FIG. 1A

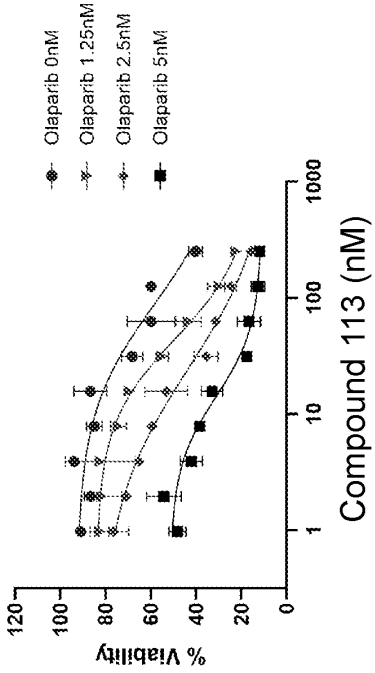

PolQi + Olaparib
Olaparib 0nM
Olaparib 1.25nM
Olaparib 2.5nM
Olaparib 5nM
% Viability
120
100
80
60
40
20
0
1
10
100
1000
Compound 113 (nM)

FIG. 1B

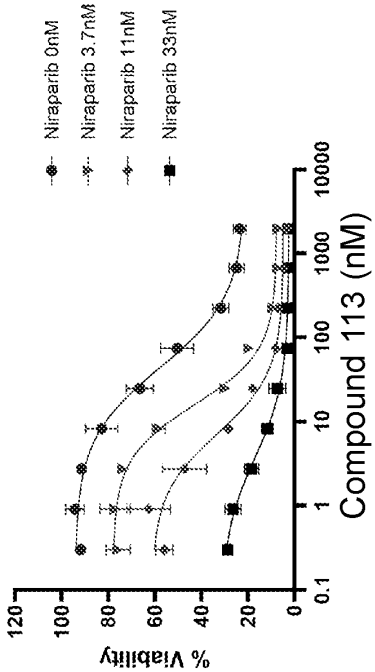

PolQi + Niraparib
Niraparib 0nM
Niraparib 3.7nM
Niraparib 11nM
Niraparib 33nM
% Viability
120
100
80
60
40
20
0
0.1
1
10
100
1000
10000
Compound 113 (nM)

FIG. 2

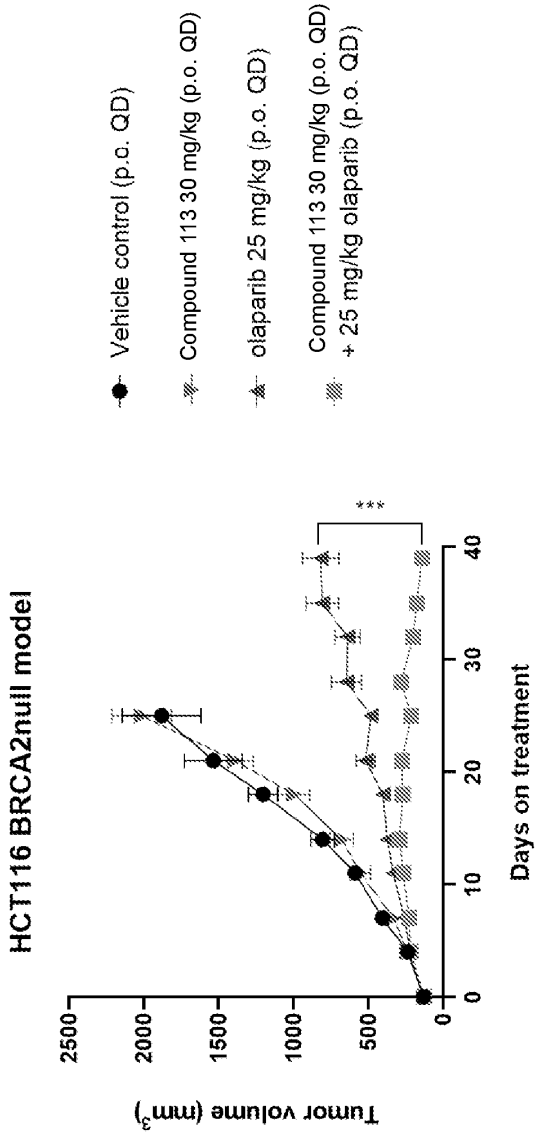

HCT116 BRCA2null model
Vehicle control (p.o. QD)
Compound 113 30 mg/kg (p.o. QD)
olaparib 25 mg/kg (p.o. QD)
Compound 113 30 mg/kg (p.o. QD)
+ 25 mg/kg olaparib (p.o. QD)
***
Tumor volume (mm3)
2500
2000
1500
1000
500
0
0
10
20
30
40
Days on treatment

