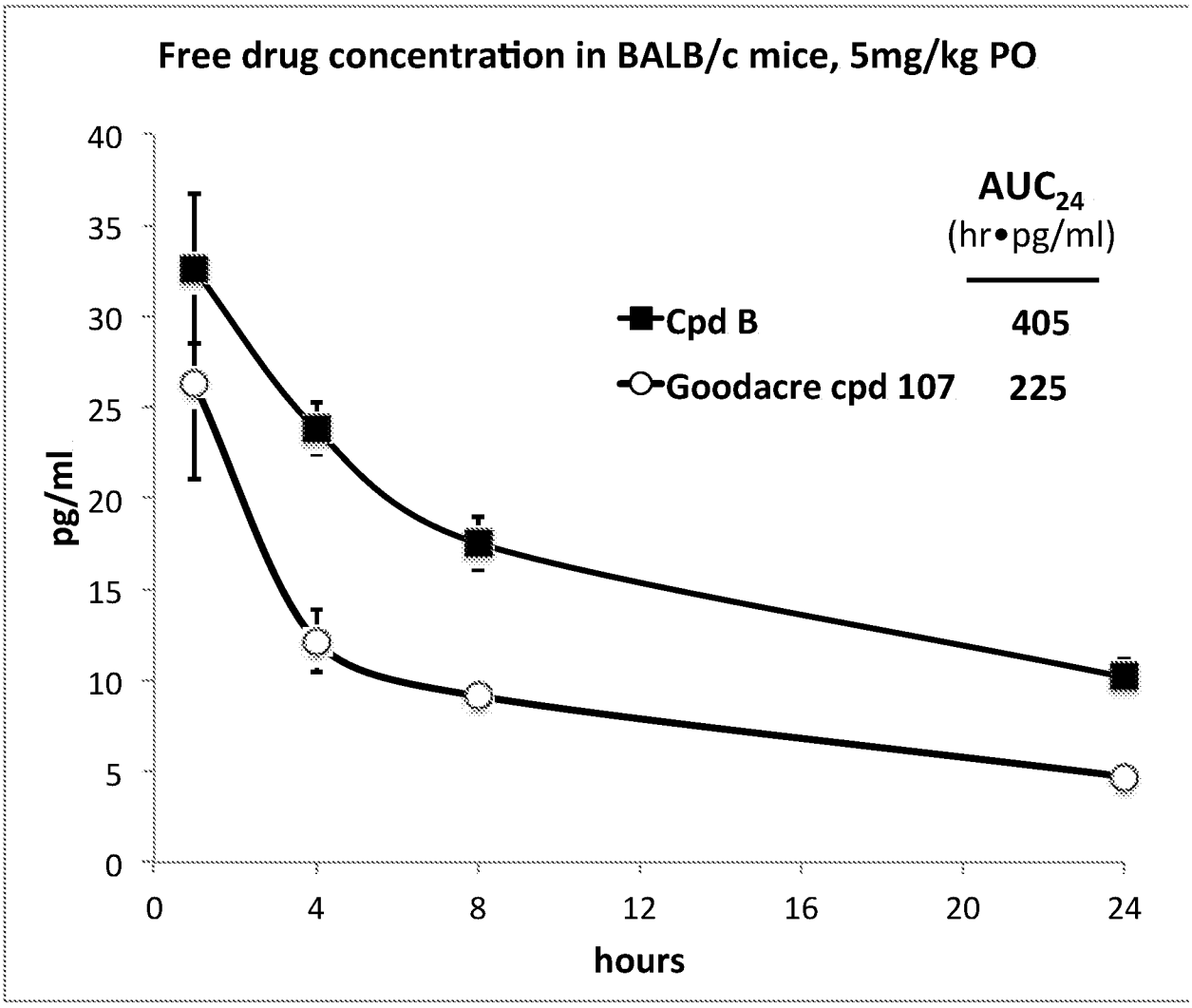

Free drug concentration in BALB/c mice, 5mg/kg PO
pg/ml
hours
AUC24
(hr•pg/ml)
Cpd B 405
Goodacre cpd 107 225
0
5
10
15
20
25
30
35
40
0
4
8
12
16
20
24

