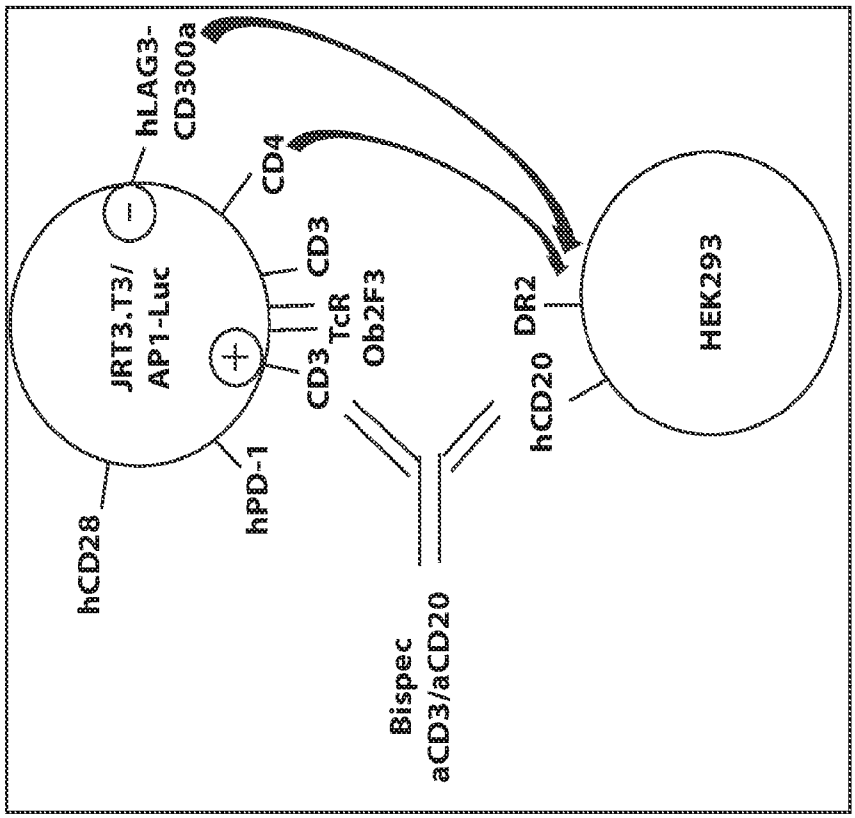

Figure 1A

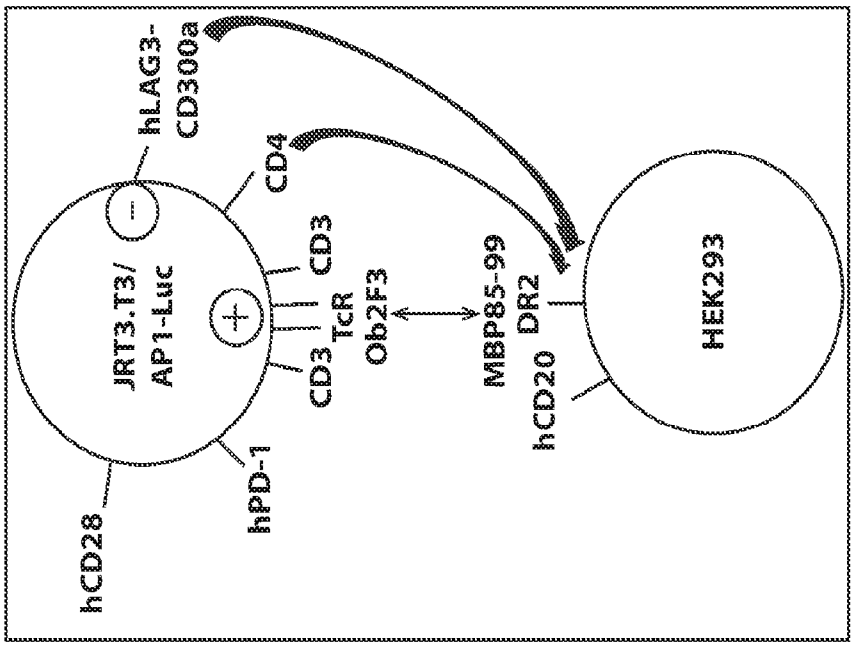

Figure 1B

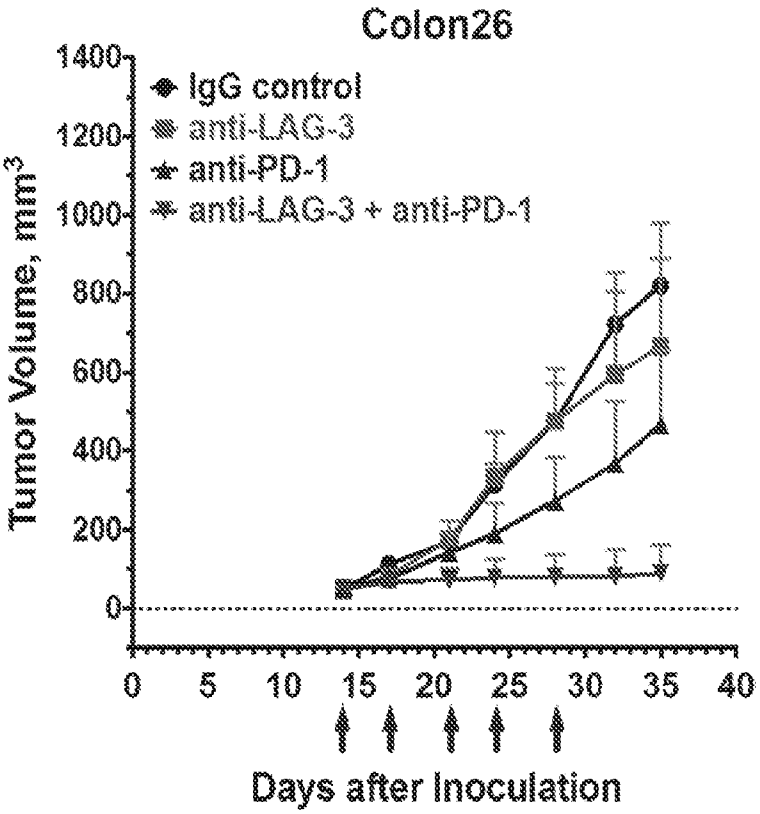
Colon26
IgG control
anti-LAG-3
anti-PD-1
anti-LAG-3 + anti-PD-1
Tumor Volume, mm3
1400
1200
1000
800
600
400
200
0
0
5
10
15
20
25
30
35
40
Days after Inoculation

Figure 2A

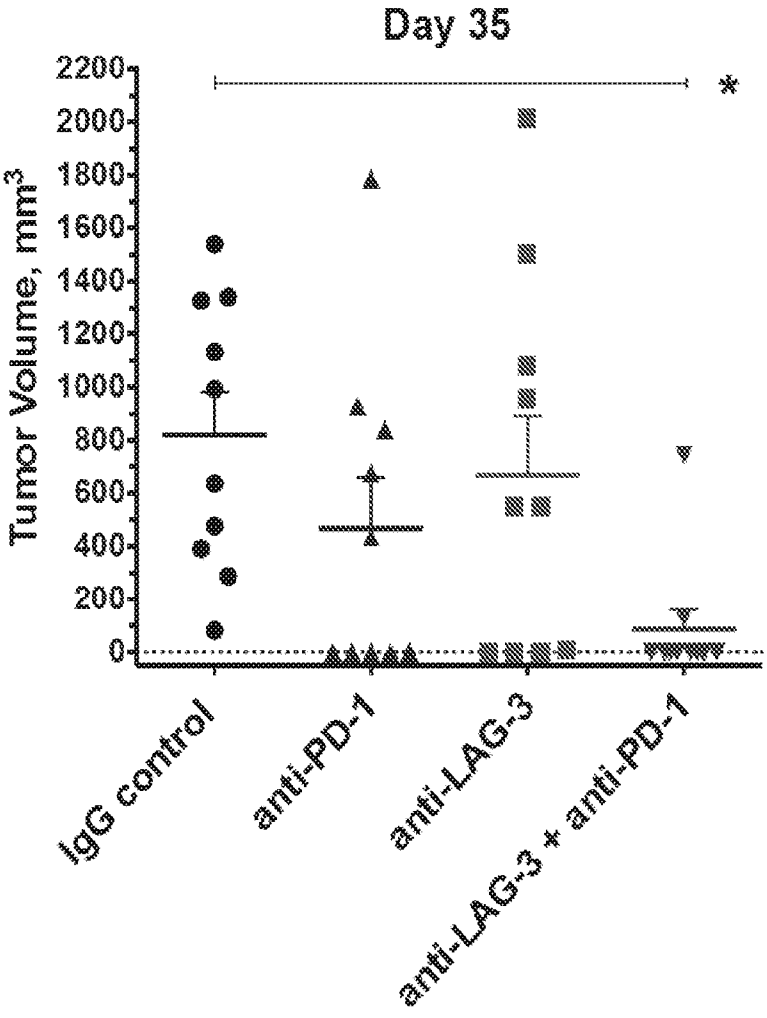
Day 35
Tumor Volume, mm3
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
*
IgG control
anti-PD-1
anti-LAG-3
anti-LAG-3 + anti-PD-1

