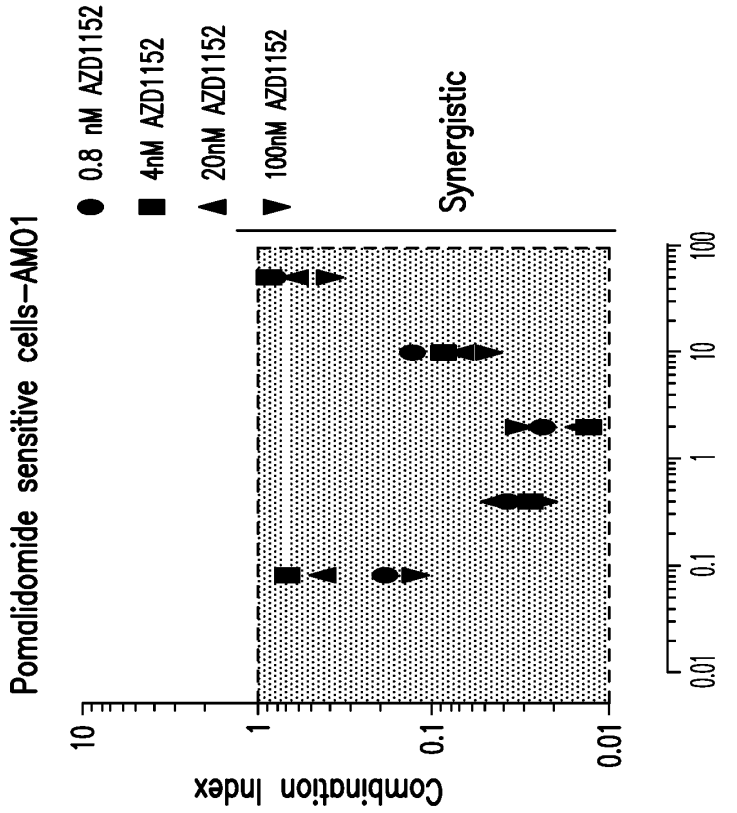

Pomalidomide sensitive cells–AMO1
0.8 nM AZD1152
4nM AZD1152
20nM AZD1152
100nM AZD1152
Synergistic
Combination Index
10
1
0.1
0.01
0.01
0.1
1
10
100
Compound 2 (μM)

FIG. 8A

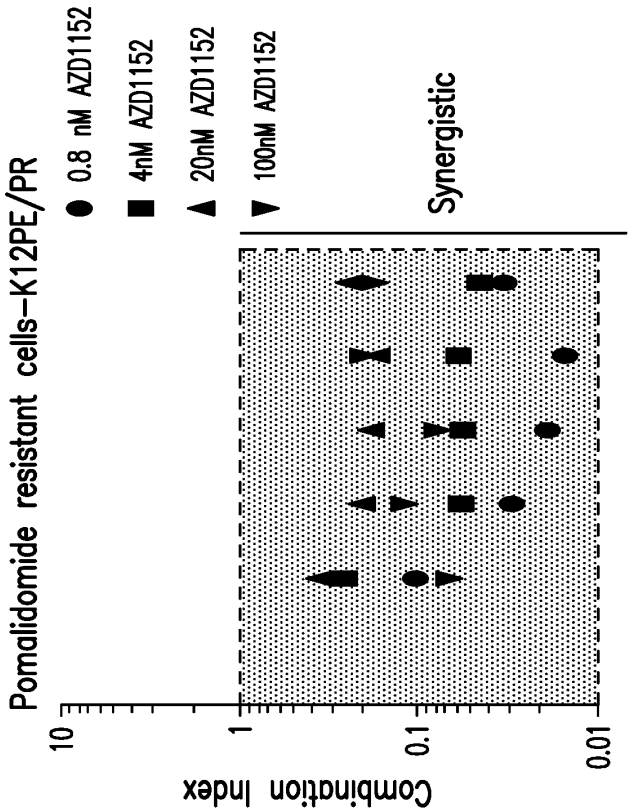

Pomalidomide resistant cells-K12PE/PR
0.8 nM AZD1152
4nM AZD1152
20nM AZD1152
100nM AZD1152
Synergistic
Combination Index
10
1
0.1
0.01
0.01
0.1
1
10
100
Compound 2 (μM)