FIG. 1A

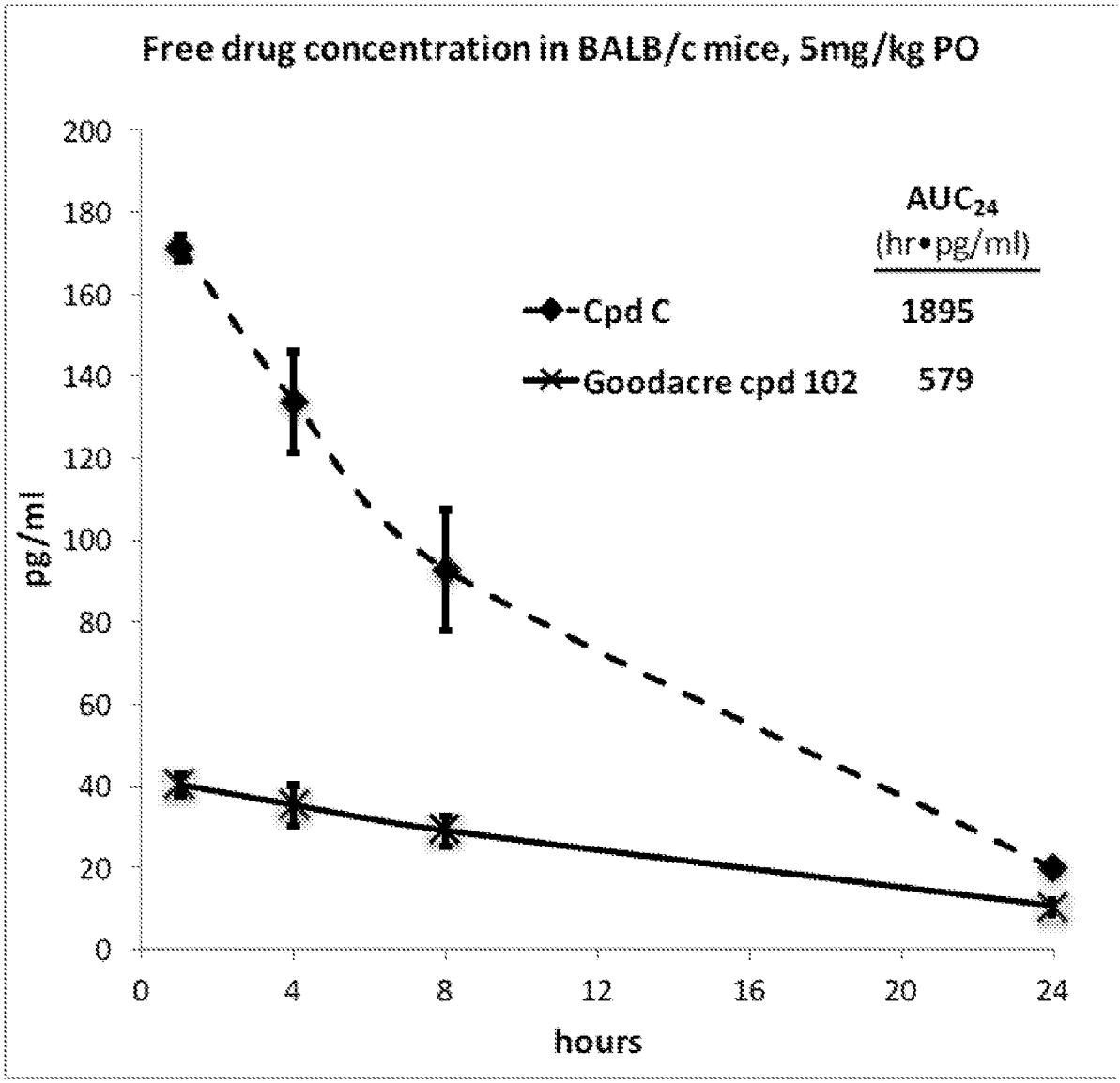

Free drug concentration in BALB/c mice, 5mg/kg PO
200
180
160
140
120
100
80
60
40
20
0
pg/ml
0
4
8
12
16
20
24
hours
AUC24
(hr•pg/ml)
Cpd C
1895
Goodacre cpd 102
579