Figure 2B

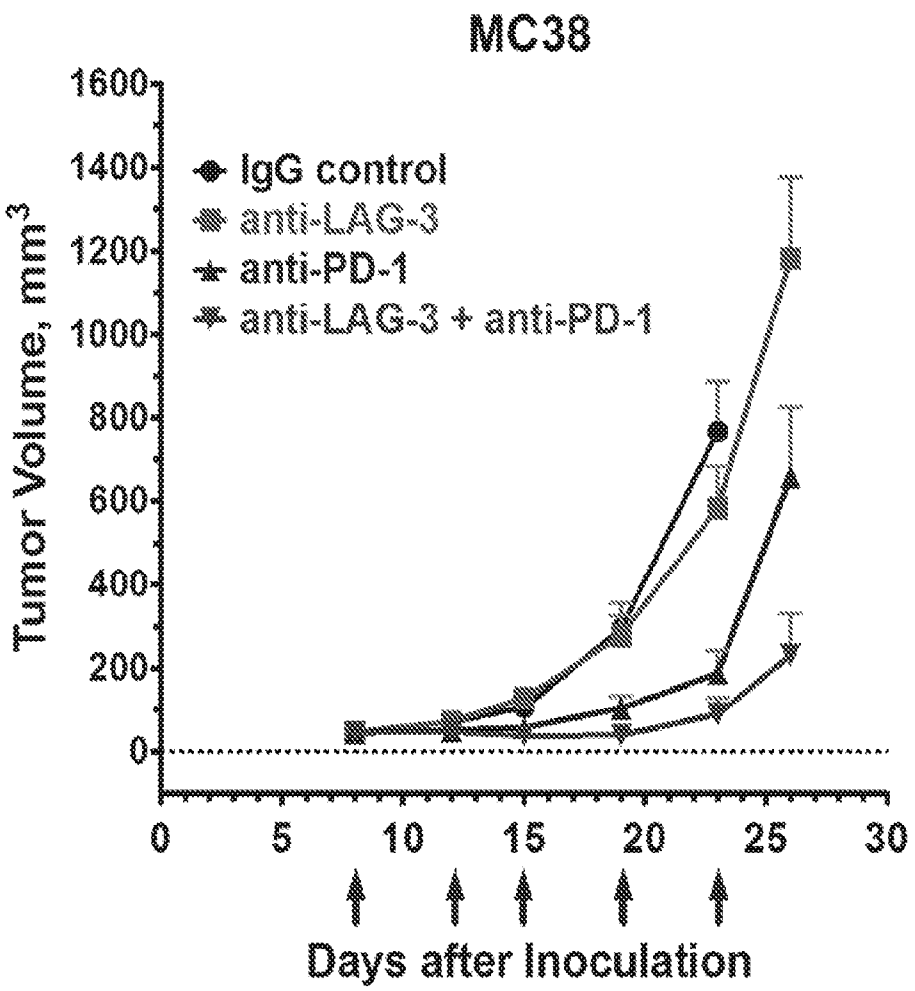
MC38
Tumor Volume, mm3
1600
1400
1200
1000
800
600
400
200
0
IgG control
anti-LAG-3
anti-PD-1
anti-LAG-3 + anti-PD-1
0
5
10
15
20
25
30
Days after Inoculation

Figure 3A

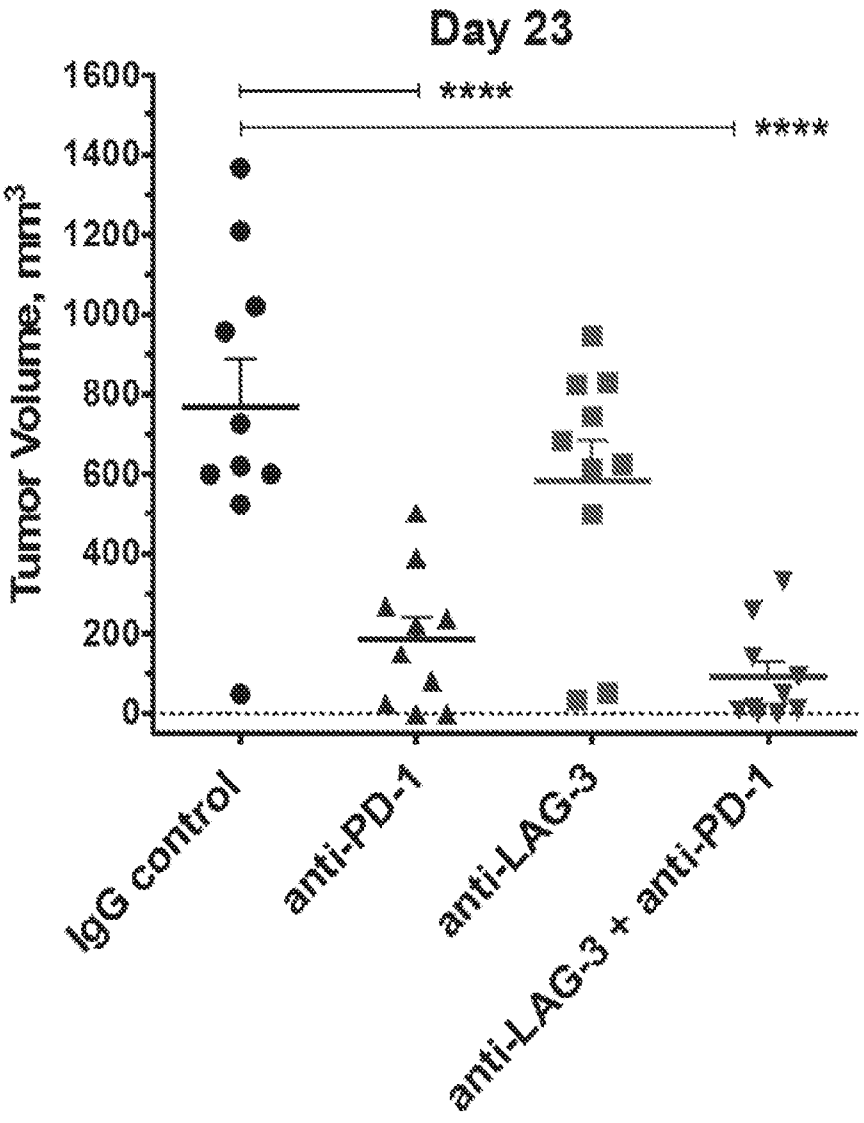
Day 23
Tumor Volume, mm3
1600
1400
1200
1000
800
600
400
200
0
****
****
IgG control
anti-PD-1
anti-LAG-3
anti-LAG-3 + anti-PD-1

Figure 3B

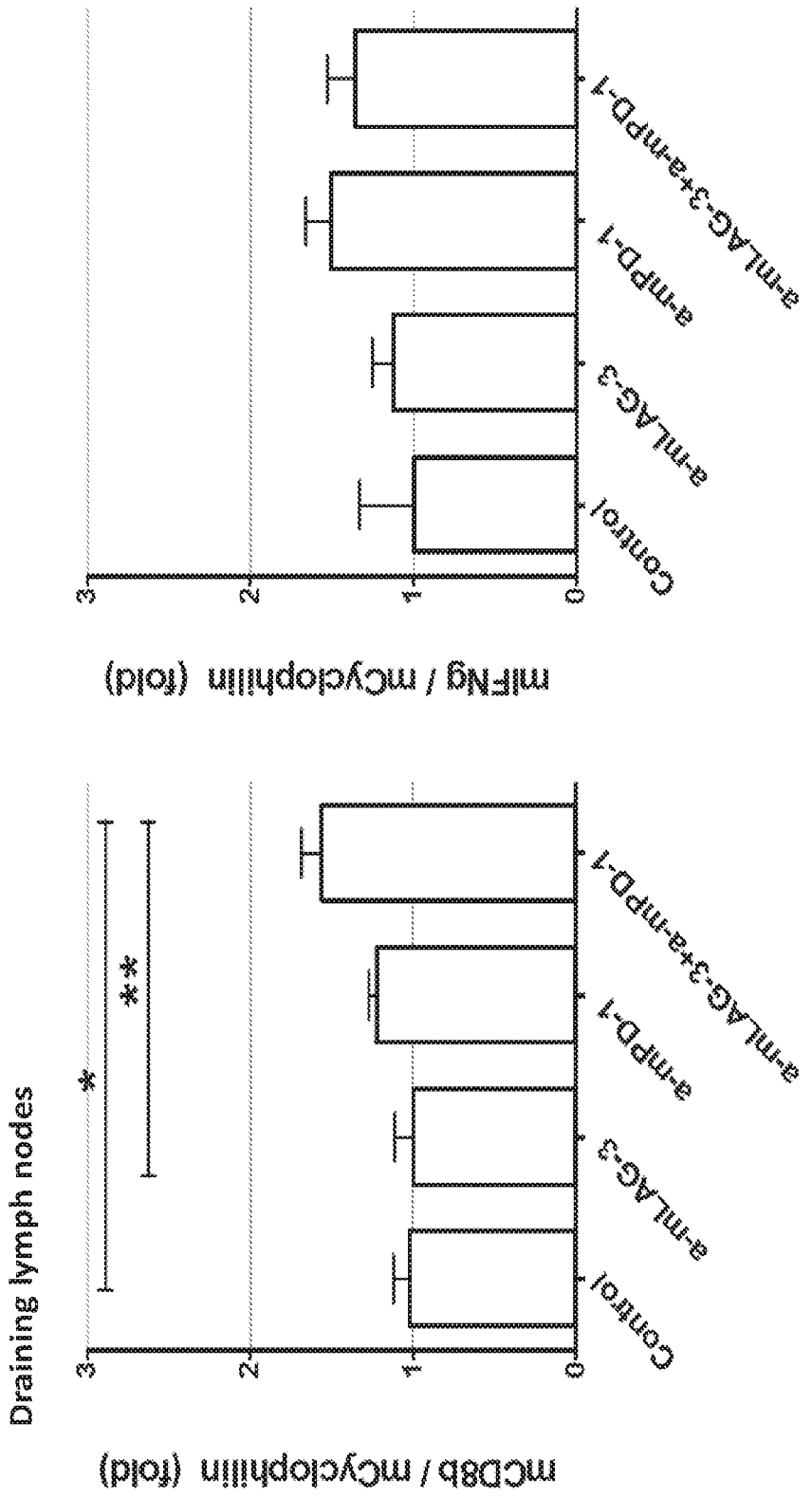
Draining lymph nodes
mCD8b / mCyclophilin (fold)
mIFNg / mCyclophilin (fold)
Control
a-mLAG-3
a-mPD-1
a-mLAG-3+a-mPD-1
0
1
2
3
*
**

