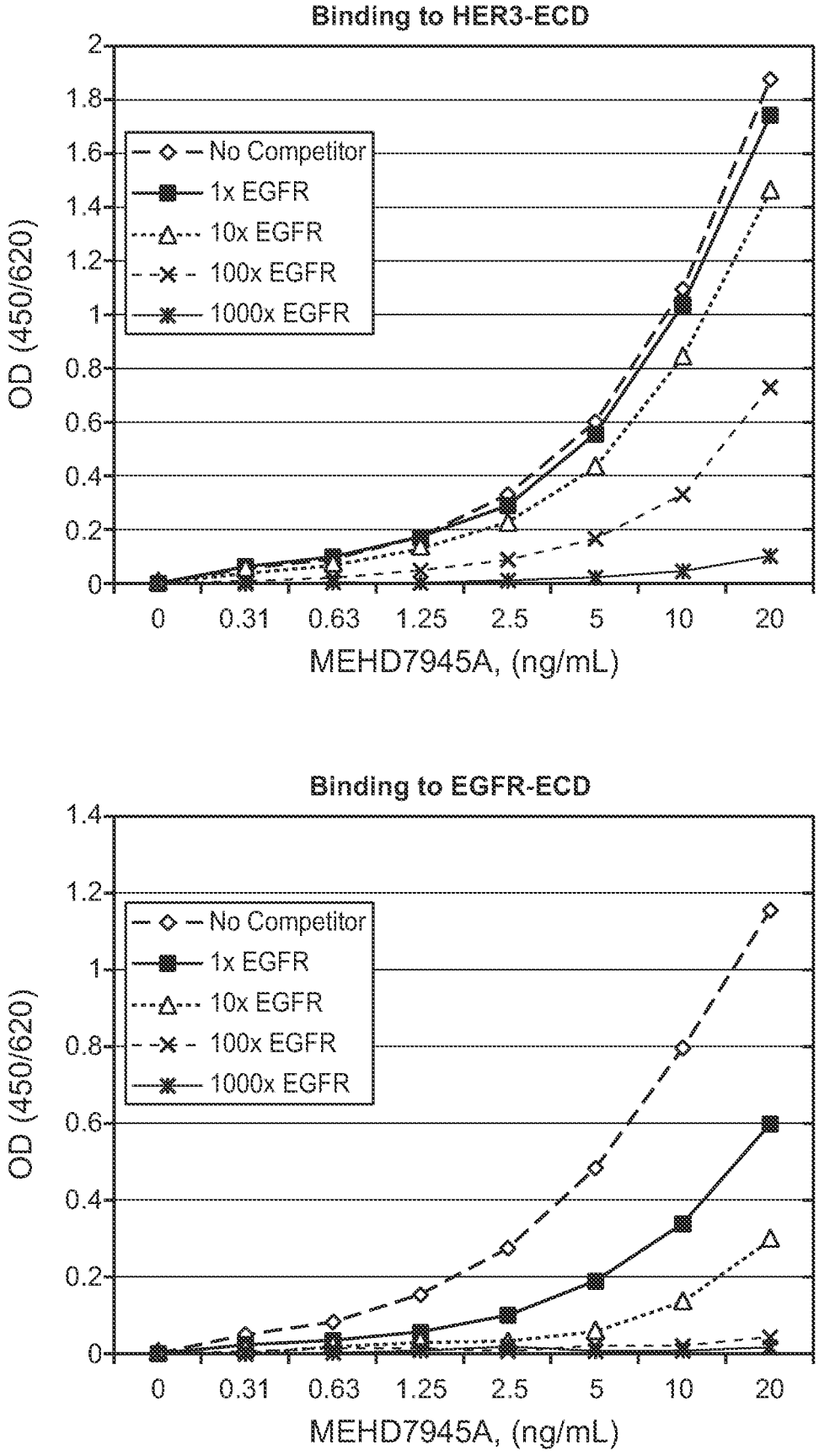
FIG. 1


Binding to HER3-ECD
OD (450/620)
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
No Competitor
1x EGFR
10x EGFR
100x EGFR
1000x EGFR
0
0.31
0.63
1.25
2.5
5
10
20
MEHD7945A, (ng/mL)
Binding to EGFR-ECD
OD (450/620)
1.4
1.2
1
0.8
0.6
0.4
0.2
0
No Competitor
1x EGFR
10x EGFR
100x EGFR
1000x EGFR
0
0.31
0.63
1.25
2.5
5
10
20
MEHD7945A, (ng/mL)

