			Synergy Score (Loewe model)	
Cell line	Indication	Sensitivity to G12C inhibitors	VS-6766 + AMG 510	VS-6766 + MRTX849
H2122	NSCLC	Moderately sensitive	43.9	46.9
H358	NSCLC	Sensitive	15.1	12.9
H2030	NSCLC	Moderately sensitive	18.8	ND
H1373	NSCLC	Sensitive	10.5	12.8
SW837	CRC	Sensitive	14.9	ND
SW1463	CRC	Moderately sensitive	11.5	ND

ND: not determined

FIG. 1A

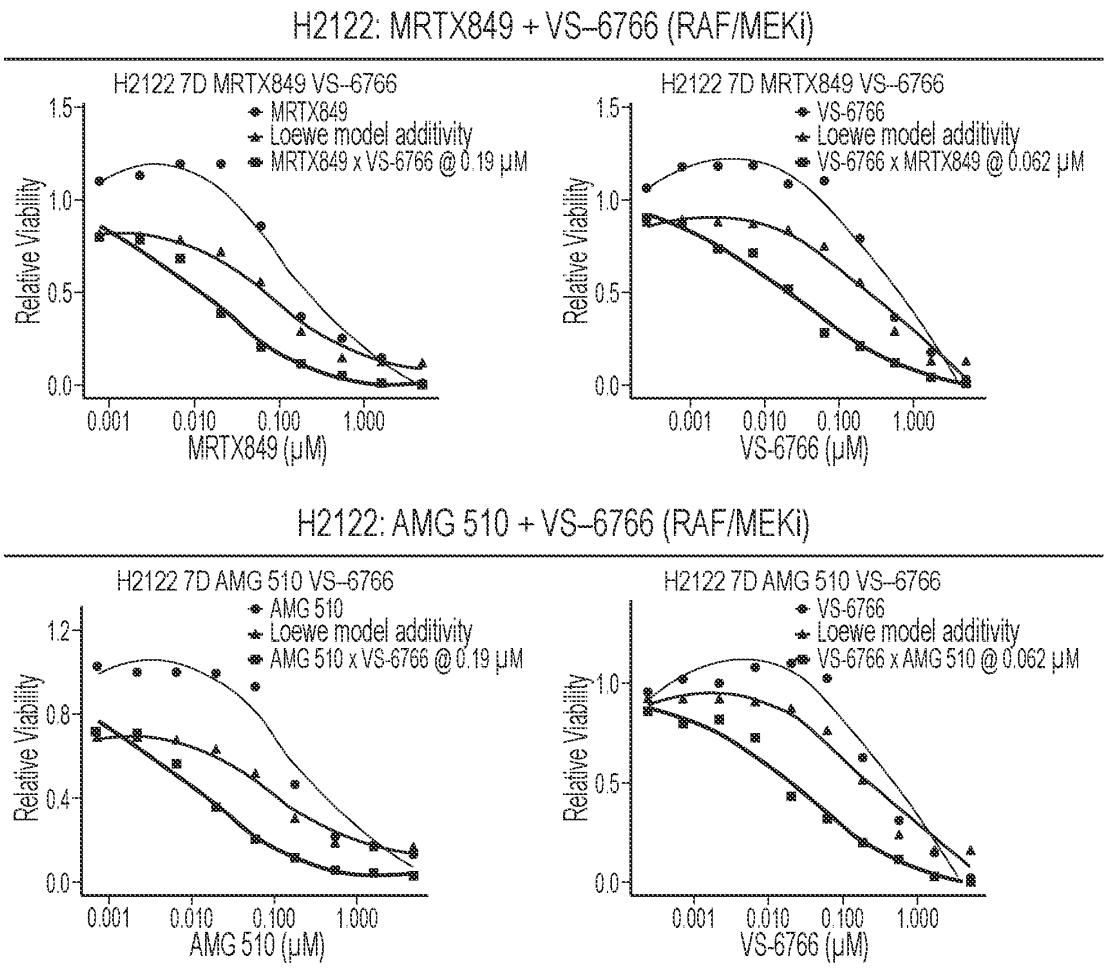


FIG. 1B

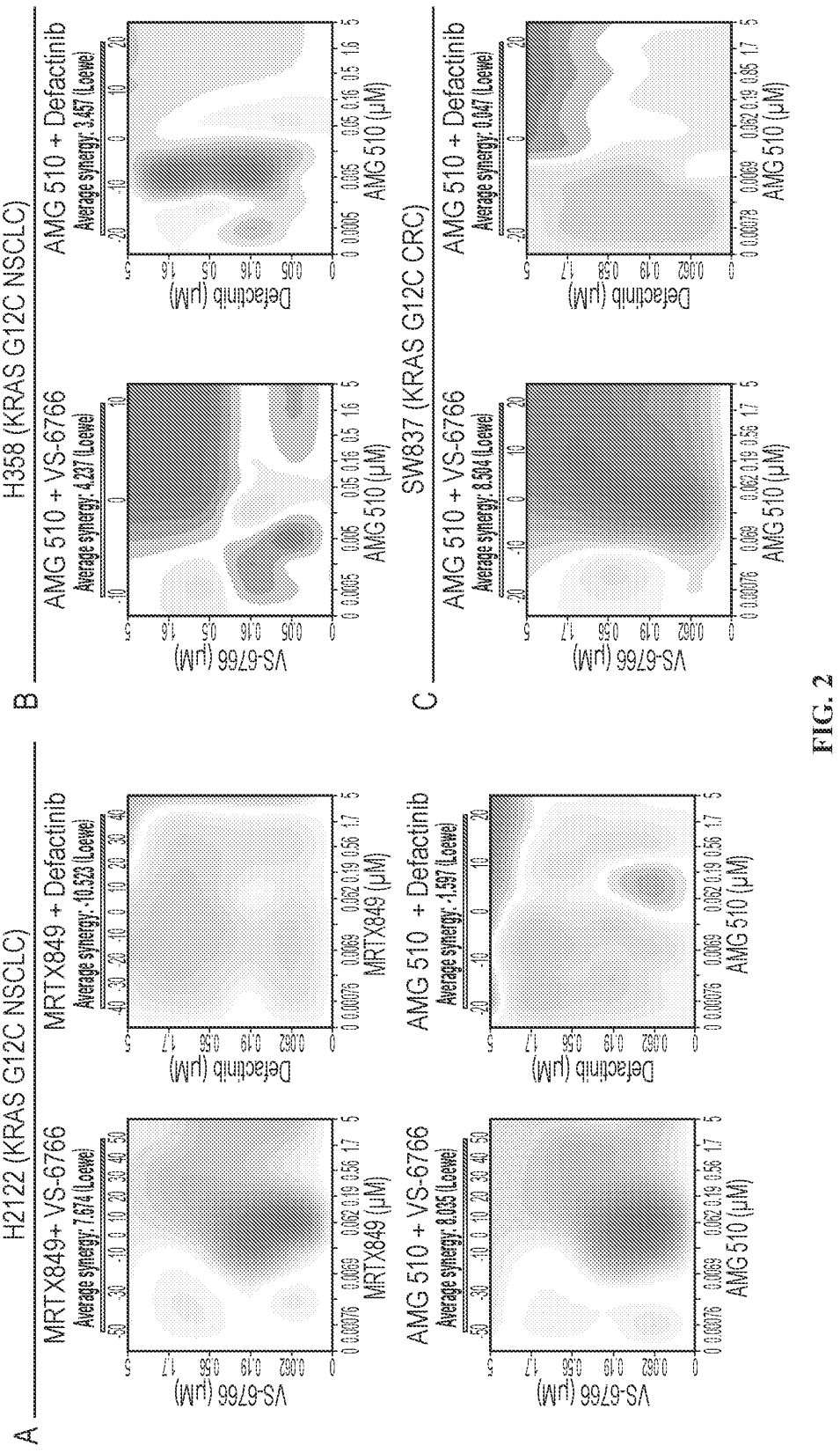

A
H2122 (KRAS G12C NSCLC)
MRTX849+ VS-6766
Average synergy: 7.674 (Loewe)
VS-6766 (µM)
MRTX849 (µM)
MRTX849 + Defactinib
Average synergy: -10.523 (Loewe)
Defactinib (µM)
AMG 510 + VS-6766
Average synergy: 8.035 (Loewe)
AMG 510 (µM)
AMG 510 + Defactinib
Average synergy: -1.597 (Loewe)
B
H358 (KRAS G12C NSCLC)
AMG 510 + VS-6766
Average synergy: 4.227 (Loewe)
AMG 510 + Defactinib
Average synergy: 3.457 (Loewe)
C
SW837 (KRAS G12C CRC)
AMG 510 + VS-6766
Average synergy: 8.504 (Loewe)
AMG 510 + Defactinib
Average synergy: 0.047 (Loewe)

