FIG. 1

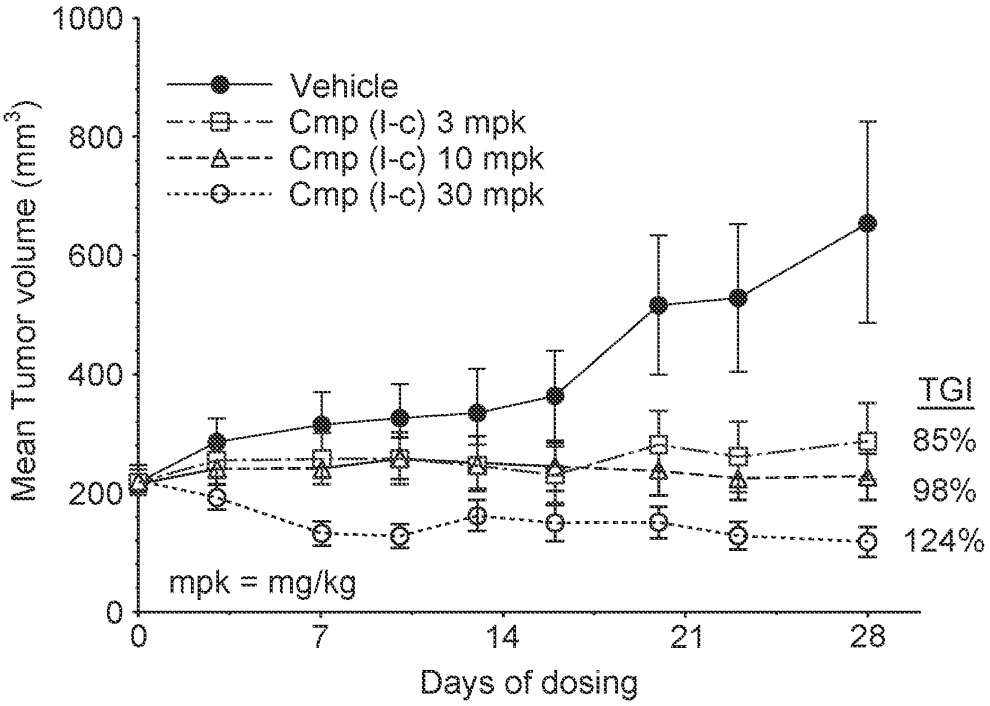

1000
800
600
400
200
0
Mean Tumor volume (mm3)
Vehicle
Cmp (I-c) 3 mpk
Cmp (I-c) 10 mpk
Cmp (I-c) 30 mpk
mpk = mg/kg
0
7
14
21
28
Days of dosing
TGI
85%
98%
124%

FIG. 2

WESTERN BLOT PD (18 hours post last dose)	% ER REDUCTION
3 mpk	95
10 mpk	97
30 mpk	94

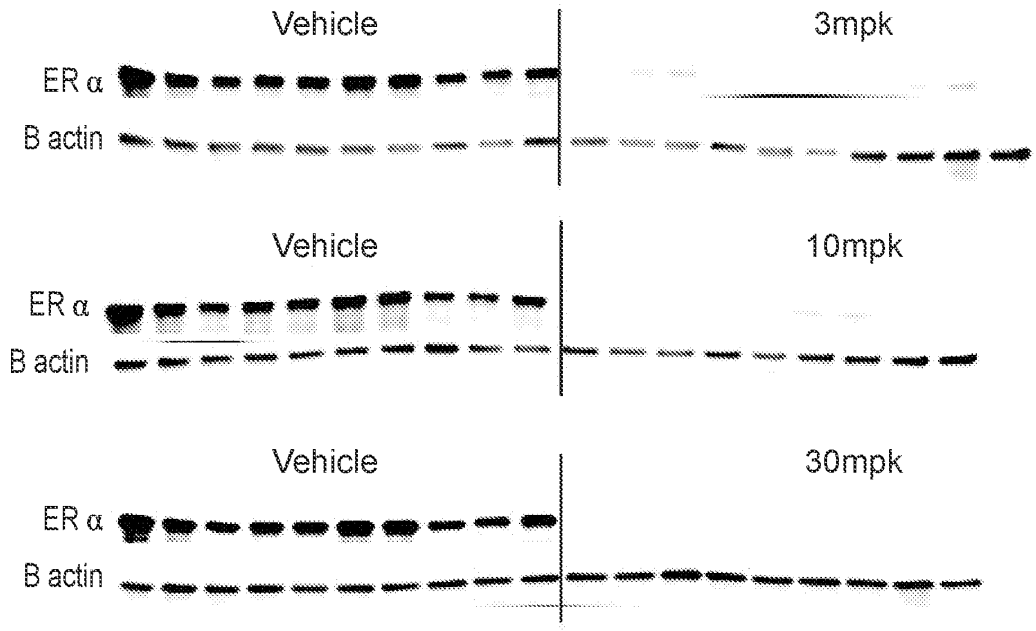


FIG. 3

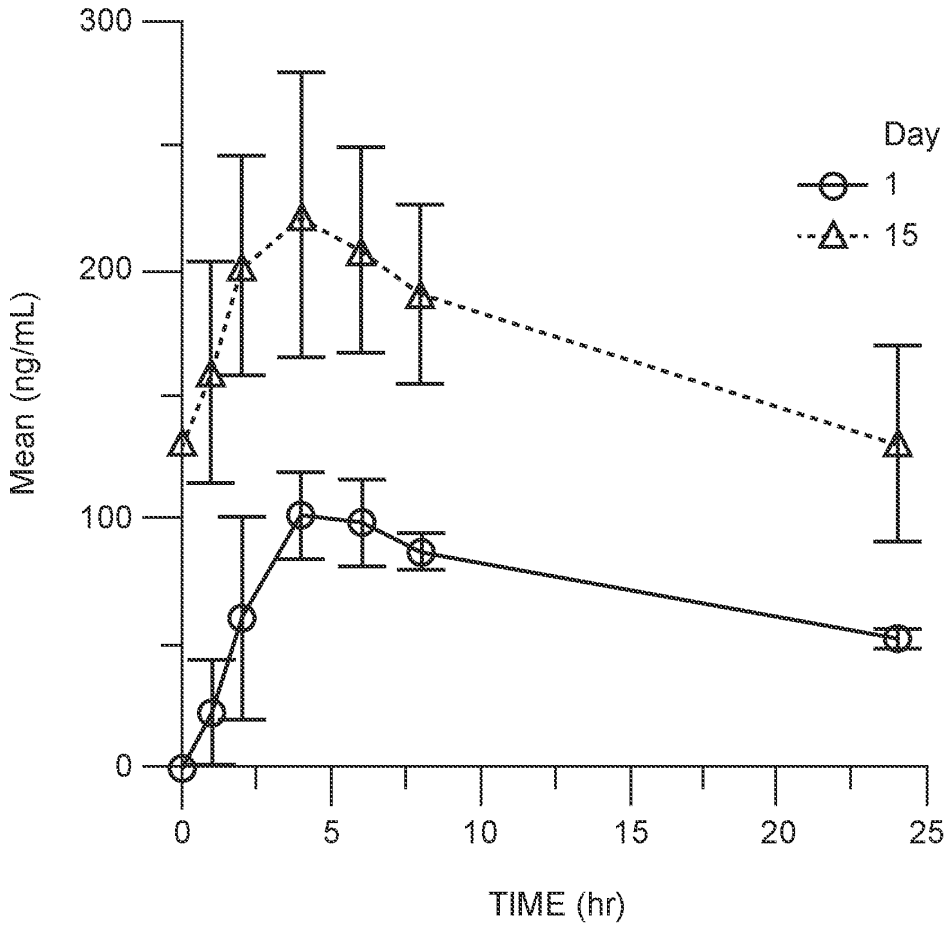


FIG. 4

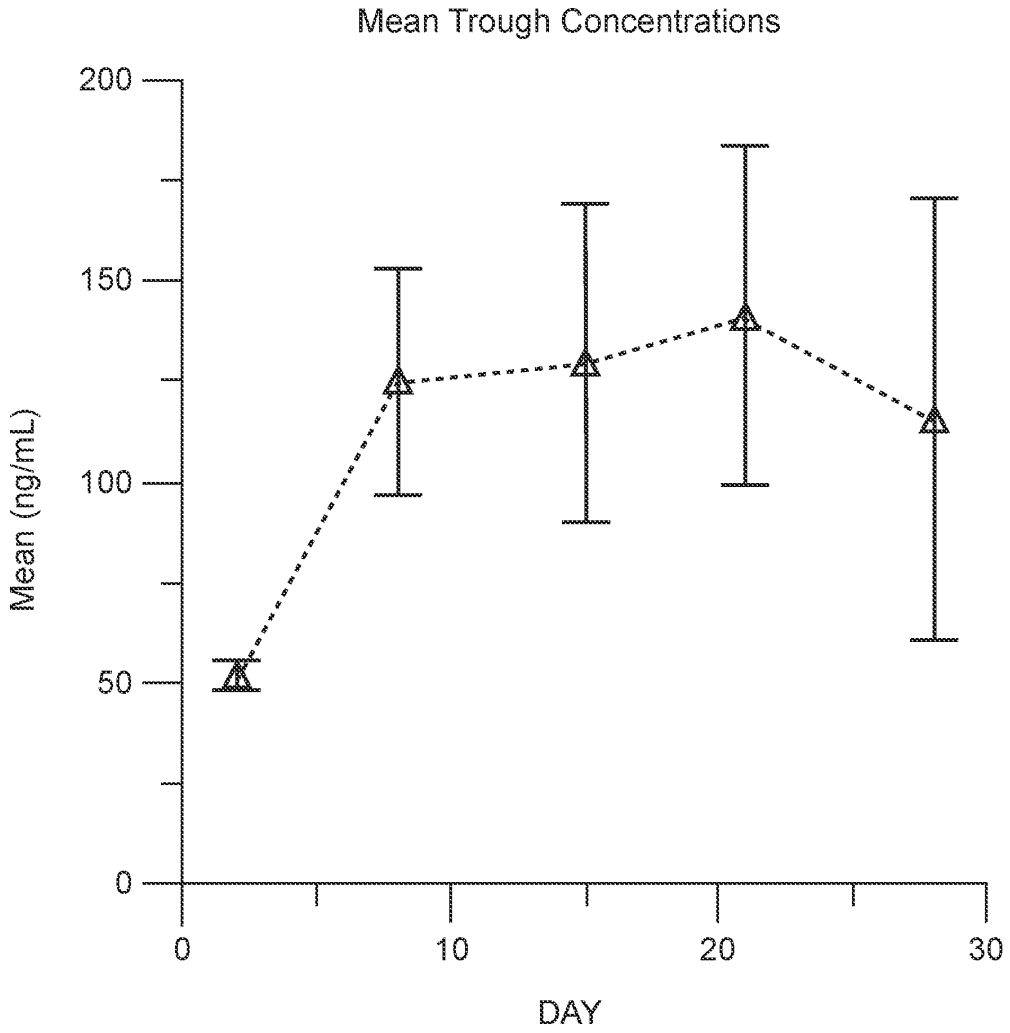

Mean Trough Concentrations
Mean (ng/mL)
200
150
100
50
0
0
10
20
30
DAY

FIG. 5

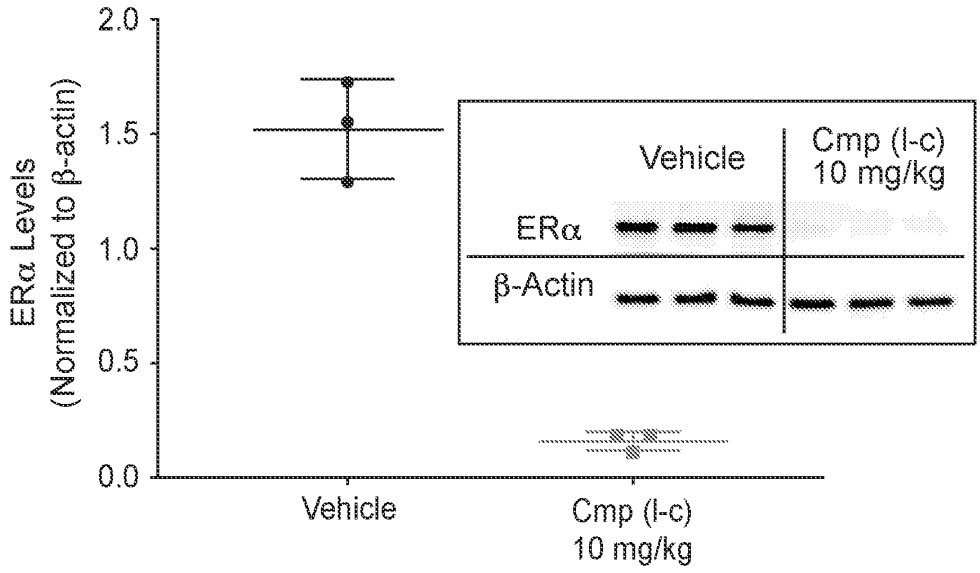

2.0
1.5
1.0
0.5
0.0
ERα Levels
(Normalized to β-actin)
Vehicle
Cmp (I-c)
10 mg/kg
Vehicle
Cmp (I-c)
10 mg/kg
ERα
β-Actin

