>gi | 47938093 | gb | AAH71557.1 | PTK7 protein tyrosine kinase 7 [Homo sapiens]

```
   1 MGAARGSPAR PRRLPLLSVL LPLLGGTQT AIVFIKQPSS QDALQGRRAL LRCEVEAPGP
  61 VHVYWLLDGA PVQDTERRFA QGSSLSFAAV DRPQDSGTFQ CVARDDVTGE EARSANASFN
 121 IKWIEAGPVV LKHPASEAEI QPQTQVTLRC HIDGHPRPTY QWFRDGTPLS DGQSNHTVSS
 181 KERNLTLRPA GPEHSGLYSC CAHSAFGQAC SSQNFTLSIA DESFARVVLA PQDVVVARYE
 241 EAMFHCQFSA QPPPSLQWLF EDETPITNRS RPPHLRRATV FANGSLLLTQ VRPRNAGIYR
 301 CIGQGQRGPP IILEATLHLA EIEDMPLFEP RVFTAGSEER VTCLPPKGLP EPSVWWEHAG
 361 VRLPTHGRVY QKGHELVLAN IAESDAGVYT CHAANLAGQR RQDVNITVAT VPSWLKKPQD
 421 SQLEEGKPGY LDCLTQATPK PTVVWYRNQM LISEDSRFEV FKNGTLRINS VEVYDGTWYR
 481 CMSSTPAGSI EAQARVQVLE KLKFTPPPQP QQCMEFDKEA TVPCSATGRE KPTIKWERAD
 541 GSSLPEWVTD NAGTLHFARV TRDDAGNYTC IASNGPQGQI RAHVQLTVAV FITFKVEPER
 601 TTVYQGHTAL LQCEAQGDPK PLIQWKGKDR ILDPTKLGPR MHIFQNGSLV IHDVAPEDSG
 661 RYTCIAGNSC NIKHTEAPLY VVDKPVPEES EGPGSPPPYK MIQTIGLSVG AAVAYIIAVL
 721 GLMFYCKKRC KAKRLQKQPE GEEPEMECLN GGPLQNGQPS AEIQEEVALT SLGSGPAATN
 781 KRHSTSDKMH FPRSSLQPIT TLGKSEFGEV FLAKAQGLEE GVAETLVLVK SLQSKDEQQQ
 841 LDFRRELEMF GKLNHANVVR LLGLCREAEP HYMVLEYVDL GDLKQFLRIS KSKDEKLKSQ
 901 PLSTKQKVAL CTQVALGMEH LSNNRFVHKD LAARNCLVSA QRQVKVSALG LSKDVYNSEY
 961 YHFRQAWVPL RWMSPEAILE GDFSTKSDVW AFGVLMWEVF THGEMPHGGQ ADDEVLADLQ
1021 AGKARLPQPE GCPSKLYRLM QRCWALSPKD RPSFSEIASA LGDSTVDSKP
```

(SEQ ID NO 73)

FIG. 1

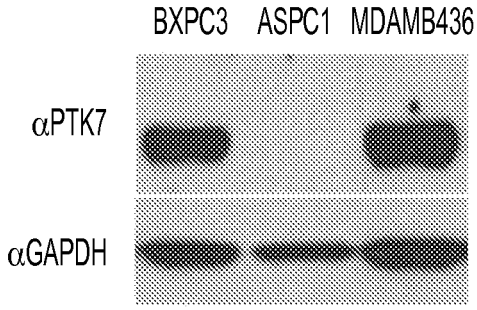

BXPC3
ASPC1
MDAMB436
αPTK7
αGAPDH

FIG. 2A

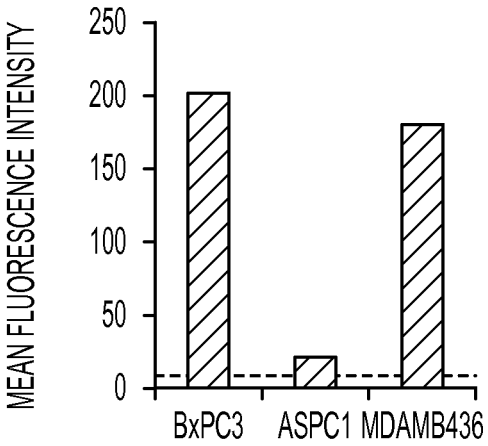

MEAN FLUORESCENCE INTENSITY
250
200
150
100
50
0
BxPC3
ASPC1
MDAMB436

FIG. 2B

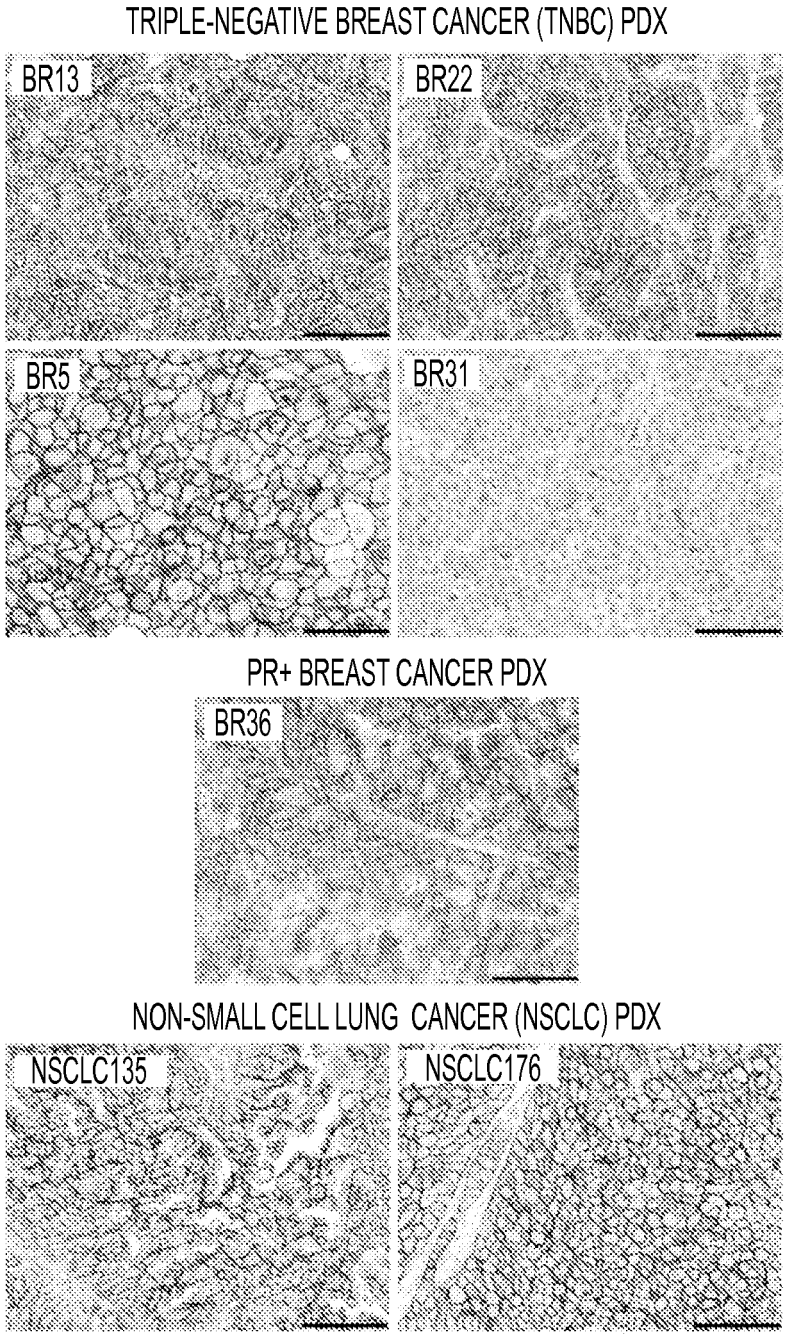

TRIPLE-NEGATIVE BREAST CANCER (TNBC) PDX
BR13
BR22
BR5
BR31
PR+ BREAST CANCER PDX
BR36
NON-SMALL CELL LUNG CANCER (NSCLC) PDX
NSCLC135
NSCLC176

