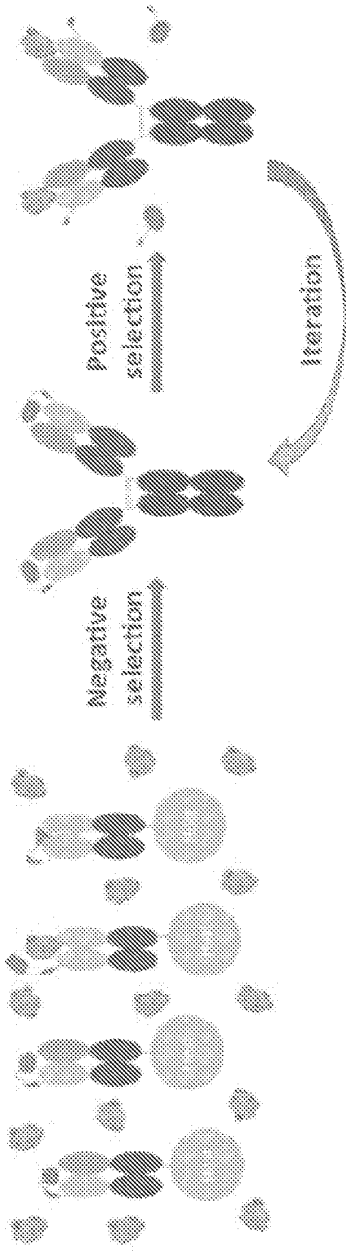


FIG. 1

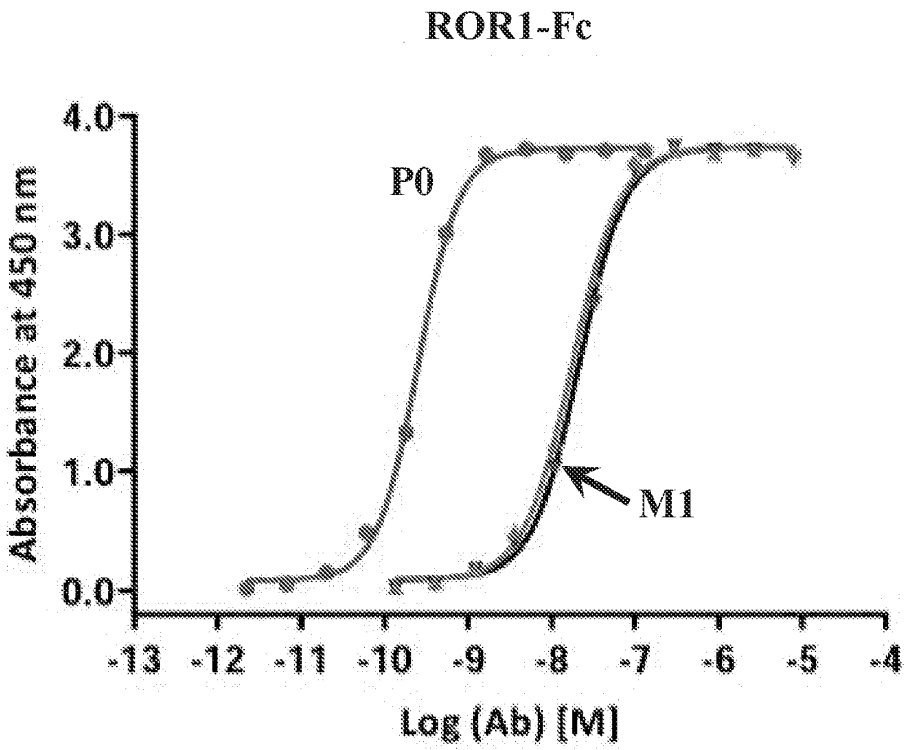

ROR1-Fc
Absorbance at 450 nm
4.0
3.0
2.0
1.0
0.0
P0
M1
-13
-12
-11
-10
-9
-8
-7
-6
-5
-4
Log (Ab) [M]

FIG. 2A

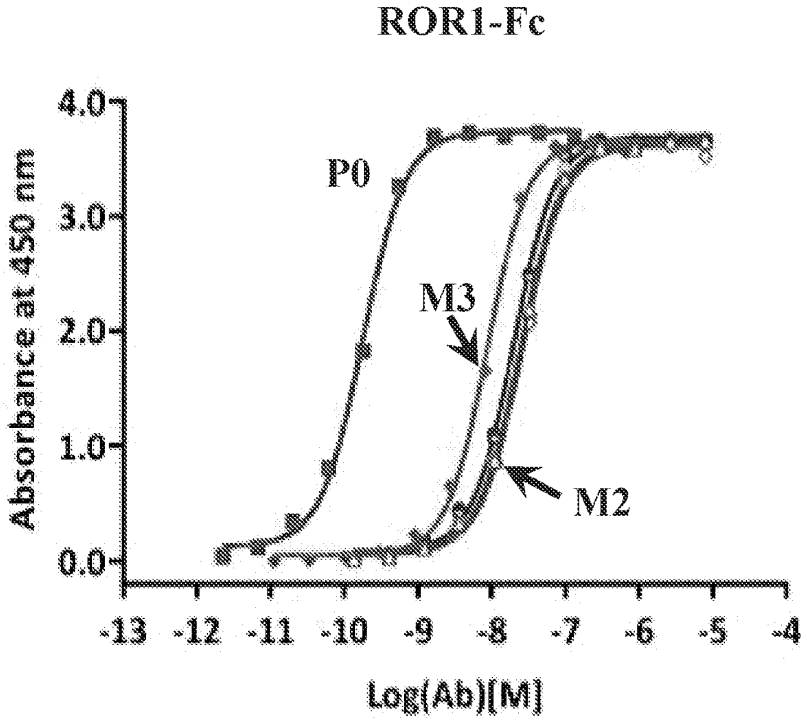

ROR1-Fc
Absorbance at 450 nm
4.0
3.0
2.0
1.0
0.0
P0
M3
M2
-13
-12
-11
-10
-9
-8
-7
-6
-5
-4
Log(Ab)[M]

FIG. 2B

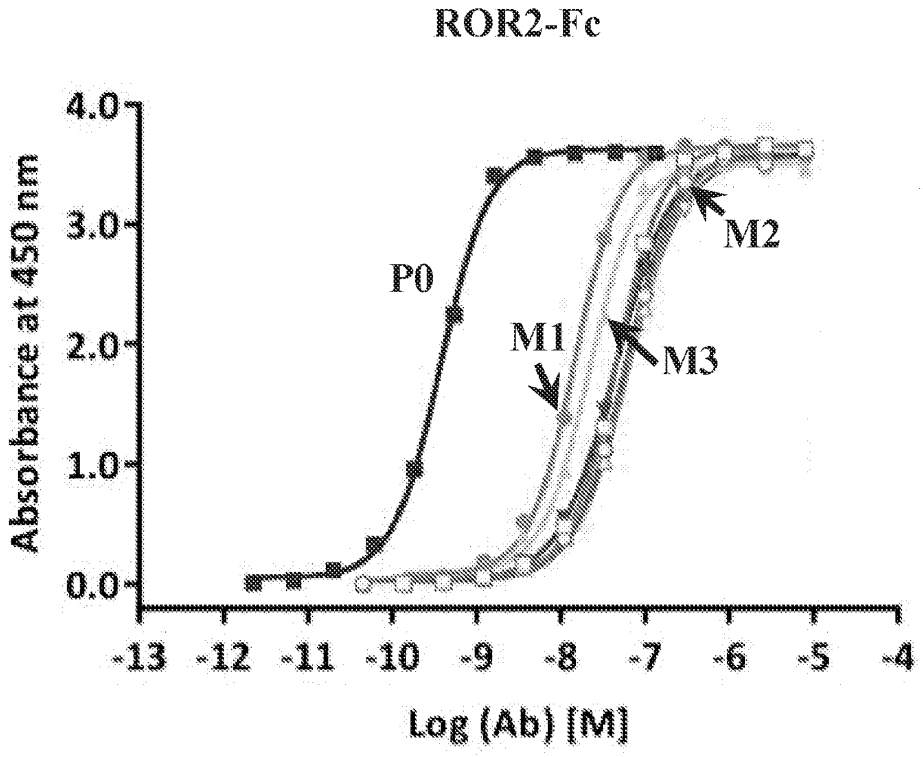

ROR2-Fc
Absorbance at 450 nm
4.0
3.0
2.0
1.0
0.0
P0
M1
M2
M3
-13
-12
-11
-10
-9
-8
-7
-6
-5
-4
Log (Ab) [M]

FIG. 2C

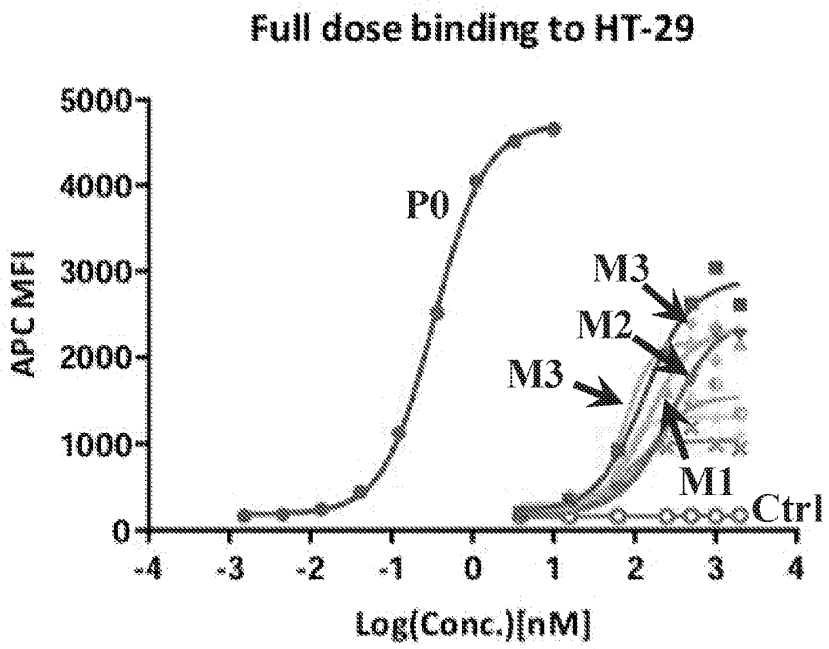

Full dose binding to HT-29
APC MFI
5000
4000
3000
2000
1000
0
P0
M3
M2
M3
M1
Ctrl
-4
-3
-2
-1
0
1
2
3
4
Log(Conc.)[nM]

FIG. 2D

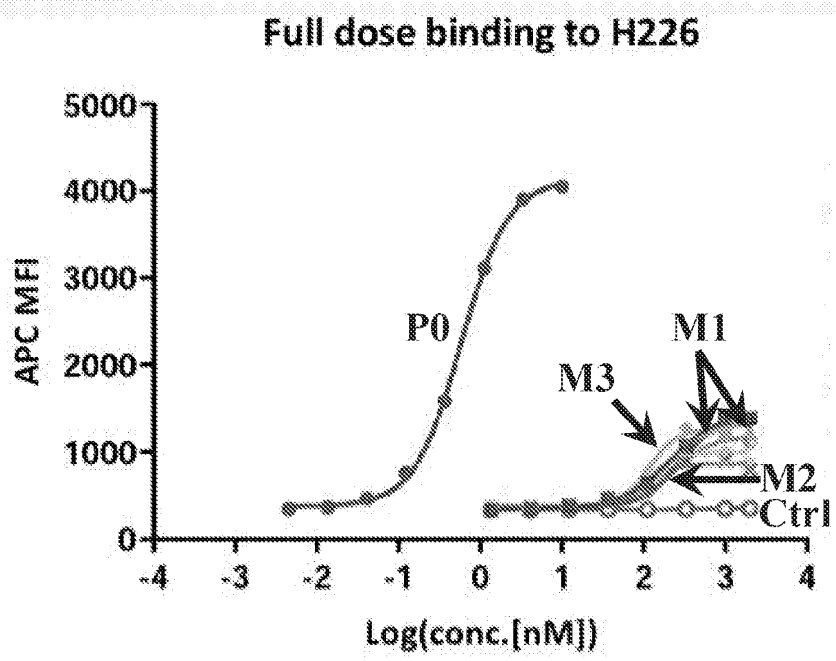

Full dose binding to H226
APC MFI
5000
4000
3000
2000
1000
0
-4
-3
-2
-1
0
1
2
3
4
Log(conc.[nM])
P0
M1
M3
M2
Ctrl

FIG. 2E

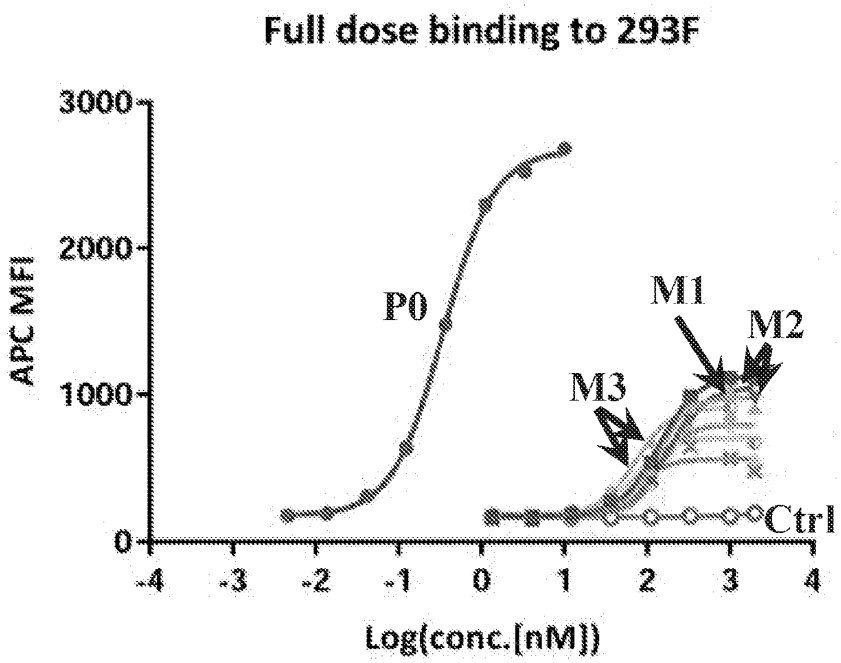

Full dose binding to 293F
APC MFI
3000
2000
1000
0
-4
-3
-2
-1
0
1
2
3
4
Log(conc.[nM])
P0
M1
M2
M3
Ctrl

