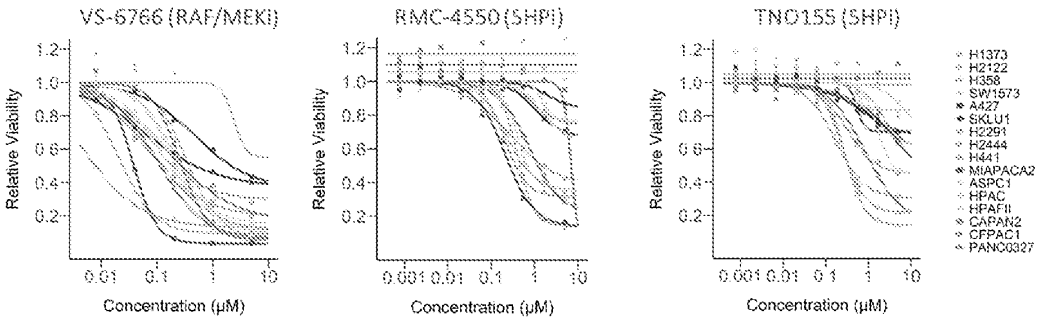


FIG. 1A

Cell Line	Cancer type	KRASmut	IC50 VS-6766 (μM)	IC50 TNO155 (μM)	IC50 RMC-4550 (μM)
H1373	lung	G12C	0.156	0.348	0.558
H2122	lung	G12C	0.767	>5	>5
H358	lung	G12C	0.842	0.334	0.456
SW1573	lung	G12C	>5	>5	>5
A427	lung	G12D	>5	>5	>5
SKLU1	lung	G12D	3.412	>5	>5
H2291	lung	G12V	0.095	1.802	1.499
H2444	lung	G13V	0.188	>5	>5
H441	lung	G13V	0.011	0.342	0.358
MIAPACA2	pancreas	G12C	0.025	>5	0.267
ASPC1	pancreas	G12D	0.209	>5	>5
HPAC	pancreas	G12D	0.169	3.976	0.681
HPAFII	pancreas	G12D	0.239	>5	>5
CAPAN2	pancreas	G12V	0.207	>5	>5
CFPAC1	pancreas	G12V	0.376	>5	>5
PANC0327	pancreas	G12V	0.678	1.238	1.209

FIG. 1B

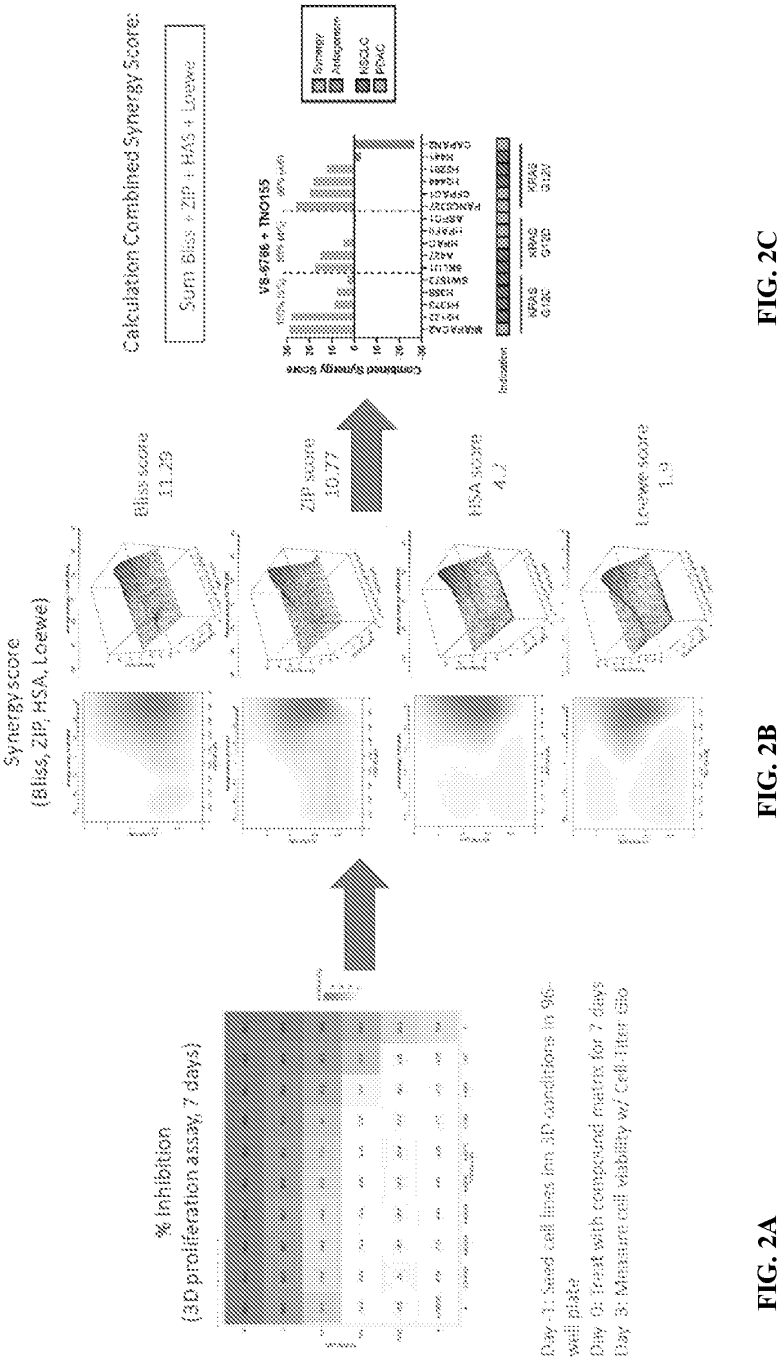


FIG. 2A

FIG. 2B

FIG. 2C

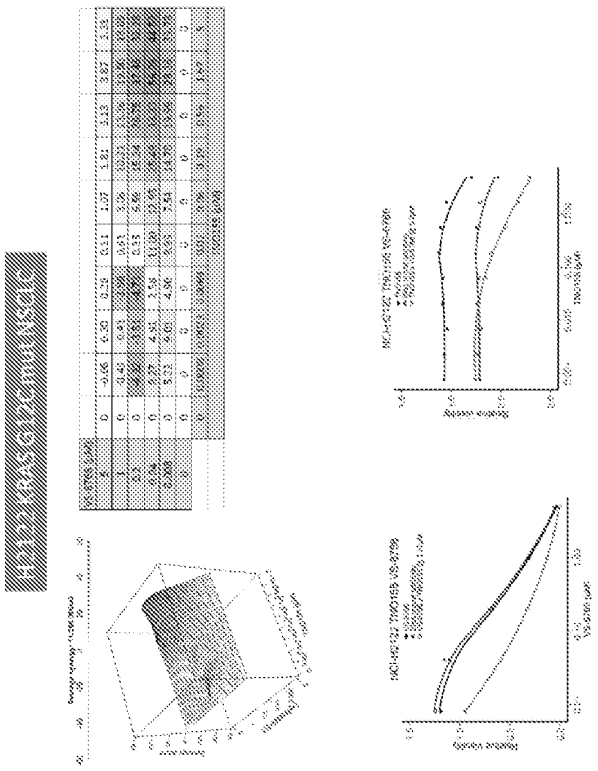


FIG. 3B

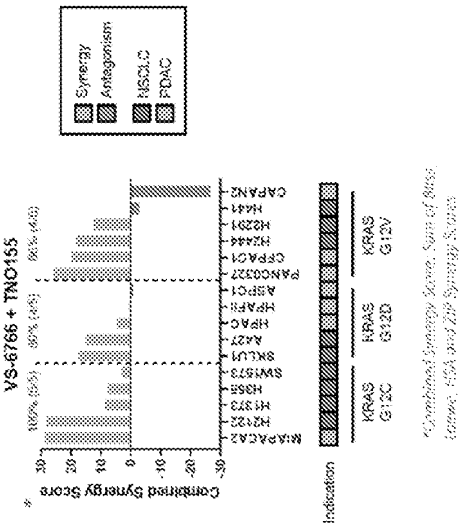

VS-6766 + TNO155
Combined Synergy Score
Synergy
Antagonism
NSCLC
PDAC
KRAS G12C
KRAS G12D
KRAS G12V
Indication
*Combined Synergy Score: Sum of Bliss Loewe, HSA and ZIP Synergy Scores