FIG. 3

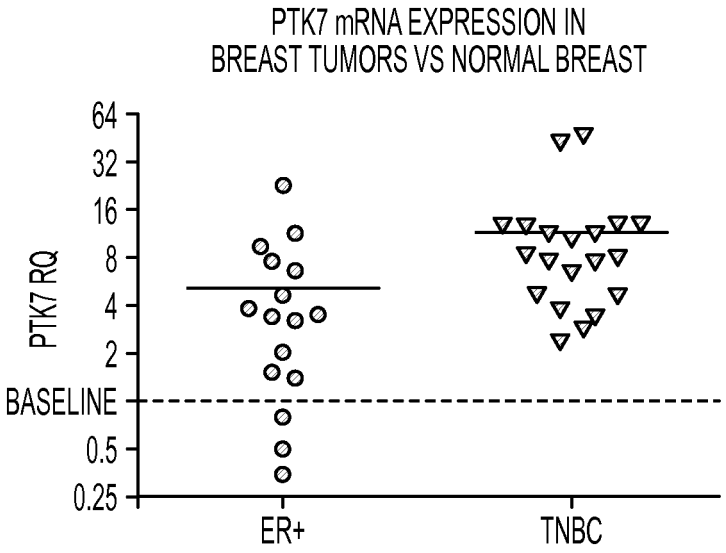

PTK7 mRNA EXPRESSION IN
BREAST TUMORS VS NORMAL BREAST
PTK7 RQ
64
32
16
8
4
2
BASELINE
0.5
0.25
ER+
TNBC

FIG. 4A

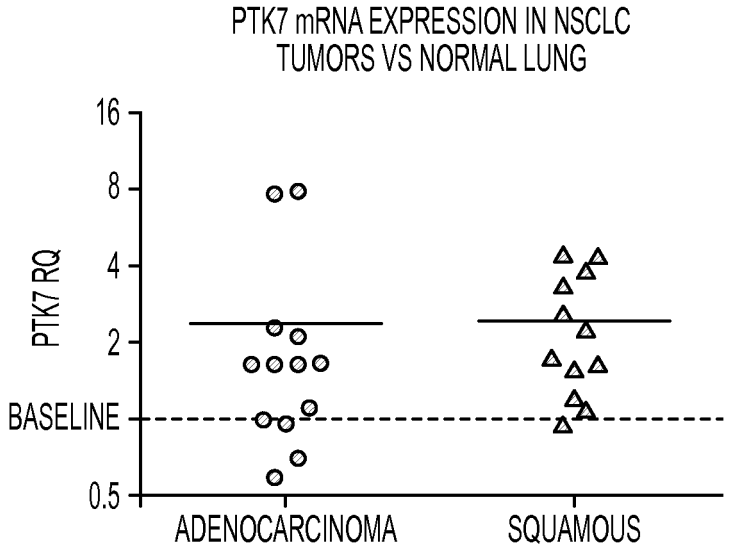

PTK7 mRNA EXPRESSION IN NSCLC
TUMORS VS NORMAL LUNG
PTK7 RQ
16
8
4
2
BASELINE
0.5
ADENOCARCINOMA
SQUAMOUS

FIG. 4B

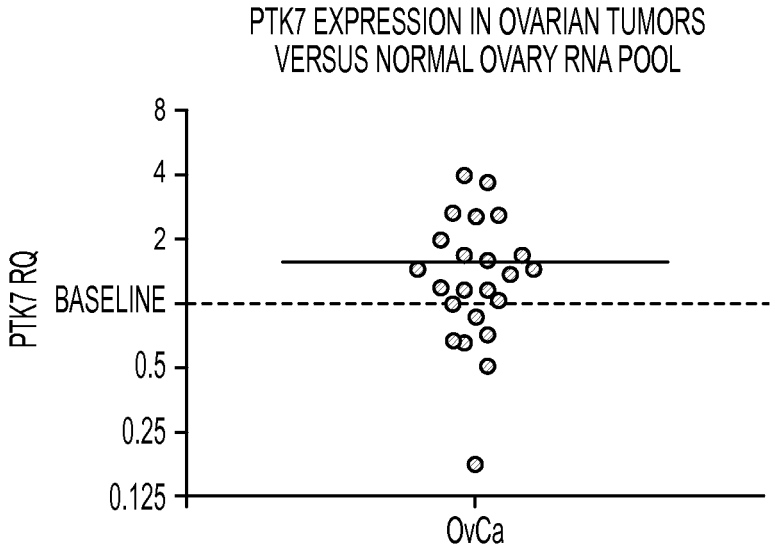

PTK7 EXPRESSION IN OVARIAN TUMORS
VERSUS NORMAL OVARY RNA POOL
PTK7 RQ
8
4
2
BASELINE
0.5
0.25
0.125
OvCa

FIG. 4C

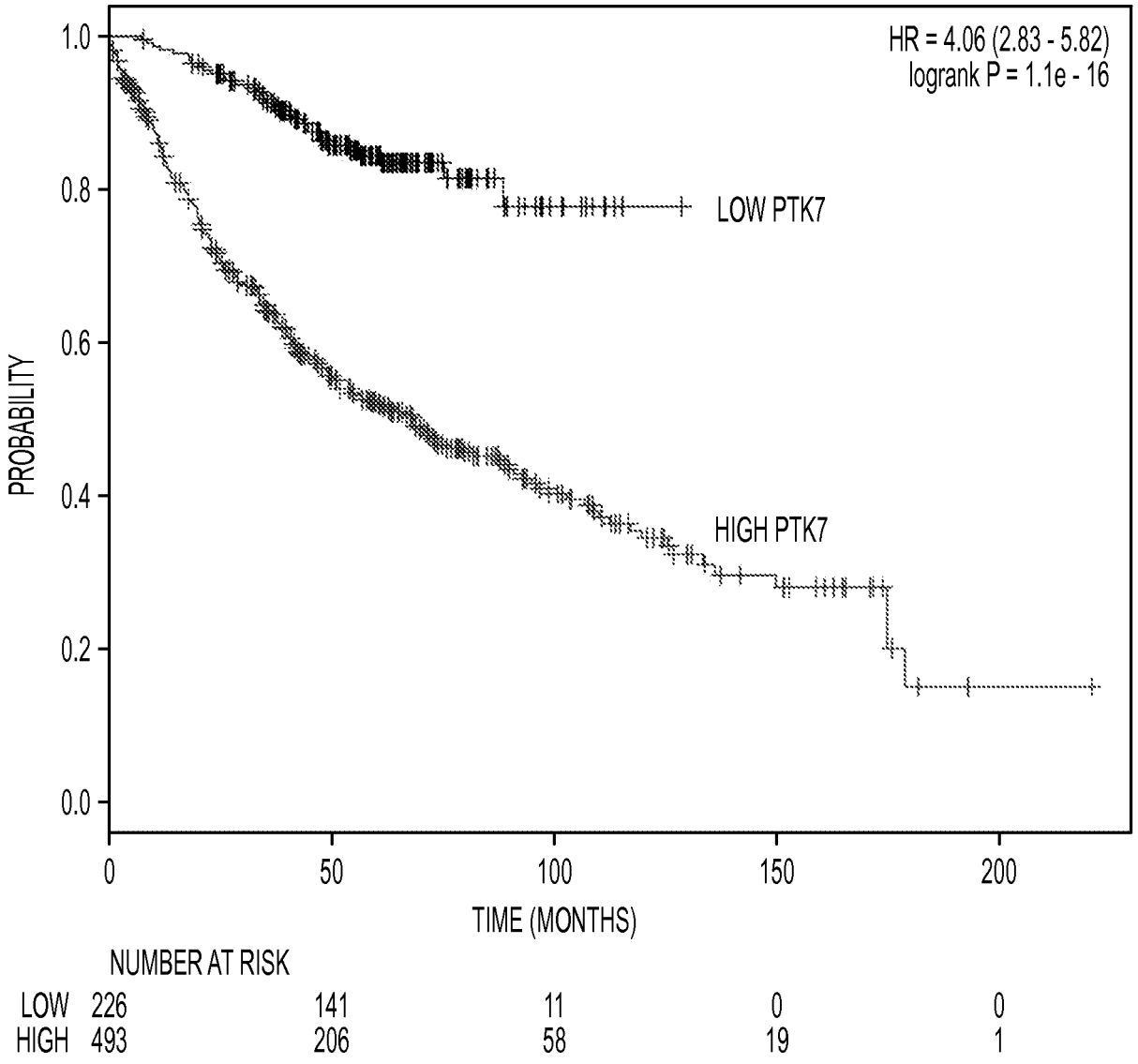

HR = 4.06 (2.83 - 5.82)
logrank P = 1.1e - 16
LOW PTK7
HIGH PTK7
PROBABILITY
1.0
0.8
0.6
0.4
0.2
0.0
0
50
100
150
200
TIME (MONTHS)
NUMBER AT RISK
LOW 226 141 11 0 0
HIGH 493 206 58 19 1