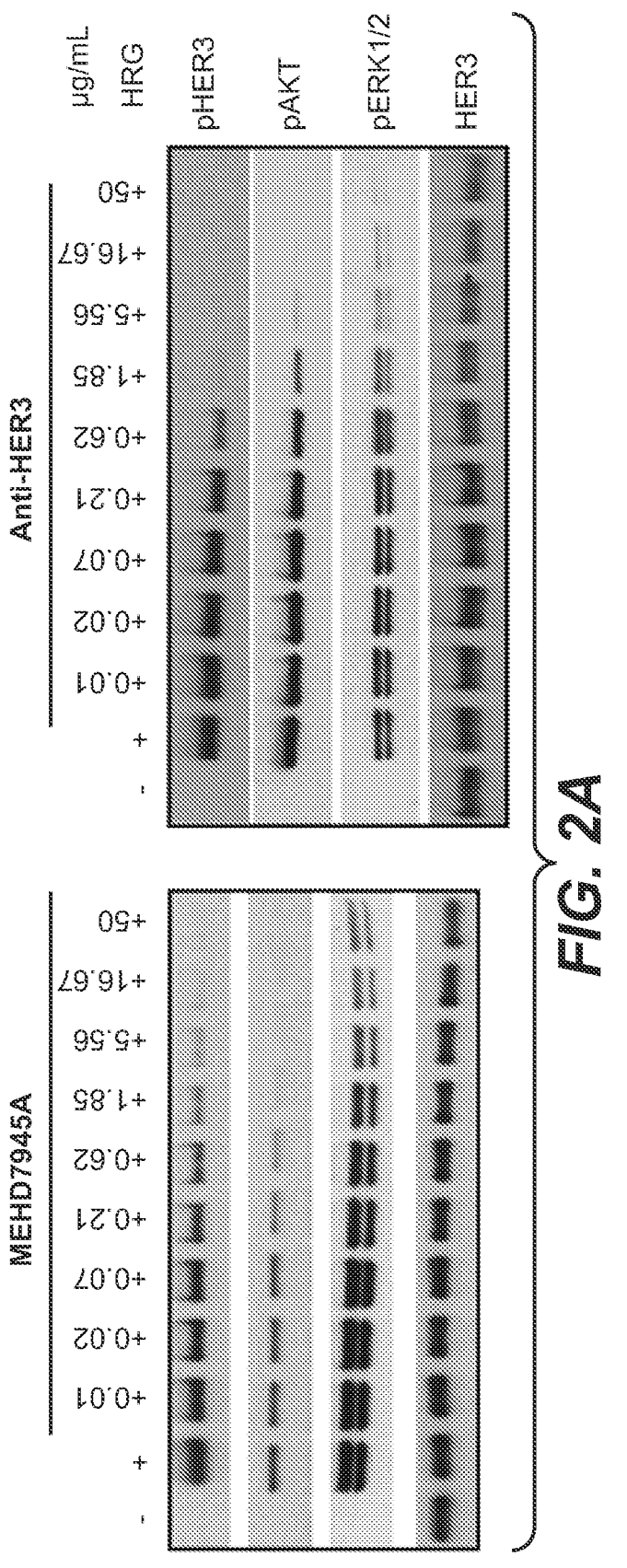

Anti-HER3
MEHD7945A
µg/mL
HRG
-
+
+0.01
+0.02
+0.07
+0.21
+0.62
+1.85
+5.56
+16.67
+50
pHER3
pAKT
pERK1/2
HER3

FIG. 2A

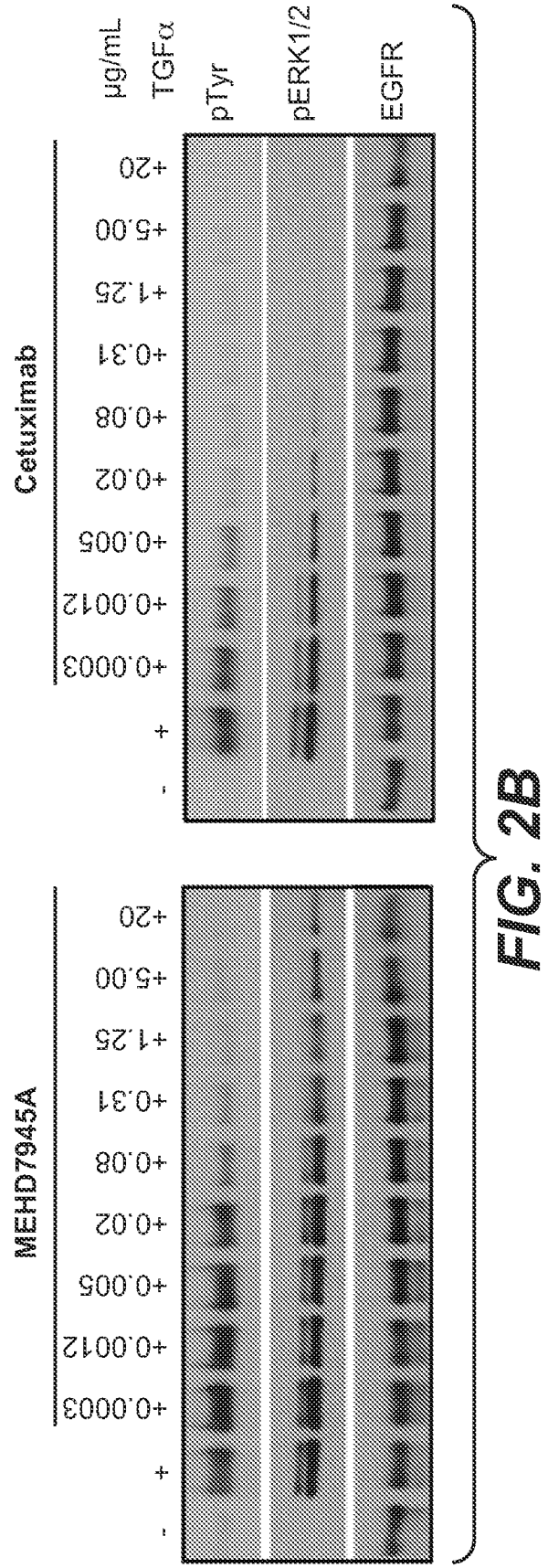

Cetuximab
MEHD7945A
µg/mL
TGFα
-
+
+0.0003
+0.0012
+0.005
+0.02
+0.08
+0.31
+1.25
+5.00
+20
pTyr
pERK1/2
EGFR

