

FIG. 1A

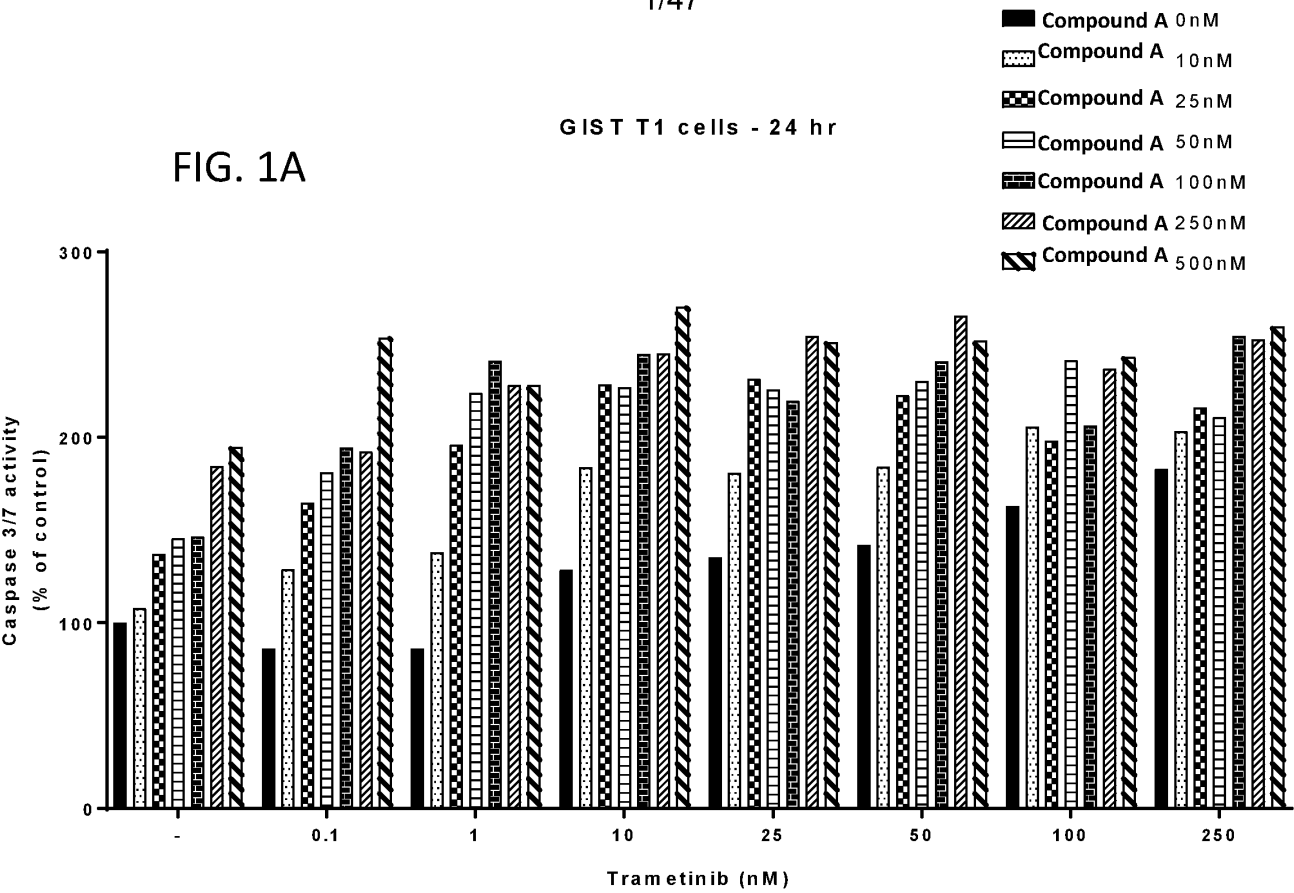
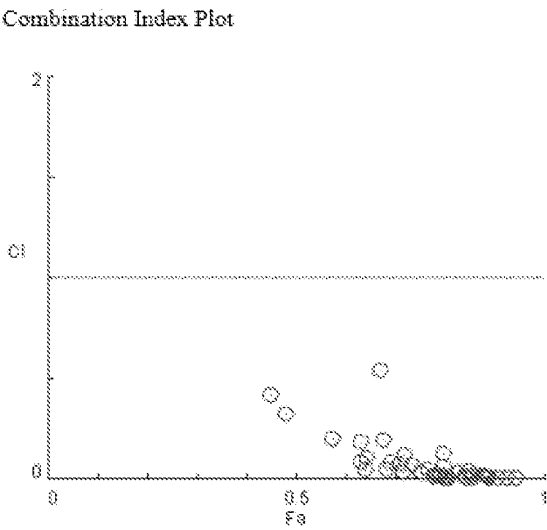


FIG. 1B Combination index by Chou Talalay analysis

CI	Compound A 10nM	Compound A 25nM	Compound A 50nM	Compound A 100nM	Compound A 250nM	Compound A 500nM
Trametinib 0.1nM	0.41635	0.20181	0.18684	0.19377	0.53669	0.01446
Trametinib 1nM	0.32337	0.04483	0.01746	0.00975	0.06517	0.13033
Trametinib 10nM	0.04689	0.00672	0.01463	0.00706	0.01761	0.0012
Trametinib 25nM	0.08445	0.00557	0.01592	0.0473	0.00679	0.01911
Trametinib 50nM	0.1024	0.01154	0.01213	0.01019	0.00149	0.01747
Trametinib 100nM	0.03211	0.0835	0.00501	0.12226	0.03448	0.0413
Trametinib 250nM	0.07868	0.03424	0.07228	0.00273	0.00836	0.007

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism



GIST T1 cells - 48 hr

FIG. 1C

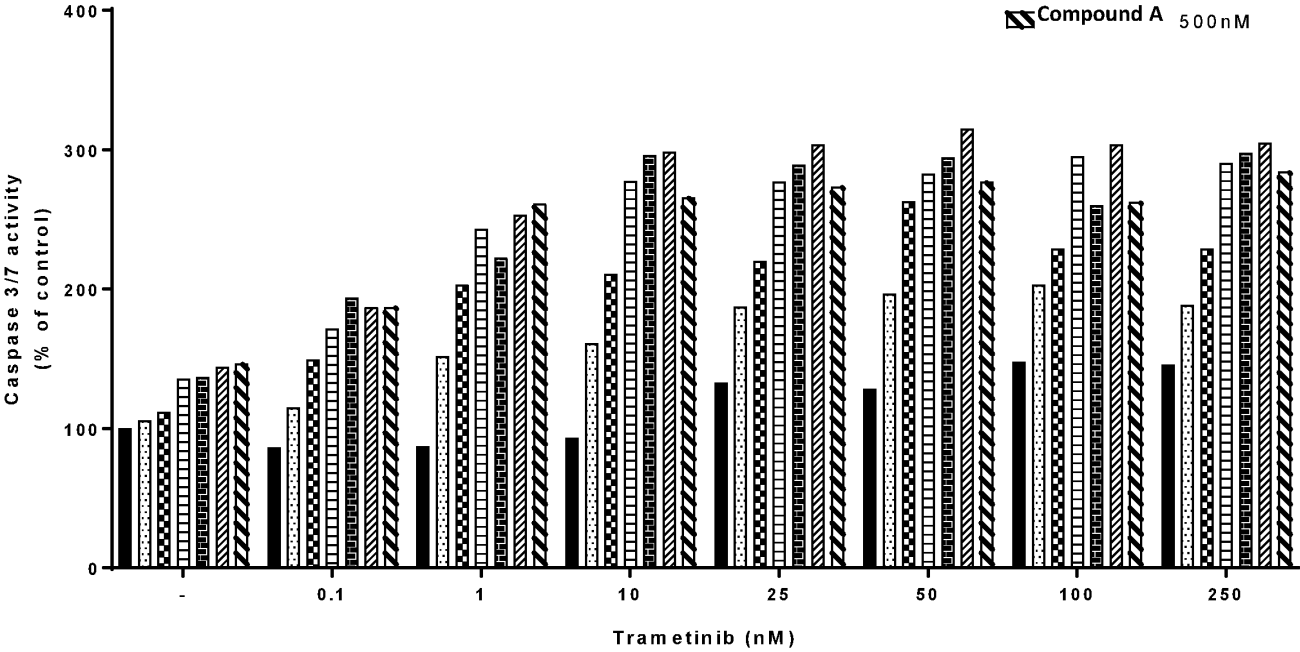
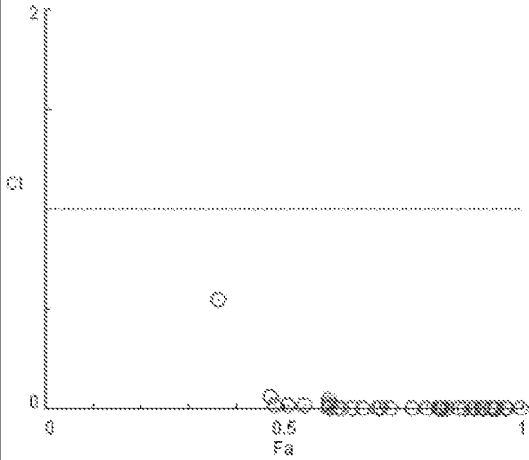


FIG. 1D Combination index by Chou Talalay analysis

CI	Compound A 10nM	Compound A 25nM	Compound A 50nM	Compound A 100nM	Compound A 250nM	Compound A 500nM
Trametinib 0.1nM	0.544	0.06109	0.01804	0.00494	0.02246	0.04491
Trametinib 1nM	0.02154	5.23E-04	1.55E-05	3.09E-04	2.10E-05	1.29E-05
Trametinib 10nM	0.01666	2.97E-04	7.82E-08	9.90E-10	9.00E-10	6.44E-06
Trametinib 25nM	0.0022	1.33E-04	8.55E-08	9.57E-09	5.70E-11	1.63E-06
Trametinib 50nM	0.00133	6.05E-07	2.55E-08	1.79E-09	1.10E-21	8.28E-07
Trametinib 100nM	0.00116	8.38E-05	7.50E-10	3.55E-06	5.70E-11	1.09E-05
Trametinib 250nM	0.01223	1.51E-04	4.04E-09	5.00E-10	3.10E-11	1.69E-07

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism

Combination Index Plot



PCT/US2019/016148

Compound A 0nM

Compound A 10nM

Compound A 25nM

Compound A 50nM

Compound A 100nM

Compound A 250nM

Compound A 500nM

GIST T1/D816E cells - 24 hr

FIG. 1E

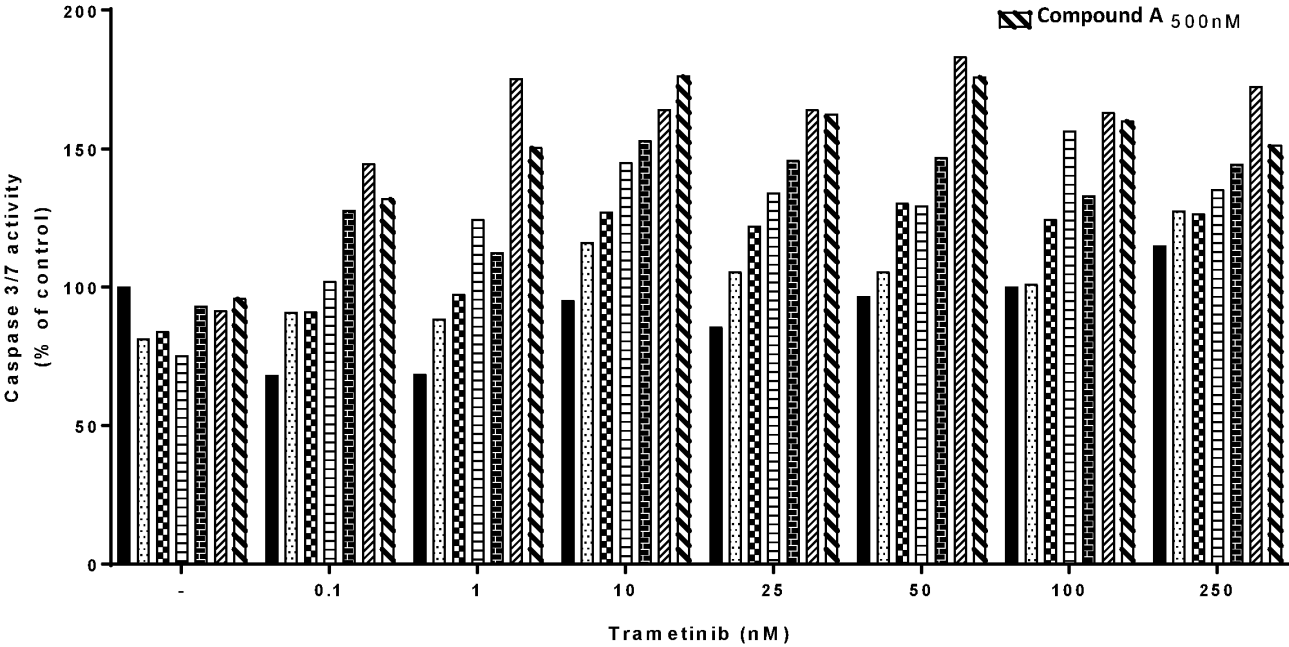


FIG. 1F Combination index by Chou Talalay analysis

CI index	Compound A 10nM	Compound A 25nM	Compound A 50nM	Compound A 100nM	Compound A 250nM	Compound A 500nM
Trametinib 0.1nM	0.05427	0.11928	0.0195	0.000143	8.28E-06	0.000253
Trametinib 1nM	0.18113	0.0469	0.02853	0.00535	7.11E-08	8.34E-06
Trametinib 10nM	0.01105	0.00199	0.000117	3.21E-05	5.07E-06	5.61E-07
Trametinib 25nM	0.14462	0.01078	0.00166	0.000258	1.26E-05	1.64E-05
Trametinib 50nM	0.28757	0.00592	0.00668	0.000438	7.57E-07	2.91E-06
Trametinib 100nM	1.18272	0.02898	0.000185	0.00772	5.94E-05	9.92E-05
Trametinib 250nM	0.04532	0.05299	0.01351	0.00313	0.000029	0.00106

CI<1 = synergy

CI=1 = additive effect

CI>1 = antagonism

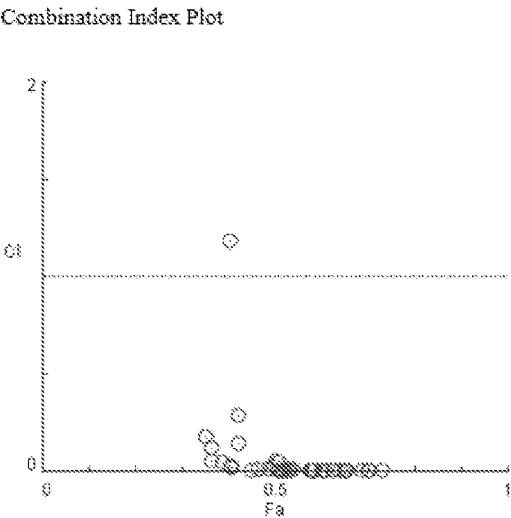


FIG. 1G

Compound A and trametinib
combination in GIST-T1/T670I

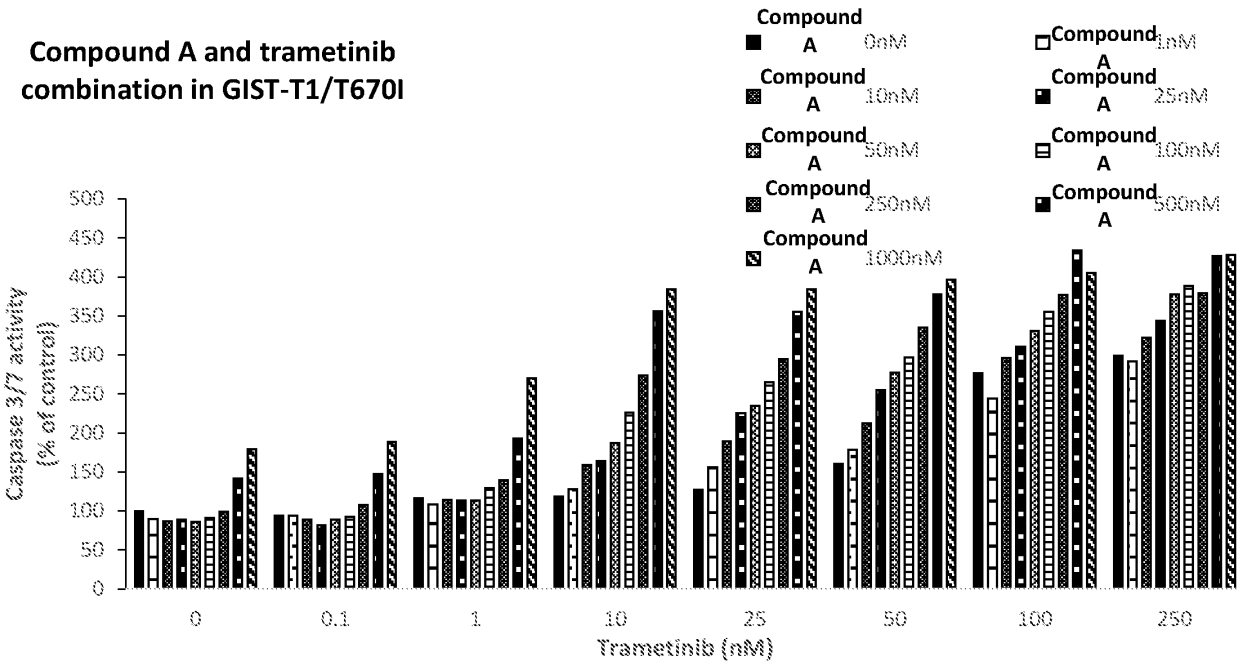


FIG. 1H Combination index by Chou Talalay analysis

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism

CI	Compound A 10nM	Compound A 25nM	Compound A 50nM	Compound A 100nM	Compound A 250nM	Compound A 500nM	Compound A 1000nM
Trametinib 1 nM	0.89607	1.05715	1.20054	0.54408	0.42371	0.03244	0.00155
Trametinib 10 nM	1.04701	0.8501	0.32966	0.07514	0.0131	5.13E-04	1.32E-04
Trametinib 25 nM	0.74569	0.19466	0.13966	0.04476	0.01521	0.00128	3.14E-04
Trametinib 50 nM	0.63181	0.12923	0.05747	0.02767	0.00618	8.94E-04	3.39E-04
Trametinib 100 nM	0.0564	0.03232	0.01456	0.00513	0.00183	5.78E-05	4.17E-04
Trametinib 250 nM	0.05133	0.02117	0.00447	0.00255	0.00425	2.46E-04	2.20E-04

Combination Index Plot

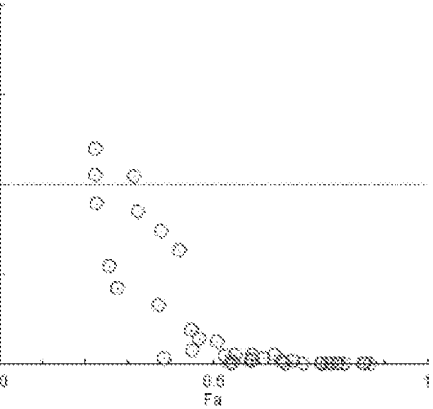


FIG. 2A

Compound B and trametinib in GIST-T1

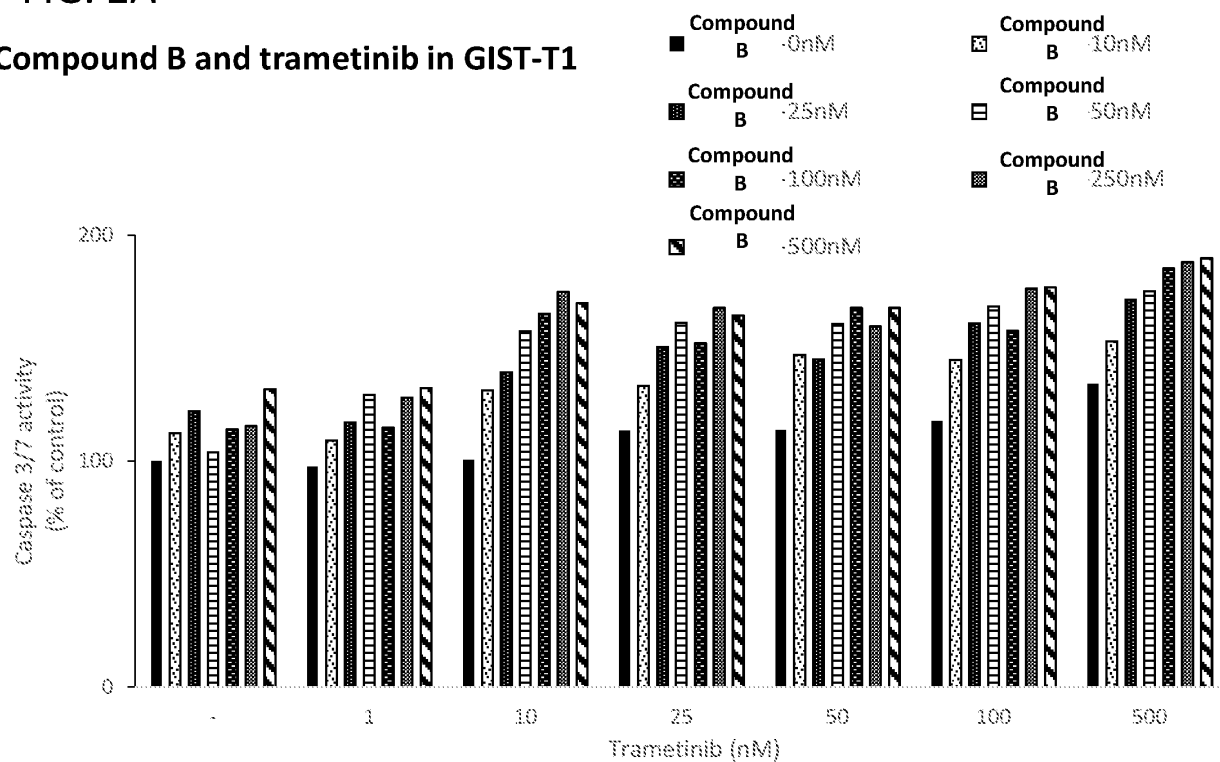


FIG. 2B Combination index by Chou Talalay analysis

CI Index	Compound B 10nM	Compound B 25nM	Compound B 50nM	Compound B 100nM	Compound B 250nM	Compound B 500nM
Trametinib 1nM	1.39845	0.30024	0.01632	2.30138	0.10126	0.064
Trametinib 10nM	0.02443	0.00825	6.55E-04	2.14E-04	4.87E-05	1.10E-04
Trametinib 25nM	0.04489	0.00449	9.92E-04	0.00355	3.69E-04	5.99E-04
Trametinib 50nM	0.014	0.0184	0.00206	7.38E-04	0.00246	7.39E-04
Trametinib 100nM	0.03929	0.00411	0.00137	0.00631	4.00E-04	3.70E-04
Trametinib 500nM	0.06136	0.00435	0.00244	4.54E-04	2.94E-04	2.15E-04

