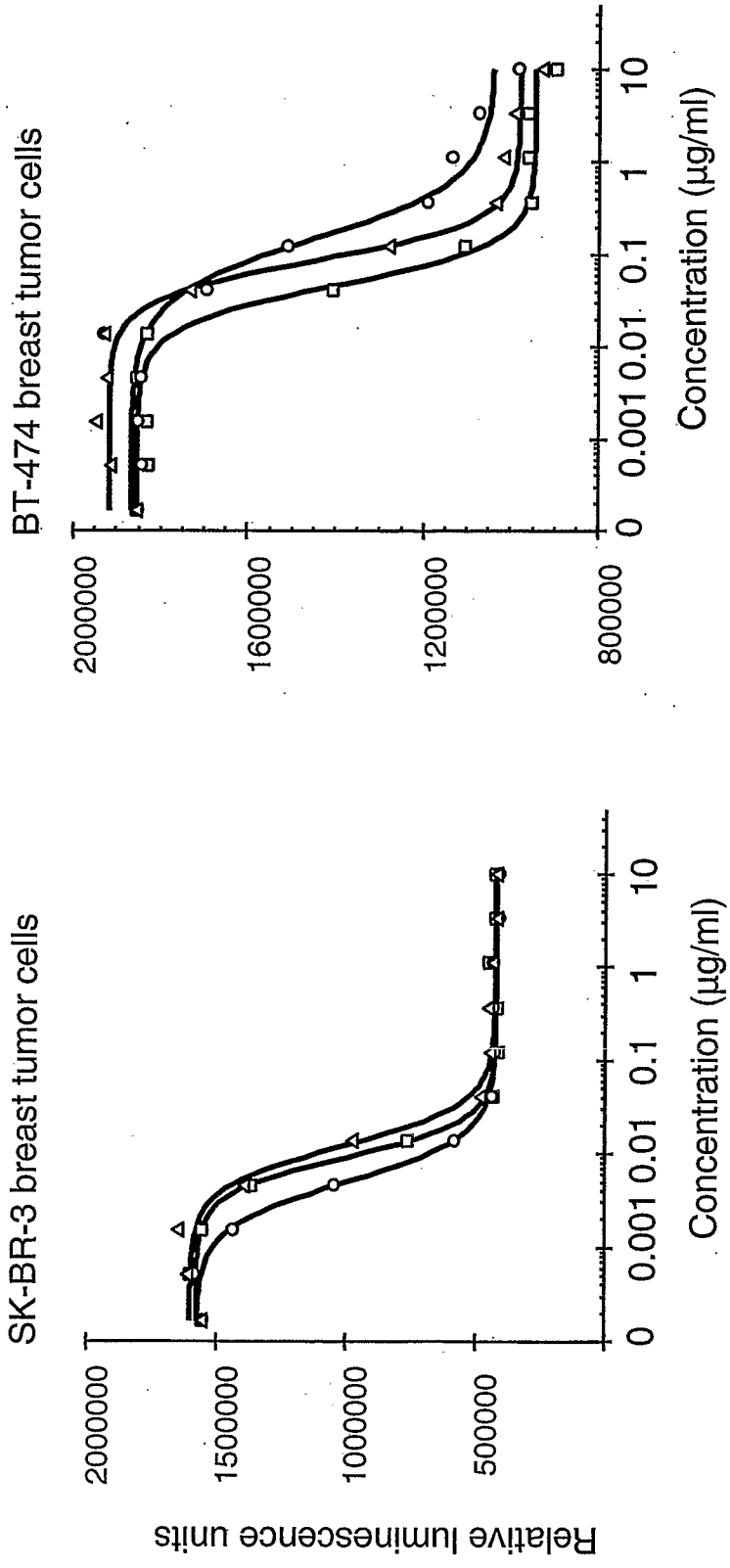



Figure 1




Figure 2

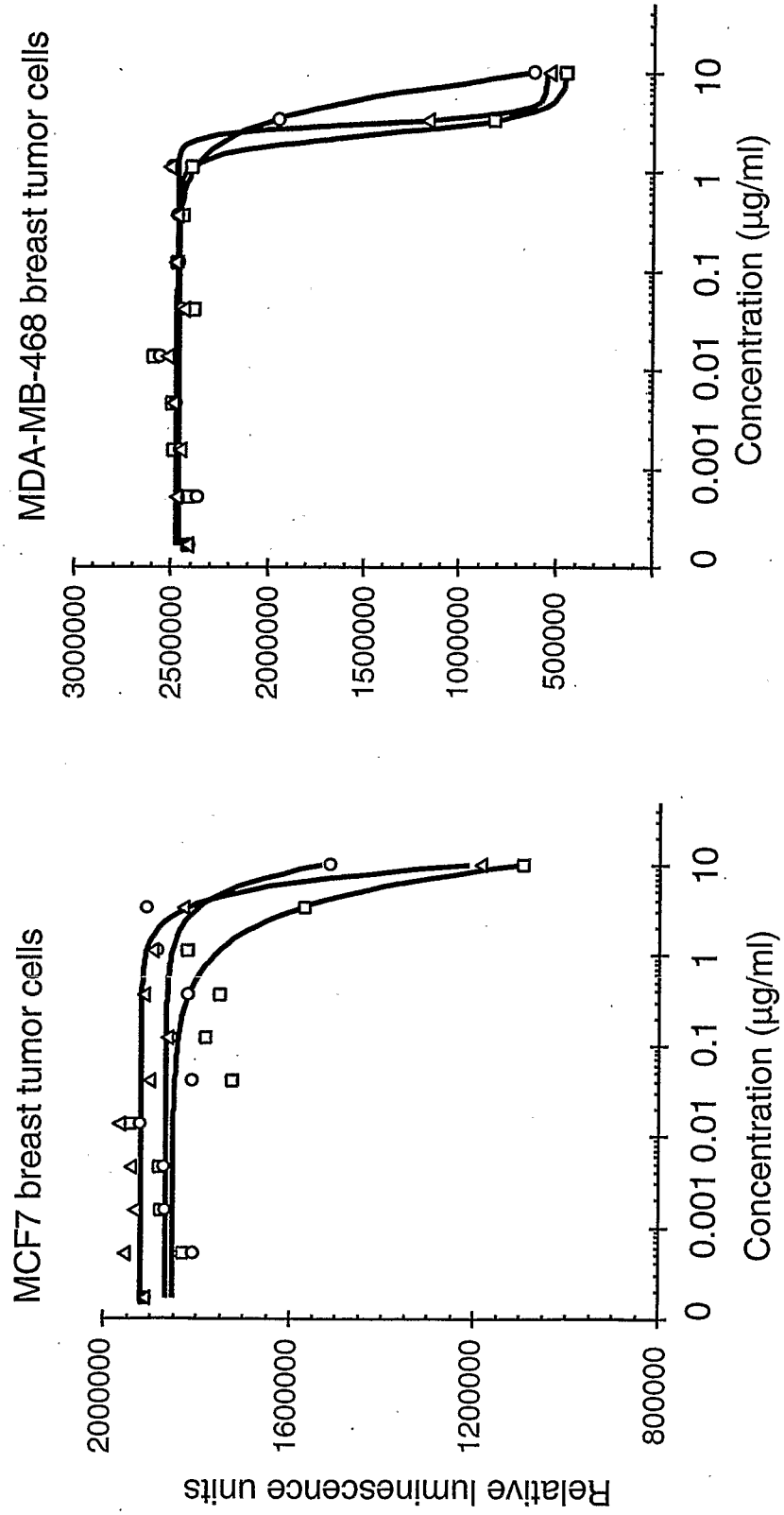



Figure 3




Figure 4

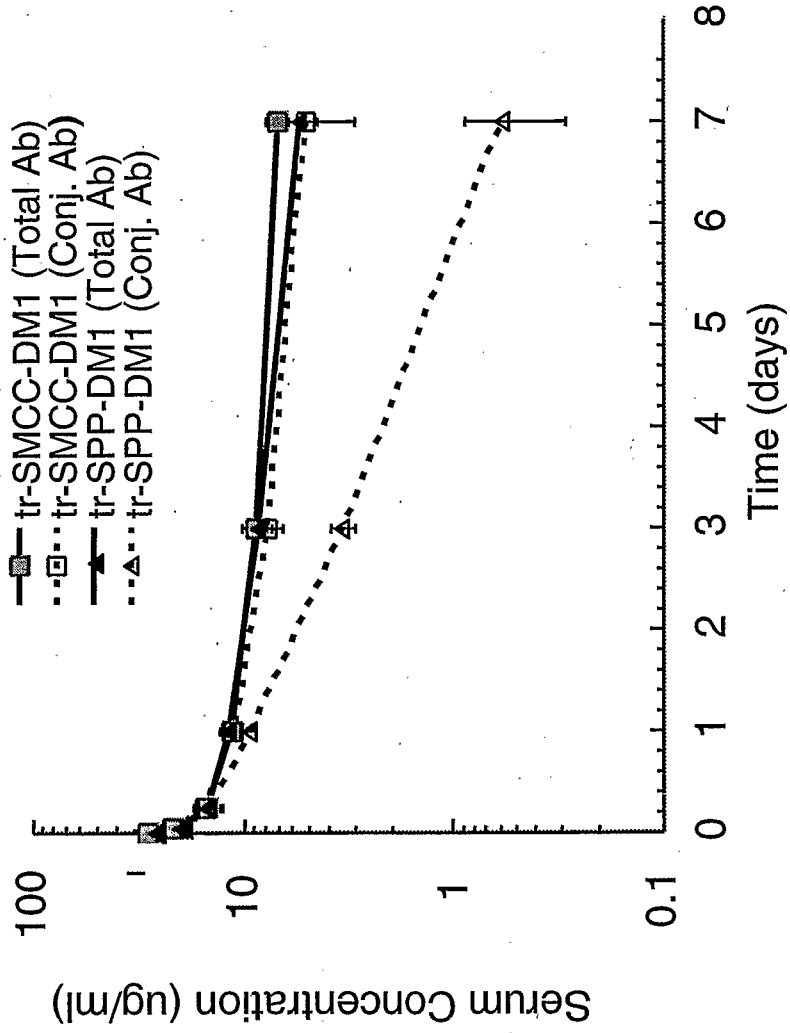

tr-SMCC-DM1 (Total Ab)
tr-SMCC-DM1 (Conj. Ab)
tr-SPP-DM1 (Total Ab)
tr-SPP-DM1 (Conj. Ab)
