FIGURE 1

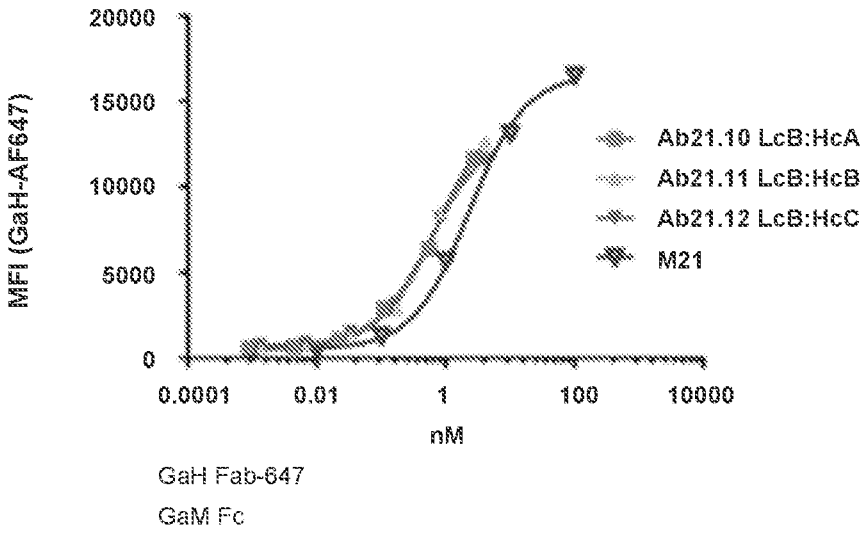

20000
15000
10000
5000
0
MFI (GaH-AF647)
0.0001
0.01
1
100
10000
nM
Ab21.10 LcB:HcA
Ab21.11 LcB:HcB
Ab21.12 LcB:HcC
M21
GaH Fab-647
GaM Fc

FIGURE 2

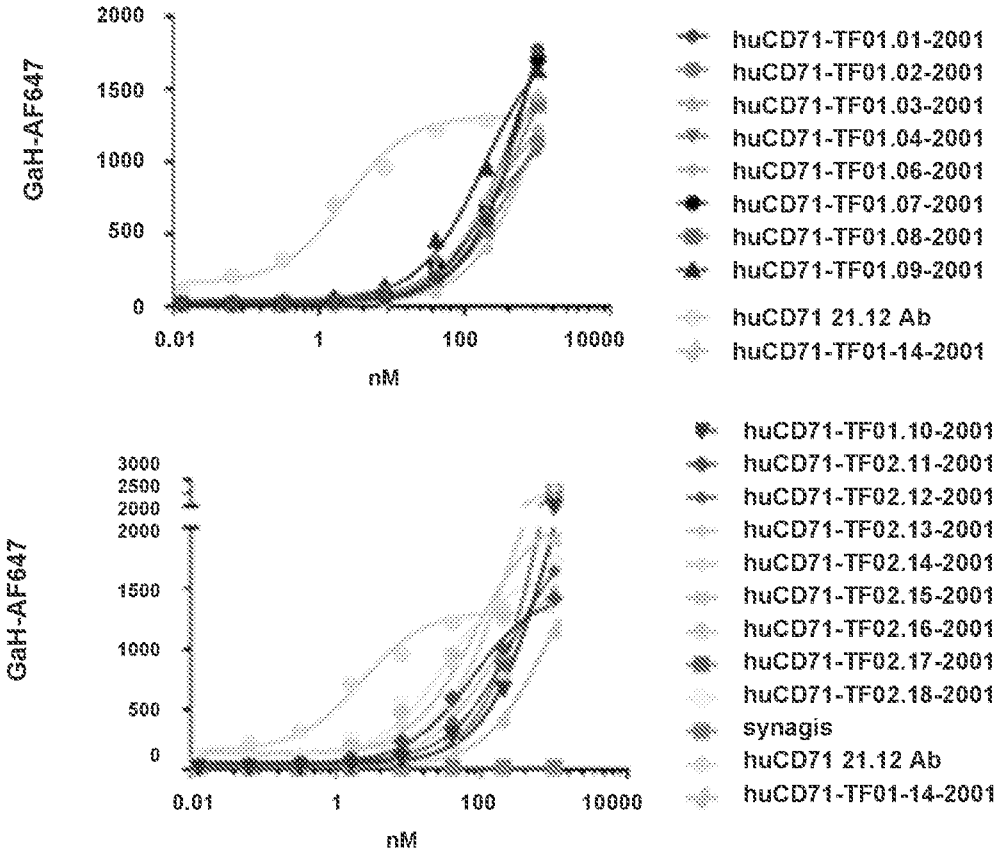

GaH-AF647
2000
1500
1000
500
0
0.01
1
100
10000
nM
huCD71-TF01.01-2001
huCD71-TF01.02-2001
huCD71-TF01.03-2001
huCD71-TF01.04-2001
huCD71-TF01.06-2001
huCD71-TF01.07-2001
huCD71-TF01.08-2001
huCD71-TF01.09-2001
huCD71 21.12 Ab
huCD71-TF01-14-2001
GaH-AF647
3000
2500
2000
2000
1500
1000
500
0
0.01
1
100
10000
nM
huCD71-TF01.10-2001
huCD71-TF02.11-2001
huCD71-TF02.12-2001
huCD71-TF02.13-2001
huCD71-TF02.14-2001
huCD71-TF02.15-2001
huCD71-TF02.16-2001
huCD71-TF02.17-2001
huCD71-TF02.18-2001
synagis
huCD71 21.12 Ab
huCD71-TF01-14-2001

FIGURE 2, cont'd

Activatable Antibody	K_{app}	fold masking
huCD71 TF01.01-2001	994.7	432
huCD71 TF01.02-2001	420.5	183
huCD71 TF01.03-2001	320.9	140
huCD71 TF01.04-2001	198.7	86
huCD71 TF01.06-2001	245.4	107
huCD71 TF01.07-2001	545.3	237
huCD71 TF01.08-2001	458.8	199
huCD71 TF02.09-2001	183.3	80
huCD71 TF02.10-2001	974. 3	424
huCD71 TF02.11-2001	74.5	32
huCD71 TF02.12-2001	265.6	115
huCD71 TF02.13-2001	127.4	55
huCD71 TF02.14-2001	227.2	99
huCD71 TF02.15-2001	654.8	285
huCD71 TF02.16-2001	79.93	35
huCD71 TF02.17-2001	885.5	385
huCD71 TF02.18-2001	32.04	14
huCD71 TF01-2001	809.5	352
huCD71 21.12 Ab	2.288	1

FIGURE 3A

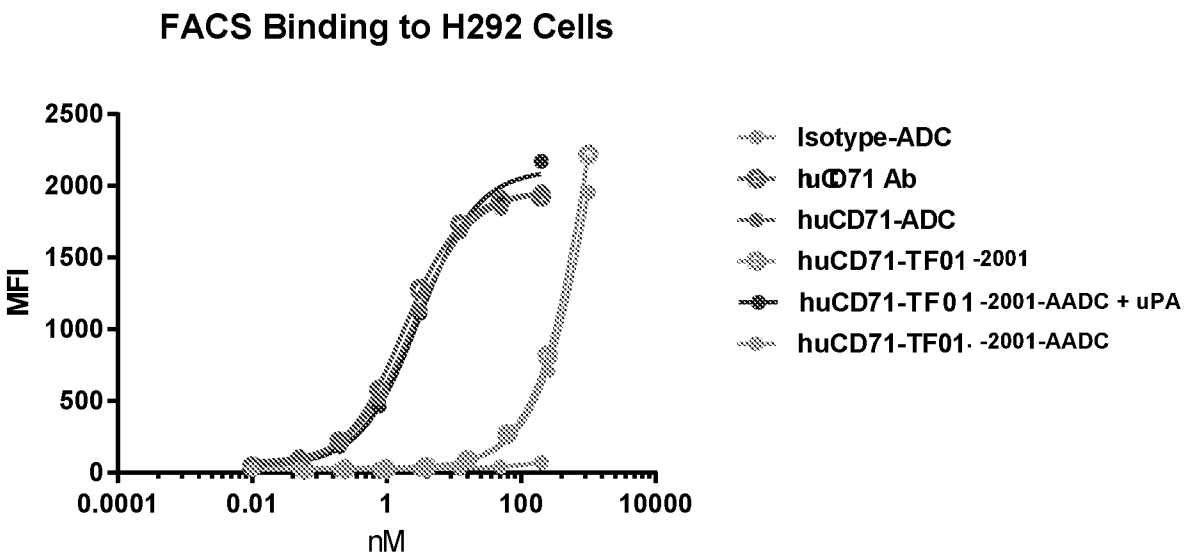


FIGURE 3B

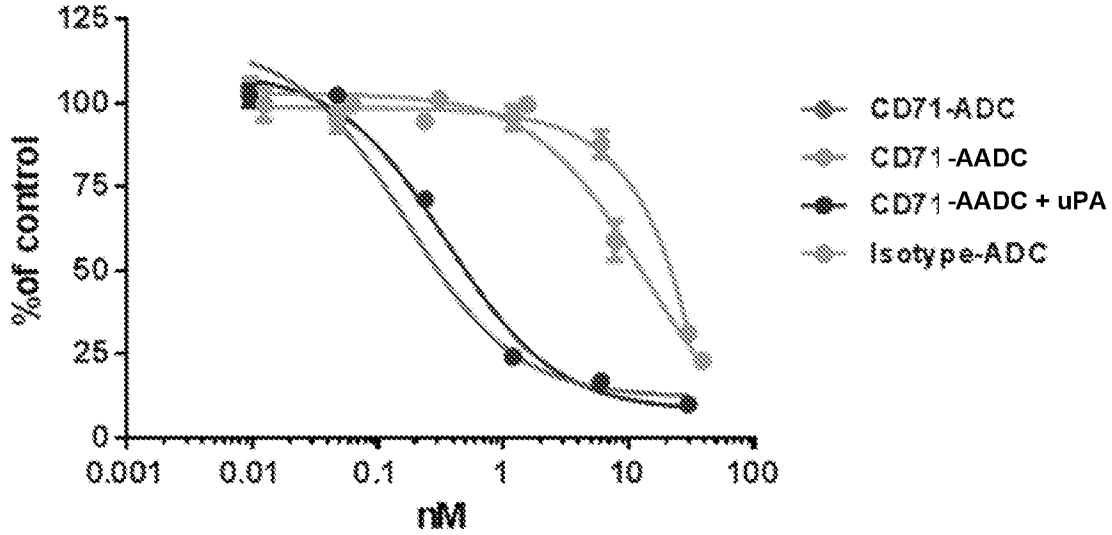


FIGURE 4

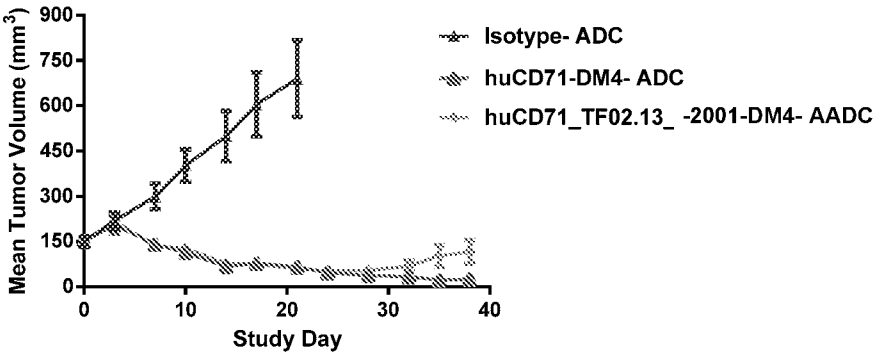

Mean Tumor Volume (mm3)
900
750
600
450
300
150
0
0
10
20
30
40
Study Day
Isotype- ADC
huCD71-DM4- ADC
huCD71_TF02.13_ -2001-DM4- AADC

FIGURE 5

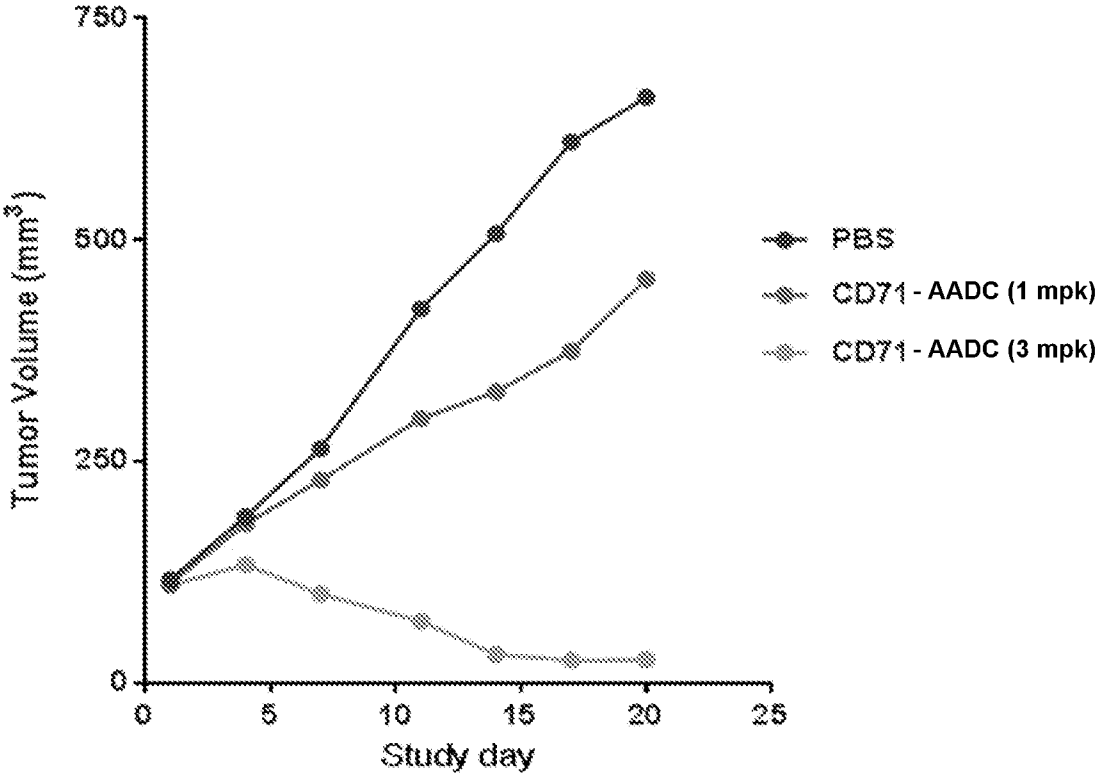

750
500
250
0
Tumor Volume (mm3)
0
5
10
15
20
25
Study day
PBS
CD71 - AADC (1 mpk)
CD71 - AADC (3 mpk)

FIGURE 6A

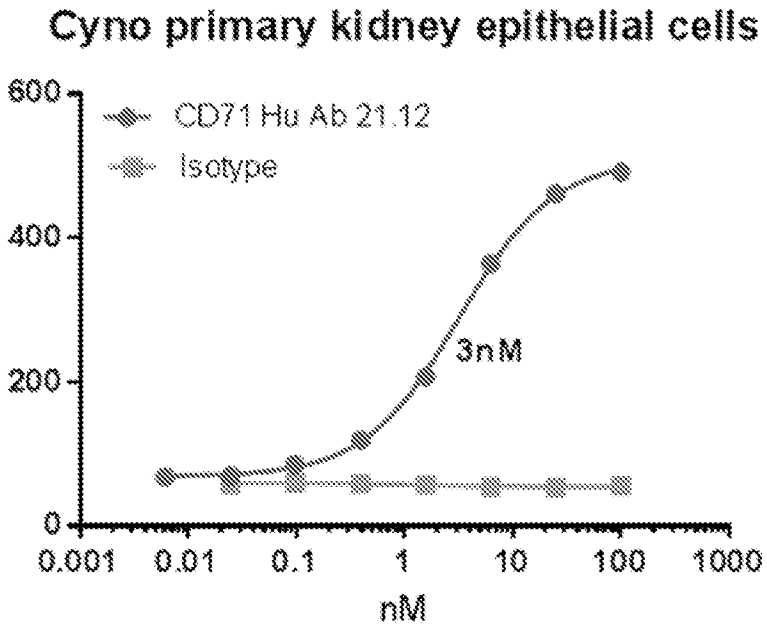


FIGURE 6B

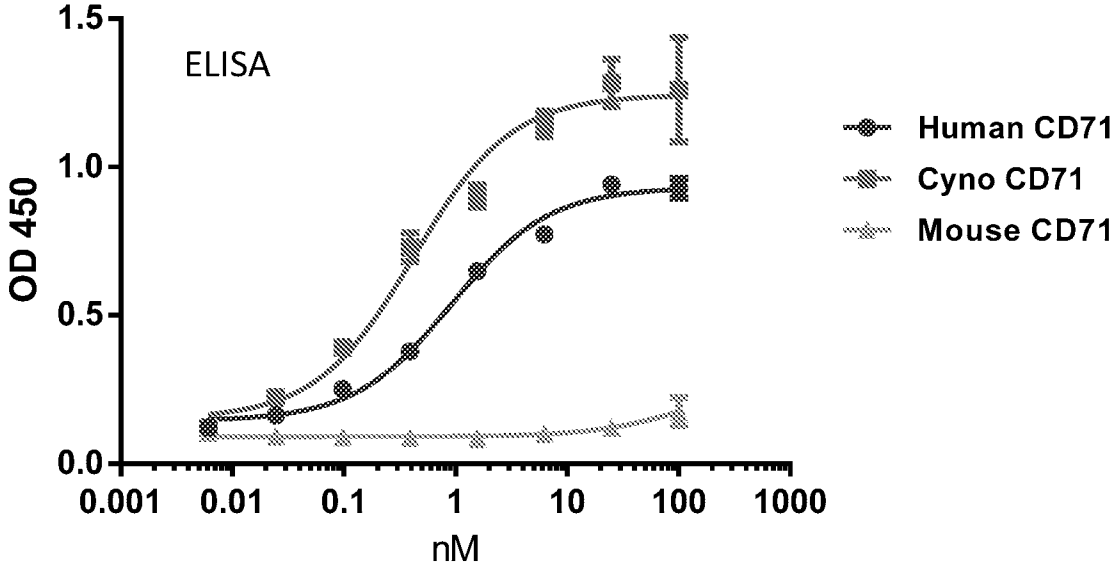


FIGURE 6C

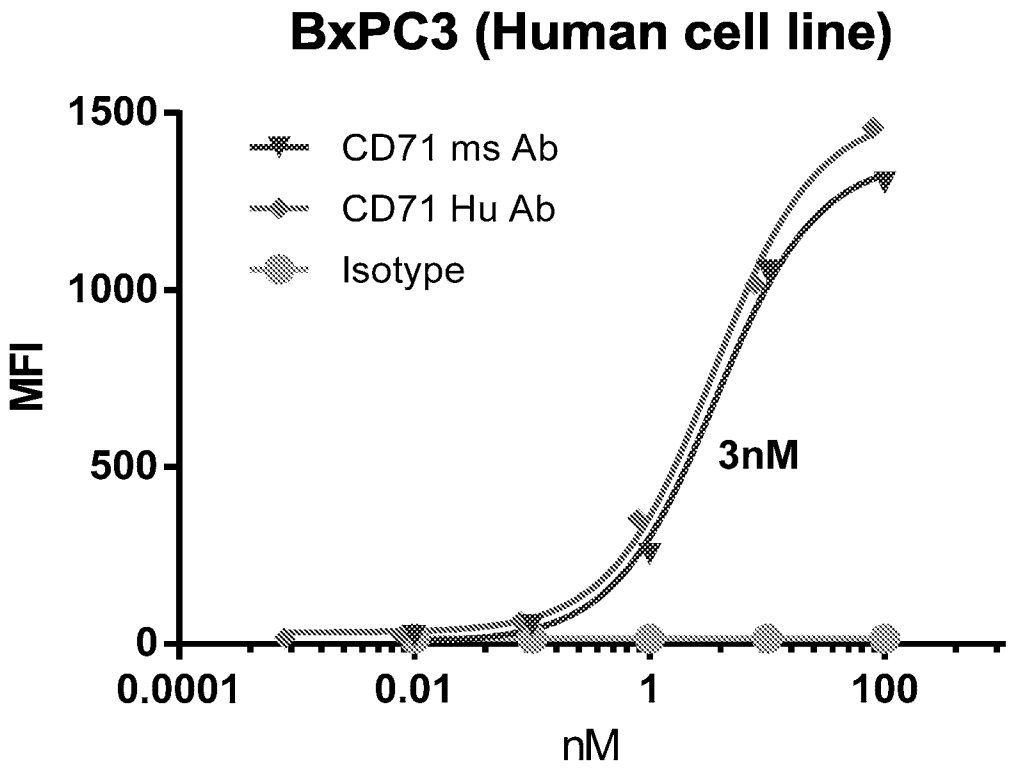

BxPC3 (Human cell line)
1500
1000
500
0
MFI
CD71 ms Ab
CD71 Hu Ab
Isotype
3nM
0.0001
0.01
1
100
nM

FIGURE 7

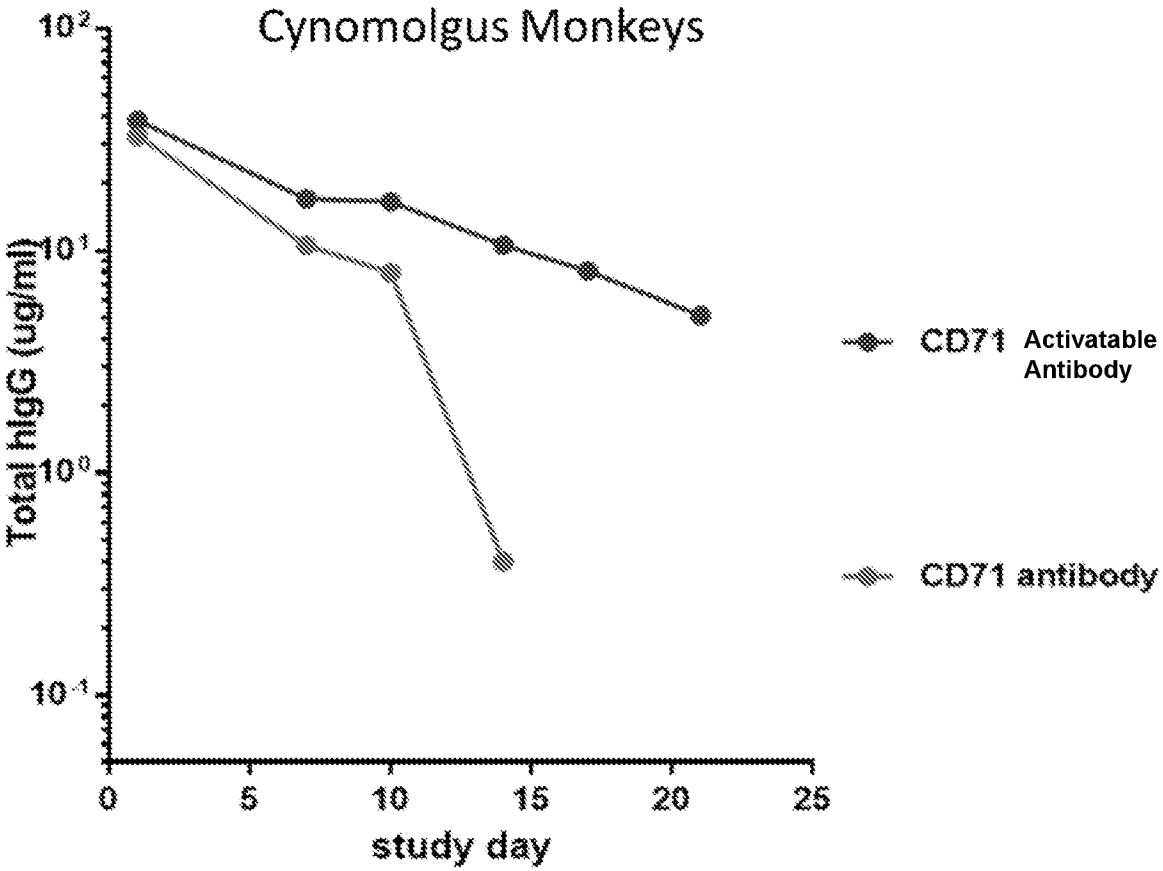

Cynomolgus Monkeys
Total hIgG (ug/ml)
10^2
10^1
10^0
10^{-1}
0
5
10
15
20
25
study day
CD71 Activatable Antibody
CD71 antibody

