```
huEFNA4 iso b NP_872631.1  MRLLPLLRTVLWAAFLGSPLRGGSSLRHVVYWNSSNPRLLRGDAVVELGL
huEFNA4 iso c NP_872632.2  MRLLPLLRTVLWAAFLGSPLRGGSSLRHVVYWNSSNPRLLRGDAVVELGL
huEFNA4 iso a NP_005218.1  MRLLPLLRTVLWAAFLGSPLRGGSSLRHVVYWNSSNPRLLRGDAVVELGL

huEFNA4 iso b NP_872631.1  NDYLDIVCPHYEGPGPPEGPETFALYMVDWPGYESCQAEGPRAYKRWVCS
huEFNA4 iso c NP_872632.2  NDYLDIVCPHYEGPGPPEGPETFALYMVDWPGYESCQAEGPRAYKRWVCS
huEFNA4 iso a NP_005218.1  NDYLDIVCPHYEGPGPPEGPETFALYMVDWPGYESCQAEGPRAYKRWVCS

huEFNA4 iso b NP_872631.1  LPFGHVQFSEKIQRFTPFSLGFEFLPGETYYYISVPTPESSGQCLRLQVS
huEFNA4 iso c NP_872632.2  LPFGHVQFSEKIQRFTPFSLGFEFLPGETYYYISVPTPESSGQCLRLQVS
huEFNA4 iso a NP_005218.1  LPFGHVQFSEKIQRFTPFSLGFEFLPGETYYYISVPTPESSGQCLRLQVS

huEFNA4 iso b NP_872631.1  VCCKERR-ARVLPRSPGGGGIPAACTGGANSDRQDGALMGEIRGSEVTLA
huEFNA4 iso c NP_872632.2  VCCKERN-LPSHPKEP-- -E-----SSQDPLEEEGSLLPALGVPIQTDK
huEFNA4 iso a NP_005218.1  VCCKERKSESAHPVGSPGESG----TSGWRGGDTPSPLCLLLLLLLLILR

huEFNA4 iso b NP_872631.1  GACPLITG (SEQ ID NO: 3)
huEFNA4 iso c NP_872632.2  MEH----- (SEQ ID NO: 4)
huEFNA4 iso a NP_005218.1  LLRIL--- (SEQ ID NO: 2)
```

FIG. 1

CLONE	ISOTYPE	VH	DH	JH	CDRH1 SEQ ID NOS: 65-76	CDRH2 SEQ ID NOS: 77-88	CDRH3 SEQ ID NOS: 89-100	VL	JL	CDRL1 SEQ ID NOS: 101-112	CDRL2 SEQ ID NOS: 113-124	CDRL3 SEQ ID NOS: 125-136
E2	IgG1/K	VHJ558	P1	JH3	GYTFTDYE	FDPETGNT	ARGYPAWFGY	IGKV1-110	JK1	QSLAHTNGNTY	KVSNMRFS	SQDTHVPPT
E5	IgG1/K	IGHV2-6	NONE	JH3	GFSLTTYG	IWGGGST	ASDWAY	IGKV6-15	JK2	QNVGTN	SASYRYS	QQYKRYPYT
E8	NOT DONE	VHJ558	IGHD6-1	JH4	GYTFTNYW	IDPSDSYI	ARERLSHAMDY	IGVK9-128	JK2	QDIKSY	YATSLAD	LQHGESPYT
E15	IgG1/K	IGHV5-6	DSP2.9	JH3	GFTFSTYG	ISSGGTYT	TRHDPNDGYYFLFAY	IGKV6-b	JK5	QSVGNN	YASNRYT	QQHYSSPLT
E22	IgG2b/K	VHJ558	DFL16.1e	JH4	GYTFTGYY	IYPGNFNT	AREDGSPYYAMDY	IGKV1-110	JK1	QSLVHSNGNTF	RVSNRFS	FQATHVPWT
E31	IgG1/K	VHJ558	DFL16.1	JH4	GYTFTRDW	IHPYDSET	VTFIKTMVDTYYYAMDY	IGKV1-135	JK1	QSLLHSDGKTY	LVSNLDS	WQGTHFPQT
E47	IgG1/K	IGHV1-26	P1inv	JH2	GYTFTYFY	INPNNGGT	ARWVGTHYFDY	IGKV21-7	JK1	QSVSSSSYTY	FASNLES	QHSWEIPPT
E60	IgG2a/K	IGHV1-39	DQ52a.2	JH4	GYSFTVYN	INPYYGGT	ARGGKTGTYYYVMDY	IGKV12-44	JK5	ENIDSY	AATLLAD	QHYYSTLT
E73	IgG1/K	IGHV3-6	DSP2.13	JH2	GYSITSGYY	ISYDGRN	AREGYGDYPFDY	IGKV21-7	JK1	QSVSSSSYSY	YASNLES	QHSWEIPRT
E76	IgG2b/K	J558.87.193	DFL16.1e	JH4	GYTFTGYY	IYPGNFNT	AREDGSPYYAMDY	IGKV1-110	JK1	QSLVHSNGNTF	RVSNRFS	FQATHVPWT
E91	IgG2b/K	IGHV1-64	P8inv	JH4	GYTFTSYW	IHPNSDTI	ATPERRRAMDY	IGKV4-74	JK4	SSLSSSY	STSFLAS	QQYDSSPFT
E105	IgG1/K	VH3660	DSP2.2	JH3	GASITSGY	INYSGNT	ARSTMITTGAWFAY	IGKV6-32	JK5	QSVSKD	YASNRYT	QQDYSSPLT

