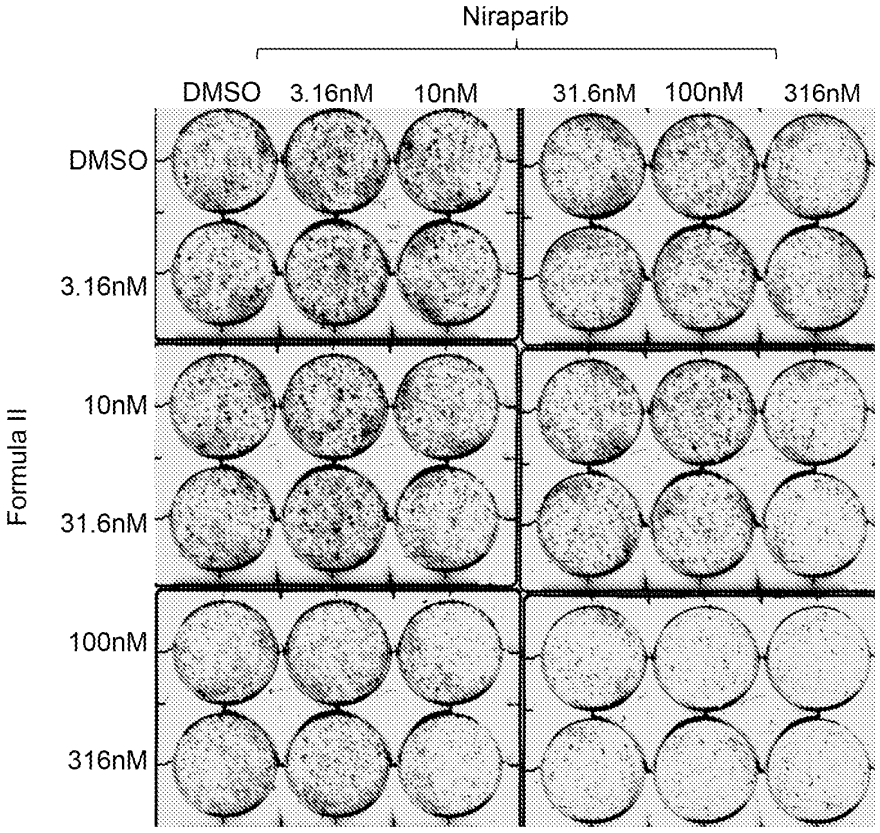
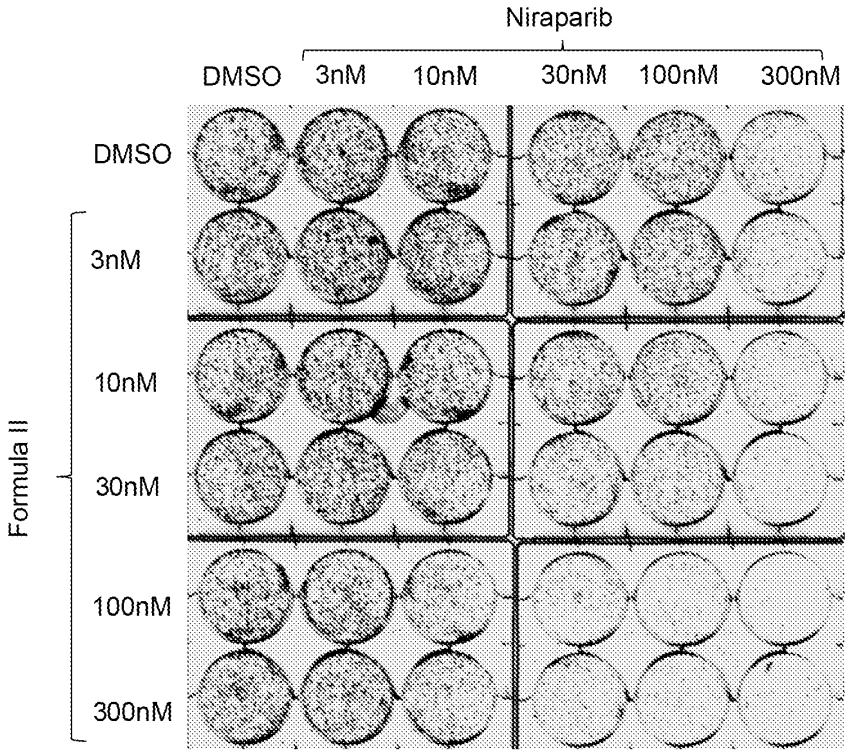


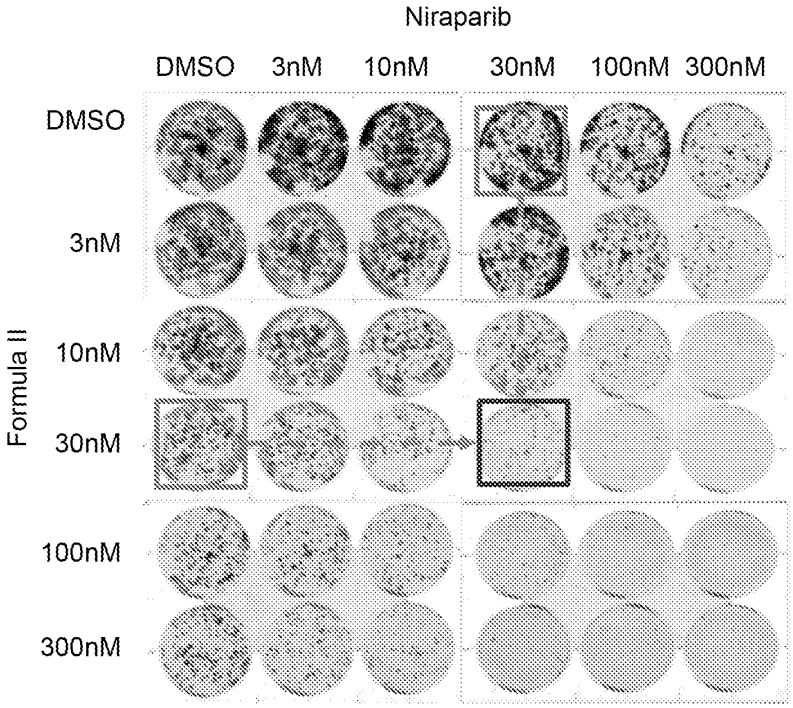
		Niraparib					
		DMSO	3.16nM	10nM	31.6nM	100nM	316nM
Formula II	DMSO	100	131	111	114	99	62
	3.16nM	115	123	115	107	94	56
	10nM	106	128	94	94	77	50
	31.6nM	96	126	79	87	69	30
	100nM	89	85	66	41	26	21
	316nM	74	75	46	34	26	19

FIG. 1



		Niraparib					
		DMSO	3nM	10nM	30nM	100nM	300nM
Formula II	DMSO	100	93	85	74	49	18
	3nM	83	94	75	72	50	14
	10nM	88	87	76	57	34	13
	30nM	75	73	60	32	17	9
	100nM	69	53	34	19	11	8
	300nM	52	42	24	15	9	7

FIG. 2



		Niraparib Conc(nM)					
		0	3	10	30	100	300
Formula II (nM)	0	100	97	64	61	35	11
	3	89	82	65	56	28	7
	10	65	59	36	26	9	4
	30	46	32	12	6	3	2
	100	14	10	6	3	2	2
	300	15	7	6	3	2	2

FIG. 3

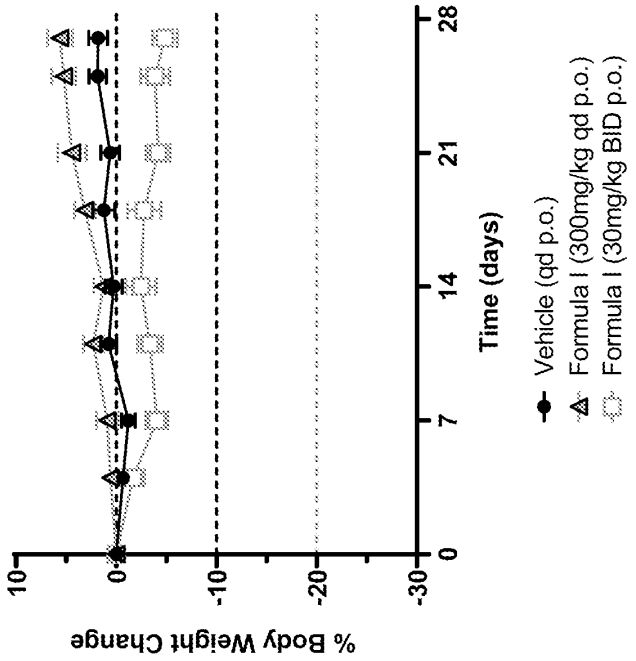

% Body Weight Change
10
0
-10
-20
-30
0
7
14
21
28
Time (days)
Vehicle (qd p.o.)
Formula I (300mg/kg qd p.o.)
Formula I (30mg/kg BID p.o.)

FIG. 4B

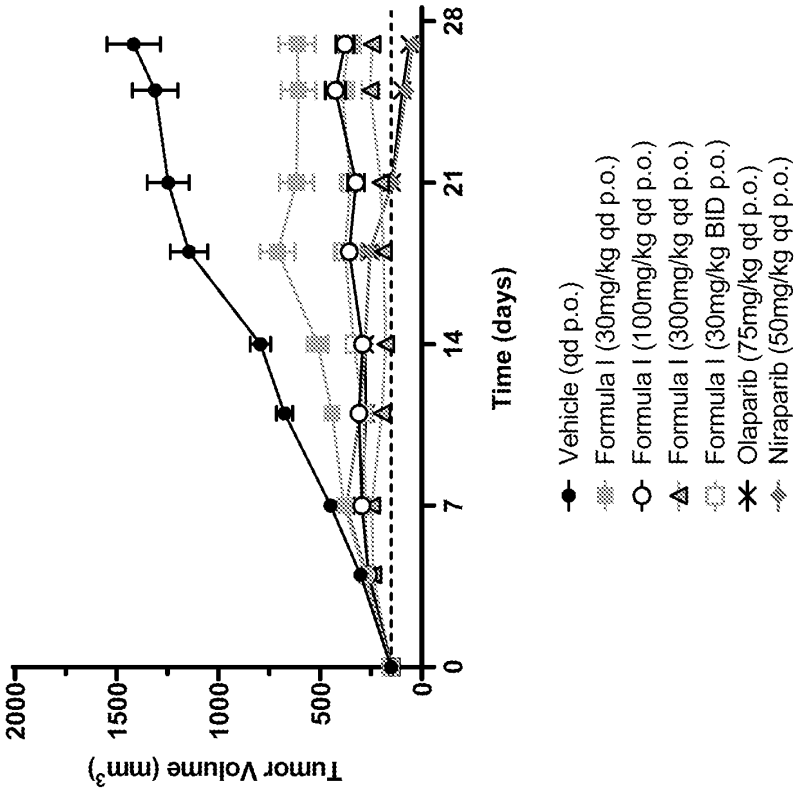

Tumor Volume (mm3)
2000
1500
1000
500
0
0
7
14
21
28
Time (days)
Vehicle (qd p.o.)
Formula I (30mg/kg qd p.o.)
Formula I (100mg/kg qd p.o.)
Formula I (300mg/kg qd p.o.)
Formula I (30mg/kg BID p.o.)
Olaparib (75mg/kg qd p.o.)
Niraparib (50mg/kg qd p.o.)

FIG. 4A

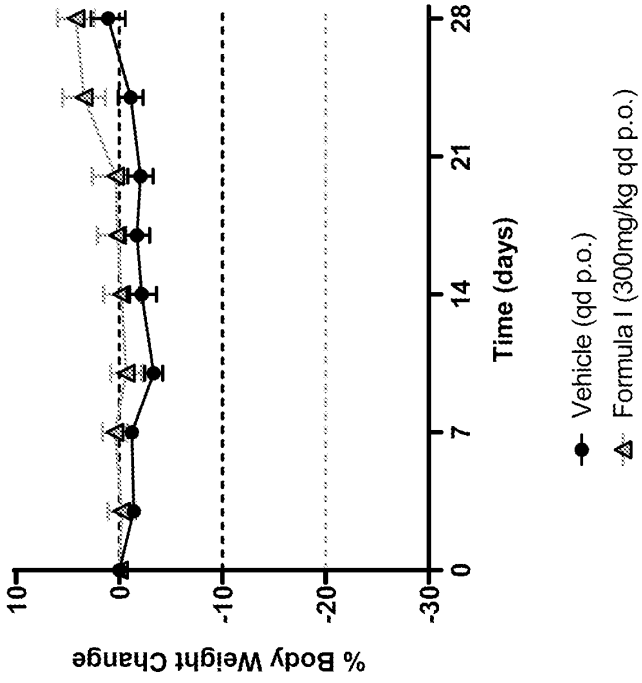

% Body Weight Change
10
0
-10
-20
-30
0
7
14
21
28
Time (days)
Vehicle (qd p.o.)
Formula I (300mg/kg qd p.o.)

FIG. 5B

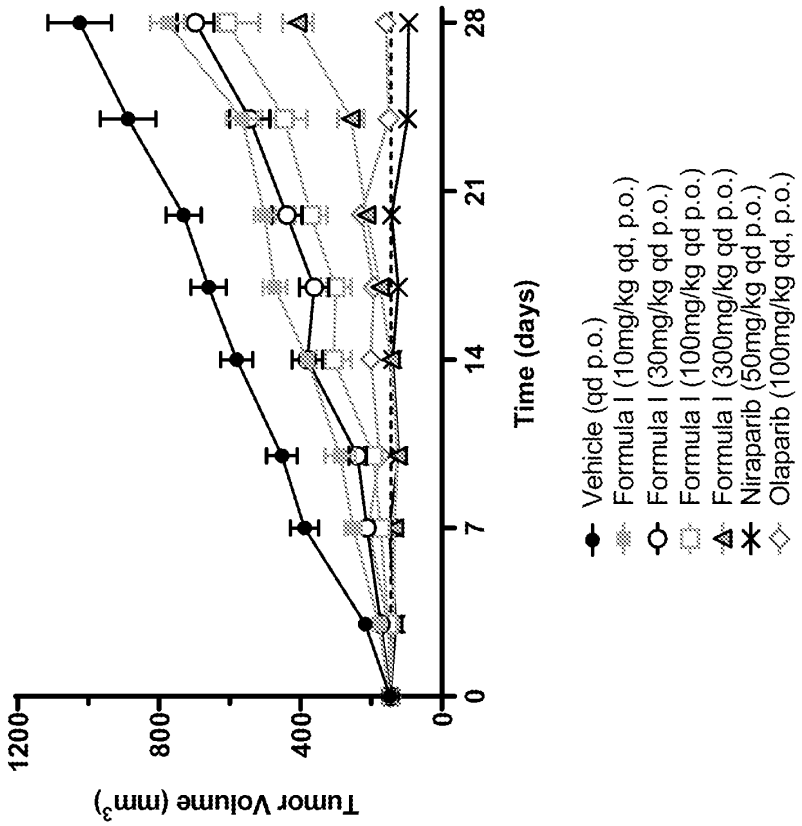

Tumor Volume (mm3)
1200
800
400
0
0
7
14
21
28
Time (days)
Vehicle (qd p.o.)
Formula I (10mg/kg qd, p.o.)
Formula I (30mg/kg qd p.o.)
Formula I (100mg/kg qd p.o.)
Formula I (300mg/kg qd p.o.)
Niraparib (50mg/kg qd p.o.)
Olaparib (100mg/kg qd, p.o.)

FIG. 5A

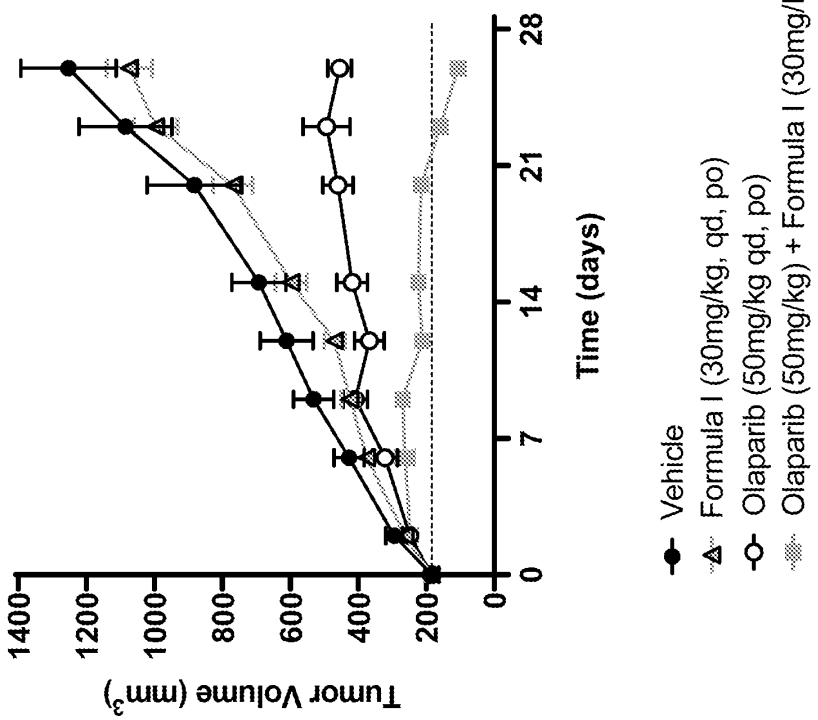

Tumor Volume (mm3)
1400
1200
1000
800
600
400
200
0
0
7
14
21
28
Time (days)
Vehicle
Formula I (30mg/kg, qd, po)
Olaparib (50mg/kg qd, po)
Olaparib (50mg/kg) + Formula I (30mg/kg)

FIG. 6A

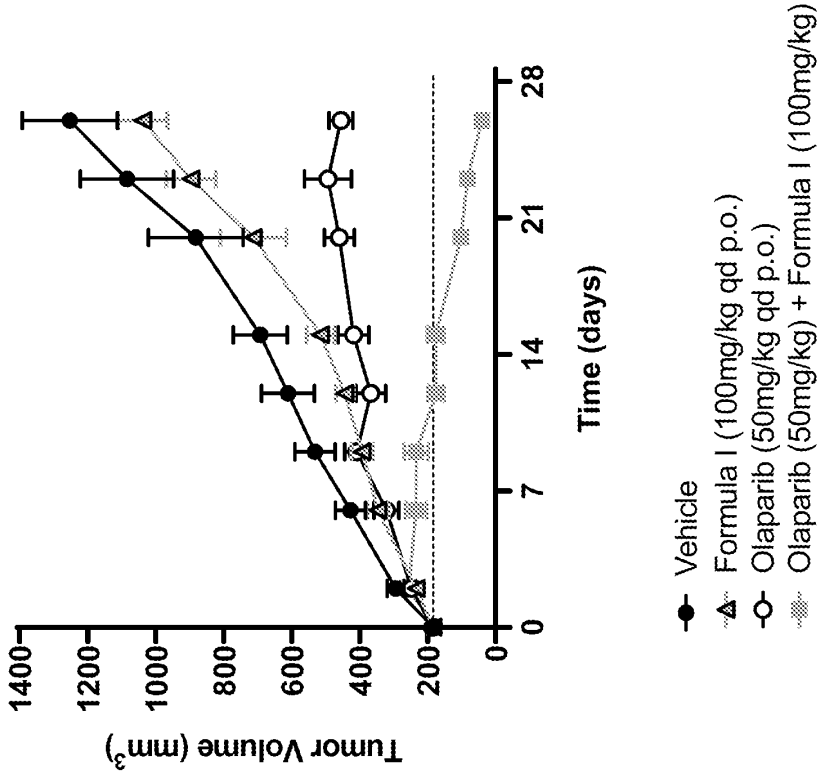

Tumor Volume (mm3)
1400
1200
1000
800
600
400
200
0
0
7
14
21
28
Time (days)
Vehicle
Formula I (100mg/kg qd p.o.)
Olaparib (50mg/kg qd p.o.)
Olaparib (50mg/kg) + Formula I (100mg/kg)

FIG. 6B

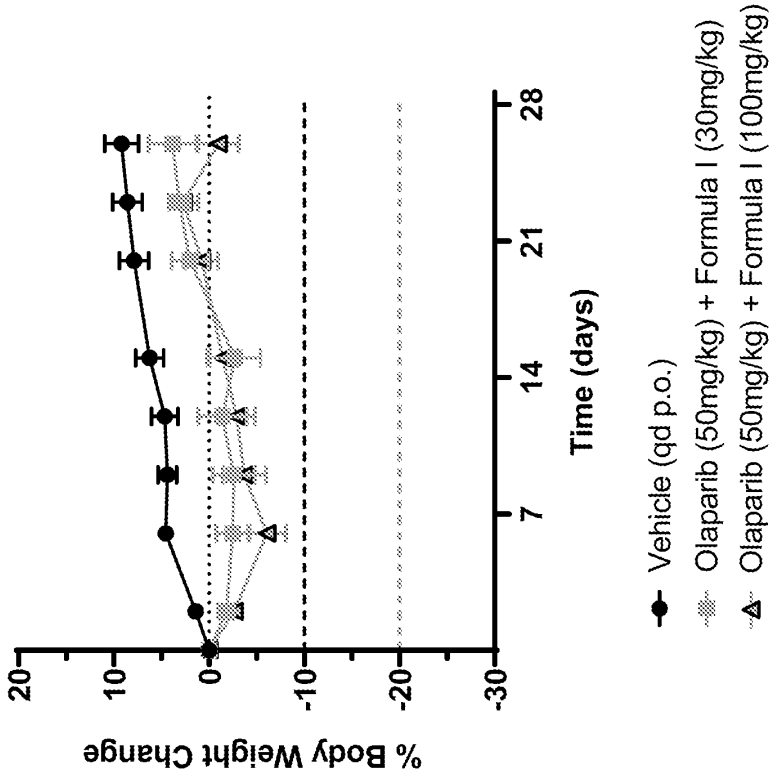

% Body Weight Change
20
10
0
-10
-20
-30
7
14
21
28
Time (days)
Vehicle (qd p.o.)
Olaparib (50mg/kg) + Formula I (30mg/kg)
Olaparib (50mg/kg) + Formula I (100mg/kg)

