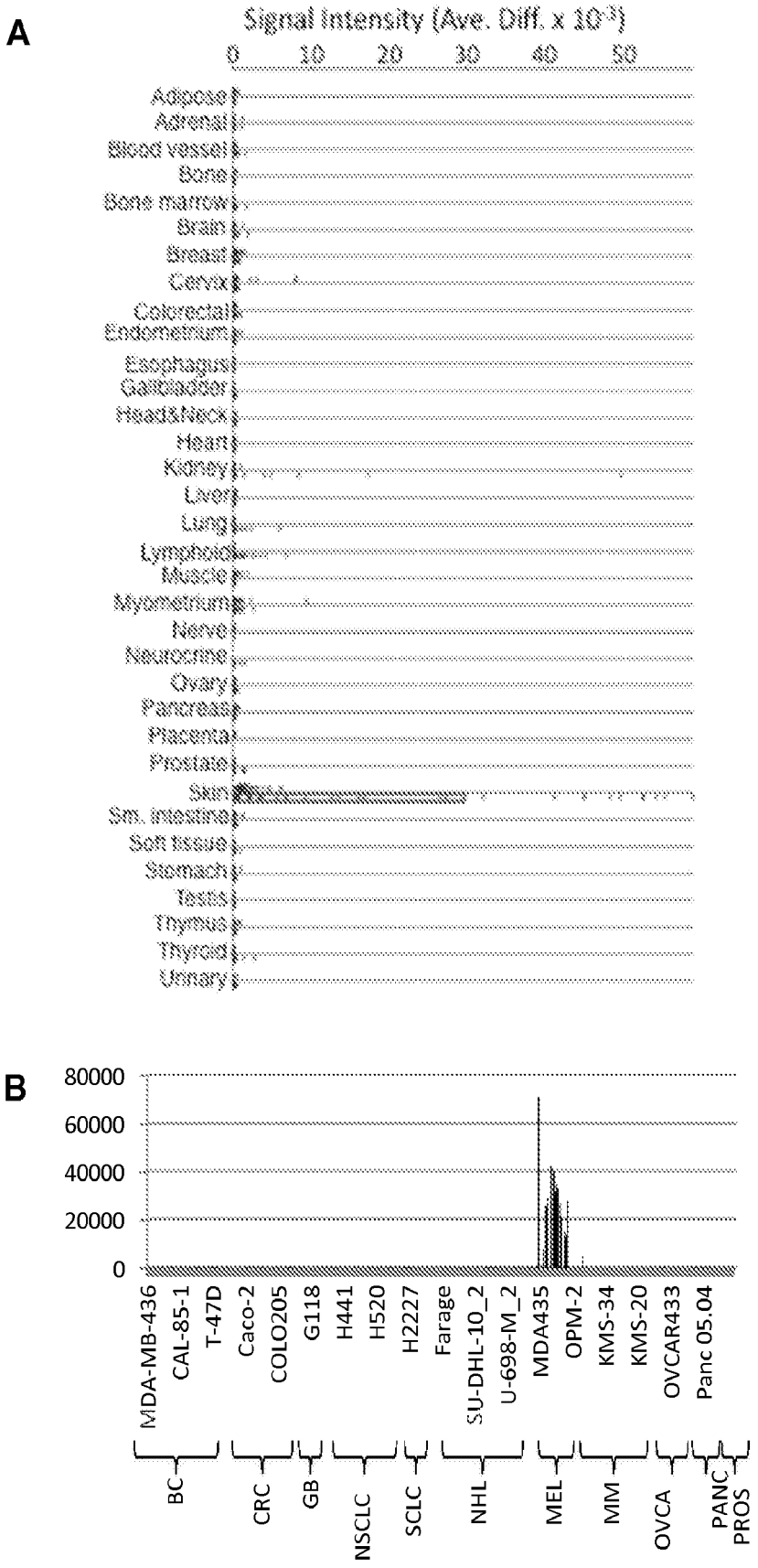

A
Signal Intensity (Ave. Diff. x 10-3)
0
10
20
30
40
50
Adipose
Adrenal
Blood vessel
Bone
Bone marrow
Brain
Breast
Cervix
Colorectal
Endometrium
Esophagus
Gallbladder
Head&Neck
Heart
Kidney
Liver
Lung
Lymphoid
Muscle
Myometrium
Nerve
Neurocrine
Ovary
Pancreas
Placenta
Prostate
Skin
Sm. Intestine
Soft tissue
Stomach
Testis
Thymus
Thyroid
Urinary
B
80000
60000
40000
20000
0
MDA-MB-436
CAL-85-1
T-47D
Caco-2
COLO205
G118
H441
H520
H2227
Farage
SU-DHL-10_2
U-698-M_2
MDA435
OPM-2
KMS-34
KMS-20
OVCAR433
Panc 05.04
BC
CRC
GB
NSCLC
SCLC
NHL
MEL
MM
OVCA
PANC
PROS

FIG. 1

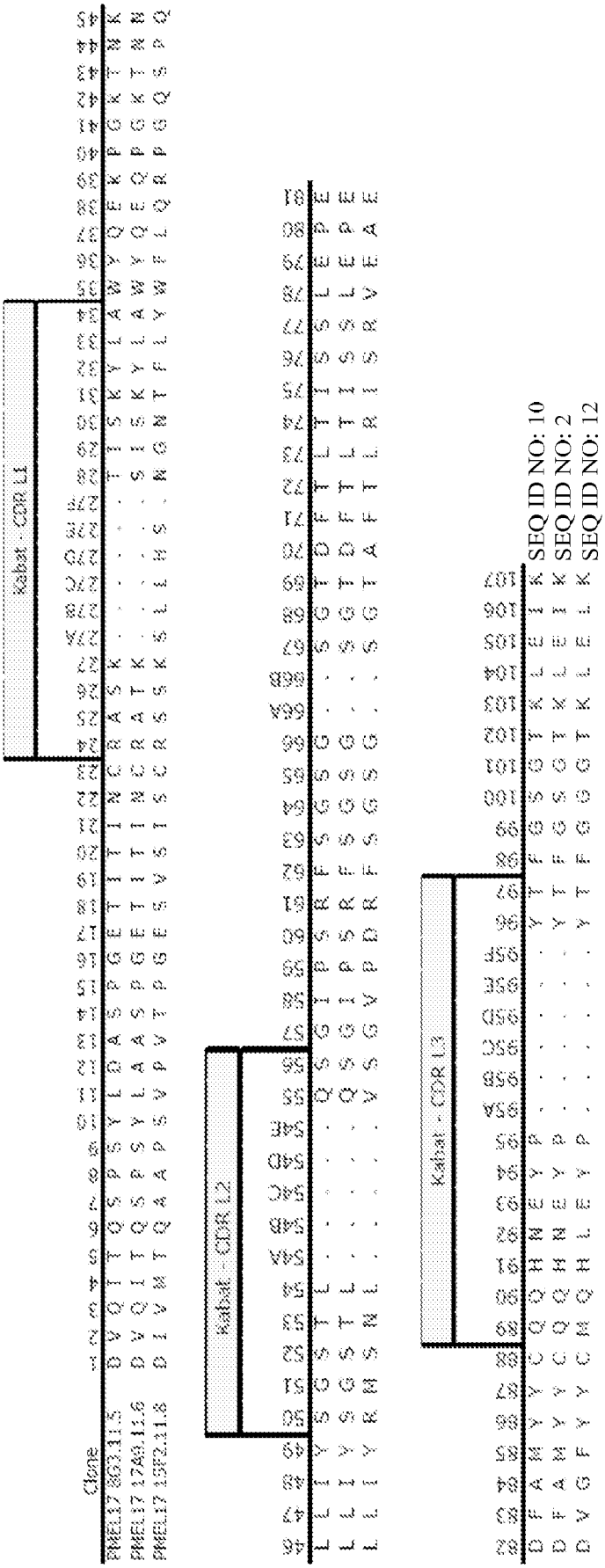

Kabat - CDR L1
Kabat - CDR L2
Kabat - CDR L3
SEQ ID NO: 10
SEQ ID NO: 2
SEQ ID NO: 12