FIG. 3A

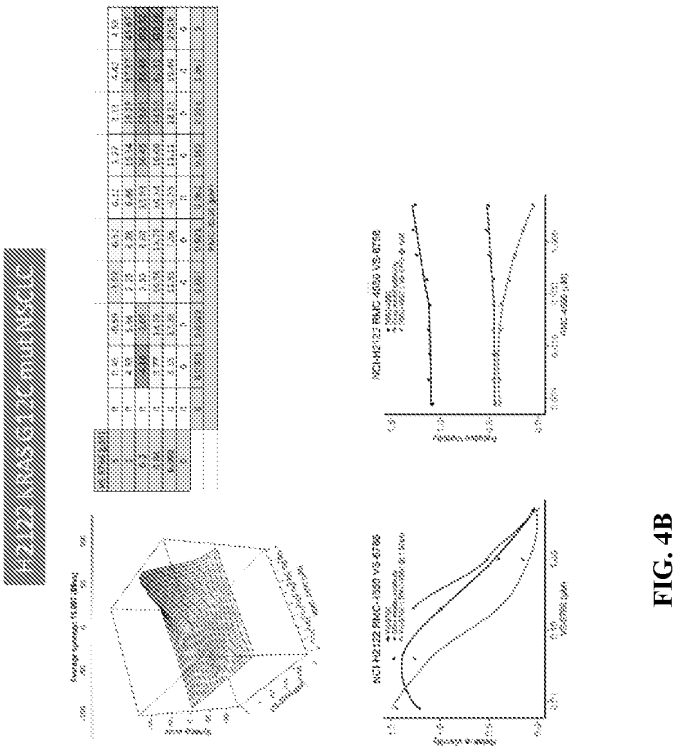


FIG. 4B

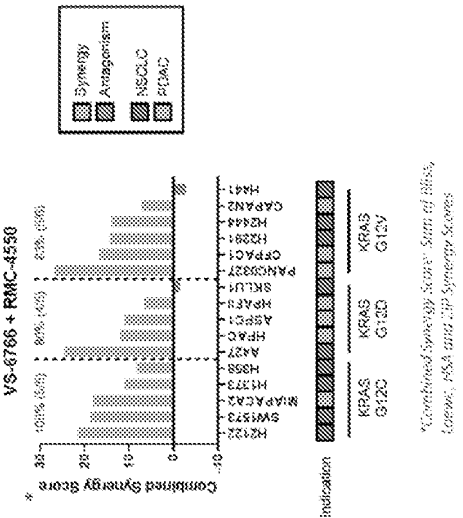


FIG. 4A

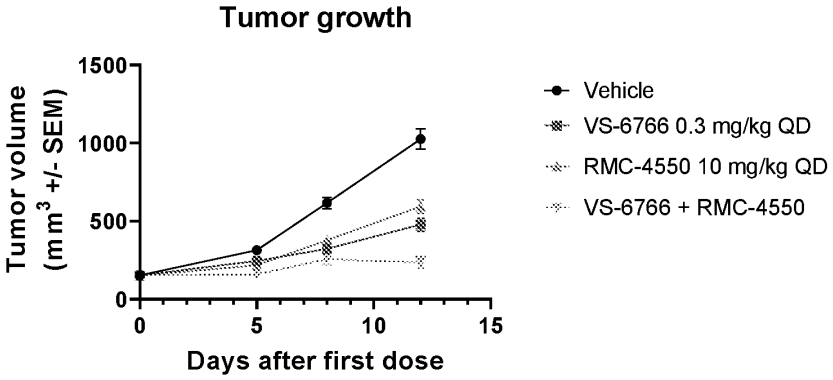

Tumor growth
Tumor volume (mm3 +/- SEM)
1500
1000
500
0
0
5
10
15
Days after first dose
Vehicle
VS-6766 0.3 mg/kg QD
RMC-4550 10 mg/kg QD
VS-6766 + RMC-4550

FIG. 5A

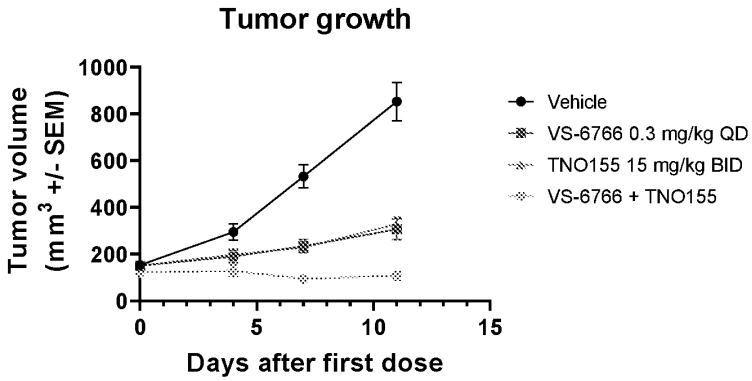

Tumor growth
Tumor volume (mm3 +/- SEM)
1000
800
600
400
200
0
0
5
10
15
Days after first dose
Vehicle
VS-6766 0.3 mg/kg QD
TNO155 15 mg/kg BID
VS-6766 + TNO155

FIG. 5B

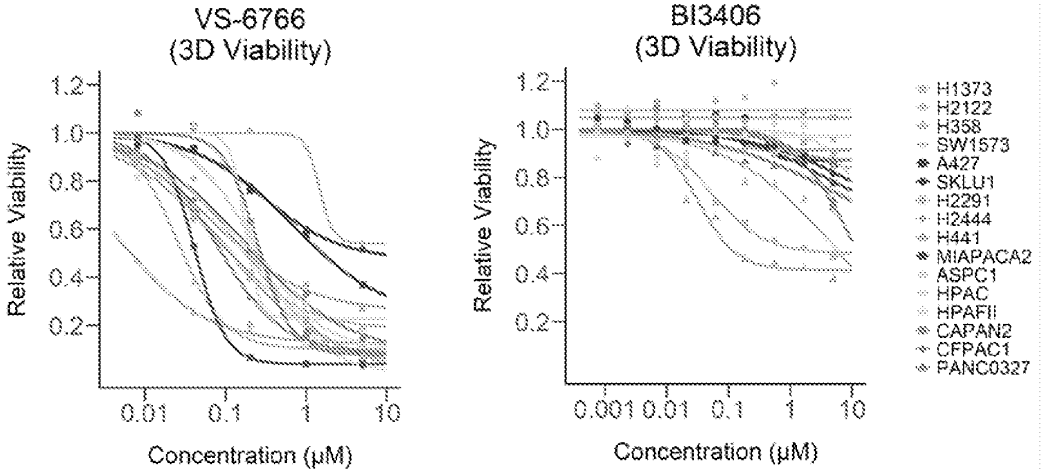


FIG. 6A

Cell Line	Cancer type	KRASmut	IC50 VS-6766 (μM)	IC50 BI-3406 (μM)
H1373	lung	G12C	0.156	1.393
H2122	lung	G12C	0.767	>5
H358	lung	G12C	0.042	>5
SW1573	lung	G12C	>5	>5
A427	lung	G12D	>5	>5
SKLU1	lung	G12D	3.412	>5
H2291	lung	G12V	0.095	>5
H2444	lung	G12V	0.188	>5
H441	lung	G12V	0.011	0.113
MIAPACA2	pancreas	G12C	0.025	>5
ASPC1	pancreas	G12D	0.209	>5
HPAC	pancreas	G12D	0.169	>5
HPAFII	pancreas	G12D	0.239	>5
CAPAN2	pancreas	G12V	0.207	>5
CFPAC1	pancreas	G12V	0.376	>5
PANC0327	pancreas	G12V	0.078	>5