CI<1 = synergy

CI=1 = additive effect

CI>1 = antagonism

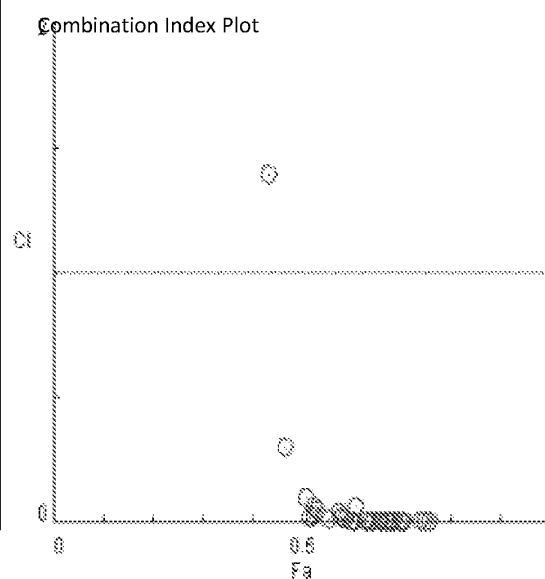


FIG. 2C

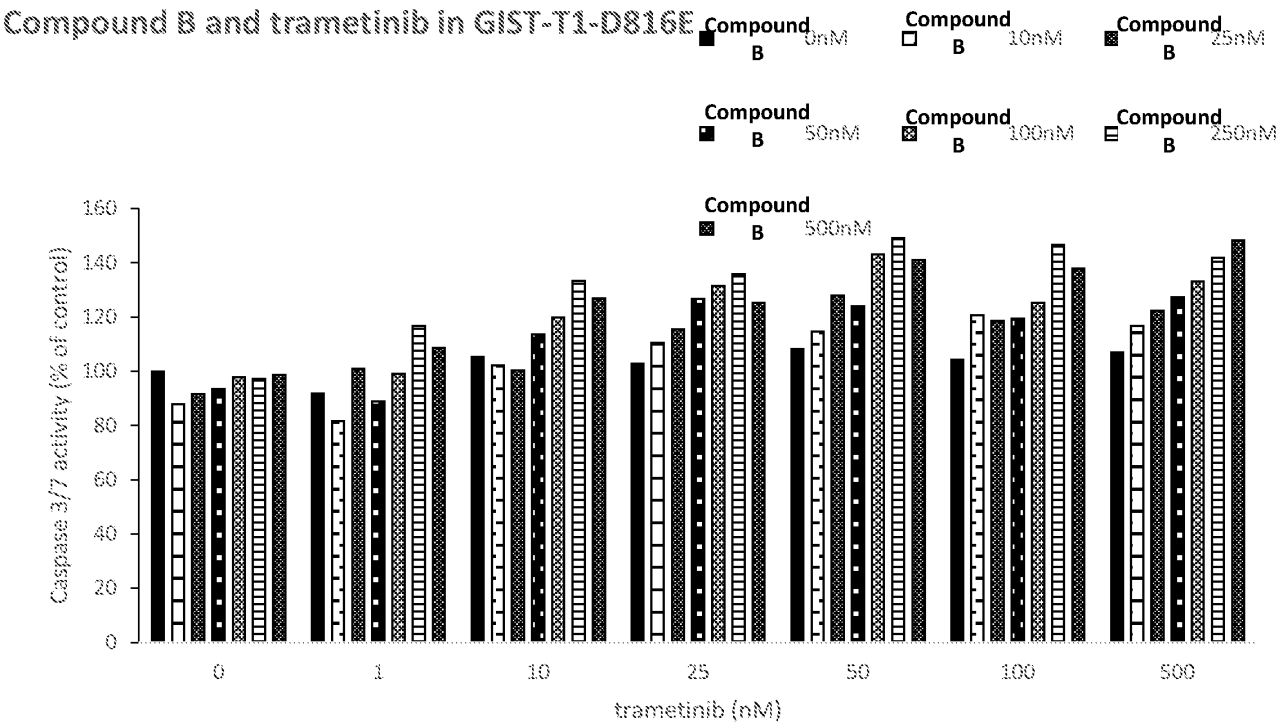


FIG. 2D Combination index by Chou Talalay analysis

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism

CI	Compound B 10nM	Compound B 25nM	Compound B 50nM	Compound B 100nM	Compound B 250nM	Compound B 500nM
Trametinib 1 nM	665.864	0.12785	26.2251	0.45772	0.00161	0.04969
Trametinib 10 nM	0.54776	1.20639	0.00454	4.57E-04	6.01E-06	1.07E-04
Trametinib 25 nM	0.03782	0.0046	4.67E-05	8.93E-06	2.92E-06	2.39E-04
Trametinib 50 nM	0.01217	4.63E-05	2.61E-04	1.36E-07	2.74E-08	9.66E-07
Trametinib 100 nM	0.00188	0.00445	0.0033	3.10E-04	8.20E-08	3.44E-06
Trametinib 500 nM	0.04614	0.00446	5.99E-04	4.82E-05	1.36E-06	1.23E-07

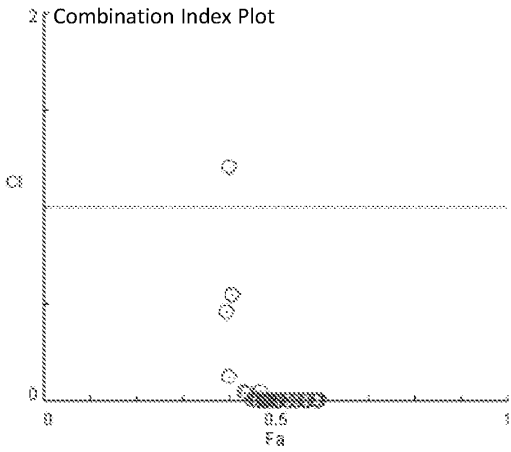


FIG. 2E

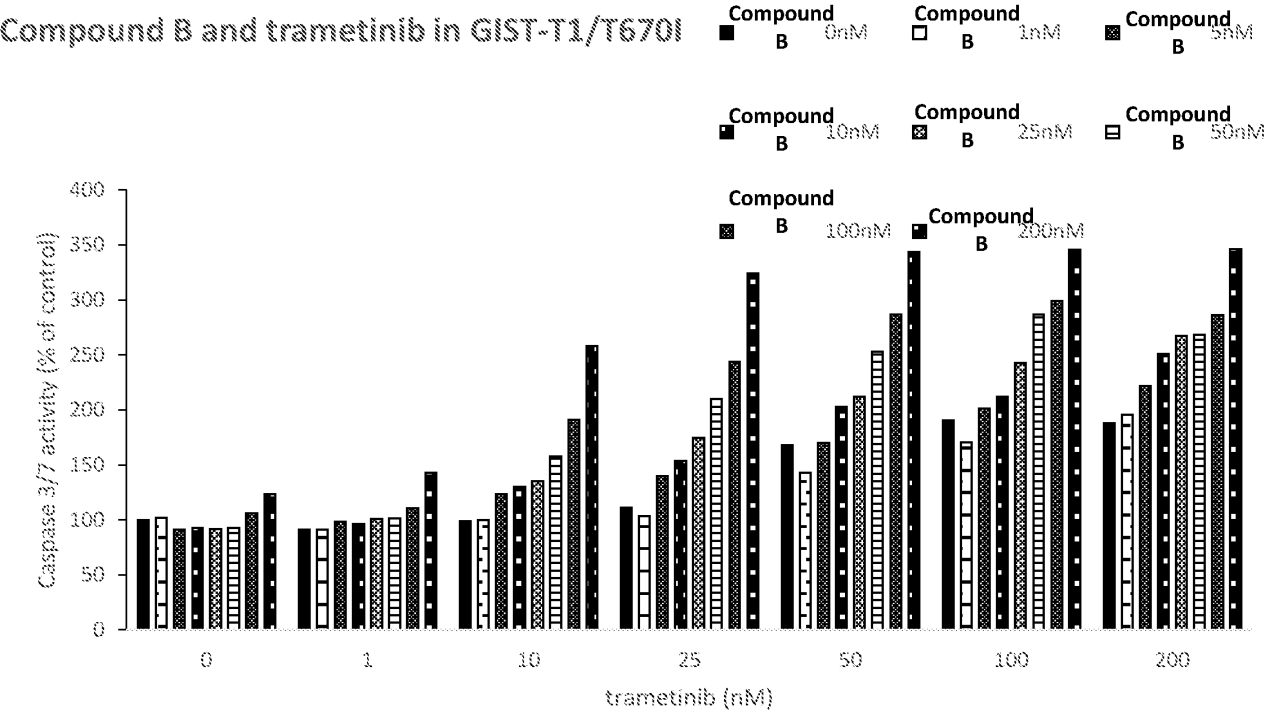


FIG. 2F Combination index by Chou Talalay analysis

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism

CI	Compound B 1nM	Compound B 5nM	Compound B 10nM	Compound B 25nM	Compound B 50nM	Compound B 100nM	Compound B 200nM
Trametinib 1 nM	1.14152	0.68225	1.61409	0.98075	1.71864	0.29552	0.03118
Trametinib 10 nM	2.69122	0.75205	0.55106	0.43683	0.16308	0.04278	0.0037
Trametinib 25 nM	5.2964	0.89005	0.48271	0.20367	0.05226	0.01535	7.67E-04
Trametinib 50 nM	1.55676	0.48782	0.13831	0.09887	0.02177	0.00642	6.93E-04
Trametinib 100 nM	0.95619	0.29266	0.19773	0.06368	0.01283	0.00935	0.00127
Trametinib 200 nM	0.72063	0.27355	0.09362	0.05242	0.04964	0.02614	0.0108

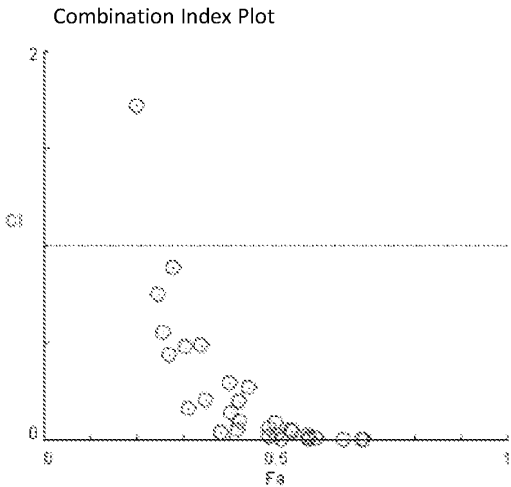


FIG. 3A

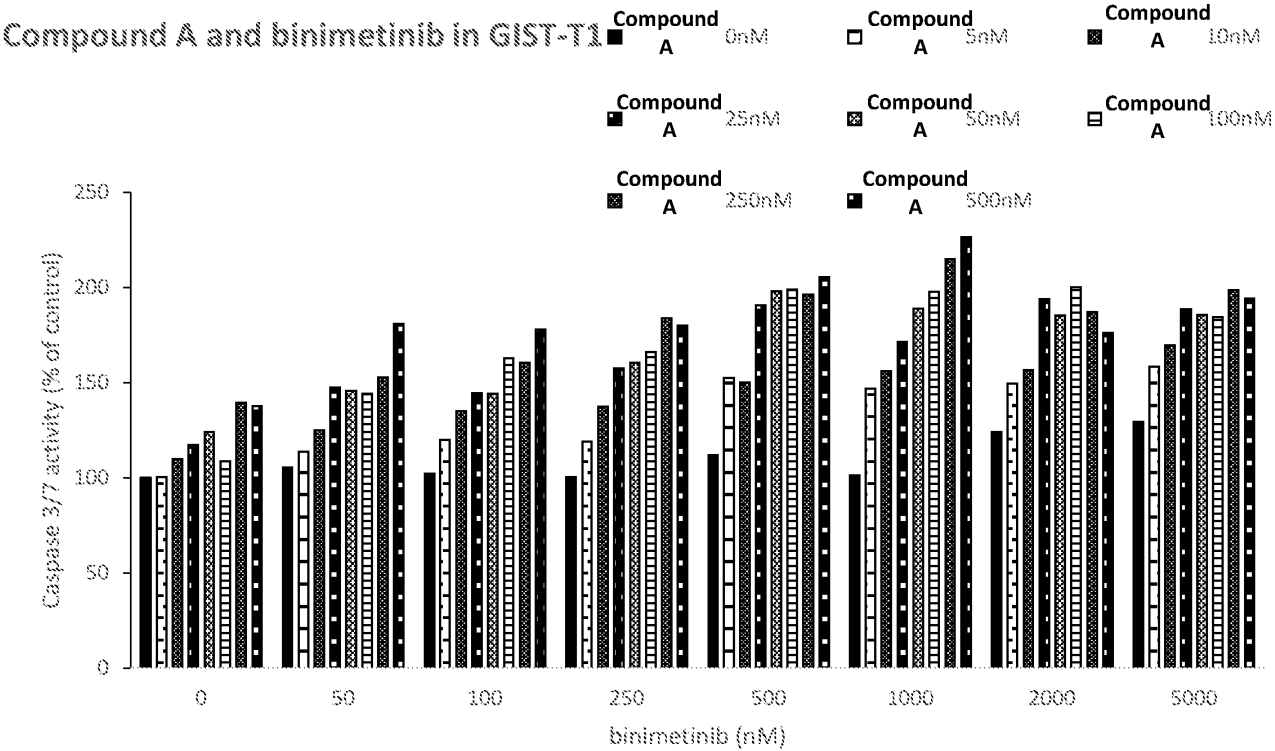


FIG. 3B Combination index by Chou Talalay analysis

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism

CI	Compound A 0nM	Compound A 5nM	Compound A 10nM	Compound A 25nM	Compound A 50nM	Compound A 100nM	Compound A 250nM
Binimetinib 50 nM	0.33162	0.11367	0.01361	0.03539	0.08336	0.05317	0.0021
Binimetinib 100 nM	0.13977	0.03047	0.02054	0.04202	0.00686	0.0182	0.00352
Binimetinib 250 nM	0.2221	0.00601	0.00355	0.0046	0.00416	5.34E-04	0.00246
Binimetinib 500 nM	0.00186	0.00463	2.11E-05	1.03E-05	1.45E-05	5.78E-05	2.16E-05
Binimetinib 1000 nM	0.00584	0.0022	4.83E-04	5.74E-05	2.16E-05	9.19E-07	5.62E-08
Binimetinib 2000 nM	0.00526	0.00249	1.18E-05	1.11E-04	1.39E-05	3.10E-04	0.00447
Binimetinib 5000 nM	0.00224	4.19E-04	3.22E-05	1.09E-04	2.53E-04	3.75E-05	2.22E-04

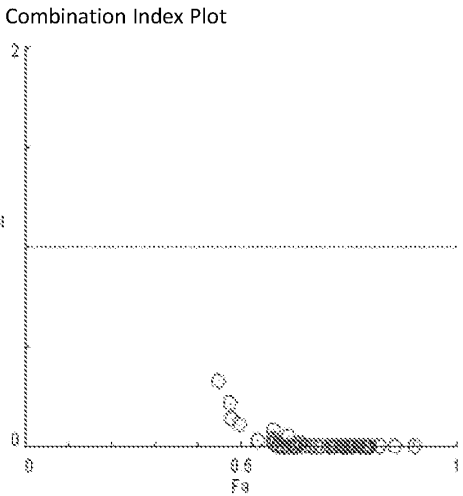


FIG. 3C

Compound A and binimetinib in G1S7-T1-D816E

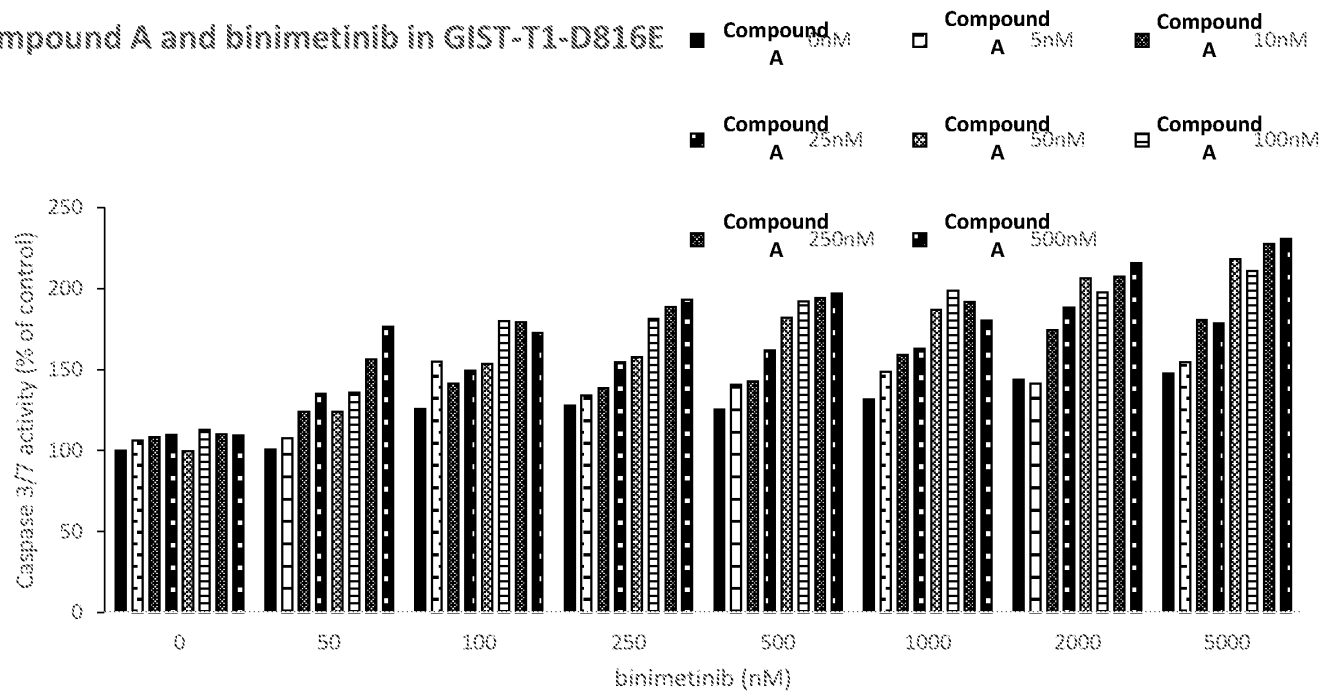


FIG. 3D Combination index by Chou Talalay analysis

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism

CI	Compound A 5nM	Compound A 10nM	Compound A 25nM	Compound A 50nM	Compound A 100nM	Compound A 250nM	Compound A 500nM
Binimetinib 50 nM	1.44226	0.18041	0.04953	0.18041	0.04533	0.00368	2.70E-04
Binimetinib 100 nM	0.00887	0.04581	0.018	0.01068	3.28E-04	3.65E-04	9.10E-04
Binimetinib 250 nM	0.27864	0.16365	0.02359	0.01571	6.58E-04	2.18E-04	1.05E-04
Binimetinib 500 nM	0.25046	0.19724	0.0189	0.00118	2.38E-04	1.70E-04	1.06E-04
Binimetinib 1000 nM	0.19128	0.05539	0.03323	0.0011	1.63E-04	5.17E-04	0.00294
Binimetinib 2000 nM	0.91612	0.0148	0.00181	7.43E-05	3.72E-04	5.74E-05	8.87E-06
Binimetinib 5000 nM	0.4718	0.01468	0.01892	1.25E-05	7.15E-05	6.91E-07	2.20E-07

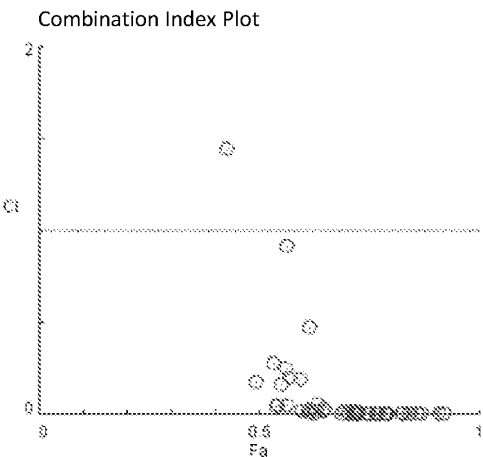


FIG. 3E

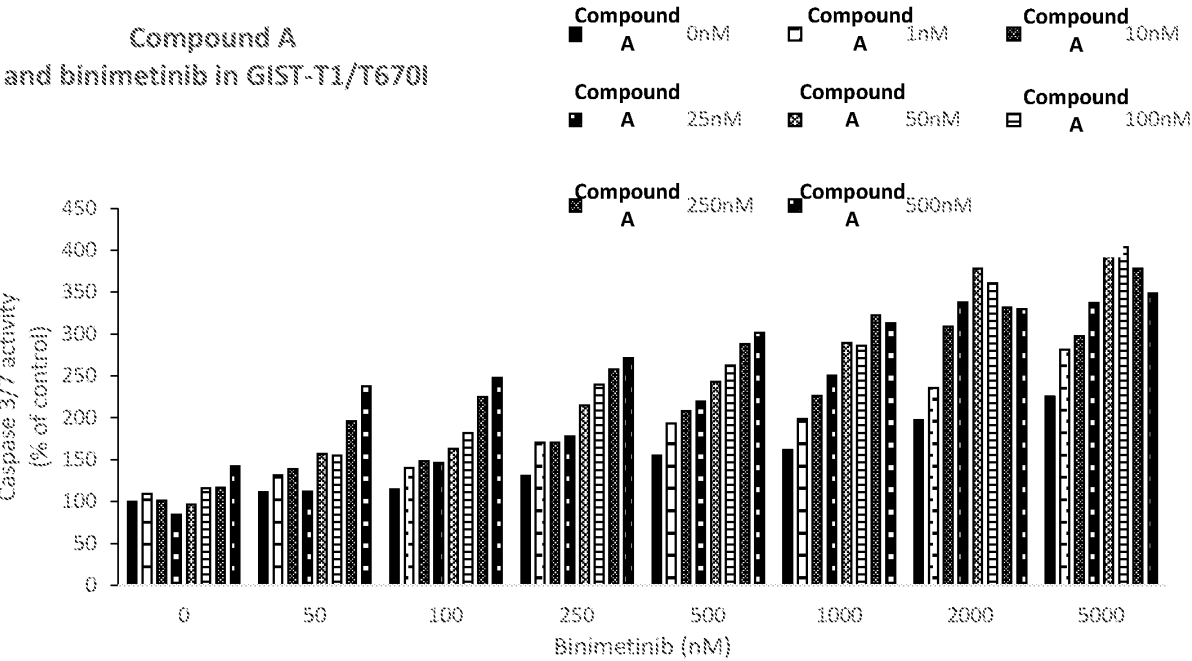


FIG. 3F Combination index by Chou Talalay analysis

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism

CI	Compound A 5nM	Compound A 10nM	Compound A 25nM	Compound A 50nM	Compound A 100nM	Compound A 250nM	Compound A 500nM
Binimetinib 50 nM	0.26759	0.19769	0.97922	0.09229	0.1009	0.02216	0.00492
Binimetinib 100 nM	0.37303	0.26335	0.28329	0.31079	0.07363	0.01588	0.00691
Binimetinib 250 nM	0.27979	0.27979	0.21379	0.05549	0.02307	0.0121	0.00751
Binimetinib 500 nM	0.2403	0.14108	0.0946	0.04058	0.02056	0.00922	0.00547
Binimetinib 1000 nM	0.40206	0.1466	0.06912	0.01474	0.01722	0.00394	0.00588
Binimetinib 2000 nM	0.21654	0.01366	0.00386	4.15E-04	0.0012	0.00506	0.00572
Binimetinib 5000 nM	0.10041	0.05372	0.01007	3.42E-04	1.38E-04	0.00104	0.00569

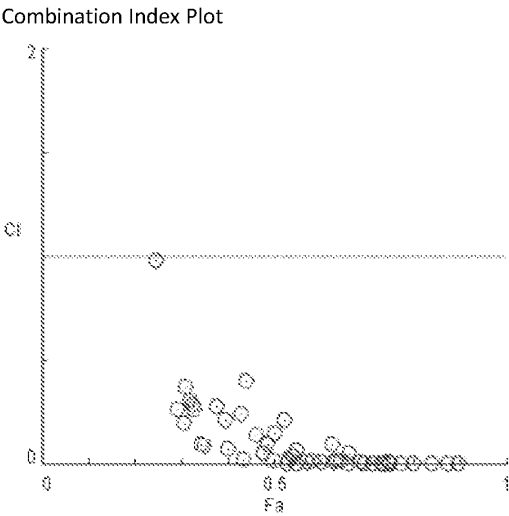
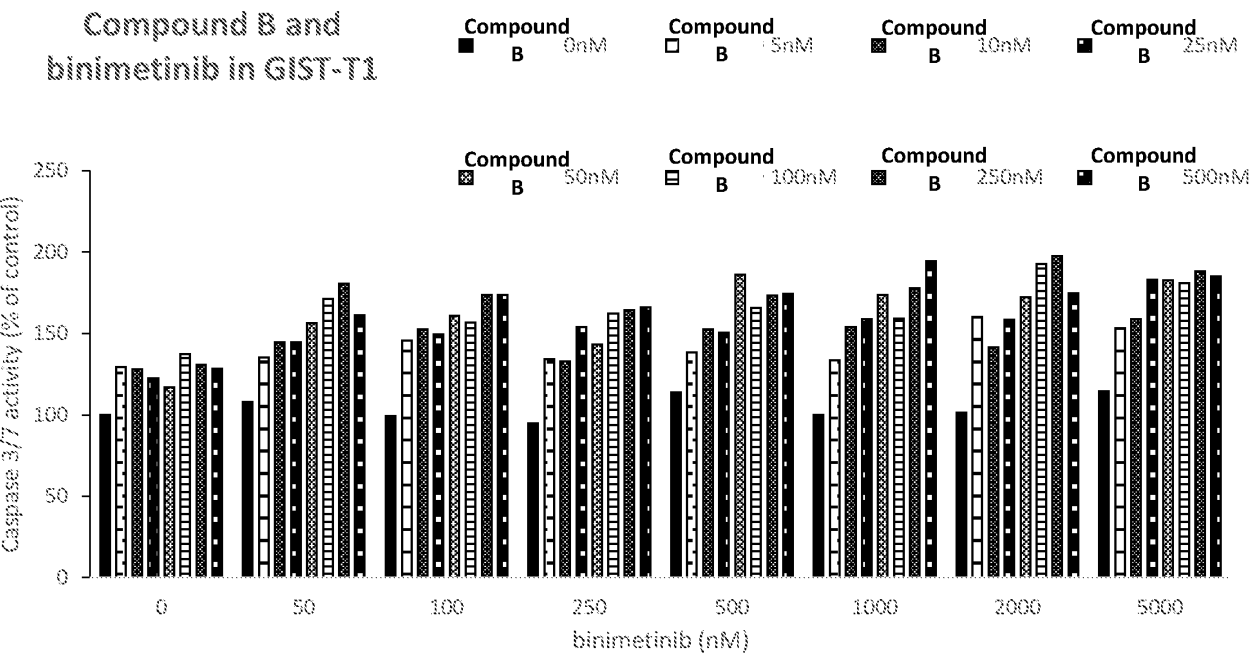