FIGURE 8

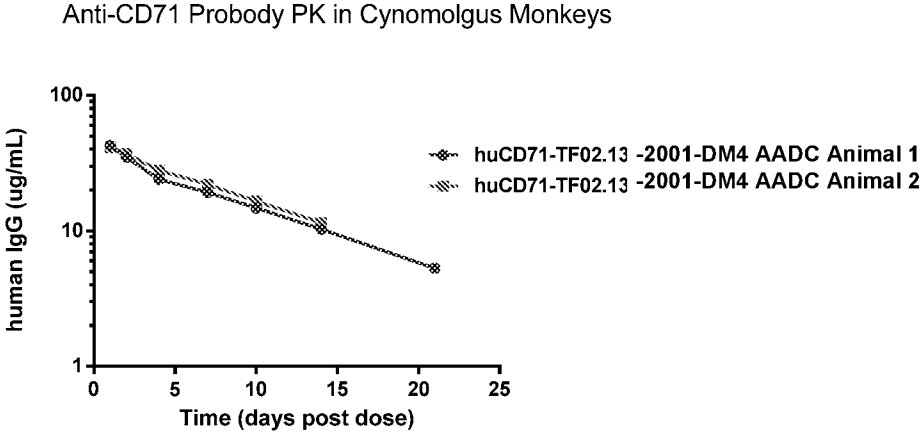

Anti-CD71 Probody PK in Cynomolgus Monkeys
human IgG (ug/mL)
100
10
1
0
5
10
15
20
25
Time (days post dose)
huCD71-TF02.13 -2001-DM4 AADC Animal 1
huCD71-TF02.13 -2001-DM4 AADC Animal 2

FIGURE 9

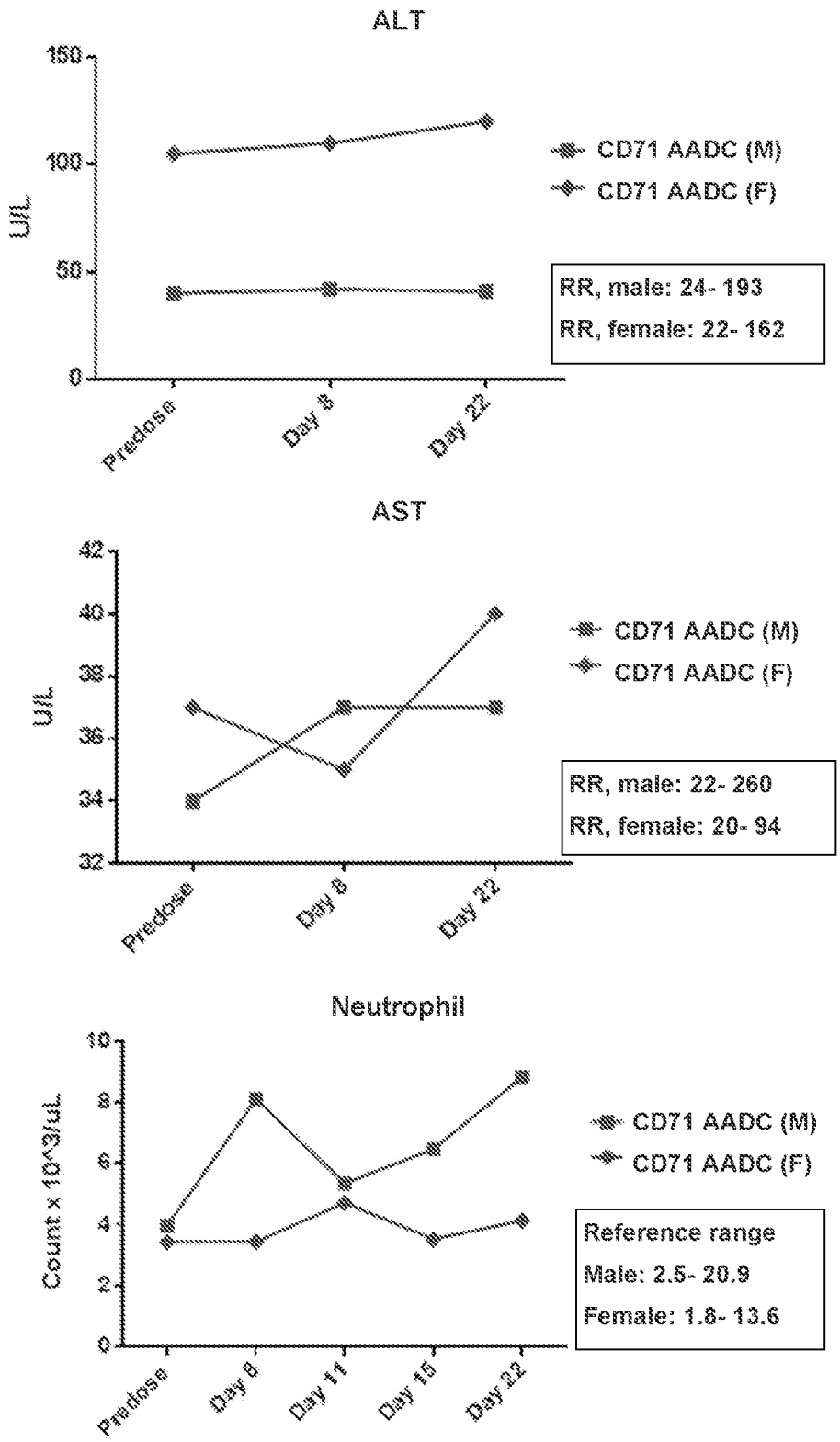

ALT
U/L
150
100
50
0
Predose
Day 8
Day 22
CD71 AADC (M)
CD71 AADC (F)
RR, male: 24- 193
RR, female: 22- 162
AST
U/L
42
40
38
36
34
32
Predose
Day 8
Day 22
CD71 AADC (M)
CD71 AADC (F)
RR, male: 22- 260
RR, female: 20- 94
Neutrophil
Count x 10^3/uL
10
8
6
4
2
0
Predose
Day 8
Day 11
Day 15
Day 22
CD71 AADC (M)
CD71 AADC (F)
Reference range
Male: 2.5- 20.9
Female: 1.8- 13.6

FIGURE 10

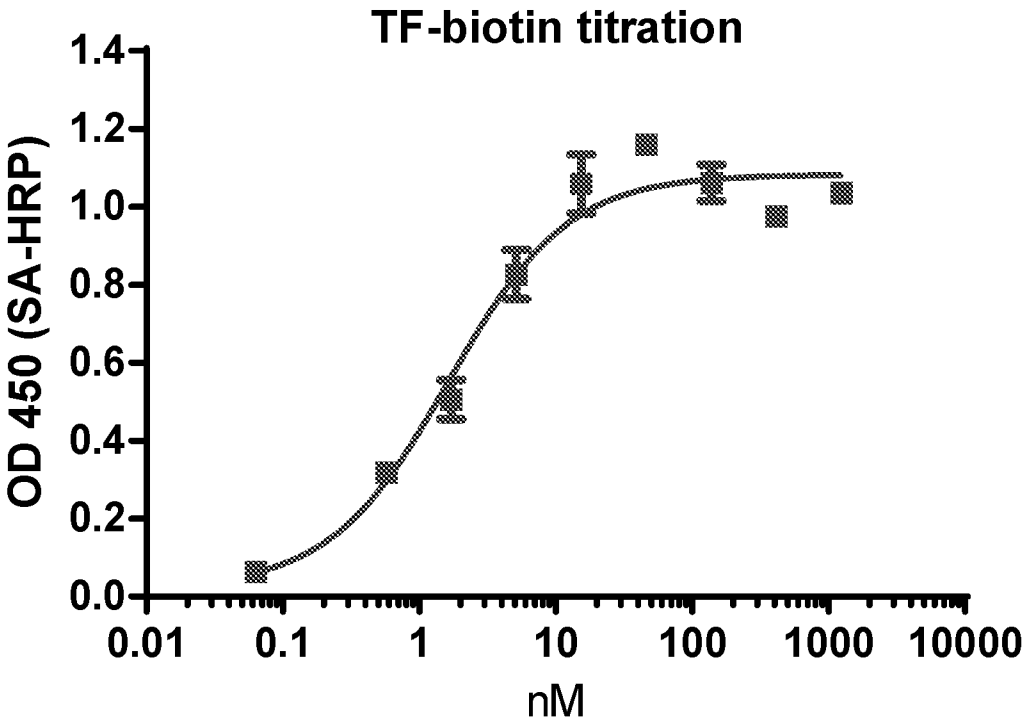

TF-biotin titration
OD 450 (SA-HRP)
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0.01
0.1
1
10
100
1000
10000
nM

FIGURE 11A

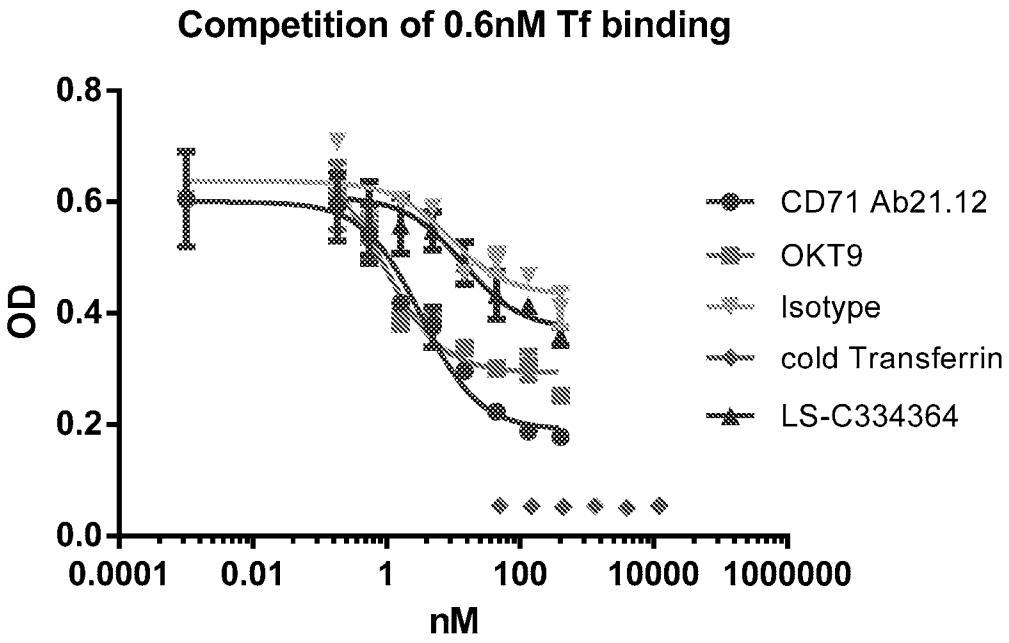

Competition of 0.6nM Tf binding
OD
0.8
0.6
0.4
0.2
0.0
0.0001
0.01
1
100
10000
1000000
nM
CD71 Ab21.12
OKT9
Isotype
cold Transferrin
LS-C334364

FIGURE 11B

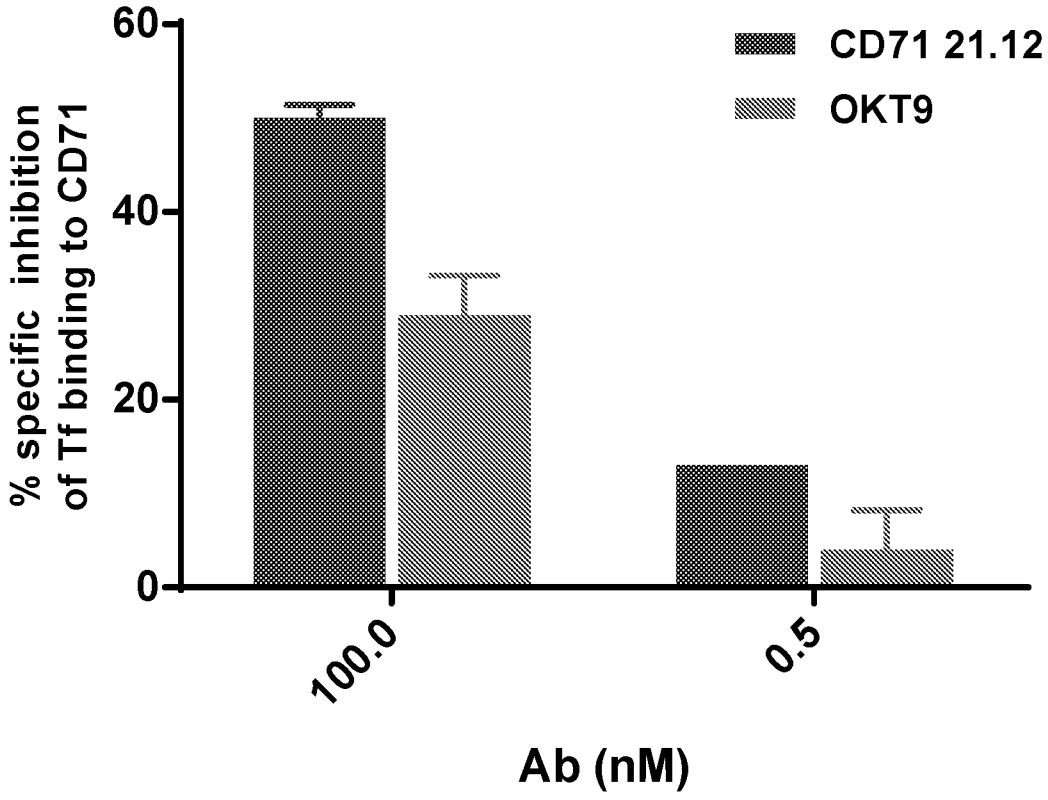

60
40
20
0
% specific inhibition of Tf binding to CD71
CD71 21.12
OKT9
100.0
0.5
Ab (nM)

FIGURE 12A

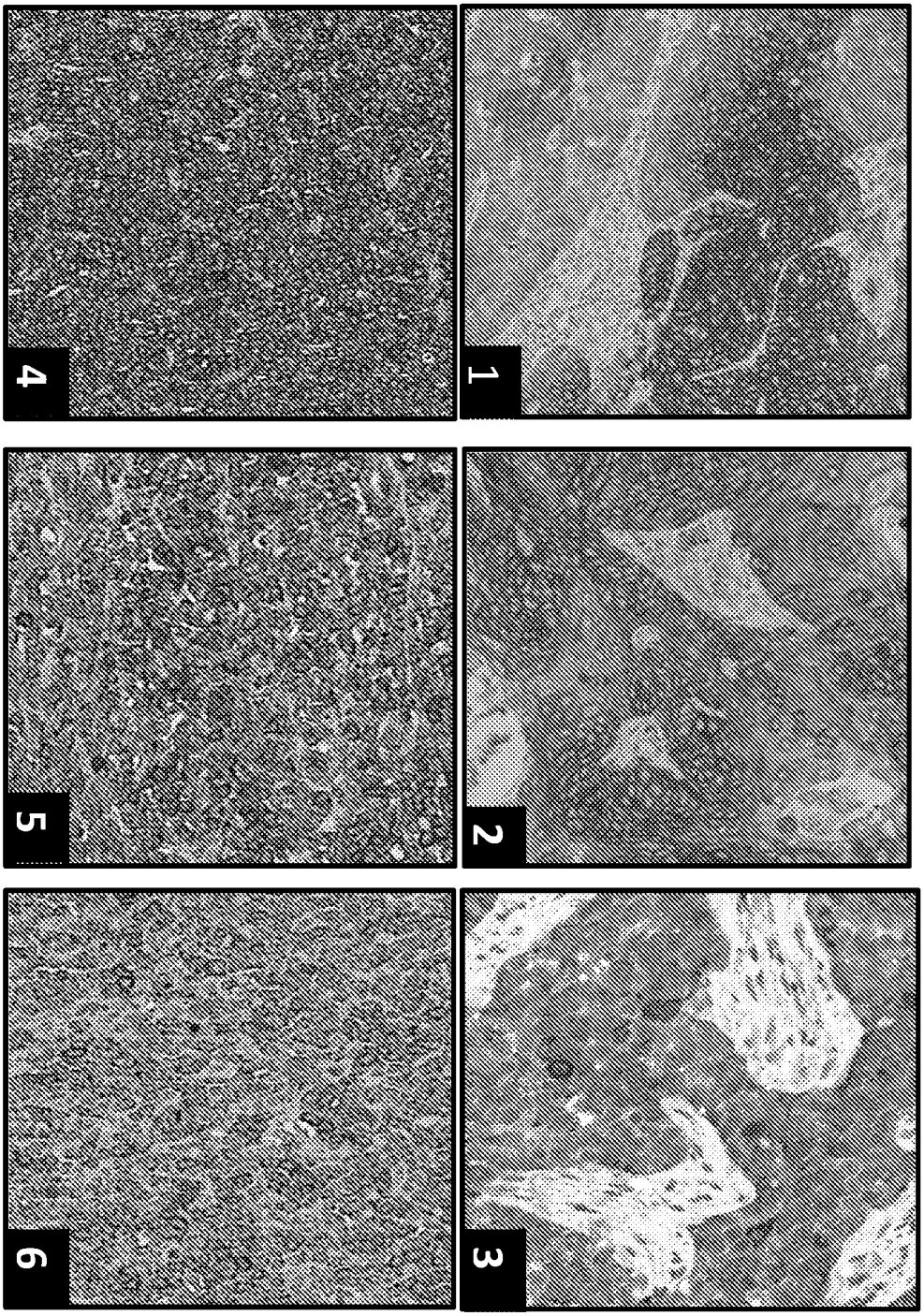


FIGURE 12B

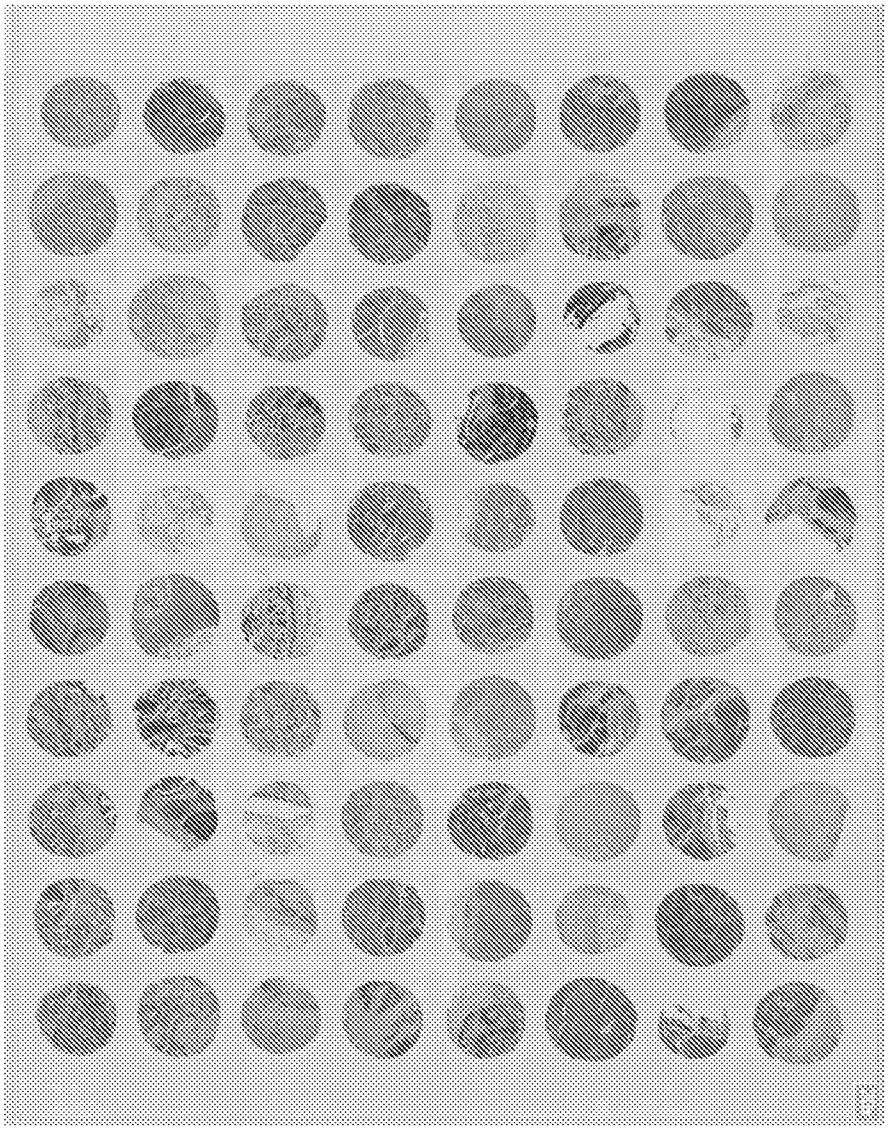


FIGURE 12C

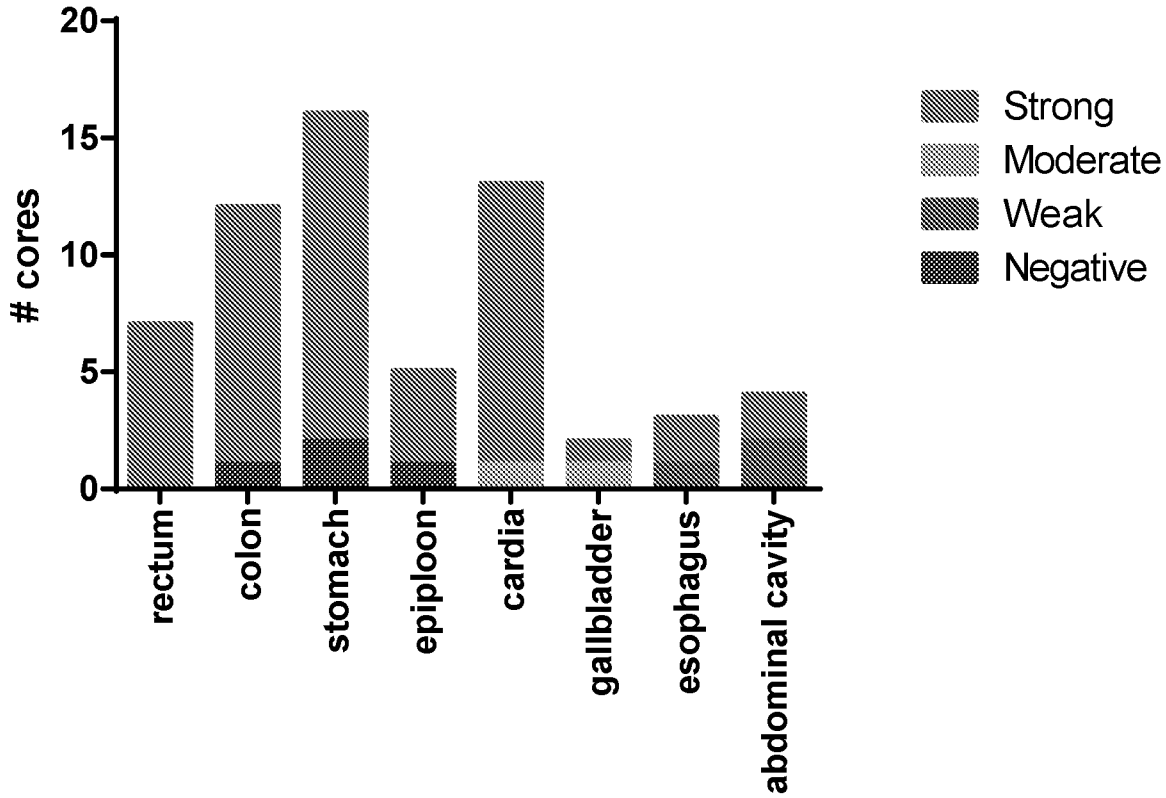

20
15
10
5
0
cores
rectum
colon
stomach
epiploon
cardia
gallbladder
esophagus
abdominal cavity
Strong
Moderate
Weak
Negative

FIGURE 13A

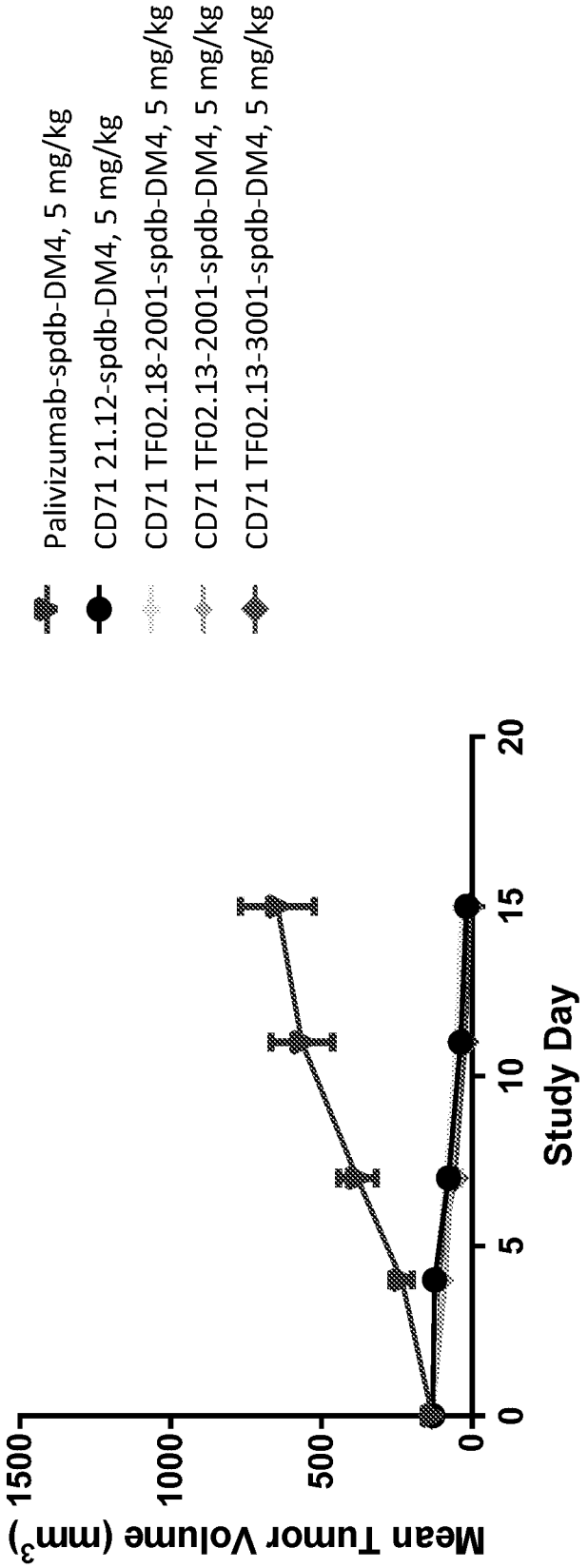

Palivizumab-spdb-DM4, 5 mg/kg
CD71 21.12-spdb-DM4, 5 mg/kg
CD71 TF02.18-2001-spdb-DM4, 5 mg/kg
CD71 TF02.13-2001-spdb-DM4, 5 mg/kg
CD71 TF02.13-3001-spdb-DM4, 5 mg/kg
Mean Tumor Volume (mm3)
1500
1000
500
0
0
5
10
15
20
Study Day