FIG. 6B

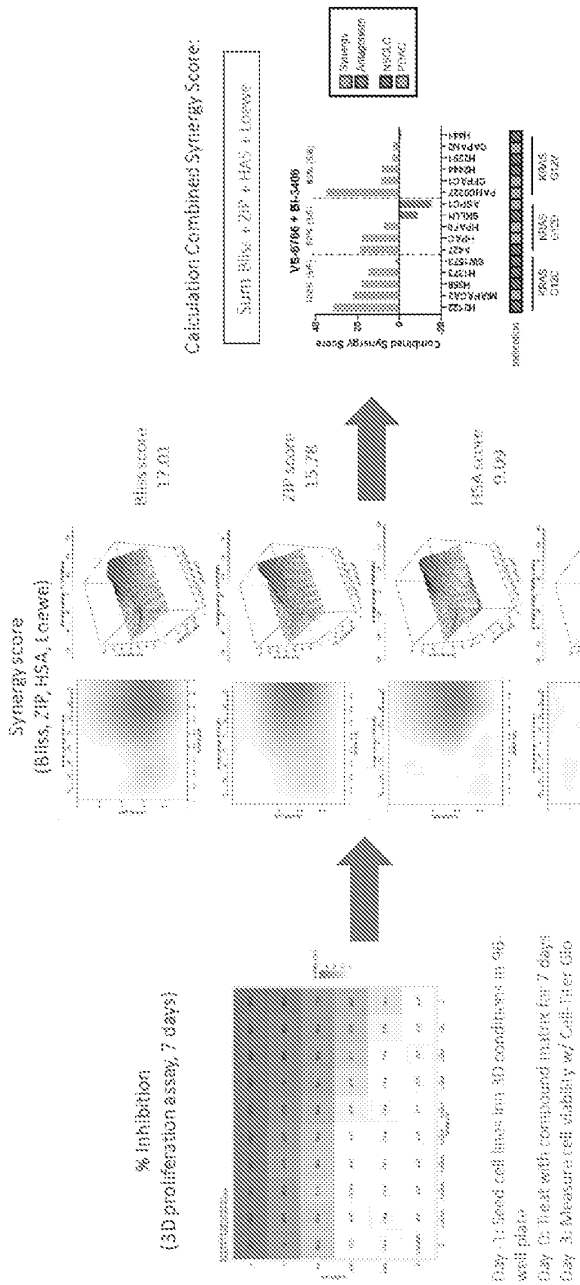


FIG. 7A

FIG. 7B

FIG. 7C

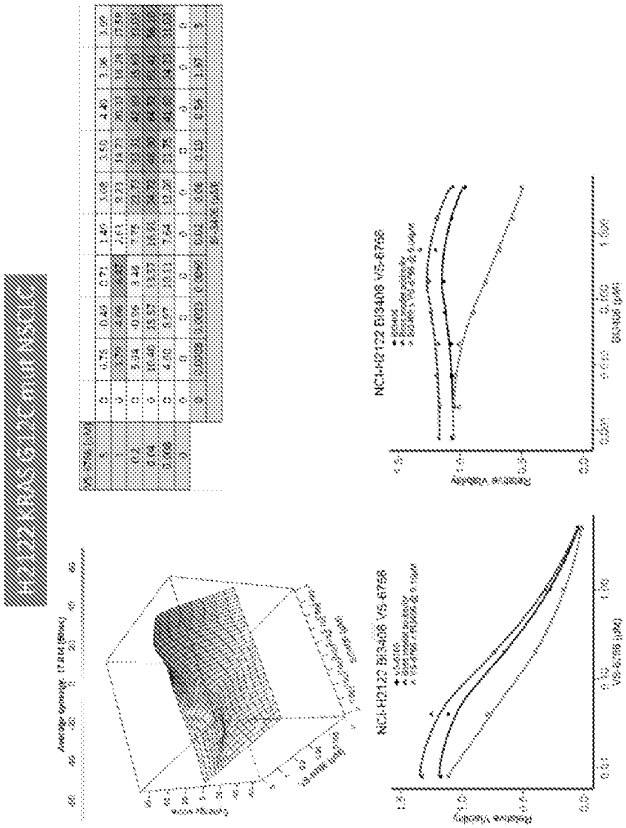


FIG. 8B

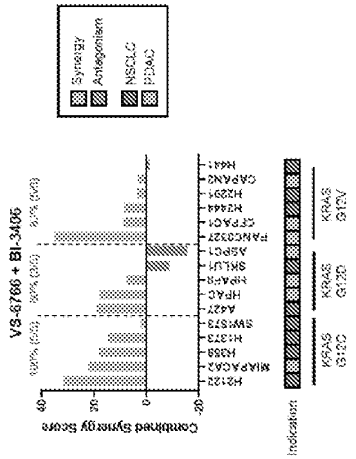


FIG. 8A

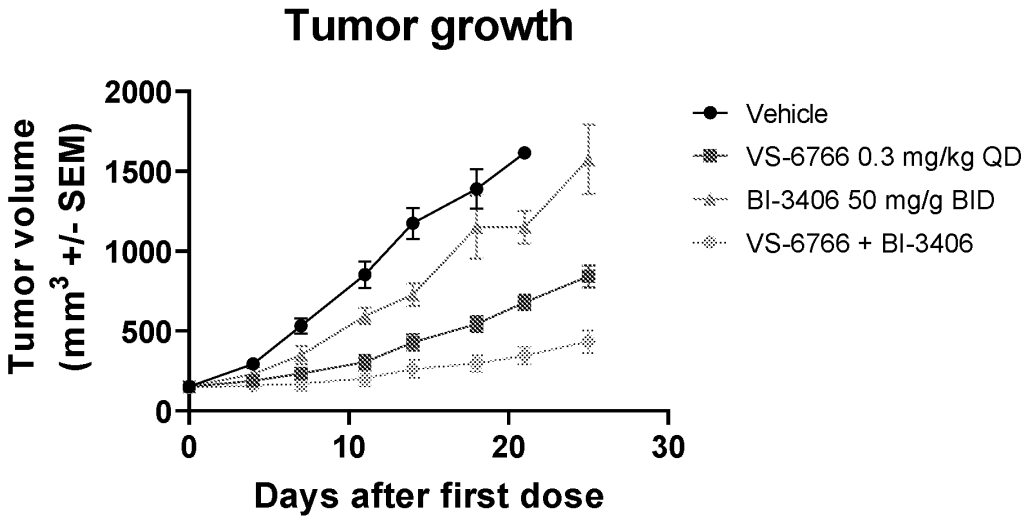

Tumor growth
Tumor volume (mm3 +/- SEM)
2000
1500
1000
500
0
0
10
20
30
Days after first dose
Vehicle
VS-6766 0.3 mg/kg QD
BI-3406 50 mg/g BID
VS-6766 + BI-3406

FIG. 9

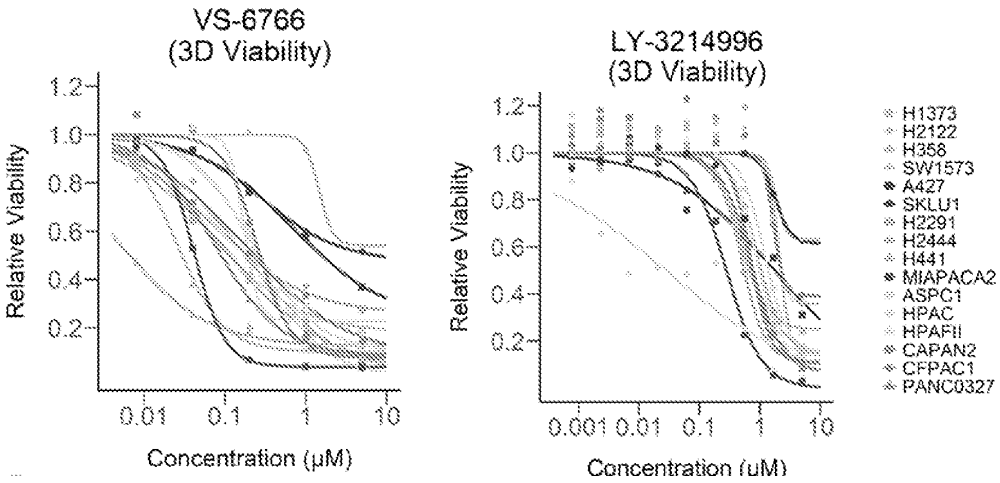


FIG. 10A

Cell Line	Cancer type	KRASmut	IC50 VS-6766 (μM)	IC50 LY-3214996 (μM)
H1373	lung	G12C	0.156	2.278
H2122	lung	G12C	0.767	2.223
H358	lung	G12C	0.042	1.056
SW1573	lung	G12C	>5	>5
A427	lung	G12D	>5	1.751
SKLU1	lung	G12D	3.412	>5
H2291	lung	G12V	0.095	0.691
H2444	lung	G12V	0.188	0.547
H441	lung	G12V	0.011	0.668
MIAPACA2	pancreas	G12C	0.025	0.278
ASPC1	pancreas	G12D	0.209	1.372
HPAC	pancreas	G12D	0.169	0.027
HPAFII	pancreas	G12D	0.239	0.970
CAPAN2	pancreas	G12V	0.207	0.766
CFPAC1	pancreas	G12V	0.376	2.269
PANC0327	pancreas	G12V	0.078	0.772