FIG. 4A



Combination index by Chou Talalay analysis

FIG. 4B

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism

CI	Compound B 5nM	Compound B 10nM	Compound B 25nM	Compound B 50nM	Compound B 100nM	Compound B 250nM	Compound B 500nM
Binimetinib 50 nM	4.65E-06	1.70E-11	3.20E-11	4.90E-19	7.80E-28	2.00E-34	5.50E-22
Binimetinib 100 nM	1.40E-12	4.60E-17	1.40E-14	1.10E-21	3.70E-19	4.30E-29	5.80E-29
Binimetinib 250 nM	1.39E-05	1.87E-04	1.80E-17	3.80E-10	4.30E-22	4.00E-23	5.50E-24
Binimetinib 500 nM	4.02E-08	5.20E-17	2.20E-17	4.50E-39	1.40E-23	4.00E-28	8.40E-29
Binimetinib 1000 nM	4.15E-05	1.80E-17	7.80E-20	5.80E-28	6.50E-20	3.80E-31	4.10E-54
Binimetinib 2000 nM	5.10E-20	1.44E-09	3.00E-19	7.20E-27	3.00E-49	7.20E-68	1.80E-28
Binimetinib 5000 nM	1.30E-16	4.80E-19	4.90E-35	1.20E-34	5.80E-33	7.00E-41	3.70E-37

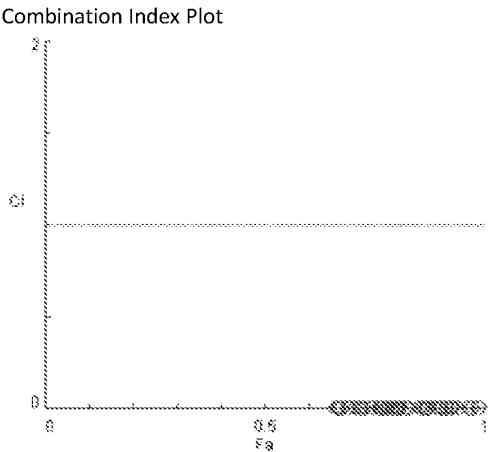


FIG. 4C

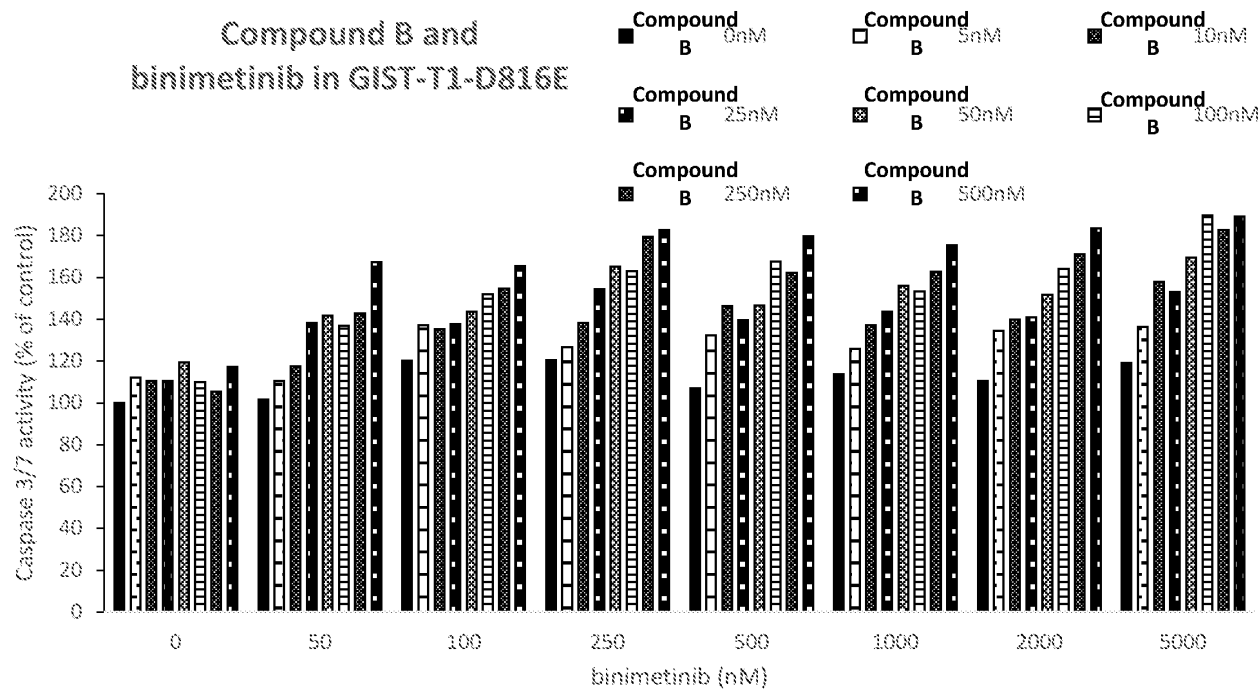


FIG. 4D Combination index by Chou Talalay analysis

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism

CI	Compound B 5nM	Compound B 10nM	Compound B 25nM	Compound B 50nM	Compound B 100nM	Compound B 250nM	Compound B 500nM
Binimetinib 50 nM	1606.78	0.00356	9.50E-11	3.40E-12	3.40E-10	1.10E-12	9.80E-25
Binimetinib 100 nM	4.70E-10	2.81E-09	2.70E-10	1.20E-12	2.60E-16	1.60E-17	3.10E-23
Binimetinib 250 nM	9.63E-06	4.80E-10	3.90E-17	1.00E-22	1.80E-21	6.80E-33	3.20E-36
Binimetinib 500 nM	1.64E-07	4.10E-13	3.20E-10	3.30E-13	9.80E-24	1.00E-20	5.80E-33
Binimetinib 1000nM	8.87E-05	4.71E-09	1.20E-11	3.30E-17	5.90E-16	9.50E-21	6.10E-29
Binimetinib 2000 nM	9.56E-08	8.80E-10	2.90E-10	6.50E-15	4.00E-21	1.40E-25	5.70E-36
Binimetinib 5000nM	4.83E-08	1.70E-17	4.50E-15	4.00E-24	3.00E-44	6.30E-35	6.30E-43

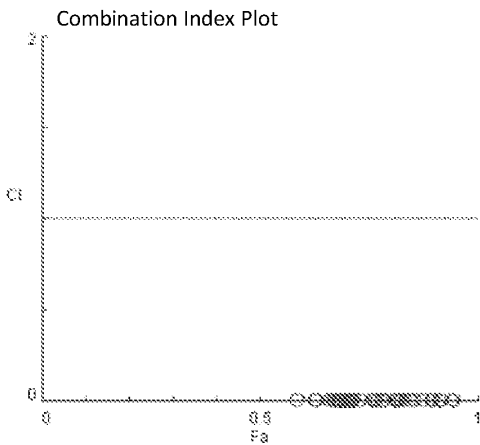


FIG. 4E

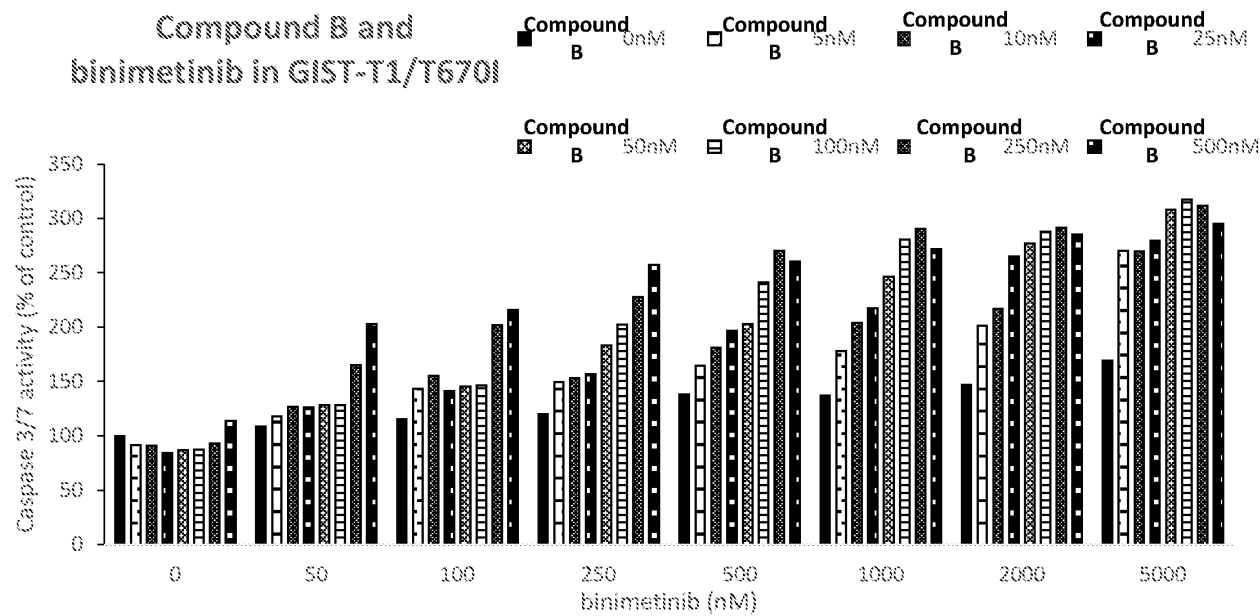


FIG. 4F Combination index by Chou Talalay analysis

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism

CI	Compound B 5nM	Compound B 10nM	Compound B 25nM	Compound B 50nM	Compound B 100nM	Compound B 250nM	Compound B 500nM
Binimetinib 50 nM	0.34963	0.16862	0.17353	1.08713	0.15037	0.00828	4.63E-04
Binimetinib 100 nM	0.0904	0.03897	0.10661	0.07671	0.06878	0.00101	3.34E-04
Binimetinib 250 nM	0.13837	0.10561	0.07858	0.01969	0.00238	3.25E-04	2.35E-05
Binimetinib 500 nM	0.0897	0.02509	0.00754	0.00476	1.96E-04	1.17E-05	3.46E-05
Binimetinib 1000 nM	0.06371	0.00878	0.00298	2.52E-04	7.39E-06	2.35E-06	2.08E-05
Binimetinib 2000 nM	0.02182	0.00631	8.43E-05	2.32E-05	6.49E-06	3.90E-06	8.47E-06
Binimetinib 5000 nM	1.21E-04	1.26E-04	4.19E-05	7.69E-07	1.09E-07	3.77E-07	5.71E-06

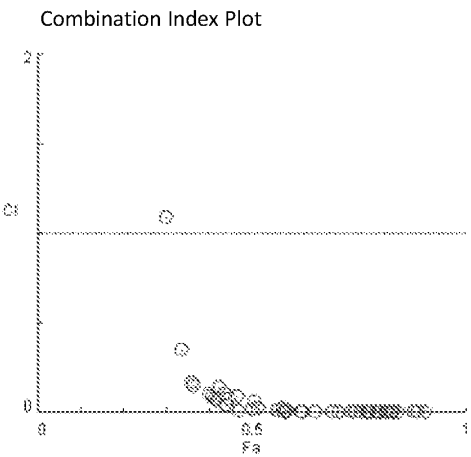


FIG. 5A

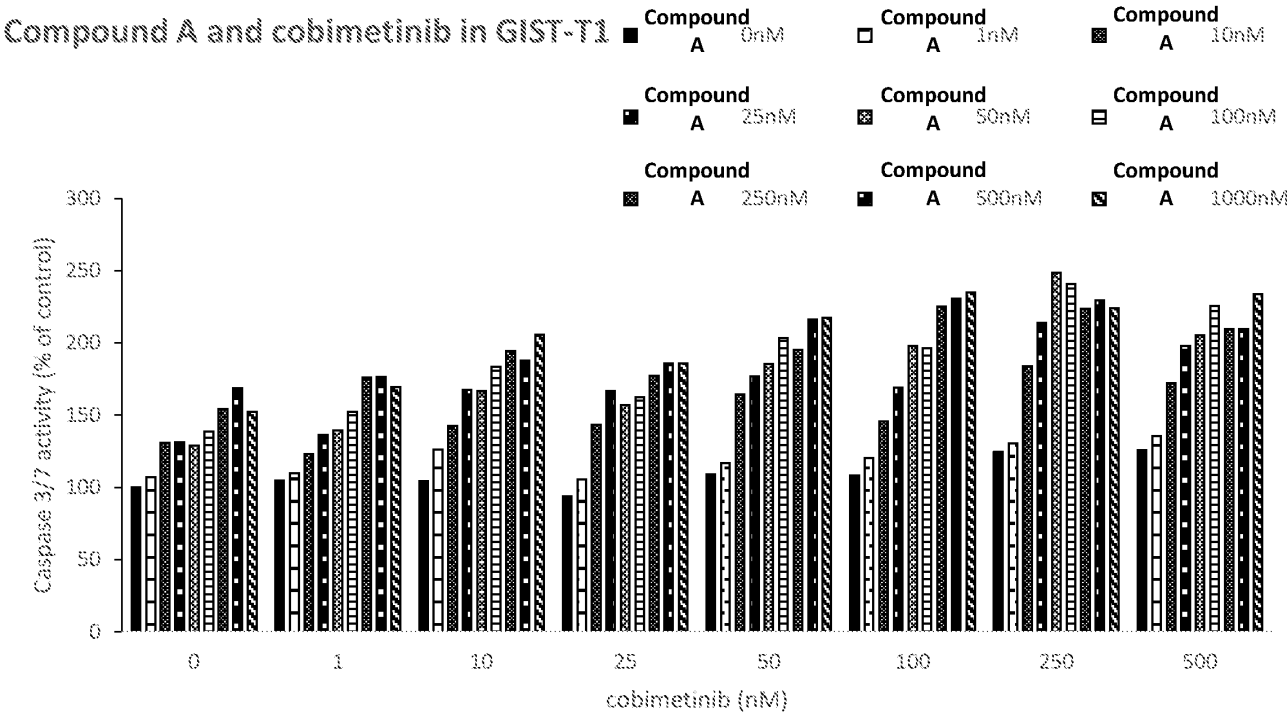


FIG. 5B Combination index by Chou Talalay analysis

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism

CI	Compound A 1nM	Compound A 10nM	Compound A 25nM	Compound A 50nM	Compound A 100nM	Compound A 200nM	Compound A 500nM	Compound A 1000nM
Cobimetinib 1 nM	0.79708	1.31592	0.55315	0.75613	0.30708	0.04872	0.09745	0.42662
Cobimetinib 10 nM	0.0855	0.0977	0.01338	0.02833	0.00855	0.0069	0.02772	0.00822
Cobimetinib 25 nM	3.4939	0.09192	0.01338	0.08493	0.0949	0.04362	0.03441	0.06882
Cobimetinib 50 nM	0.50545	0.00754	0.00461	0.00363	0.00107	0.00621	0.00138	0.00249
Cobimetinib 100 nM	0.34962	0.0678	0.01067	9.52E-04	0.00223	2.74E-04	3.13E-04	4.17E-04
Cobimetinib 250 nM	0.08223	8.55E-04	8.95E-05	5.31E-06	2.27E-05	3.37E-04	3.47E-04	0.00122
Cobimetinib 500 nM	0.04575	0.00305	4.76E-04	4.33E-04	1.04E-04	0.00135	0.00271	4.62E-04

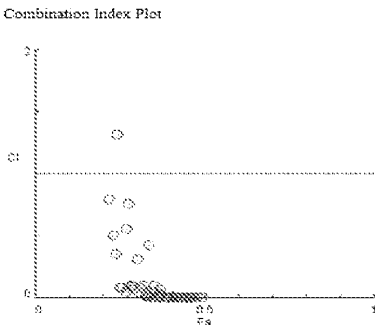


FIG. 5C

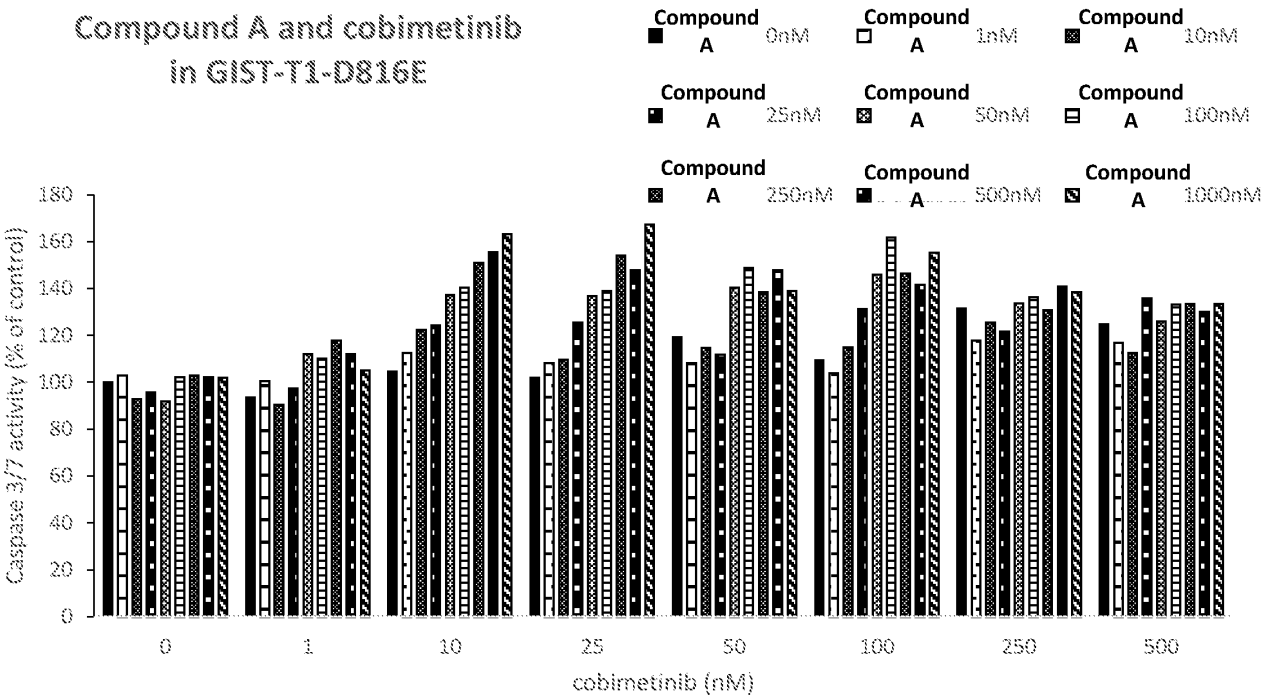


FIG. 5D Combination index by Chou Talalay analysis

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism

CI	Compound A 1nM	Compound A 10nM	Compound A 25nM	Compound A 50nM	Compound A 100nM	Compound A 200nM	Compound A 500nM	Compound A 1000nM
Cobimetinib 1 nM	0.18534	438696	4.76549	0.02461	0.03479	0.00915	0.02461	0.08008
Cobimetinib 10 nM	0.23568	0.04233	0.03138	0.00324	0.00193	3.04E-04	1.35E-04	3.08E-05
Cobimetinib 25 nM	1.17886	0.94861	0.0607	0.00882	0.00598	4.44E-04	0.00129	3.77E-05
Cobimetinib 50 nM	2.46263	0.79943	1.28476	0.00963	0.00227	0.01361	0.00259	0.01248
Cobimetinib 100 nM	10.3649	1.46703	0.09078	0.00705	4.08E-04	0.00675	0.01549	0.00135
Cobimetinib 250 nM	2.28677	0.60705	1.15264	0.15427	0.09612	0.25807	0.04413	0.06806
Cobimetinib 500 nM	5.42979	11.784	0.20954	1.11463	0.33621	0.30855	0.56228	0.30855

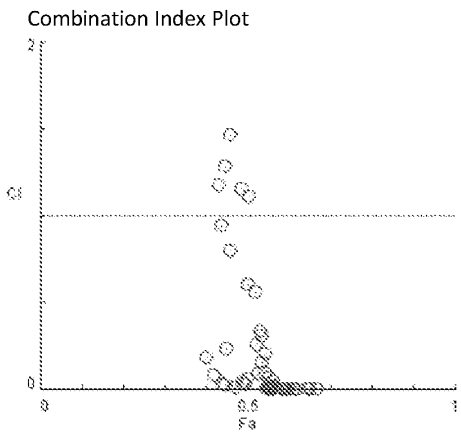


FIG. 5E

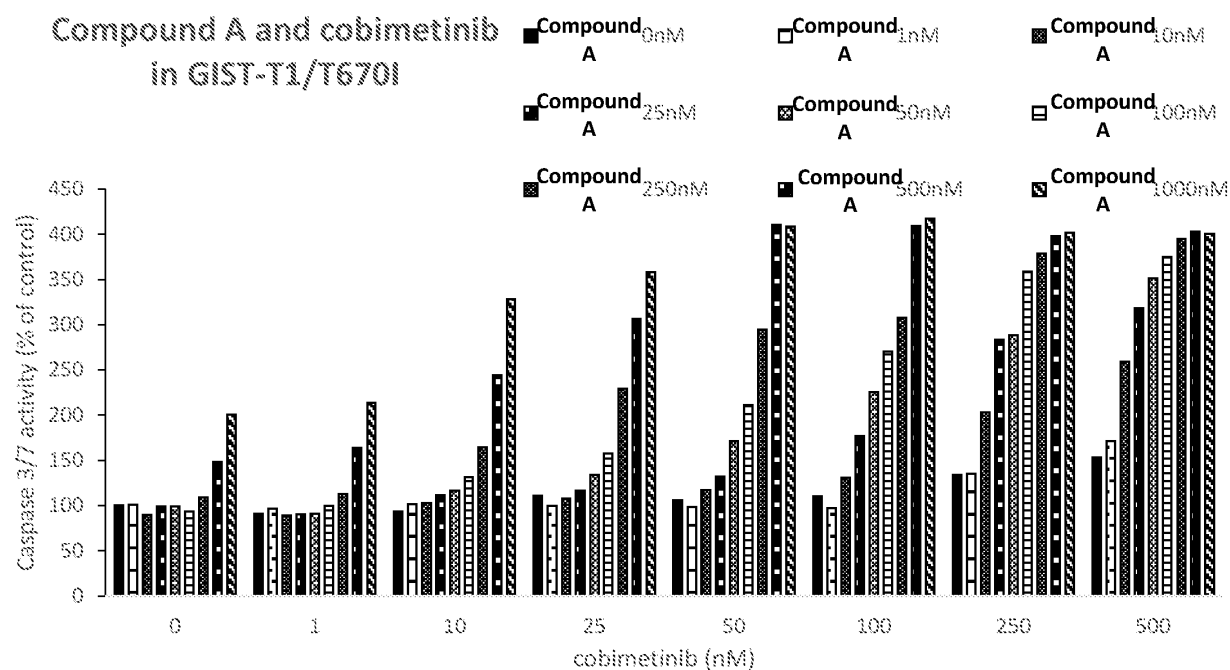


FIG. 5F

Combination index by Chou Talalay analysis

CI<1 = synergy
 CI=1 = additive effect
 CI>1 = antagonism

CI	Compound A 1nM	Compound A 10nM	Compound A 25nM	Compound A 50nM	Compound A 100nM	Compound A 200nM	Compound A 500nM	Compound A 1000nM
Cobimetinib 1 nM	0.26554	2.67726	5.76653	10.5467	7.71672	4.89163	0.13285	0.0072
Cobimetinib 10 nM	0.9985	1.33769	0.84391	0.86036	0.39351	0.06559	4.54E-04	2.51E-06
Cobimetinib 25 nM	2.8673	1.43276	0.75657	0.22264	0.04996	6.46E-04	6.27E-06	2.47E-07
Cobimetinib 50 nM	6.77934	0.90654	0.2524	0.01232	0.00104	7.27E-06	8.00E-10	1.99E-09
Cobimetinib 100 nM	16.1737	0.4255	0.00853	2.79E-04	1.89E-05	3.10E-06	9.50E-10	7.40E-10
Cobimetinib 250 nM	0.62392	0.0019	5.23E-06	4.56E-06	3.00E-08	1.07E-08	3.20E-09	4.13E-09
Cobimetinib 500 nM	0.04617	5.14E-05	5.56E-07	4.53E-08	1.19E-09	2.52E-09	1.94E-09	5.19E-09

