Fig. 1

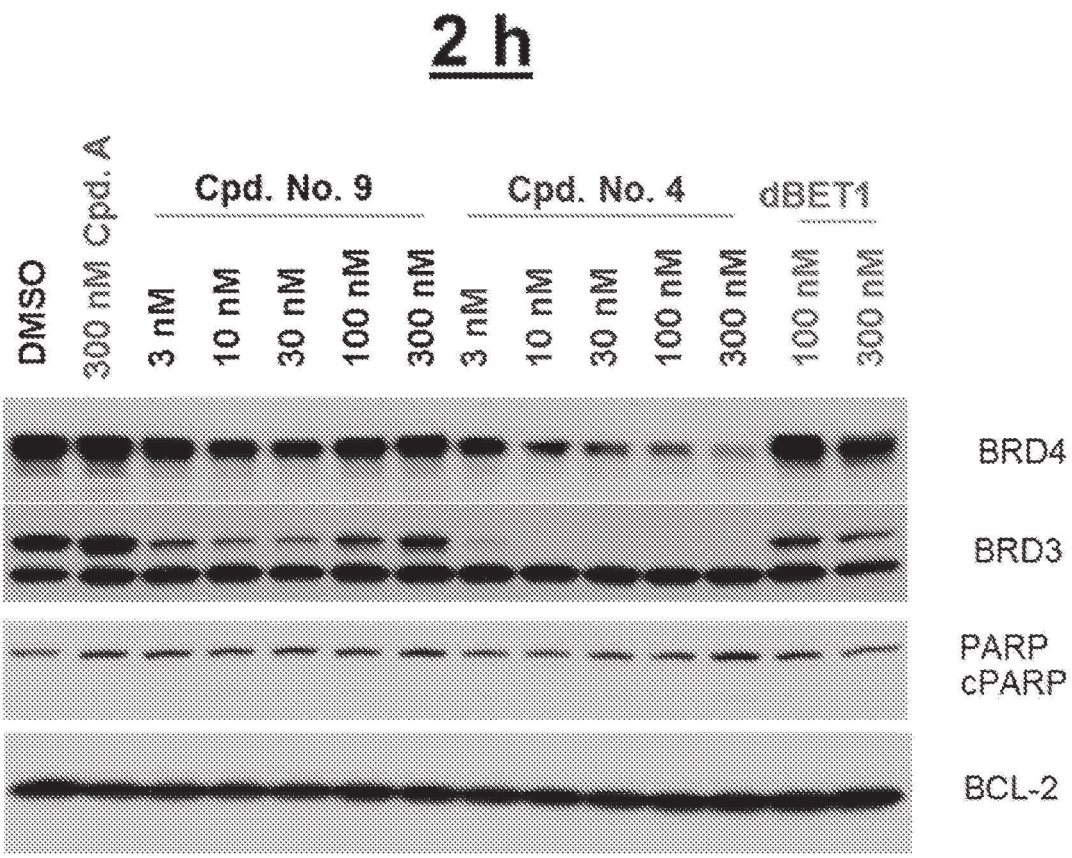

2 h
DMSO
300 nM Cpd. A
Cpd. No. 9
3 nM
10 nM
30 nM
100 nM
300 nM
Cpd. No. 4
3 nM
10 nM
30 nM
100 nM
300 nM
dBET1
100 nM
300 nM
BRD4
BRD3
PARP
cPARP
BCL-2

Fig. 2

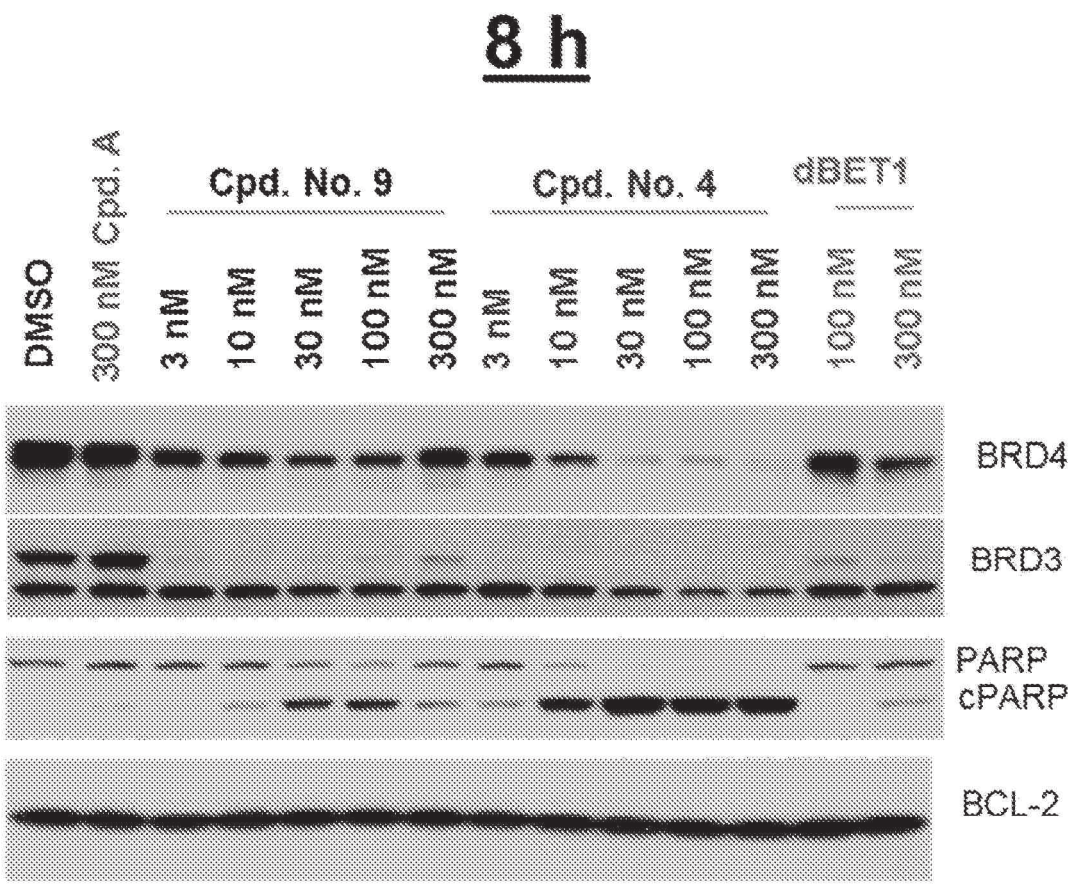

8 h
DMSO
300 nM Cpd. A
Cpd. No. 9
3 nM
10 nM
30 nM
100 nM
300 nM
Cpd. No. 4
3 nM
10 nM
30 nM
100 nM
300 nM
dBET1
100 nM
300 nM
BRD4
BRD3
PARP
cPARP
BCL-2

