FIG. 1

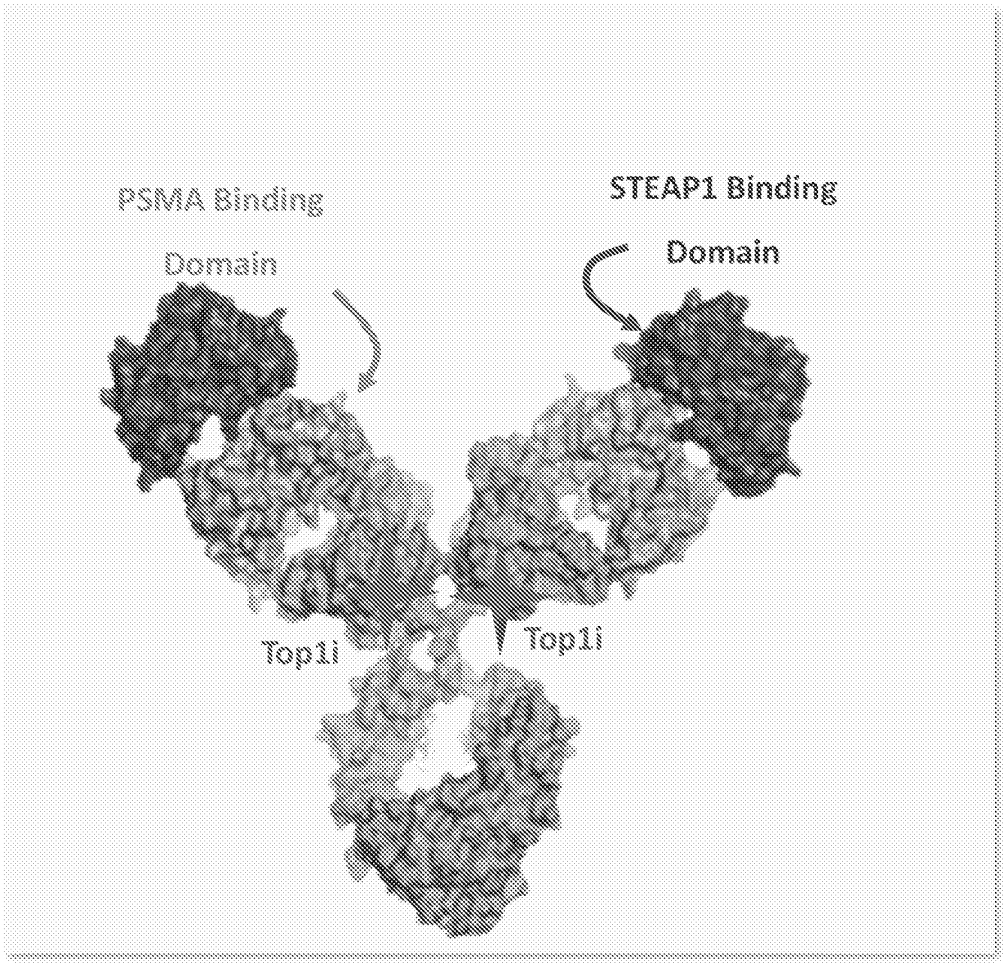


FIG. 2A

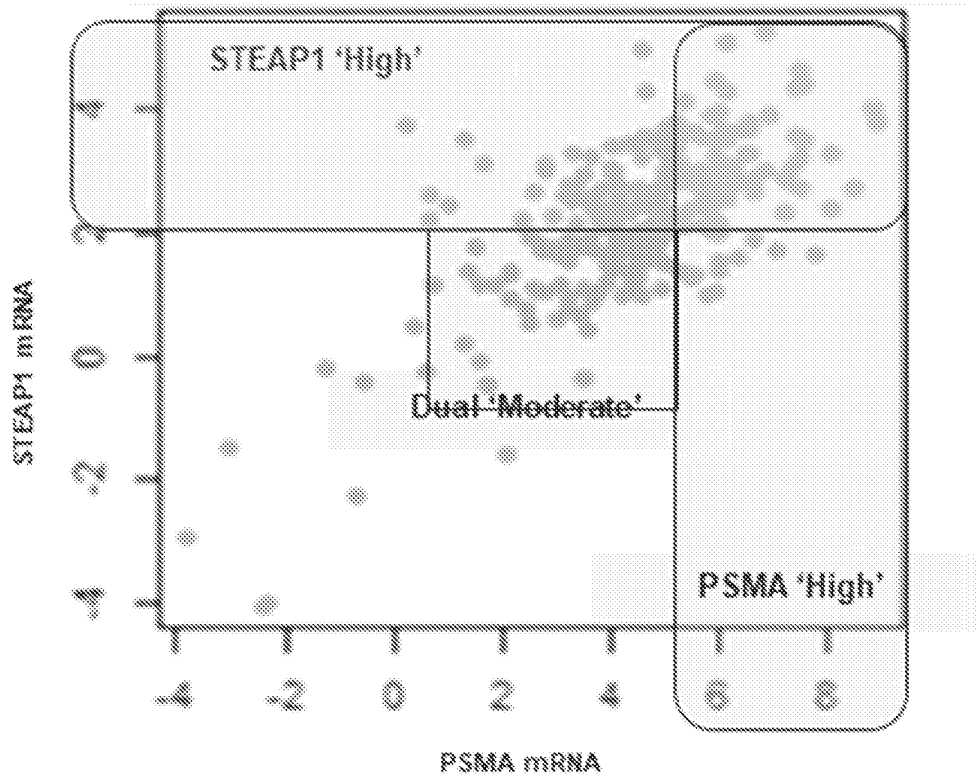
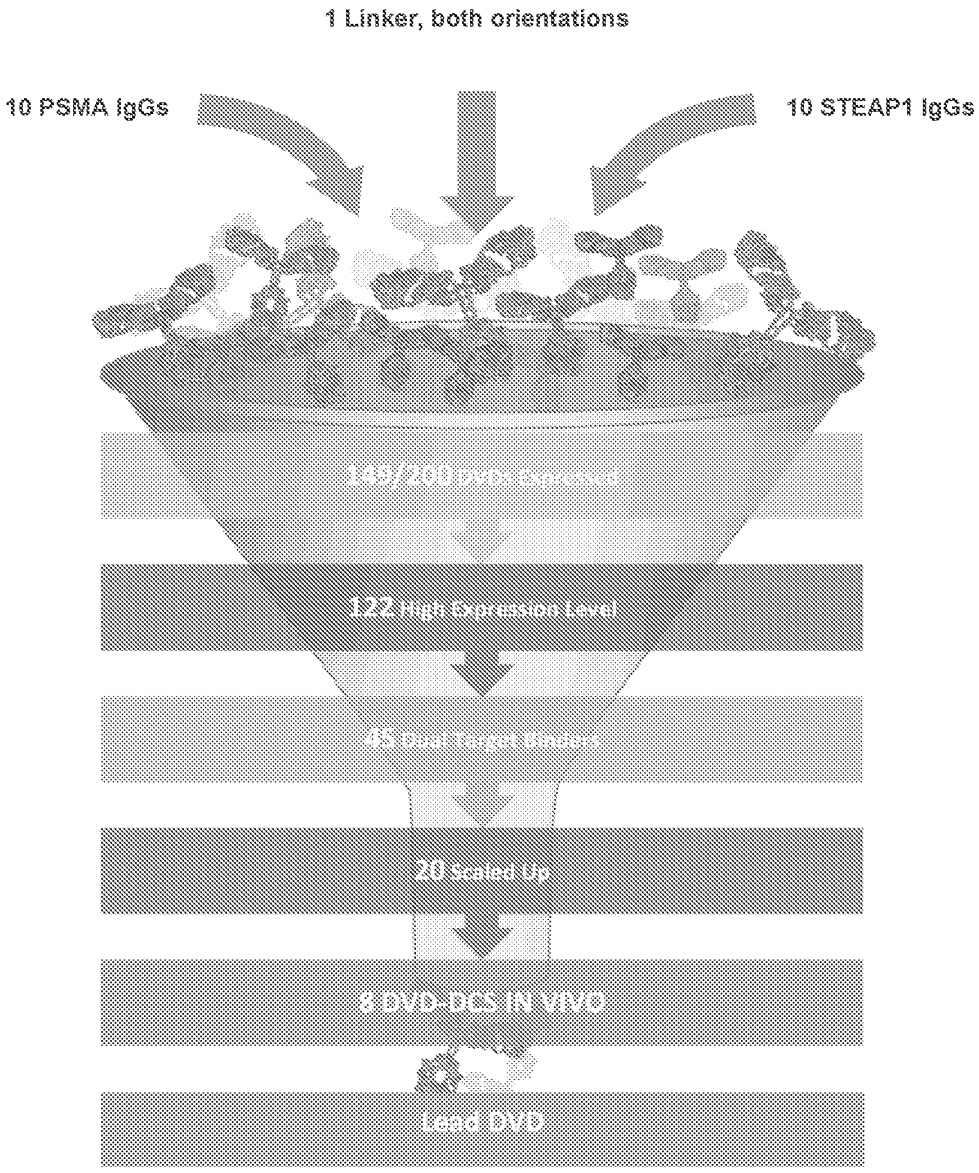