Combination Index Plot

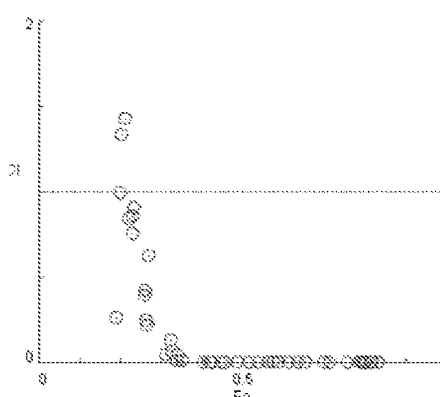


FIG. 6A

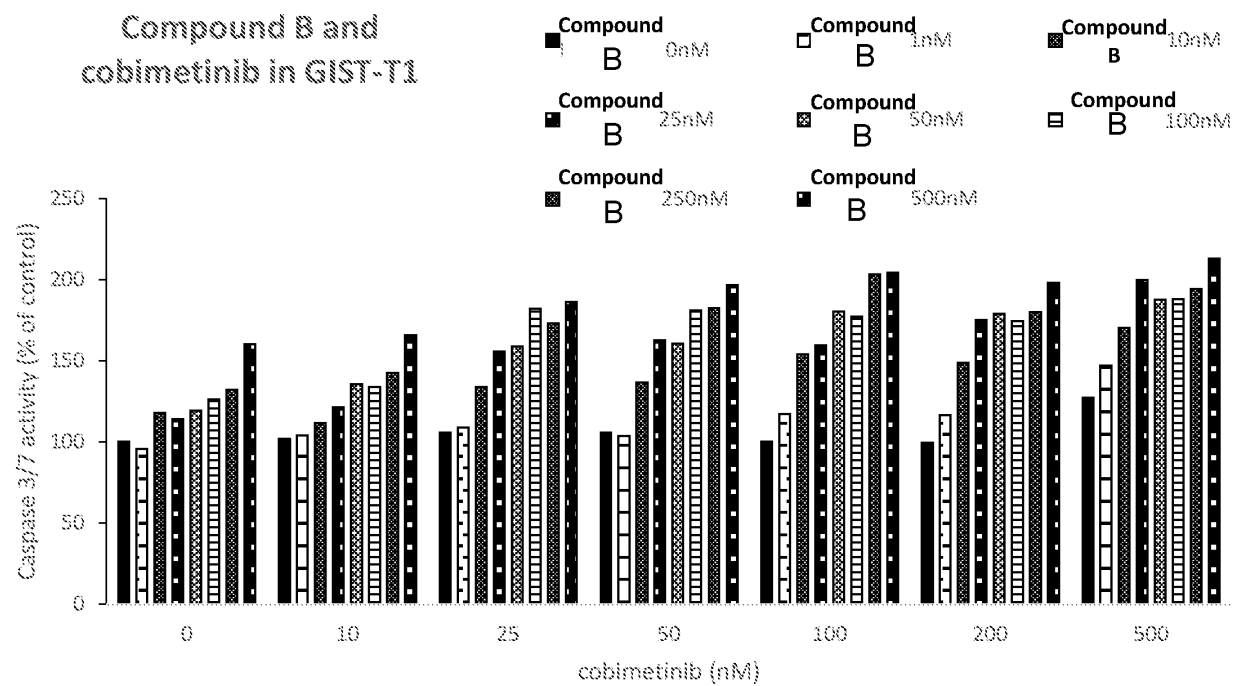


FIG. 6B

Combination index by Chou Talalay analysis

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism

CI	Compound B 1nM	Compound B 10nM	Compound B 25nM	Compound B 50nM	Compound B 100nM	Compound B 200nM	Compound B 500nM
Cobimetinib 10 nM	0.56205	1.23447	0.95172	0.33923	0.8499	0.57466	0.05953
Cobimetinib 25 nM	0.37301	0.08307	0.01254	0.01607	0.000825	0.00764	0.00181
Cobimetinib 50 nM	1.76547	0.06105	0.00477	0.01282	0.000975	0.00158	0.0002
Cobimetinib 100 nM	0.17549	0.00644	0.0073	0.000551	0.00193	1.34E-05	2.54E-05
Cobimetinib 200 nM	0.3168	0.01266	0.000656	0.000703	0.00317	0.00249	0.000126
Cobimetinib 500 nM	0.00186	0.000613	4.14E-06	0.000144	0.000251	0.000131	8.3E-07

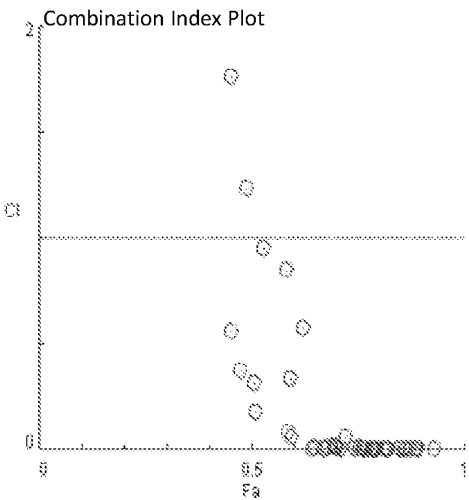
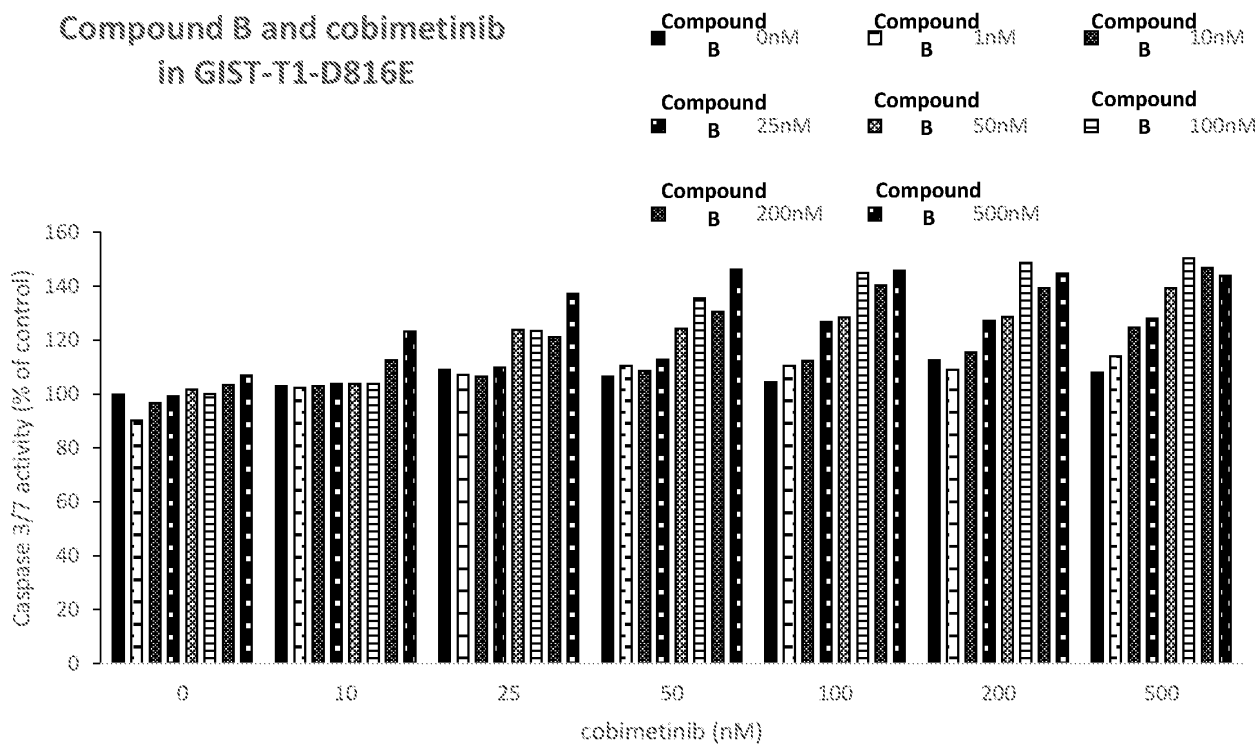


FIG. 6C



Combination index by Chou Talalay analysis

FIG. 6D

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism

CI	Compound B 1nM	Compound B 10nM	Compound B 25nM	Compound B 50nM	Compound B 100nM	Compound B 200nM	Compound B 500nM
Cobimetinib 10 nM	1.78658	1.4423	33.0169	1.15037	7.15955	0.03569	0.000619
Cobimetinib 25 nM	0.37205	0.54877	0.09771	7.19E-05	0.000137	0.000781	3.5E-07
Cobimetinib 50 nM	0.12042	0.36756	0.0391	8.29E-05	2.14E-07	6.79E-06	7.2E-10
Cobimetinib 100 nM	0.24051	0.09661	2.61E-05	1.04E-05	4.2E-10	2.11E-08	1.07E-09
Cobimetinib 200 nM	1.00074	0.03502	3.02E-05	1.47E-05	1.8E-11	3.89E-08	2.34E-09
Cobimetinib 500 nM	0.1855	0.000379	4.48E-05	1.86E-08	4.1E-12	1.8E-10	3.97E-09

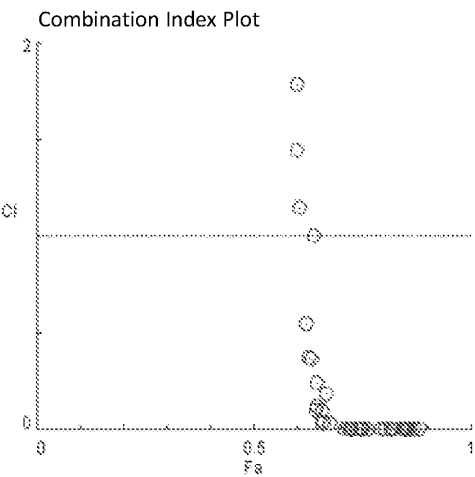


FIG. 6E

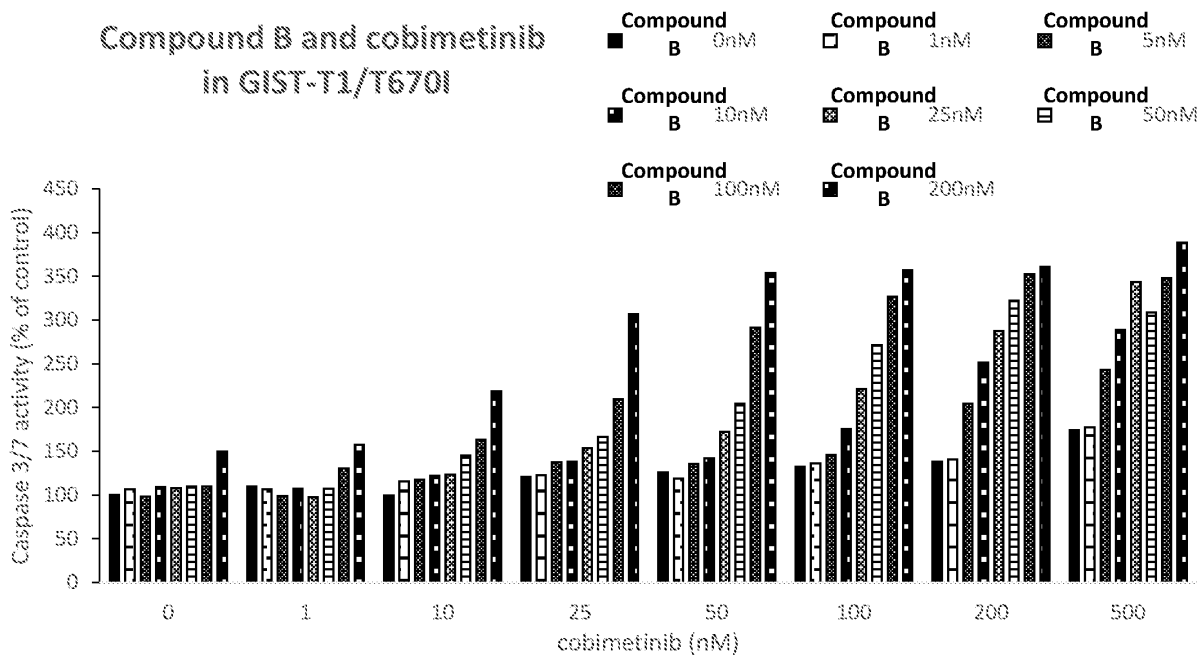


FIG. 6F

Combination index by Chou Talalay analysis

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism

CI	Compound B 1nM	Compound B 5nM	Compound B 10nM	Compound B 25nM	Compound B 50nM	Compound B 100nM	Compound B 200nM
Cobimetinib 1 nM	0.41369	3.735	1.55347	21.4235	6.74637	0.24978	0.00783
Cobimetinib 10 nM	1.03215	0.85167	0.54699	0.59718	0.05047	0.00877	6.73E-05
Cobimetinib 25 nM	1.09419	0.2284	0.22022	0.04847	0.0152	3.62E-04	1.23E-07
Cobimetinib 50 nM	3.39319	0.55609	0.29001	0.01725	0.00105	8.66E-07	3.52E-09
Cobimetinib 100 nM	1.04878	0.40707	0.02628	5.35E-04	9.31E-06	8.64E-08	5.25E-09
Cobimetinib 200 nM	1.33157	0.00418	9.39E-05	5.03E-06	2.57E-07	1.63E-08	6.70E-09
Cobimetinib 500 nM	0.10996	4.48E-04	1.11E-05	9.15E-08	2.16E-06	5.98E-08	8.60E-10

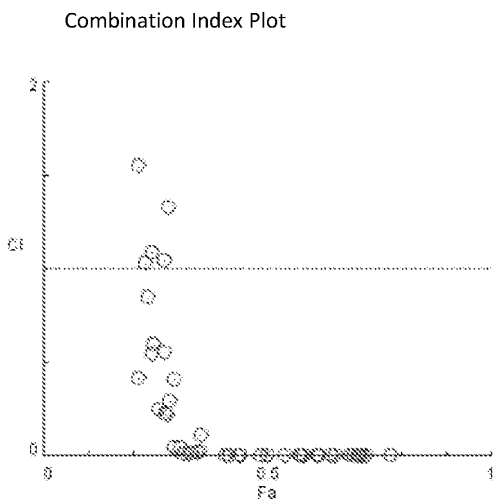


FIG. 7A

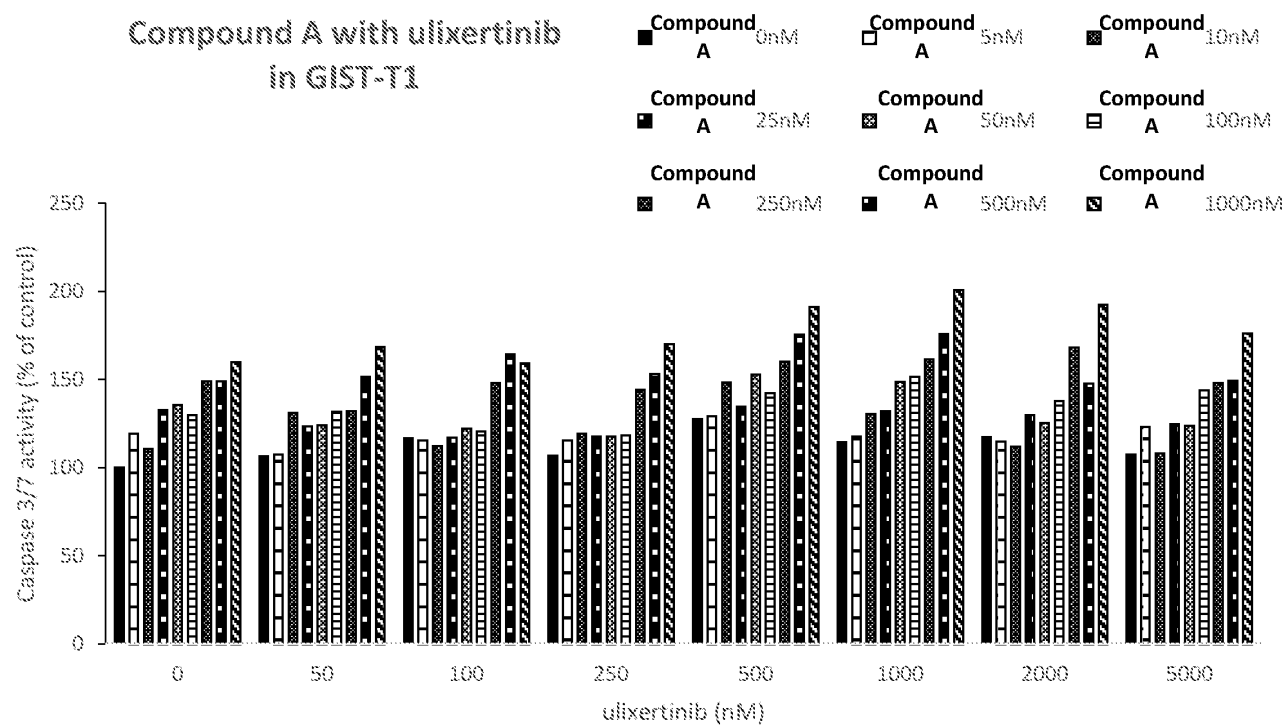


FIG. 7B

Combination index by Chou Talalay analysis

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism

CI	Compound A 5nM	Compound A 5nM	Compound A 10nM	Compound A 25nM	Compound A 50nM	Compound A 100nM	Compound A 200nM	Compound A 500nM	Compound A 1000nM
Ulixertinib 50nM	397033	12152.7	0.29353	2.00594	3.73337	2.73202	6.357	0.83994	0.143
Ulixertinib 100nM	15.0853	1.23598	7.30524	4.9472	4.97932	12.3642	0.67675	0.13312	0.57025
Ulixertinib 250nM	1.3E+11	1.29932	1.48118	4.60126	9.20222	16.5094	1.16864	0.67302	0.1129
Ulixertinib 500nM	0.14288	0.18202	0.0261	0.44394	0.06984	0.60244	0.12257	0.0243	0.00367
Ulixertinib 1000nM	0.05213	0.92137	0.30425	0.6357	0.13049	0.16799	0.10139	0.02333	6.50E-04
Ulixertinib 2000nM	9233.7	1.87274	70.9971	0.84709	3.23328	1.15347	0.03718	1.45611	0.00291
Ulixertinib 5000nM	0.7266	0.43113	274131	1.73715	3.87011	0.50263	0.67675	1.12708	0.0448

Combination Index Plot

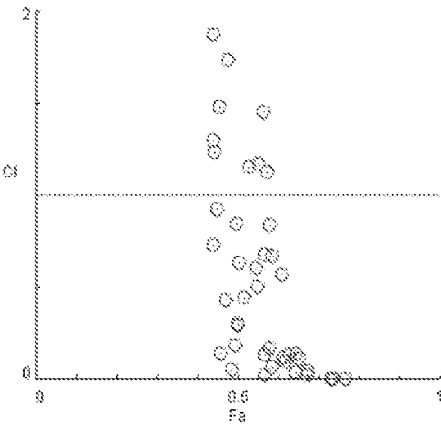


FIG. 7C

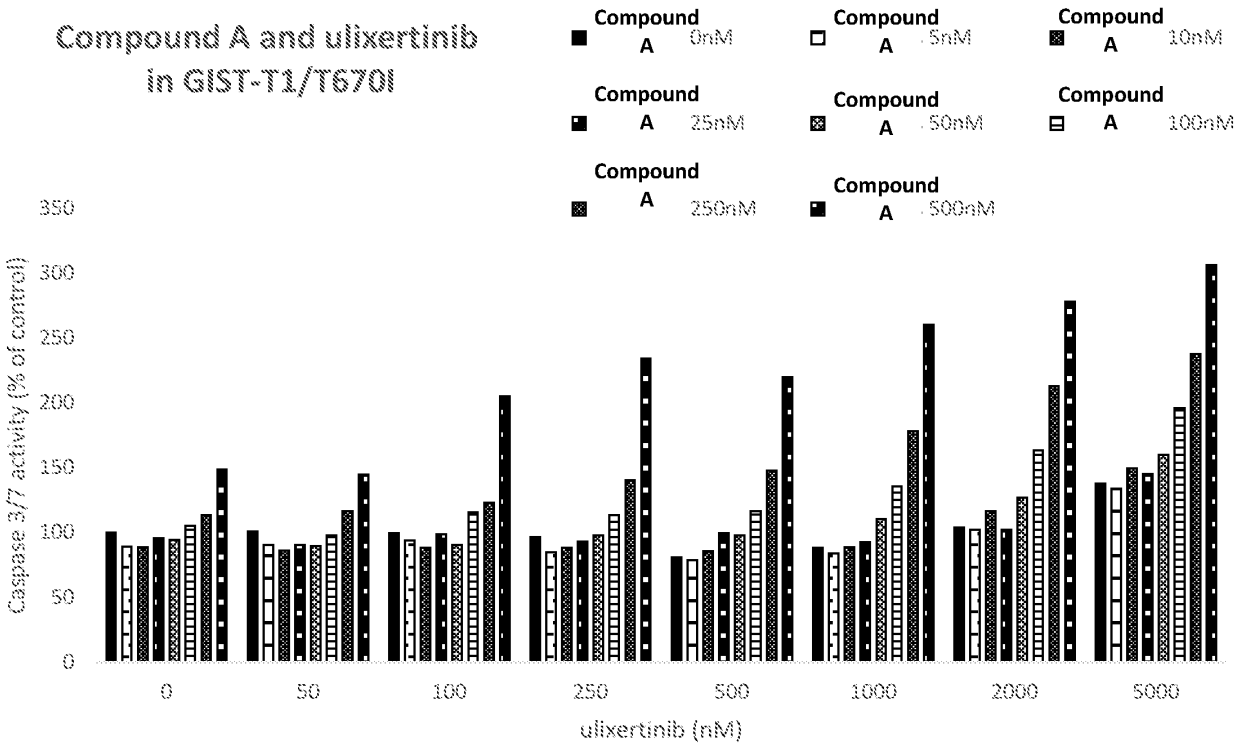


FIG. 7D

Combination index by Chou Talalay analysis

CI<1 = synergy
CI=1 = additive effect
CI>1 = antagonism

CI	Compound A 5nM	Compound A 10nM	Compound A 25nM	Compound A 50nM	Compound A 100nM	Compound A 200nM	Compound A 500nM
Ulixertinib 50nM	1.31834	3.57672	2.90308	5.56256	3.88493	1.36233	0.3461
Ulixertinib 100nM	1.10711	3.91925	1.11824	5.40429	0.75024	0.75332	0.00559
Ulixertinib 250nM	17.7013	8.33131	4.13239	2.71447	0.87632	0.19479	9.10E-04
Ulixertinib 500nM	175.181	27.9521	1.87828	0.83106	0.68648	0.11088	0.00217
Ulixertinib 1000nM	87.5534	27.0813	11.9376	3.57	0.14557	0.013	1.83E-04
Ulixertinib 2000nM	2.74177	0.20886	3.54357	0.1633	0.01821	0.00135	6.21E-05
Ulixertinib 5000nM	0.02425	0.00614	0.01896	0.01184	0.00199	2.93E-04	9.86E-06

