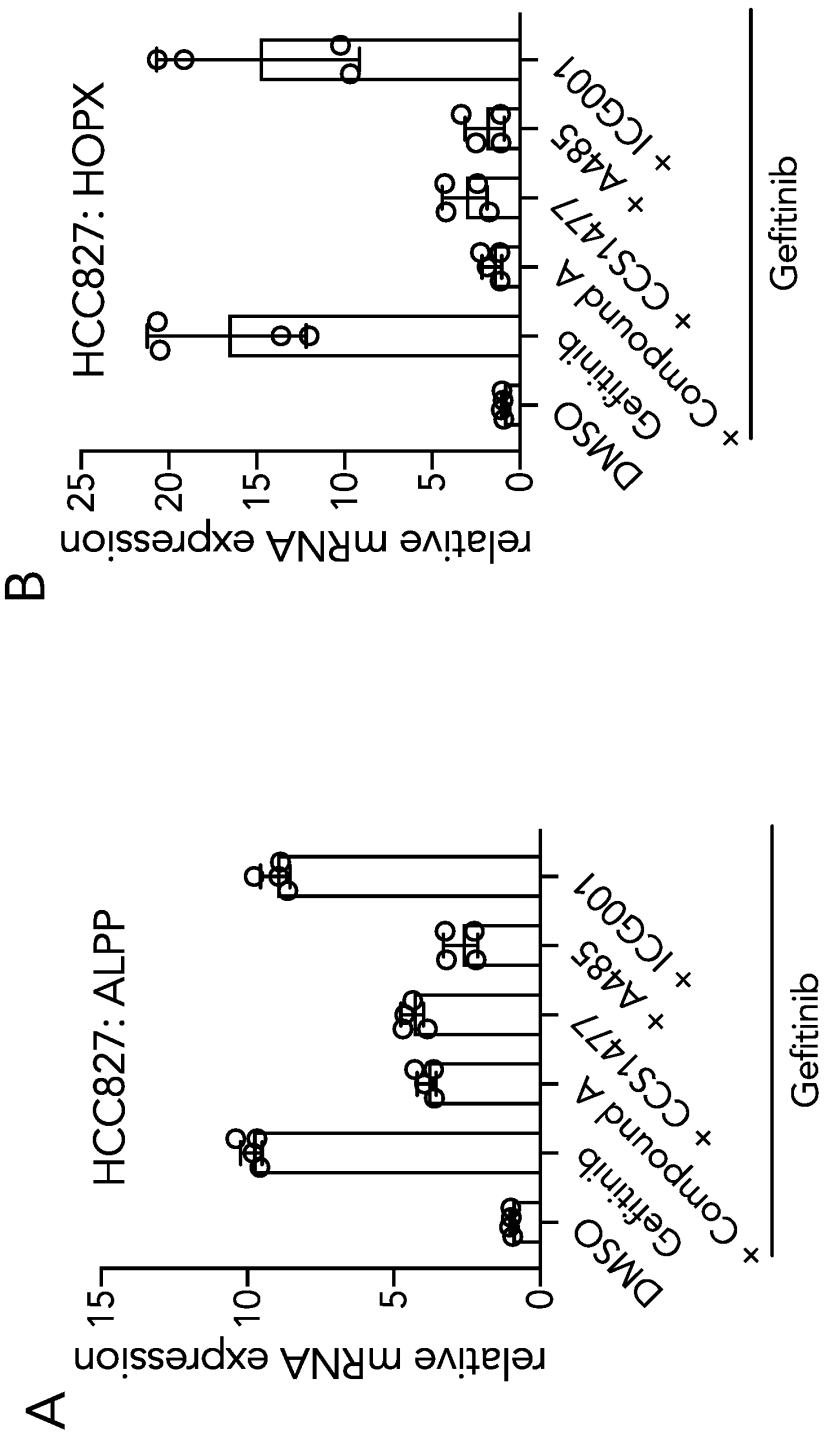

A
HCC827: ALPP
relative mRNA expression
0
5
10
15
DMSO
Gefitinib
+ Compound A
+ CCS1477
+ A485
+ ICG001
Gefitinib
B
HCC827: HOPX
relative mRNA expression
0
5
10
15
20
25
DMSO
Gefitinib
+ Compound A
+ CCS1477
+ A485
+ ICG001
Gefitinib

FIG. 1 A, B

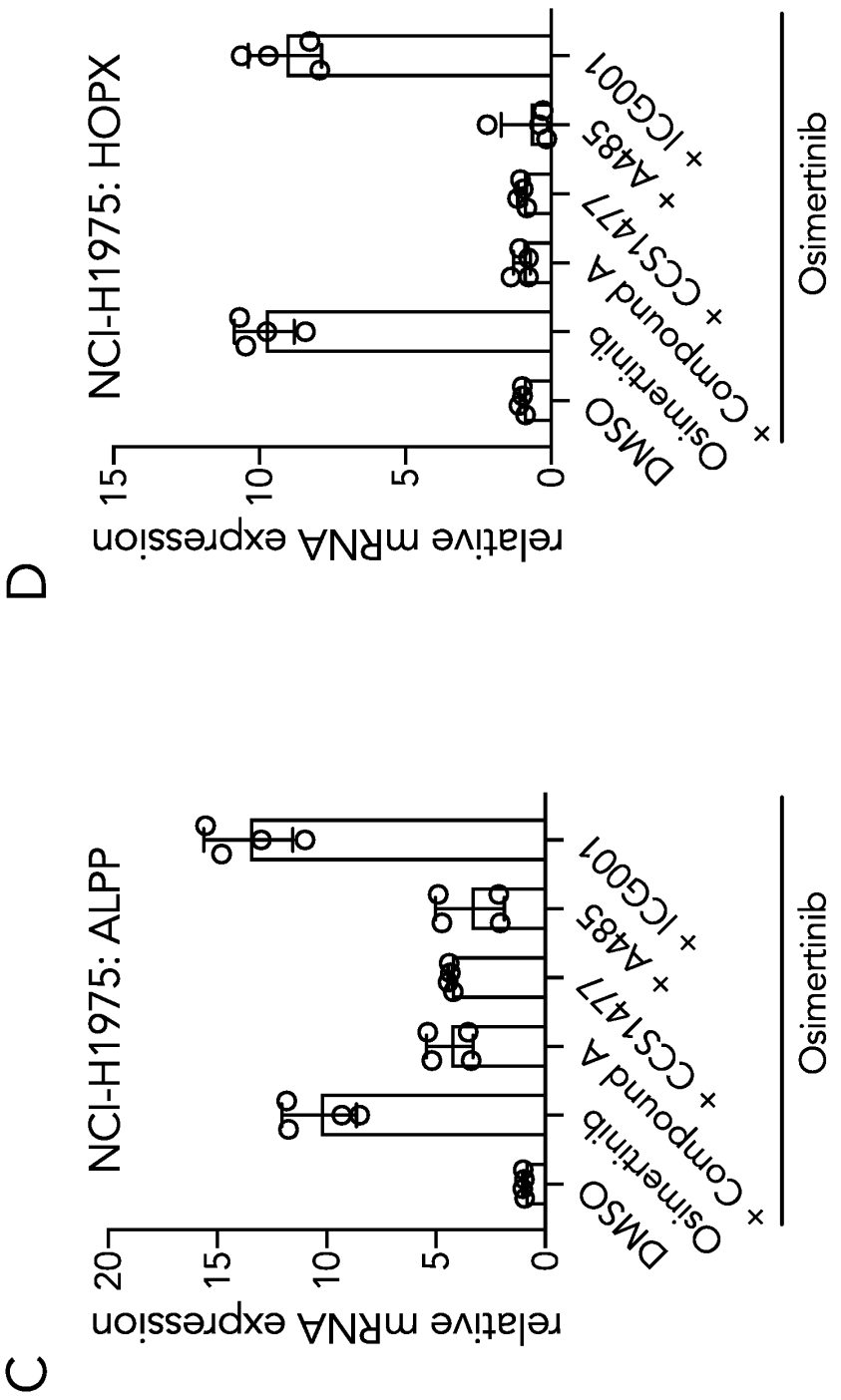

C
NCI-H1975: ALPP
relative mRNA expression
20
15
10
5
0
DMSO
Osimertinib
Osimertinib + Compound A + CCS1477 + A485 + ICG001
Osimertinib
D
NCI-H1975: HOPX
relative mRNA expression
15
10
5
0
DMSO
Osimertinib
Osimertinib + Compound A + CCS1477 + A485 + ICG001
Osimertinib

