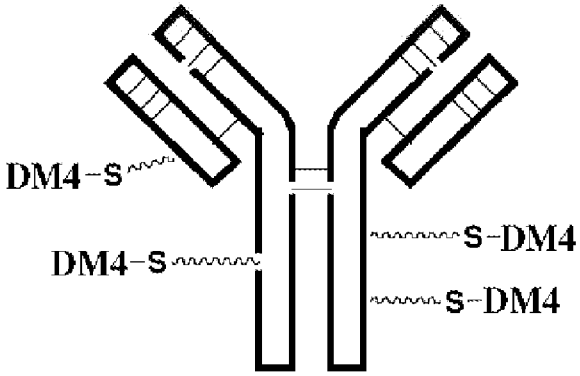
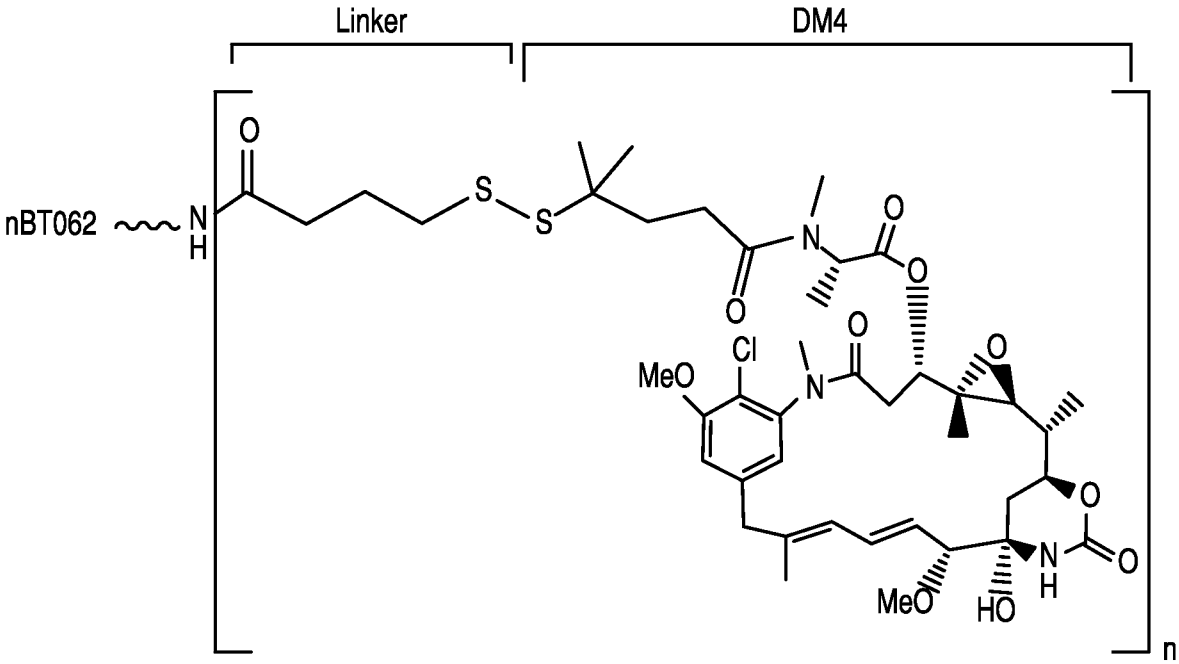
FIG. 1





*n is approximately 3.5 drug linked per antibody molecule

FIG. 2

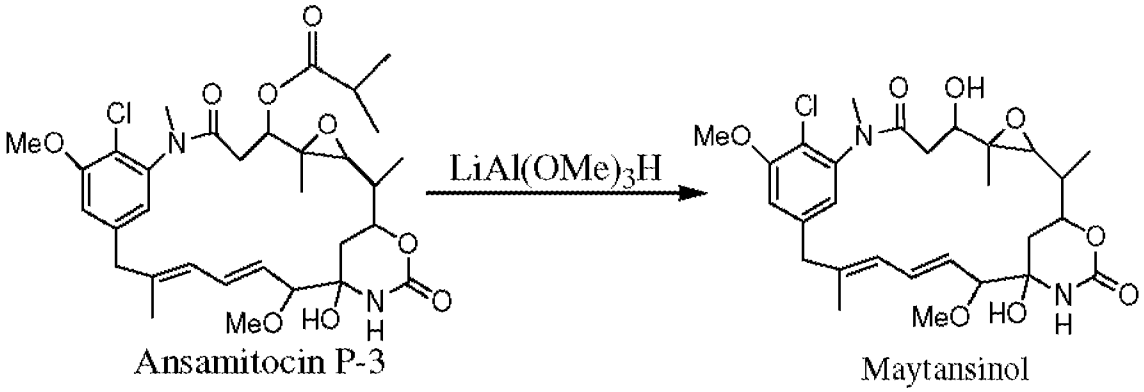
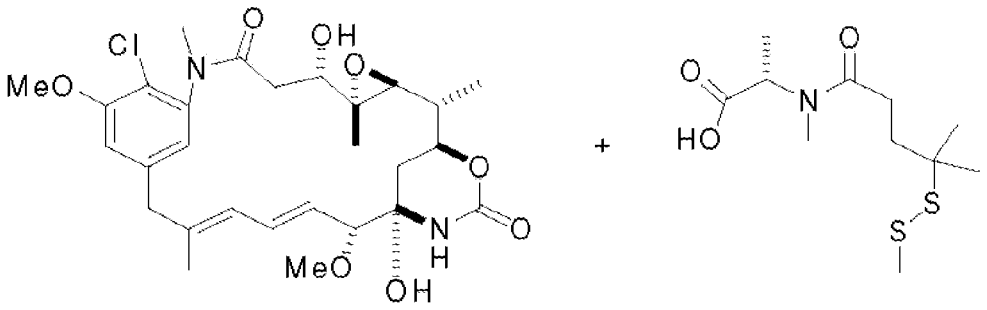


FIG. 3

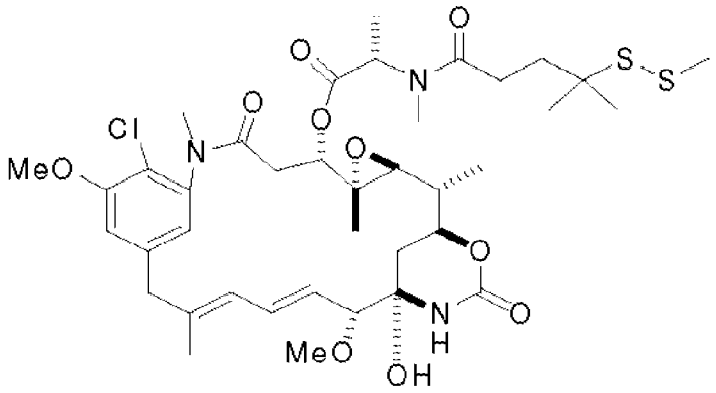


Maytansinol

DM4 Side Chain

Step I

1) DCC, $ZnCl_2$, CH_2Cl_2
2) Chromatography

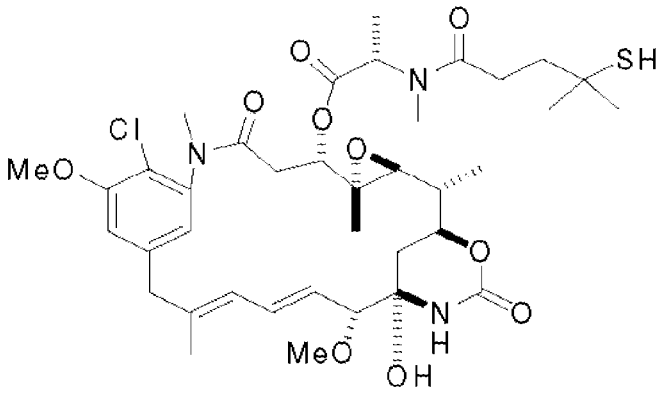


L-DM4-SMe

FIG. 4

Step II

1) DTT, DME, phosphate buffer
2) Chromatography



L-DM4

DCC: 1,3-dicyclohexylcarbodiimide
DTT: Dithiothreitol
DME: 1,2-Dimethoxyetha

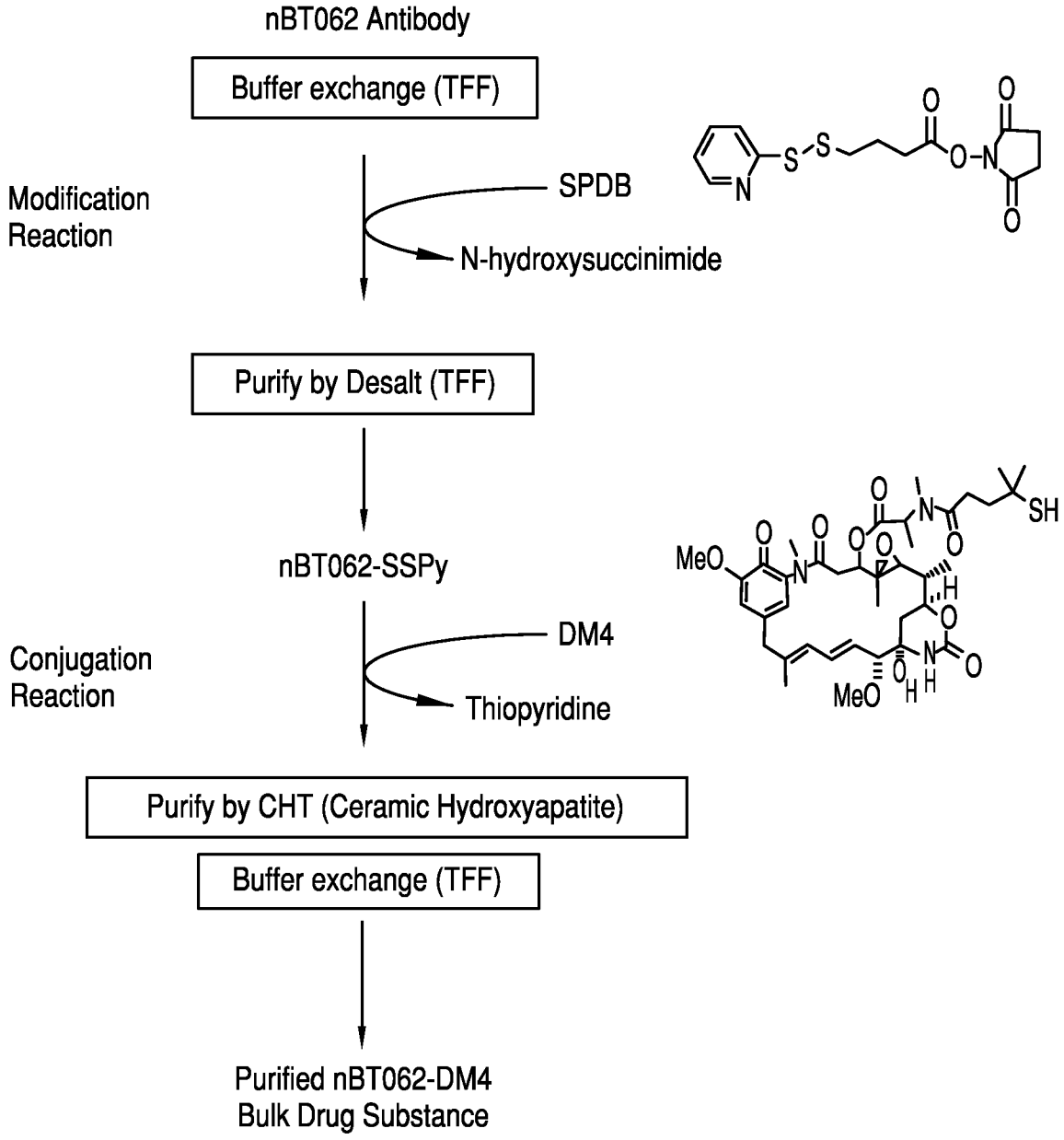

nBT062 Antibody
Buffer exchange (TFF)
Modification Reaction
SPDB
N-hydroxysuccinimide
Purify by Desalt (TFF)
nBT062-SSPy
Conjugation Reaction
DM4
Thiopyridine
Purify by CHT (Ceramic Hydroxyapatite)
Buffer exchange (TFF)
Purified nBT062-DM4
Bulk Drug Substance
MeO
SH

FIG. 5

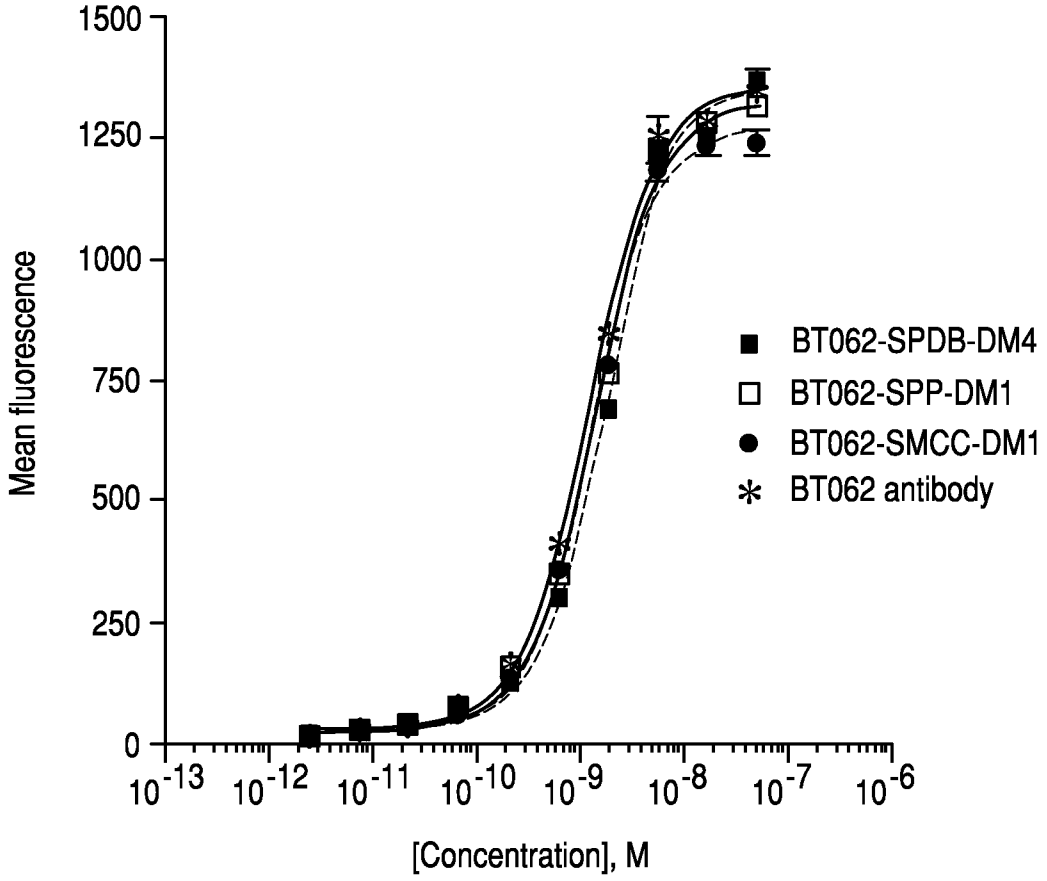

1500
1250
1000
750
500
250
0
Mean fluorescence
10-13
10-12
10-11
10-10
10-9
10-8
10-7
10-6
[Concentration], M
BT062-SPDB-DM4
BT062-SPP-DM1
BT062-SMCC-DM1
BT062 antibody

