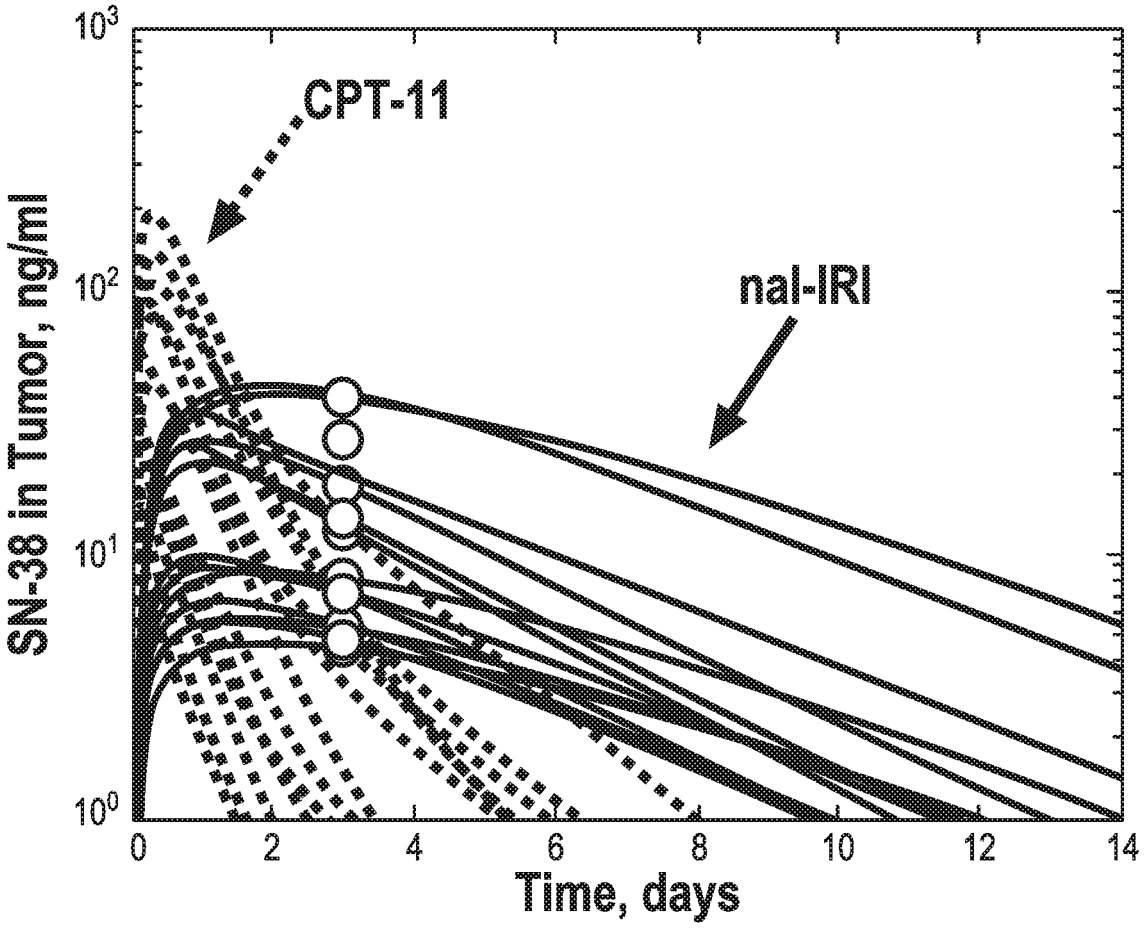

CPT-11
nal-IRI
SN-38 in Tumor, ng/ml
Time, days
10^3
10^2
10^1
10^0
0
2
4
6
8
10
12
14

FIG. 1A

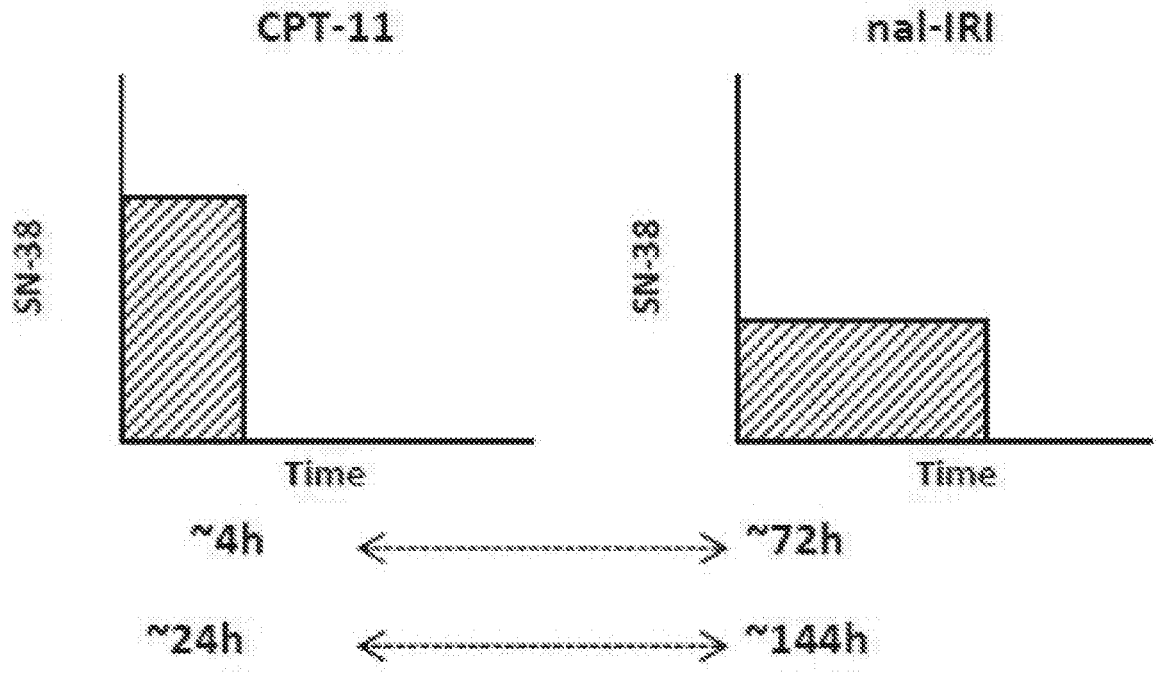

CPT-11
nal-IRI
SN-38
SN-38
Time
Time
~4h
~72h
~24h
~144h

FIG. 1B

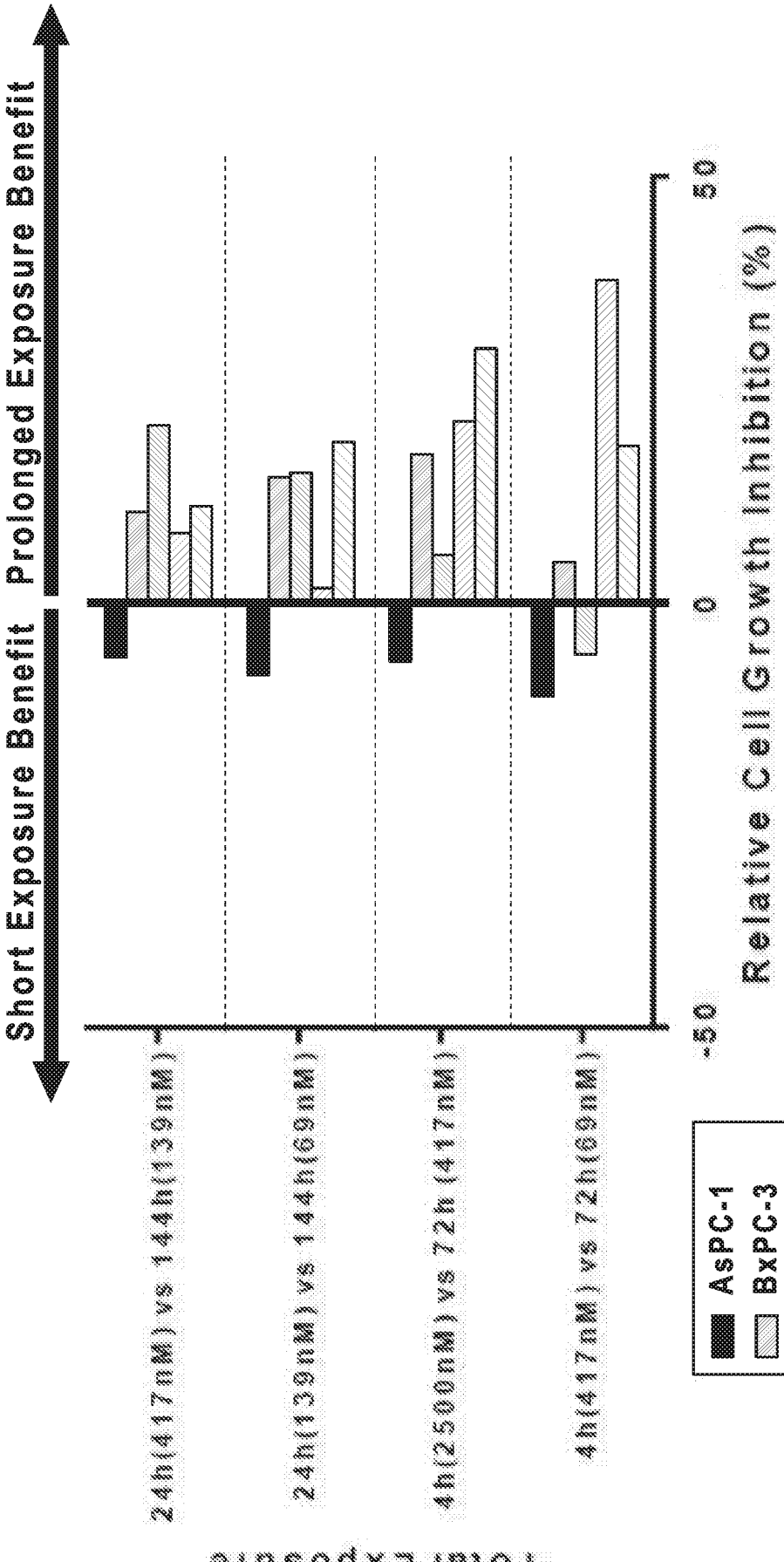

Short Exposure Benefit
Prolonged Exposure Benefit
Total Exposure
24h(417nM) vs 144h(139nM)
24h(139nM) vs 144h(69nM)
4h(2500nM) vs 72h(417nM)
4h(417nM) vs 72h(69nM)
-50
0
50
Relative Cell Growth Inhibition (%)
AsPC-1
BxPC-3
Capan-2
CFPAC-1
MiaPaCa-2

FIG. 1C

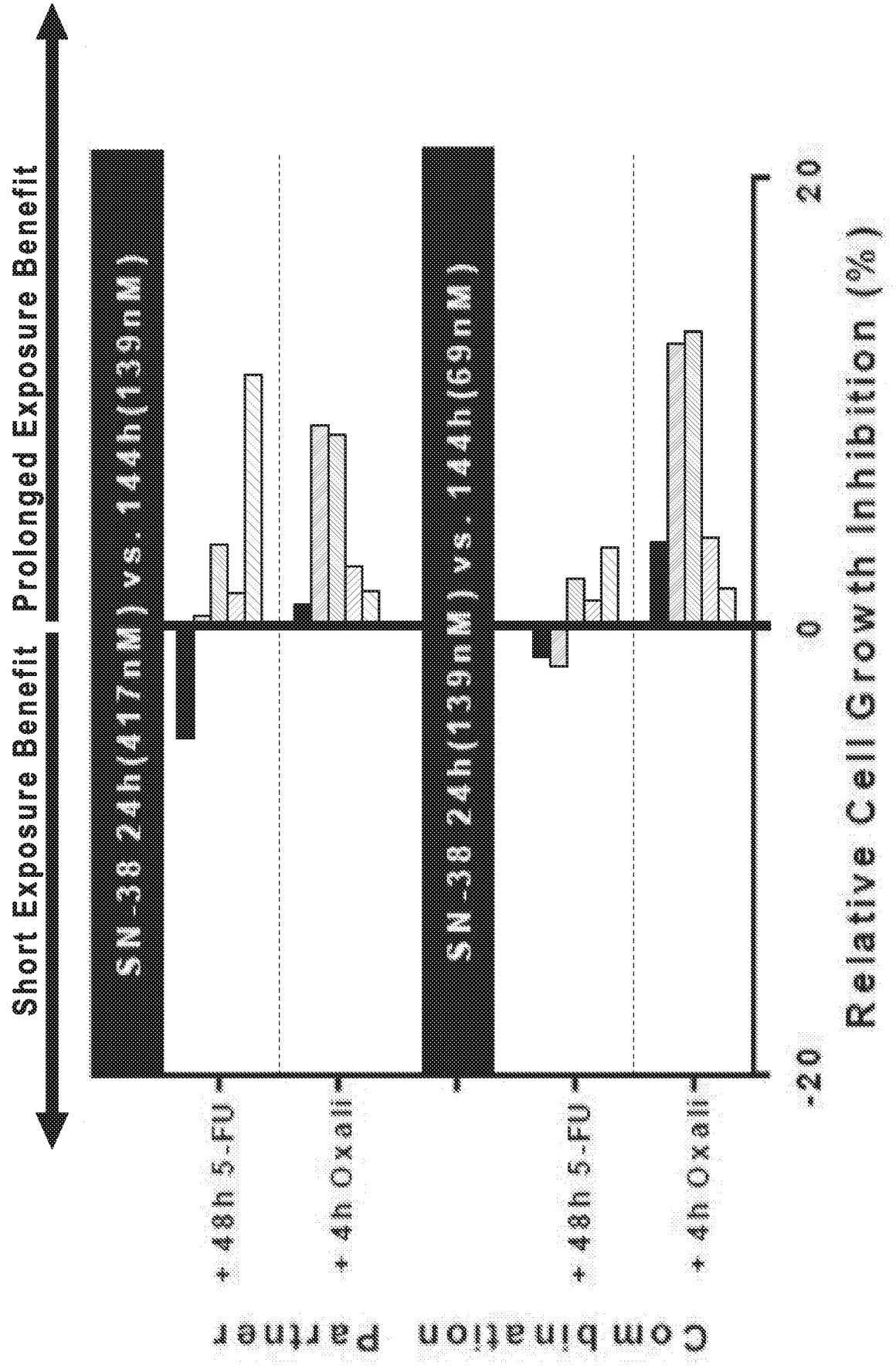

Short Exposure Benefit
Prolonged Exposure Benefit
SN-38 24h(417nM) vs. 144h(139nM)
SN-38 24h(139nM) vs. 144h(69nM)
+ 48h 5-FU
+ 4h Oxali
+ 48h 5-FU
+ 4h Oxali
Combination Partner
-20
0
20
Relative Cell Growth Inhibition (%)