FIG. 3

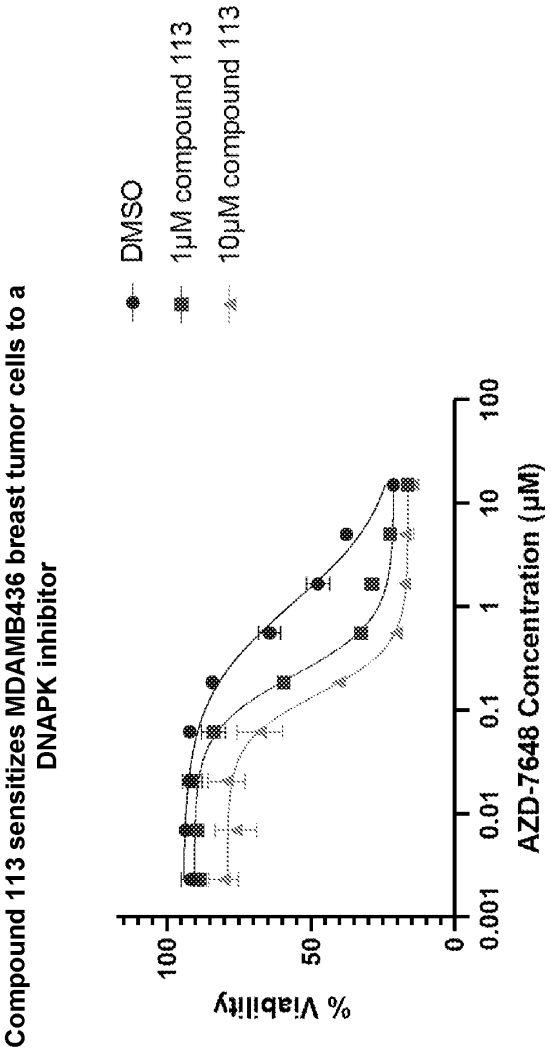

Compound 113 sensitizes MDAMB436 breast tumor cells to a DNAPK inhibitor
DMSO
1µM compound 113
10µM compound 113
% Viability
100
50
0
0.001
0.01
0.1
1
10
100
AZD-7648 Concentration (µM)

FIG. 4

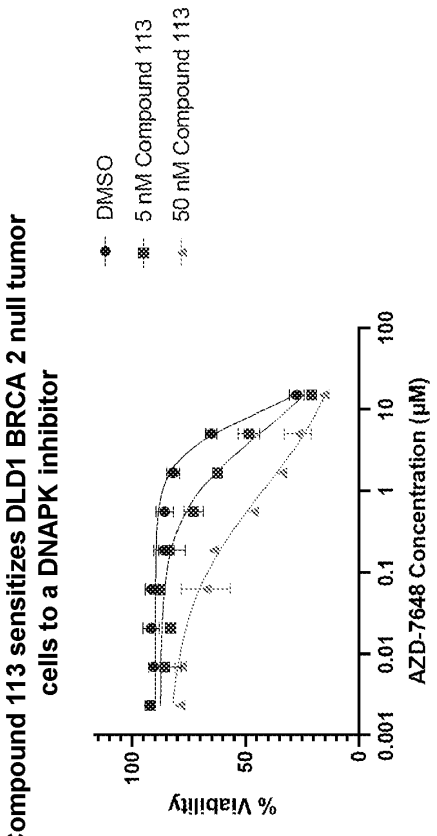

Compound 113 sensitizes DLD1 BRCA 2 null tumor cells to a DNAPK inhibitor
DMSO
5 nM Compound 113
50 nM Compound 113
% Viability
100
50
0
0.001
0.01
0.1
1
10
100
AZD-7648 Concentration (µM)