FIG. 1 C, D

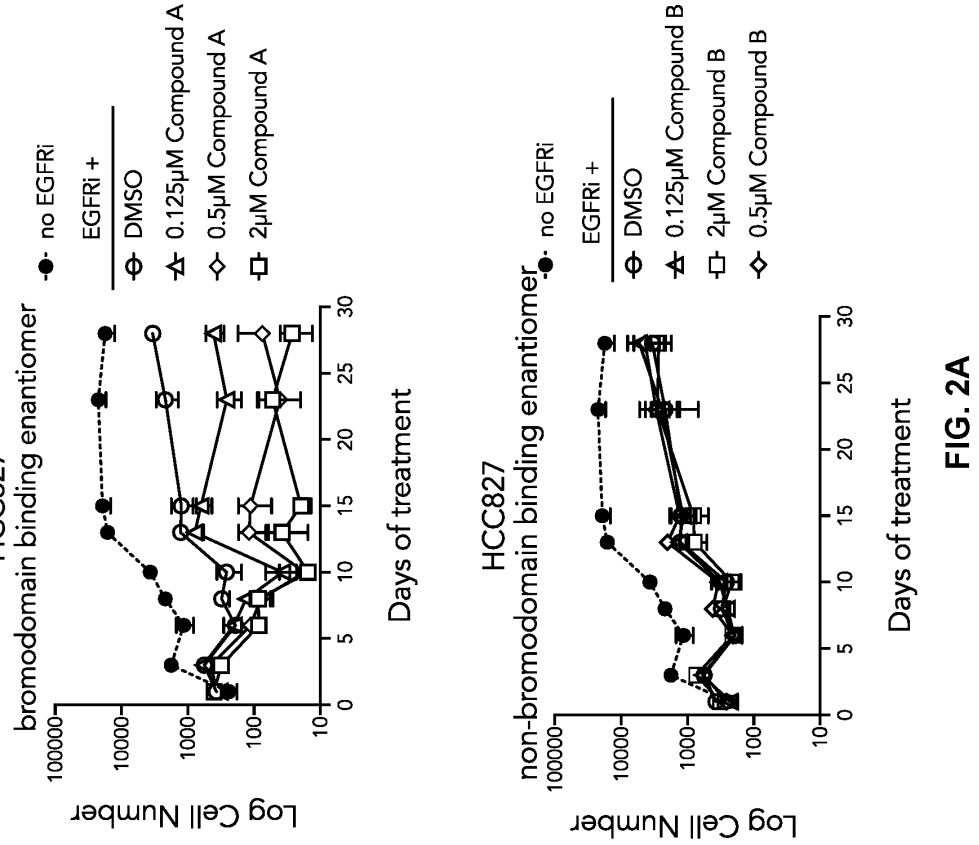

HCC827
bromodomain binding enantiomer
no EGFRi
EGFRi +
DMSO
0.125µM Compound A
0.5µM Compound A
2µM Compound A
Log Cell Number
Days of treatment
HCC827
non-bromodomain binding enantiomer
no EGFRi
EGFRi +
DMSO
0.125µM Compound B
2µM Compound B
0.5µM Compound B
Log Cell Number
Days of treatment

FIG. 2A

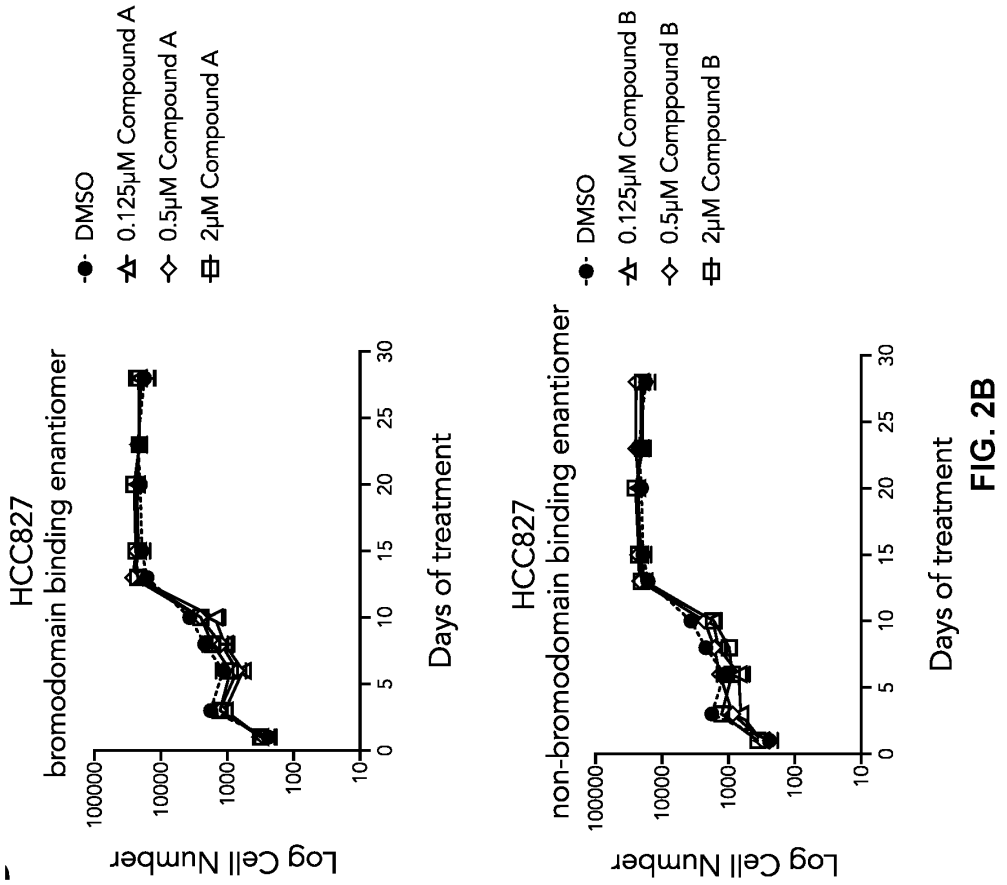

HCC827
bromodomain binding enantiomer
DMSO
0.125µM Compound A
0.5µM Compound A
2µM Compound A
Log Cell Number
100000
10000
1000
100
10
0
5
10
15
20
25
30
Days of treatment
HCC827
non-bromodomain binding enantiomer
DMSO
0.125µM Compound B
0.5µM Compound B
2µM Compound B
Log Cell Number
Days of treatment