FIG. 1B

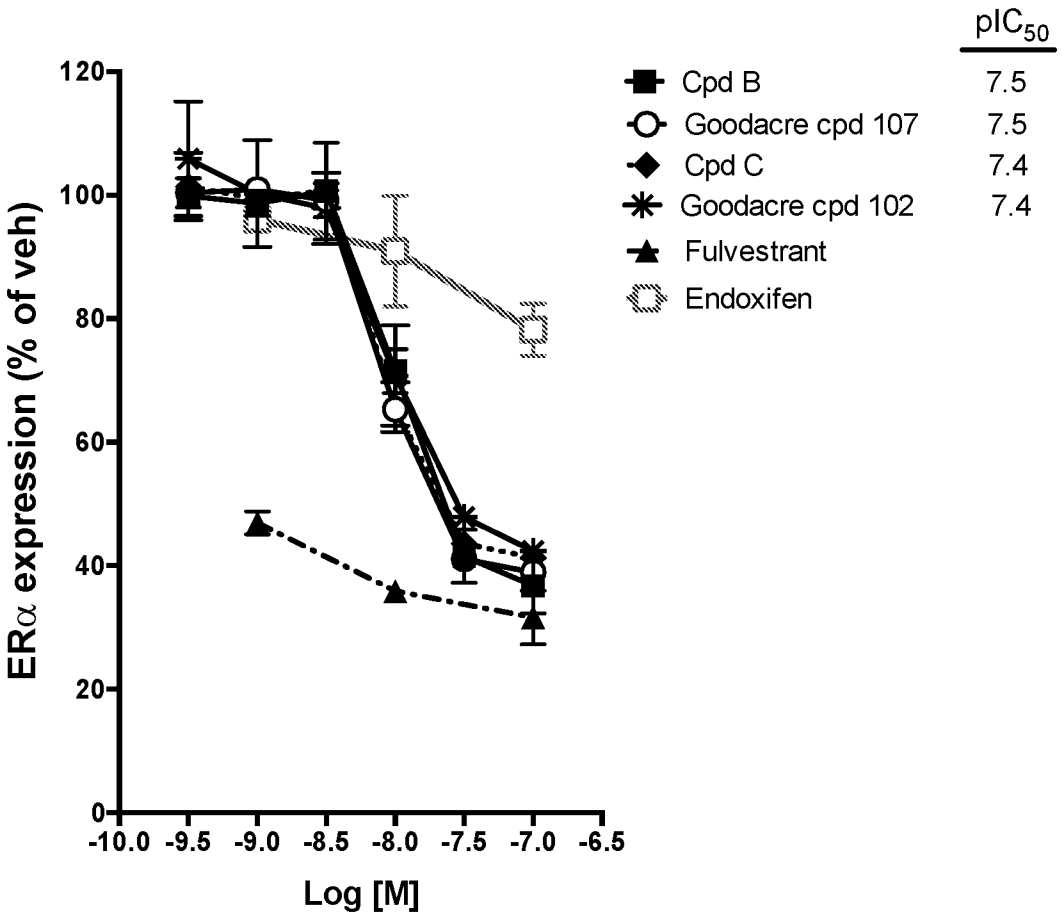

pIC50
Cpd B 7.5
Goodacre cpd 107 7.5
Cpd C 7.4
Goodacre cpd 102 7.4
Fulvestrant
Endoxifen
ERα expression (% of veh)
120
100
80
60
40
20
0
-10.0 -9.5 -9.0 -8.5 -8.0 -7.5 -7.0 -6.5
Log [M]