FIG. 5

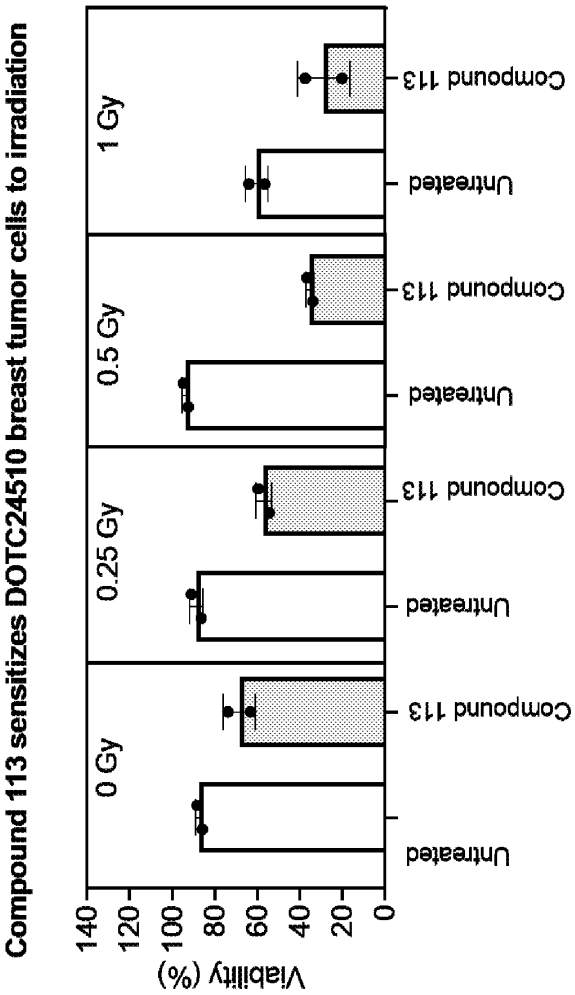

Compound 113 sensitizes DOTC24510 breast tumor cells to irradiation
Viability (%)
140
120
100
80
60
40
20
0
0 Gy
0.25 Gy
0.5 Gy
1 Gy
Untreated
Compound 113
Untreated
Compound 113
Untreated
Compound 113
Untreated
Compound 113

FIG. 6A

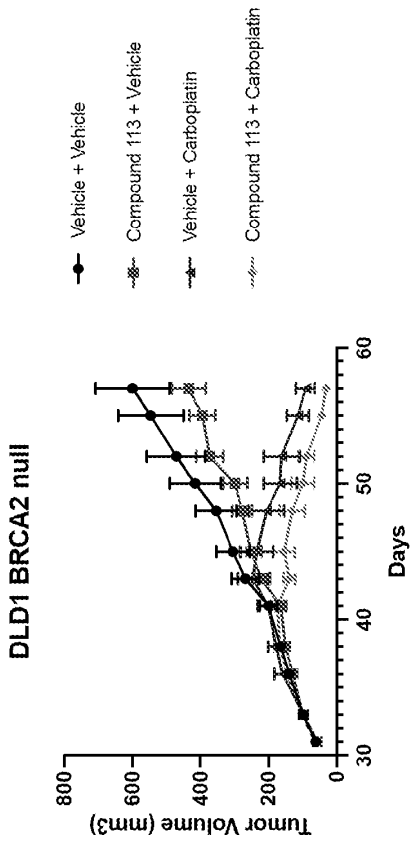

DLD1 BRCA2 null
Vehicle + Vehicle
Compound 113 + Vehicle
Vehicle + Carboplatin
Compound 113 + Carboplatin
Tumor Volume (mm3)
0
200
400
600
800
30
40
50
60
Days