FIG. 2B

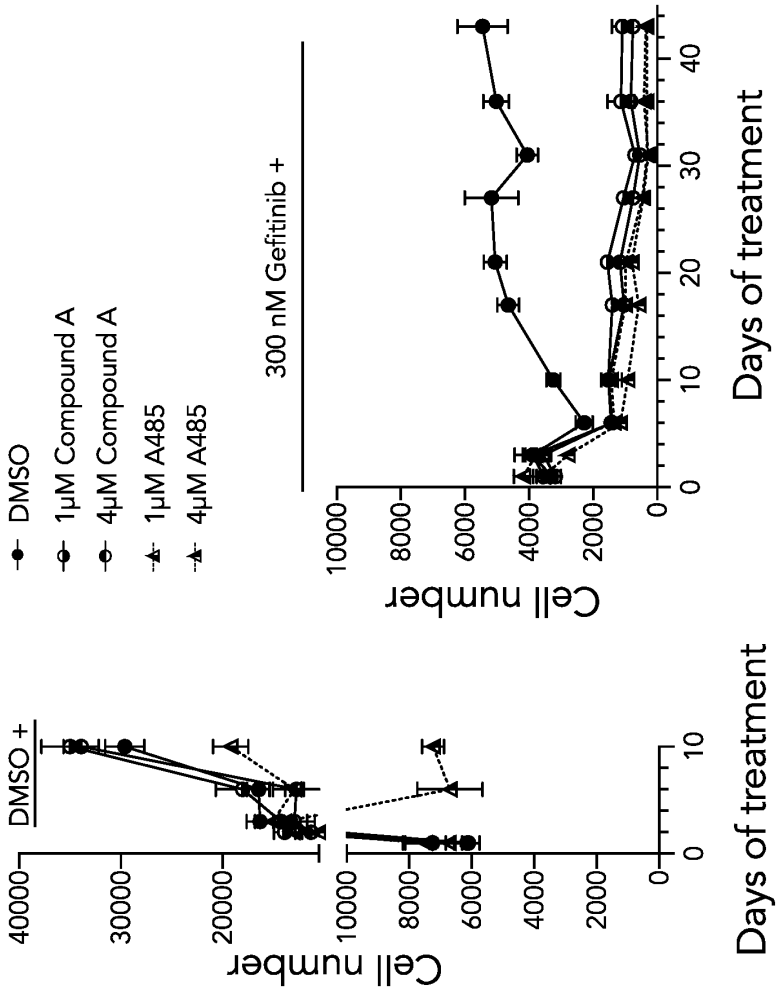

DMSO
1µM Compound A
4µM Compound A
1µM A485
4µM A485
DMSO +
300 nM Gefitinib +
Cell number
Days of treatment
40000
30000
20000
10000
8000
6000
4000
2000
0
10
20
30
40

FIG. 3A

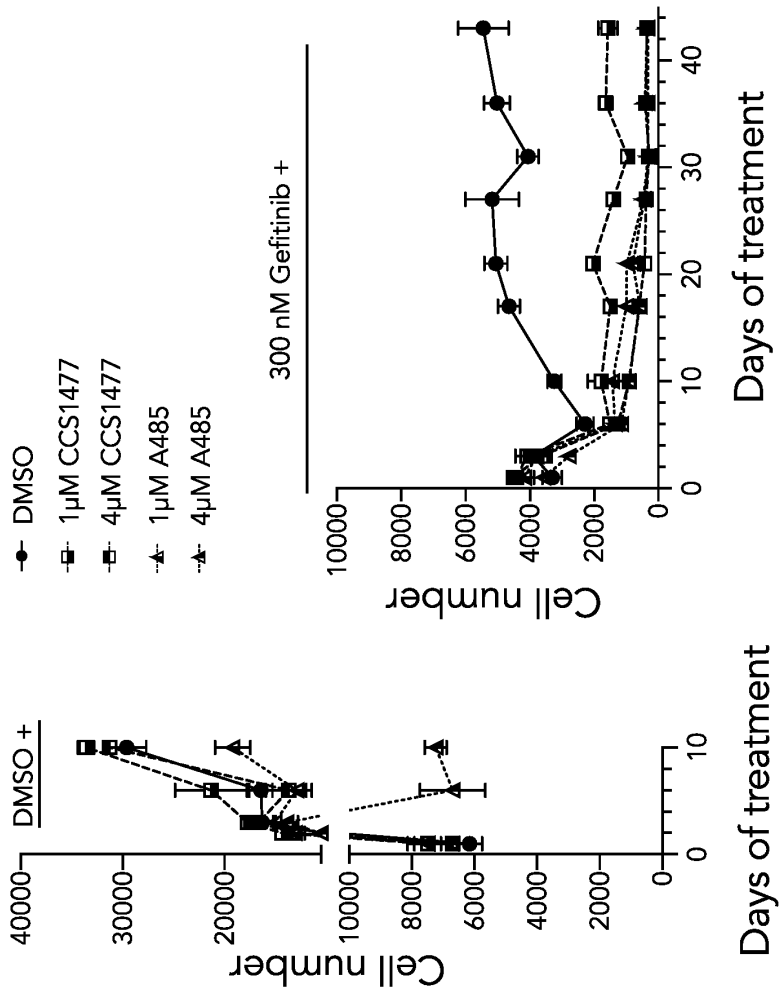

DMSO
1µM CCS1477
4µM CCS1477
1µM A485
4µM A485
DMSO +
300 nM Gefitinib +
Cell number
Days of treatment
40000
30000
20000
10000
8000
6000
4000
2000
0
10
20
30
40

FIG. 3B

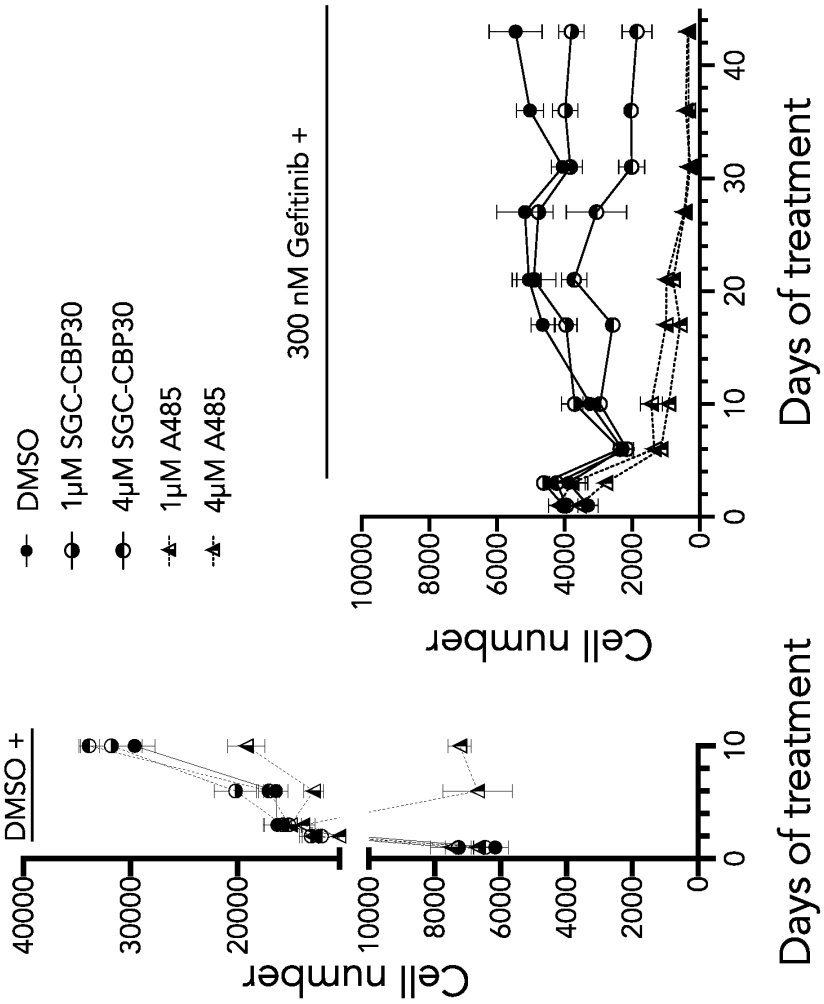

DMSO
1µM SGC-CBP30
4µM SGC-CBP30
1µM A485
4µM A485
DMSO +
300 nM Gefitinib +
Cell number
Days of treatment
40000
30000
20000
10000
8000
6000
4000
2000
0
10
20
30
40