Serum Concentration (ug/ml)
100
10
1
0.1
0
1
2
3
4
5
6
7
8
Time (days)

Figure 5

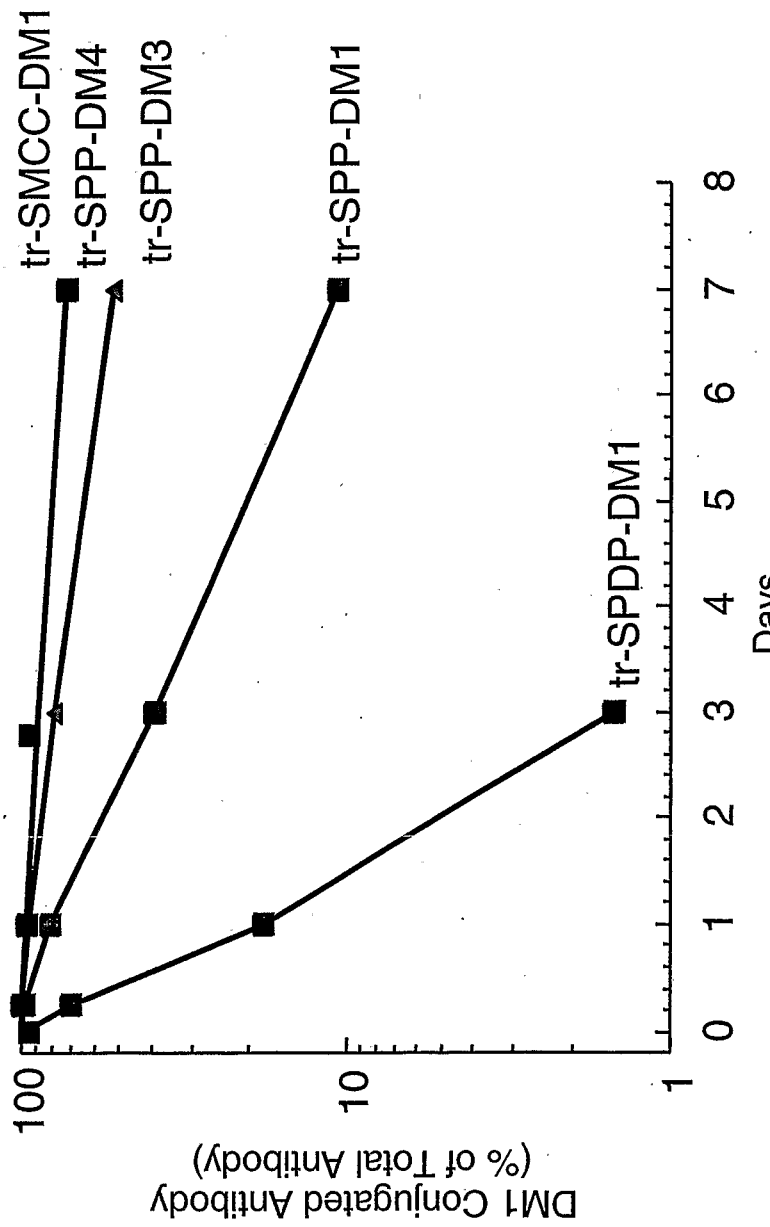

tr-SMCC-DM1
tr-SPP-DM4
tr-SPP-DM3
tr-SPP-DM1
tr-SPDP-DM1
100
10
1
0
1
2
3
4
5
6
7
8
Days
DM1 Conjugated Antibody
(% of Total Antibody)