Combination Index Plot

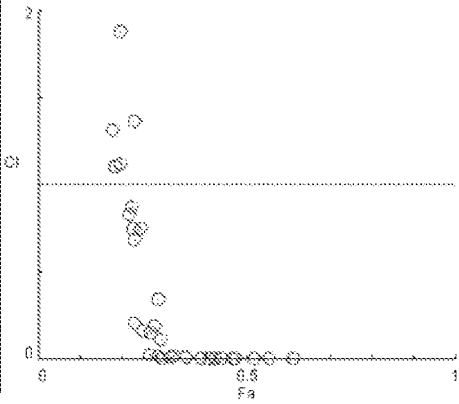


FIG. 8A

GIST-T1

2 wk drug treatment, 9 day recovery

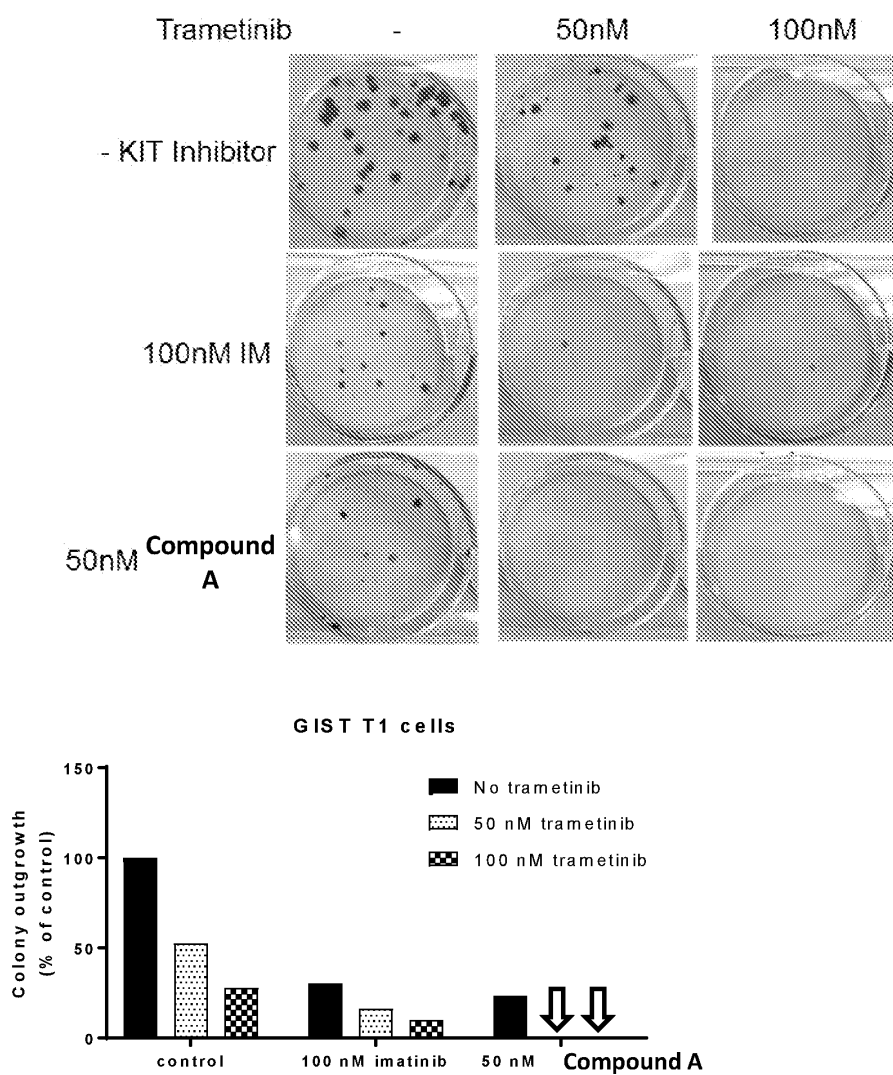
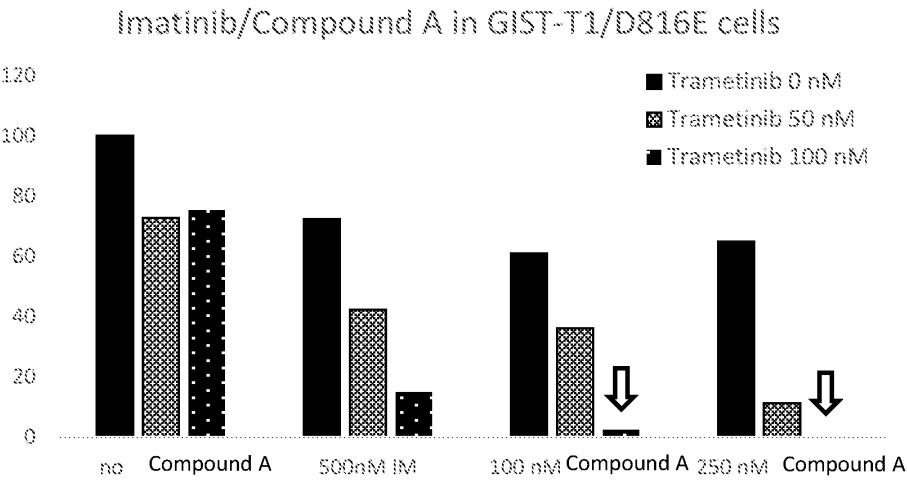
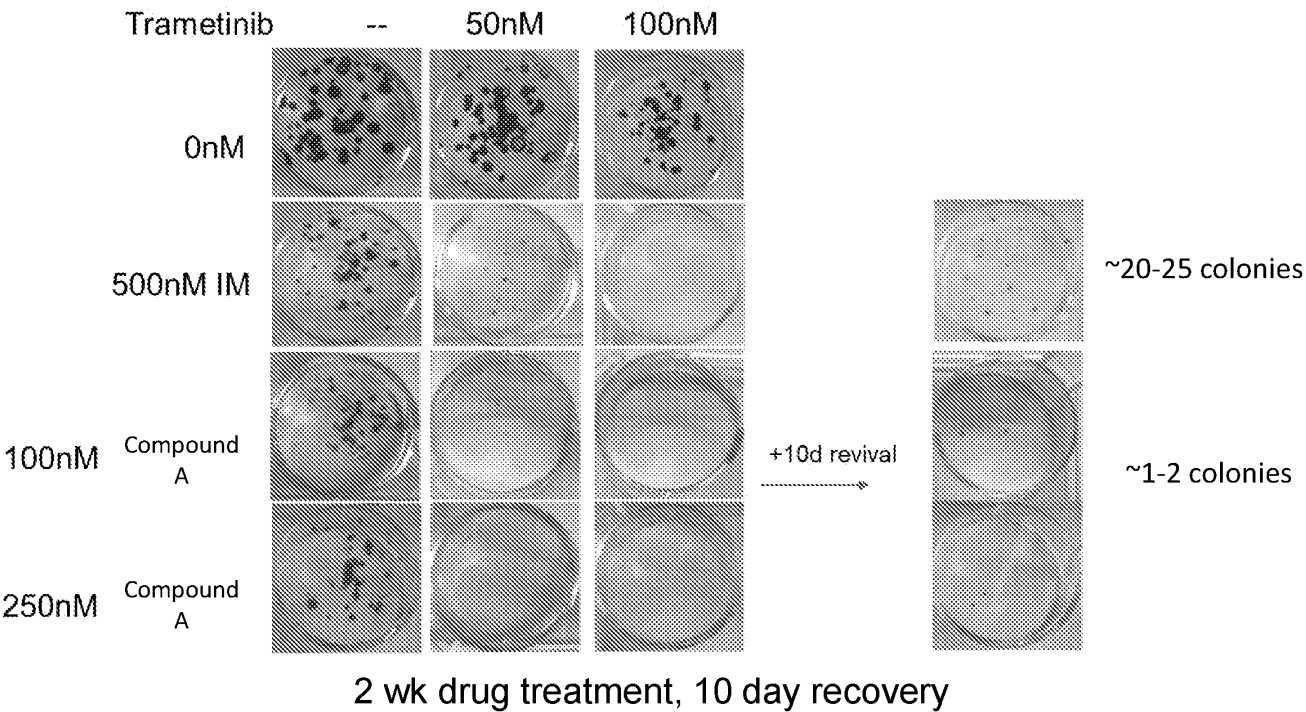


FIG. 8B

GIST-T1/D816E



24/47
GIST-T1/D816E

FIG. 8C

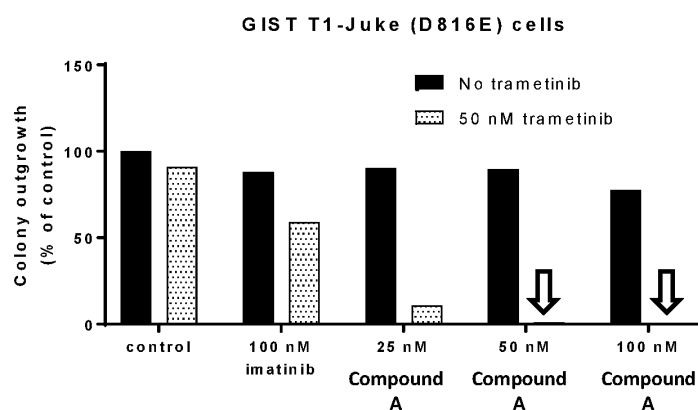
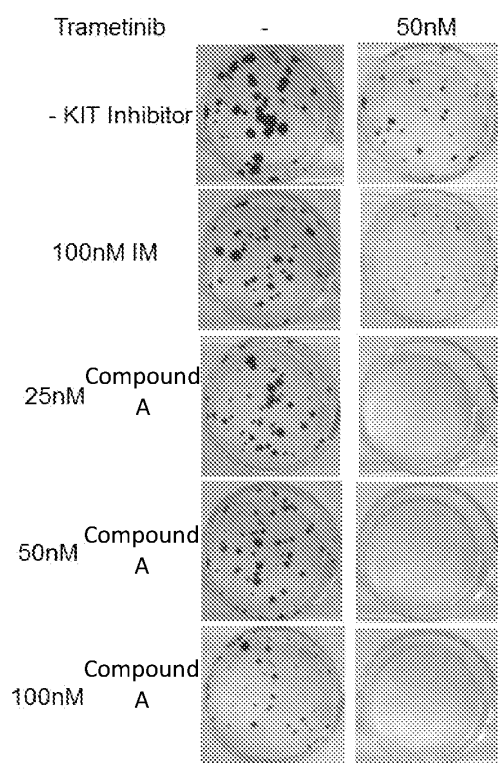
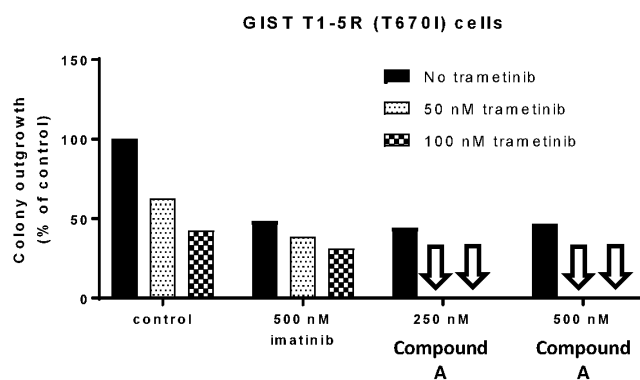
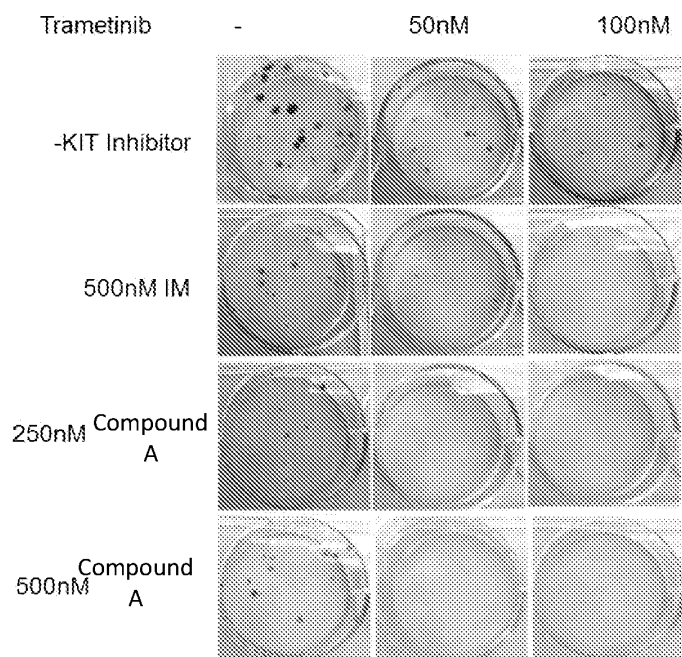


FIG. 8D

GIST-T1/T670I



2 wk drug treatment, 10 day recovery

Fig. 9A

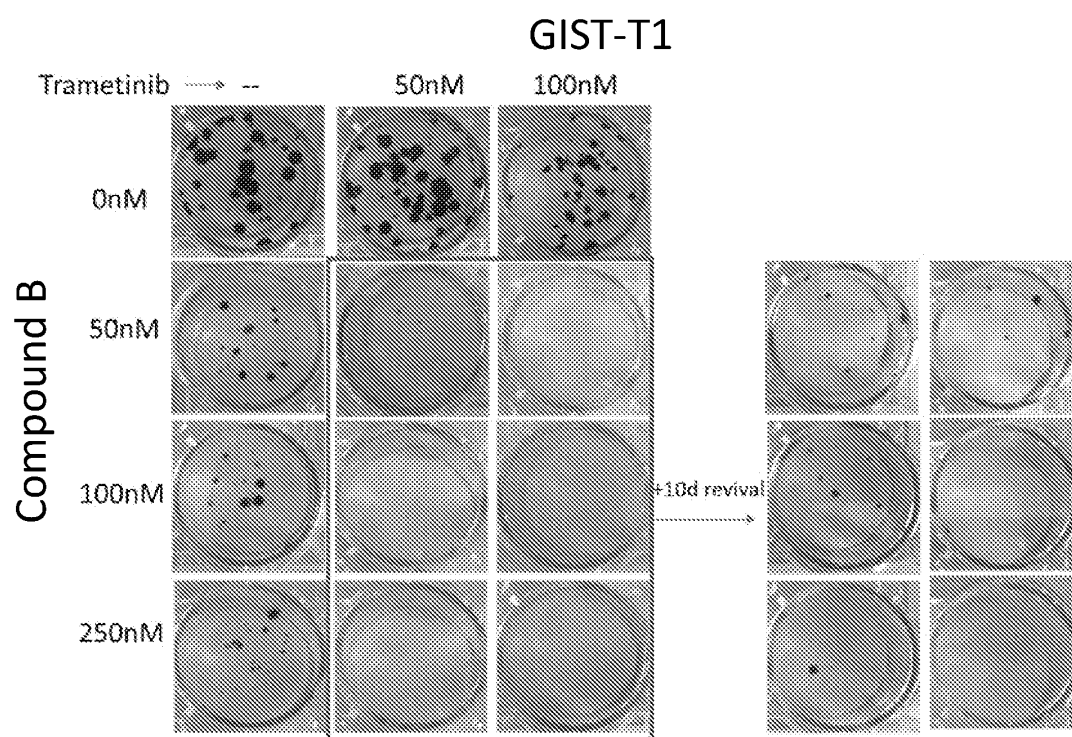
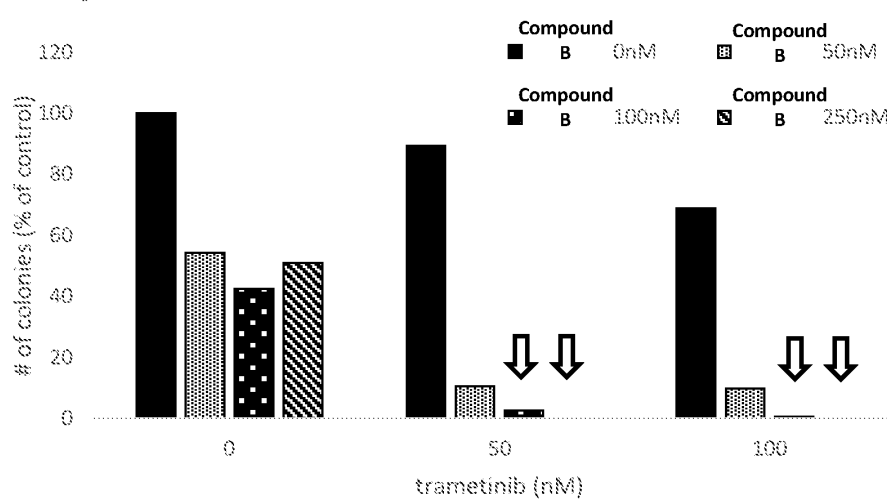
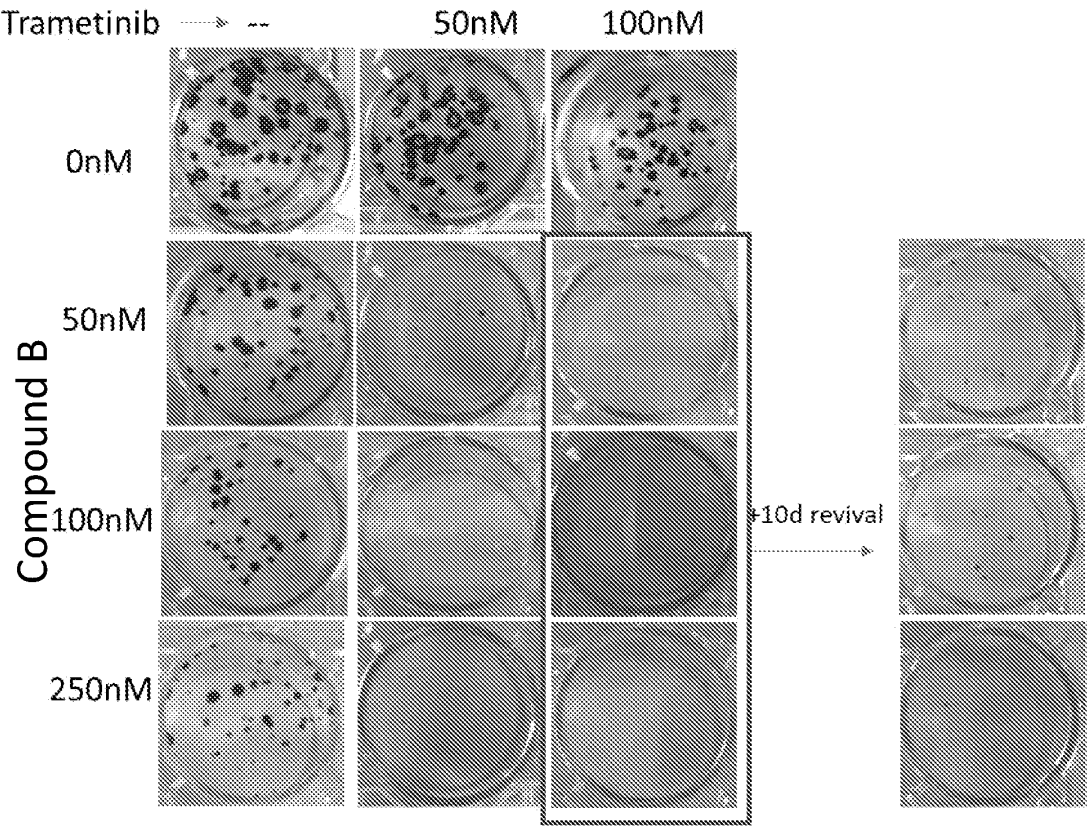
**Compound B and trametinib in GIST-T1**

Fig. 9B

GIST-T1/D816E



Compound B with trametinib
in GIST-T1/D816E

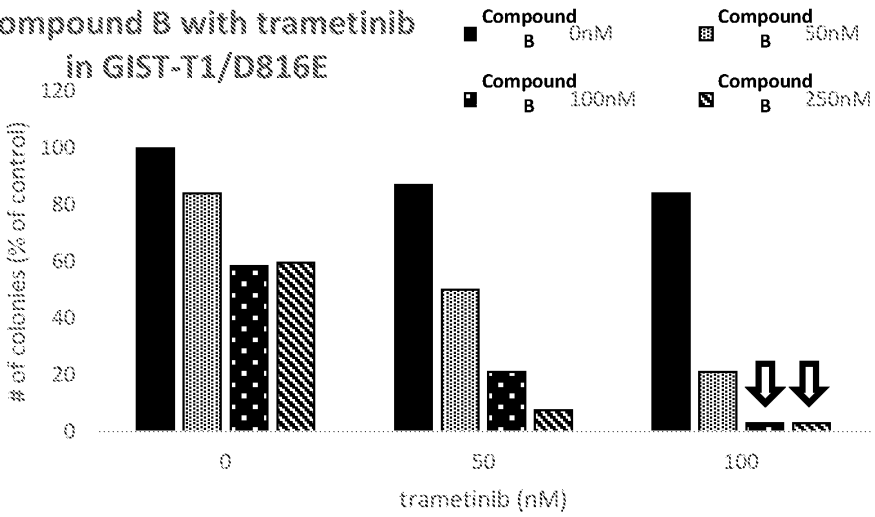


Fig. 9C

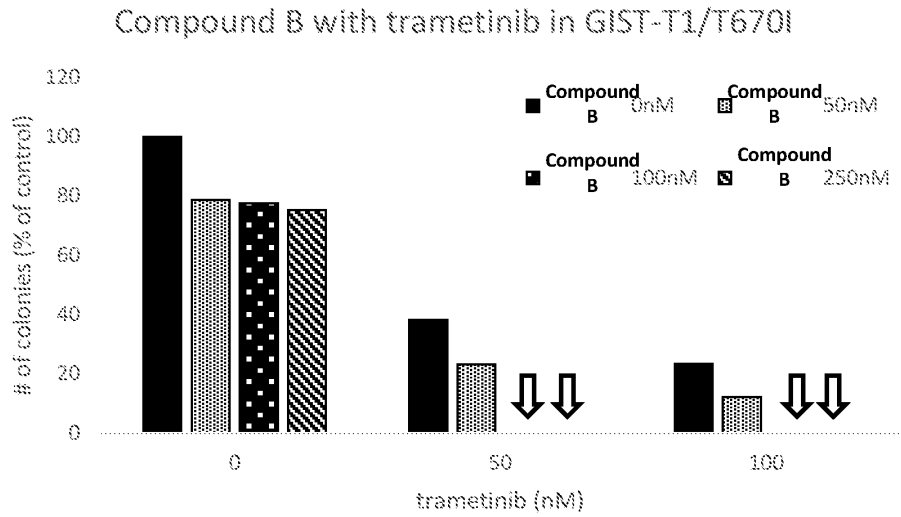
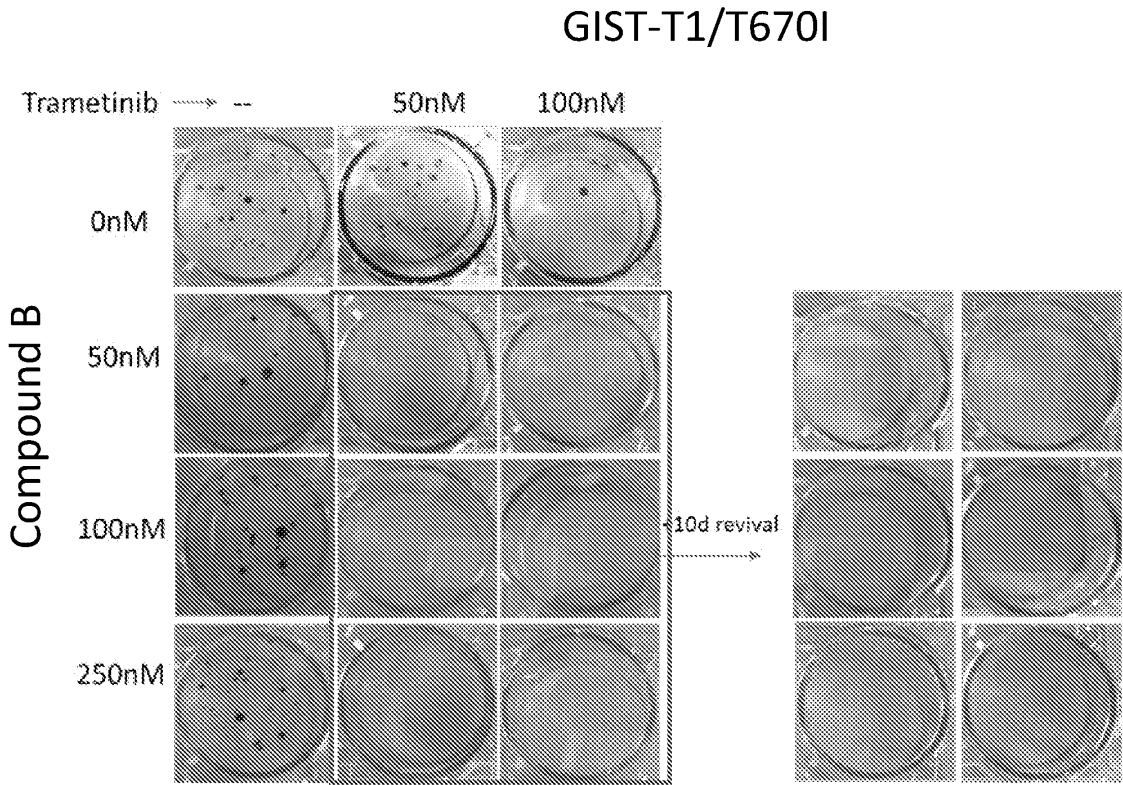