Fig. 3

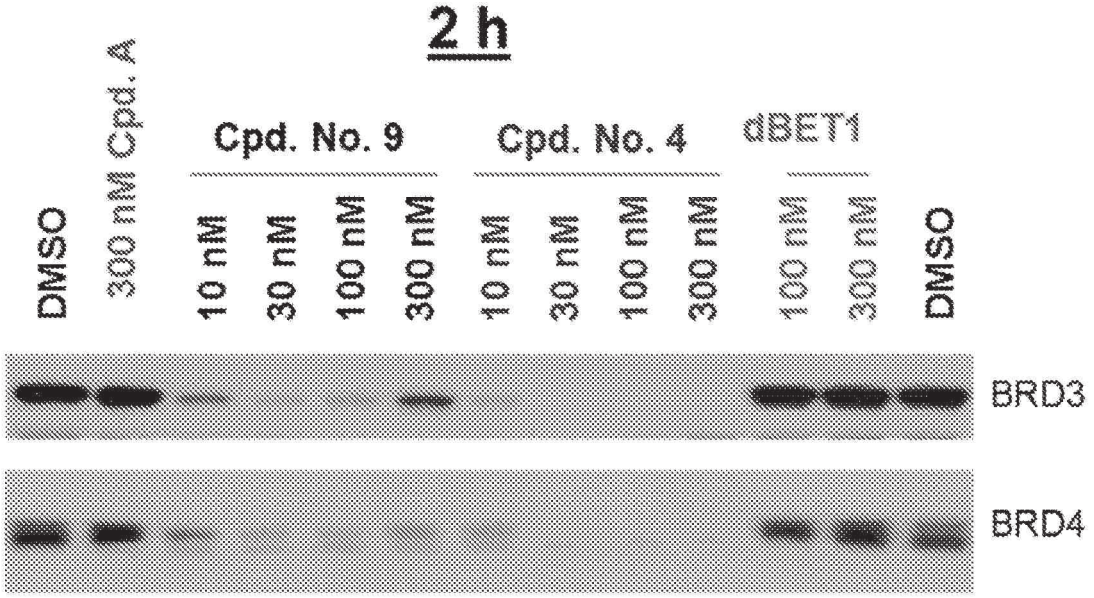

2 h
DMSO
300 nM Cpd. A
Cpd. No. 9
10 nM
30 nM
100 nM
300 nM
Cpd. No. 4
10 nM
30 nM
100 nM
300 nM
dBET1
100 nM
300 nM
DMSO
BRD3
BRD4

Fig. 4

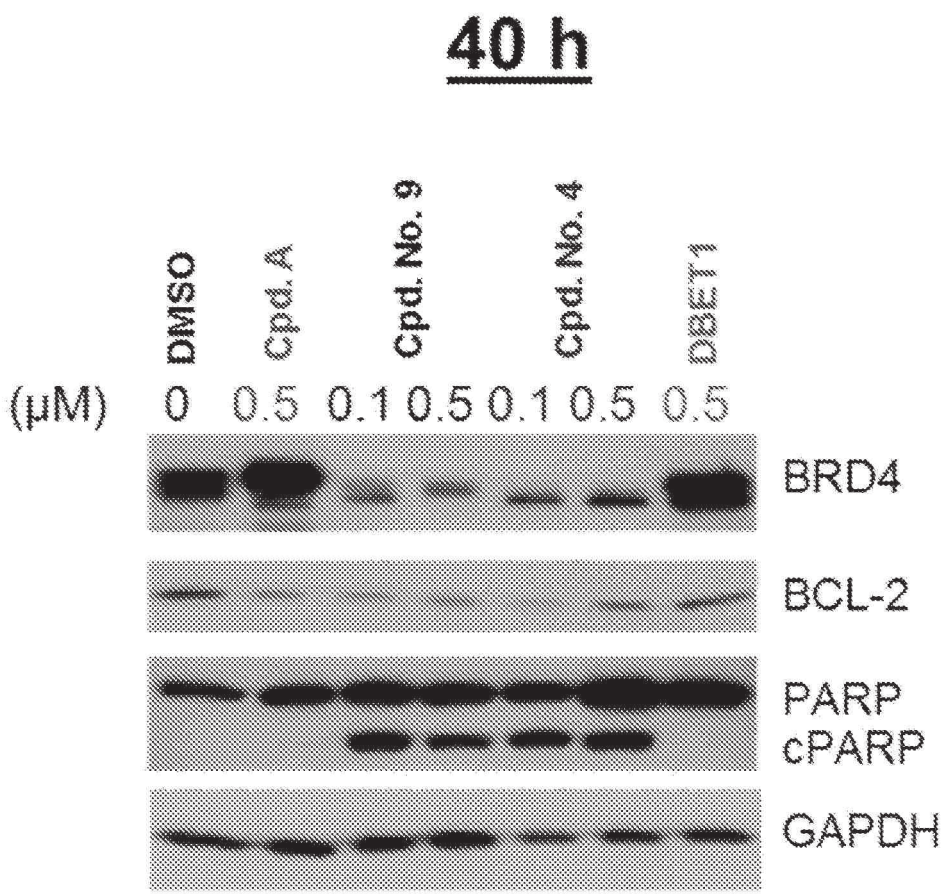

40 h
DMSO
Cpd. A
Cpd. No. 9
Cpd. No. 4
DBET1
(μM)
0
0.5
0.1
0.5
0.1
0.5
0.5
BRD4
BCL-2
PARP
cPARP
GAPDH