FIG. 2B

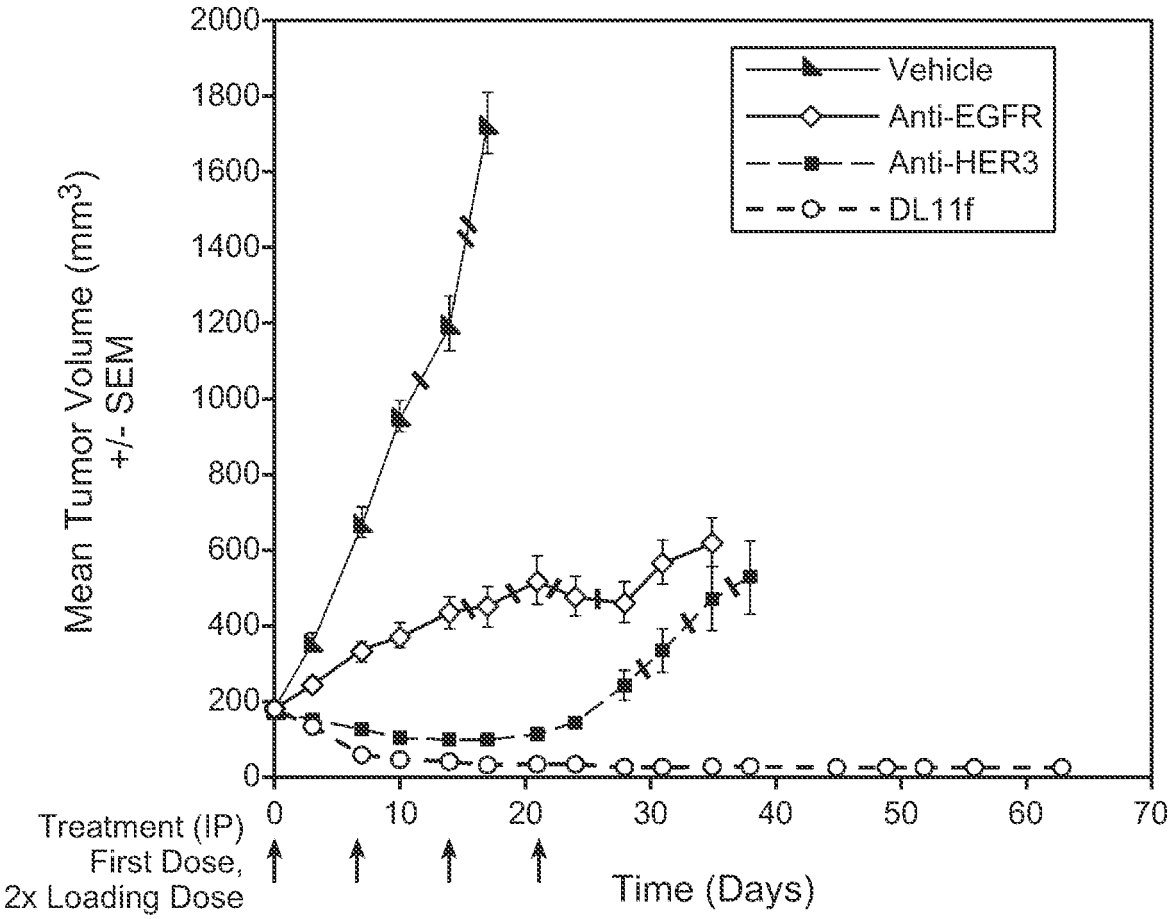

Mean Tumor Volume (mm3)
+/- SEM
2000
1800
1600
1400
1200
1000
800
600
400
200
0
Vehicle
Anti-EGFR
Anti-HER3
DL11f
Treatment (IP)
First Dose,
2x Loading Dose
0
10
20
30
40
50
60
70
Time (Days)

FIG. 3

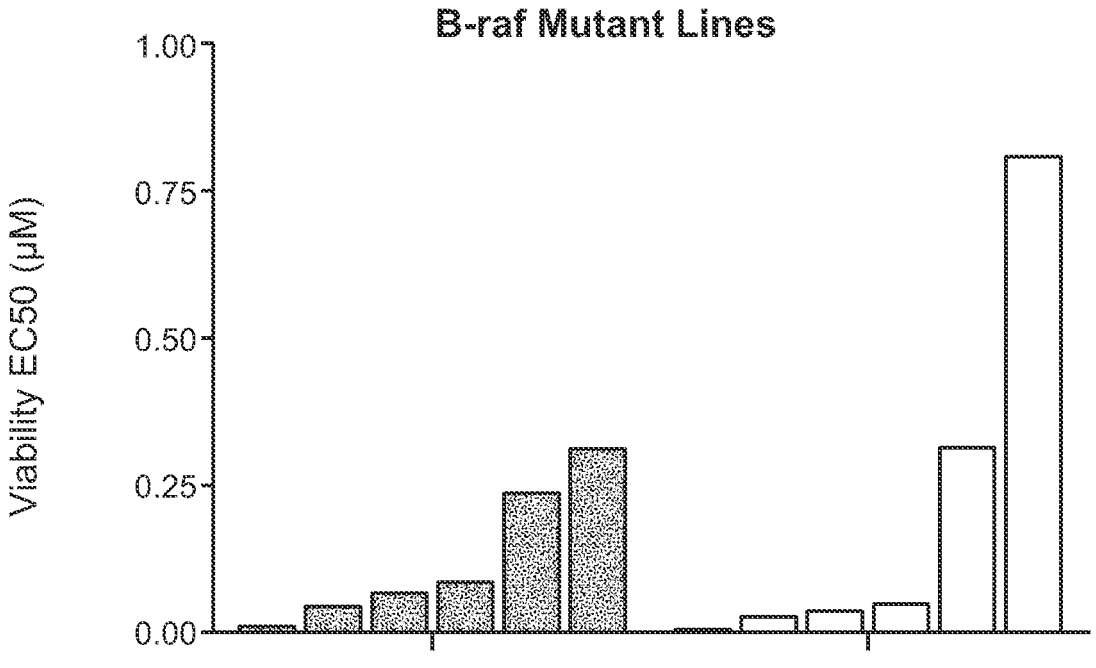

B-raf Mutant Lines
Viability EC50 (μM)
1.00
0.75
0.50
0.25
0.00

FIG. 5

Model	phenotype	Cetuximab	MEHD7945A	anti-HER3	Cetuximab + anti-HER3
NCI-H292	NSCLC	+++	+++	-	n/a
NCI-H1975	NSCLC	+++	+++	-	n/a
SW948	CRC	++	++	+	n/a
OVXF550	ovarian	++	++	++	++
A431	epidermoid	+++	+++	++	n/a
Cal27	HNSCC	+++	+++	++	n/a
FaDu	HNSCC	++	+++	+++	n/a
LXF983	NSCLC	++	+++	++	+++
MAXF449	breast	-	+++	+++	+++
A549	NSCLC	-	++	+	+++
Calu-3	NSCLC	-	++	+	++
BxPC3	pancreas	-	++	+	n/a

