FIG. 1

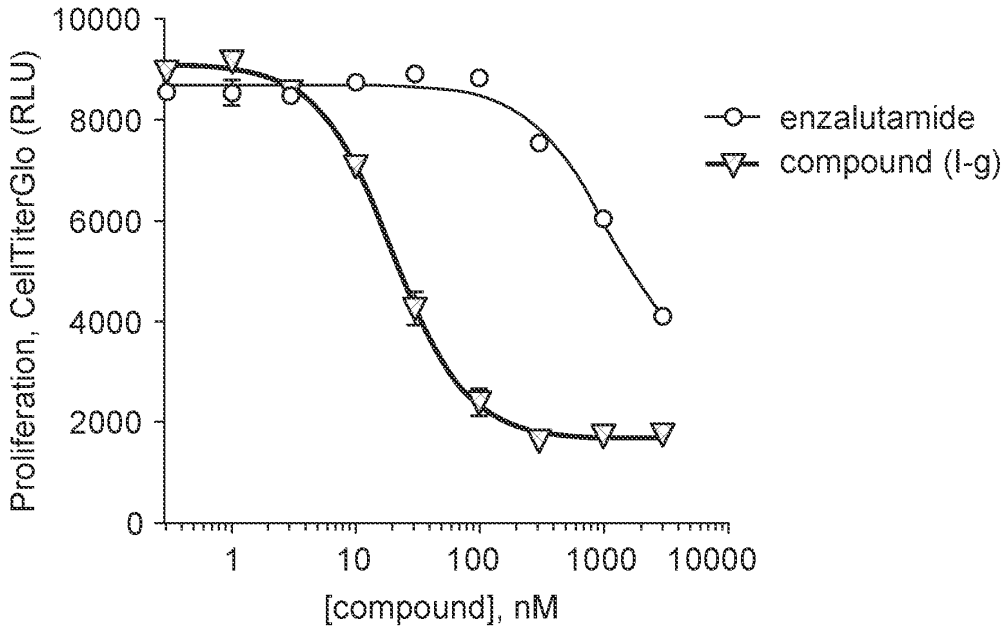

10000
8000
6000
4000
2000
0
Proliferation, CellTiterGlo (RLU)
1
10
100
1000
10000
[compound], nM
enzalutamide
compound (I-g)