Figure 6

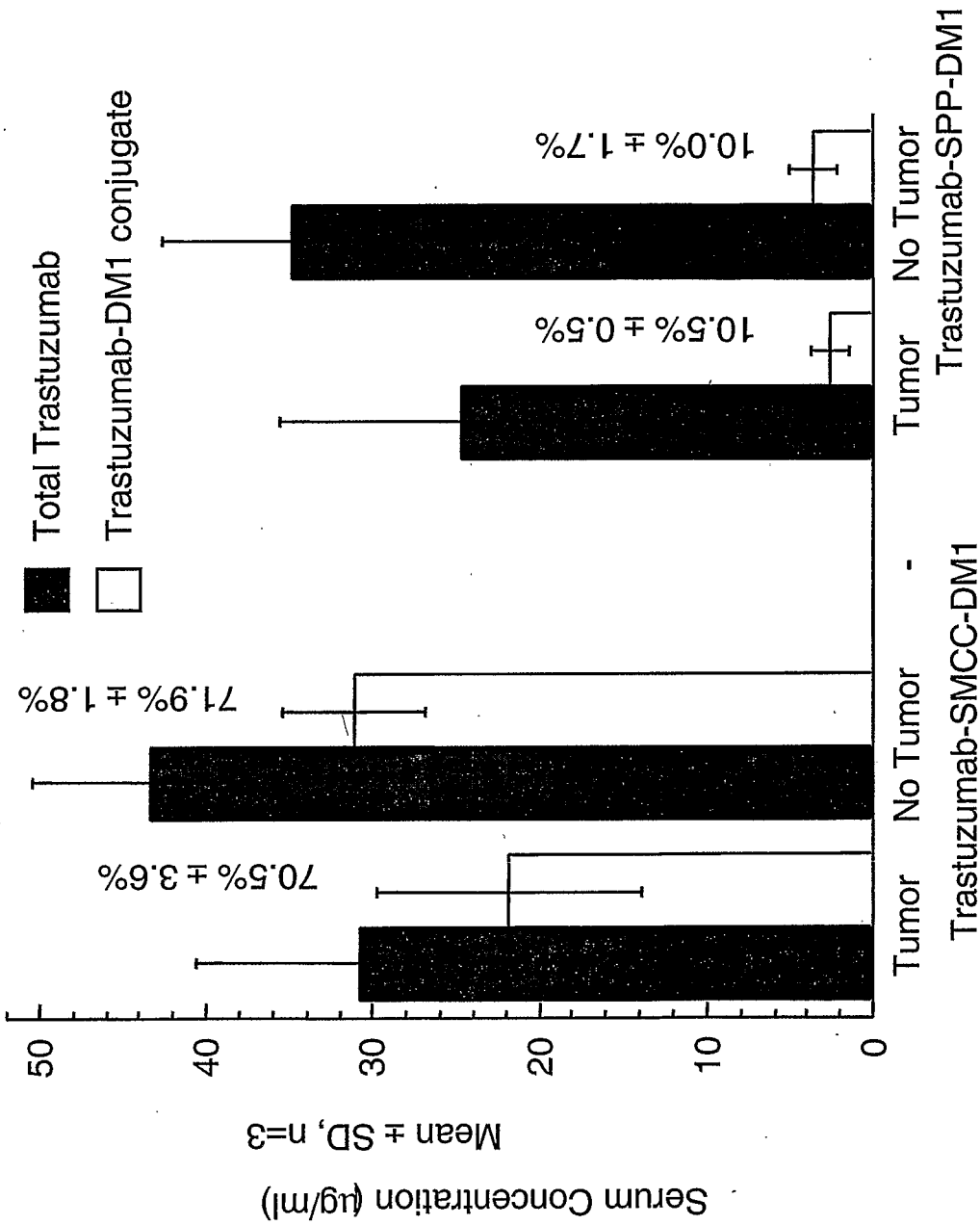

Serum Concentration (µg/ml)
Mean ± SD, n=3
0
10
20
30
40
50
Total Trastuzumab
Trastuzumab-DM1 conjugate
70.5% ± 3.6%
71.9% ± 1.8%
10.5% ± 0.5%
10.0% ± 1.7%
Tumor
No Tumor
Trastuzumab-SMCC-DM1
Tumor
No Tumor
Trastuzumab-SPP-DM1

**Figure 7**

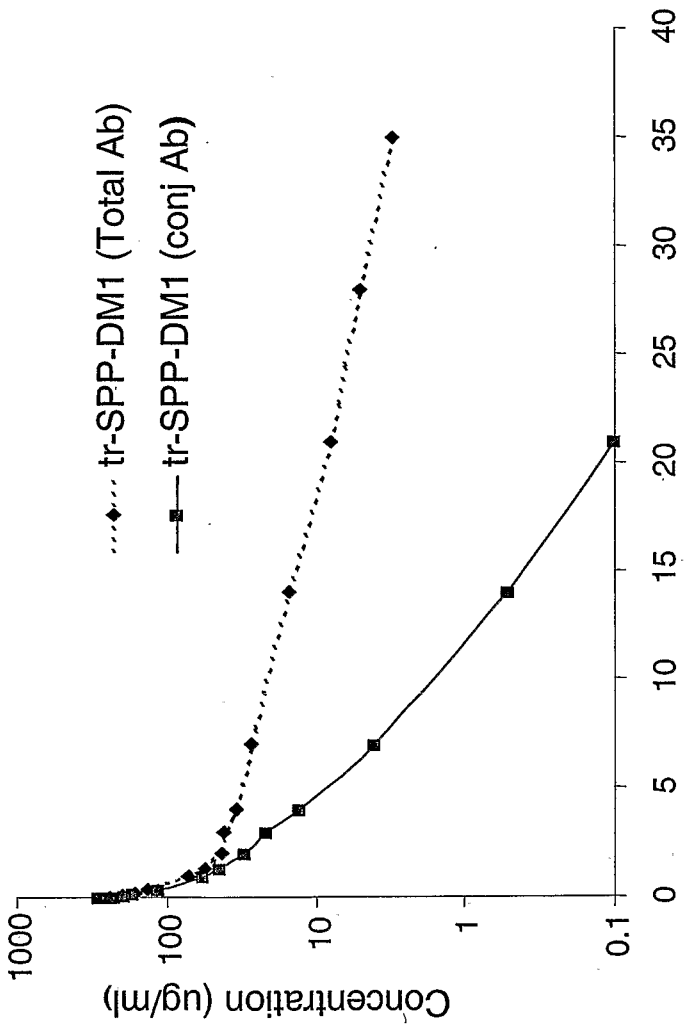

tr-SPP-DM1 (Total Ab)
tr-SPP-DM1 (conj Ab)
Concentration (ug/ml)
1000
100
10
1
0.1
0
5
10
15
20
25
30
35
40
Time (days)