FIG. 6B

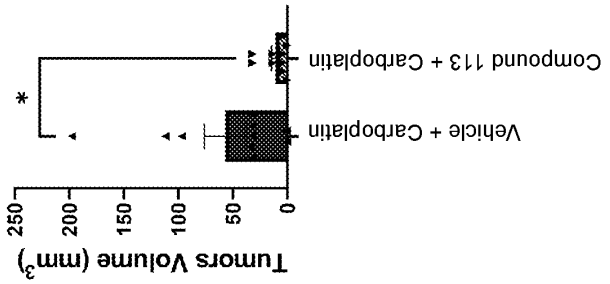

Day 35
Tumors Volume (mm3)
0
50
100
150
200
250
Vehicle + Carboplatin
Compound 113 + Carboplatin

FIG. 7B

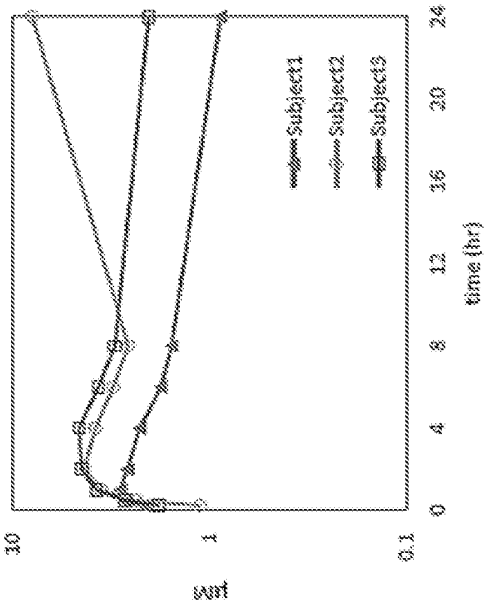

Subject1
Subject2
Subject3
time (hr)
0
4
8
12
16
20
24
μM
10
1
0.1

FIG. 7A

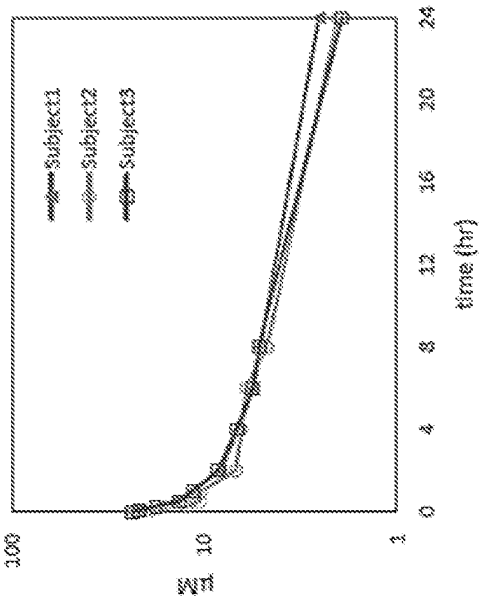

Subject1