FIG. 2

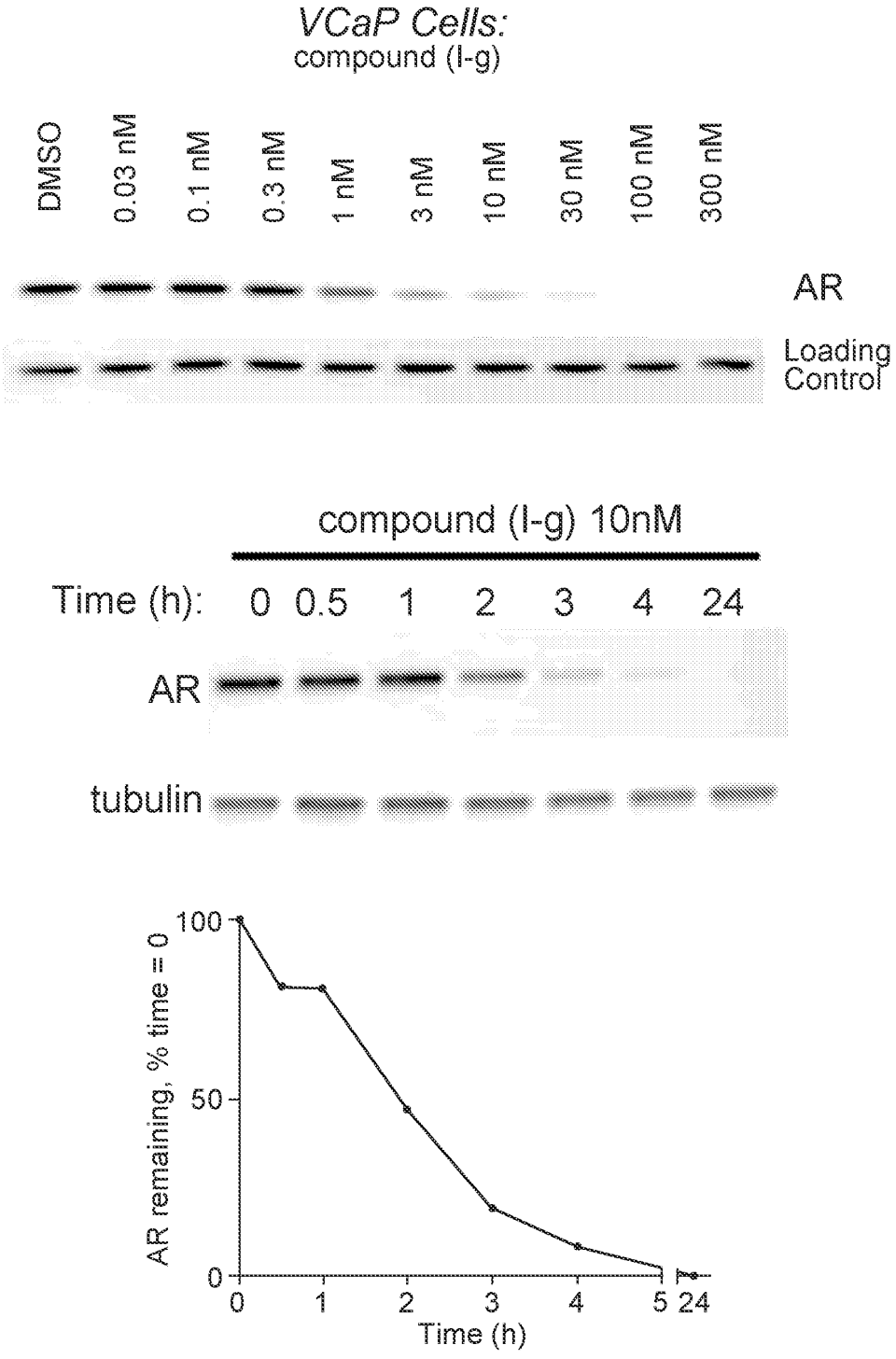

VCaP Cells:
compound (I-g)
DMSO
0.03 nM
0.1 nM
0.3 nM
1 nM
3 nM
10 nM
30 nM
100 nM
300 nM
AR
Loading Control
compound (I-g) 10nM
Time (h): 0 0.5 1 2 3 4 24
AR
tubulin
AR remaining, % time = 0
100
50
0
0 1 2 3 4 5 24
Time (h)

FIG. 3

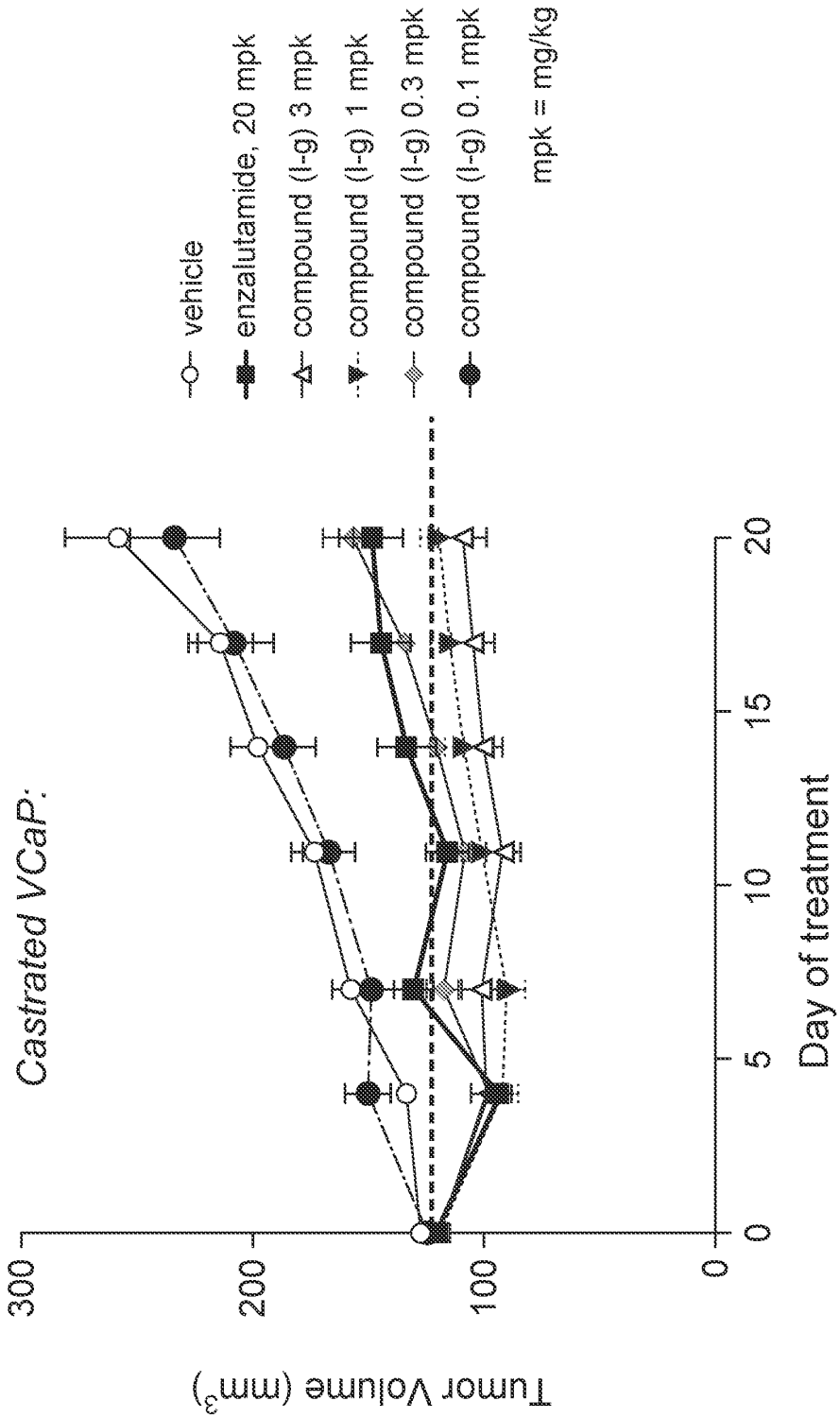

Castrated VCaP:
vehicle
enzalutamide, 20 mpk
compound (I-g) 3 mpk
compound (I-g) 1 mpk
compound (I-g) 0.3 mpk
compound (I-g) 0.1 mpk
mpk = mg/kg
Tumor Volume (mm3)
300
200
100
0
0
5
10
15
20
Day of treatment