FIG. 2F

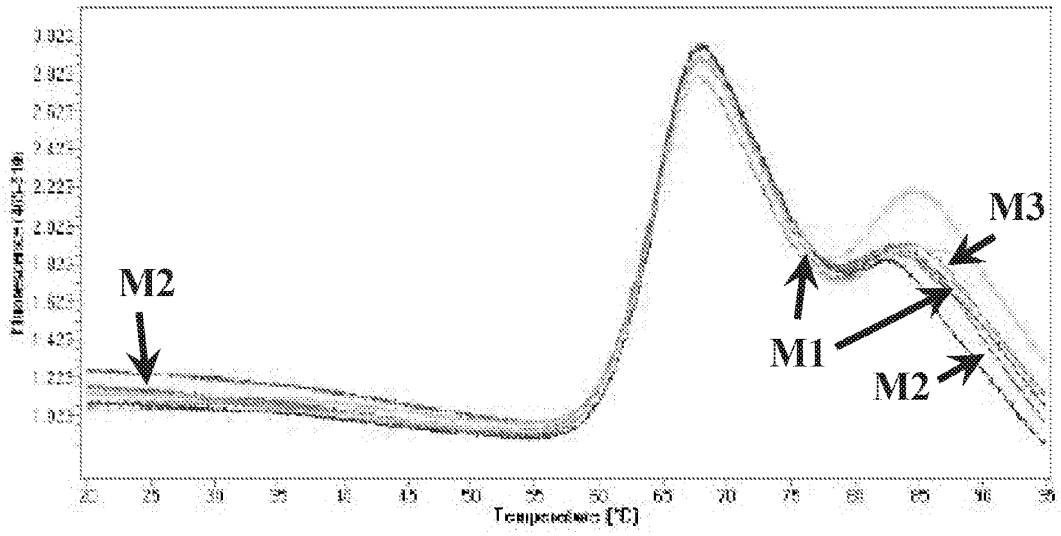


FIG. 3A

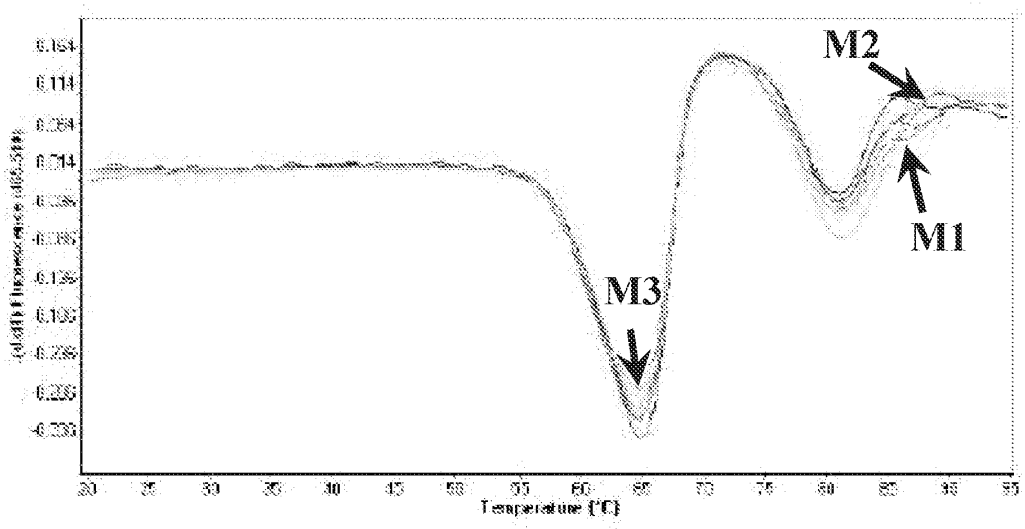


FIG. 3B

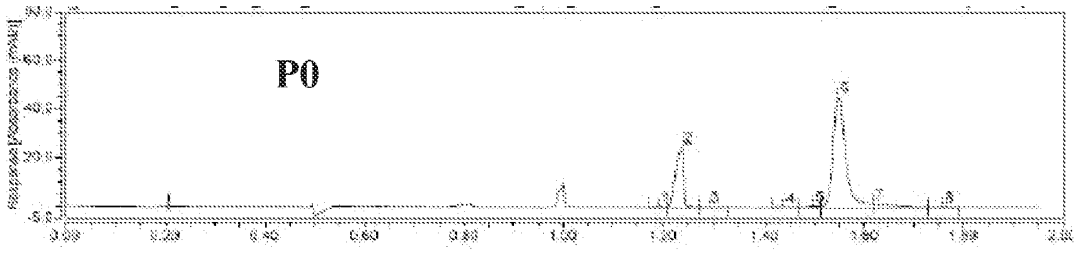


FIG. 4A

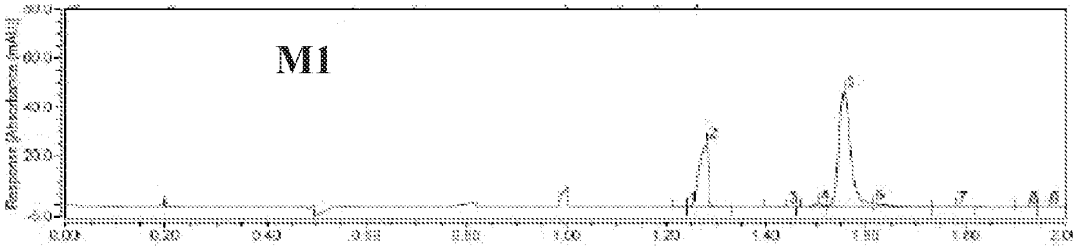


FIG. 4B

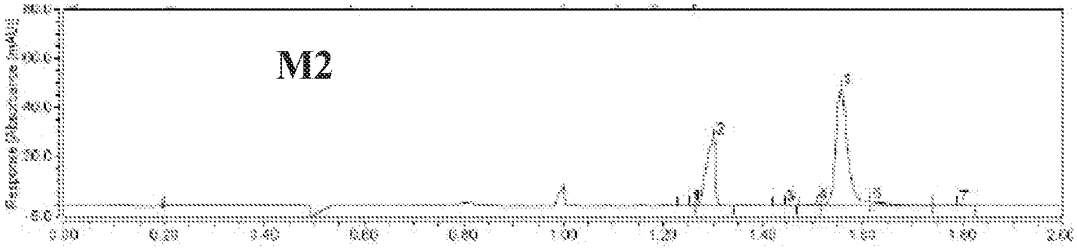


FIG. 4C

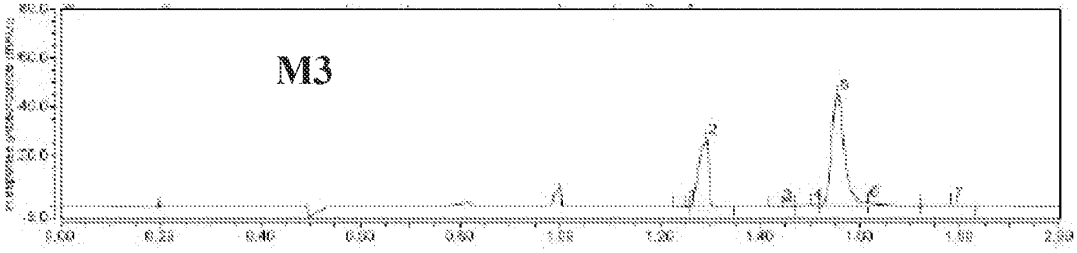


FIG. 4D

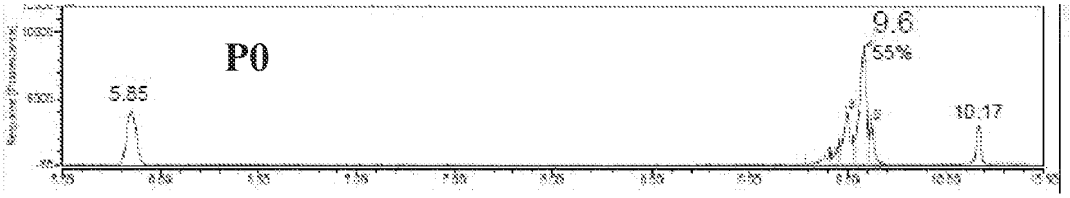


FIG. 5A

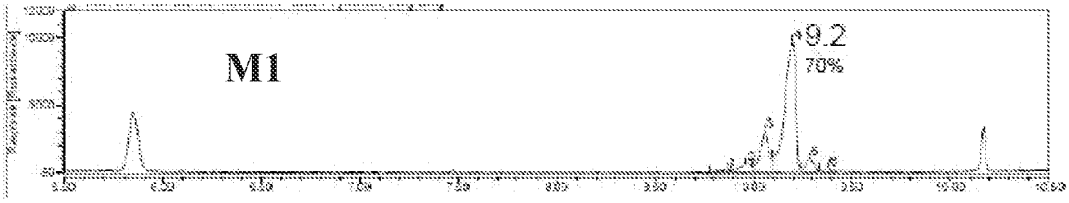


FIG. 5B

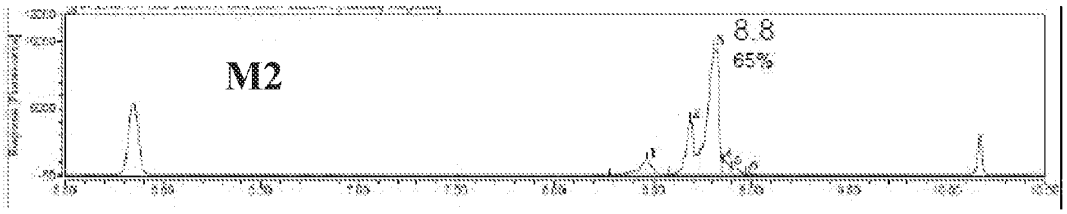


FIG. 5C

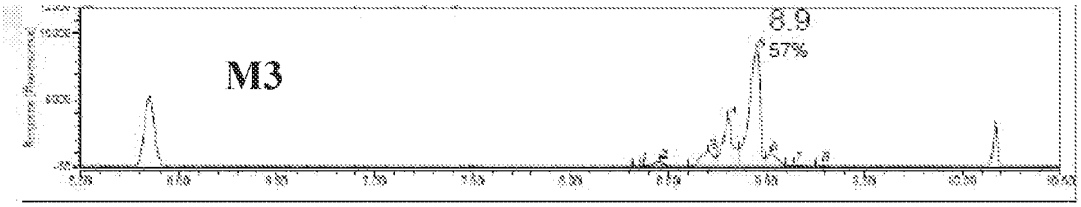


FIG. 5D

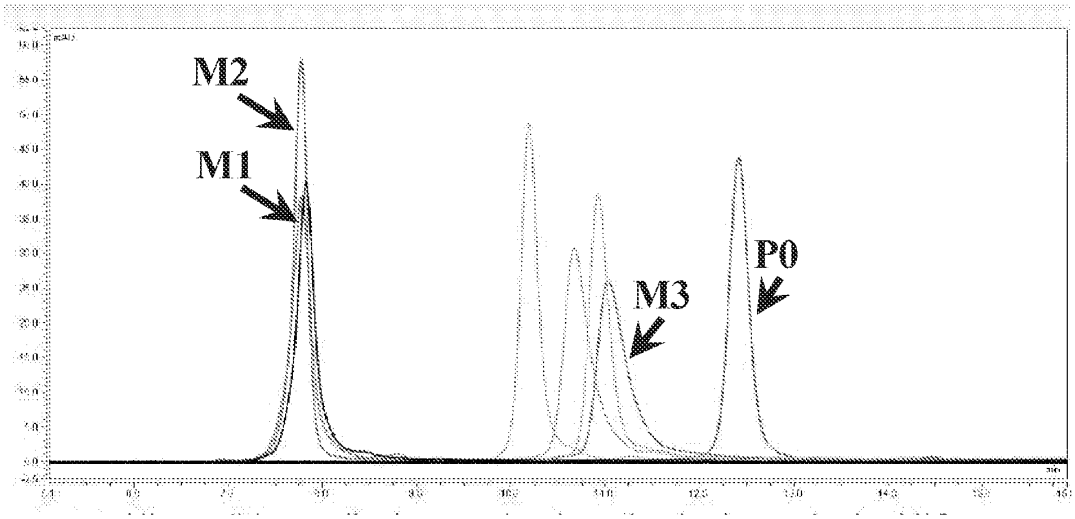