Fig. 5

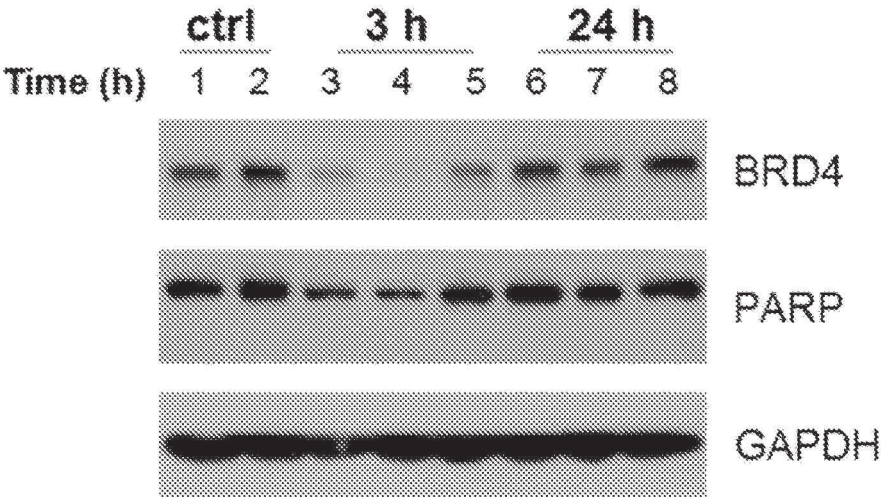


Fig. 6

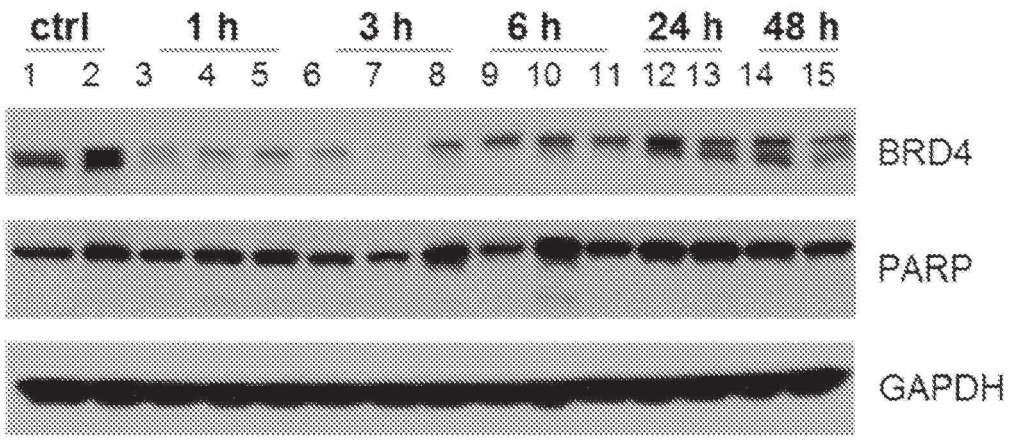

ctrl
1 h
3 h
6 h
24 h
48 h
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
BRD4
PARP
GAPDH

Fig. 7

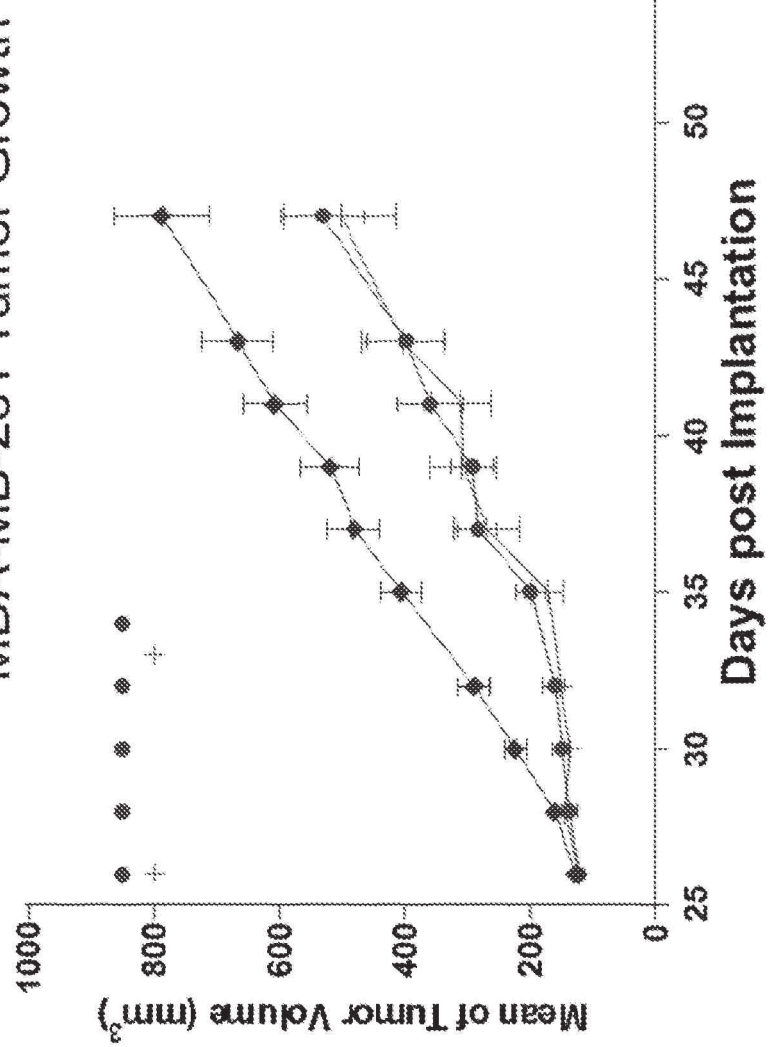

MDA-MB-231 Tumor Growth
Vehicle Control
Cpd. No. 9 10 mg/kg q2D IV 10% PCP
Cpd. No. 9 10 mg/kg qW IV 10% PCP
Mean of Tumor Volume (mm3)
1000
800
600
400
200
0
25
30
35
40
45
50
55
Days post Implantation