FIG. 4

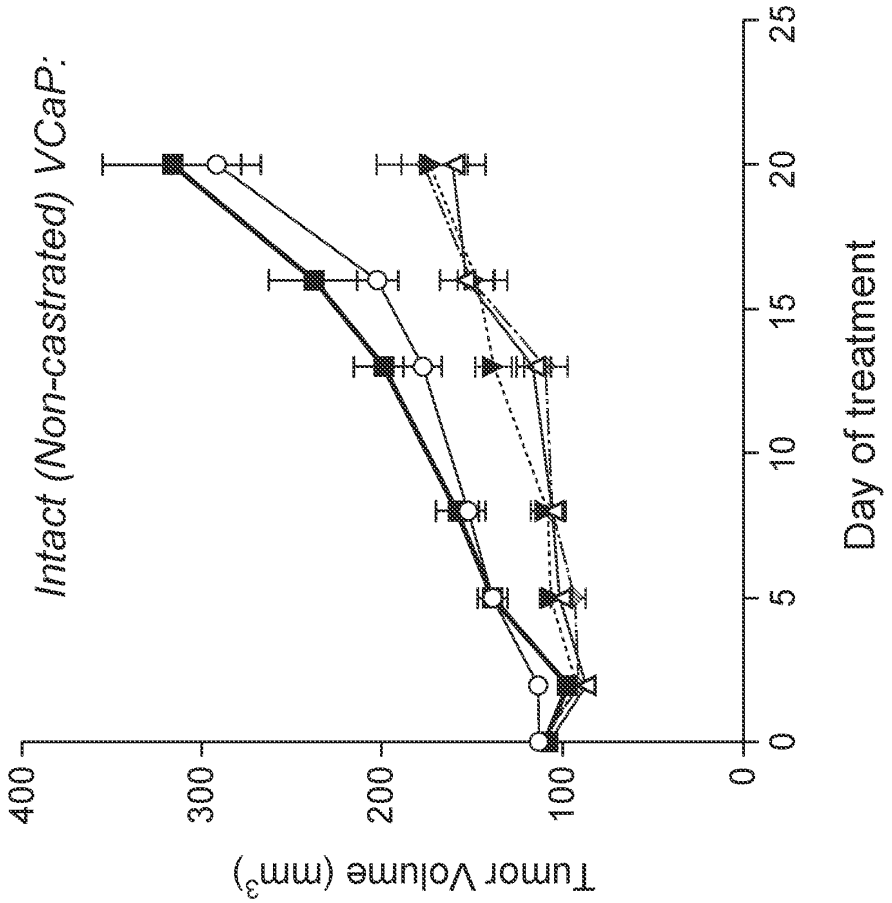

Intact (Non-castrated) VCaP;
vehicle
enzalutamide, 20 mpk
compound (I-g) 10 mpk
compound (I-g) 3 mpk
compound (I-g) 1 mpk
Tumor Volume (mm3)
400
300
200
100
0
0
5
10
15
20
25
Day of treatment

FIG. 5

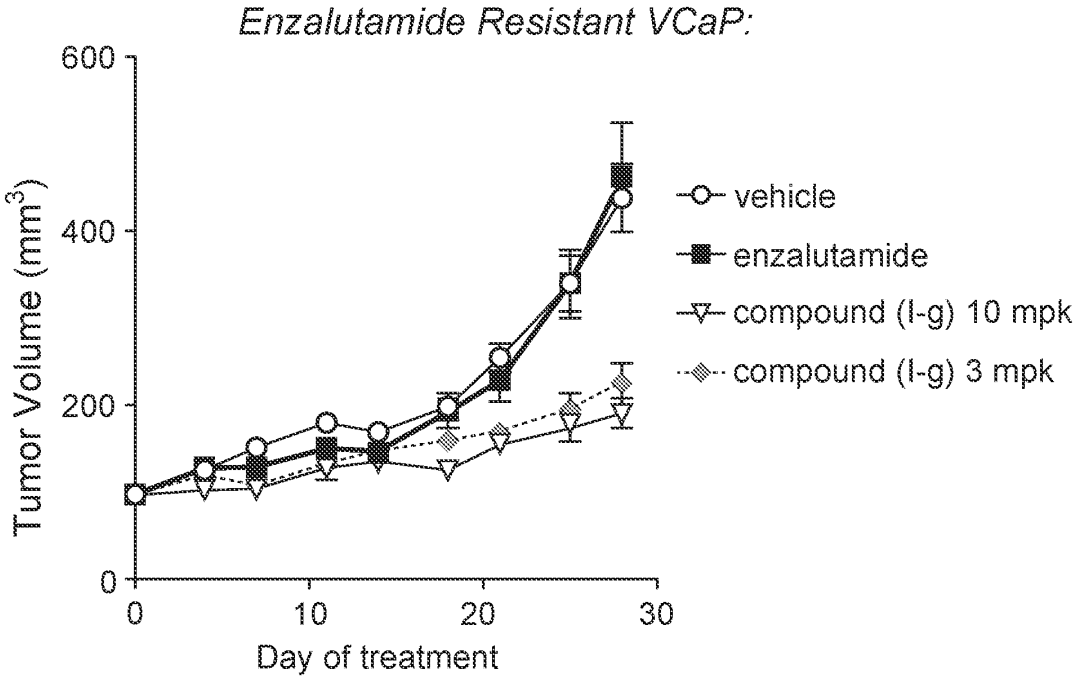

Enzalutamide Resistant VCaP:
600
400
200
0
Tumor Volume (mm3)
0
10
20
30
Day of treatment
vehicle
enzalutamide
compound (I-g) 10 mpk
compound (I-g) 3 mpk