FIGURE 13B

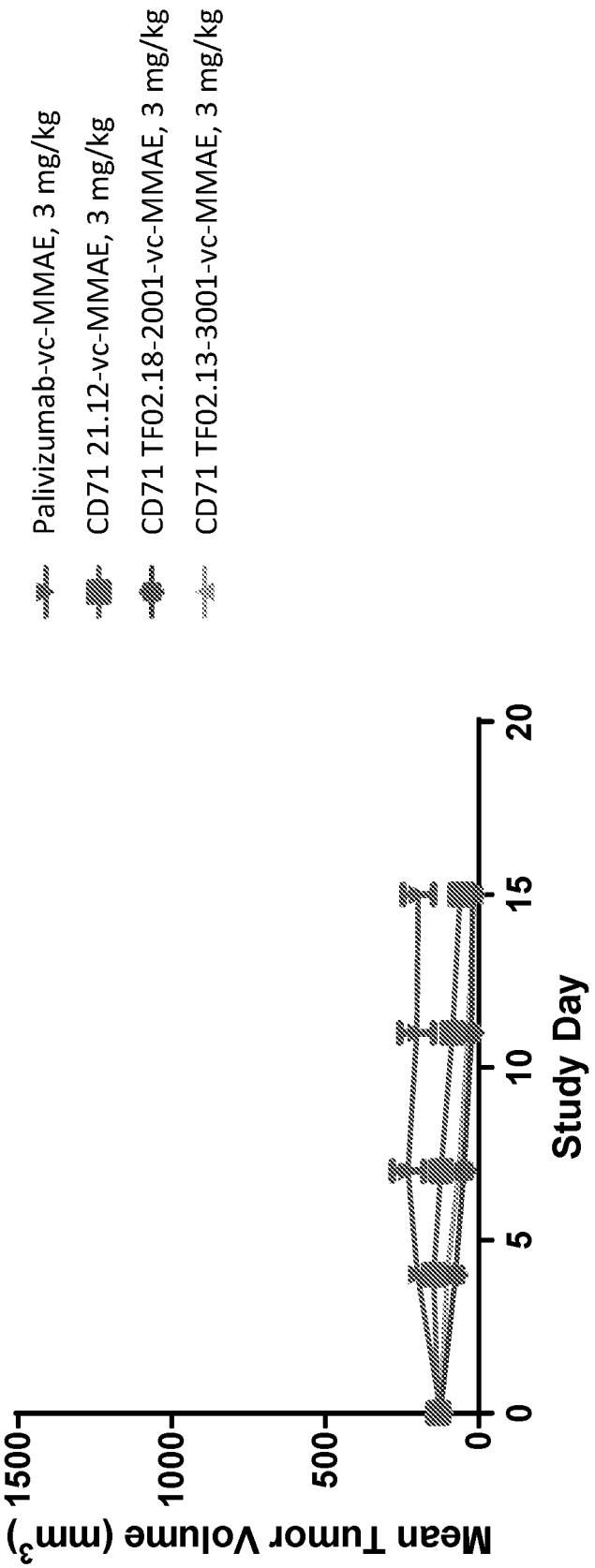

Palivizumab-vc-MMAE, 3 mg/kg
CD71 21.12-vc-MMAE, 3 mg/kg
CD71 TF02.18-2001-vc-MMAE, 3 mg/kg
CD71 TF02.13-3001-vc-MMAE, 3 mg/kg
Mean Tumor Volume (mm3)
1500
1000
500
0
0
5
10
15
20
Study Day

FIGURE 13C

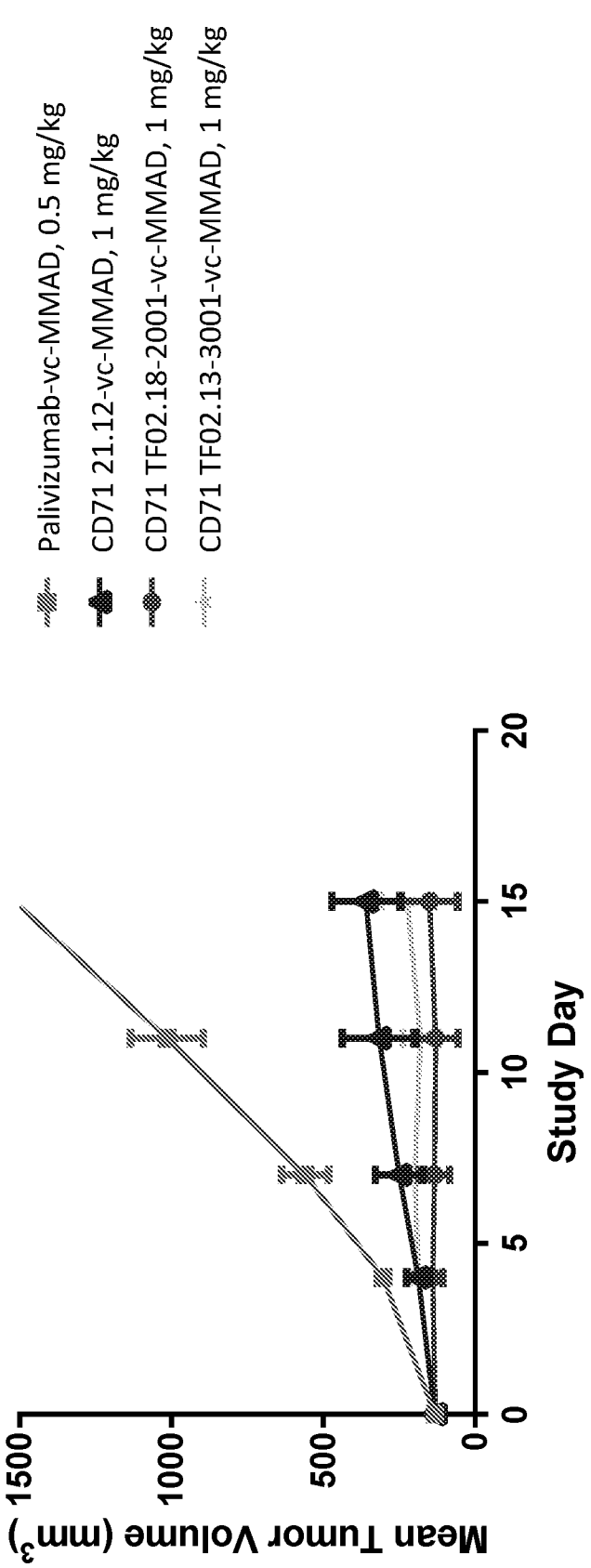

Palivizumab-vc-MMAD, 0.5 mg/kg
CD71 21.12-vc-MMAD, 1 mg/kg
CD71 TF02.18-2001-vc-MMAD, 1 mg/kg
CD71 TF02.13-3001-vc-MMAD, 1 mg/kg
Mean Tumor Volume (mm3)
1500
1000
500
0
0
5
10
15
20
Study Day

FIGURE 14A

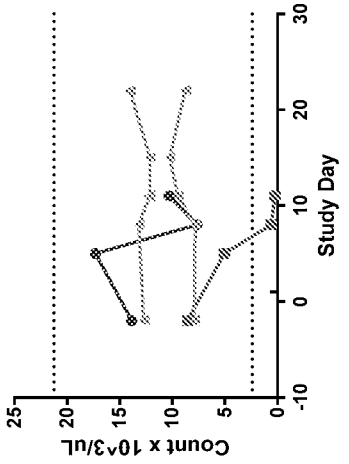


FIGURE 14B

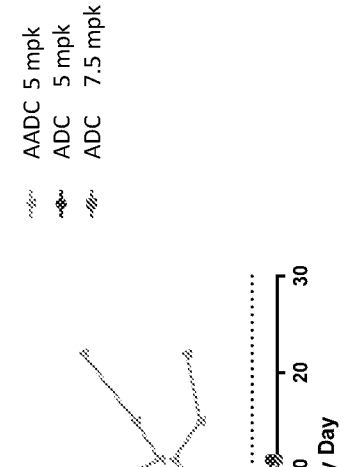


FIGURE 14C

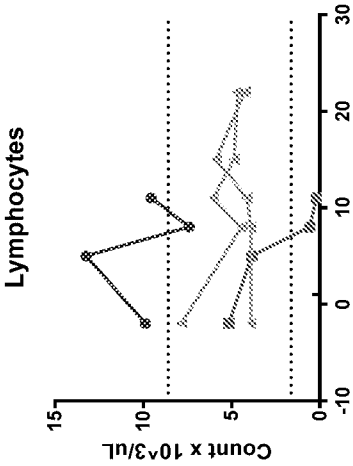


FIGURE 14D

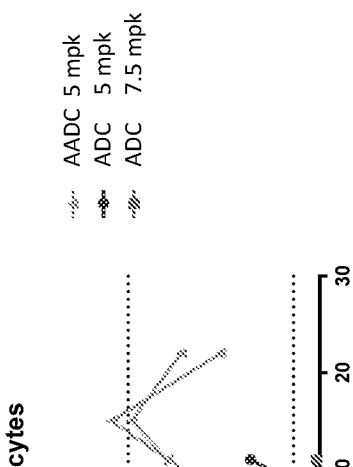


FIGURE 14E

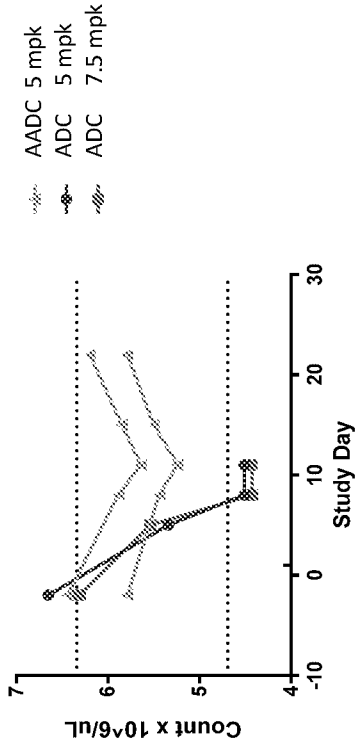
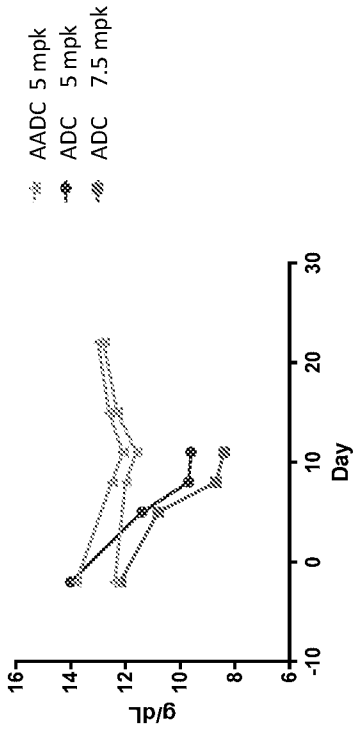


FIGURE 14F



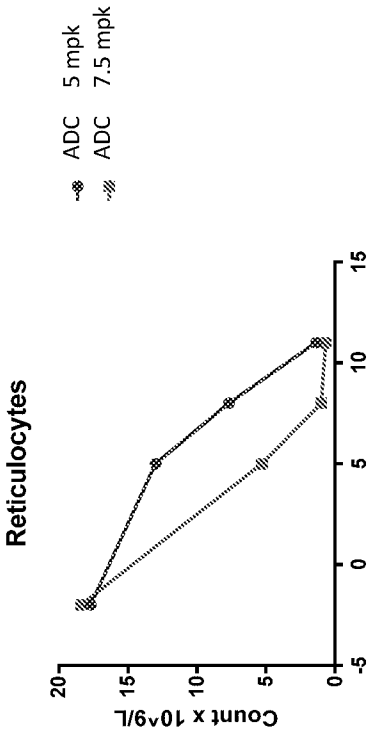


FIGURE 14G

FIGURE 15

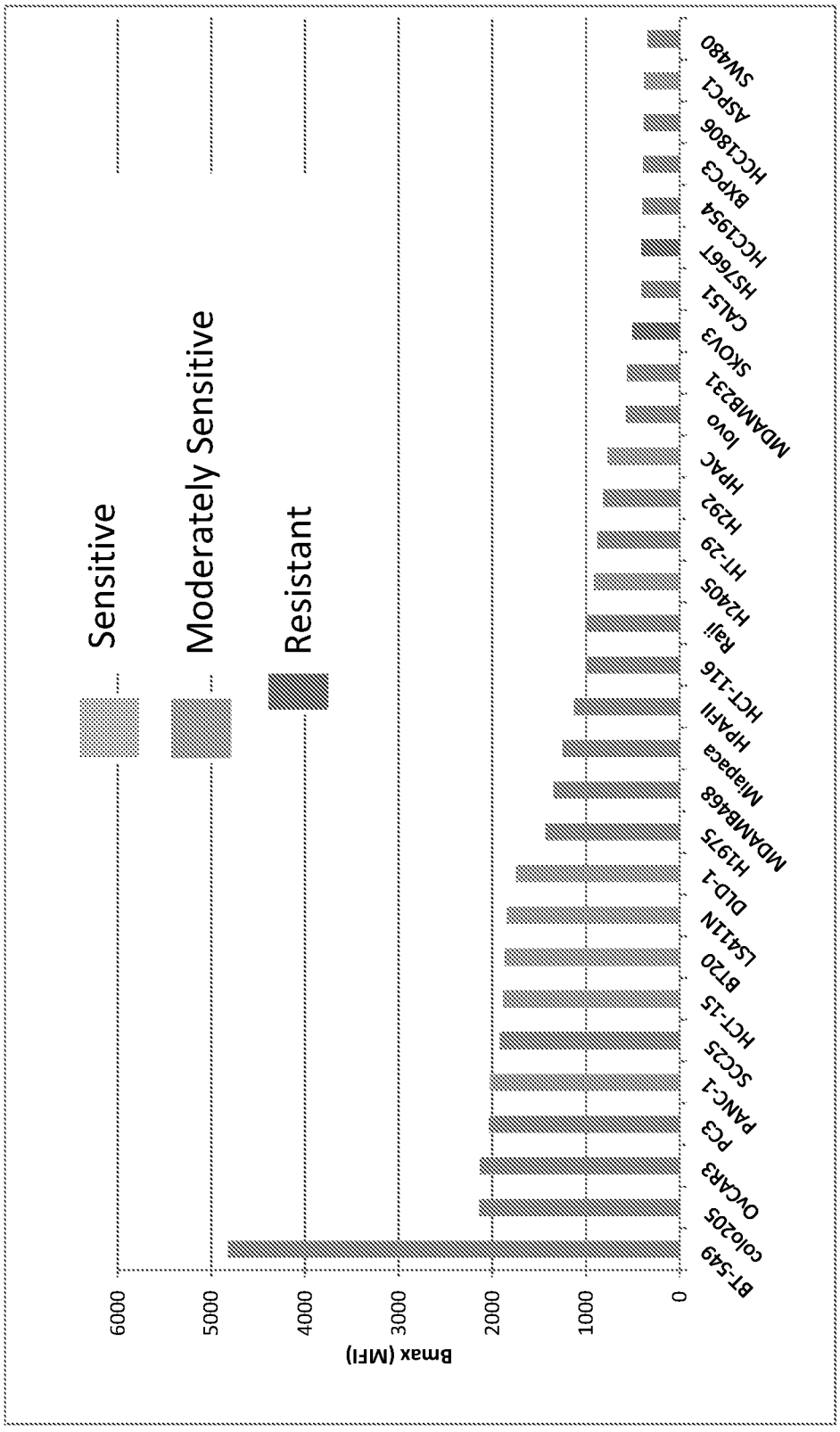

Sensitive
Moderately Sensitive
Resistant
Bmax (MFI)
6000
5000
4000
3000
2000
1000
0
BT-549
colo205
OVCAR3
PC3
PANC-1
SCC25
HCT-15
BT20
LS411N
DLD-1
H1975
MDAMB468
Miapaca
HPAFII
HCT-116
Raji
H2405
HT-29
H292
HPAC
Iovo
MDAMB231
SKOV3
CAL51
HS766T
HCC1954
BxPC3
HCC1806
ASPC1
SW480

FIGURE 16A: HT29 Cells

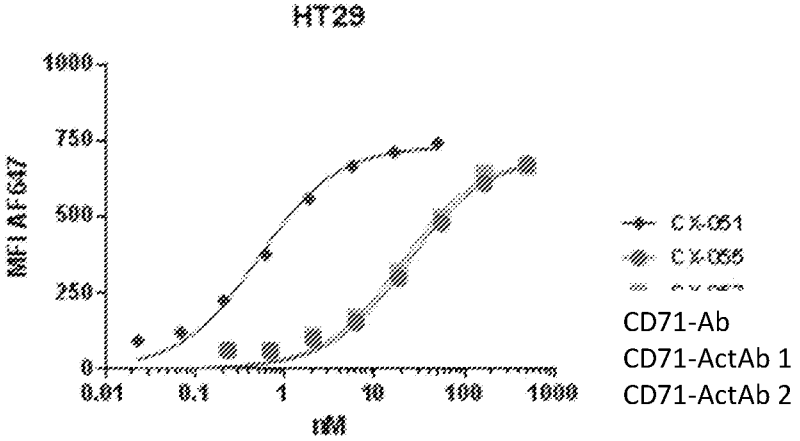


FIGURE 16B: BXPc3 Cells

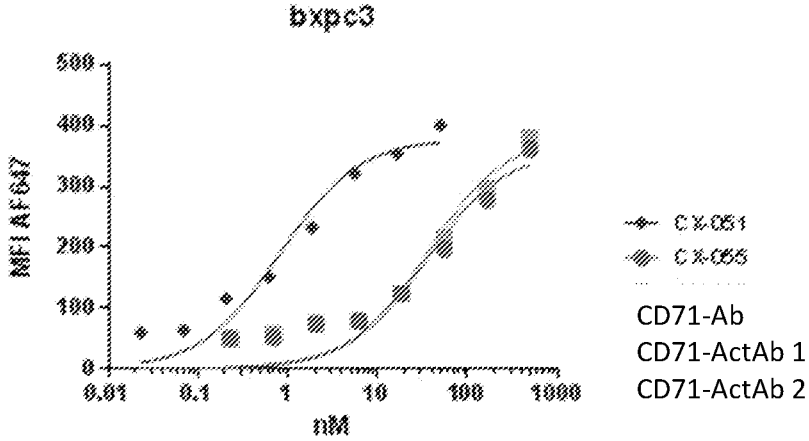


FIGURE 16C: Fadu Cells

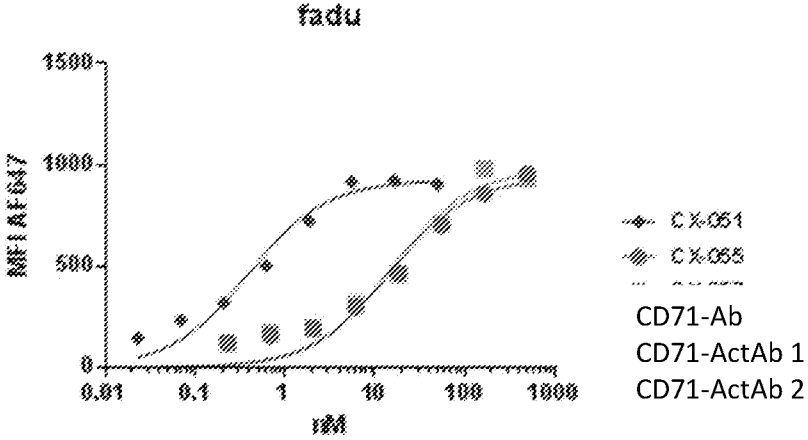


FIGURE 16D: MDA MB231 Cells

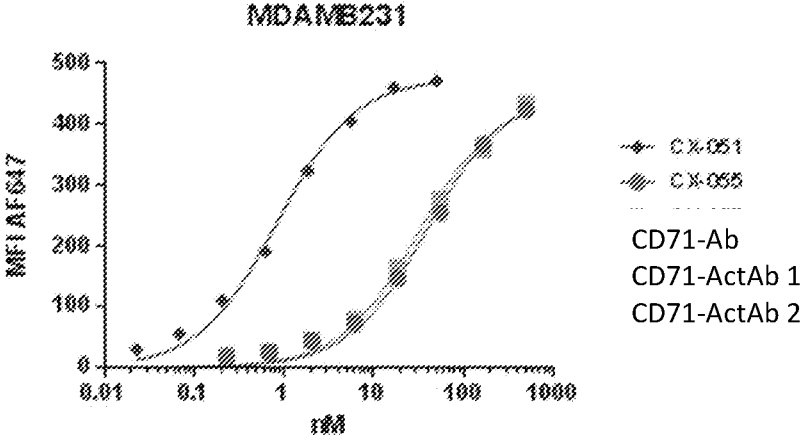


FIGURE 17A

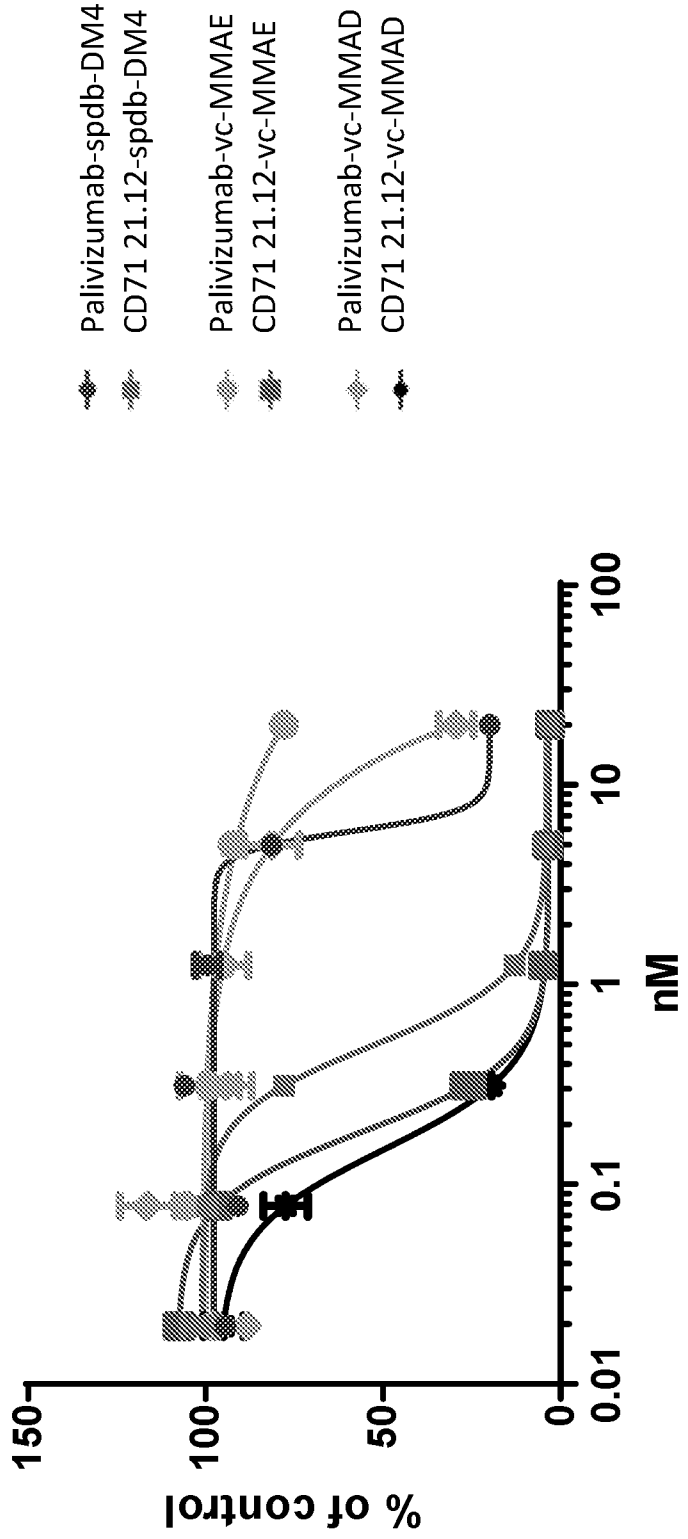

Palivizumab-spdb-DM4
CD71 21.12-spdb-DM4
Palivizumab-vc-MMAE
CD71 21.12-vc-MMAE
Palivizumab-vc-MMAD
CD71 21.12-vc-MMAD
HT29 cells
% of control
150
100
50
0
0.01
0.1
1
10
100
nM