FIG. 5

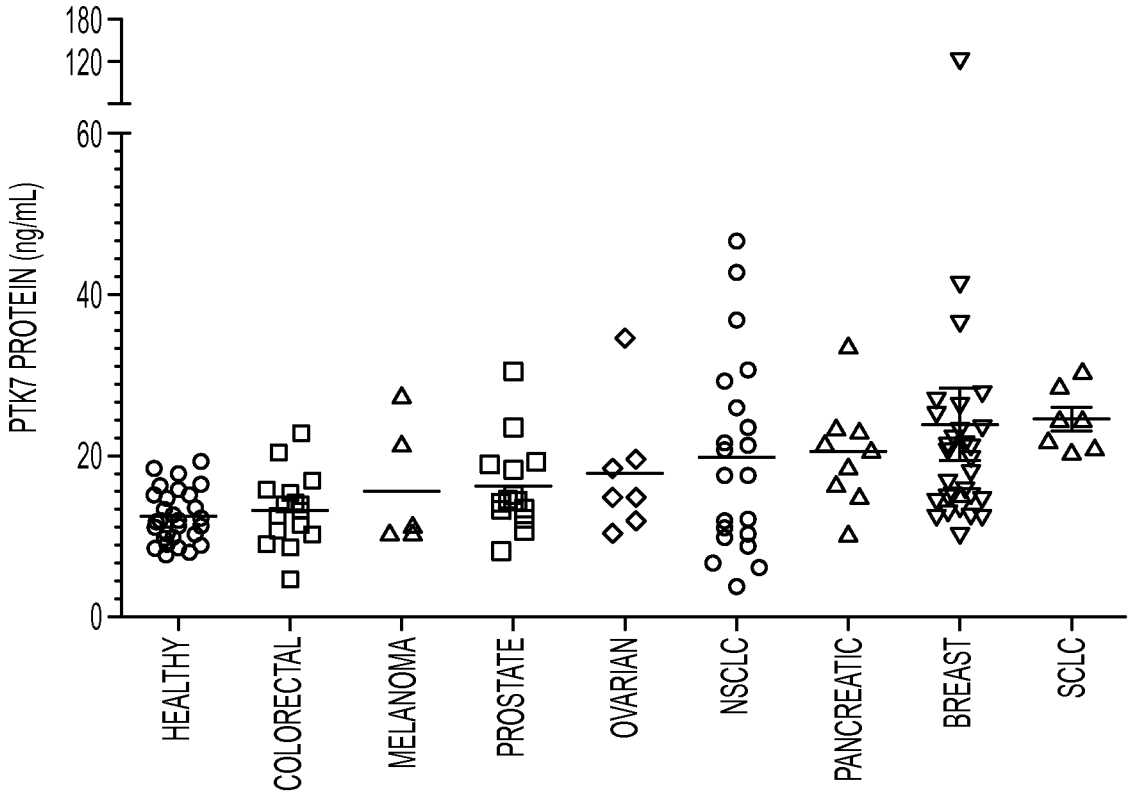

180
120
60
40
20
0
PTK7 PROTEIN (ng/mL)
HEALTHY
COLORECTAL
MELANOMA
PROSTATE
OVARIAN
NSCLC
PANCREATIC
BREAST
SCLC

FIG. 6

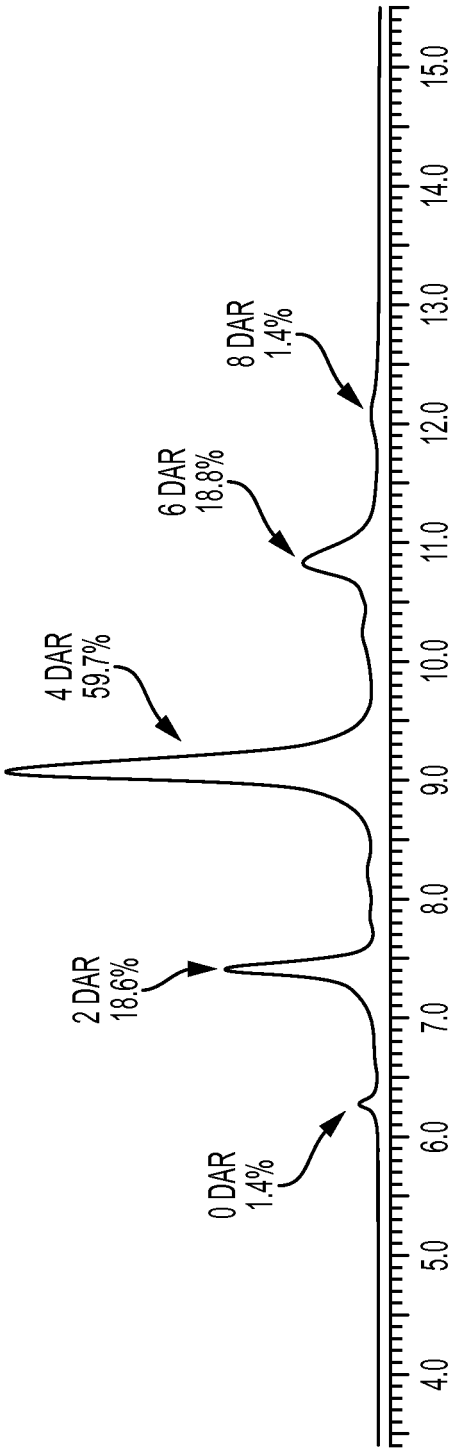

0 DAR
1.4%
2 DAR
18.6%
4 DAR
59.7%
6 DAR
18.8%
8 DAR
1.4%
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
15.0
MINUTES

FIG. 7

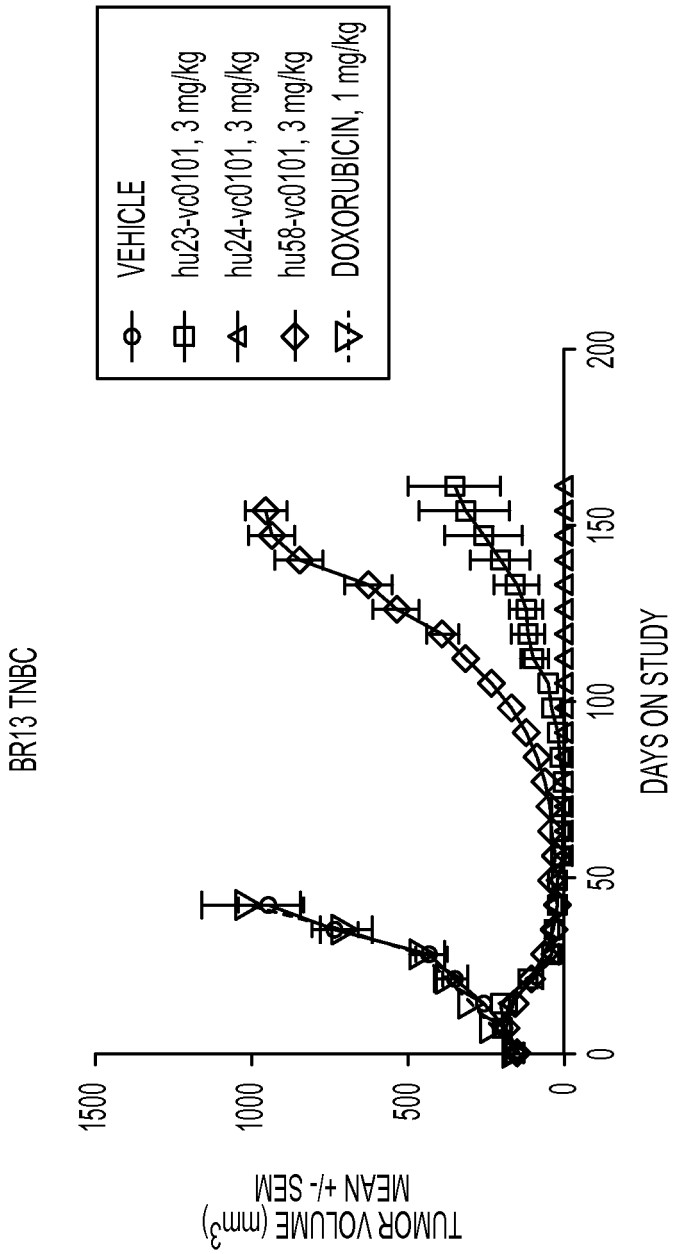

BR13 TNBC
VEHICLE
hu23-vc0101, 3 mg/kg
hu24-vc0101, 3 mg/kg
hu58-vc0101, 3 mg/kg
DOXORUBICIN, 1 mg/kg
TUMOR VOLUME (mm3)
MEAN +/- SEM
DAYS ON STUDY
0
500
1000
1500
0
50
100
150
200

FIG. 8

EFFICACY OF anti-PTK7 ADCs IN THE BR13 TNBC PDX.

DAY	VEHICLE	10mg/kg hu24-vc0101	10mg/kg hu23-mc8261	3mg/kg hu23-mc8261	10mg/kg hu24-mc8261	3mg/kg hu24-mc8261	10mg/kg hu58-mc8261	3mg/kg hu58-mc8261
0	144 ± 13	192 ± 23	157 ± 11	162 ± 8	196 ± 26	160 ± 12	163 ± 14	153 ± 8
7	255 ± 22	203 ± 30	205 ± 12	188 ± 11	248 ± 23	196 ± 21	233 ± 15	230 ± 20
14	349 ± 40	136 ± 14	142 ± 12	203 ± 13	243 ± 30	188 ± 23	249 ± 20	277 ± 29
21	428 ± 48	36 ± 6	148 ± 21	125 ± 12	166 ± 19	150 ± 15	301 ± 24	366 ± 26
28	650 ± 62	20 ± 5	169 ± 19	159 ± 15	158 ± 23	187 ± 25	525 ± 77	463 ± 51
35	734 ± 74	4 ± 2	286 ± 41	207 ± 26	216 ± 41	237 ± 37	717 ± 78	599 ± 55
42	940 ± 105	6 ± 3	404 ± 53	286 ± 40	276 ± 53	310 ± 46	GT	688 ± 64
49	GT	5 ± 2	629 ± 83	394 ± 54	419 ± 97	435 ± 76	GT	GT
56	GT	3 ± 3	776 ± 54	611 ± 63	582 ± 130	587 ± 95	GT	GT
63	GT	3 ± 2	935 ± 115	700 ± 76	798 ± 53	650 ± 102	GT	GT
70	GT	0 ± 0	1166 ± 81	1024 ±100	1107 ± 240	924 ± 117	GT	GT
77	GT	4 ± 2	GT	GT	1215 ± 207	GT	GT	GT
84	GT	3 ± 2	GT	GT	GT	GT	GT	GT
91	GT	3 ± 3	GT	GT	GT	GT	GT	GT
98	GT	5 ± 5	GT	GT	GT	GT	GT	GT
105	GT	5 ± 5	GT	GT	GT	GT	GT	GT
112	GT	9 ± 9	GT	GT	GT	GT	GT	GT
119	GT	10 ± 10	GT	GT	GT	GT	GT	GT
126	GT	11 ± 11	GT	GT	GT	GT	GT	GT
133	GT	1 ± 1	GT	GT	GT	GT	GT	GT
140	GT	0 ± 0	GT	GT	GT	GT	GT	GT
147	GT	0 ± 0	GT	GT	GT	GT	GT	GT
154	GT	0 ± 0	GT	GT	GT	GT	GT	GT
161	GT	0 ± 0	GT	GT	GT	GT	GT	GT
168	GT	5 ± 5	GT	GT	GT	GT	GT	GT
175	GT	9 ± 9	GT	GT	GT	GT	GT	GT
182	GT	10 ± 10	GT	GT	GT	GT	GT	GT
189	GT	15 ± 15	GT	GT	GT	GT	GT	GT
196	GT	19 ± 19	GT	GT	GT	GT	GT	GT
203	GT	28 ± 28	GT	GT	GT	GT	GT	GT
210	GT	30 ± 30	GT	GT	GT	GT	GT	GT
217	GT	34 ± 34	GT	GT	GT	GT	GT	GT
224	GT	65 ± 65	GT	GT	GT	GT	GT	GT
231	GT	0 ± 0	GT	GT	GT	GT	GT	GT