FIG. 8D

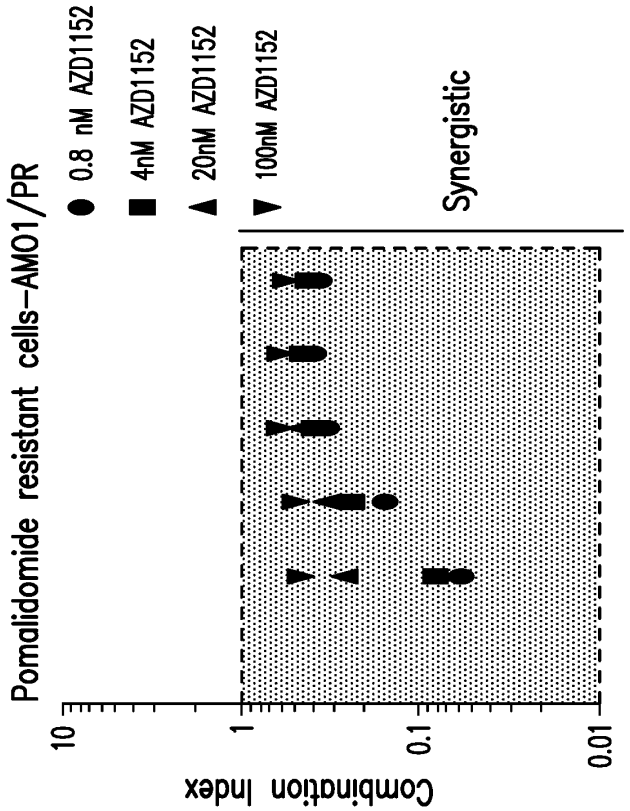

Pomalidomide resistant cells-AMO1/PR
0.8 nM AZD1152
4nM AZD1152
20nM AZD1152
100nM AZD1152
Synergistic
Combination Index
10
1
0.1
0.01
0.01
0.1
1
10
100
Compound 2 (μM)

FIG. 8C

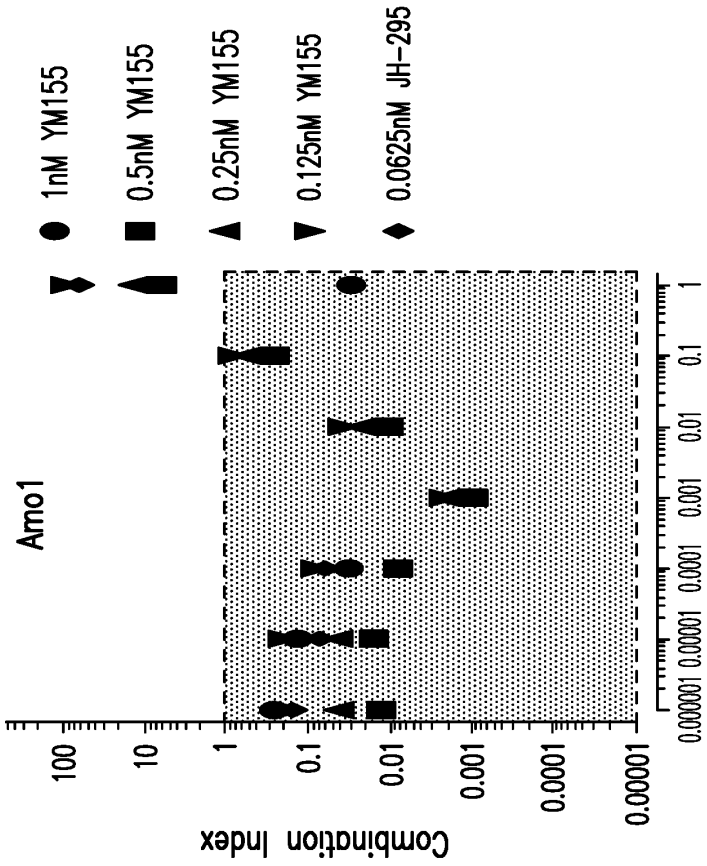

1nM YM155
0.5nM YM155
0.25nM YM155
0.125nM YM155
0.0625nM JH-295
Amo1
Combination Index
100
10
1
0.1
0.01
0.001
0.0001
0.00001
0.000001 0.00001 0.0001 0.001 0.01 0.1 1
Compound 2 (μM)

FIG. 9B

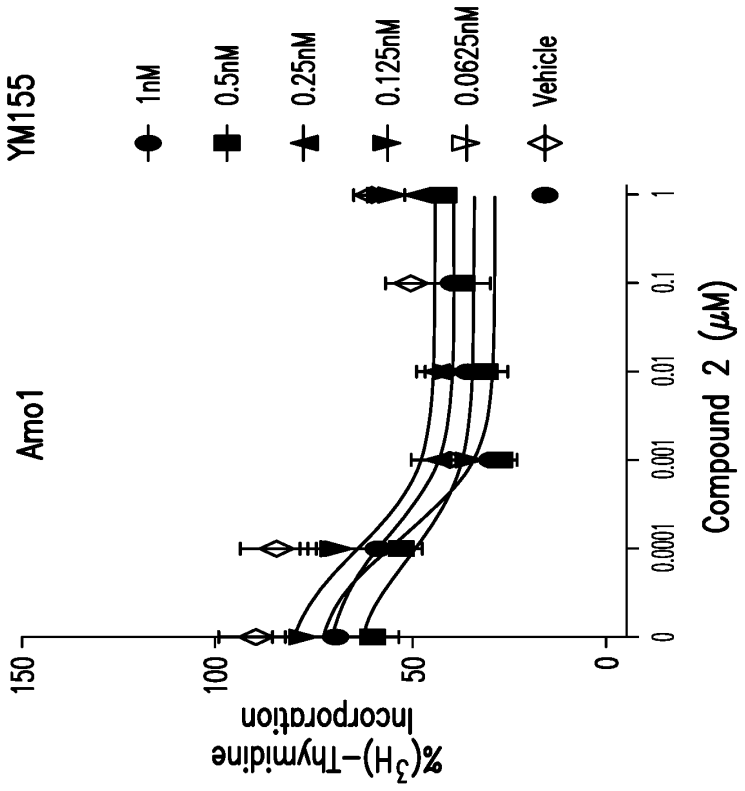

YM155
1nM
0.5nM
0.25nM
0.125nM
0.0625nM
Vehicle
Amo1
%(³H)-Thymidine Incorporation
150
100
50
0
0 0.0001 0.001 0.01 0.1 1
Compound 2 (μM)