FIG. 6

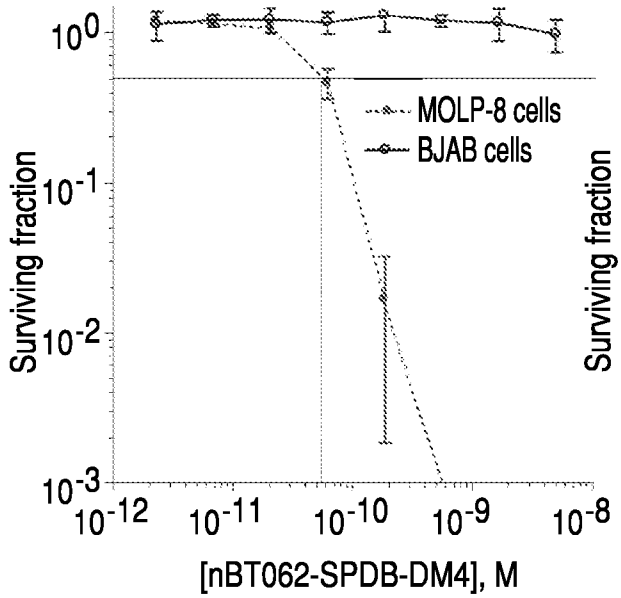


FIG. 7A

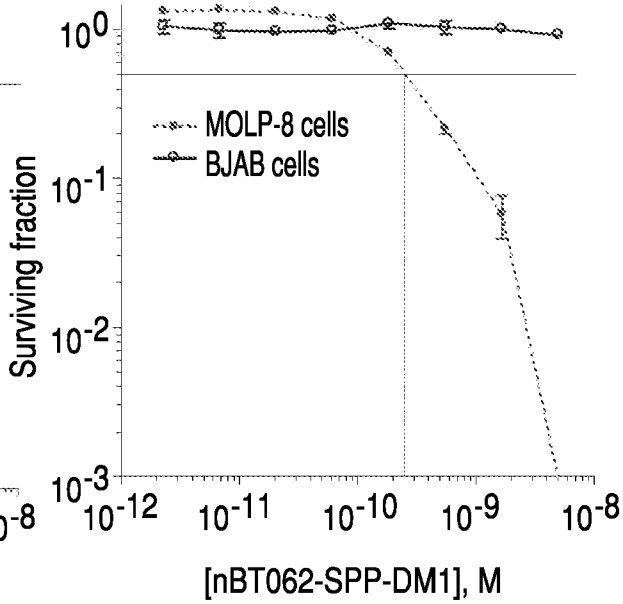


FIG. 7B

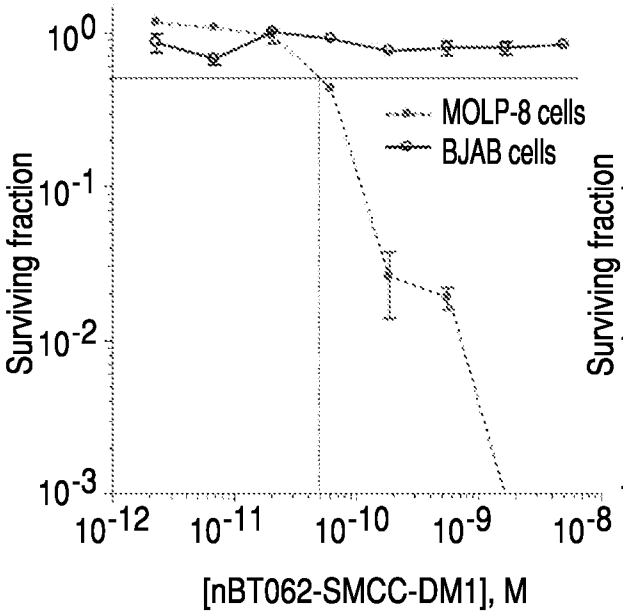


FIG. 7C

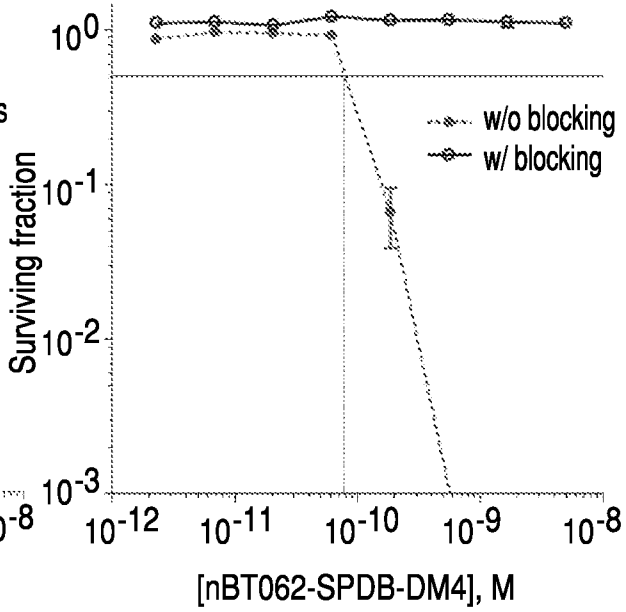


FIG. 7D

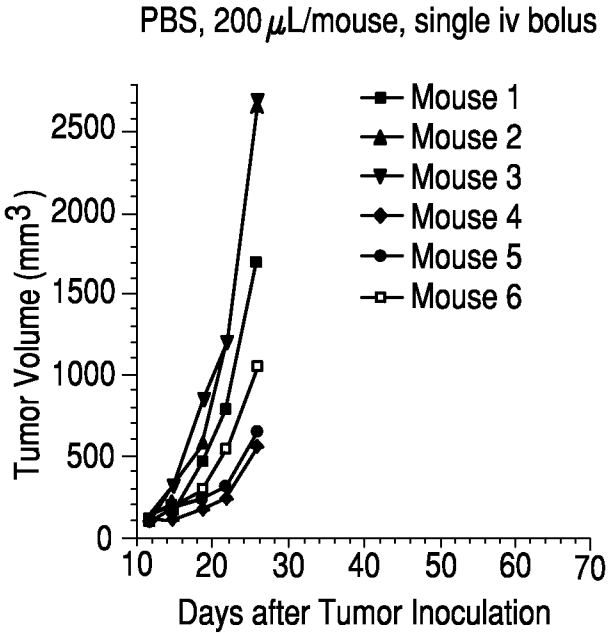


FIG. 8A

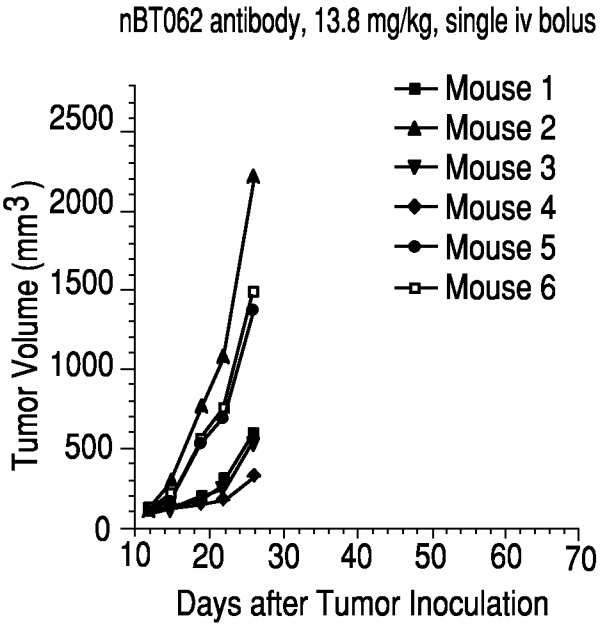


FIG. 8B

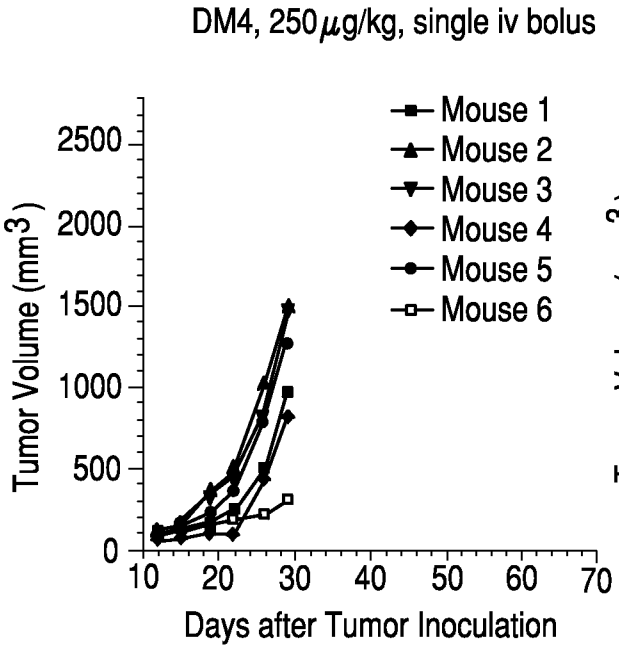


FIG. 8C

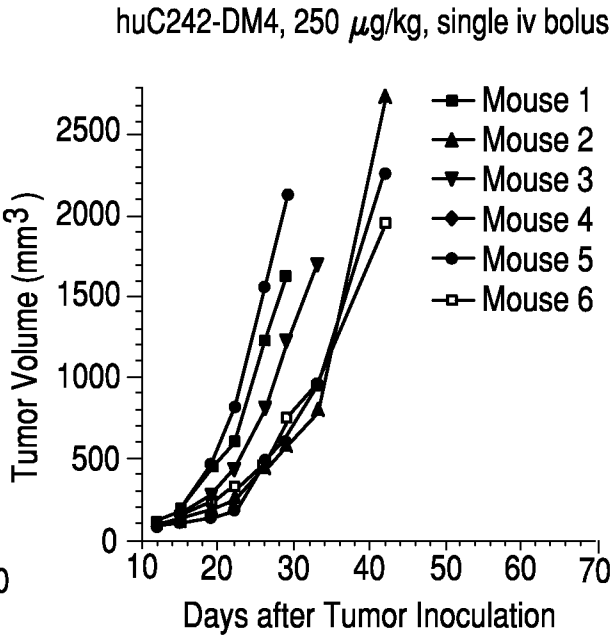


FIG. 8D

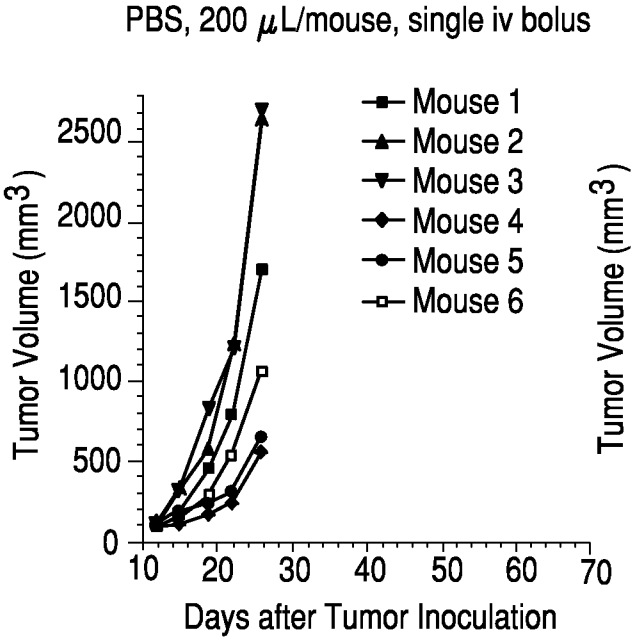


FIG. 9A

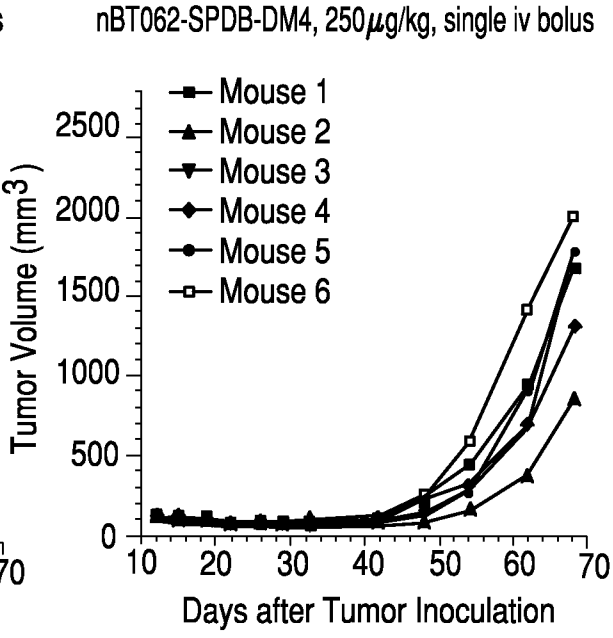


FIG. 9B

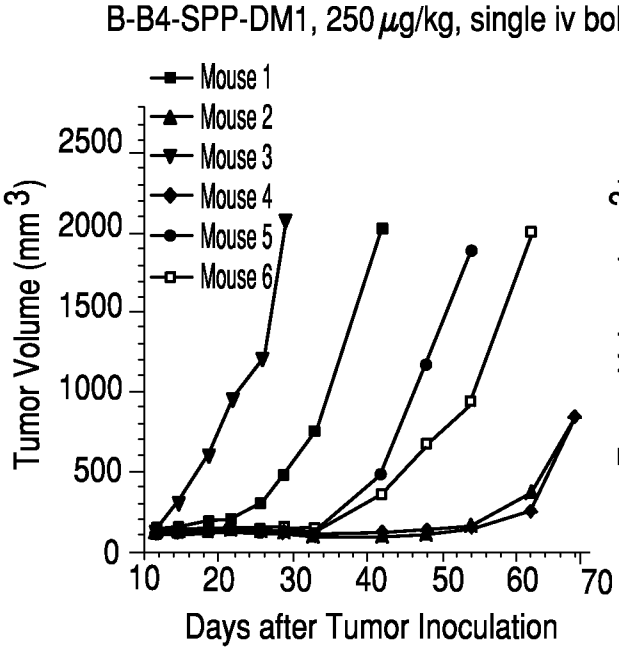


FIG. 9C

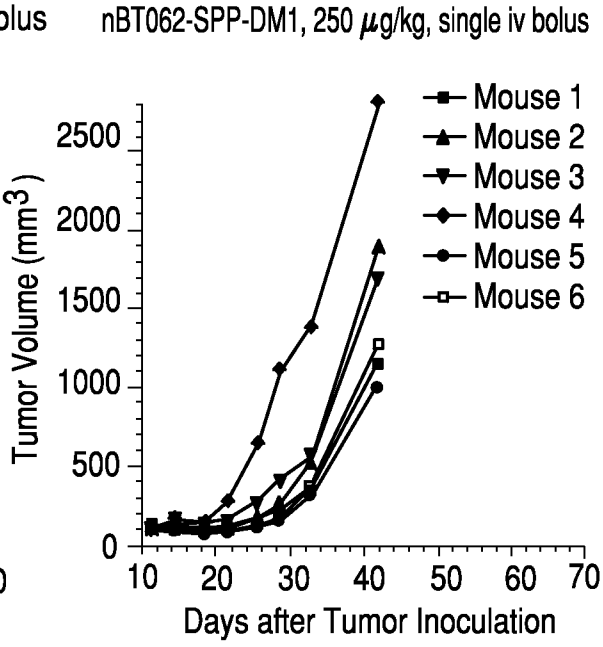


FIG. 9D

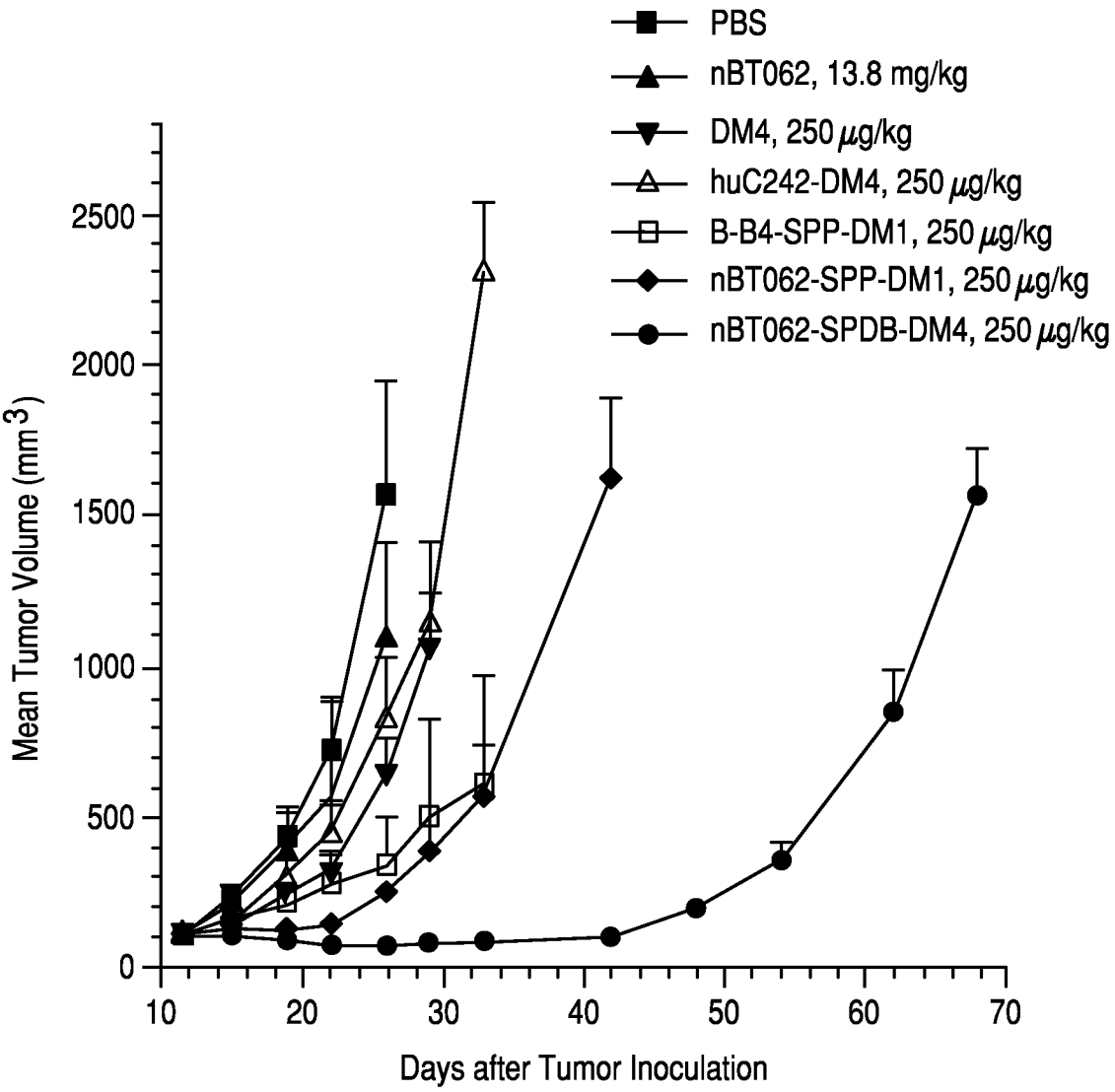

PBS
nBT062, 13.8 mg/kg
DM4, 250 μg/kg