FIG. 10B

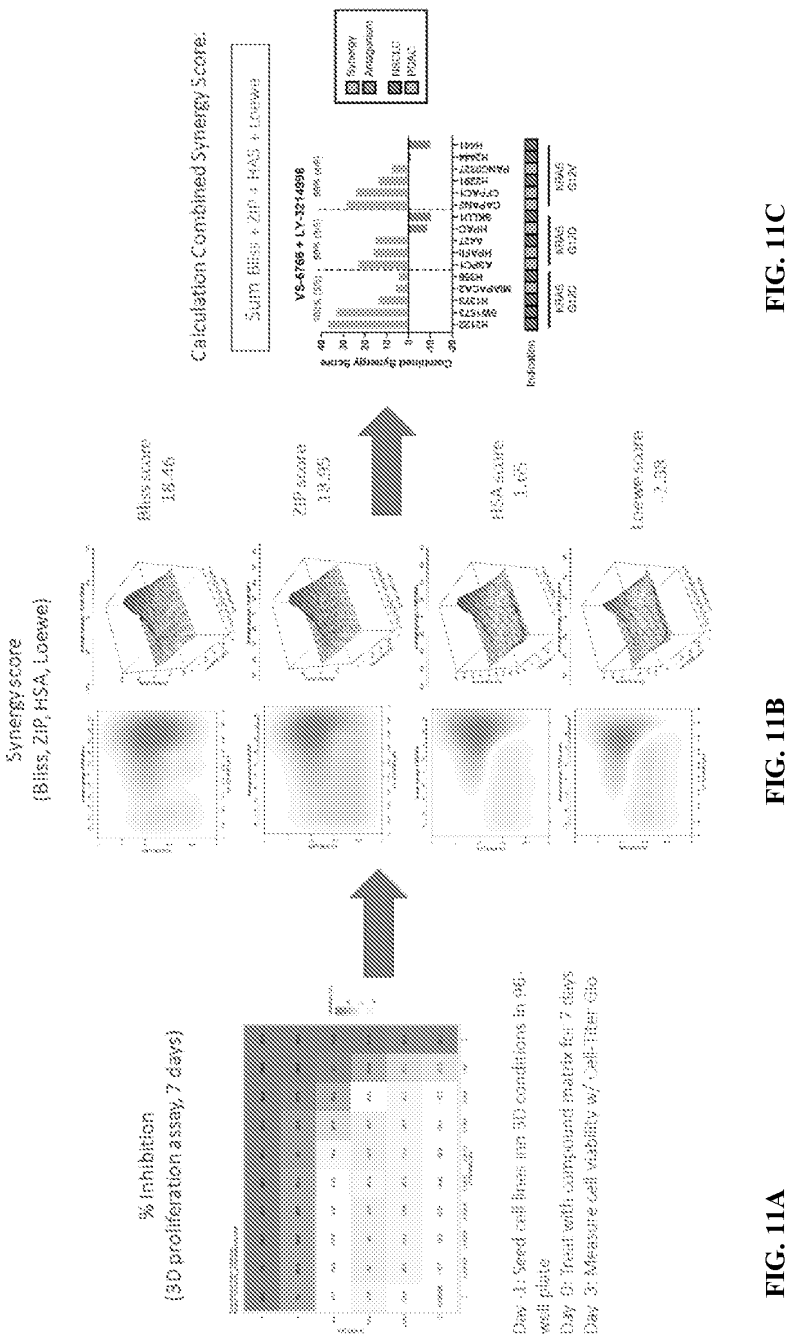


FIG. 11A

FIG. 11B

FIG. 11C

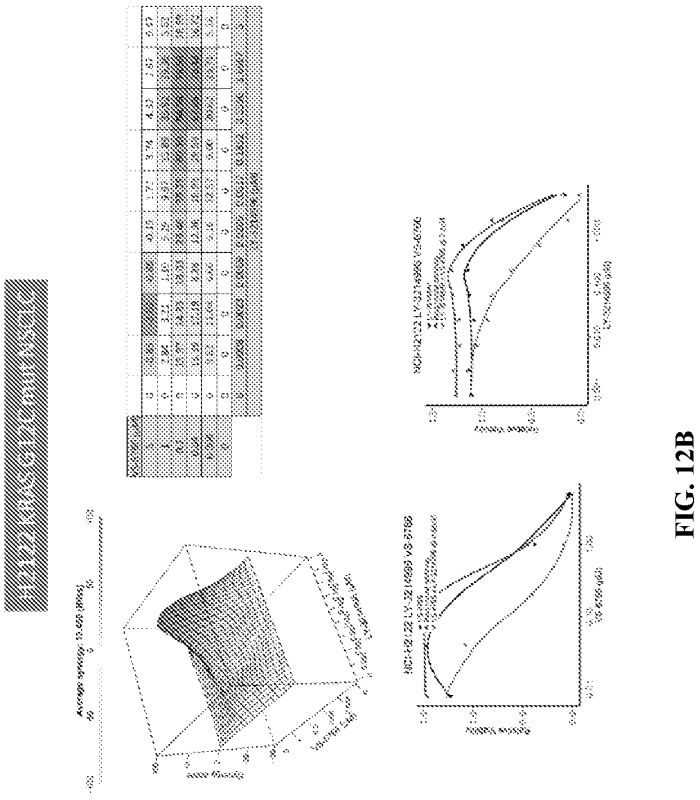


FIG. 12B

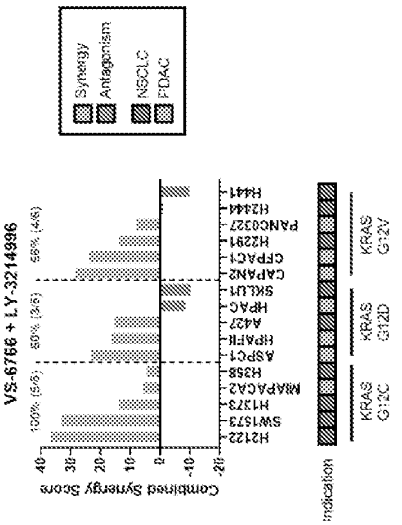


FIG. 12A

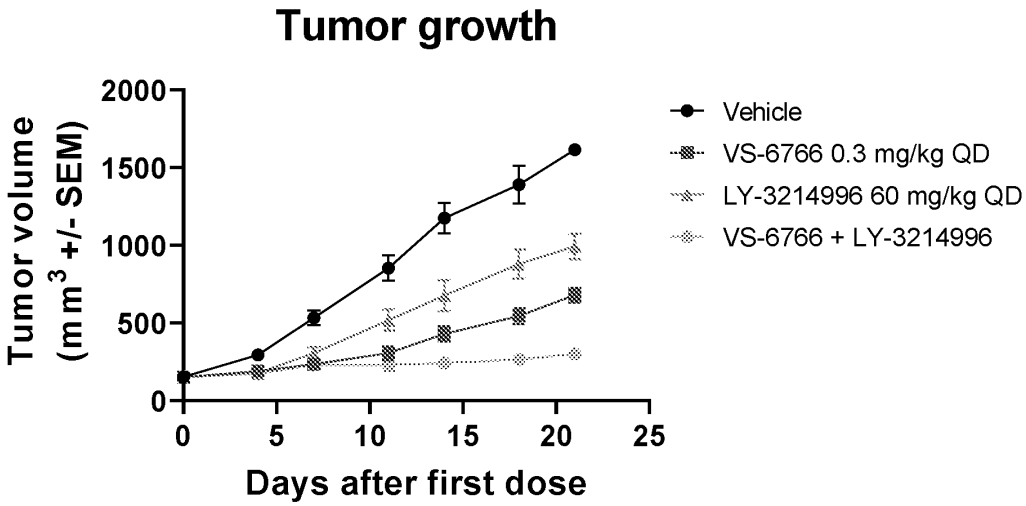

Tumor growth
Tumor volume (mm3 +/- SEM)
2000
1500
1000
500
0
0
5
10
15
20
25
Days after first dose
Vehicle
VS-6766 0.3 mg/kg QD
LY-3214996 60 mg/kg QD
VS-6766 + LY-3214996

FIG. 13

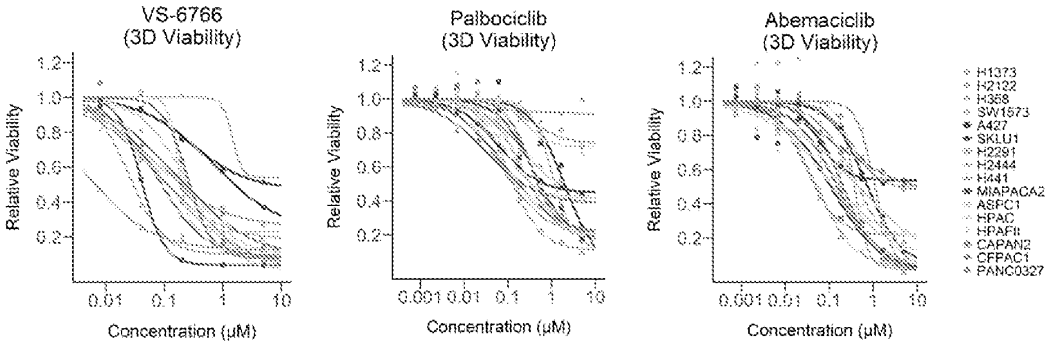


FIG. 14A

Cell Line	Cancer type	KRASmut	IC50 VS-6766 (μM)	IC50 Palbociclib (μM)	IC50 Abemaciclib (μM)
H1373	lung	G12C	0.156	1.420	0.456
H2122	lung	G12C	0.767	1.204	0.375
H358	lung	G12C	0.042	0.134	0.052
SW1573	lung	G12C	>5	0.313	0.119
A427	lung	G12D	>5	1.954	0.751
SKLU1	lung	G12D	3.412	0.704	>5
H2291	lung	G12V	0.095	>5	4.110
H2444	lung	G12V	0.188	>5	1.104
H441	lung	G12V	0.011	0.127	0.048
MIAPACA2	pancreas	G12C	0.025	0.540	0.108
ASPC1	pancreas	G12D	0.209	>5	0.459
HPAC	pancreas	G12D	0.169	0.339	0.126
HPAFII	pancreas	G12D	0.239	0.331	0.190
CAPAN2	pancreas	G12V	0.207	0.486	0.207
CFPAC1	pancreas	G12V	0.376	0.171	0.153
PANC0327	pancreas	G12V	0.078	0.224	>5