FIG. 3C

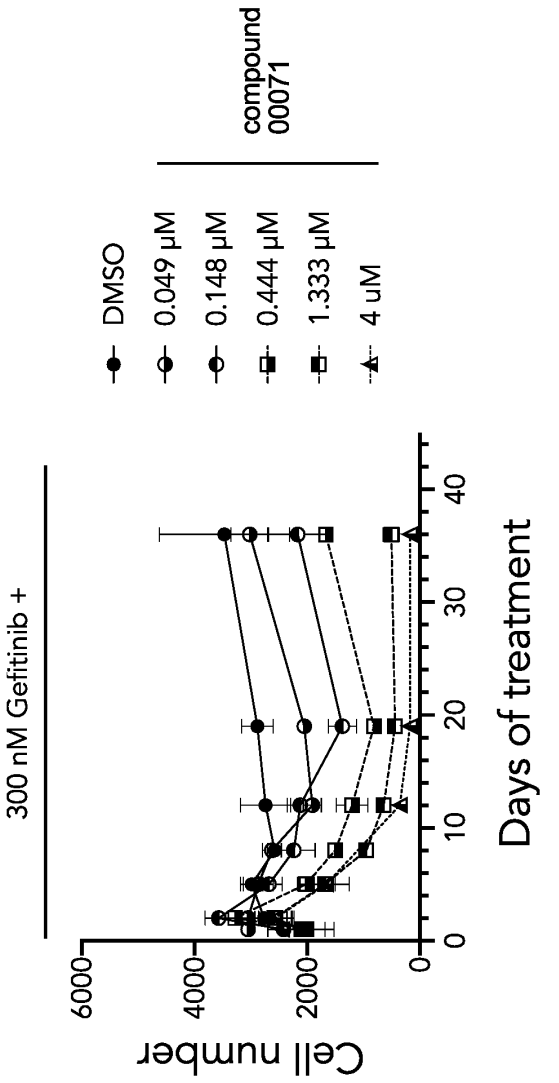

300 nM Gefitinib +
compound 00071
DMSO
0.049 µM
0.148 µM
0.444 µM
1.333 µM
4 uM
Cell number
0
2000
4000
6000
0
10
20
30
40
Days of treatment

FIG. 3D

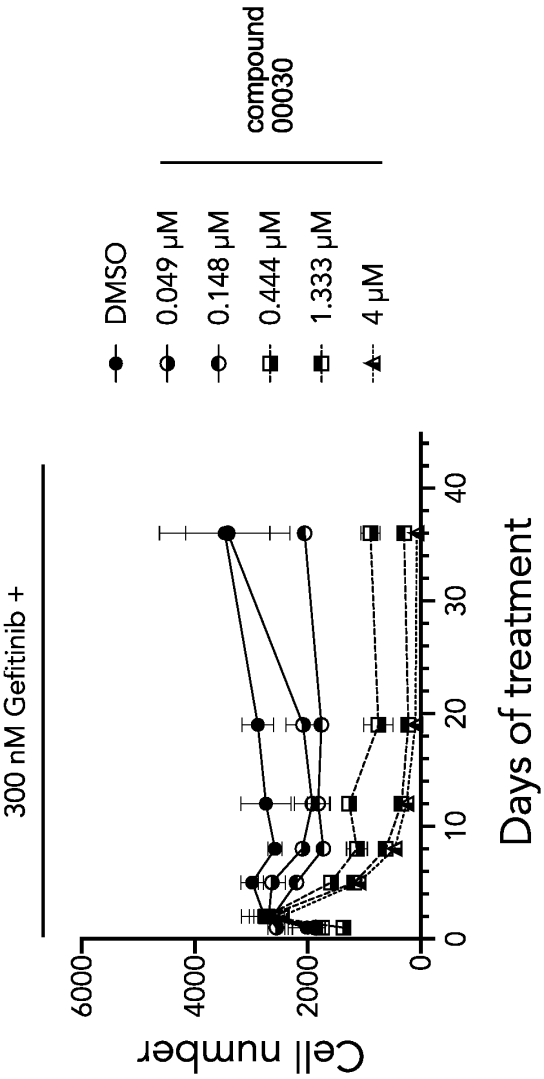

300 nM Gefitinib +
Cell number
6000
4000
2000
0
0
10
20
30
40
Days of treatment
DMSO
0.049 µM
0.148 µM
0.444 µM
1.333 µM
4 µM
compound 00030

FIG. 3E

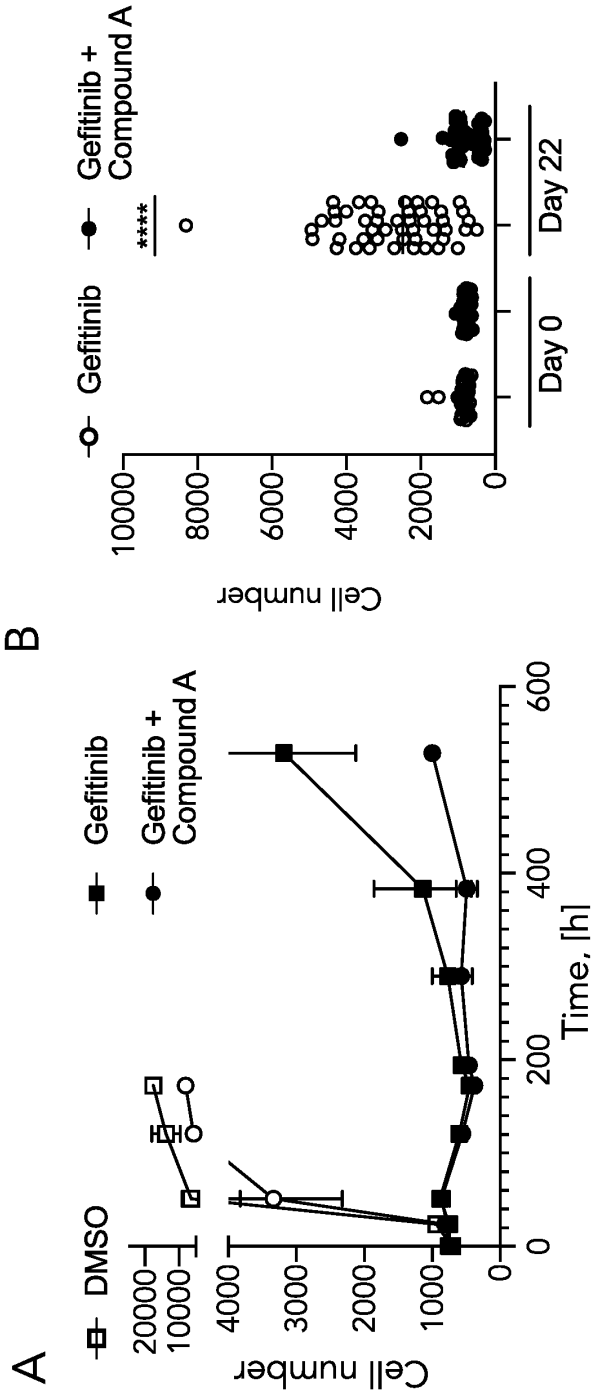

A
DMSO
Gefitinib
Gefitinib + Compound A
Cell number
Time, [h]
B
Gefitinib
Gefitinib + Compound A
****
Cell number
Day 0
Day 22

FIG. 4 A, B


C
Cells, log fold of Day 0
1.0
0.5
0.0
-0.5
-1.0
300 nM Gefitinib
300 nM Gefitinib + 1µM Compound A