Figure 4A

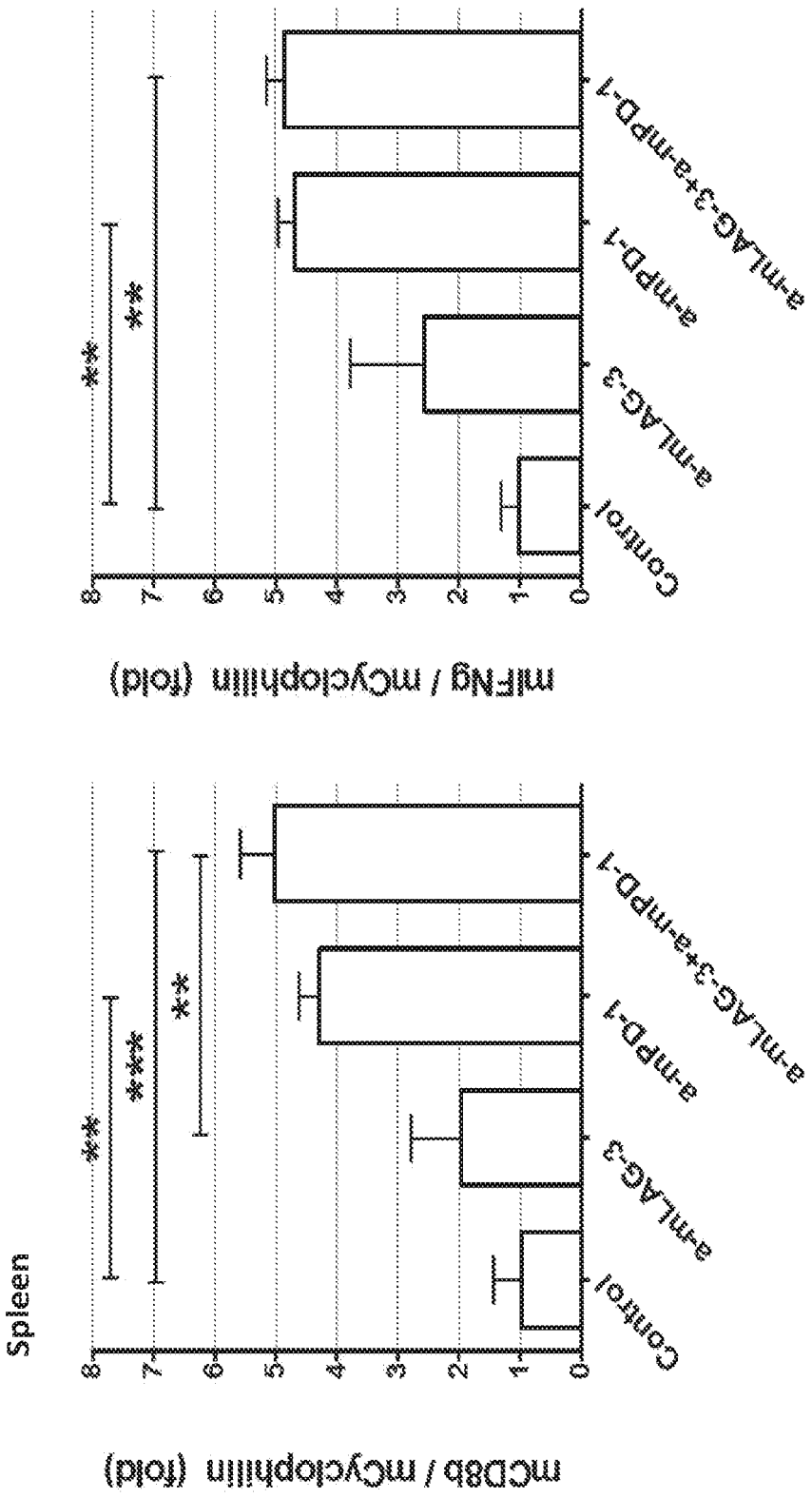
Spleen
mCD8b / mCyclophilin (fold)
mIFNg / mCyclophilin (fold)
Control
a-mLAG-3
a-mPD-1
a-mLAG-3+a-mPD-1
0
1
2
3
4
5
6
7
8
**
****
**
***
**

Figure 4B

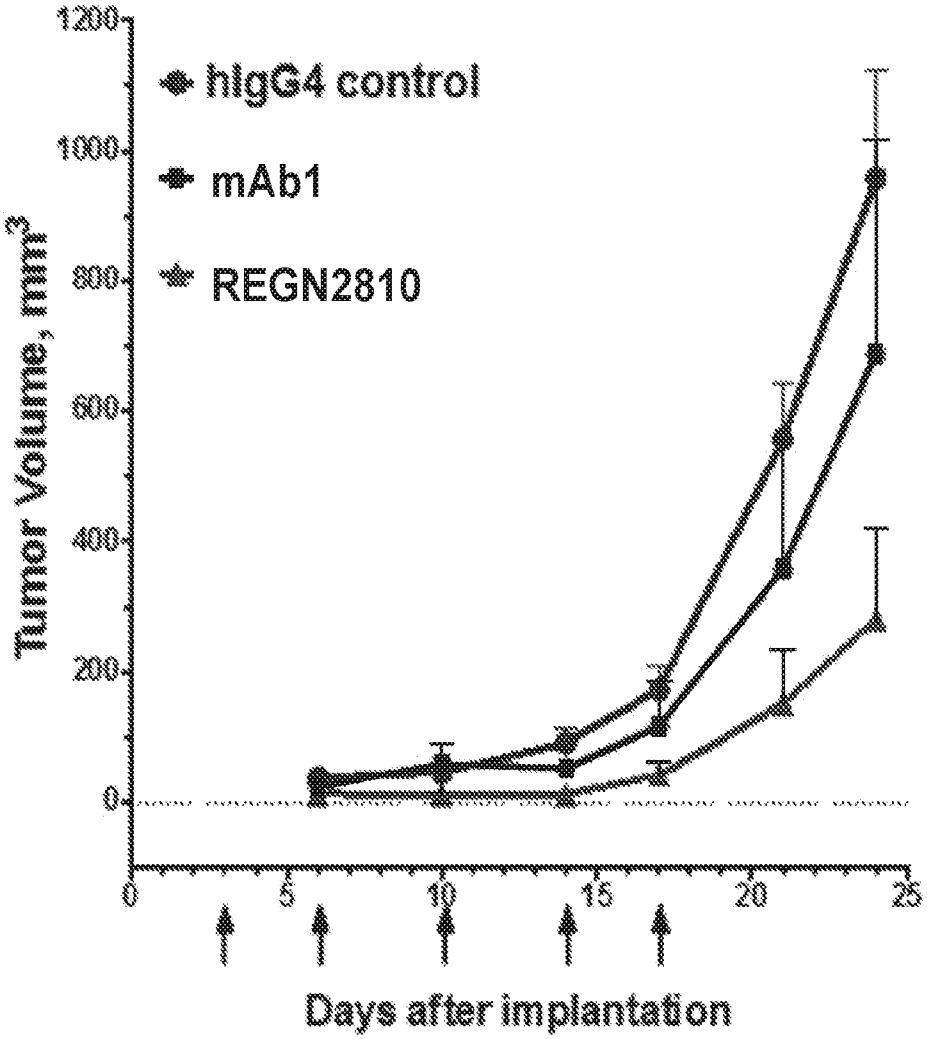
1200
1000
800
600
400
200
0
Tumor Volume, mm3
hIgG4 control
mAb1
REGN2810
0
5
10
15
20
25
Days after implantation