FIG. 2

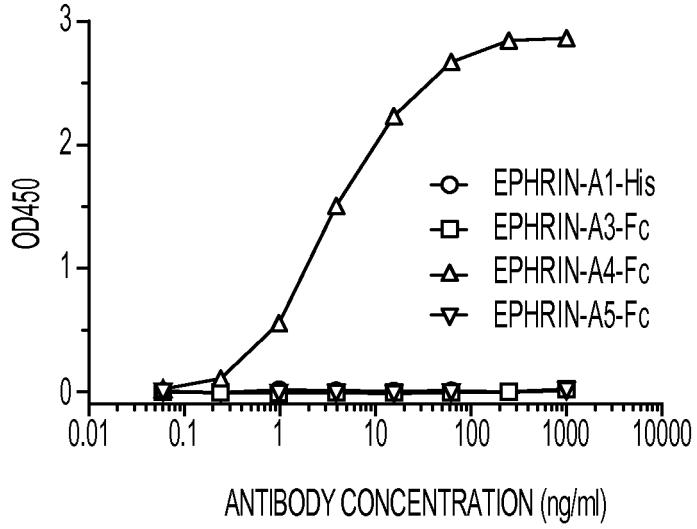

OD450
3
2
1
0
0.01
0.1
1
10
100
1000
10000
EPHRIN-A1-His
EPHRIN-A3-Fc
EPHRIN-A4-Fc
EPHRIN-A5-Fc
ANTIBODY CONCENTRATION (ng/ml)

FIG. 3A

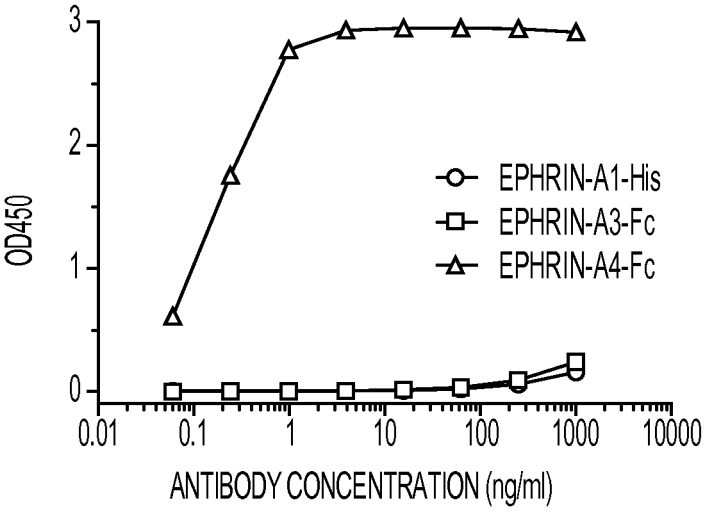

OD450
3
2
1
0
0.01
0.1
1
10
100
1000
10000
EPHRIN-A1-His
EPHRIN-A3-Fc
EPHRIN-A4-Fc
ANTIBODY CONCENTRATION (ng/ml)

FIG. 3B

AcBut-CM

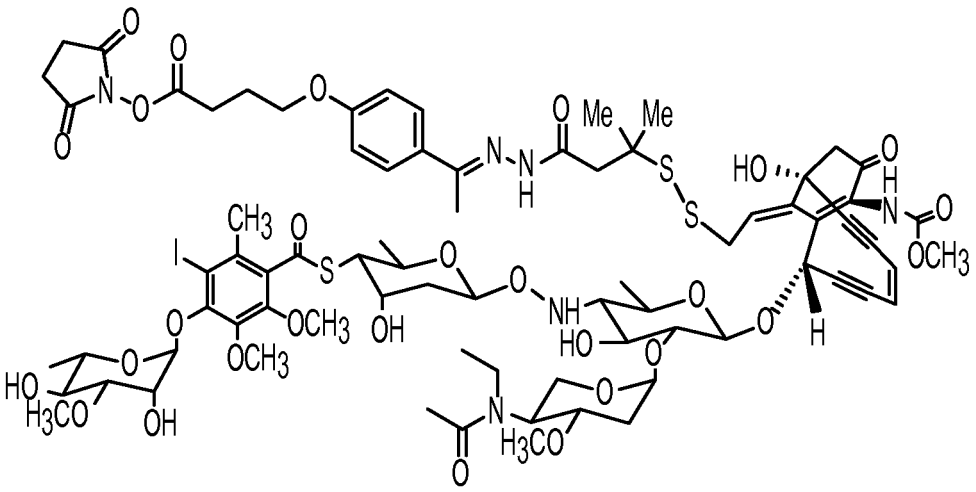


FIG. 4A

AcBut-CM CONJUGATED TO AN ANTIBODY (X)