FIGURE 17B

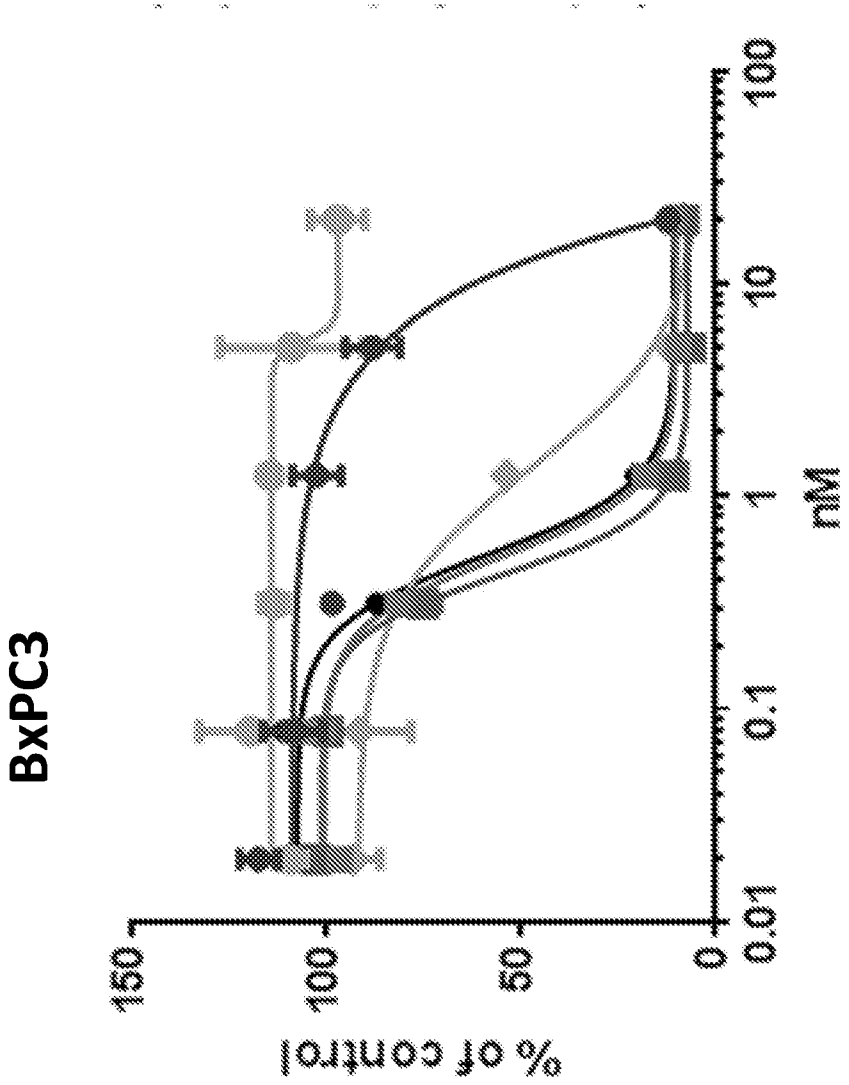

Palivizumab-spdb-DM4
CD71 21.12-spdb-DM4
Palivizumab-vc-MMAE
CD71 21.12-vc-MMAE
Palivizumab-vc-MMAD
CD71 21.12-vc-MMAD
BxPC3
% of control
150
100
50
0
0.01
0.1
1
10
100
nM

FIGURE 17C

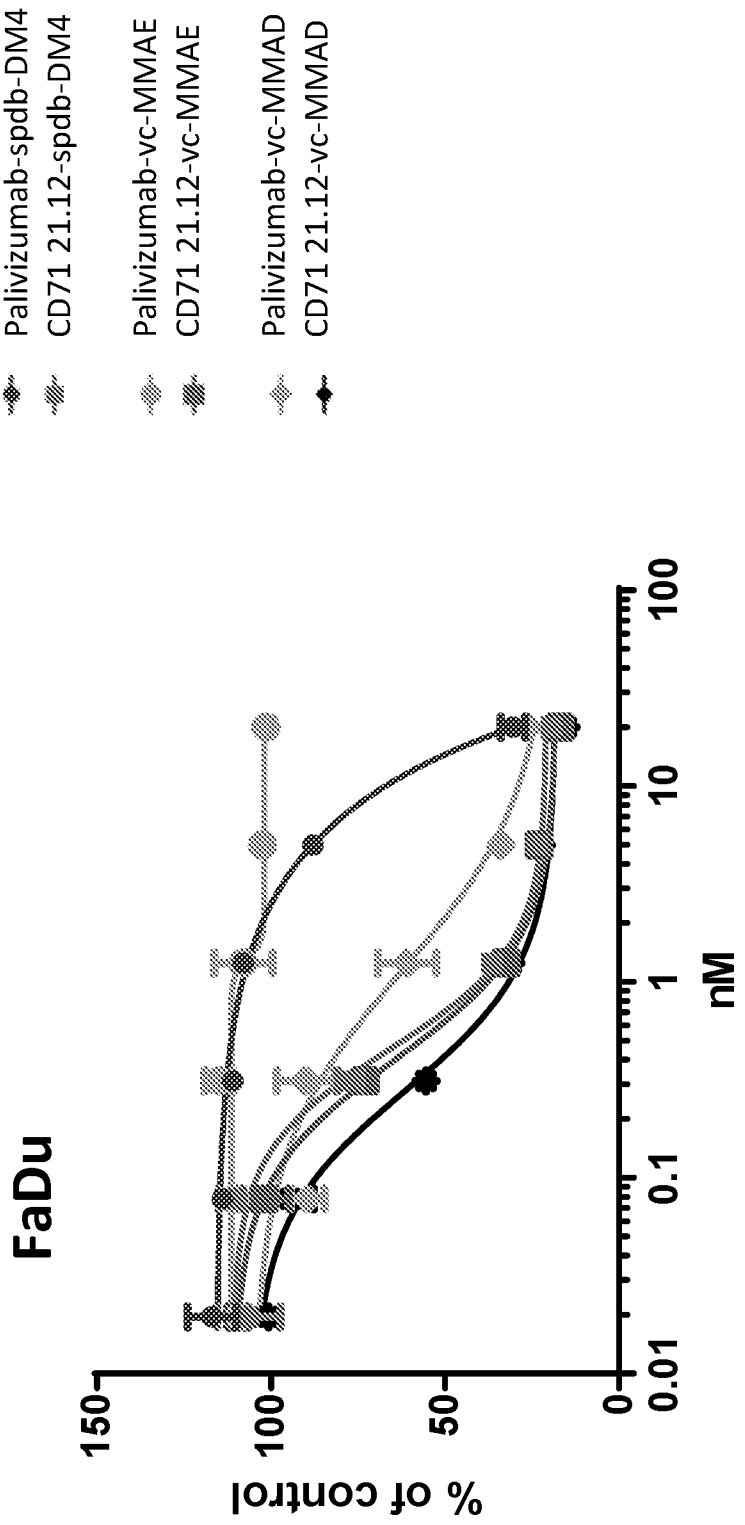

Palivizumab-spdb-DM4
CD71 21.12-spdb-DM4
Palivizumab-vc-MMAE
CD71 21.12-vc-MMAE
Palivizumab-vc-MMAD
CD71 21.12-vc-MMAD
FaDu
% of control
150
100
50
0
0.01
0.1
1
10
100
nM

FIGURE 17D

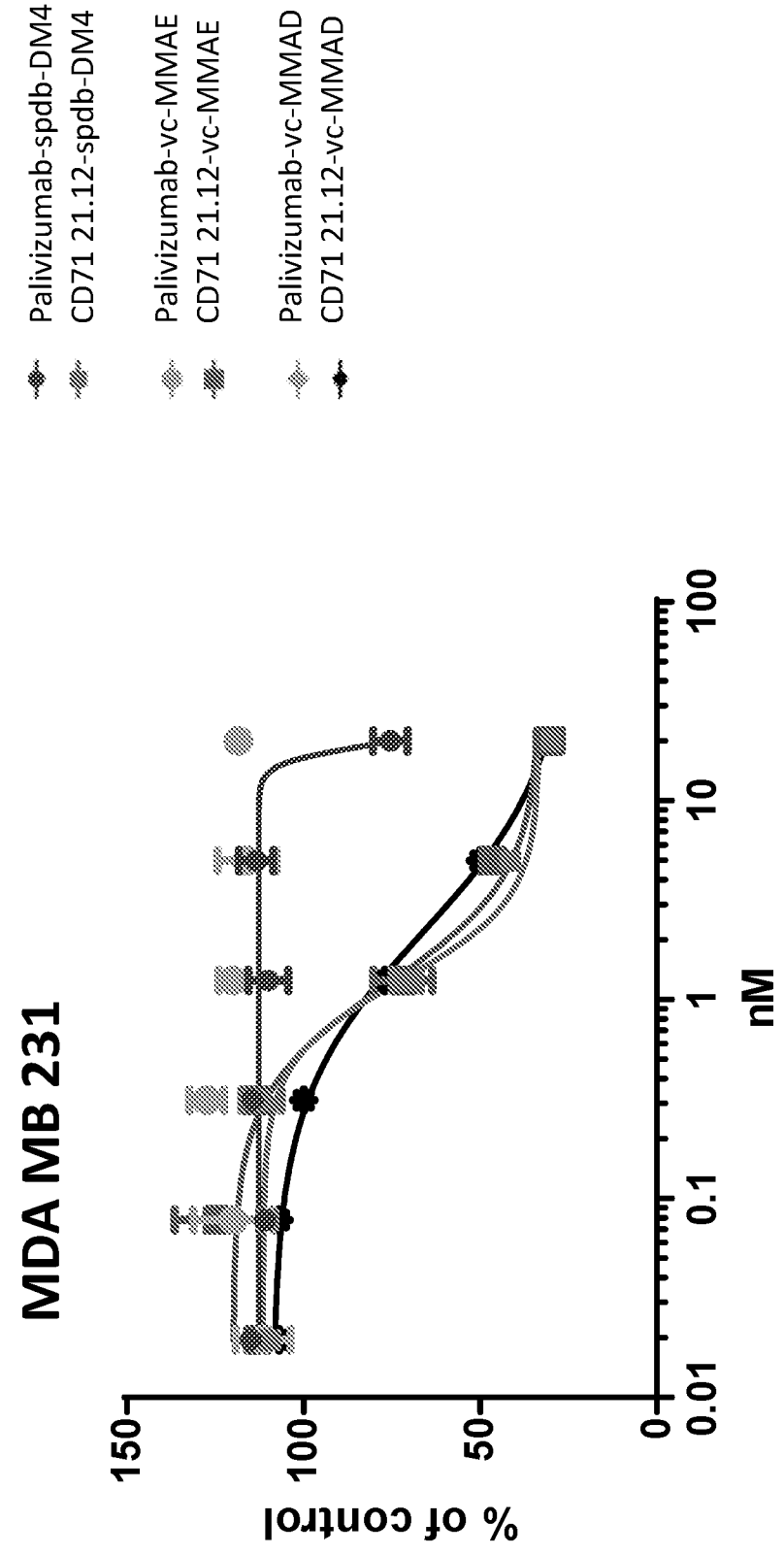

Palivizumab-spdb-DM4
CD71 21.12-spdb-DM4
Palivizumab-vc-MMAE
CD71 21.12-vc-MMAE
Palivizumab-vc-MMAD
CD71 21.12-vc-MMAD
MDA MB 231
% of control
150
100
50
0
0.01
0.1
1
10
100
nM

FIGURE 18

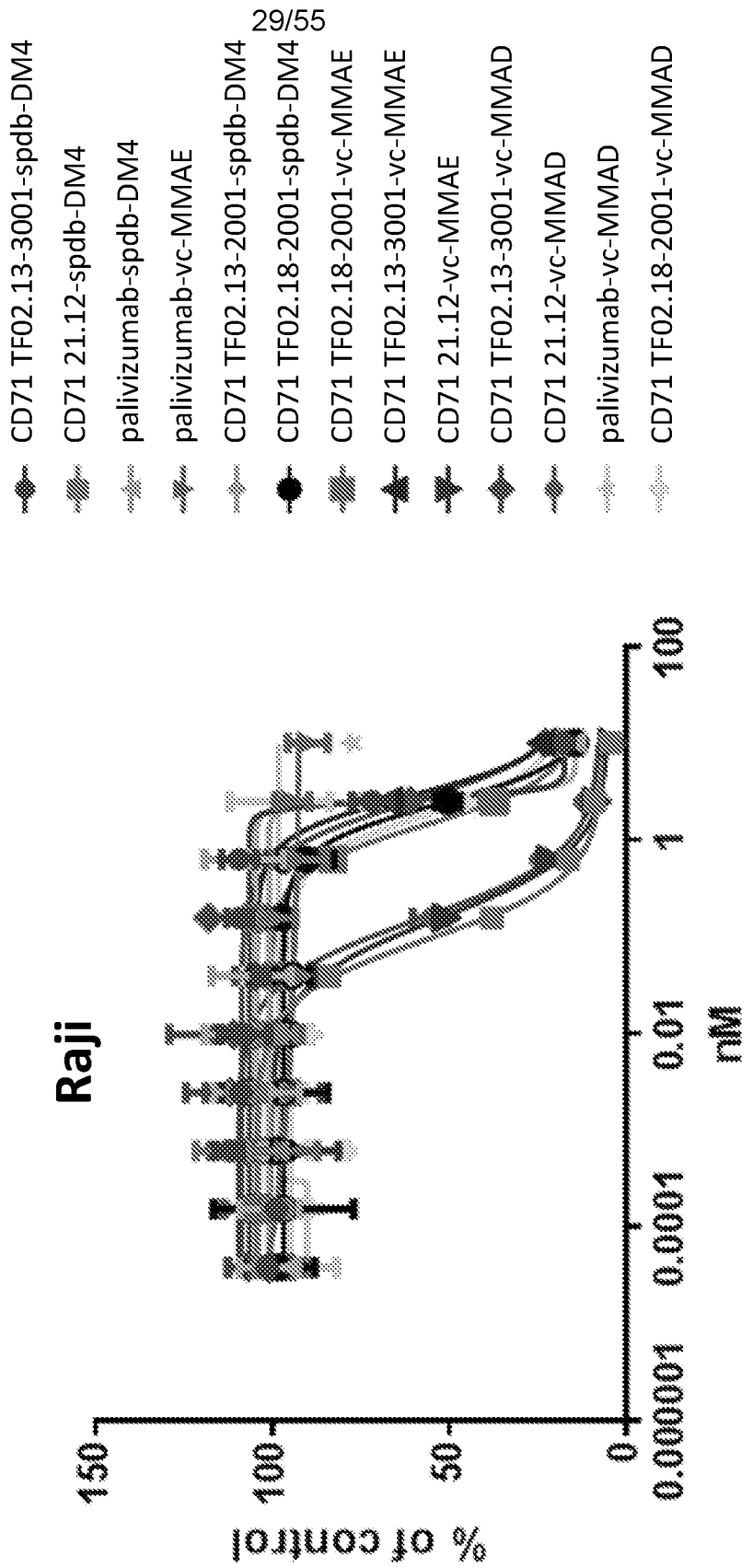

Raji
% of control
150
100
50
0
0.000001
0.0001
0.01
1
100
nM
CD71 TF02.13-3001-spdb-DM4
CD71 21.12-spdb-DM4
palivizumab-spdb-DM4
palivizumab-vc-MMAE
CD71 TF02.13-2001-spdb-DM4
CD71 TF02.18-2001-spdb-DM4
CD71 TF02.18-2001-vc-MMAE
CD71 TF02.13-3001-vc-MMAE
CD71 21.12-vc-MMAE
CD71 TF02.13-3001-vc-MMAD
CD71 21.12-vc-MMAD
palivizumab-vc-MMAD
CD71 TF02.18-2001-vc-MMAD

FIGURE 19

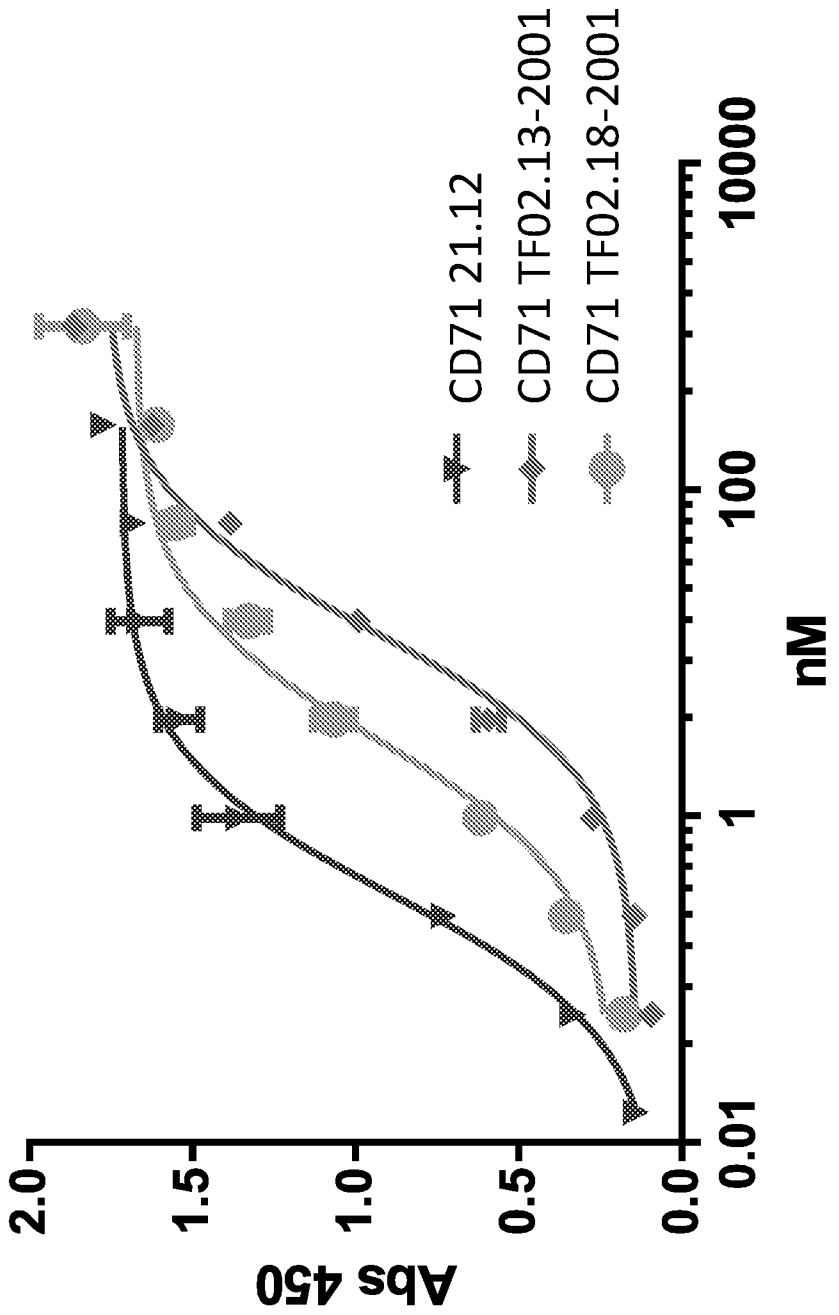

Abs 450
2.0
1.5
1.0
0.5
0.0
0.01
1
100
10000
nM
CD71 21.12
CD71 TF02.13-2001
CD71 TF02.18-2001