FIG. 9A

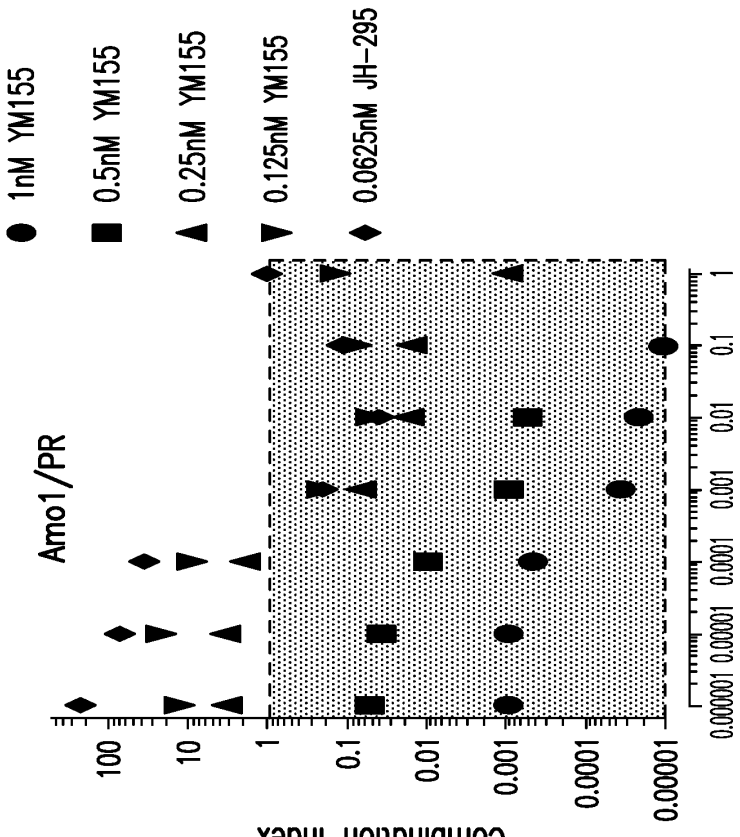

1nM YM155
0.5nM YM155
0.25nM YM155
0.125nM YM155
0.0625nM JH-295
Amo1/PR
Combination Index
100
10
1
0.1
0.01
0.001
0.0001
0.00001
0.000001
0.00001
0.0001
0.001
0.01
0.1
1
Compound 2 (μM)

FIG. 9D

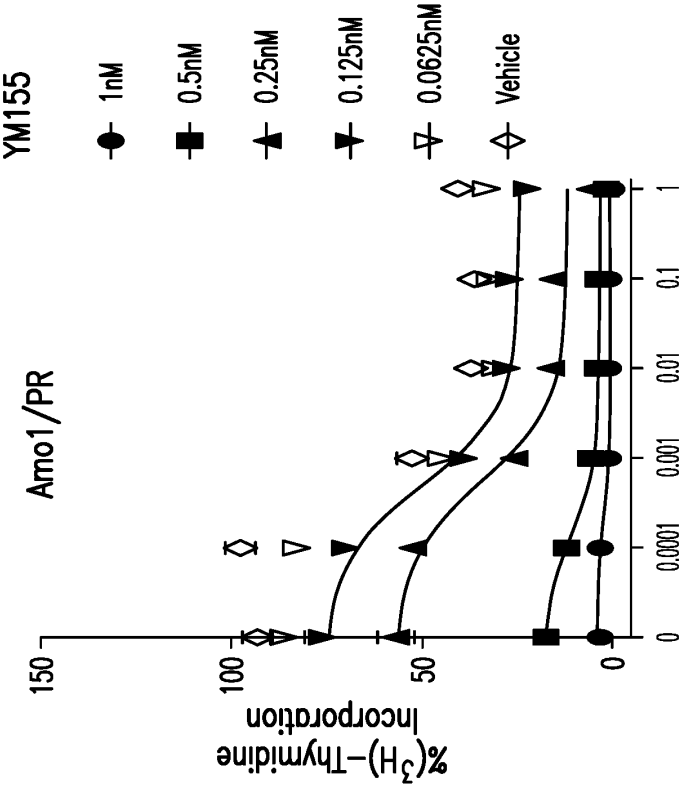

YM155
1nM
0.5nM
0.25nM
0.125nM
0.0625nM
Vehicle
Amo1/PR
%(³H)-Thymidine Incorporation
150
100
50
0
0
0.0001
0.001
0.01
0.1
1
Compound 2 (μM)