STEAP1 'High'
Dual 'Moderate'
PSMA 'High'
STEAP1 mRNA
PSMA mRNA
4
2
0
-2
-4
-4
-2
0
2
4
6
8

FIG. 2B


1 Linker, both orientations
10 PSMA IgGs
10 STEAP1 IgGs
149/200 pairs Expressed
122 High Expression Level
45 Dual Target Binders
20 Scaled Up
8 DVD-DCS IN VIVO
Lead DVD

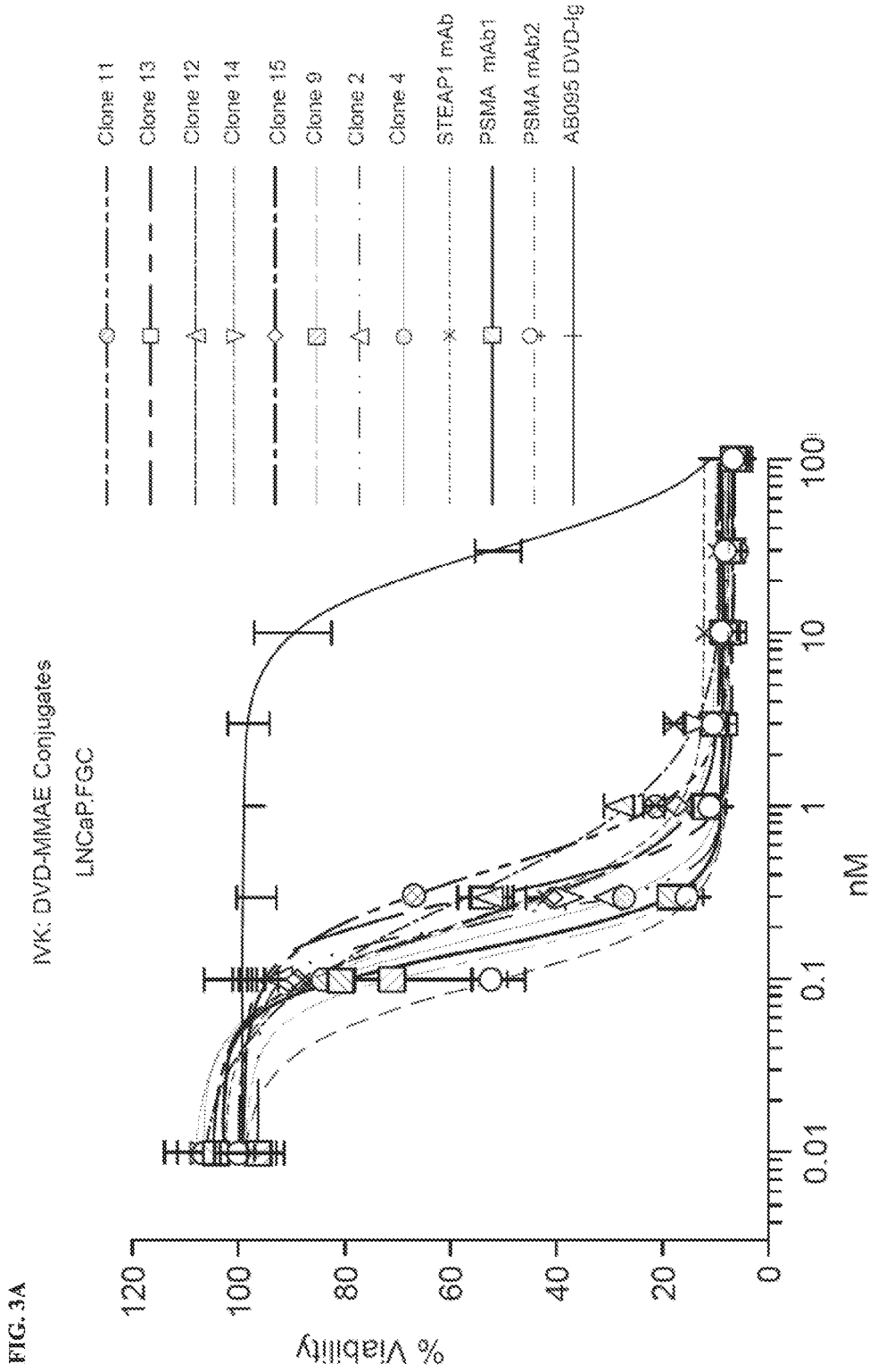

IVK: DVD-MMAE Conjugates
LNCaP.FGC
Clone 11
Clone 13
Clone 12
Clone 14
Clone 15
Clone 9
Clone 2
Clone 4
STEAP1 mAb
PSMA mAb1
PSMA mAb2
AB095 DVD-Ig
% Viability
120
100
80
60
40
20
0
0.01
0.1
1
10
100
nM