Figure 8

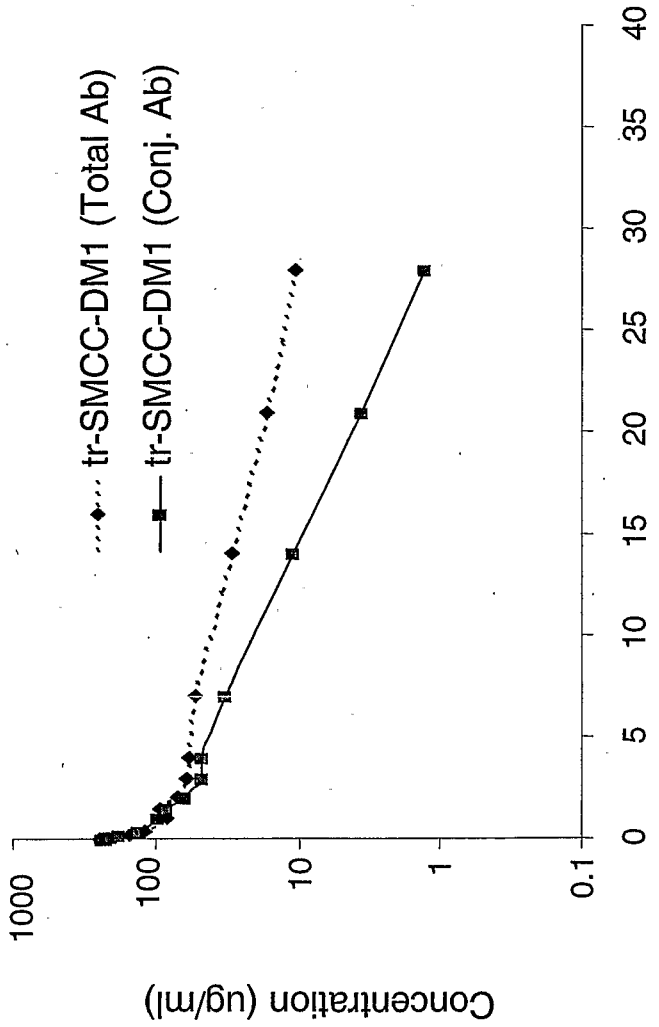

tr-SMCC-DM1 (Total Ab)
tr-SMCC-DM1 (Conj. Ab)
Concentration (ug/ml)
1000
100
10
1
0.1
0
5
10
15
20
25
30
35
40
Time (days)

**Figure 9**

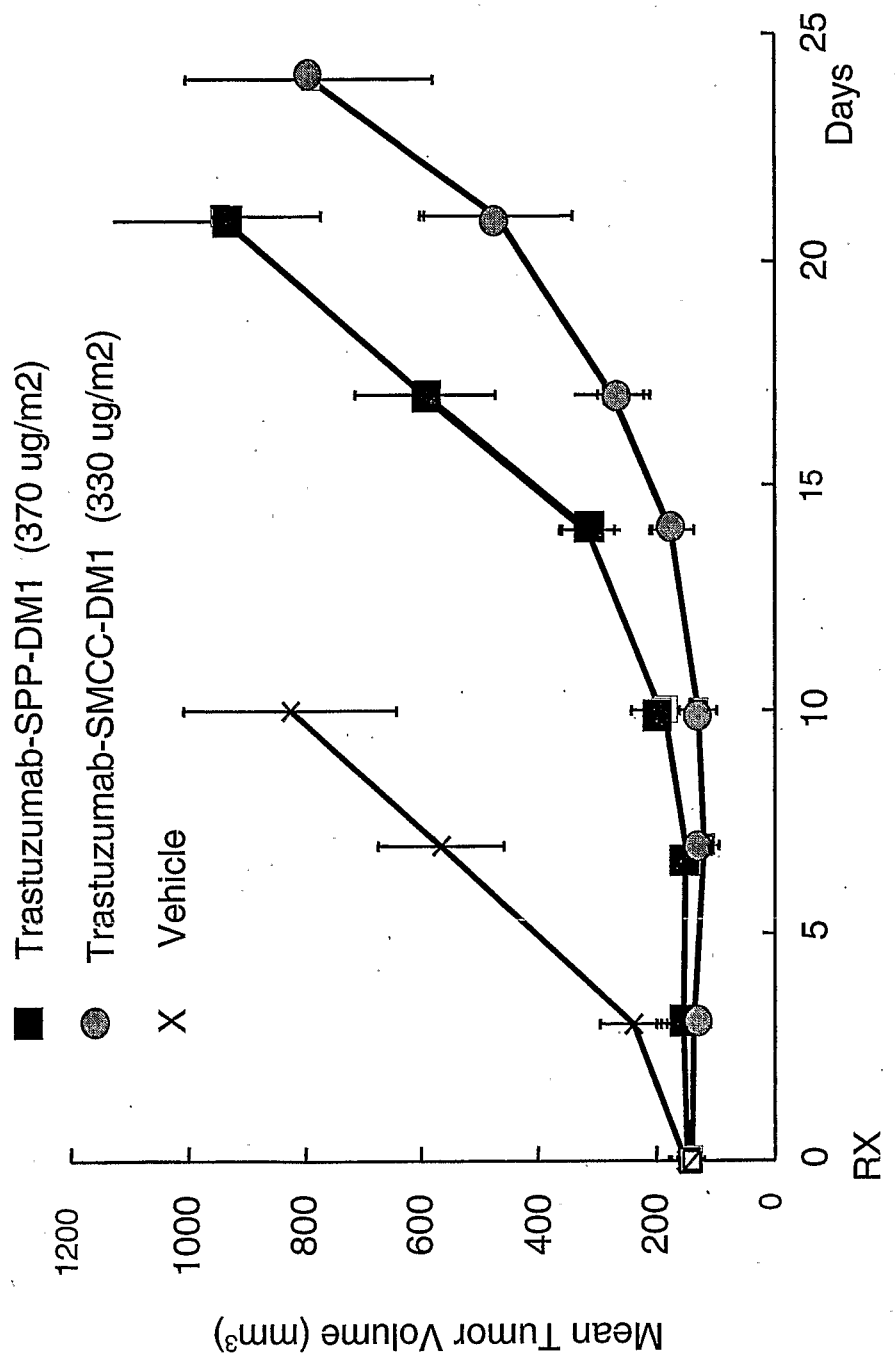

Trastuzumab-SPP-DM1 (370 ug/m2)
Trastuzumab-SMCC-DM1 (330 ug/m2)
Vehicle
Mean Tumor Volume (mm3)
1200
1000
800
600
400
200
0
0
5
10
15
20
25
Days
RX