FIG. 2

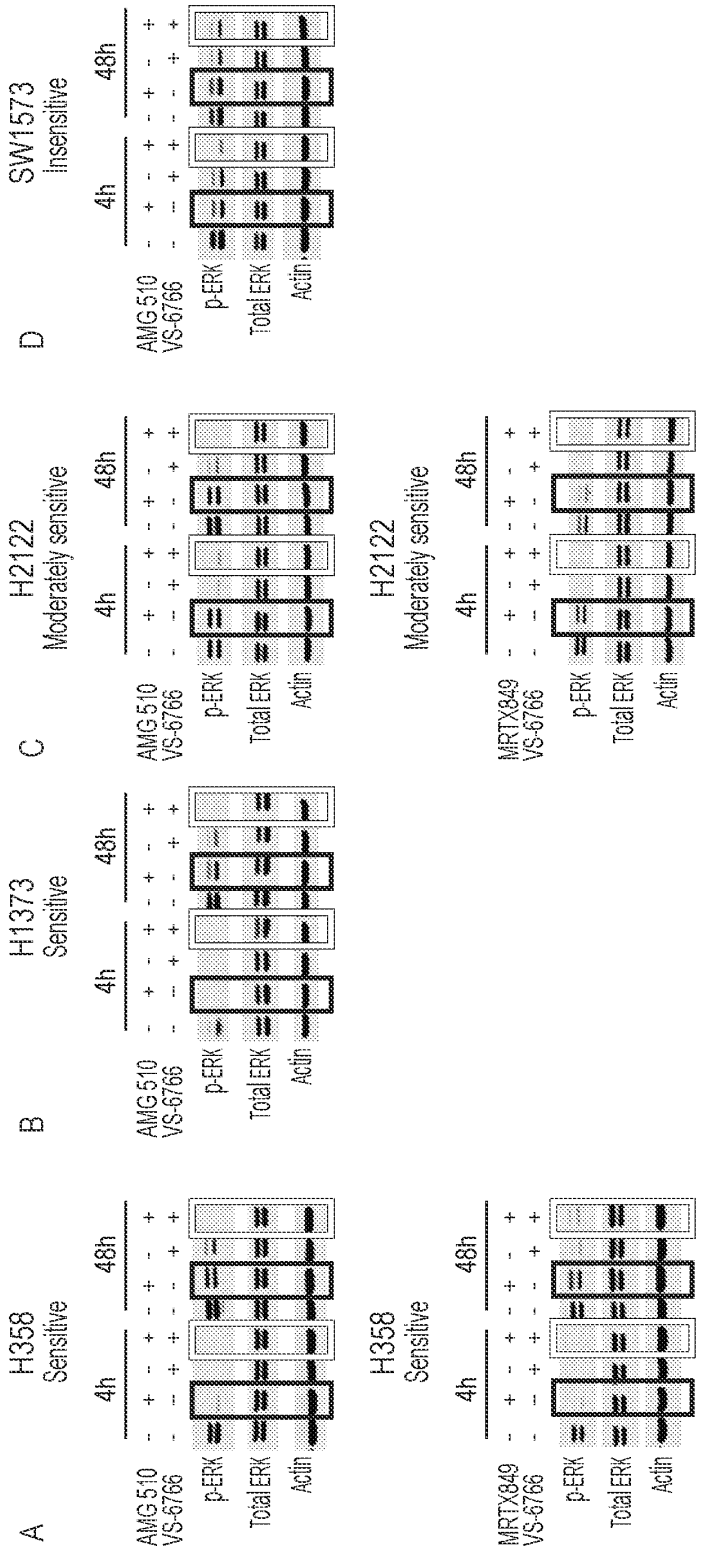

A
H358
Sensitive
4h
48h
AMG 510
VS-6766
MRTX849
p-ERK
Total ERK
Actin
B
H1373
Sensitive
C
H2122
Moderately sensitive
D
SW1573
Insensitive

FIG. 3

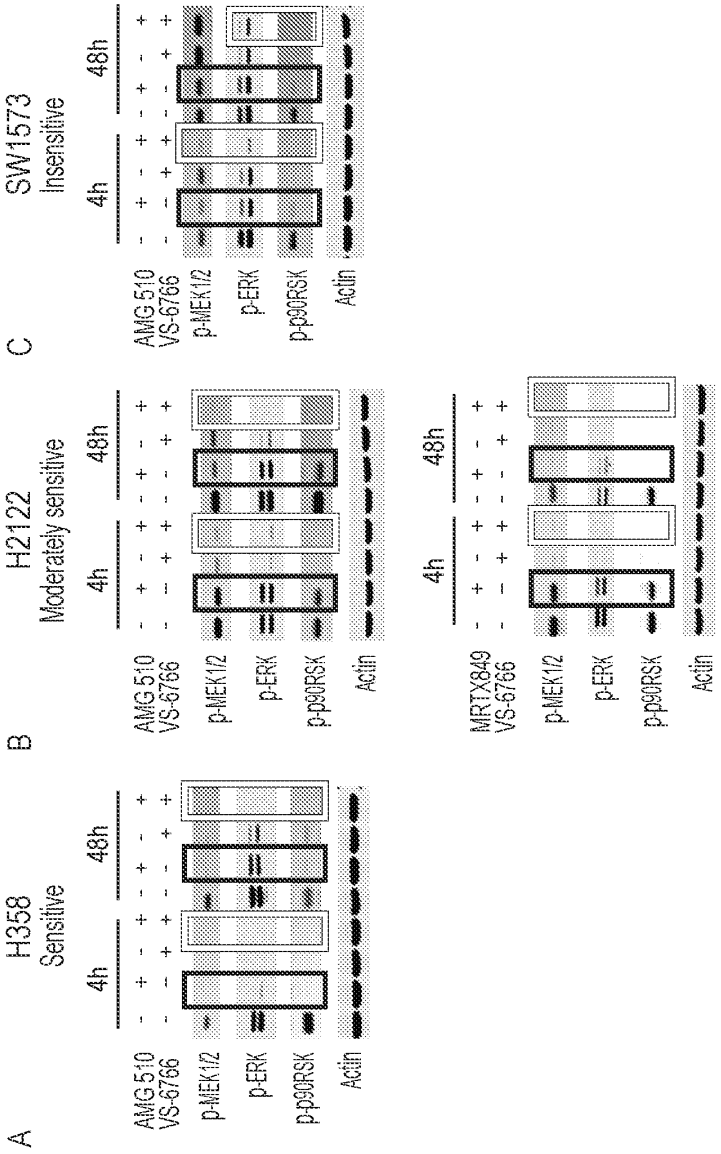

A
H358
Sensitive
4h
48h
AMG 510
VS-6766
p-MEK1/2
p-ERK
p-p90RSK
Actin
B
H2122
Moderately sensitive
4h
48h
AMG 510
VS-6766
p-MEK1/2
p-ERK
p-p90RSK
Actin
MRTX849
VS-6766
p-MEK1/2
p-ERK
p-p90RSK
Actin
C
SW1573
Insensitive
4h
48h
AMG 510
VS-6766
p-MEK1/2
p-ERK
p-p90RSK
Actin