FIG. 6

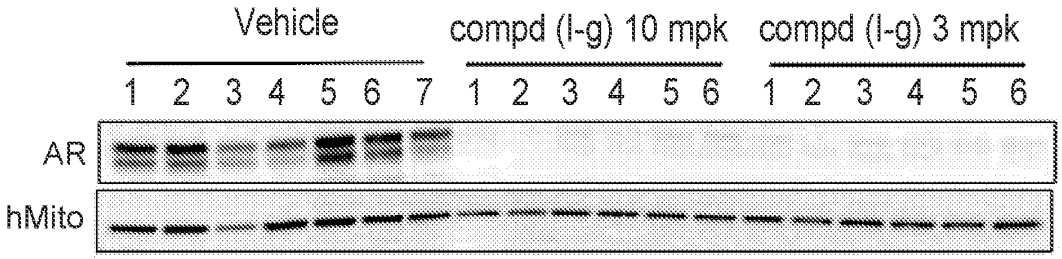

Vehicle
compd (I-g) 10 mpk
compd (I-g) 3 mpk
1 2 3 4 5 6 7 1 2 3 4 5 6 1 2 3 4 5 6
AR
hMito

FIG. 7

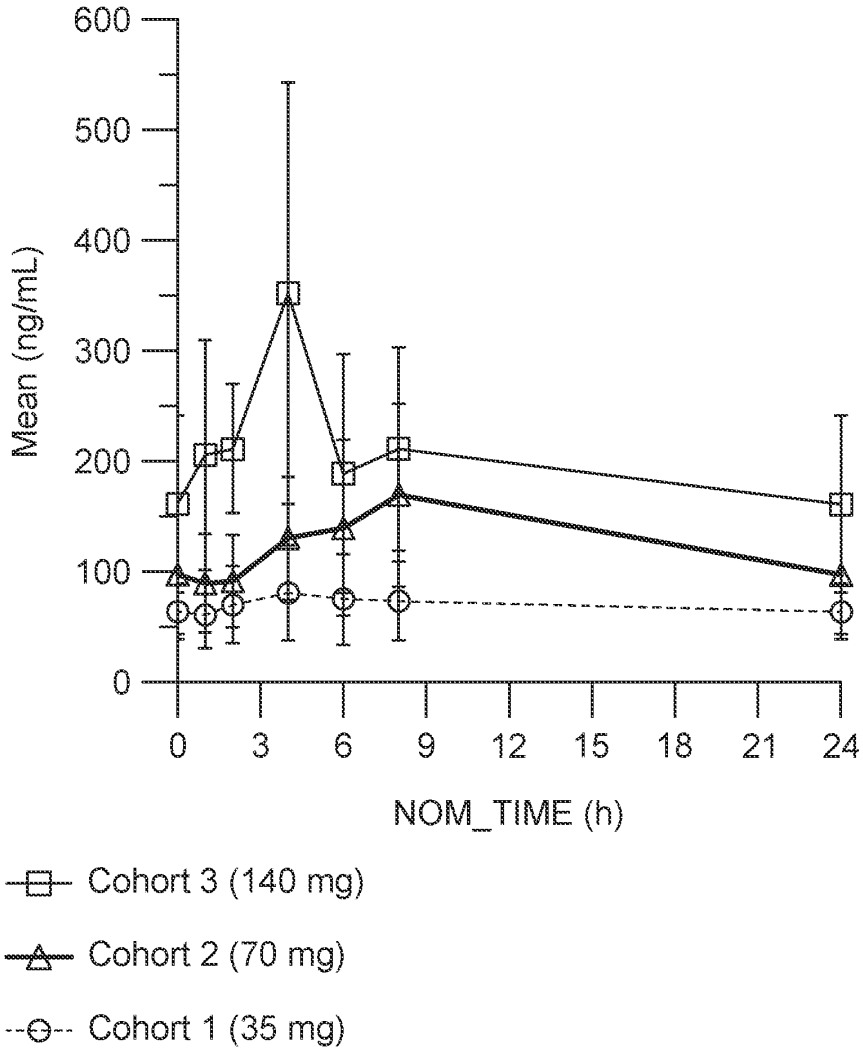
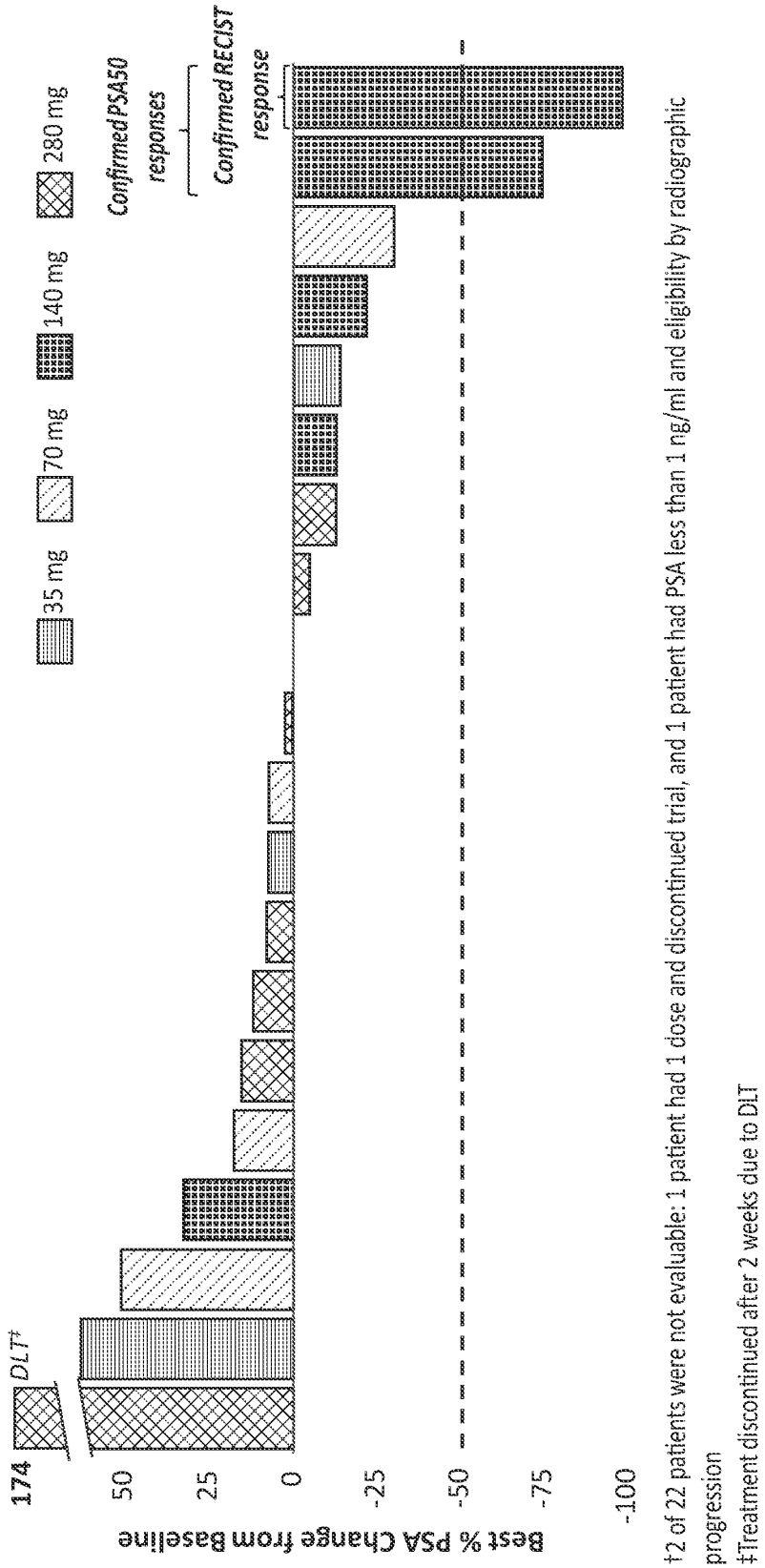