FIGURE 20A

Model LY2214

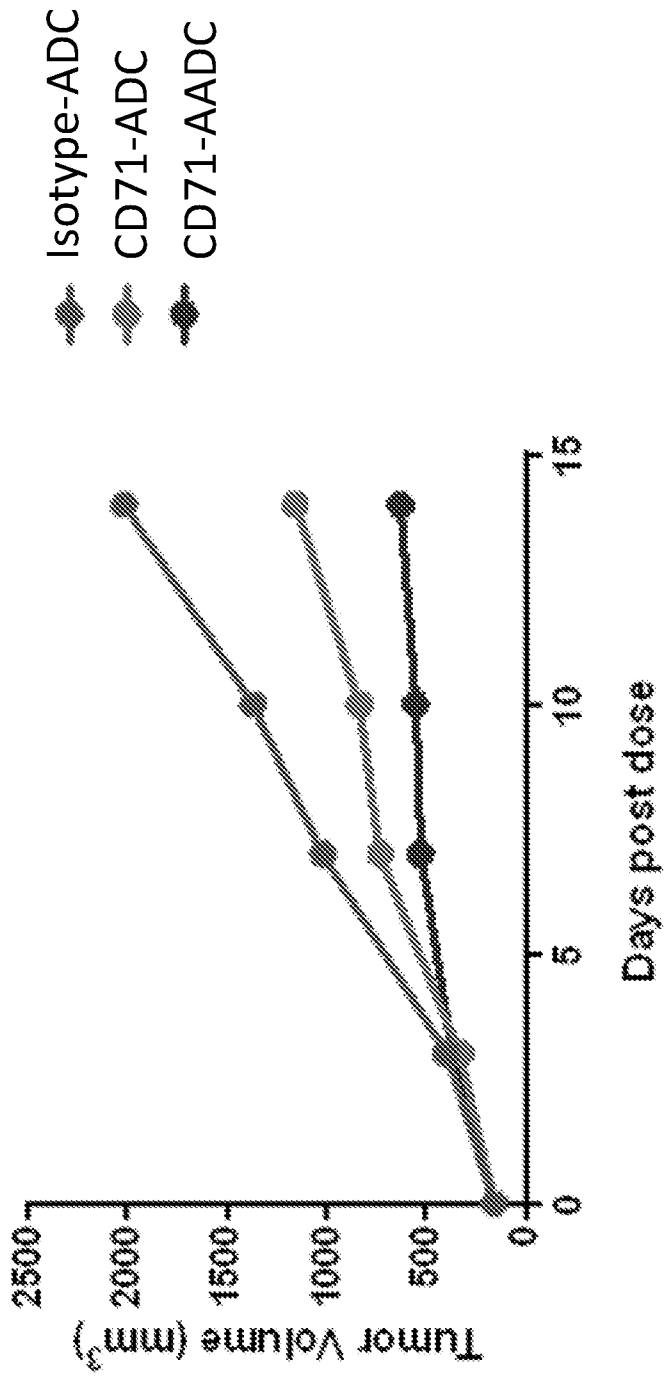


FIGURE 20B

Model LY0257

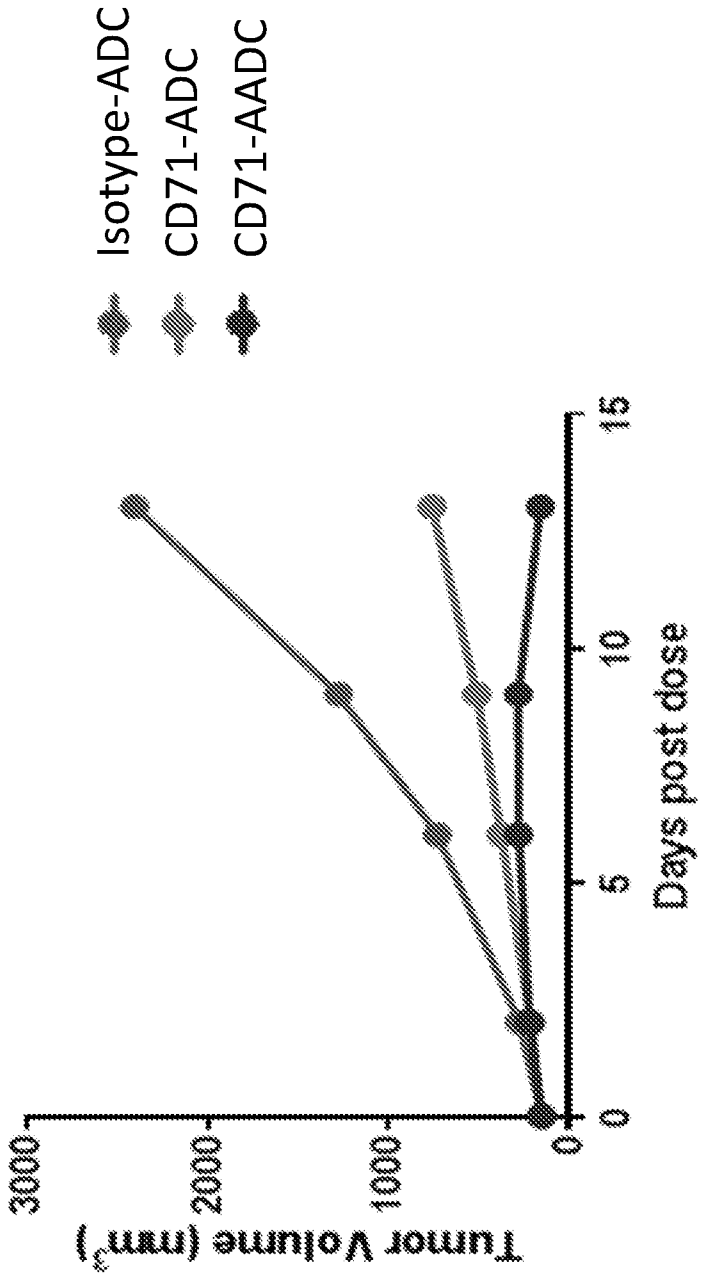


FIGURE 21A

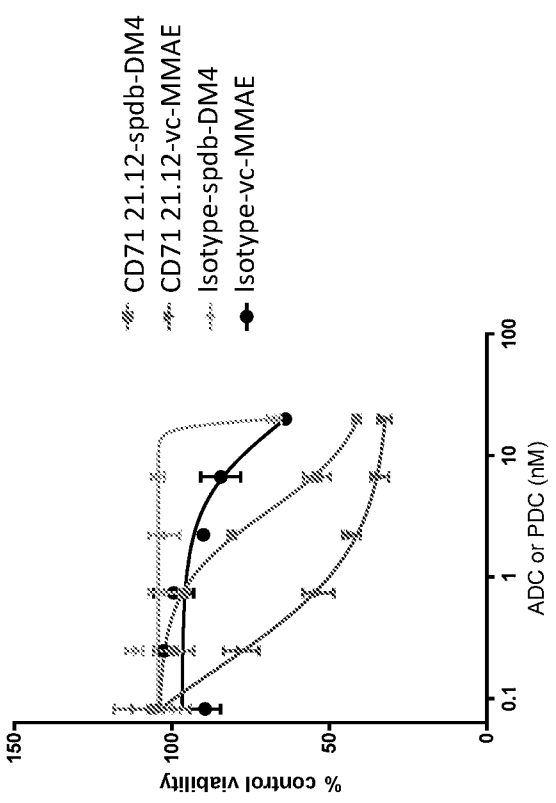


FIGURE 21B

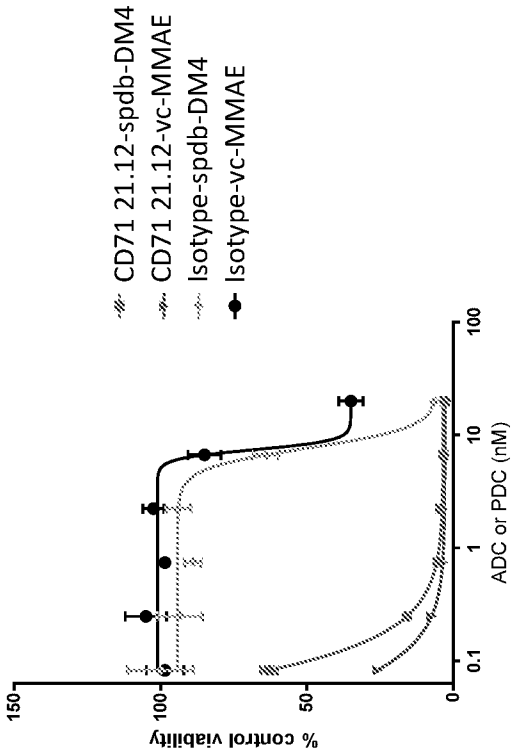


FIGURE 21C

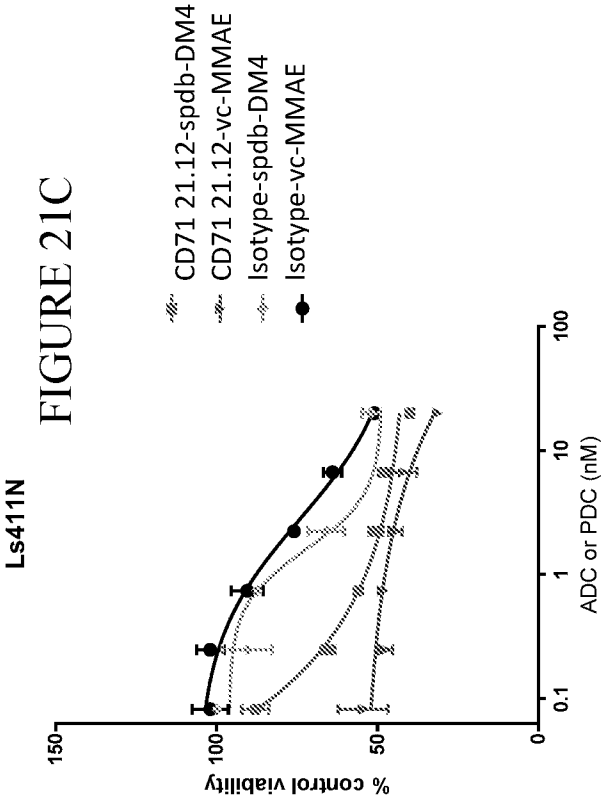


FIGURE 21D

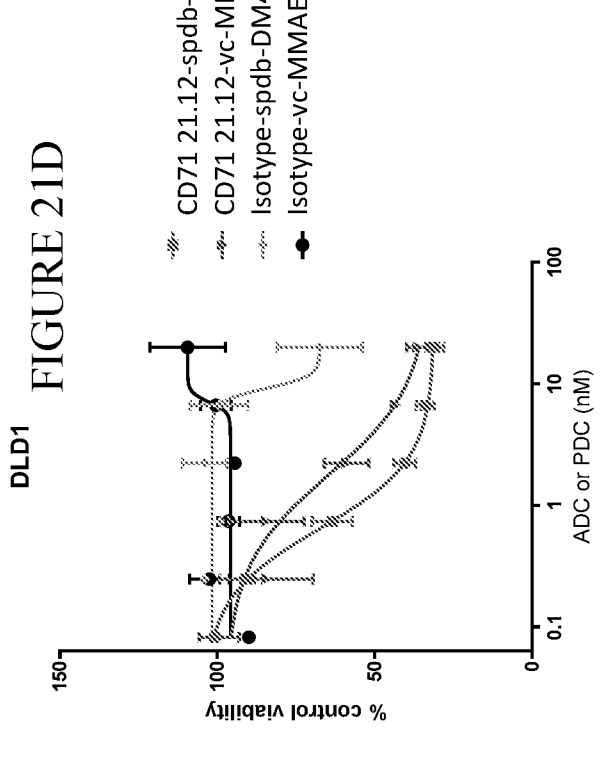


FIGURE 21E

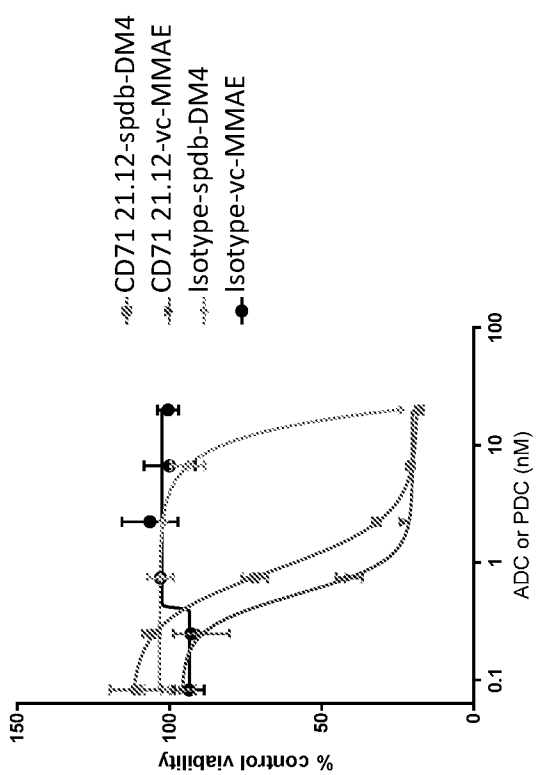


FIGURE 21F

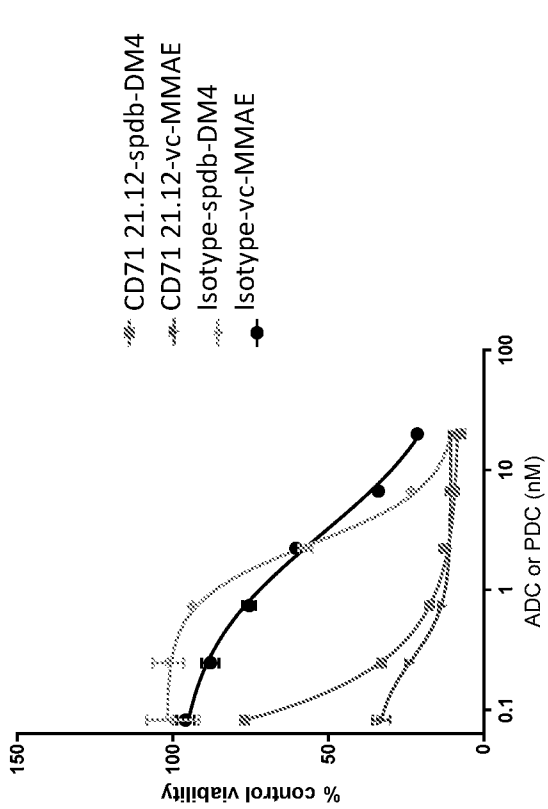


FIGURE 21G

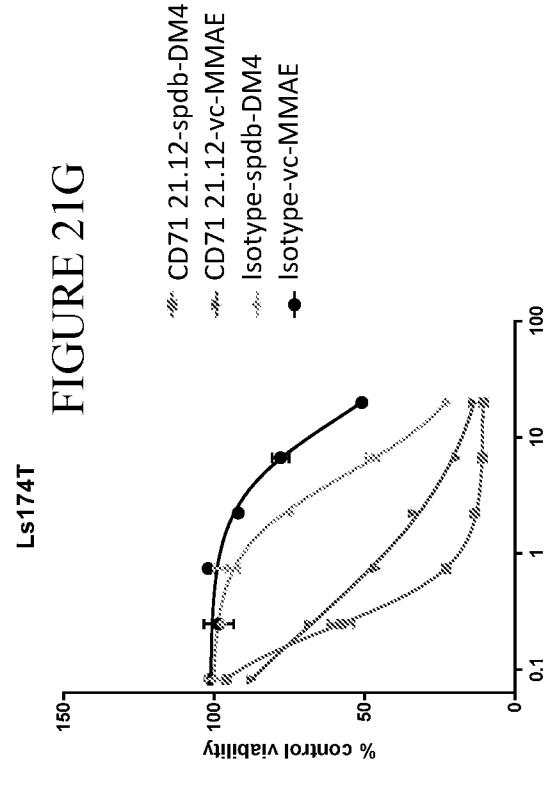


FIGURE 21H

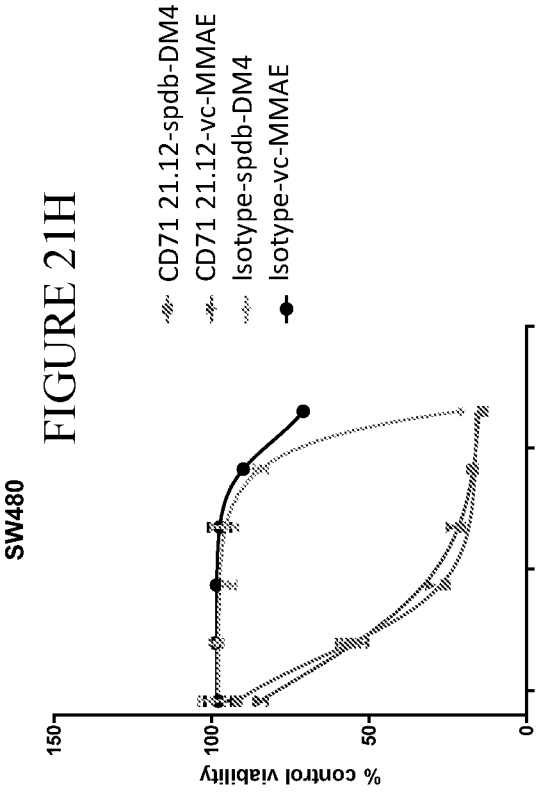


FIGURE 22A

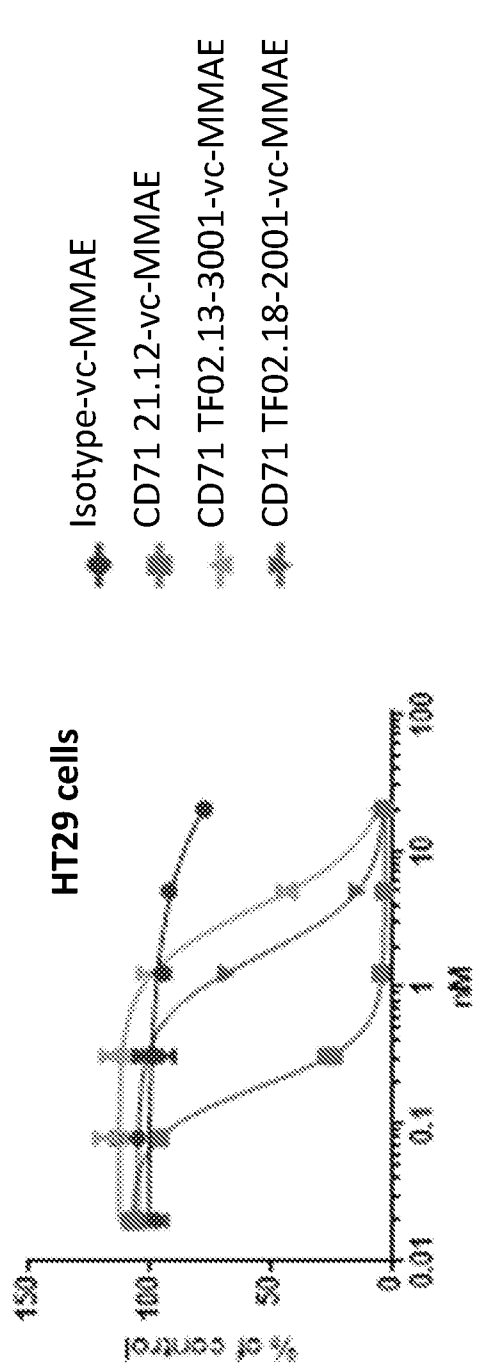


FIGURE 22B

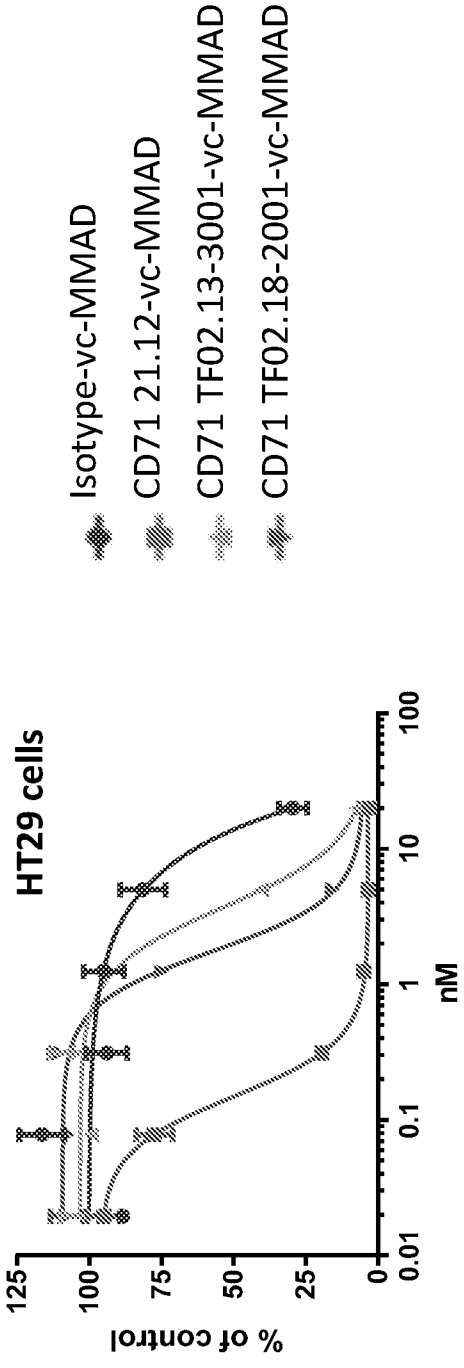


FIGURE 23A

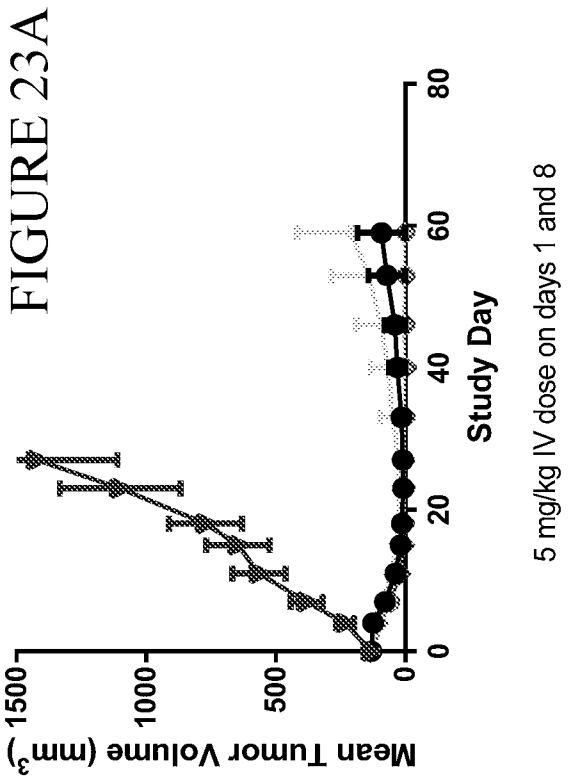


FIGURE 23B

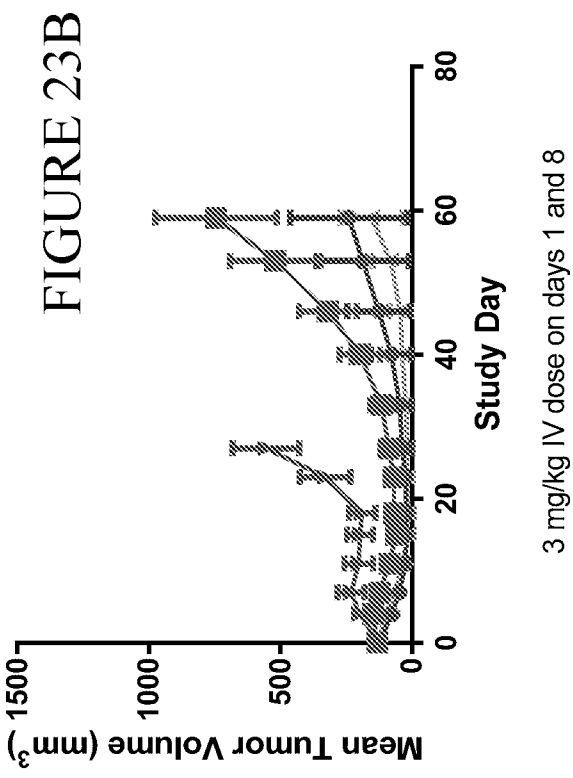


FIGURE 24A

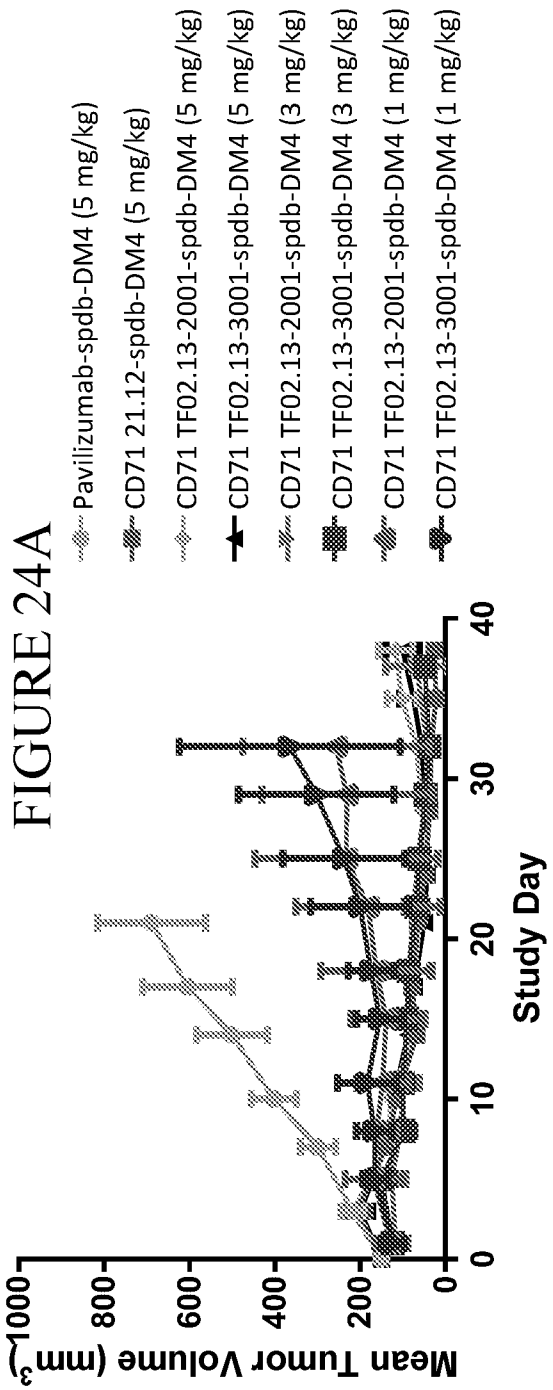


FIGURE 24B

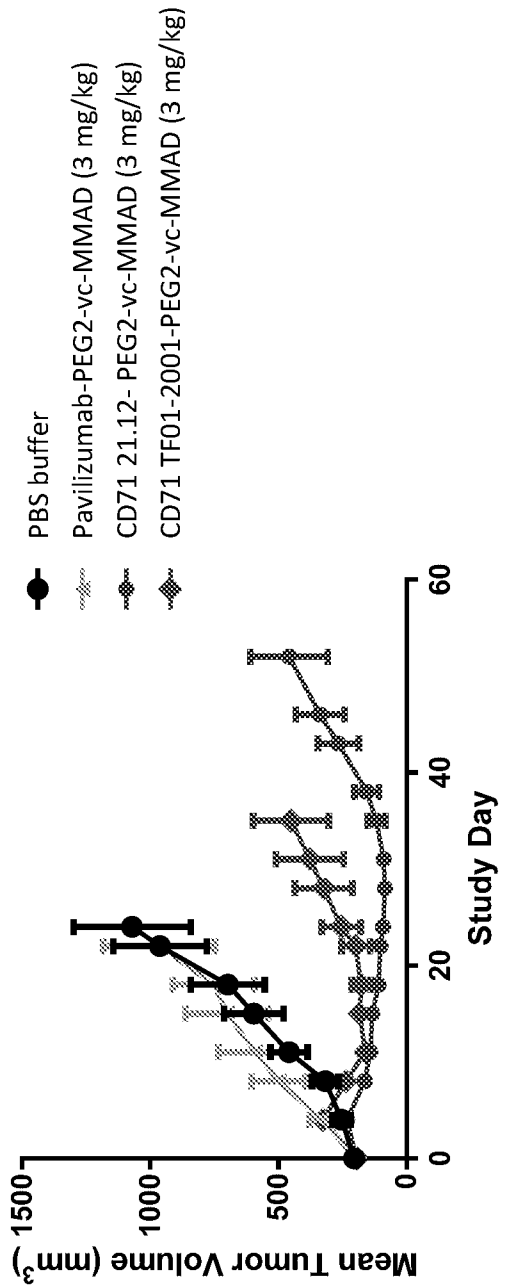


FIGURE 25

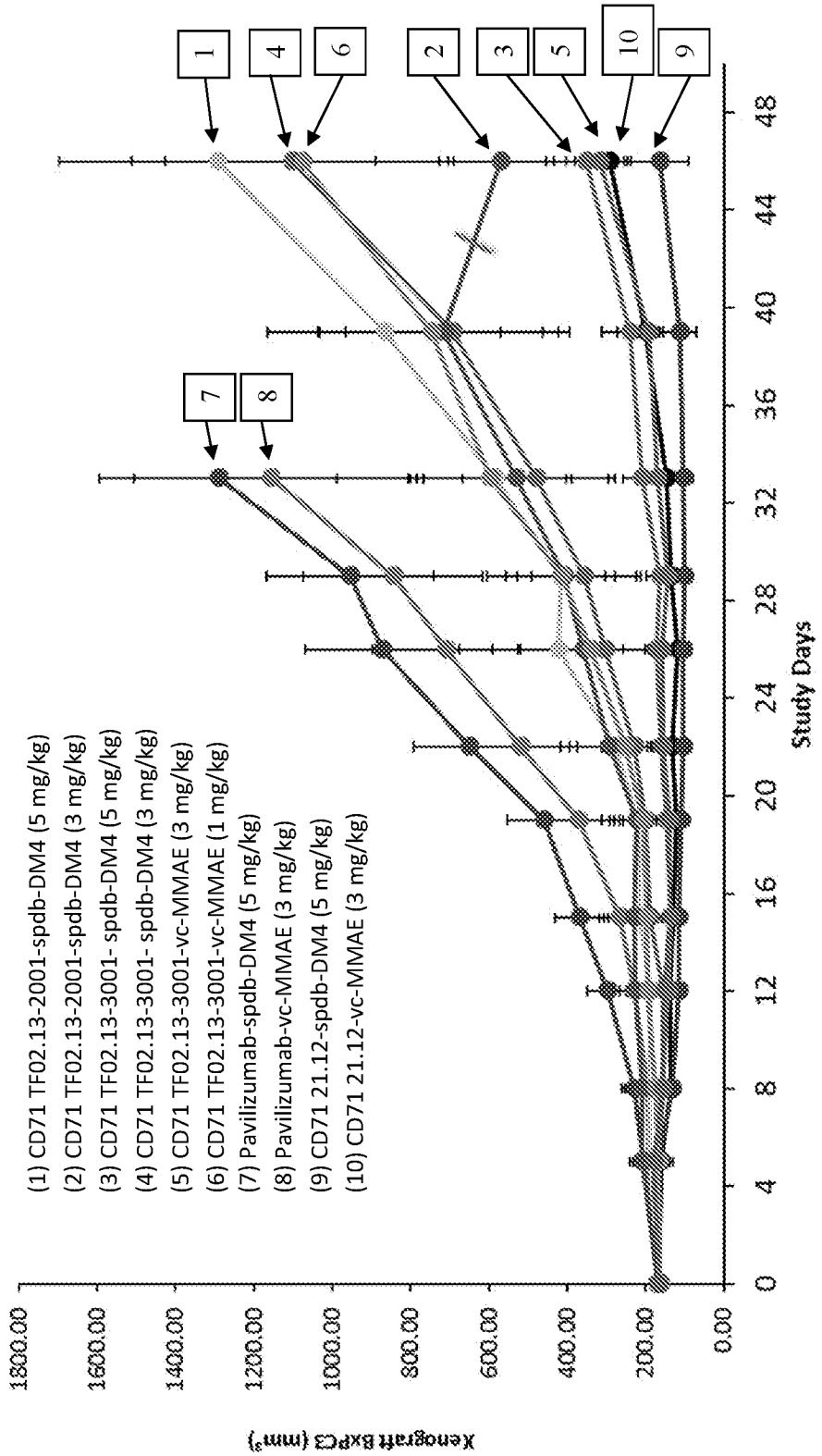

Xenograft BxPC3 (mm³)
1800.00
1600.00
1400.00
1200.00
1000.00
800.00
600.00
400.00
200.00
0.00
0
4
8
12
16
20
24
28
32
36
40
44
48
Study Days
(1) CD71 TF02.13-2001-spdb-DM4 (5 mg/kg)
(2) CD71 TF02.13-2001-spdb-DM4 (3 mg/kg)
(3) CD71 TF02.13-3001- spdb-DM4 (5 mg/kg)
(4) CD71 TF02.13-3001- spdb-DM4 (3 mg/kg)
(5) CD71 TF02.13-3001-vc-MMAE (3 mg/kg)
(6) CD71 TF02.13-3001-vc-MMAE (1 mg/kg)
(7) Pavilizumab-spdb-DM4 (5 mg/kg)
(8) Pavilizumab-vc-MMAE (3 mg/kg)
(9) CD71 21.12-spdb-DM4 (5 mg/kg)
(10) CD71 21.12-vc-MMAE (3 mg/kg)
1
4
6
2
3
5
10
9
7
8