FIG. 4

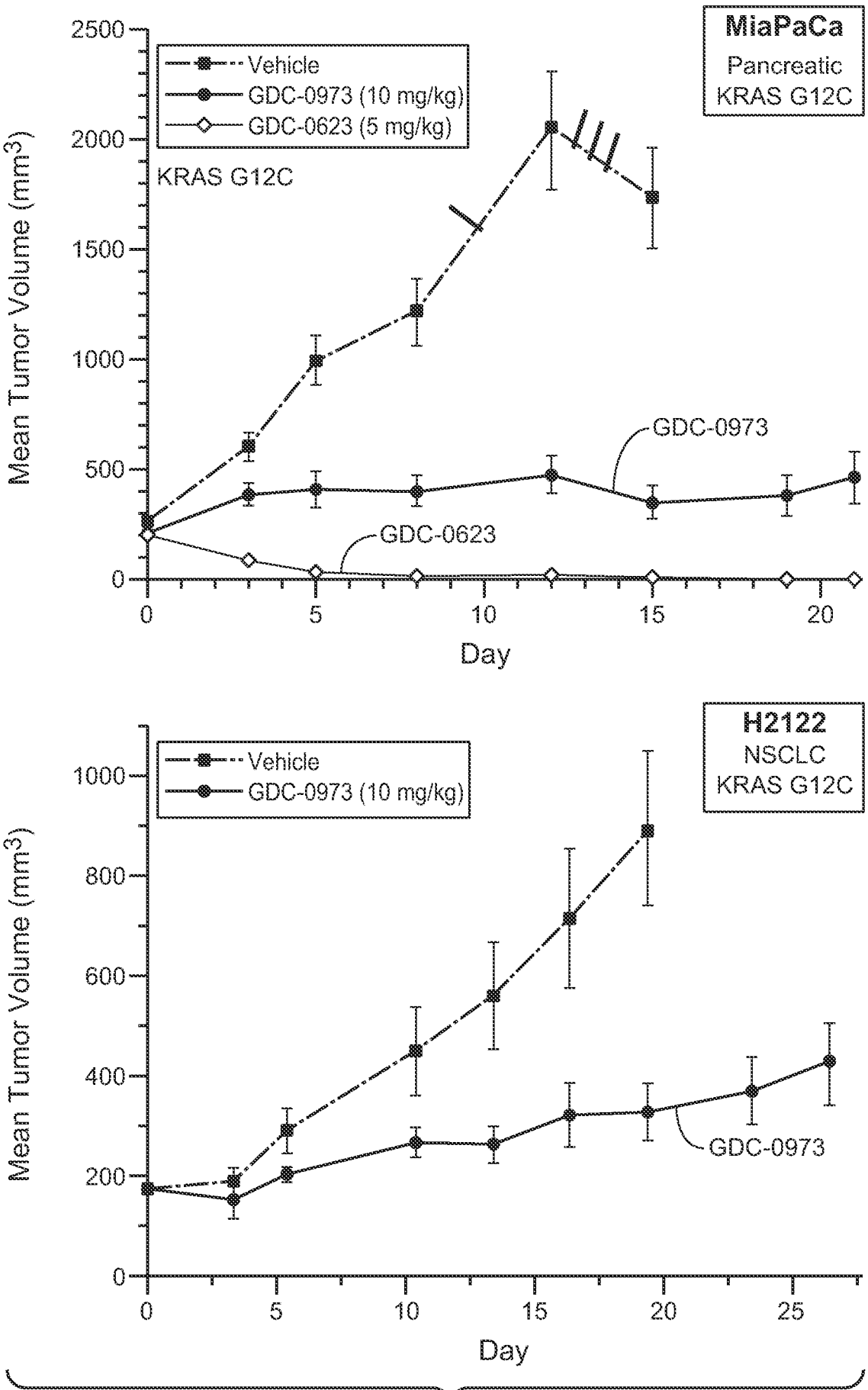

MiaPaCa
Pancreatic
KRAS G12C
Vehicle
GDC-0973 (10 mg/kg)
GDC-0623 (5 mg/kg)
KRAS G12C
Mean Tumor Volume (mm3)
2500
2000
1500
1000
500
0
GDC-0973
GDC-0623
0
5
10
15
20
Day
H2122
NSCLC
KRAS G12C
Vehicle
GDC-0973 (10 mg/kg)
Mean Tumor Volume (mm3)
1000
800
600
400
200
0
GDC-0973
0
5
10
15
20
25
Day