huC242-DM4, 250 μg/kg
B-B4-SPP-DM1, 250 μg/kg
nBT062-SPP-DM1, 250 μg/kg
nBT062-SPDB-DM4, 250 μg/kg
Mean Tumor Volume (mm3)
0
500
1000
1500
2000
2500
10
20
30
40
50
60
70
Days after Tumor Inoculation

FIG. 10

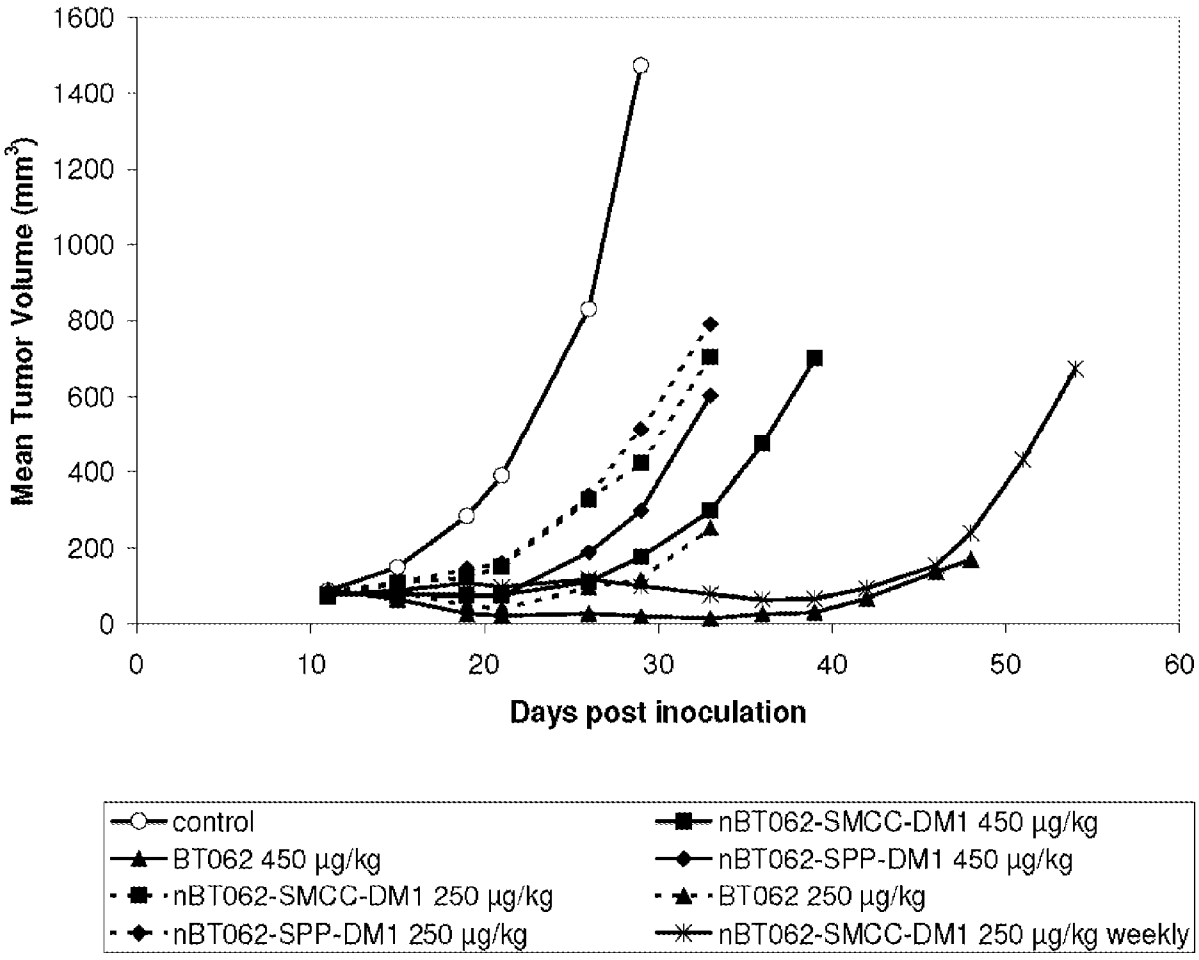

1600
1400
1200
1000
800
600
400
200
0
Mean Tumor Volume (mm3)
0
10
20
30
40
50
60
Days post inoculation
control
BT062 450 µg/kg
nBT062-SMCC-DM1 250 µg/kg
nBT062-SPP-DM1 250 µg/kg
nBT062-SMCC-DM1 450 µg/kg
nBT062-SPP-DM1 450 µg/kg
BT062 250 µg/kg
nBT062-SMCC-DM1 250 µg/kg weekly

FIG. 11A

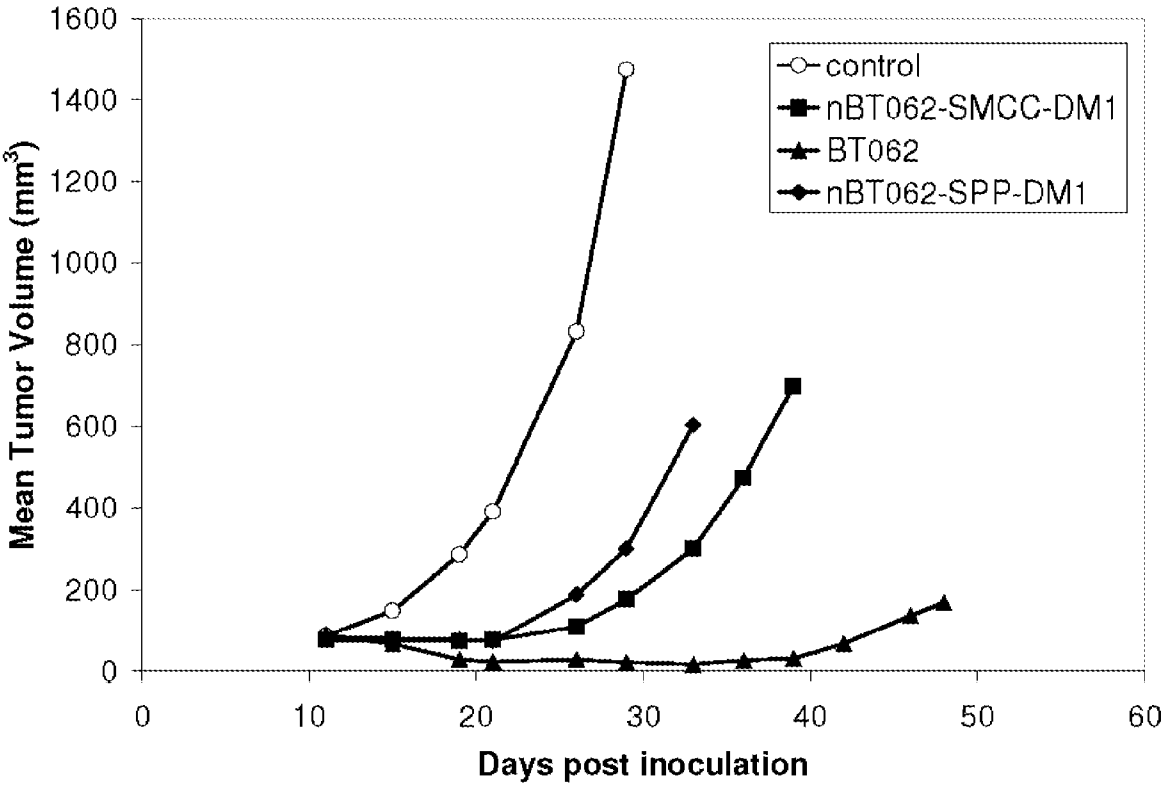

1600
1400
1200
1000
800
600
400
200
0
Mean Tumor Volume (mm3)
0
10
20
30
40
50
60
Days post inoculation
control
nBT062-SMCC-DM1
BT062
nBT062-SPP-DM1