FIG. 6C

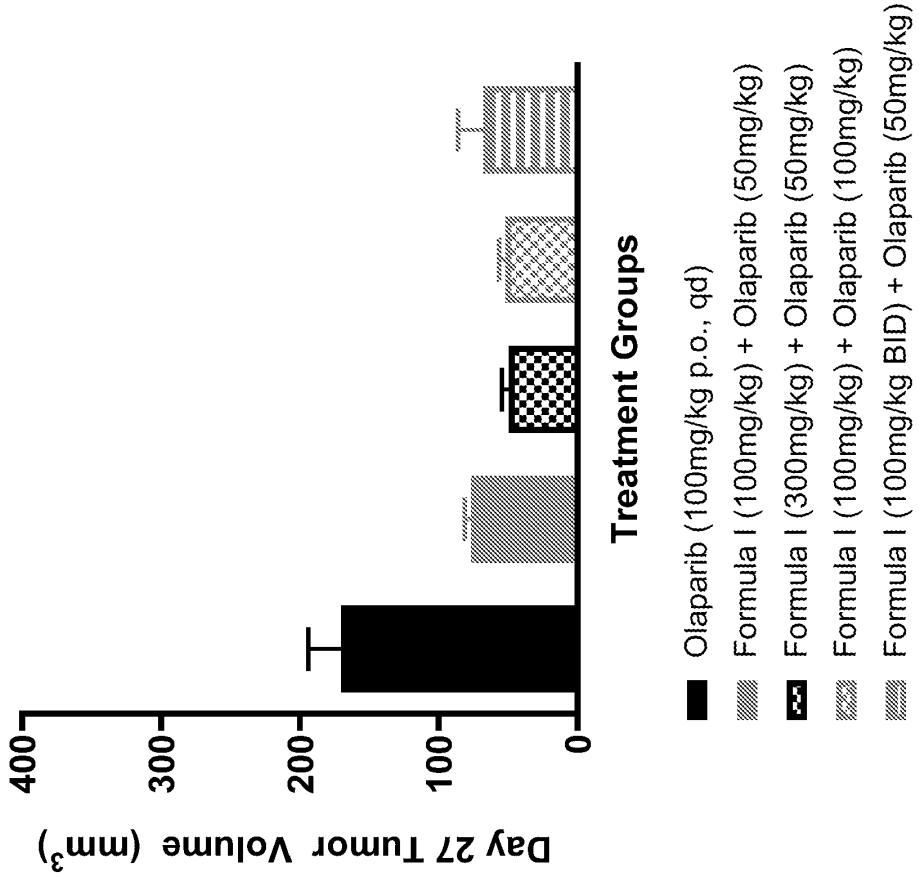

Day 27 Tumor Volume (mm3)
400
300
200
100
0
Treatment Groups
Olaparib (100mg/kg p.o., qd)
Formula I (100mg/kg) + Olaparib (50mg/kg)
Formula I (300mg/kg) + Olaparib (50mg/kg)
Formula I (100mg/kg) + Olaparib (100mg/kg)
Formula I (100mg/kg BID) + Olaparib (50mg/kg)

FIG. 6D

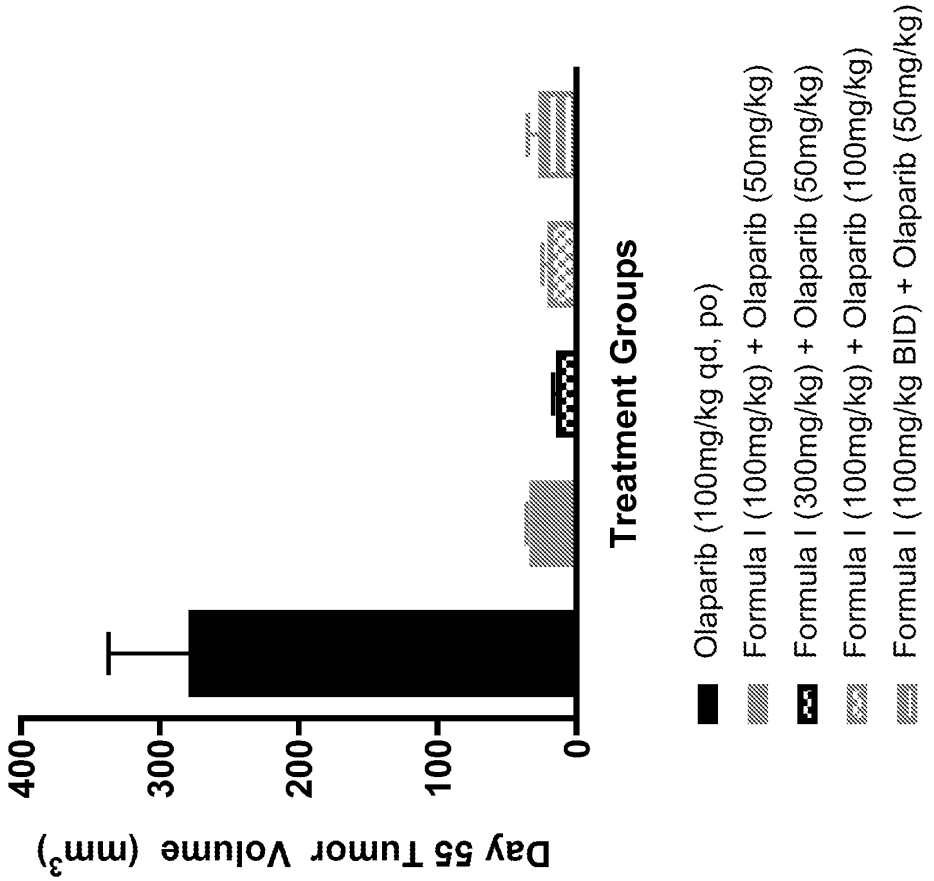

Day 55 Tumor Volume (mm3)
400
300
200
100
0
Treatment Groups
Olaparib (100mg/kg qd, po)
Formula I (100mg/kg) + Olaparib (50mg/kg)
Formula I (300mg/kg) + Olaparib (50mg/kg)
Formula I (100mg/kg) + Olaparib (100mg/kg)
Formula I (100mg/kg BID) + Olaparib (50mg/kg)

FIG. 6E

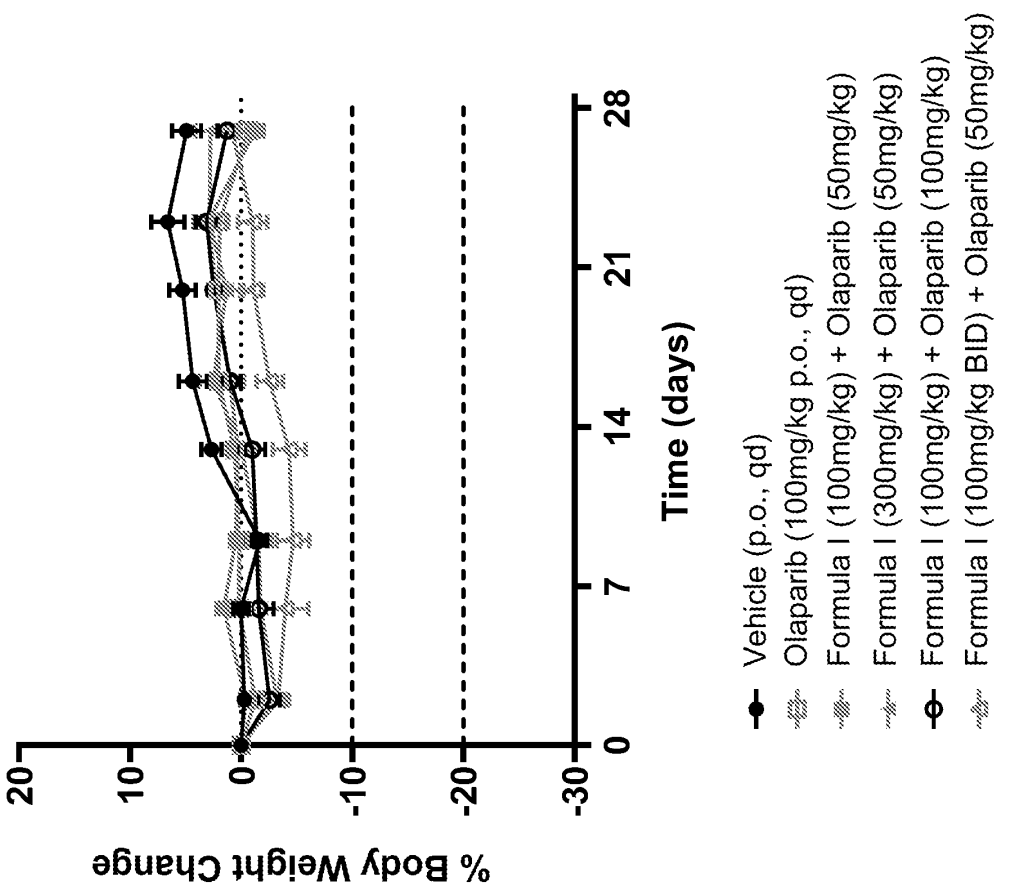

% Body Weight Change
20
10
0
-10
-20
-30
0
7
14
21
28
Time (days)
Vehicle (p.o., qd)
Olaparib (100mg/kg p.o., qd)
Formula I (100mg/kg) + Olaparib (50mg/kg)
Formula I (300mg/kg) + Olaparib (50mg/kg)
Formula I (100mg/kg) + Olaparib (100mg/kg)
Formula I (100mg/kg BID) + Olaparib (50mg/kg)

FIG. 6F

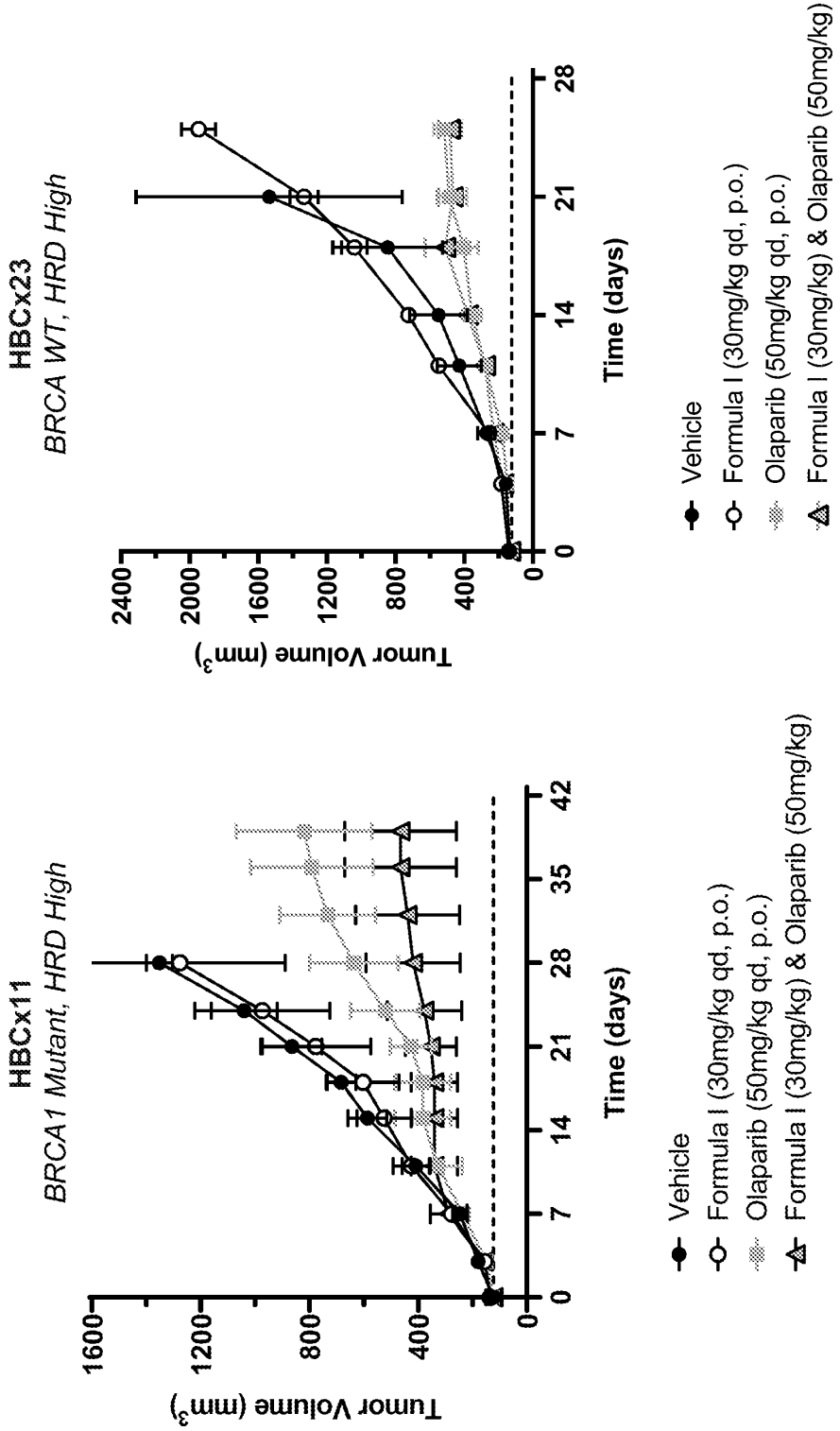

HBCx11
BRCA1 Mutant, HRD High
Tumor Volume (mm³)
1600
1200
800
400
0
0
7
14
21
28
35
42
Time (days)
Vehicle
Formula I (30mg/kg qd, p.o.)
Olaparib (50mg/kg qd, p.o.)
Formula I (30mg/kg) & Olaparib (50mg/kg)
HBCx23
BRCA WT, HRD High
Tumor Volume (mm³)
2400
2000
1600
1200
800
400
0
0
7
14
21
28
Time (days)
Vehicle
Formula I (30mg/kg qd, p.o.)
Olaparib (50mg/kg qd, p.o.)
Formula I (30mg/kg) & Olaparib (50mg/kg)

FIG. 7A

FIG. 7B

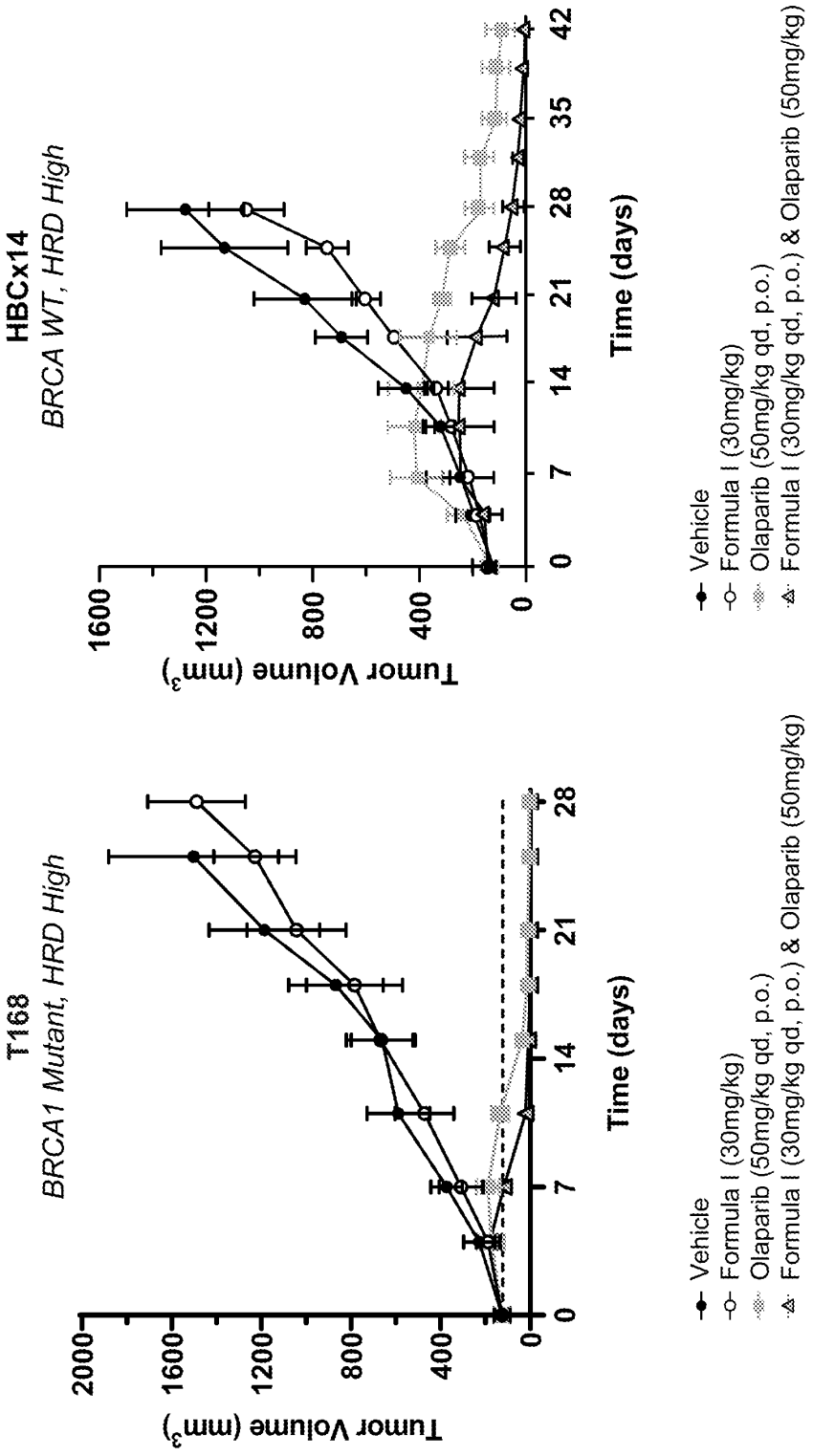

T168
BRCA1 Mutant, HRD High
Tumor Volume (mm³)
2000
1600
1200
800
400
0
0
7
14
21
28
Time (days)
Vehicle
Formula I (30mg/kg)
Olaparib (50mg/kg qd, p.o.)
Formula I (30mg/kg qd, p.o.) & Olaparib (50mg/kg)
HBCx14
BRCA WT, HRD High
Tumor Volume (mm³)
1600
1200
800
400
0
0
7
14
21
28
35
42
Time (days)
Vehicle
Formula I (30mg/kg)
Olaparib (50mg/kg qd, p.o.)
Formula I (30mg/kg qd, p.o.) & Olaparib (50mg/kg)

FIG. 7C

FIG. 7D

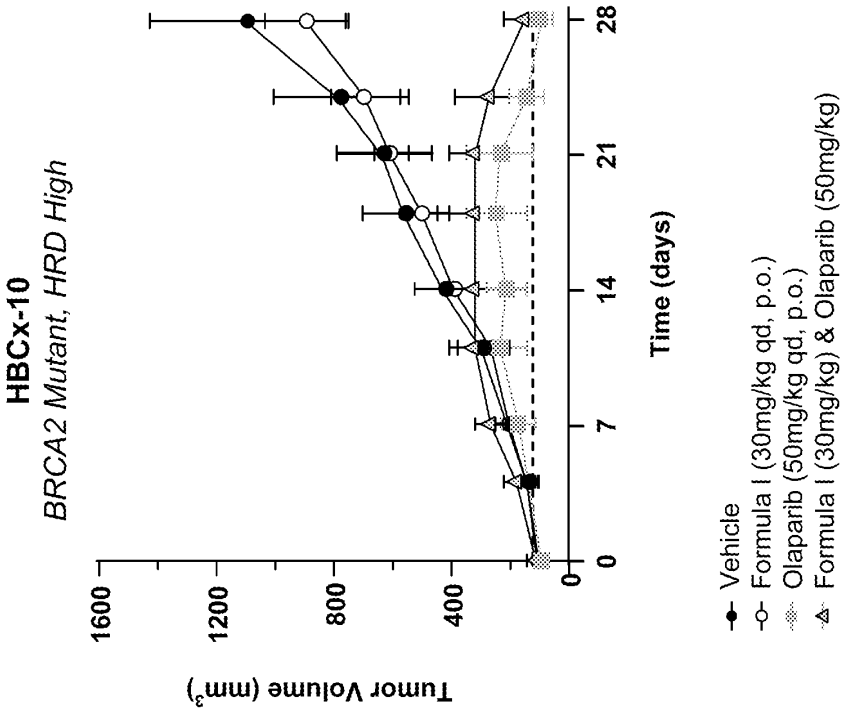

HBCx-10
BRCA2 Mutant, HRD High
Tumor Volume (mm³)
1600
1200
800
400
0
0
7
14
21
28
Time (days)
Vehicle
Formula I (30mg/kg qd, p.o.)
Olaparib (50mg/kg qd, p.o.)
Formula I (30mg/kg) & Olaparib (50mg/kg)

FIG. 7E

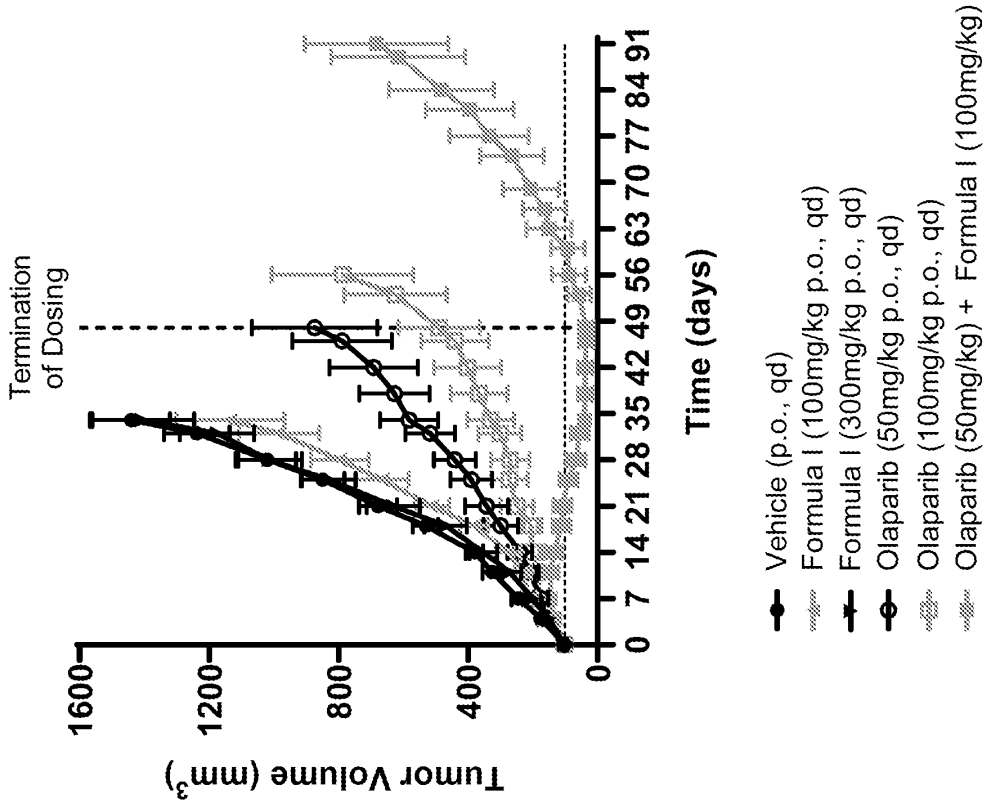

Termination of Dosing
Tumor Volume (mm³)
1600
1200
800
400
0
0 7 14 21 28 35 42 49 56 63 70 77 84 91
Time (days)
Vehicle (p.o., qd)
Formula I (100mg/kg p.o., qd)
Formula I (300mg/kg p.o., qd)
Olaparib (50mg/kg p.o., qd)
Olaparib (100mg/kg p.o., qd)
Olaparib (50mg/kg) + Formula I (100mg/kg)