FIG. 1D

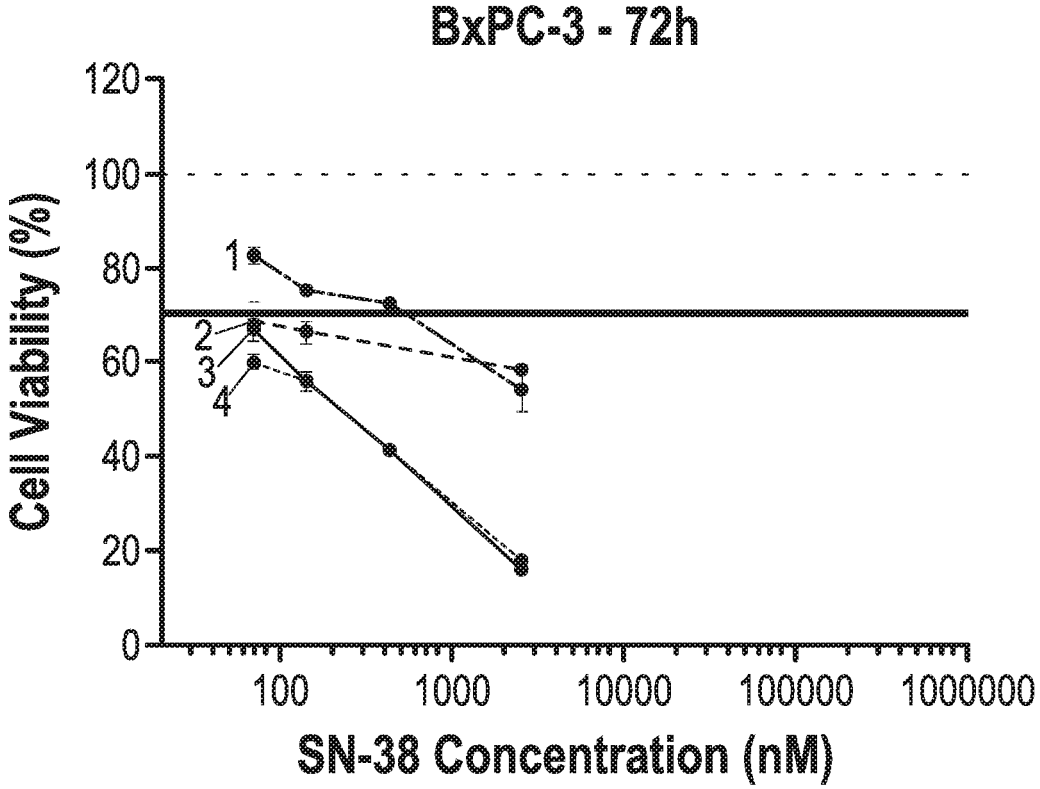

BxPC-3 - 72h
Cell Viability (%)
120
100
80
60
40
20
0
1
2
3
4
100
1000
10000
100000
1000000
SN-38 Concentration (nM)

FIG. 2A

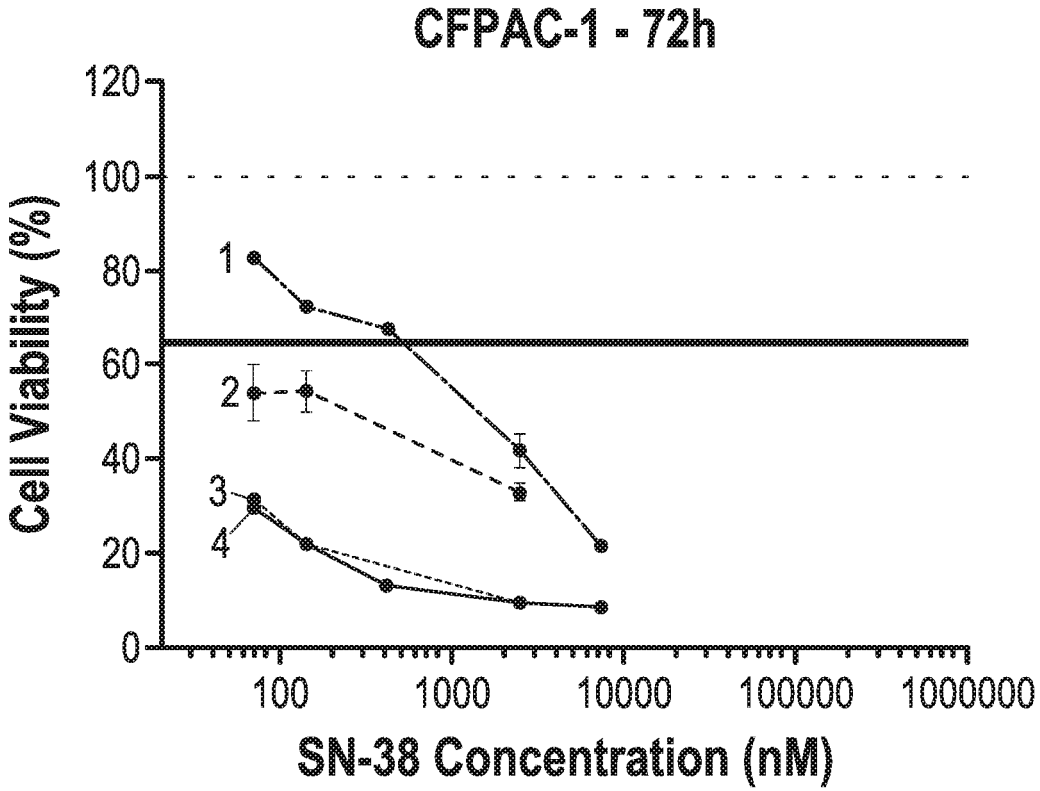

CFPAC-1 - 72h
Cell Viability (%)
120
100
80
60
40
20
0
1
2
3
4
100
1000
10000
100000
1000000
SN-38 Concentration (nM)

FIG. 2B

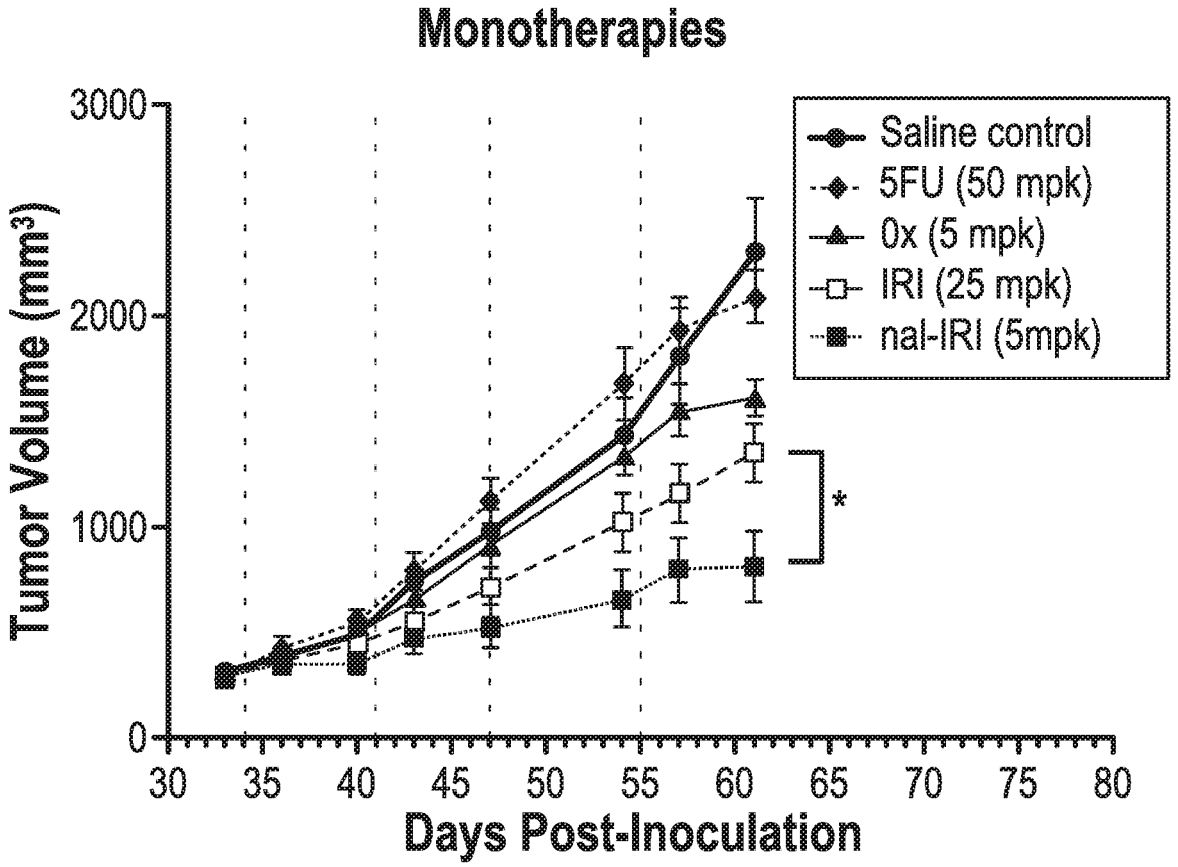

Monotherapies
Tumor Volume (mm³)
3000
2000
1000
0
30
35
40
45
50
55
60
65
70
75
80
Days Post-Inoculation
Saline control
5FU (50 mpk)
0x (5 mpk)
IRI (25 mpk)
nal-IRI (5mpk)
*