FIG. 11B

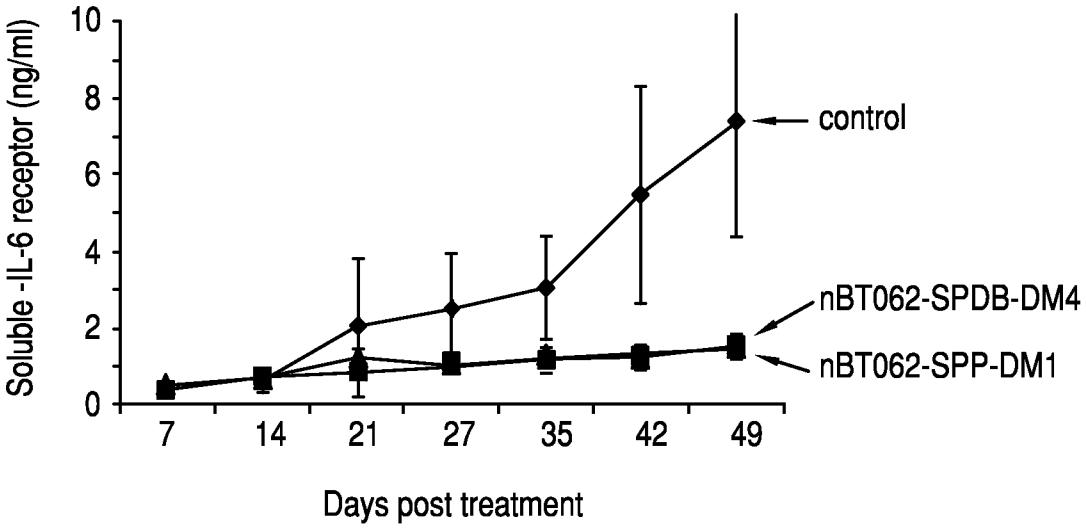

Soluble -IL-6 receptor (ng/ml)
10
8
6
4
2
0
7
14
21
27
35
42
49
Days post treatment
control
nBT062-SPDB-DM4
nBT062-SPP-DM1

FIG. 12

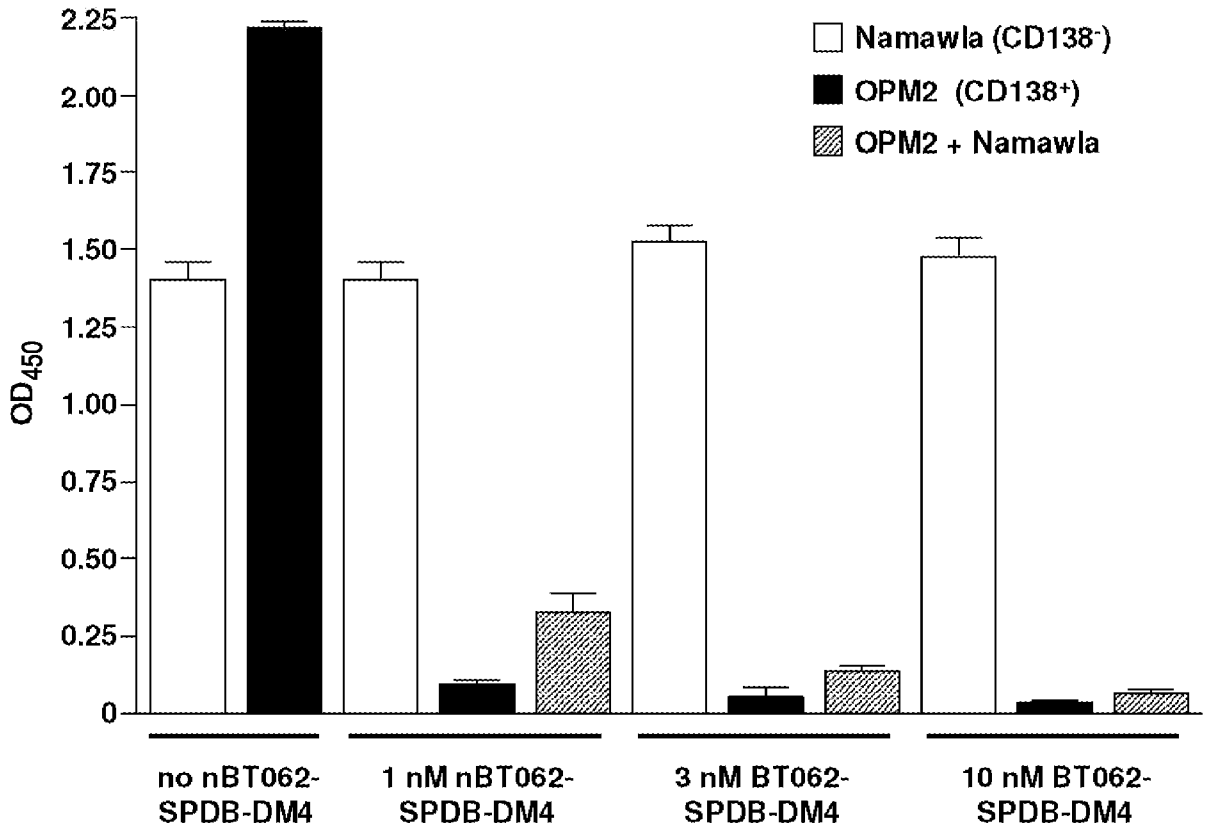
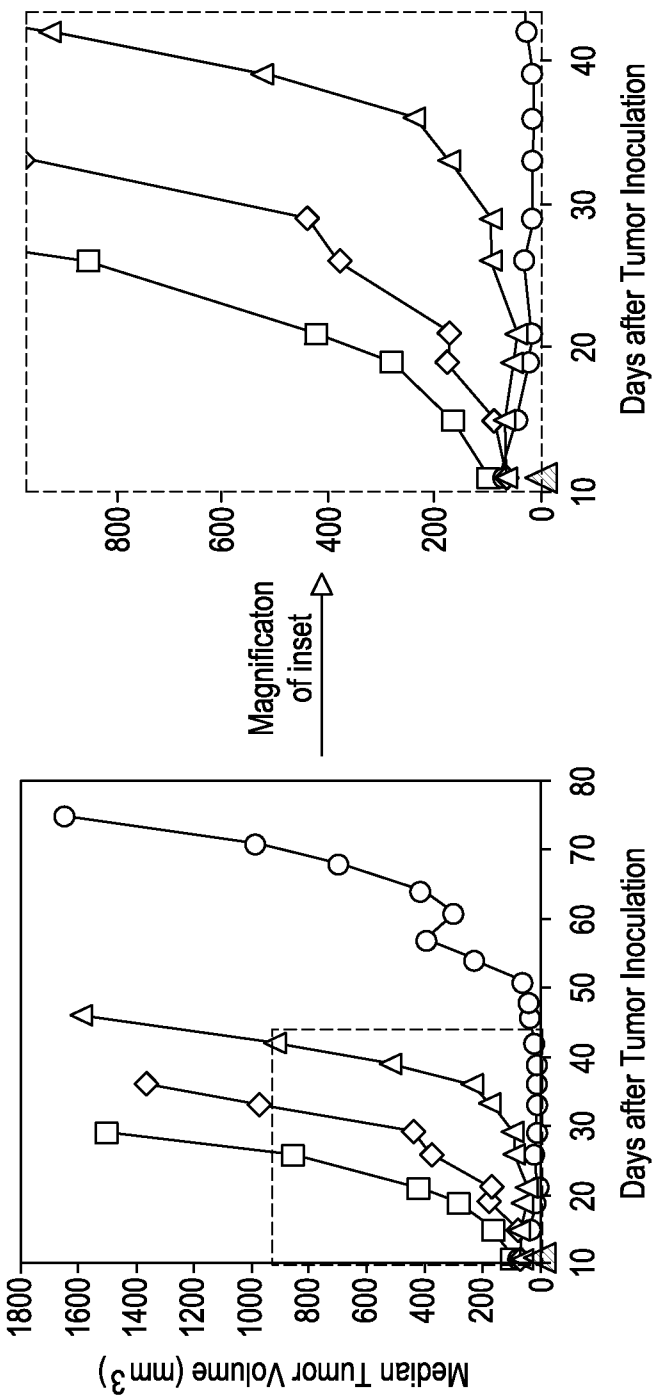

2.25
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0
OD450
Namawla (CD138-)
OPM2 (CD138+)
OPM2 + Namawla
no nBT062-SPDB-DM4
1 nM nBT062-SPDB-DM4
3 nM BT062-SPDB-DM4
10 nM BT062-SPDB-DM4

FIG. 13

FIG. 14


Median Tumor Volume (mm3)
1800
1600
1400
1200
1000
800
600
400
200
0
10
20
30
40
50
60
70
80
Days after Tumor Inoculation
Magnificaton of inset
800
600
400
200
0
10
20
30
40
Days after Tumor Inoculation
PBS
450 μg/kg*
250 μg/kg*
100 μg/kg*
Injection

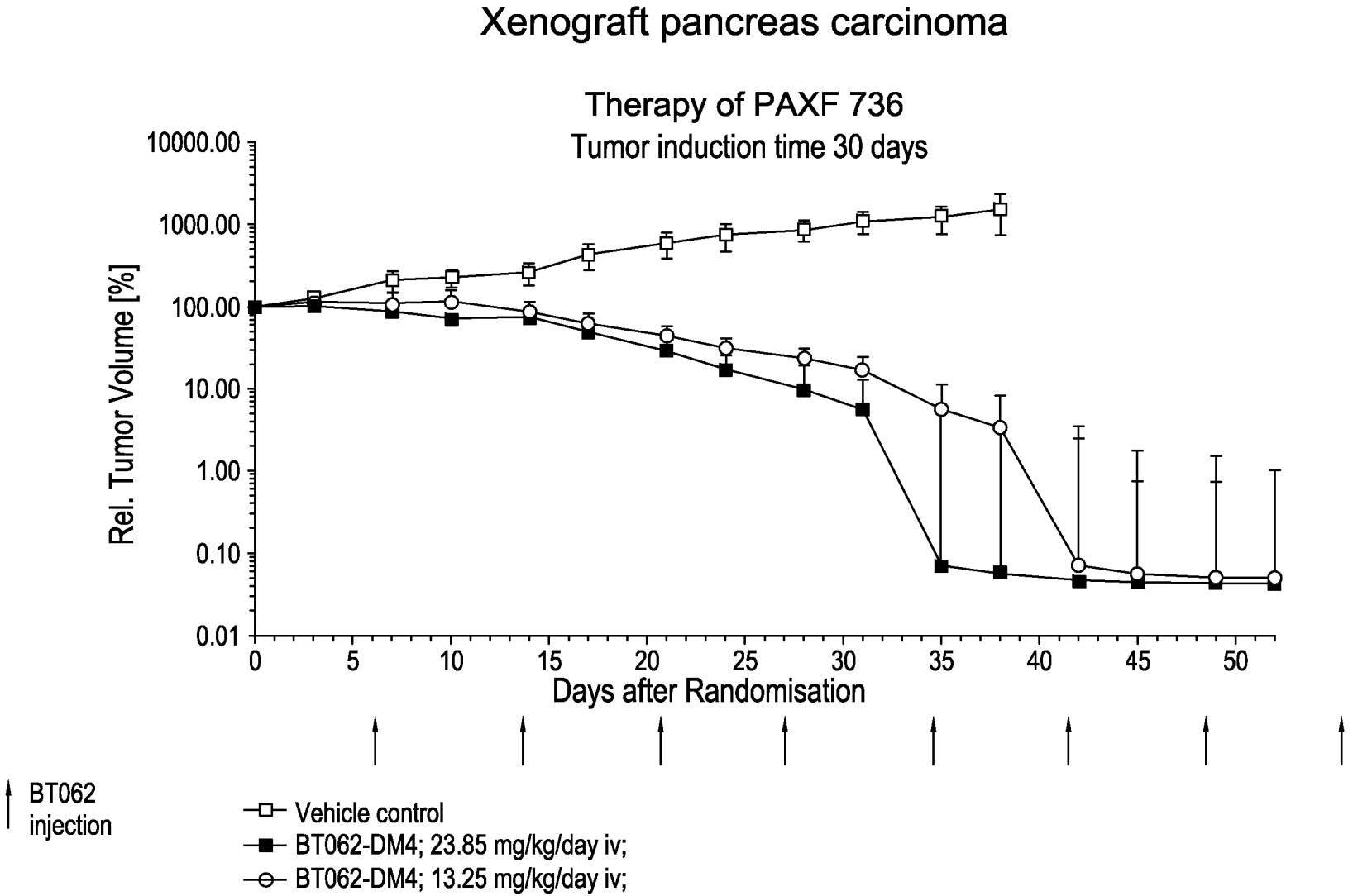

Xenograft pancreas carcinoma
Therapy of PAXF 736
Tumor induction time 30 days
Rel. Tumor Volume [%]
10000.00
1000.00
100.00
10.00
1.00
0.10
0.01
0
5
10
15
20
25
30
35
40
45
50
Days after Randomisation
BT062 injection
Vehicle control
BT062-DM4; 23.85 mg/kg/day iv;
BT062-DM4; 13.25 mg/kg/day iv;