FIG. 8A

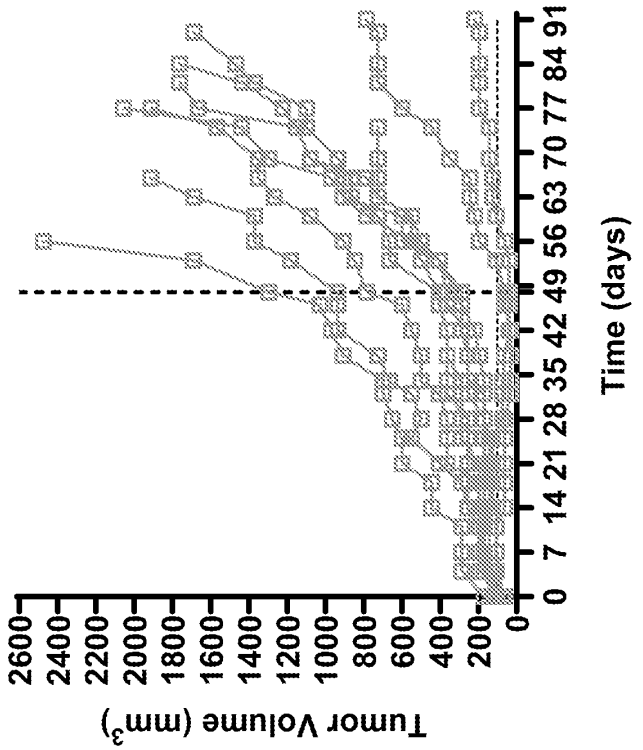

Tumor Volume (mm3)
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
0 7 14 21 28 35 42 49 56 63 70 77 84 91
Time (days)

FIG. 8C

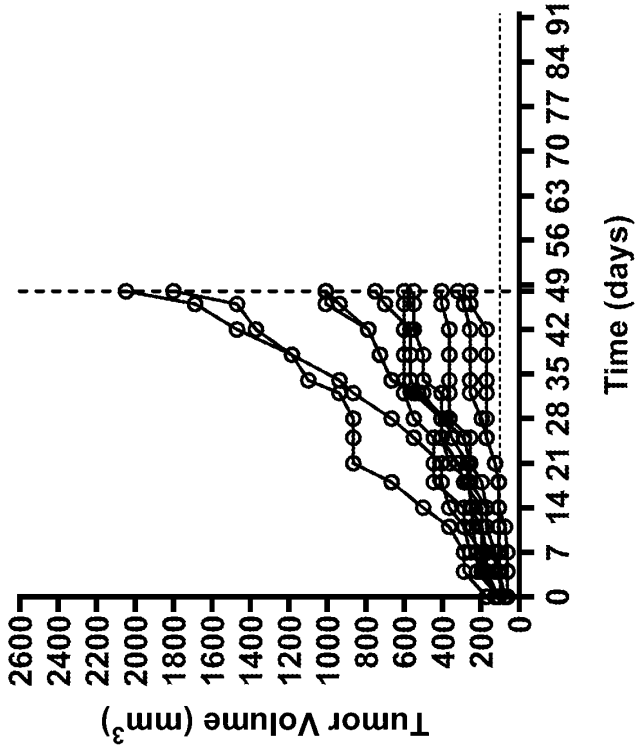

Tumor Volume (mm3)
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
0 7 14 21 28 35 42 49 56 63 70 77 84 91
Time (days)

FIG. 8B

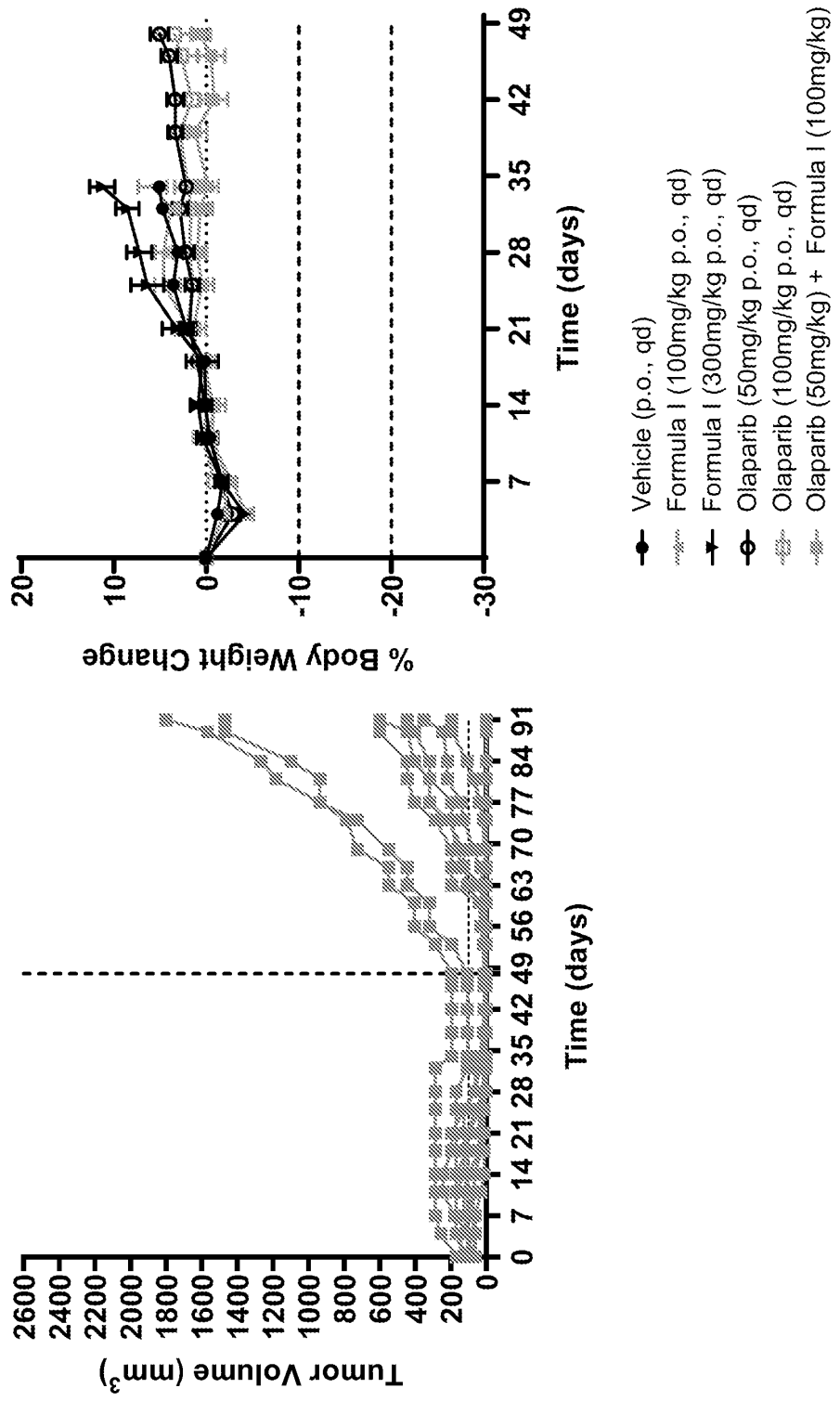

Tumor Volume (mm3)
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
0 7 14 21 28 35 42 49 56 63 70 77 84 91
Time (days)
% Body Weight Change
20
10
0
-10
-20
-30
7 14 21 28 35 42 49
Time (days)
Vehicle (p.o., qd)
Formula I (100mg/kg p.o., qd)
Formula I (300mg/kg p.o., qd)
Olaparib (50mg/kg p.o., qd)
Olaparib (100mg/kg p.o., qd)
Olaparib (50mg/kg) + Formula I (100mg/kg)

FIG. 8D

FIG. 8E

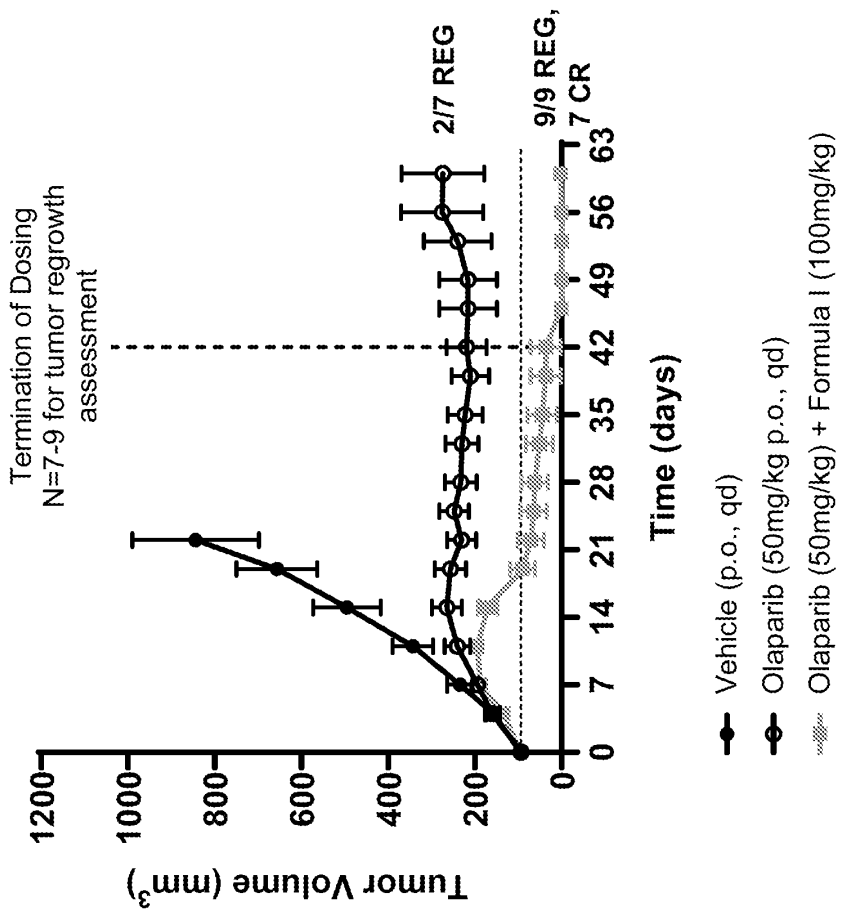

Termination of Dosing
N=7-9 for tumor regrowth assessment
2/7 REG
9/9 REG, 7 CR
Tumor Volume (mm3)
1200
1000
800
600
400
200
0
0
7
14
21
28
35
42
49
56
63
Time (days)
Vehicle (p.o., qd)
Olaparib (50mg/kg p.o., qd)
Olaparib (50mg/kg) + Formula I (100mg/kg)

FIG. 9A

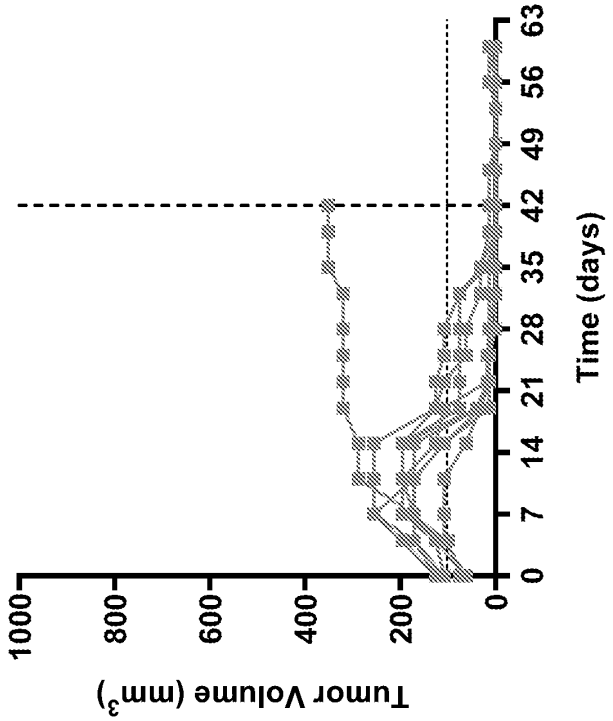

Tumor Volume (mm³)
1000
800
600
400
200
0
0
7
14
21
28
35
42
49
56
63
Time (days)

FIG. 9C

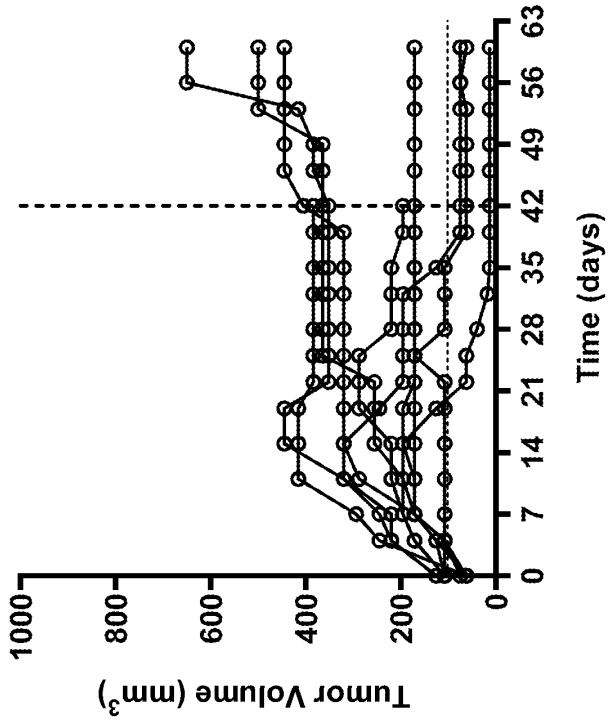

Tumor Volume (mm³)
1000
800
600
400
200
0
0
7
14
21
28
35
42
49
56
63
Time (days)

FIG. 9B

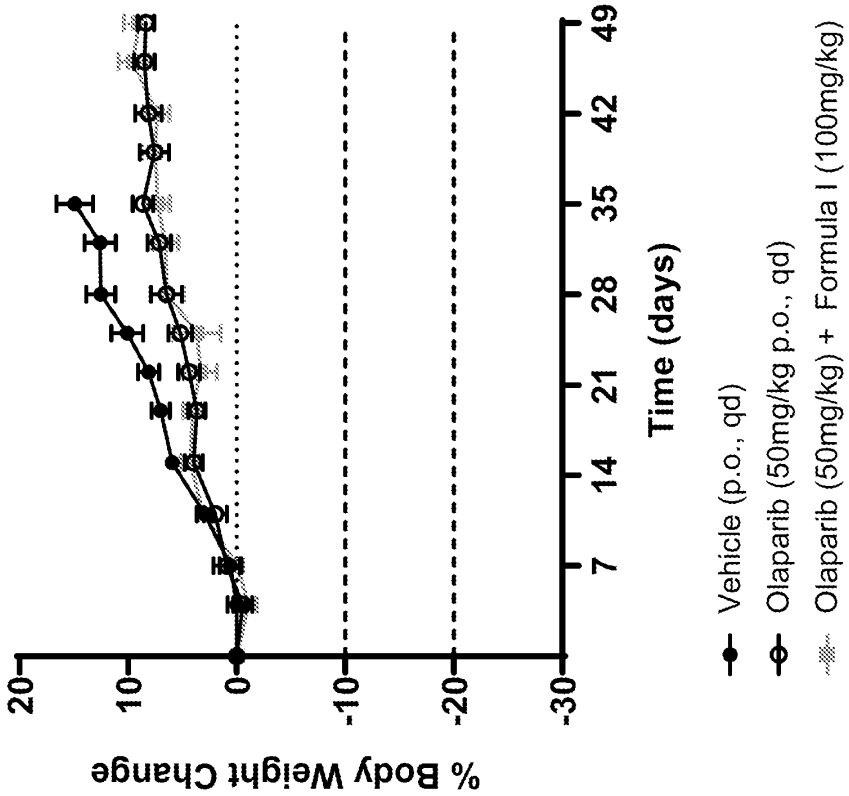

% Body Weight Change
20
10
0
-10
-20
-30
7
14
21
28
35
42
49
Time (days)
Vehicle (p.o., qd)
Olaparib (50mg/kg p.o., qd)
Olaparib (50mg/kg) + Formula I (100mg/kg)

FIG. 9D

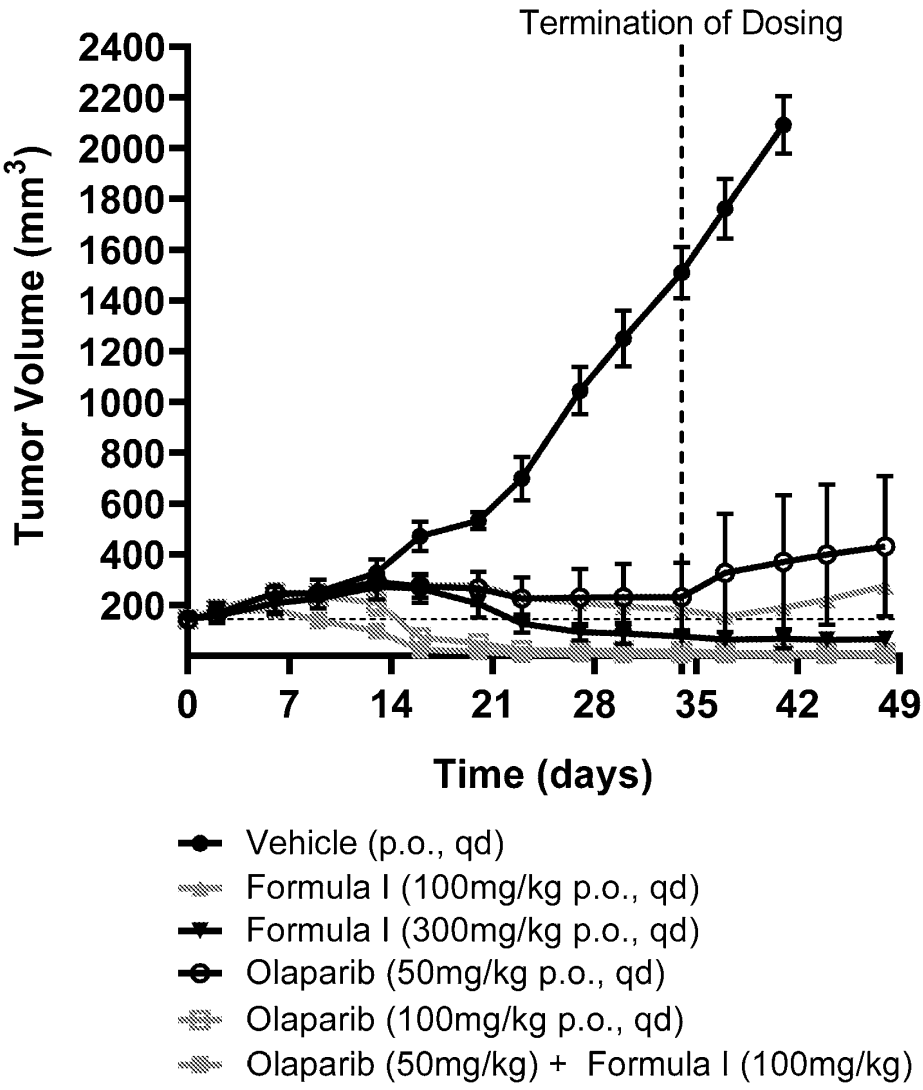

Termination of Dosing
Tumor Volume (mm3)
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
7
14
21
28
35
42
49
Time (days)
Vehicle (p.o., qd)
Formula I (100mg/kg p.o., qd)
Formula I (300mg/kg p.o., qd)
Olaparib (50mg/kg p.o., qd)
Olaparib (100mg/kg p.o., qd)
Olaparib (50mg/kg) + Formula I (100mg/kg)