FIG. 3A

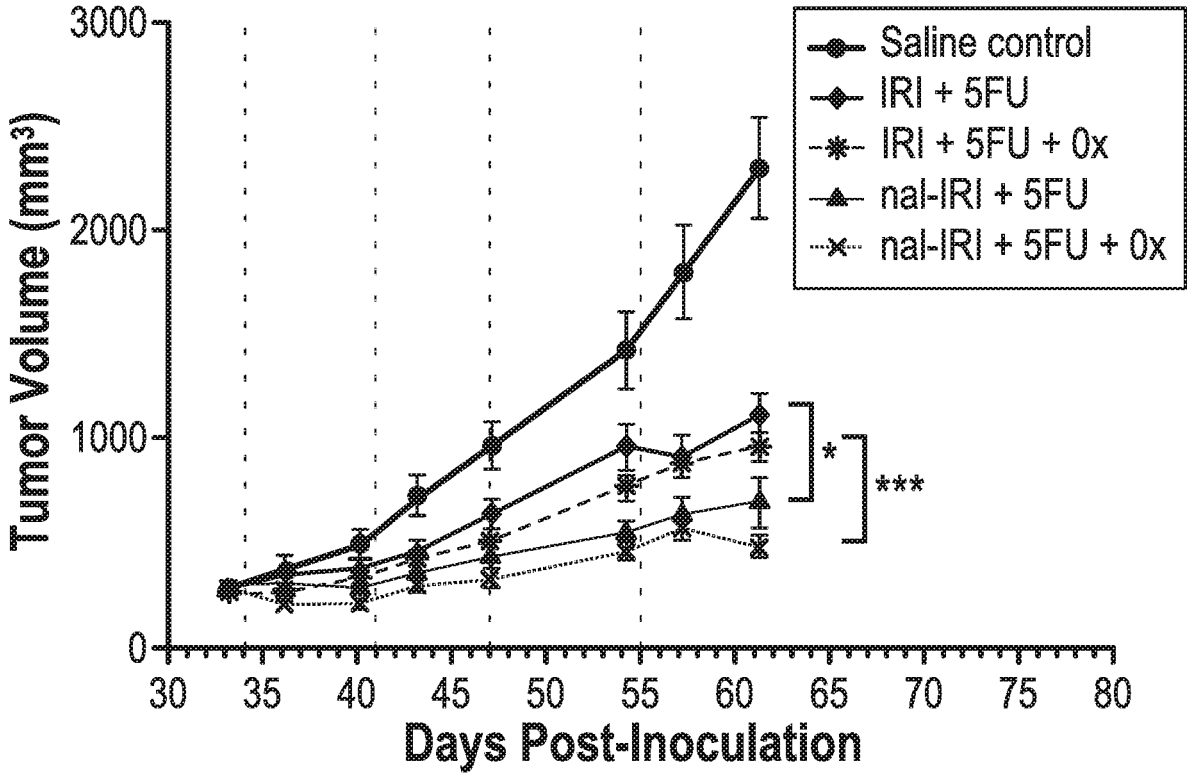

Tumor Volume (mm³)
3000
2000
1000
0
30
35
40
45
50
55
60
65
70
75
80
Days Post-Inoculation
Saline control
IRI + 5FU
IRI + 5FU + 0x
nal-IRI + 5FU
nal-IRI + 5FU + 0x
*
***

FIG. 3B

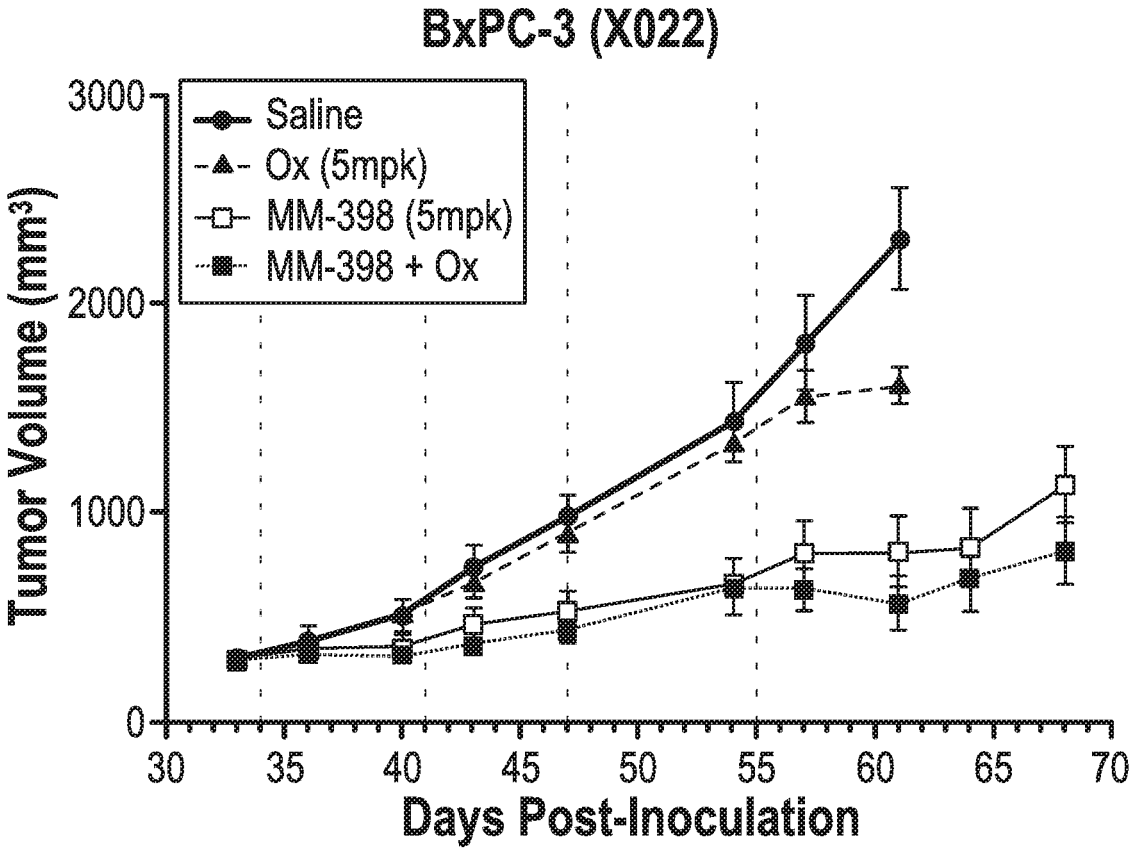

BxPC-3 (X022)
Saline
Ox (5mpk)
MM-398 (5mpk)
MM-398 + Ox
Tumor Volume (mm³)
3000
2000
1000
0
30
35
40
45
50
55
60
65
70
Days Post-Inoculation

FIG. 4A

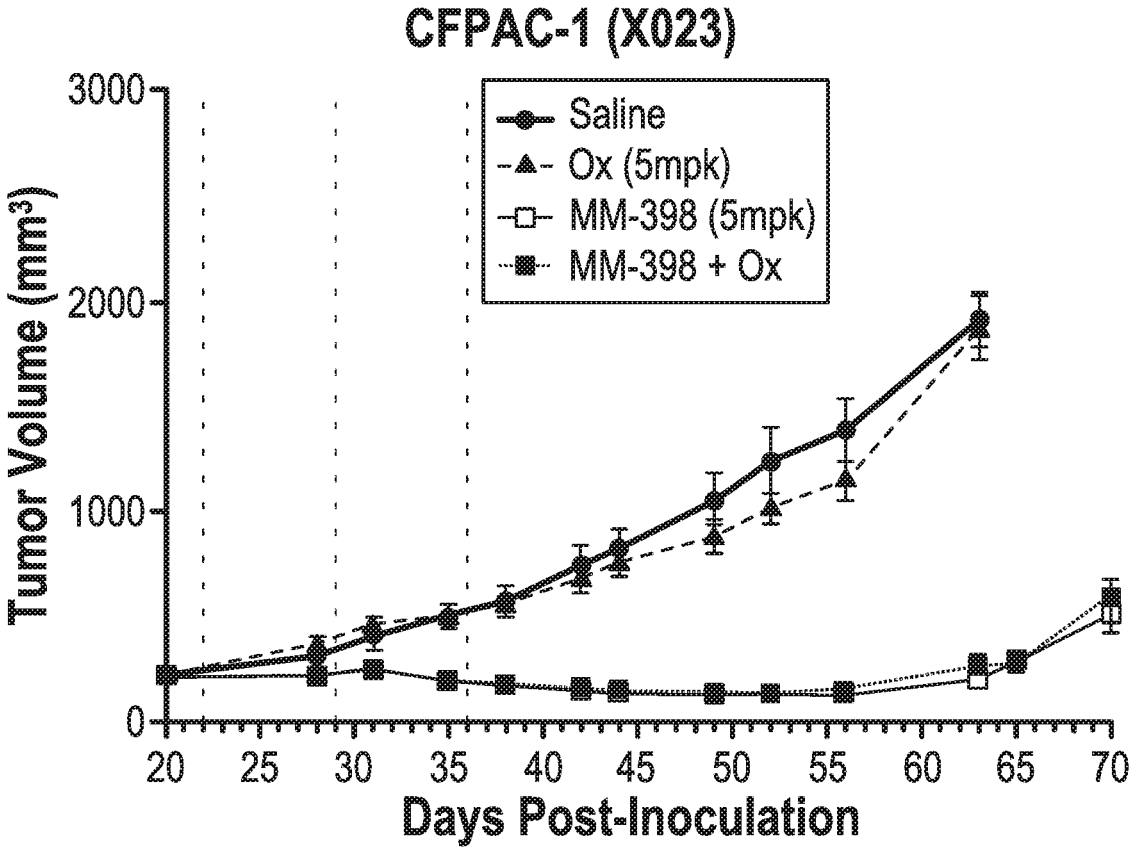

CFPAC-1 (X023)
Saline
Ox (5mpk)
MM-398 (5mpk)
MM-398 + Ox
Tumor Volume (mm³)
3000
2000
1000
0
20
25
30
35
40
45
50
55
60
65
70
Days Post-Inoculation

FIG. 4B

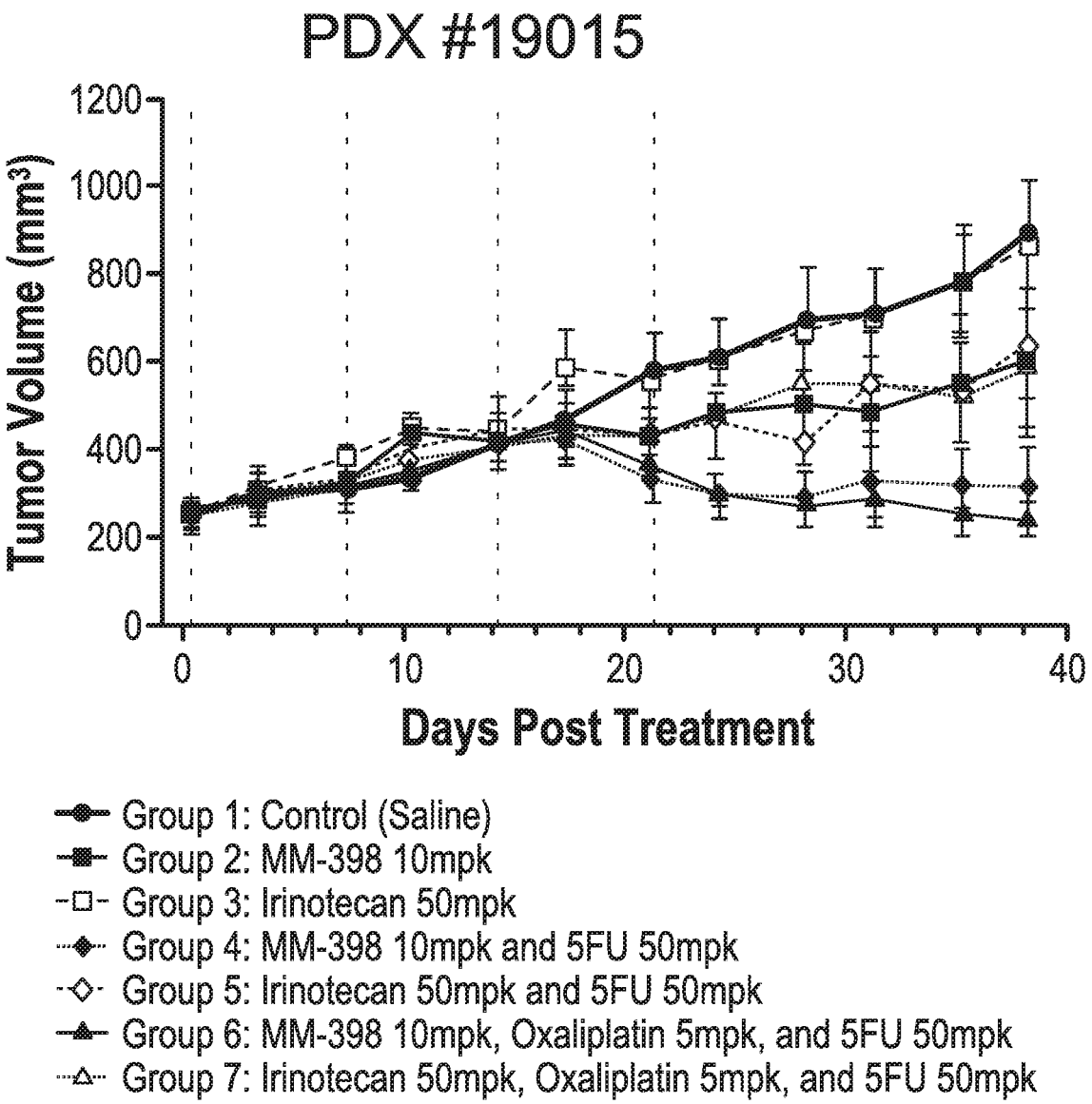

PDX #19015
Tumor Volume (mm3)
1200
1000
800
600
400
200
0
0
10
20
30
40
Days Post Treatment
Group 1: Control (Saline)
Group 2: MM-398 10mpk
Group 3: Irinotecan 50mpk
Group 4: MM-398 10mpk and 5FU 50mpk
Group 5: Irinotecan 50mpk and 5FU 50mpk
Group 6: MM-398 10mpk, Oxaliplatin 5mpk, and 5FU 50mpk
Group 7: Irinotecan 50mpk, Oxaliplatin 5mpk, and 5FU 50mpk