FIG. 3A

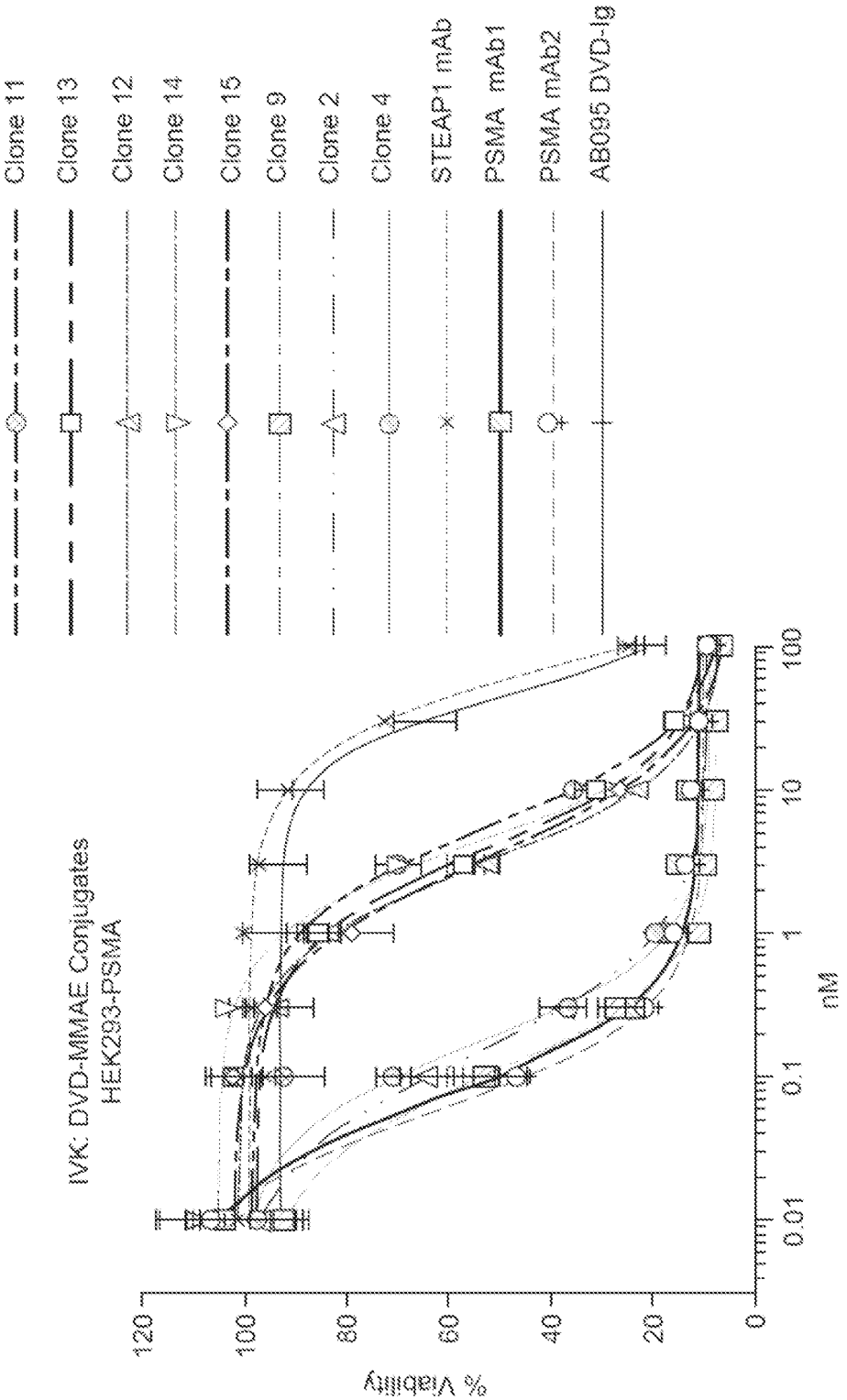

Clone 11
Clone 13
Clone 12
Clone 14
Clone 15
Clone 9
Clone 2
Clone 4
STEAP1 mAb
PSMA mAb1
PSMA mAb2
AB095 DVD-Ig
IVK: DVD-MMAE Conjugates
HEK293-PSMA
% Viability
120
100
80
60
40
20
0
0.01
0.1
1
10
100
nM

FIG. 3B

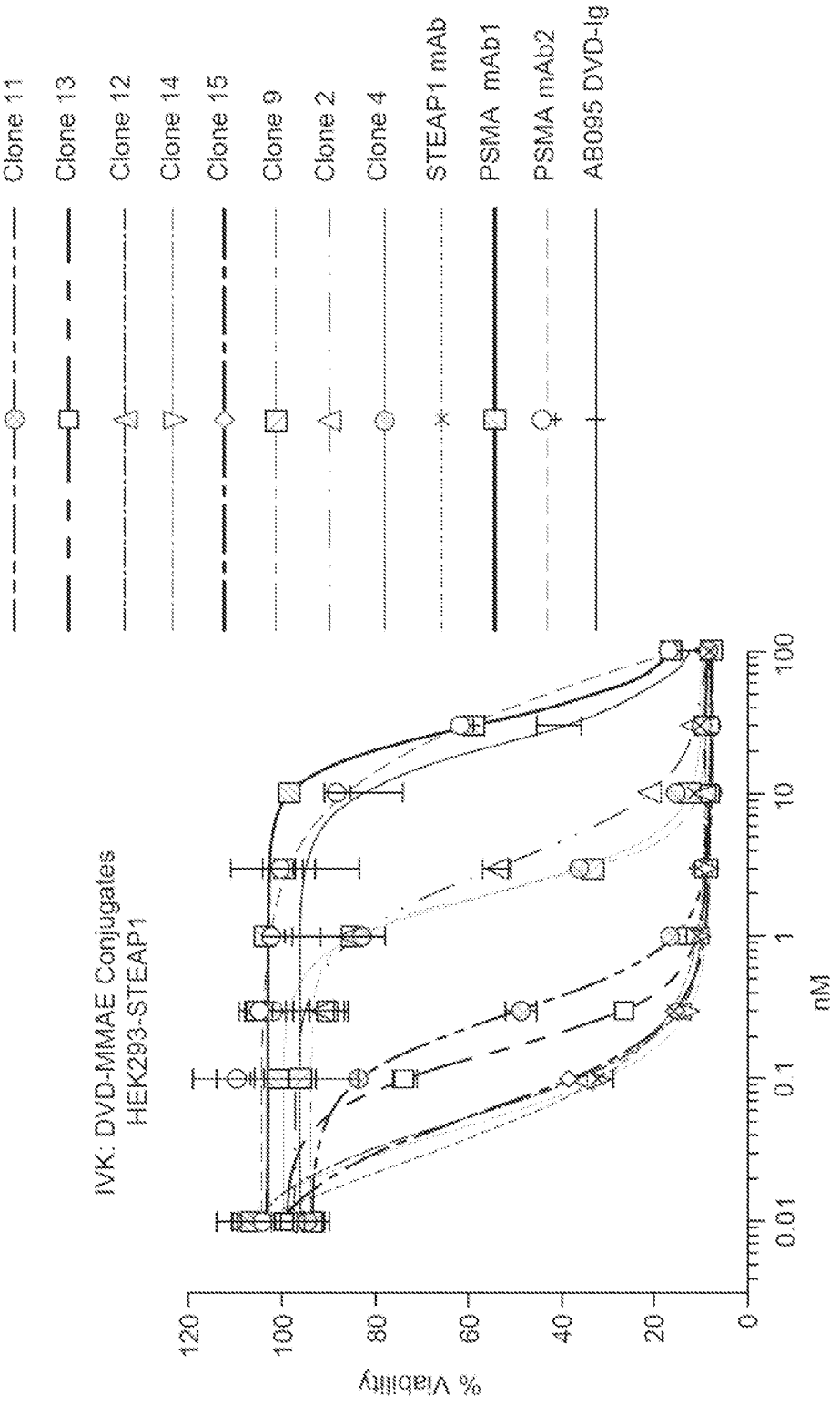

Clone 11
Clone 13
Clone 12
Clone 14
Clone 15
Clone 9
Clone 2
Clone 4
STEAP1 mAb
PSMA mAb1
PSMA mAb2
AB095 DVD-Ig
IVK: DVD-MMAE Conjugates
HEK293-STEAP1
% Viability
120
100
80
60
40
20
0
0.01
0.1
1
10
100
nM