600
500
400
300
200
100
0
Mean (ng/mL)
0
3
6
9
12
15
18
21
24
NOM_TIME (h)
Cohort 3 (140 mg)
Cohort 2 (70 mg)
Cohort 1 (35 mg)

FIG. 8




†2 of 22 patients were not evaluable: 1 patient had 1 dose and discontinued trial, and 1 patient had PSA less than 1 ng/ml and eligibility by radiographic progression
‡Treatment discontinued after 2 weeks due to DLT

FIG. 9

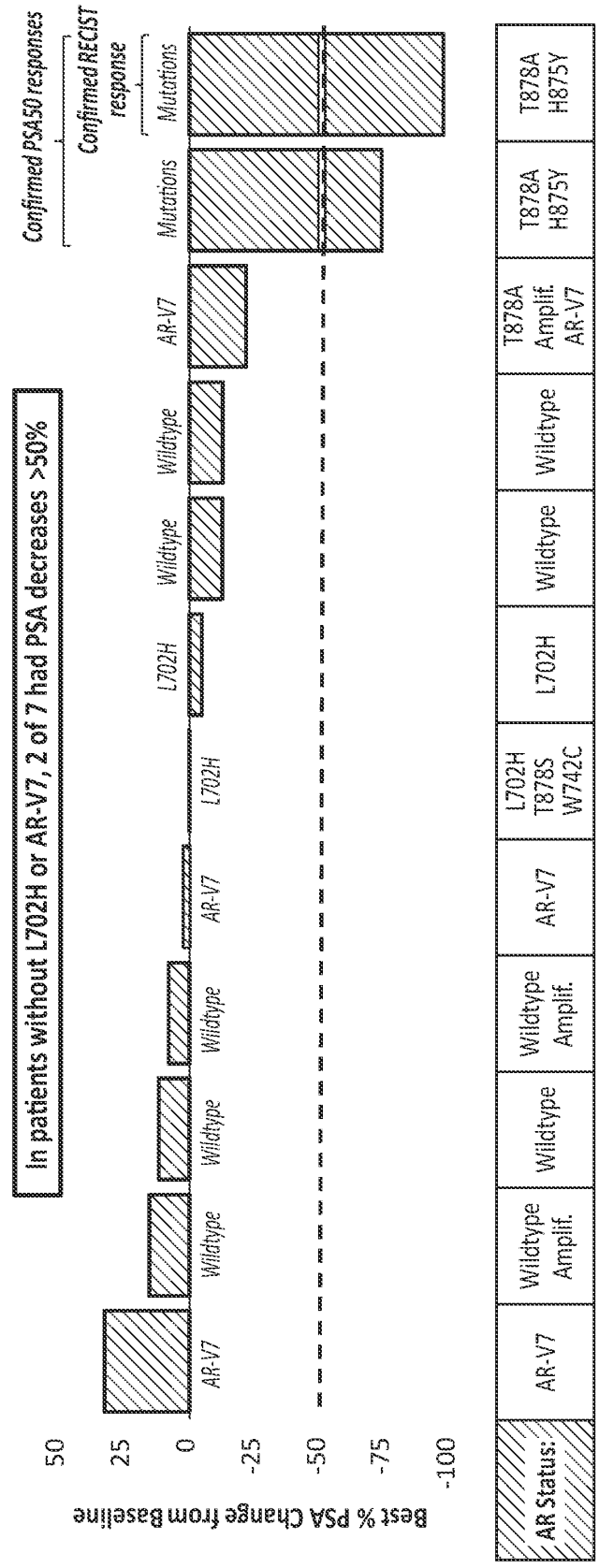

In patients without L702H or AR-V7, 2 of 7 had PSA decreases >50%
Confirmed PSA50 responses
Confirmed RECIST response
Mutations
Mutations
Best % PSA Change from Baseline
50
25
0
-25
-50
-75
-100
AR-V7
Wildtype
Wildtype
Wildtype
Wildtype
AR-V7
L702H
L702H
Wildtype
Wildtype
AR-V7
AR Status:
AR-V7
Wildtype Amplif.
Wildtype
Wildtype Amplif.
AR-V7
L702H T878S W742C
L702H
Wildtype
Wildtype
T878A Amplif. AR-V7
T878A H875Y
T878A H875Y

FIG. 10

Confirmed PSA Responder; Non-Evaluable by RECIST

Patient history:

- 69 y.o. male
- Diagnosed 2006 with non-metastatic prostate cancer (nmHSPC)
- Blastic bone metastases including the sternum, left first rib, T3, T10 vertebral bodies
- No measurable disease to evaluate

Prior therapy included:

- Bicalutamide (HSPC)
- Docetaxel (HSPC)
- Abiraterone
- Radium
- Enzalutamide

Biomarker status:

- AR H875Y and T878A mutations (associated with resistance to abiraterone and enzalutamide)

Response:

- PSA 74% reduction
- No radiographic progression
- Duration of Compound (I-g) – 30 weeks and ongoing

FIG. 11A

**Confirmed RECIST Partial Response in a Patient with a PCWG3 PSA Response**

**Patient history:**

- 72 y.o. male
- Diagnosed 2010 with metastatic prostate cancer (mHSPC)
- Metastatic sites: adrenal gland, aortocaval nodes, bone-spine, pelvis

**Prior therapy:**

- Bicalutamide
- Enzalutamide
- Provenge
- Abiraterone
- Cabazitaxel

**Biomarker status:**

- AR H875Y and T878A mutations (associated with resistance to abiraterone and enzalutamide)

**Response:**

- PSA reduction 97%
- Duration of Compound (I-g) 18 weeks and ongoing

FIG. 11B




BASELINE CT SCAN

FIG. 11C




AFTER 4 CYCLES

FIG. 12

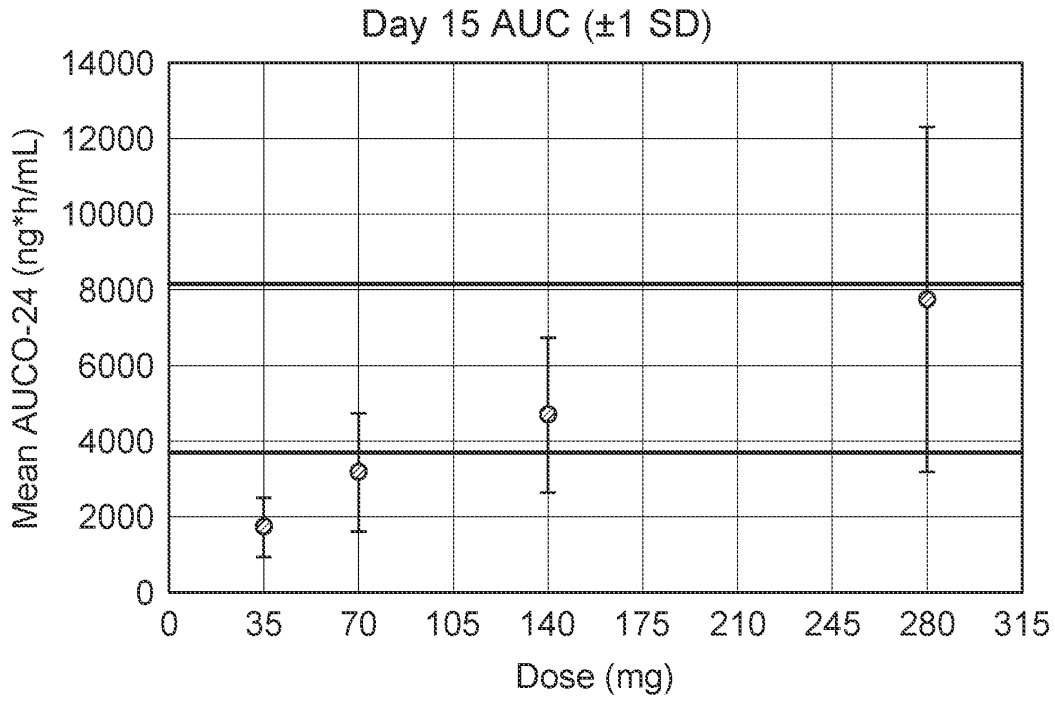

Day 15 AUC (±1 SD)
Mean AUCO-24 (ng*h/mL)
14000
12000
10000
8000
6000
4000
2000
0
0
35
70
105
140
175
210
245
280
315
Dose (mg)