FIG. 9

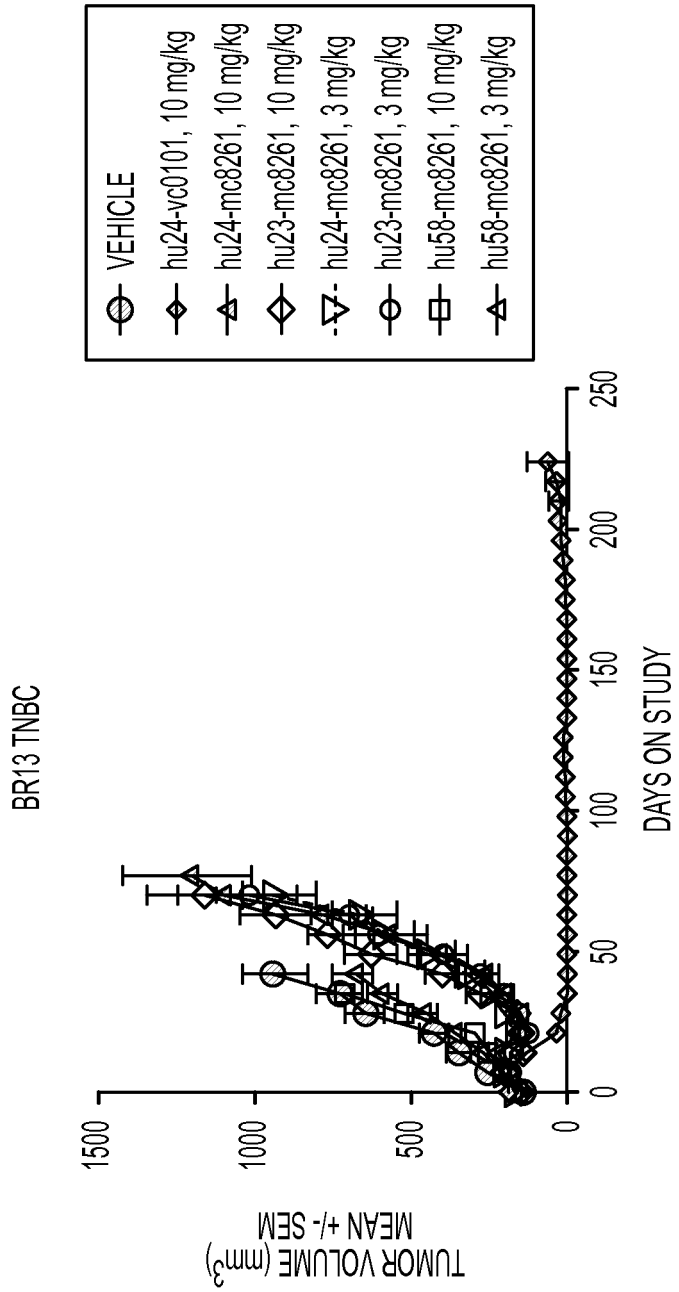

BR13 TNBC
VEHICLE
hu24-vc0101, 10 mg/kg
hu24-mc8261, 10 mg/kg
hu23-mc8261, 10 mg/kg
hu24-mc8261, 3 mg/kg
hu23-mc8261, 3 mg/kg
hu58-mc8261, 10 mg/kg
hu58-mc8261, 3 mg/kg
TUMOR VOLUME (mm3)
MEAN +/- SEM
1500
1000
500
0
0
50
100
150
200
250
DAYS ON STUDY

FIG. 10

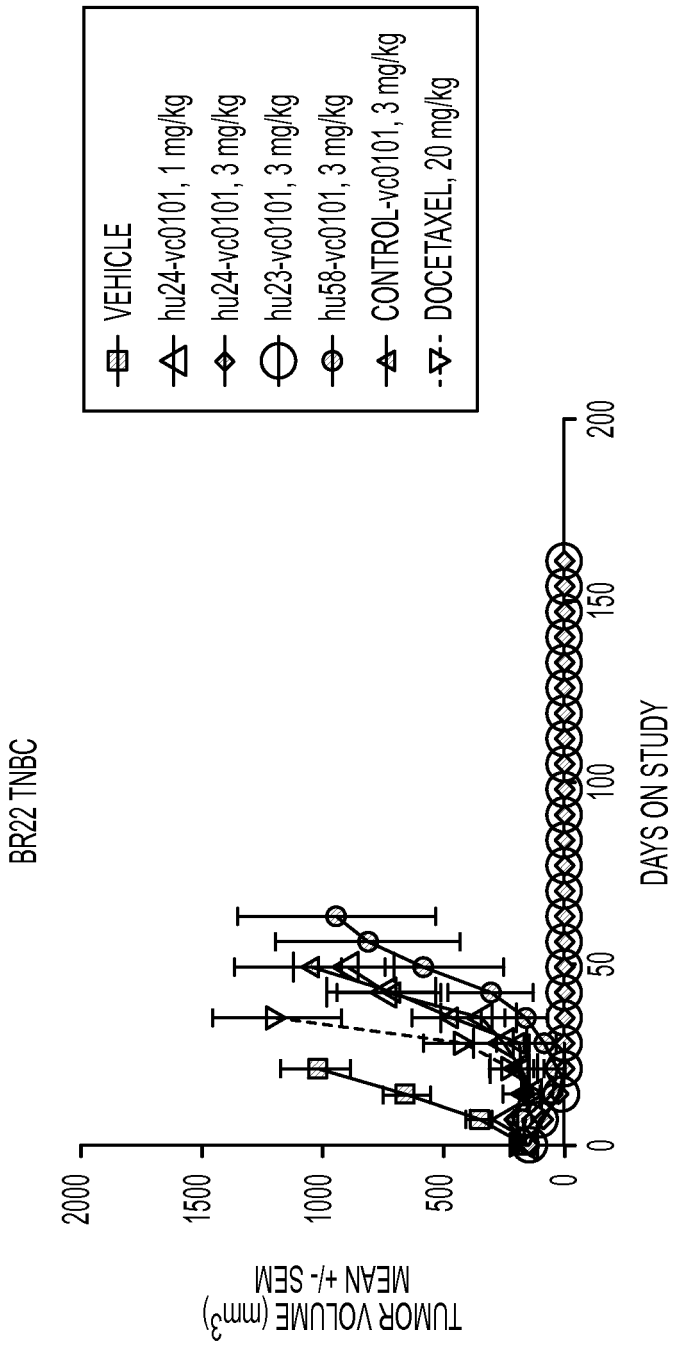

BR22 TNBC
VEHICLE
hu24-vc0101, 1 mg/kg
hu24-vc0101, 3 mg/kg
hu23-vc0101, 3 mg/kg
hu58-vc0101, 3 mg/kg
CONTROL-vc0101, 3 mg/kg
DOCETAXEL, 20 mg/kg
TUMOR VOLUME (mm3)
MEAN +/- SEM
2000
1500
1000
500
0
0
50
100
150
200
DAYS ON STUDY

FIG. 11

EFFICACY OF anti-PTK7 ADCs IN THE BR22 TNBC PDX.

DAY	VEHICLE	10mg/kg hu23-vc0101	10mg/kg hu23-mc8261	3mg/kg hu23-mc8261	10mg/kg hu24-mc8261	3mg/kg hu24-mc8261	1mg/kg hu24-mc8261	10mg/kg hu58-mc8261	3mg/kg hu58-mc8261
0	195 ± 17	166 ± 24	164 ± 19	156 ± 12	188 ± 13	185 ± 10	184 ± 13	164 ± 17	149 ± 12
7	376 ± 43	69 ± 14	258 ± 50	335 ± 41	359 ± 24	315 ± 17	413 ± 44	289 ± 35	370 ± 19
14	564 ± 54	12 ± 3	364 ± 40	360 ± 59	588 ± 42	633 ± 55	750 ± 69	563 ± 69	672 ± 39
21	819 ± 97	0 ± 0	701 ± 106	916 ± 93	878 ± 79	1265 ± 218	1134 ± 112	1133 ± 133	984 ± 65
28	GT	0 ± 0	1189 ± 176	1534 ± 112	GT	GT	GT	GT	1555 ± 121
35	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
42	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
49	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
56	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
63	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
70	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
77	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
84	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
91	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
98	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
105	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
112	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
119	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
126	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
133	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
140	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
147	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
154	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
161	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
168	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
175	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
182	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
189	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT
196	GT	0 ± 0	GT	GT	GT	GT	GT	GT	GT