FIG. 3C

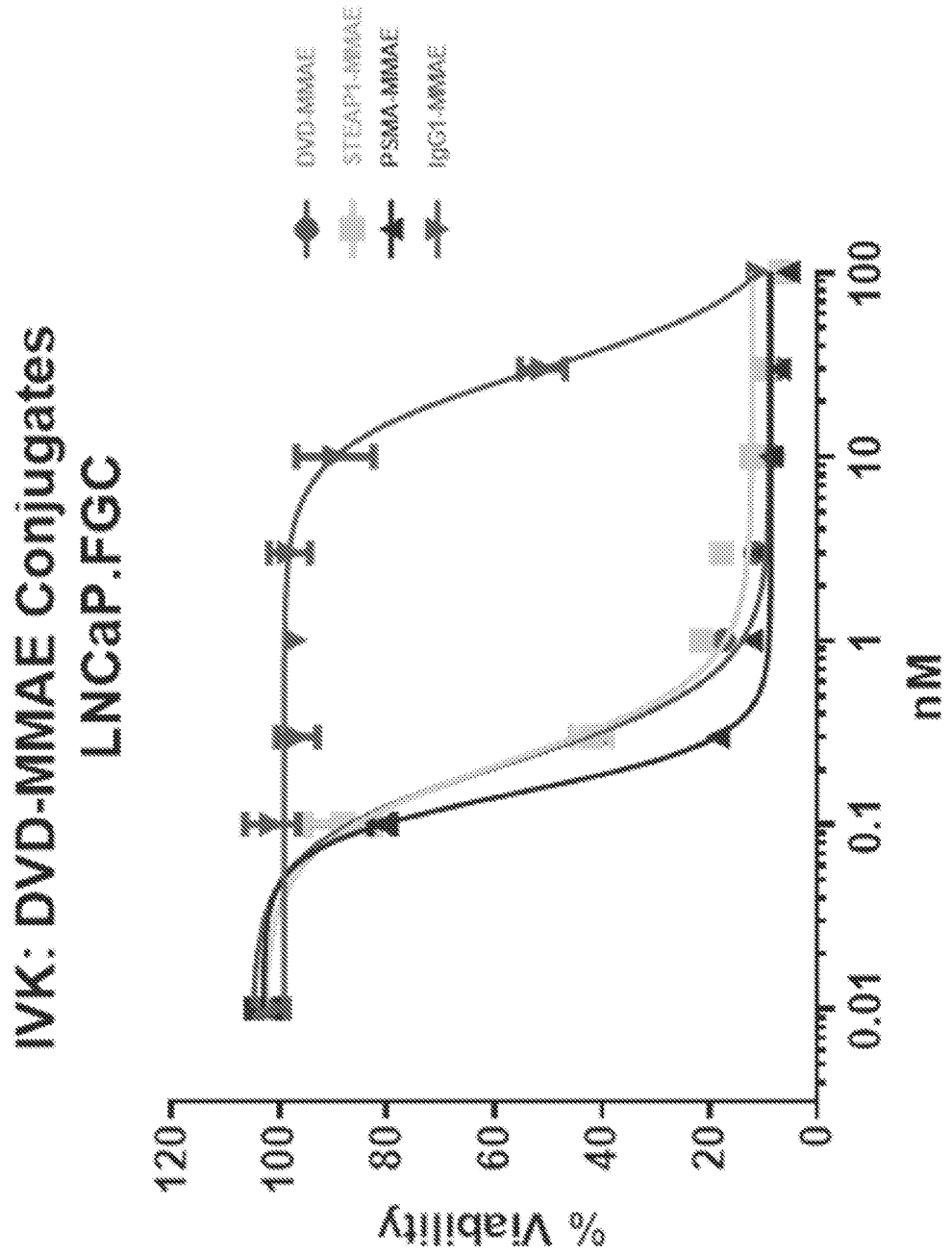

IVK: DVD-MMAE Conjugates
LNCaP.FGC
DVD-MMAE
STEAP1-MMAE
PSMA-MMAE
IgG1-MMAE
% Viability
120
100
80
60
40
20
0
0.01
0.1
1
10
100
nM

FIG. 3D

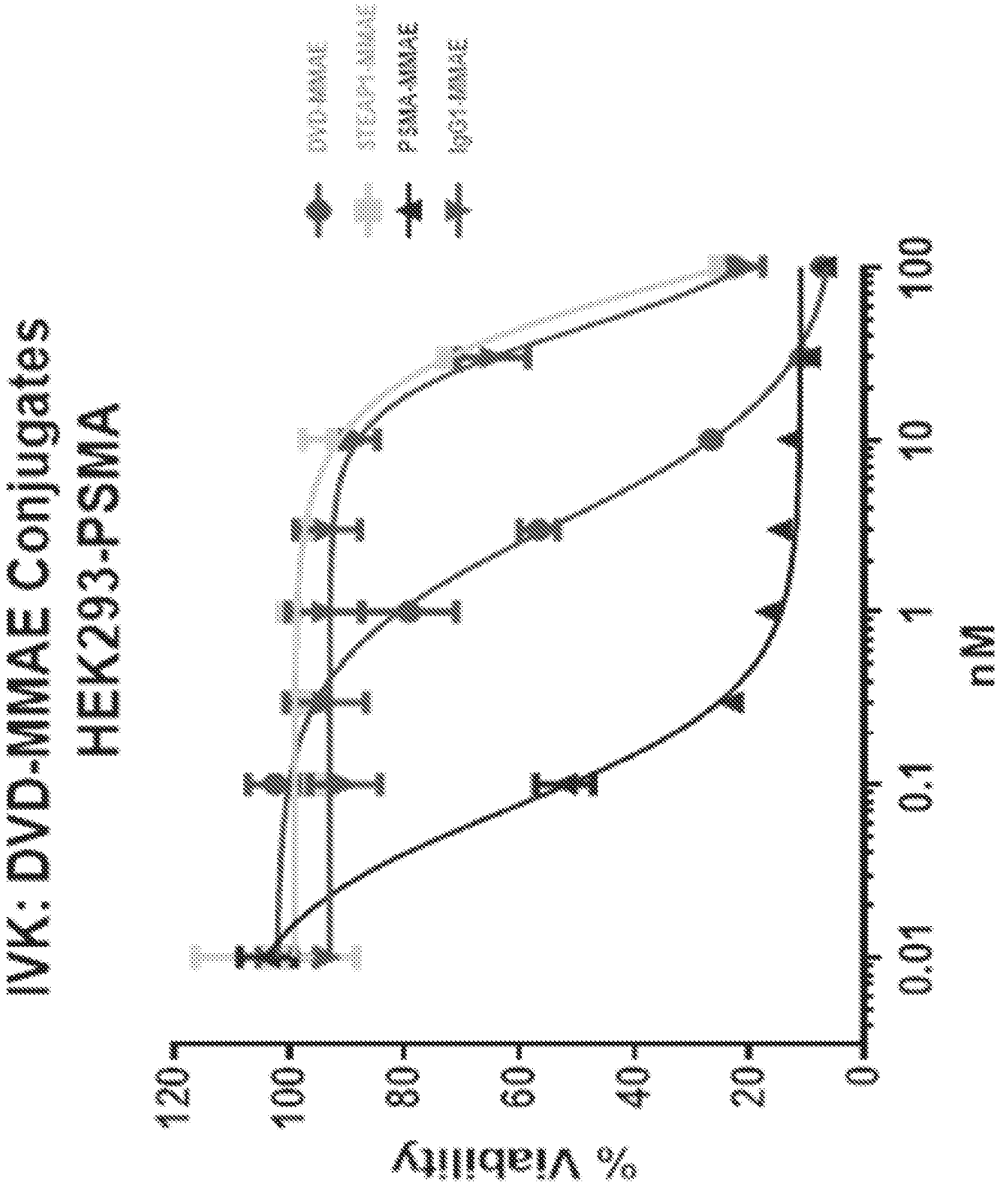

IVK: DVD-MMAE Conjugates
HEK293-PSMA
DVD-MMAE
STEAP1-MMAE
PSMA-MMAE
IgG1-MMAE
% Viability
120
100
80
60
40
20
0
0.01
0.1
1
10
100
nM