FIG. 6

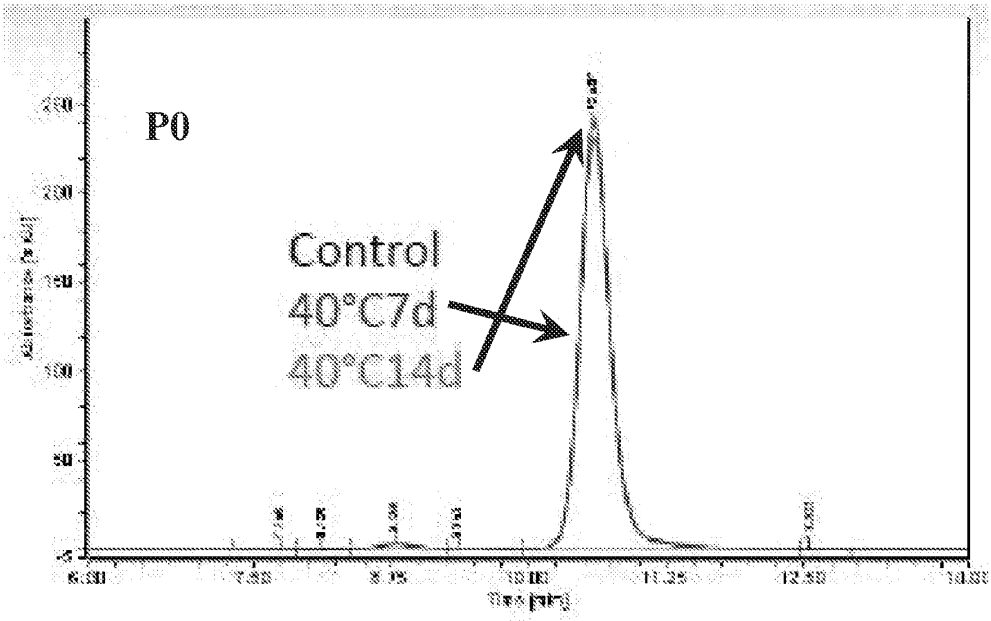


FIG. 7A

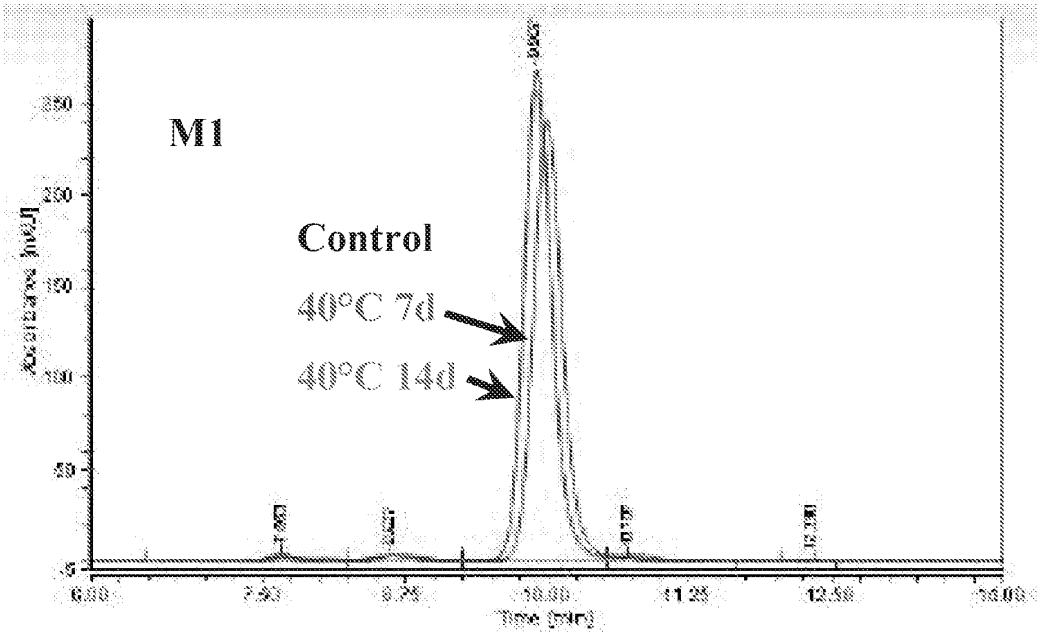


FIG. 7B

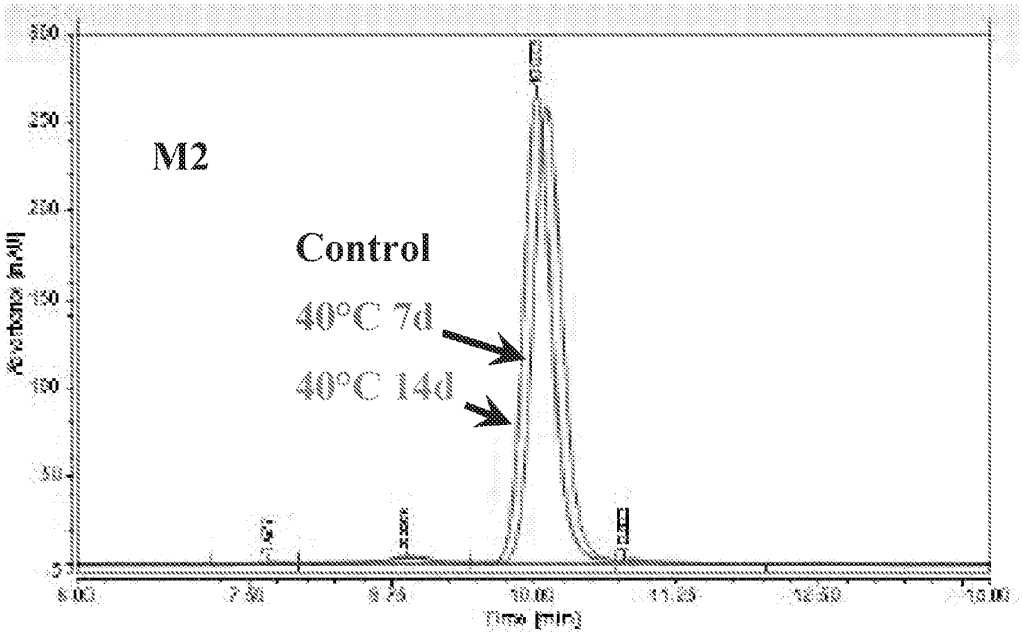


FIG. 7C

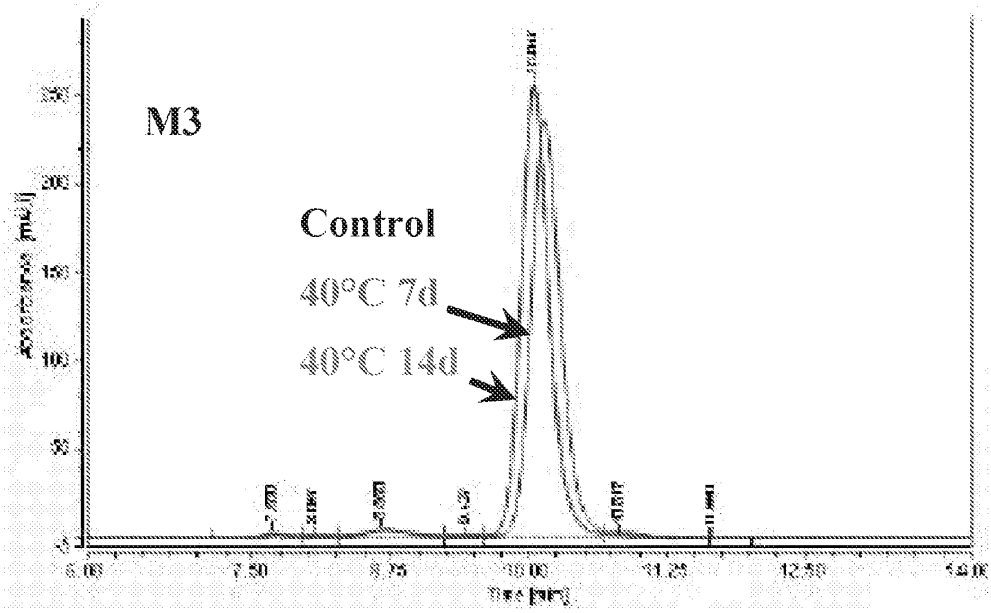


FIG. 7D

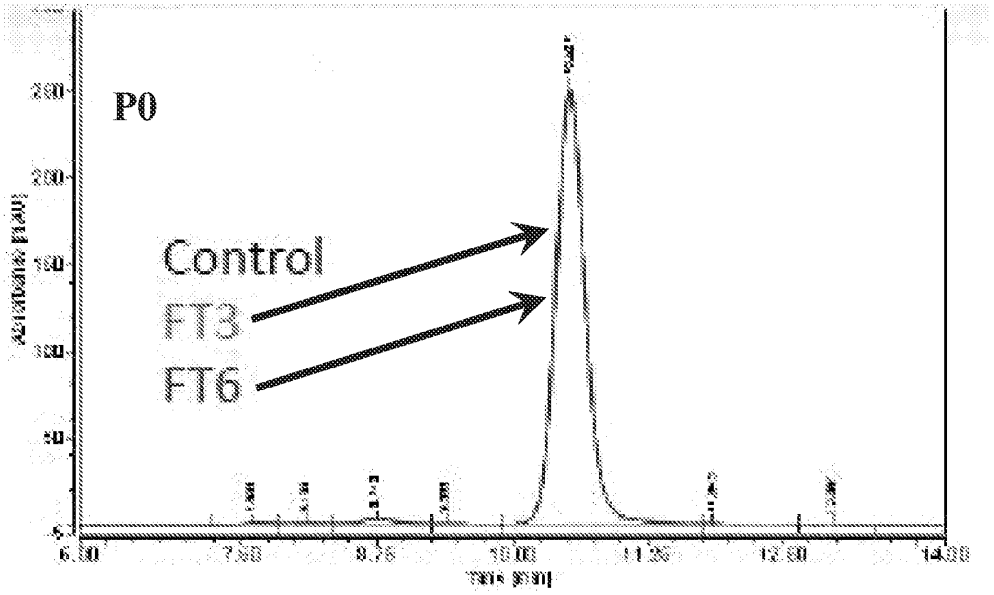


FIG. 8A

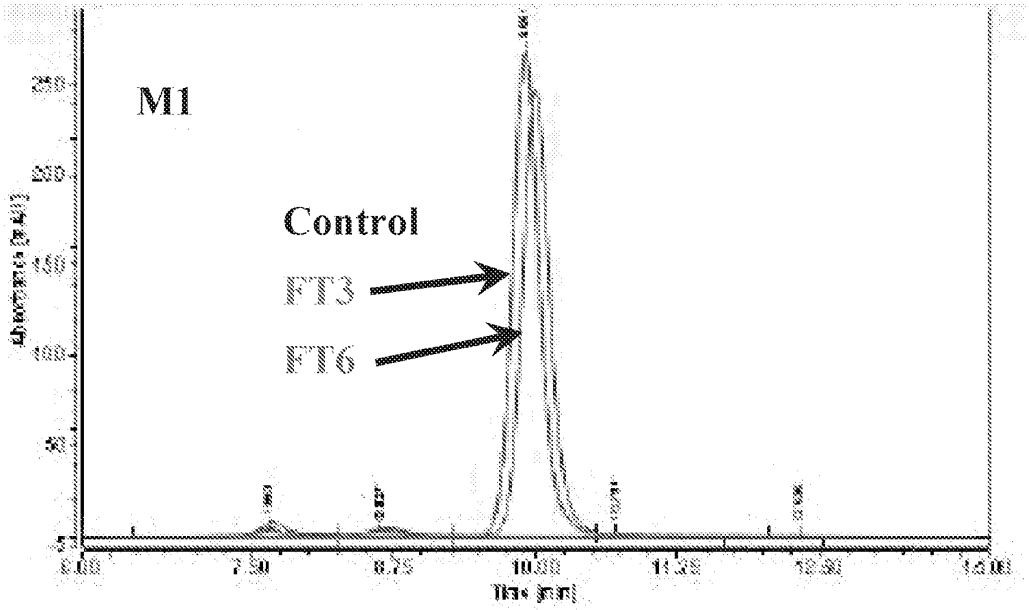


FIG. 8B

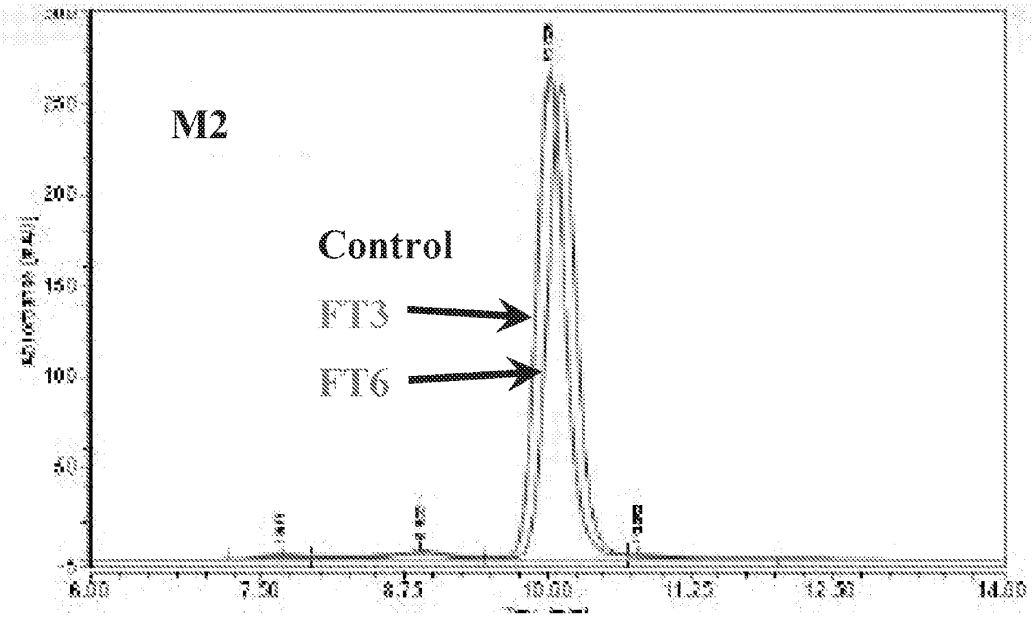


FIG. 8C

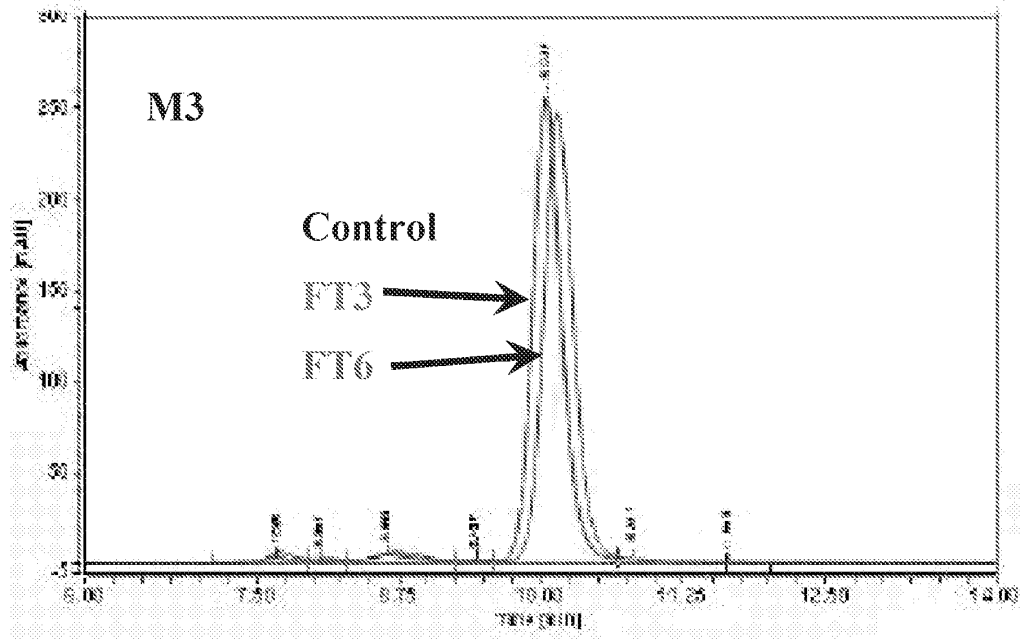


FIG. 8D

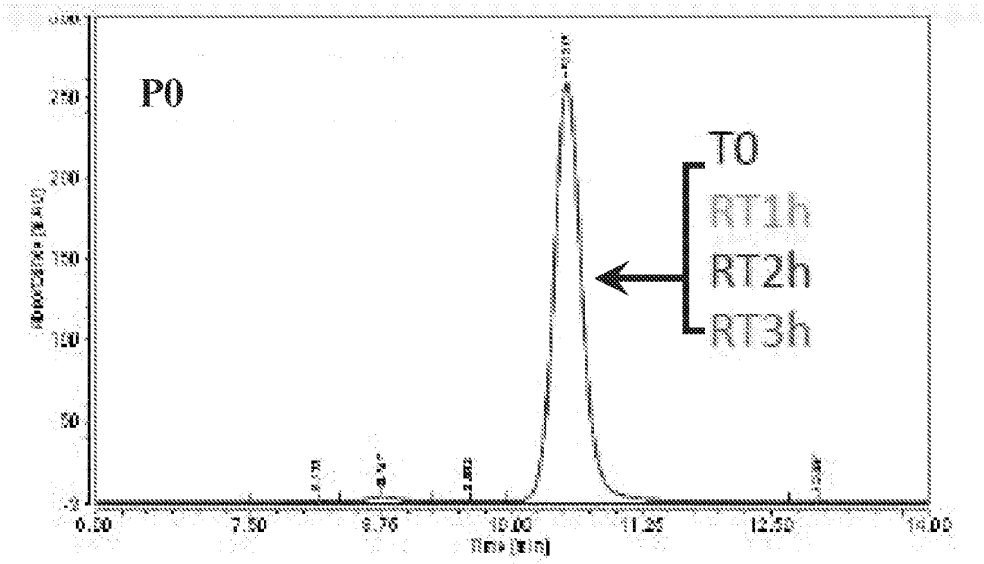


FIG. 9A

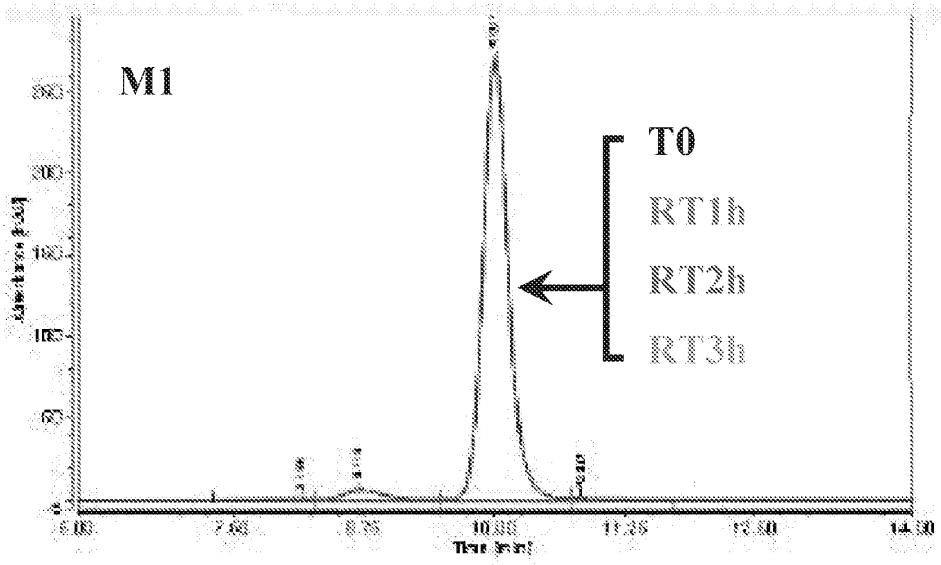


FIG. 9B

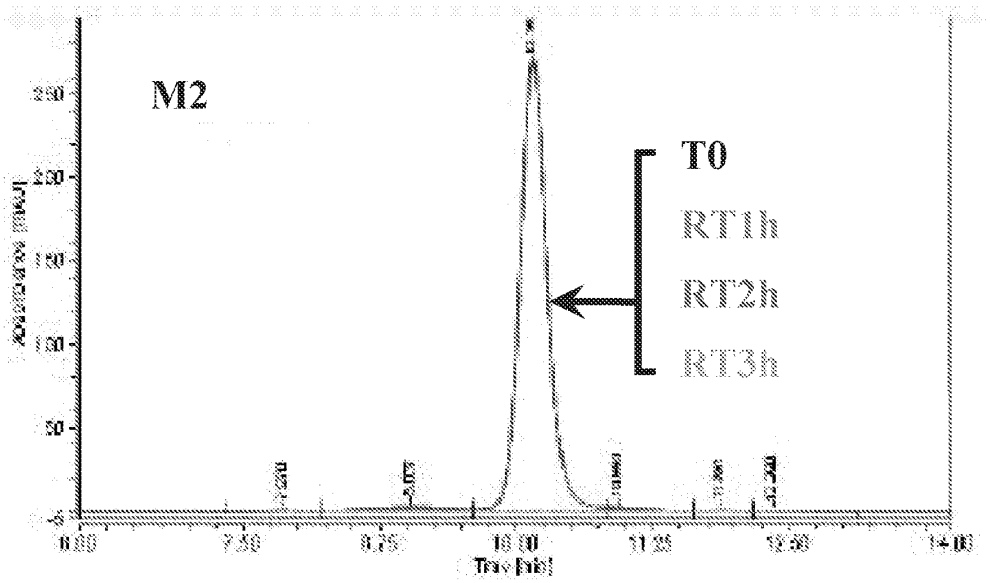