FIG. 2

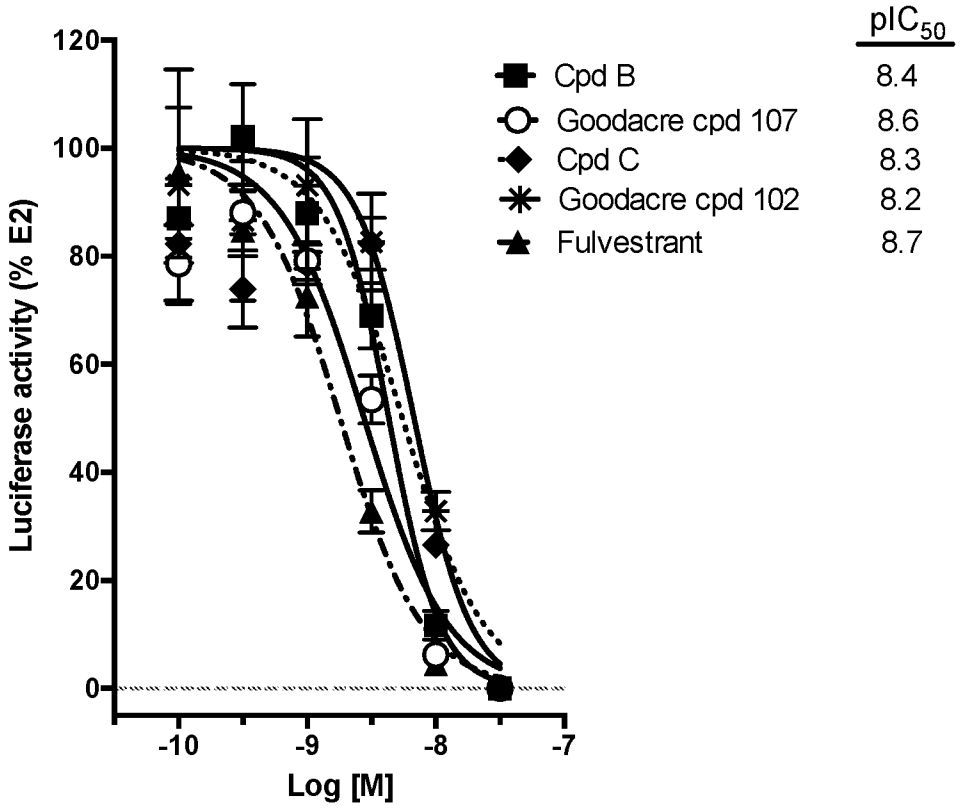

pIC50
Cpd B 8.4
Goodacre cpd 107 8.6
Cpd C 8.3
Goodacre cpd 102 8.2
Fulvestrant 8.7
Luciferase activity (% E2)
120
100
80
60
40
20
0
-10
-9
-8
-7
Log [M]