Figure 10

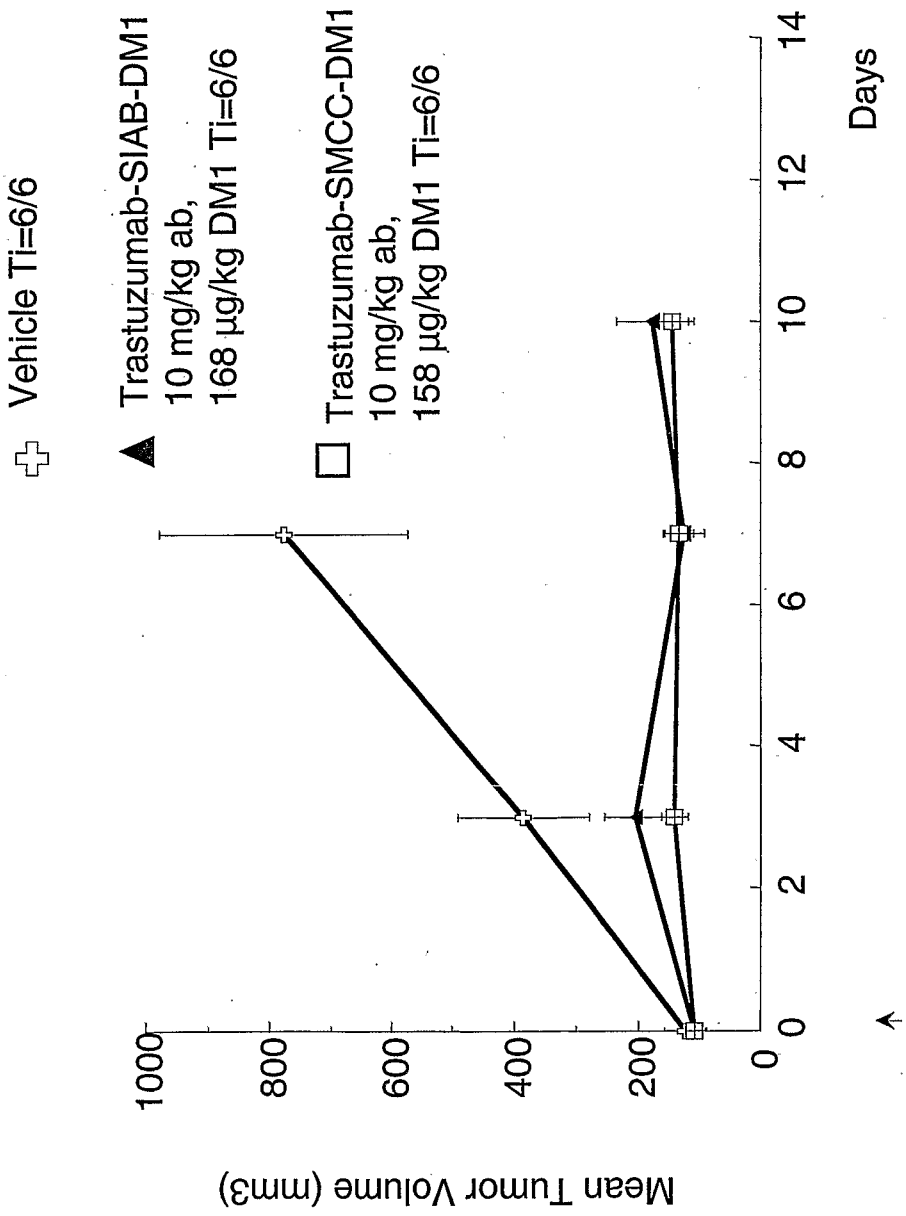

Vehicle Ti=6/6
Trastuzumab-SIAB-DM1
10 mg/kg ab,
168 µg/kg DM1 Ti=6/6
Trastuzumab-SMCC-DM1
10 mg/kg ab,
158 µg/kg DM1 Ti=6/6
Mean Tumor Volume (mm3)
1000
800
600
400
200
0
0
2
4
6
8
10
12
14
Days
RX