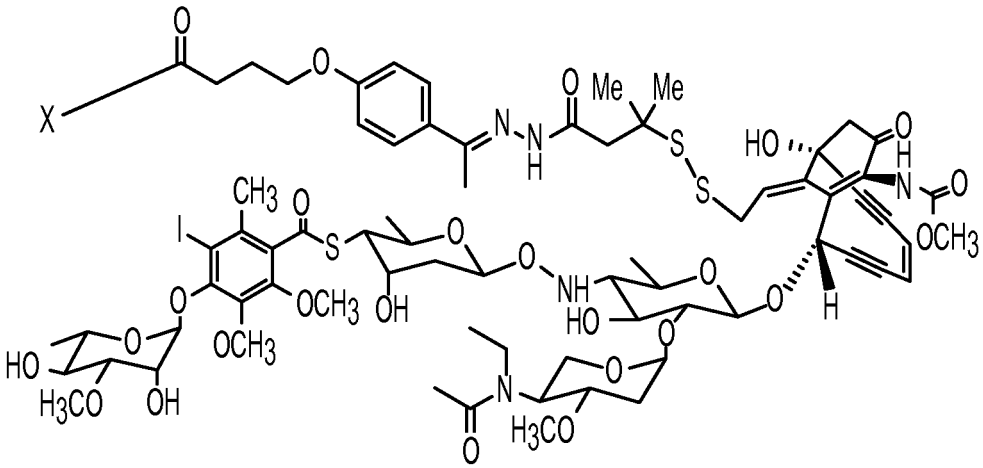


FIG. 4B

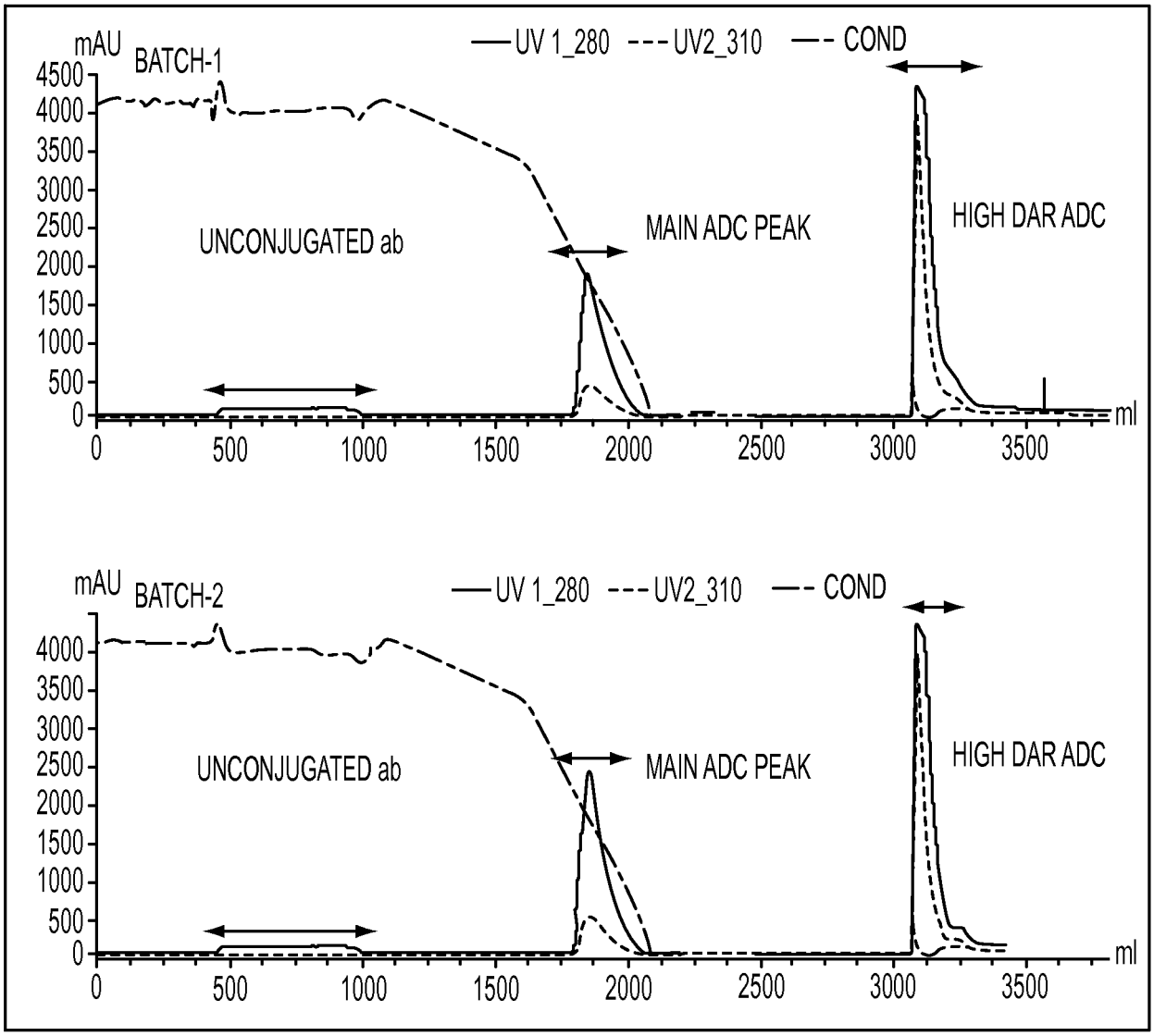

mAU
BATCH-1
UV 1_280
UV2_310
COND
4500
4000
3500
3000
2500
2000
1500
1000
500
0
UNCONJUGATED ab
MAIN ADC PEAK
HIGH DAR ADC
0
500
1000
1500
2000
2500
3000
3500
ml
mAU
BATCH-2
UV 1_280
UV2_310
COND
4000
3500
3000
2500
2000
1500
1000
500
0
UNCONJUGATED ab
MAIN ADC PEAK
HIGH DAR ADC
0
500
1000
1500
2000
2500
3000
3500
ml