FIG. 12

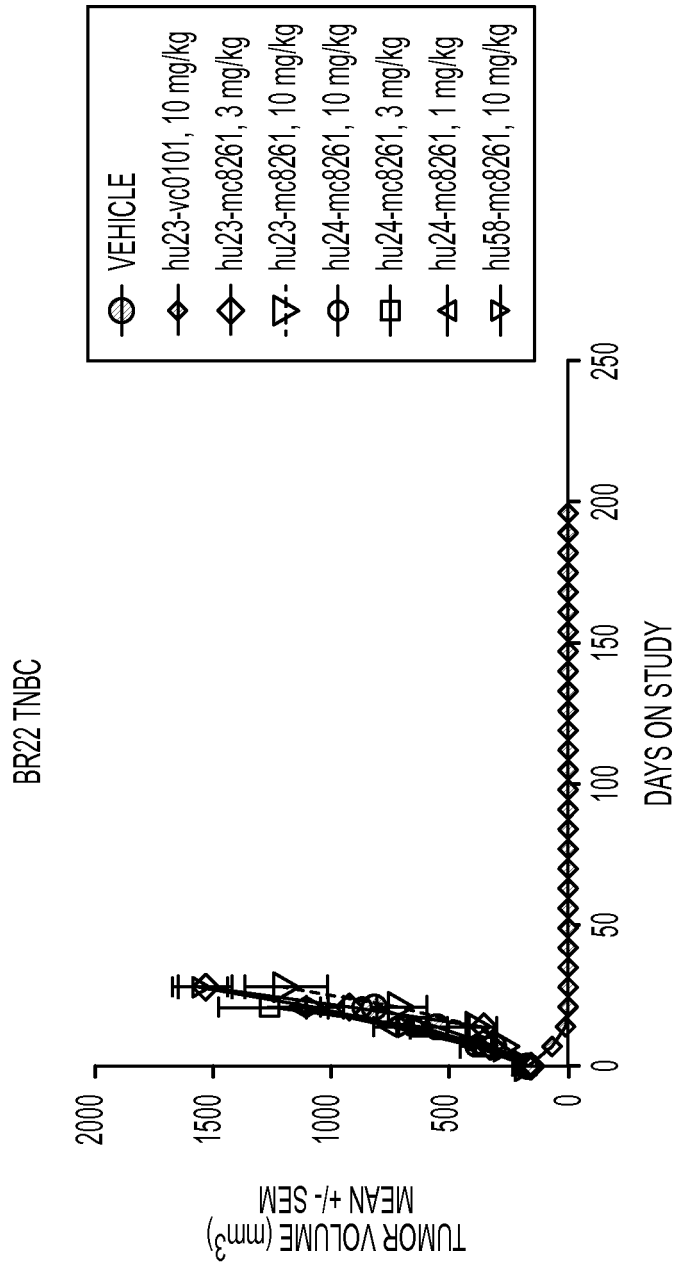

BR22 TNBC
VEHICLE
hu23-vc0101, 10 mg/kg
hu23-mc8261, 3 mg/kg
hu23-mc8261, 10 mg/kg
hu24-mc8261, 10 mg/kg
hu24-mc8261, 3 mg/kg
hu24-mc8261, 1 mg/kg
hu58-mc8261, 10 mg/kg
TUMOR VOLUME (mm3)
MEAN +/- SEM
2000
1500
1000
500
0
0
50
100
150
200
250
DAYS ON STUDY

FIG. 13

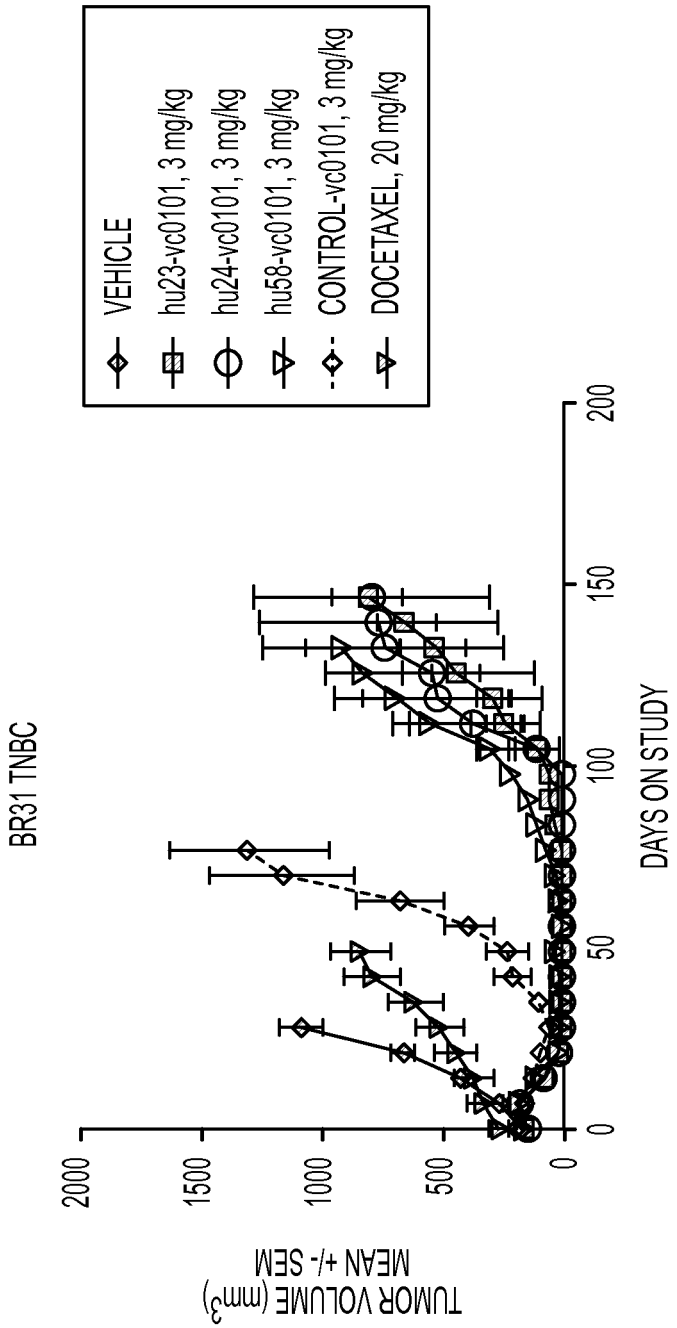

BR31 TNBC
TUMOR VOLUME (mm^3) MEAN +/- SEM
2000
1500
1000
500
0
0
50
100
150
200
DAYS ON STUDY
VEHICLE
hu23-vc0101, 3 mg/kg
hu24-vc0101, 3 mg/kg
hu58-vc0101, 3 mg/kg
CONTROL-vc0101, 3 mg/kg
DOCETAXEL, 20 mg/kg

FIG. 14

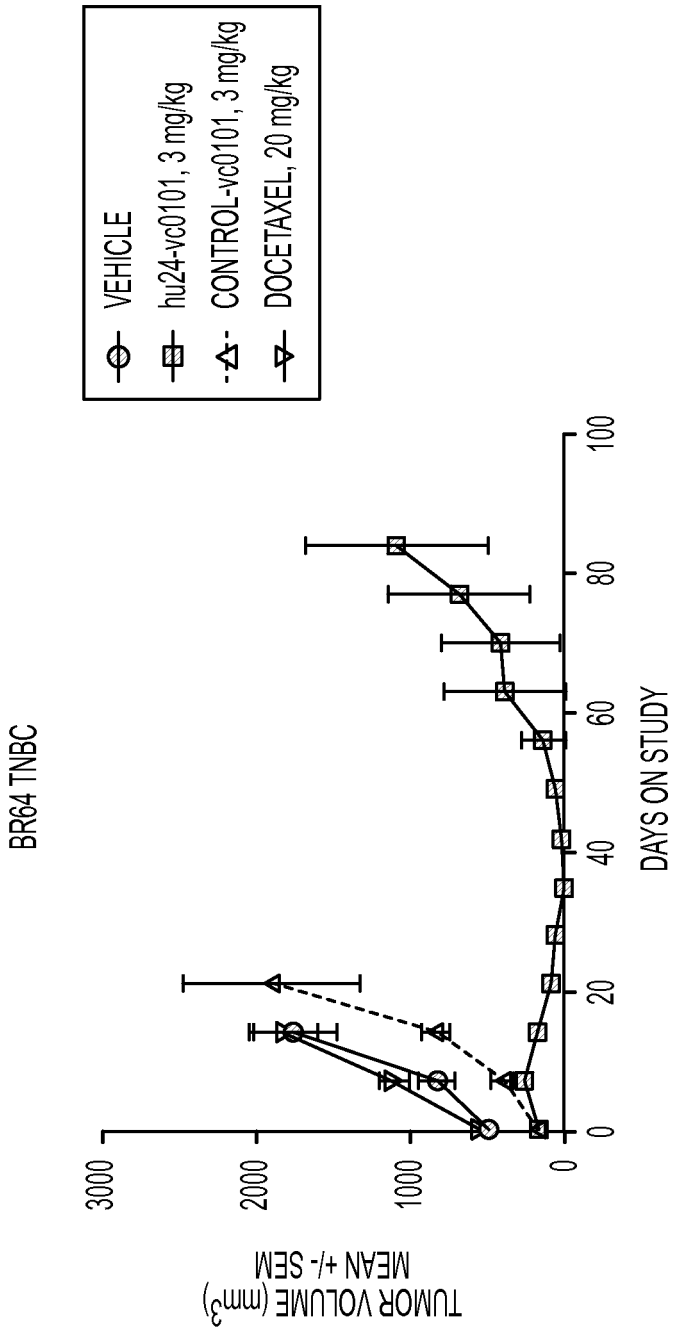

BR64 TNBC
VEHICLE
hu24-vc0101, 3 mg/kg
CONTROL-vc0101, 3 mg/kg
DOCETAXEL, 20 mg/kg
TUMOR VOLUME (mm3)
MEAN +/- SEM
3000
2000
1000
0
0
20
40
60
80
100
DAYS ON STUDY