FIG. 6

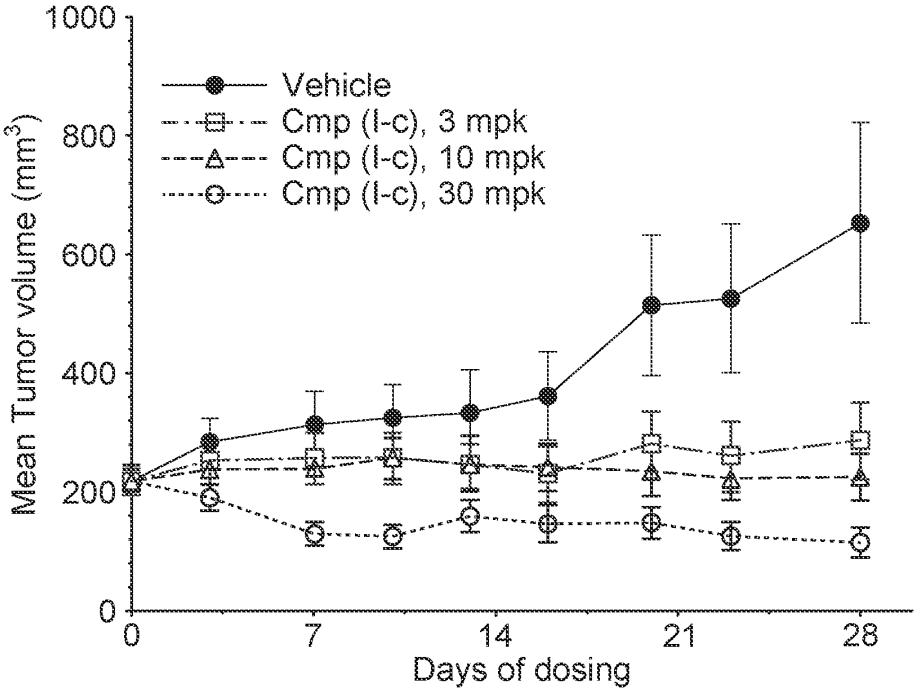

Vehicle
Cmp (I-c), 3 mpk
Cmp (I-c), 10 mpk
Cmp (I-c), 30 mpk
Mean Tumor volume (mm3)
1000
800
600
400
200
0
0
7
14
21
28
Days of dosing

FIG. 7

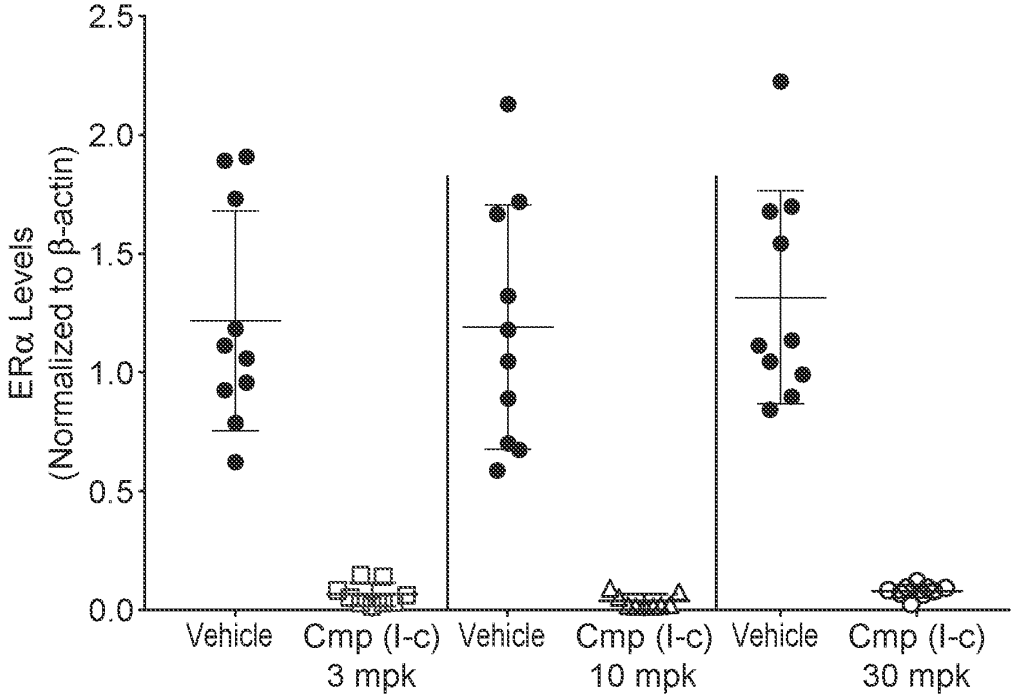

ERα Levels
(Normalized to β-actin)
2.5
2.0
1.5
1.0
0.5
0.0
Vehicle
Cmp (I-c)
3 mpk
Vehicle
Cmp (I-c)
10 mpk
Vehicle
Cmp (I-c)
30 mpk

FIG. 8

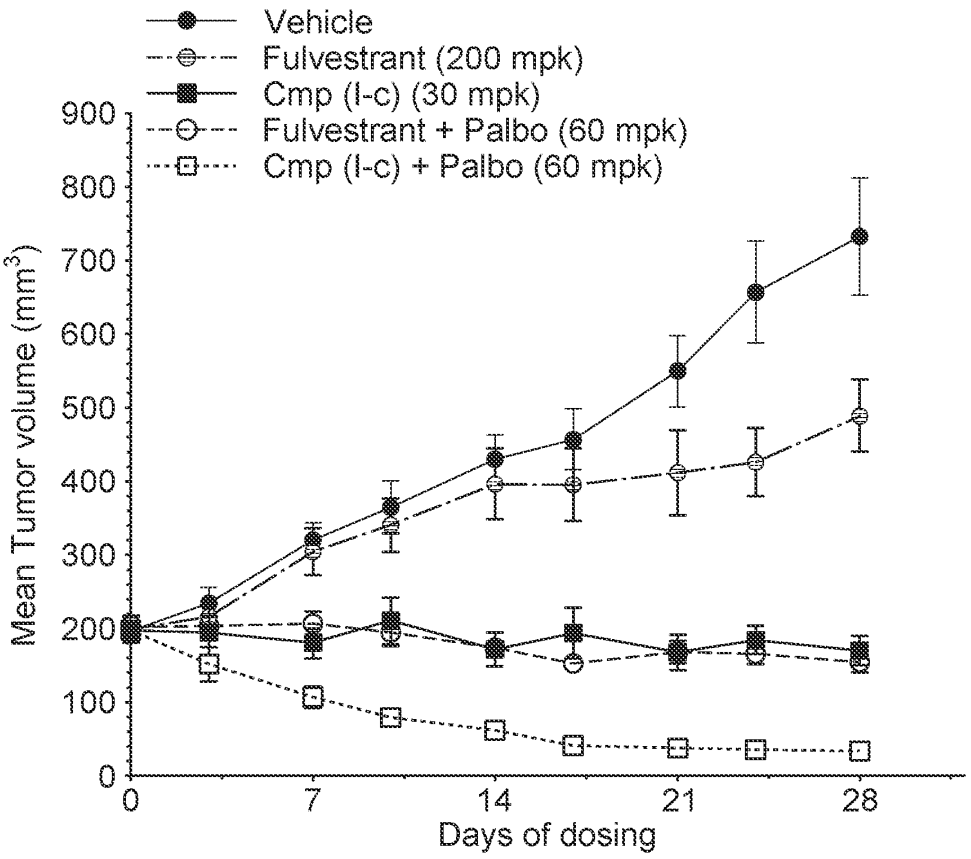

Vehicle
Fulvestrant (200 mpk)
Cmp (I-c) (30 mpk)
Fulvestrant + Palbo (60 mpk)
Cmp (I-c) + Palbo (60 mpk)
Mean Tumor volume (mm3)
900
800
700
600
500
400
300
200
100
0
0
7
14
21
28
Days of dosing

FIG. 9

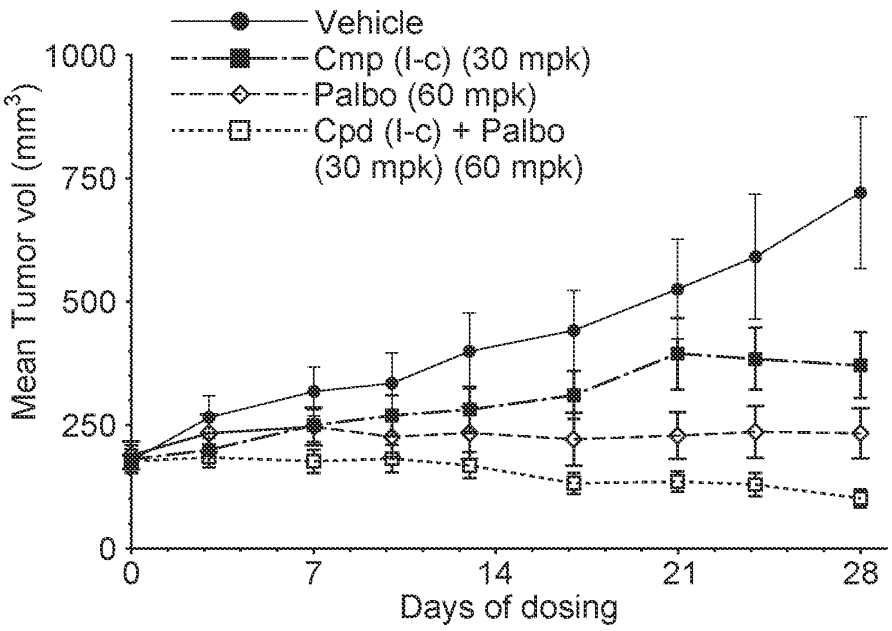

Vehicle
Cmp (I-c) (30 mpk)
Palbo (60 mpk)
Cpd (I-c) + Palbo
(30 mpk) (60 mpk)
Mean Tumor vol (mm3)
1000
750
500
250
0
0
7
14
21
28
Days of dosing