FIG. 10A

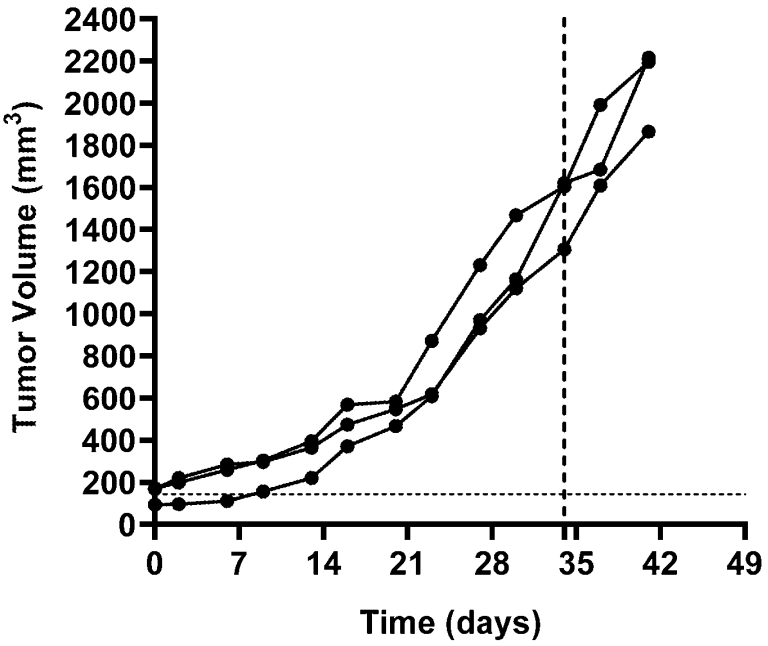


FIG. 10B

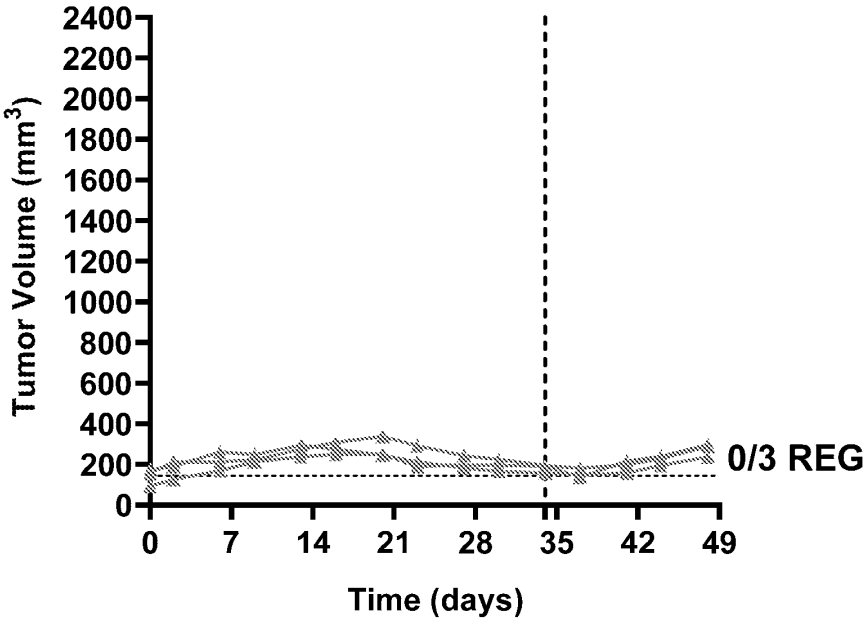


FIG. 10C

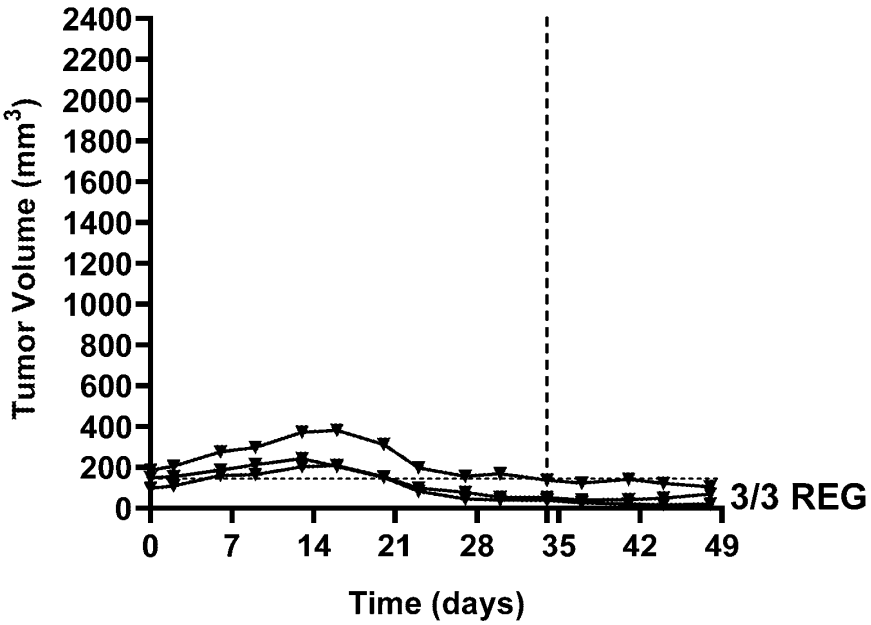


FIG. 10D

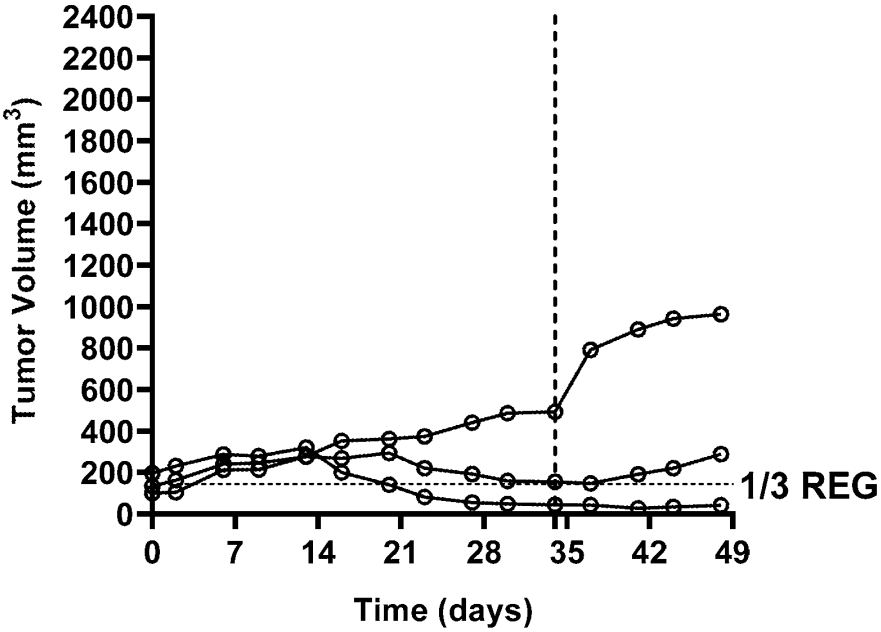


FIG. 10E

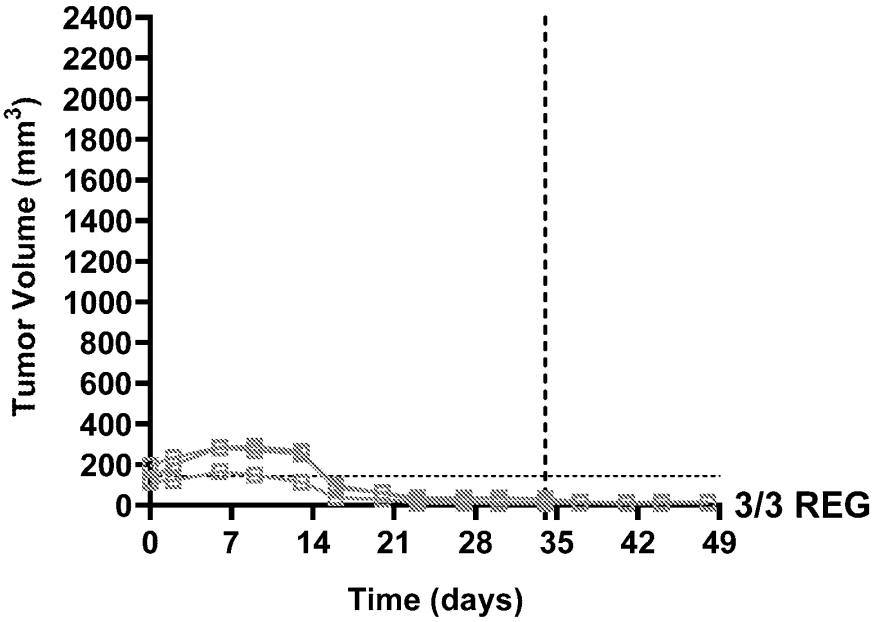


FIG. 10F

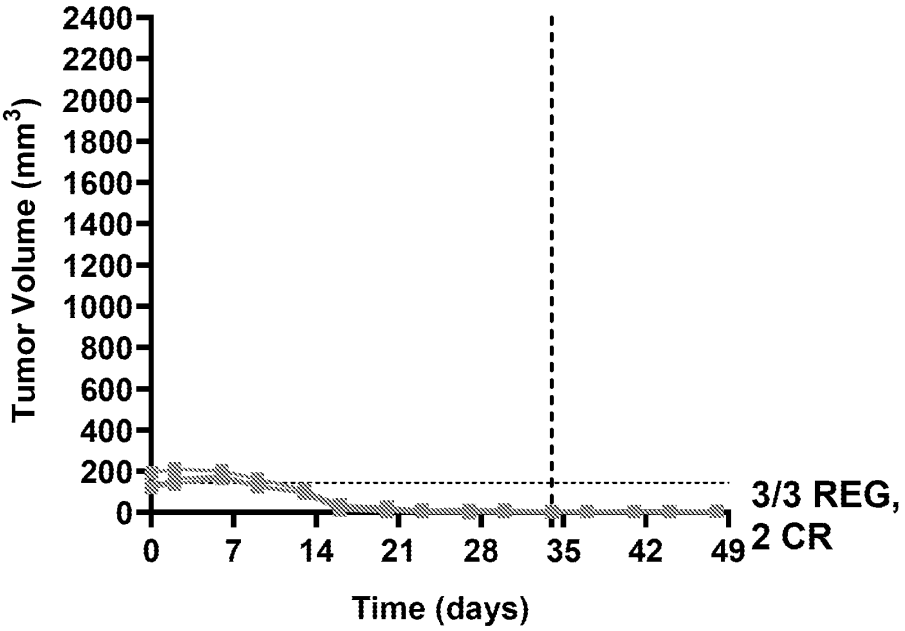


FIG. 10G

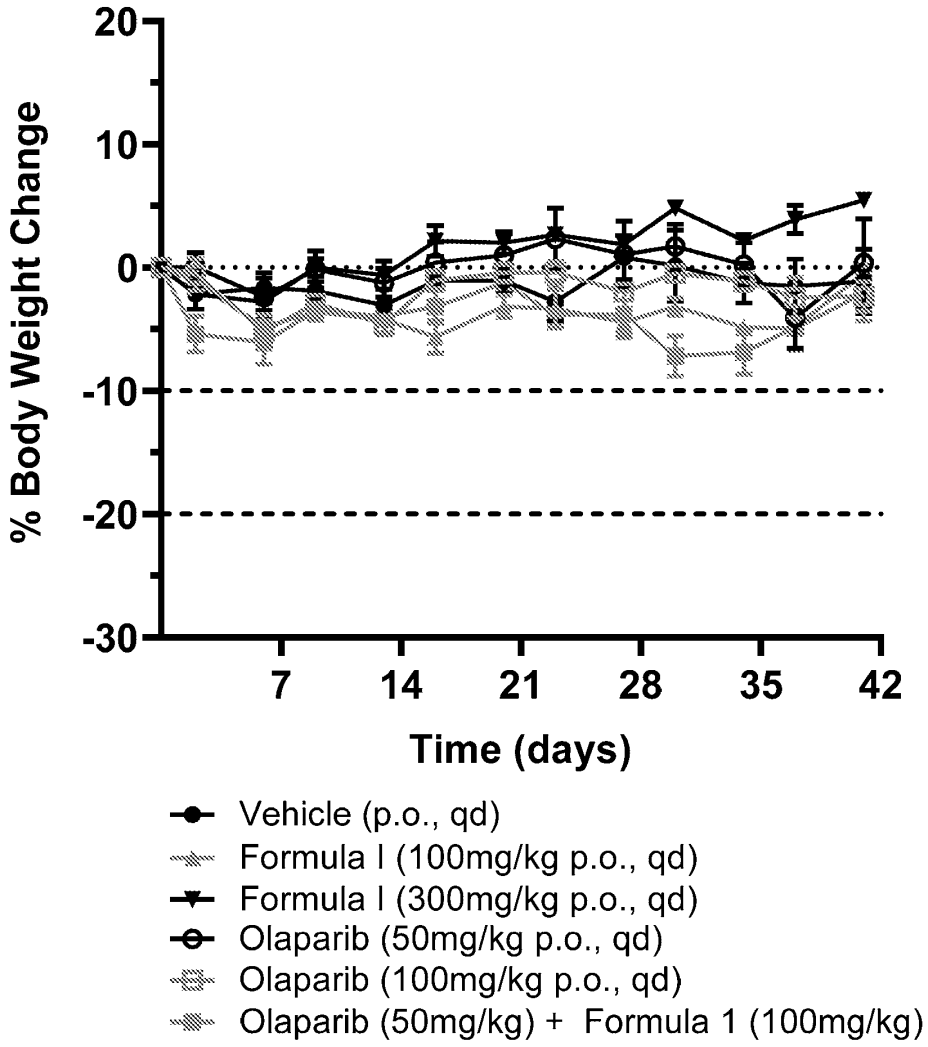

20
10
0
-10
-20
-30
% Body Weight Change
7
14
21
28
35
42
Time (days)
Vehicle (p.o., qd)
Formula I (100mg/kg p.o., qd)
Formula I (300mg/kg p.o., qd)
Olaparib (50mg/kg p.o., qd)
Olaparib (100mg/kg p.o., qd)
Olaparib (50mg/kg) + Formula 1 (100mg/kg)

FIG. 10H

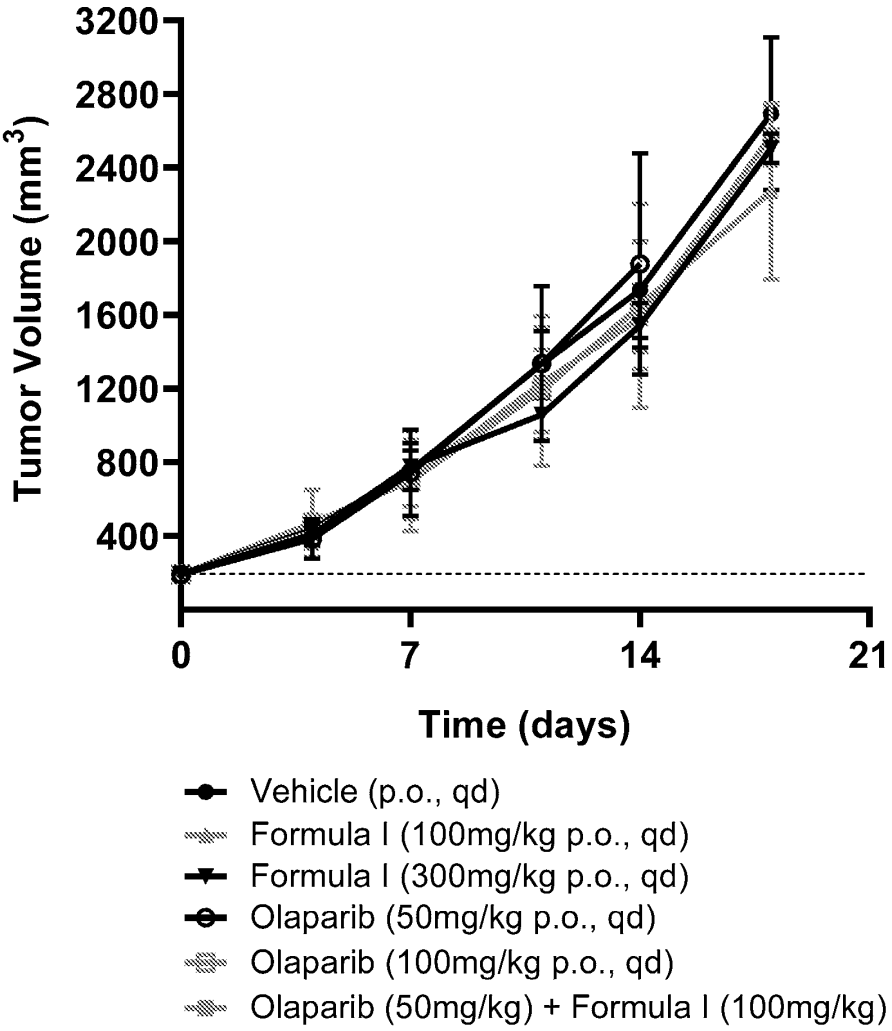

3200
2800
2400
2000
1600
1200
800
400
Tumor Volume (mm3)
0
7
14
21
Time (days)
Vehicle (p.o., qd)
Formula I (100mg/kg p.o., qd)
Formula I (300mg/kg p.o., qd)
Olaparib (50mg/kg p.o., qd)
Olaparib (100mg/kg p.o., qd)
Olaparib (50mg/kg) + Formula I (100mg/kg)

FIG. 11A

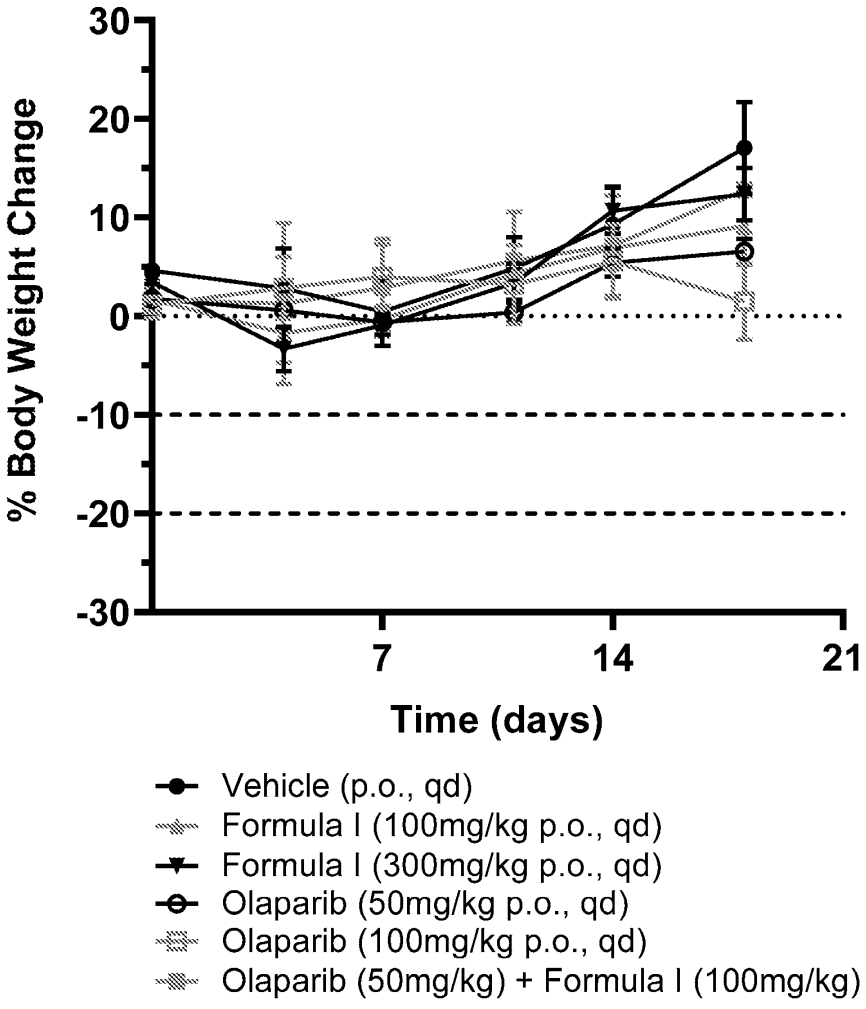

30
20
10
0
-10
-20
-30
% Body Weight Change
7
14
21
Time (days)
Vehicle (p.o., qd)
Formula I (100mg/kg p.o., qd)
Formula I (300mg/kg p.o., qd)
Olaparib (50mg/kg p.o., qd)
Olaparib (100mg/kg p.o., qd)
Olaparib (50mg/kg) + Formula I (100mg/kg)

FIG. 11B

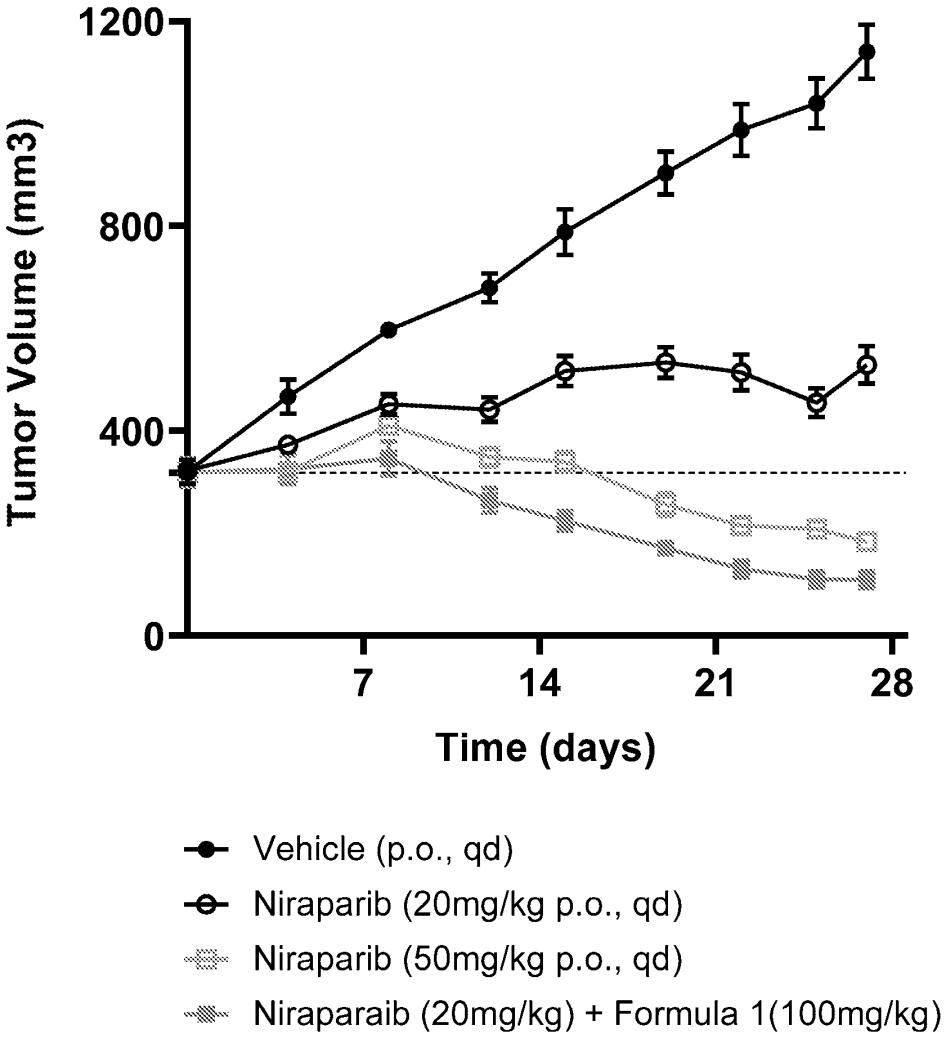

1200
800
400
0
Tumor Volume (mm3)
7
14
21
28
Time (days)
Vehicle (p.o., qd)
Niraparib (20mg/kg p.o., qd)
Niraparib (50mg/kg p.o., qd)
Niraparaib (20mg/kg) + Formula 1(100mg/kg)