Fig. 8

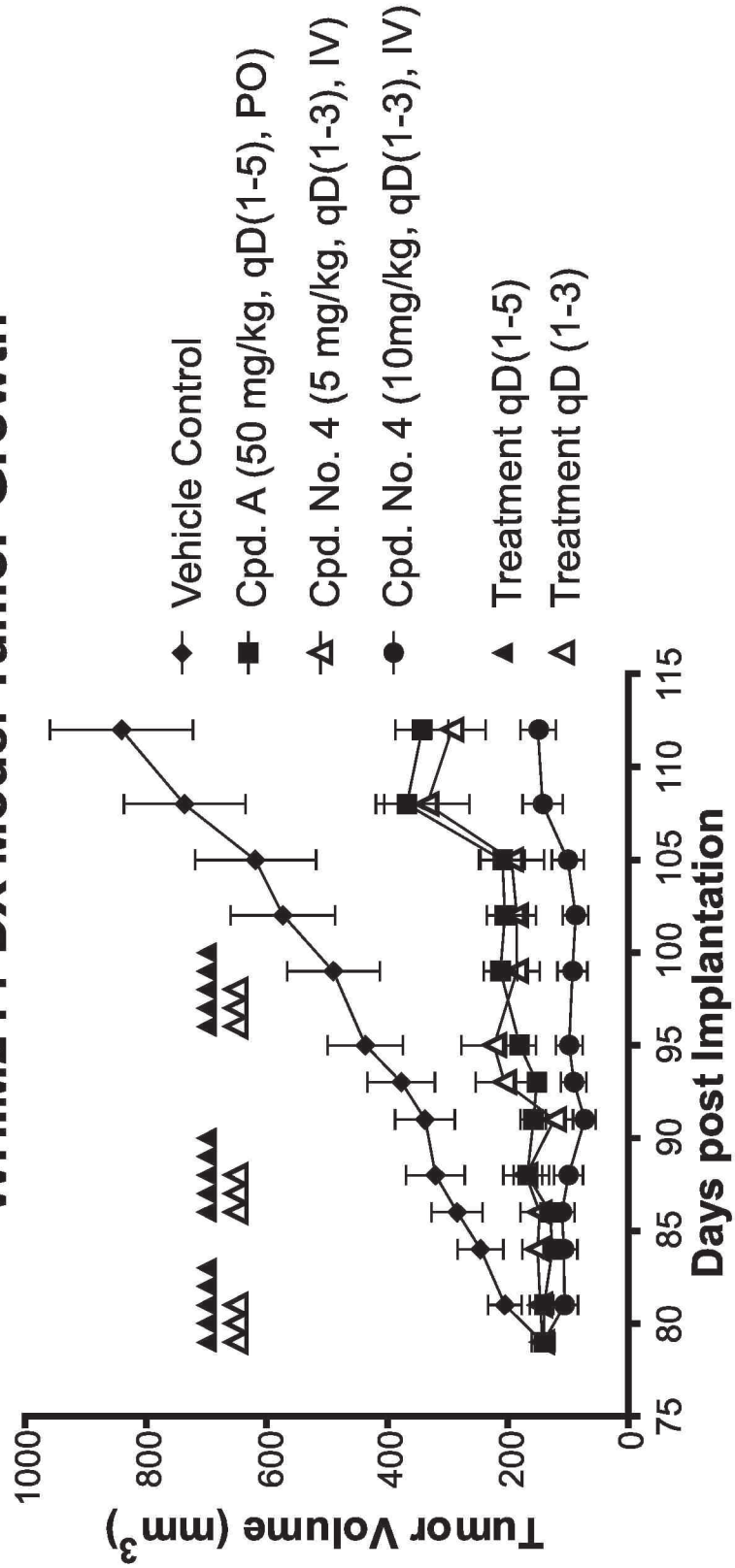

WHIM24 PDX Model Tumor Growth
Vehicle Control
Cpd. A (50 mg/kg, qD(1-5), PO)
Cpd. No. 4 (5 mg/kg, qD(1-3), IV)
Cpd. No. 4 (10mg/kg, qD(1-3), IV)
Treatment qD(1-5)
Treatment qD (1-3)
Tumor Volume (mm3)
1000
800
600
400
200
0
75
80
85
90
95
100
105
110
115
Days post Implantation