FIG. 10

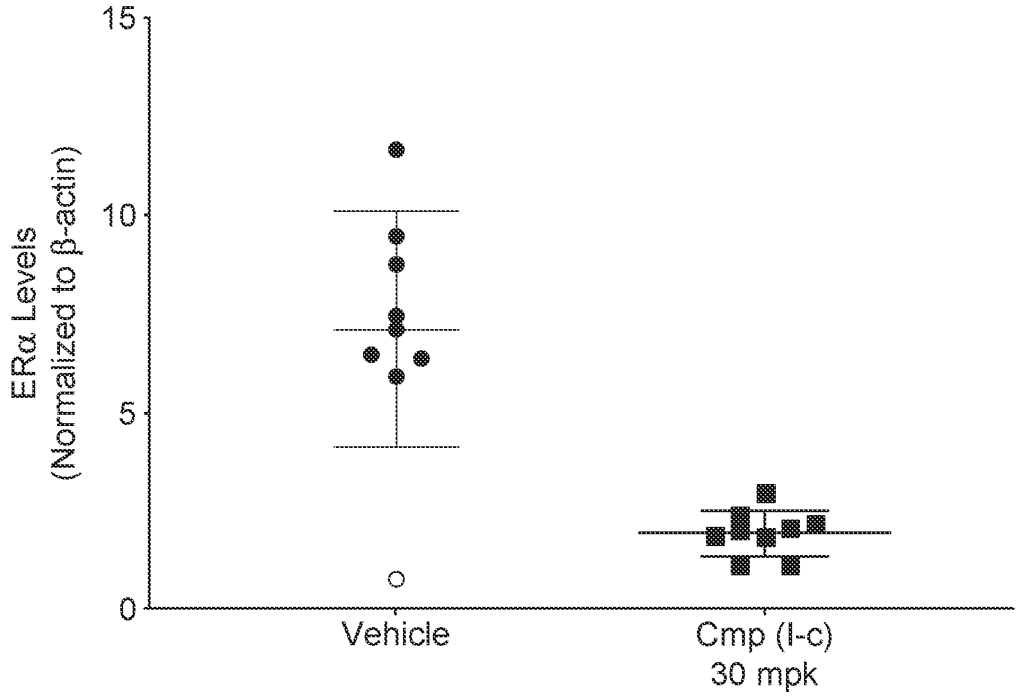

ERα Levels
(Normalized to β-actin)
15
10
5
0
Vehicle
Cmp (I-c)
30 mpk

FIG. 11

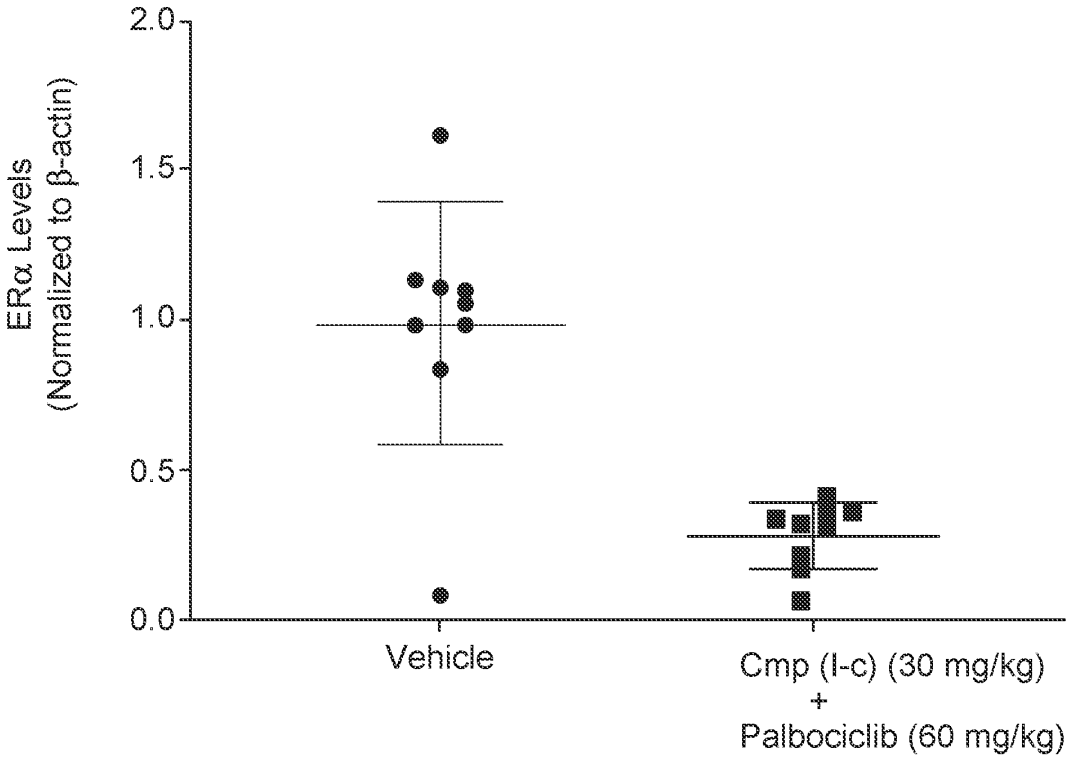

ERα Levels
(Normalized to β-actin)
2.0
1.5
1.0
0.5
0.0
Vehicle
Cmp (I-c) (30 mg/kg)
+
Palbociclib (60 mg/kg)

FIG. 12

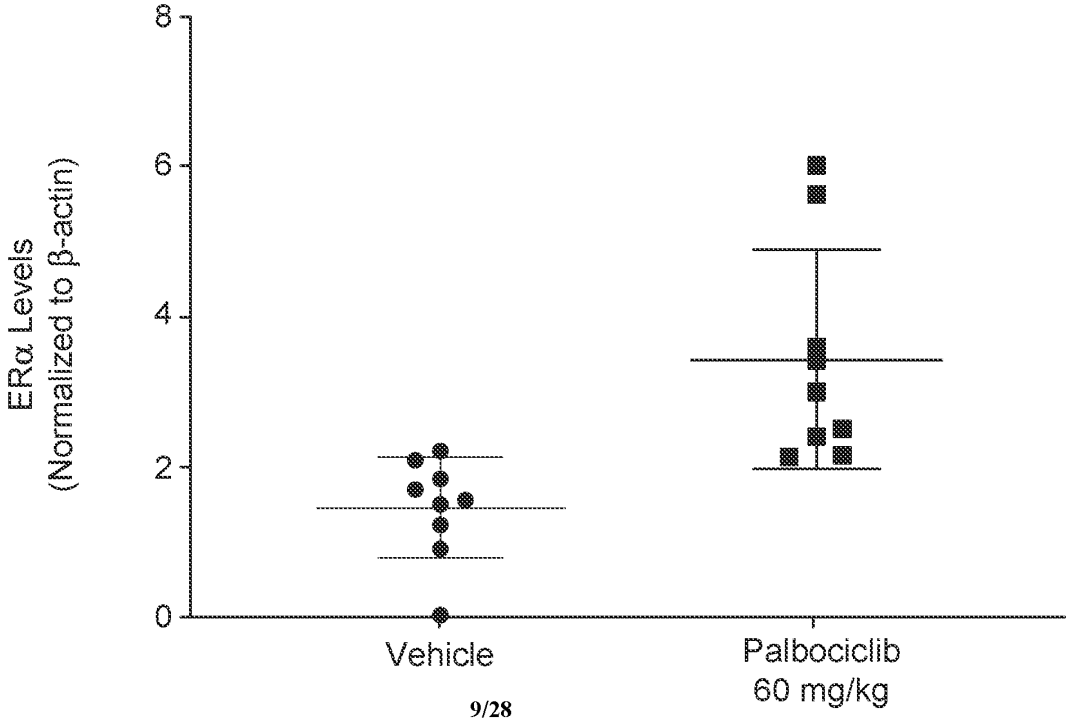

ERα Levels
(Normalized to β-actin)
8
6
4
2
0
Vehicle
Palbociclib
60 mg/kg

FIG. 13

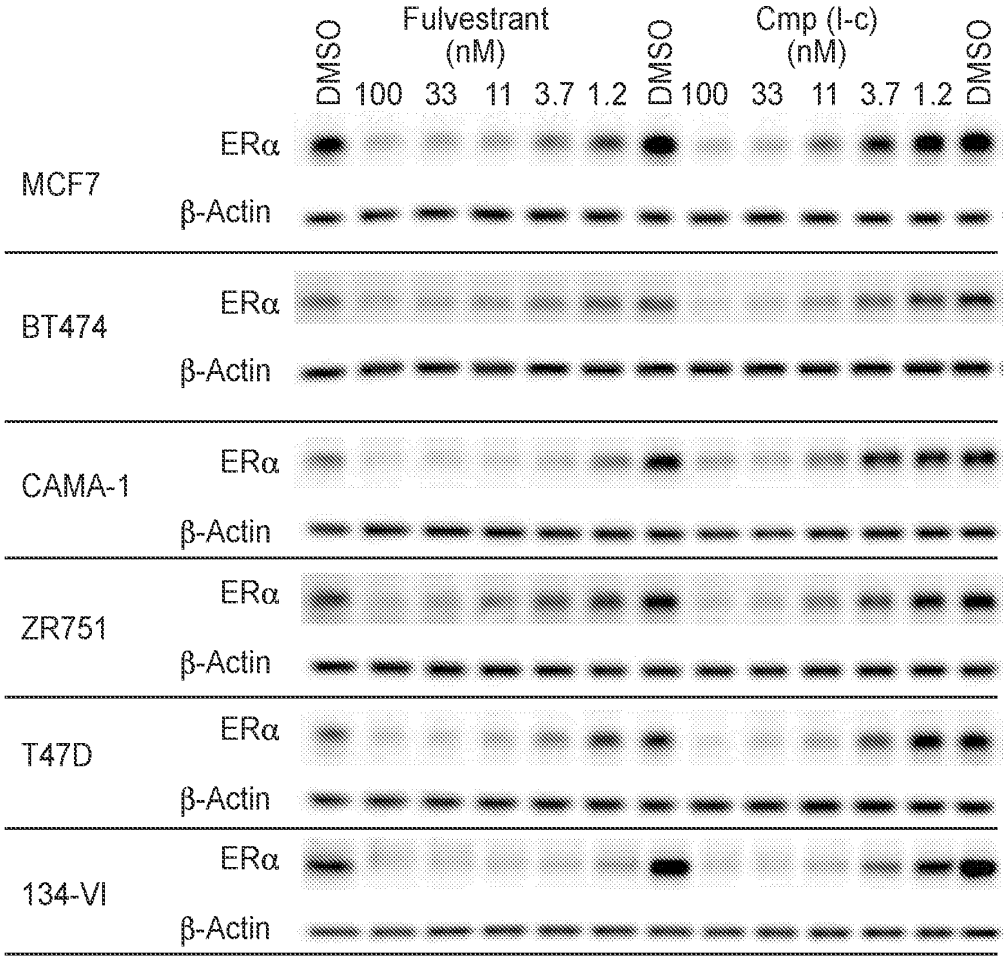

DMSO
Fulvestrant (nM)
100
33
11
3.7
1.2
DMSO
Cmp (I-c) (nM)
100
33
11
3.7
1.2
DMSO
MCF7
ERα
β-Actin
BT474
ERα
β-Actin
CAMA-1
ERα
β-Actin
ZR751
ERα
β-Actin
T47D
ERα
β-Actin
134-VI
ERα
β-Actin