FIG. 15

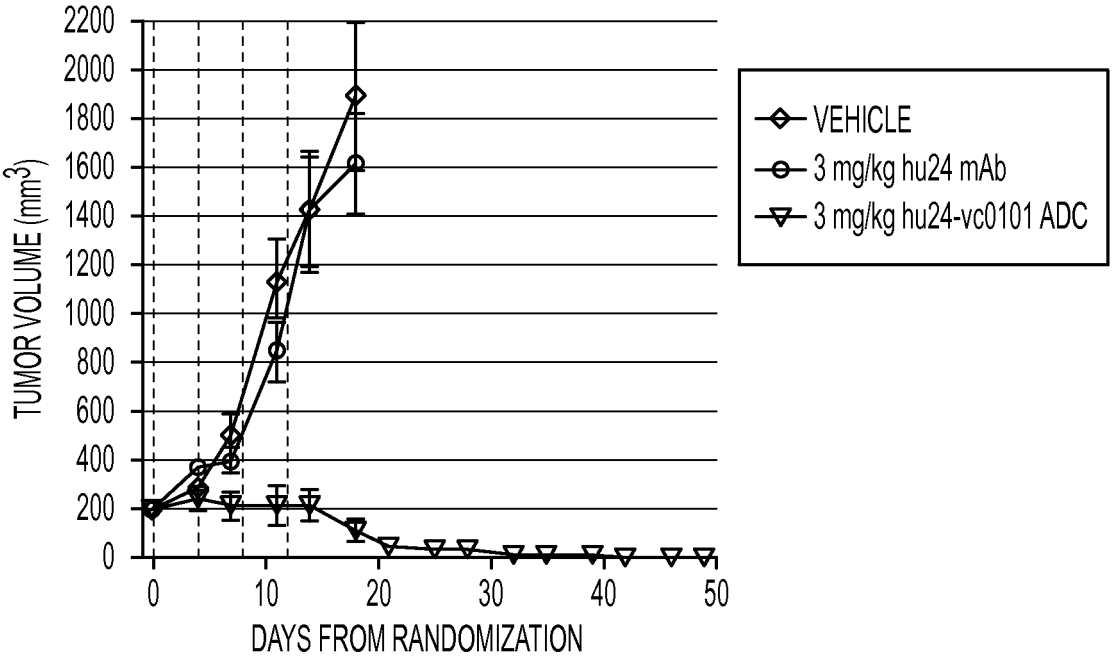

2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
TUMOR VOLUME (mm3)
0
10
20
30
40
50
DAYS FROM RANDOMIZATION
VEHICLE
3 mg/kg hu24 mAb
3 mg/kg hu24-vc0101 ADC

FIG. 16

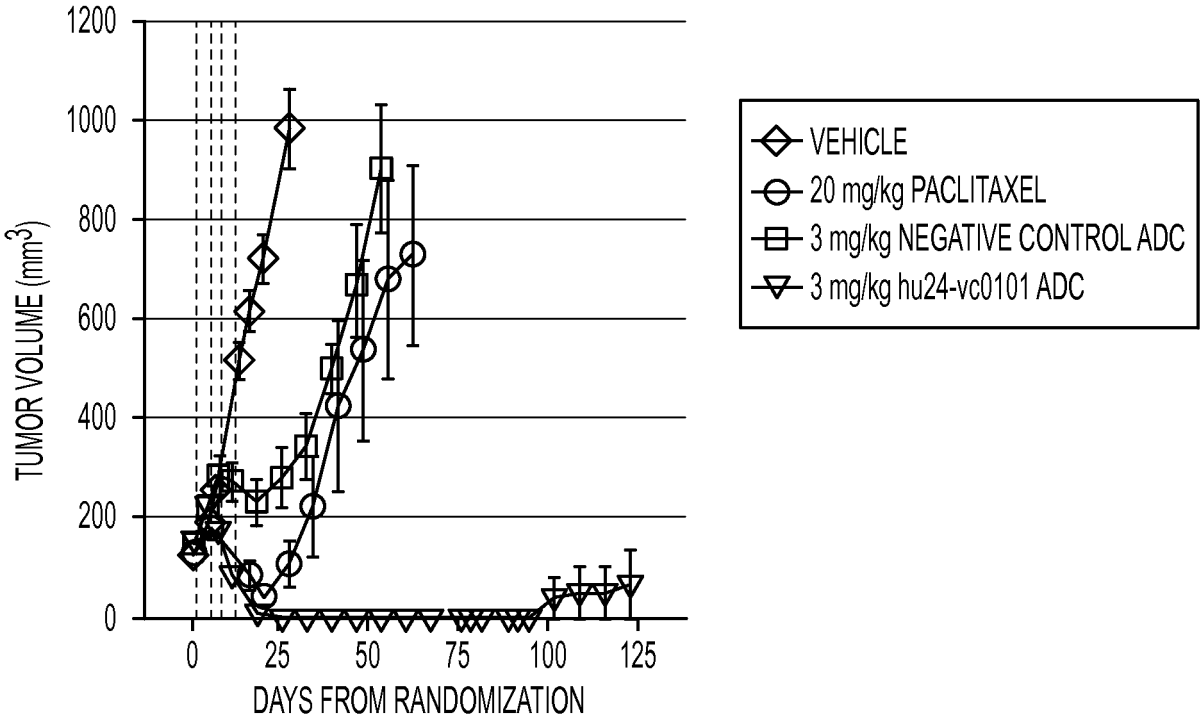

1200
1000
800
600
400
200
0
TUMOR VOLUME (mm3)
0
25
50
75
100
125
DAYS FROM RANDOMIZATION
VEHICLE
20 mg/kg PACLITAXEL
3 mg/kg NEGATIVE CONTROL ADC
3 mg/kg hu24-vc0101 ADC