FIG. 15

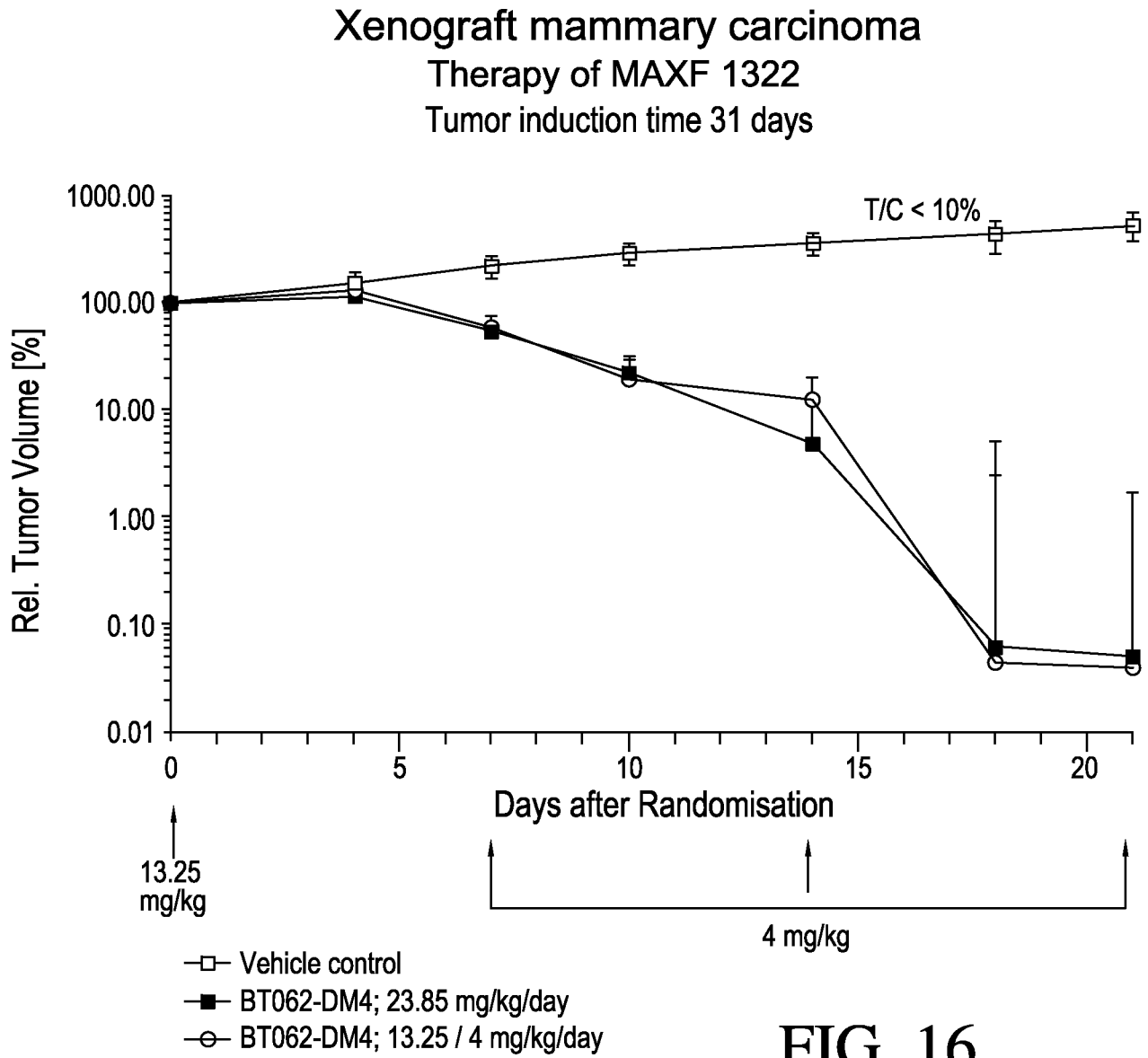

Xenograft mammary carcinoma
Therapy of MAXF 1322
Tumor induction time 31 days
Rel. Tumor Volume [%]
1000.00
100.00
10.00
1.00
0.10
0.01
T/C < 10%
0
5
10
15
20
Days after Randomisation
13.25
mg/kg
4 mg/kg
Vehicle control
BT062-DM4; 23.85 mg/kg/day
BT062-DM4; 13.25 / 4 mg/kg/day

FIG. 16

FIG. 17

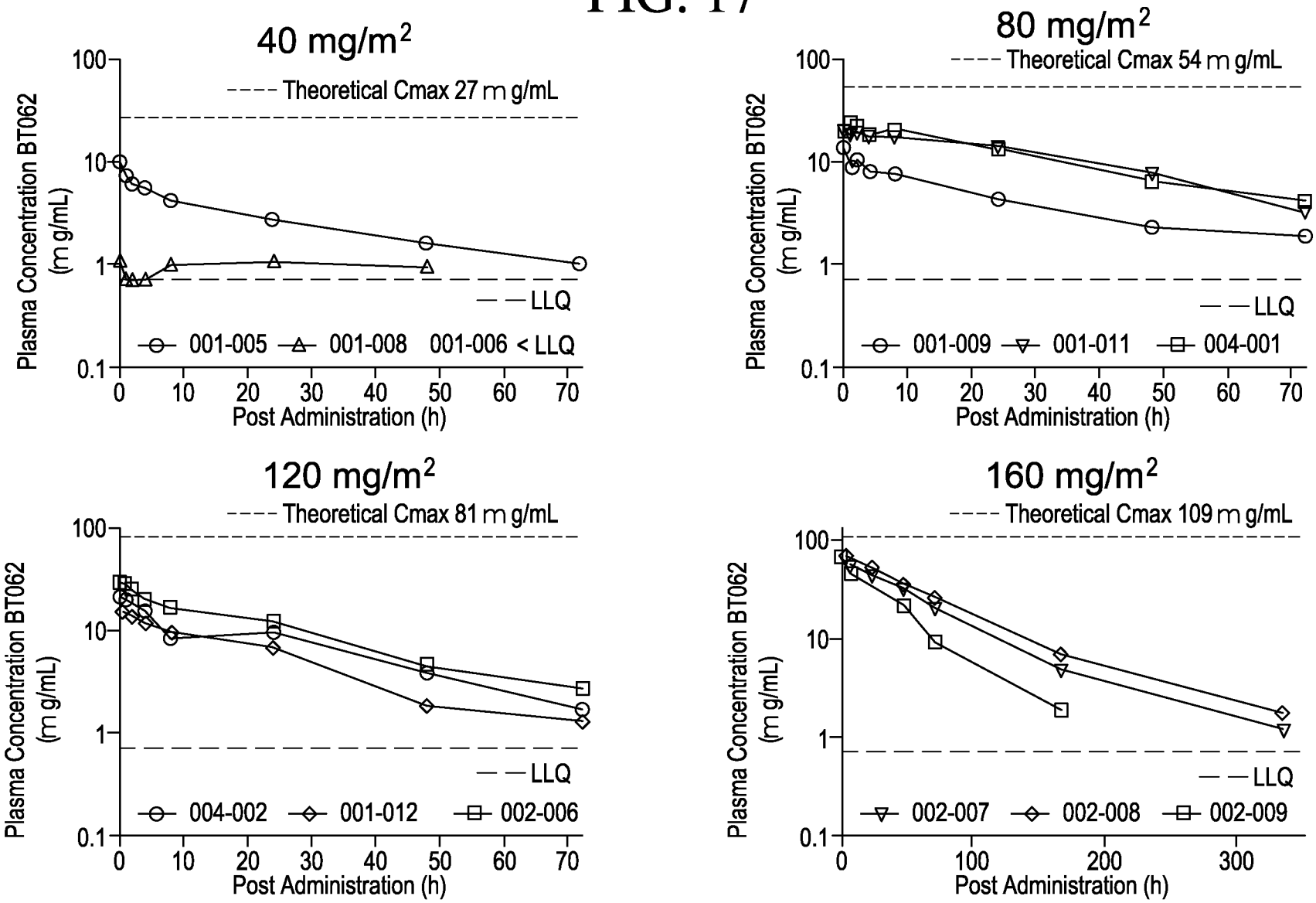

40 mg/m2
Theoretical Cmax 27 m g/mL
LLQ
001-005
001-008
001-006 < LLQ
80 mg/m2
Theoretical Cmax 54 m g/mL
LLQ
001-009
001-011
004-001
120 mg/m2
Theoretical Cmax 81 m g/mL
LLQ
004-002
001-012
002-006
160 mg/m2
Theoretical Cmax 109 m g/mL
LLQ
002-007
002-008
002-009
Plasma Concentration BT062 (m g/mL)
Post Administration (h)

FIG. 18

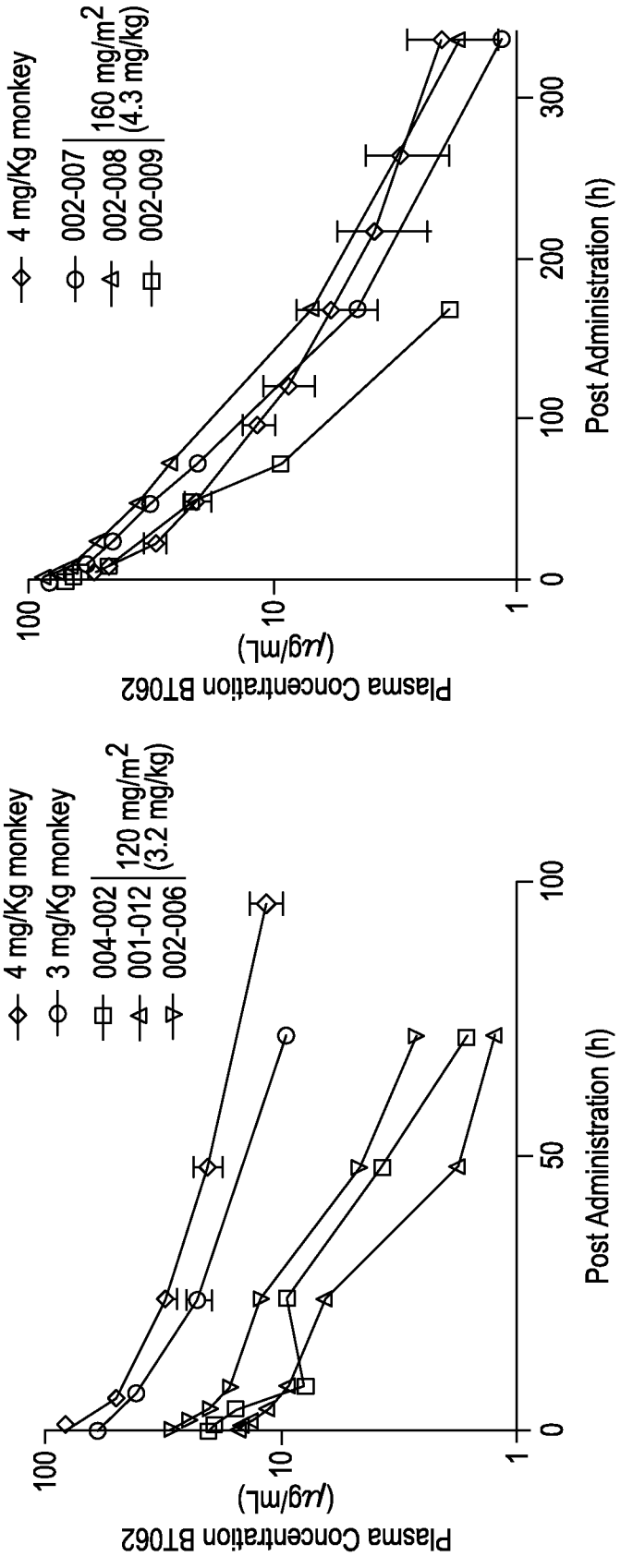

Plasma Concentration BT062
(μg/mL)
100
10
1
0
50
100
Post Administration (h)
4 mg/Kg monkey
3 mg/Kg monkey
004-002
001-012
002-006
120 mg/m2
(3.2 mg/kg)
Plasma Concentration BT062
(μg/mL)
100
10
1
0
100
200
300
Post Administration (h)
4 mg/Kg monkey
002-007
002-008
002-009
160 mg/m2
(4.3 mg/kg)