FIG. 5A

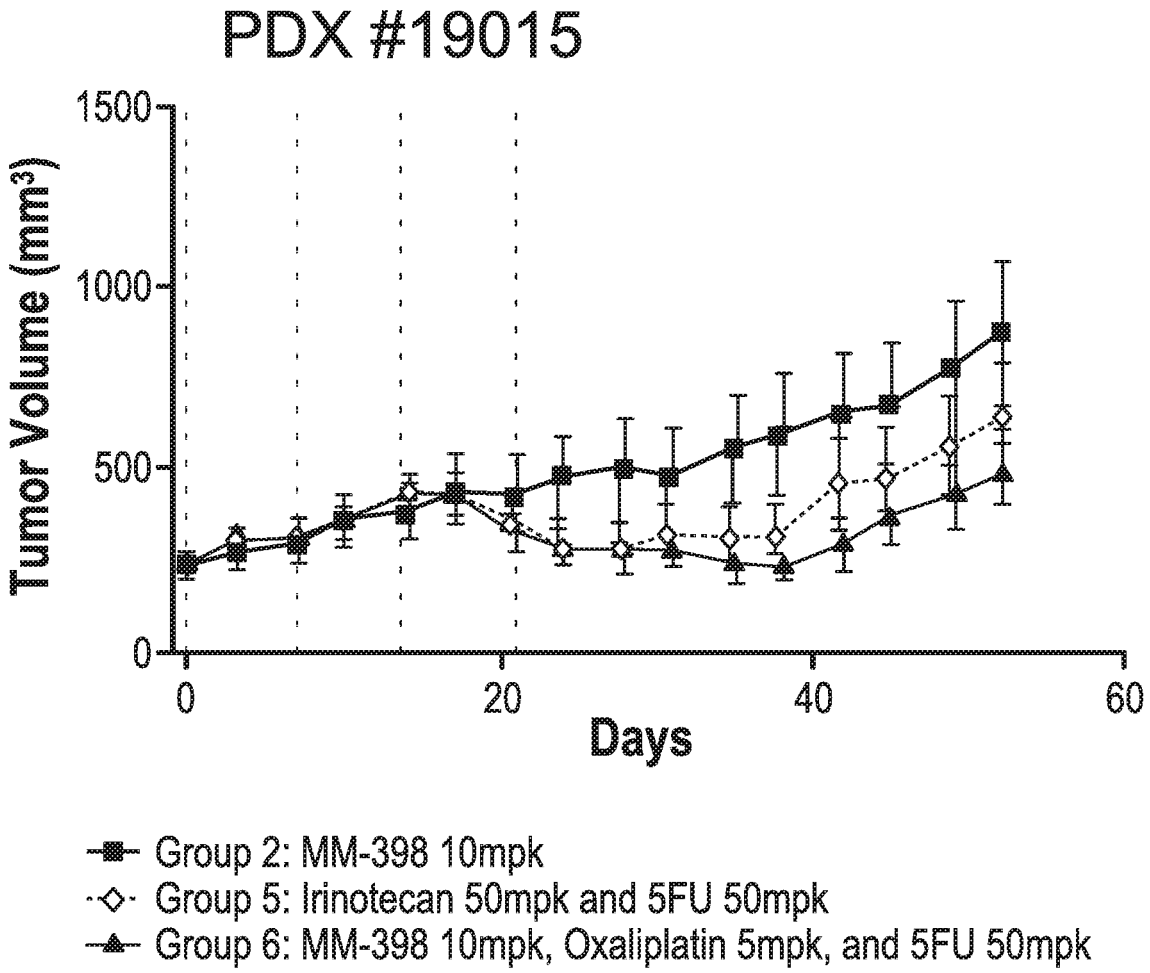

PDX #19015
Tumor Volume (mm3)
1500
1000
500
0
0
20
40
60
Days
Group 2: MM-398 10mpk
Group 5: Irinotecan 50mpk and 5FU 50mpk
Group 6: MM-398 10mpk, Oxaliplatin 5mpk, and 5FU 50mpk

FIG. 5B

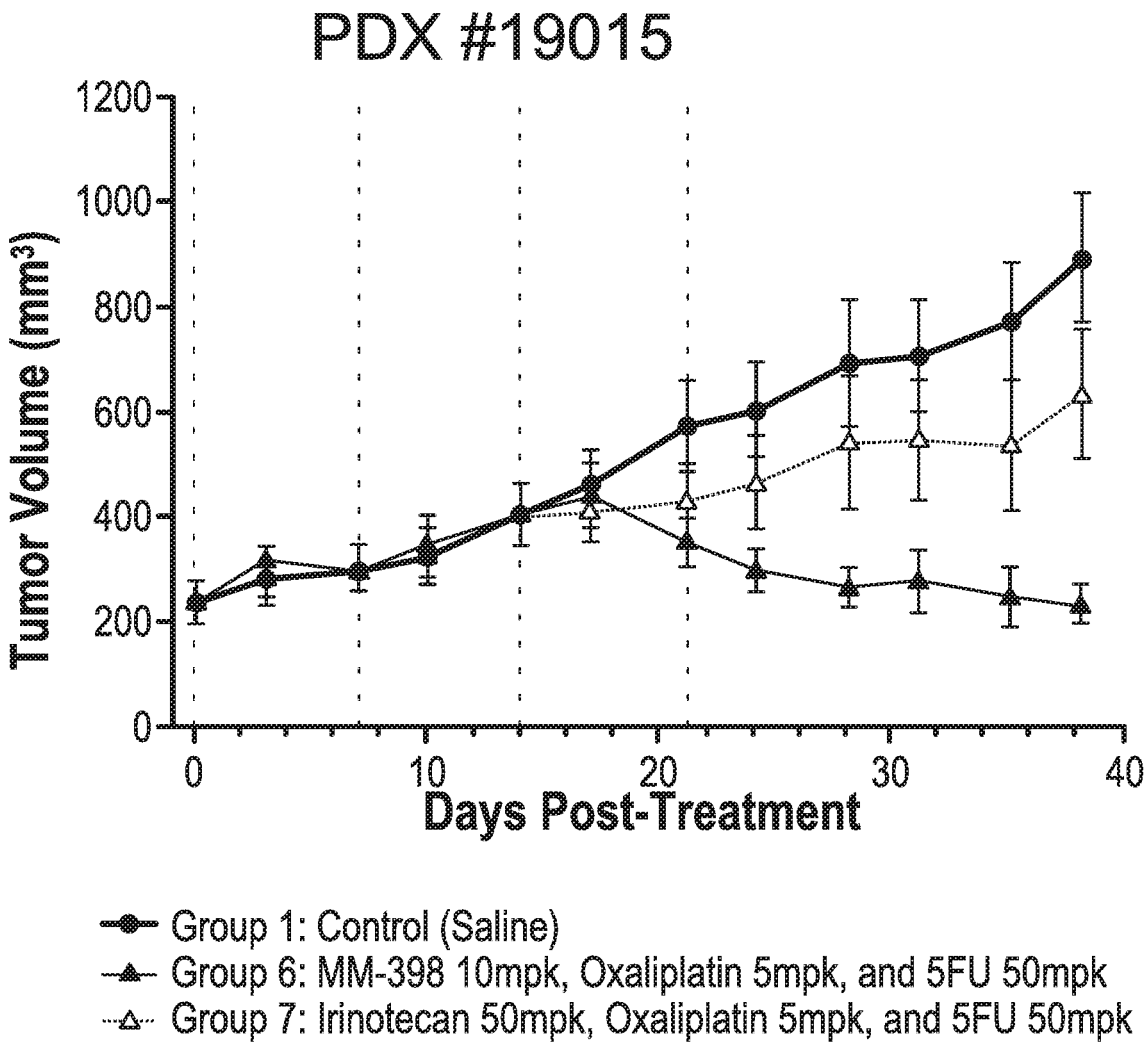

PDX #19015
Tumor Volume (mm3)
1200
1000
800
600
400
200
0
0
10
20
30
40
Days Post-Treatment
Group 1: Control (Saline)
Group 6: MM-398 10mpk, Oxaliplatin 5mpk, and 5FU 50mpk
Group 7: Irinotecan 50mpk, Oxaliplatin 5mpk, and 5FU 50mpk

FIG. 5C

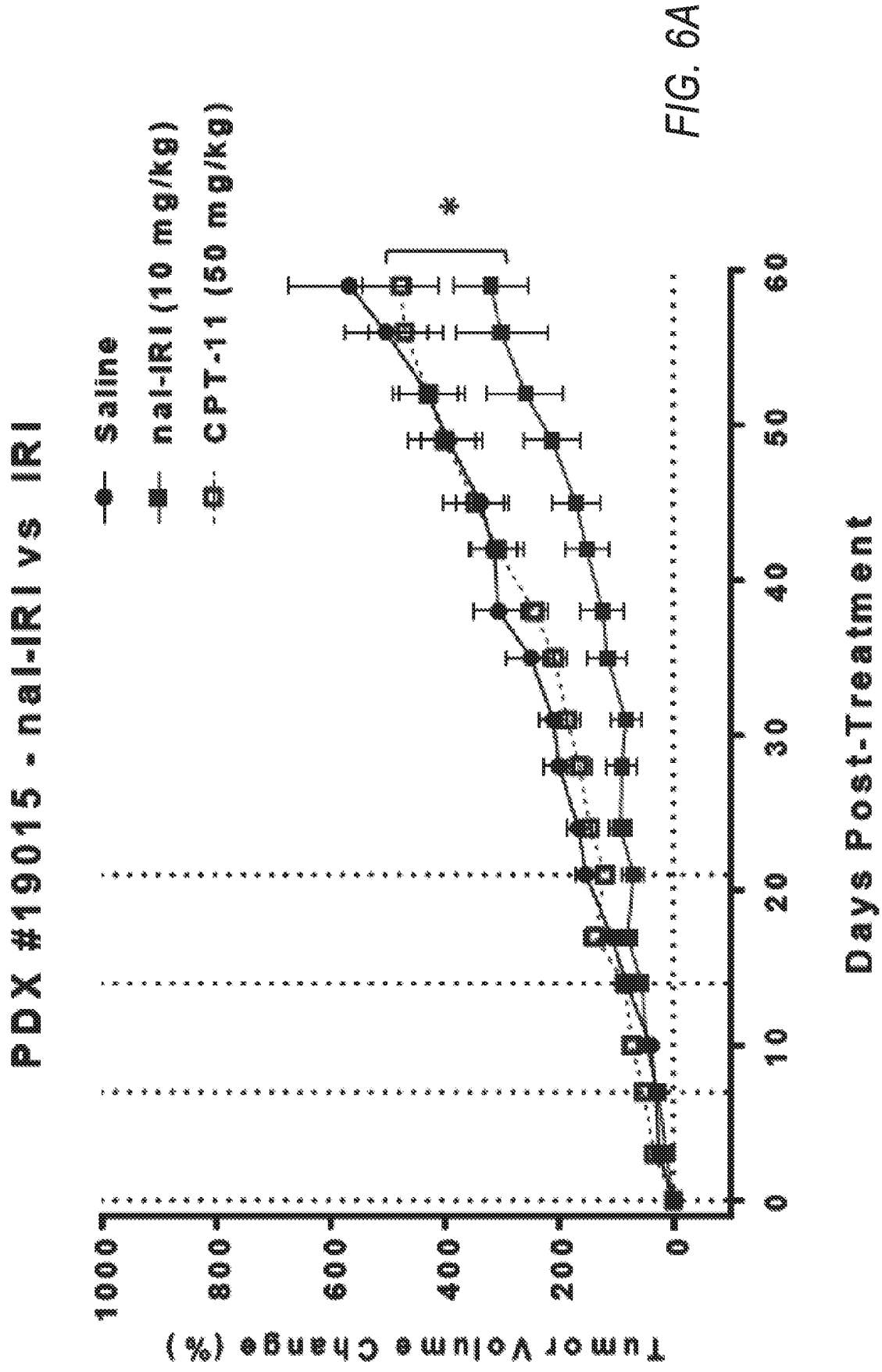

PDX #19015 - nal-IRI vs IRI
Saline
nal-IRI (10 mg/kg)
CPT-11 (50 mg/kg)
*
Tumor Volume Change (%)
1000
800
600
400
200
0
0
10
20
30
40
50
60
Days Post-Treatment