FIG. 2A

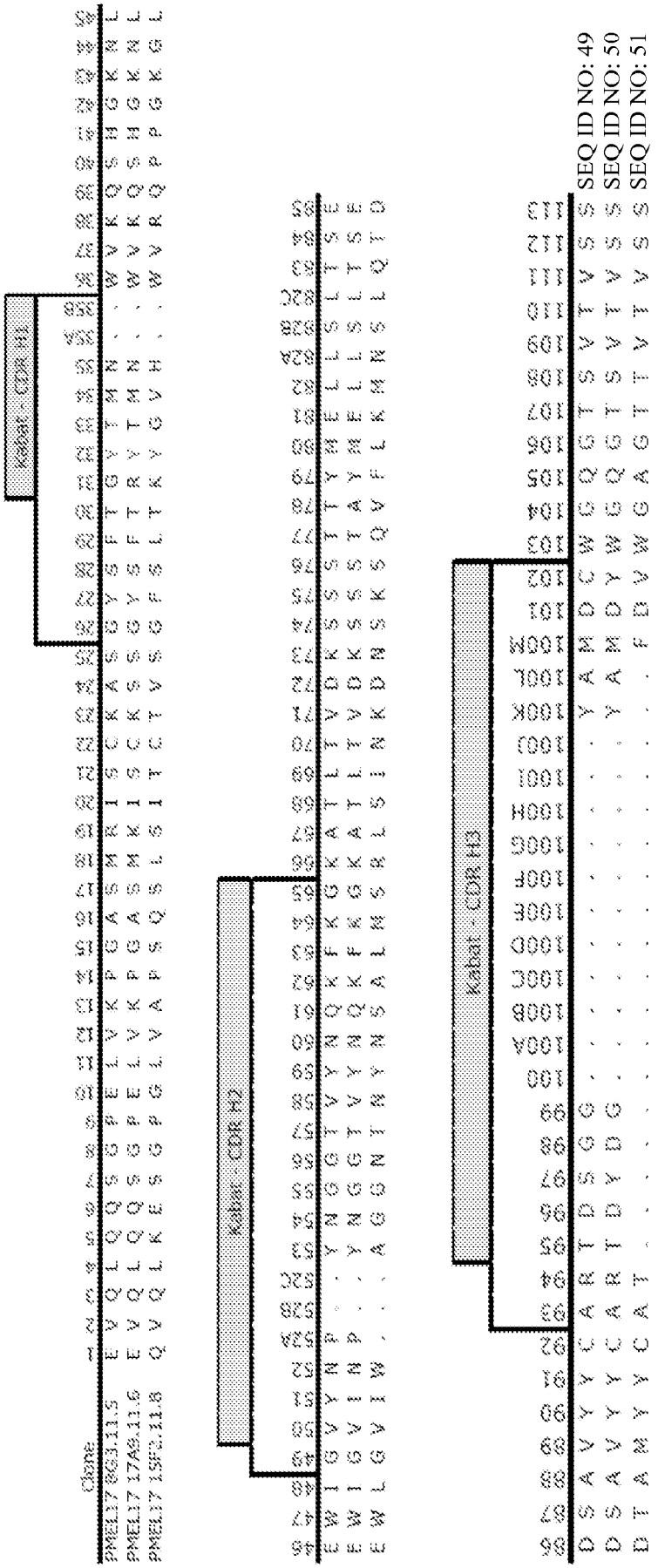

Clone
PMEL17 863.11.5
PMEL17 17A9.11.6
PMEL17 15F2.11.8
Kabat - CDR H1
Kabat - CDR H2
Kabat - CDR H3
SEQ ID NO: 49
SEQ ID NO: 50
SEQ ID NO: 51

FIG. 2B

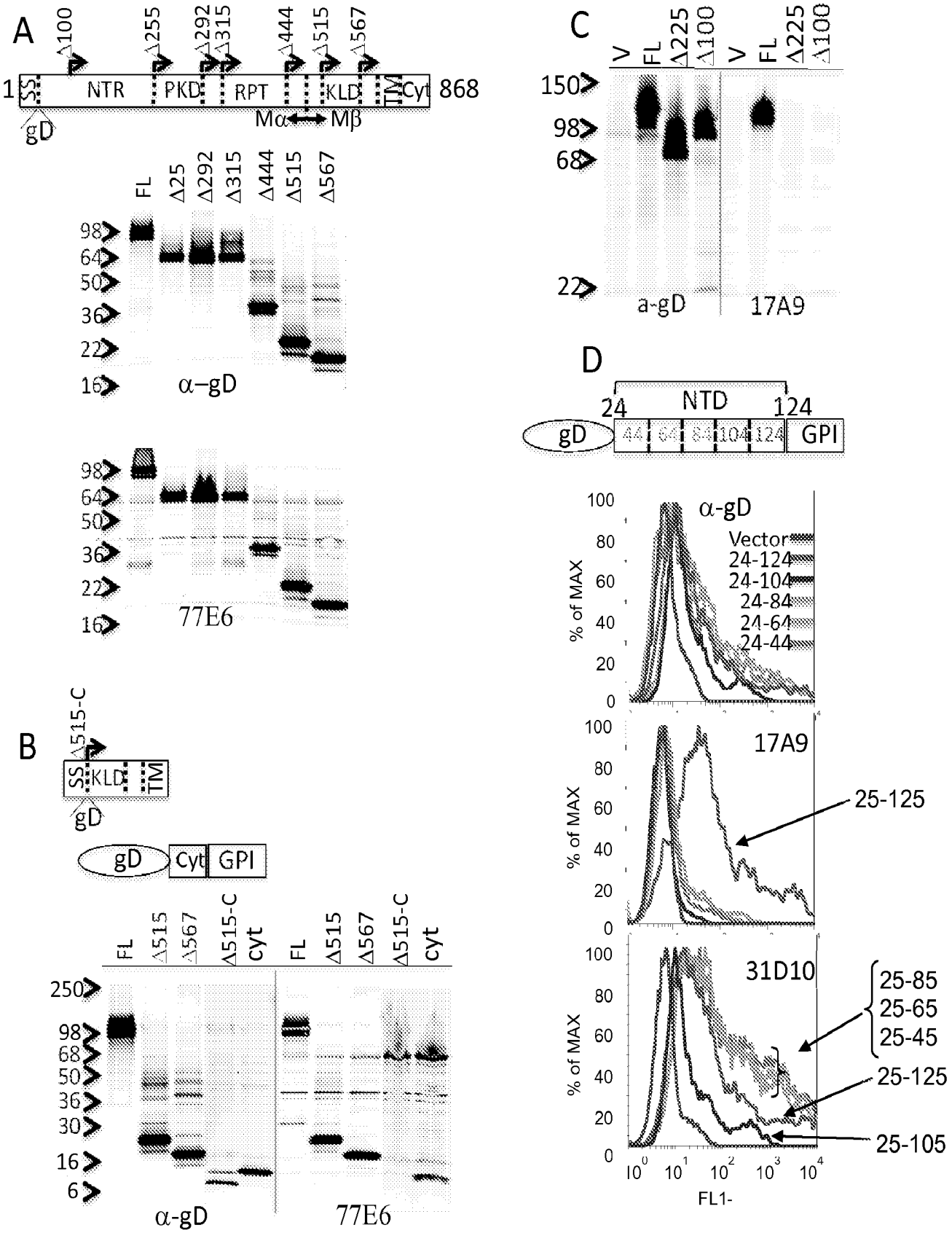

A
Δ100
Δ255
Δ292
Δ315
Δ444
Δ515
Δ567
1
SS
NTR
PKD
RPT
KLD
TM
Cyt
868
gD
Mα
Mβ
FL
Δ25
Δ292
Δ315
Δ444
Δ515
Δ567
98
64
50
36
22
16
α–gD
77E6
B
Δ515-C
SS
KLD
TM
gD
gD
Cyt
GPI
FL
Δ515
Δ567
Δ515-C
cyt
250
98
68
50
36
30
16
6
α-gD
77E6
C
V
FL
Δ225
Δ100
150
98
68
22
a-gD
17A9
D
24
NTD
124
gD
44
64
84
104
124
GPI
α-gD
Vector
24-124
24-104
24-84
24-64
24-44
% of MAX
17A9
25-125
31D10
25-85
25-65
25-45
25-125
25-105
FL1-