FIG. 14B

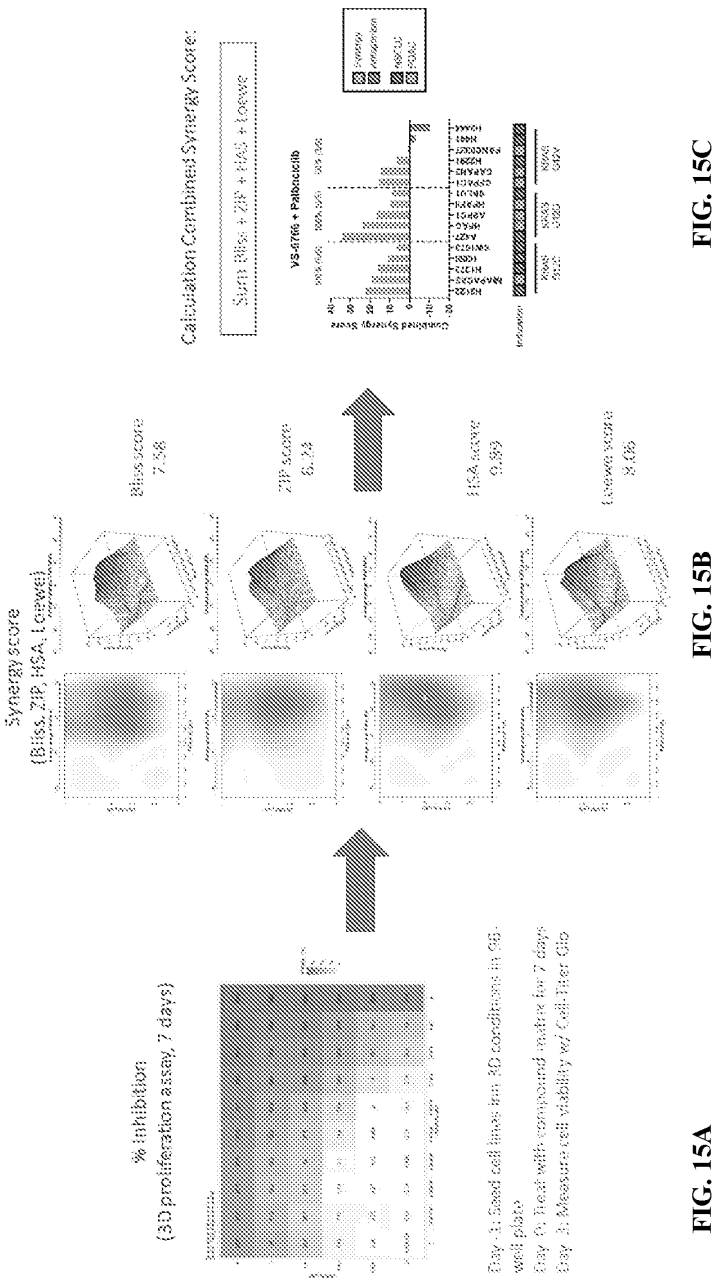


FIG. 15A

FIG. 15B

FIG. 15C

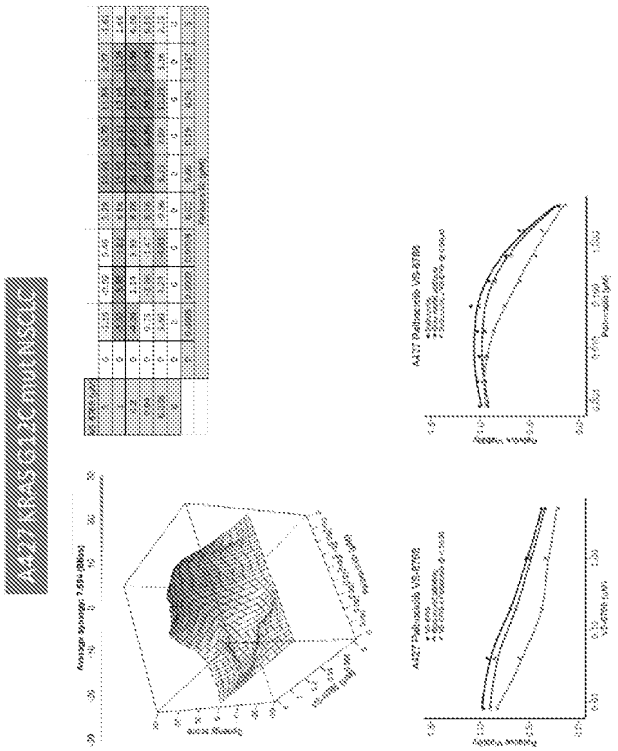


FIG. 16B

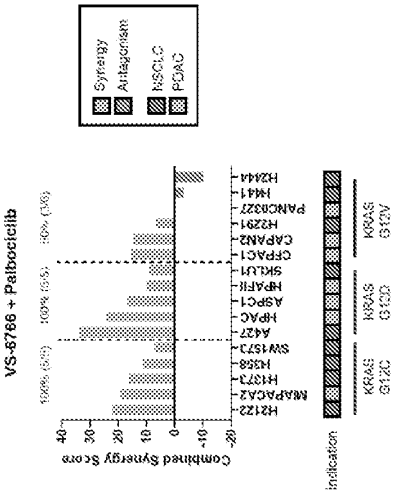


FIG. 16A

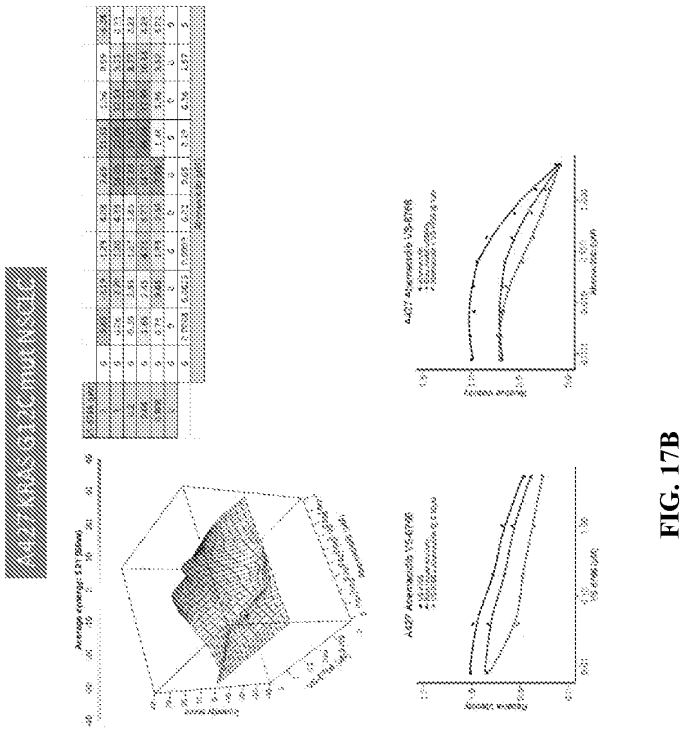


FIG. 17B

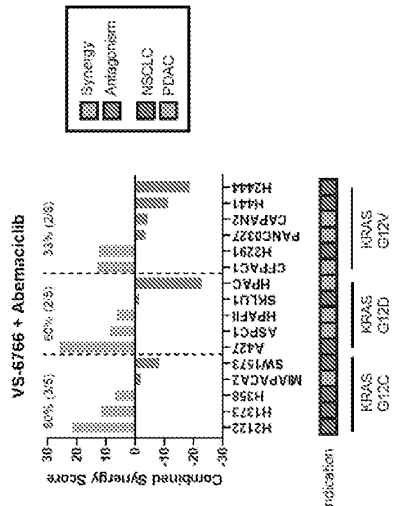


FIG. 17A

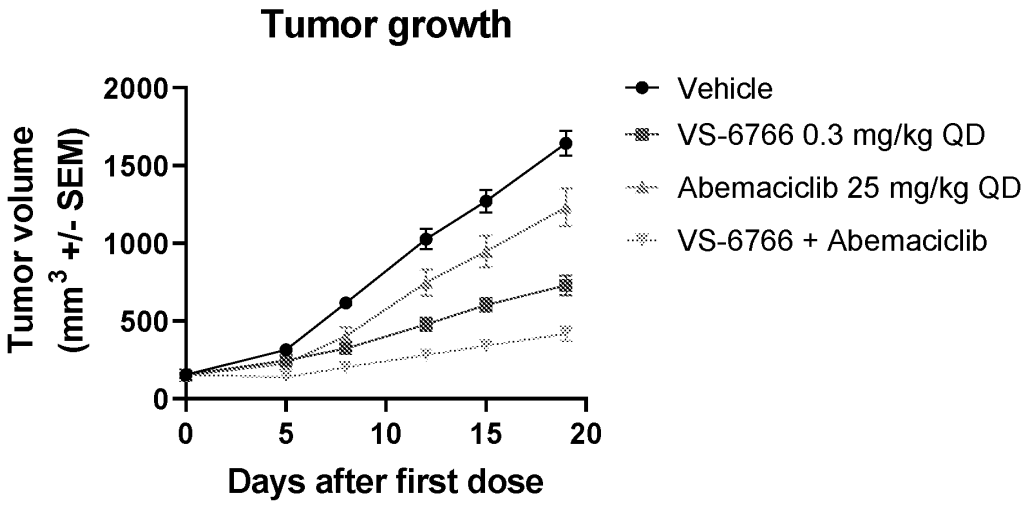

Tumor growth
Tumor volume (mm3 +/- SEM)
2000
1500
1000
500
0
0
5
10
15
20
Days after first dose
Vehicle
VS-6766 0.3 mg/kg QD
Abemaciclib 25 mg/kg QD
VS-6766 + Abemaciclib

FIG. 18

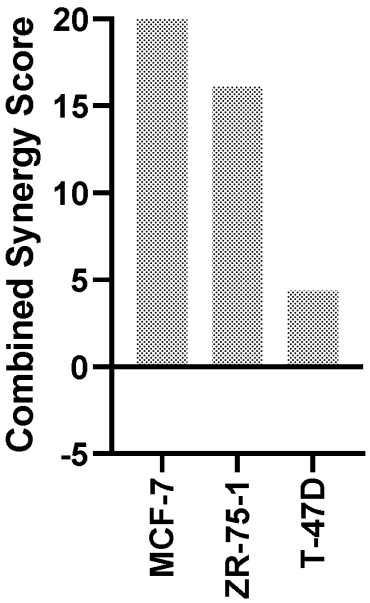


FIG. 19A

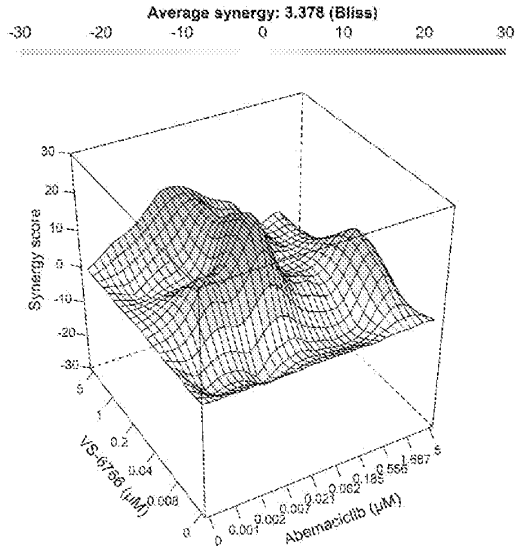


FIG. 19B

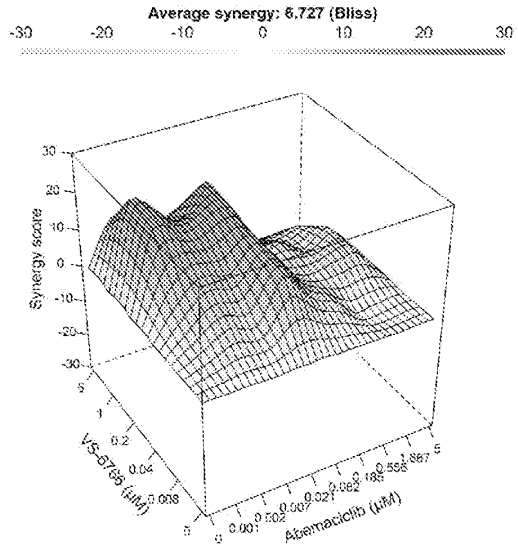


FIG. 19C

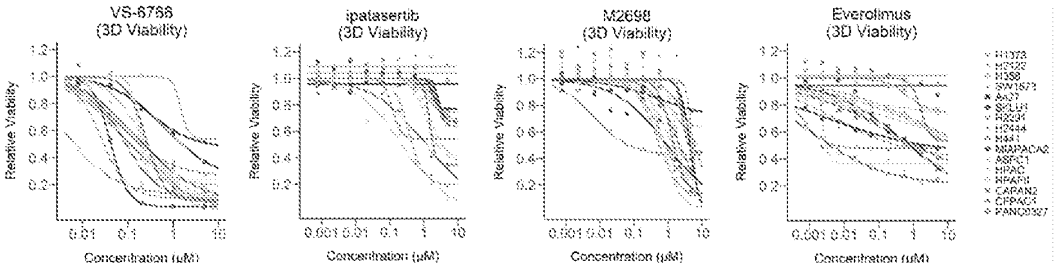


FIG. 20A

Cell Line	Cancer type	KRASmut	IC50 VS-6766 (μM)	IC50 ipatasertib (μM)	IC50 M2698 (μM)	IC50 Everolimus (μM)
H1373	lung	G12C	0.156	>5	>5	>5
H2122	lung	G12C	0.297	>5	>5	>5
H358	lung	G12C	0.042	>5	>5	>5
SW1573	lung	G12C	>5	0.969	0.560	0.347
A427	lung	G12D	>5	>5	4.367	>5
SKLU1	lung	G12D	3.417	>5	>5	2.387
H2291	lung	G12V	0.995	>5	>5	>5
H2444	lung	G12V	0.198	>5	0.837	0.068
H441	lung	G12V	0.011	>5	0.072	0.662
MIAPACA2	pancreas	G12C	0.035	>5	0.926	0.779
ASPC1	pancreas	G12D	0.209	2.445	2.018	>5
HPAC	pancreas	G12D	0.169	0.224	0.731	0.013
HPAFII	pancreas	G12D	0.239	3.989	1.305	>5
CAPAN2	pancreas	G12V	0.207	>5	4.050	>5
CFPAC1	pancreas	G12V	0.376	1.860	1.498	0.104
PANC0327	pancreas	G12V	0.078	1.176	2.171	1.359