FIG. 6A

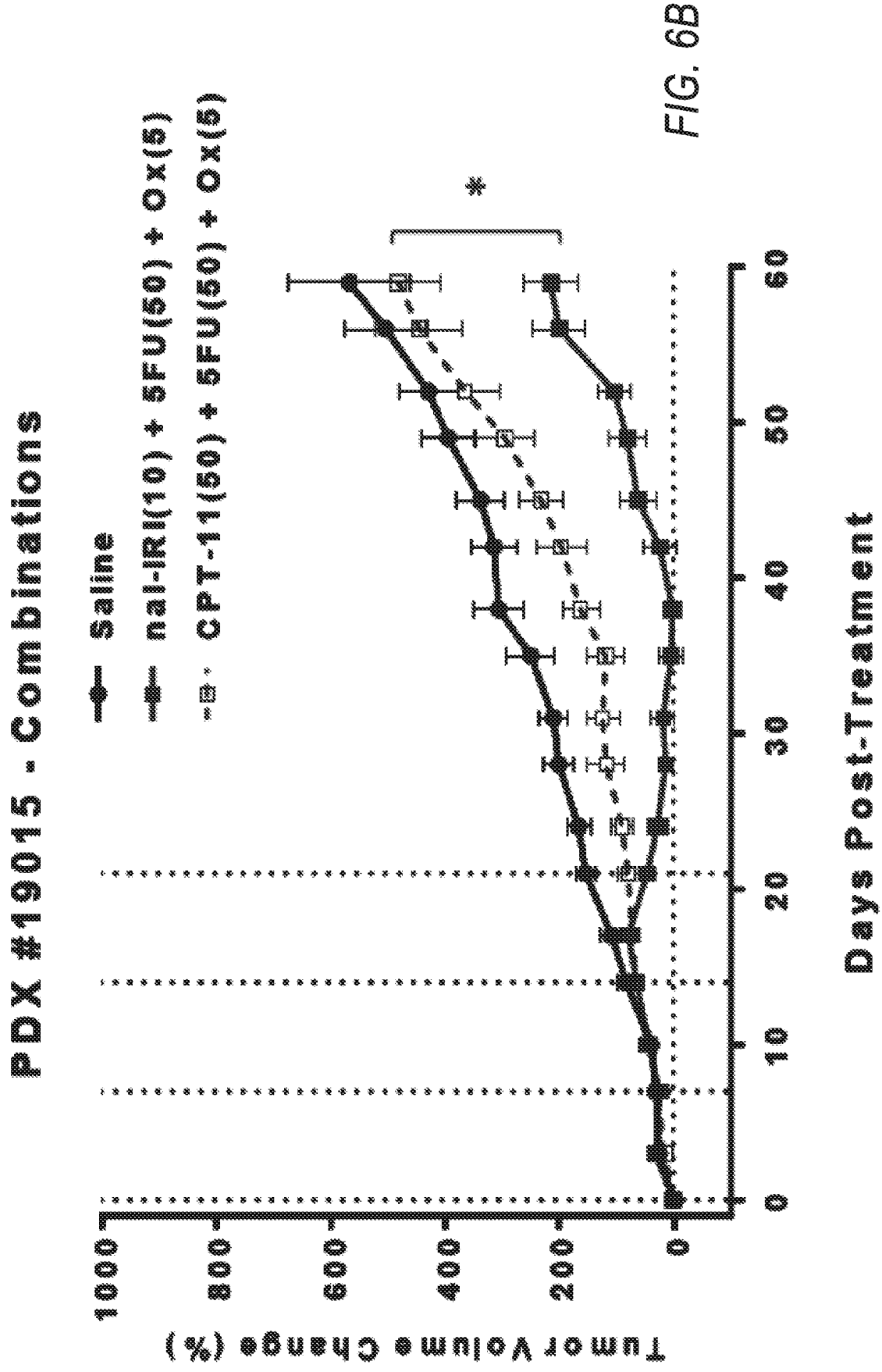

PDX #19015 - Combinations
Saline
nal-IRI(10) + 5FU(50) + Ox(5)
CPT-11(50) + 5FU(50) + Ox(5)
*
Tumor Volume Change (%)
1000
800
600
400
200
0
0
10
20
30
40
50
60
Days Post-Treatment

FIG. 6B

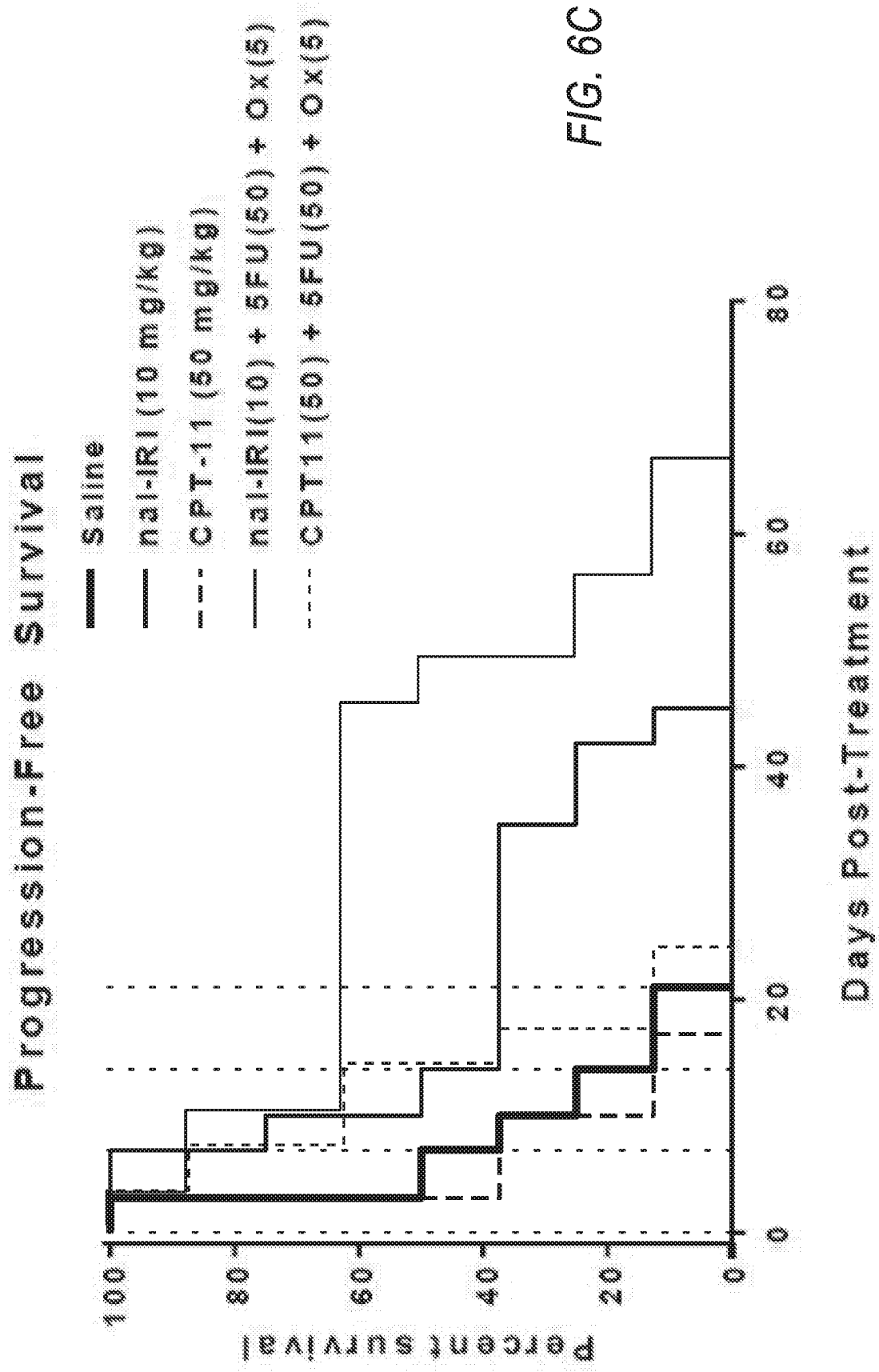

Progression-Free Survival
Saline
nal-IRI (10 mg/kg)
CPT-11 (50 mg/kg)
nal-IRI(10) + 5FU(50) + Ox(5)
CPT11(50) + 5FU(50) + Ox(5)
Percent survival
100
80
60
40
20
0
0
20
40
60
80
Days Post-Treatment

FIG. 6C

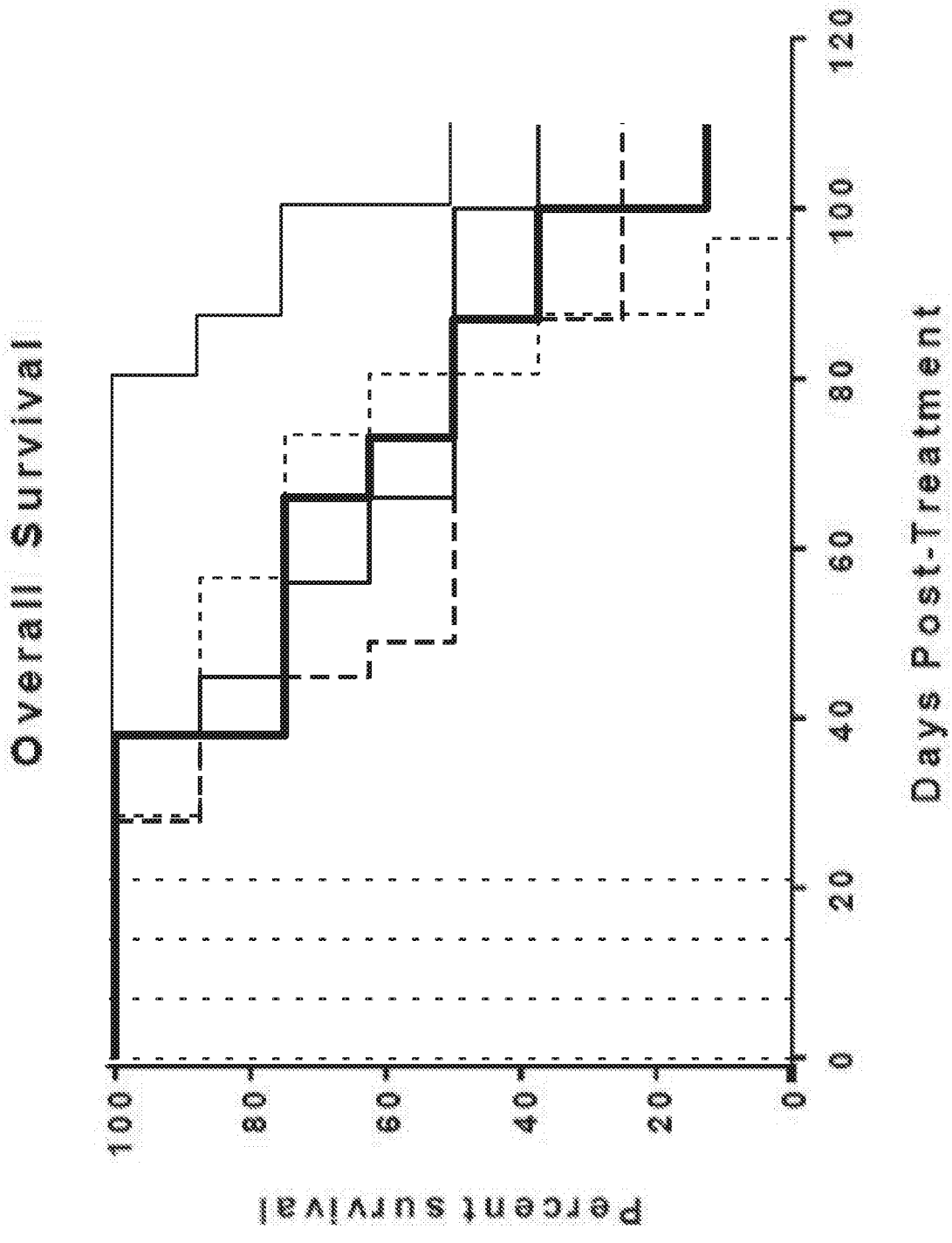

Overall Survival
Percent survival
100
80
60
40
20
0
0
20
40
60
80
100
120
Days Post-Treatment

FIG. 6D

G1 – Control
G2 – MM-398 10 mpk
G3 – Irinotecan 50 mg/kg
G4 – MM-398 10 mpk + 5FU 50 mpk
G5 – Irinotecan 50 mpk + 5FU 50 mpk
G6 – MM-398 10 mpk + 5FU 50 mpk + Ox 5 mpk
G7 – Irinotecan 50 mpk + 5FU 50 mpk + Ox 5 mpk