FIG. 12A

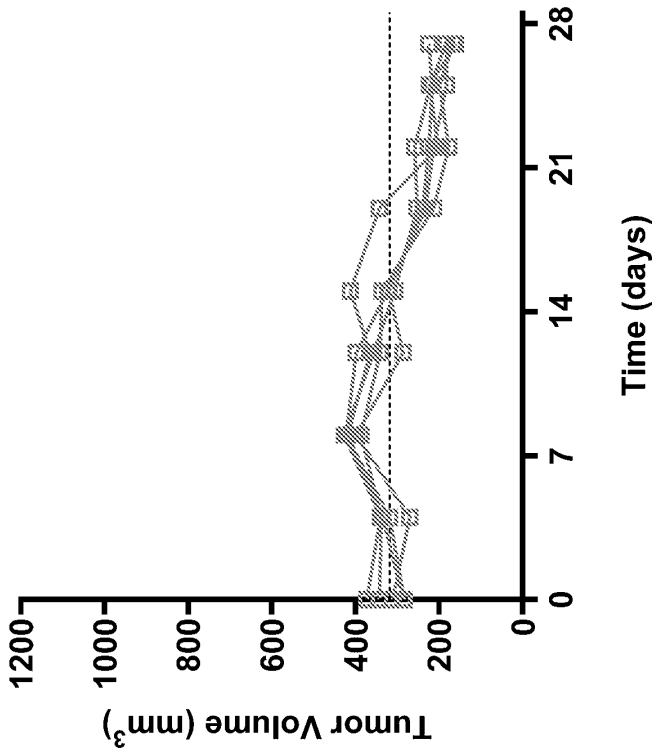


FIG. 12C

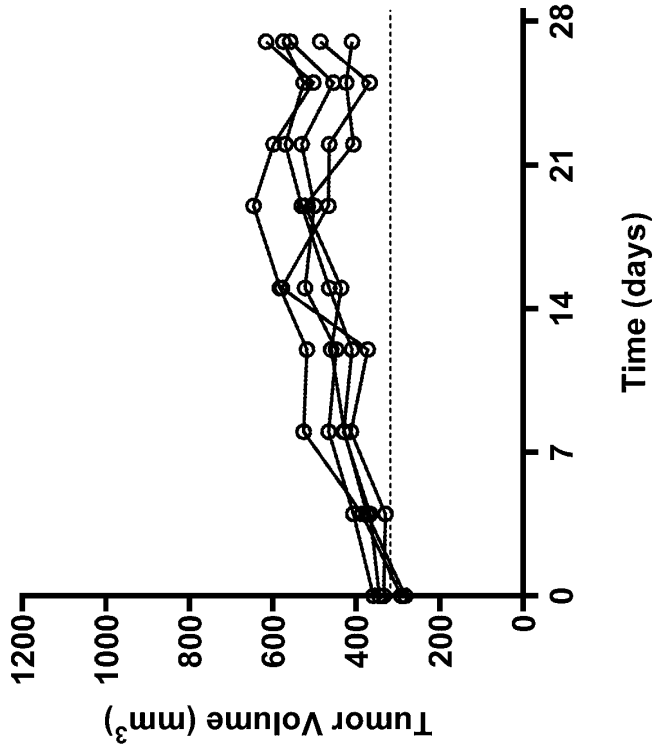


FIG. 12B

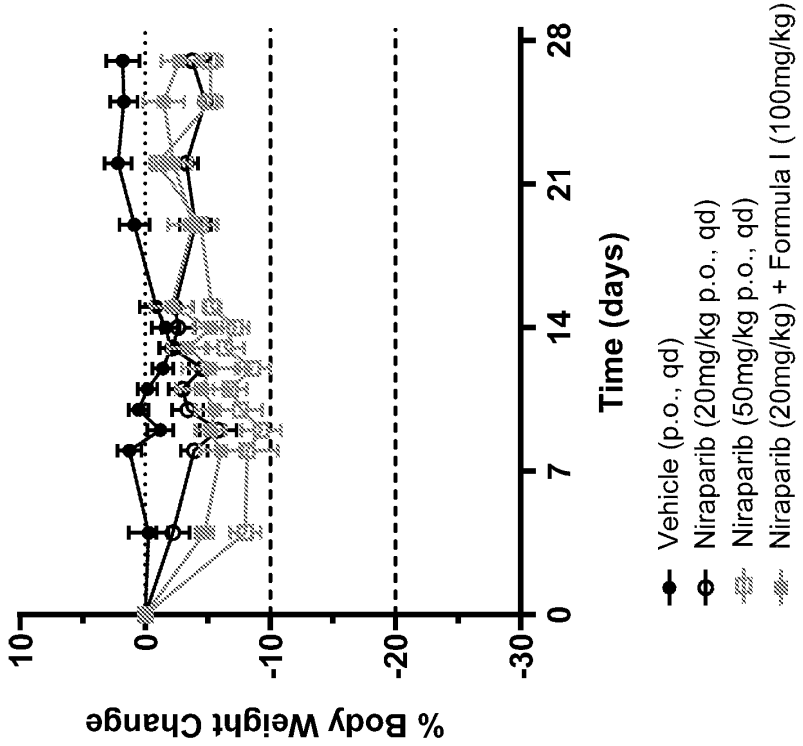


FIG. 12E

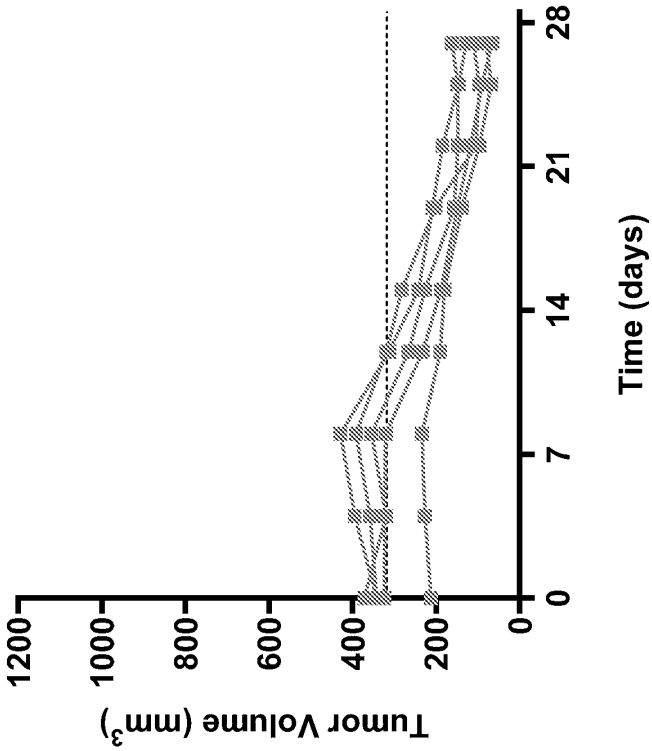
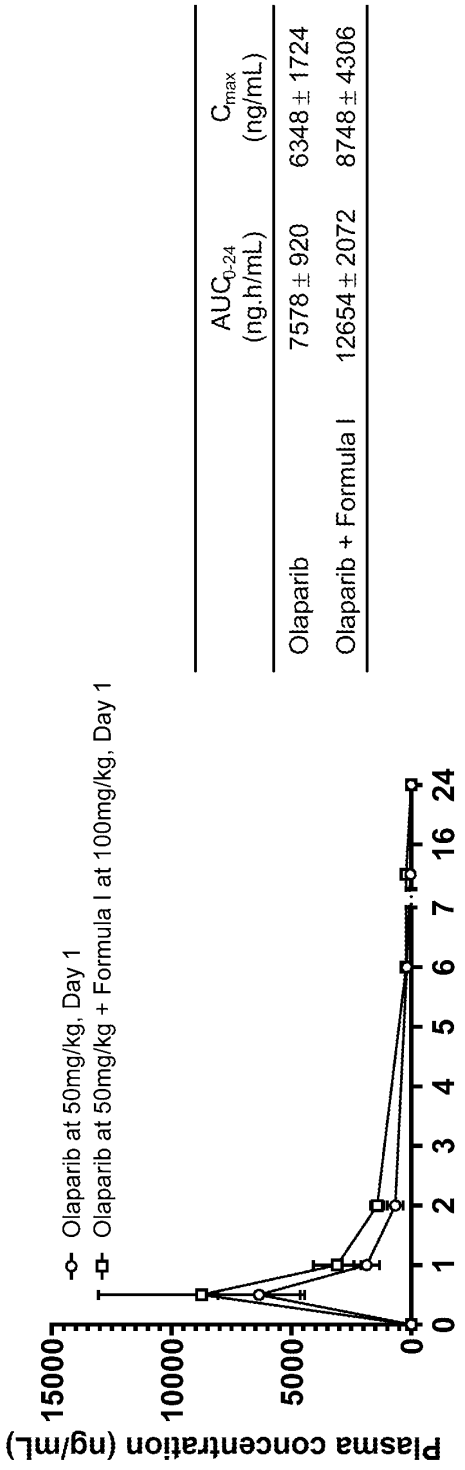
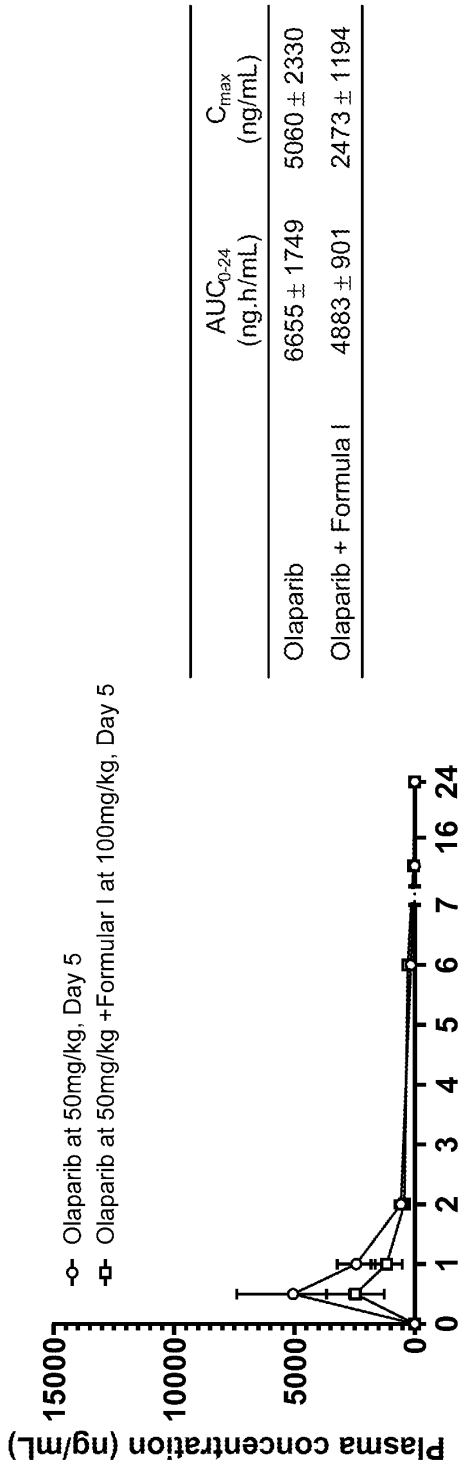


FIG. 12D



	AUC_{0-24} (ng.h/mL)	C_{max} (ng/mL)
Olaparib	7578 ± 920	6348 ± 1724
Olaparib + Formula I	12654 ± 2072	8748 ± 4306

FIG. 13A



	AUC_{0-24} (ng.h/mL)	C_{max} (ng/mL)
Olaparib	6655 ± 1749	5060 ± 2330
Olaparib + Formula I	4883 ± 901	2473 ± 1194

FIG. 13B

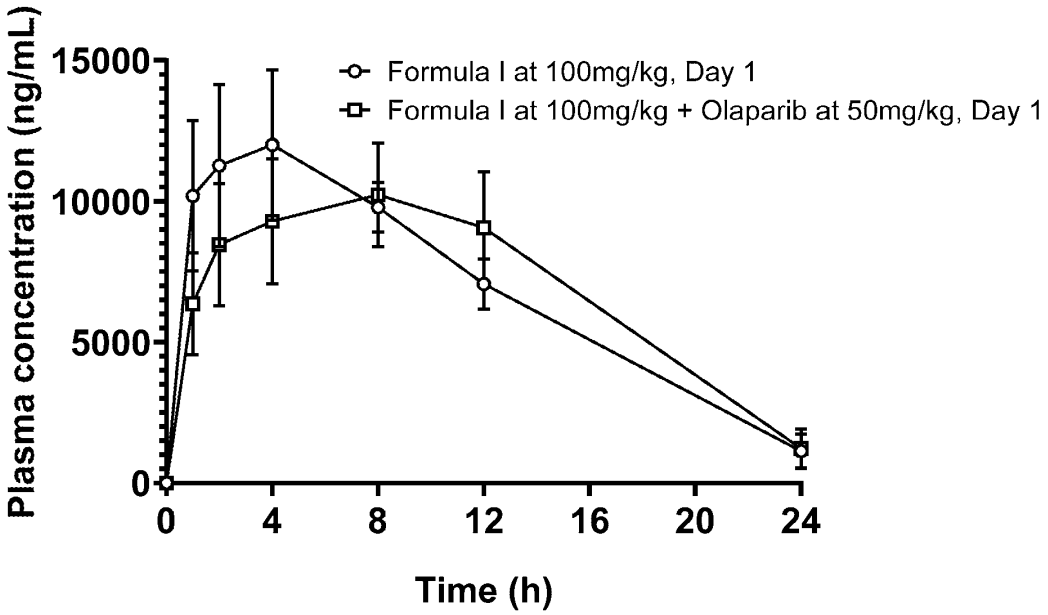


FIG. 13C

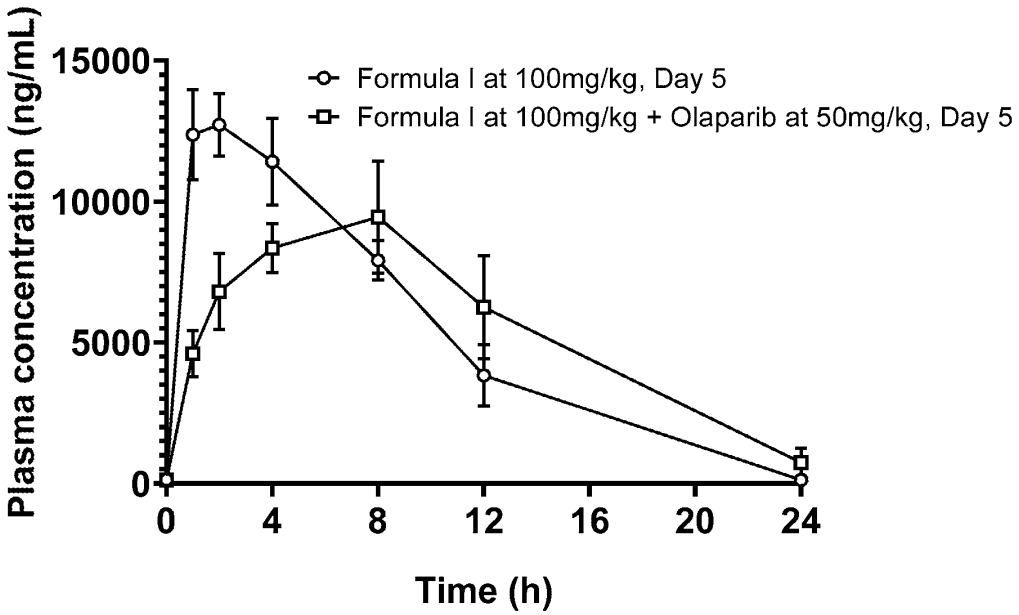
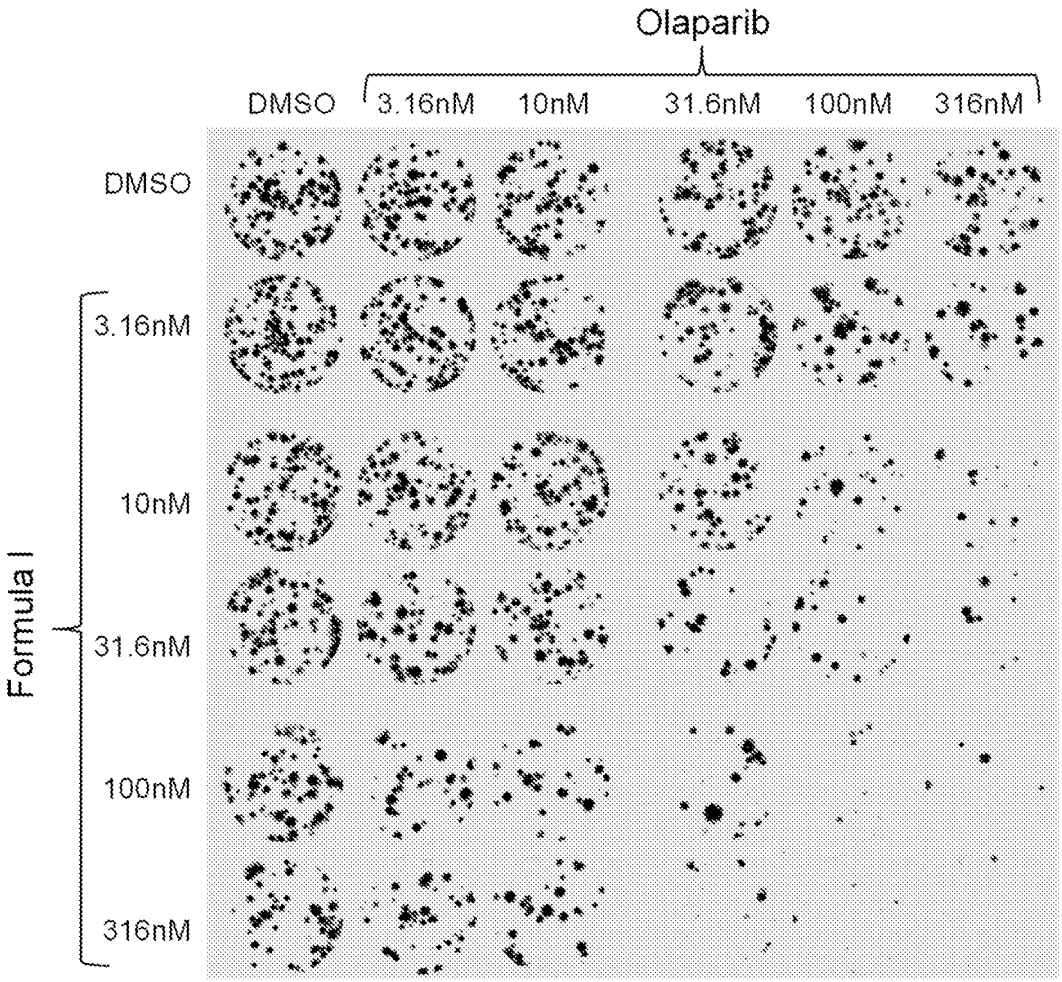


FIG. 13D



		Olaparib					
		DMSO	3.16nM	10nM	31.6nM	100nM	316nM
Formula I	DMSO	100	93	86	97	91	80
	3.16nM	97	97	92	97	78	63
	10nM	102	97	94	83	40	22
	31.6nM	93	94	78	52	39	19
	100nM	87	61	50	15	2	2
	316nM	75	57	56	4	1	0

FIG. 14

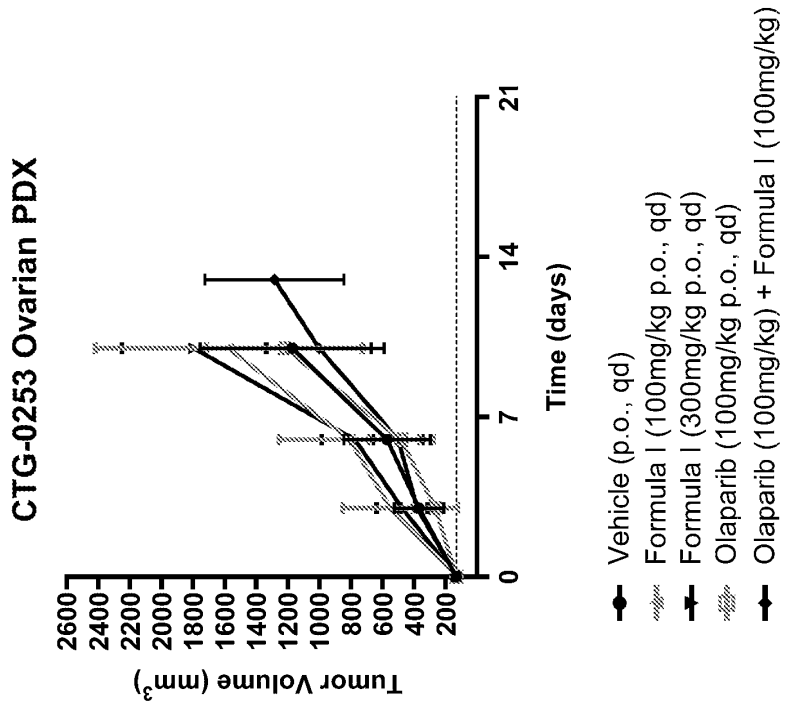

CTG-0253 Ovarian PDX
Tumor Volume (mm3)
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
7
14
21
Time (days)
Vehicle (p.o., qd)
Formula I (100mg/kg p.o., qd)
Formula I (300mg/kg p.o., qd)
Olaparib (100mg/kg p.o., qd)
Olaparib (100mg/kg) + Formula I (100mg/kg)