FIG. 9C

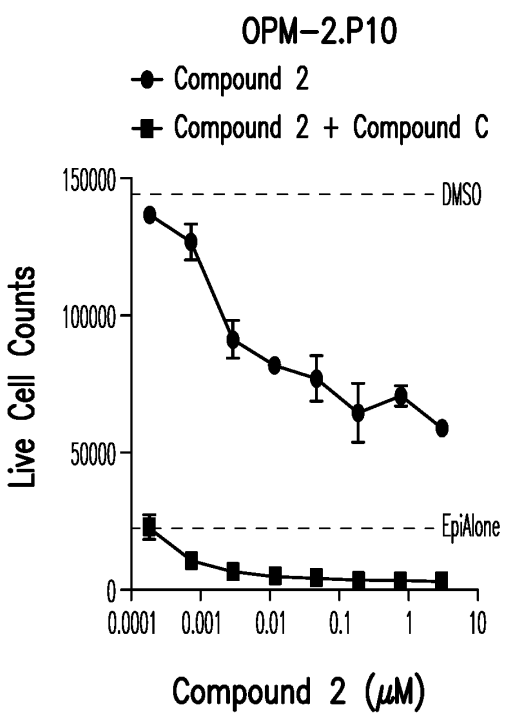


FIG. 10A

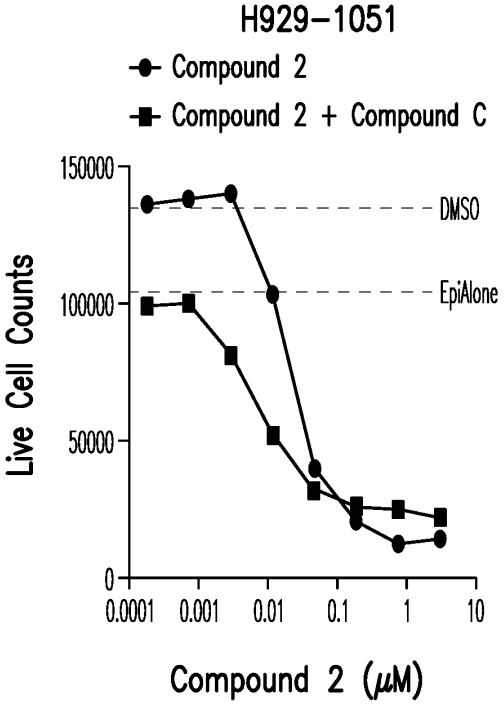


FIG. 10B

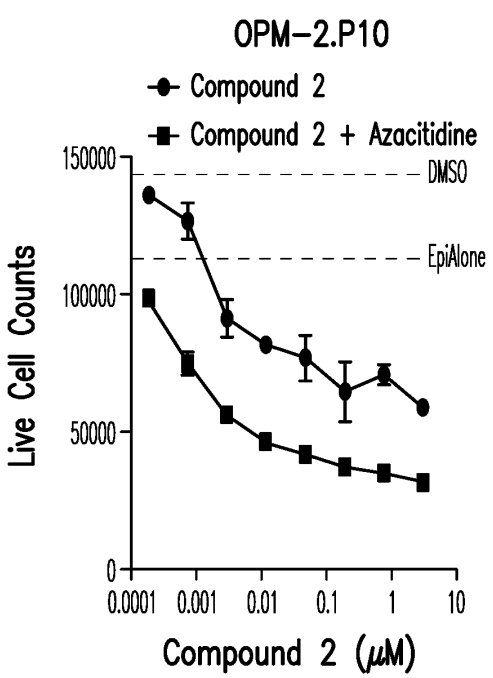


FIG. 11A

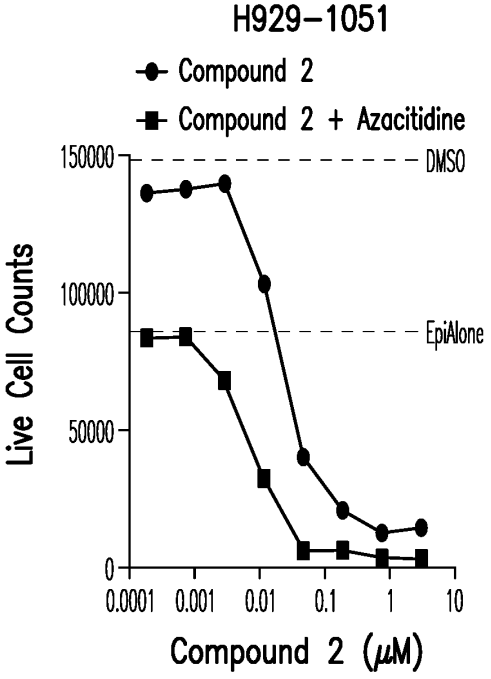