FIG. 3

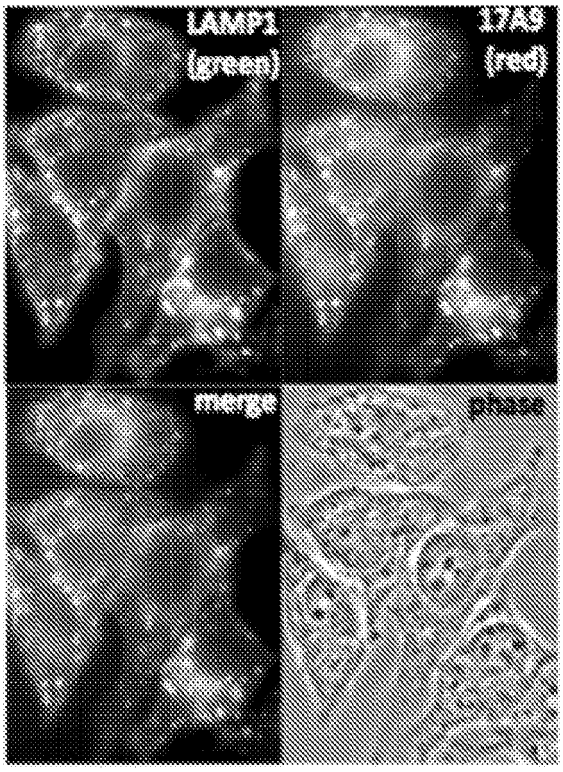

LAMP1
(green)
17A3
(red)
merge
phase

FIG. 4

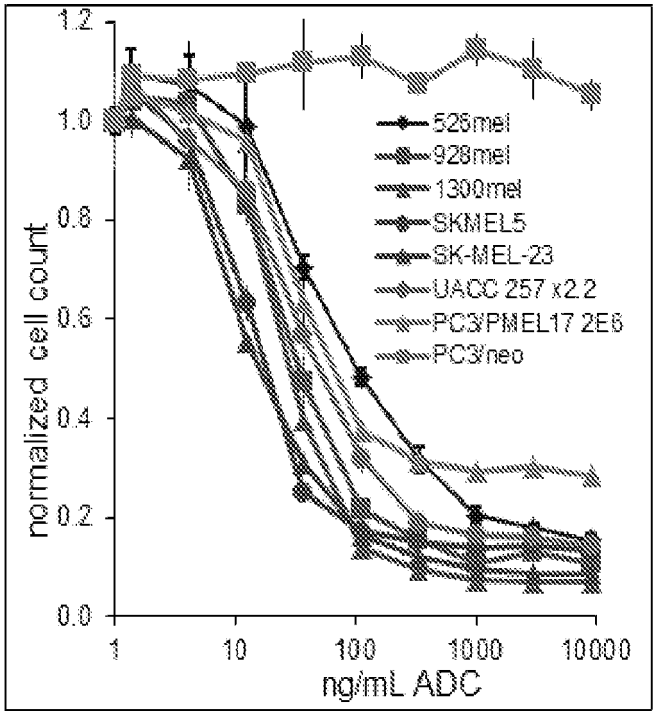

normalized cell count
ng/mL ADC
526mel
928mel
1300mel
SKMEL5
SK-MEL-23
UACC 257 x2.2
PC3/PMEL17 2E6
PC3/neo

FIG. 5

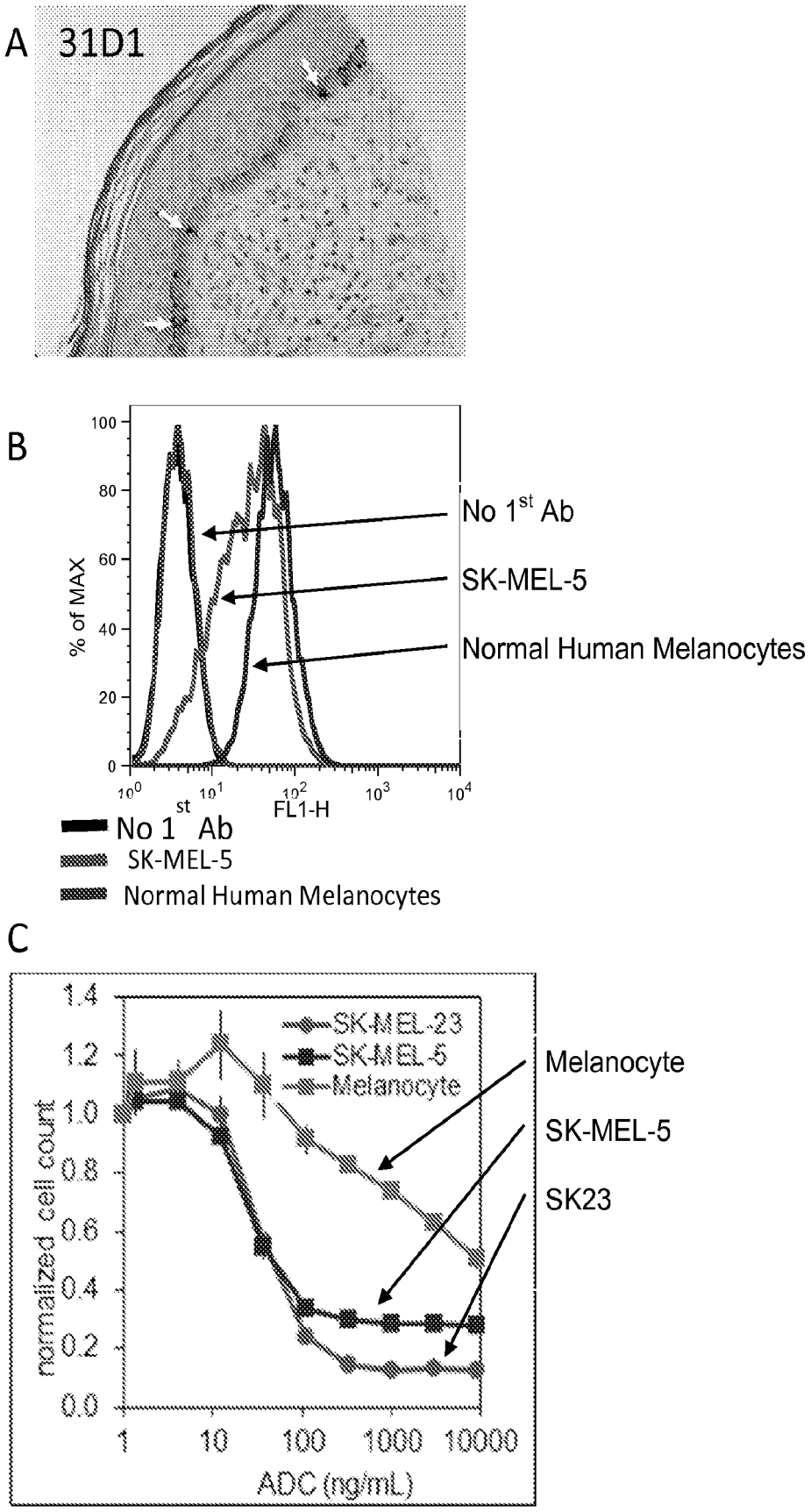
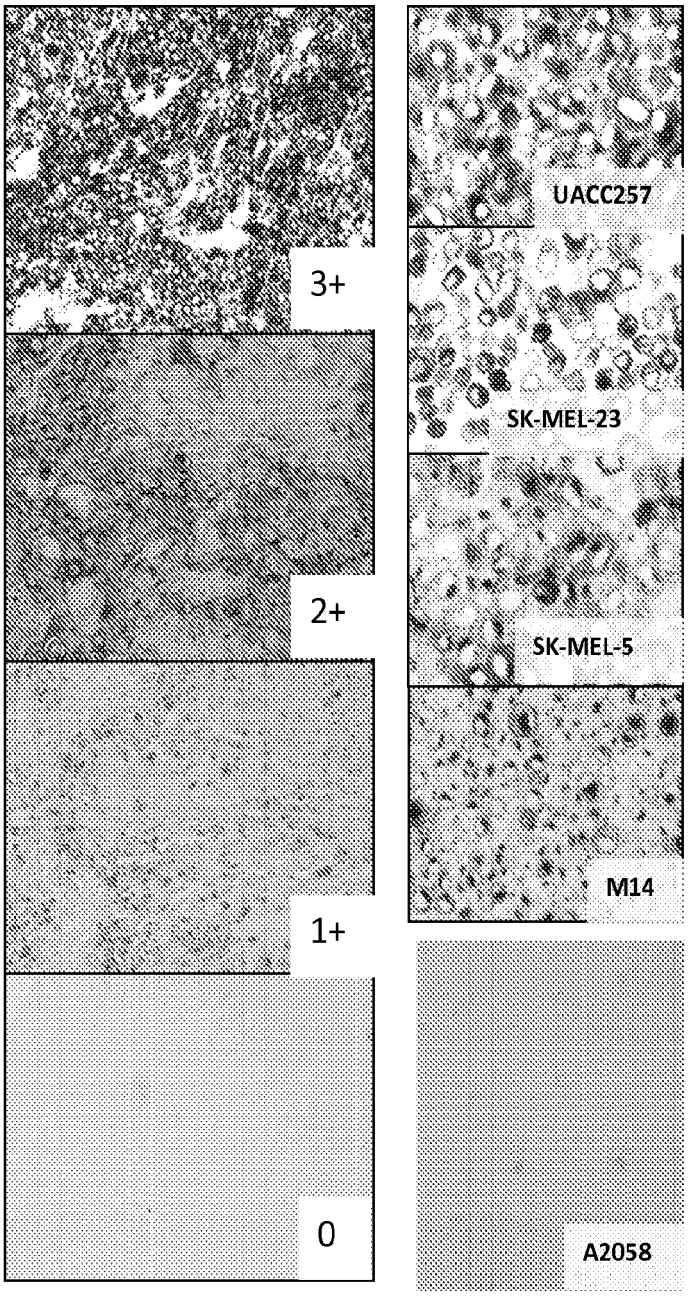