Figure 5A

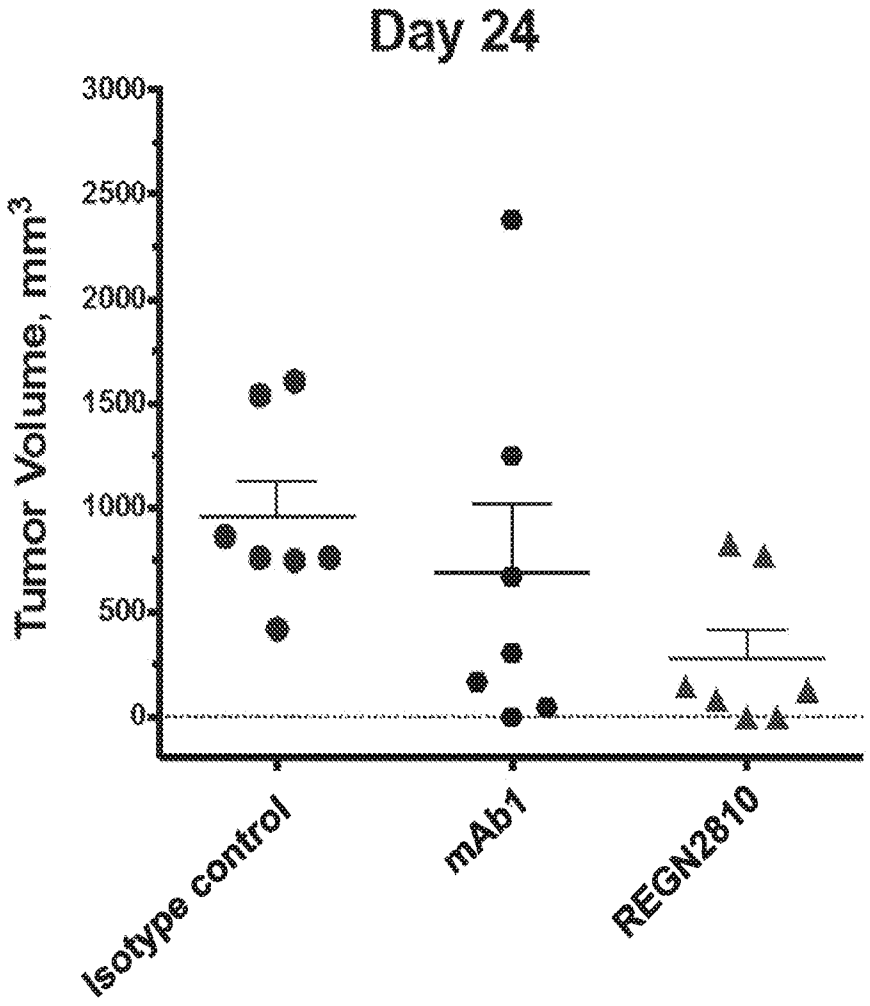
Day 24
Tumor Volume, mm3
3000
2500
2000
1500
1000
500
0
Isotype control
mAb1
REGN2810

Figure 5B

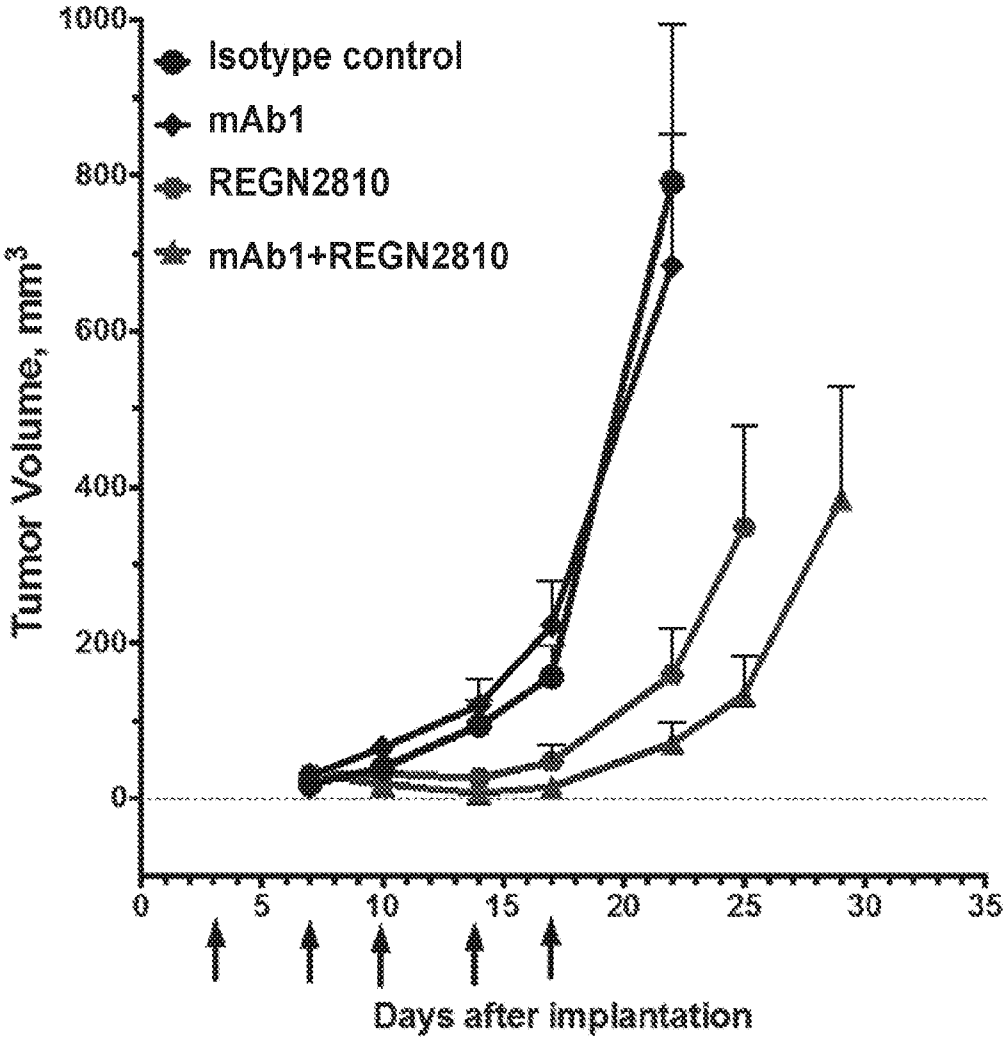
1000
800
600
400
200
0
Tumor Volume, mm3
Isotype control
mAb1
REGN2810
mAb1+REGN2810
0
5
10
15
20
25
30
35
Days after implantation

Figure 6A

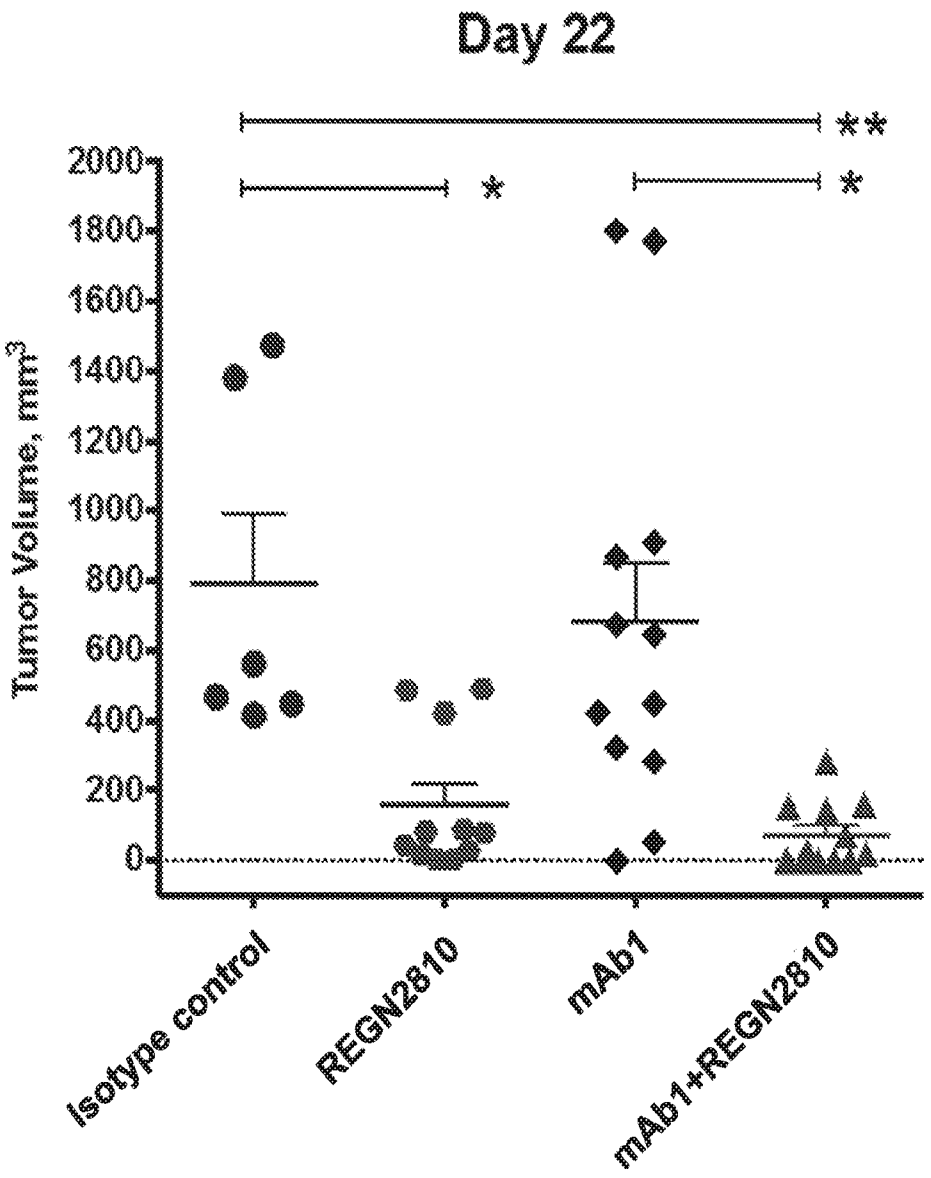
Day 22
**
*
*
2000
1800
1600
1400
1200
1000
800
600
400
200
0
Tumor Volume, mm3
Isotype control
REGN2810
mAb1
mAb1+REGN2810