FIG. 11B

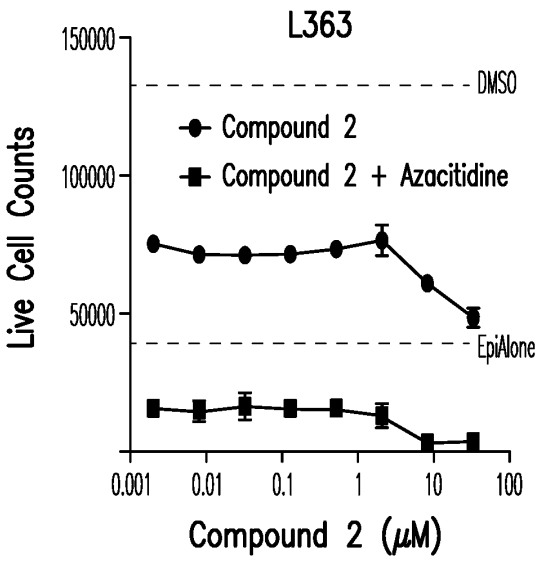


FIG. 11C

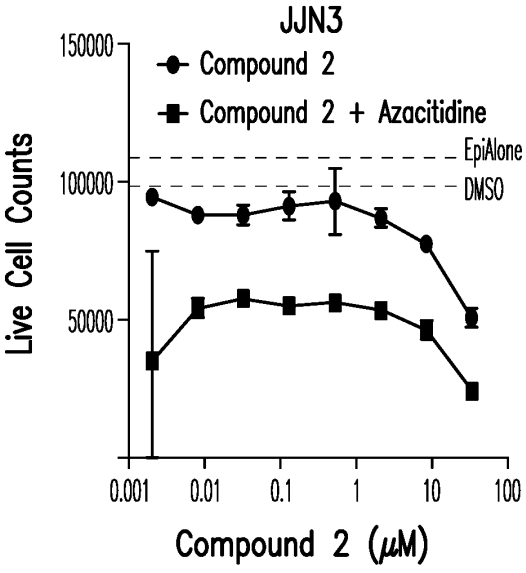


FIG. 11D

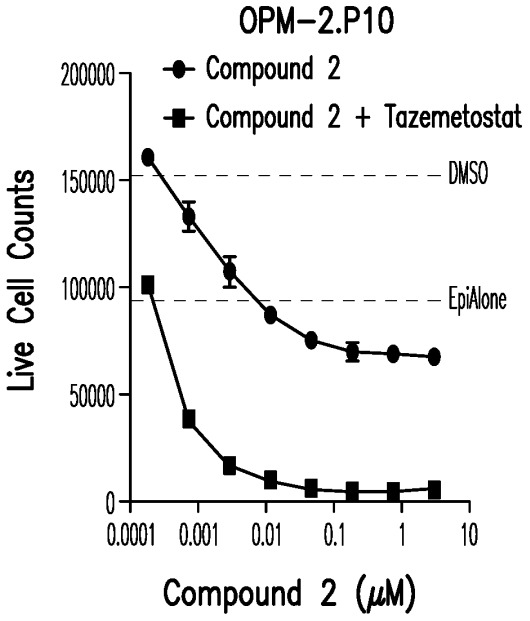


FIG. 12A

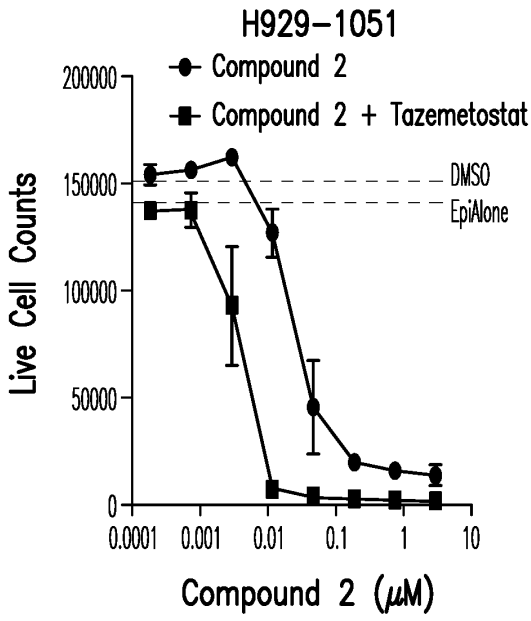