FIG. 5

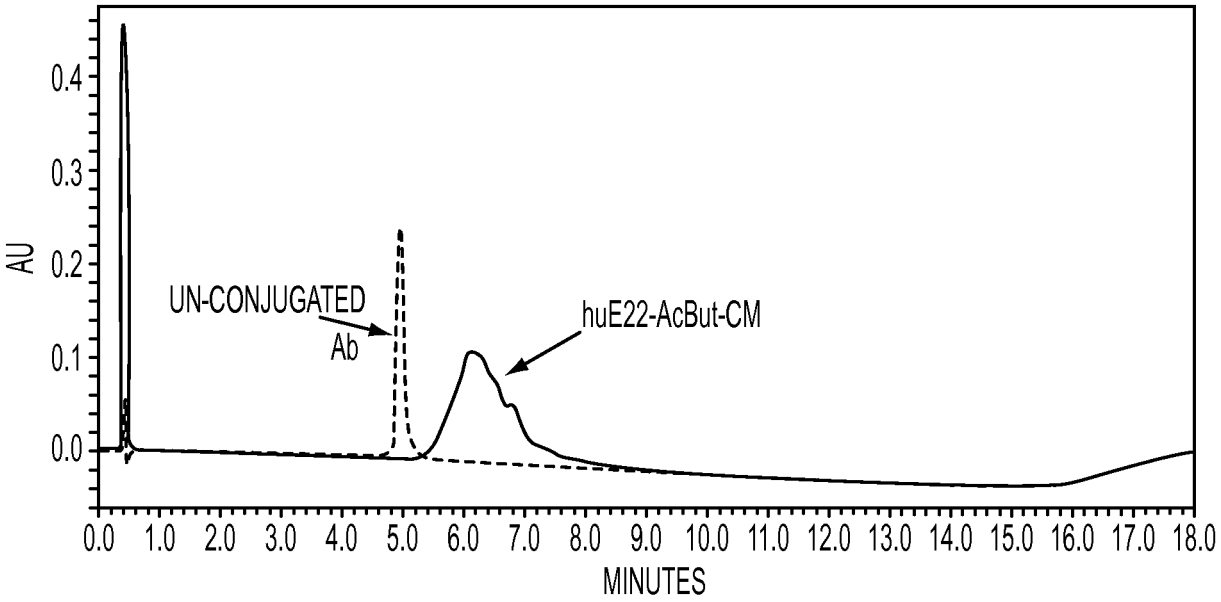

AU
0.4
0.3
0.2
0.1
0.0
UN-CONJUGATED
Ab
huE22-AcBut-CM
0.0 1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0 9.0 10.0 11.0 12.0 13.0 14.0 15.0 16.0 17.0 18.0
MINUTES