FIG. 3E

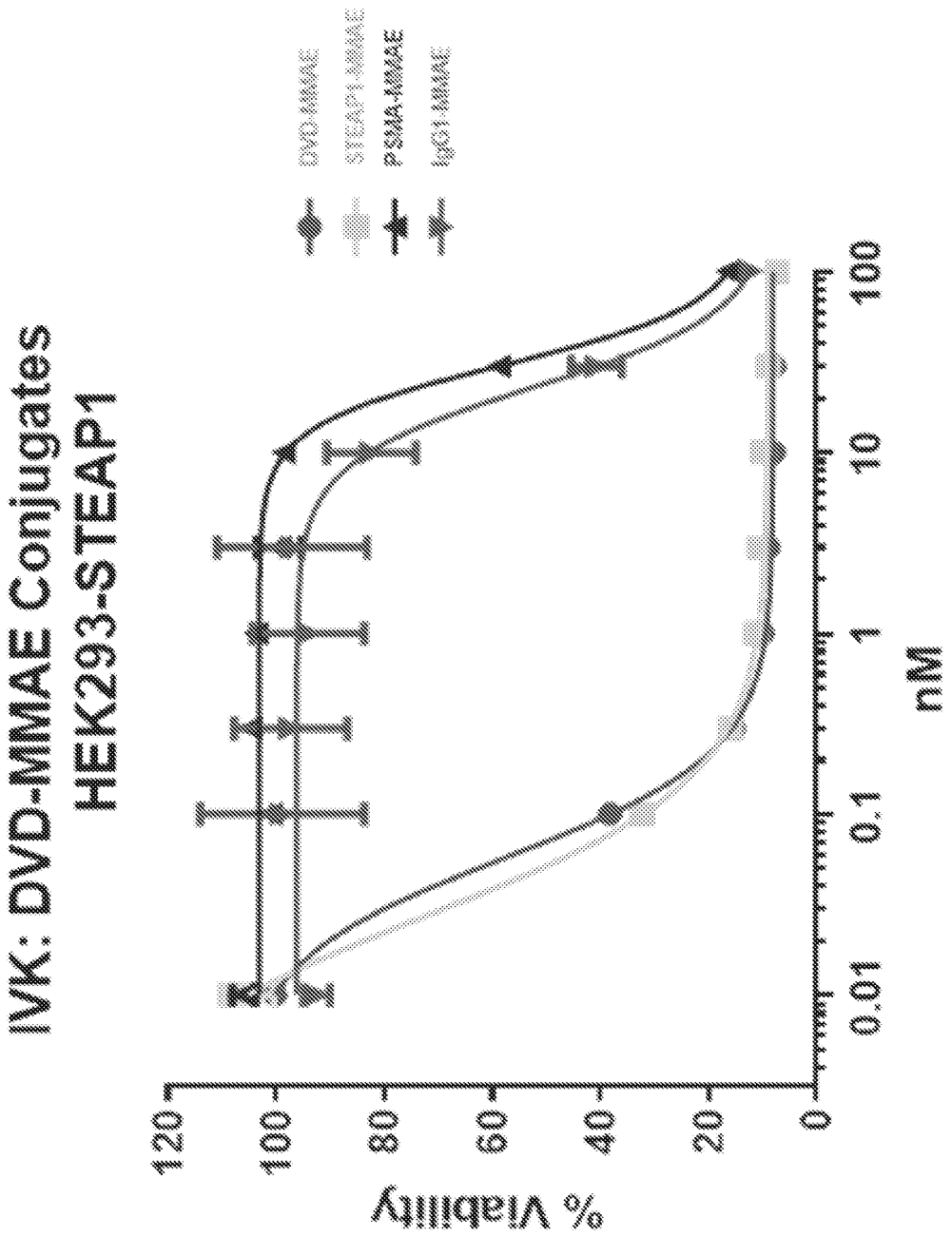

IVK: DVD-MMAE Conjugates
HEK293-STEAP1
DVD-MMAE
STEAP1-MMAE
P-SMA-MMAE
IgG1-MMAE
% Viability
120
100
80
60
40
20
0
0.01
0.1
1
10
100
nM

FIG. 3F

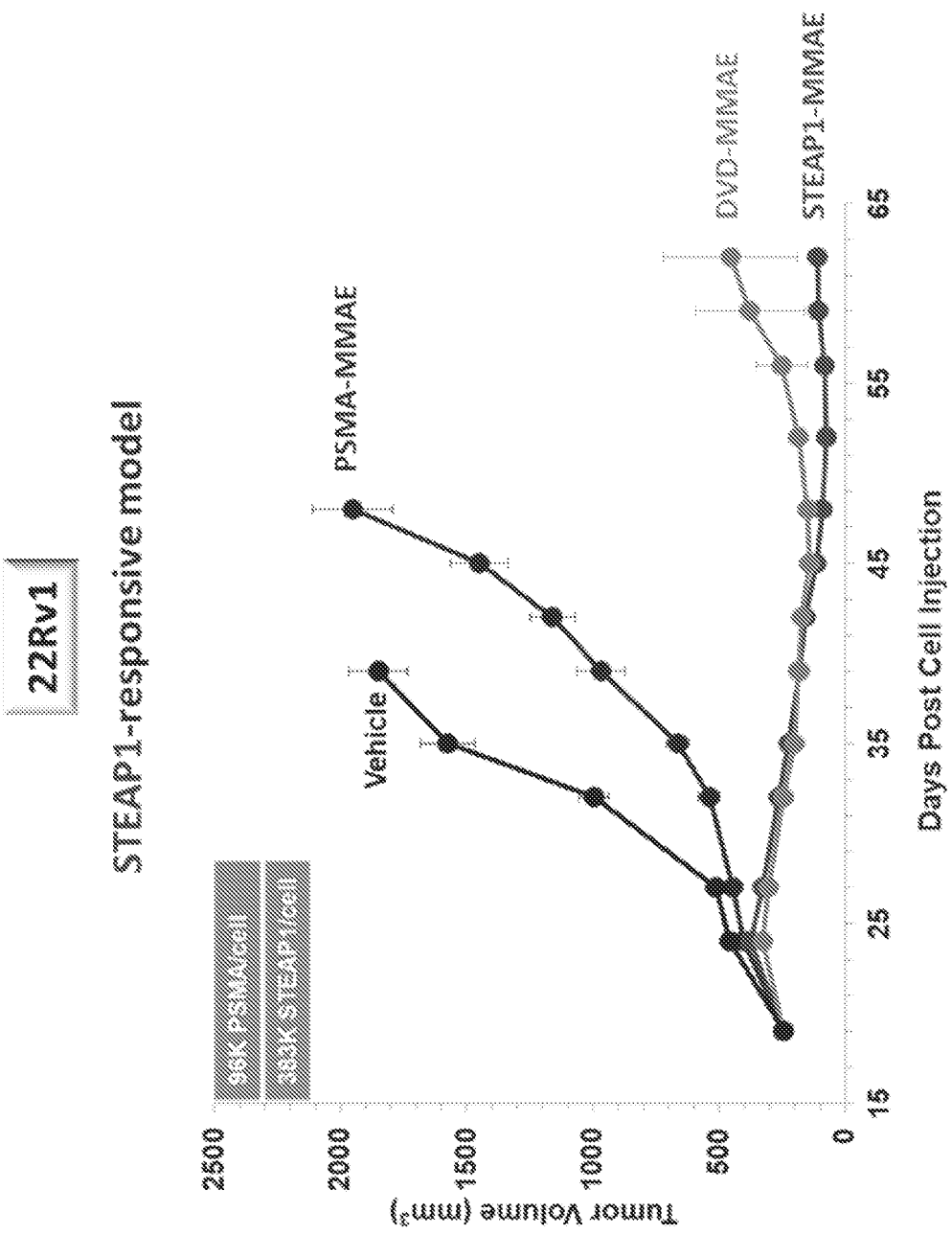

22Rv1
STEAP1-responsive model
96K PSMA/cell
383K STEAP1/cell
Vehicle
PSMA-MMAE
DVD-MMAE
STEAP1-MMAE
Tumor Volume (mm³)
2500
2000
1500
1000
500
0
15
25
35
45
55
65
Days Post Cell Injection