Fig. 9

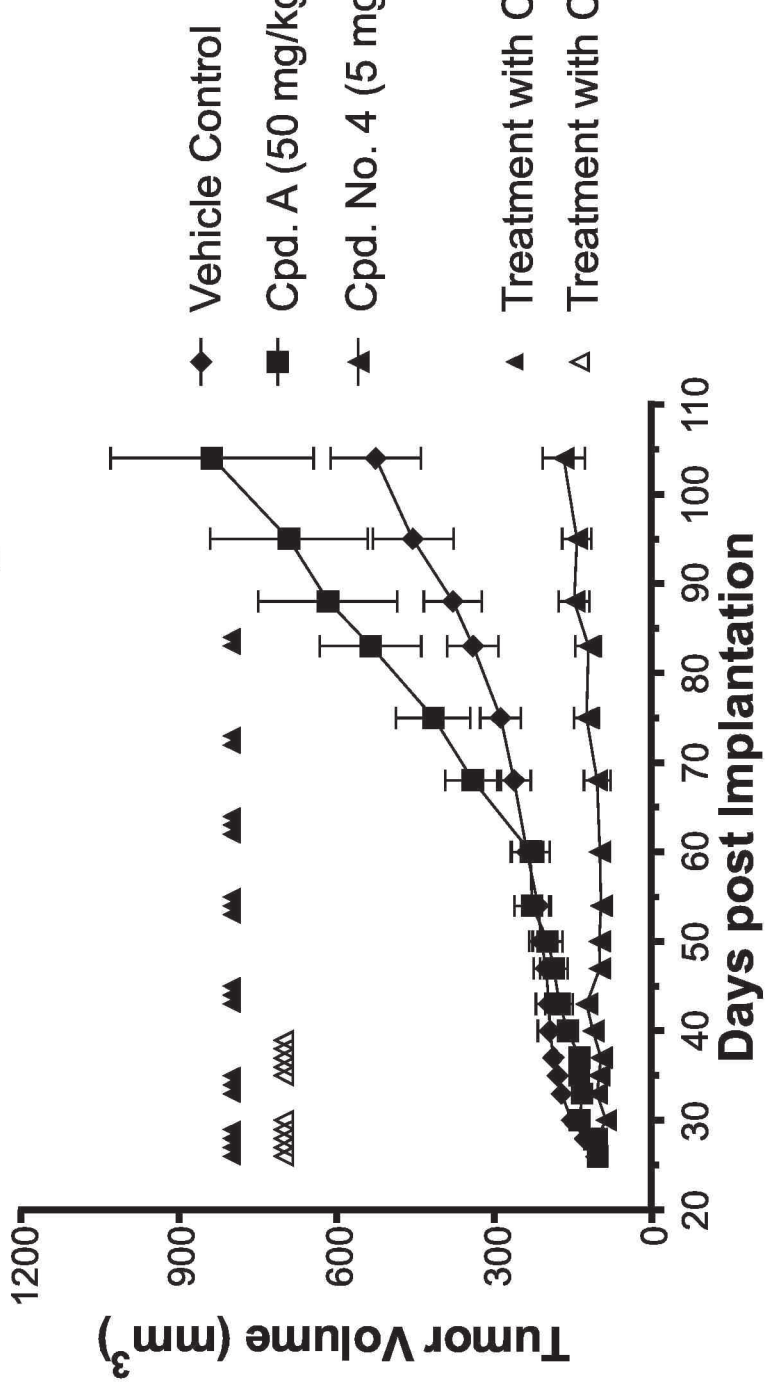

MDA-MB-453 Xenograft Tumor Growth
Tumor Volume (mm3)
1200
900
600
300
0
20
30
40
50
60
70
80
90
100
110
Days post Implantation
Vehicle Control
Cpd. A (50 mg/kg, PO)
Cpd. No. 4 (5 mg/kg, IV)
Treatment with Cpd. No. 4
Treatment with Cpd. A

Fig. 10

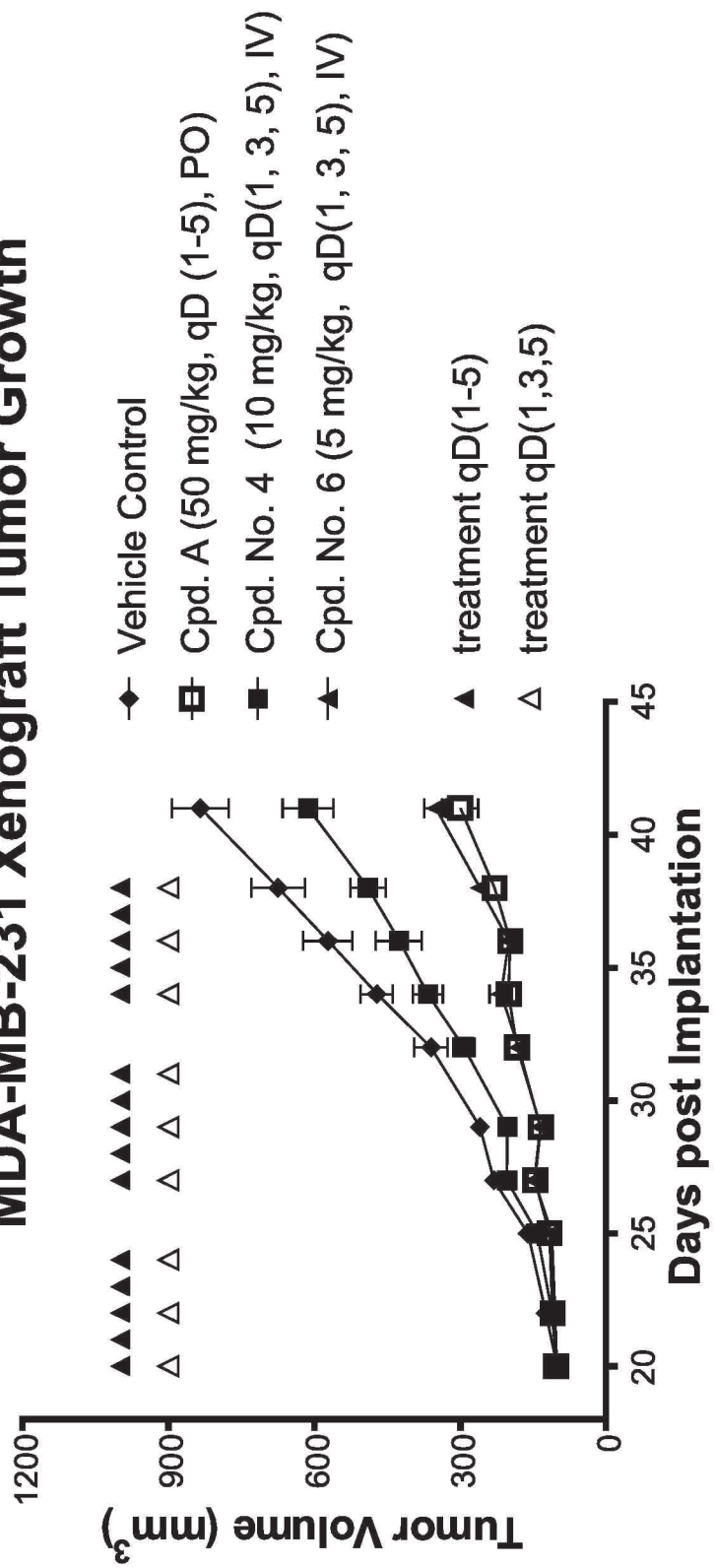

MDA-MB-231 Xenograft Tumor Growth
Vehicle Control
Cpd. A (50 mg/kg, qD (1-5), PO)
Cpd. No. 4 (10 mg/kg, qD(1, 3, 5), IV)
Cpd. No. 6 (5 mg/kg, qD(1, 3, 5), IV)
treatment qD(1-5)
treatment qD(1,3,5)
Tumor Volume (mm3)
1200
900
600
300
0
20
25
30
35
40
45
Days post Implantation