Figure 11

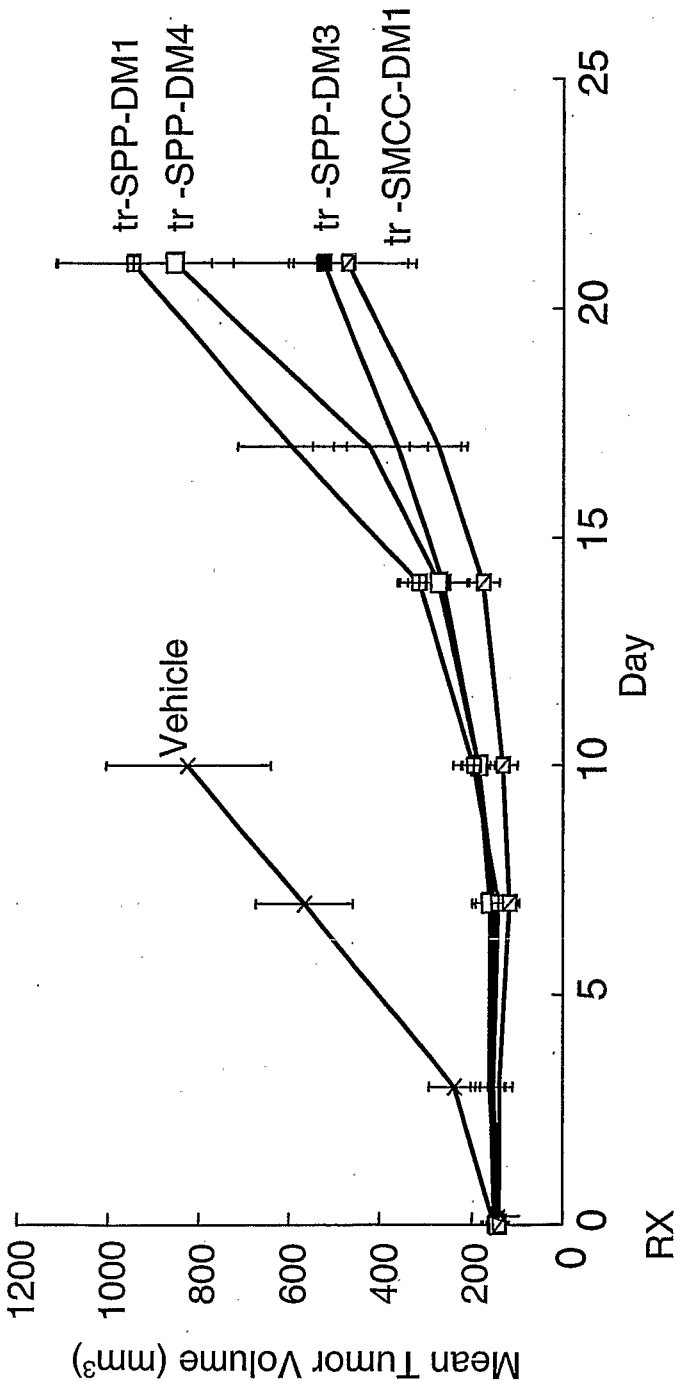

Mean Tumor Volume (mm3)
1200
1000
800
600
400
200
0
RX
0
5
10
15
20
25
Day
Vehicle
tr-SPP-DM1
tr -SPP-DM4
tr -SPP-DM3
tr -SMCC-DM1

Figure 12

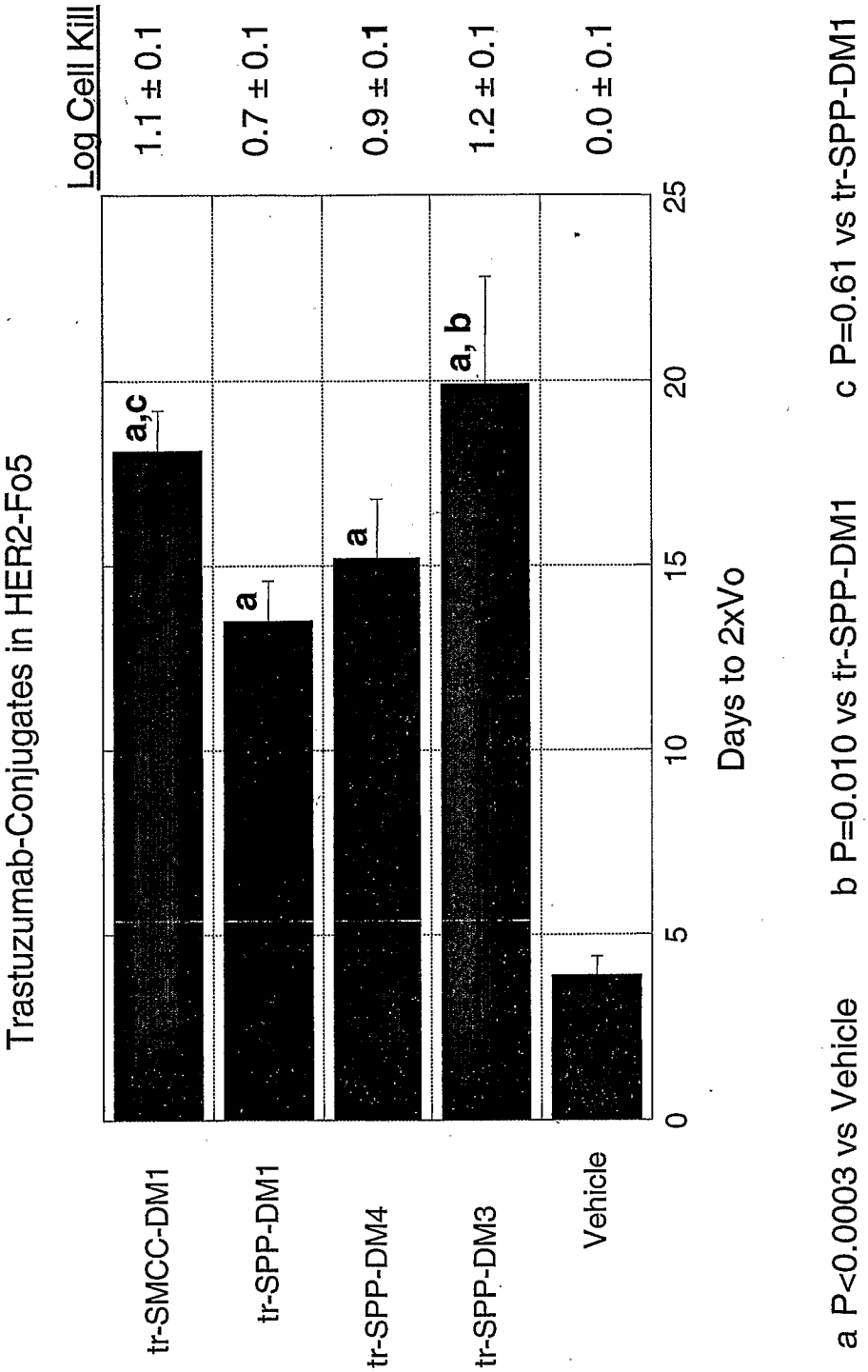

Trastuzumab-Conjugates in HER2-Fo5
Log Cell Kill
1.1 ± 0.1
0.7 ± 0.1
0.9 ± 0.1
1.2 ± 0.1
0.0 ± 0.1
a,c
a
a
a, b
tr-SMCC-DM1
tr-SPP-DM1
tr-SPP-DM4
tr-SPP-DM3
Vehicle
0
5
10
15
20
25
Days to 2xVo
a P<0.0003 vs Vehicle
b P=0.010 vs tr-SPP-DM1
c P=0.61 vs tr-SPP-DM1