A
31D1
B
% of MAX
FL1-H
No 1st Ab
SK-MEL-5
Normal Human Melanocytes
C
normalized cell count
ADC (ng/mL)
SK-MEL-23
SK-MEL-5
Melanocyte
Melanocyte
SK-MEL-5
SK23

FIG. 6

A



B IHC scores for human melanoma (n=58)

Score	0	1	2	3
31D1	10	15	20	13
17A9	21	17	13	7

FIG. 7

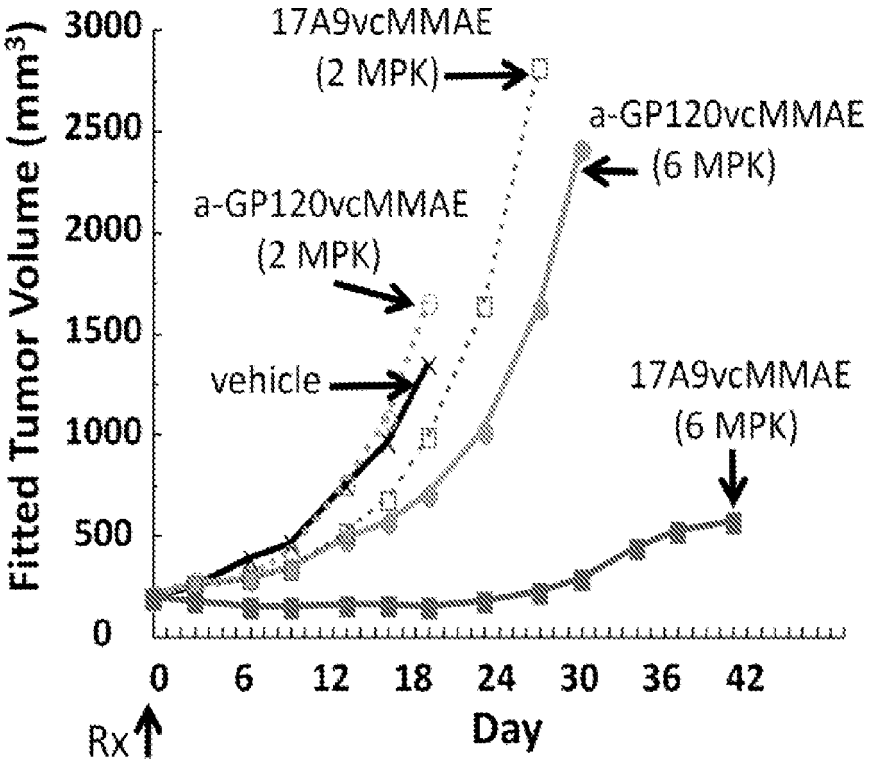

Fitted Tumor Volume (mm3)
3000
2500
2000
1500
1000
500
0
17A9vcMMAE
(2 MPK)
a-GP120vcMMAE
(6 MPK)
a-GP120vcMMAE
(2 MPK)
vehicle
17A9vcMMAE
(6 MPK)
0 6 12 18 24 30 36 42
Rx
Day