FIGURE 26A

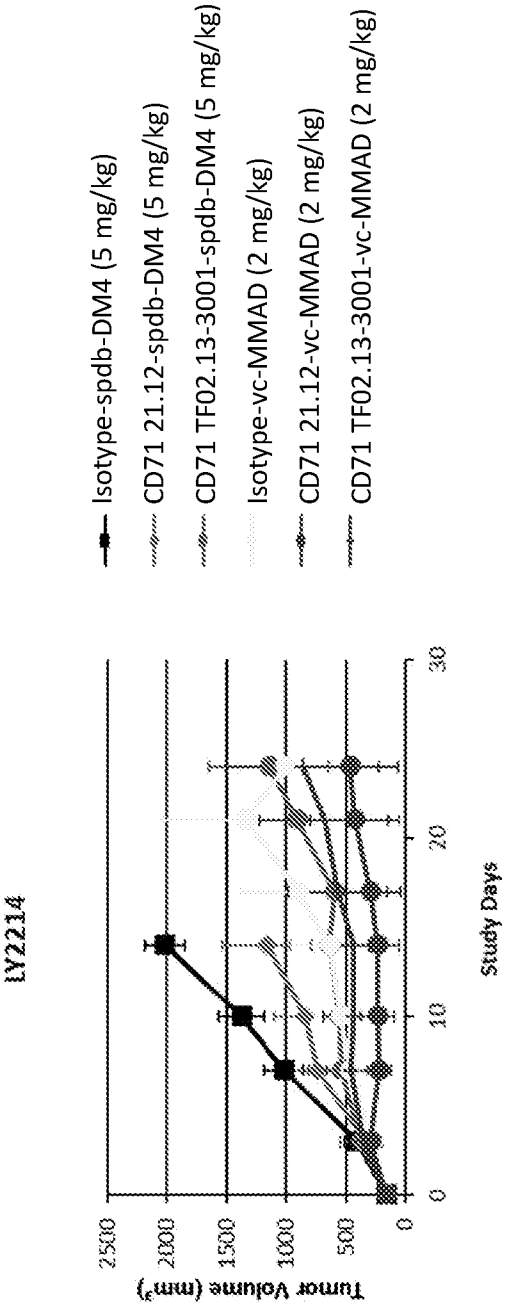


FIGURE 26B

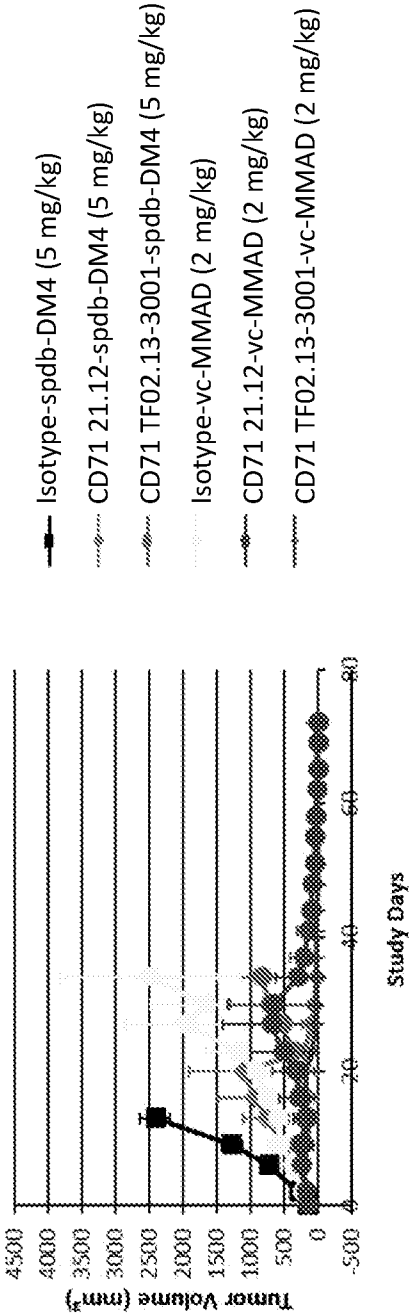


FIGURE 27A

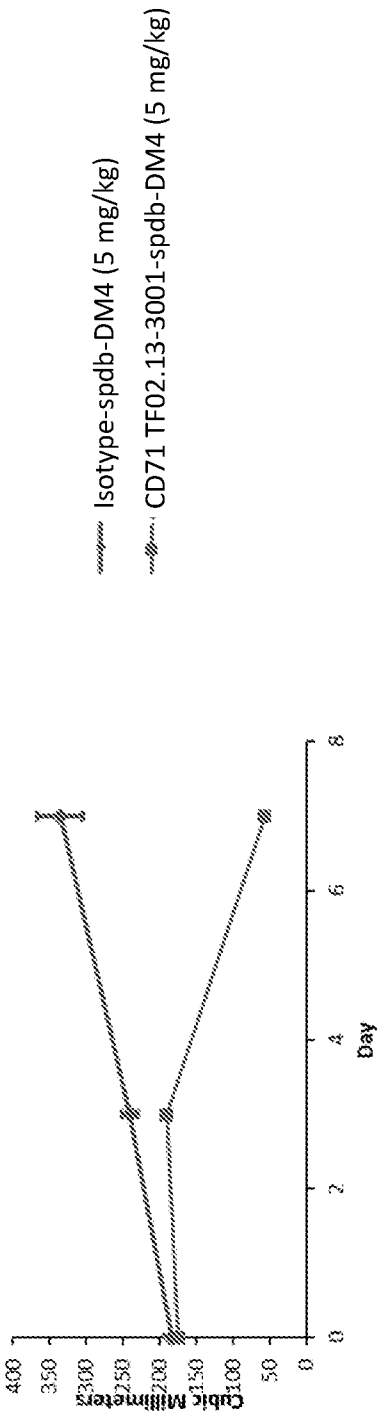


FIGURE 27B

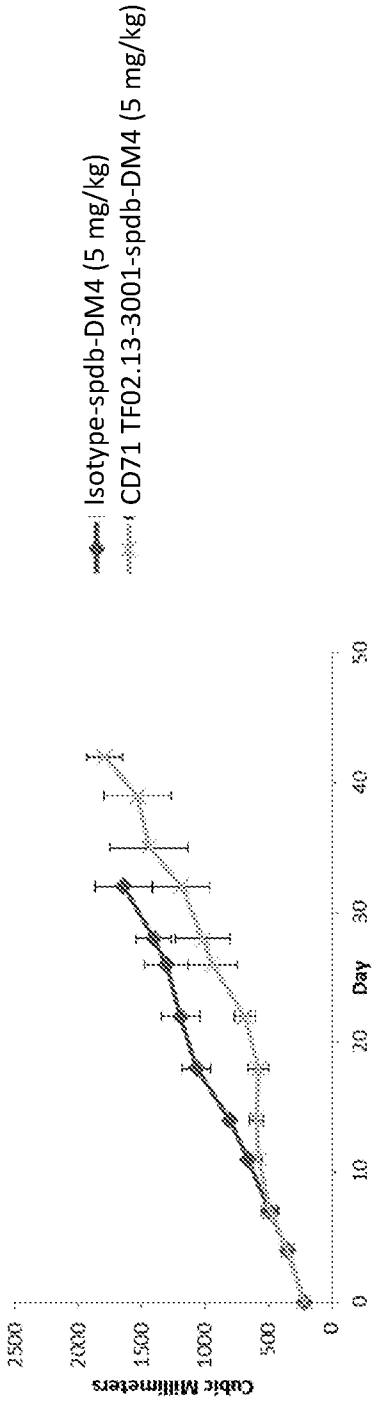


FIGURE 28

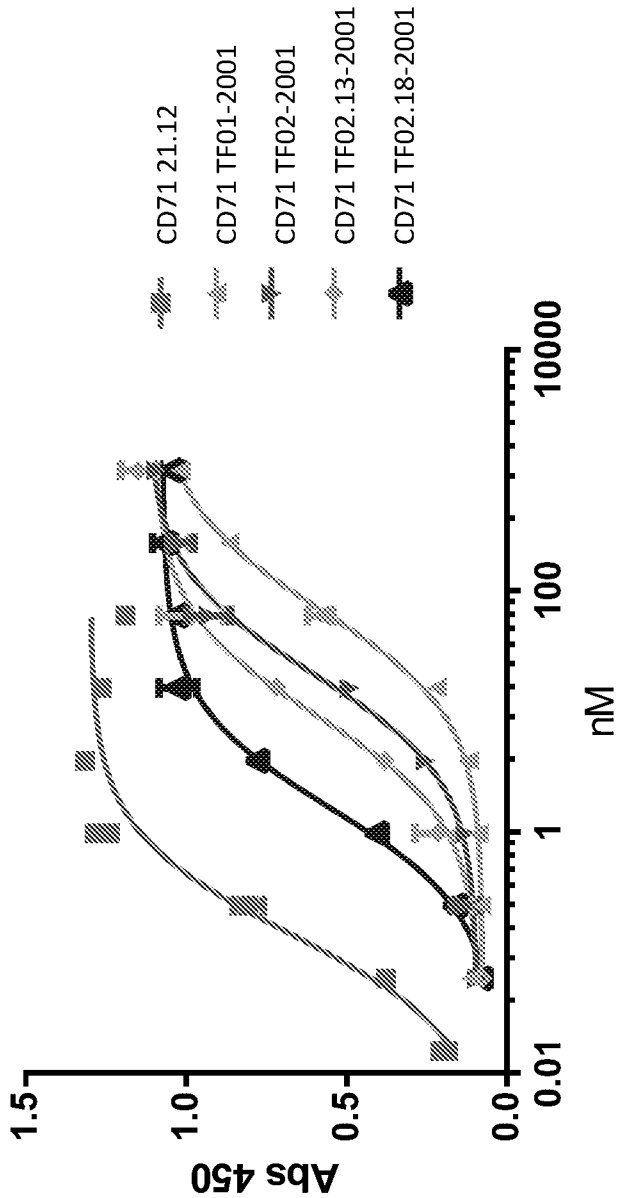

CD71 21.12
CD71 TF01-2001
CD71 TF02-2001
CD71 TF02.13-2001
CD71 TF02.18-2001
Abs 450
1.5
1.0
0.5
0.0
0.01
1
100
10000
nM

FIGURE 29A

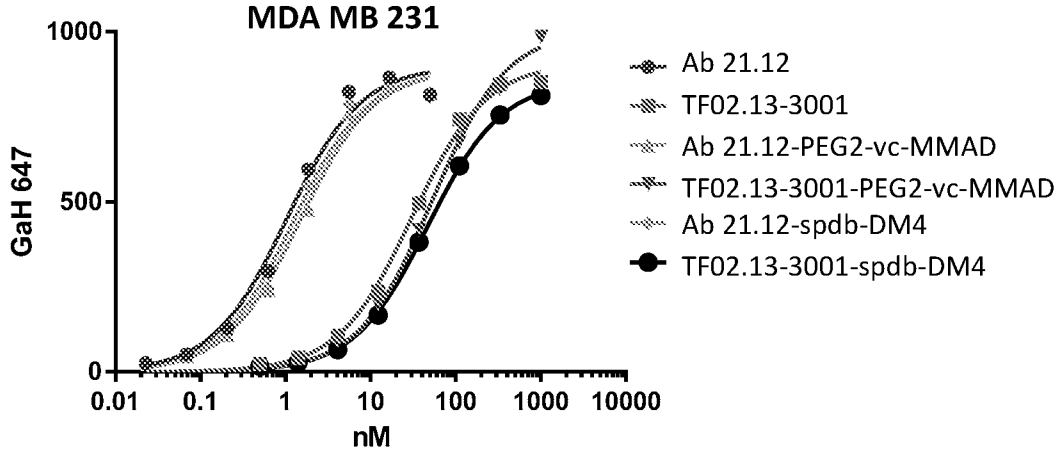


FIGURE 29B

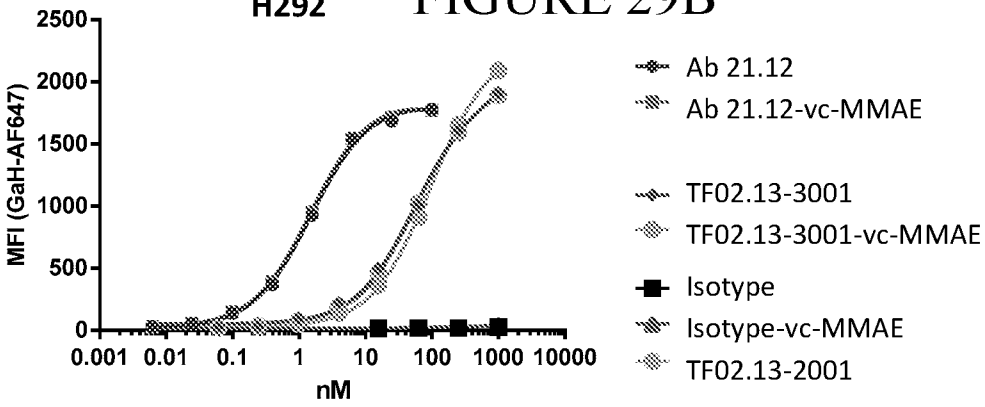


FIGURE 29C

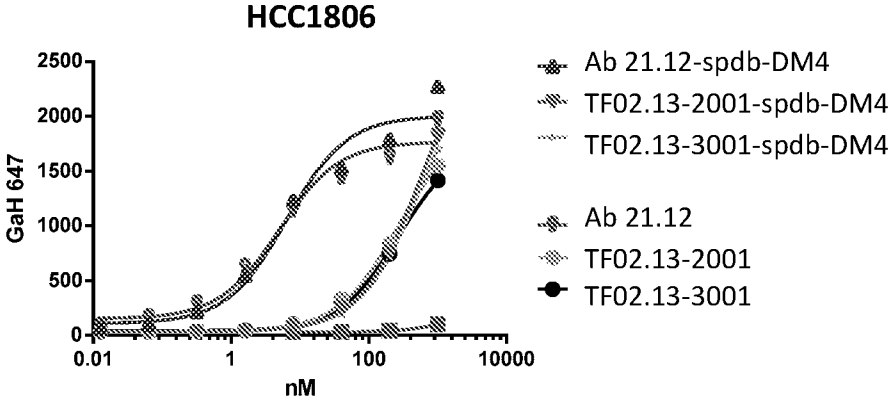


FIGURE 30A

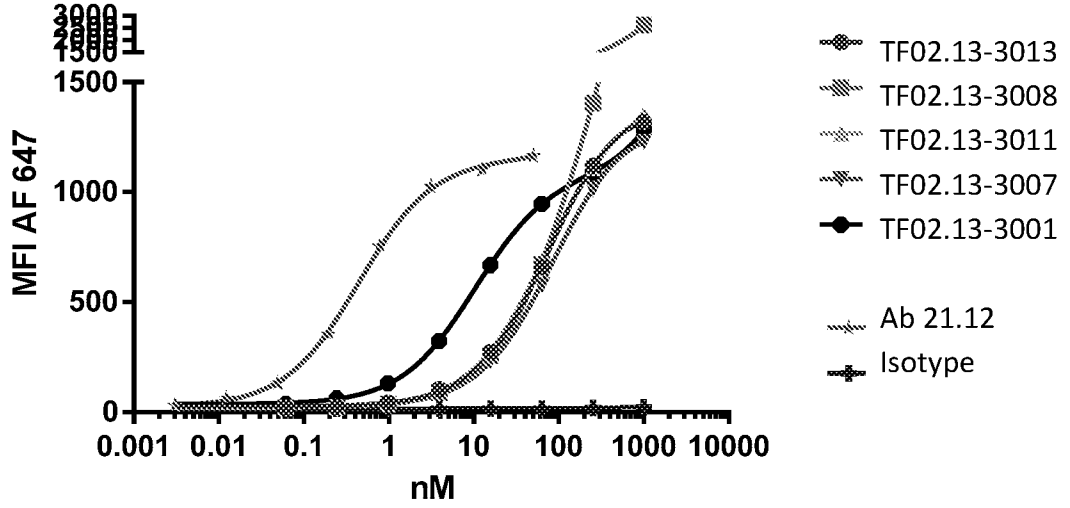


FIGURE 30B

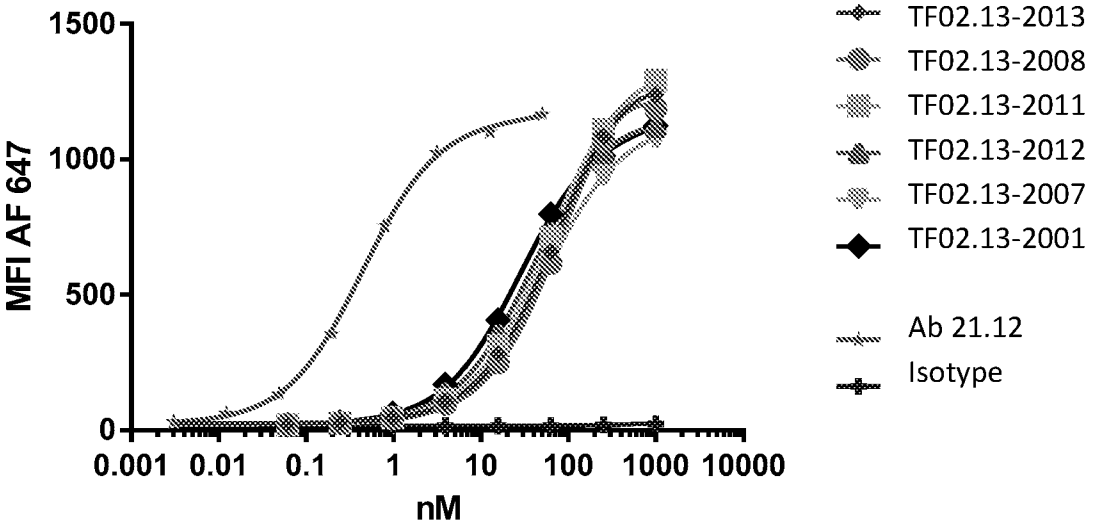


FIGURE 30C

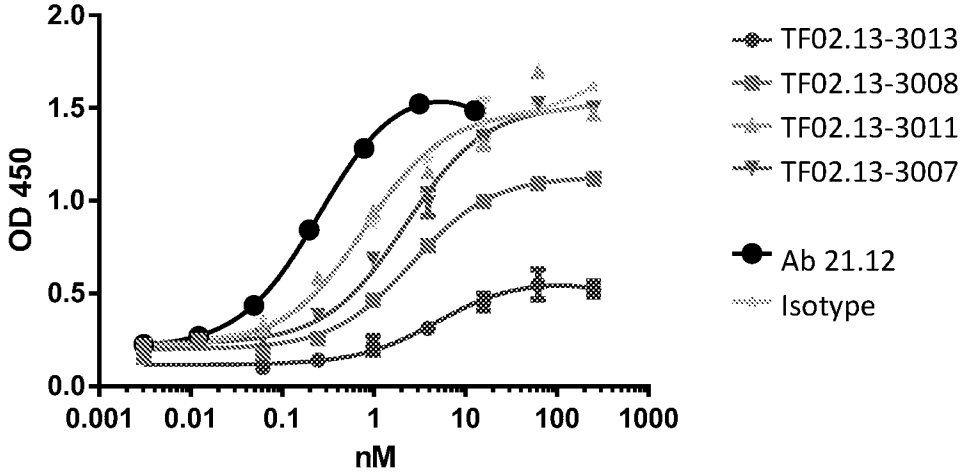


FIGURE 30D

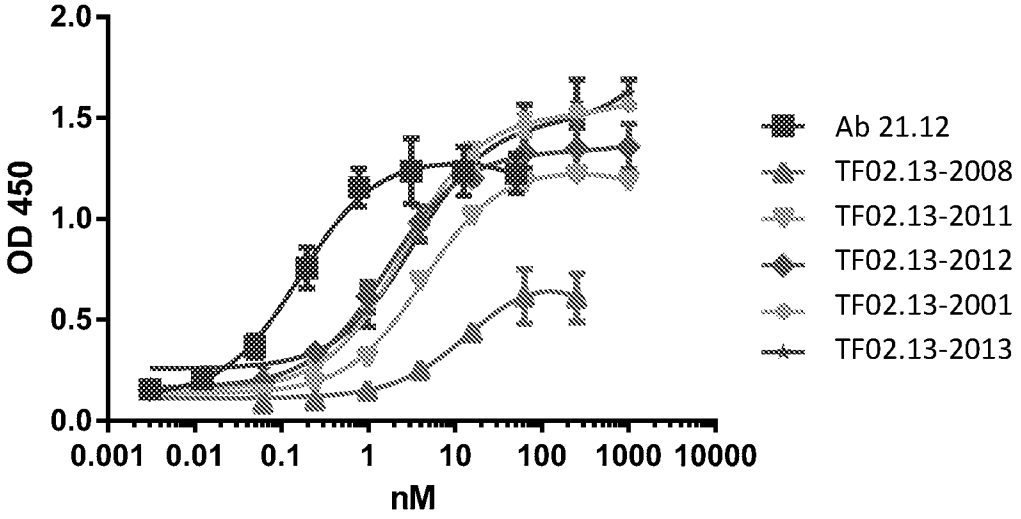