FIG. 17

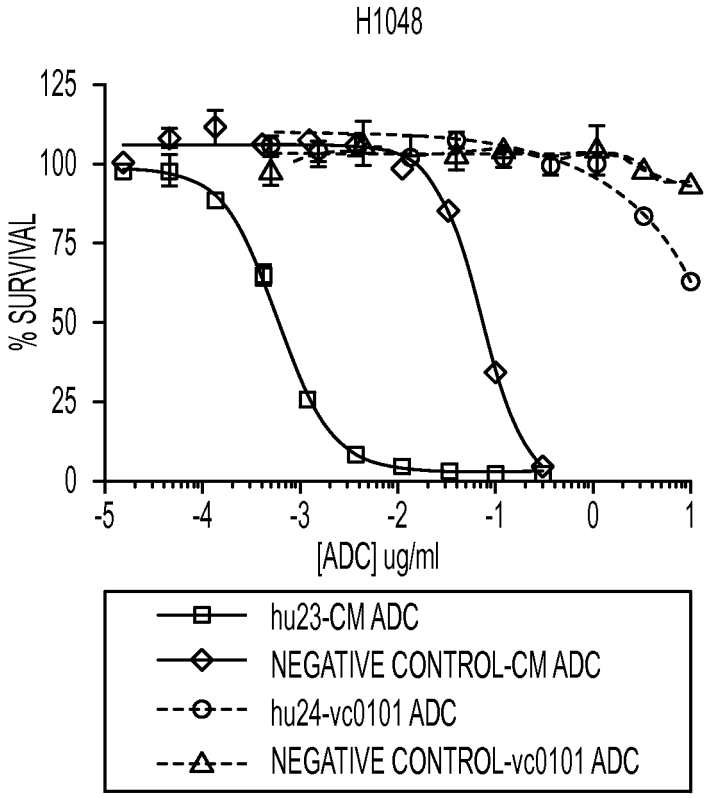


FIG. 18A

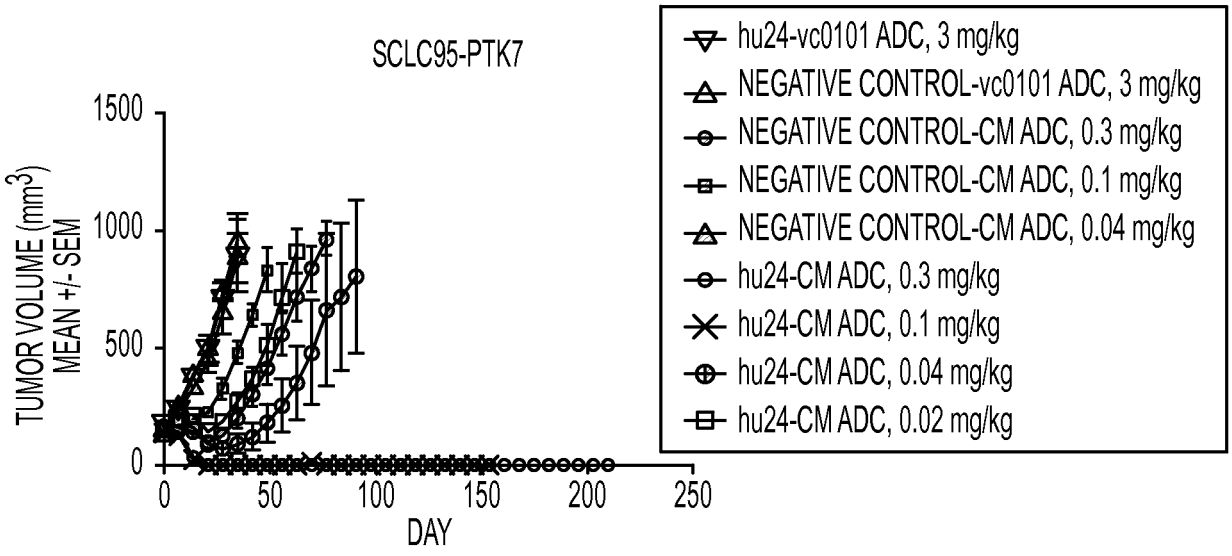


FIG. 18B

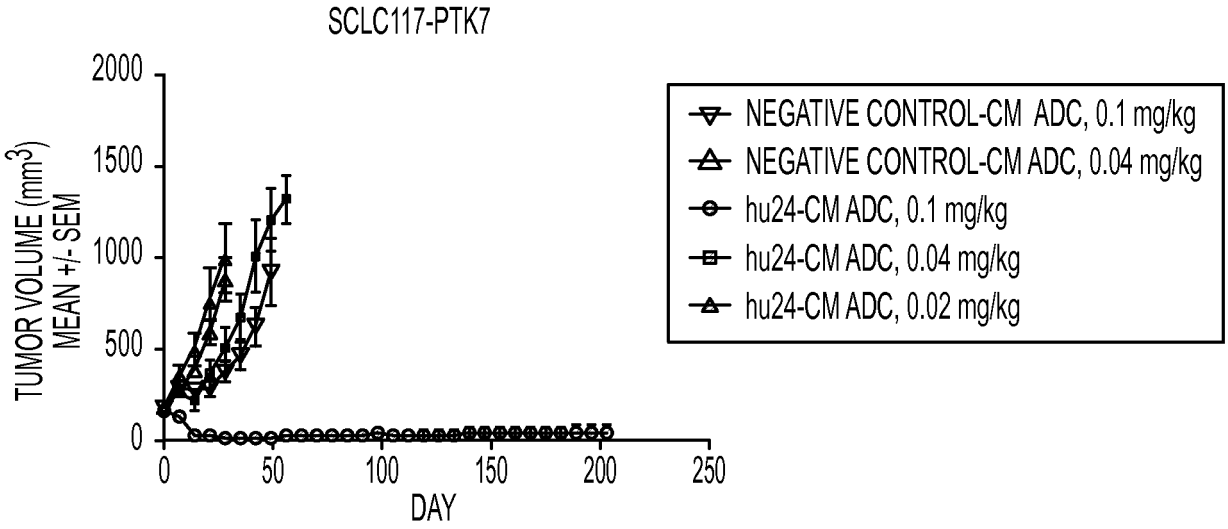


FIG. 19A

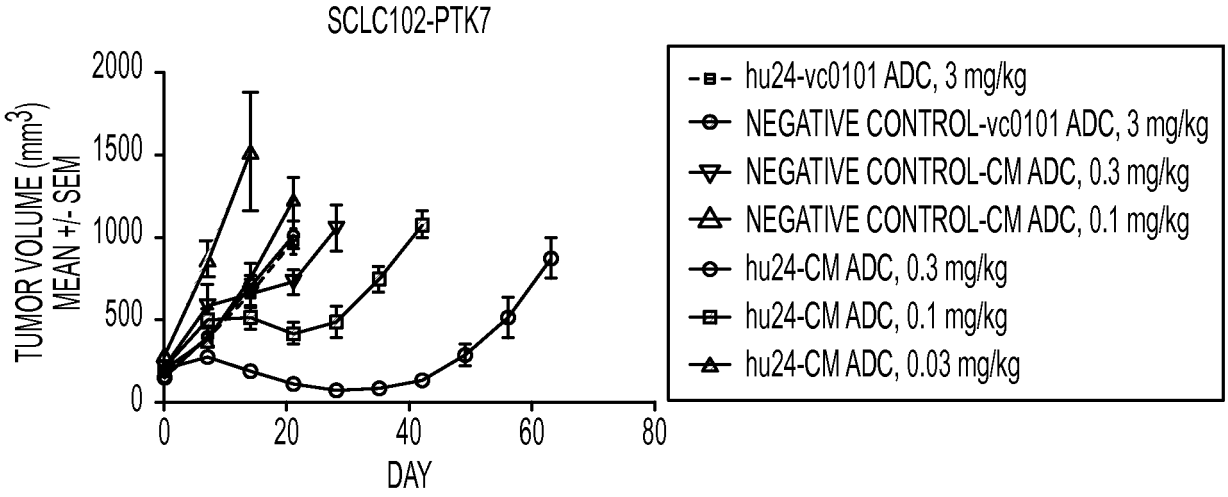


FIG. 19B

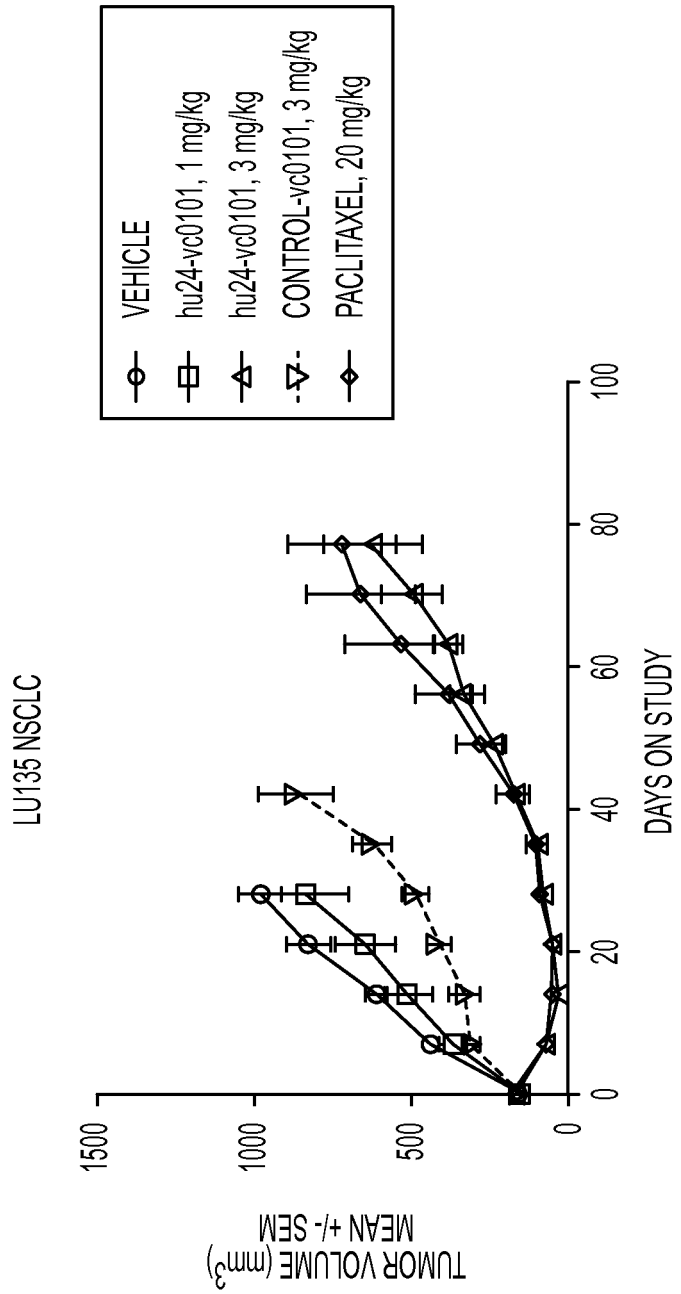

LU135 NSCLC
VEHICLE
hu24-vc0101, 1 mg/kg
hu24-vc0101, 3 mg/kg
CONTROL-vc0101, 3 mg/kg
PACLITAXEL, 20 mg/kg
TUMOR VOLUME (mm^3) MEAN +/- SEM
1500
1000
500
0
0
20
40
60
80
100
DAYS ON STUDY

FIG. 20

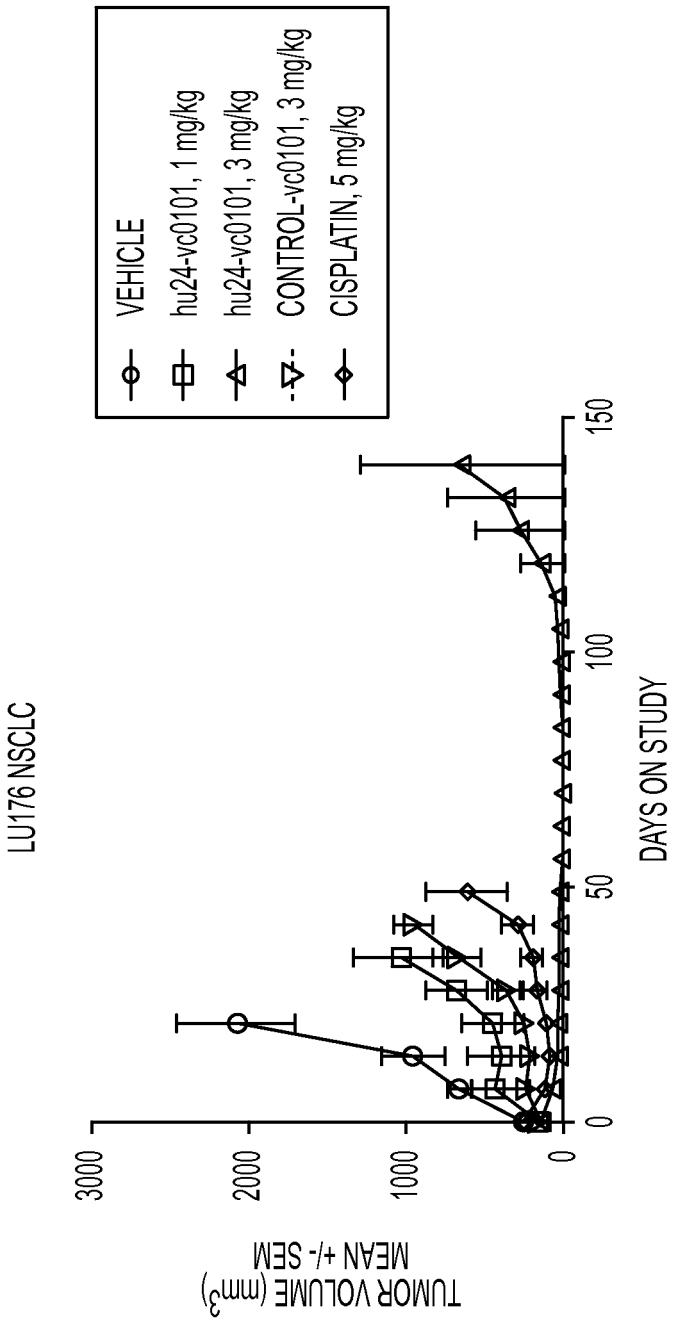

LU176 NSCLC
VEHICLE
hu24-vc0101, 1 mg/kg
hu24-vc0101, 3 mg/kg
CONTROL-vc0101, 3 mg/kg
CISPLATIN, 5 mg/kg
TUMOR VOLUME (mm^3) MEAN +/- SEM
3000
2000
1000
0
0
50
100
150
DAYS ON STUDY