Fig. 10A

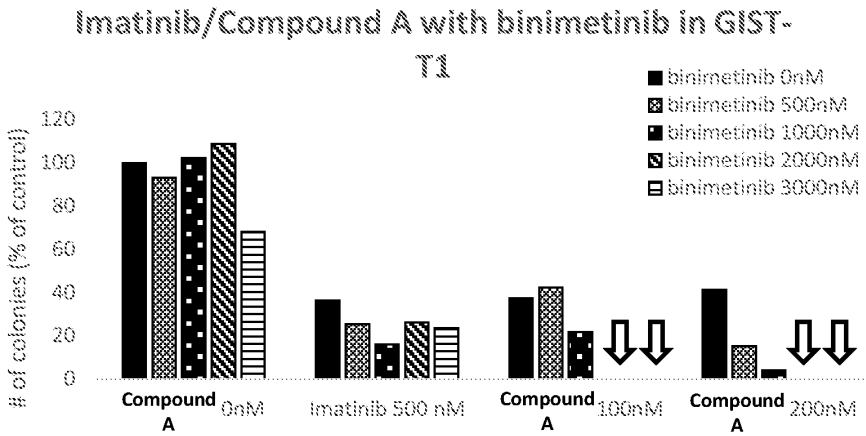
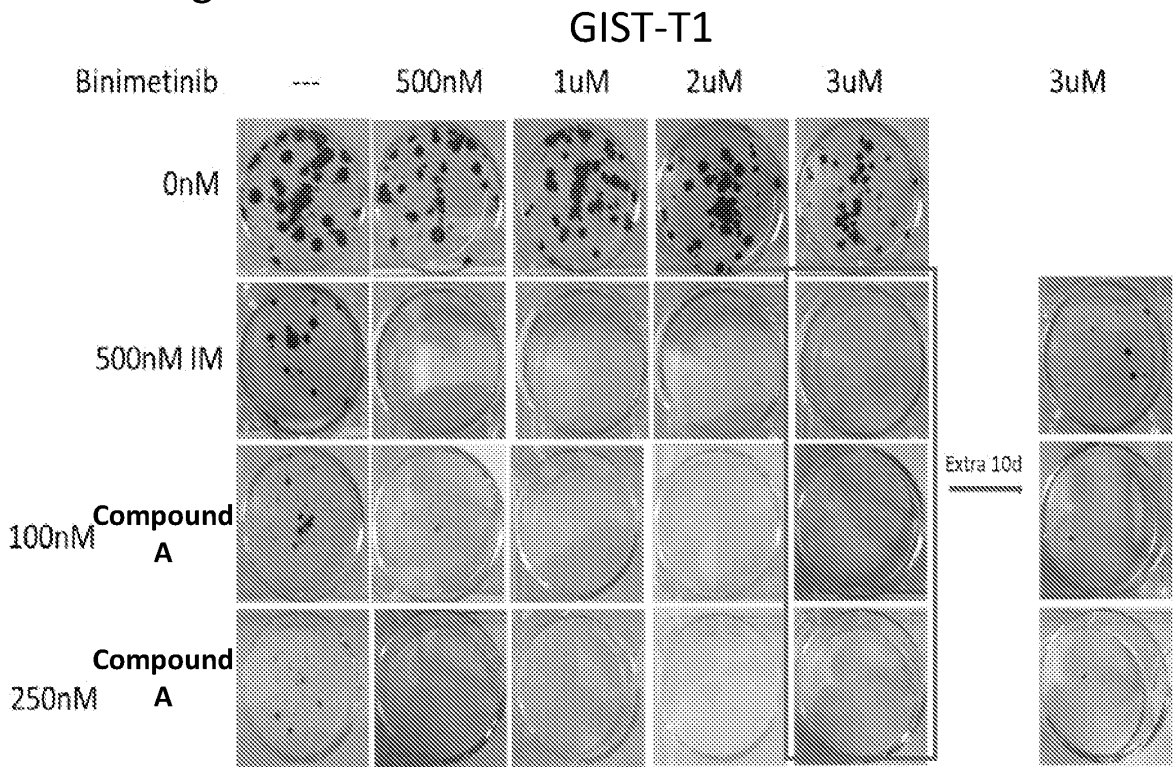
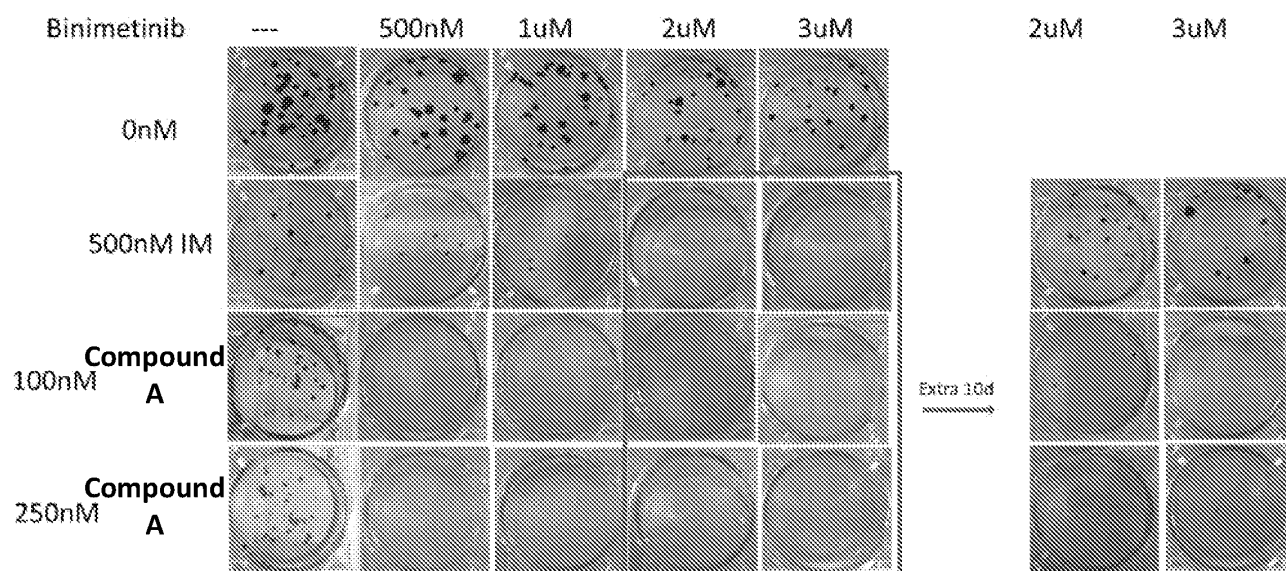


Fig. 10B

GIST-T1/D816E



Imatinib/Compound A and binimetinib in GIST-T1/D816E

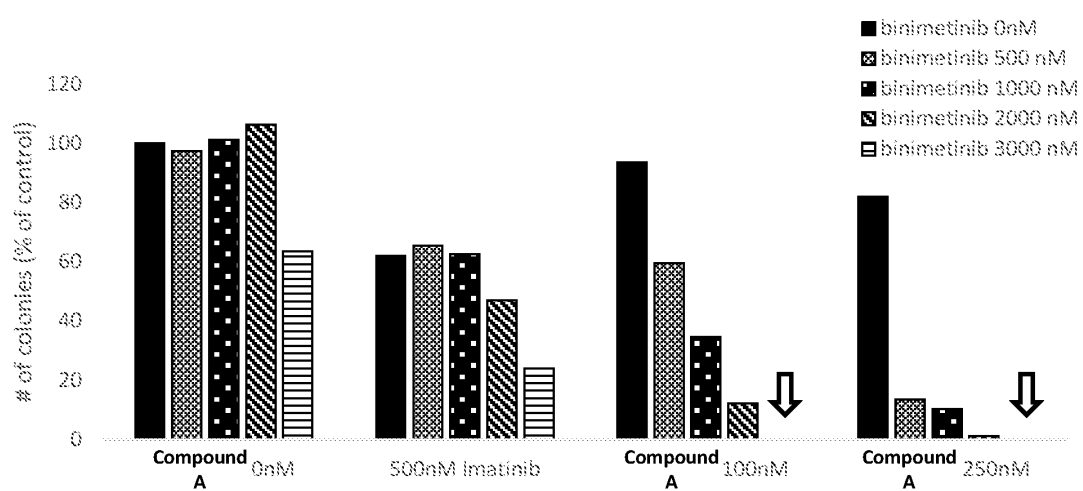
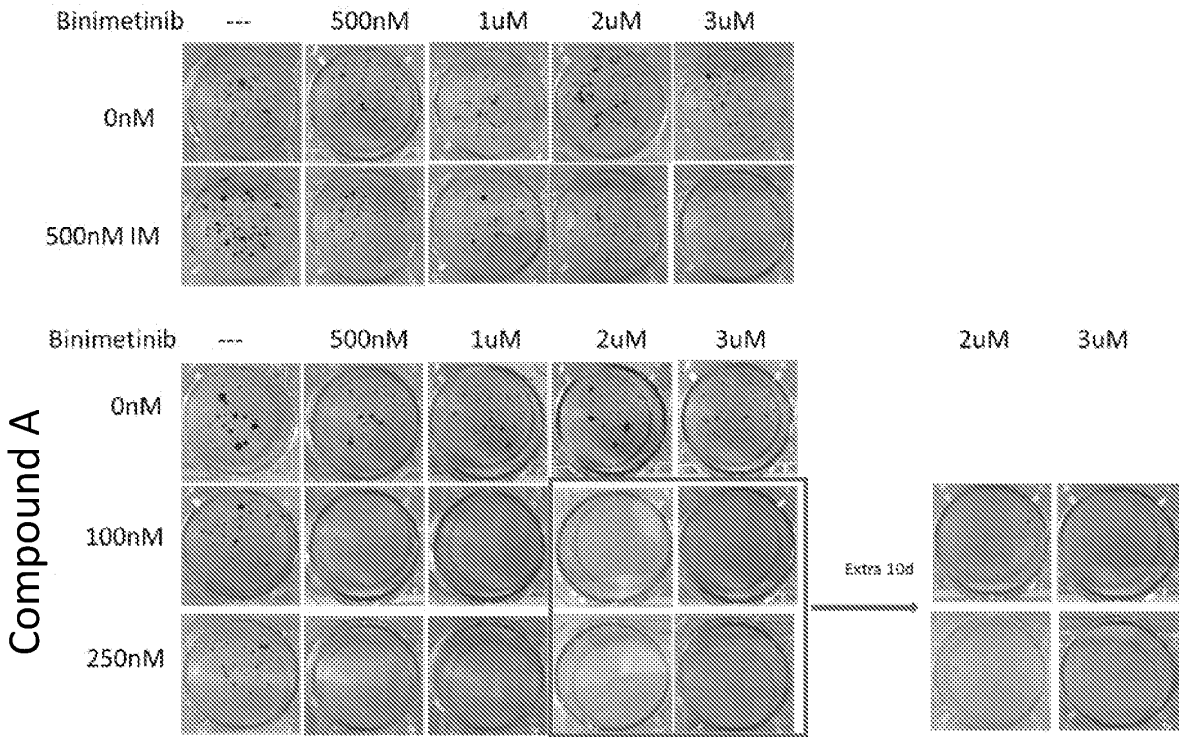


Fig. 10C

GIST-T1/T670I



Imatinib/Compound A and binimetinib in GIST-T1/T670I

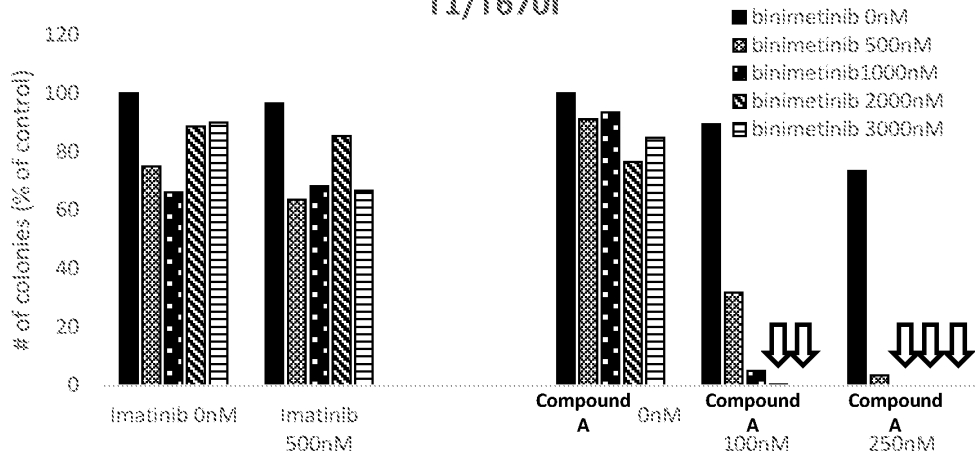
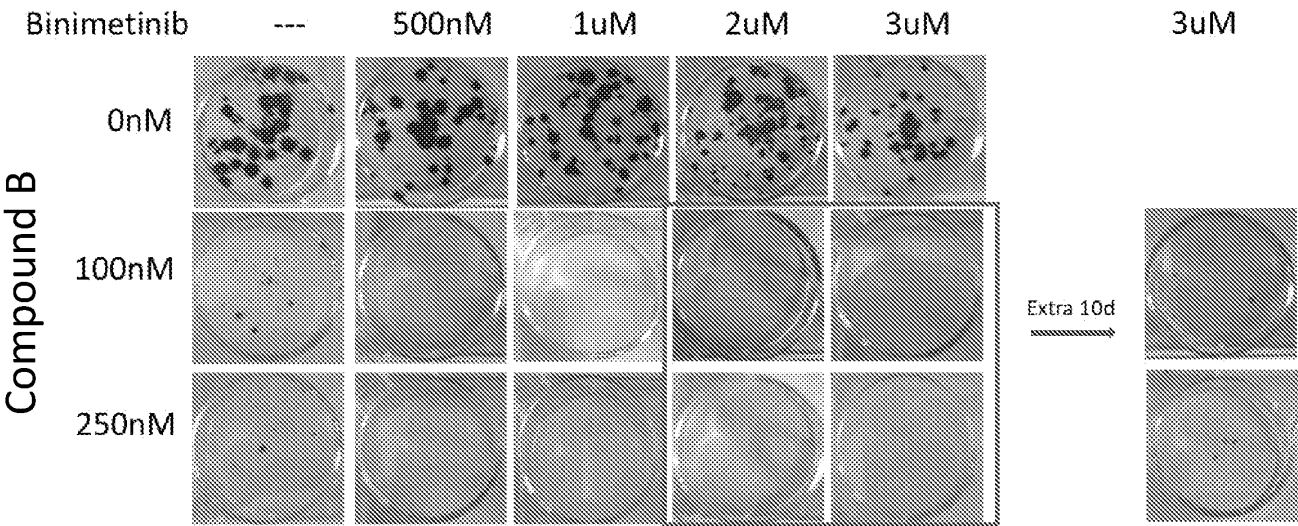


Fig. 11A

GIST-T1



Compound B and binimetinib in GIST-T1

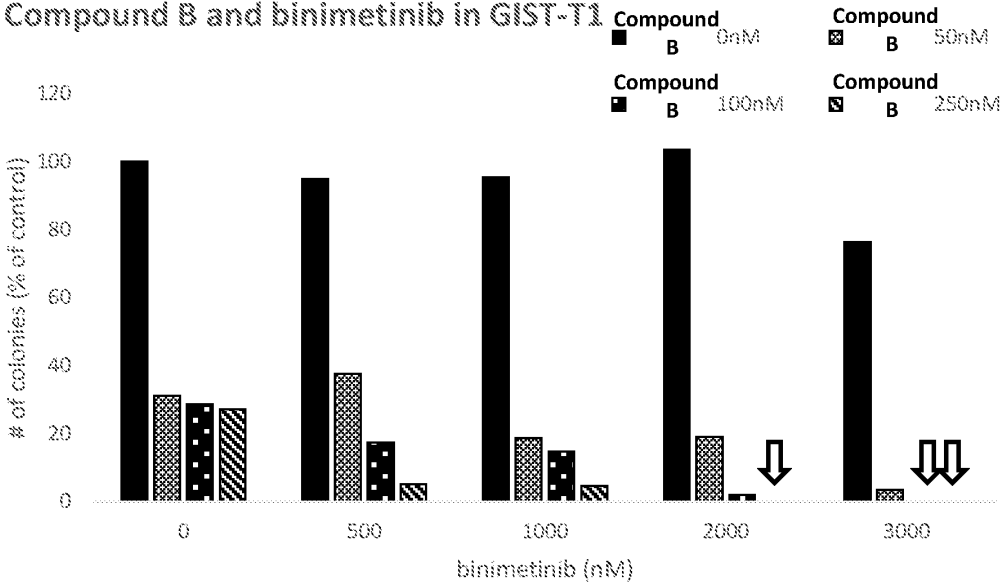


Fig. 11B

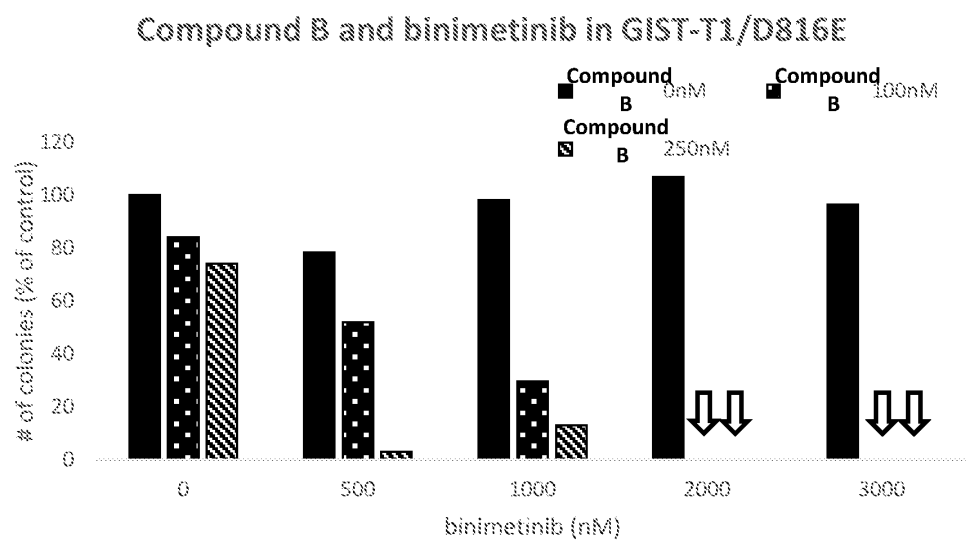
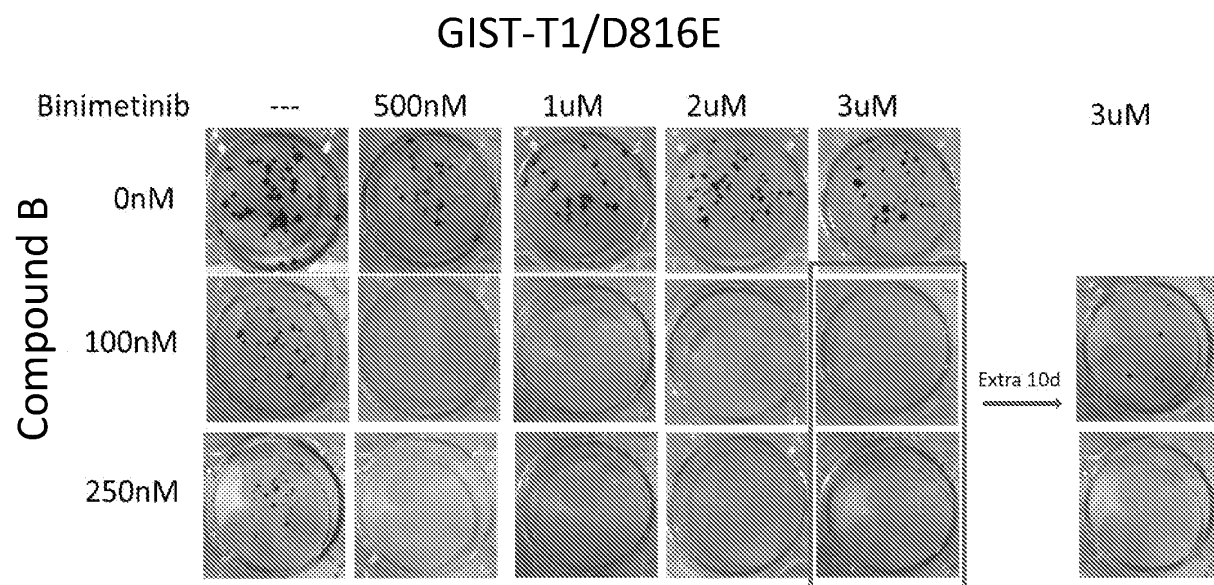
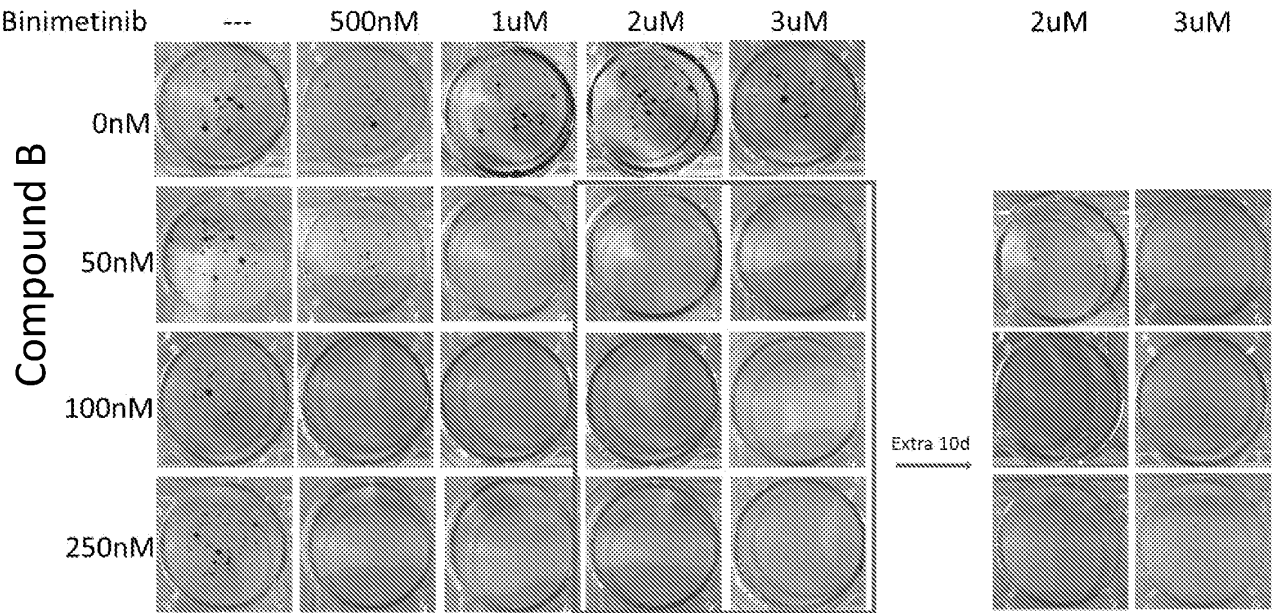


Fig. 11C

GIST-T1/T670I



Compound B and binimetinib in GIST-T1/T670I

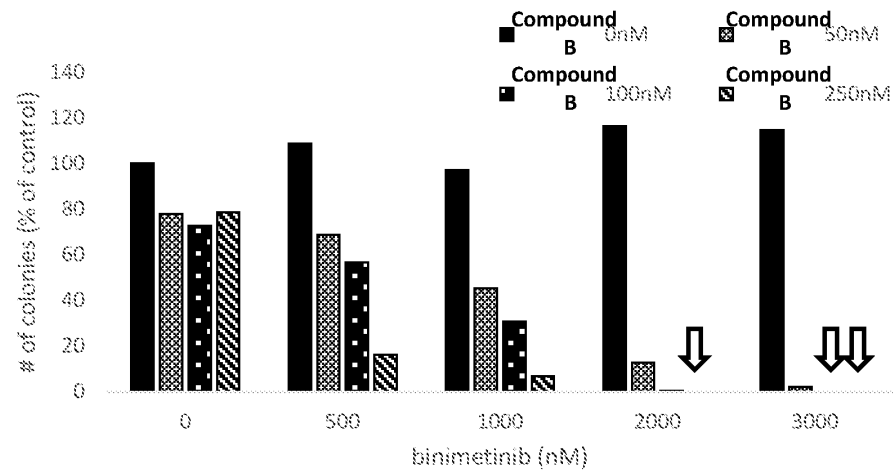
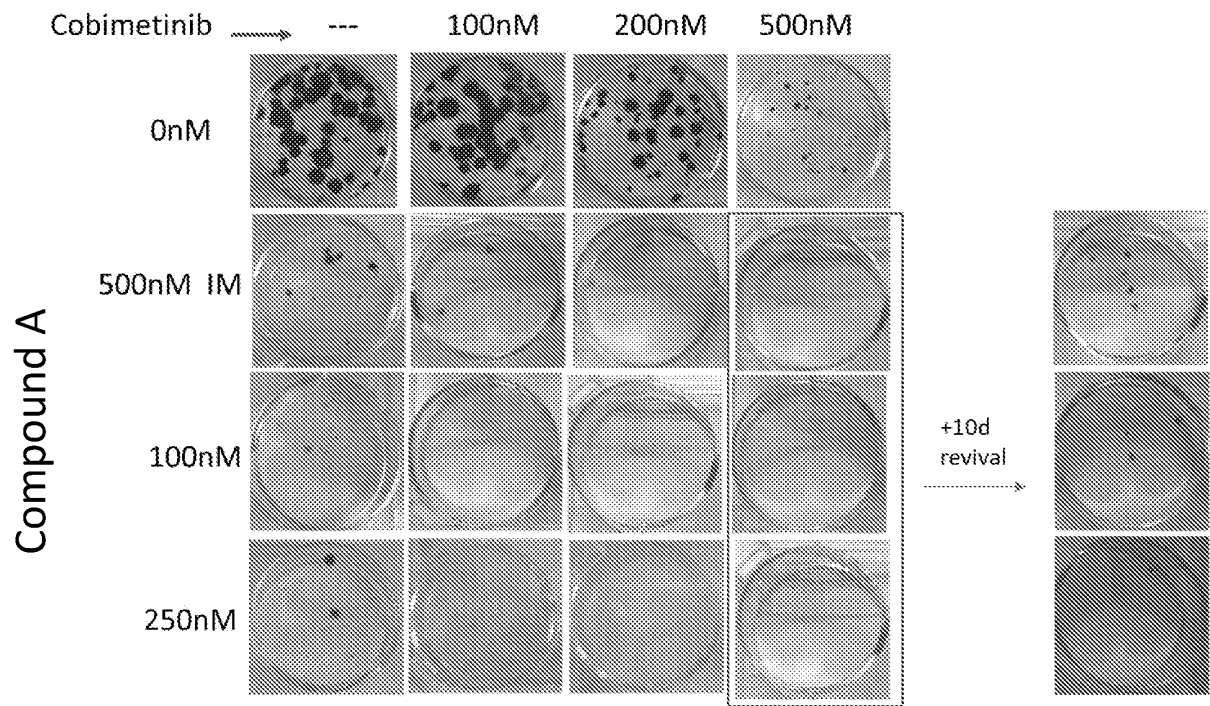