FIGURE 31A

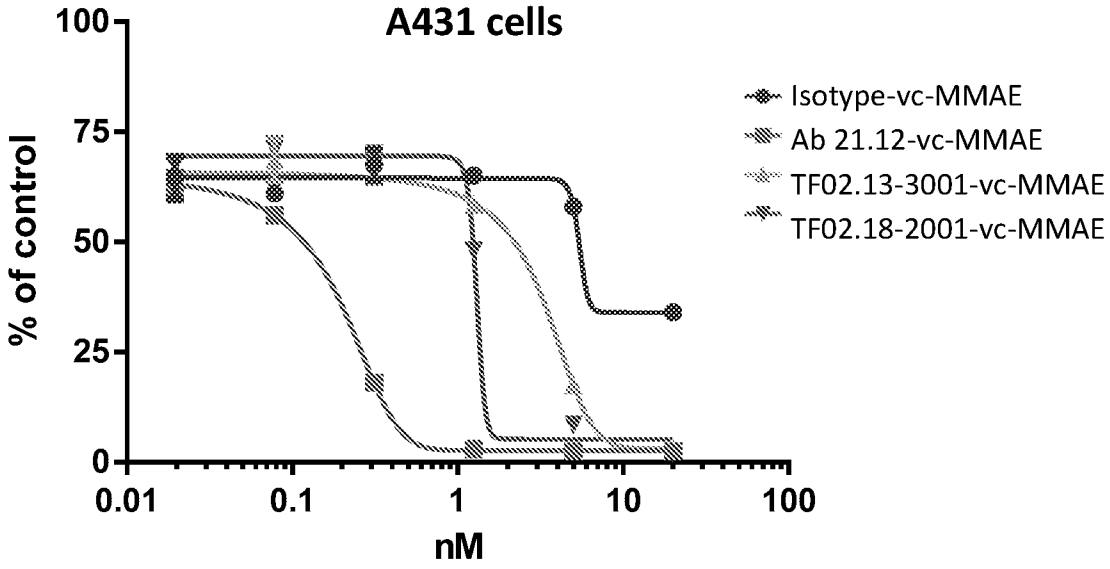


FIGURE 31B

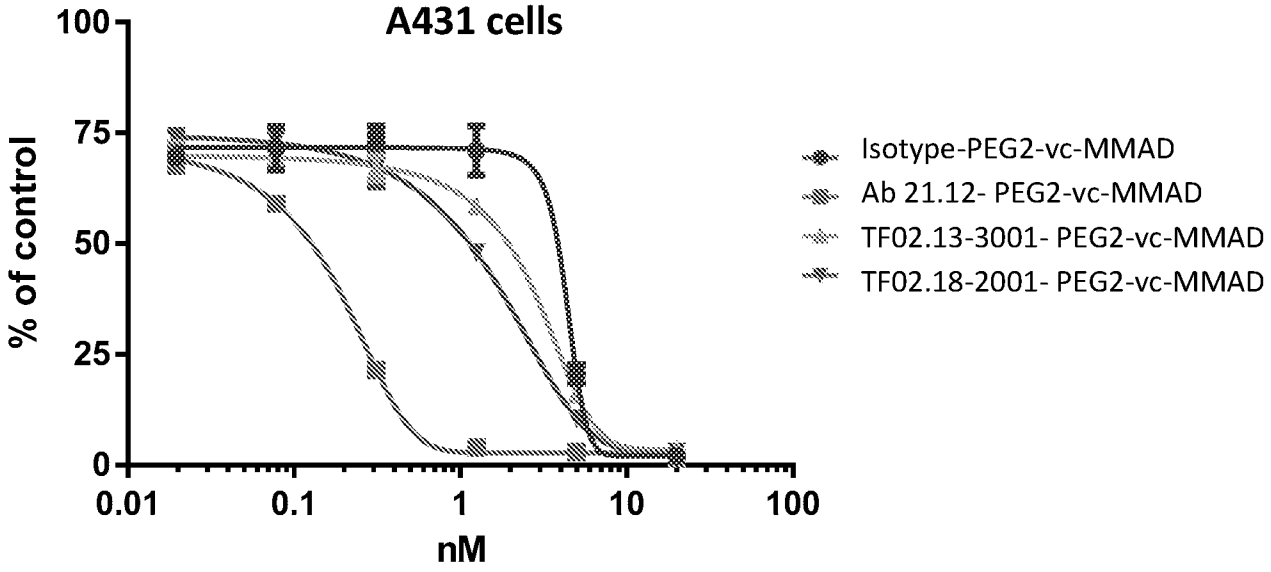


FIGURE 31C

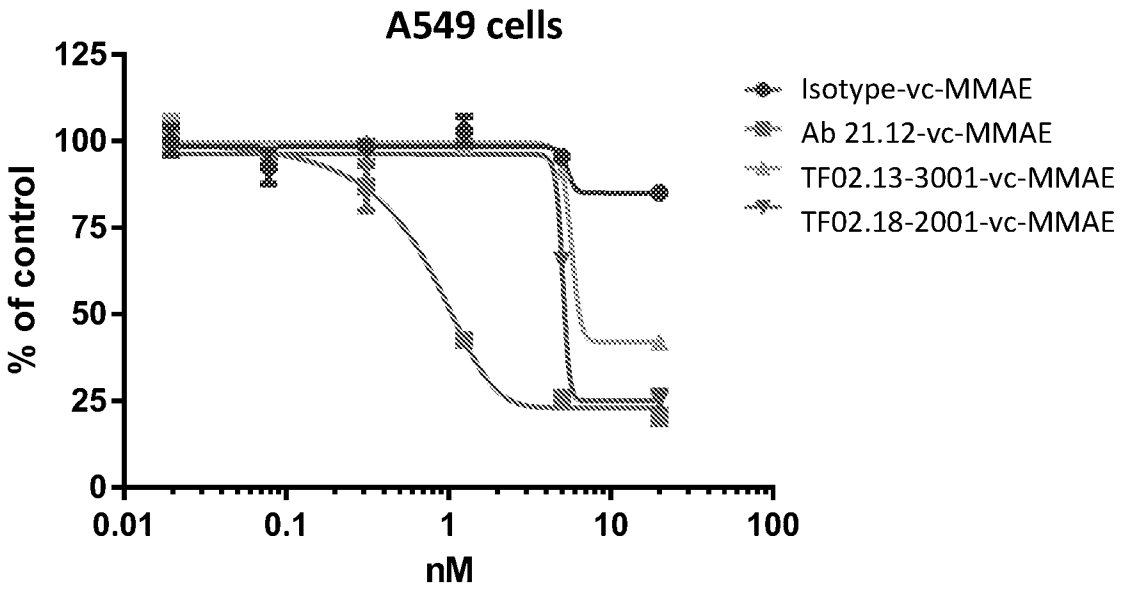


FIGURE 31D

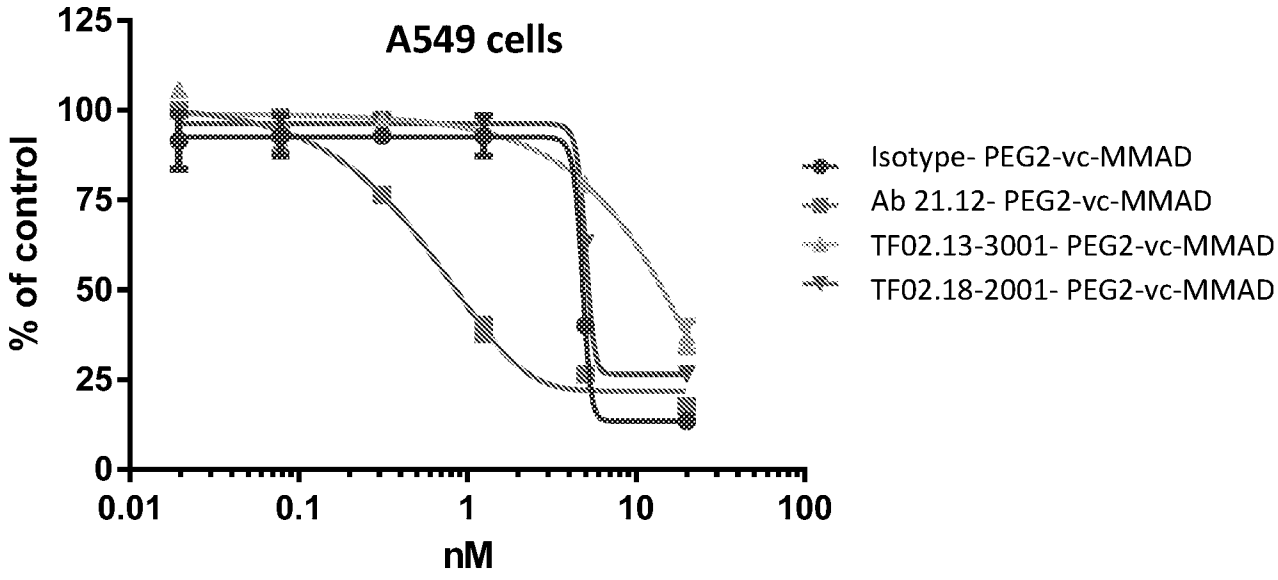


FIGURE 31E

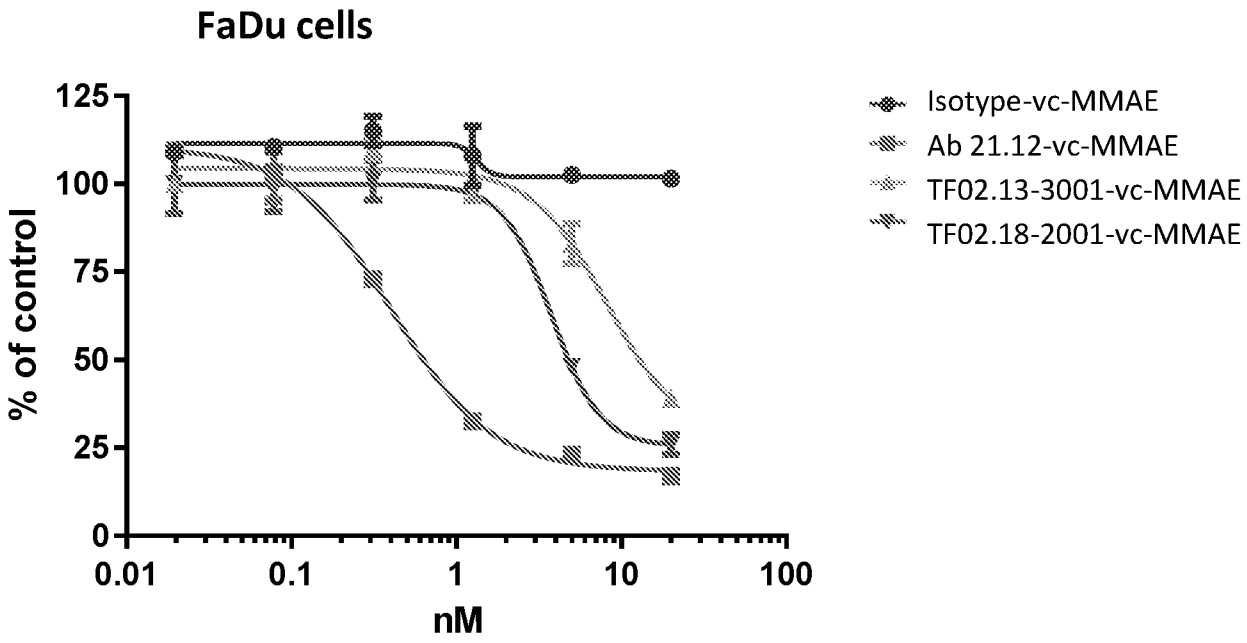


FIGURE 31F

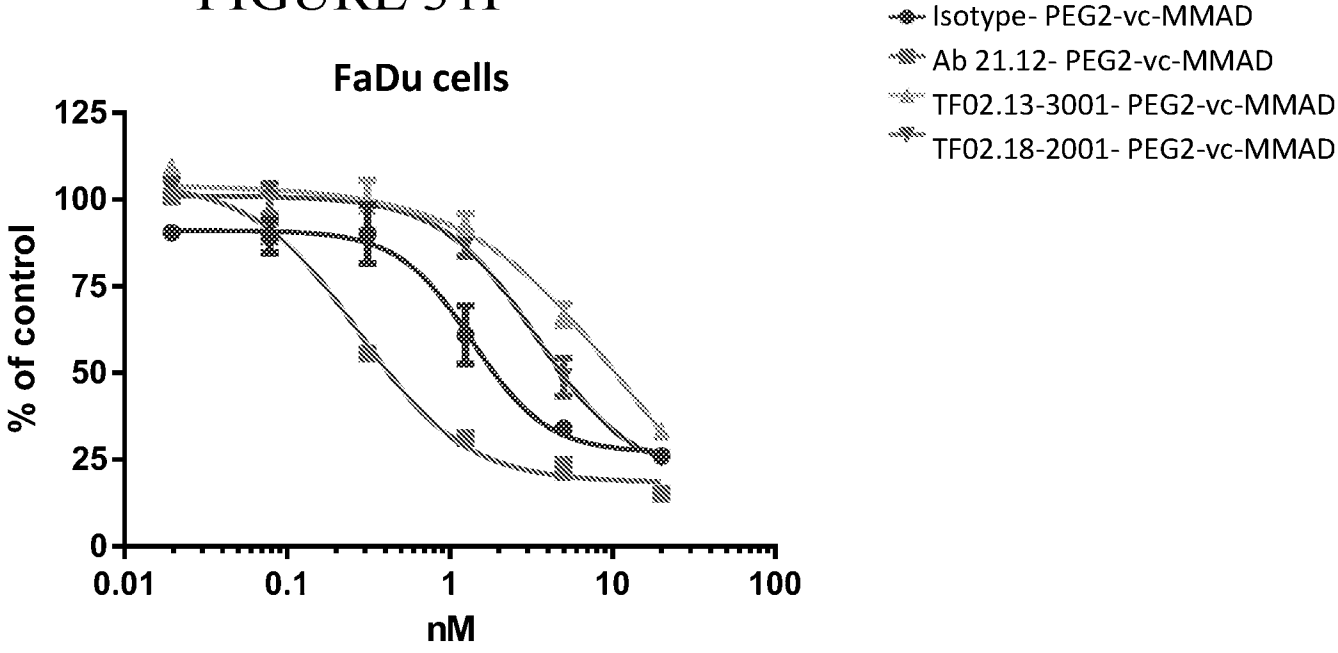


FIGURE 31G

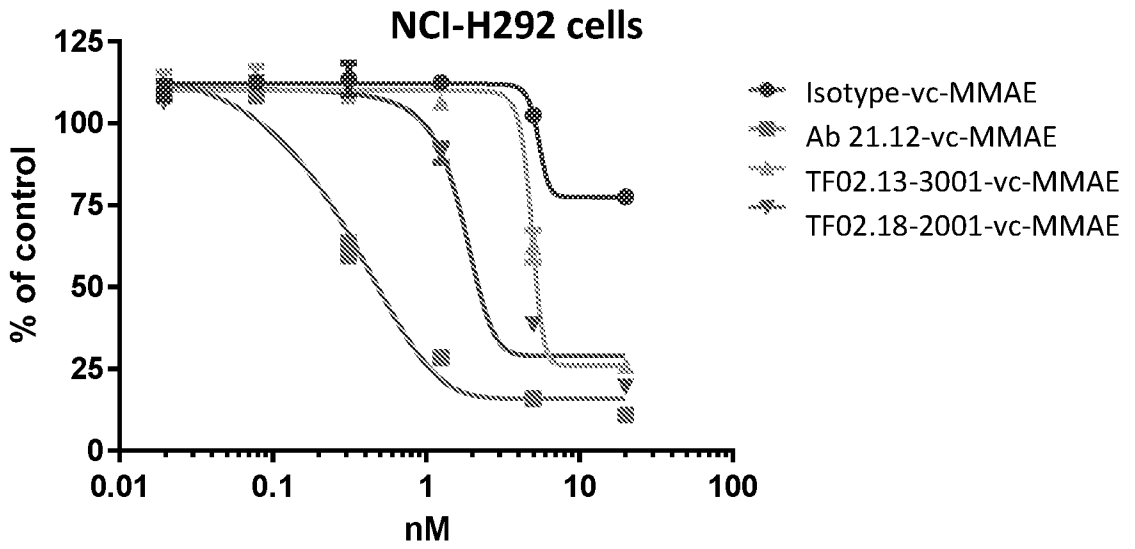


FIGURE 31H

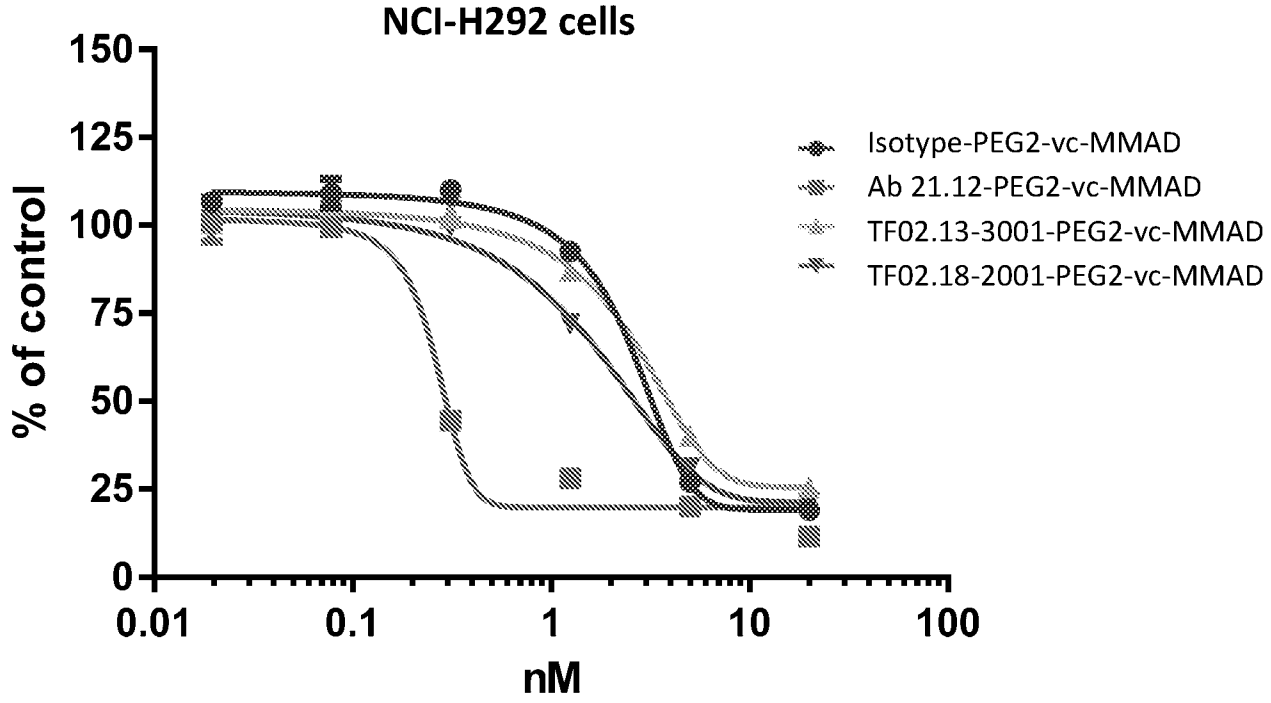


FIGURE 31I

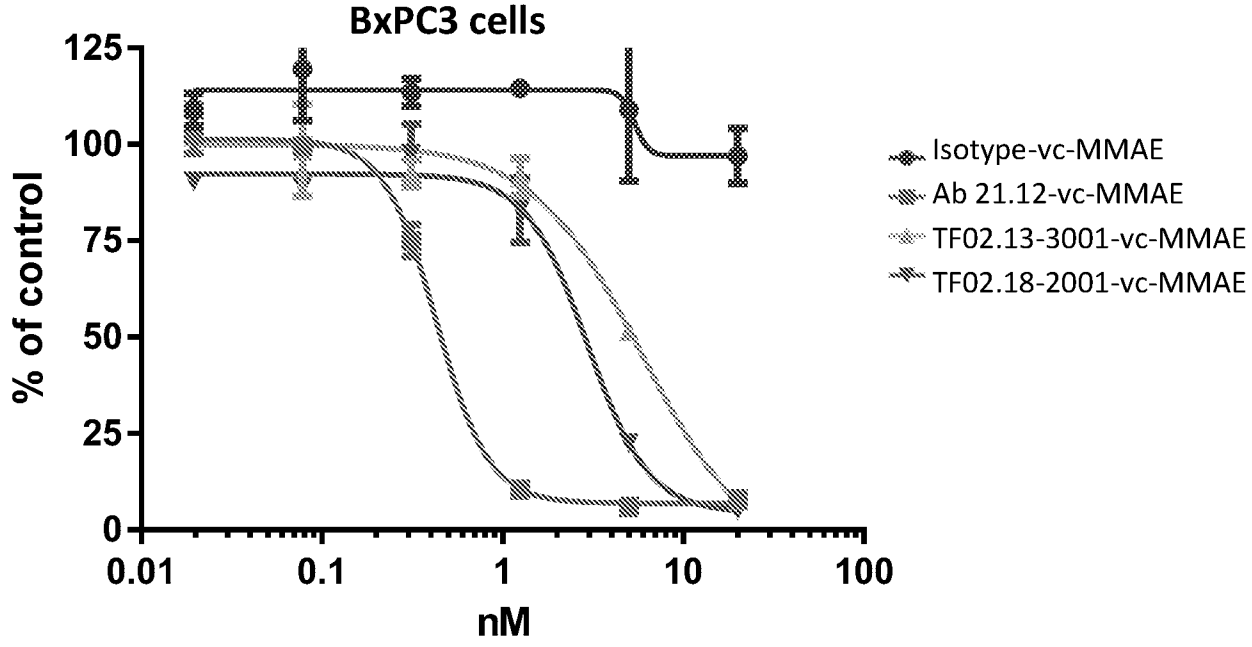


FIGURE 31J

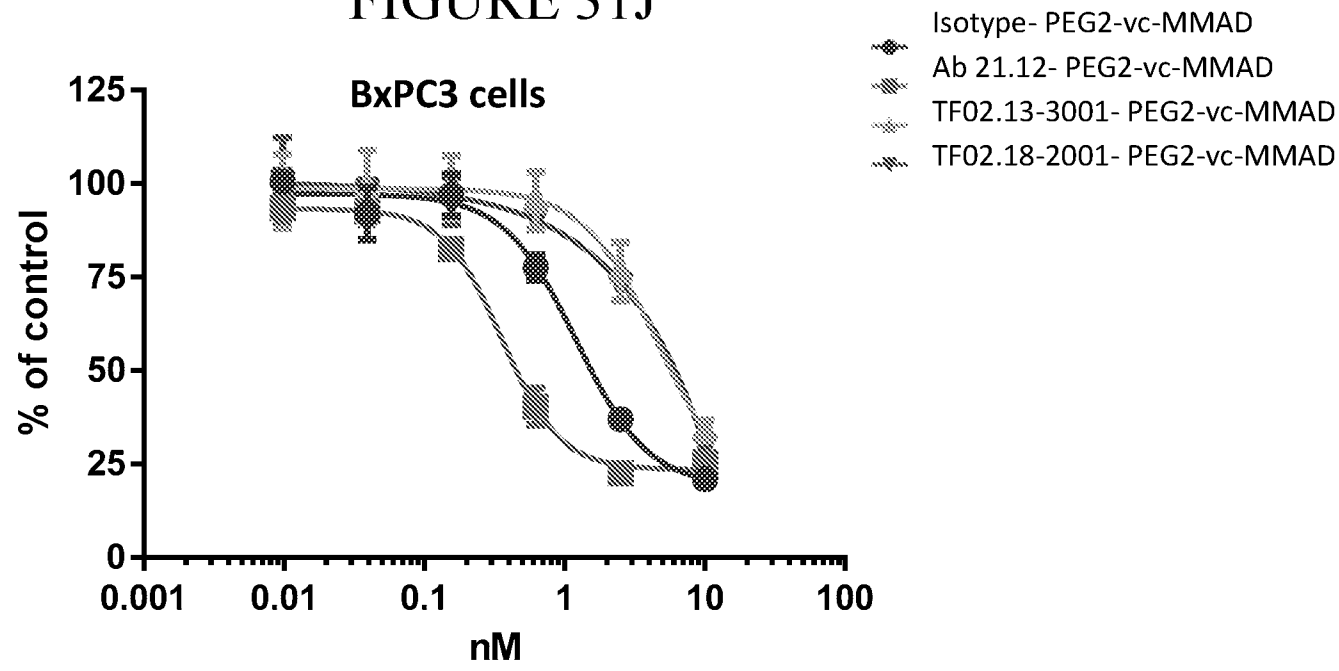


FIGURE 32A

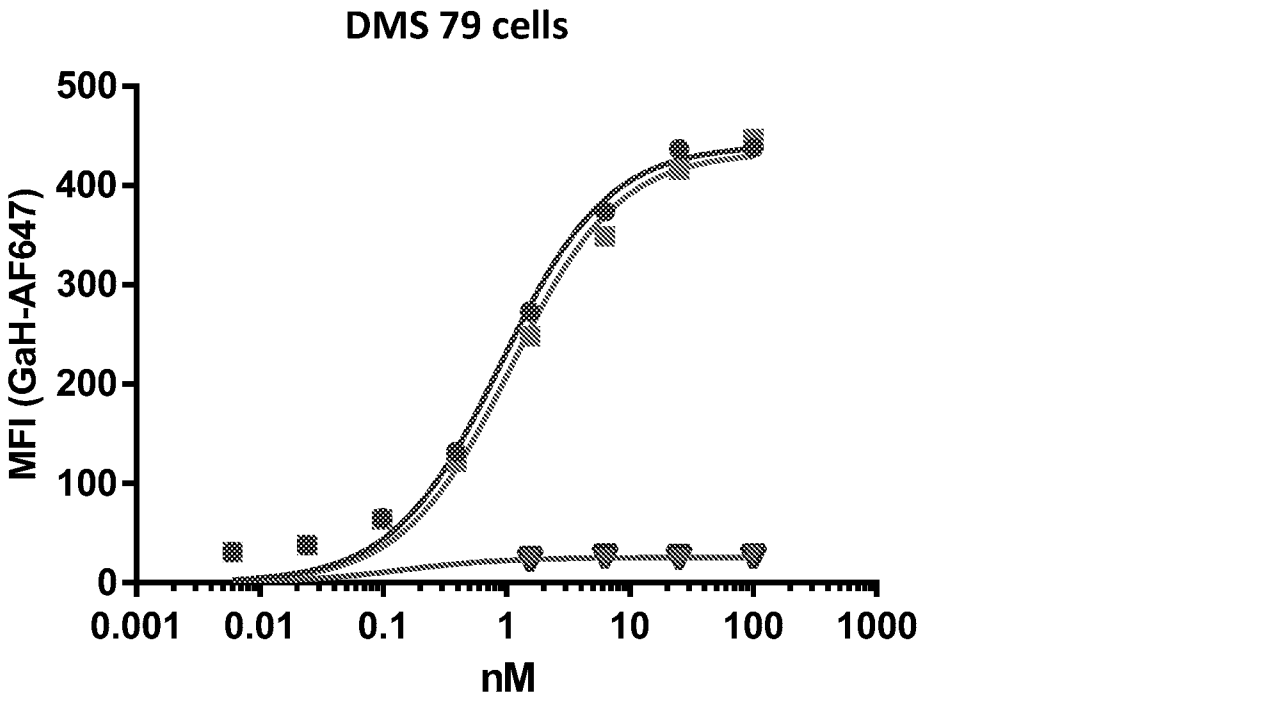


FIGURE 32B

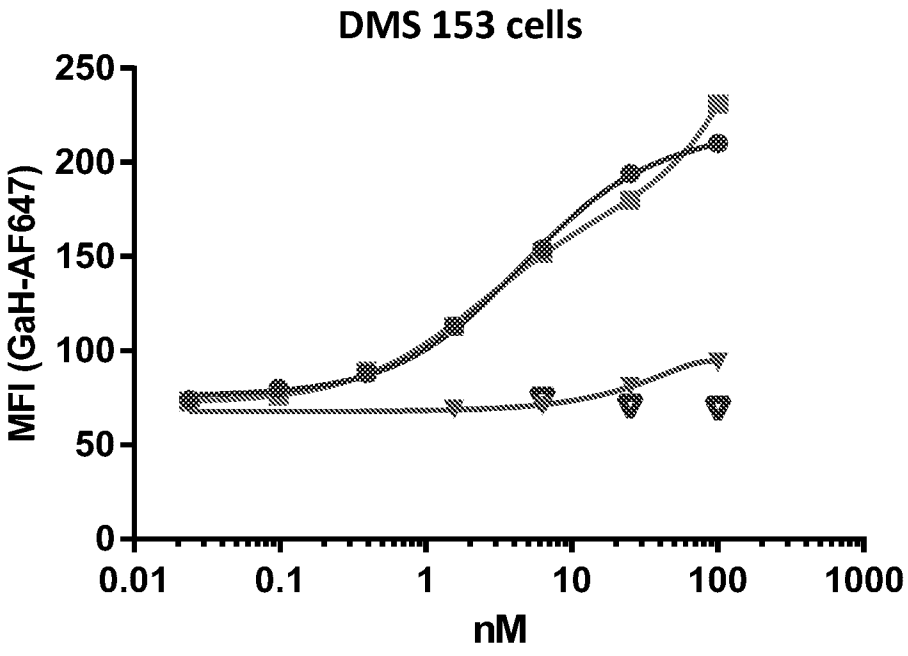


FIGURE 33A

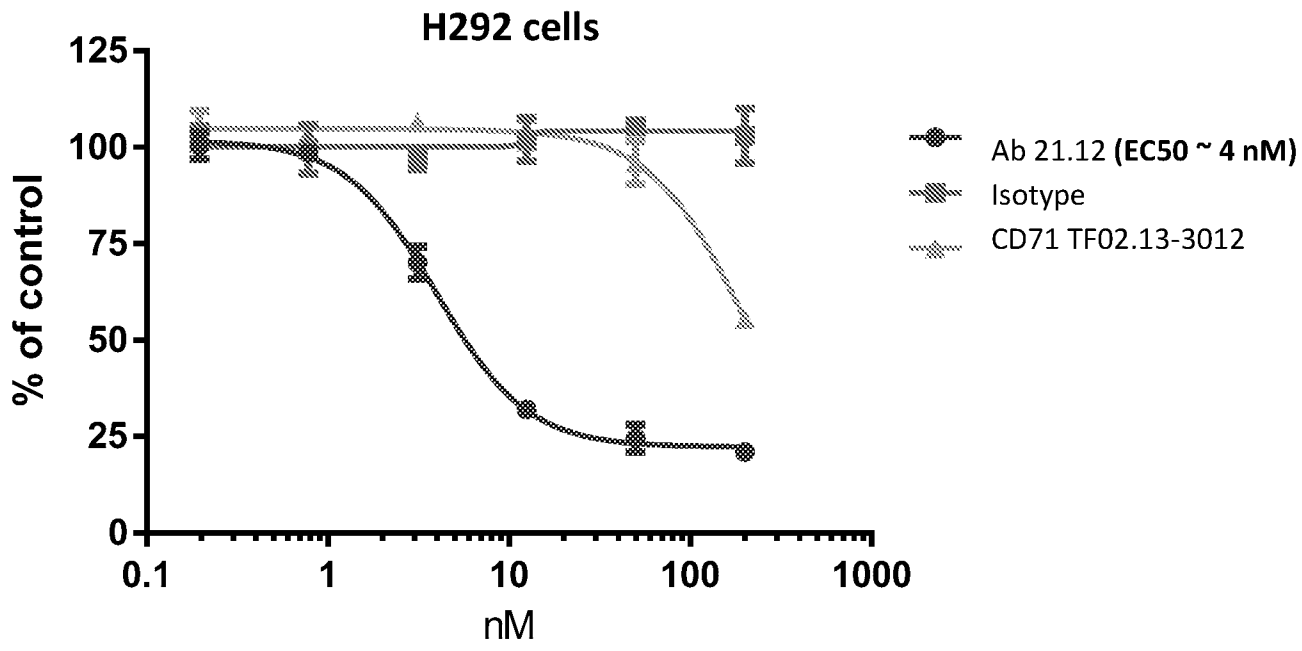


FIGURE 33B

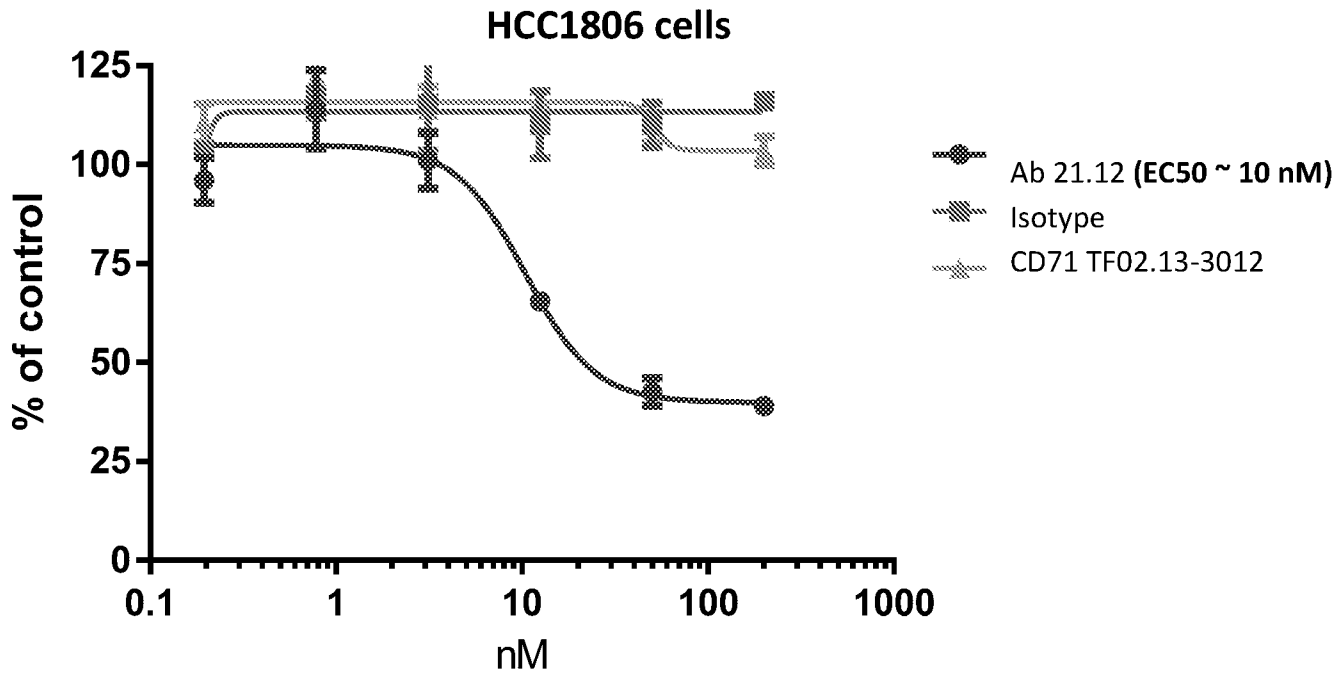


FIGURE 34