FIG. 9C

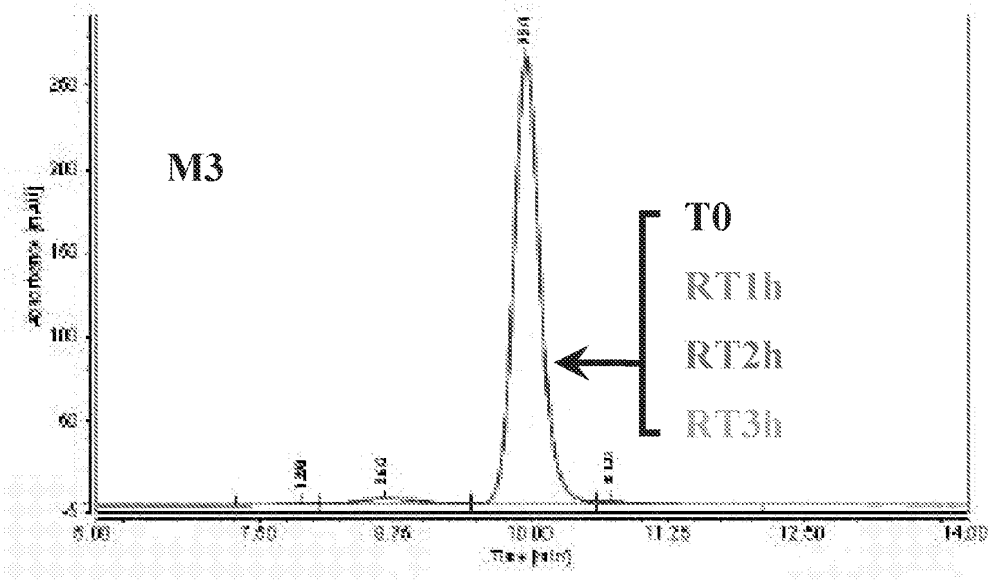


FIG. 9D

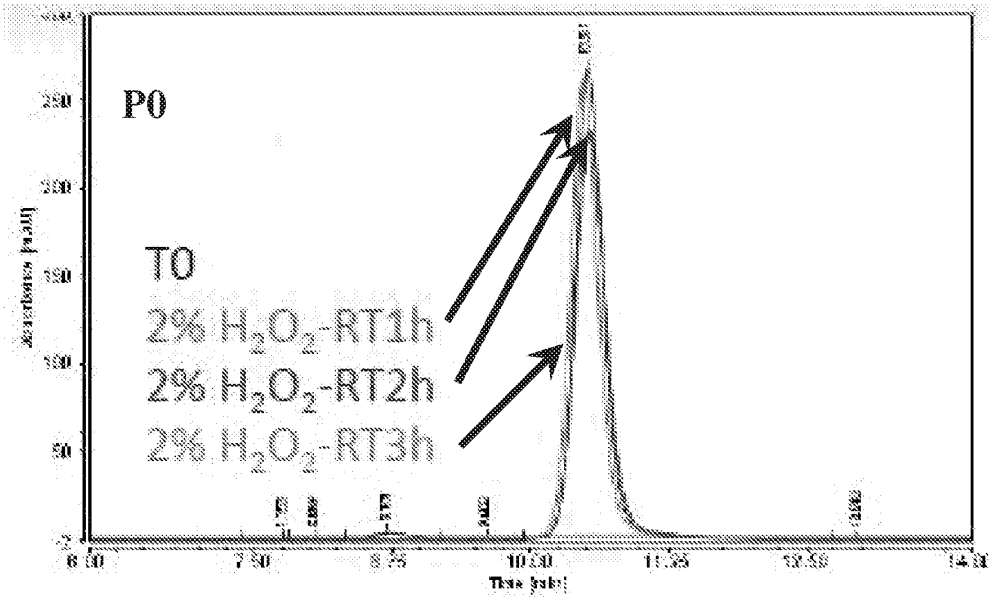


FIG. 10A

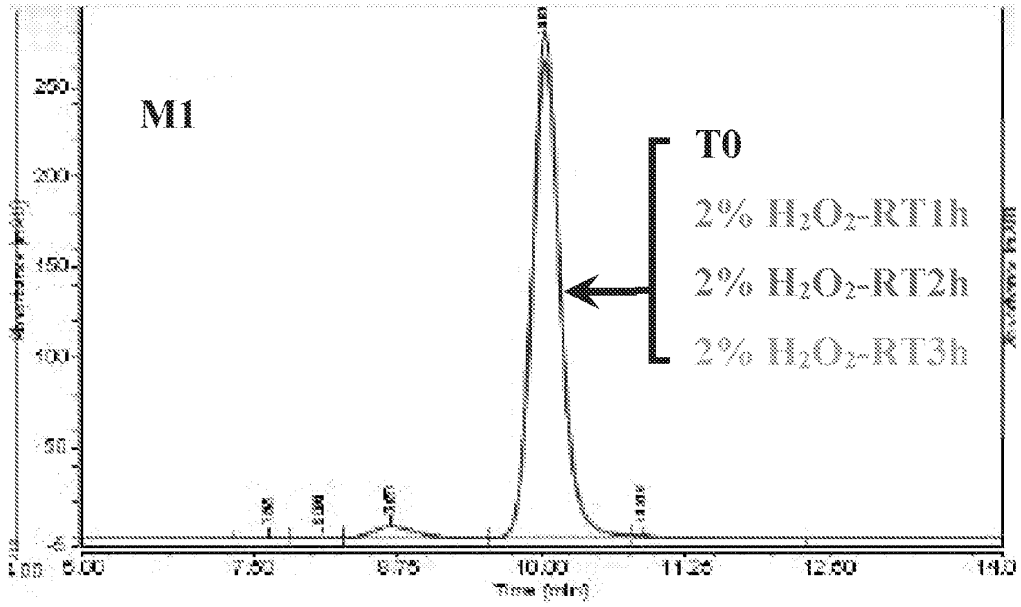


FIG. 10B

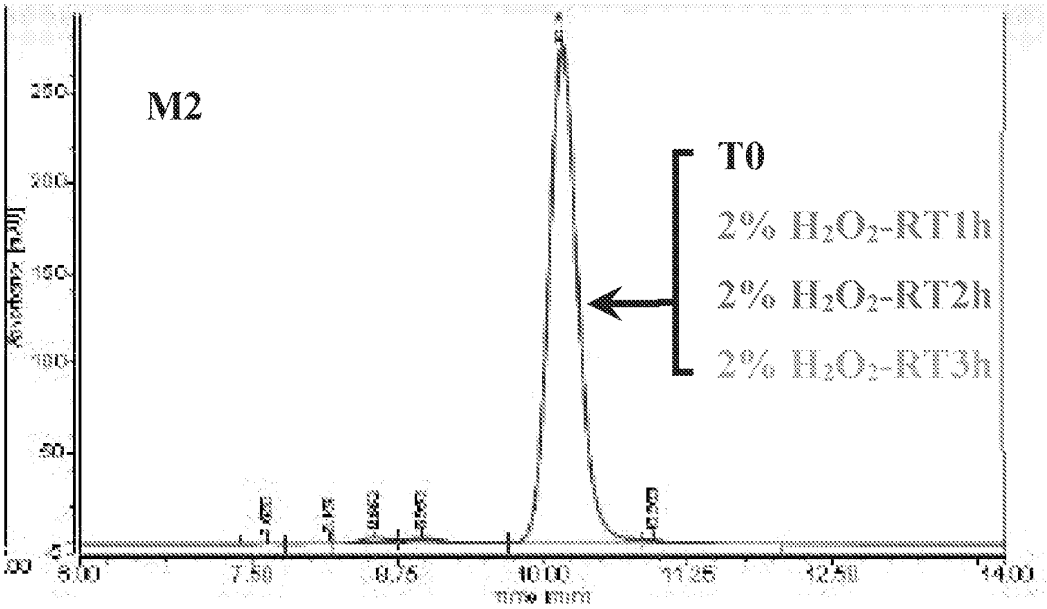


FIG. 10C

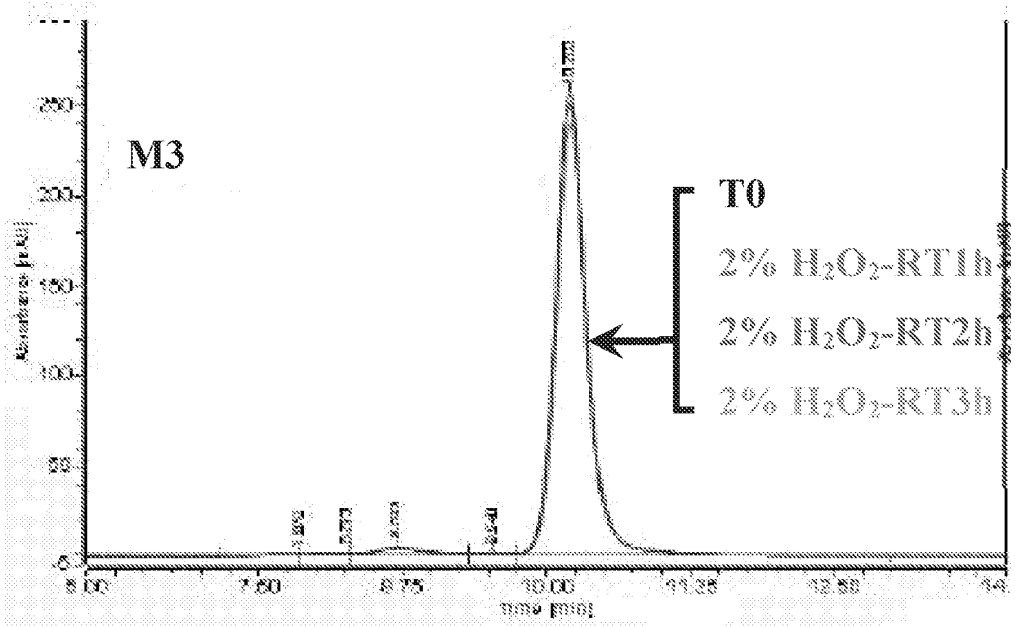


FIG. 10D

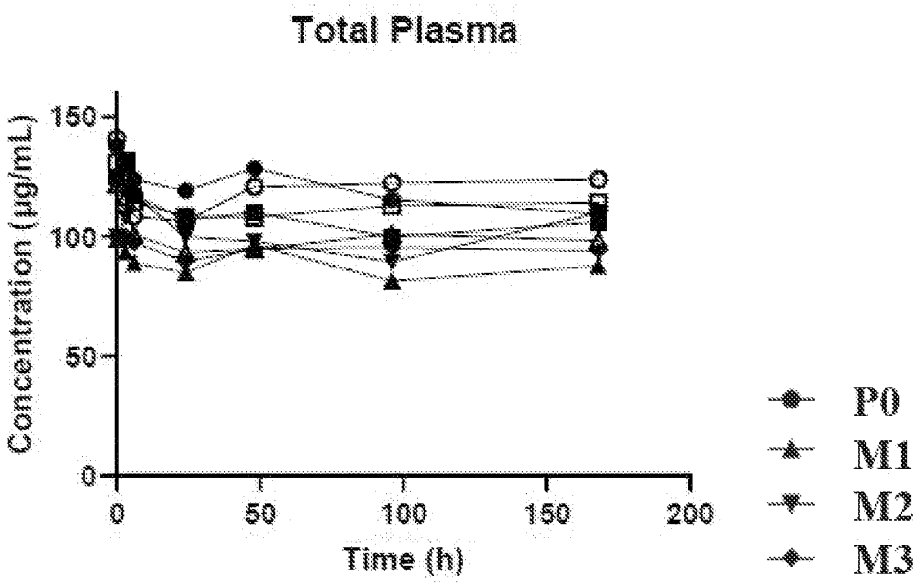


FIG. 11A

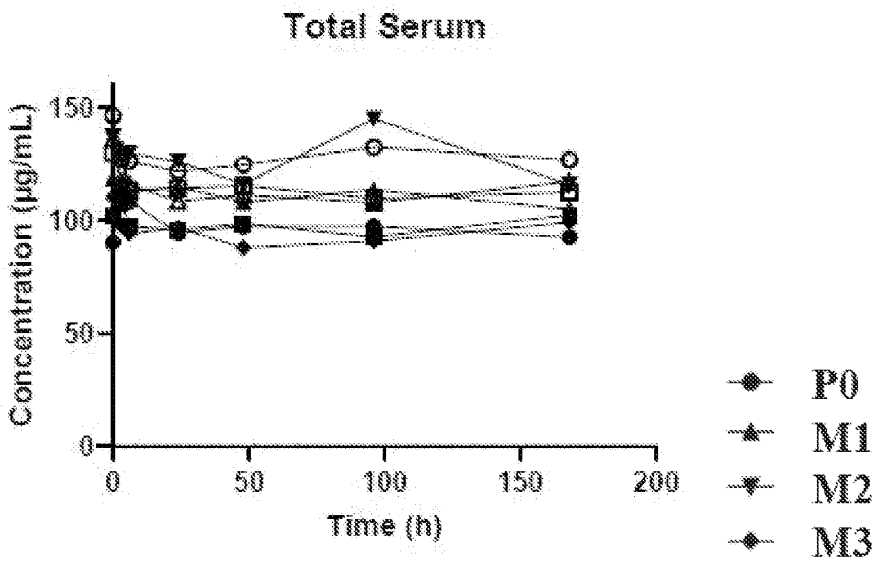


FIG. 11B

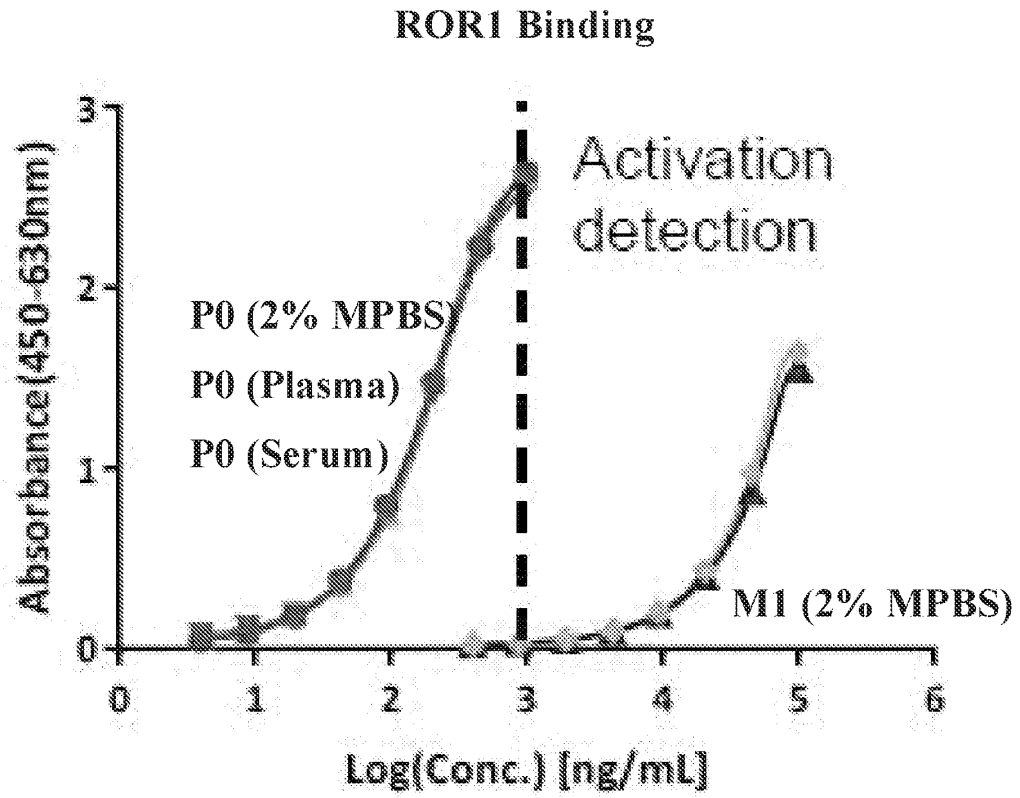

ROR1 Binding
Absorbance(450-630nm)
Log(Conc.) [ng/mL]
Activation detection
P0 (2% MPBS)
P0 (Plasma)
P0 (Serum)
M1 (2% MPBS)
0
1
2
3
4
5
6