Figure 6B

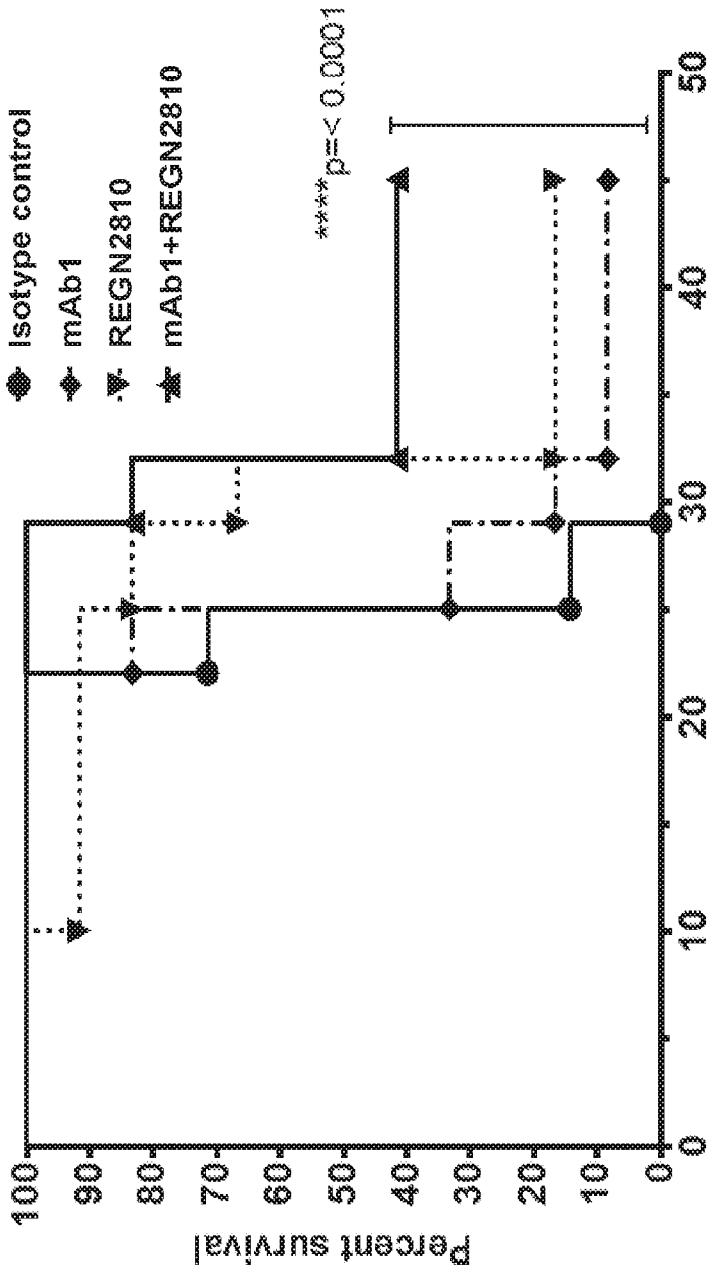
Isotype control
mAb1
REGN2810
mAb1+REGN2810
****p=< 0.0001
Percent survival
Days after implantation
0
10
20
30
40
50
0
10
20
30
40
50
60
70
80
90
100

Figure 6C

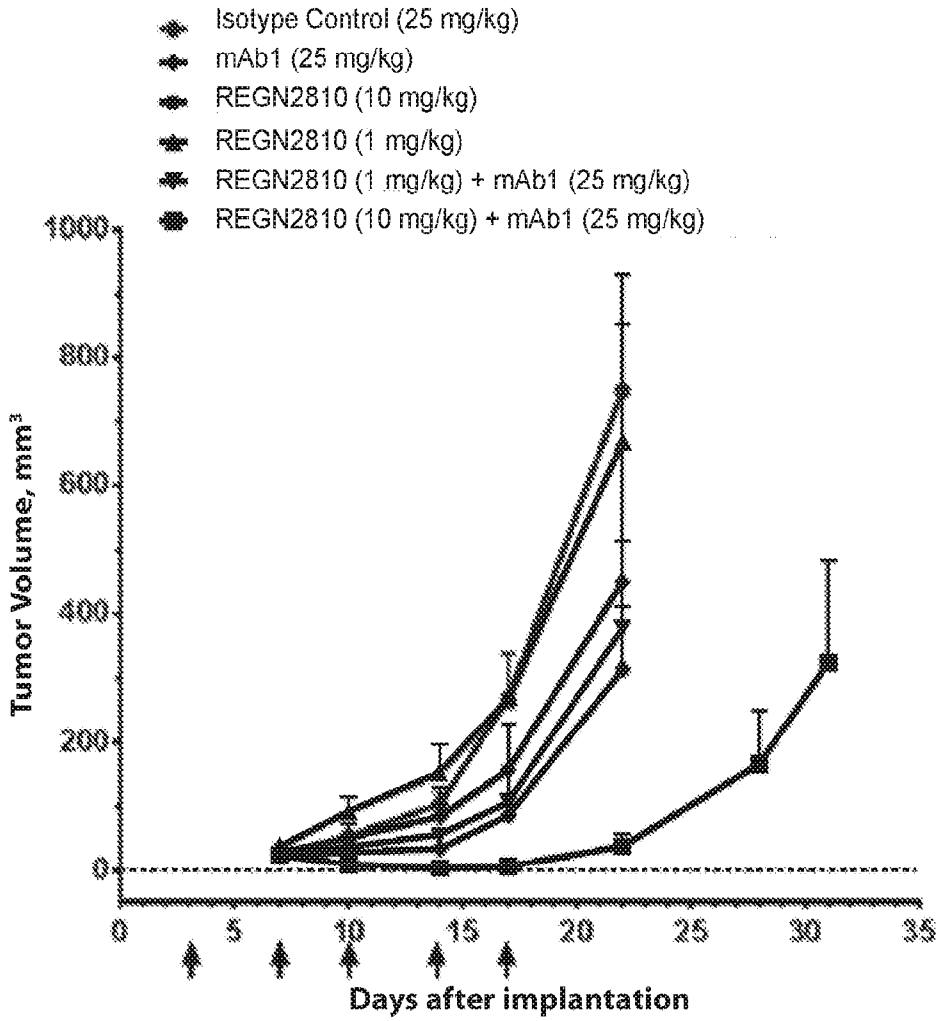
Isotype Control (25 mg/kg)
mAb1 (25 mg/kg)
REGN2810 (10 mg/kg)
REGN2810 (1 mg/kg)
REGN2810 (1 mg/kg) + mAb1 (25 mg/kg)
REGN2810 (10 mg/kg) + mAb1 (25 mg/kg)
Tumor Volume, mm³
1000
800
600
400
200
0
0
5
10
15
20
25
30
35
Days after implantation

Figure 7A

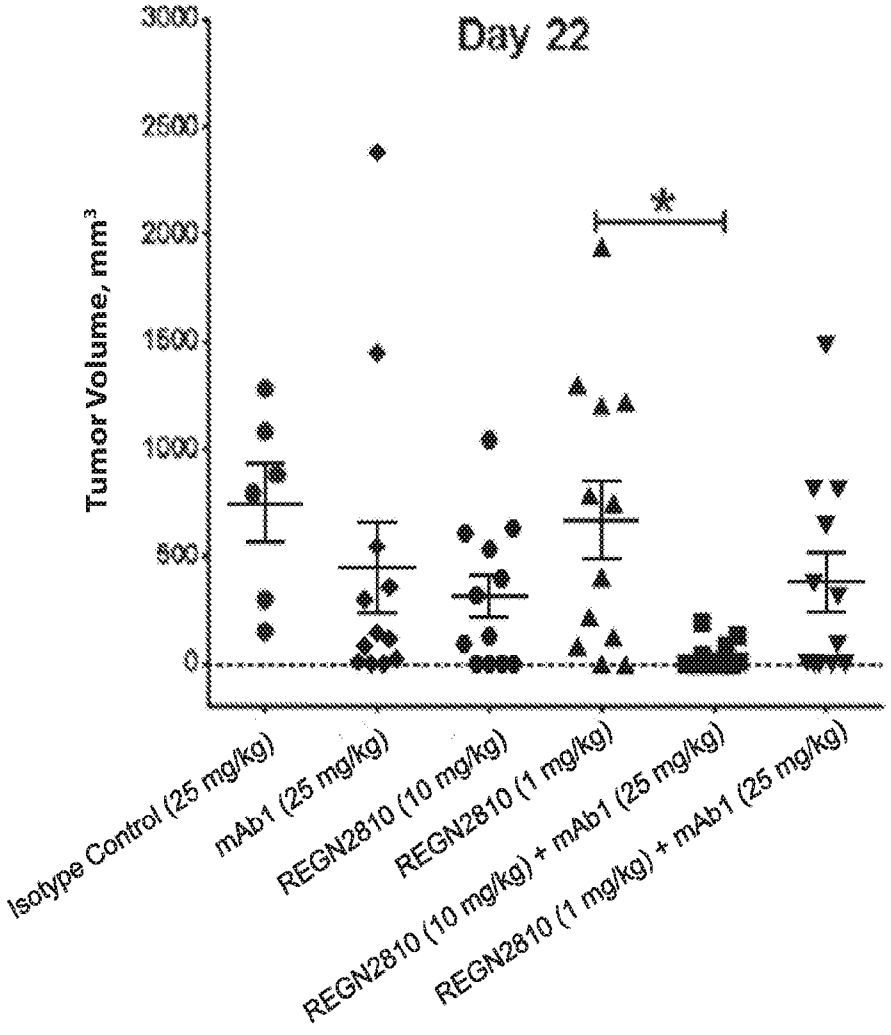
Day 22
Tumor Volume, mm3
3000
2500
2000
1500
1000
500
0
*
Isotype Control (25 mg/kg)
mAb1 (25 mg/kg)
REGN2810 (10 mg/kg)
REGN2810 (1 mg/kg)
REGN2810 (10 mg/kg) + mAb1 (25 mg/kg)
REGN2810 (1 mg/kg) + mAb1 (25 mg/kg)