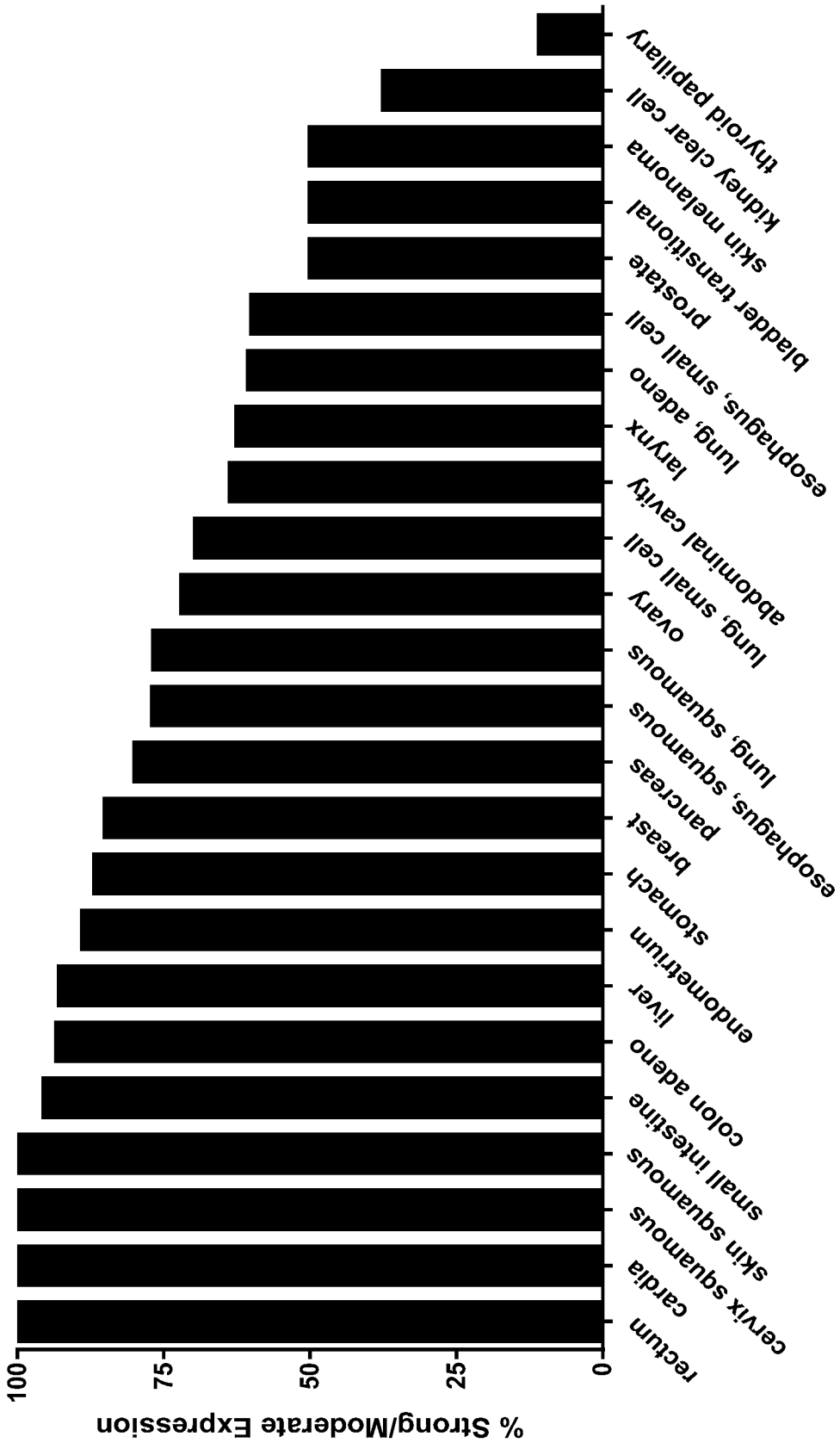

% Strong/Moderate Expression
100
75
50
25
0
rectum
cardia
cervix squamous
skin squamous
small intestine
colon adeno
liver
endometrium
stomach
breast
pancreas
esophagus, squamous
lung, squamous
ovary
lung, small cell
abdominal cavity
larynx
lung, adeno
esophagus, small cell
prostate
bladder transitional
skin melanoma
kidney clear cell
thyroid papillary

FIGURE 35

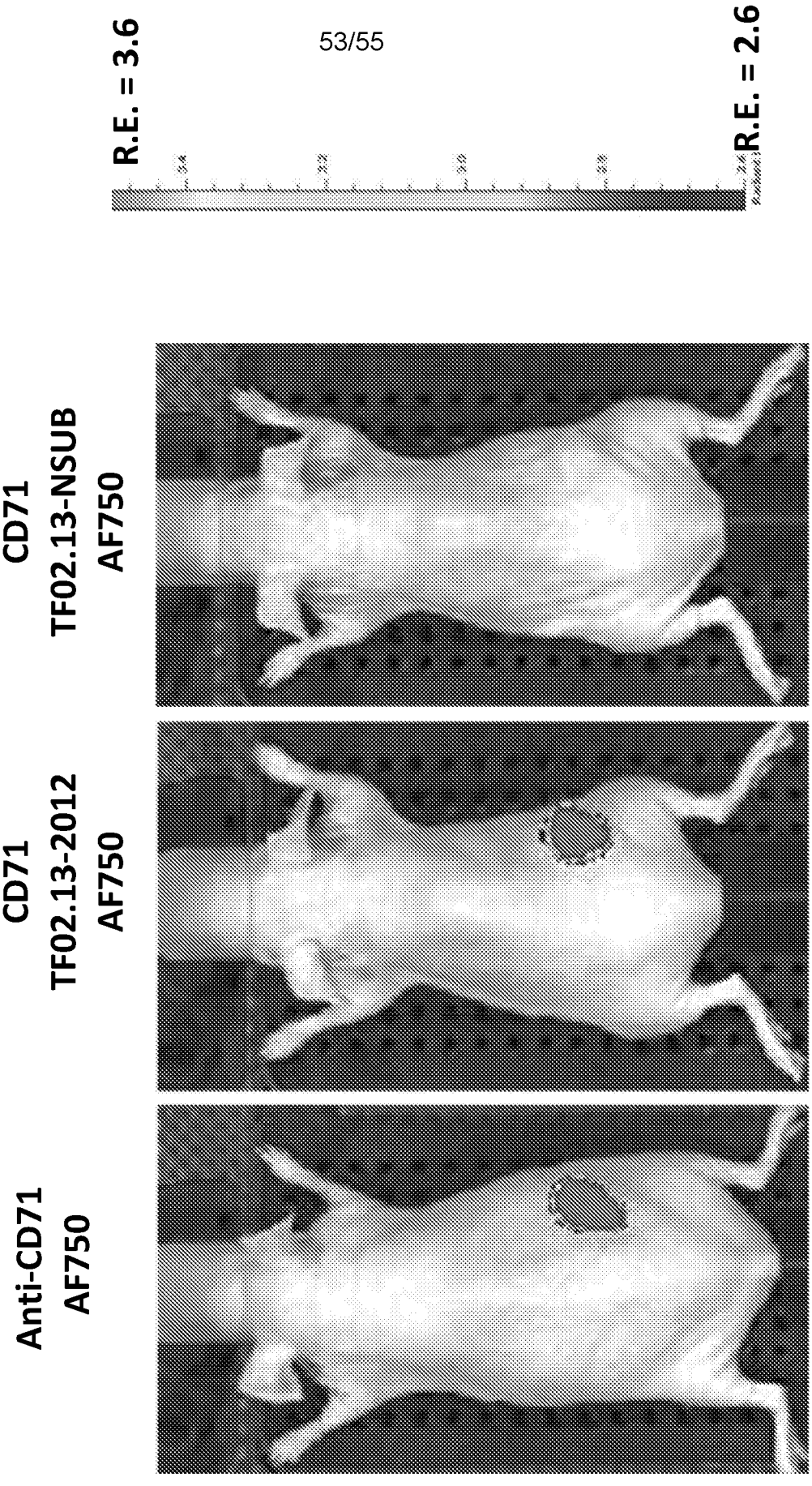
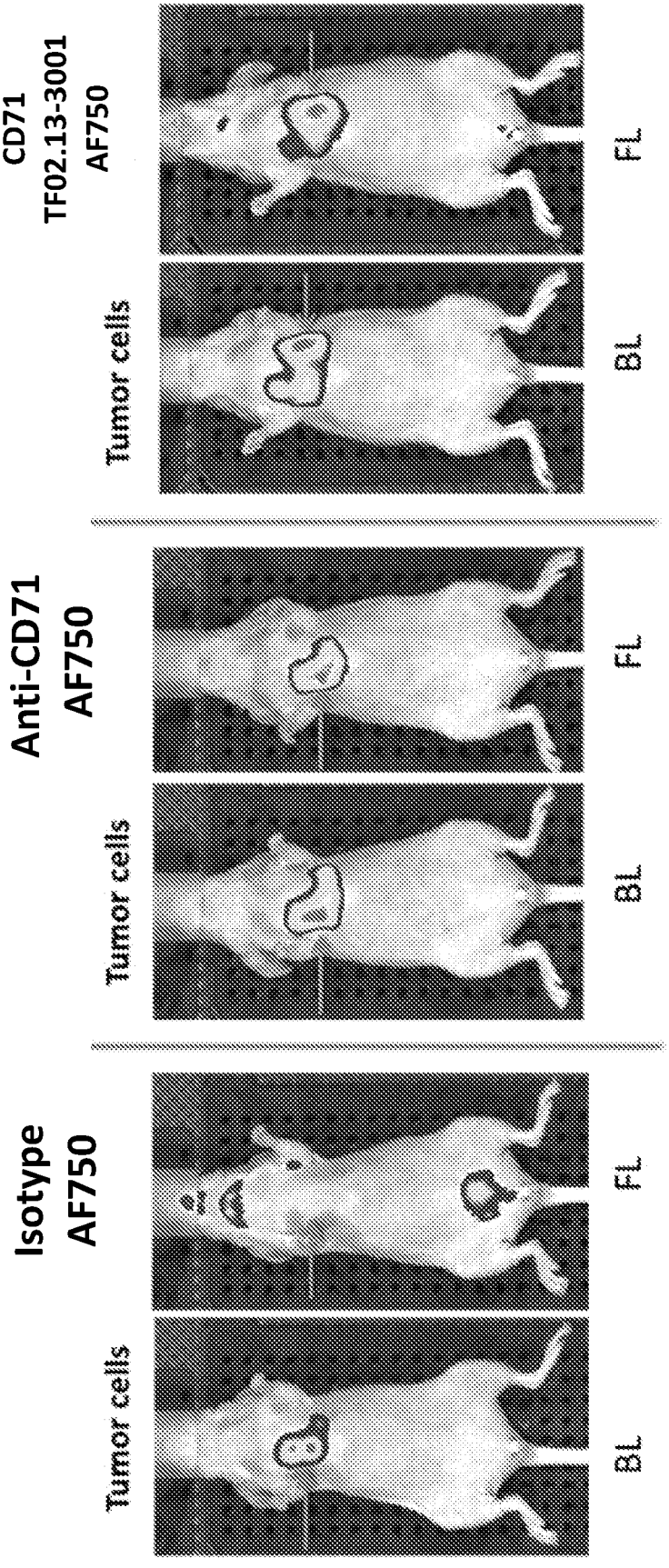
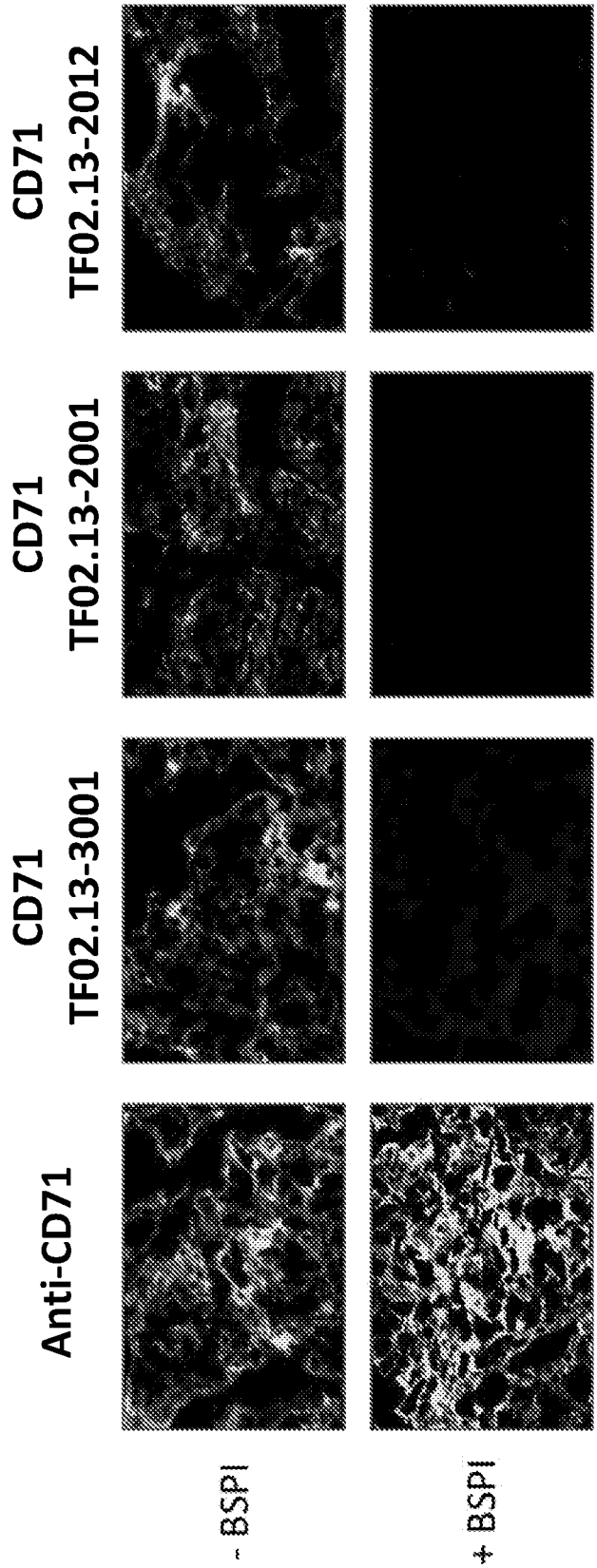

R.E. = 3.6
R.E. = 2.6
CD71
TF02.13-NSUB
AF750
CD71
TF02.13-2012
AF750
Anti-CD71
AF750

FIGURE 36



BL: bioluminescent imaging
FL: fluorescent imaging

FIGURE 37


Anti-CD71
CD71 TF02.13-3001
CD71 TF02.13-2001
CD71 TF02.13-2012
- BSPI
+ BSPI