FIG. 11C

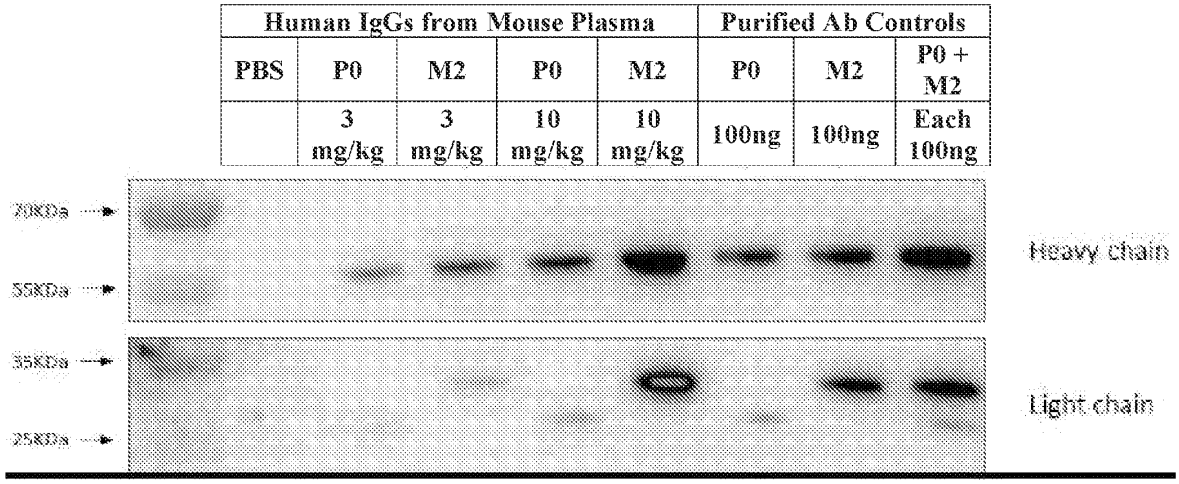


FIG. 12

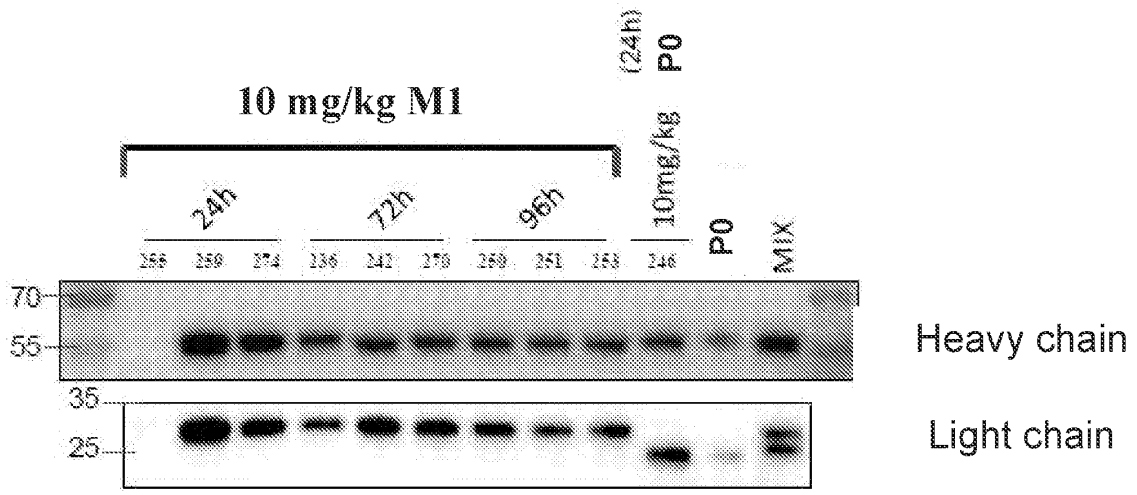


FIG. 13A

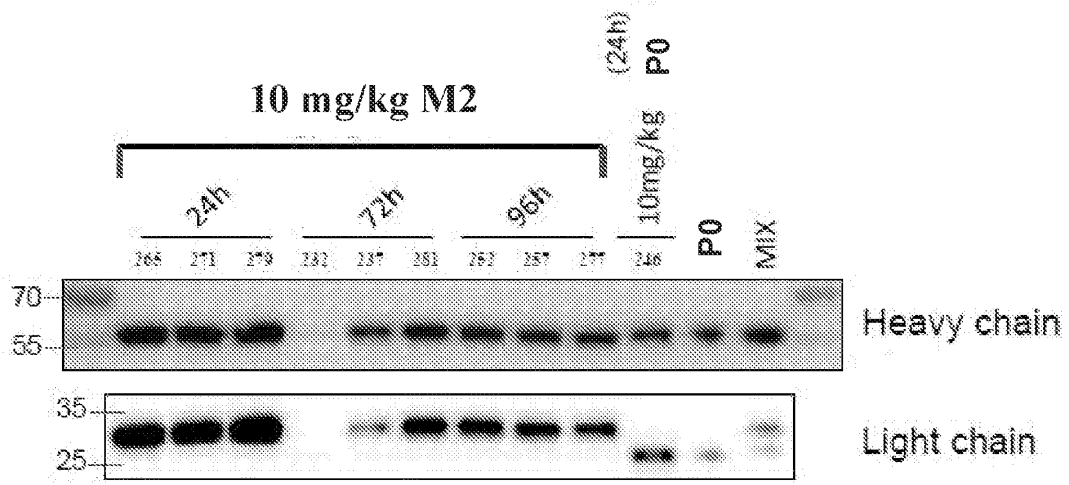


FIG. 13B

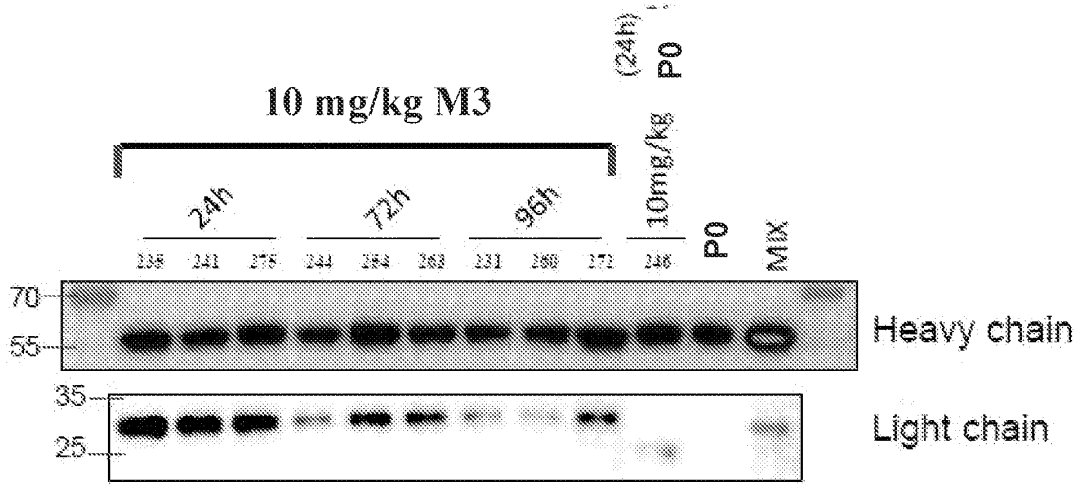


FIG. 13C

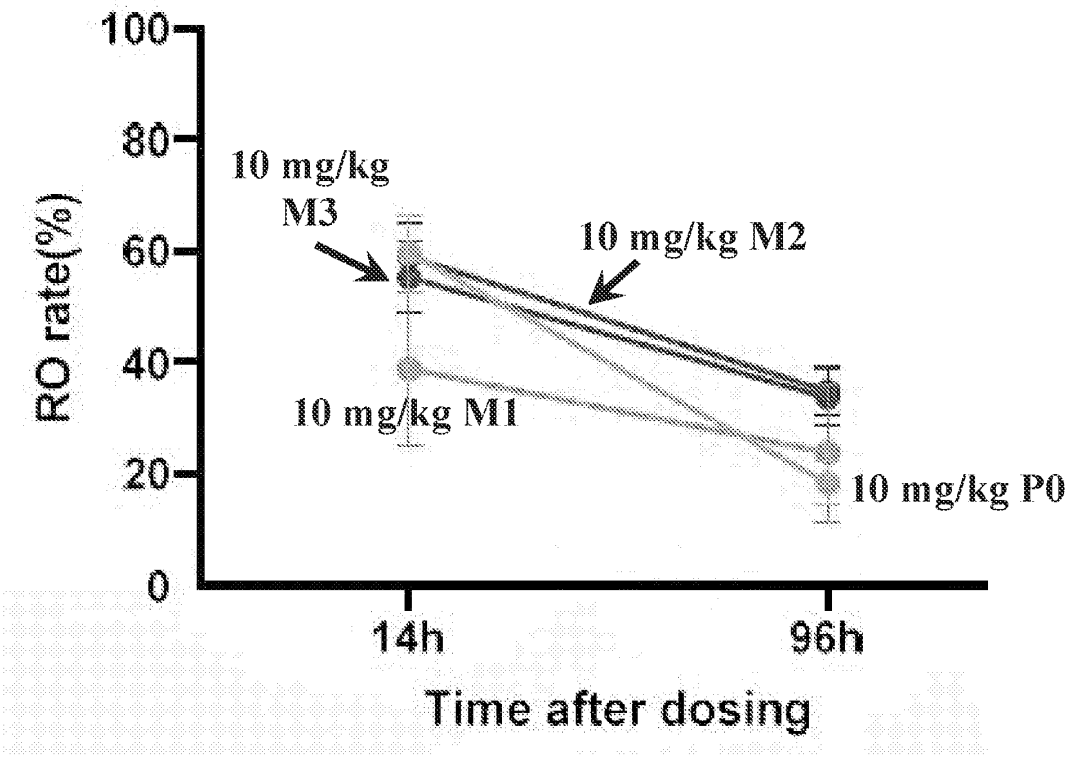

100
80
60
40
20
0
RO rate(%)
10 mg/kg
M3
10 mg/kg M2
10 mg/kg M1
10 mg/kg P0
14h
96h
Time after dosing