FIG. 14

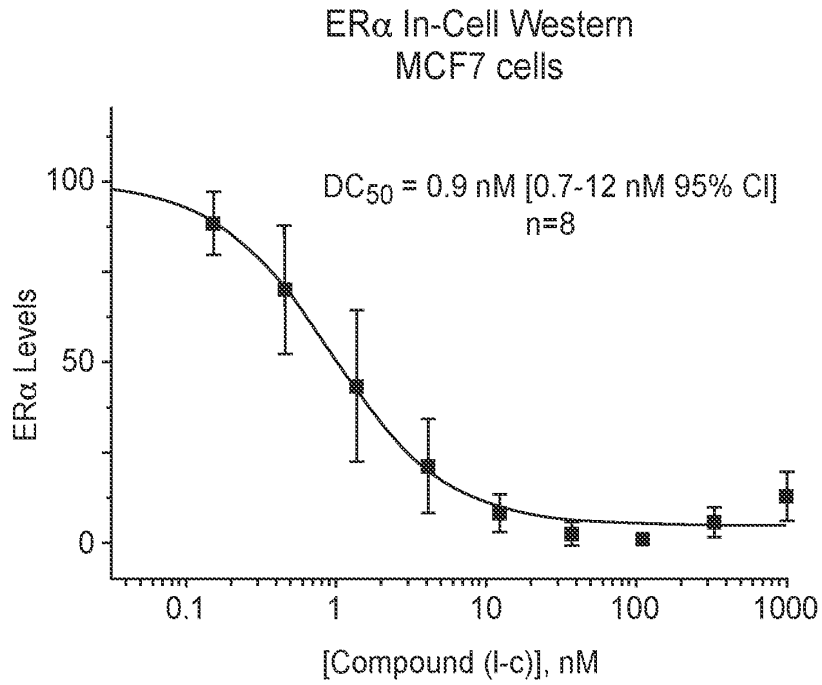

ERα In-Cell Western
MCF7 cells
DC50 = 0.9 nM [0.7-12 nM 95% CI]
n=8
ERα Levels
100
50
0
0.1
1
10
100
1000
[Compound (I-c)], nM

FIG. 15

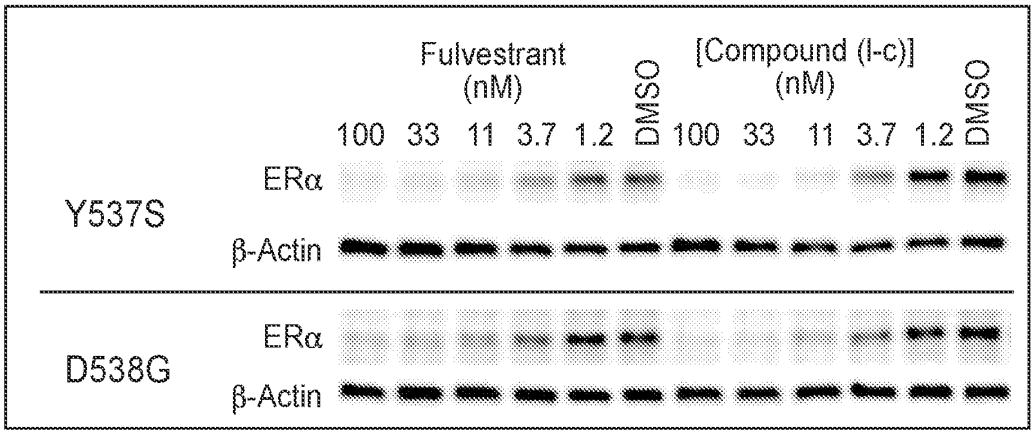

Fulvestrant (nM)
[Compound (I-c)] (nM)
100 33 11 3.7 1.2 DMSO 100 33 11 3.7 1.2 DMSO
Y537S
ERα
β-Actin
D538G
ERα
β-Actin

FIG. 16

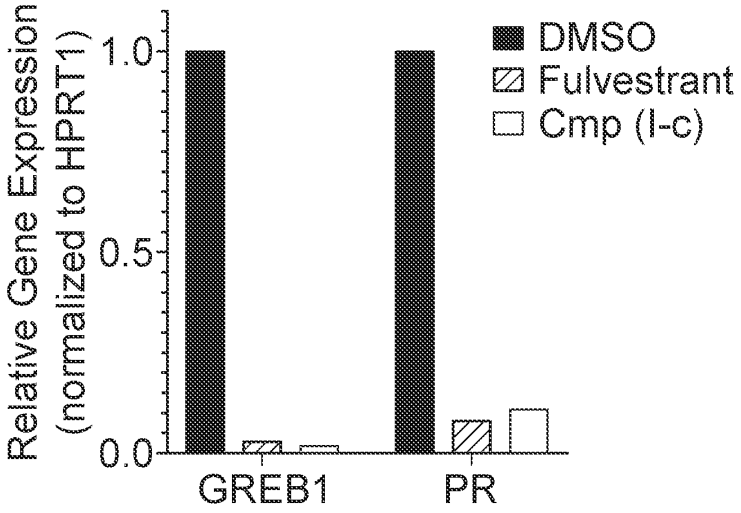

Relative Gene Expression
(normalized to HPRT1)
1.0
0.5
0.0
GREB1
PR
DMSO
Fulvestrant
Cmp (I-c)

FIG. 17

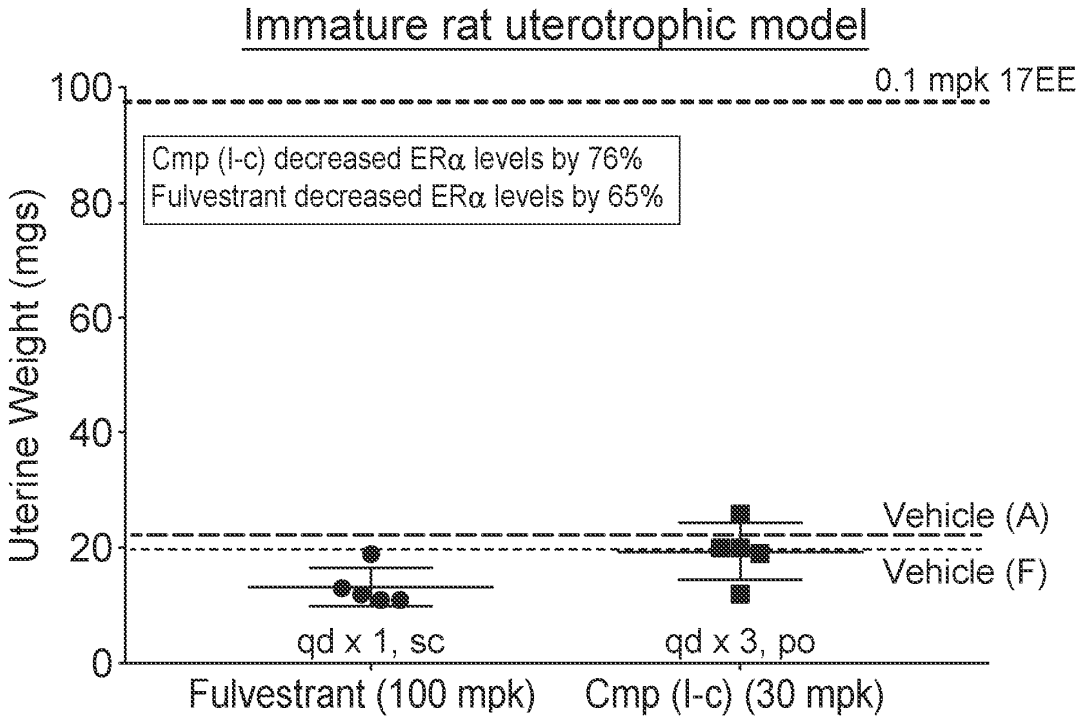

Immature rat uterotrophic model
0.1 mpk 17EE
Cmp (I-c) decreased ERα levels by 76%
Fulvestrant decreased ERα levels by 65%
Uterine Weight (mgs)
100
80
60
40
20
0
Vehicle (A)
Vehicle (F)
qd x 1, sc
qd x 3, po
Fulvestrant (100 mpk)
Cmp (I-c) (30 mpk)

FIG. 18

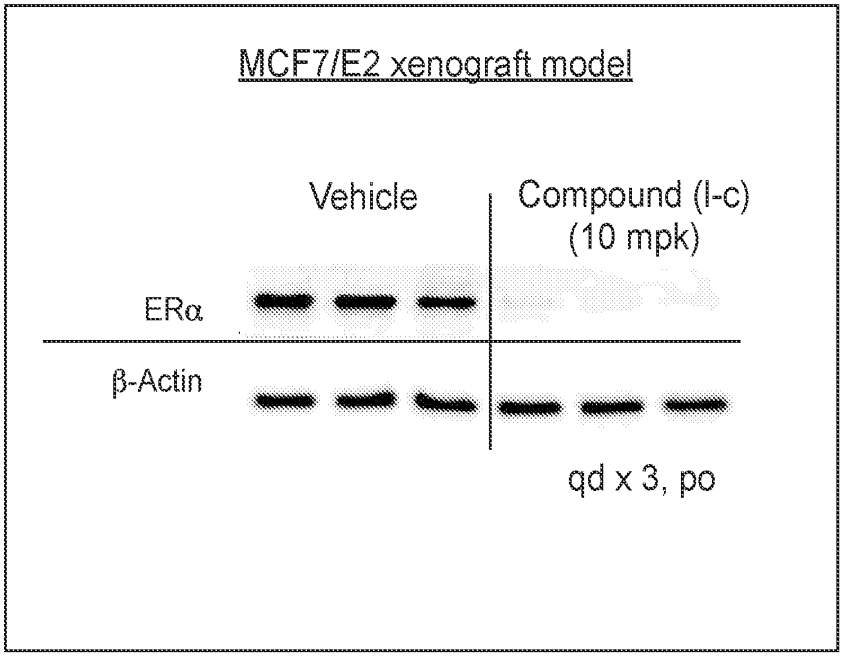

MCF7/E2 xenograft model
Vehicle
Compound (I-c)
(10 mpk)
ERα
β-Actin
qd x 3, po

FIG. 19

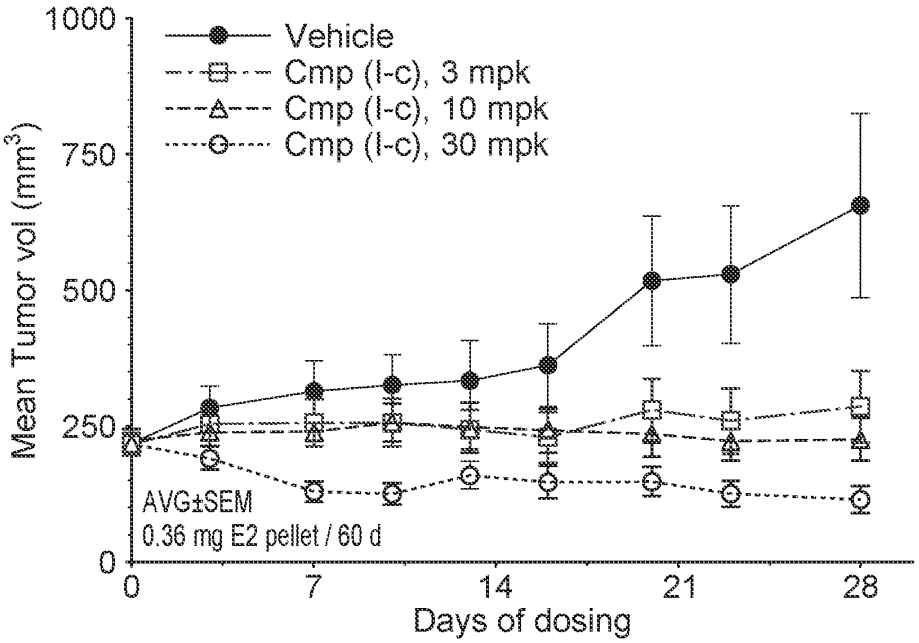

Vehicle
Cmp (I-c), 3 mpk
Cmp (I-c), 10 mpk
Cmp (I-c), 30 mpk
Mean Tumor vol (mm3)
1000
750
500
250
0
AVG±SEM
0.36 mg E2 pellet / 60 d
0
7
14
21
28
Days of dosing