FIG. 6

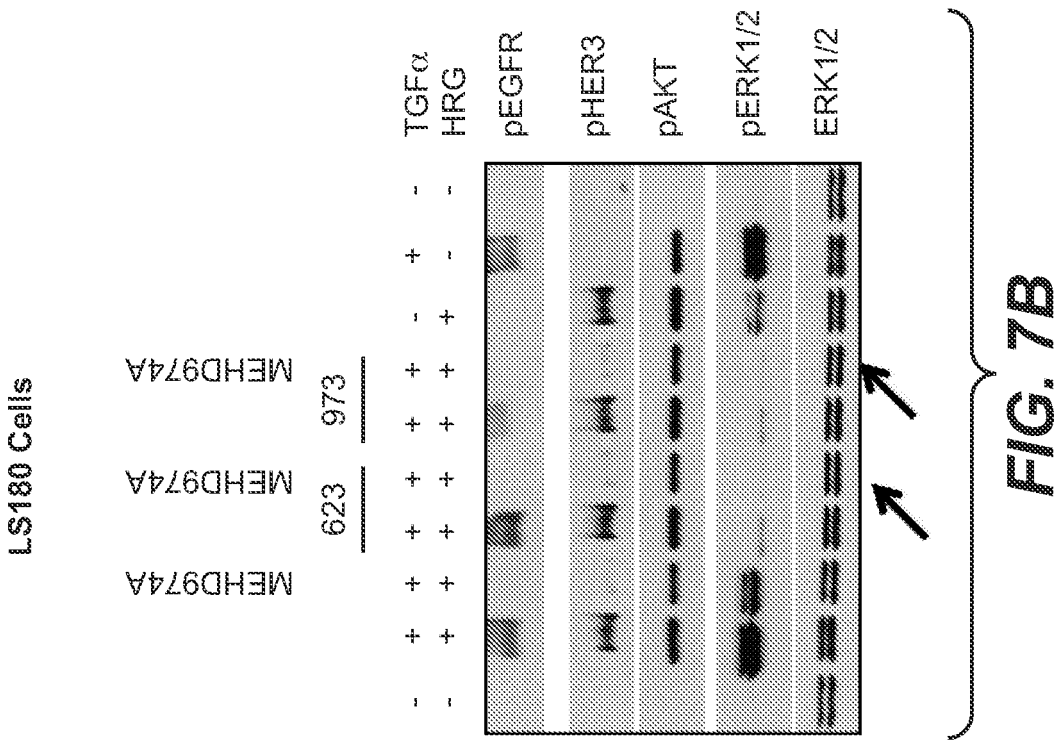

LS180 Cells
MEHD974A
MEHD974A
MEHD974A
623
973
TGFα
HRG
pEGFR
pHER3
pAKT
pERK1/2
ERK1/2

FIG. 7B

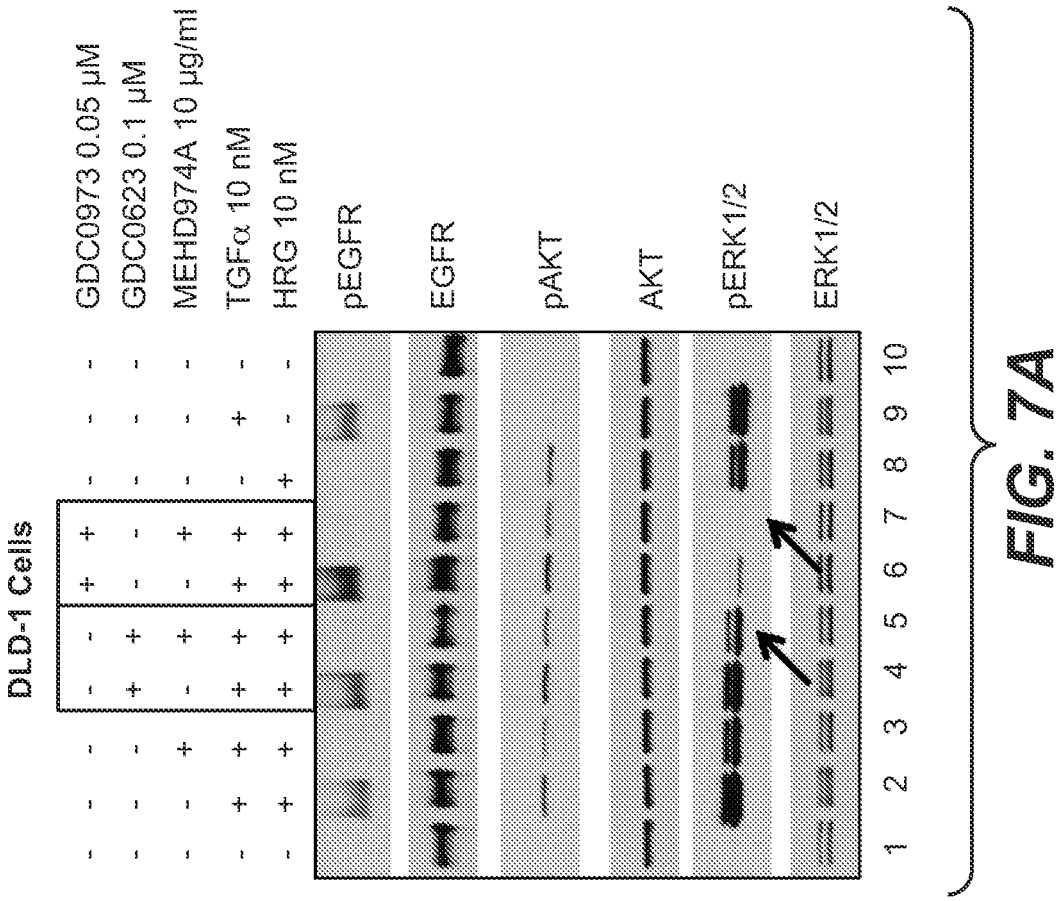

DLD-1 Cells
GDC0973 0.05 µM
GDC0623 0.1 µM
MEHD974A 10 µg/ml
TGFα 10 nM
HRG 10 nM
pEGFR
EGFR
pAKT
AKT
pERK1/2
ERK1/2
1 2 3 4 5 6 7 8 9 10

FIG. 7A

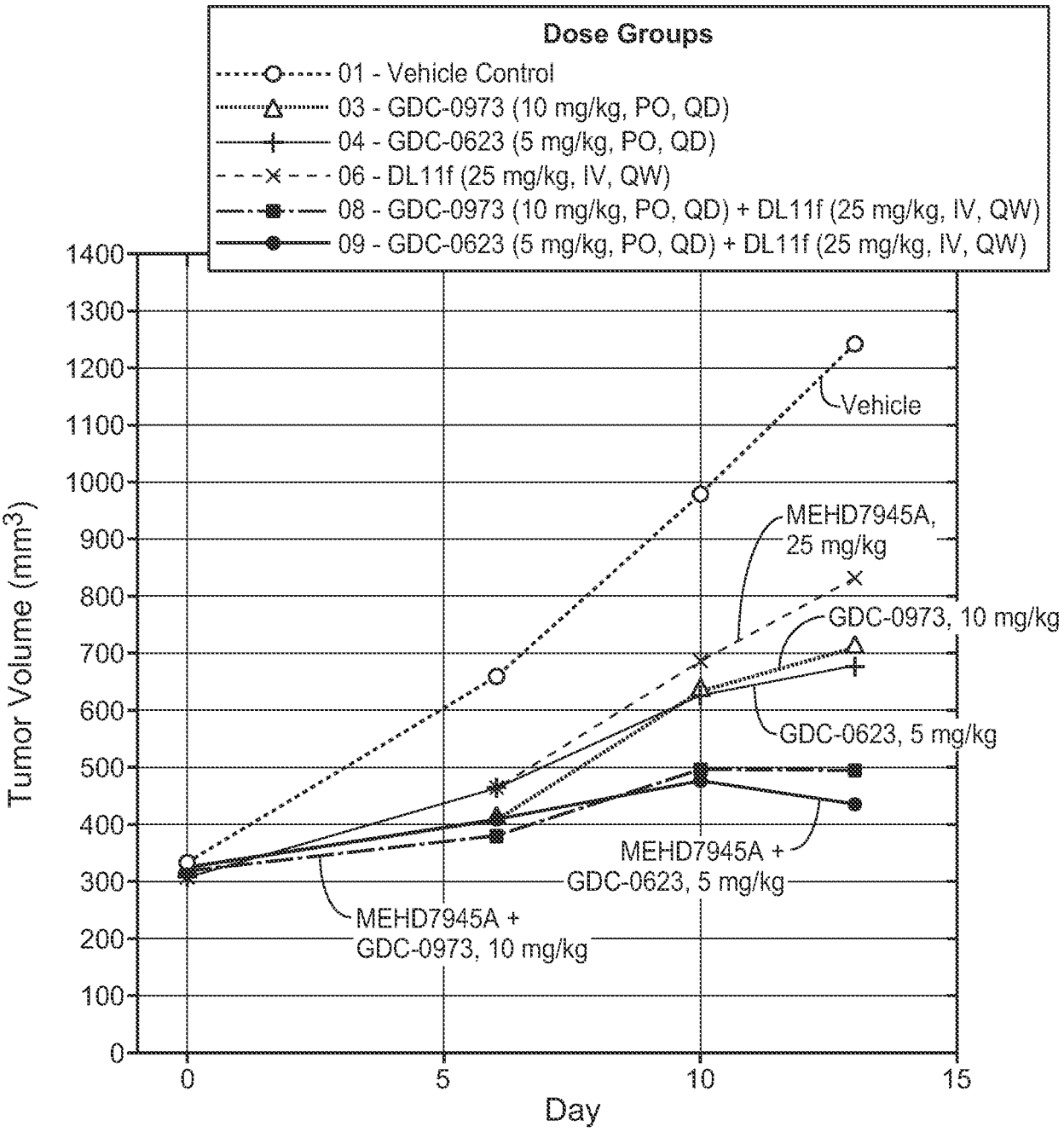

Dose Groups
01 - Vehicle Control
03 - GDC-0973 (10 mg/kg, PO, QD)
04 - GDC-0623 (5 mg/kg, PO, QD)
06 - DL11f (25 mg/kg, IV, QW)
08 - GDC-0973 (10 mg/kg, PO, QD) + DL11f (25 mg/kg, IV, QW)
09 - GDC-0623 (5 mg/kg, PO, QD) + DL11f (25 mg/kg, IV, QW)
Tumor Volume (mm3)
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
0
5
10
15
Day
Vehicle
MEHD7945A, 25 mg/kg
GDC-0973, 10 mg/kg
GDC-0623, 5 mg/kg
MEHD7945A + GDC-0623, 5 mg/kg
MEHD7945A + GDC-0973, 10 mg/kg