FIG. 4C

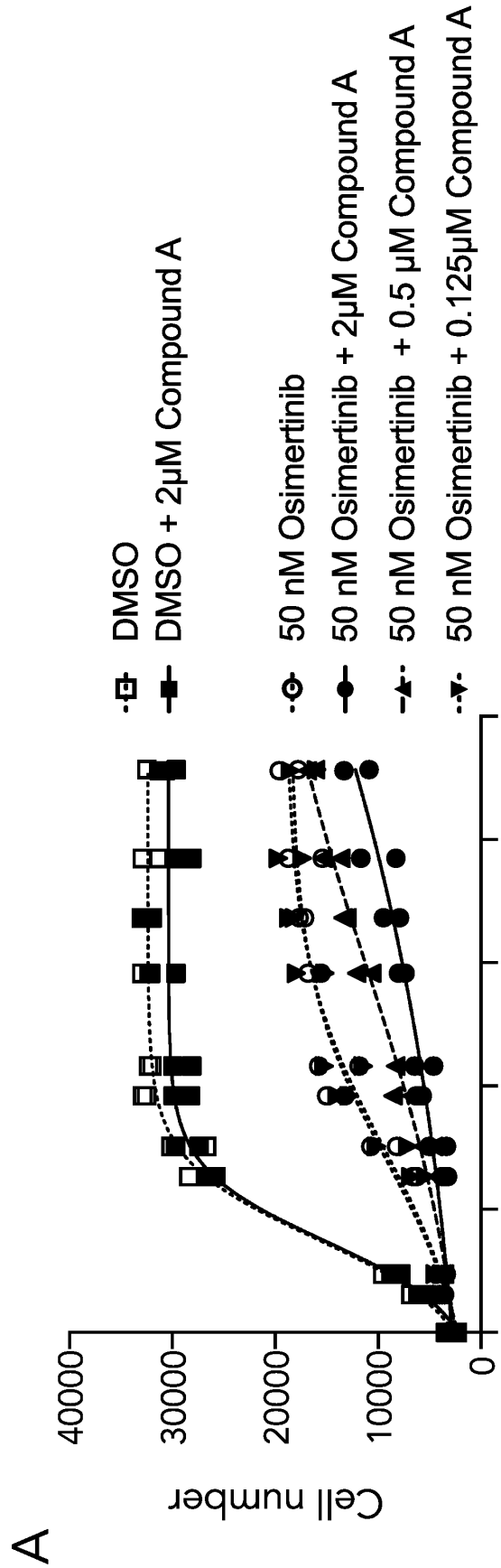

A
Cell number
40000
30000
20000
10000
0
0
100
200
300
400
500
Time, [h]
DMSO
DMSO + 2µM Compound A
50 nM Osimertinib
50 nM Osimertinib + 2µM Compound A
50 nM Osimertinib + 0.5 µM Compound A
50 nM Osimertinib + 0.125µM Compound A

FIG. 5A

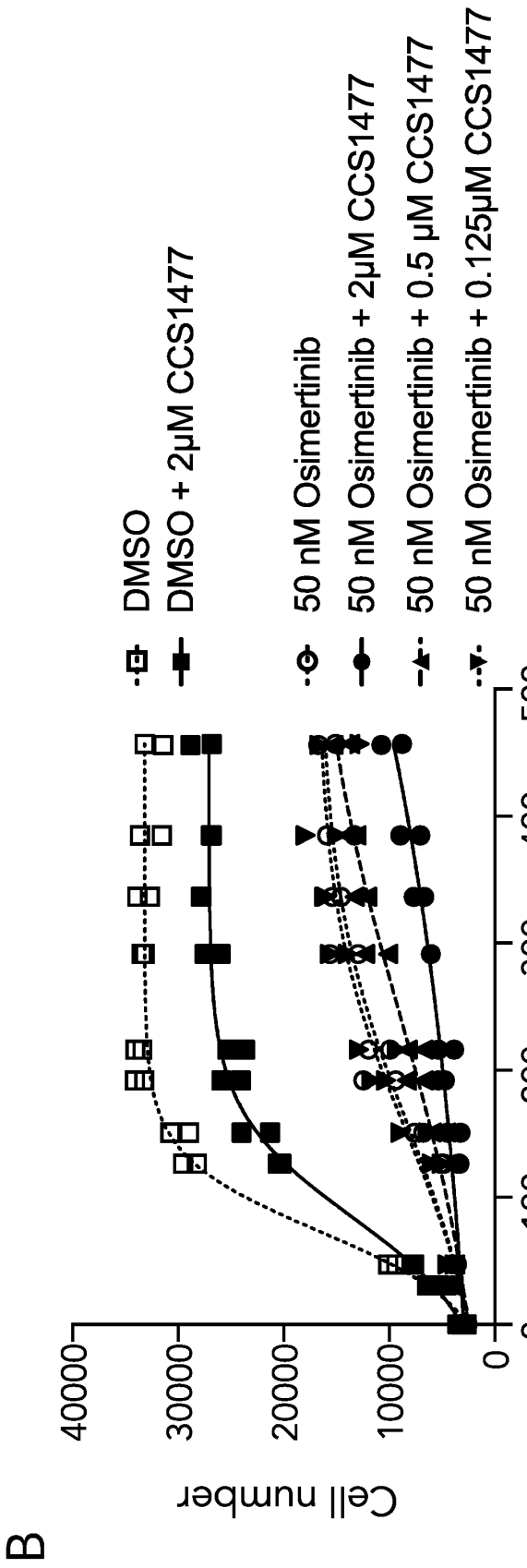

B
Cell number
40000
30000
20000
10000
0
0
100
200
300
400
500
Time, [h]
DMSO
DMSO + 2µM CCS1477
50 nM Osimertinib
50 nM Osimertinib + 2µM CCS1477
50 nM Osimertinib + 0.5 µM CCS1477
50 nM Osimertinib + 0.125µM CCS1477

FIG. 5B

A

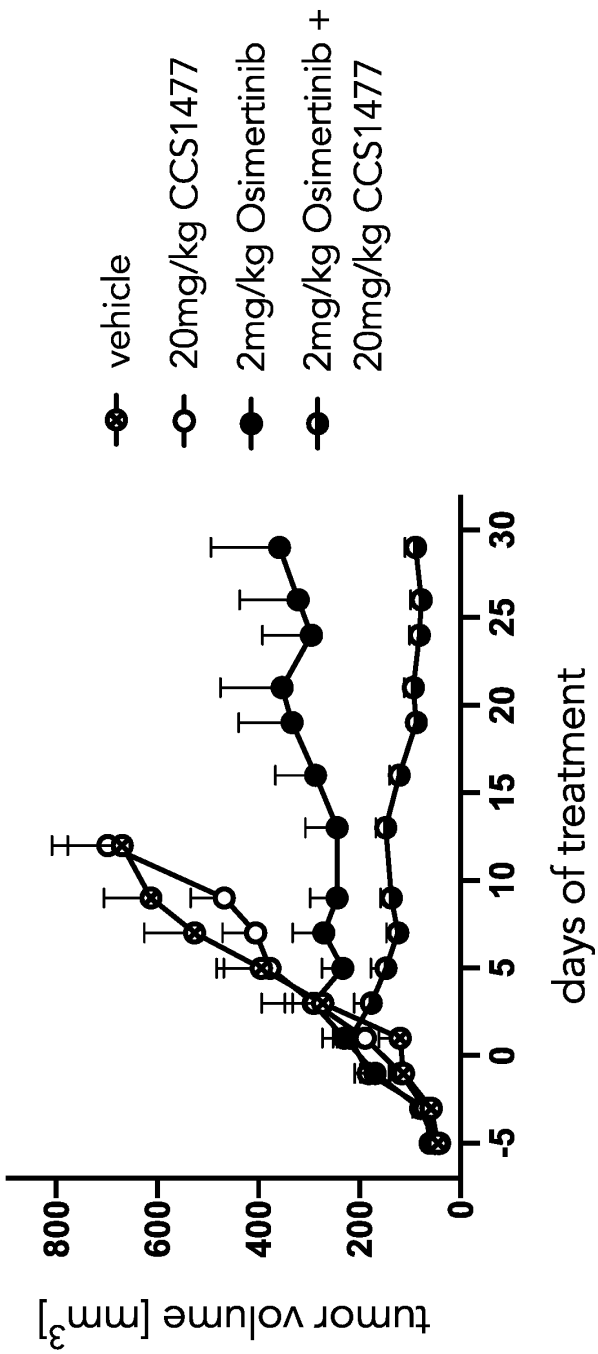

vehicle
20mg/kg CCS1477
2mg/kg Osimertinib
2mg/kg Osimertinib +
20mg/kg CCS1477
tumor volume [mm3]
800
600
400
200
0
-5
0
5
10
15
20
25
30
days of treatment