FIG. 15A

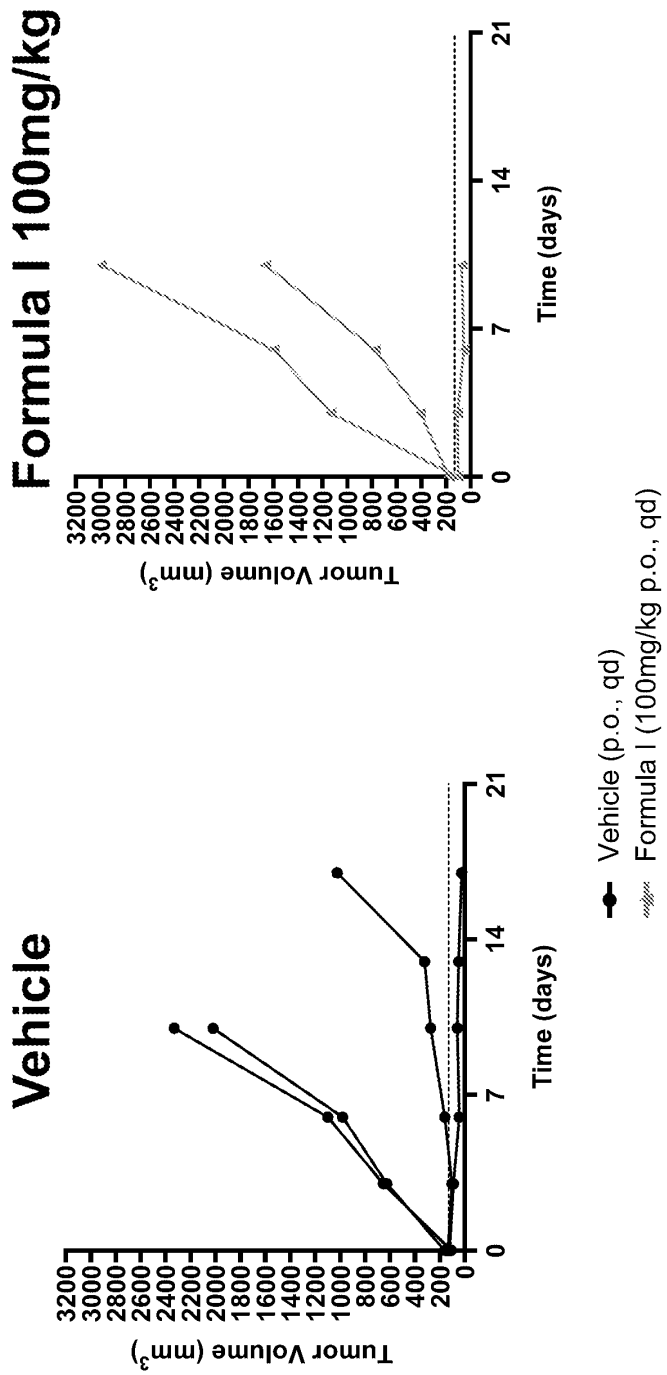


FIG. 15B

FIG. 15C

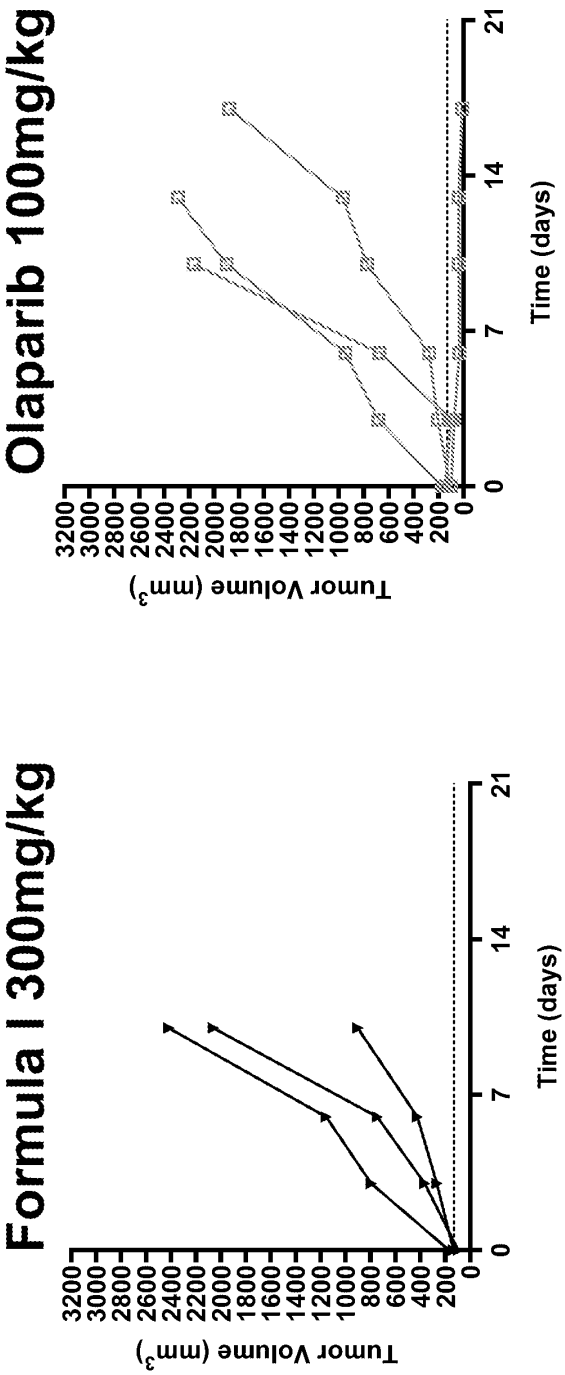


FIG. 15D

FIG. 15E

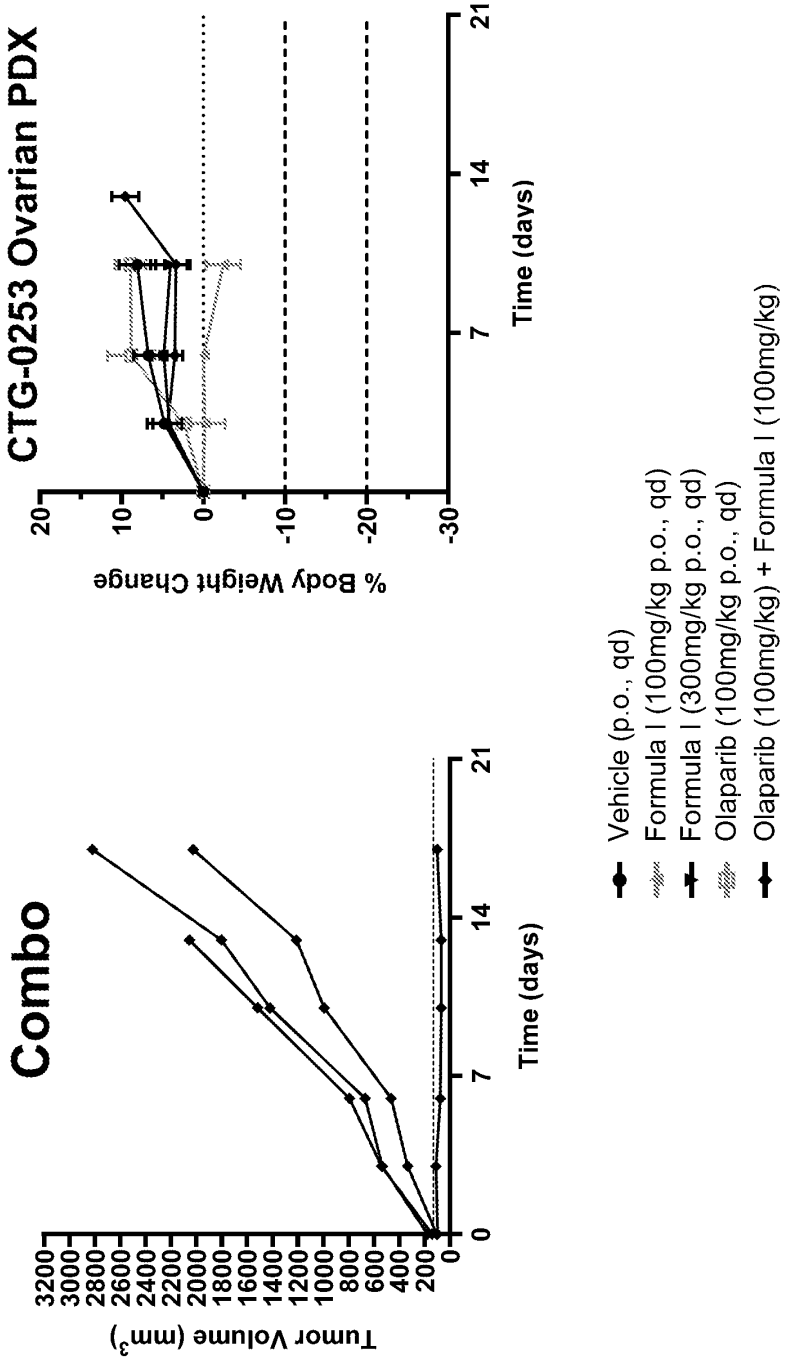


FIG. 15F

FIG. 15G

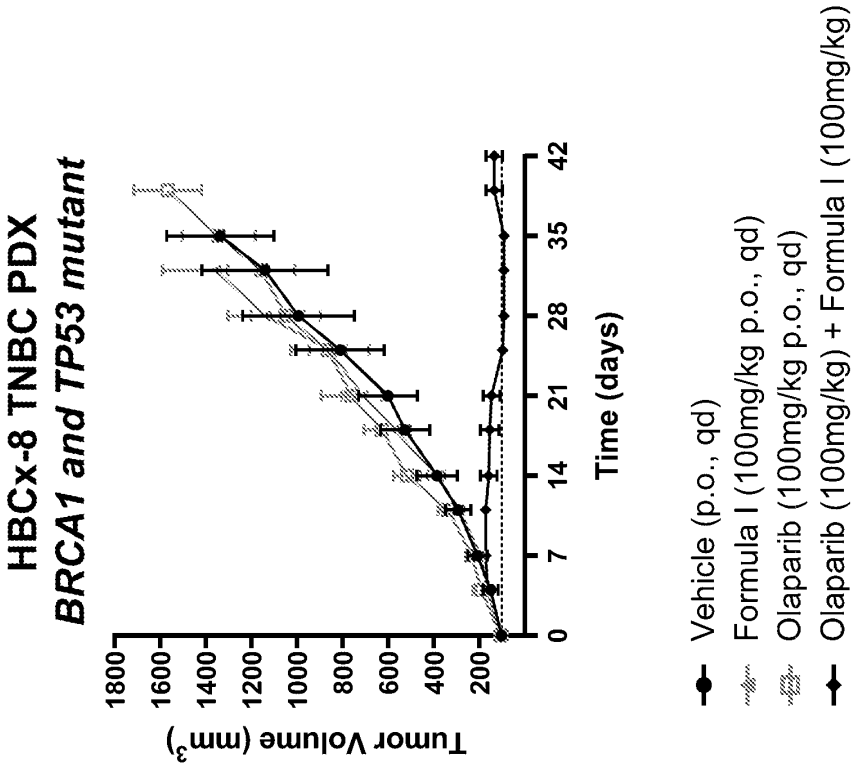

HBCx-8 TNBC PDX
BRCA1 and TP53 mutant
Tumor Volume (mm3)
1800
1600
1400
1200
1000
800
600
400
200
0
7
14
21
28
35
42
Time (days)
Vehicle (p.o., qd)
Formula I (100mg/kg p.o., qd)
Olaparib (100mg/kg p.o., qd)
Olaparib (100mg/kg) + Formula I (100mg/kg)

FIG. 16A

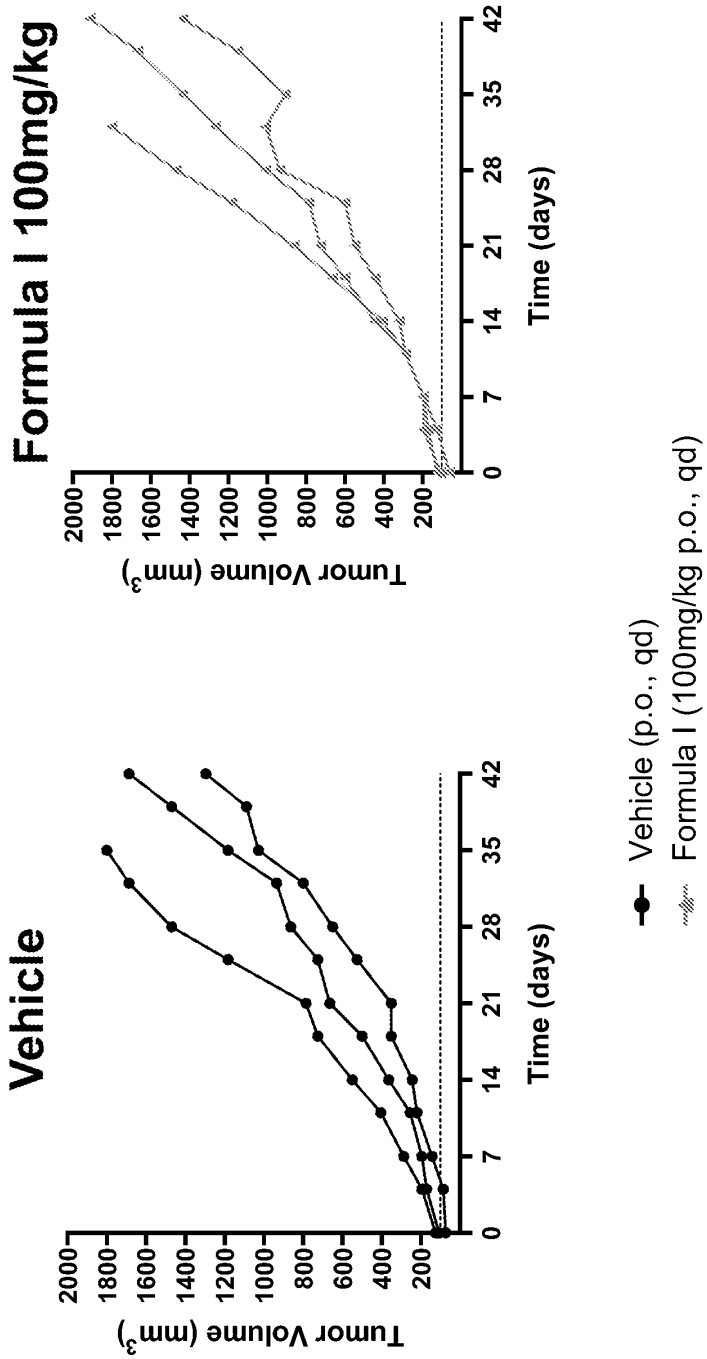


FIG. 16B

FIG. 16C

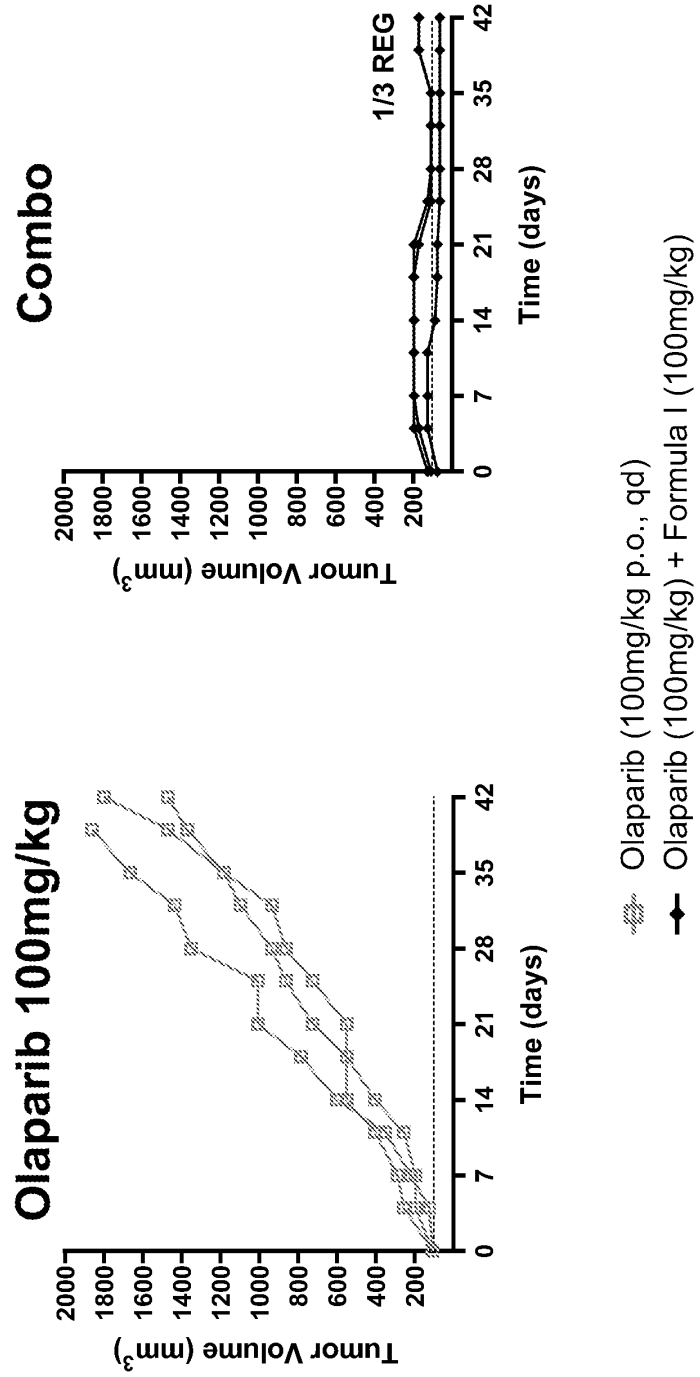


FIG. 16D

FIG. 16E

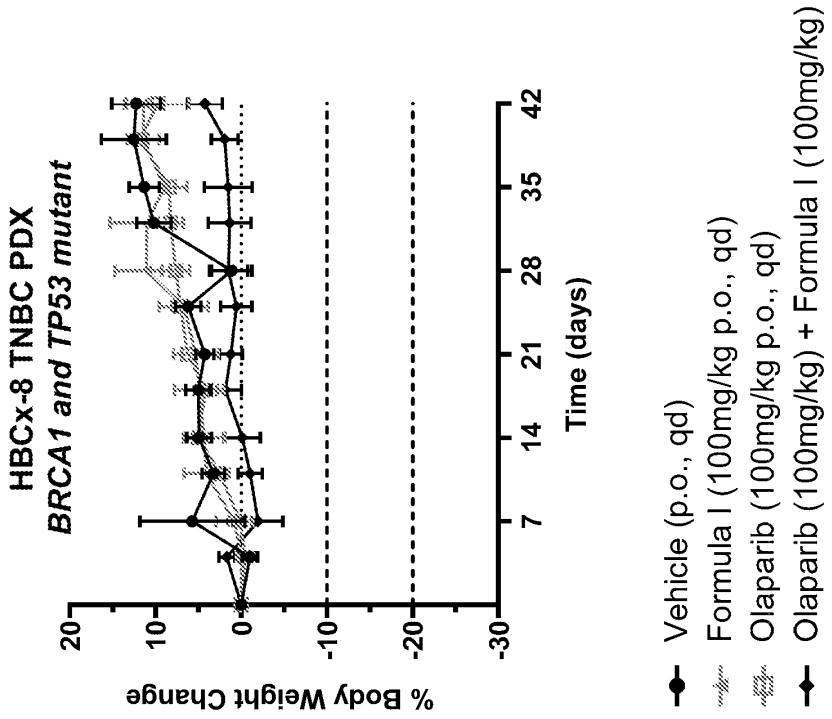

HBCx-8 TNBC PDX
BRCA1 and TP53 mutant
% Body Weight Change
20
10
0
-10
-20
-30
7
14
21
28
35
42
Time (days)
Vehicle (p.o., qd)
Formula I (100mg/kg p.o., qd)
Olaparib (100mg/kg p.o., qd)
Olaparib (100mg/kg) + Formula I (100mg/kg)