Fig. 11

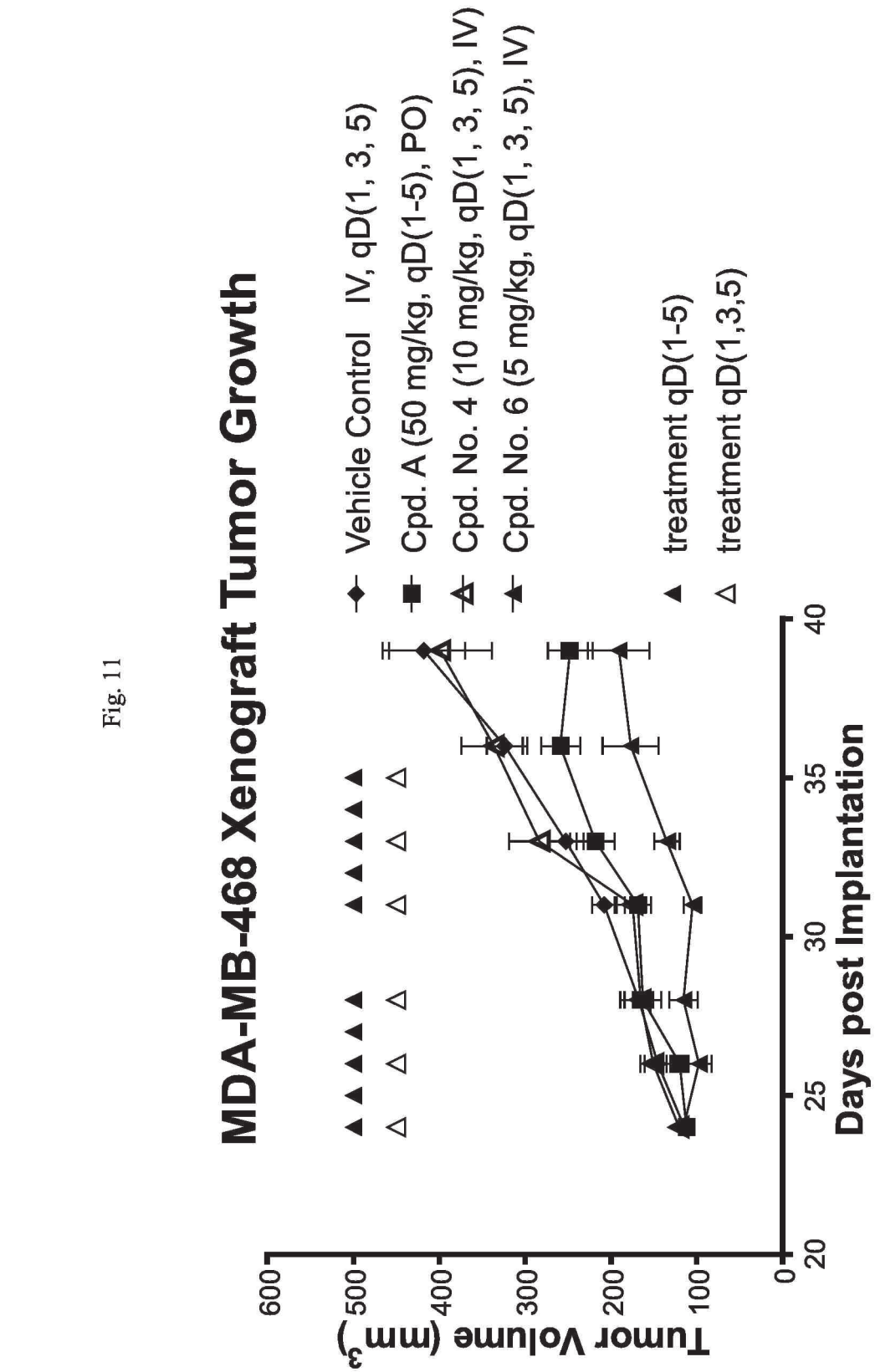

MDA-MB-468 Xenograft Tumor Growth
Vehicle Control IV, qD(1, 3, 5)
Cpd. A (50 mg/kg, qD(1-5), PO)
Cpd. No. 4 (10 mg/kg, qD(1, 3, 5), IV)
Cpd. No. 6 (5 mg/kg, qD(1, 3, 5), IV)
treatment qD(1-5)
treatment qD(1,3,5)
Tumor Volume (mm3)
Days post Implantation
0
100
200
300
400
500
600
20
25
30
35
40