FIG. 8

```
rat      -MGVQRRCFLPVLVLGALLALGSIEGSRNQNWHGVSRQLVTKVWNKQLYPEWTEVQGSNC 59
mouse    -MGVQRRSFLPVLVLSALLAVGALEGSRNQDWLGVPRQLVTKTWNRQLYPEWTEVQGSNC 59
human    MDLVLKRCLLHLAVIGALLAVGATKVPRNQDWLGVSRQLRTKAWNRQLYPEWTEAQRLDC 60
cyno     ----------------------KGPRNQDWLGVSRQLRTKAWNRQLYPEWTEAQRLDC 36
                                : .*****:* **.*** **.**::********.*  :*

rat      WRGGQVSLKVRNDGPTLVGANTSFSIALHFPGSQKVLPDGQVIWVNNTIINGSQVWGGQP 119
mouse    WRGGQVSLRVINDGPTLVGANASFSIALHFPGSQKVLPDGQVIWANNTIINGSQVWGGQP 119
human    WRGGQVSLKVSNDGPTLIGANASFSIALNFPGSQKVLPDGQVIWVNNTIINGSQVWGGQP 120
cyno     WRGGQVSLKVSNDGPTLIGANASFSIALNFPGSQKVLPDGQVIWVNNTIINGSQVWGGQP 96
         ********** ********:*****:**********************.**********

rat      VYPREPDDACIFPDGGPCPSGPKPPRRSFVYVWKTWGQYWQVLGGPESKLSIPTGHARLG 179
mouse    VYPQEPDDACVFPDGGPCPSGPKPPKRSFVYVWKTWGKYWQVLGGPVSRLSIATGHAKLG 179
human    VYPQETDDACIFPDGGPCPSGSWSQKRSFVYVWKTWGQYWQVLGGPVSGLSIGTGRAMLG 180
cyno     VYPQETDDACIFPDGGPCPSGPWSQKRSFVYVWKTWGQYWQVLGGPVSGLSIGTGRAMLG 156
         ***:*.*****:********** . :*********** * *** **:* **

rat      THTMEVTVYHRRGSQSYVPLAHSSSTFTIT---------------------------- 209
mouse    THTMEVTVYHRRGSQSYVPLAHASSTFTITDQVPFSVSVSQLQALDGETKHFLRNHPLIF 239
human    THTMEVTVYHRRGSRSYVPLAHSSSAFTITDQVPFSVSVSQLRALDGGNKHFLRNQPLTF 240
cyno     THTMEVTVYHRRGSRSYVPLAHSSSAFTITDQVPFSVSVSQLRALDGGNKHFLRNQPLTF 216
         ********** *********:**:*********++++++++++  ++++  ++++++ ++ +

rat      ---------------------------------------------------------- 
mouse    ALQLHDPSGYLAEADLSYTWDFGDGTGTLISRALDVTHTYLESGSVTAQVVLQAAIPLVS 299
human    ALQLHDPSGYLAEADLSYTWDFGDSSGTLISRALVVTHTYLEPGPVTAQVVLQAAIPLTS 300
cyno     ALQLHDPSGYLAEADLSYTWDFGDSSGTLISRALVVTHTYLEPGPVTAQVVLQAAIPLTS 276
         ++++++++++++++++++++++++++++++  ++++++++ +++++++ + ++++++++++++ +

rat      ---------------------------------------------------------- 
mouse    CGSSPVPGTTDGYMPTAEAPGTTSRQGTTTKVVGTTPGQMPTTQPSGTTVVQMPTTEVTA 359
human    CGSSPVPGTTDGHRPTAEAPNTTAGQVPTTEVVGTTPGQAPTAEPSGTTSVQVPTTEVIS 360
cyno     CGSSPVPGTTDGHRPTAEAPDTTAGRGPTTEVVGTTPGQVPTTQPSGTTSVQVPTTEVIS 336
         ++++++++++++  ++++++ ++     ++ ++++++++ ++  +++++ ++ +++++

rat   SEQ ID NO: 29
mouse SEQ ID NO: 31
human SEQ ID NO: 26
cyno  SEQ ID NO: 28
```

FIG. 9A

```
rat     ----------------------------------------------------------
mouse   TTSEQMLTSA----------VIDTTLAEVSTTEGTGTTPTRPSGTTVA---------- 397
human   TAPVQMPTAESTGMTPEKVPVSEVMGTTLAEMSTPEATGMTPAEVSIVVLSGTTAAQVTT 420
cyno    TTPVQMPTAESTGTTPEKVPVSEVMGTTLAEMSTPEAIGMTPAEVSIVVPSGTTAAQVTT 396
        +   ++ +                +   +++++ ++ +   + ++    +

rat     ----------------------------GSVSRLLDDTDTIMLVKRQVPLDCVLYRY 238
mouse   ----------QATTTEGPDASPLLPTQSSTGSISPLLDDTDTIMLVKRQVPLDCVLYRY 446
human   TEWVETTARELPIPEPEGPDASSIMSTESITGSLGPLLDGTATLRLVKRQVPLDCVLYRY 480
cyno    TEWVETTAGELPTPEPEGPDTSSIMSTESITGSLGPLLDGTATLRLEKRQVPLDCVLYRY 456
                   ++++ +    + +  **:. ***.* *: * **************

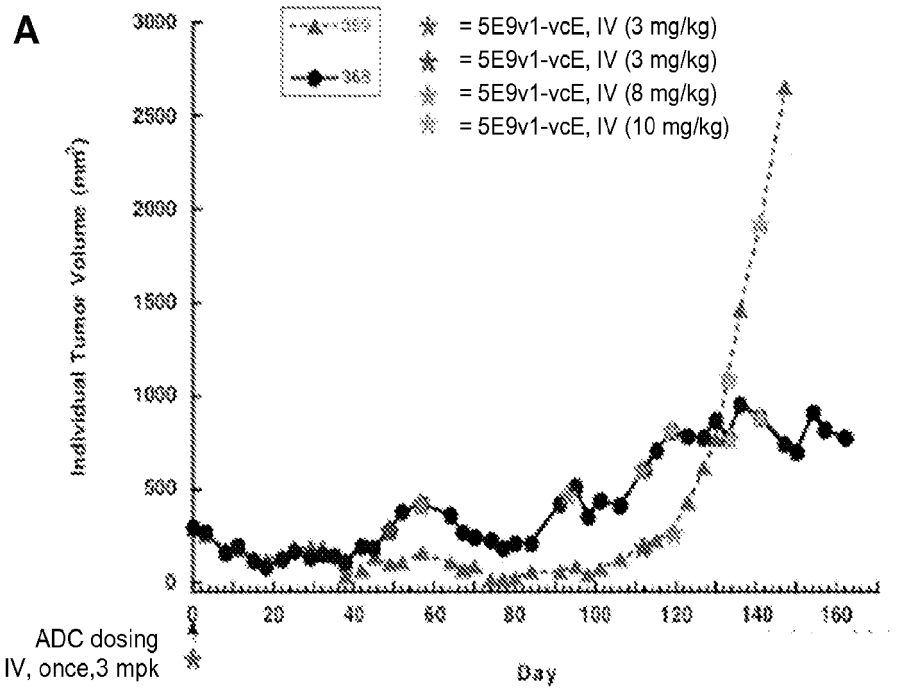
rat     GSFSLTLDIVQGIESAEILQAVPSSEGDAFELTVSCRGGLPKEACMDISSPGCQPPAQRL 298
mouse   GSFSLALDIVQGIESAEILQAVPFSEGDAFELTVSCQGGLPKEACMDISSPGCQPPAQRL 506
human   GSFSVTLDIVQGIESAEILQAVPSGEGDAFELTVSCQGGLPKEACMEISSPGCQPPAQRL 540
cyno    GSFSVTLDIVQGIESAEILQVVPSSEGDAFELTVSCQGGLPTEACMEISSPGCQPPAQQL 516
        ****::*************.** .**********:****.****:************:*

rat     CQPVPPSPDCQLVLHQILKGGLGTYCLNVSLADANSLAVASTQLVVPGQEGSLGQAPLLV 358
mouse   CQSVPPSPDCQLVLHQVLKGGSGTYCLNVSLADANSLAVASTQLVVPGQDGGLGQAPLLV 566
human   CQPVLPSPACQLVLHQILKGGSGTYCLNVSLADTNSLAVVSTQLIMPGQEAGLGQVPLIV 600
cyno    CQPVPPSPACQLVLYQILKGGLGTYCLNVSLADANSLAVVSTQLIVPGQEAGLGQAPLFV 576
        **.* *** *****:*:**** **********:******.****::***:.. ***.**:*

rat     GVLLVLVAVVLASLIYRHRLKKQD-SVSQTPHGSTHWLRLPPVFCARRLGESSPLLSGQQ 417
mouse   GILLVLVAVVLASLIHRHRLKKQG-SVSQMPHGSTHWLRLPPVFRARGLGENSPLLSGQQ 625
human   GILLVLMAVVLASLIYRRRLMKQDFSVPQLPHSSSHWLRLPRIFCSCPIGENSPLLSGQQ 660
cyno    GILLVLMAVVLASLIYRRRLMKQAFSIPQLPHGSSHWLRLPRIFRSCPIGENSPLLSGQE 636
        *:*****:**********:*:** **  *:.* **.*:******* :* :  :**.********:

rat     V 418  SEQ ID NO: 29
mouse   V 626  SEQ ID NO: 31
human   V 661  SEQ ID NO: 26
cyno    V 637  SEQ ID NO: 28
        *
```