Figure 7B

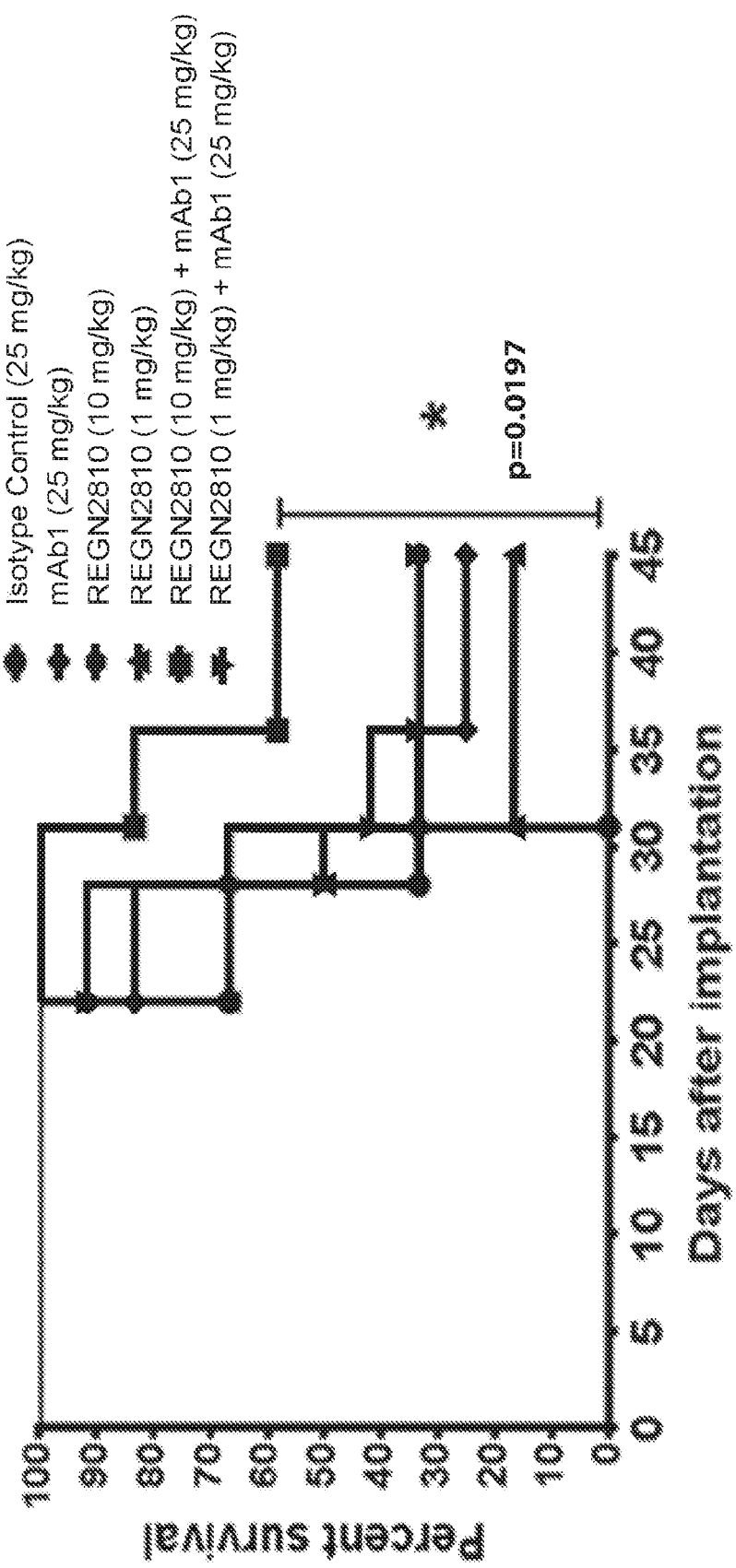
Isotype Control (25 mg/kg)
mAb1 (25 mg/kg)
REGN2810 (10 mg/kg)
REGN2810 (1 mg/kg)
REGN2810 (10 mg/kg) + mAb1 (25 mg/kg)
REGN2810 (1 mg/kg) + mAb1 (25 mg/kg)
*
p=0.0197
Percent survival
100
90
80
70
60
50
40
30
20
10
0
0
5
10
15
20
25
30
35
40
45
Days after implantation

Figure 7C

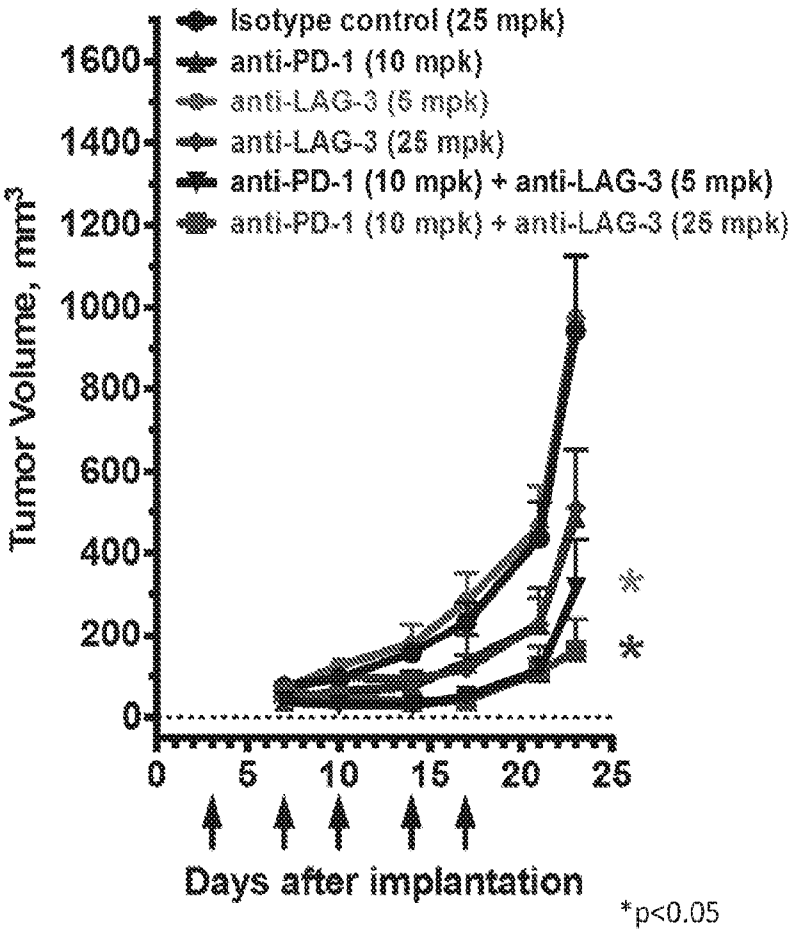
Isotype control (25 mpk)
anti-PD-1 (10 mpk)
anti-LAG-3 (5 mpk)
anti-LAG-3 (25 mpk)
anti-PD-1 (10 mpk) + anti-LAG-3 (5 mpk)
anti-PD-1 (10 mpk) + anti-LAG-3 (25 mpk)
Tumor Volume, mm3
1600
1400
1200
1000
800
600
400
200
0
0
5
10
15
20
25
Days after implantation
*
*
*p<0.05