Fig. 12

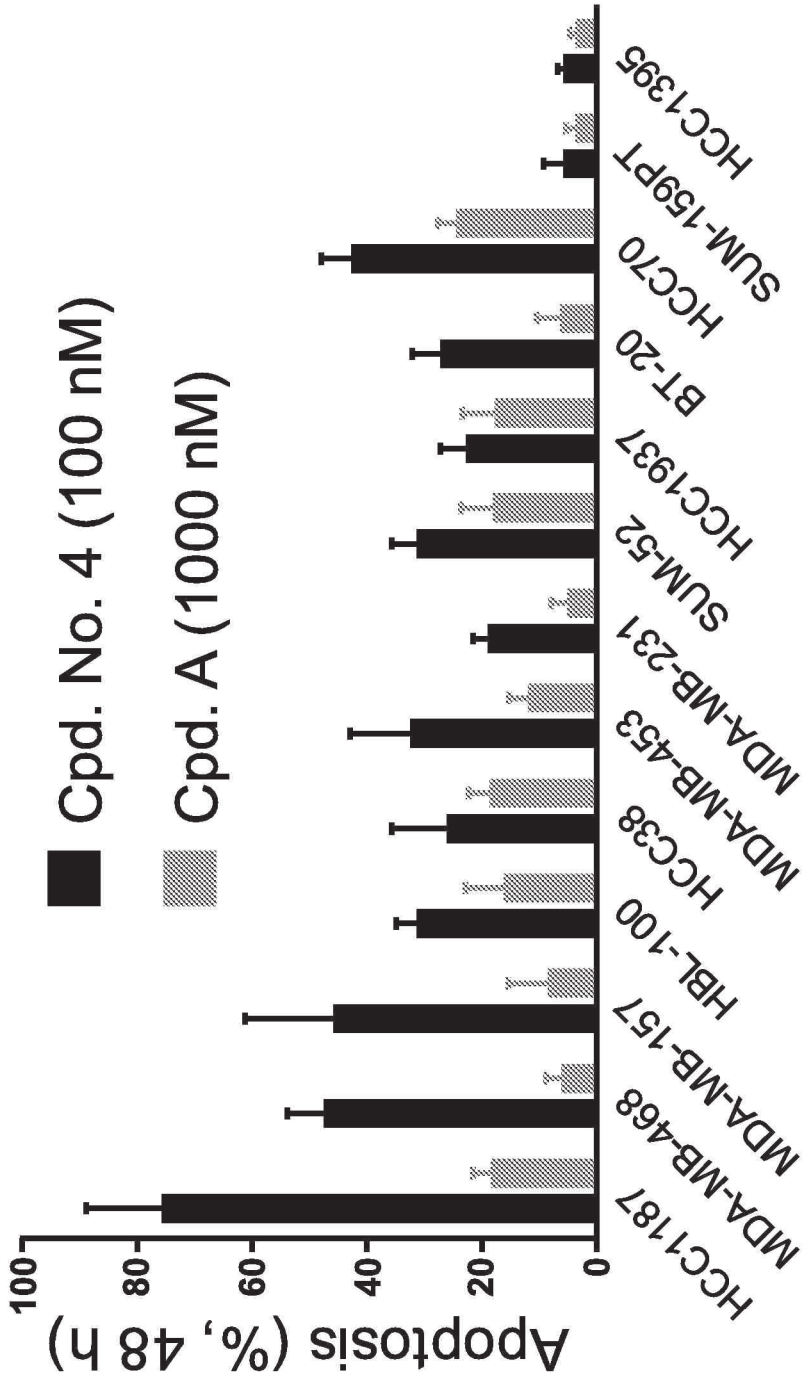

Cpd. No. 4 (100 nM)
Cpd. A (1000 nM)
Apoptosis (%, 48 h)
0
20
40
60
80
100
HCC1187
MDA-MB-468
MDA-MB-157
HBL-100
HCC38
MDA-MB-453
MDA-MB-231
SUM-52
HCC1937
BT-20
HCC70
SUM-159PT
HCC1395

Fig. 13

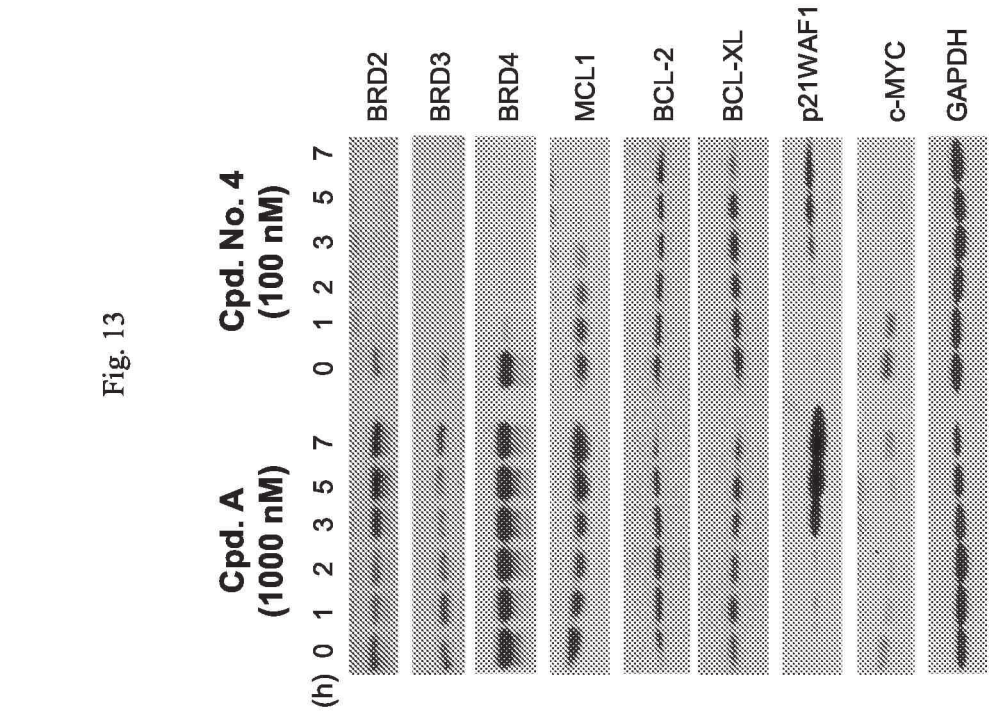
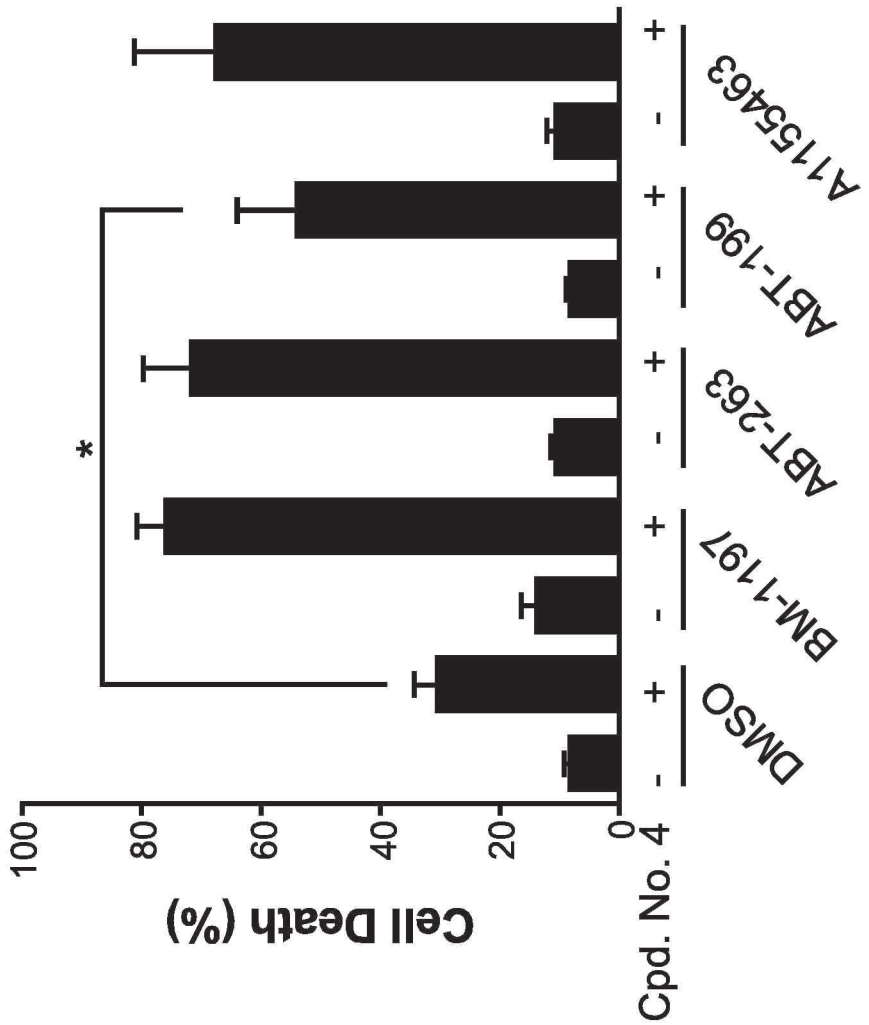