FIG. 13

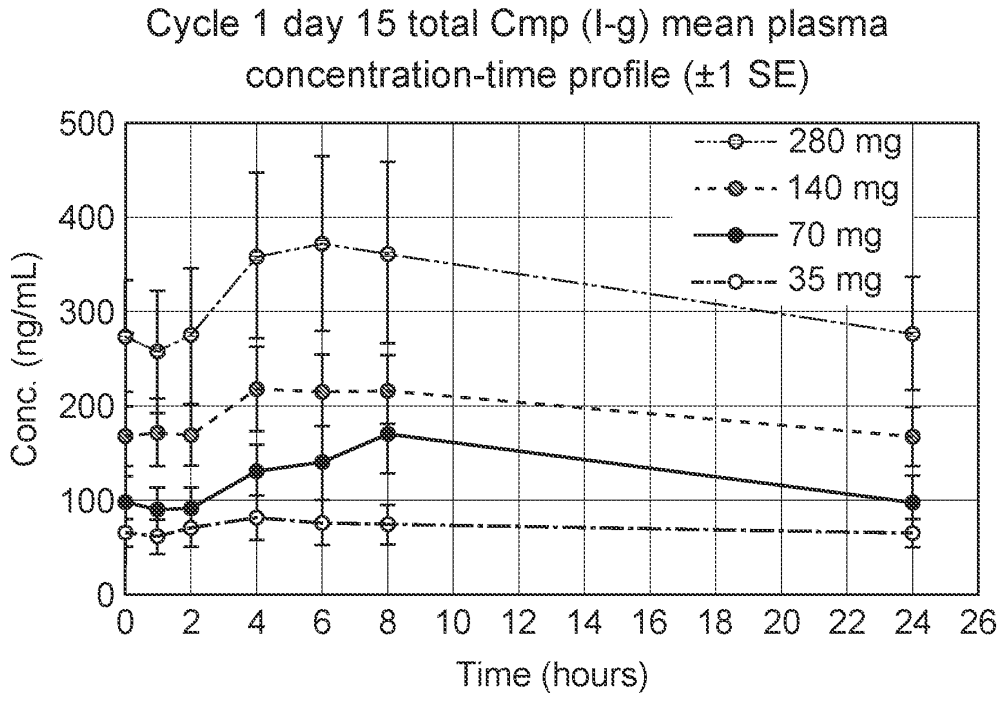

Cycle 1 day 15 total Cmp (I-g) mean plasma concentration-time profile (±1 SE)
Conc. (ng/mL)
500
400
300
200
100
0
0
2
4
6
8
10
12
14
16
18
20
22
24
26
Time (hours)
280 mg
140 mg
70 mg
35 mg