**Figure 13**

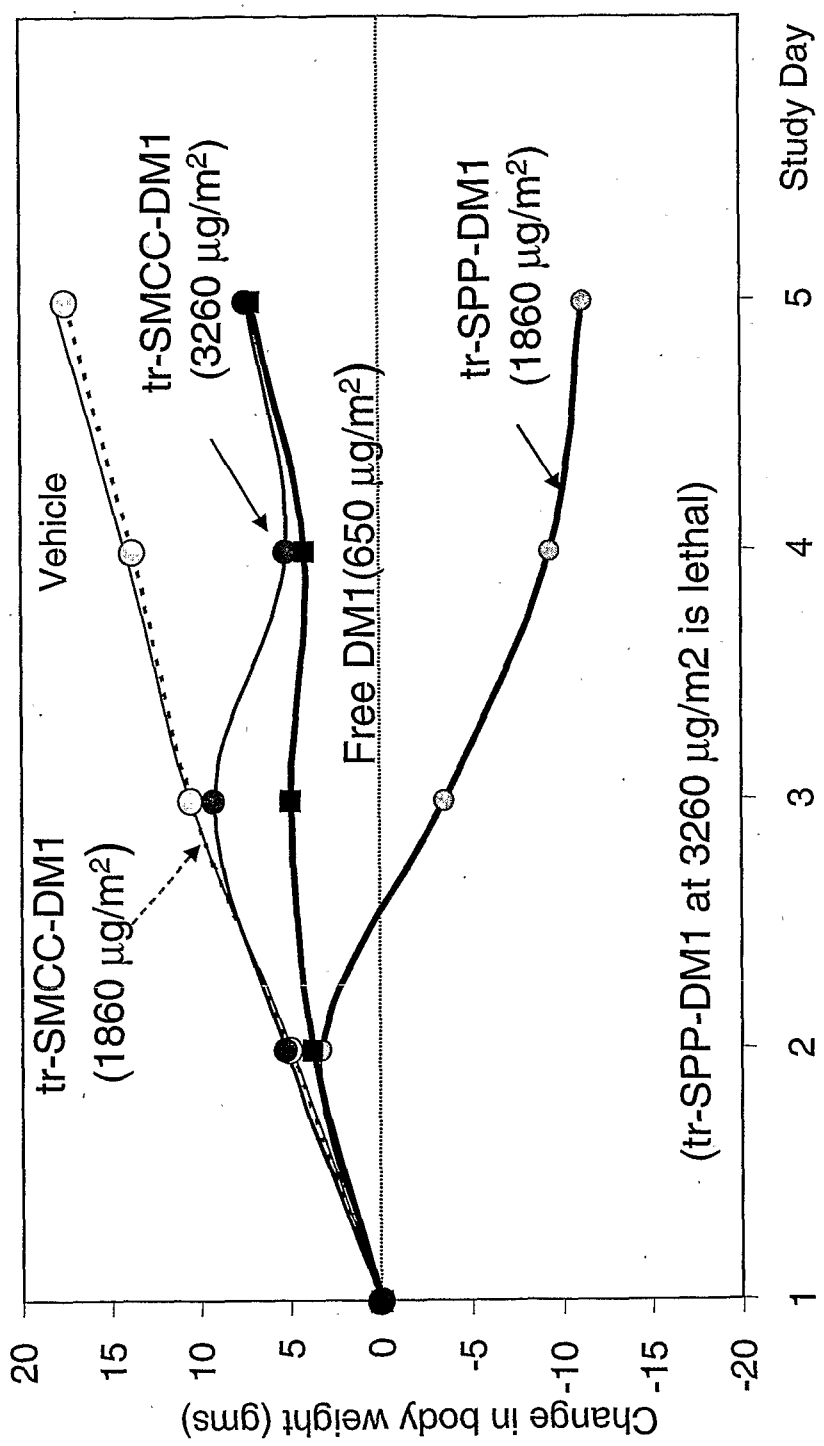

Change in body weight (gms)
20
15
10
5
0
-5
-10
-15
-20
1
2
3
4
5
Study Day
Vehicle
tr-SMCC-DM1
(3260 µg/m²)
Free DM1(650 µg/m²)
tr-SPP-DM1
(1860 µg/m²)
tr-SMCC-DM1
(1860 µg/m²)
(tr-SPP-DM1 at 3260 µg/m2 is lethal)

**Figure 14**

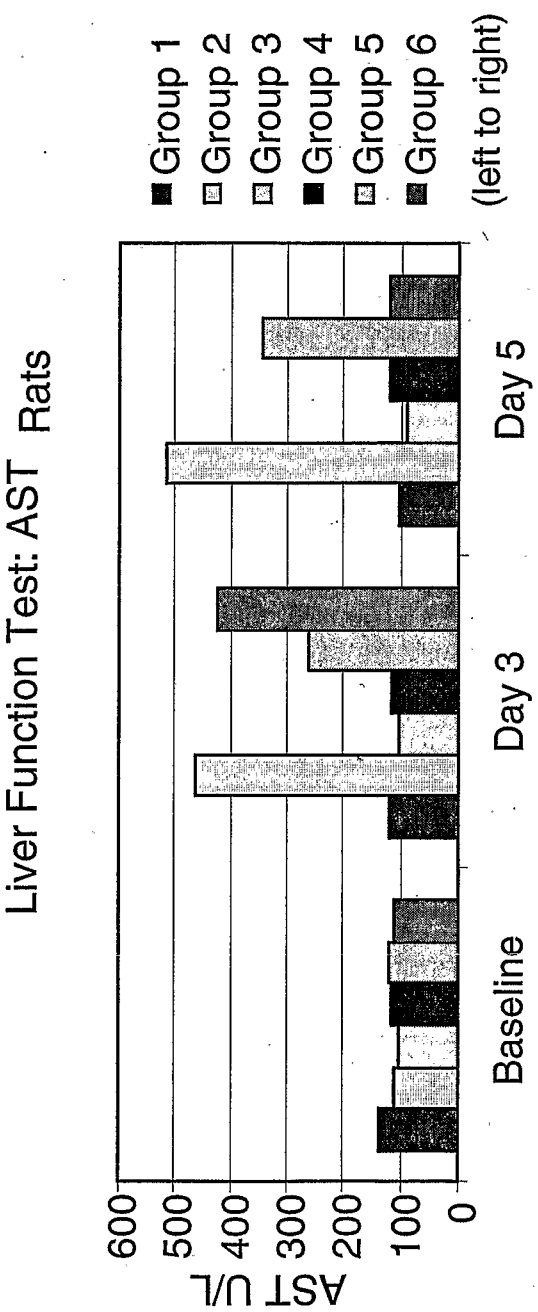

Liver Function Test: AST Rats
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
(left to right)
AST U/L
600
500
400
300
200
100
0
Baseline
Day 3
Day 5
Group 1: Vehicle
Group 2: tr-SPP-DM1, 22.3mg/kg
Group 3: tr-SMCC-DM1, 10mg/kg
Group 4: tr-SMCC-DM1, 25mg/kg
Group 5: tr-SMCC-DM1, 50mg/kg
Group 6, free DM1