FIG. 20

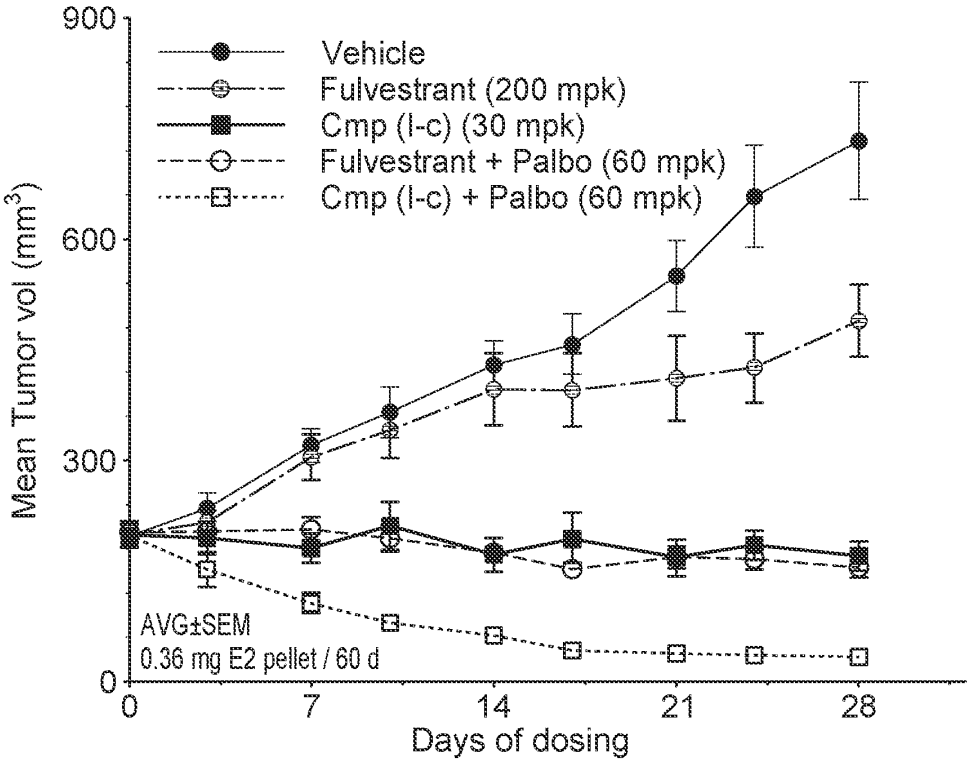

Vehicle
Fulvestrant (200 mpk)
Cmp (I-c) (30 mpk)
Fulvestrant + Palbo (60 mpk)
Cmp (I-c) + Palbo (60 mpk)
Mean Tumor vol (mm3)
900
600
300
0
AVG±SEM
0.36 mg E2 pellet / 60 d
0
7
14
21
28
Days of dosing

FIG. 21

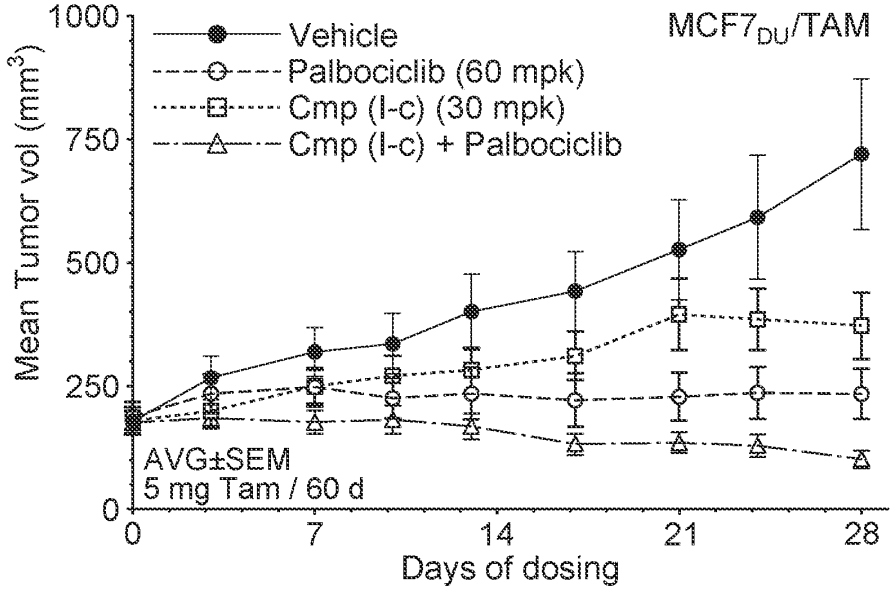
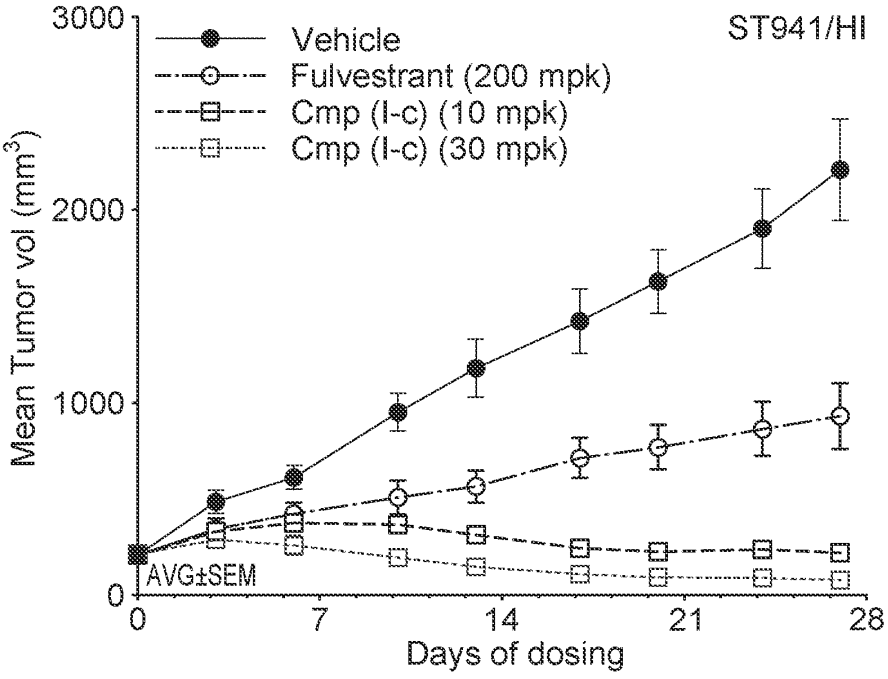

Vehicle
Palbociclib (60 mpk)
Cmp (I-c) (30 mpk)
Cmp (I-c) + Palbociclib
MCF7DU/TAM
Mean Tumor vol (mm3)
1000
750
500
250
0
AVG±SEM
5 mg Tam / 60 d
0
7
14
21
28
Days of dosing

FIG. 22


Vehicle
Fulvestrant (200 mpk)
Cmp (I-c) (10 mpk)
Cmp (I-c) (30 mpk)
ST941/HI
Mean Tumor vol (mm3)
3000
2000
1000
0
AVG±SEM
0
7
14
21
28
Days of dosing