Subject2
Subject3
time (hr)
0
4
8
12
16
20
24
μM
100
10
1

FIG. 7C

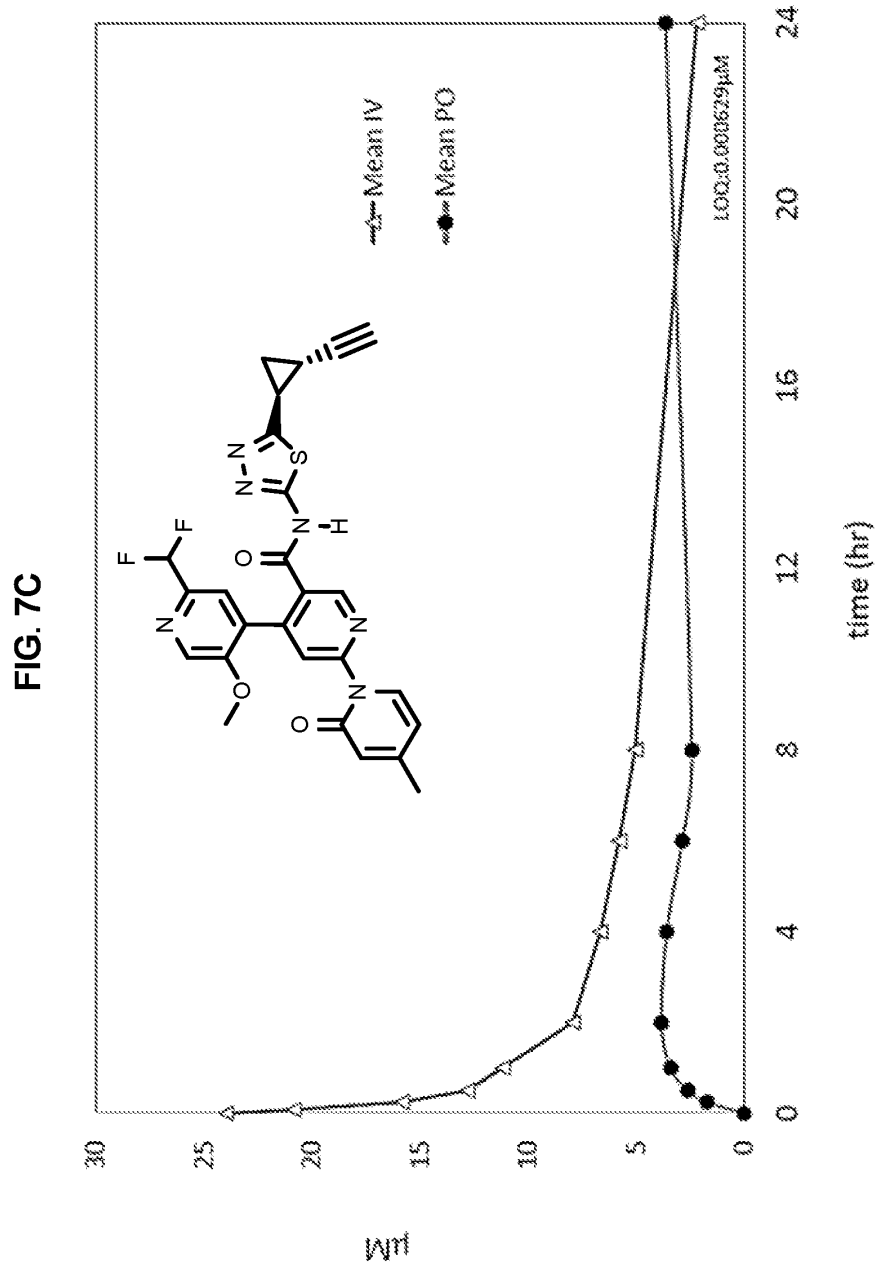

Mean IV
Mean PO
LOQ:0.000629μM
time (hr)
μM
0
4
8
12
16
20
24
0
5
10
15
20
25
30

FIG. 8B

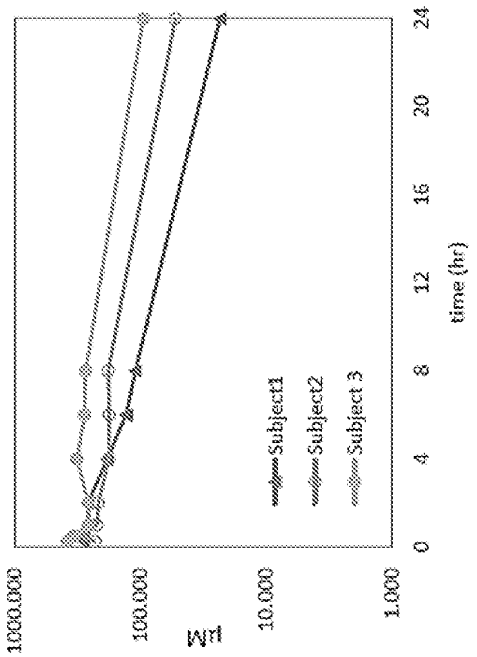

1000.000
100.000
10.000
1.000
µM
0
4
8
12
16
20
24
time (hr)
Subject1
Subject2
Subject 3