FIG. 9B


A
= 5E9v1-vcE, IV (3 mg/kg)
= 5E9v1-vcE, IV (3 mg/kg)
= 5E9v1-vcE, IV (8 mg/kg)
= 5E9v1-vcE, IV (10 mg/kg)
Individual Tumor Volume (mm³)
3000
2500
2000
1500
1000
500
0
0
20
40
60
80
100
120
140
160
Day
ADC dosing
IV, once,3 mpk

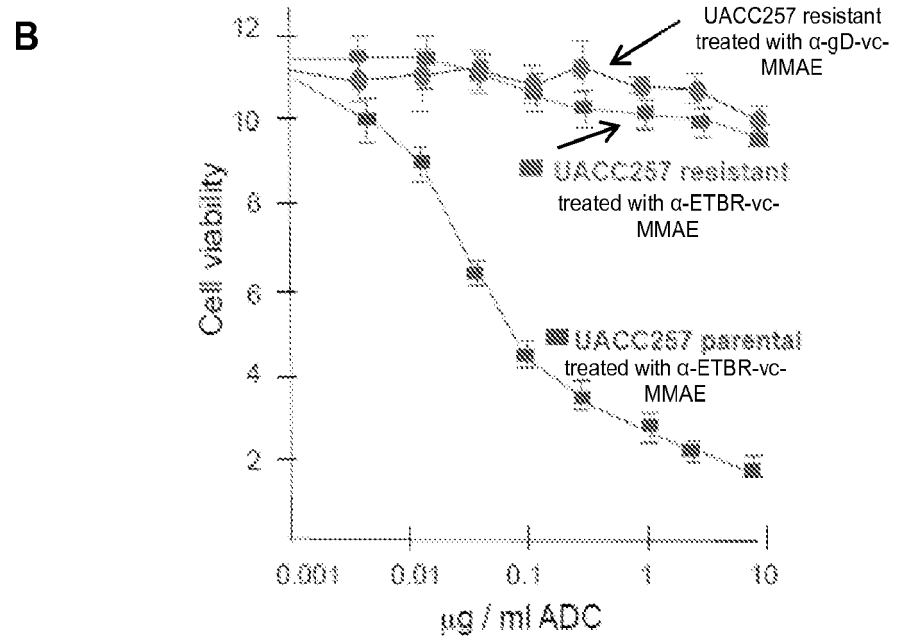

B
UACC257 resistant
treated with α-gD-vc-
MMAE
UACC257 resistant
treated with α-ETBR-vc-
MMAE
UACC257 parental
treated with α-ETBR-vc-
MMAE
Cell viability
12
10
8
6
4
2
0.001
0.01
0.1
1
10
µg / ml ADC

FIG. 10

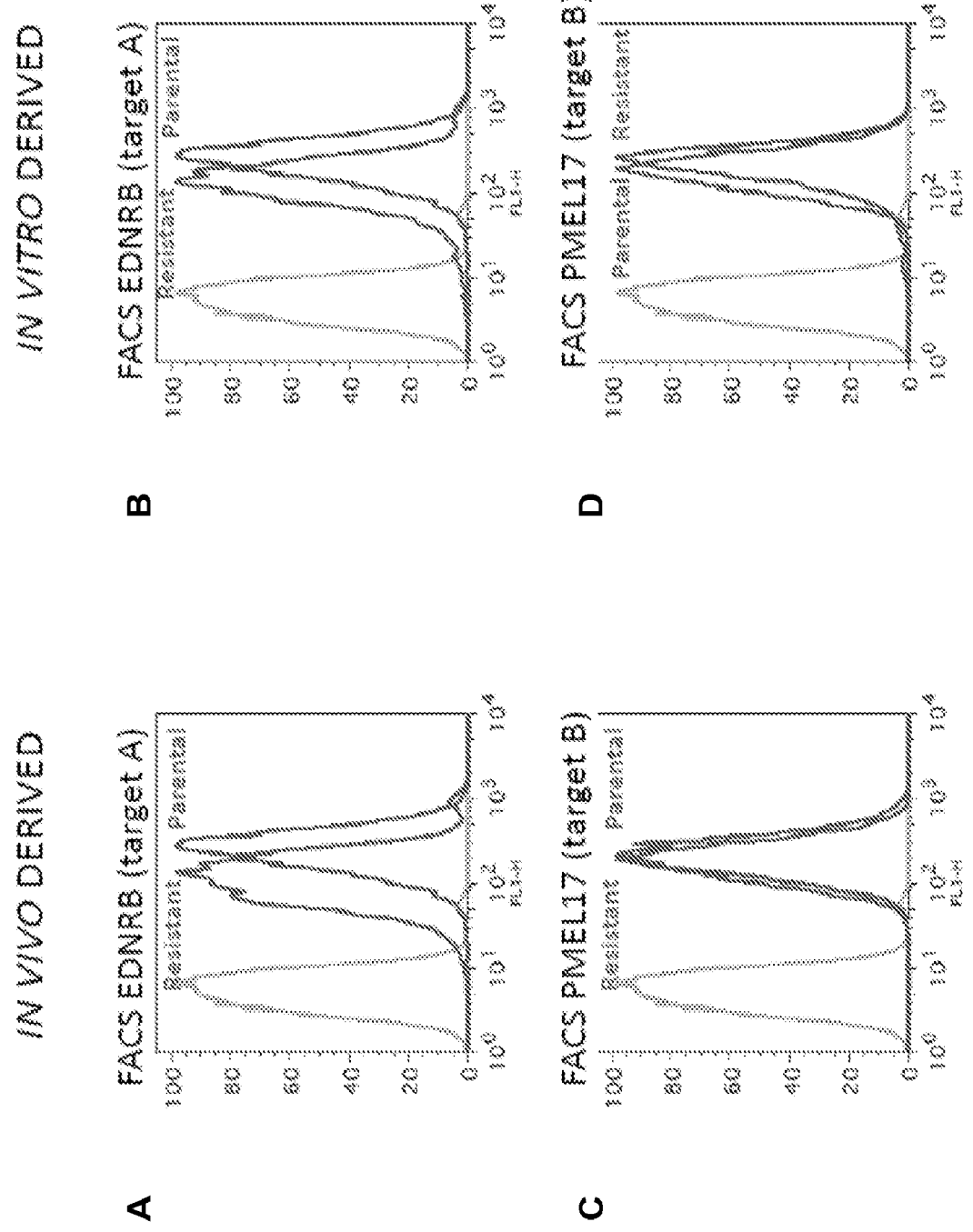

IN VIVO DERIVED
IN VITRO DERIVED
A
FACS EDNRB (target A)
Resistant
Parental
B
FACS EDNRB (target A)
Resistant
Parental
C
FACS PMEL17 (target B)
Resistant
Parental
D
FACS PMEL17 (target B)
Resistant
Parental