Fig. 12A GIST-T1



Imatinib/Compound A with cobimetinib in GIST-T1

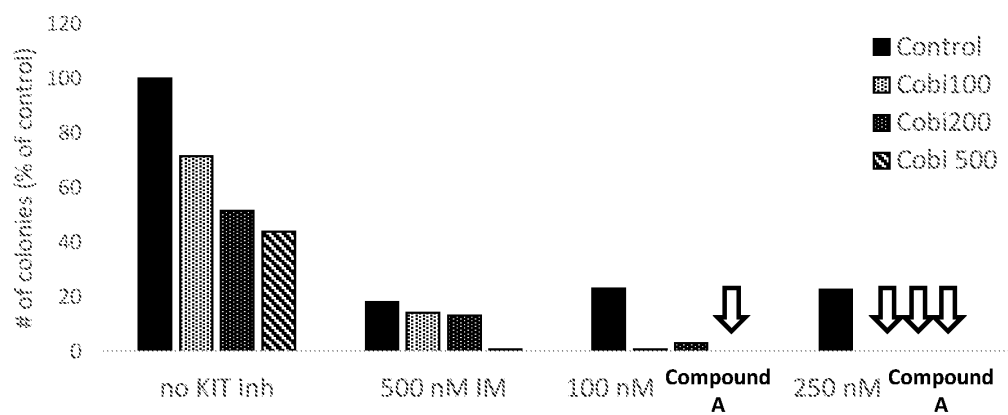
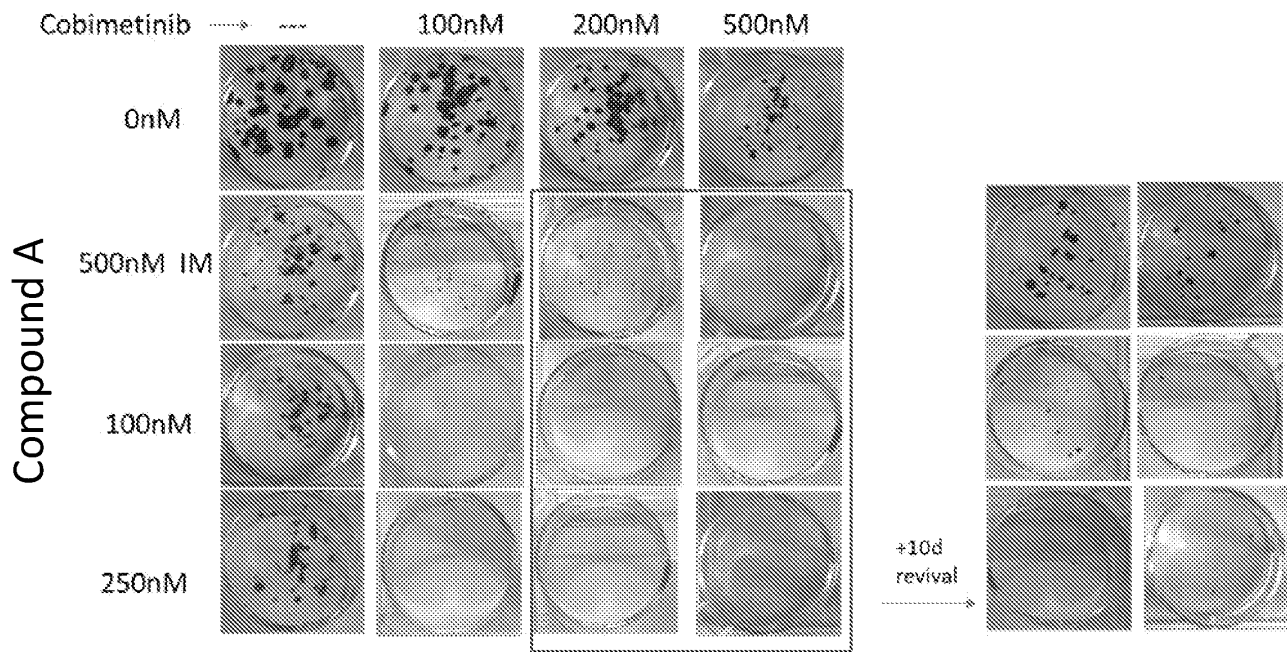


Fig. 12B

GIST-T1/D816E



Imatinib/Compound A with cobimetinib in GIST-T1/D816E

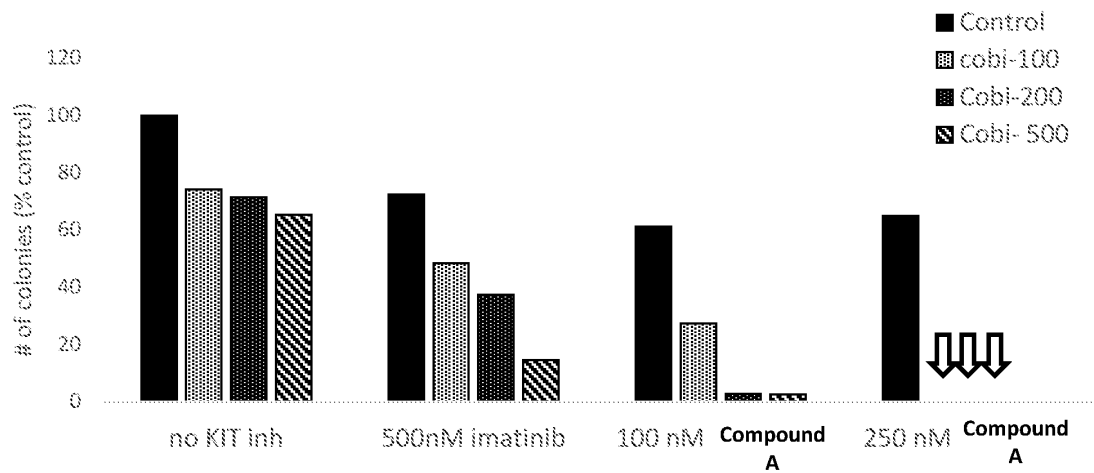


Fig. 12C GIST-T1/T670I

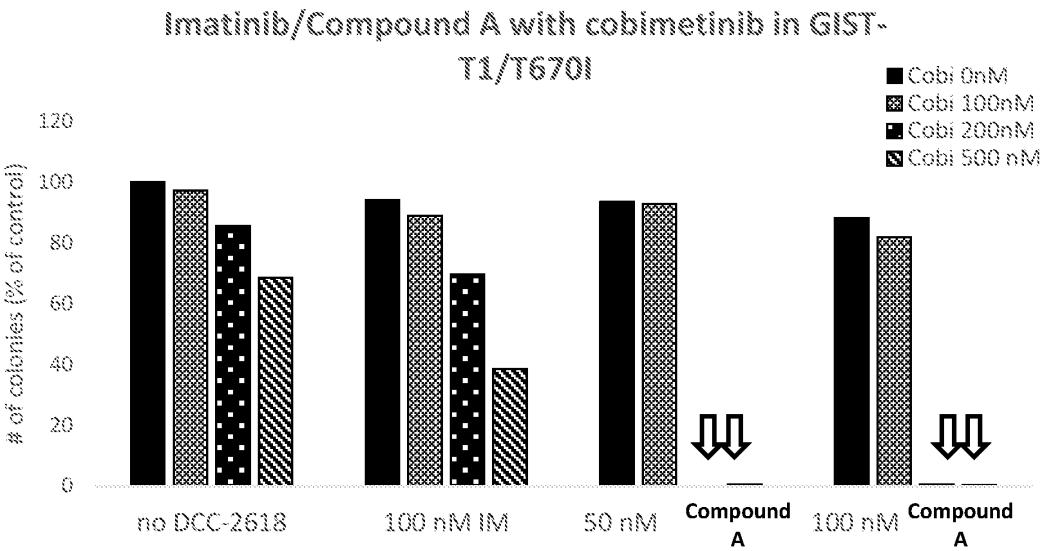
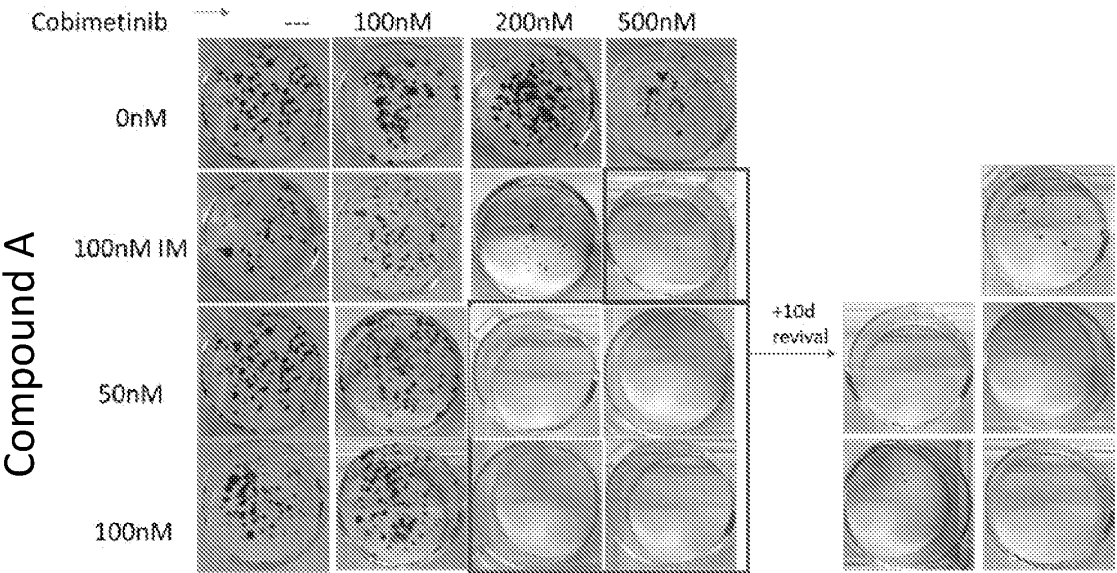


Fig. 13A

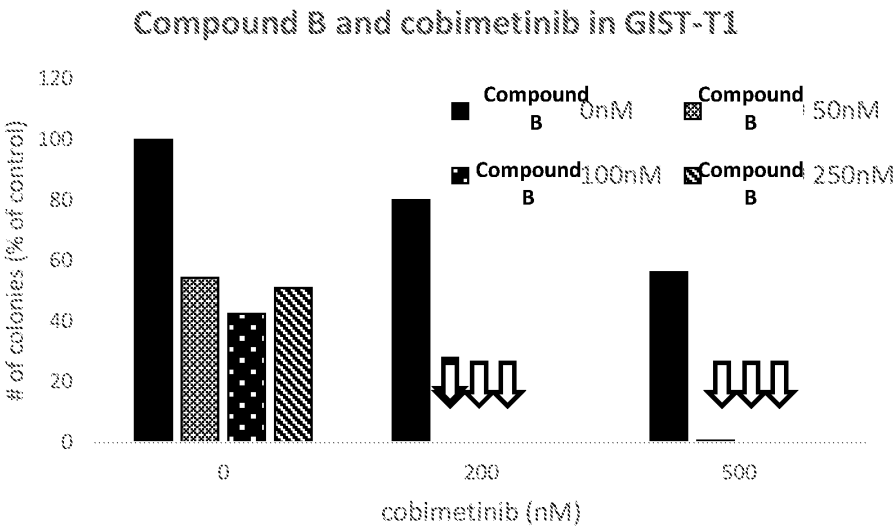
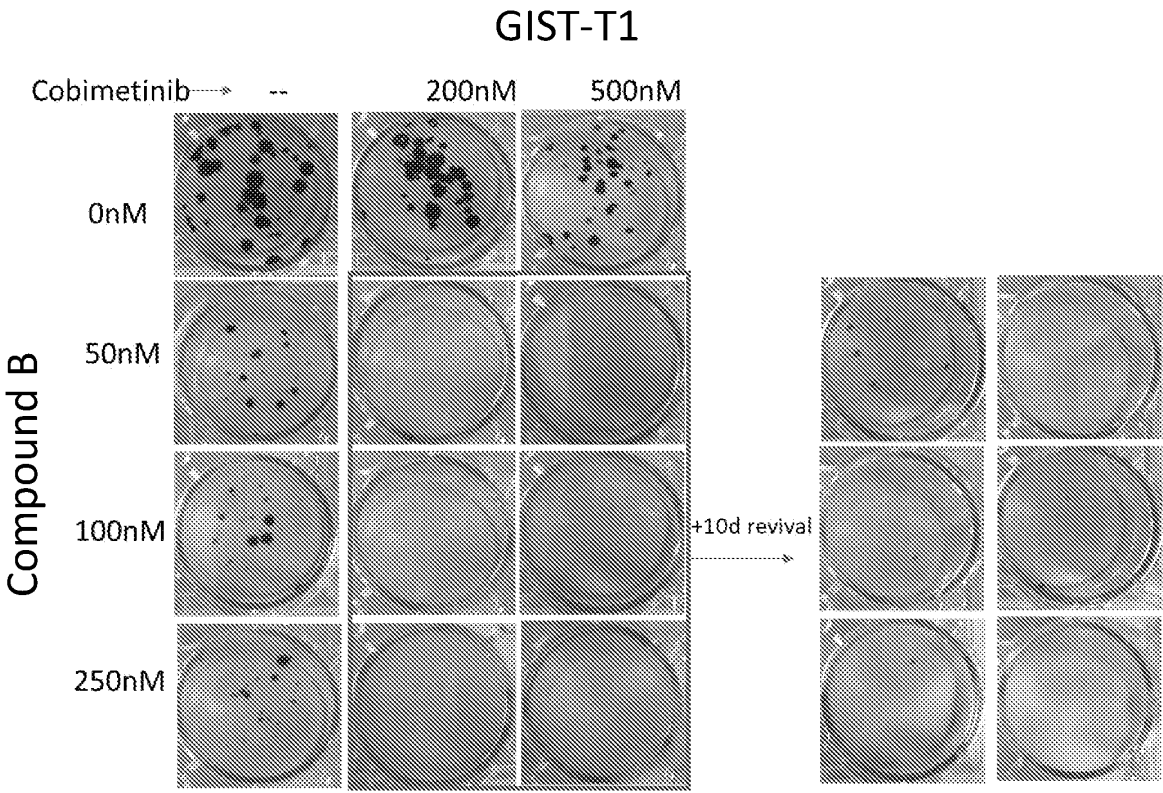
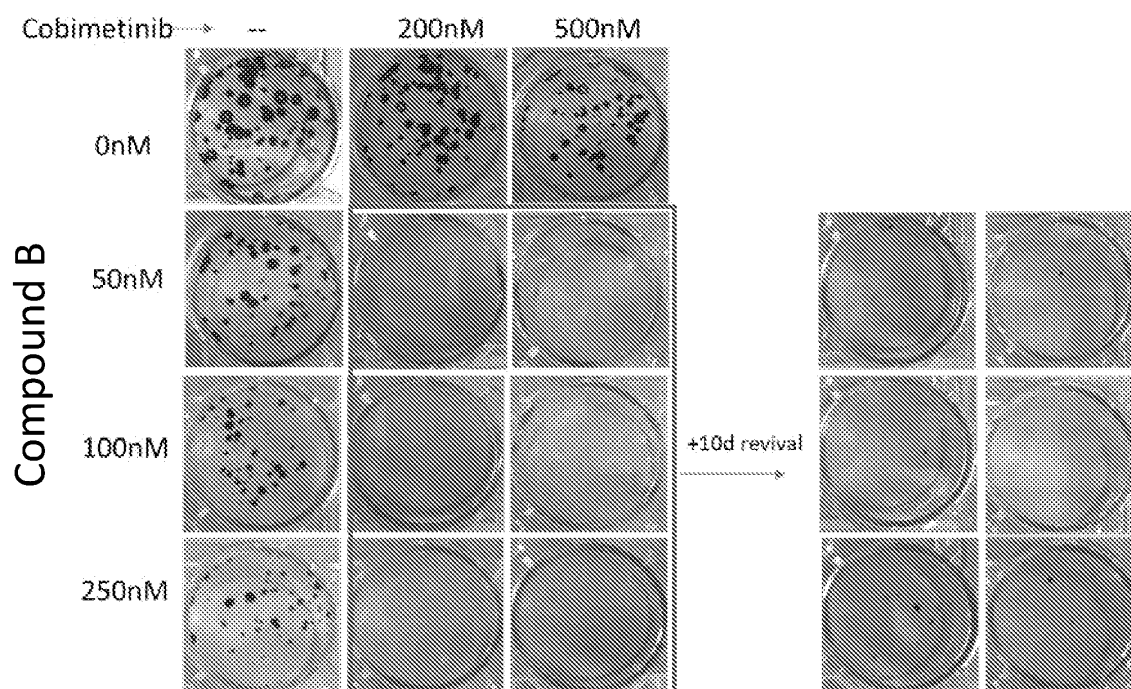


Fig. 13B

GIST-T1/D816E



Compound B with cobimetinib in GIST-T1/D816E

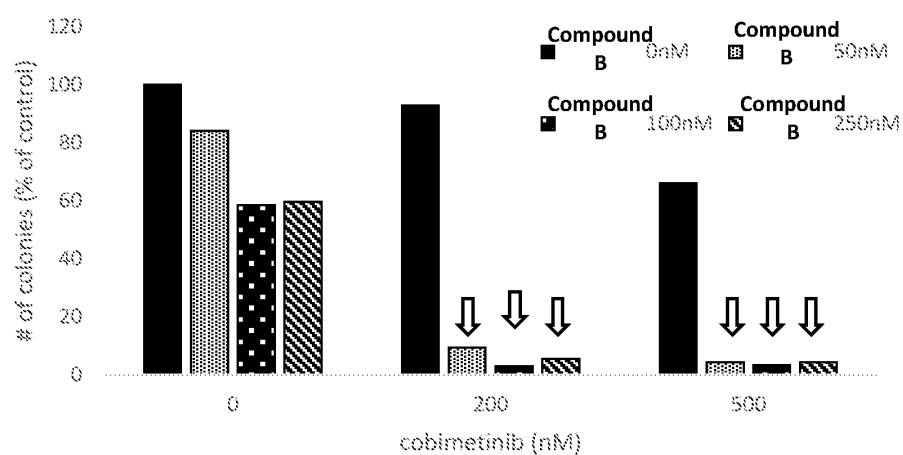
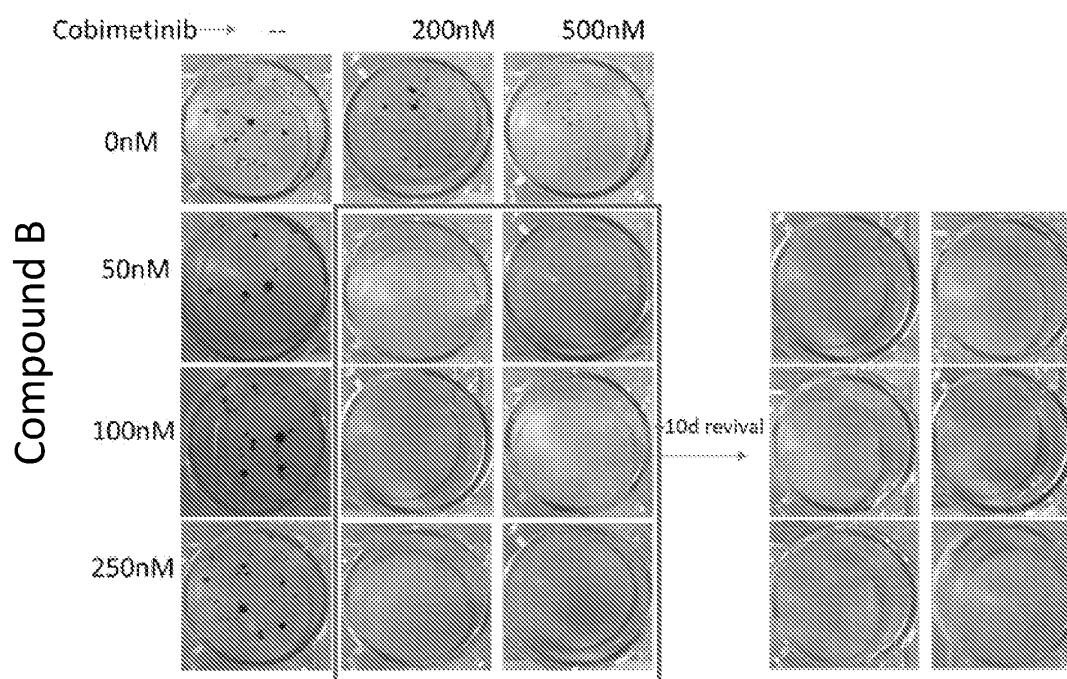


Fig. 13C

GIST-T1/T670I



Compound B with cobimetinib in GIST-T1/T670I

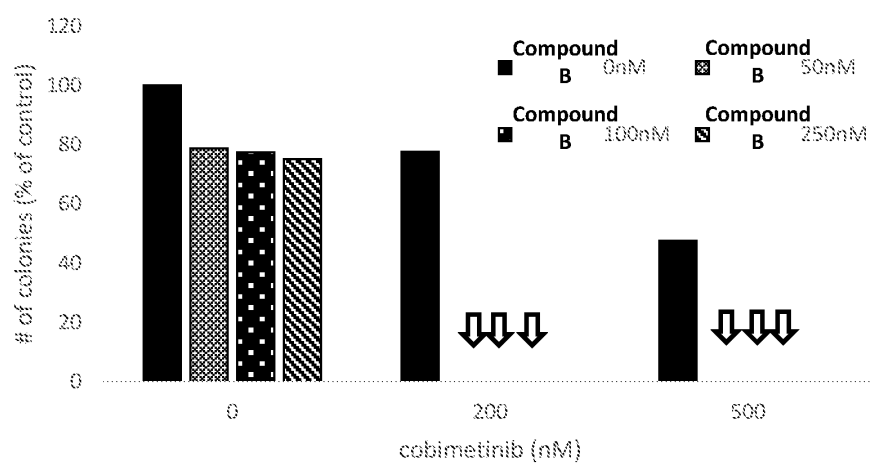
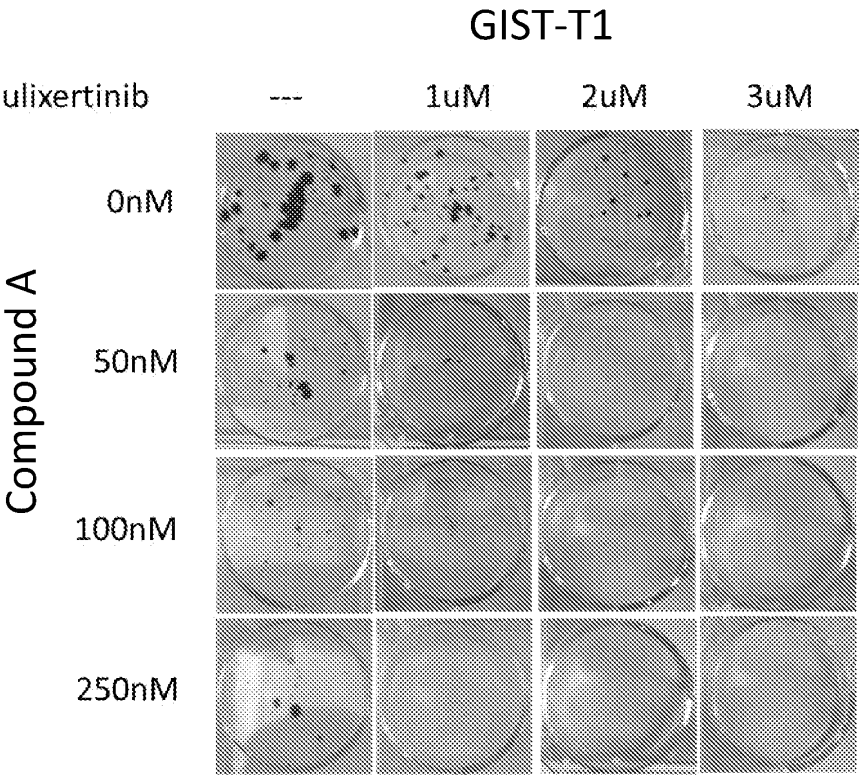