FIG. 3

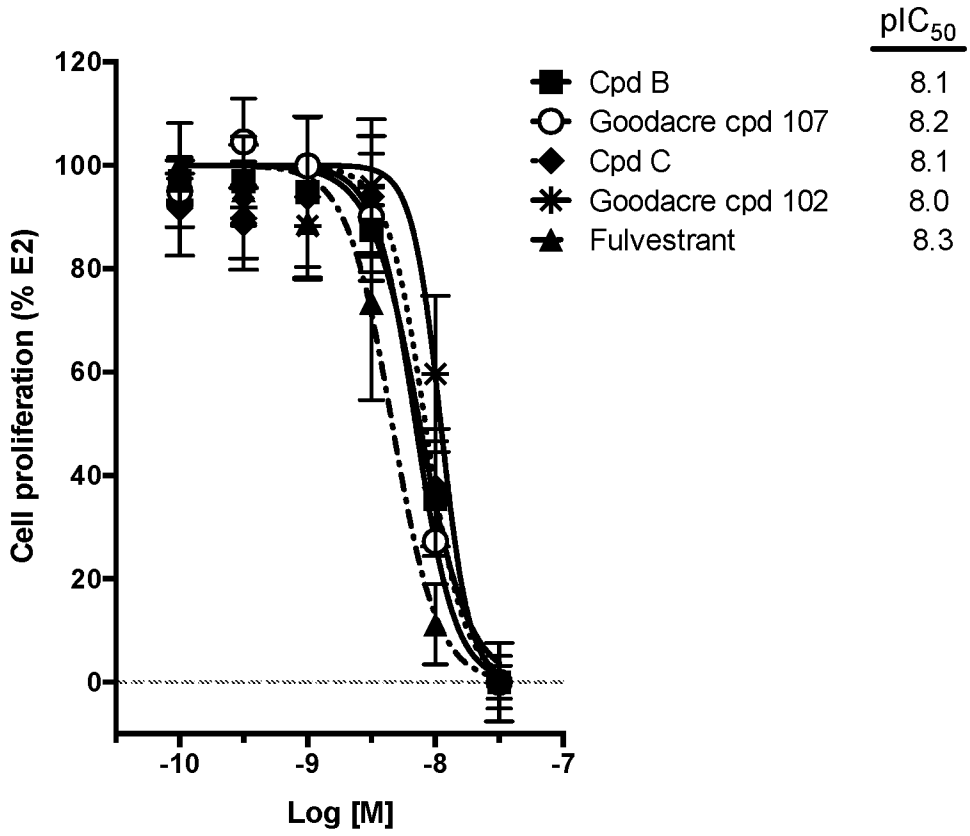

pIC50
Cpd B 8.1
Goodacre cpd 107 8.2
Cpd C 8.1
Goodacre cpd 102 8.0
Fulvestrant 8.3
Cell proliferation (% E2)
120
100
80
60
40
20
0
-10
-9
-8
-7
Log [M]