FIG. 14

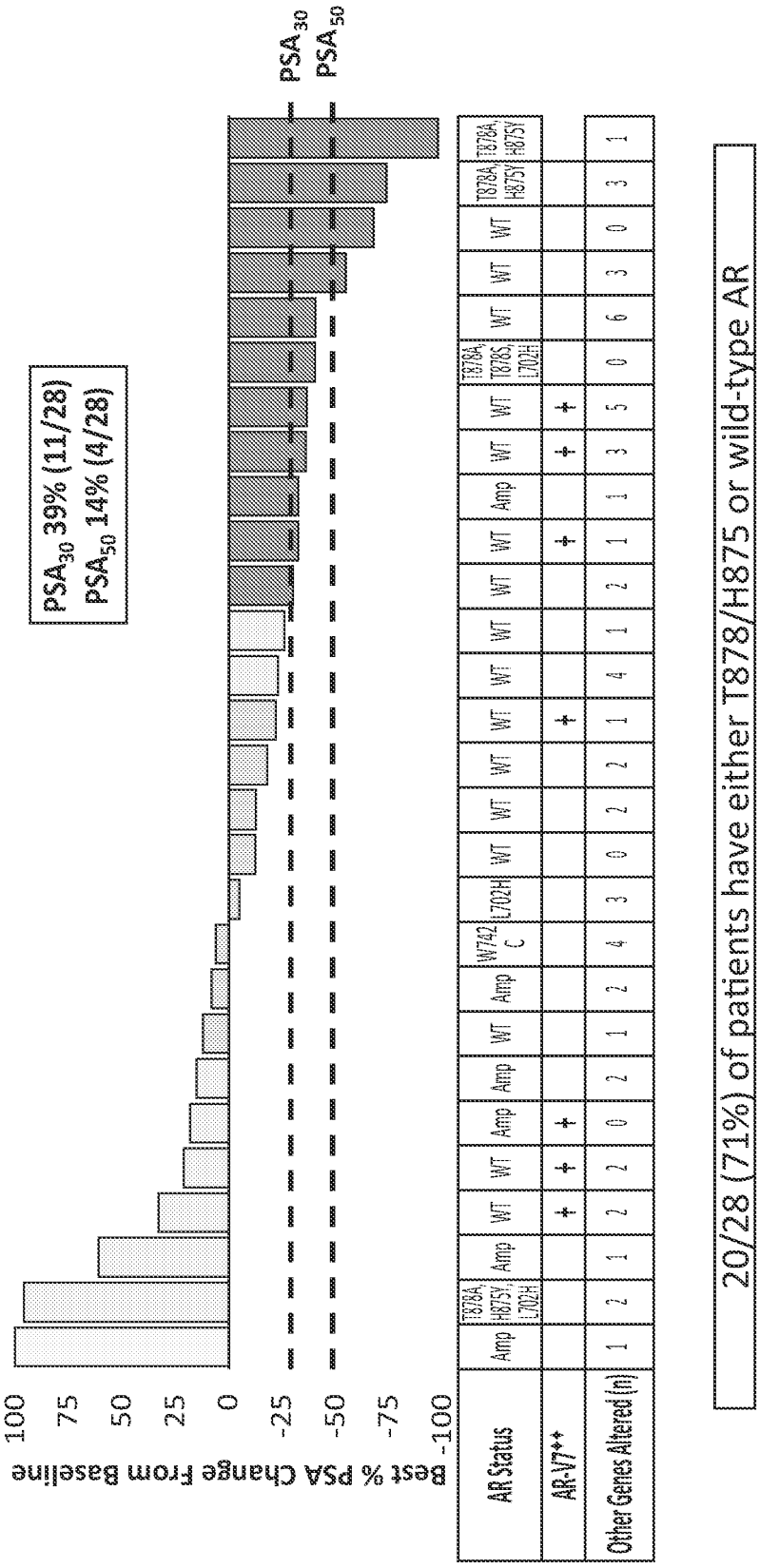
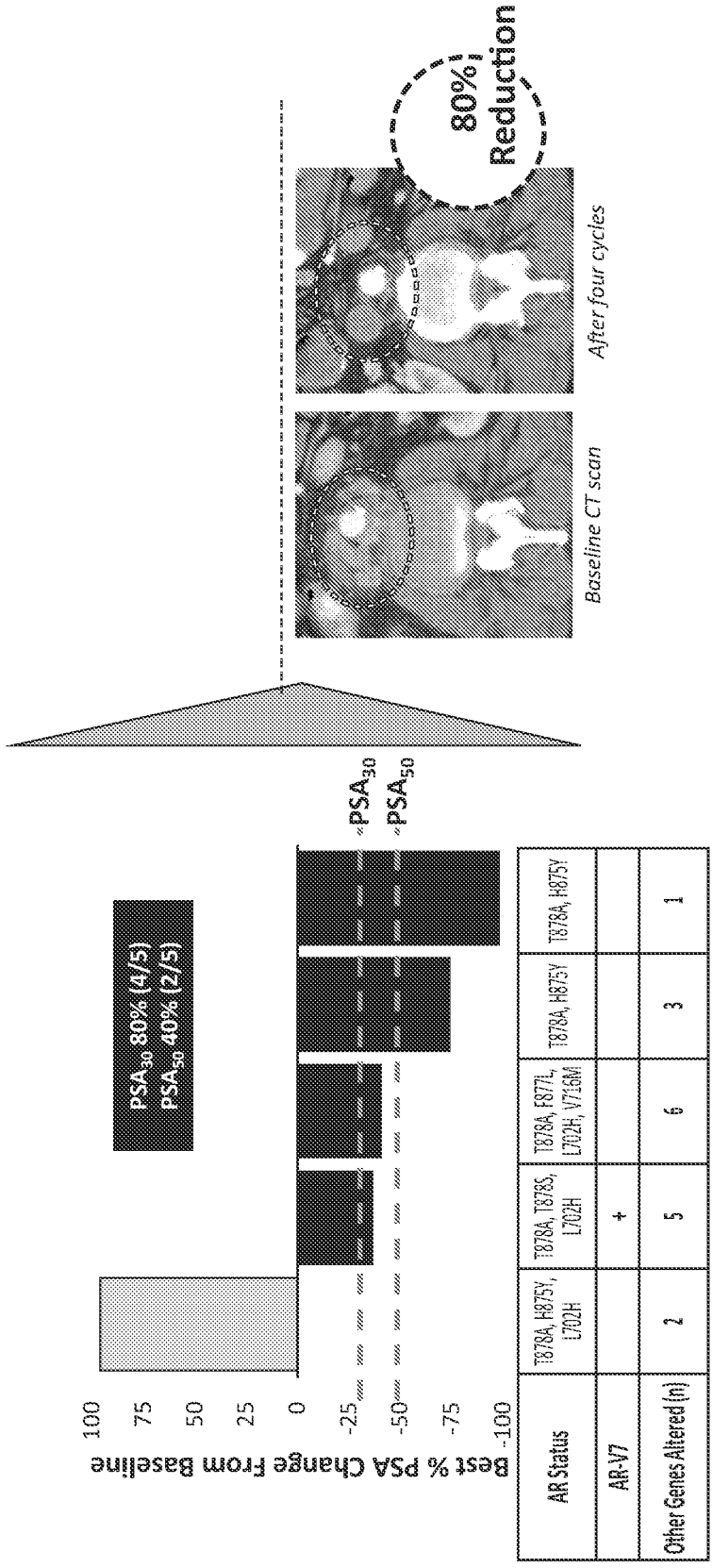

PSA30
PSA50
PSA30 39% (11/28)
PSA50 14% (4/28)
Best % PSA Change from Baseline
100
75
50
25
0
-25
-50
-75
-100
AR Status
AR-V7++
Other Genes Altered (n)
Amp
T878A, H875Y, L702H
Amp
WT
WT
Amp
Amp
WT
Amp
W742C
L702H
WT
WT
WT
WT
WT
WT
WT
WT
Amp
WT
T878A, T878S, L702H
WT
WT
T878A, H875Y
T878A, H875Y
20/28 (71%) of patients have either T878/H875 or wild-type AR

FIG. 15


80% Reduction
Baseline CT scan
After four cycles
PSA30
PSA50
PSA30 80% (4/5)
PSA50 40% (2/5)
Best % PSA Change From Baseline
100
75
50
25
0
-25
-50
-75
-100
AR Status
AR-V7
Other Genes Altered (n)
T878A, H875Y, L702H
T878A, T878S, L702H
T878A, F877L, L702H, V716M
T878A, H875Y
T878A, H875Y
+
2
5
6
3
1