FIG. 20B

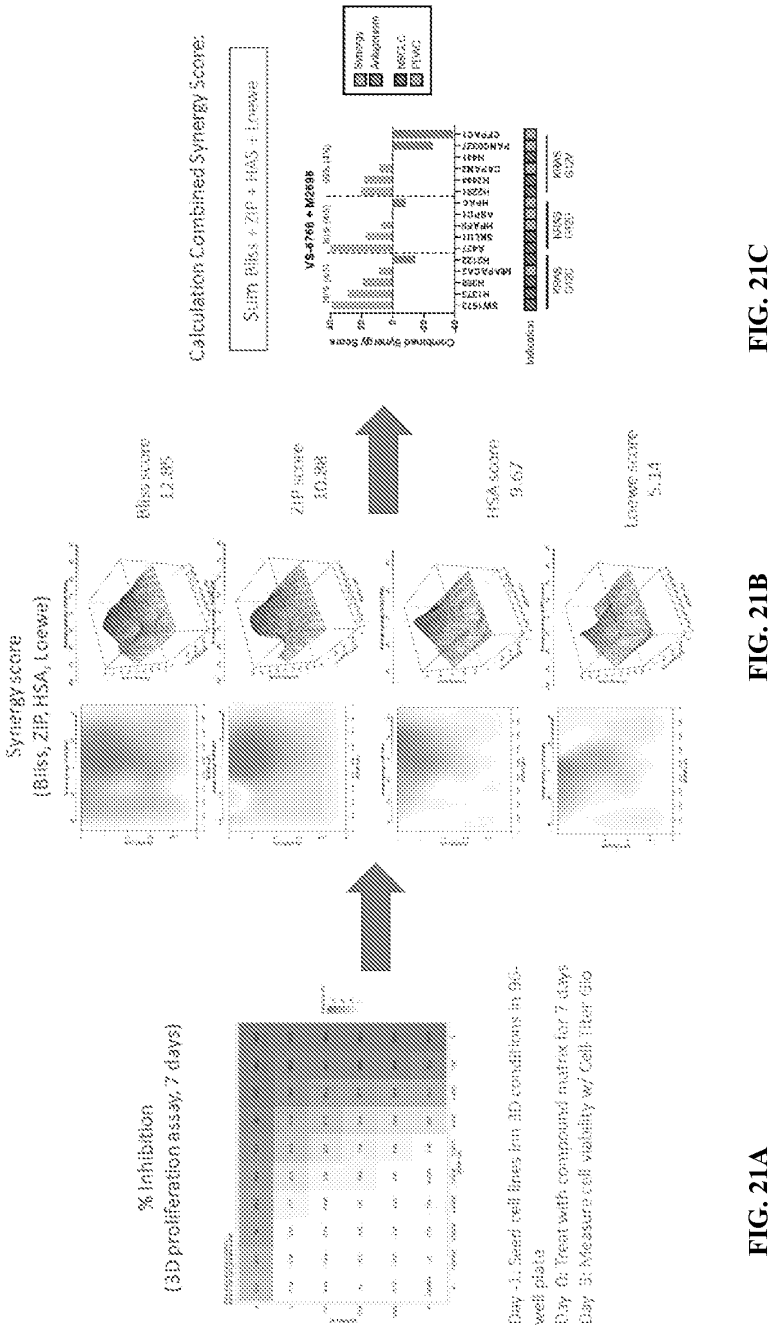


FIG. 21A

FIG. 21B

FIG. 21C

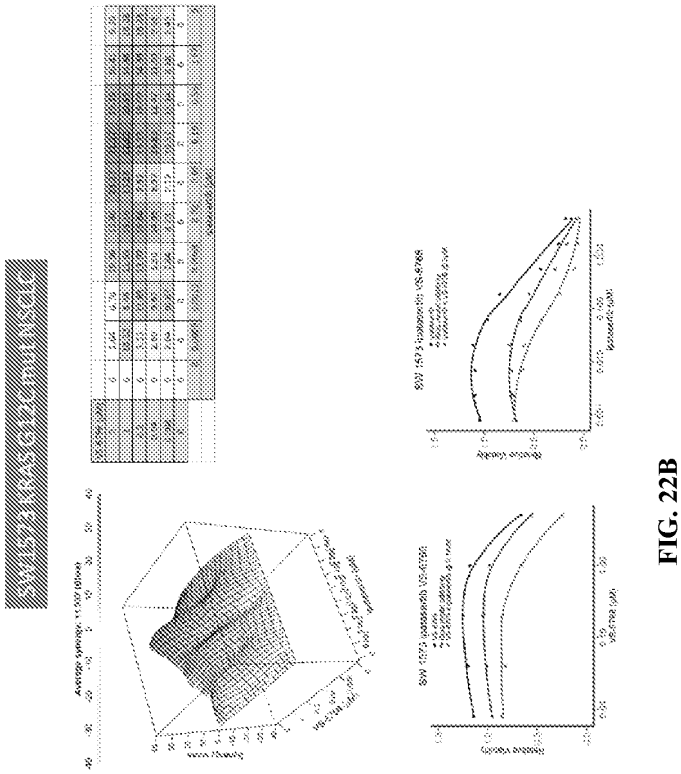


FIG. 22B

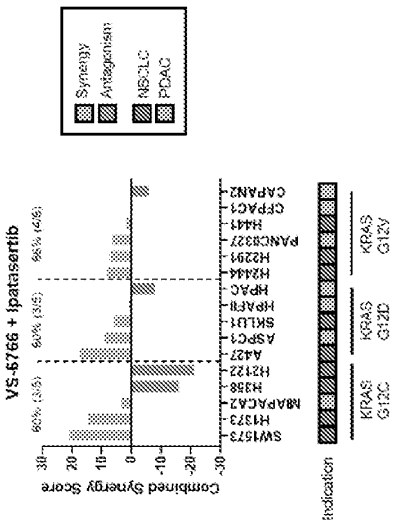


FIG. 22A

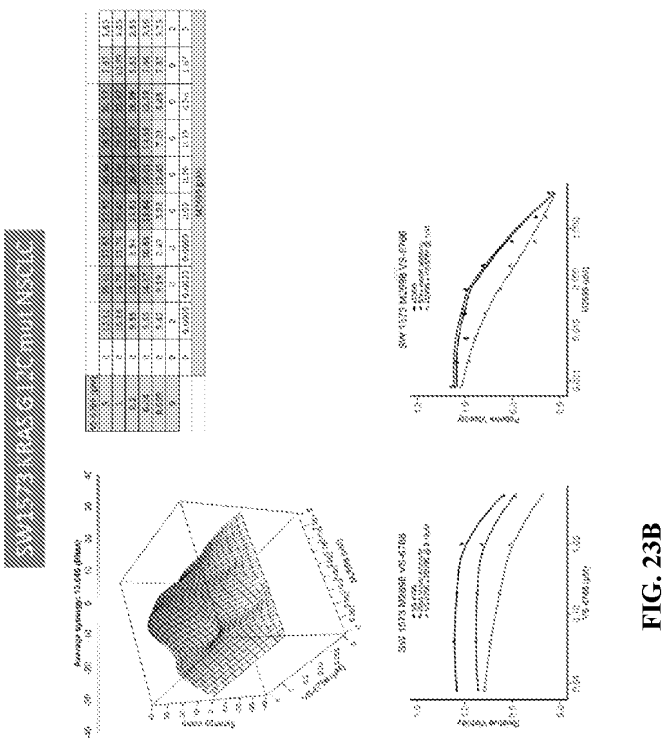


FIG. 23B

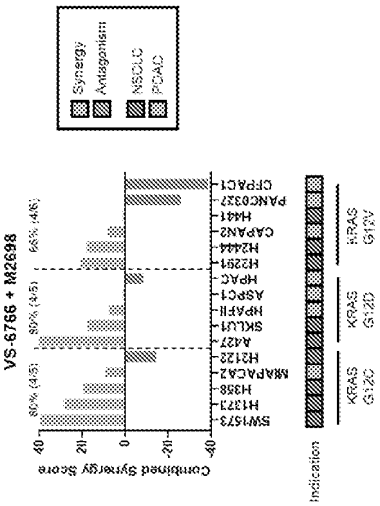


FIG. 23A

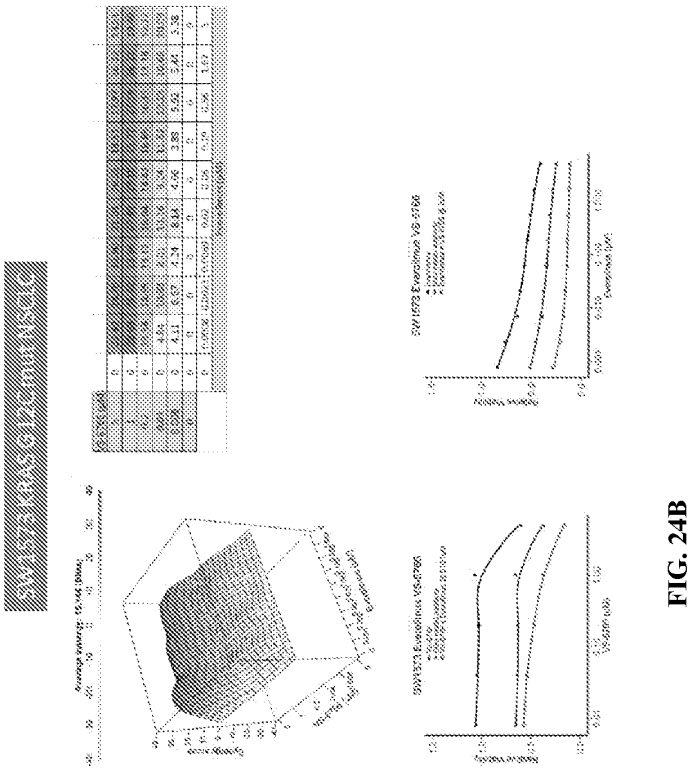


FIG. 24B

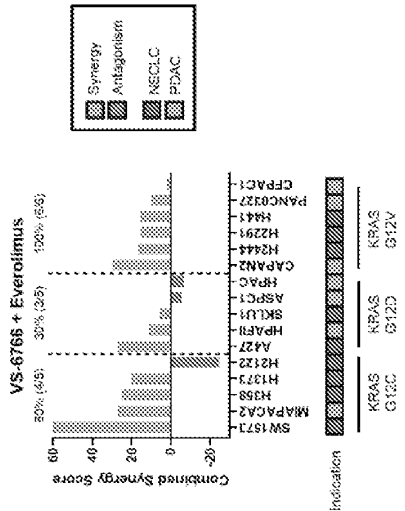


FIG. 24A

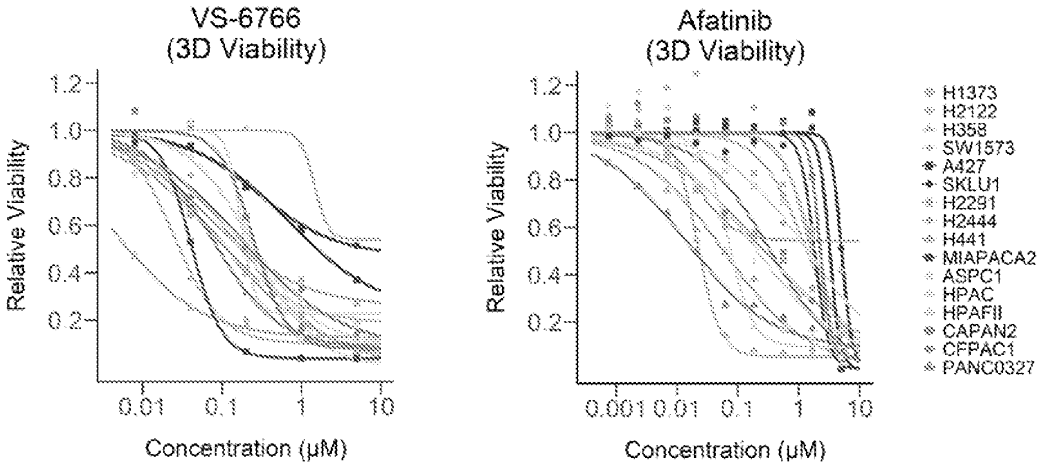


FIG. 25A

Cell Line	Cancer type	KRASmut	IC50 VS-6766 (μM)	IC50 Afatinib (μM)
H1373	lung	G12C	0.156	1.360
H2122	lung	G12C	0.767	1.775
H358	lung	G13C	0.042	0.033
SW1573	lung	G12C	>5	1.572
A427	lung	G12D	>5	3.227
SKLU1	lung	G12D	3.412	5.051
H2291	lung	G12V	0.095	0.276
H2444	lung	G12V	0.188	>5
H441	lung	G12V	0.011	0.058
MIAPACA2	pancreas	G12C	0.025	1.816
ASPC1	pancreas	G12D	0.209	1.396
HPAC	pancreas	G12D	0.189	0.076
HPAFII	pancreas	G12D	0.239	0.209
CAPAN2	pancreas	G12V	0.207	2.262
CFPAC1	pancreas	G12V	0.376	0.343
PANC0327	pancreas	G12V	0.078	0.019