FIG. 4

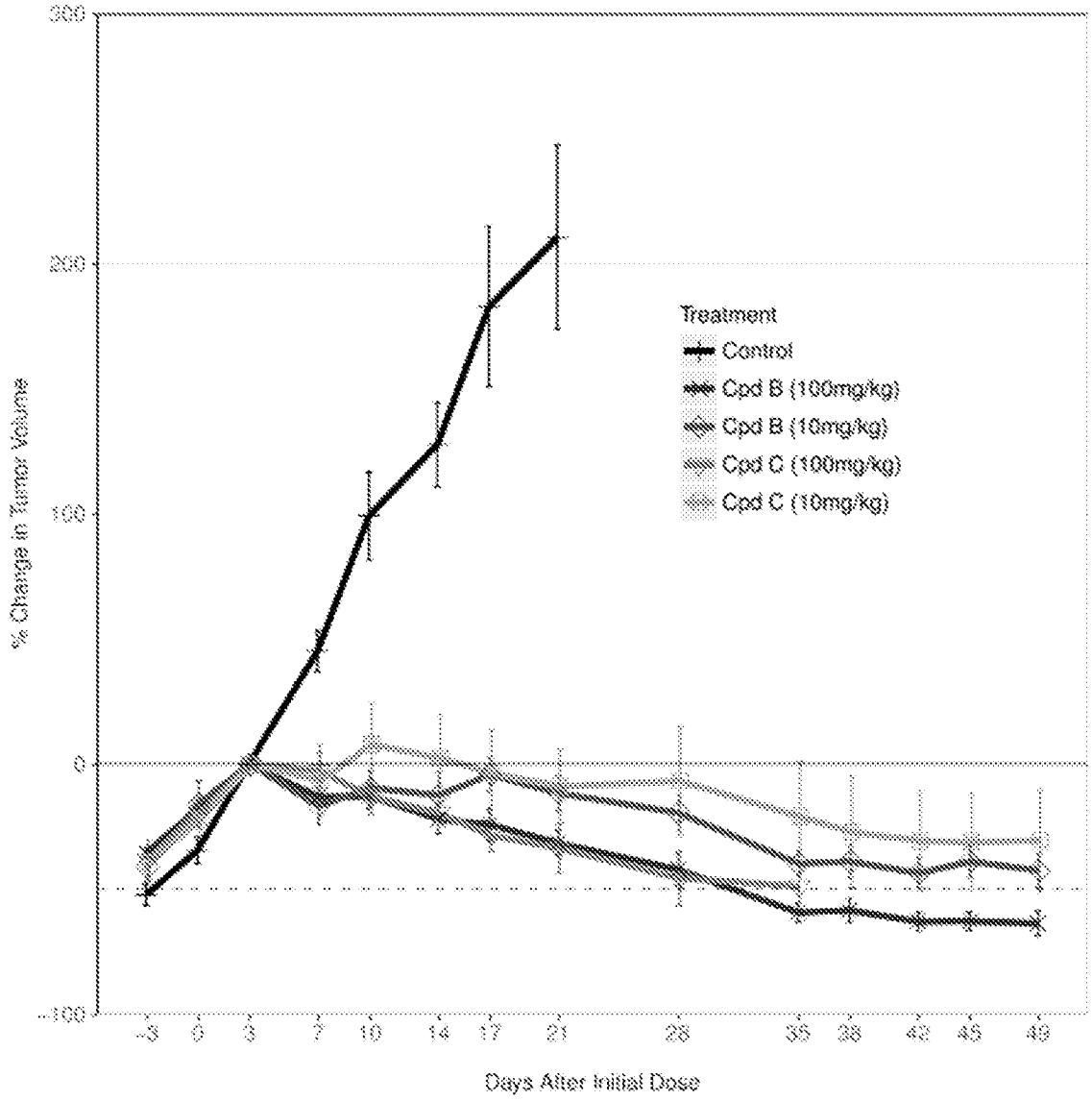

300
200
100
0
-100
% Change in Tumor Volume
Treatment
Control
Cpd B (100mg/kg)
Cpd B (10mg/kg)
Cpd C (100mg/kg)
Cpd C (10mg/kg)
-3
0
3
7
10
14
17
21
28
35
38
42
45
49
Days After Initial Dose