FIG. 4A

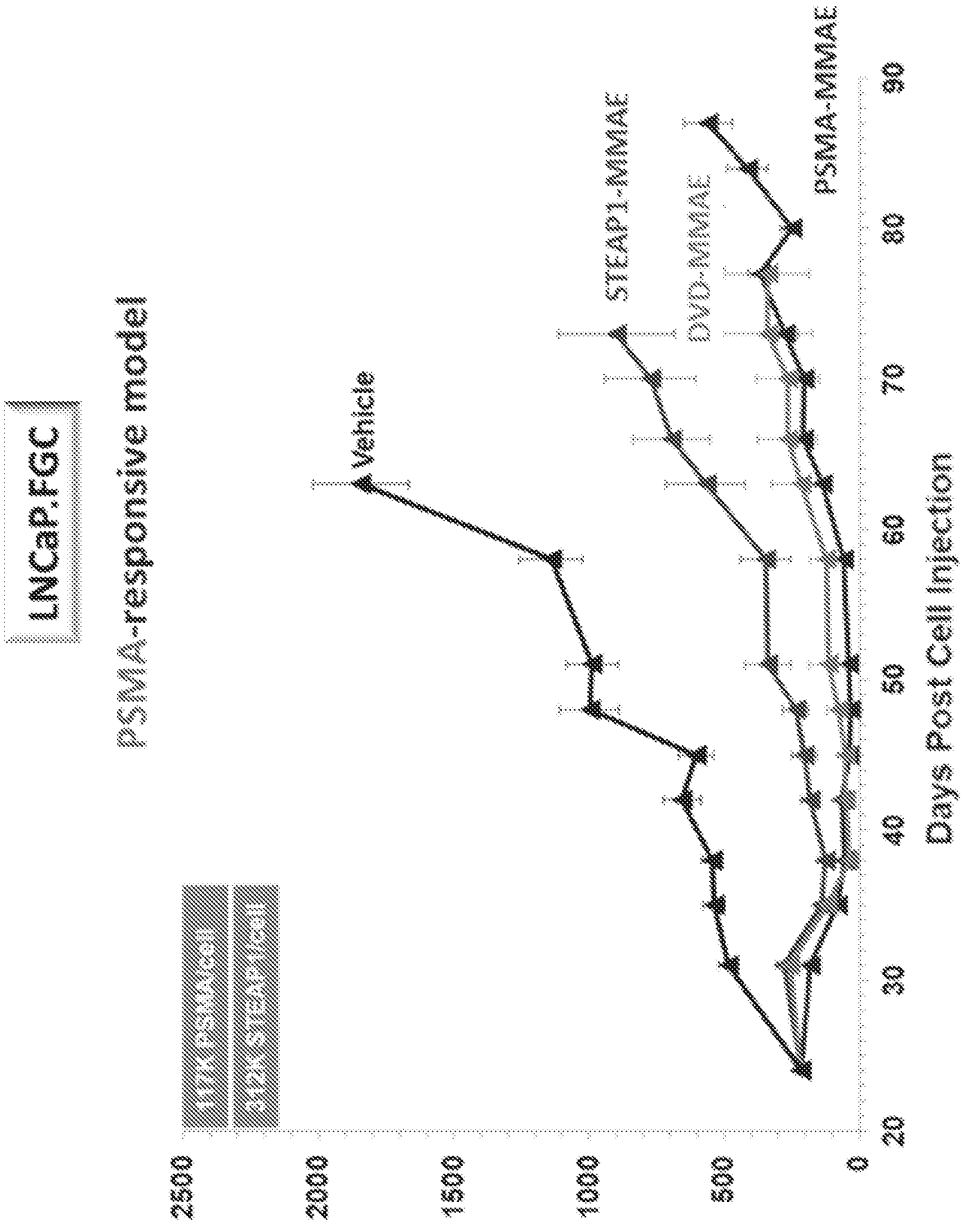

LNCaP.FGC
PSMA-responsive model
117K PSMA/cell
312K STEAP1/cell
Vehicle
STEAP1-MMAE
DVD-MMAE
PSMA-MMAE
2500
2000
1500
1000
500
0
20
30
40
50
60
70
80
90
Days Post Cell Injection

FIG. 4B

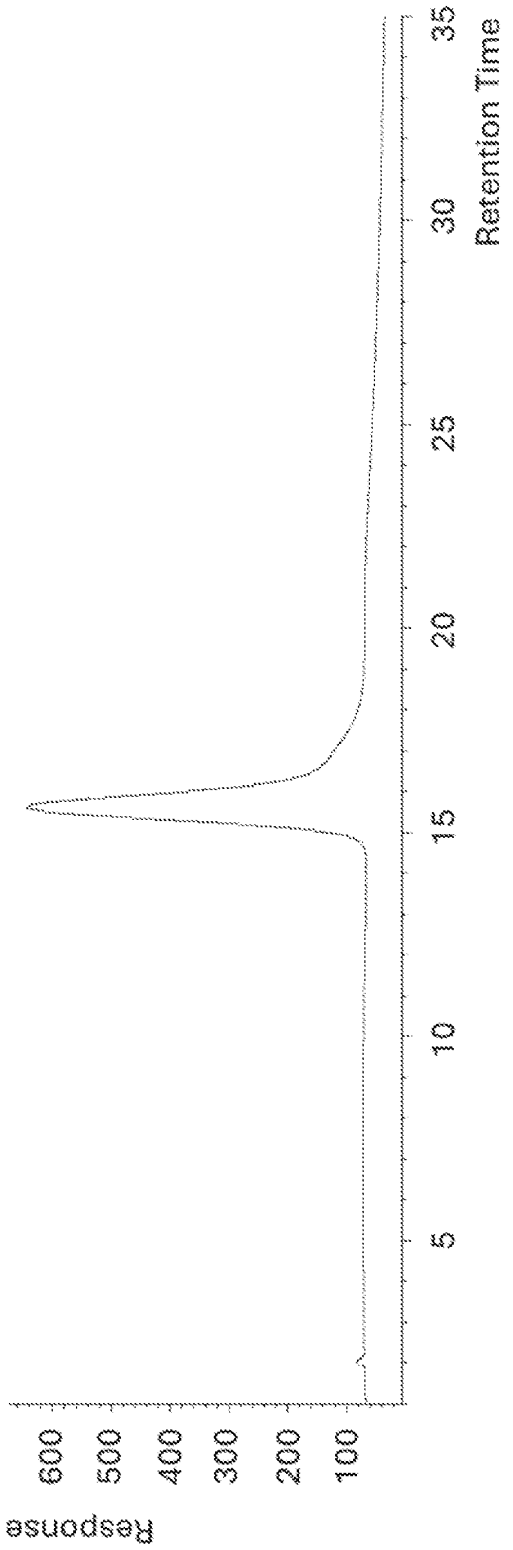

Response
600
500
400
300
200
100
5
10
15
20
25
30
35
Retention Time

FIG. 5A

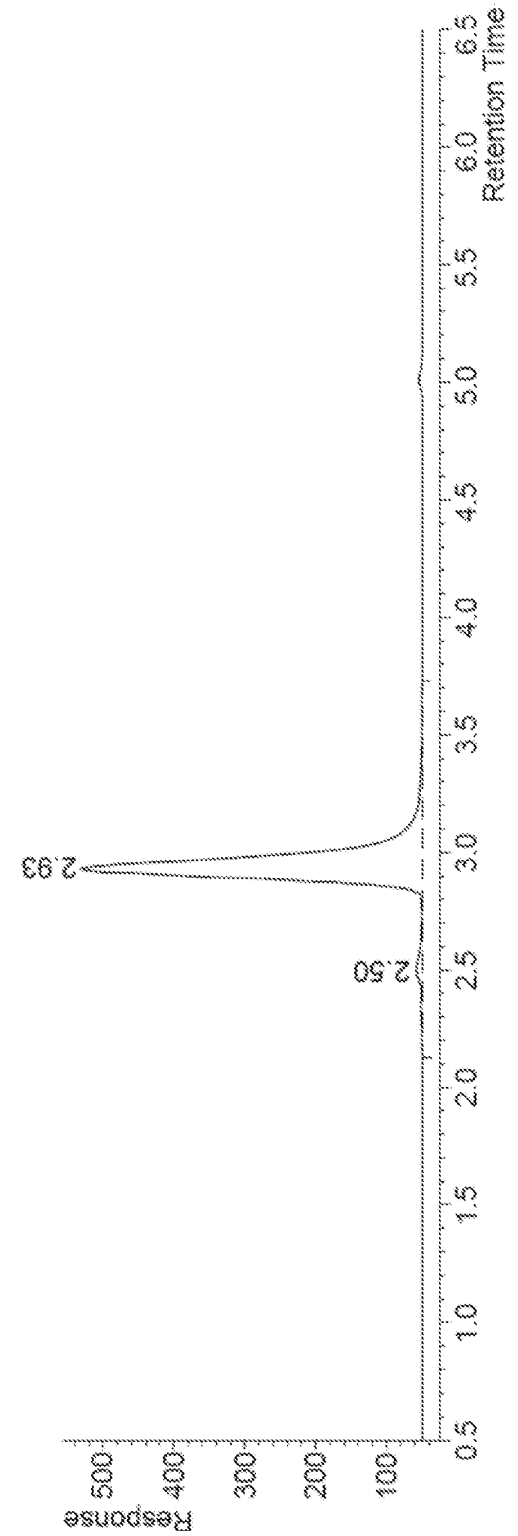

Response
500
400
300
200
100
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
Retention Time
2.93
2.50