FIG. 6

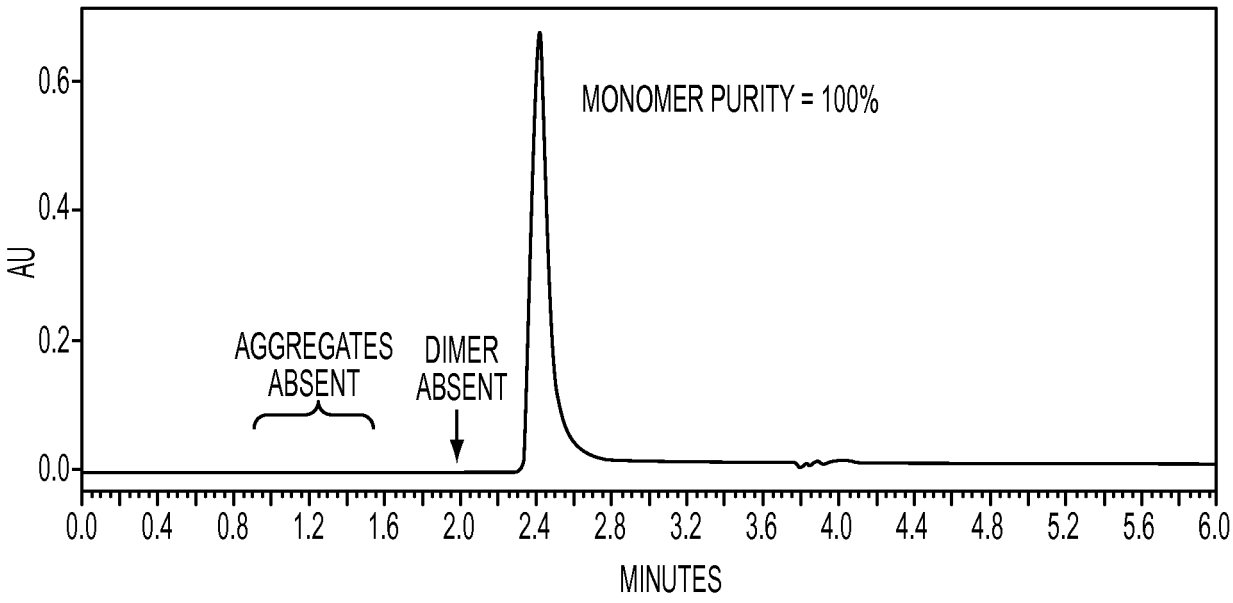

AU
0.6
0.4
0.2
0.0
MONOMER PURITY = 100%
AGGREGATES
ABSENT
DIMER
ABSENT
0.0 0.4 0.8 1.2 1.6 2.0 2.4 2.8 3.2 3.6 4.0 4.4 4.8 5.2 5.6 6.0
MINUTES

FIG. 7

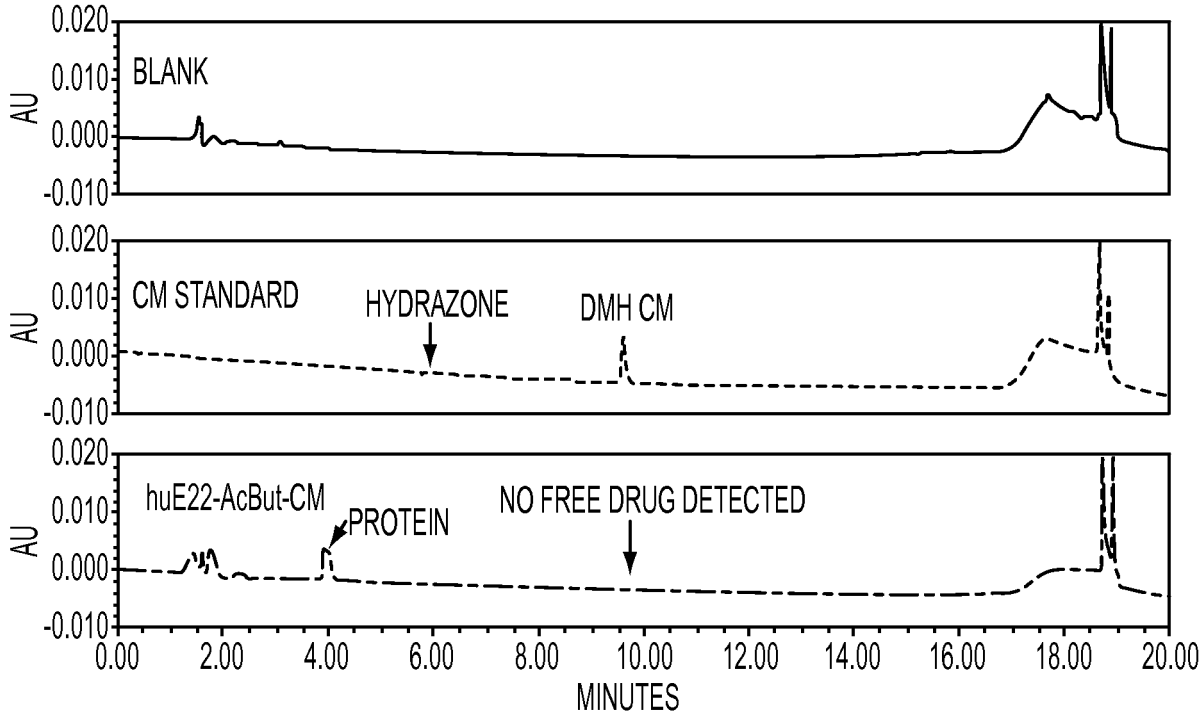

BLANK
CM STANDARD
HYDRAZONE
DMH CM
huE22-AcBut-CM
PROTEIN
NO FREE DRUG DETECTED
AU
0.020
0.010
0.000
-0.010
0.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
20.00
MINUTES