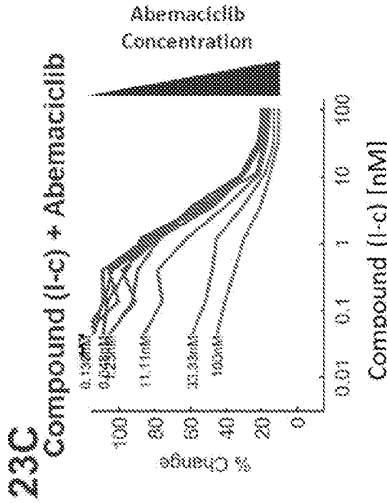


FIG. 23C

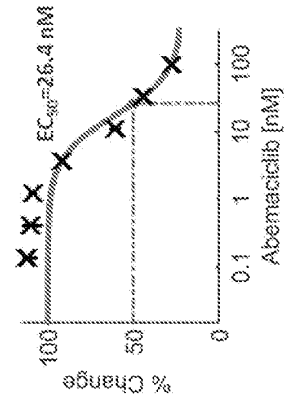


FIG. 23B

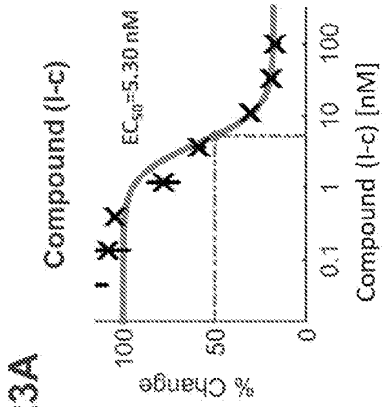


FIG. 23A

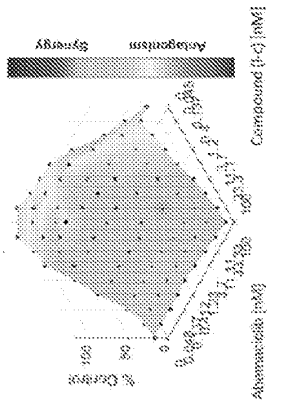


FIG. 23F

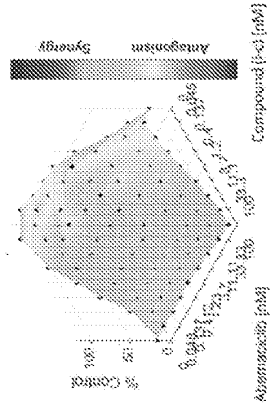


FIG. 23E

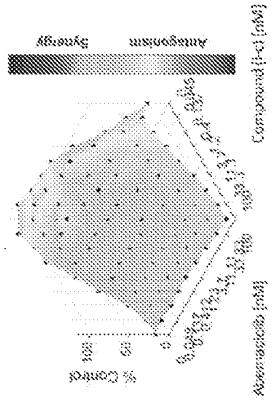


FIG. 23D

FIG. 24A

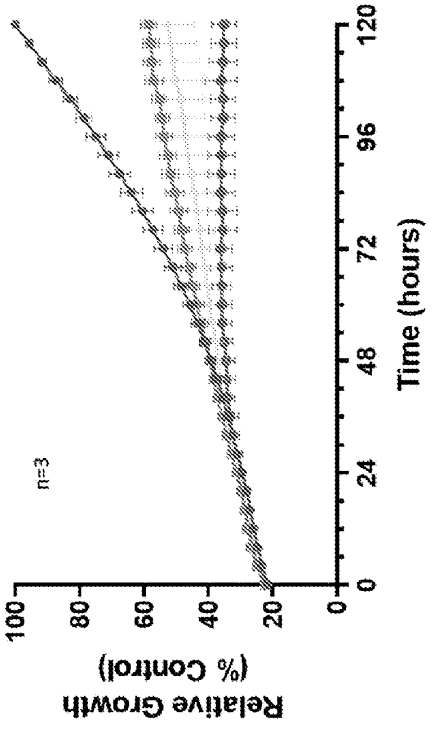


FIG. 24B

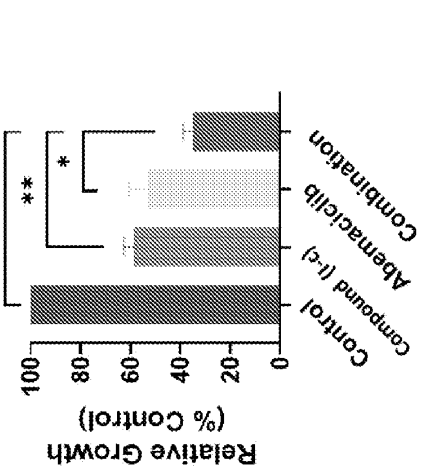


FIG. 25A

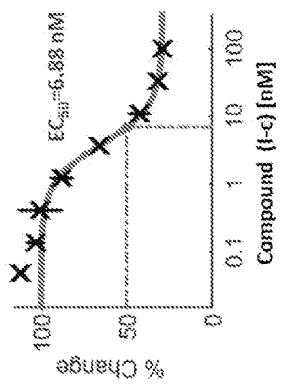


FIG. 25B

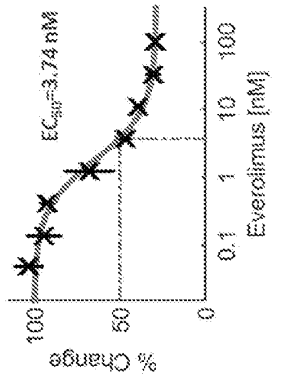


FIG. 25C

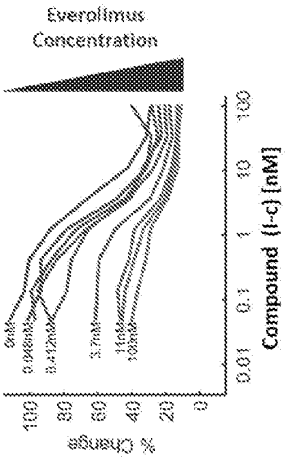


FIG. 25D

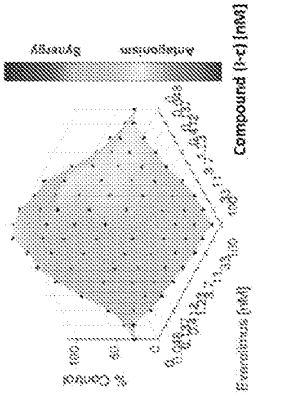


FIG. 25E

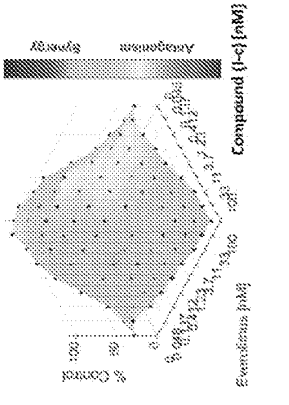
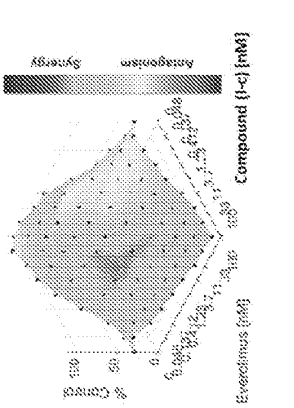
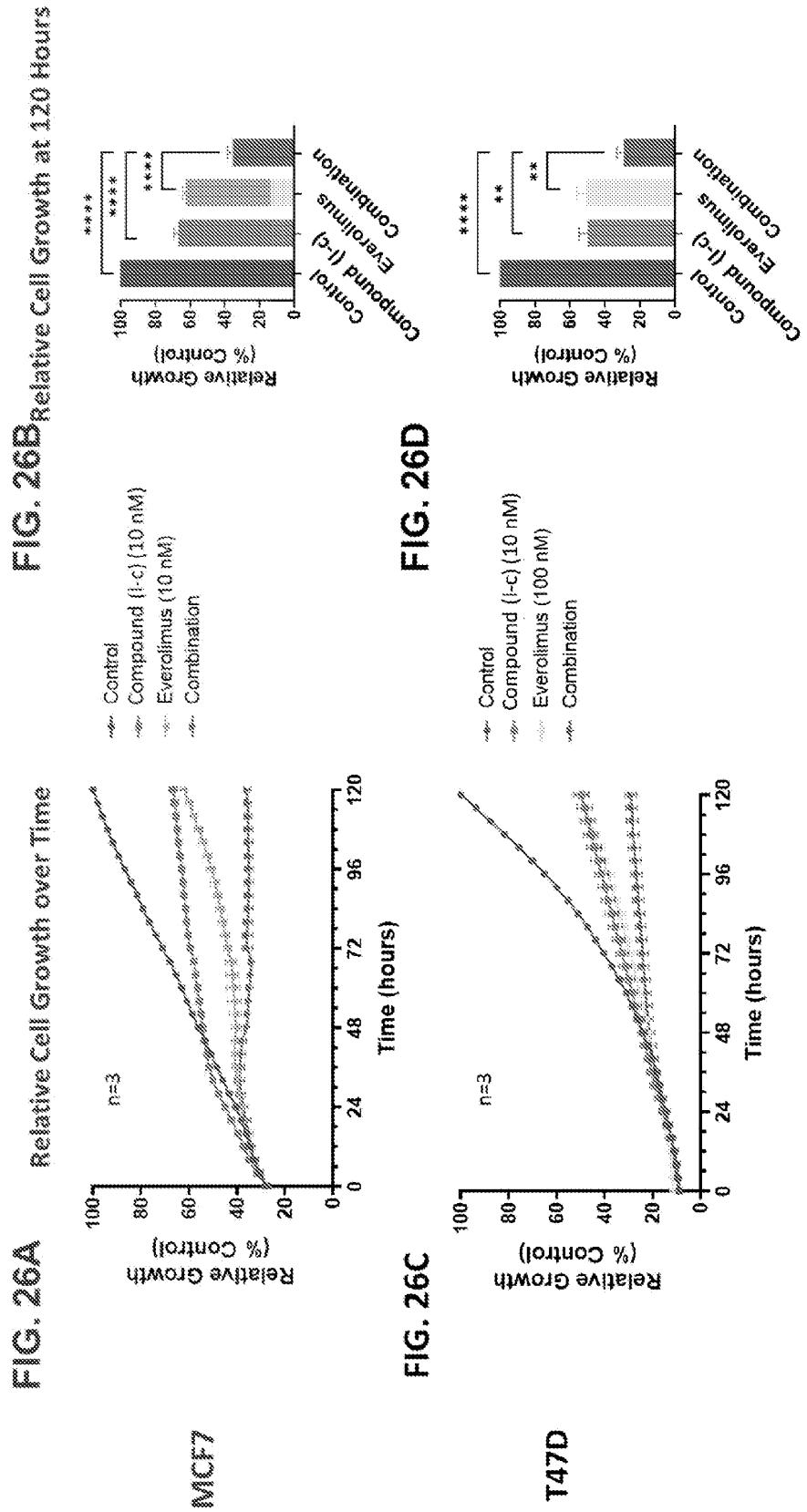


FIG. 25F




FIG. 26A
Relative Cell Growth over Time
MCF7
n=3
Relative Growth (% Control)
Time (hours)
Control
Compound (i-c) (10 nM)
Everolimus (10 nM)
Combination
FIG. 26B
Relative Cell Growth at 120 Hours
Relative Growth (% Control)
Control
Compound (i-c)
Everolimus
Combination
****
FIG. 26C
T47D
n=3
Relative Growth (% Control)
Time (hours)
Control
Compound (i-c) (10 nM)
Everolimus (100 nM)
Combination
FIG. 26D
Relative Growth (% Control)
Control
Compound (i-c)
Everolimus
Combination
****
**

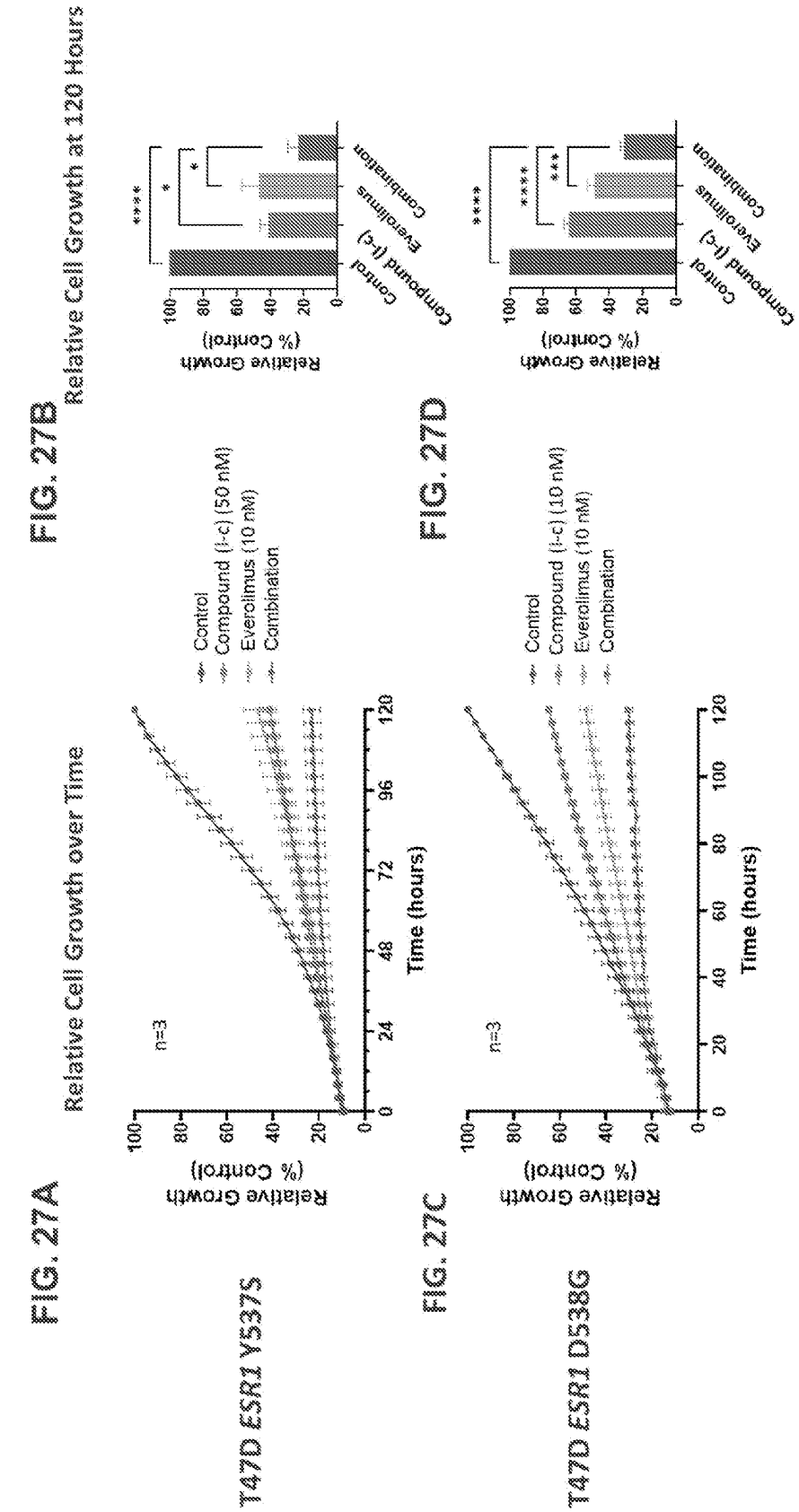

FIG. 27A
Relative Cell Growth over Time
T47D ESR1 Y537S
n=3
Relative Growth (% Control)
Time (hours)
Control
Compound (I-c) (50 nM)
Everolimus (10 nM)
Combination
FIG. 27B
Relative Cell Growth at 120 Hours
Relative Growth (% Control)
Control
Compound (I-c)
Everolimus
Combination
****
*
*
FIG. 27C
T47D ESR1 D538G
n=3
Relative Growth (% Control)
Time (hours)
Control
Compound (I-c) (10 nM)
Everolimus (10 nM)
Combination
FIG. 27D
Relative Growth (% Control)
Control
Compound (I-c)
Everolimus
Combination
****
****
***