FIG. 11

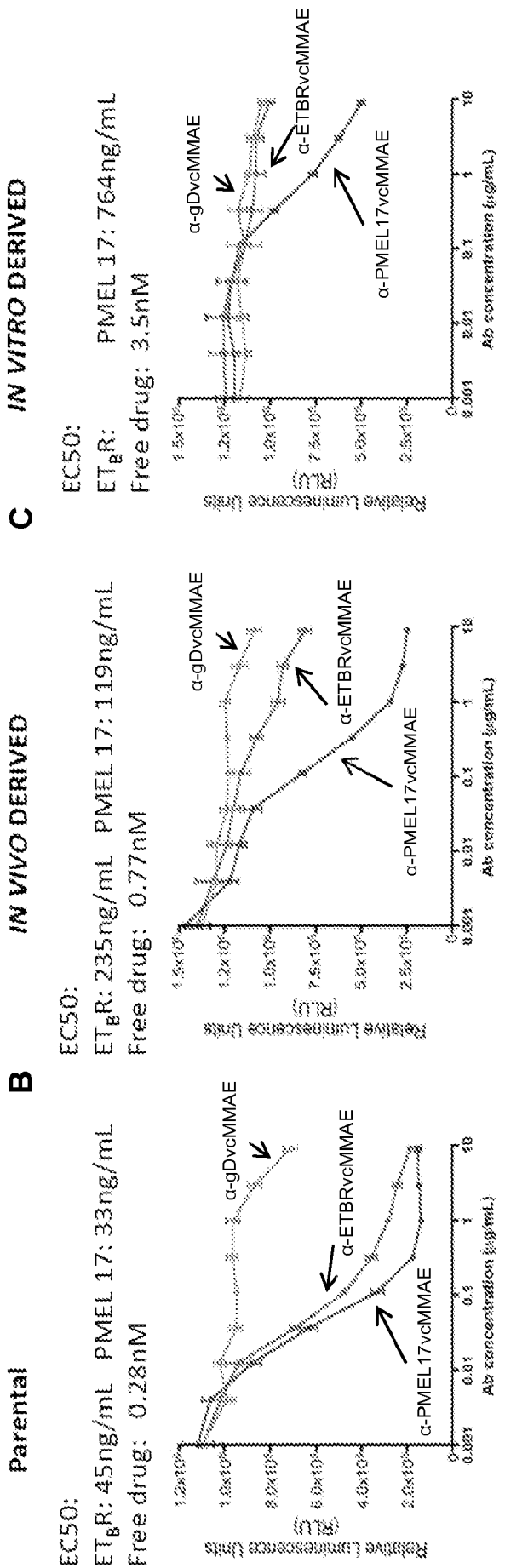

A
Parental
EC50:
ETBR: 45ng/mL PMEL 17: 33ng/mL
Free drug: 0.28nM
B
IN VIVO DERIVED
EC50:
ETBR: 235ng/mL PMEL 17: 119ng/mL
Free drug: 0.77nM
C
IN VITRO DERIVED
EC50:
ETBR: PMEL 17: 764ng/mL
Free drug: 3.5nM
α-gDvcMMAE
α-ETBRvcMMAE
α-PMEL17vcMMAE
Relative Luminescence Units (RLU)
Ab concentration (μg/mL)

FIG. 12

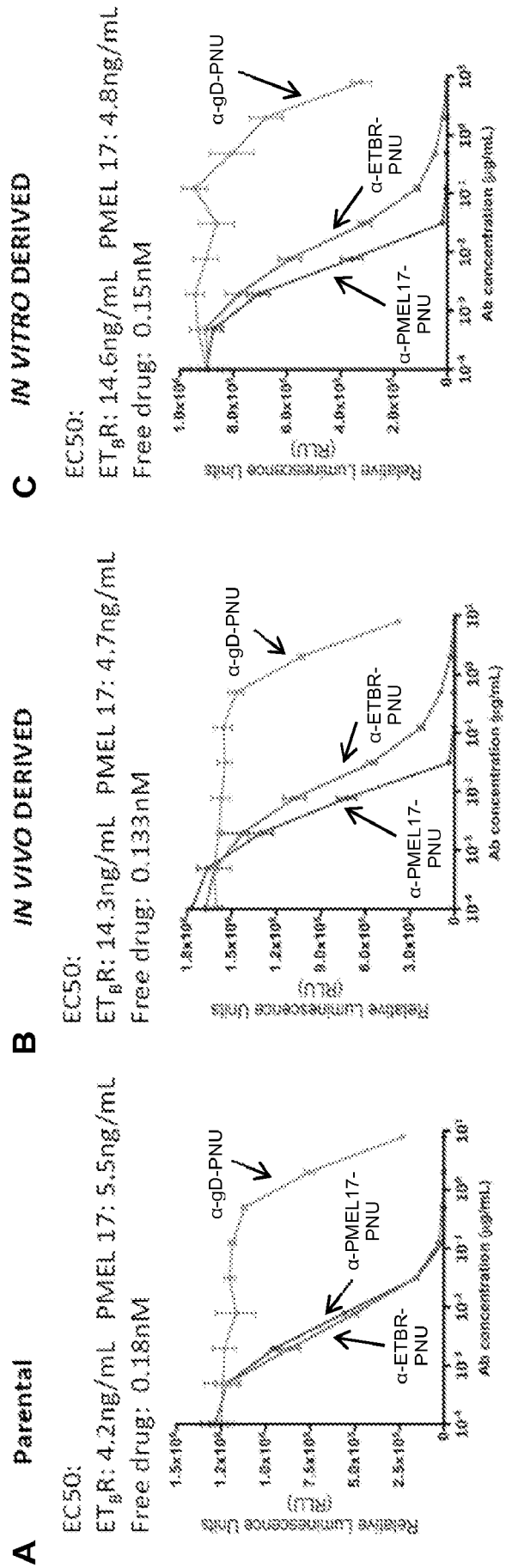

A
Parental
EC50:
ET8R: 4.2ng/mL PMEL 17: 5.5ng/mL
Free drug: 0.18nM
B
IN VIVO DERIVED
EC50:
ET8R: 14.3ng/mL PMEL 17: 4.7ng/mL
Free drug: 0.133nM
C
IN VITRO DERIVED
EC50:
ET8R: 14.6ng/mL PMEL 17: 4.8ng/mL
Free drug: 0.15nM
α-gD-PNU
α-PMEL17-PNU
α-ETBR-PNU
Relative Luminescence Units (RLU)
Ab concentration (pg/mL)