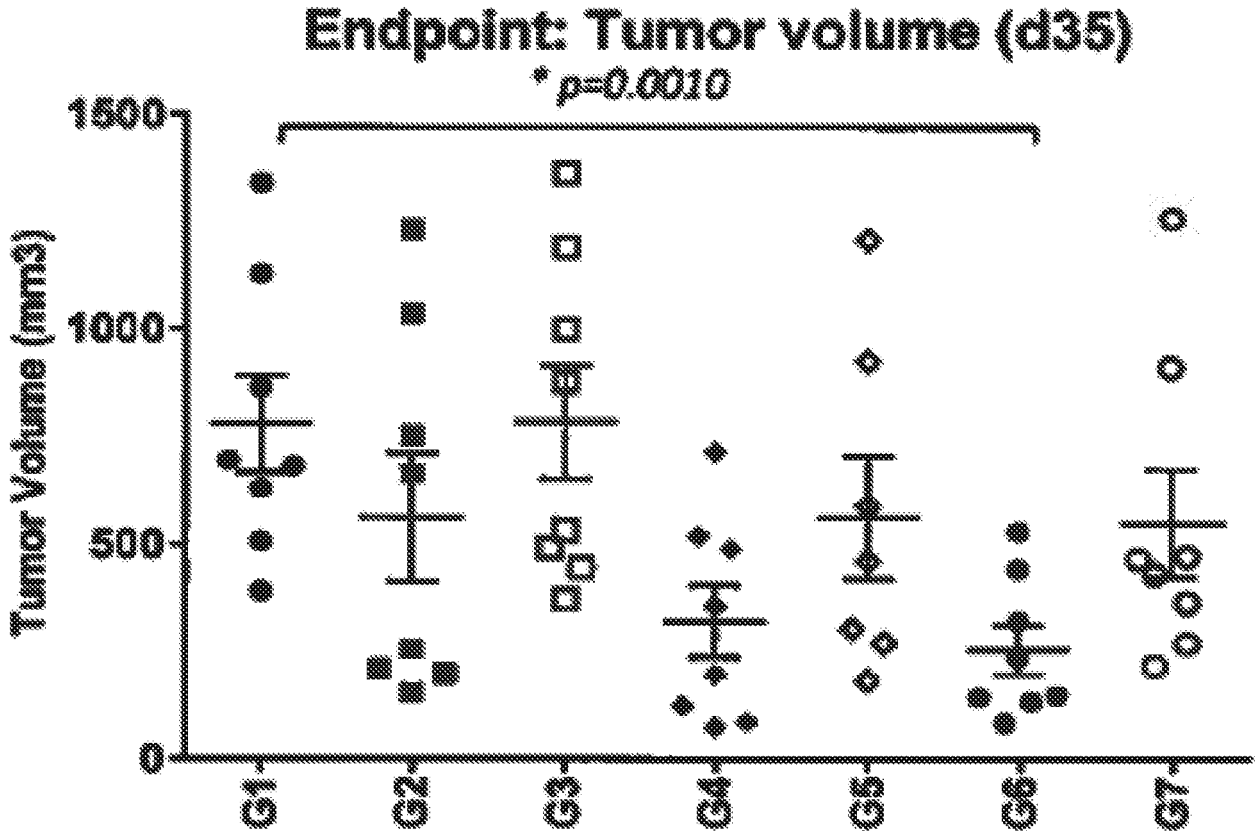


FIG. 7

	Control	MM-398	IRI	NAPOLI	FOLFIRI	NAPOX	FOLFIRINOX
Tumor Vol (mean mm^3,d35)	779	562	753	321	523	255	445
TGI (% at d35)	n/a	27.9%	3.4%	58.8%	32.9%	67.3%	42.9%
Median Days to $1000mm^3$	50.5 (n=8 of 8)	68 (6 of 8, 2 est)	43.5 (8 of 8)	70 (6 of 8, 2 est)	56 (7 of 7)	77 (8 of 8)	56 (8 of 8)
Stable Disease (-30% - +30%)	0	3	1	2	3	2	4
PR (30%-95% reduction)	0	0	0	3	0	4	0
CR (≥95% reduction)	0	0	0	0	0	0	0
Response Rate (≥30% reduction)	0%	0%	0%	38%	0%	50%	0%
Disease Control	0%	38%	13%	63%	38%	75%	50%
Rate (ORR + SD)							
Median Progression Free Survival (days)	5	12	3	36.5	10	47	14
Median OS(days)	80	83	68	100	80	105	80

FIG. 8

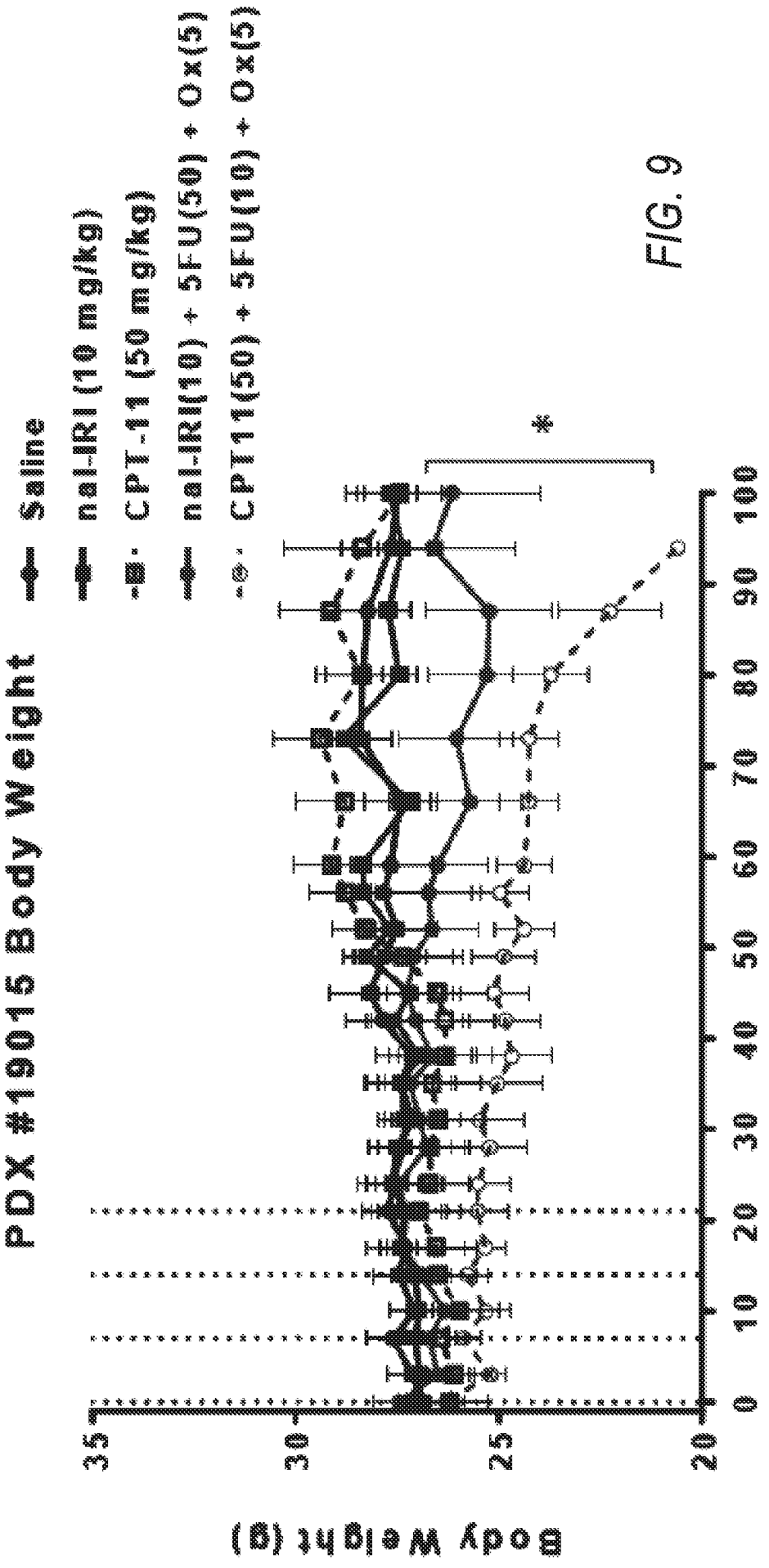

PDX #19015 Body Weight
Saline
nal-IRI (10 mg/kg)
CPT-11 (50 mg/kg)
nal-IRI(10) + 5FU(50) + Ox(5)
CPT11(50) + 5FU(10) + Ox(5)
*
Body Weight (g)
Days Post-Treatment
35
30
25
20
0
10
20
30
40
50
60
70
80
90
100

FIG. 9

FIG. 10A

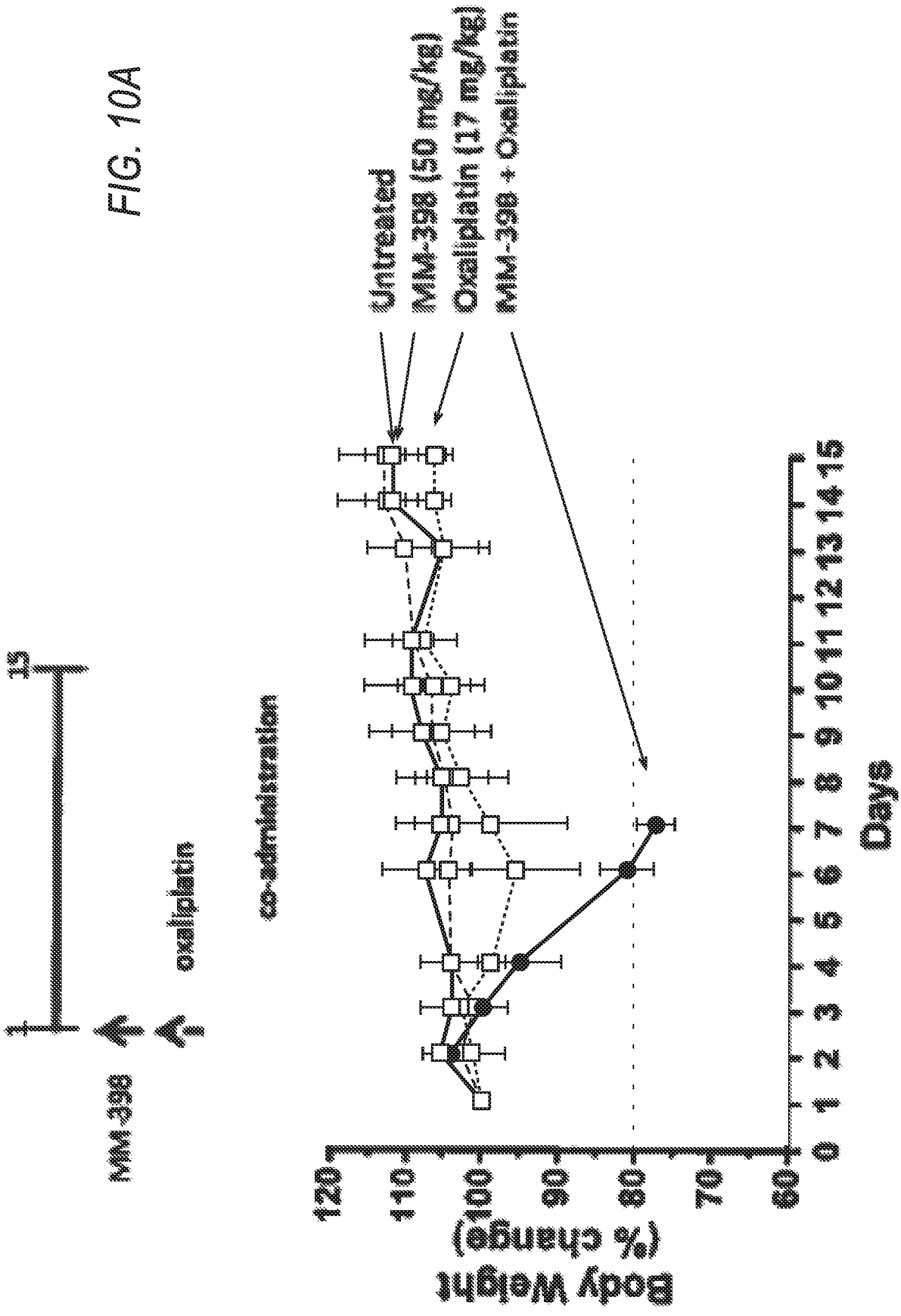
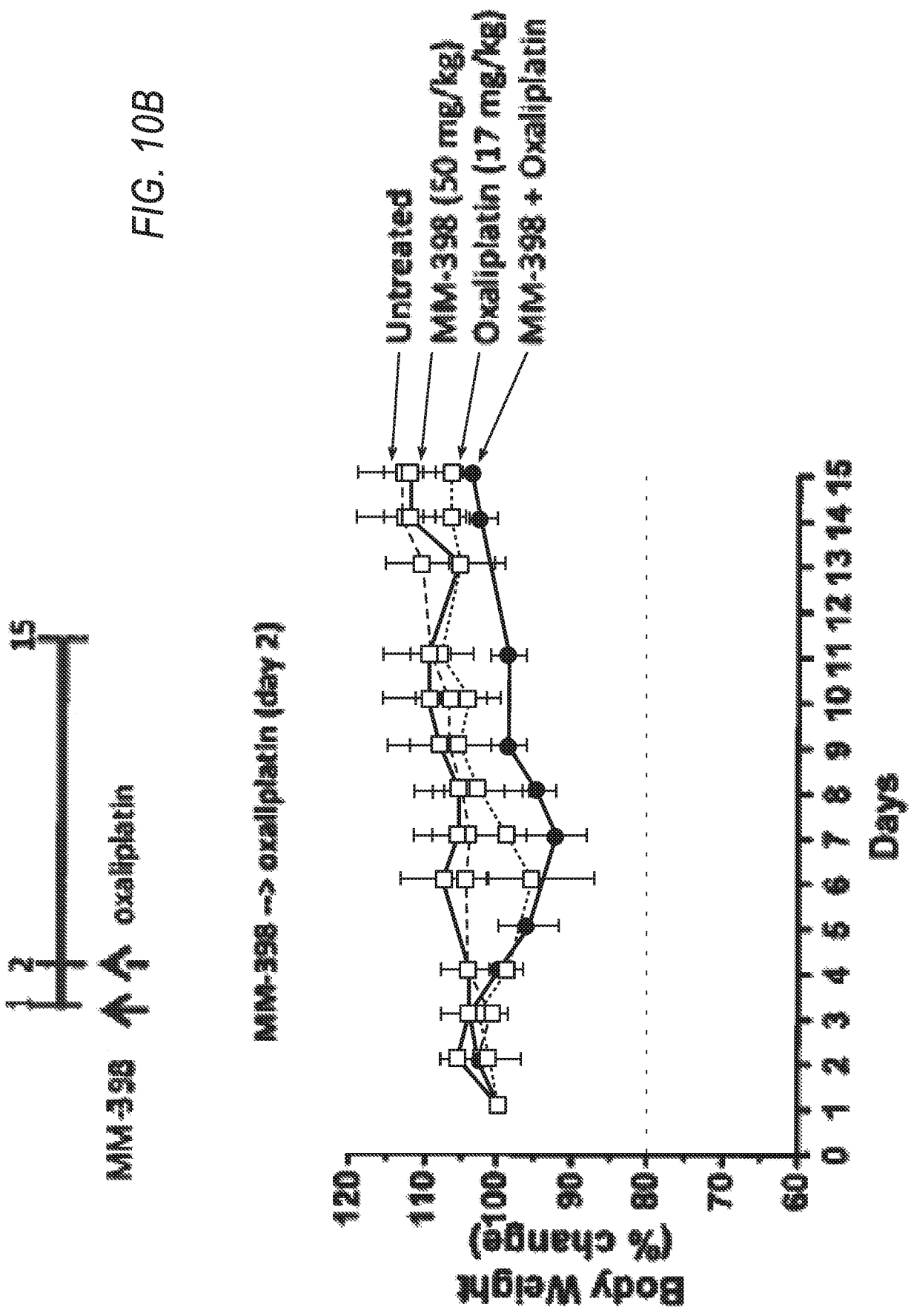