FIG. 4

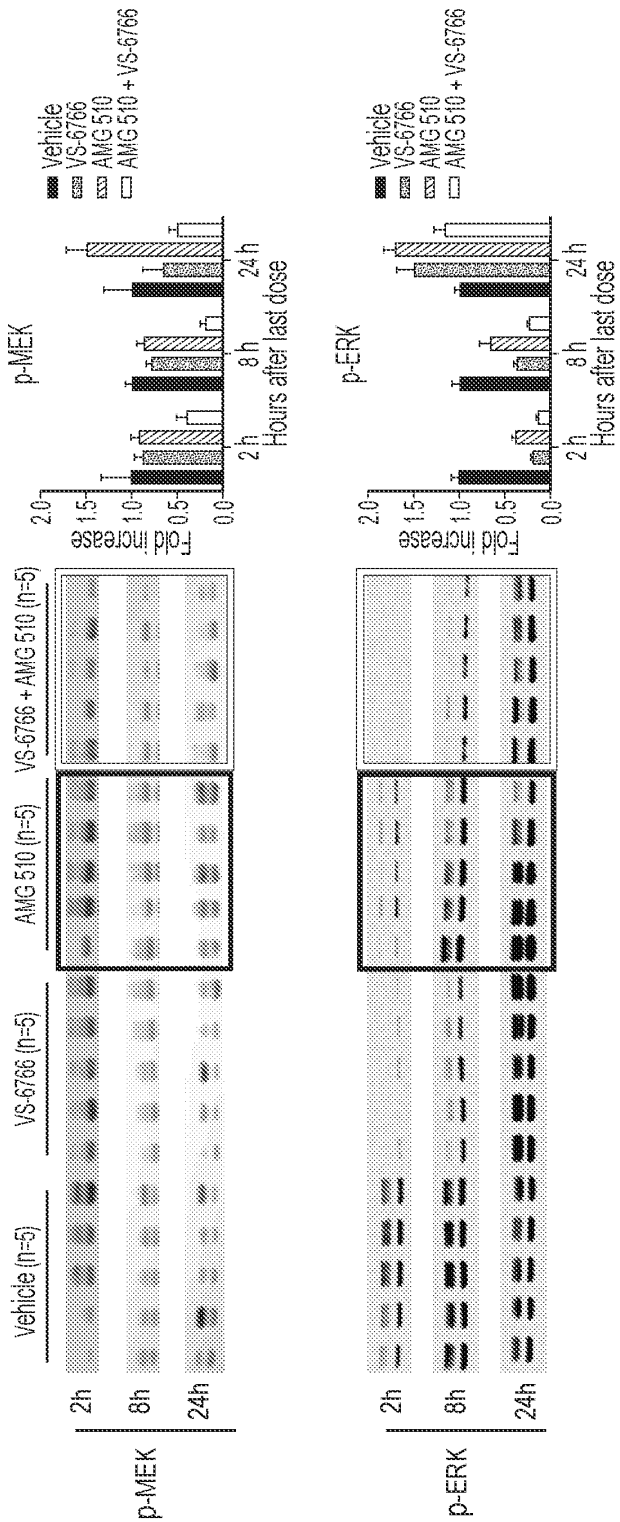

Vehicle
VS-6766
AMC 510
AMC 510 + VS-6766
p-MEK
p-ERK
Fold increase
Hours after last dose
2 h
8 h
24 h
Vehicle (n=5)
VS-6766 (n=5)
AMC 510 (n=5)
VS-6766 + AMC 510 (n=5)
2h
8h
24h