FIG. 6A

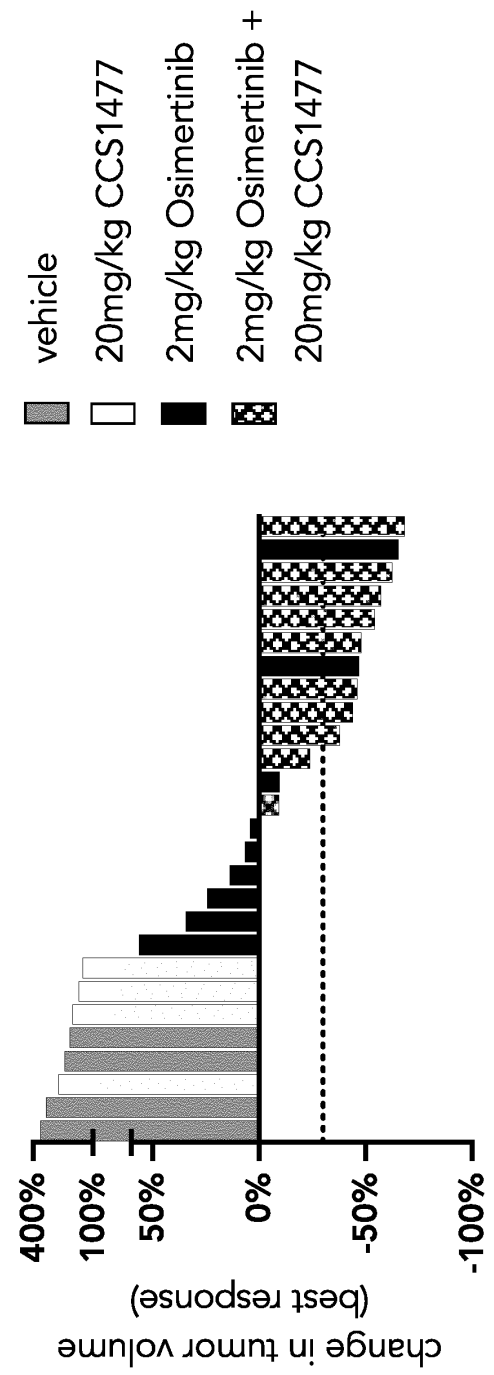

B
change in tumor volume
(best response)
400%
100%
50%
0%
-50%
-100%
vehicle
20mg/kg CCS1477
2mg/kg Osimertinib
2mg/kg Osimertinib +
20mg/kg CCS1477

FIG. 6B

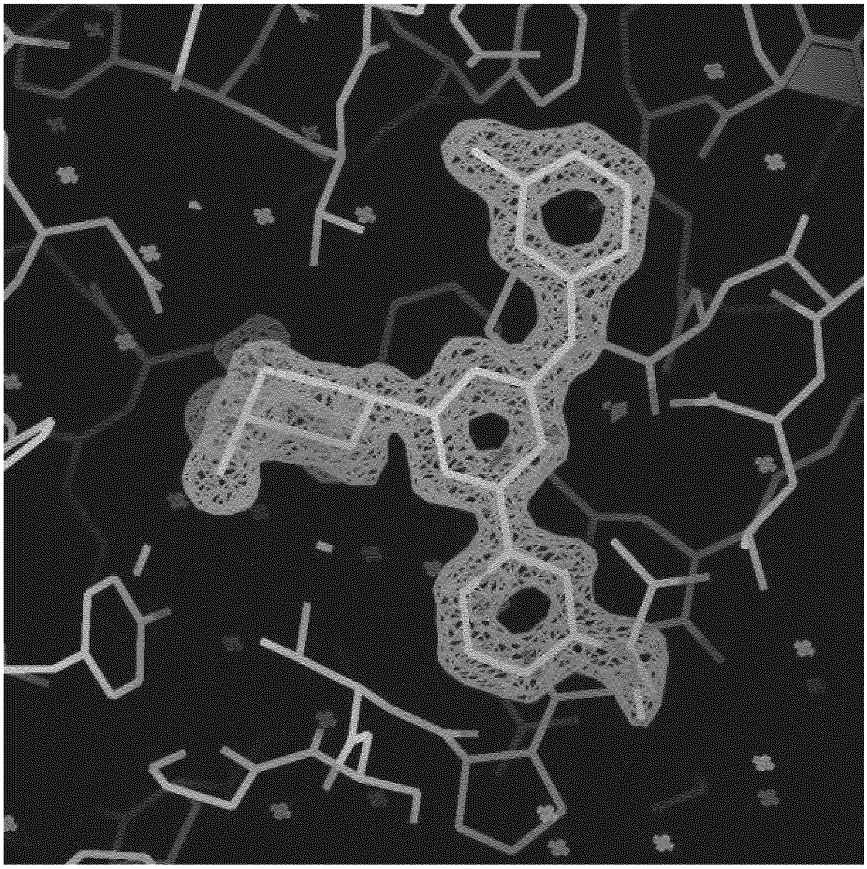


FIG. 7

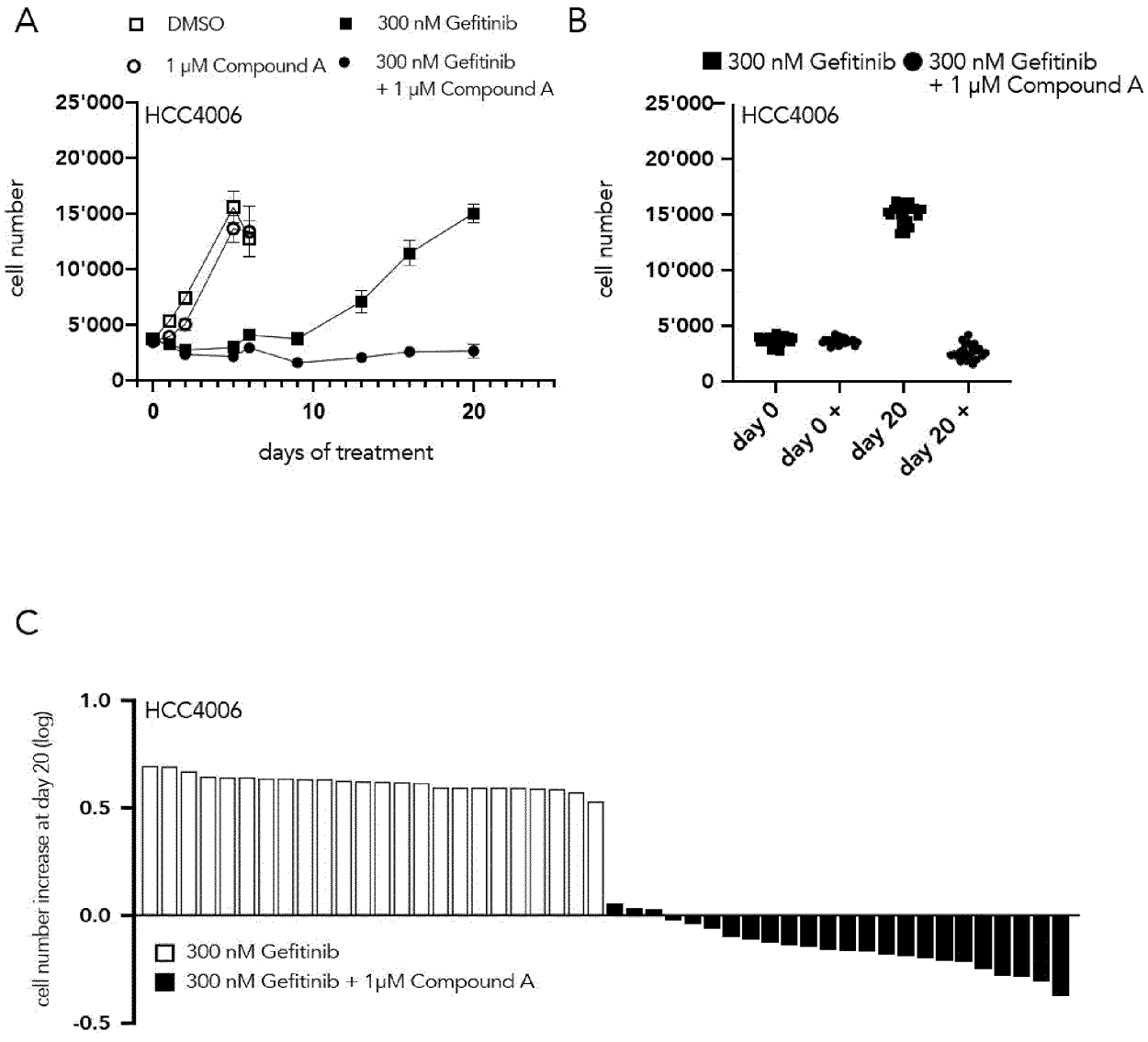

A
DMSO
1 µM Compound A
300 nM Gefitinib
300 nM Gefitinib + 1 µM Compound A
HCC4006
cell number
25'000
20'000
15'000
10'000
5'000
0
0
10
20
days of treatment
B
300 nM Gefitinib
300 nM Gefitinib + 1 µM Compound A
HCC4006
cell number
day 0
day 0 +
day 20
day 20 +
C
HCC4006
cell number increase at day 20 (log)
1.0
0.5
0.0
-0.5
300 nM Gefitinib
300 nM Gefitinib + 1µM Compound A