FIG. 5A

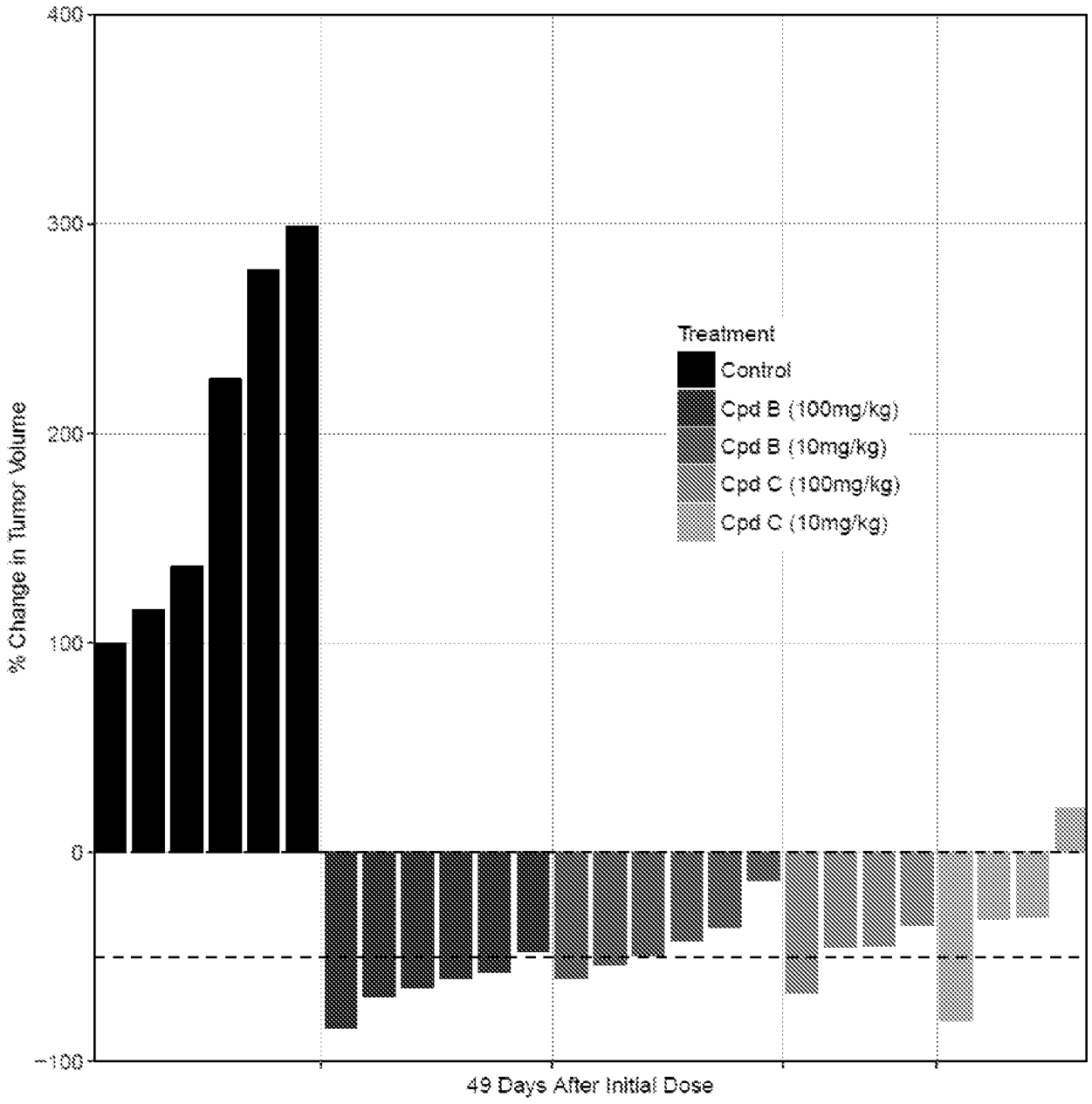

400
300
200
100
0
-100
% Change in Tumor Volume
49 Days After Initial Dose
Treatment
Control
Cpd B (100mg/kg)
Cpd B (10mg/kg)
Cpd C (100mg/kg)
Cpd C (10mg/kg)

FIG. 5B

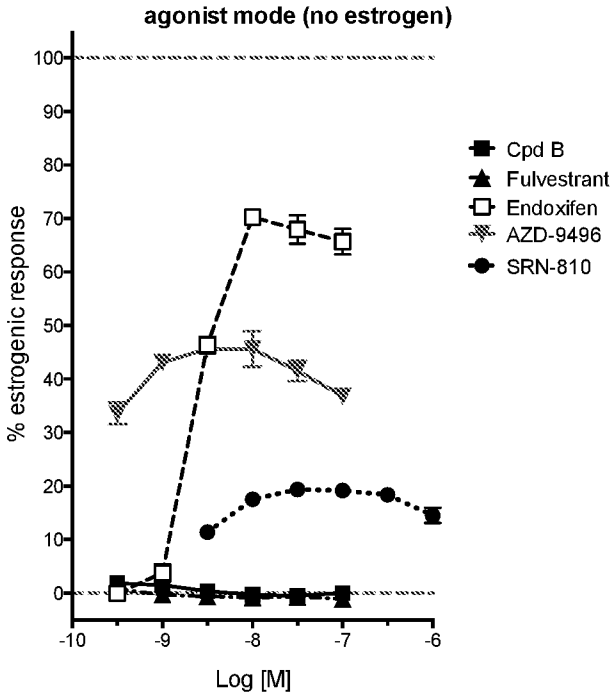

agonist mode (no estrogen)
% estrogenic response
Log [M]
Cpd B
Fulvestrant
Endoxifen
AZD-9496
SRN-810

FIG. 6A

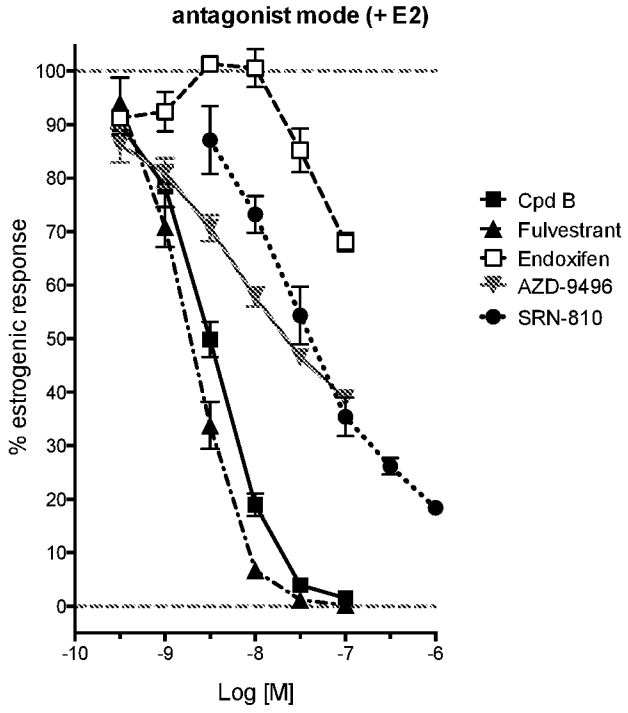
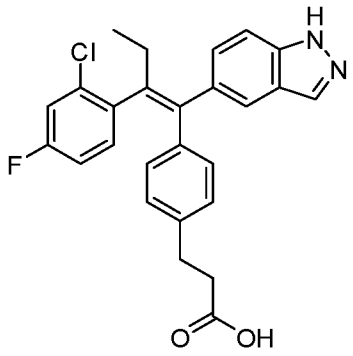
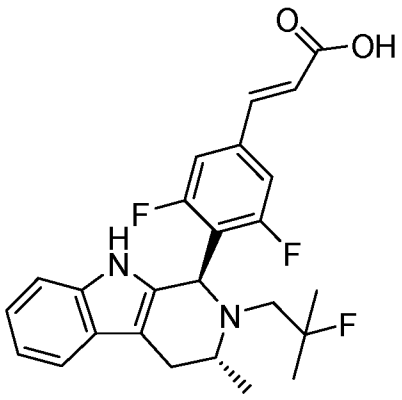