FIG. 19

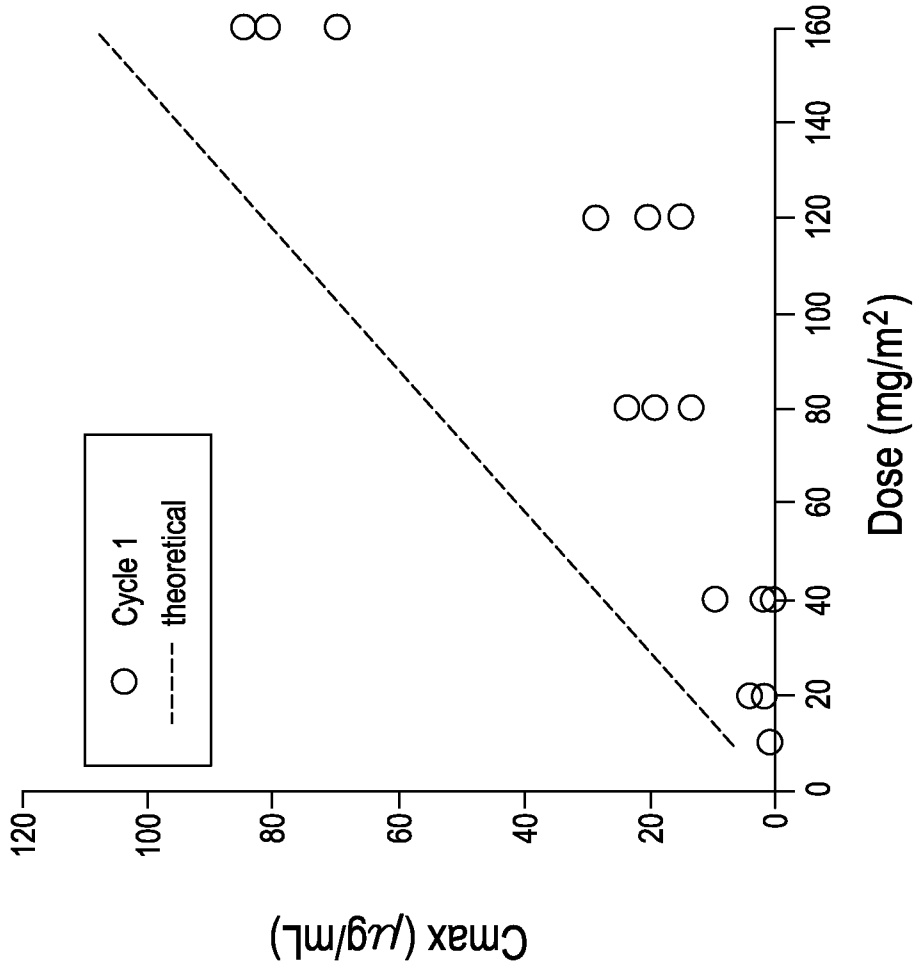

Cmax (μg/mL)
Dose (mg/m²)
Cycle 1
theoretical
0
20
40
60
80
100
120
140
160

FIG. 20

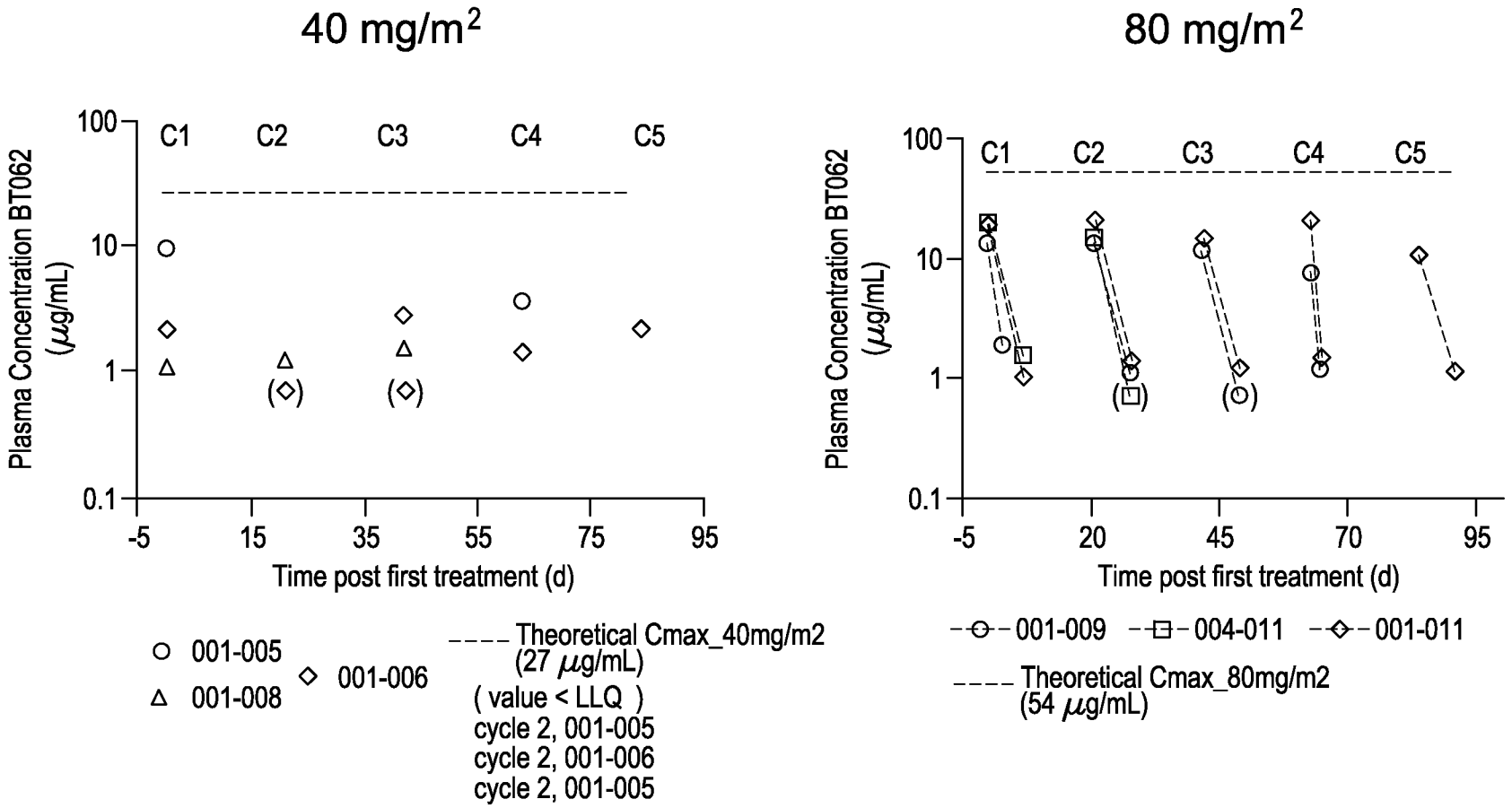

40 mg/m2
80 mg/m2
Plasma Concentration BT062 (μg/mL)
100
10
1
0.1
C1
C2
C3
C4
C5
-5
15
35
55
75
95
20
45
70
Time post first treatment (d)
001-005
001-006
001-008
001-009
004-011
001-011
Theoretical Cmax_40mg/m2 (27 μg/mL)
Theoretical Cmax_80mg/m2 (54 μg/mL)
(value < LLQ)
cycle 2, 001-005
cycle 2, 001-006
cycle 2, 001-005

FIG. 21

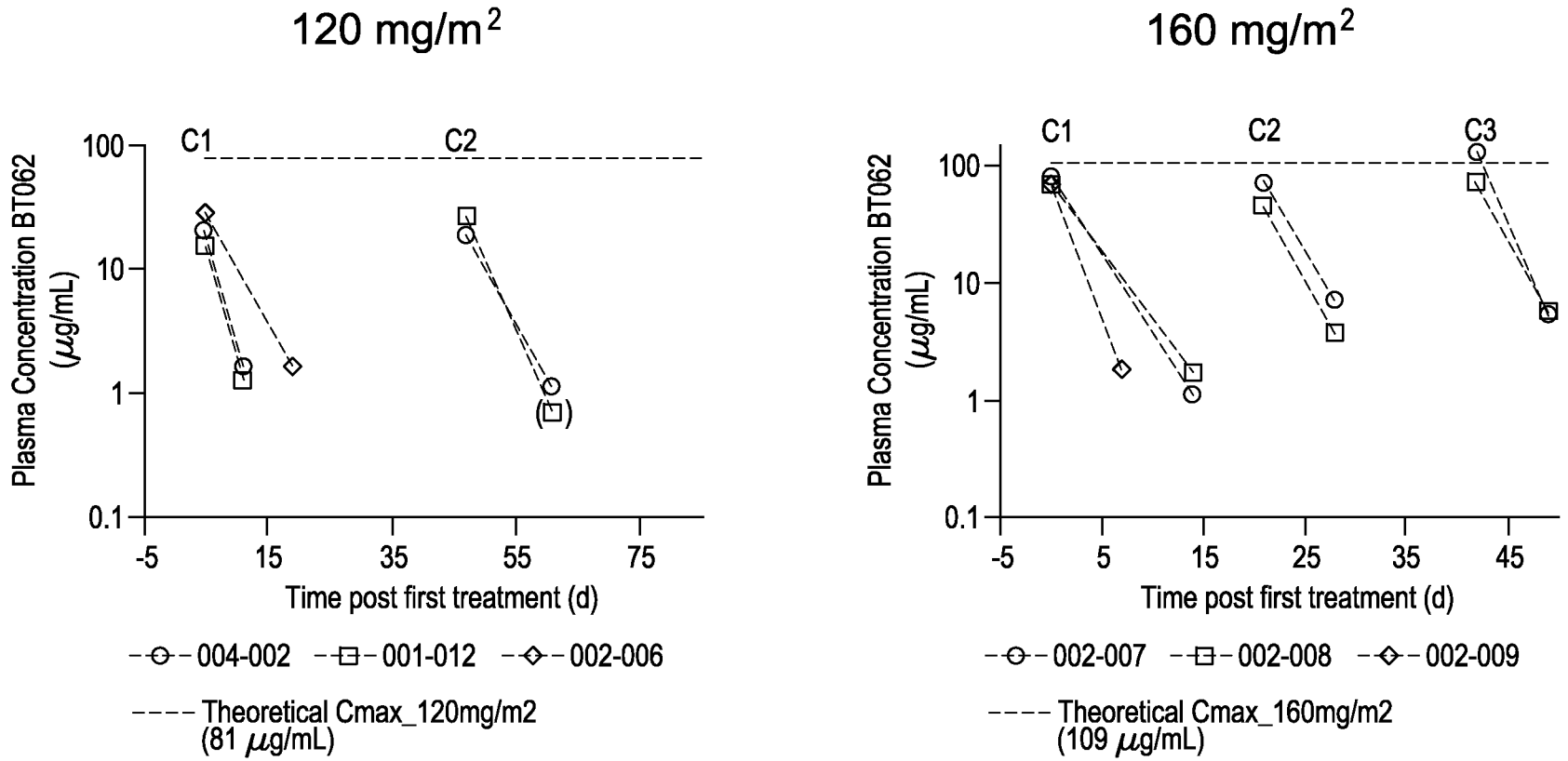

120 mg/m2
160 mg/m2
Plasma Concentration BT062 (μg/mL)
Time post first treatment (d)
C1
C2
C3
004-002
001-012
002-006
002-007
002-008
002-009
Theoretical Cmax_120mg/m2 (81 μg/mL)
Theoretical Cmax_160mg/m2 (109 μg/mL)

FIG. 22

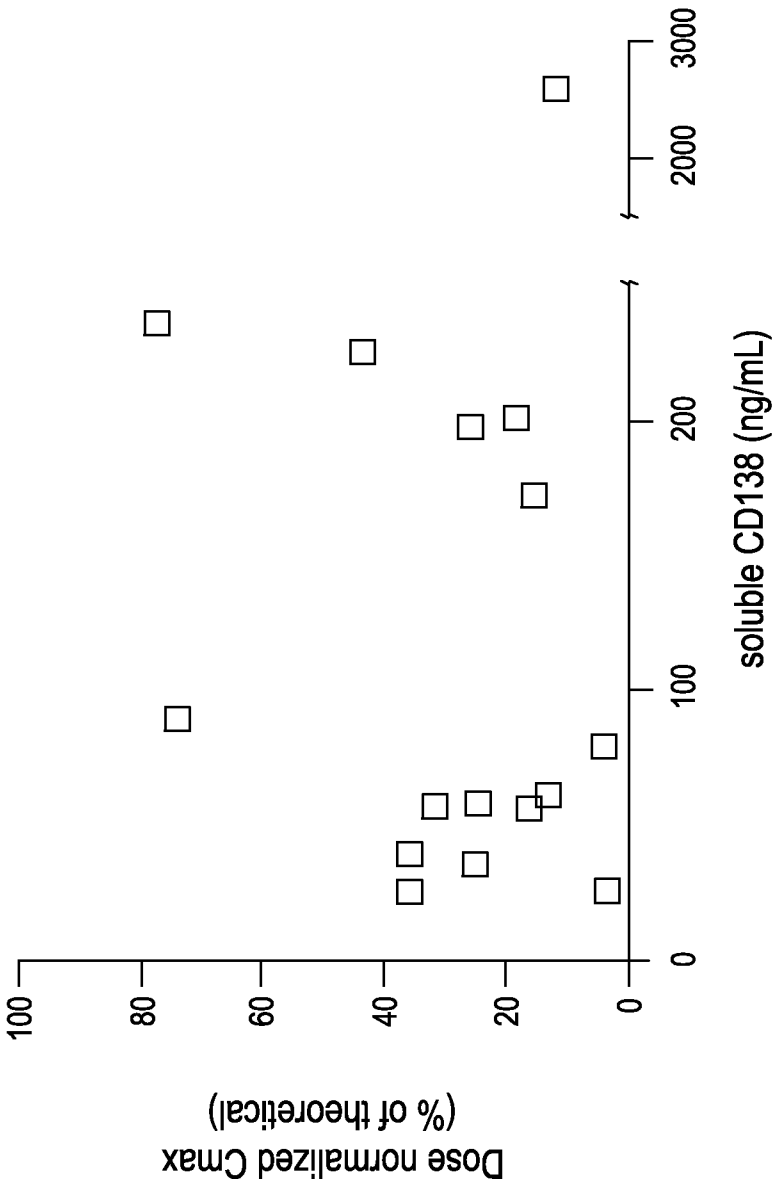
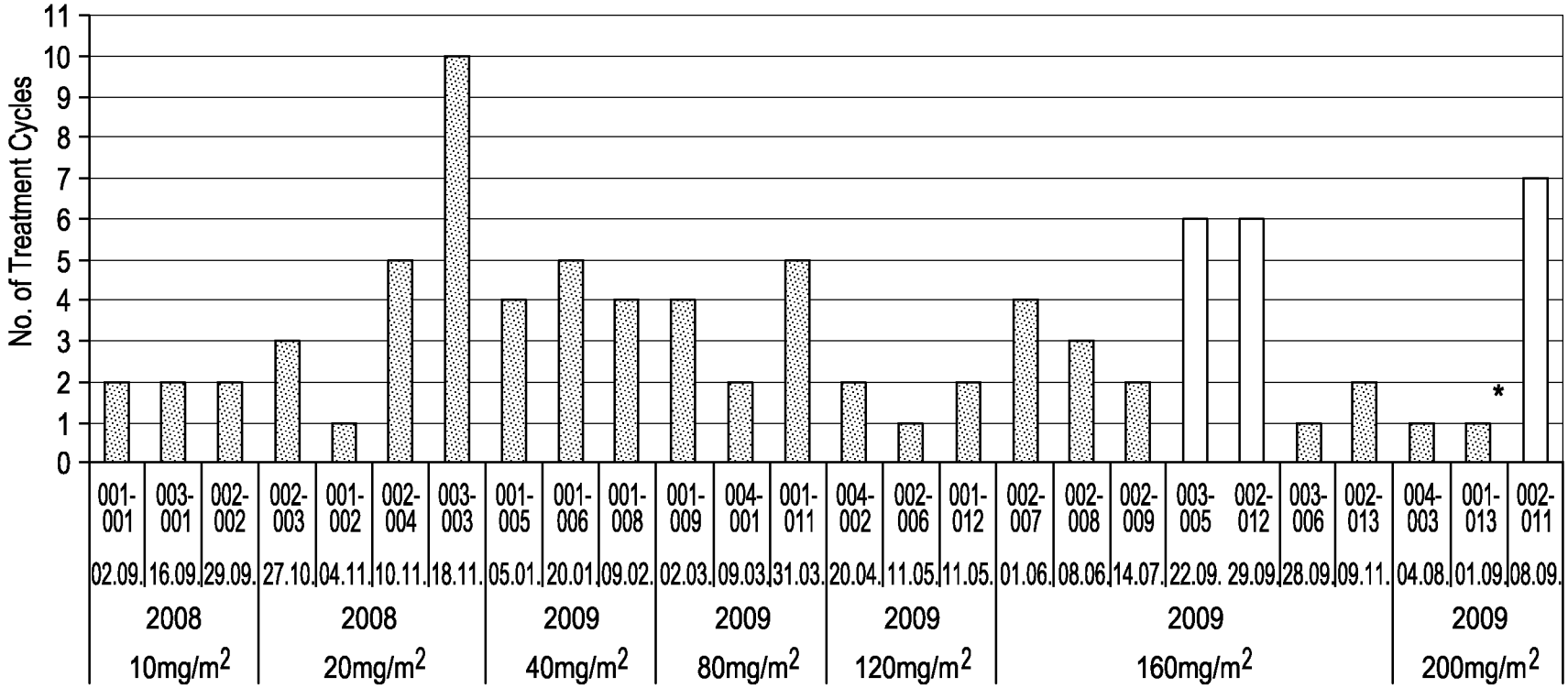