Untreated
MM-398 (50 mg/kg)
Oxaliplatin (17 mg/kg)
MM-398 + Oxaliplatin
Body Weight (% change)
120
110
100
90
80
70
60
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Days
MM-398
oxaliplatin
co-administration
1
13

FIG. 10B


1
2
15
MM-398
oxaliplatin
MM-398 --> oxaliplatin (day 2)
Untreated
MM-398 (50 mg/kg)
Oxaliplatin (17 mg/kg)
MM-398 + Oxaliplatin
Body Weight (% change)
120
110
100
90
80
70
60
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Days

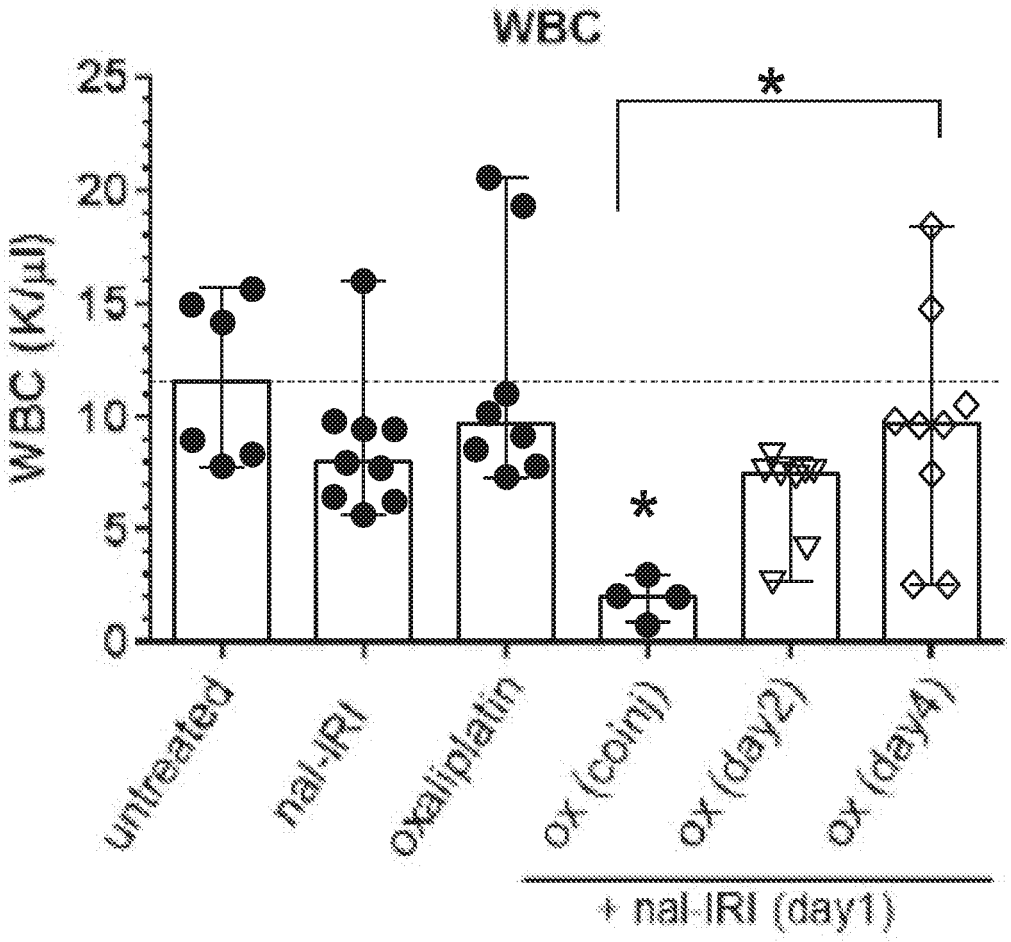


FIG. 11A

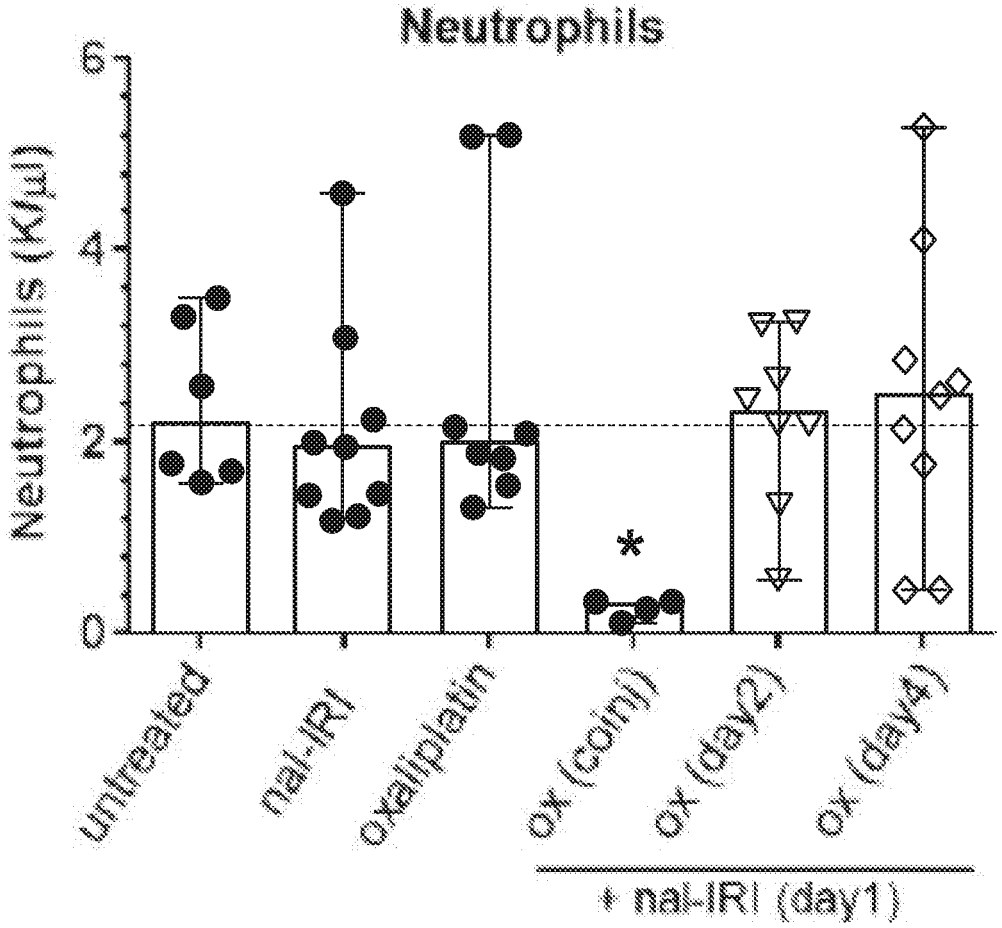