antagonist mode (+ E2)
% estrogenic response
Log [M]
Cpd B
Fulvestrant
Endoxifen
AZD-9496
SRN-810

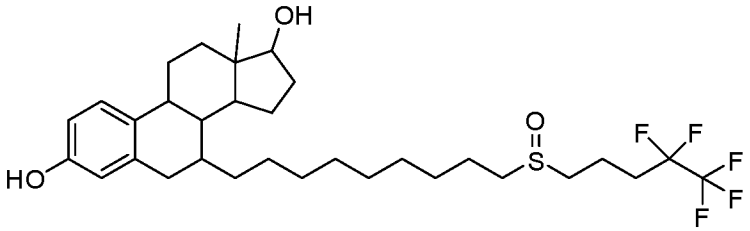
FIG. 6B



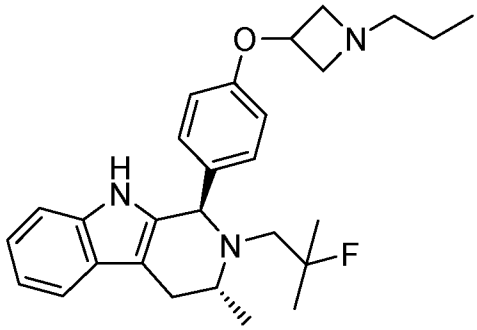
ARN-810



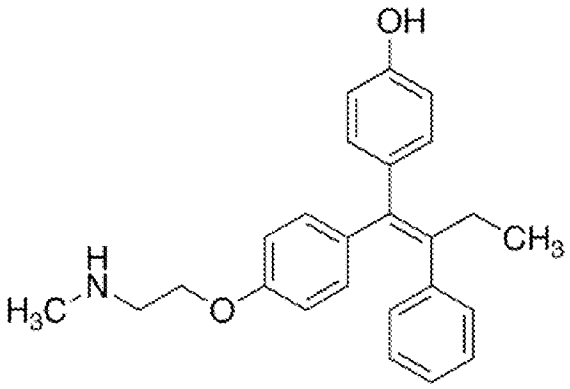
AZ9496



Fulvestrant



Compound **B**



Endoxifen

FIG. 6C

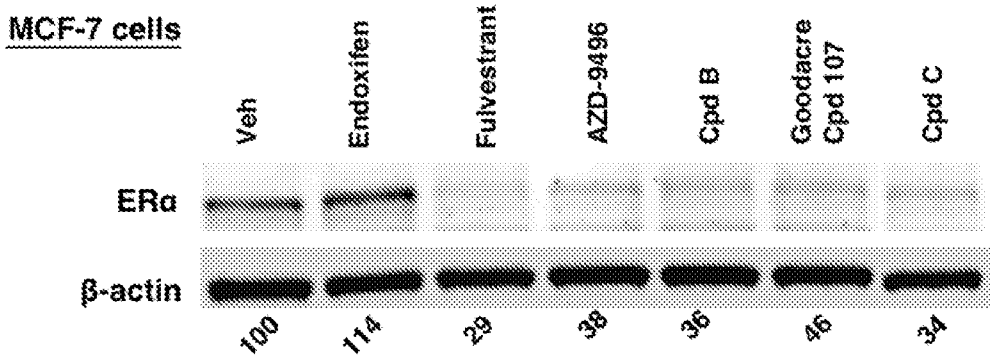

MCF-7 cells
Veh
Endoxifen
Fulvestrant
AZD-9496
Cpd B
Goodacre Cpd 107
Cpd C
ERα
β-actin
100
114
29
38
36
46
34

FIG. 7