FIG. 13

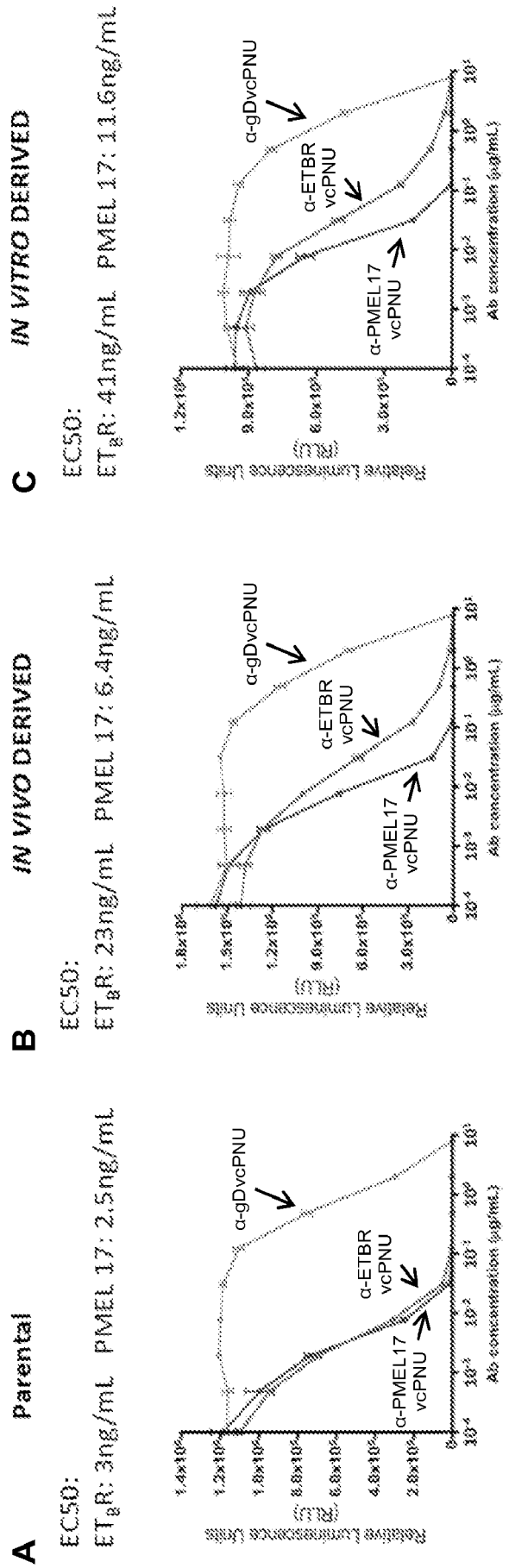
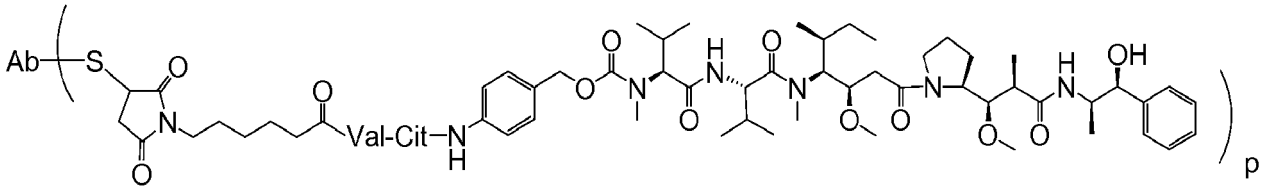
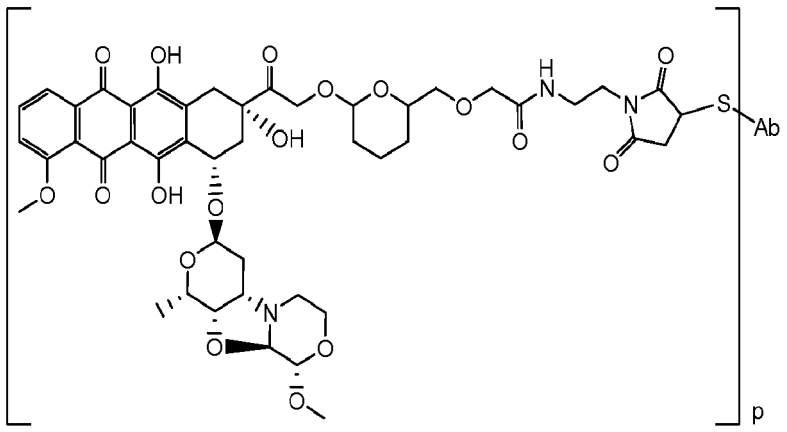

A
Parental
EC50:
ETBR: 3ng/mL PMEL 17: 2.5ng/mL
B
IN VIVO DERIVED
EC50:
ETBR: 23ng/mL PMEL 17: 6.4ng/mL
C
IN VITRO DERIVED
EC50:
ETBR: 41ng/mL PMEL 17: 11.6ng/mL
α-gDvcPNU
α-ETBR vcPNU
α-PMEL17 vcPNU
Relative Luminescence Units (RLU)
Ab concentration (μg/mL)

FIG. 14

A Ab-MC-val-cit-PAB-MMAE



B Ab-MC-acetal-PNU-159682



C Ab-MC-val-cit-PAB-PNU-159682

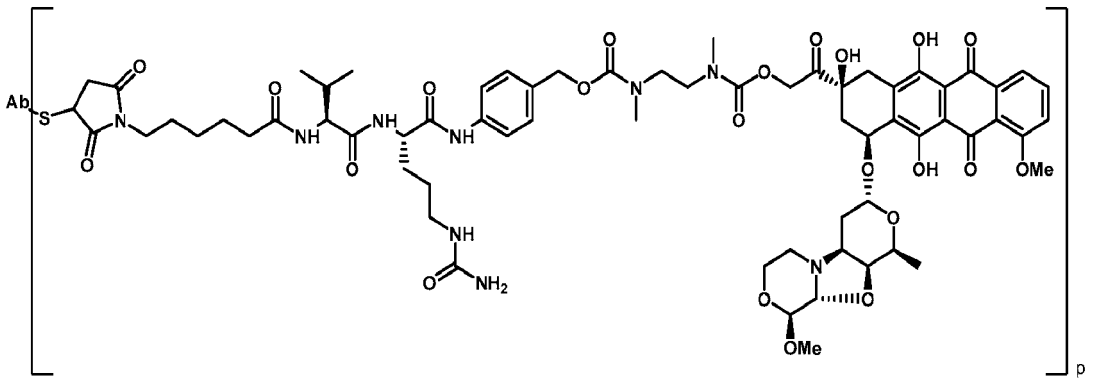
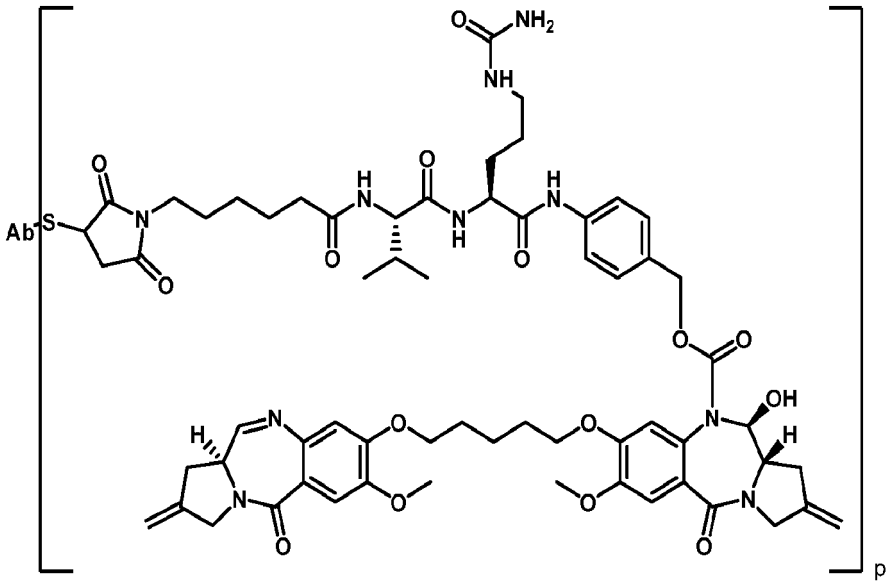


FIG. 15

D Ab-MC-val-cit-PAB-PBD



E Ab-PNU-159682

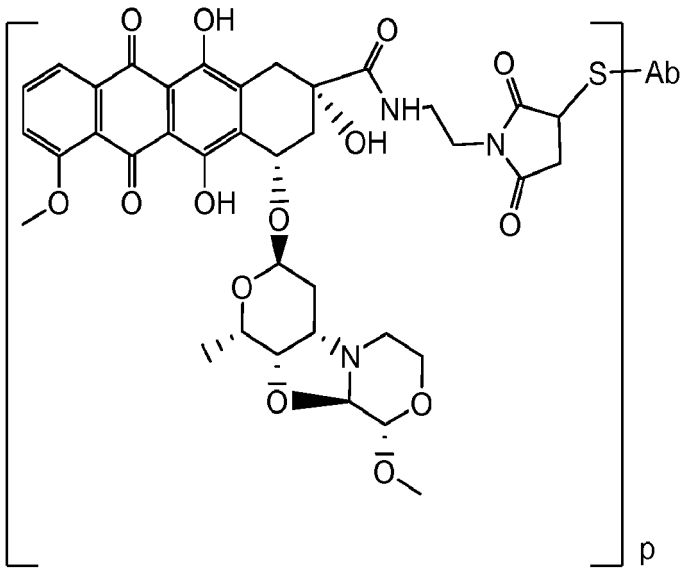


FIG. 15