FIG. 8

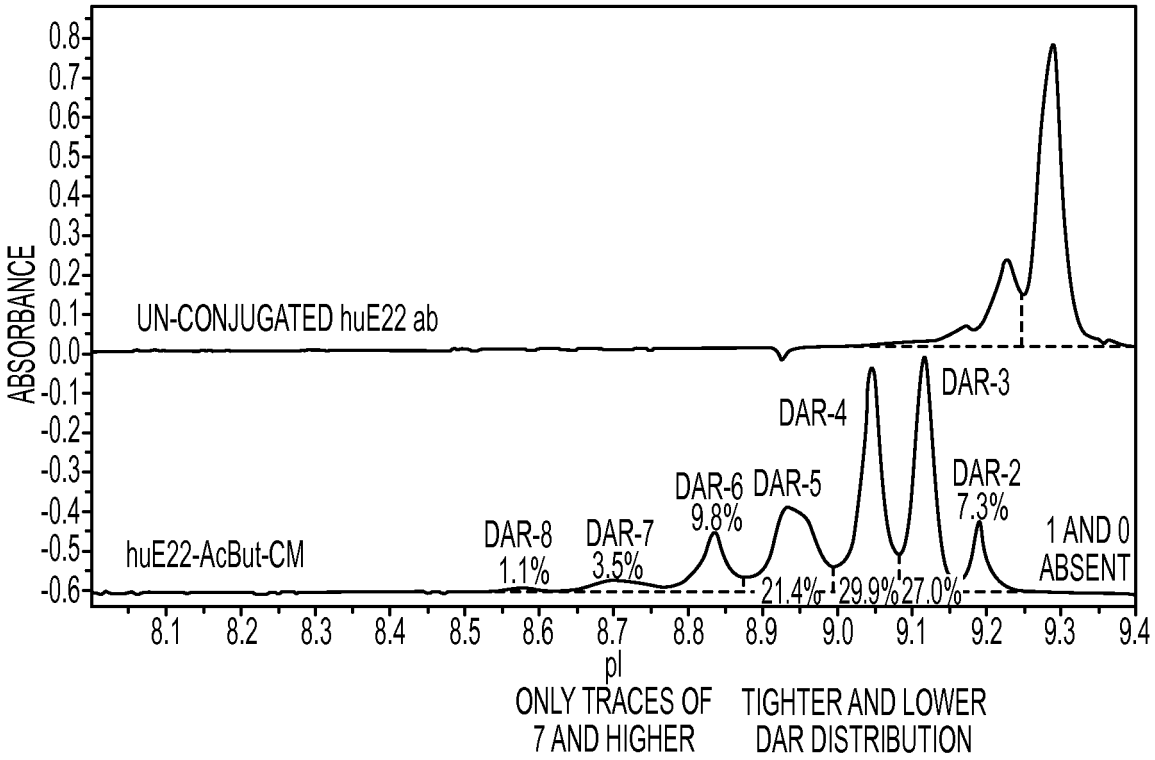

UN-CONJUGATED huE22 ab
huE22-AcBut-CM
ABSORBANCE
DAR-8
1.1%
DAR-7
3.5%
DAR-6
9.8%
DAR-5
21.4%
DAR-4
29.9%
DAR-3
27.0%
DAR-2
7.3%
1 AND 0
ABSENT
pI
ONLY TRACES OF
7 AND HIGHER
TIGHTER AND LOWER
DAR DISTRIBUTION