FIG. 8A

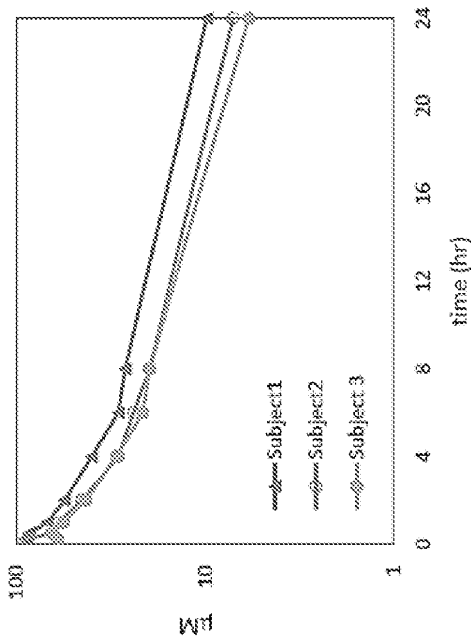
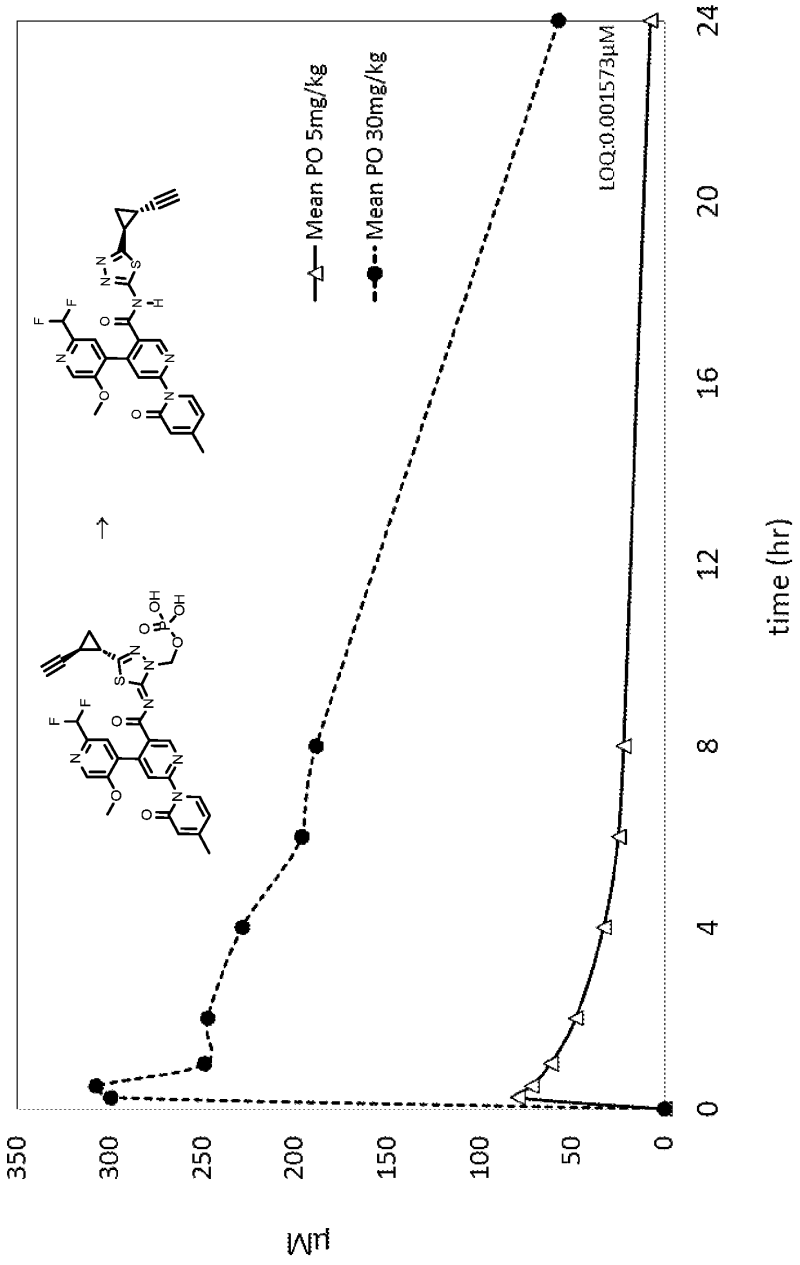

100
10
1
µM
0
4
8
12
16
20
24
time (hr)
Subject1
Subject2
Subject 3

FIG. 8C


Mean PO 5mg/kg
Mean PO 30mg/kg
LOQ:0.001573μM
μM
time (hr)
0
50
100
150
200
250
300
350
0
4
8
12
16
20
24