FIG. 14

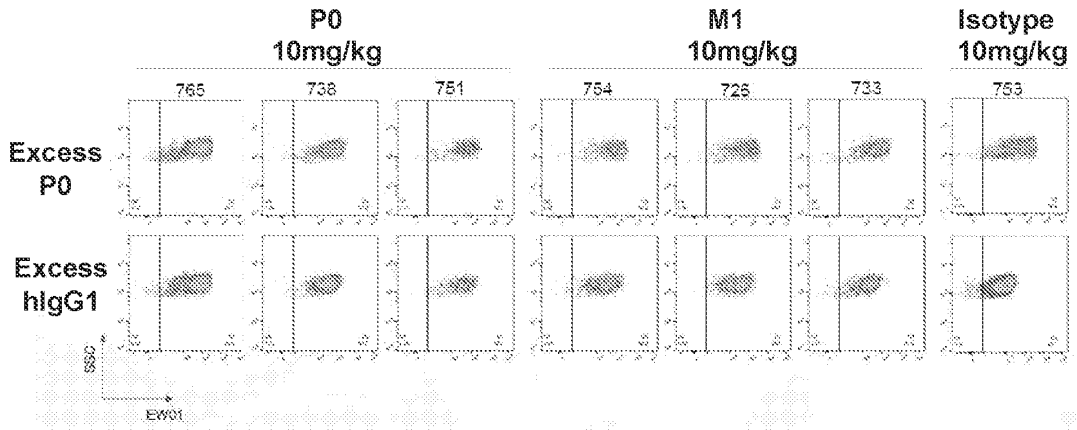


FIG. 15A

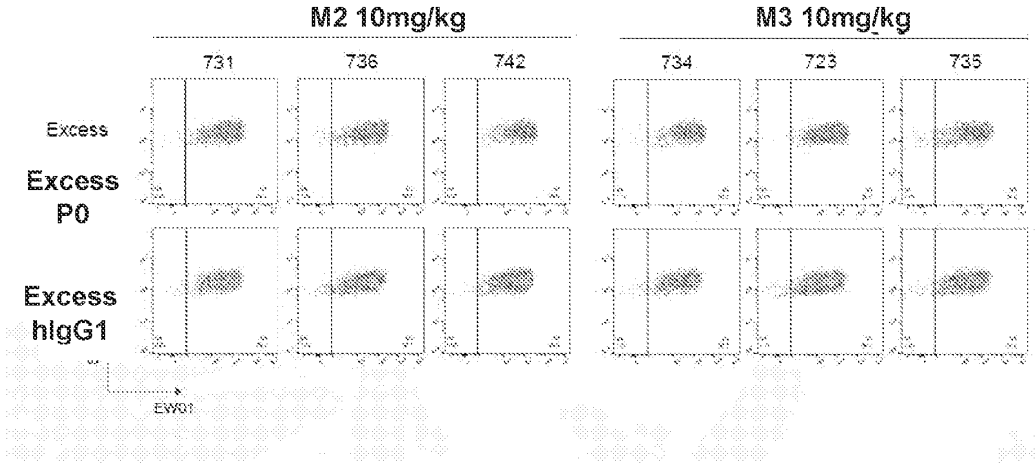


FIG. 15B

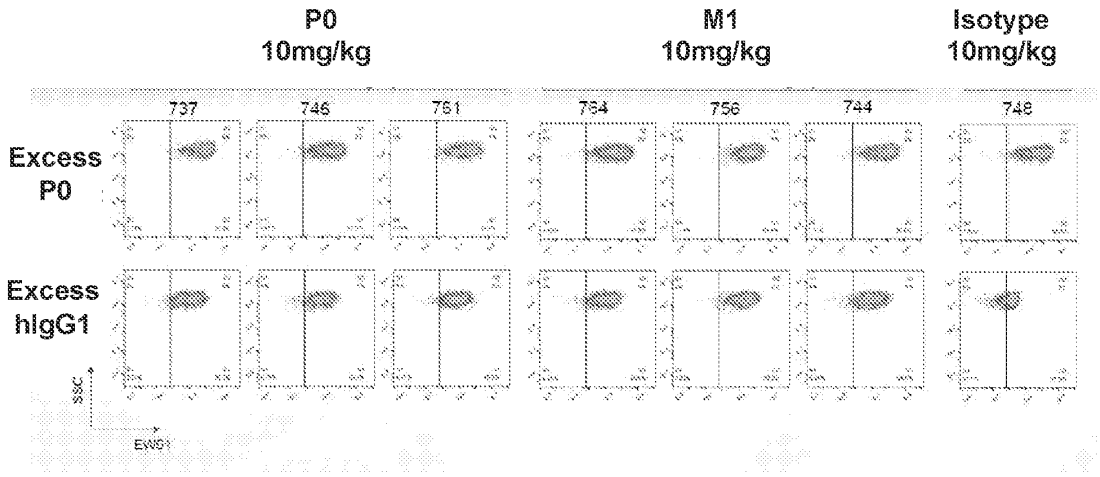


FIG. 16A

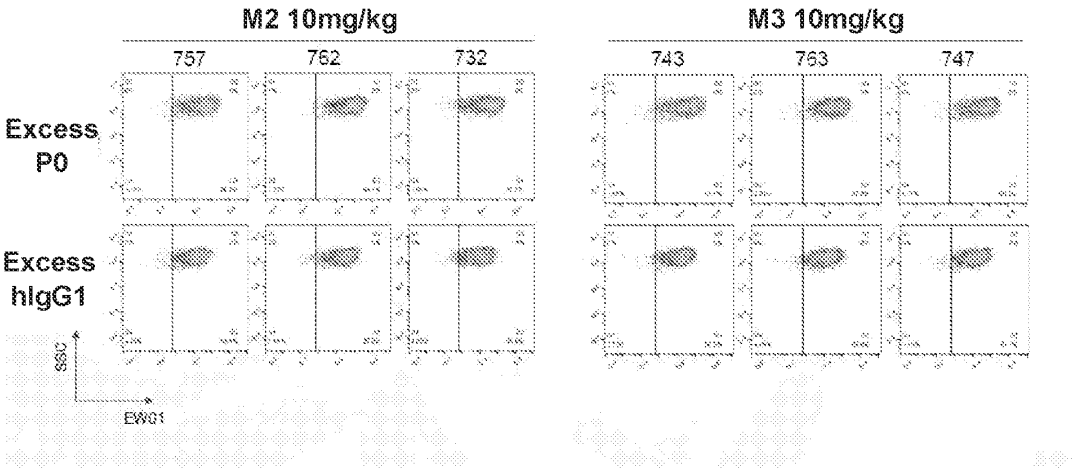


FIG. 16B

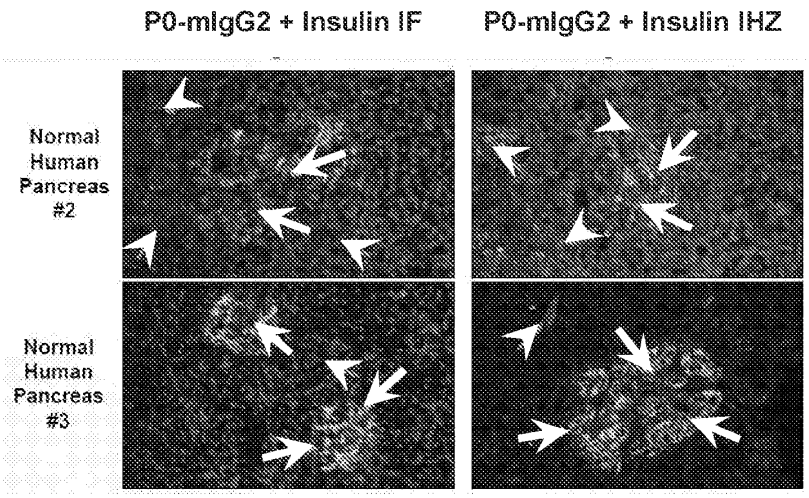


FIG. 17

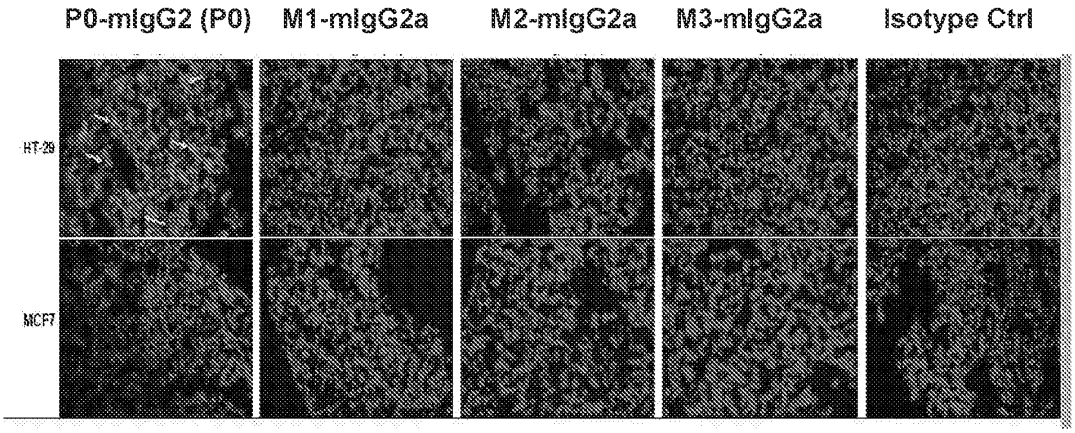


FIG. 18A

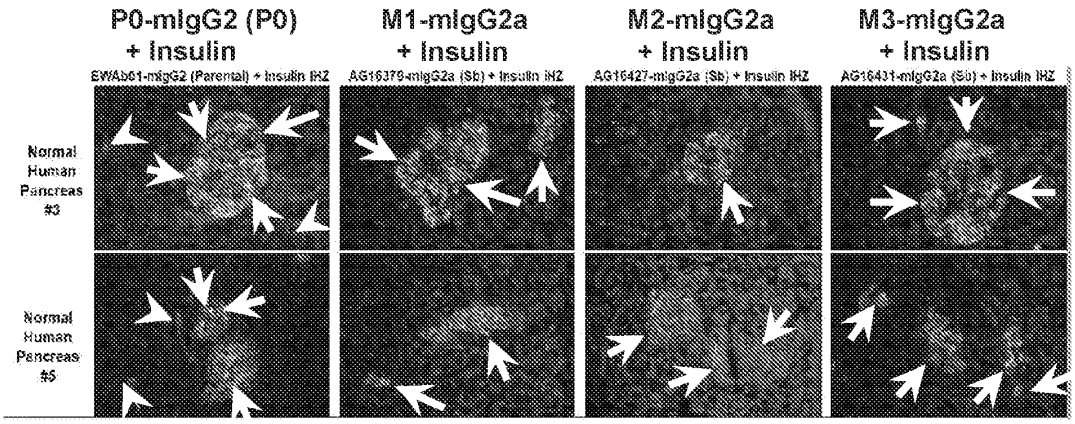


FIG. 18B

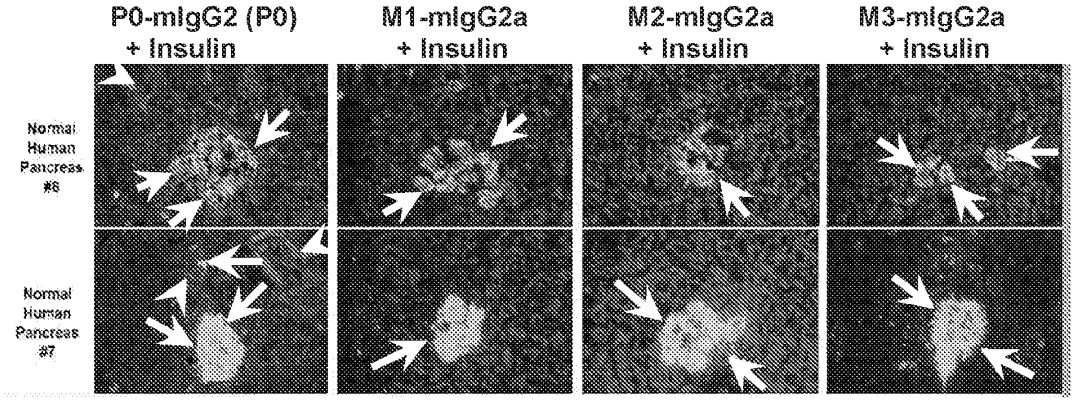


FIG. 18C

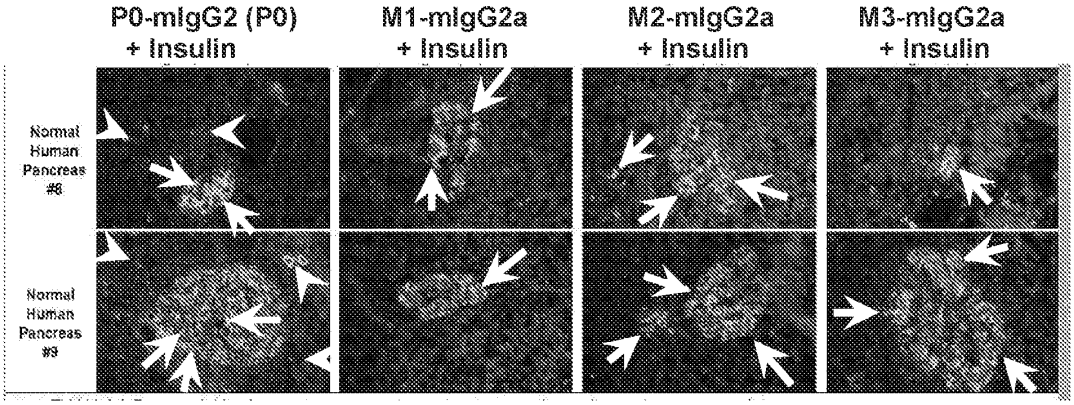


FIG. 18D

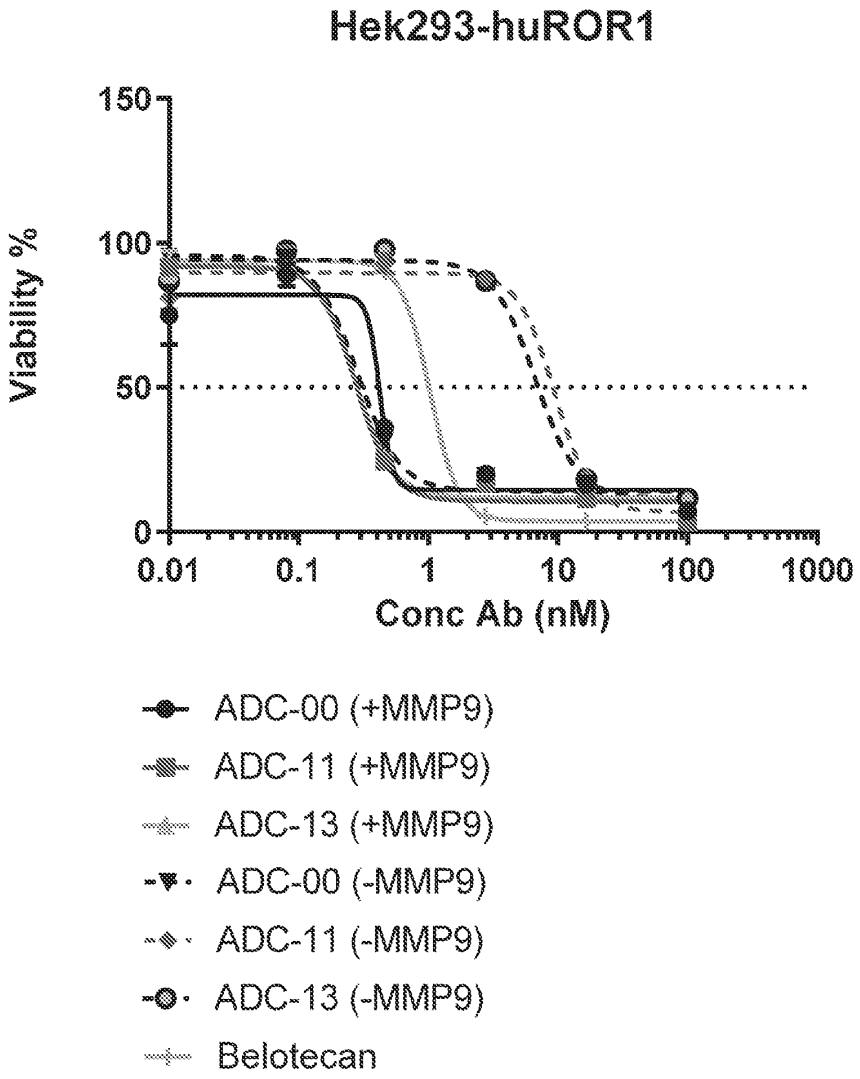

Hek293-huROR1
Viability %
150
100
50
0
0.01
0.1
1
10
100
1000
Conc Ab (nM)
ADC-00 (+MMP9)
ADC-11 (+MMP9)
ADC-13 (+MMP9)
ADC-00 (-MMP9)
ADC-11 (-MMP9)
ADC-13 (-MMP9)
Belotecan