FIG. 12B

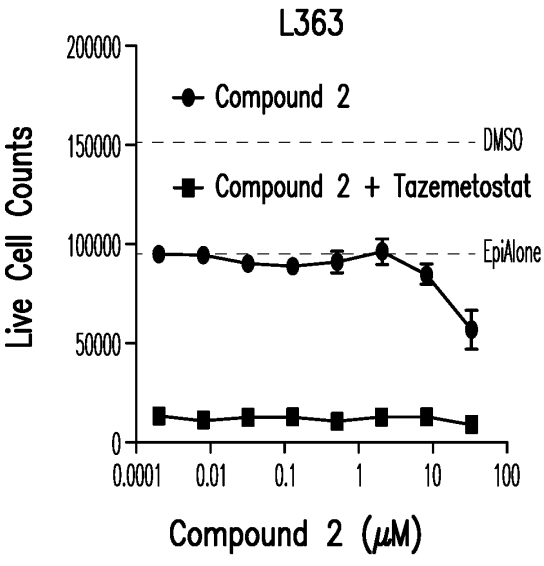


FIG. 12C

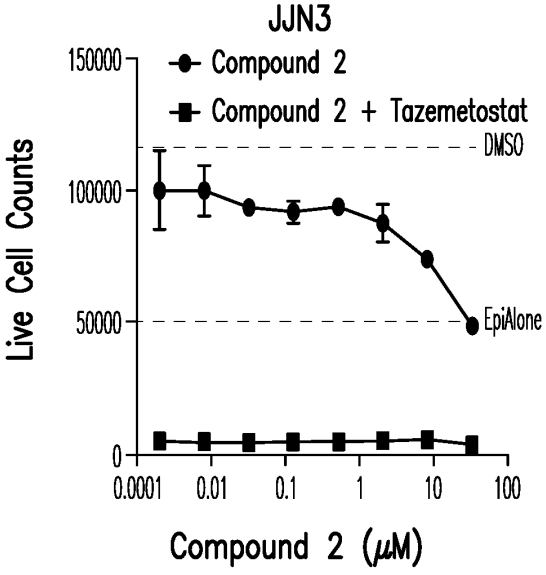


FIG. 12D

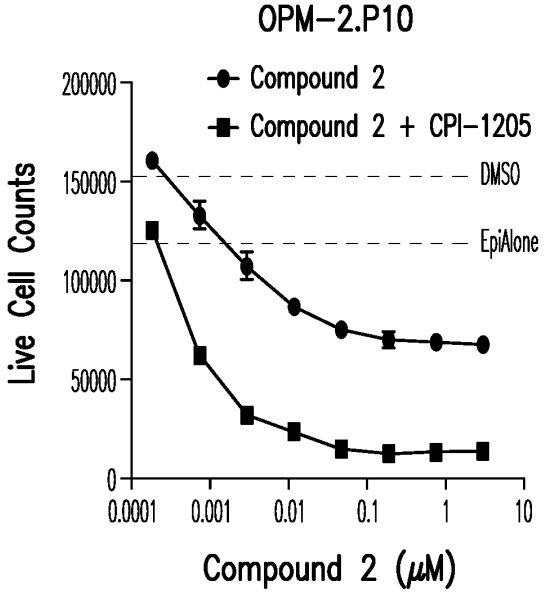


FIG. 13A

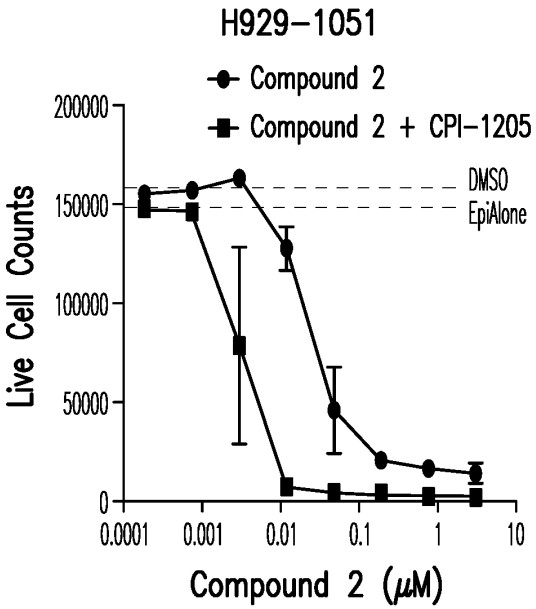


FIG. 13B