FIG. 8

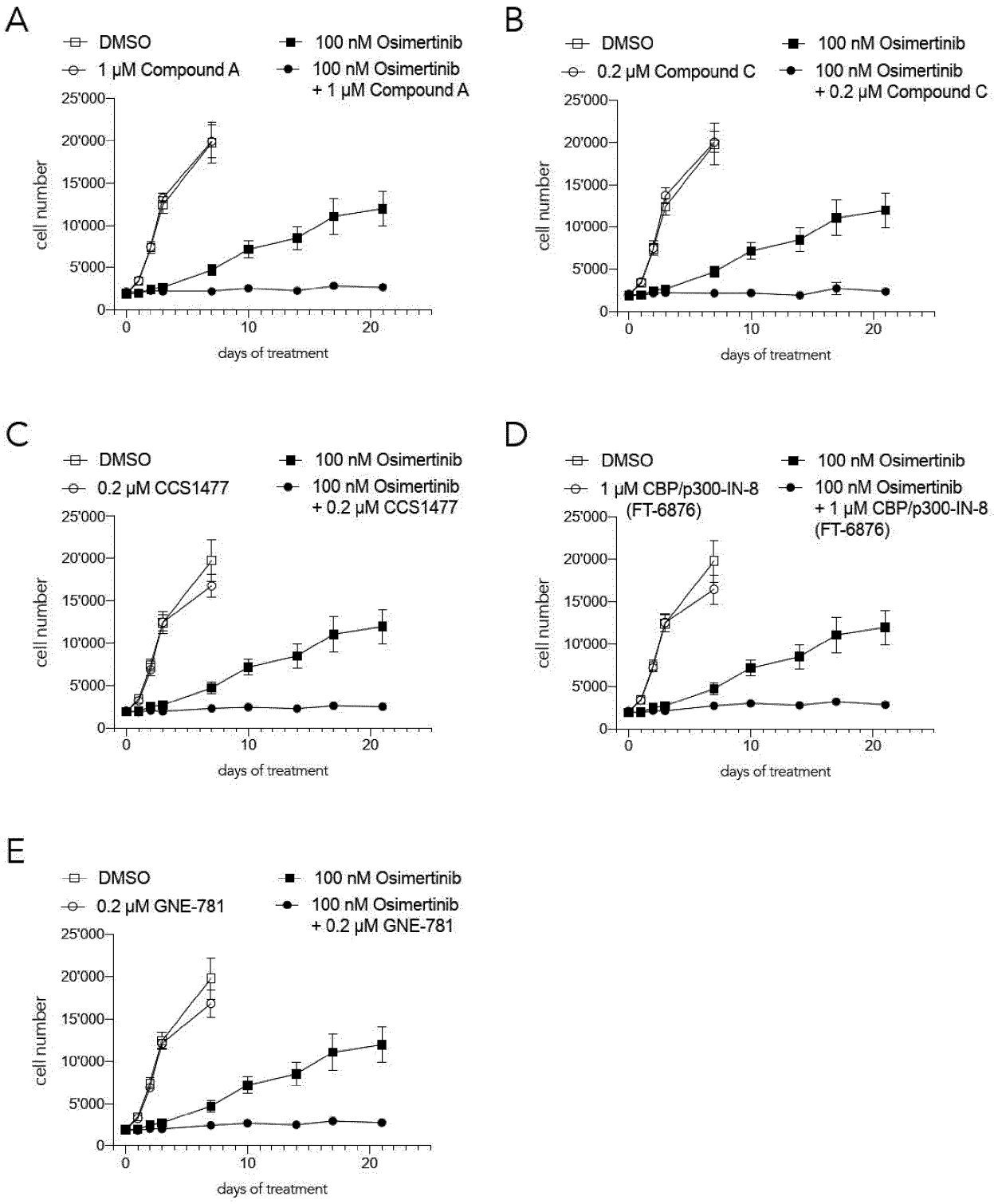

A
DMSO
1 µM Compound A
100 nM Osimertinib
100 nM Osimertinib + 1 µM Compound A
cell number
days of treatment
B
DMSO
0.2 µM Compound C
100 nM Osimertinib
100 nM Osimertinib + 0.2 µM Compound C
cell number
days of treatment
C
DMSO
0.2 µM CCS1477
100 nM Osimertinib
100 nM Osimertinib + 0.2 µM CCS1477
cell number
days of treatment
D
DMSO
1 µM CBP/p300-IN-8 (FT-6876)
100 nM Osimertinib
100 nM Osimertinib + 1 µM CBP/p300-IN-8 (FT-6876)
cell number
days of treatment
E
DMSO
0.2 µM GNE-781
100 nM Osimertinib
100 nM Osimertinib + 0.2 µM GNE-781
cell number
days of treatment