FIG. 19A

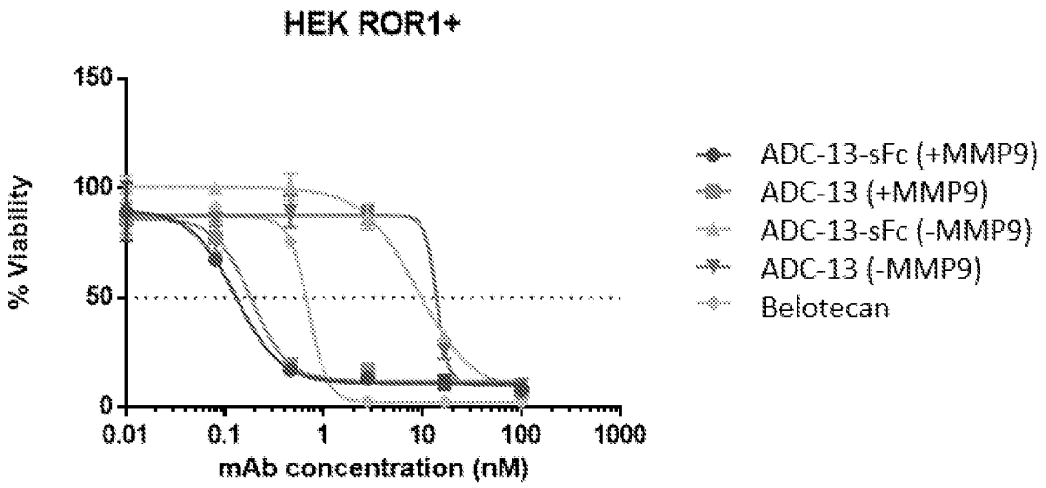


FIG. 19B

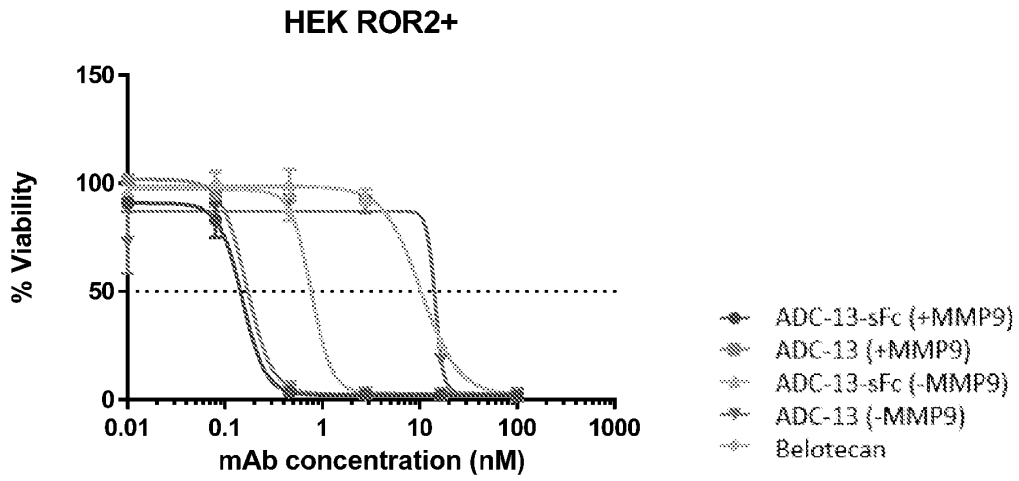


FIG. 19C

-MMP9

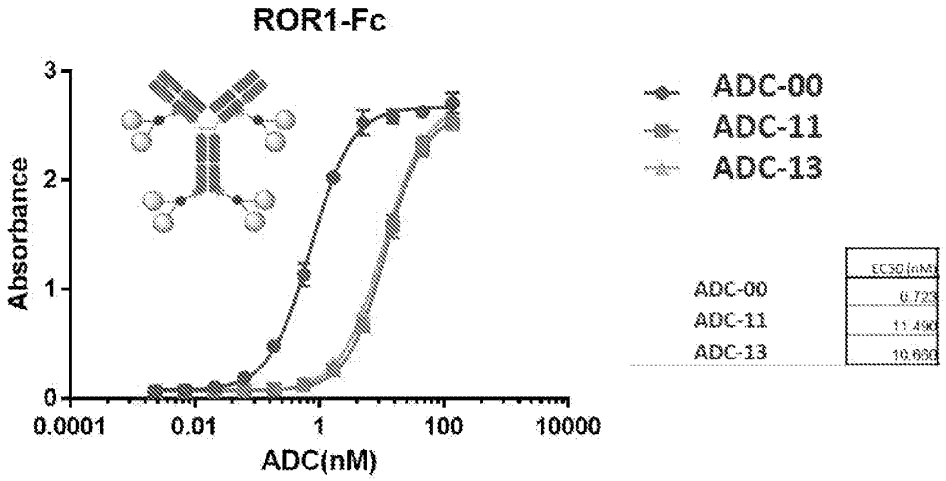


FIG. 20A

+MMP9

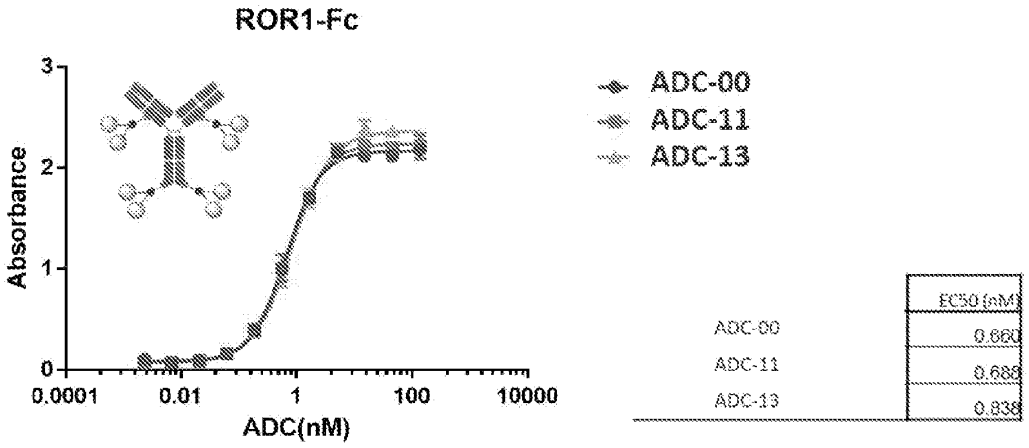


FIG. 20B

-MMP9

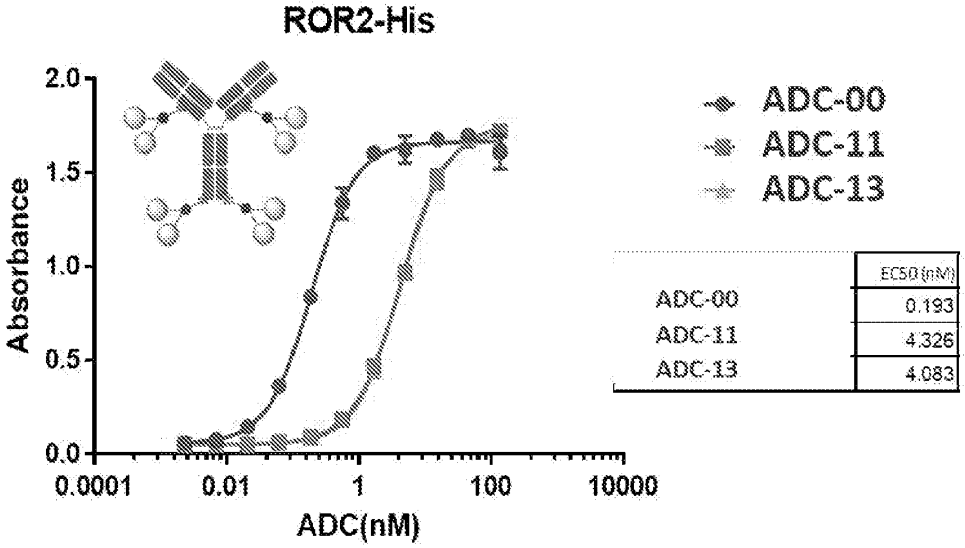


FIG. 20C

+MMP9

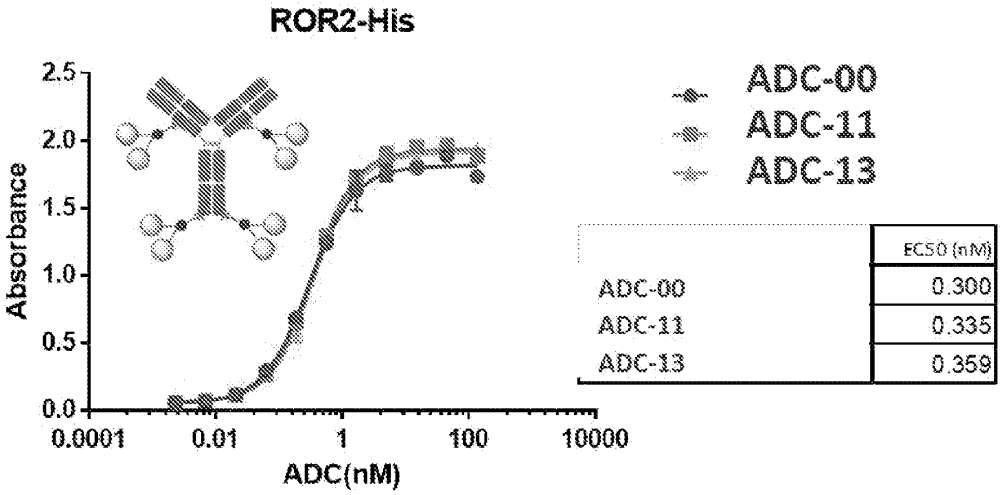


FIG. 20D

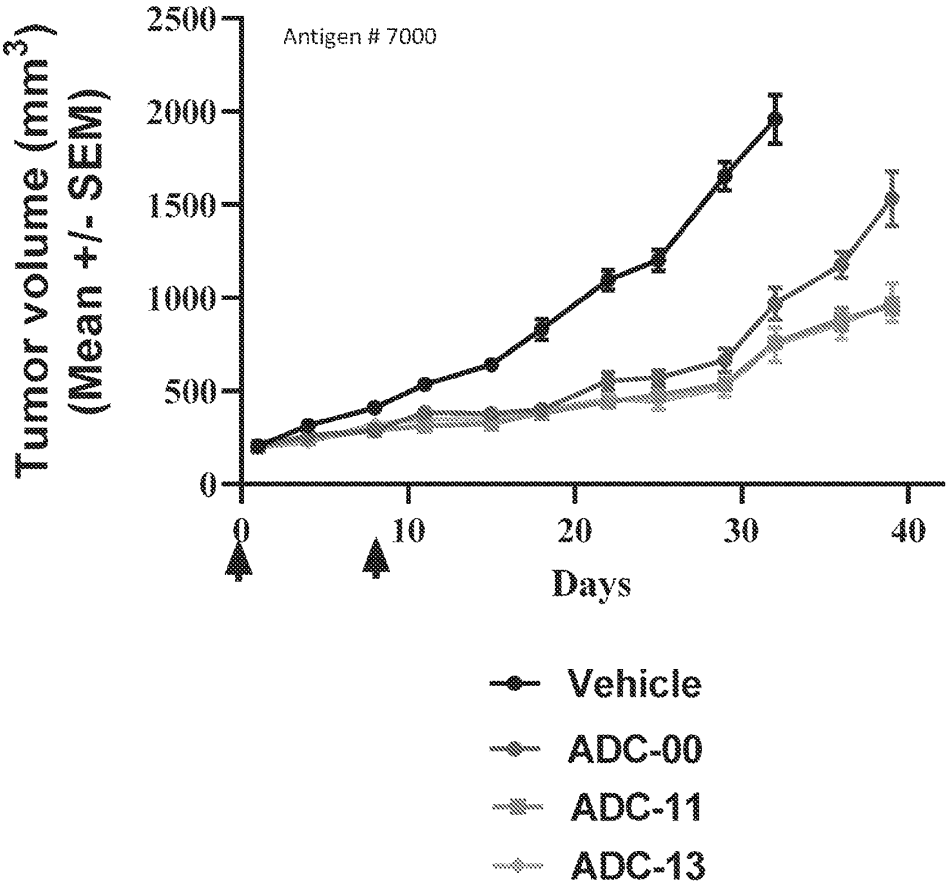

Antigen # 7000
Tumor volume (mm3)
(Mean +/- SEM)
2500
2000
1500
1000
500
0
0
10
20
30
40
Days
Vehicle
ADC-00
ADC-11
ADC-13

FIG. 21A

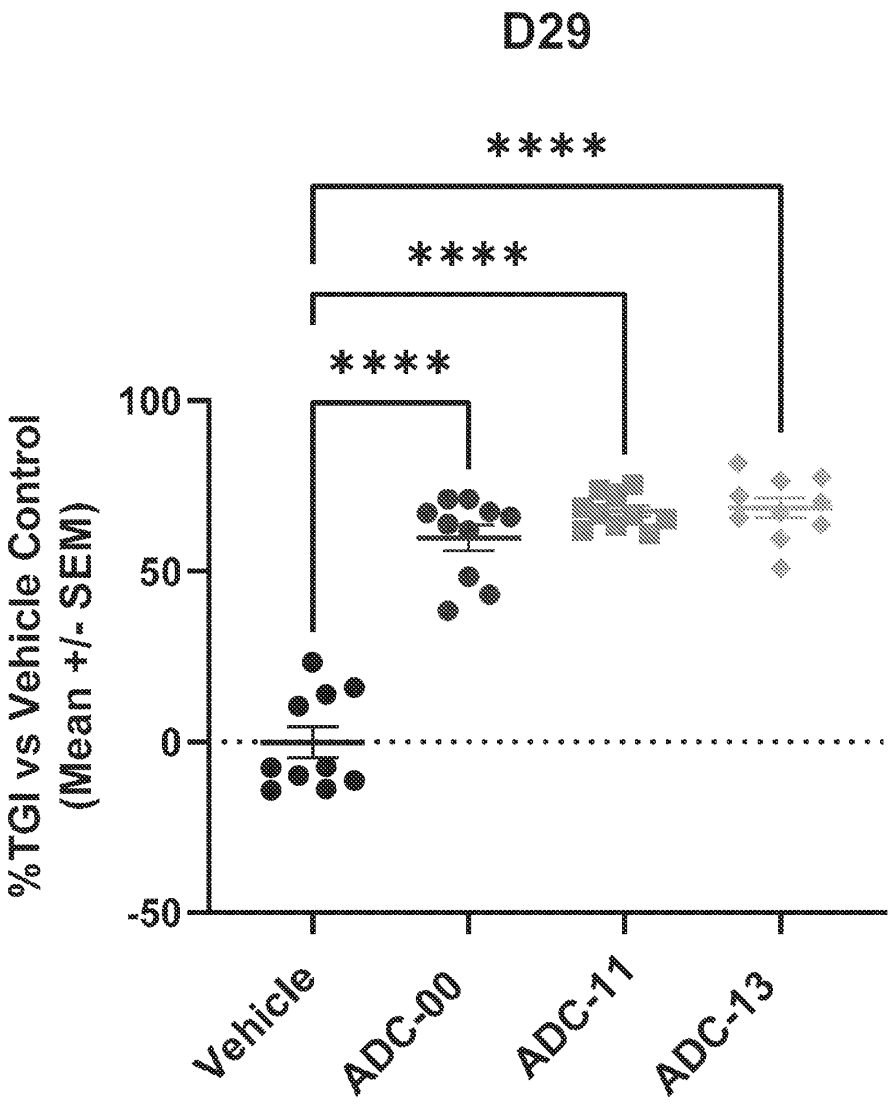

D29
****
****
****
100
50
0
-50
%TGI vs Vehicle Control
(Mean +/- SEM)
Vehicle
ADC-00
ADC-11
ADC-13

FIG. 21B

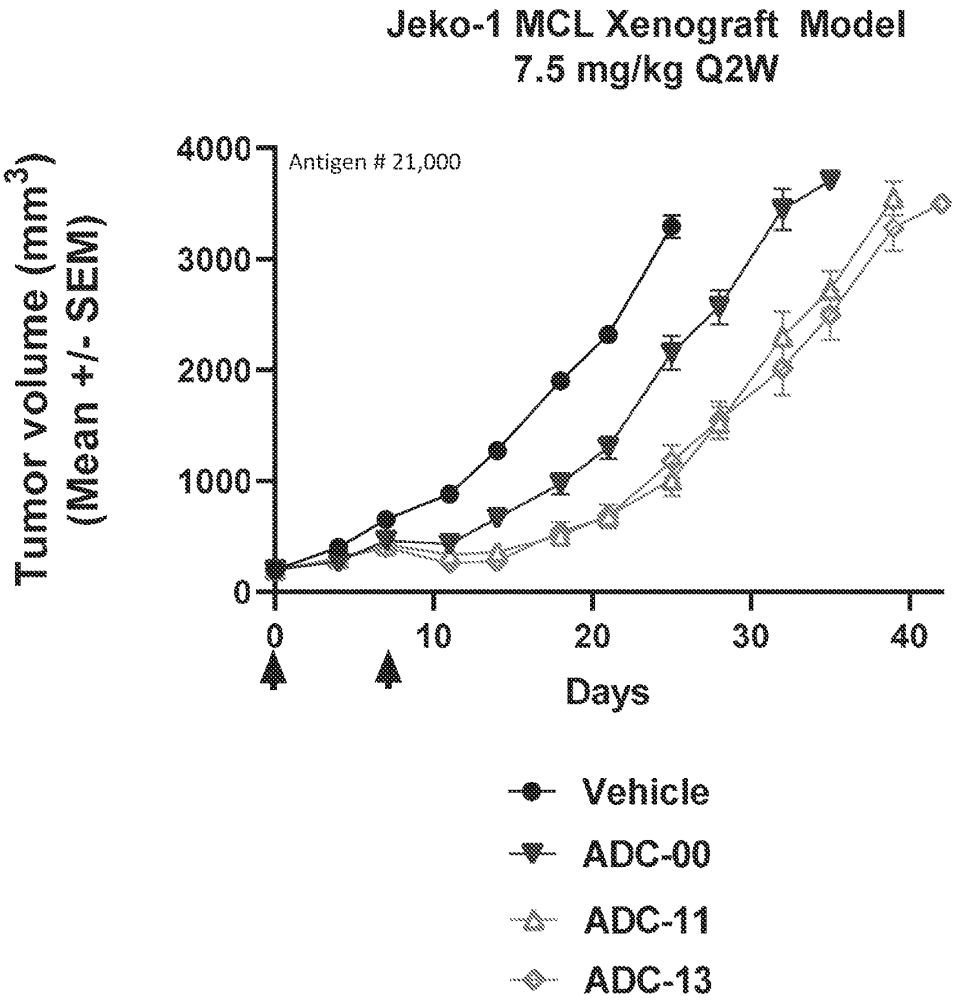

Jeko-1 MCL Xenograft Model
7.5 mg/kg Q2W
Tumor volume (mm3)
(Mean +/- SEM)
Antigen # 21,000
4000
3000
2000
1000
0
0
10
20
30
40
Days
Vehicle
ADC-00
ADC-11
ADC-13