FIG. 8

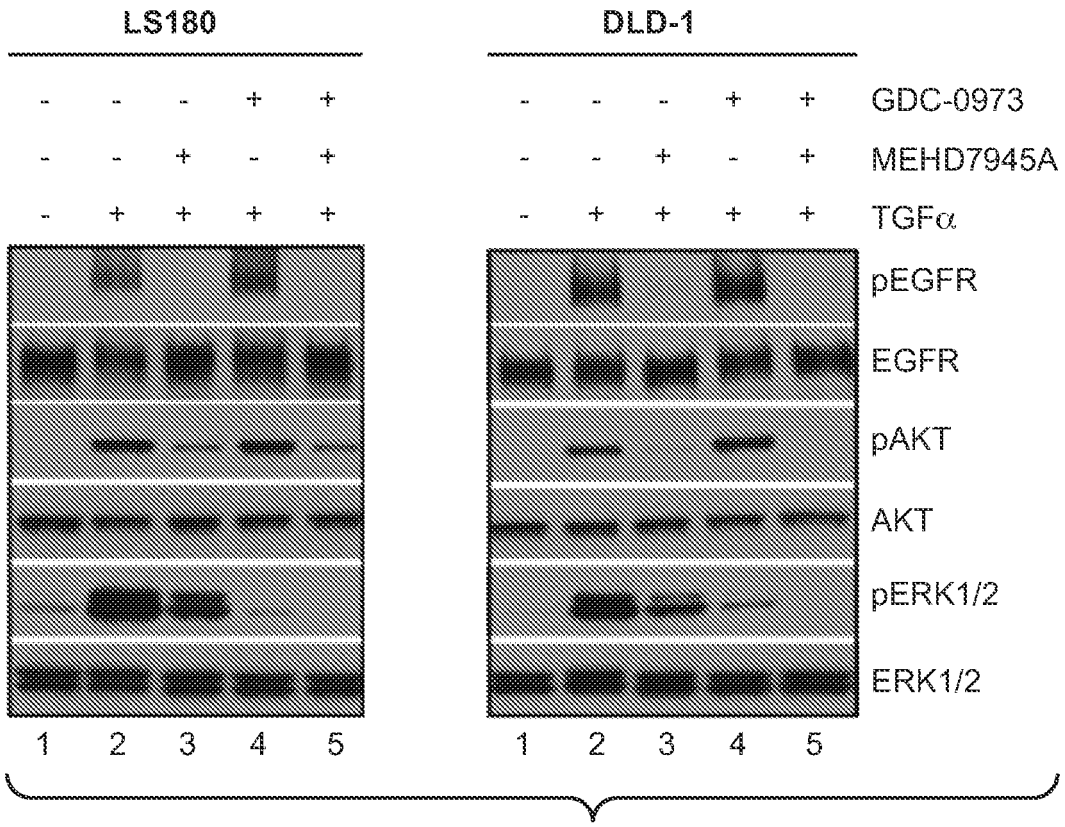

LS180
DLD-1
GDC-0973
MEHD7945A
TGFα
pEGFR
EGFR
pAKT
AKT
pERK1/2
ERK1/2
1 2 3 4 5
1 2 3 4 5

FIG. 9

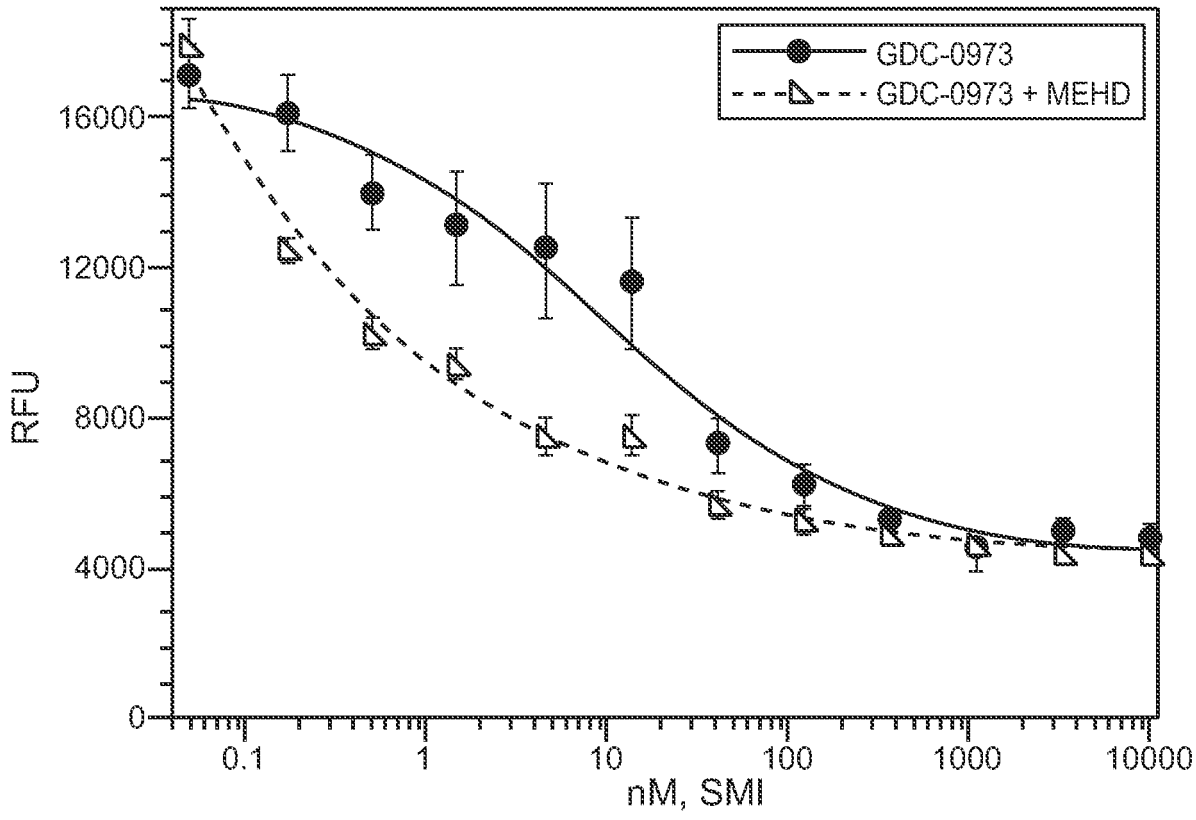

GDC-0973
GDC-0973 + MEHD
RFU
16000
12000
8000
4000
0
0.1
1
10
100
1000
10000
nM, SMI

FIG. 10

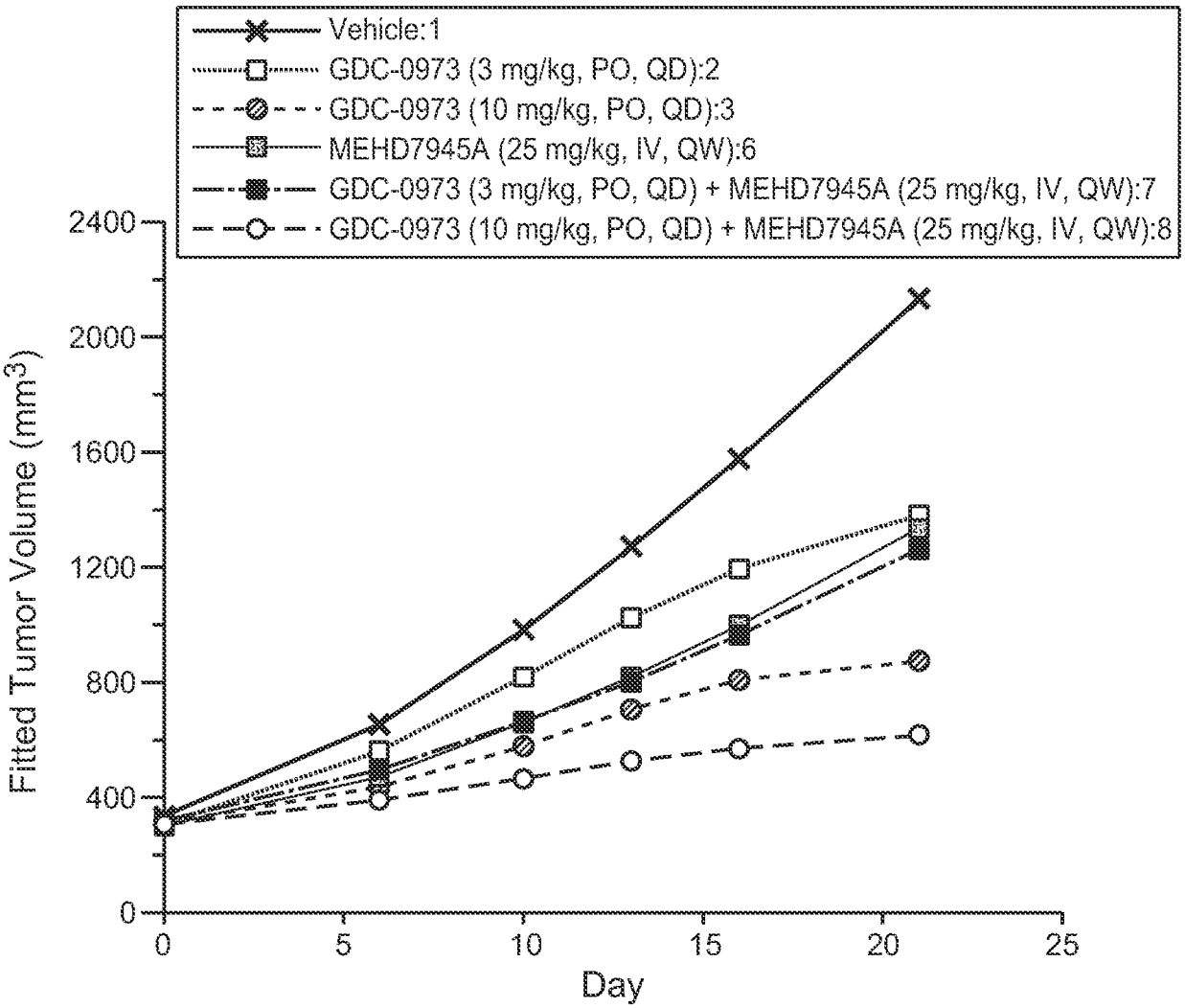


FIG. 11A

Group (n = 8)	Test Material	Dose (mg/kg)	% TGI (Estimated)	% TGI (Lower CI)	% TGI (Upper CI)
1	Vehicle (MCT) Vehicle (HB#8)	0 0	0	0	0
2	Cobimetinib	3	28	-55	64
3	Cobimetinib	10	63	16	83
6	MEHD7954A	25	44	-15	73
7	Cobimetinib MEHD7954A	3 25	48	-11	74
8	Cobimetinib MEHD7954A	10 25	79	49	92