Figure 8A

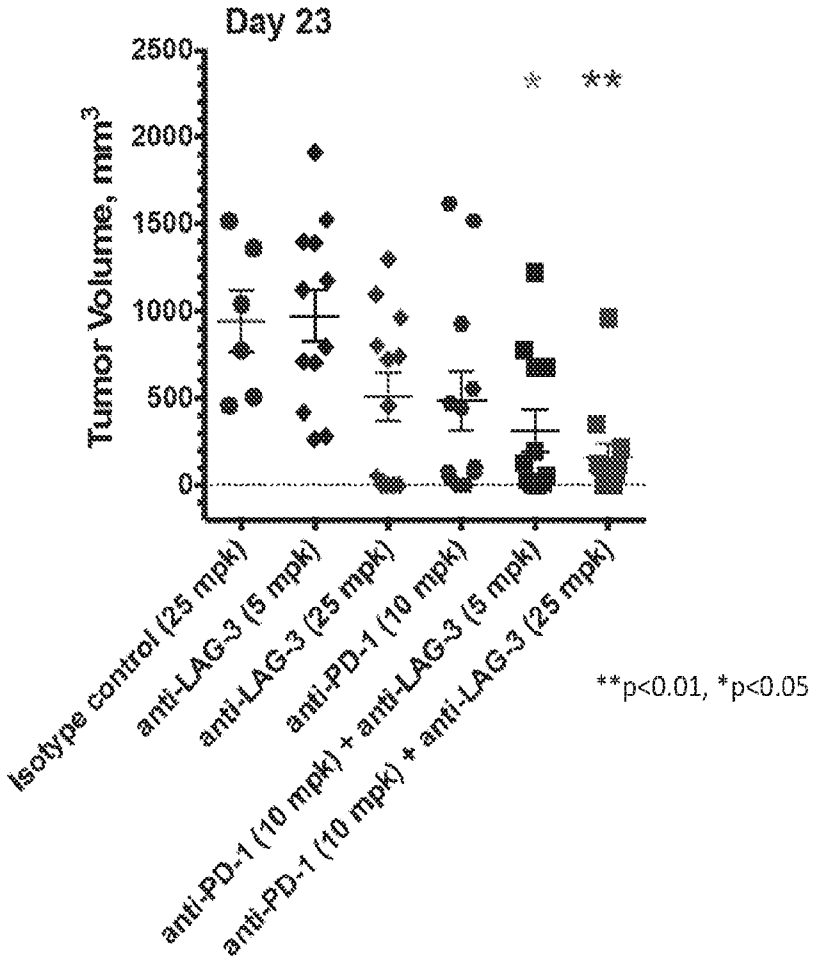
Day 23
Tumor Volume, mm3
2500
2000
1500
1000
500
0
*
**
Isotype control (25 mpk)
anti-LAG-3 (5 mpk)
anti-LAG-3 (25 mpk)
anti-PD-1 (10 mpk)
anti-PD-1 (10 mpk) + anti-LAG-3 (5 mpk)
anti-PD-1 (10 mpk) + anti-LAG-3 (25 mpk)
**p<0.01, *p<0.05

Figure 8B

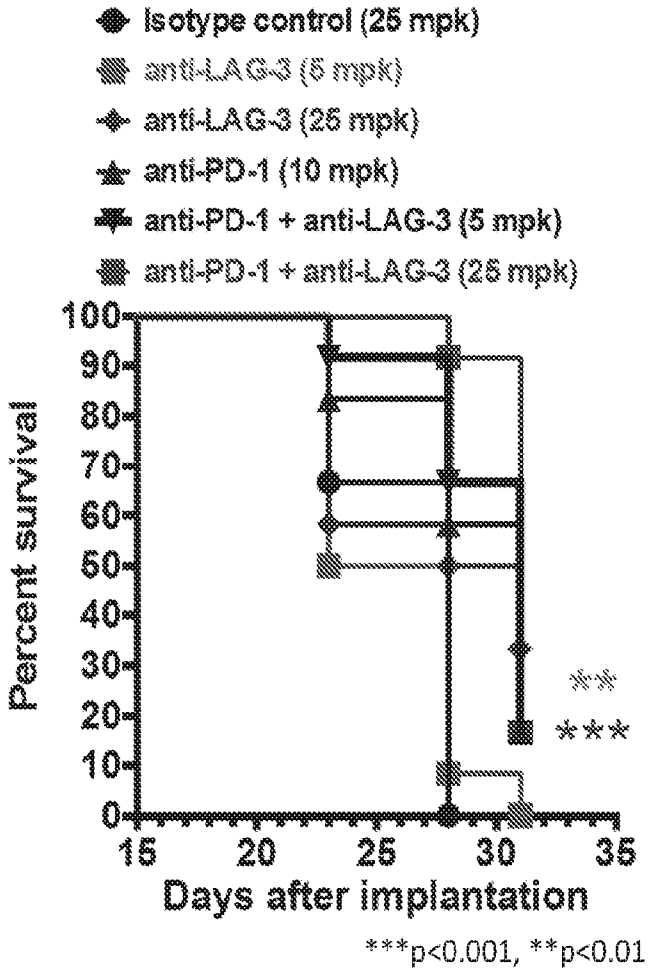
Isotype control (25 mpk)
anti-LAG-3 (5 mpk)
anti-LAG-3 (25 mpk)
anti-PD-1 (10 mpk)
anti-PD-1 + anti-LAG-3 (5 mpk)
anti-PD-1 + anti-LAG-3 (25 mpk)
Percent survival
100
90
80
70
60
50
40
30
20
10
0
15
20
25
30
35
Days after implantation
**
***
***p<0.001, **p<0.01

Figure 8C

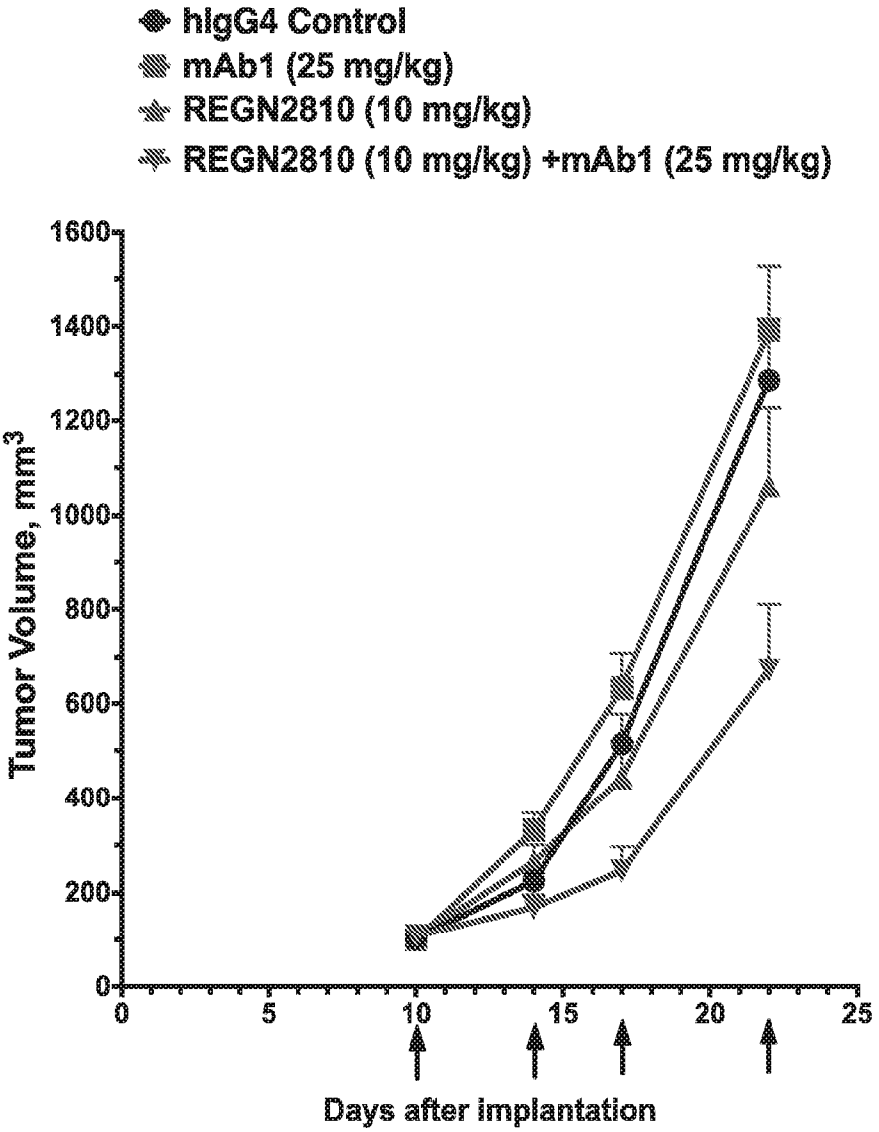
hIgG4 Control
mAb1 (25 mg/kg)
REGN2810 (10 mg/kg)
REGN2810 (10 mg/kg) +mAb1 (25 mg/kg)
Tumor Volume, mm3
1600
1400
1200
1000
800
600
400
200
0
0
5
10
15
20
25
Days after implantation