Dose normalized Cmax
(% of theoretical)
100
80
60
40
20
0
0
100
200
2000
3000
soluble CD138 (ng/mL)

FIG. 23



* = subject 02-011 received first dose at 200 mg/m^2 and all doses after 1 cycle at 160 mg/m^2

FIG. 24

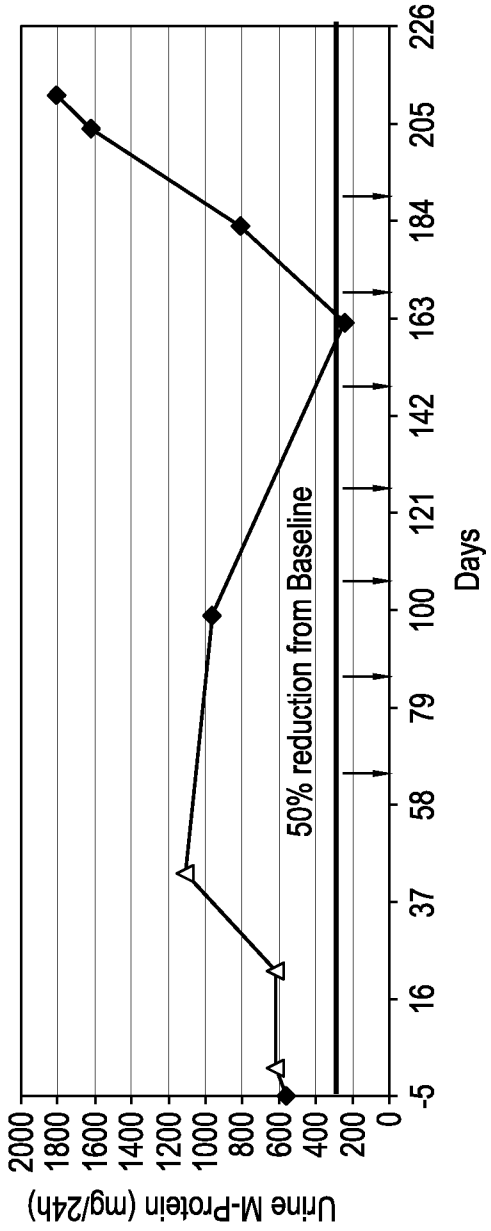

Urine M-Protein
Urine M-Protein (mg/24h)
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-5
16
37
58
79
100
121
142
163
184
205
226
Days
50% reduction from Baseline
= Treatment
=Sample
=Sample & Treatment

FIG. 25

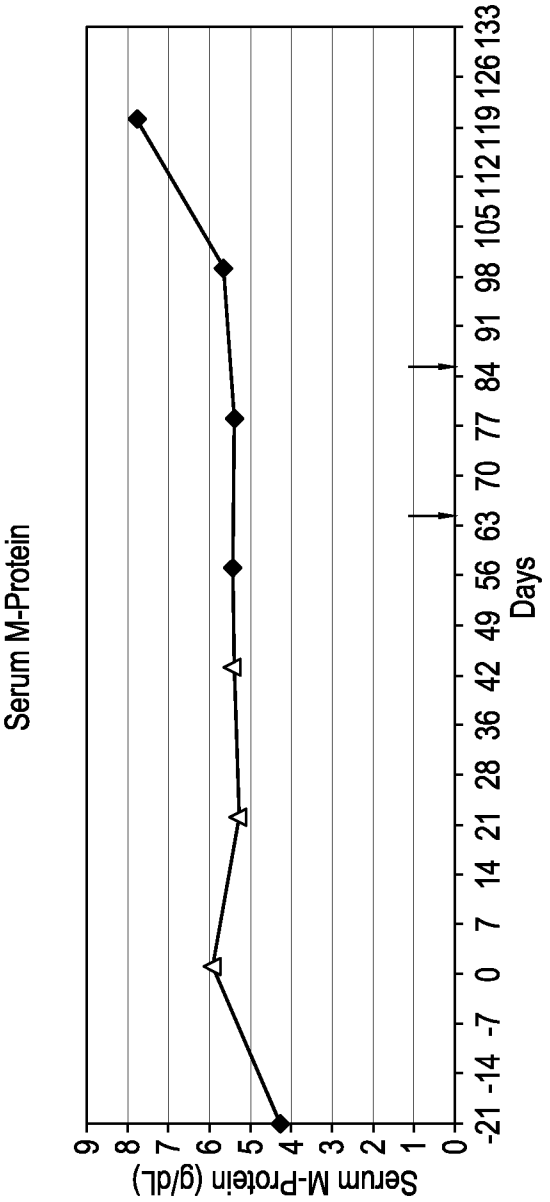

Serum M-Protein
Serum M-Protein (g/dL)
0
1
2
3
4
5
6
7
8
9
-21 -14 -7 0 7 14 21 28 36 42 49 56 63 70 77 84 91 98 105 112 119 126 133
Days
= Treatment
=Sample
=Sample & Treatment

FIG. 26

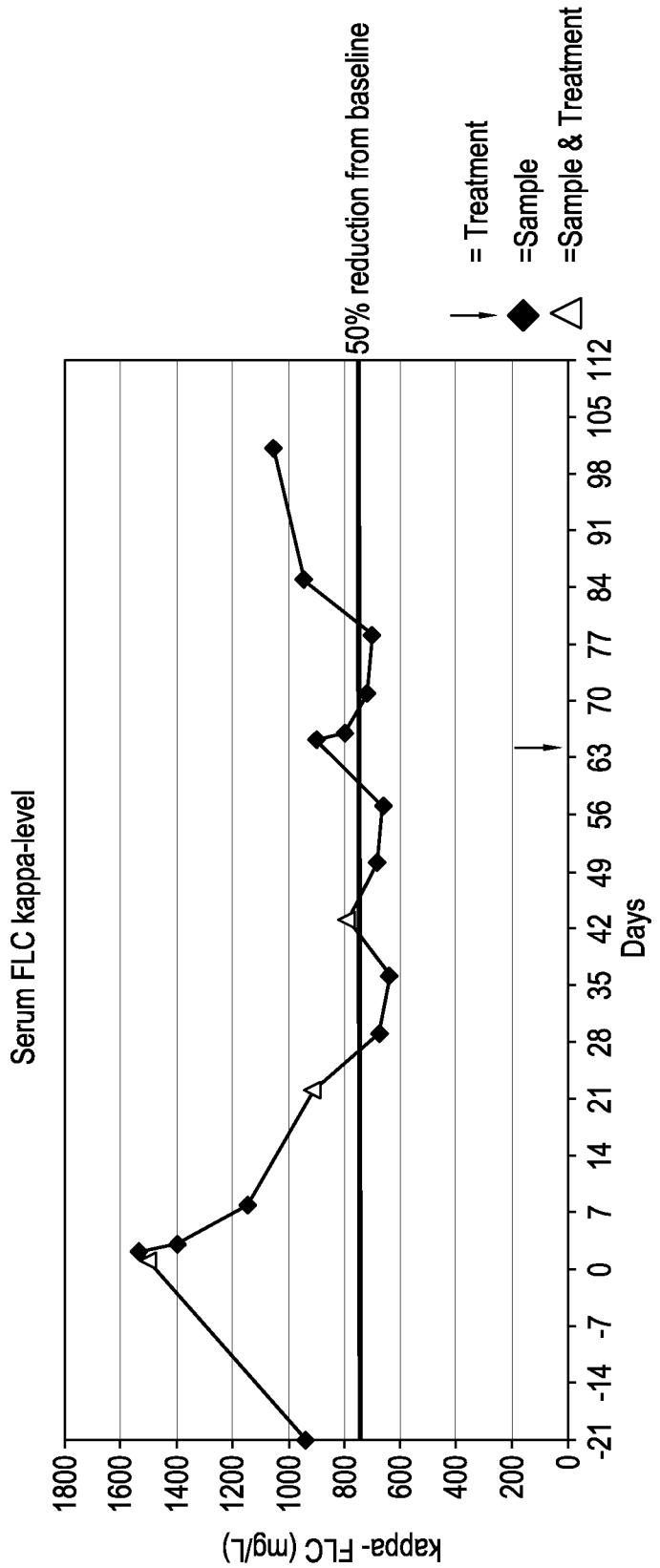
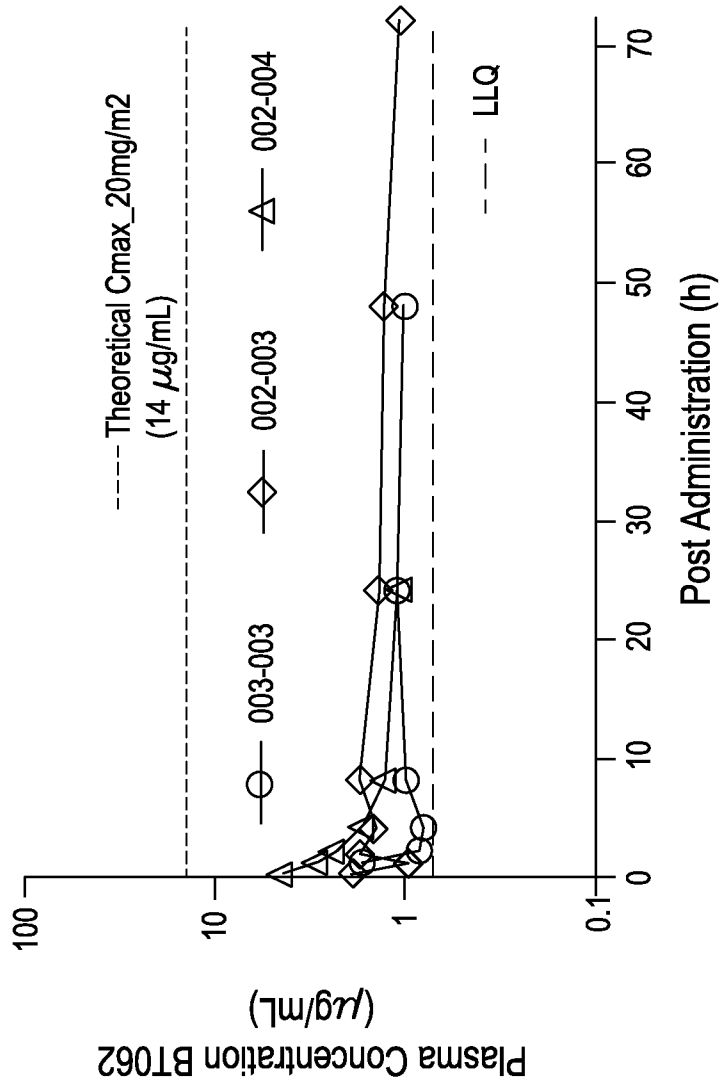

Serum FLC kappa-level
kappa- FLC (mg/L)
1800
1600
1400
1200
1000
800
600
400
200
0
-21 -14 -7 0 7 14 21 28 35 42 49 56 63 70 77 84 91 98 105 112
Days
50% reduction from baseline
= Treatment
=Sample
=Sample & Treatment

FIG. 27


Plasma Concentration BT062
(μg/mL)
100
10
1
0.1
0
10
20
30
40
50
60
70
Post Administration (h)
Theoretical Cmax_20mg/m2
(14 μg/mL)
003-003
002-003
002-004
LLQ