Cpd. A
(1000 nM)
Cpd. No. 4
(100 nM)
(h) 0 1 2 3 5 7 0 1 2 3 5 7
BRD2
BRD3
BRD4
MCL1
BCL-2
BCL-XL
p21WAF1
c-MYC
GAPDH

Fig. 14


Cell Death (%)
100
80
60
40
20
0
*
Cpd. No. 4
-
+
-
+
-
+
-
+
DMSO
BM-1197
ABT-263
ABT-199
A1155463

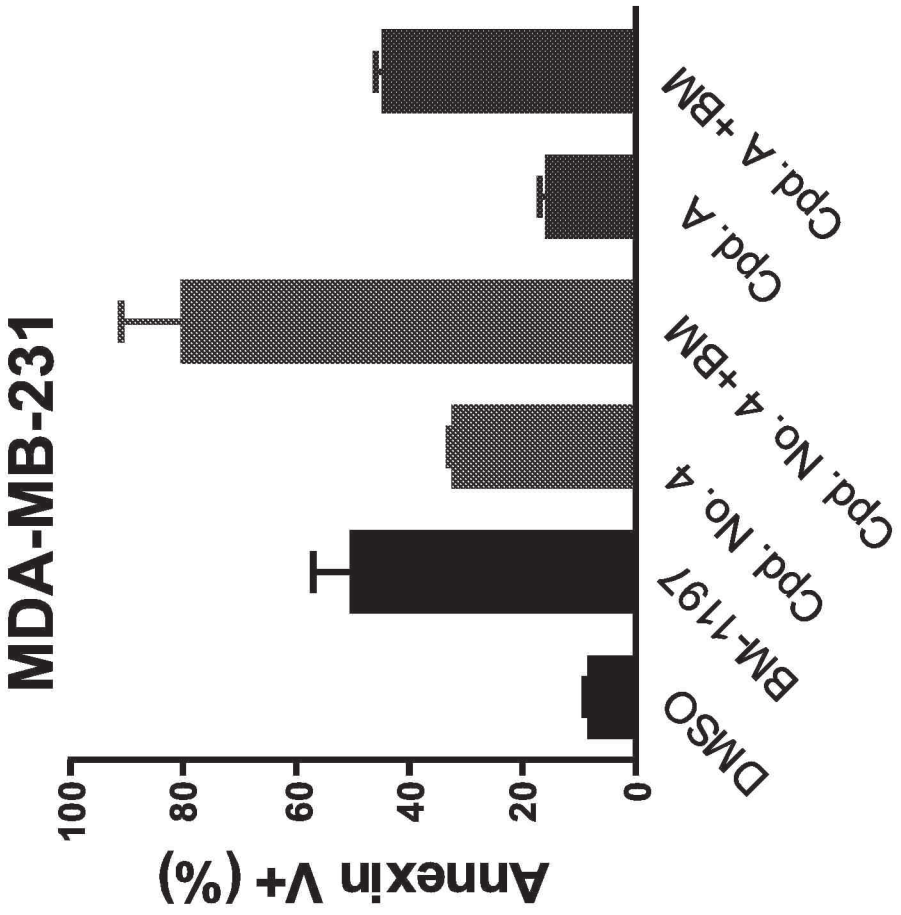
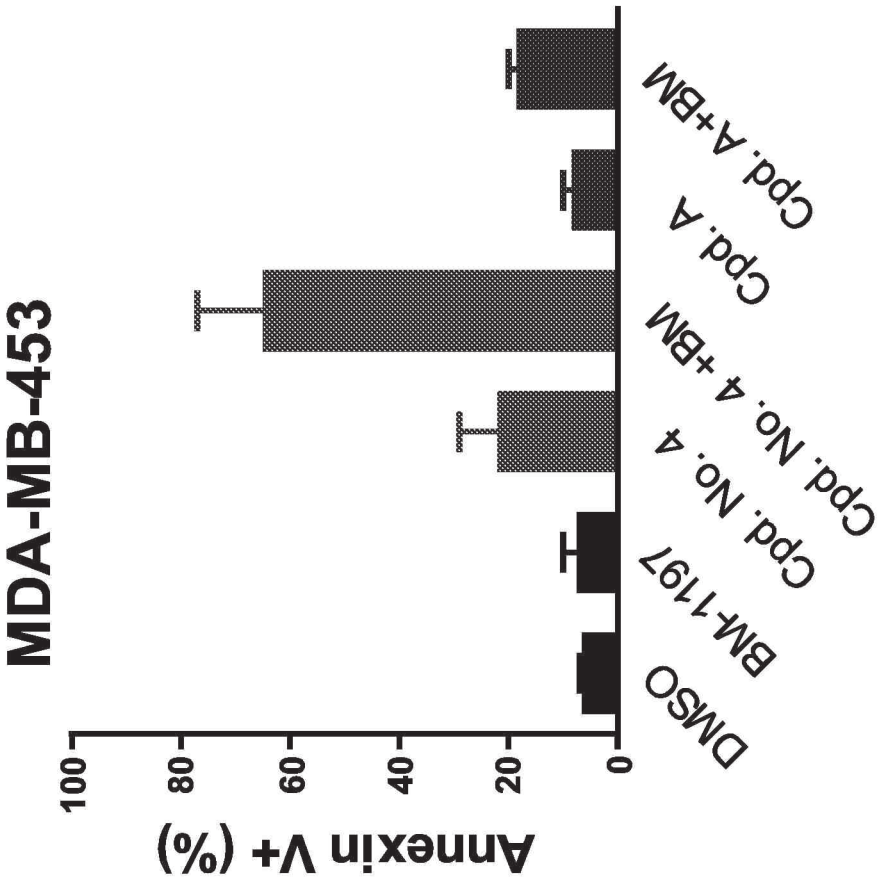

MDA-MB-231
Annexin V+ (%)
0
20
40
60
80
100
DMSO
BM-1197
Cpd. No. 4
Cpd. No. 4 +BM
Cpd. A
Cpd. A +BM

Fig. 15

Fig. 16


MDA-MB-453
Annexin V+ (%)
100
80
60
40
20
0
DMSO
BM-1197
Cpd. No. 4
Cpd. No. 4 +BM
Cpd. A
Cpd. A+BM