FIG. 22A

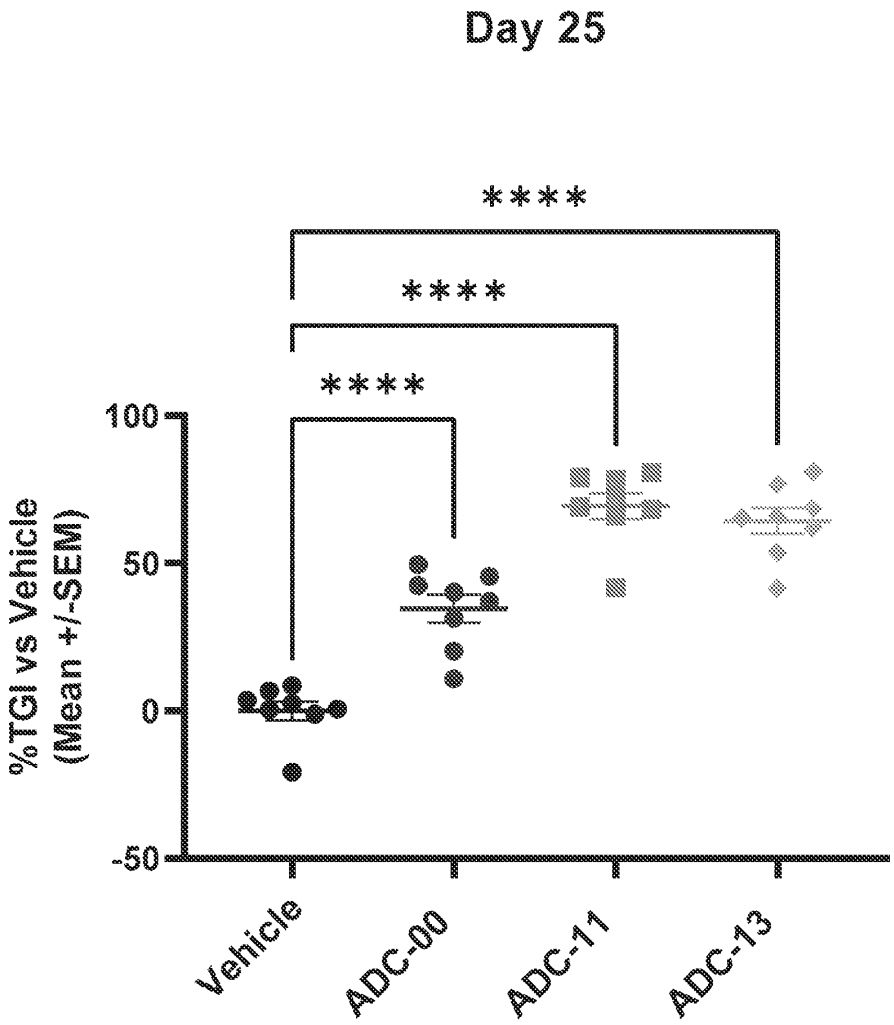

Day 25
****
****
****
100
50
0
-50
%TGI vs Vehicle
(Mean +/-SEM)
Vehicle
ADC-00
ADC-11
ADC-13

FIG. 22B

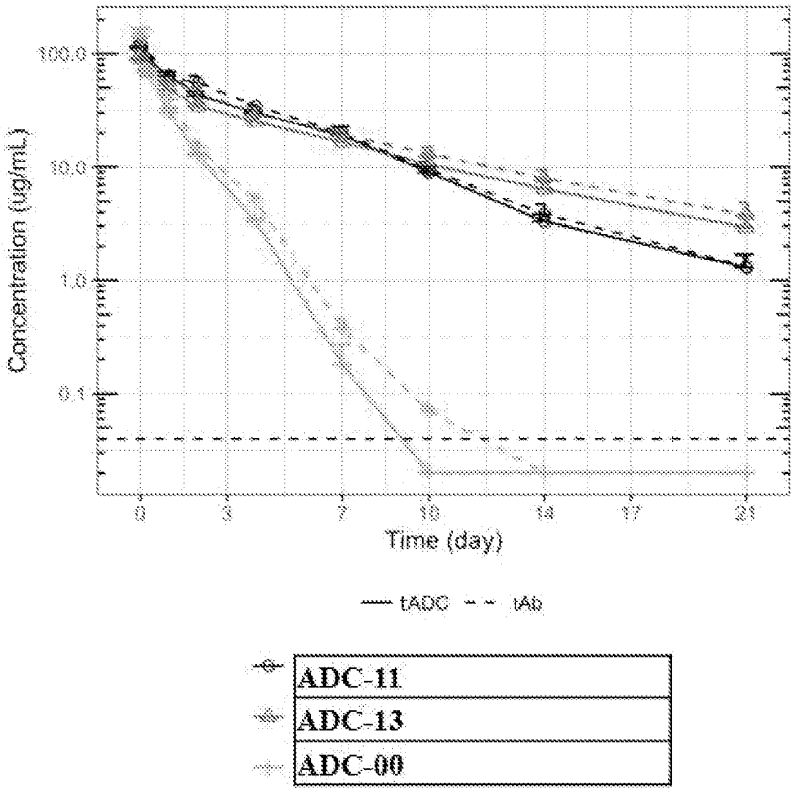

100.0
10.0
1.0
0.1
Concentration (ug/mL)
0
3
7
10
14
17
21
Time (day)
tADC
tAb
ADC-11
ADC-13
ADC-00

FIG. 23

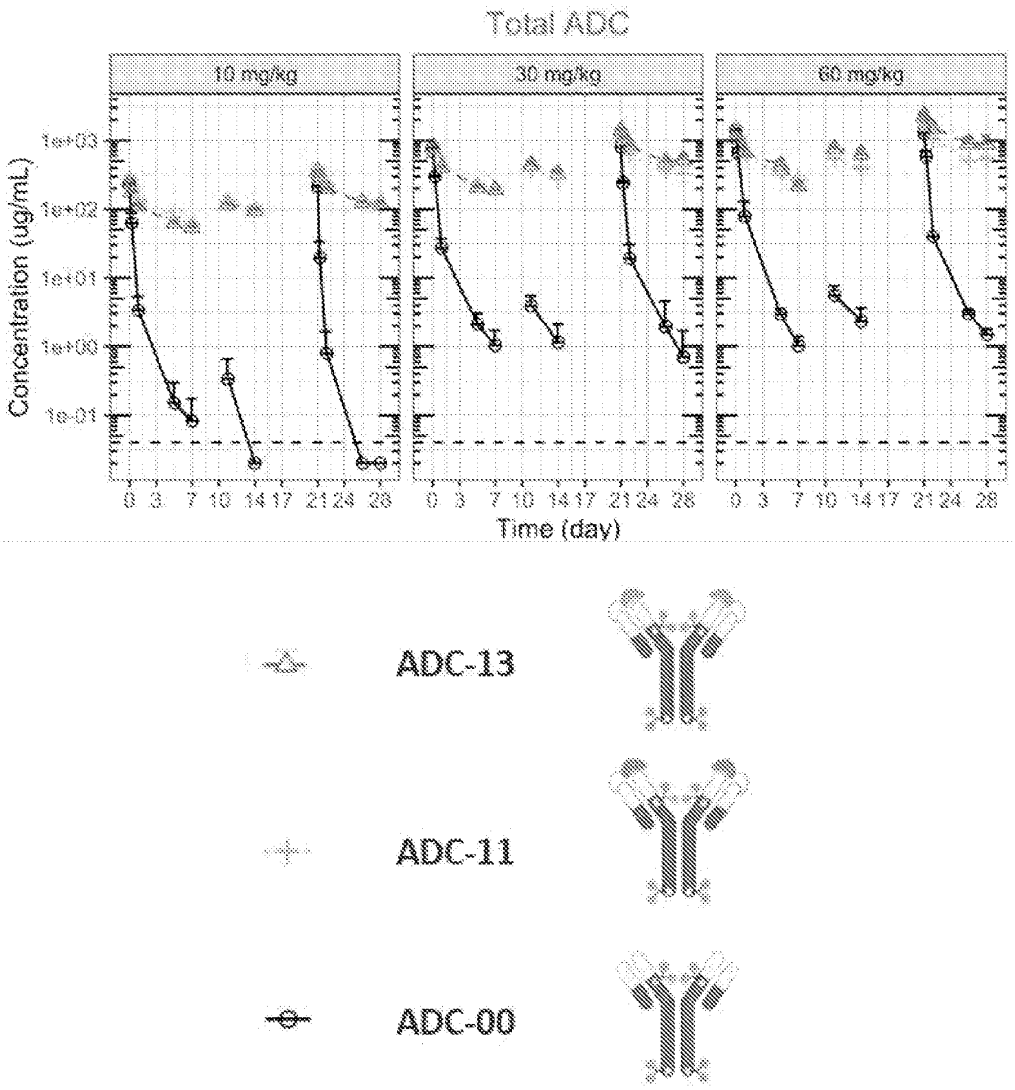
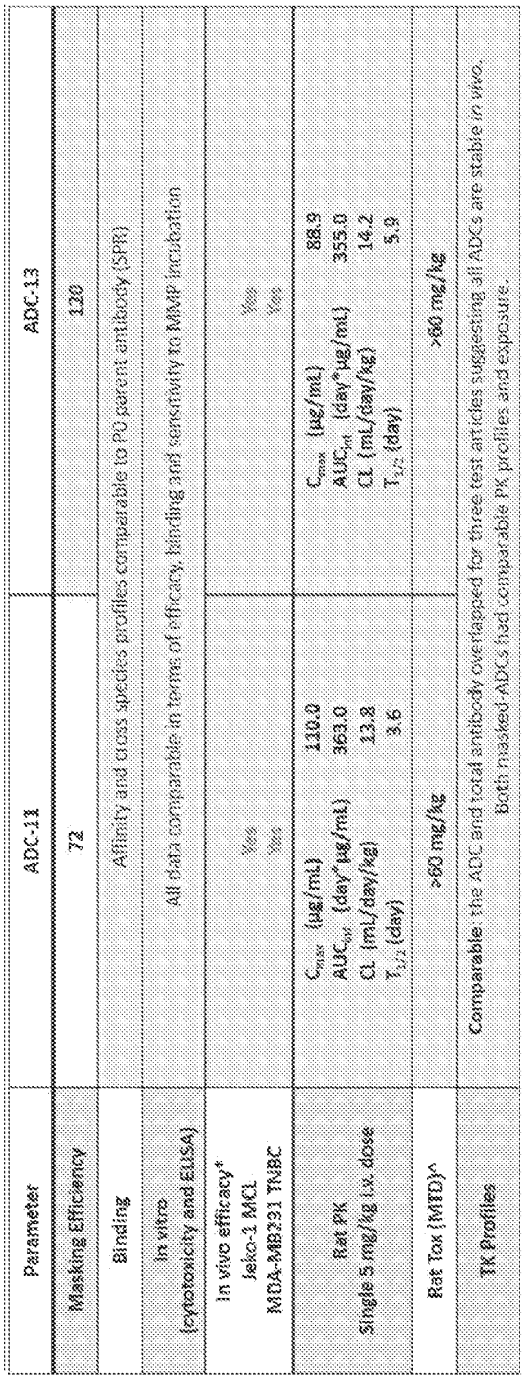

Total ADC
10 mg/kg
30 mg/kg
60 mg/kg
Concentration (ug/mL)
1e+03
1e+02
1e+01
1e+00
1e-01
0 3 7 10 14 17 21 24 28
Time (day)
ADC-13
ADC-11
ADC-00

FIG. 24



Parameter	ADC-11	ADC-13
Masking Efficiency	72	120
Binding	Affinity and cross species profiles comparable to PO parent antibody (SPR)	
In vitro (cytotoxicity and ELISA)	All data comparable in terms of efficacy, binding and sensitivity to MMP incubation	
In vivo efficacy* Jeko-1 MCL MDA-MB231 TNBC	Yes Yes	Yes Yes
Rat PK Single 5 mg/kg i.v. dose	C_{max} (µg/mL) 110.0 AUC_{inf} (day*µg/mL) 363.0 Cl (mL/day/kg) 13.8 $T_{1/2}$ (day) 3.6	C_{max} (µg/mL) 88.9 AUC_{inf} (day*µg/mL) 355.0 Cl (mL/day/kg) 14.2 $T_{1/2}$ (day) 5.9
Rat Tox (MTD)^	>60 mg/kg	>60 mg/kg
TK Profiles	Comparable the ADC and total antibody overlapped for three test articles suggesting all ADCs are stable *in vivo*. Both masked-ADCs had comparable PK profiles and exposure.	

*p < 0.05 %TGI vs isotype control
^projected

FIG. 25

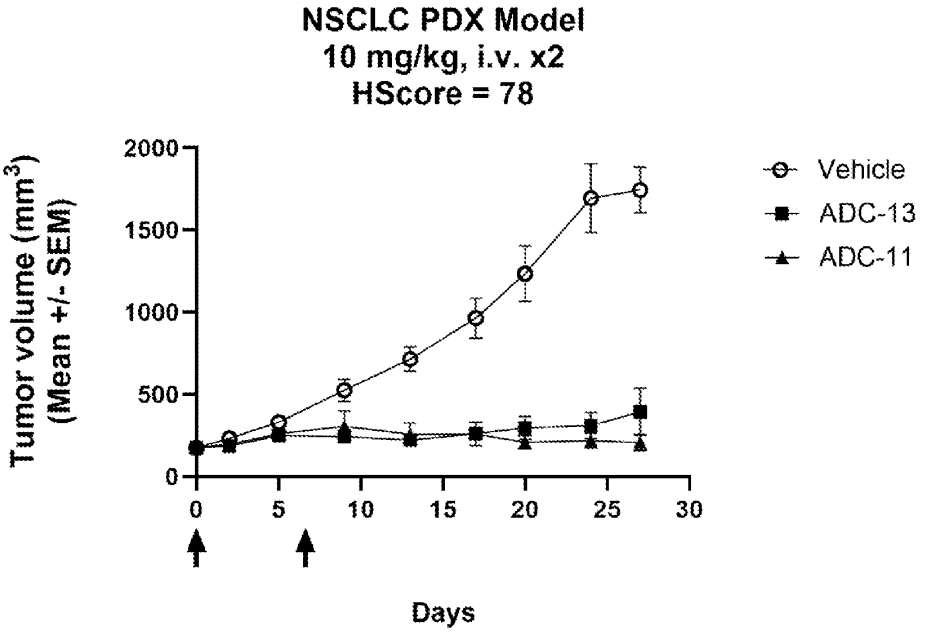

NSCLC PDX Model
10 mg/kg, i.v. x2
HScore = 78
Tumor volume (mm3)
(Mean +/- SEM)
2000
1500
1000
500
0
0
5
10
15
20
25
30
Days
Vehicle
ADC-13
ADC-11

FIG. 26