FIG. 28

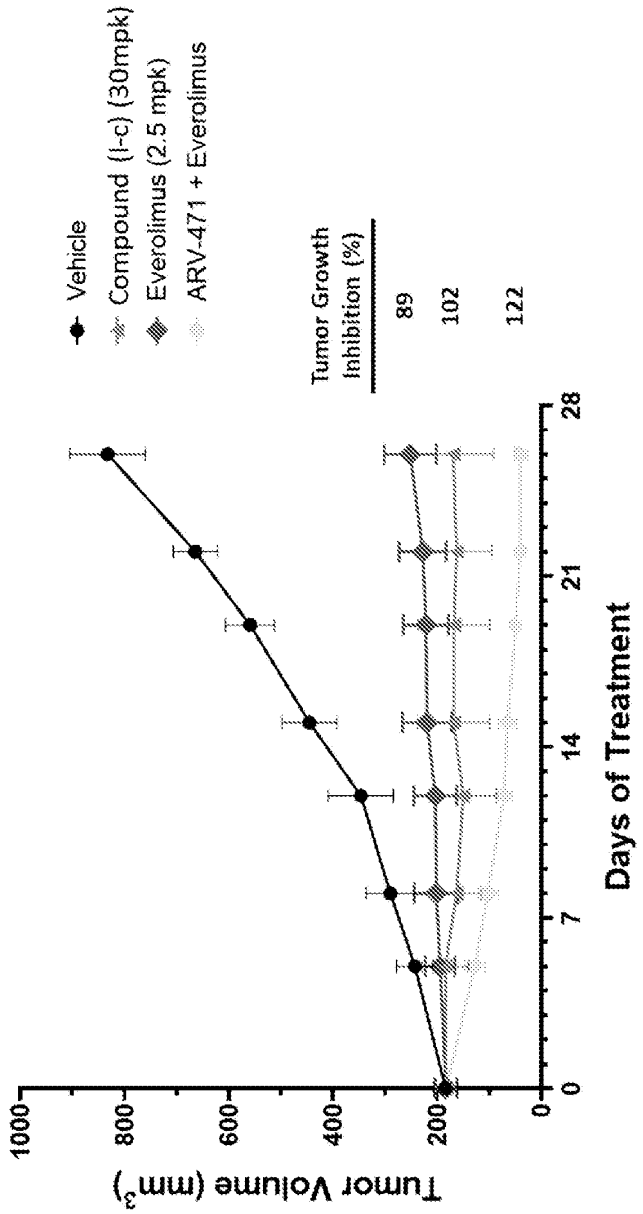

Vehicle
Compound (I-c) (30mpk)
Everolimus (2.5 mpk)
ARV-471 + Everolimus
Tumor Growth Inhibition (%)
89
102
122
Tumor Volume (mm³)
1000
800
600
400
200
0
0
7
14
21
28
Days of Treatment

FIG. 29A

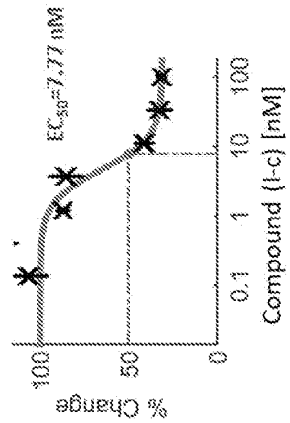


FIG. 29B

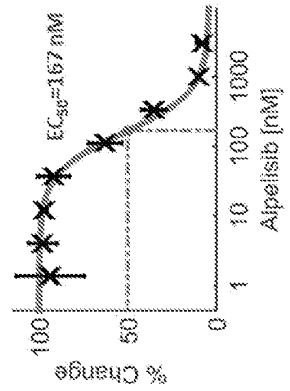


FIG. 29C

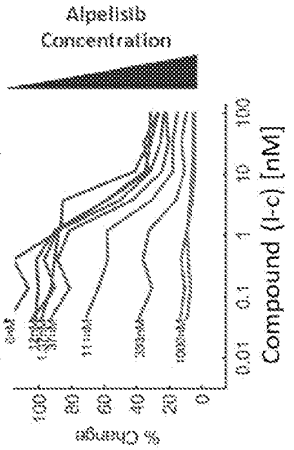


FIG. 29D

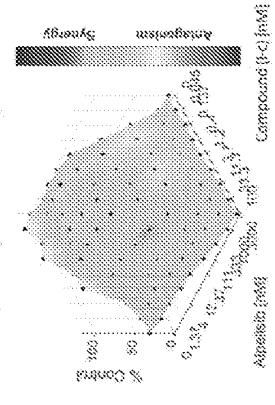


FIG. 29E

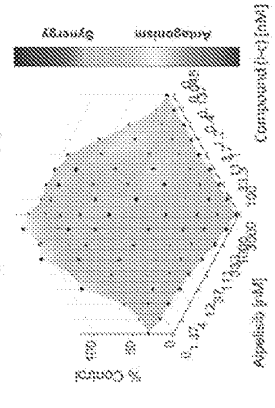
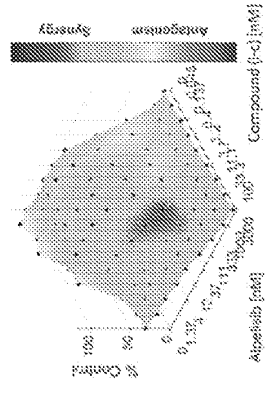


FIG. 29F



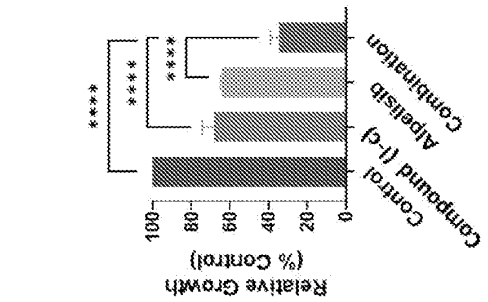


FIG. 30B

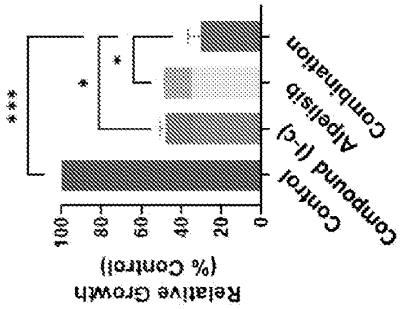


FIG. 30D

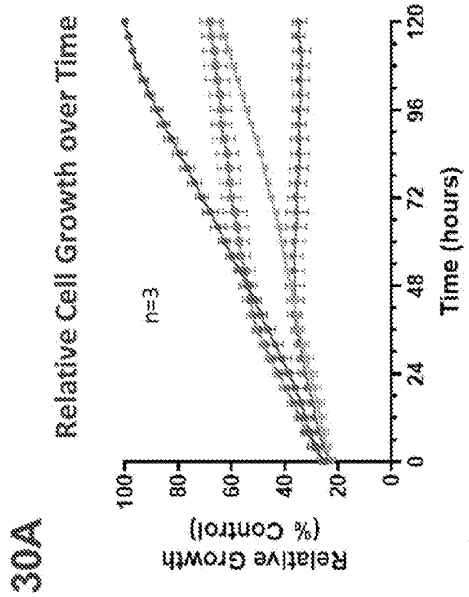


FIG. 30A

MCF7

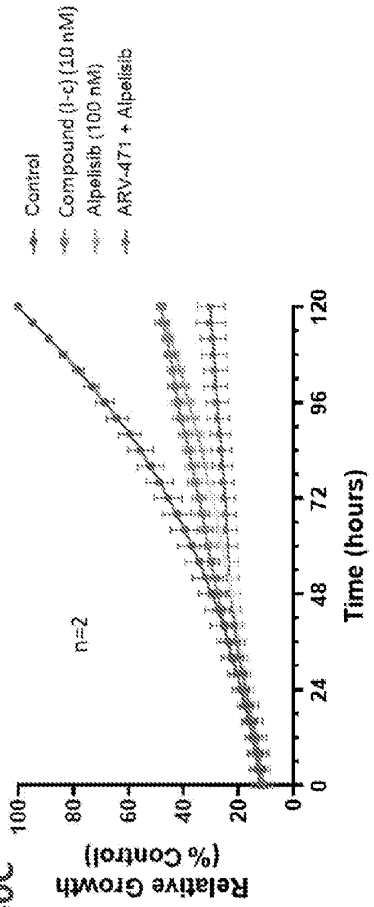


FIG. 30C

T47D

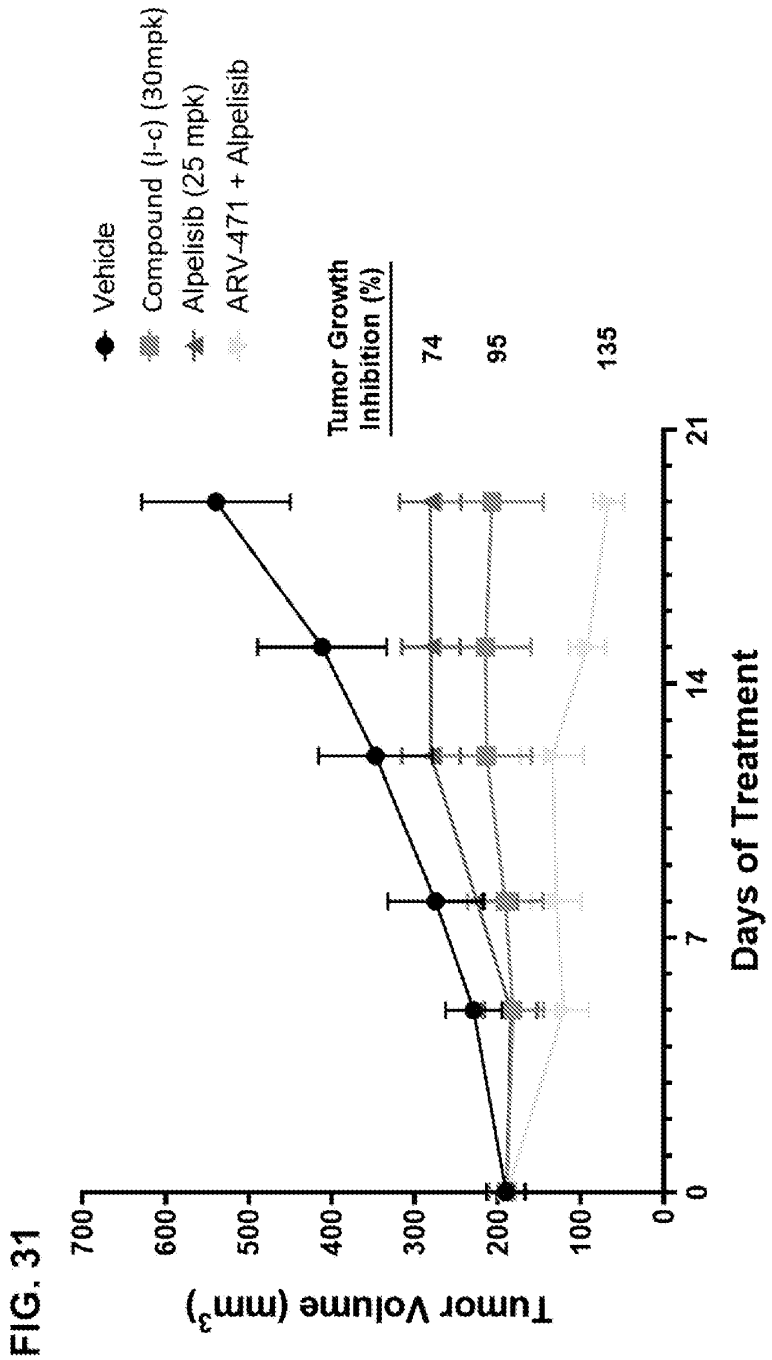

Vehicle
Compound (I-c) (30mpk)
Alpelisib (25 mpk)
ARV-471 + Alpelisib
Tumor Growth Inhibition (%)
74
95
135
Tumor Volume (mm³)
700
600
500
400
300
200
100
0
0
7
14
21
Days of Treatment