FIG. 11B

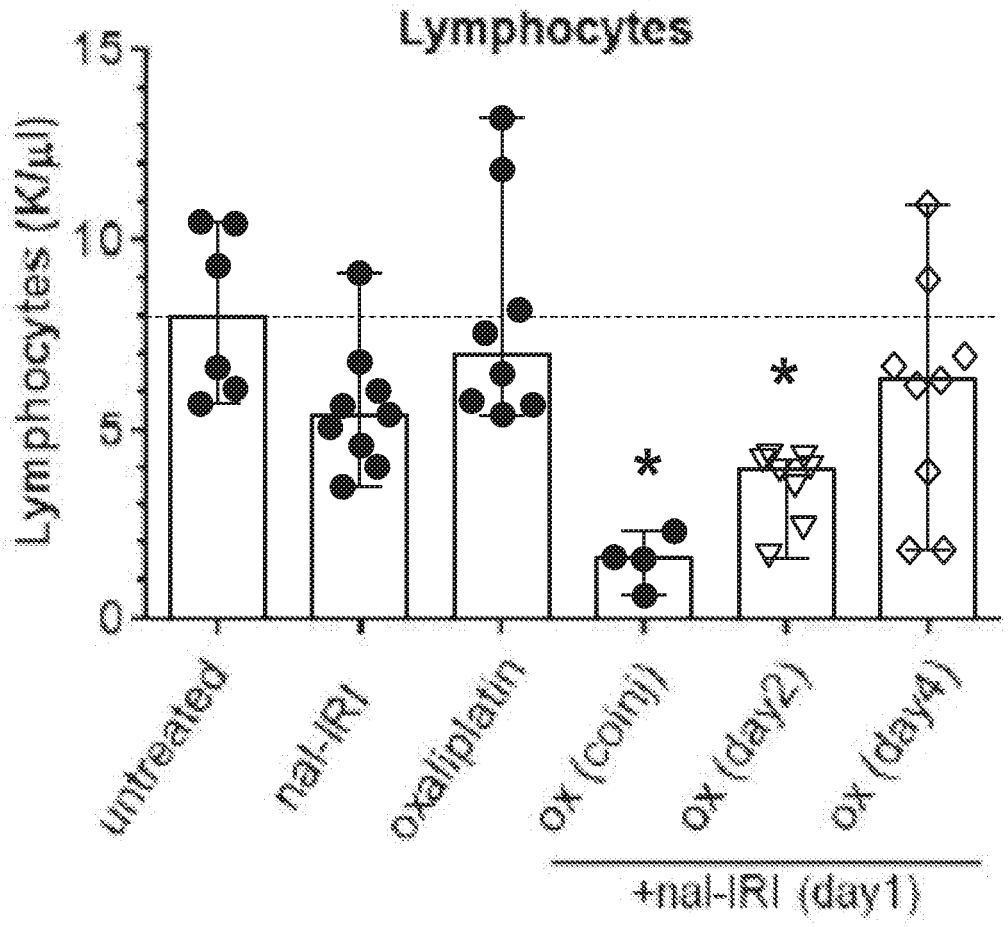


FIG. 11C

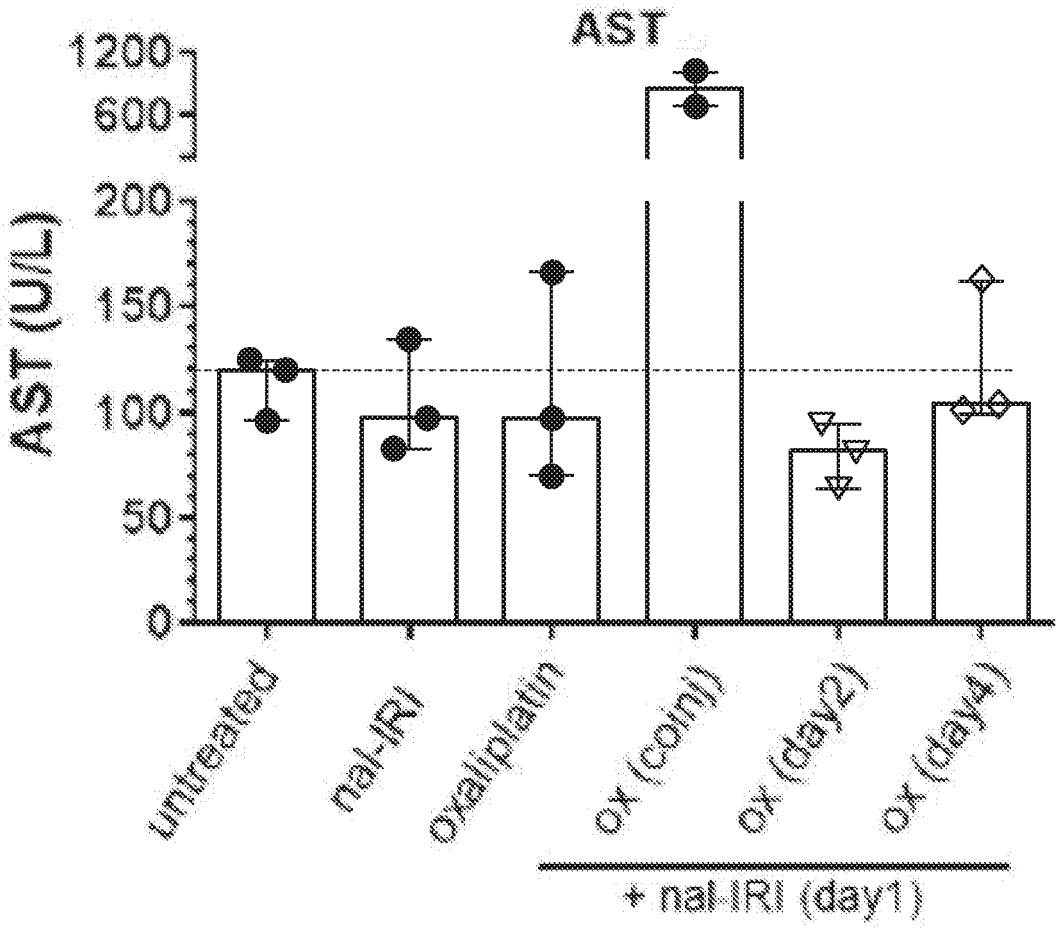


FIG. 11D

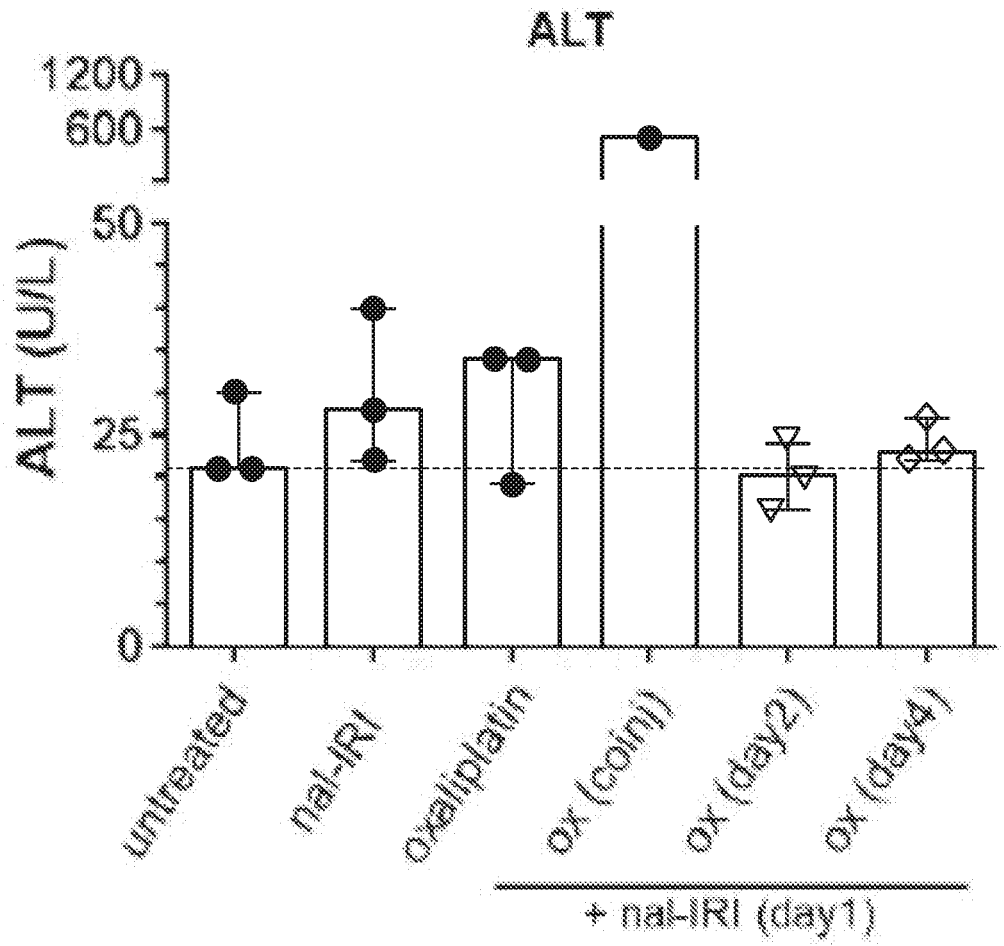


FIG. 11E

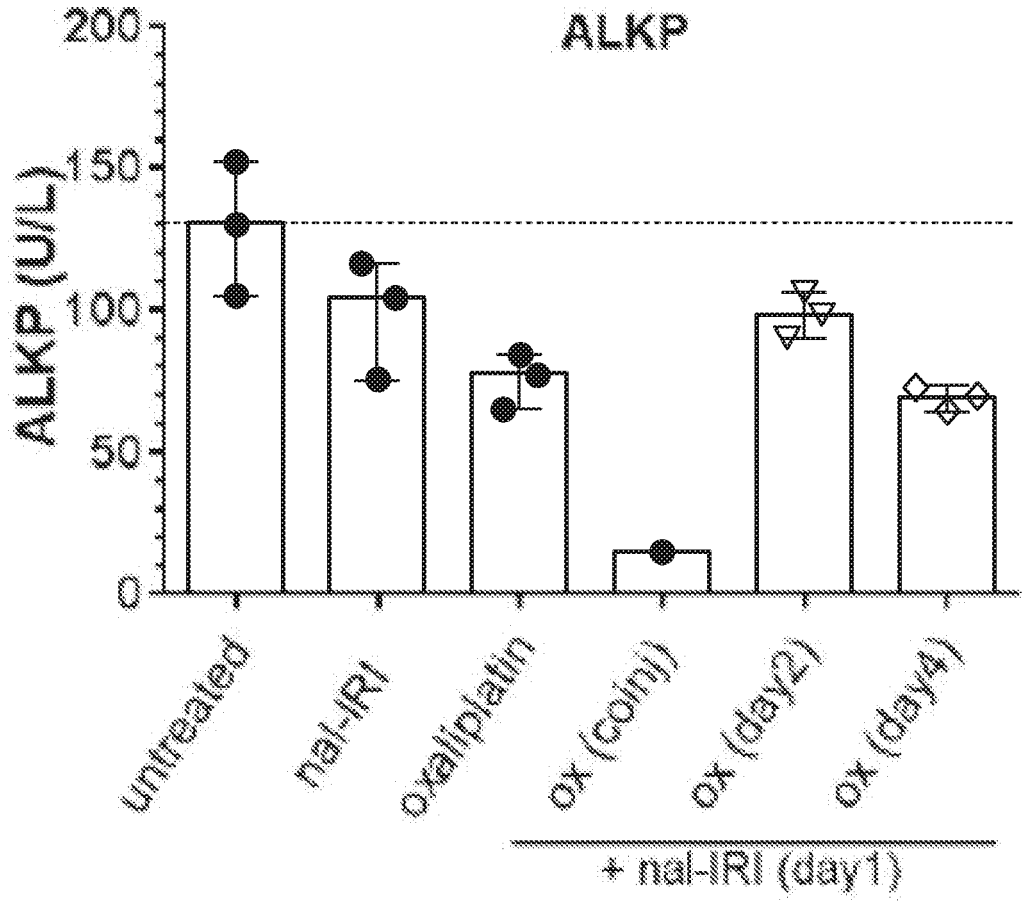


FIG. 11F

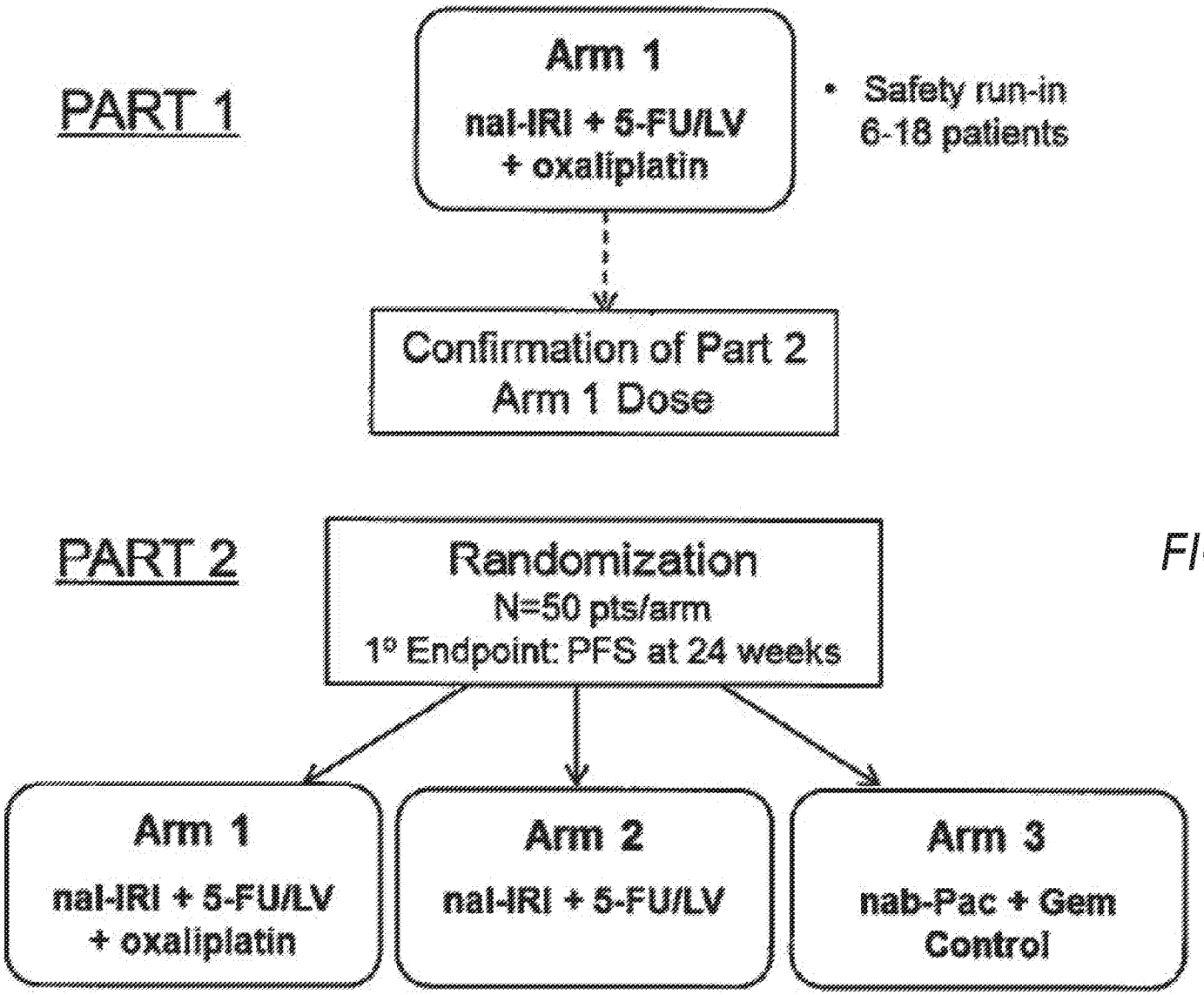

PART 1
Arm 1
nal-IRI + 5-FU/LV
+ oxaliplatin
• Safety run-in
6-18 patients
Confirmation of Part 2
Arm 1 Dose
PART 2
Randomization
N=50 pts/arm
1º Endpoint: PFS at 24 weeks
Arm 1
nal-IRI + 5-FU/LV
+ oxaliplatin
Arm 2
nal-IRI + 5-FU/LV
Arm 3
nab-Pac + Gem
Control

FIG. 12