FIG. 21

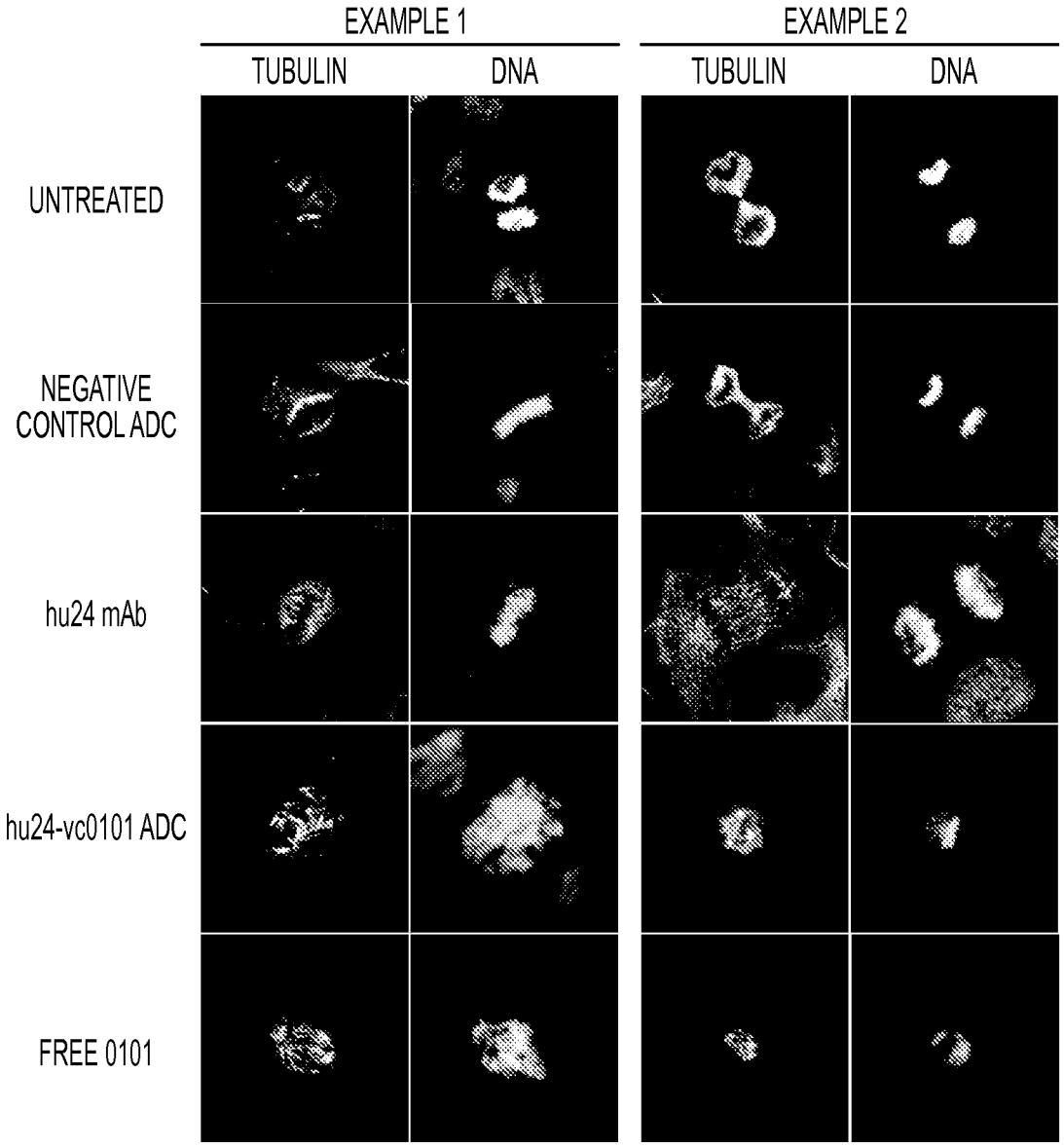

EXAMPLE 1
EXAMPLE 2
TUBULIN
DNA
TUBULIN
DNA
UNTREATED
NEGATIVE CONTROL ADC
hu24 mAb
hu24-vc0101 ADC
FREE 0101

FIG. 22

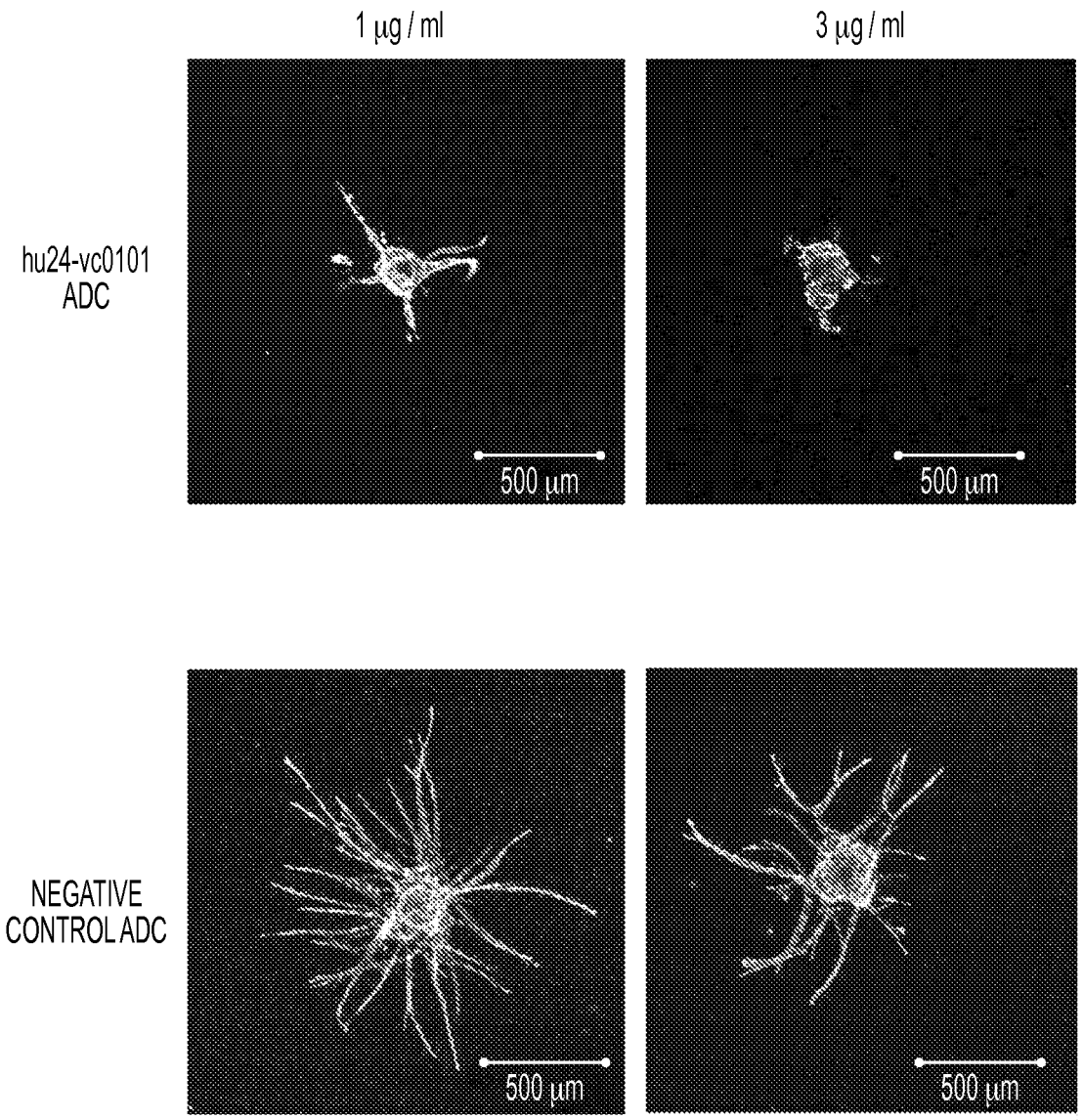

1 μg / ml
3 μg / ml
hu24-vc0101 ADC
500 μm
500 μm
NEGATIVE CONTROL ADC
500 μm
500 μm

FIG. 23