FIG. 31

FIG. 32A

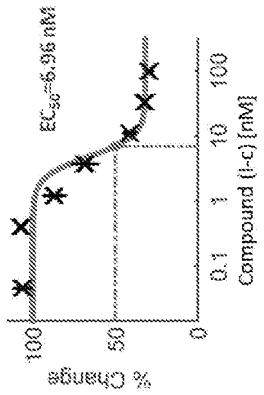


FIG. 32B

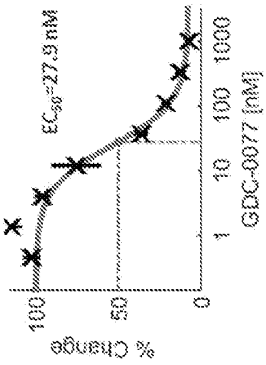


FIG. 32C

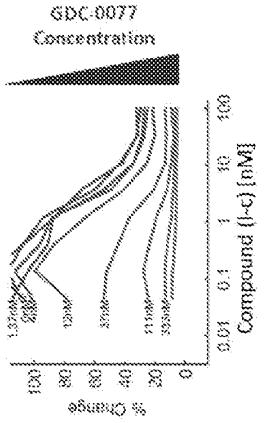


FIG. 32D

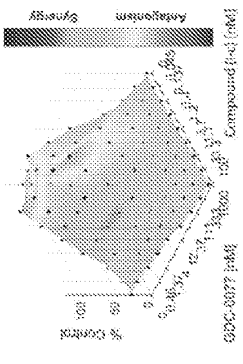


FIG. 32E

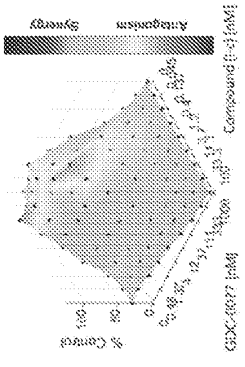
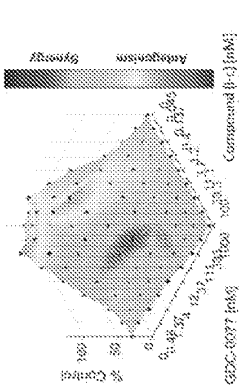


FIG. 32F



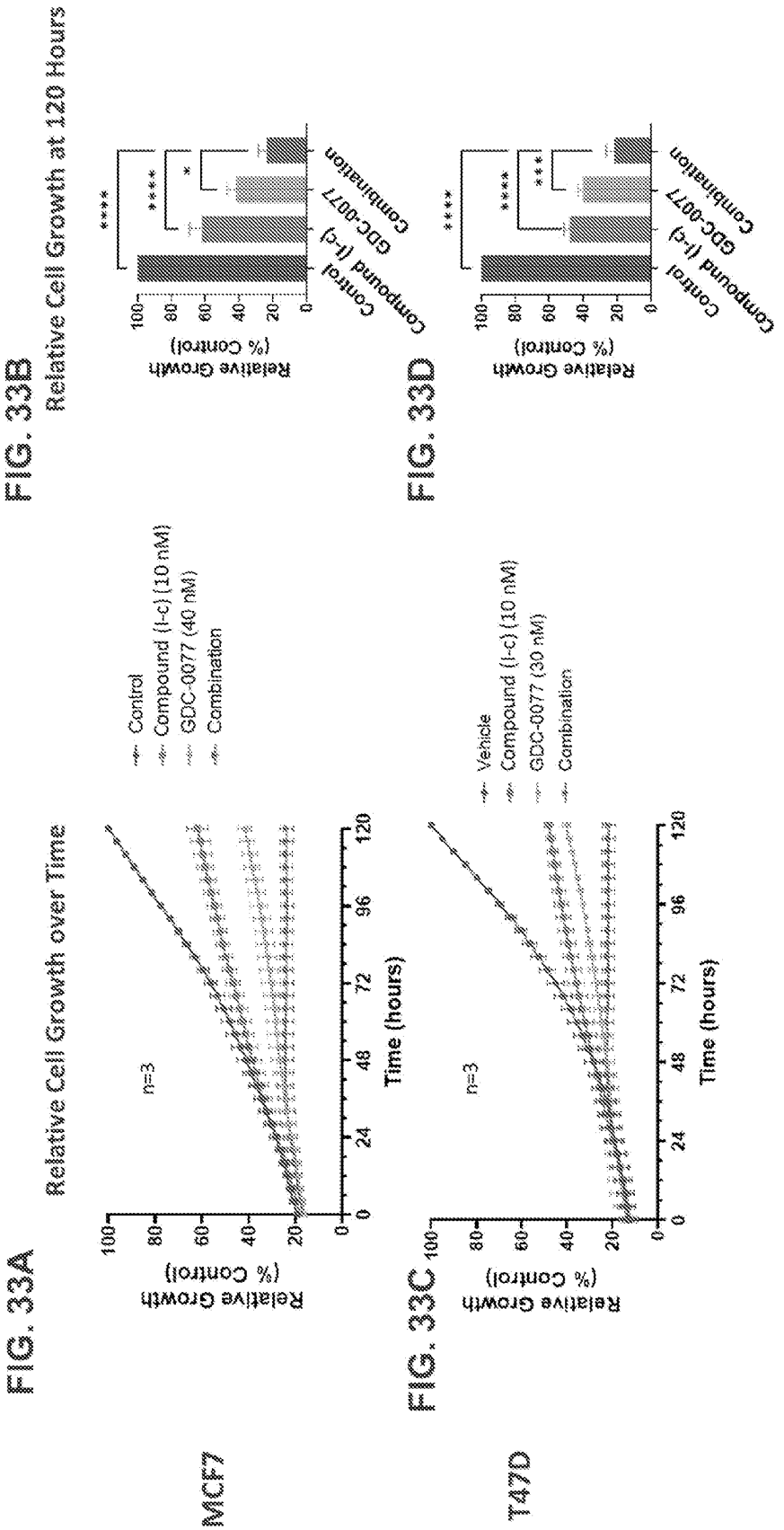

FIG. 33A
Relative Cell Growth over Time
MCF7
Control
Compound (I-c) (10 nM)
GDC-0077 (40 nM)
Combination
n=3
Relative Growth (% Control)
Time (hours)
FIG. 33B
Relative Cell Growth at 120 Hours
****
****
*
Control
Compound (I-c)
GDC-0077
Combination
FIG. 33C
T47D
Vehicle
Compound (I-c) (10 nM)
GDC-0077 (30 nM)
Combination
n=3
FIG. 33D
****
****
***

FIG. 34A

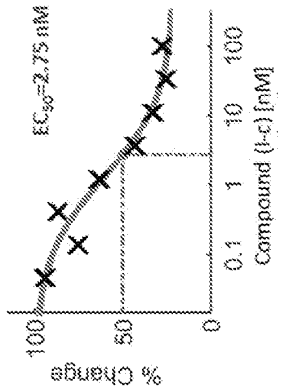


FIG. 34B

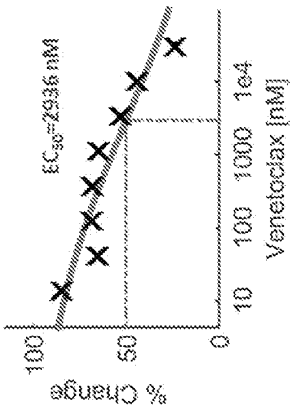


FIG. 34C

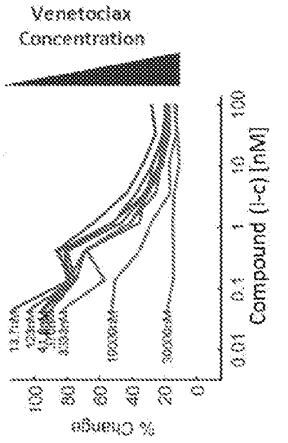


FIG. 34D

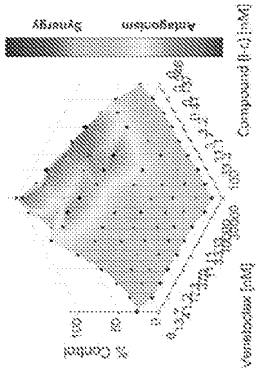


FIG. 34E

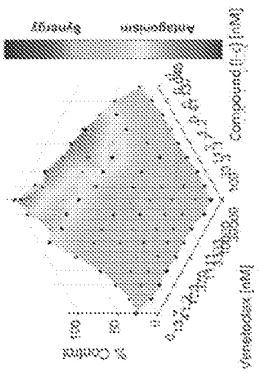


FIG. 34F

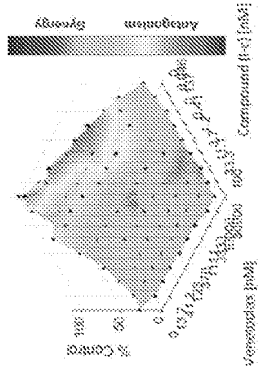


FIG. 35A

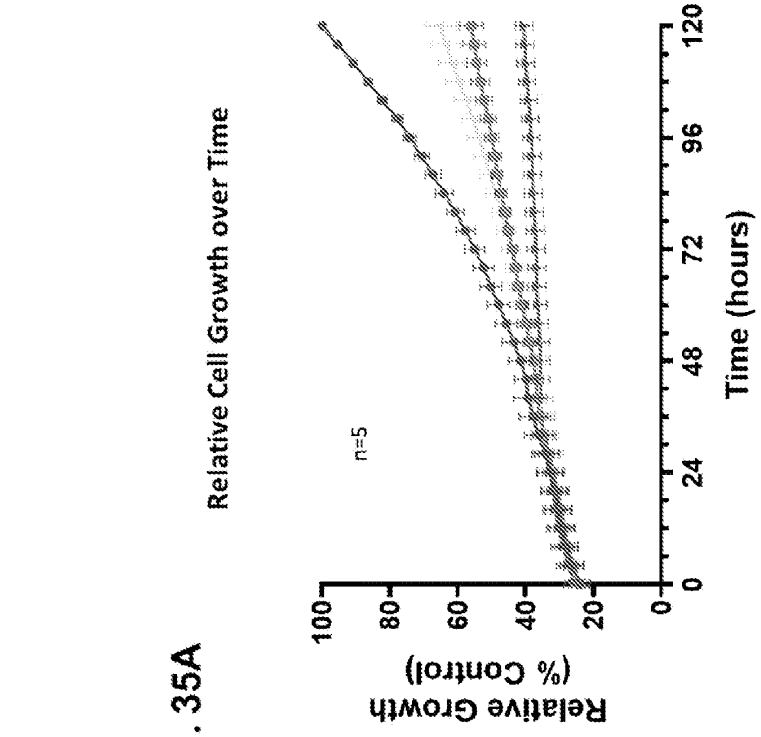


FIG. 35B