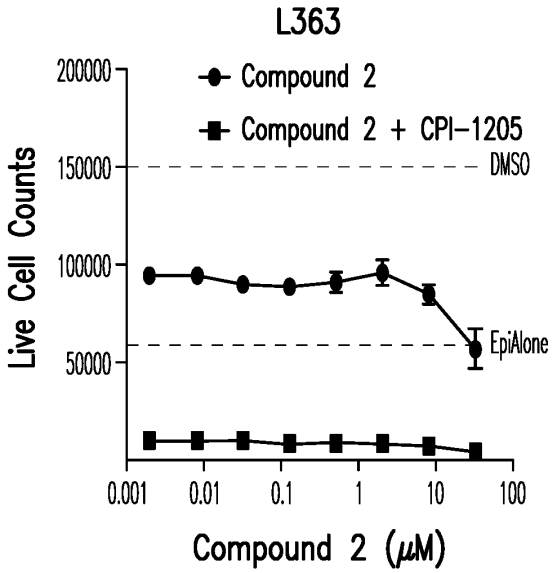


FIG. 13C

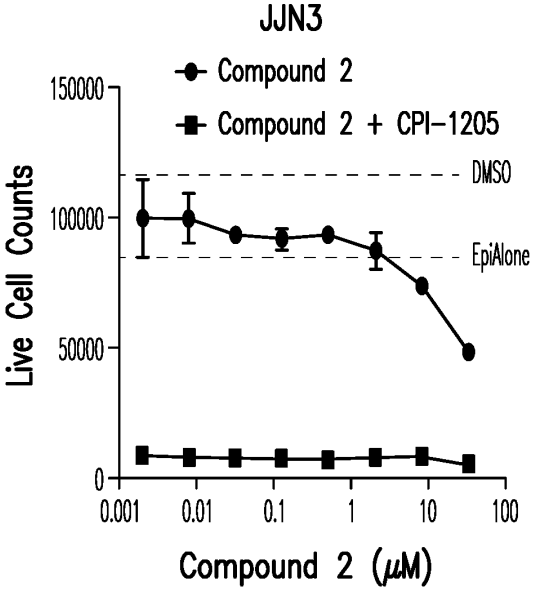


FIG. 13D

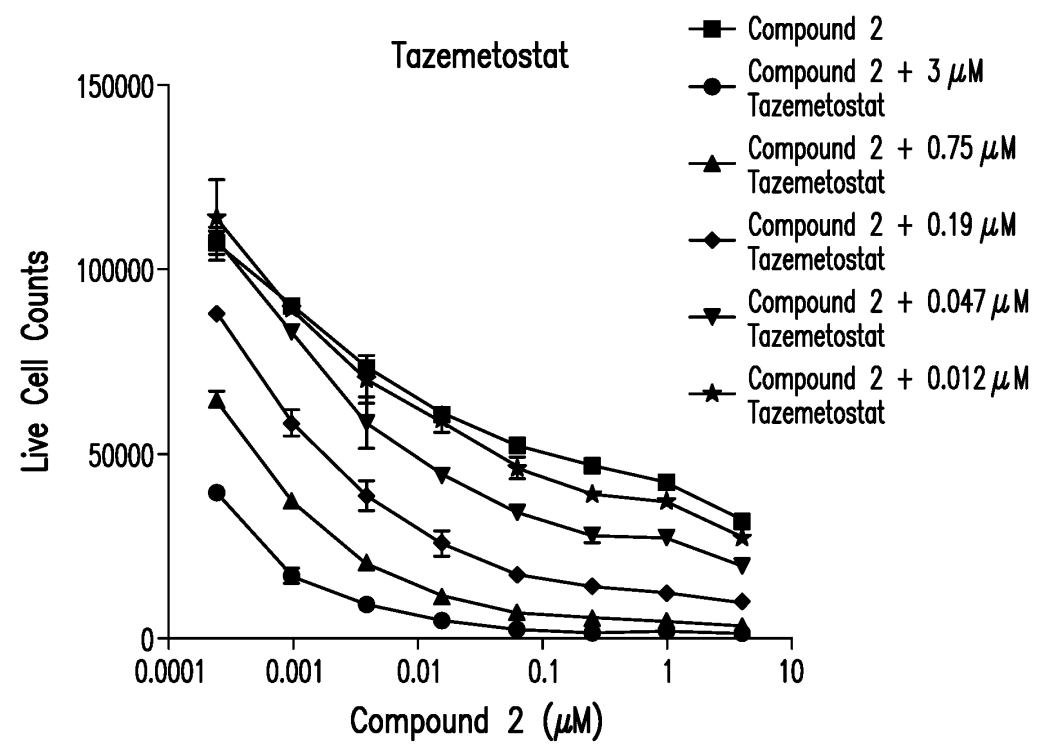


FIG. 14A

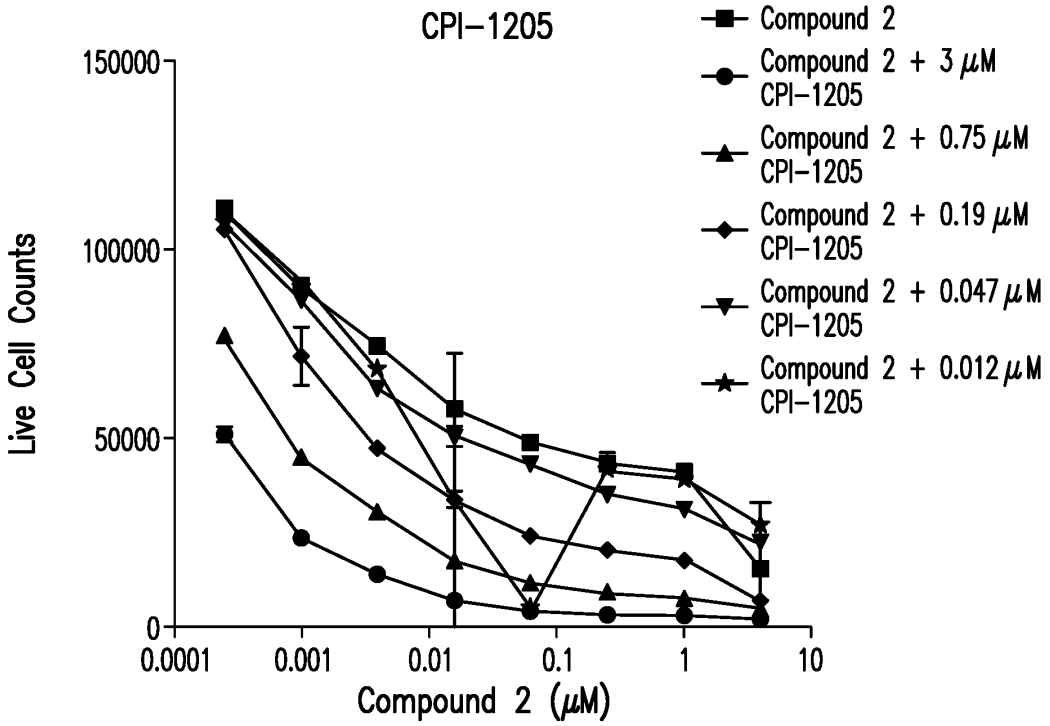


FIG. 14B