FIG. 5B

FIG. 6A

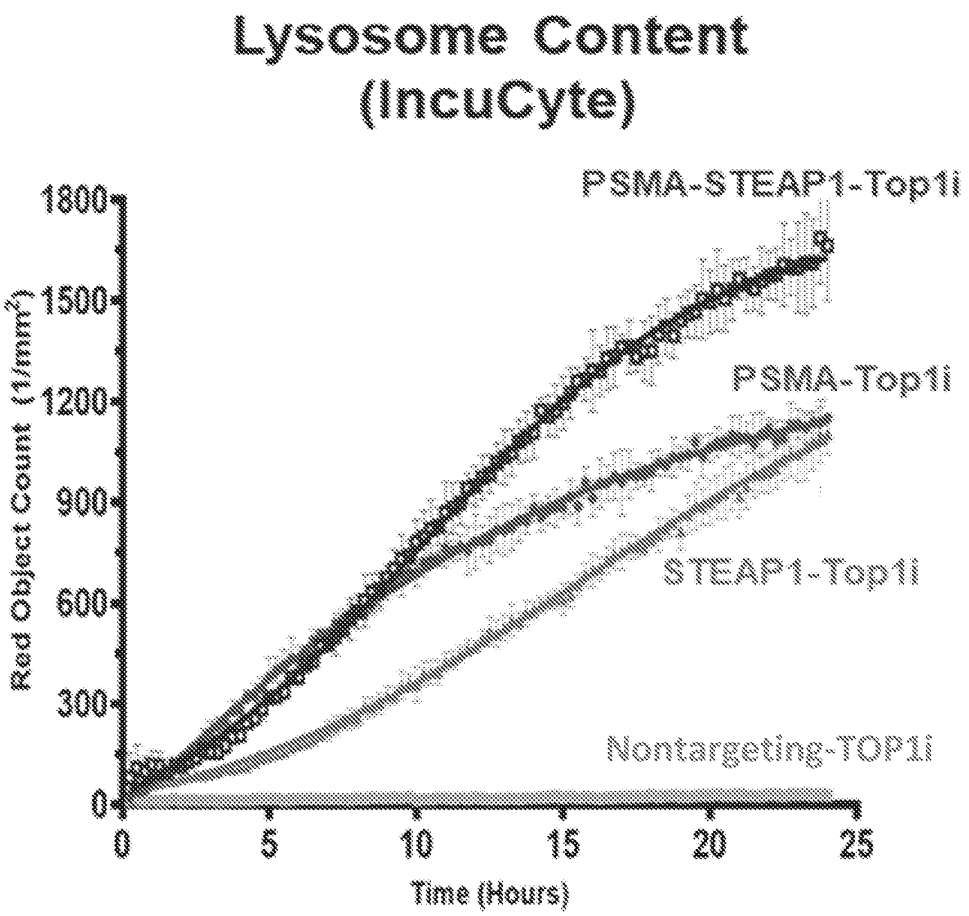

Lysosome Content
(IncuCyte)
PSMA-STEAP1-Top1i
PSMA-Top1i
STEAP1-Top1i
Nontargeting-TOP1i
Red Object Count (1/mm²)
1800
1500
1200
900
600
300
0
0
5
10
15
20
25
Time (Hours)

FIG. 6B

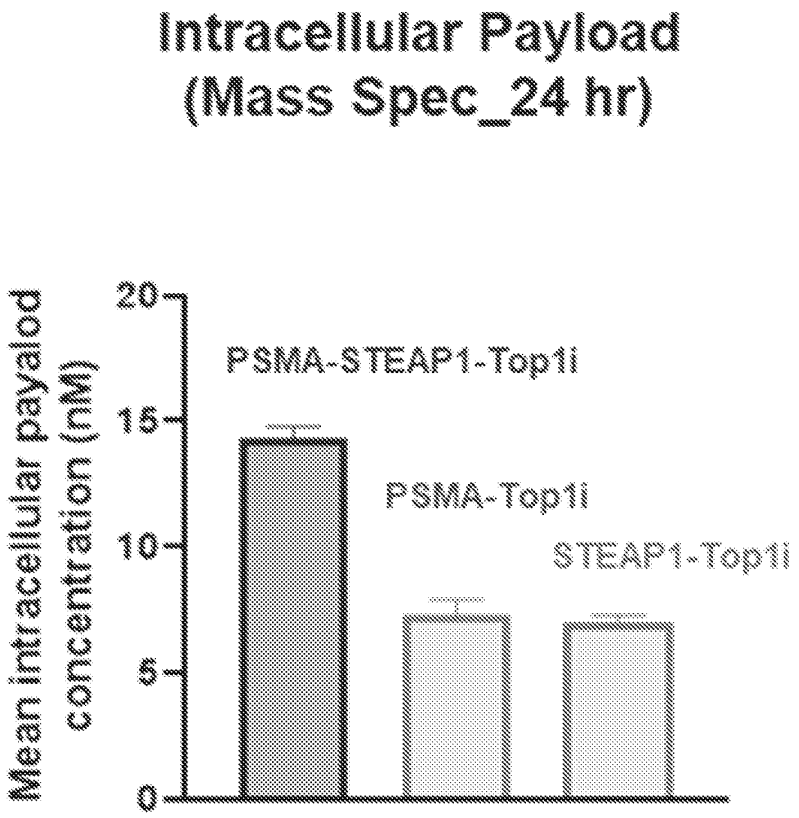
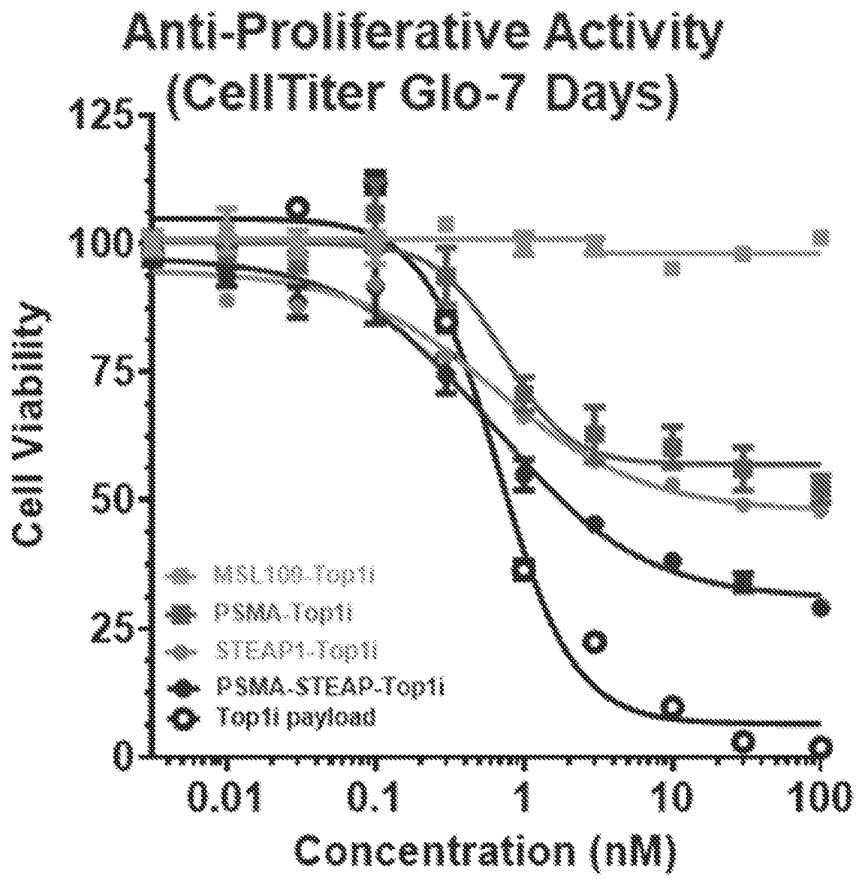

Intracellular Payload
(Mass Spec_24 hr)
Mean intracellular payalod concentration (nM)
20
15
10
5
0
PSMA-STEAP1-Top1I
PSMA-Top1I
STEAP1-Top1I

FIG. 6C


Anti-Proliferative Activity
(CellTiter Glo-7 Days)
Cell Viability
125
100
75
50
25
0
0.01
0.1
1
10
100
Concentration (nM)
MSL109-Top1i
PSMA-Top1i
STEAP1-Top1i
PSMA-STEAP-Top1i
Top1i payload