FIG. 5

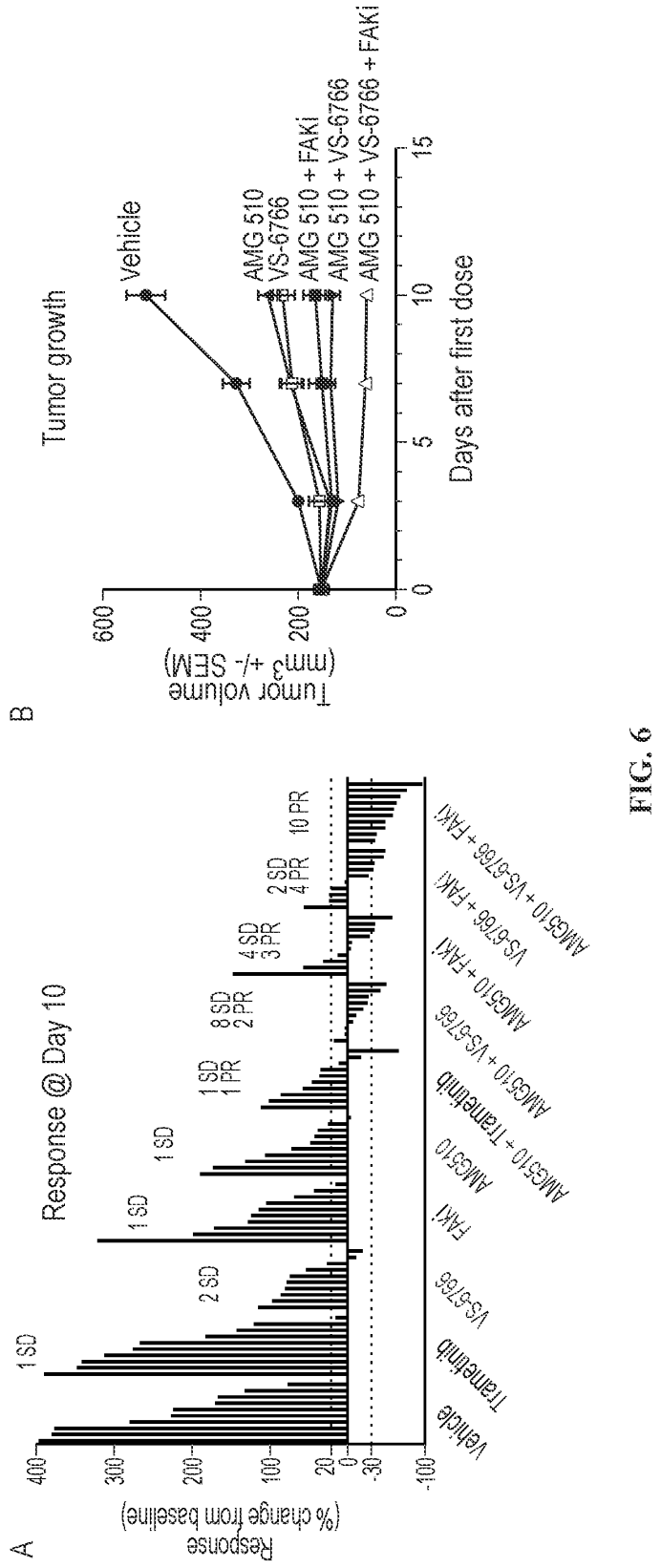

A
Response
(% change from baseline)
400
300
200
100
20
0
-30
-100
Response @ Day 10
1 SD
1 SD
2 SD
1 SD
1 SD
1 PR
8 SD
2 PR
4 SD
3 PR
2 SD
4 PR
10 PR
Vehicle
Tametinib
VS-6766
FAKi
AMG510
AMG510 + Tametinib
AMG510 + VS-6766
AMG510 + FAKi
VS-6766 + FAKi
AMG510 + VS-6766 + FAKi
B
Tumor growth
Tumor volume
(mm3 +/- SEM)
600
400
200
0
0
5
10
15
Days after first dose
Vehicle
AMG 510
VS-6766
AMG 510 + FAKi
AMG 510 + VS-6766
AMG 510 + VS-6766 + FAKi