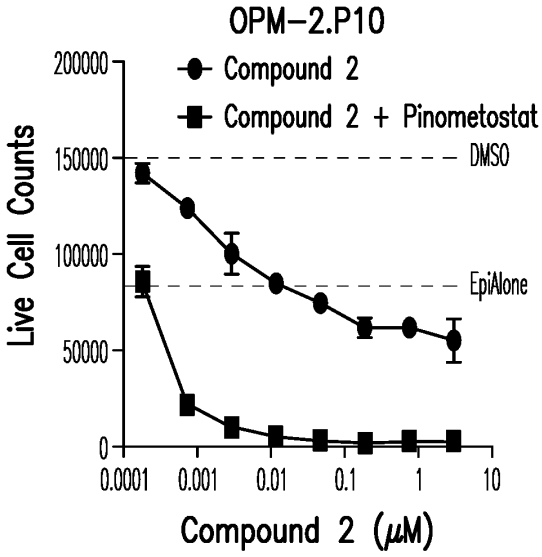


FIG. 15A

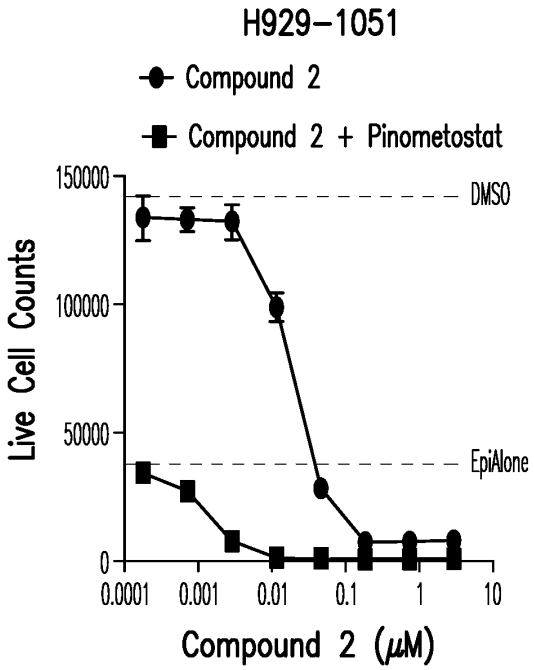


FIG. 15B

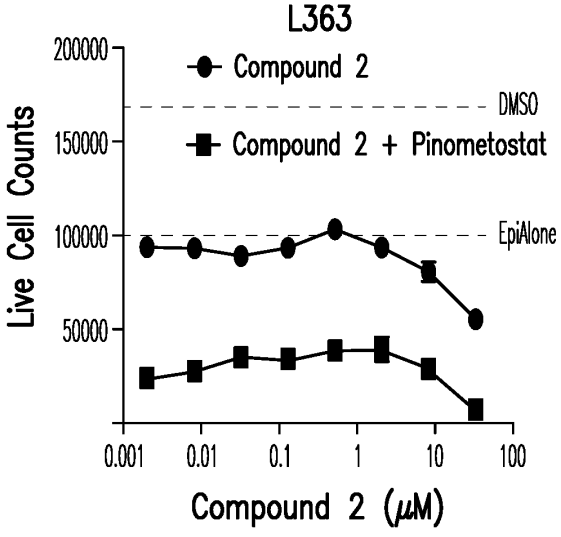


FIG. 15C

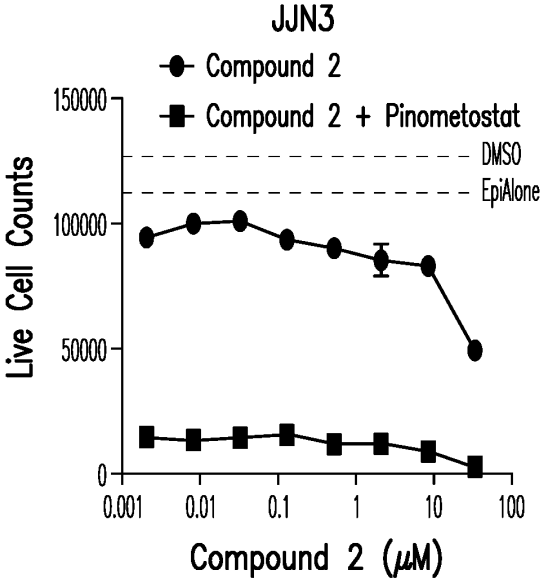


FIG. 15D