FIG. 9

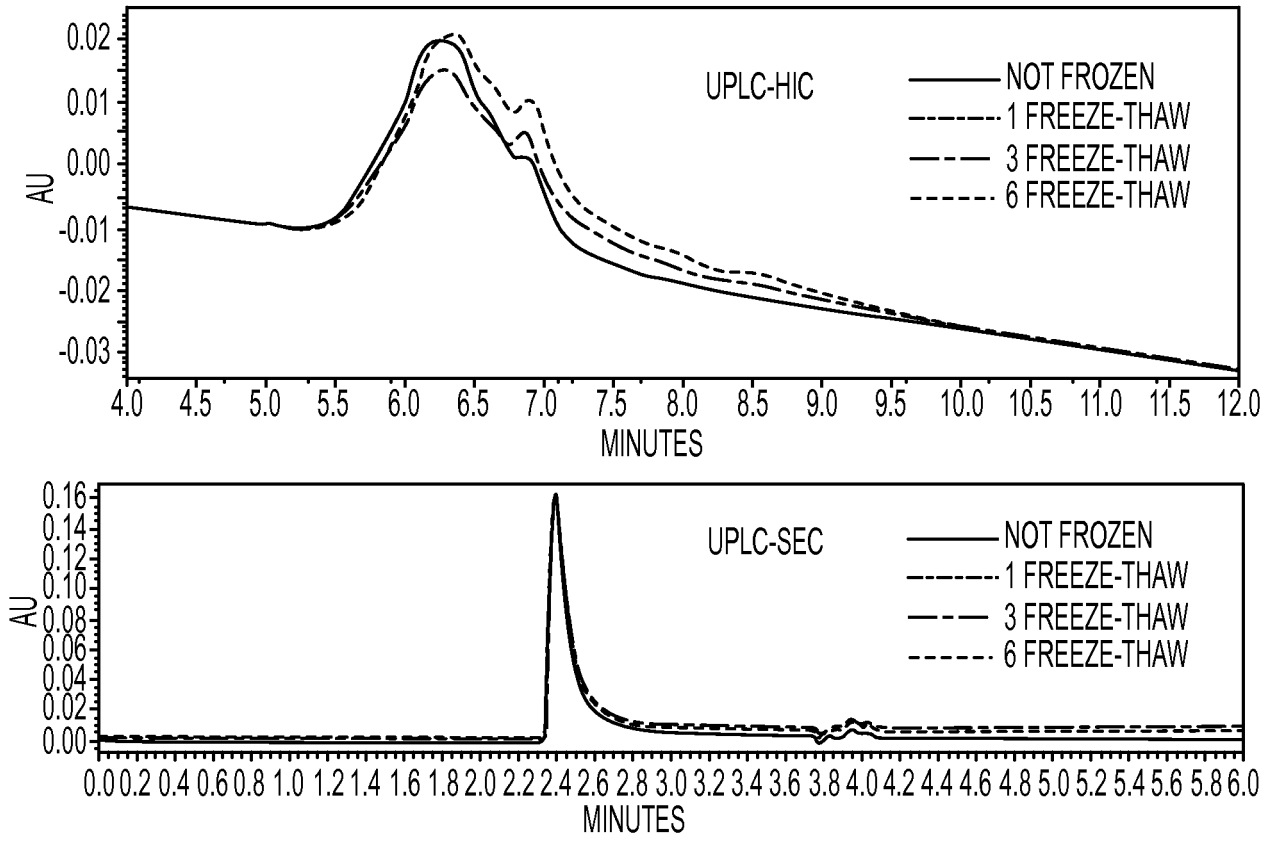

UPLC-HIC
NOT FROZEN
1 FREEZE-THAW
3 FREEZE-THAW
6 FREEZE-THAW
AU
0.02
0.01
0.00
-0.01
-0.02
-0.03
4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0 8.5 9.0 9.5 10.0 10.5 11.0 11.5 12.0
MINUTES
UPLC-SEC
NOT FROZEN
1 FREEZE-THAW
3 FREEZE-THAW
6 FREEZE-THAW
AU
0.16
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0.00
0.0 0.2 0.4 0.6 0.8 1.0 1.2 1.4 1.6 1.8 2.0 2.2 2.4 2.6 2.8 3.0 3.2 3.4 3.6 3.8 4.0 4.2 4.4 4.6 4.8 5.0 5.2 5.4 5.6 5.8 6.0
MINUTES

FIG. 10

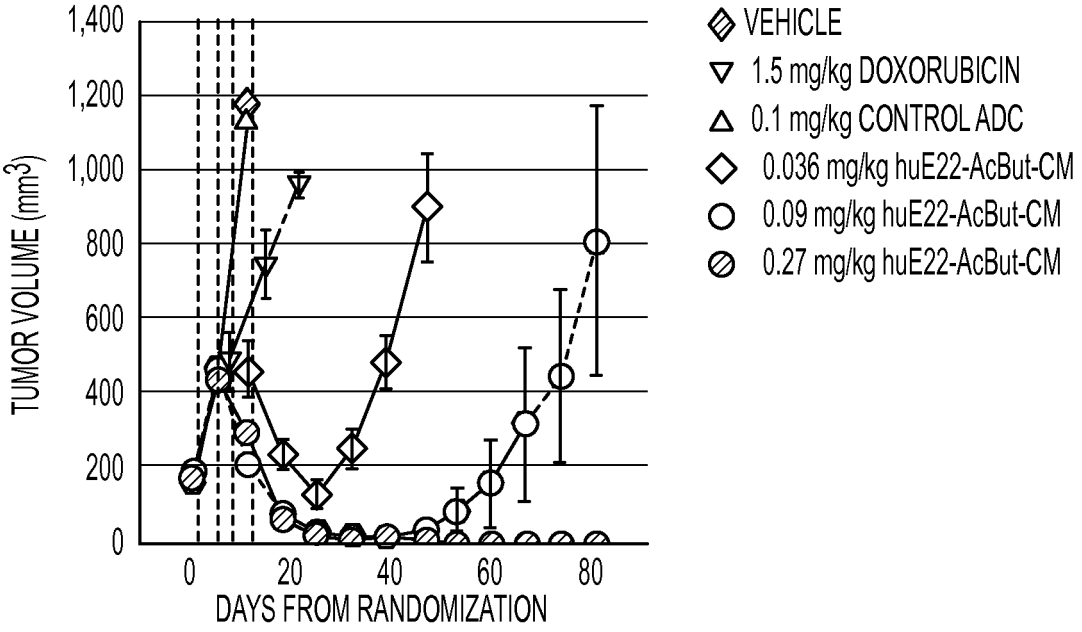

1,400
1,200
1,000
800
600
400
200
0
TUMOR VOLUME (mm3)
0
20
40
60
80
DAYS FROM RANDOMIZATION
VEHICLE
1.5 mg/kg DOXORUBICIN
0.1 mg/kg CONTROL ADC
0.036 mg/kg huE22-AcBut-CM
0.09 mg/kg huE22-AcBut-CM
0.27 mg/kg huE22-AcBut-CM