FIG. 25B

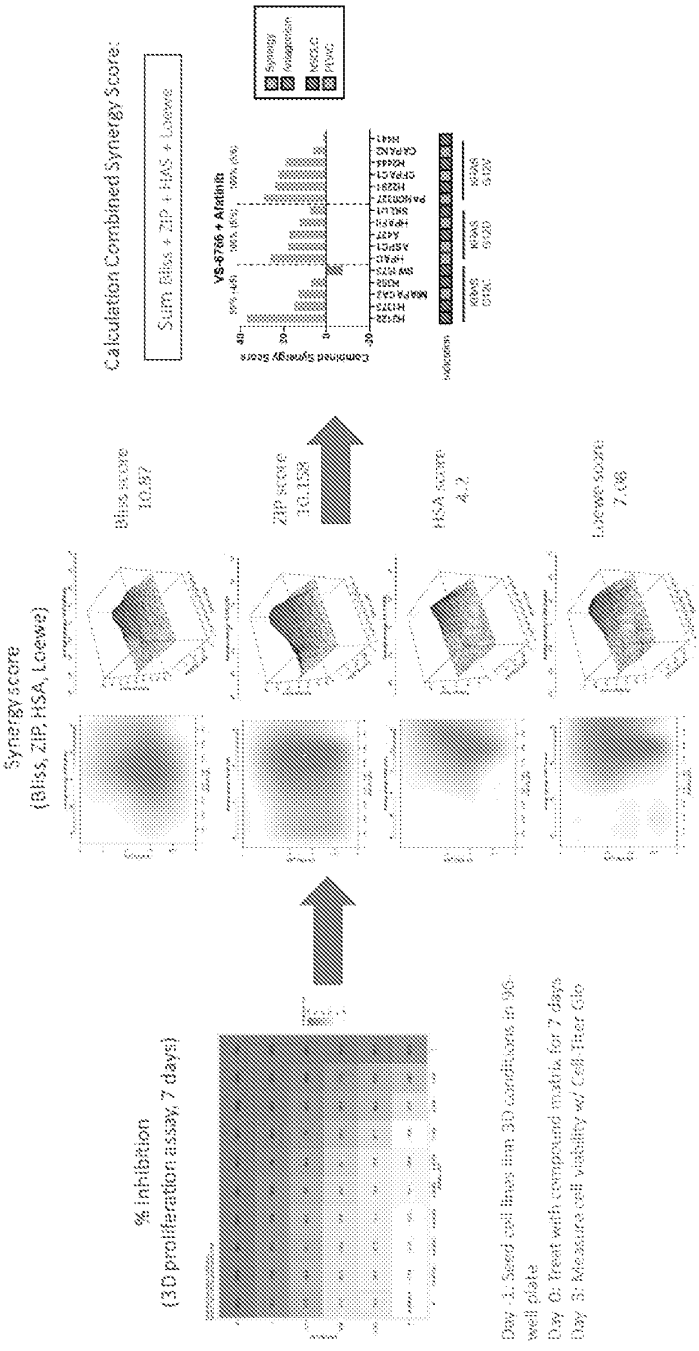


FIG. 26A

FIG. 26B

FIG. 26C

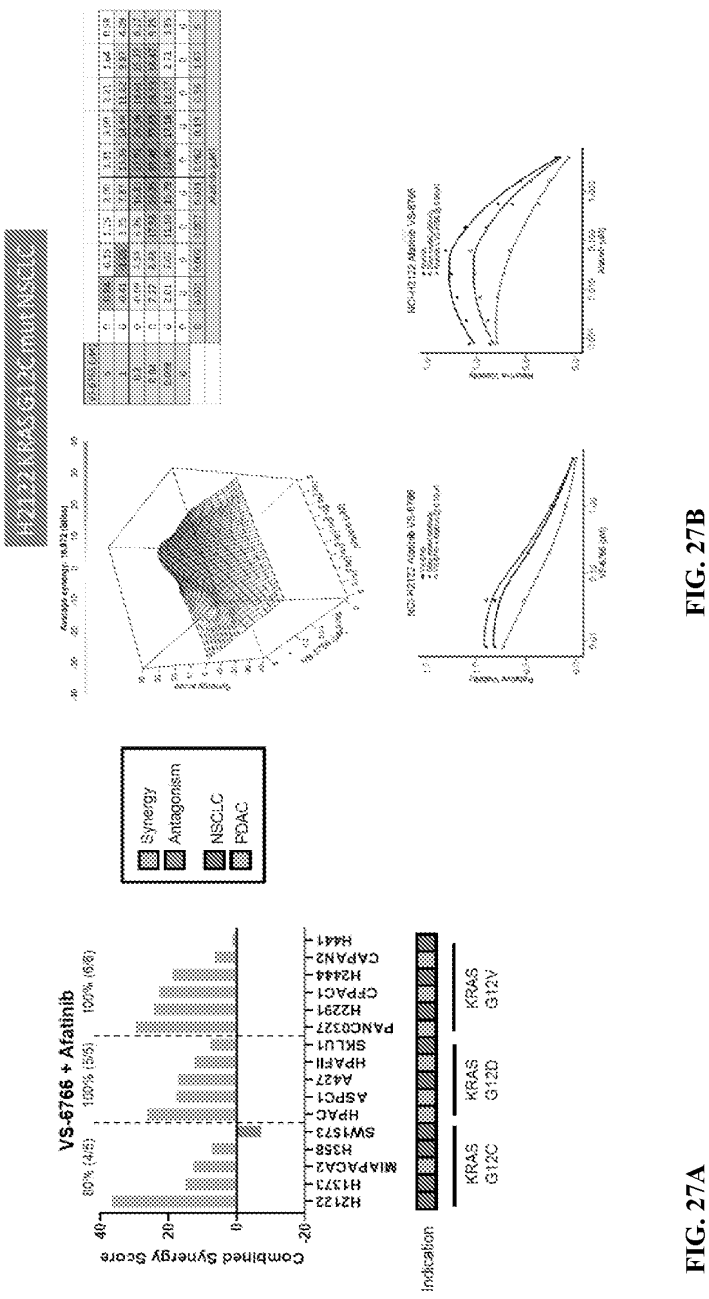


FIG. 27A

FIG. 27B

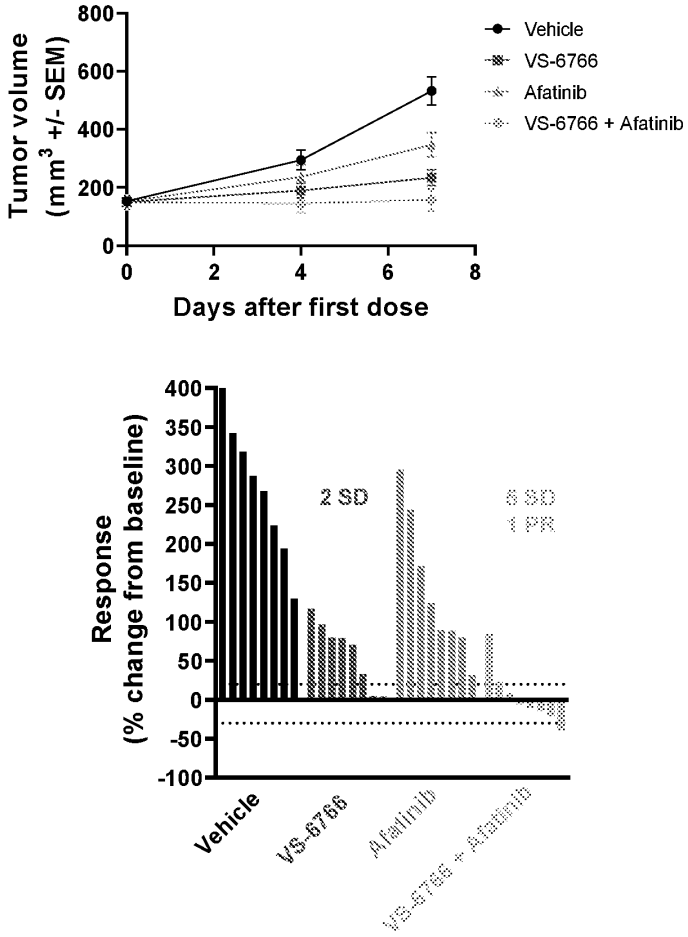
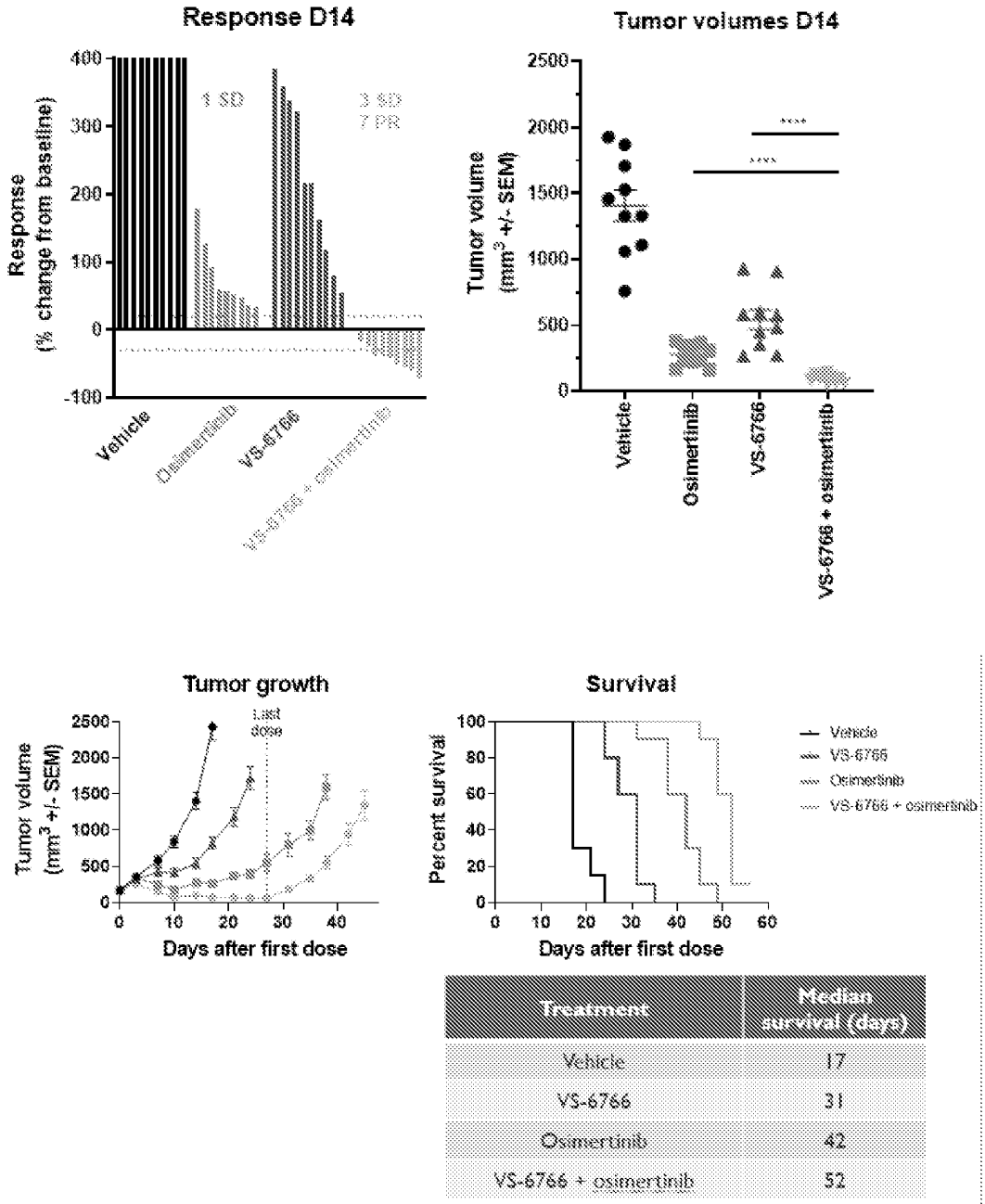
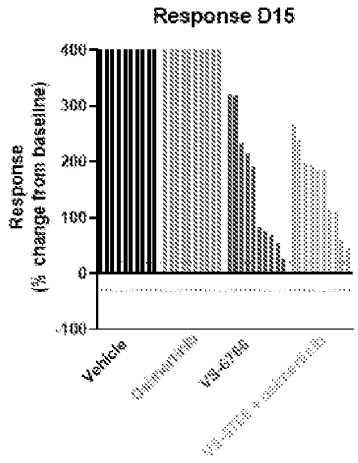

Tumor volume
(mm3 +/- SEM)
800
600
400
200
0
0
2
4
6
8
Days after first dose
Vehicle
VS-6766
Afatinib
VS-6766 + Afatinib
Response
(% change from baseline)
400
350
300