FIG. 16F

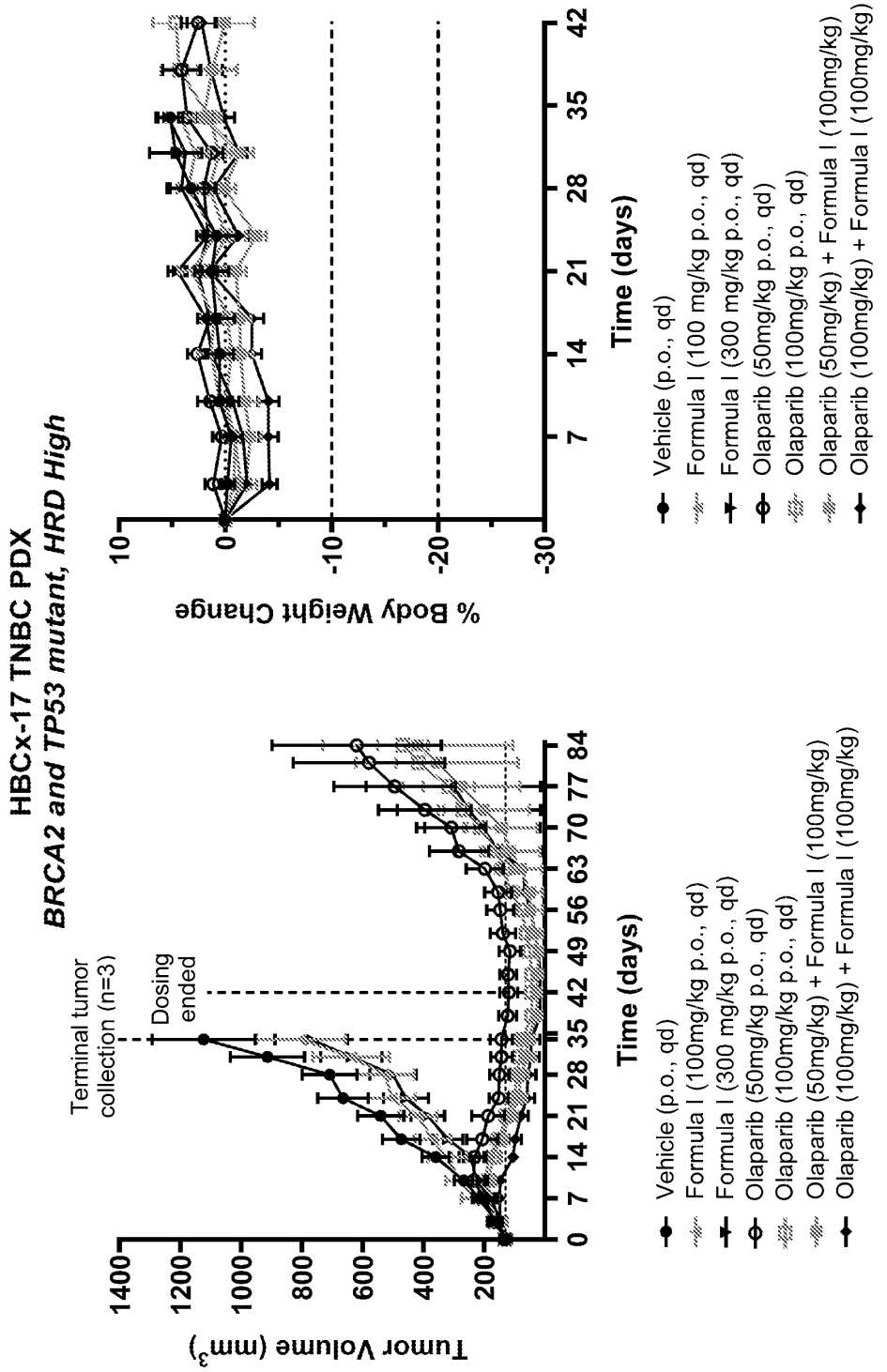


FIG. 17A

FIG. 17B

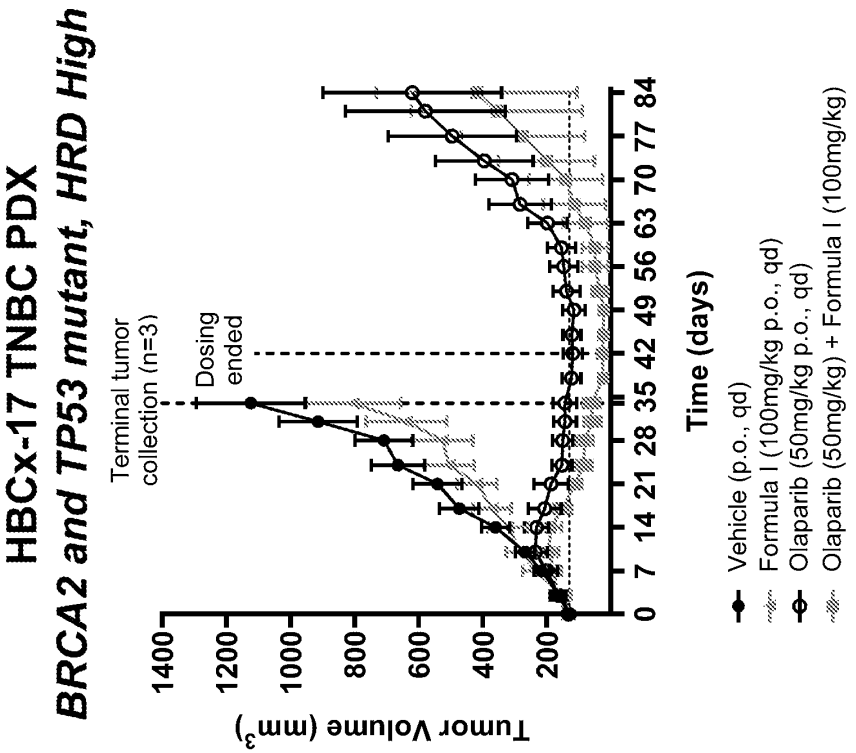

HBCx-17 TNBC PDX
BRCA2 and TP53 mutant, HRD High
Terminal tumor collection (n=3)
Dosing ended
Tumor Volume (mm3)
1400
1200
1000
800
600
400
200
0 7 14 21 28 35 42 49 56 63 70 77 84
Time (days)
Vehicle (p.o., qd)
Formula I (100mg/kg p.o., qd)
Olaparib (50mg/kg p.o., qd)
Olaparib (50mg/kg) + Formula I (100mg/kg)

FIG. 17C

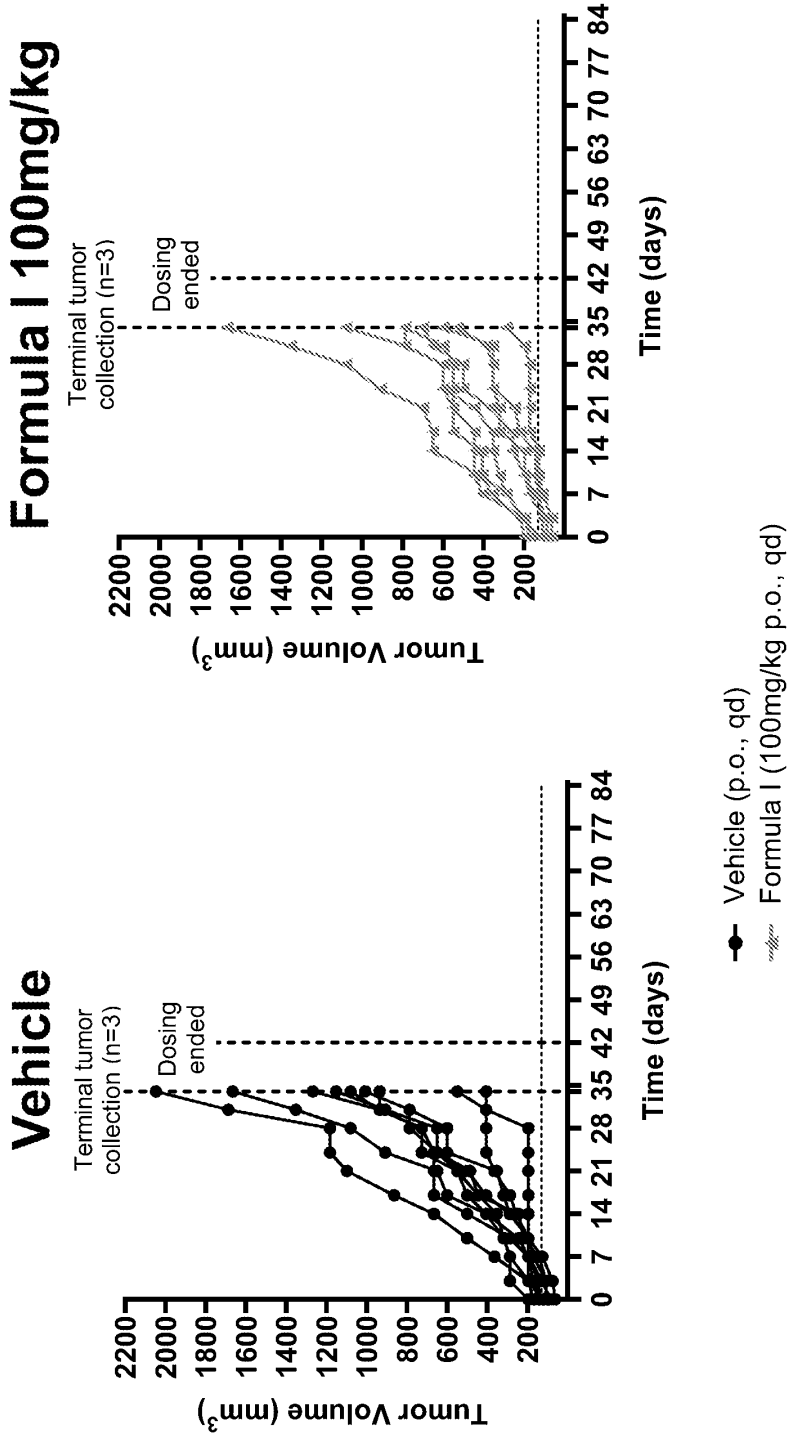


FIG. 17D

FIG. 17E

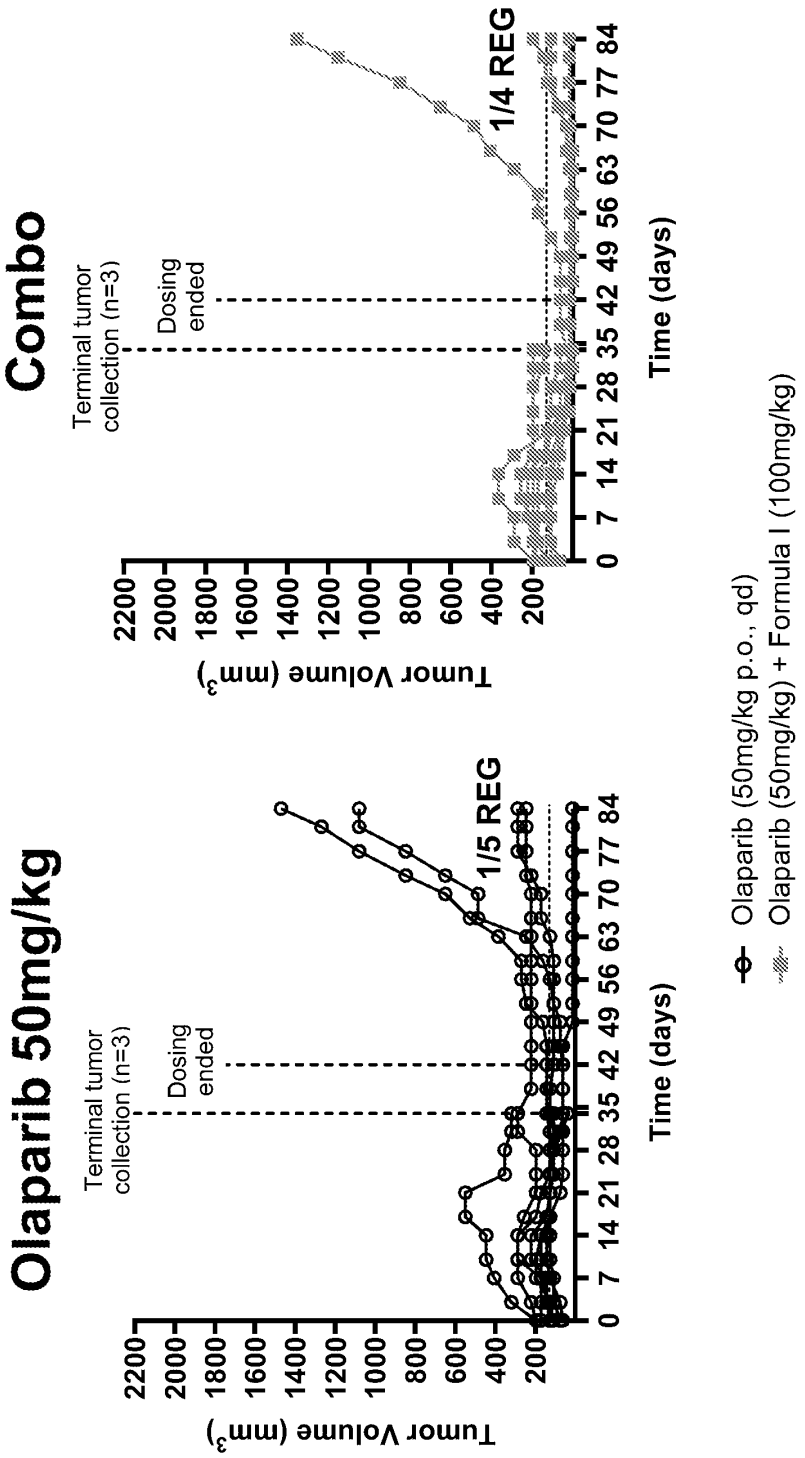


FIG. 17F

FIG. 17G

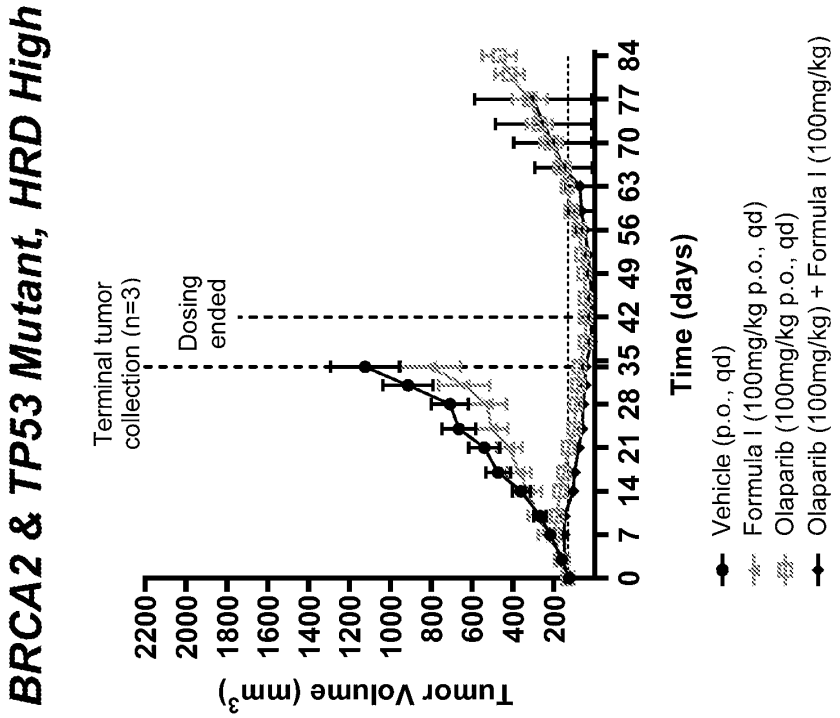

HBCx-17 TNBC PDX
BRCA2 & TP53 Mutant, HRD High
Terminal tumor collection (n=3)
Dosing ended
Tumor Volume (mm3)
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0 7 14 21 28 35 42 49 56 63 70 77 84
Time (days)
Vehicle (p.o., qd)
Formula I (100mg/kg p.o., qd)
Olaparib (100mg/kg p.o., qd)
Olaparib (100mg/kg) + Formula I (100mg/kg)

FIG. 17H

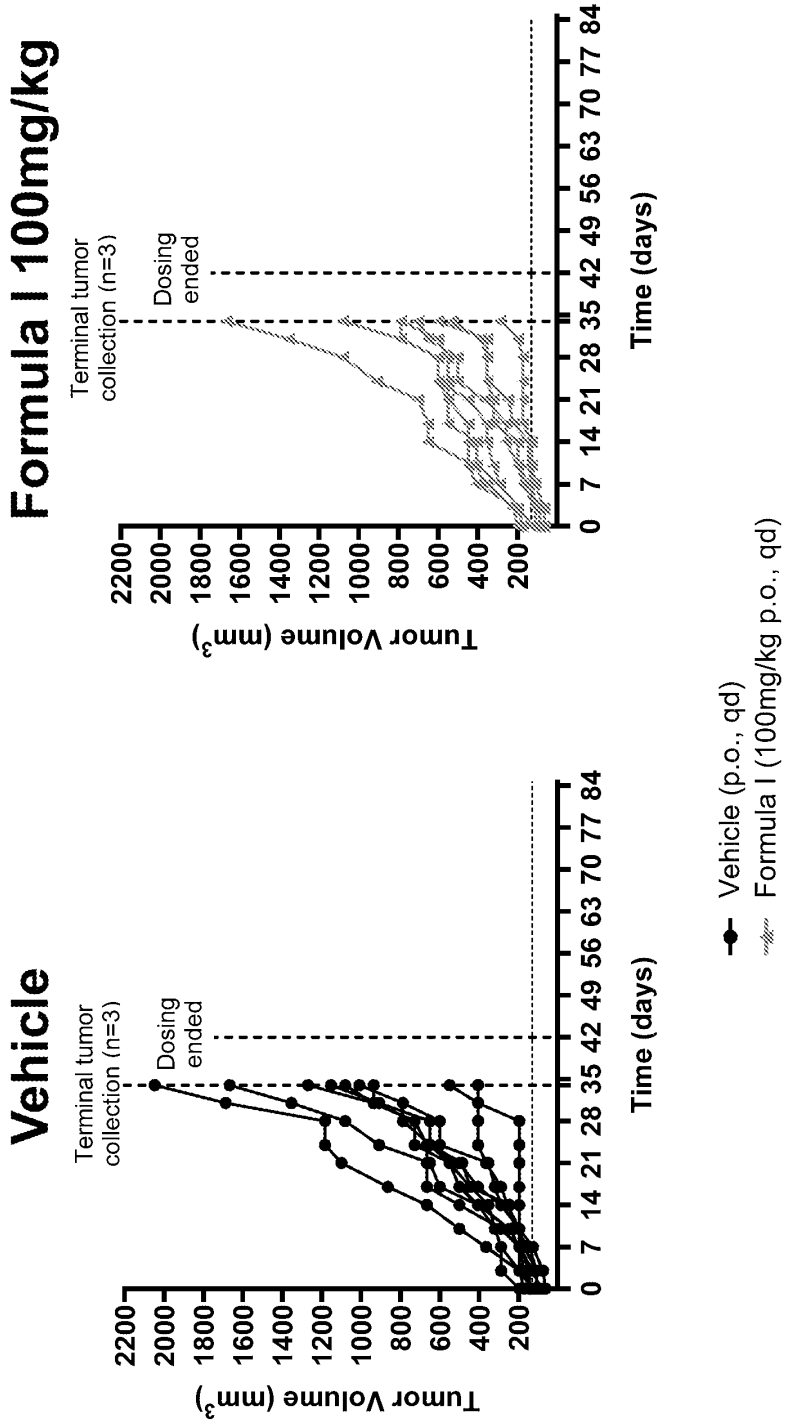


FIG. 17I

FIG. 17J

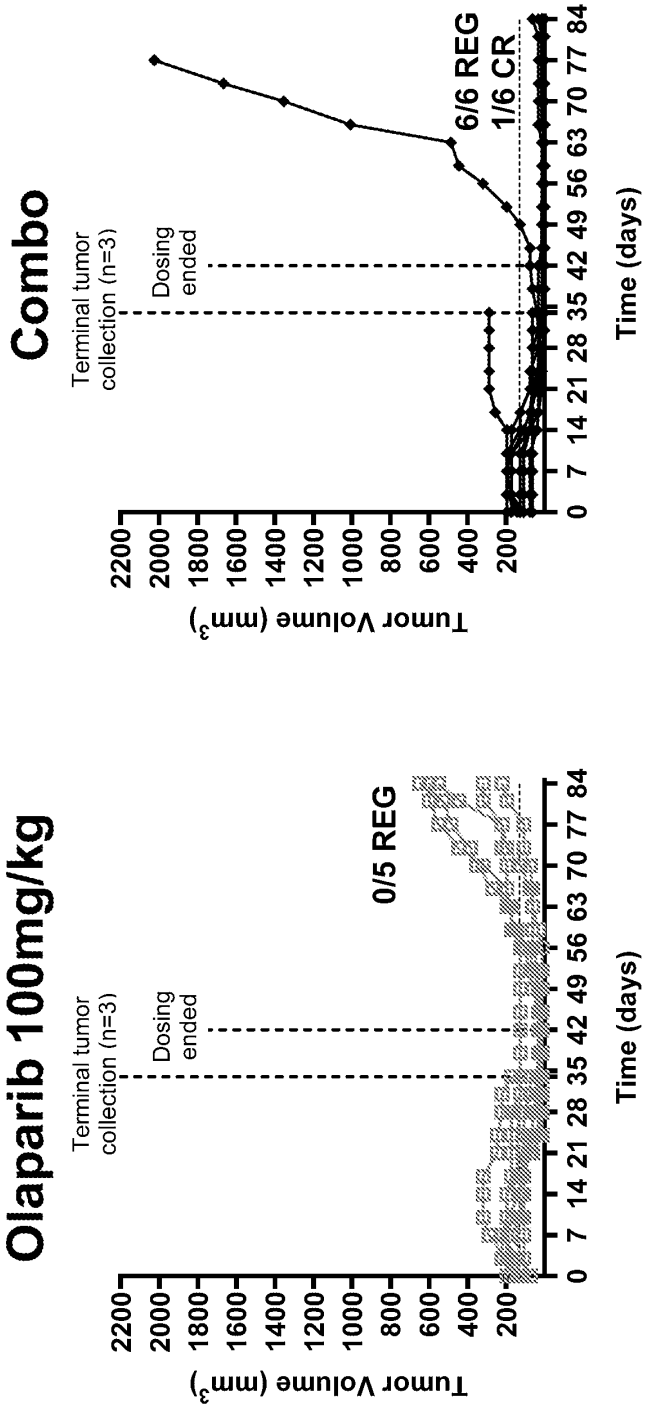


FIG. 17K

FIG. 17L

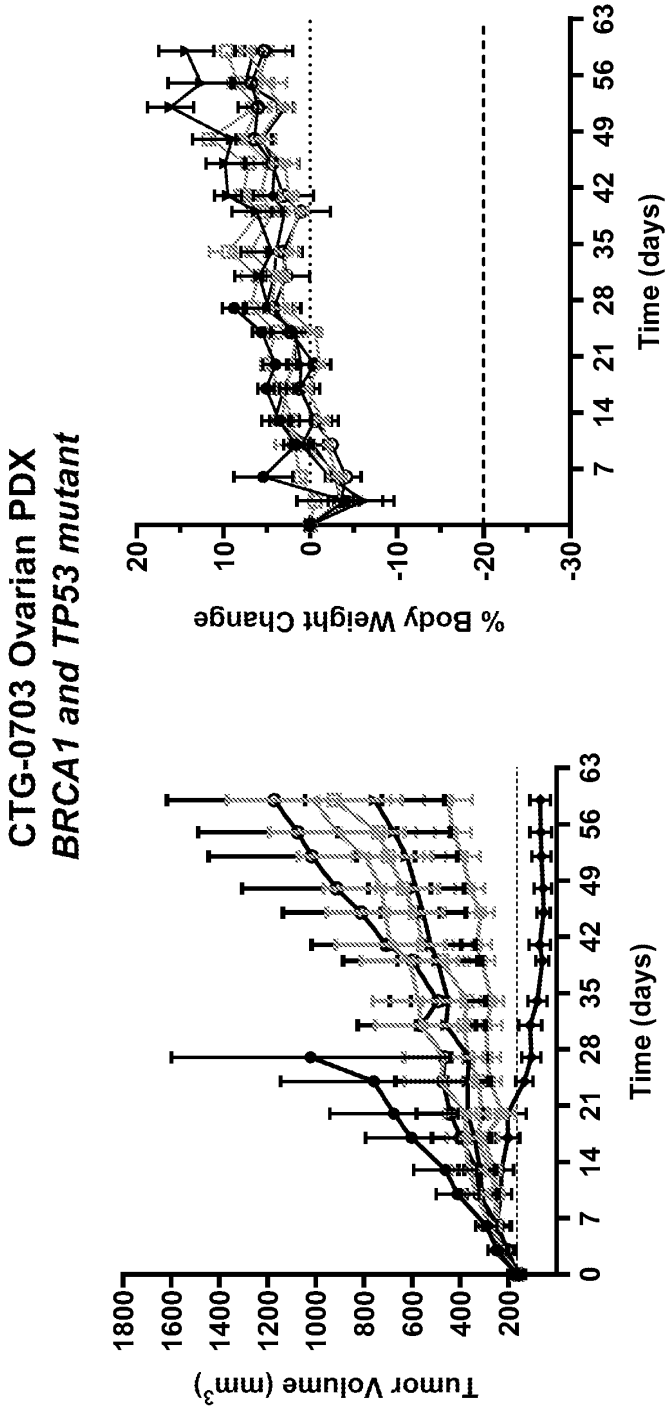


FIG. 18A

FIG. 18B

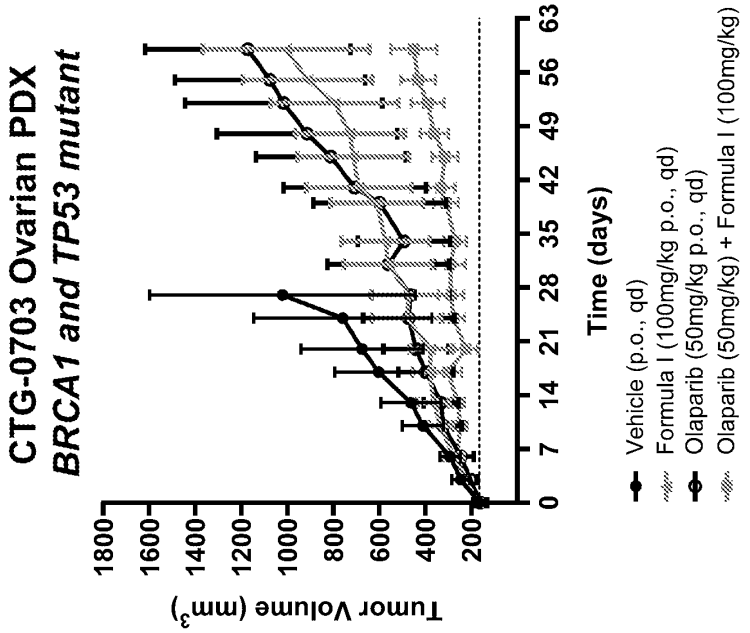

CTG-0703 Ovarian PDX
BRCA1 and TP53 mutant
Tumor Volume (mm3)
1800
1600
1400
1200
1000
800
600
400
200
0
7
14
21
28
35
42
49
56
63
Time (days)
Vehicle (p.o., qd)
Formula I (100mg/kg p.o., qd)
Olaparib (50mg/kg p.o., qd)
Olaparib (50mg/kg) + Formula I (100mg/kg)