Fig. 14A



Compound A and ulixertinib in GIST-T1

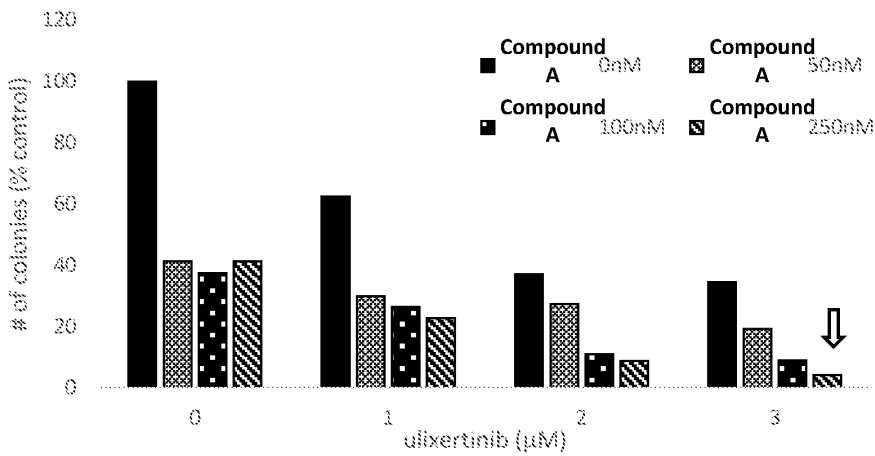


Fig. 14B

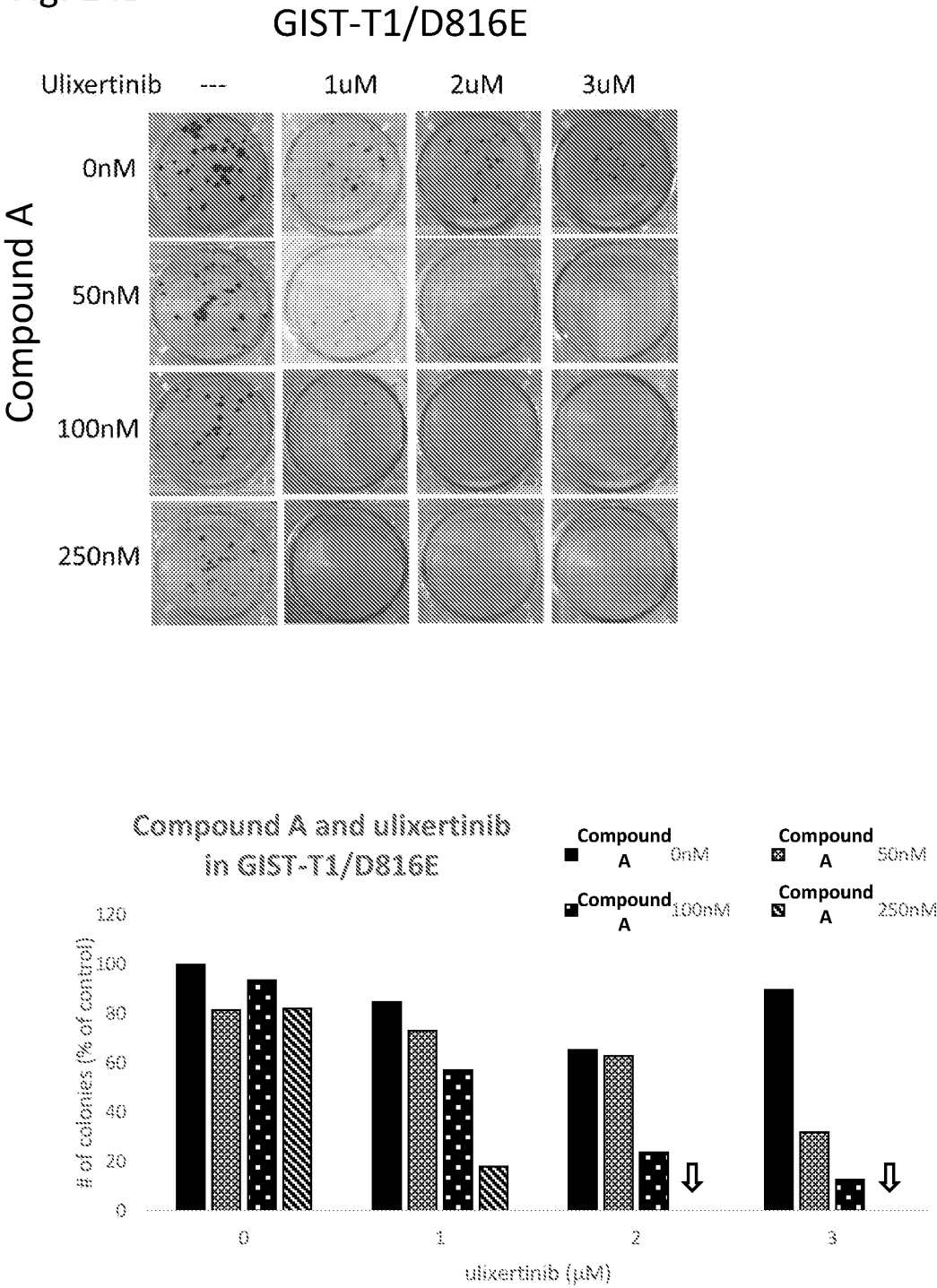
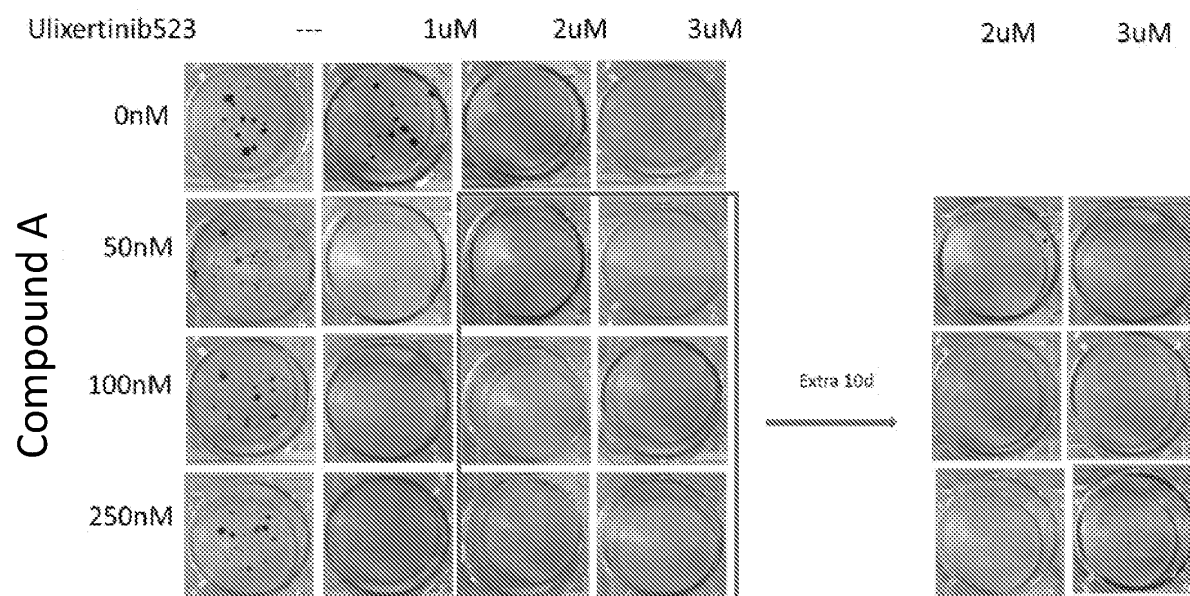


Fig. 14C

GIST-T1/T670I



Compound A and ulixertinib in GIST-T1/T670I

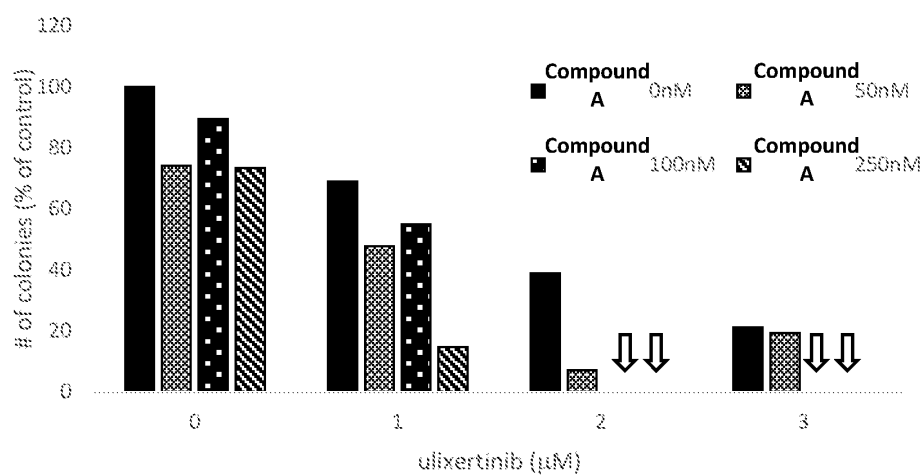


Fig. 15

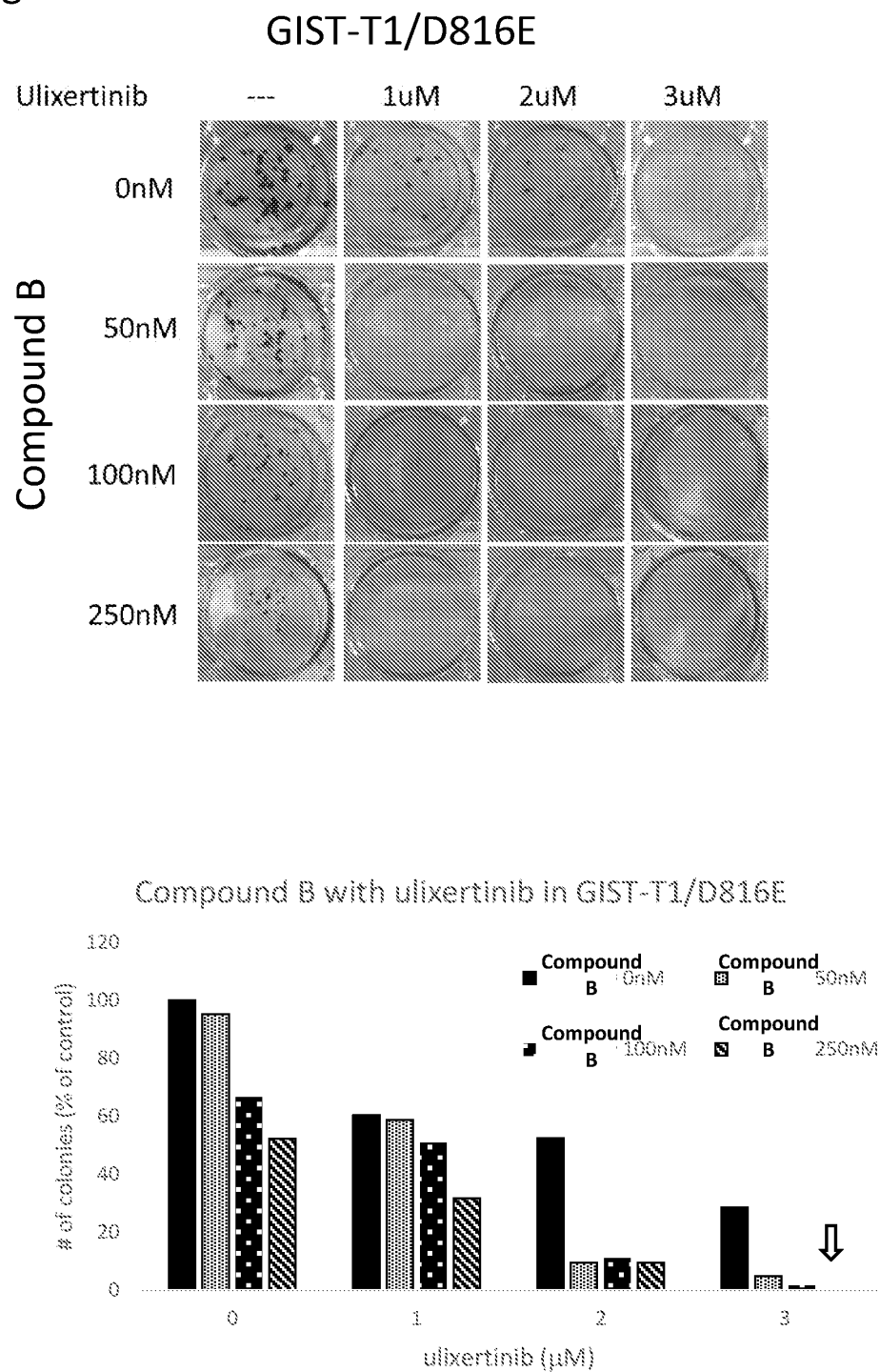


FIG. 16A GIST T1 cells - 48h

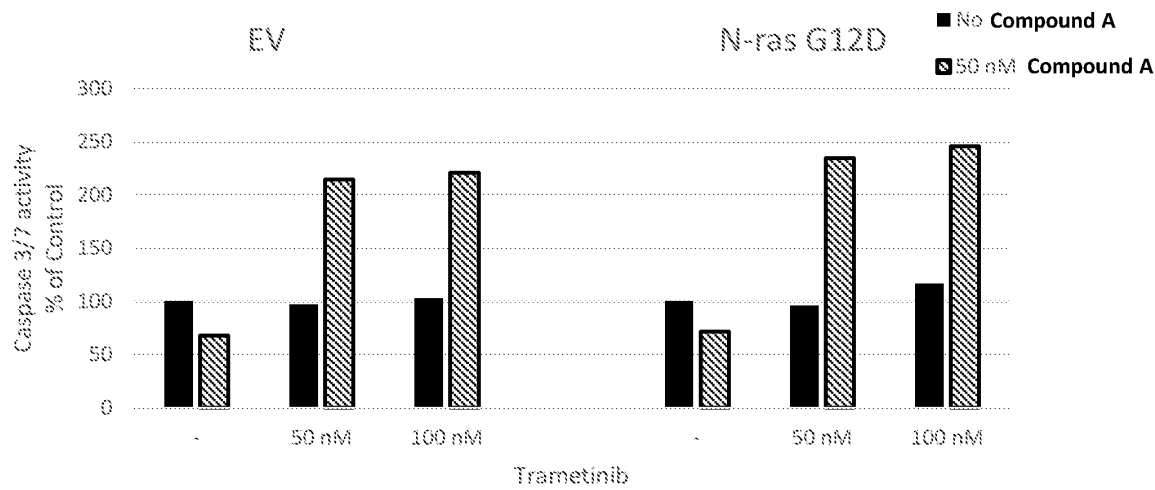


FIG. 16B.1

FIG. 16B.2

2 wk drug treatment, 10 day recovery

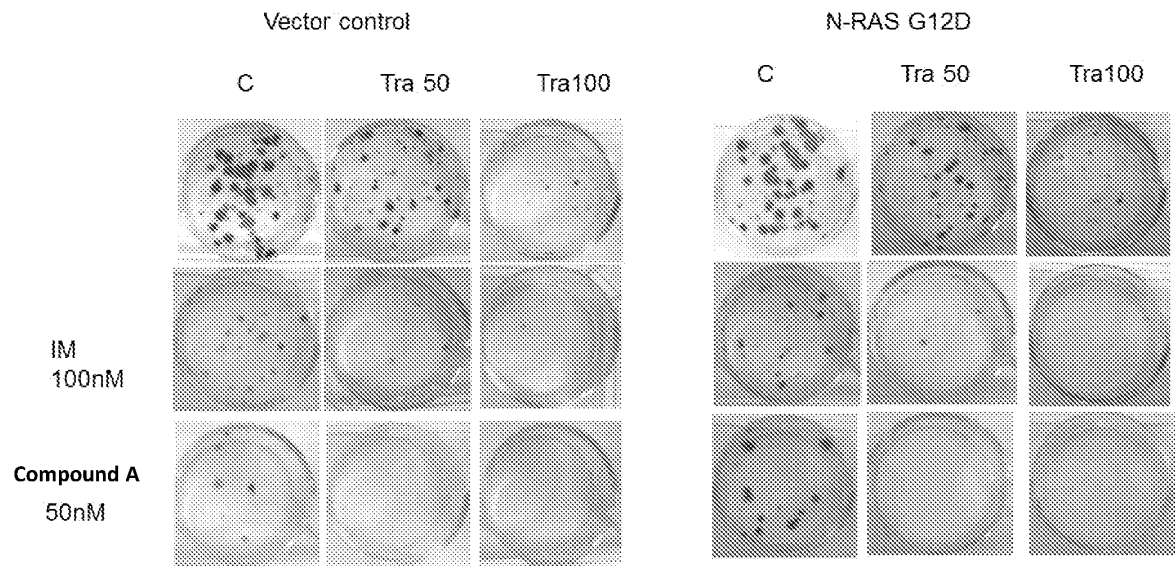


FIG. 16C.1

FIG. 16C.2

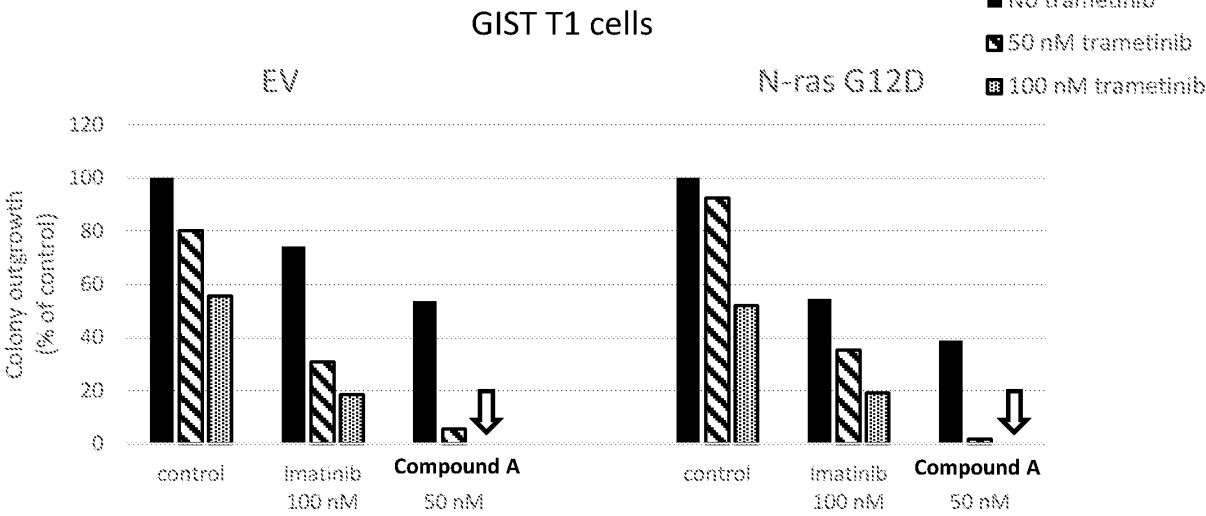


FIG. 16D

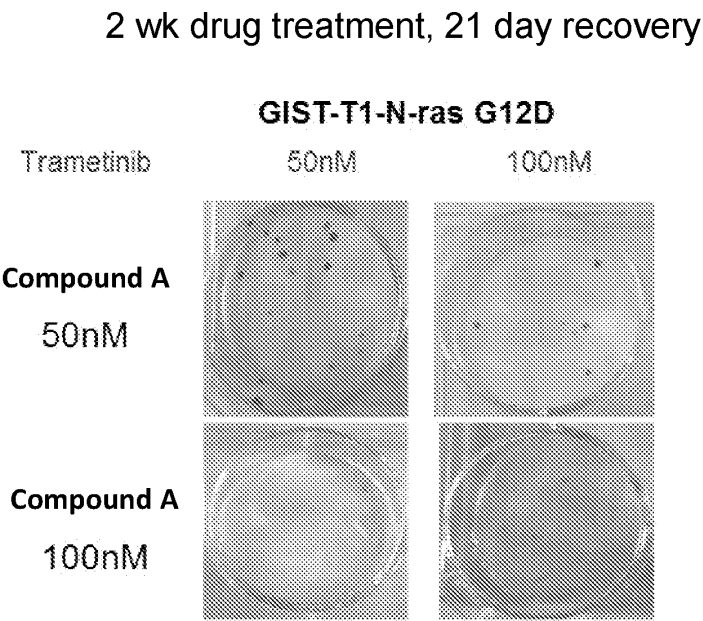


FIG. 17A

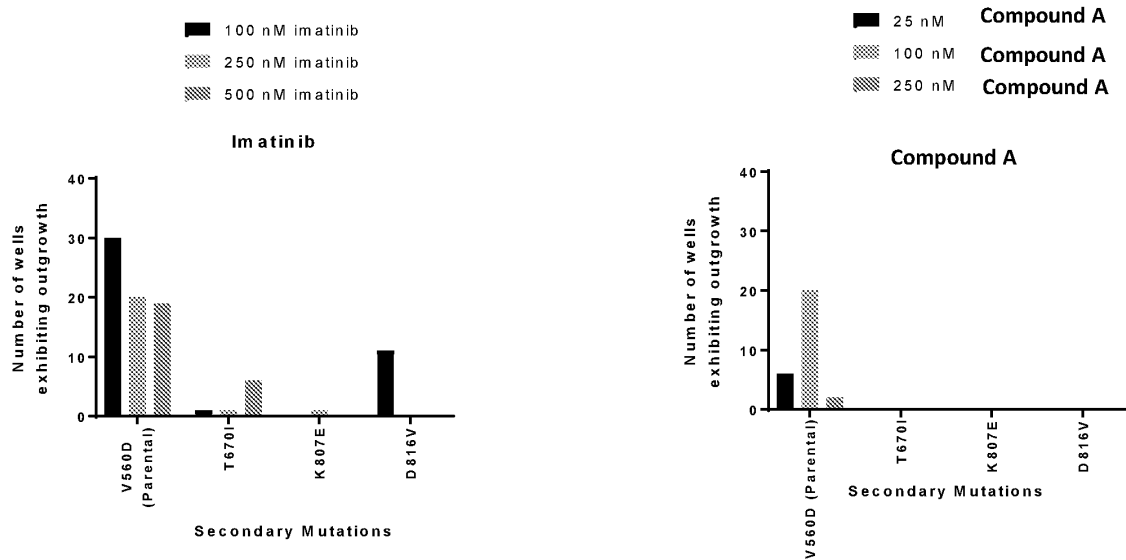


FIG. 17B

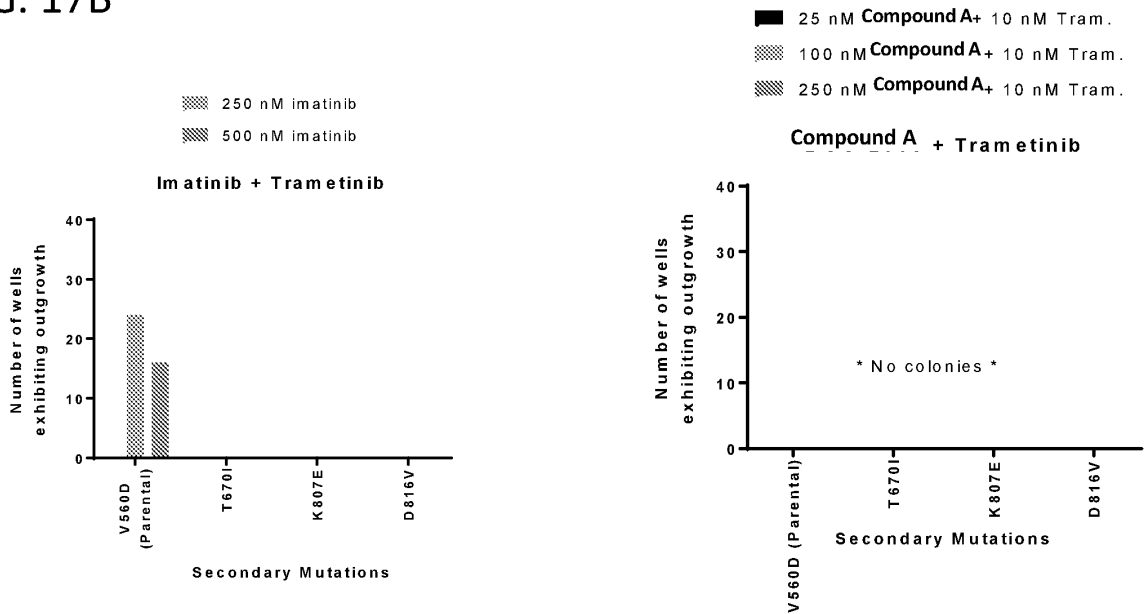


FIG. 18A

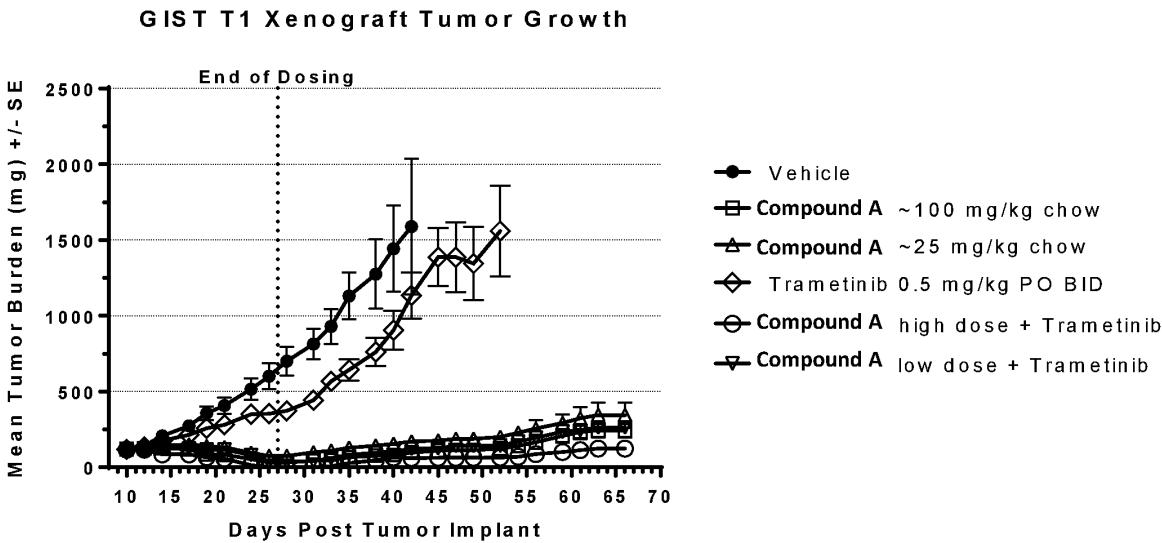


FIG. 18B