FIG. 6

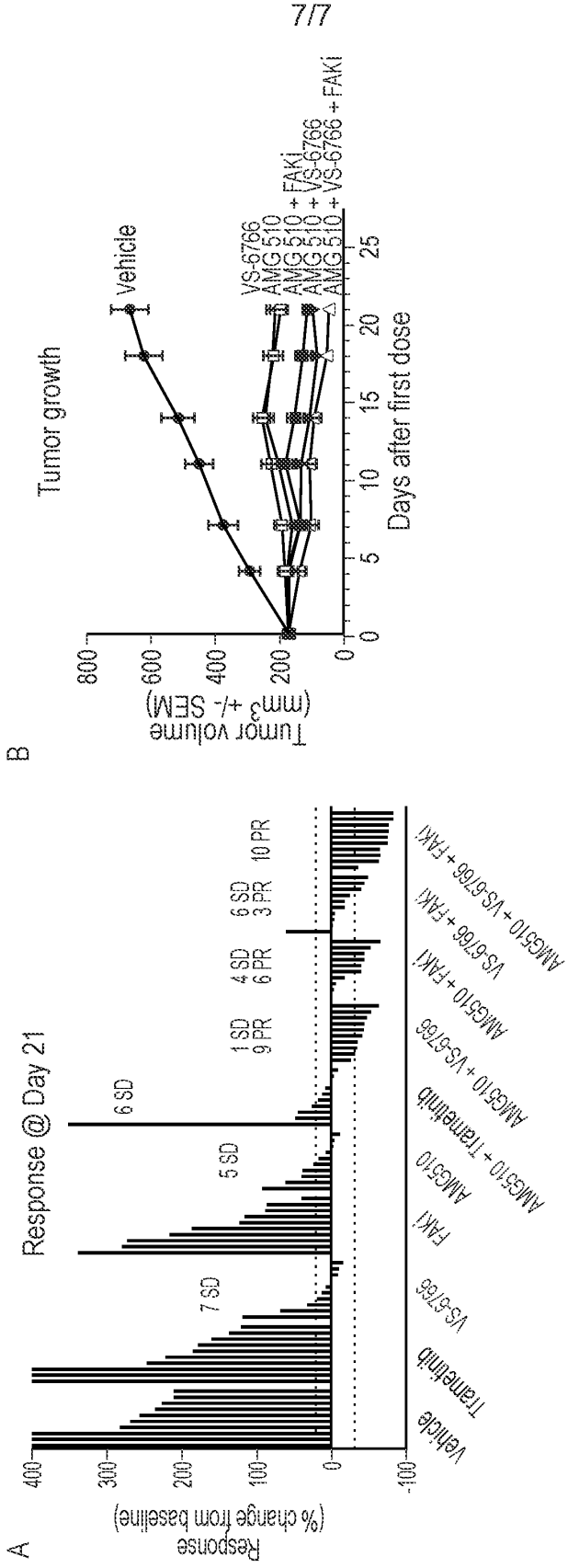

A
Response
(% change from baseline)
400
300
200
100
0
-100
Response @ Day 21
7 SD
5 SD
6 SD
1 SD
9 PR
4 SD
6 PR
6 SD
3 PR
10 PR
Vehicle
Tametinib
VS-6766
FAKi
AMG510
AMG510 + Tametinib
AMG510 + VS-6766
AMG510 + FAKi
VS-6766 + FAKi
AMG510 + VS-6766 + FAKi
B
Tumor volume
(mm3 +/- SEM)
800
600
400
200
0
Tumor growth
Vehicle
VS-6766
AMG 510
AMG510 + FAKi
AMG510 + VS-6766
AMG 510 + VS-6766 + FAKi
0
5
10
15
20
25
Days after first dose

FIG. 7