Figure 9

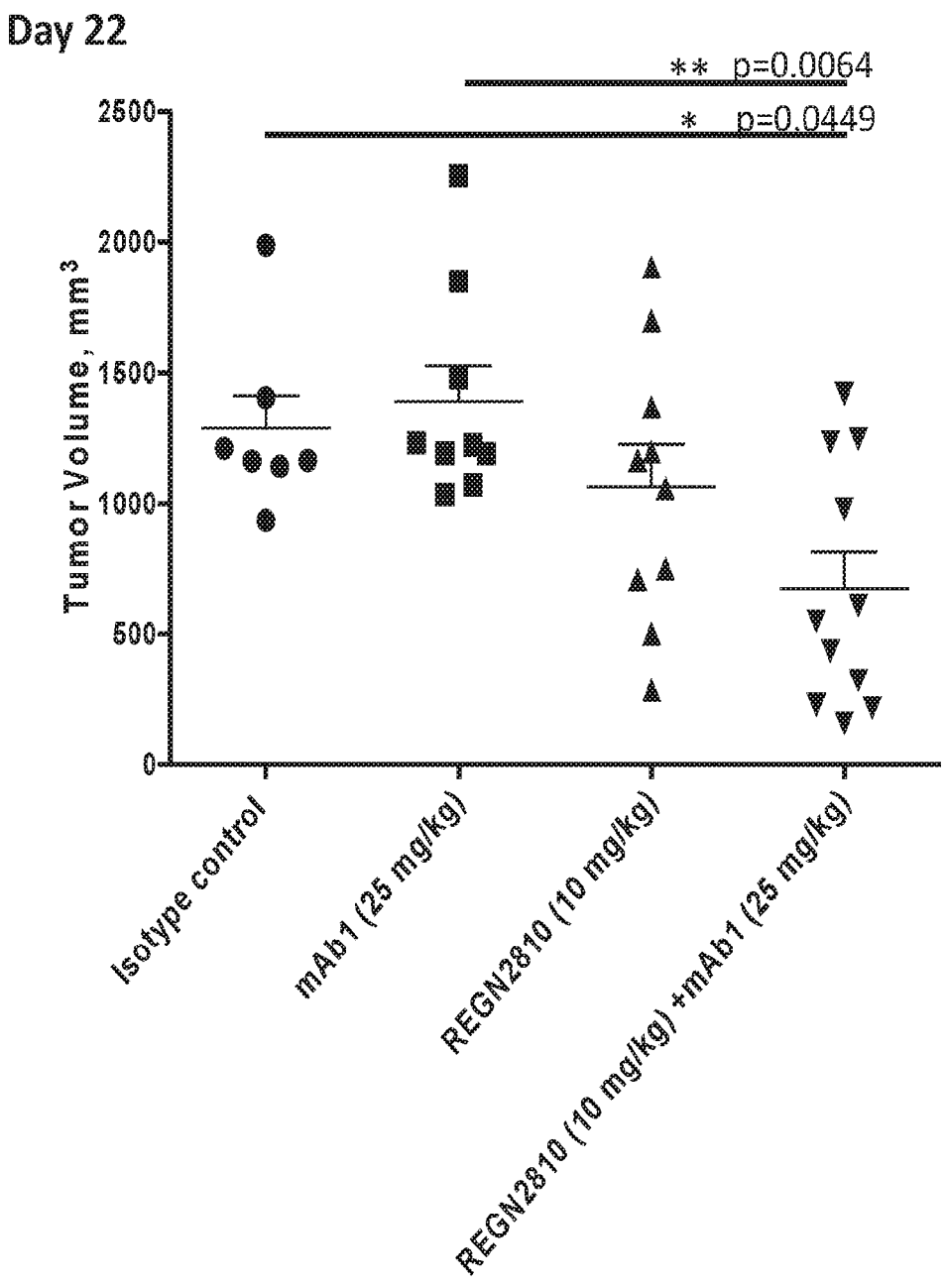
Day 22
** p=0.0064
* p=0.0449
Tumor Volume, mm3
2500
2000
1500
1000
500
0
Isotype control
mAb1 (25 mg/kg)
REGN2810 (10 mg/kg)
REGN2810 (10 mg/kg) +mAb1 (25 mg/kg)

Figure 10

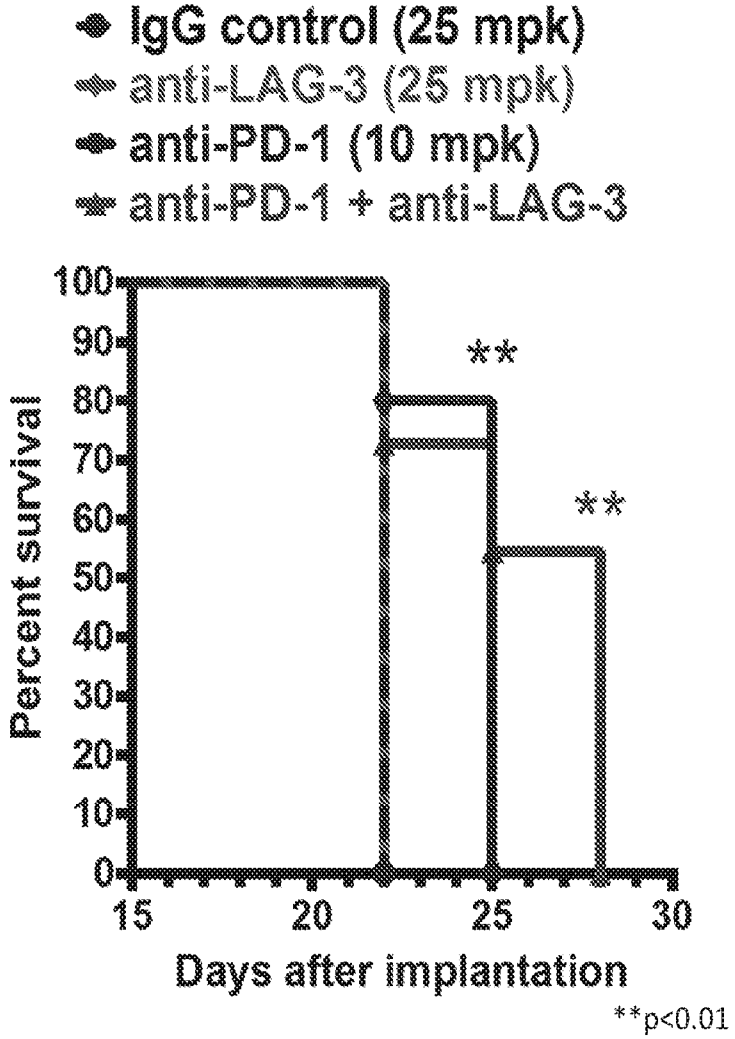
IgG control (25 mpk)
anti-LAG-3 (25 mpk)
anti-PD-1 (10 mpk)
anti-PD-1 + anti-LAG-3
Percent survival
100
90
80
70
60
50
40
30
20
10
0
15
20
25
30
Days after implantation
**
**
**p<0.01

Figure 11

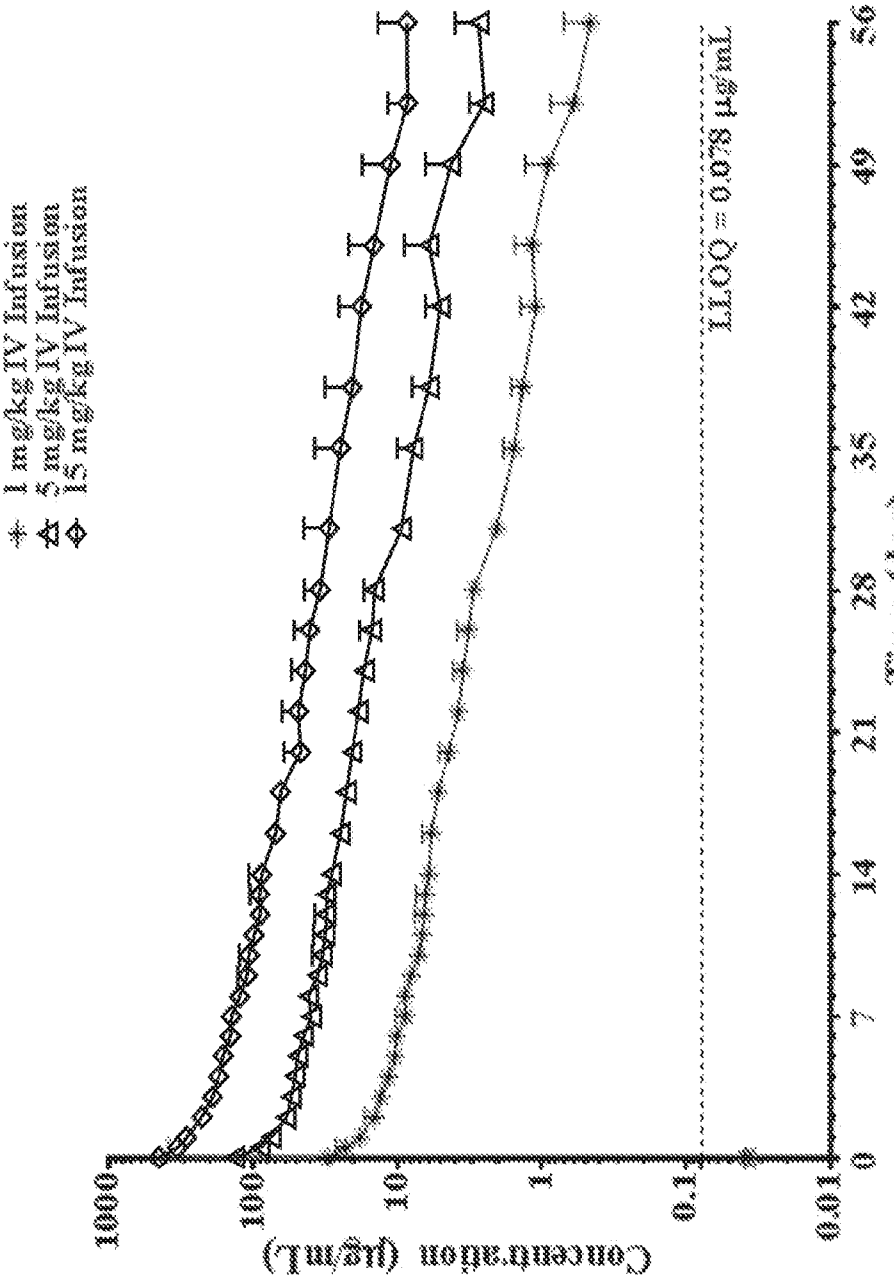
1 mg/kg IV Infusion
5 mg/kg IV Infusion
15 mg/kg IV Infusion
Concentration (µg/mL)
1000
100
10
1
0.1
0.01
LLOQ = 0.078 µg/mL
0
7
14
21
28
35
42
49
56
Time (day)

Figure 12