FIG. 9

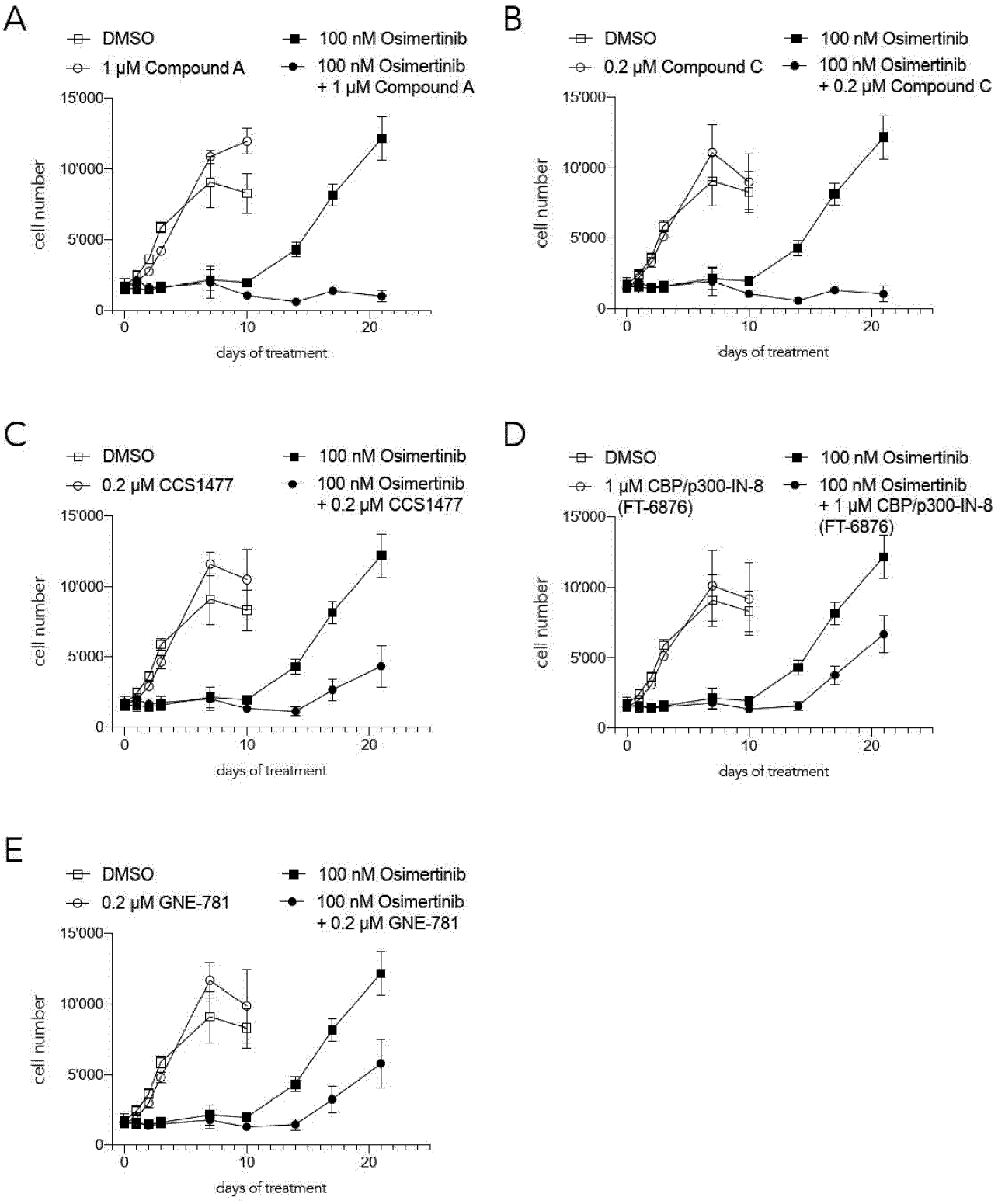

A
DMSO
1 µM Compound A
100 nM Osimertinib
100 nM Osimertinib + 1 µM Compound A
cell number
15'000
10'000
5'000
0
0
10
20
days of treatment
B
DMSO
0.2 µM Compound C
100 nM Osimertinib
100 nM Osimertinib + 0.2 µM Compound C
cell number
15'000
10'000
5'000
0
0
10
20
days of treatment
C
DMSO
0.2 µM CCS1477
100 nM Osimertinib
100 nM Osimertinib + 0.2 µM CCS1477
cell number
15'000
10'000
5'000
0
0
10
20
days of treatment
D
DMSO
1 µM CBP/p300-IN-8 (FT-6876)
100 nM Osimertinib
100 nM Osimertinib + 1 µM CBP/p300-IN-8 (FT-6876)
cell number
15'000
10'000
5'000
0
0
10
20
days of treatment
E
DMSO
0.2 µM GNE-781
100 nM Osimertinib
100 nM Osimertinib + 0.2 µM GNE-781
cell number
15'000
10'000
5'000
0
0
10
20
days of treatment

FIG. 10

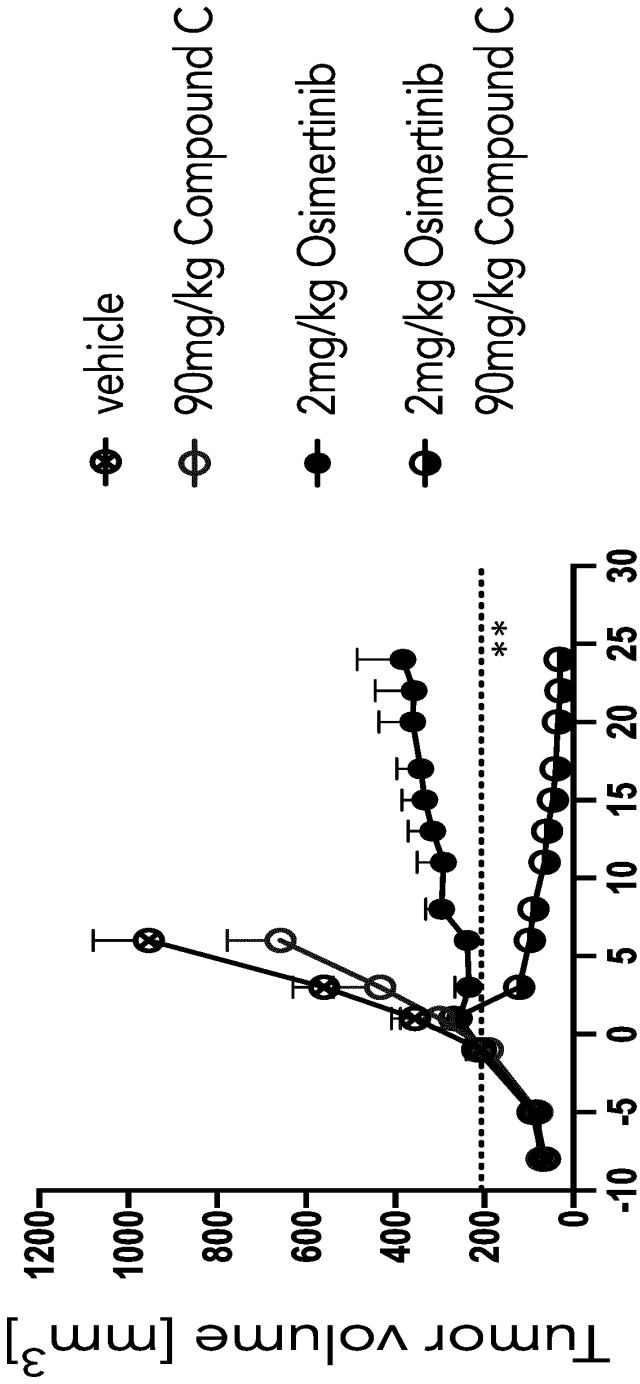

vehicle
90mg/kg Compound C
2mg/kg Osimertinib
2mg/kg Osimertinib
90mg/kg Compound C
Tumor volume [mm3]
1200
1000
800
600
400
200
0
-10
-5
0
5
10
15
20
25
30
days of treatment
**

FIG. 11A

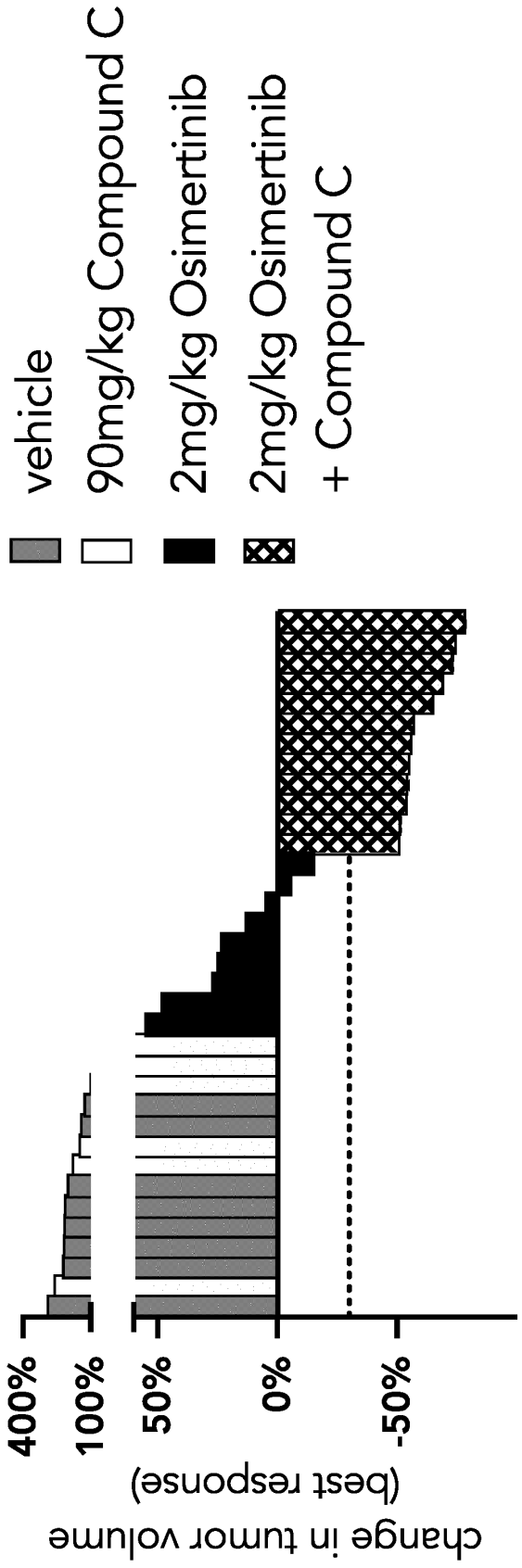

vehicle
90mg/kg Compound C
2mg/kg Osimertinib
2mg/kg Osimertinib
+ Compound C
400%
100%
50%
0%
-50%
change in tumor volume
(best response)

FIG. 11B