**Figure 15**

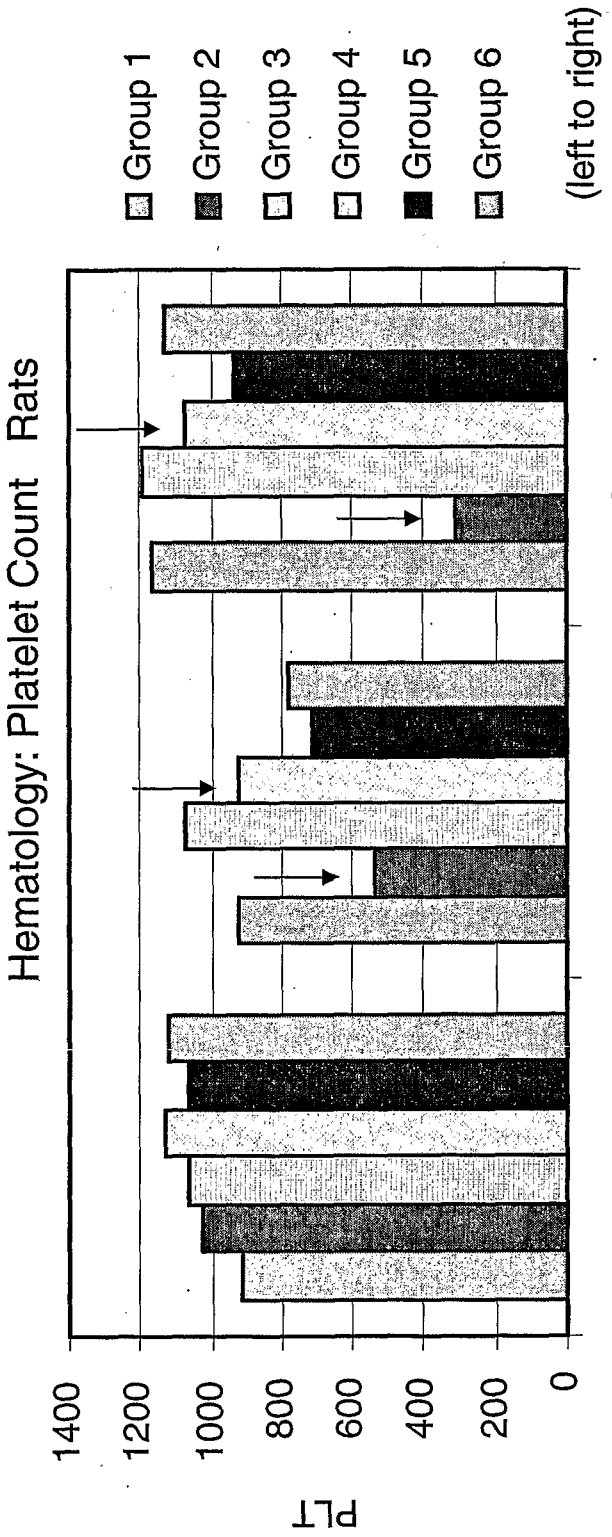

Hematology: Platelet Count Rats
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
(left to right)
PLT
1400
1200
1000
800
600
400
200
0
Baseline
Day 3
Day 5
Group 1: Vehicle
Group 2: tr-SPP-DM1, 22.3mg/kg
Group 3: tr-SMCC-DM1, 10mg/kg
Group 4: tr-SMCC-DM1, 25mg/kg
Group 5: tr-SMCC-DM1, 50mg/kg
Group 6, free DM1

**Figure 16**

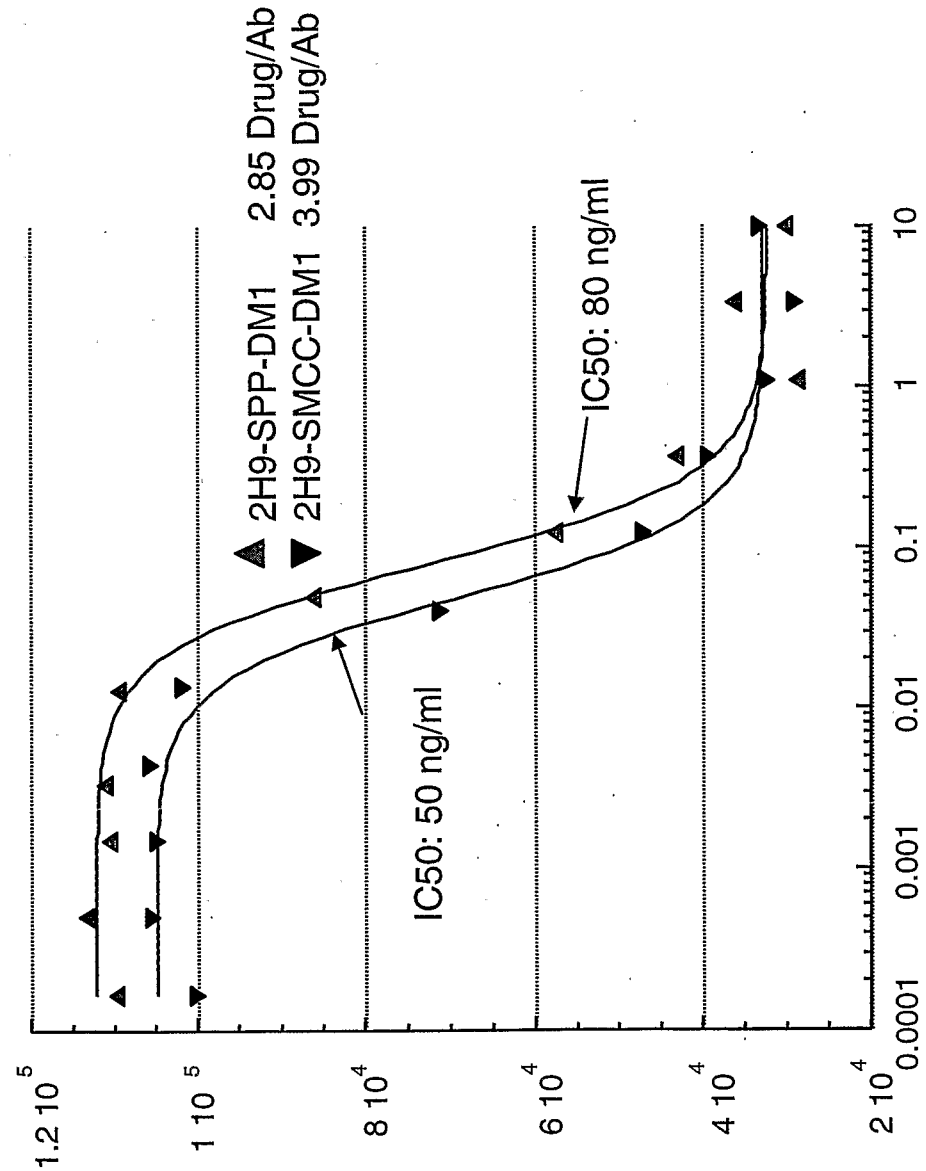

2H9-SPP-DM1 2.85 Drug/Ab
2H9-SMCC-DM1 3.99 Drug/Ab
IC50: 50 ng/ml
IC50: 80 ng/ml
1.2 10^5
1 10^5
8 10^4
6 10^4
4 10^4
2 10^4
0.0001
0.001
0.01
0.1
1
10

Figure 17