FIG. 18C

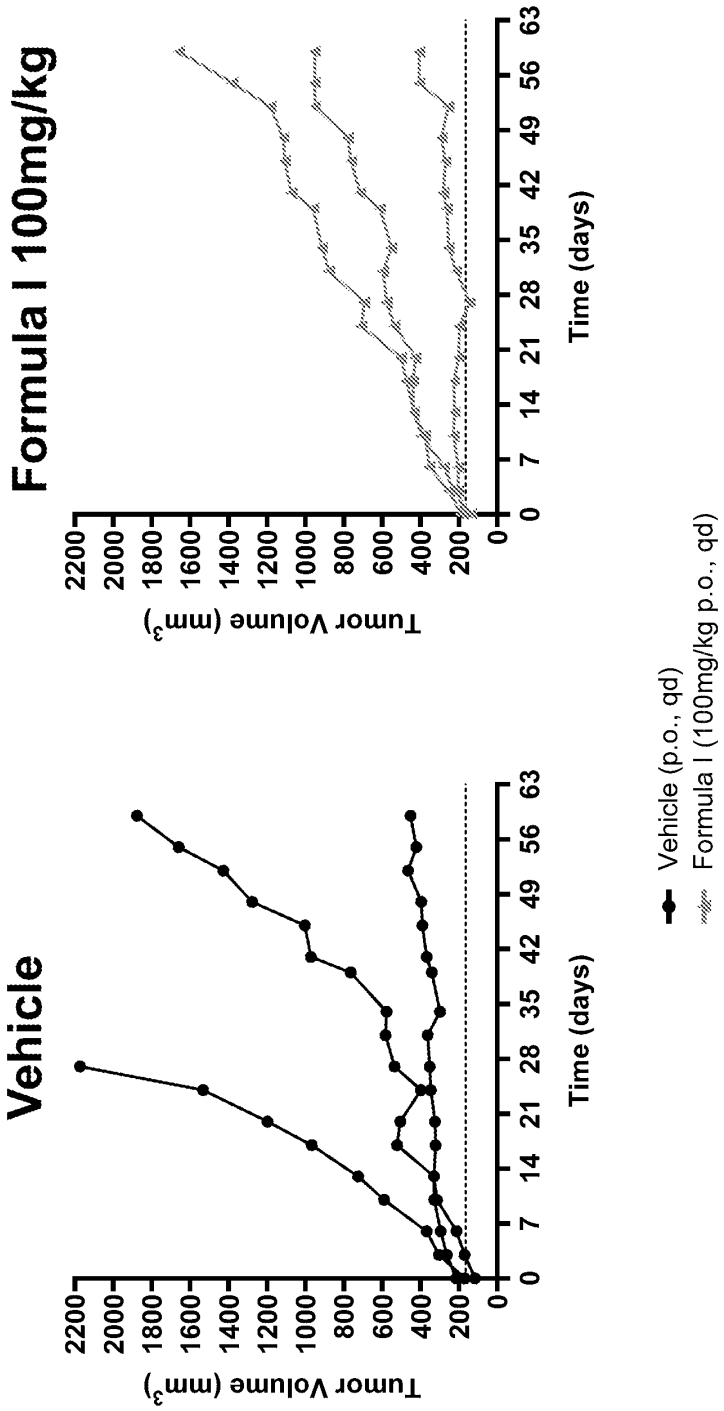


FIG. 18D

FIG. 18E

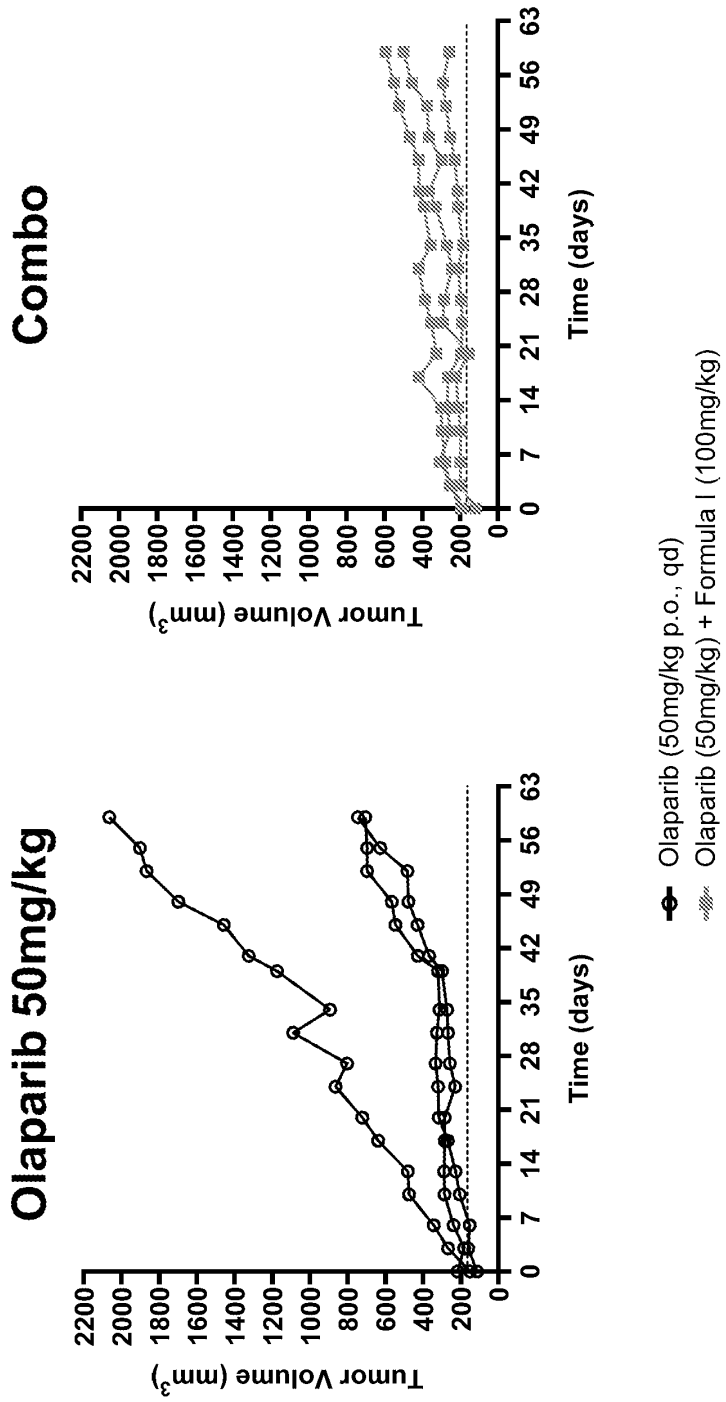


FIG. 18F

FIG. 18G

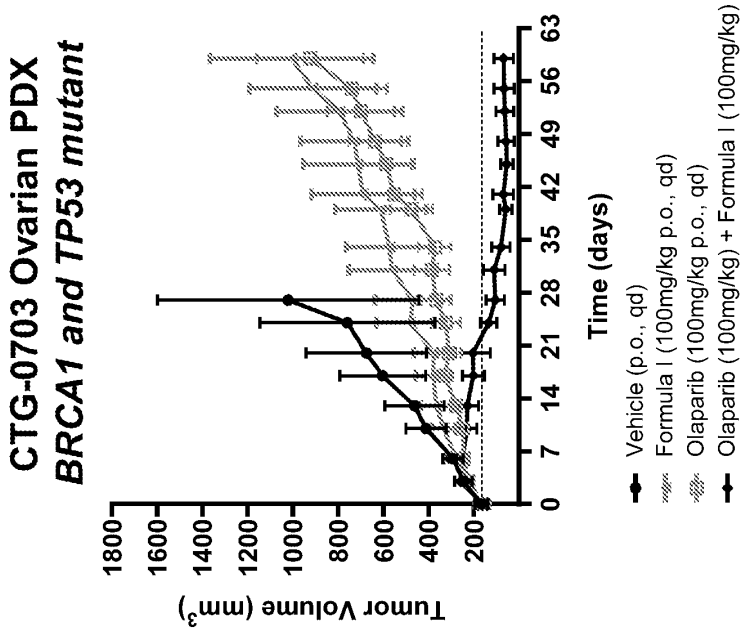

CTG-0703 Ovarian PDX
BRCA1 and TP53 mutant
Tumor Volume (mm3)
1800
1600
1400
1200
1000
800
600
400
200
0
7
14
21
28
35
42
49
56
63
Time (days)
Vehicle (p.o., qd)
Formula I (100mg/kg p.o., qd)
Olaparib (100mg/kg p.o., qd)
Olaparib (100mg/kg) + Formula I (100mg/kg)

FIG. 18H

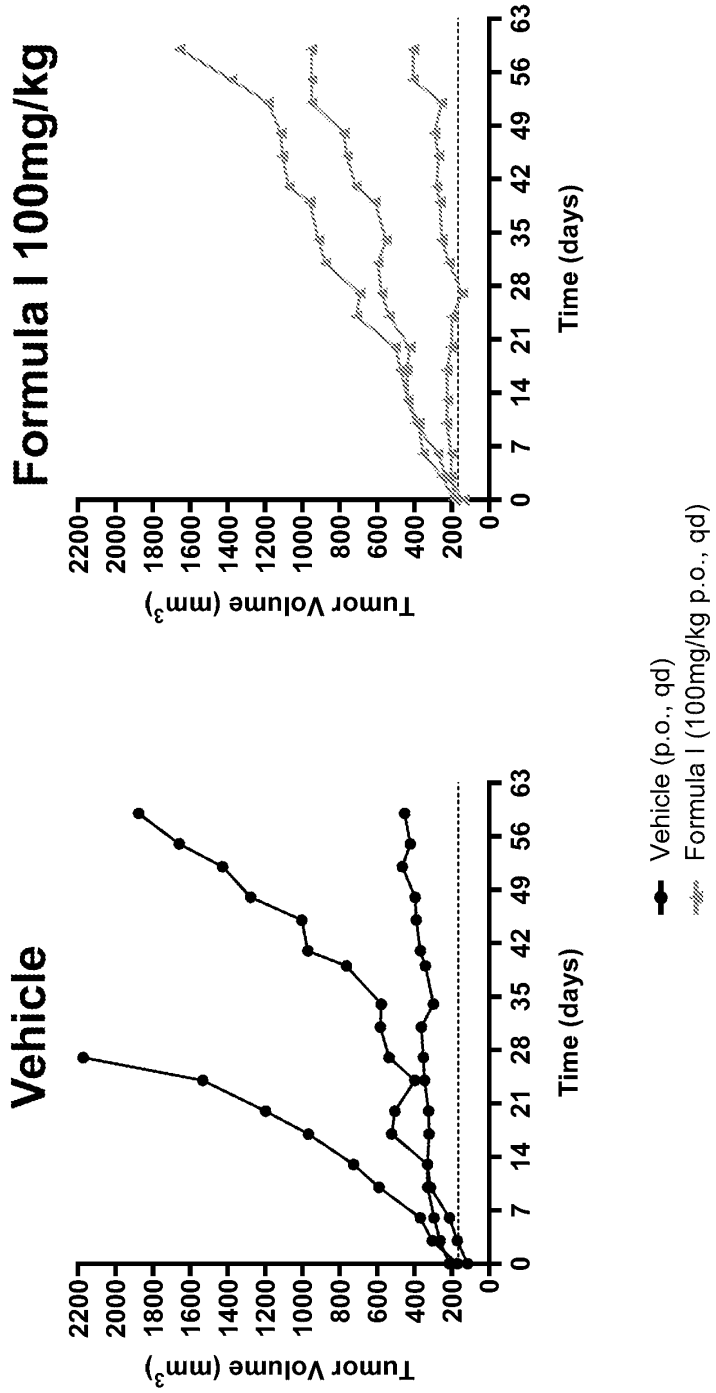


FIG. 18I

FIG. 18J

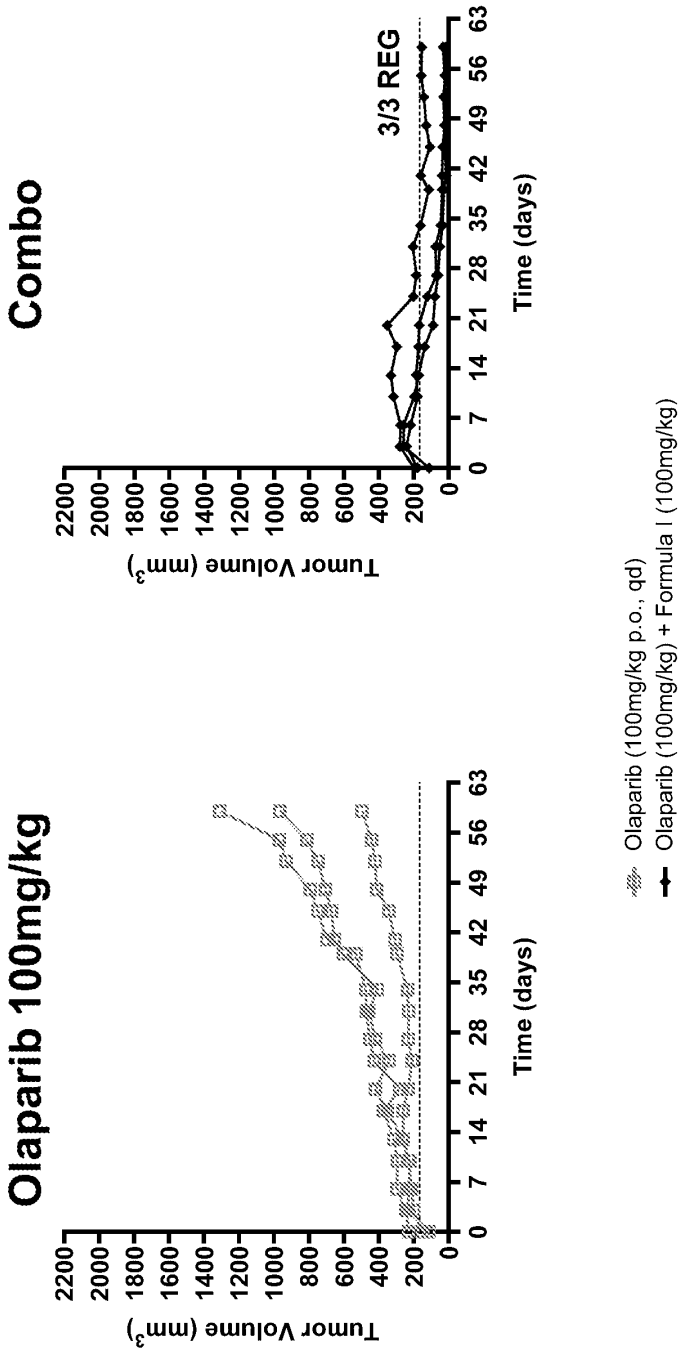


FIG. 18K

FIG. 18L

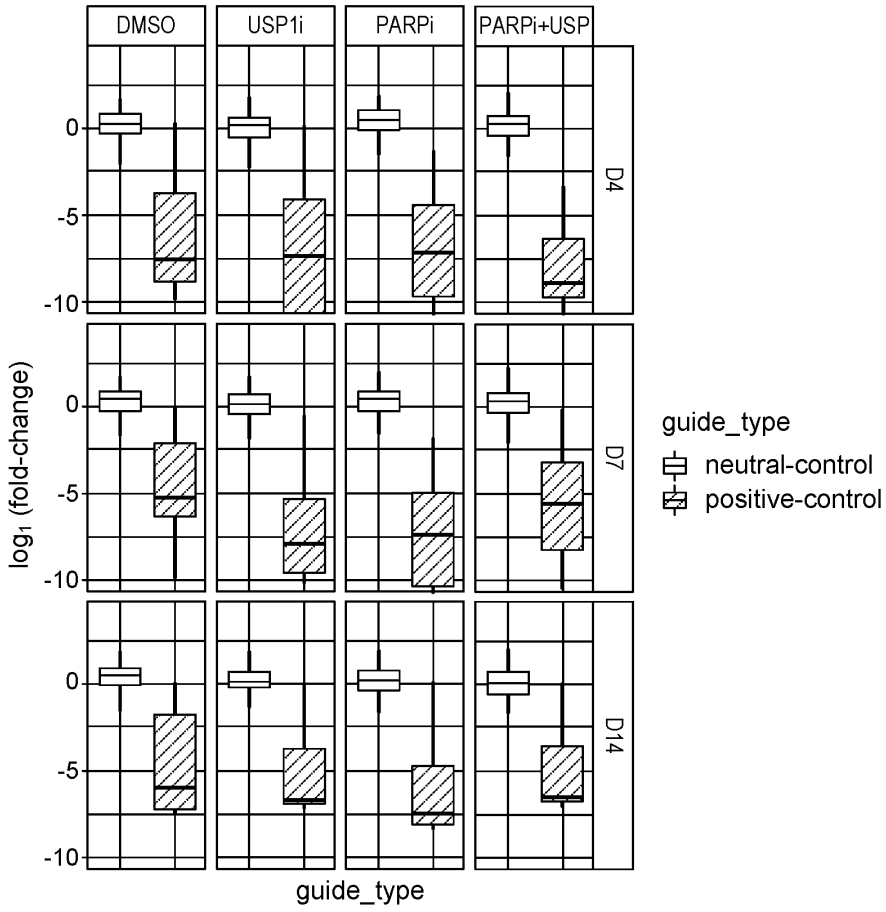

DMSO
USP1i
PARPi
PARPi+USP
D4
D7
D14
0
-5
-10
log1 (fold-change)
guide_type
guide_type
neutral-control
positive-control

FIG. 19

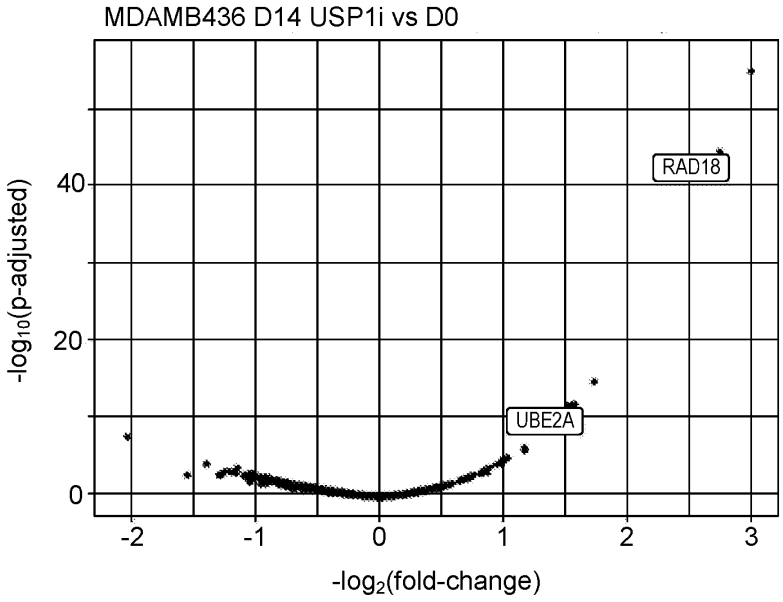

MDAMB436 D14 USP1i vs D0
RAD18
UBE2A
40
20
0
-2
-1
0
1
2
3
-log10(p-adjusted)
-log2(fold-change)

FIG. 20