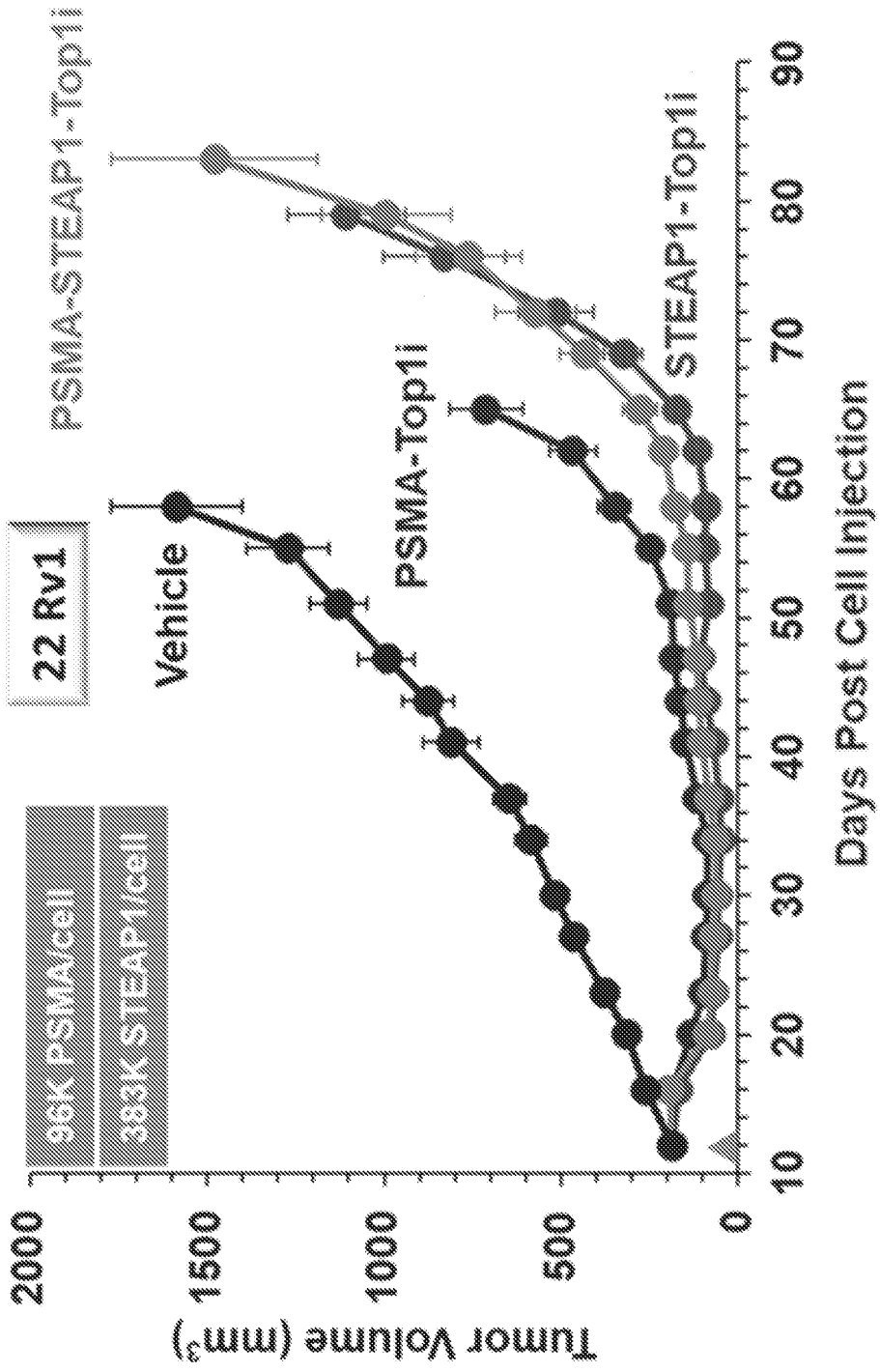

Tumor Volume (mm³)
2000
1500
1000
500
0
10
20
30
40
50
60
70
80
90
Days Post Cell Injection
22 Rv1
86K PSMA/cell
383K STEAP1/cell
Vehicle
PSMA-Top1i
STEAP1-Top1i
PSMA-STEAP1-Top1i

FIG. 7A

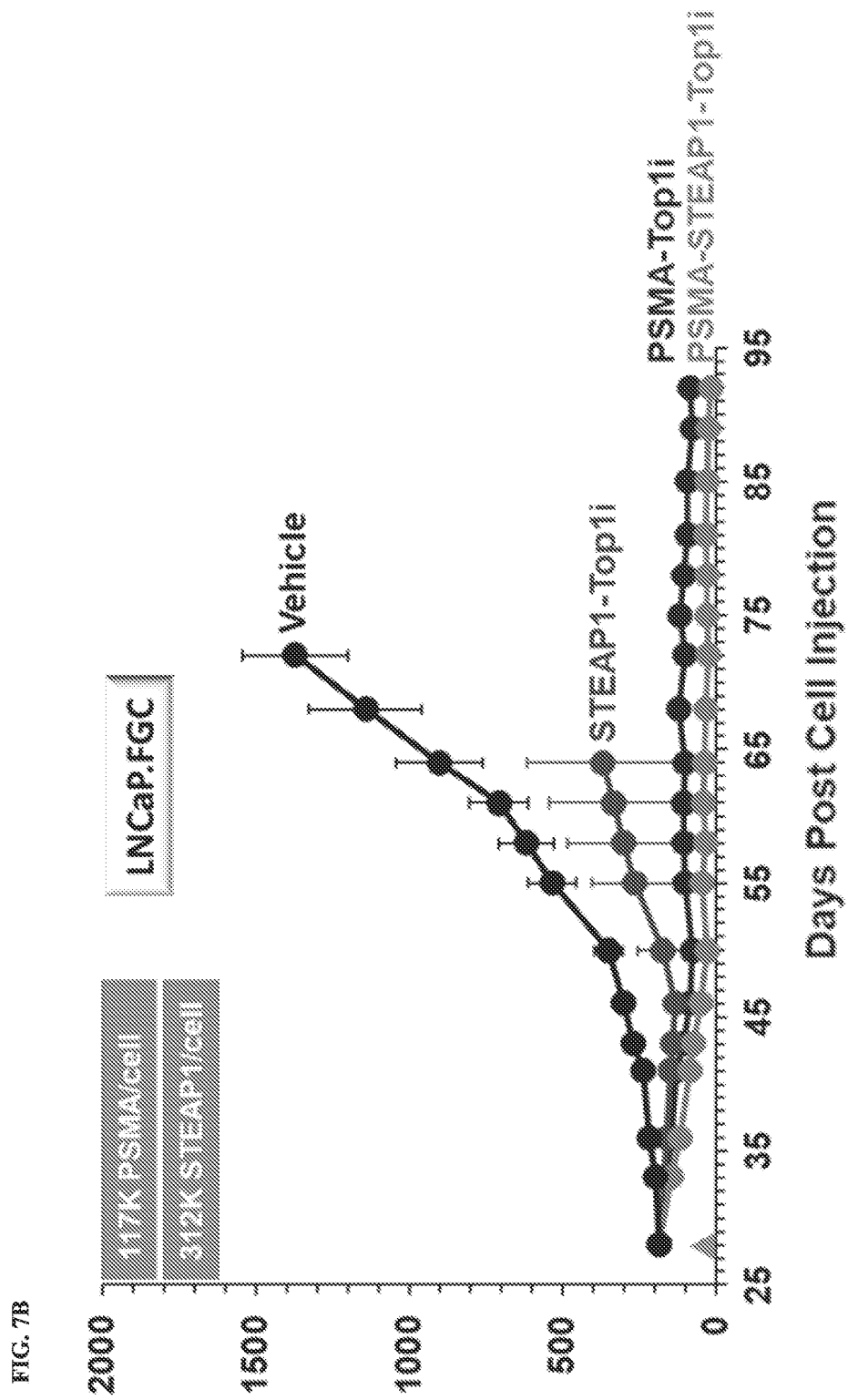

LNCaP.FGC
117K PSMA/cell
312K STEAP1/cell
Vehicle
STEAP1-Top1i
PSMA-Top1i
PSMA-STEAP1-Top1i
2000
1500
1000
500
0
25
35
45
55
65
75
85
95
Days Post Cell Injection

FIG. 7B