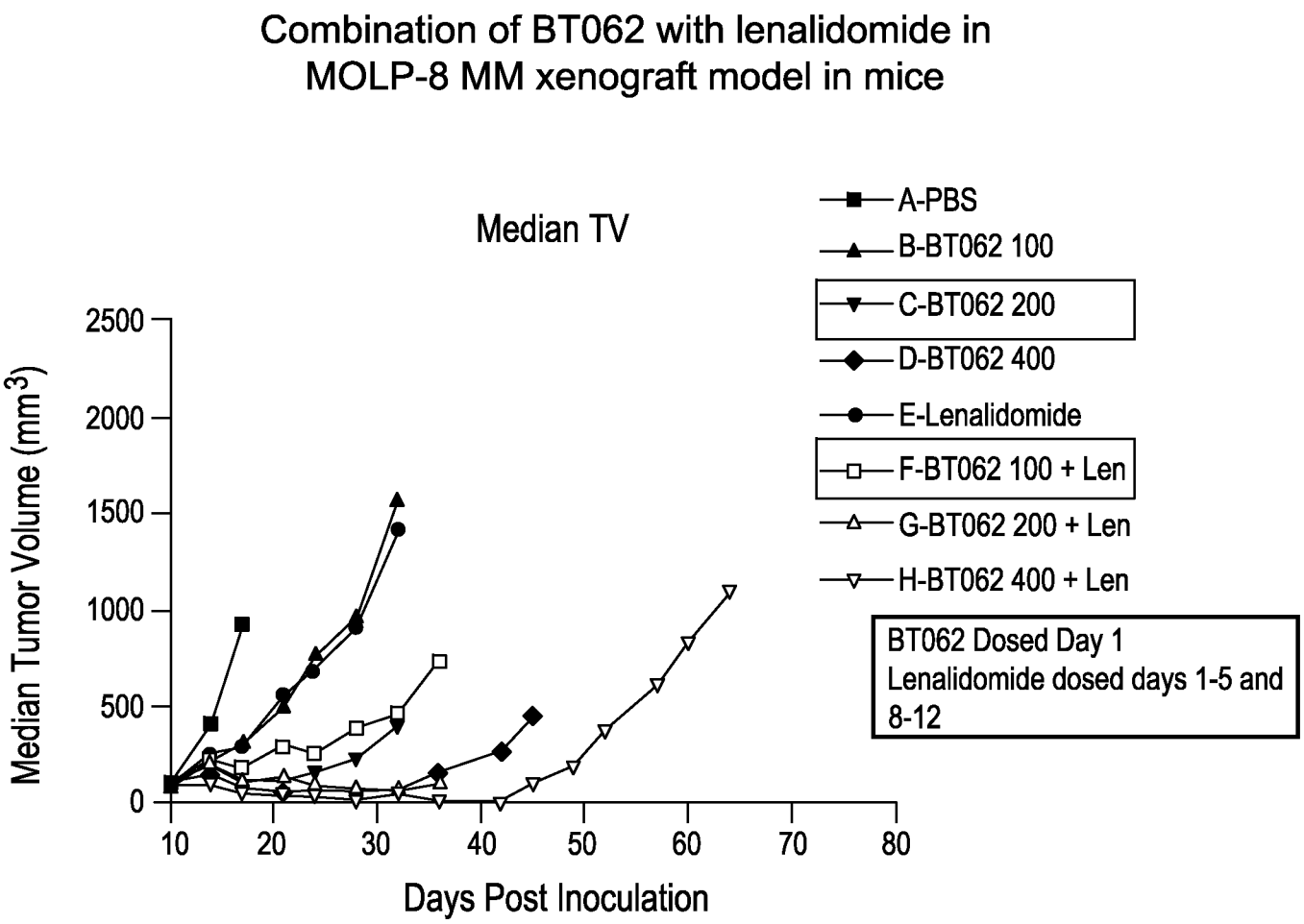

Combination of BT062 with lenalidomide in
MOLP-8 MM xenograft model in mice
Median TV
Median Tumor Volume (mm3)
2500
2000
1500
1000
500
0
10
20
30
40
50
60
70
80
Days Post Inoculation
A-PBS
B-BT062 100
C-BT062 200
D-BT062 400
E-Lenalidomide
F-BT062 100 + Len
G-BT062 200 + Len
H-BT062 400 + Len
BT062 Dosed Day 1
Lenalidomide dosed days 1-5 and
8-12

FIG. 28

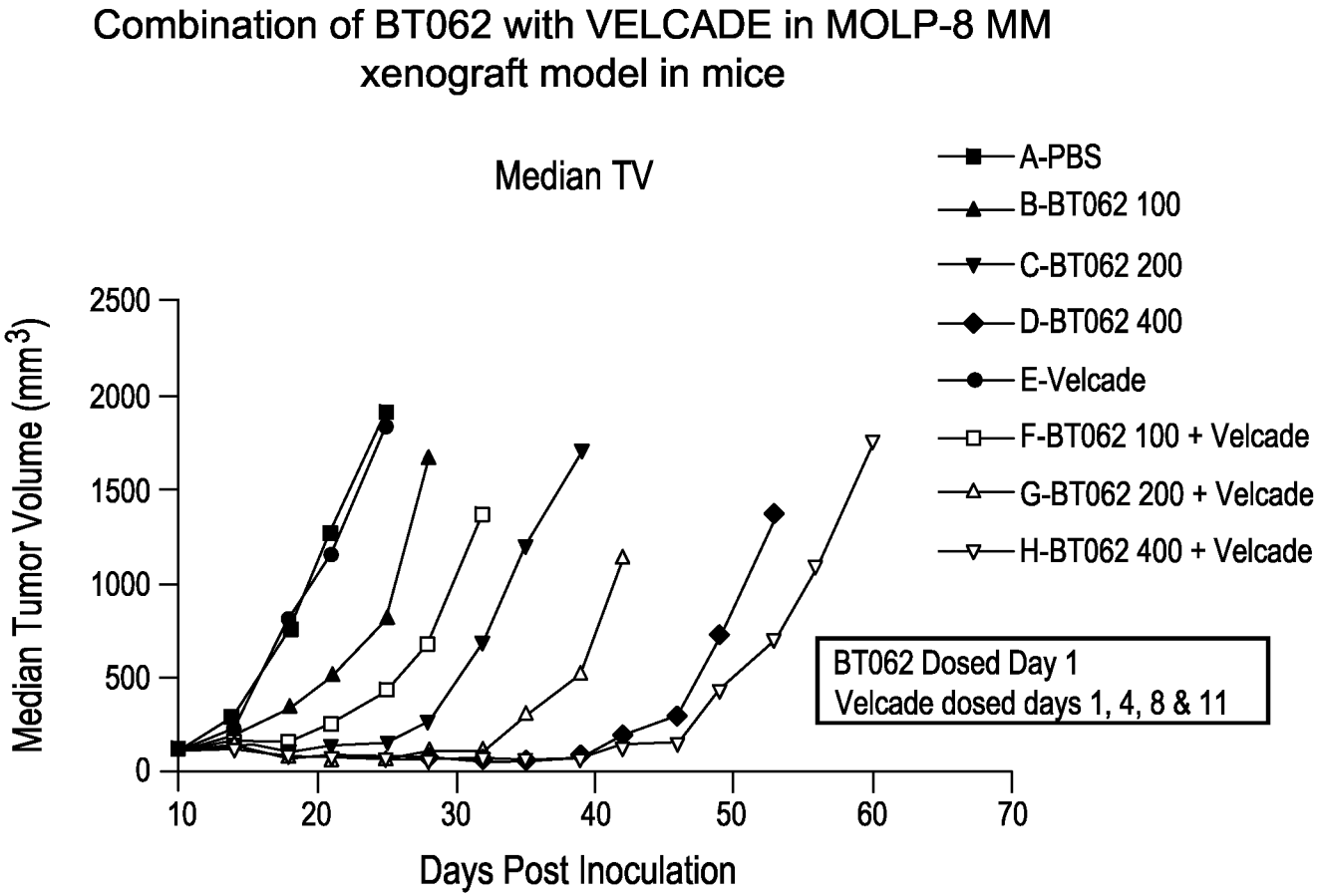

Combination of BT062 with VELCADE in MOLP-8 MM xenograft model in mice
Median TV
Median Tumor Volume (mm3)
2500
2000
1500
1000
500
0
10
20
30
40
50
60
70
Days Post Inoculation
A-PBS
B-BT062 100
C-BT062 200
D-BT062 400
E-Velcade
F-BT062 100 + Velcade
G-BT062 200 + Velcade
H-BT062 400 + Velcade
BT062 Dosed Day 1
Velcade dosed days 1, 4, 8 & 11

FIG. 29

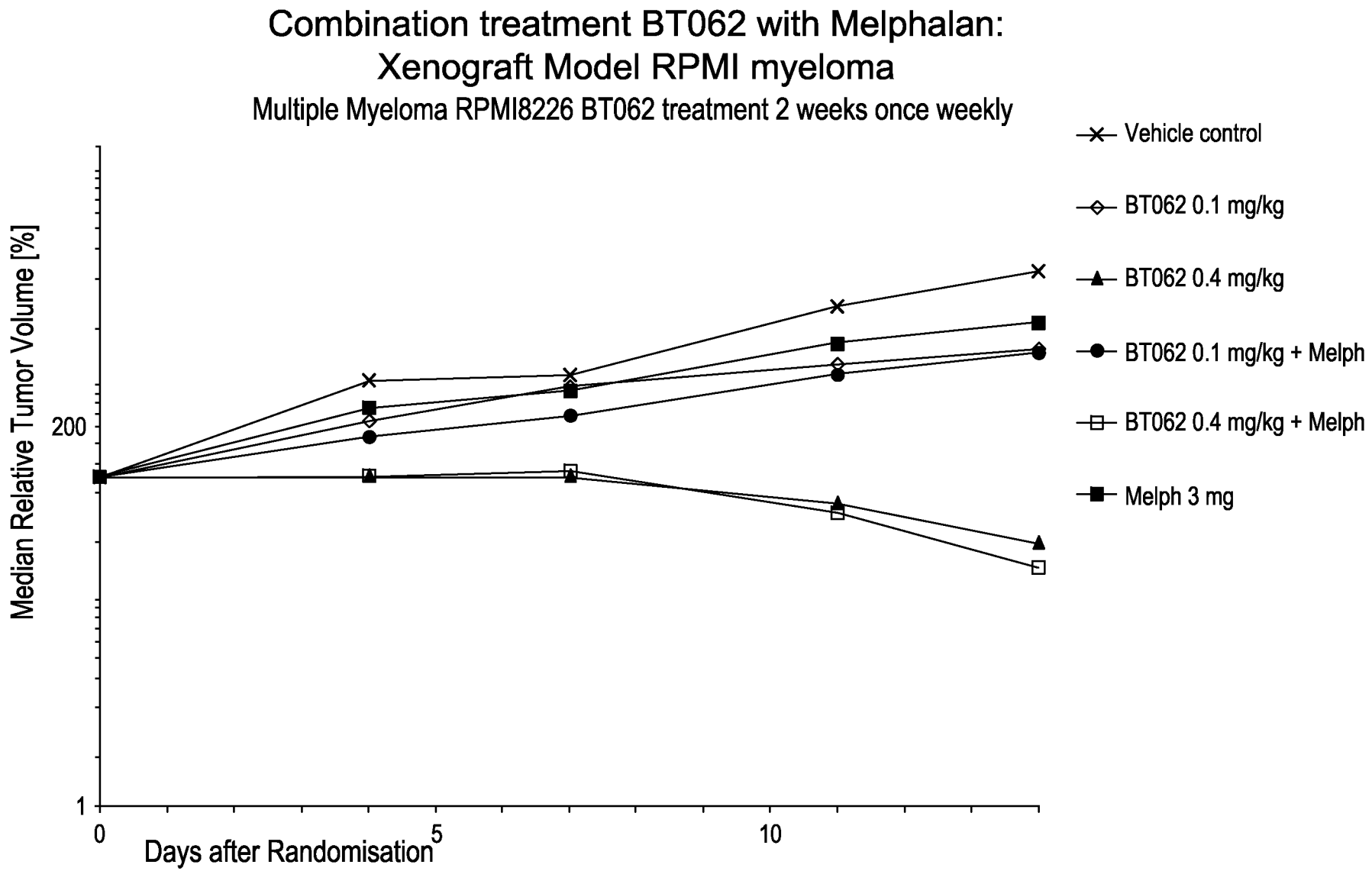

Combination treatment BT062 with Melphalan:
Xenograft Model RPMI myeloma
Multiple Myeloma RPMI8226 BT062 treatment 2 weeks once weekly
Median Relative Tumor Volume [%]
200
1
0
5
10
Days after Randomisation
Vehicle control
BT062 0.1 mg/kg
BT062 0.4 mg/kg
BT062 0.1 mg/kg + Melph
BT062 0.4 mg/kg + Melph
Melph 3 mg

FIG. 30

SEQUENCE LISTING

<110> Biotest AG
<110> ImmunoGen Inc

<120> Uses of Immunoconjugates Targeting CD138

<130> 324215.WO/JND/CJS

<150> US 61/176,069
<151> 2009-05-06

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Ser Val Lys Ile Ser Cys Lys Ala Thr Gly Tyr Thr Phe Ser Asn Tyr
            20                  25                  30

Trp Ile Glu Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp Ile
        35                  40                  45

Gly Glu Ile Leu Pro Gly Thr Gly Arg Thr Ile Tyr Asn Glu Lys Phe
    50                  55                  60

Lys Gly Lys Ala Thr Phe Thr Ala Asp Ile Ser Ser Asn Thr Val Gln
65                  70                  75                  80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Arg Asp Tyr Tyr Gly Asn Phe Tyr Tyr Ala Met Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175
```

```
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190

Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr
    210                 215                 220

Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro
225                 230                 235                 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
                245                 250                 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp
            260                 265                 270

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
        275                 280                 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val
    290                 295                 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305                 310                 315                 320

Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
                325                 330                 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
            340                 345                 350

Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
        355                 360                 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
    370                 375                 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385                 390                 395                 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys
                405                 410                 415

Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
            420                 425                 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
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Asp Arg Val Thr Ile Ser Cys Ser Ala Ser Gln Gly Ile Asn Asn Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Glu Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Pro
65                  70                  75                  80

Glu Asp Ile Gly Thr Tyr Tyr Cys Gln Gln Tyr Ser Lys Leu Pro Arg
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205

Phe Asn Arg Gly Glu Cys
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