FIG. 11B

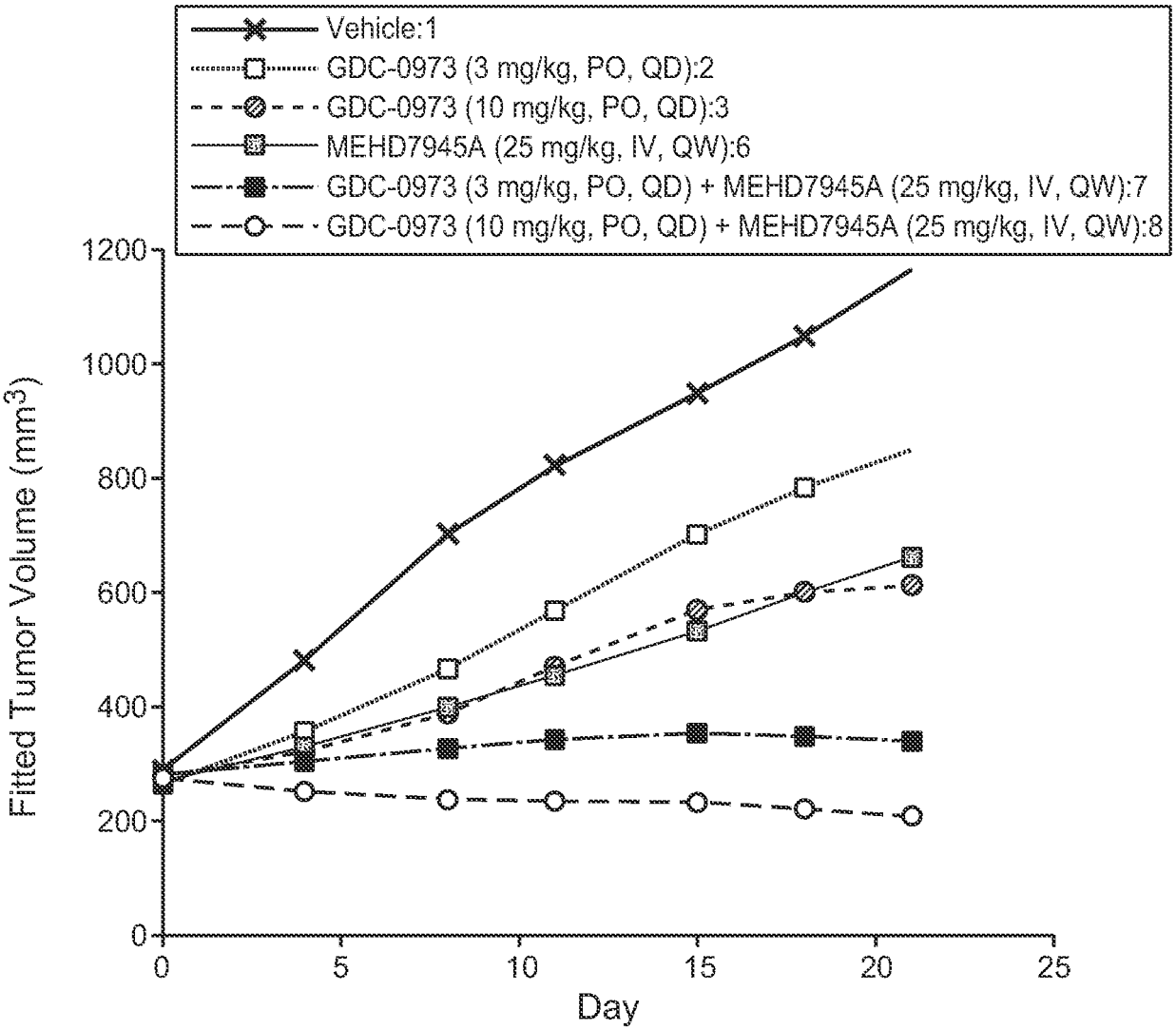


FIG. 12A

Group (n = 8)	Test Material	Dose (mg/kg)	% TGI (Estimated)	% TGI (Lower CI)	% TGI (Upper CI)
1	Vehicle (MCT) Vehicle (HB#8)	0 0	0	0	0
2	Cobimetinib	3	39	13	59
3	Cobimetinib	10	62	41	75
6	MEHD7954A	25	62	44	76
7	Cobimetinib MEHD7954A	3 25	90	78	99
8	Cobimetinib MEHD7954A	10 25	108	102	115

FIG. 12B

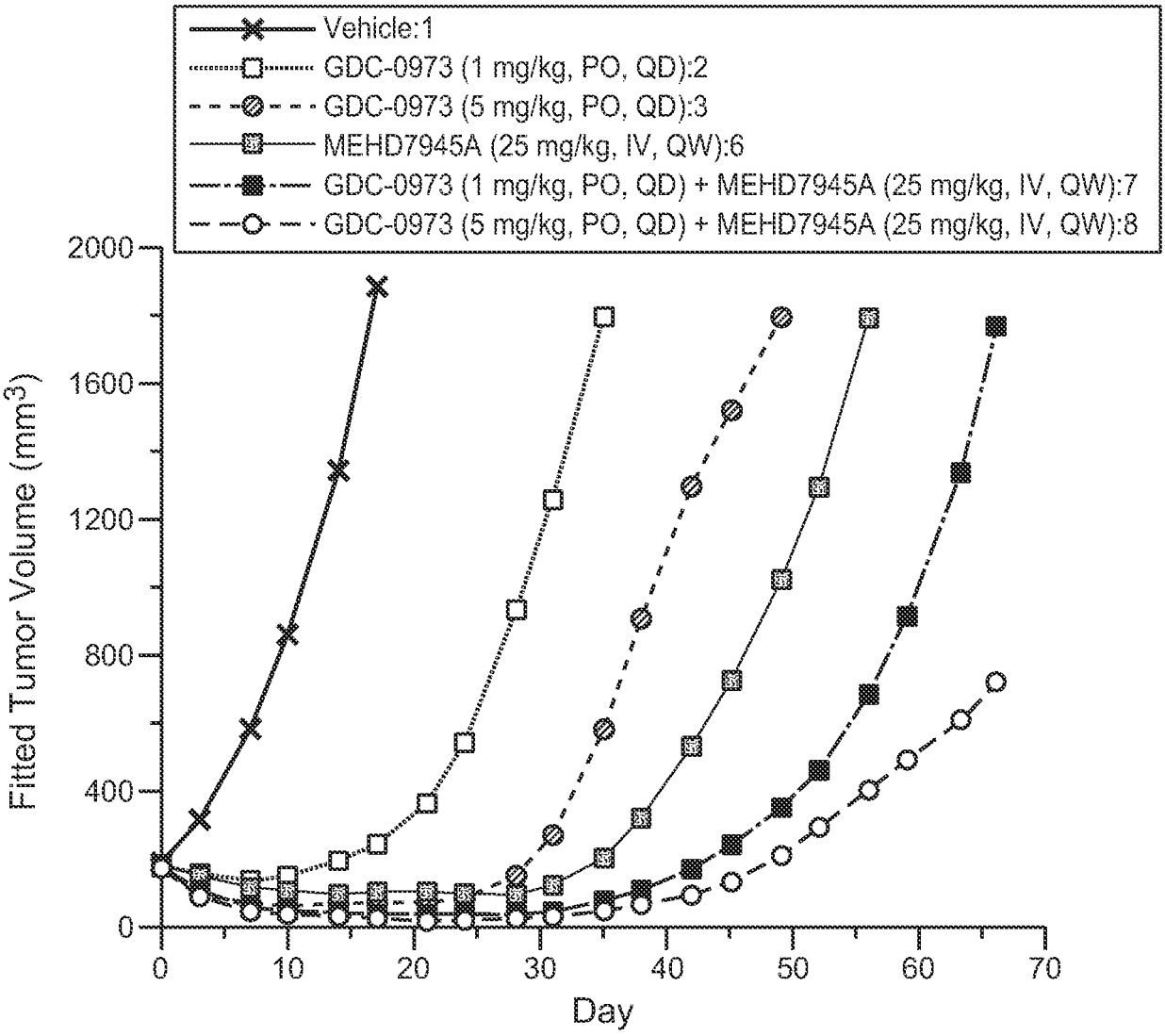

Vehicle:1
GDC-0973 (1 mg/kg, PO, QD):2
GDC-0973 (5 mg/kg, PO, QD):3
MEHD7945A (25 mg/kg, IV, QW):6
GDC-0973 (1 mg/kg, PO, QD) + MEHD7945A (25 mg/kg, IV, QW):7
GDC-0973 (5 mg/kg, PO, QD) + MEHD7945A (25 mg/kg, IV, QW):8
Fitted Tumor Volume (mm3)
2000
1600
1200
800
400
0
0
10
20
30
40
50
60
70
Day

FIG. 13A

Group (n = 10)	Test Material	Dose (mg/kg)	% TGI (Estimated)	% TGI (Lower CI)	% TGI (Upper CI)
1	Vehicle (MCT, HB#8)	0	0	0	0
2	Cobimetinib	1	88	73	98
3	Cobimetinib	5	109	104	119
6	MEHD7954A	25	107	102	116
7	Cobimetinib MEHD7954A	1 25	113	106	124
8	Cobimetinib MEHD7954A	5 25	114	106	124

FIG. 13B

Group (n = 10)	Test Material	Dose (mg/kg)	TTP x2	TTP x5	PR	CR
1	Vehicle (MCT, HB#8)	0	4.5	11.5	0	0
2	Cobimetinib	1	22	28.5	2	0
3	Cobimetinib	5	33	39	2	0
6	MEHD7954A	25	39.5	49	5	0
7	Cobimetinib MEHD7954A	1 25	50.5	60	10	0
8	Cobimetinib MEHD7954A	5 25	56	NA	7	3

FIG. 13C