250
200
150
100
50
0
-50
-100
2 SD
6 SD
1 PR
Vehicle
VS-6766
Afatinib
VS-6766 + Afatinib

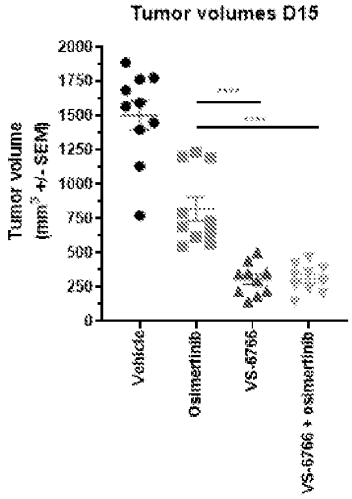
FIG. 28



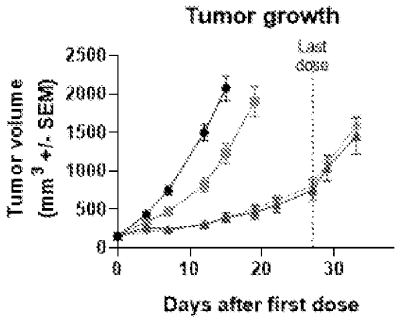
Treatment	Median survival (days)
Vehicle	17
VS-6766	31
Osimertinib	42
VS-6766 + osimertinib	52

FIG. 29





Treatment	Median survival (days)
Vehicle	15
VS-6766	38
Osimertinib	22
VS-6766 + osimertinib	36



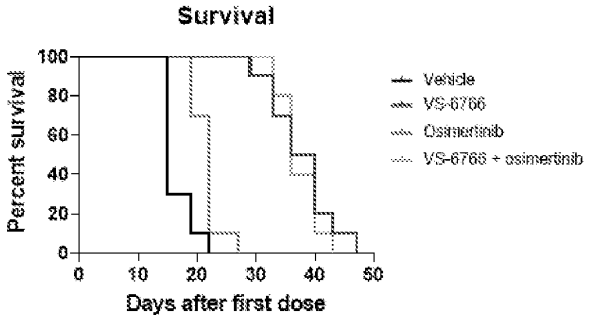


FIG. 30