FIG. 11

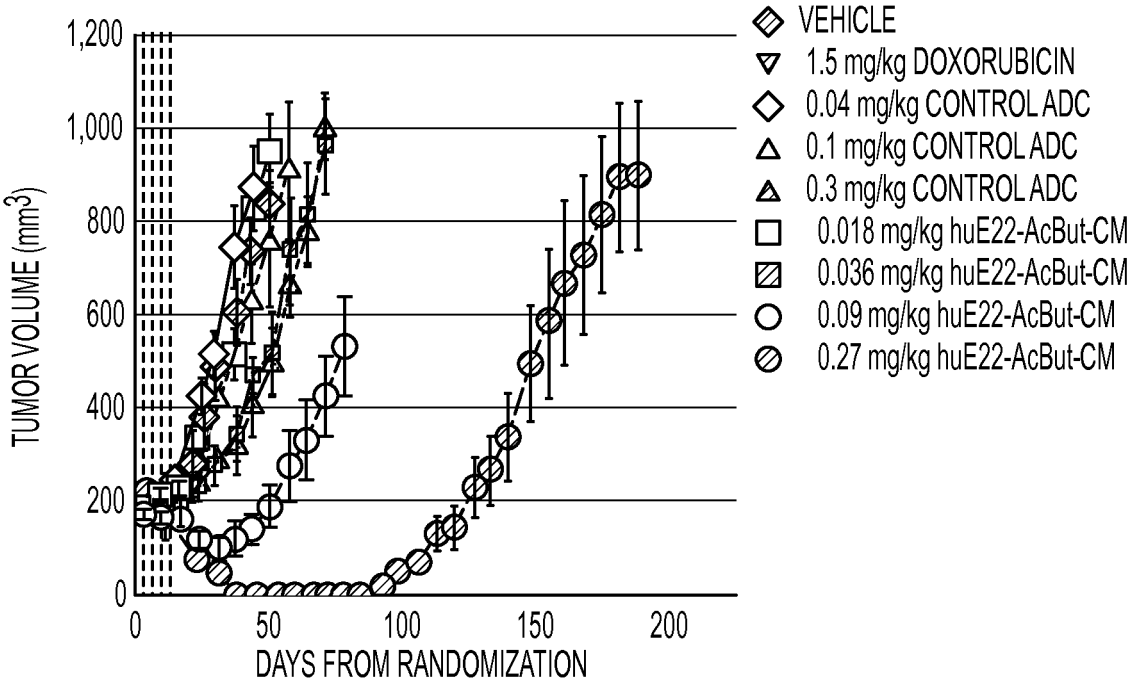

1,200
1,000
800
600
400
200
0
TUMOR VOLUME (mm3)
0
50
100
150
200
DAYS FROM RANDOMIZATION
VEHICLE
1.5 mg/kg DOXORUBICIN
0.04 mg/kg CONTROL ADC
0.1 mg/kg CONTROL ADC
0.3 mg/kg CONTROL ADC
0.018 mg/kg huE22-AcBut-CM
0.036 mg/kg huE22-AcBut-CM
0.09 mg/kg huE22-AcBut-CM
0.27 mg/kg huE22-AcBut-CM

FIG. 12

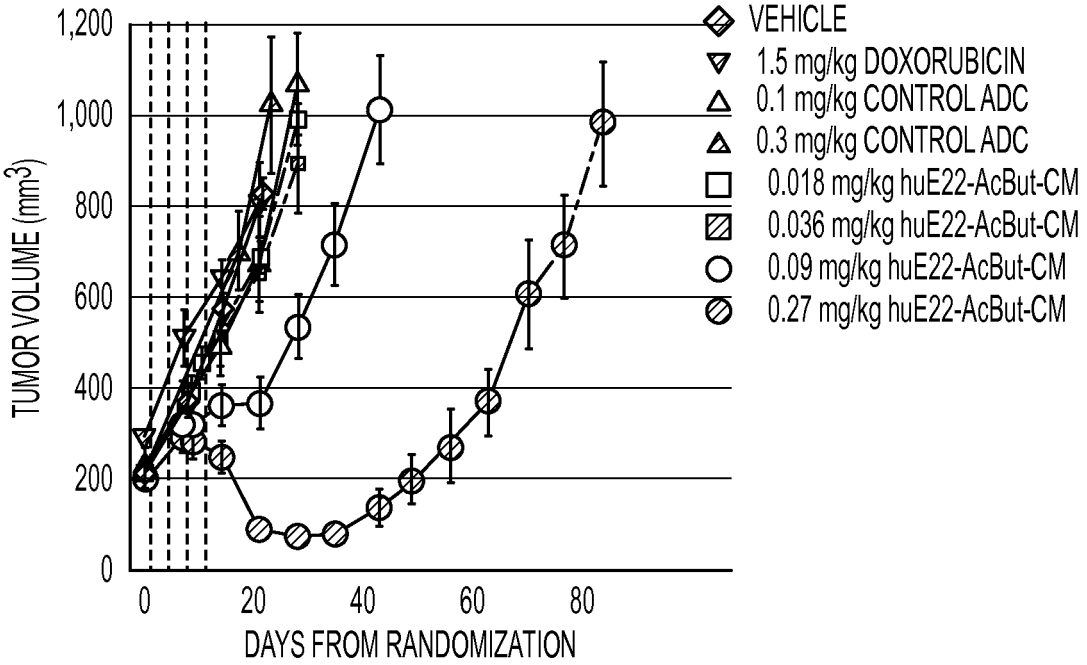

1,200
1,000
800
600
400
200
0
TUMOR VOLUME (mm3)
0
20
40
60
80
DAYS FROM RANDOMIZATION
VEHICLE
1.5 mg/kg DOXORUBICIN
0.1 mg/kg CONTROL ADC
0.3 mg/kg CONTROL ADC
0.018 mg/kg huE22-AcBut-CM
0.036 mg/kg huE22-AcBut-CM
0.09 mg/kg huE22-AcBut-CM
0.27 mg/kg huE22-AcBut-CM

FIG. 13

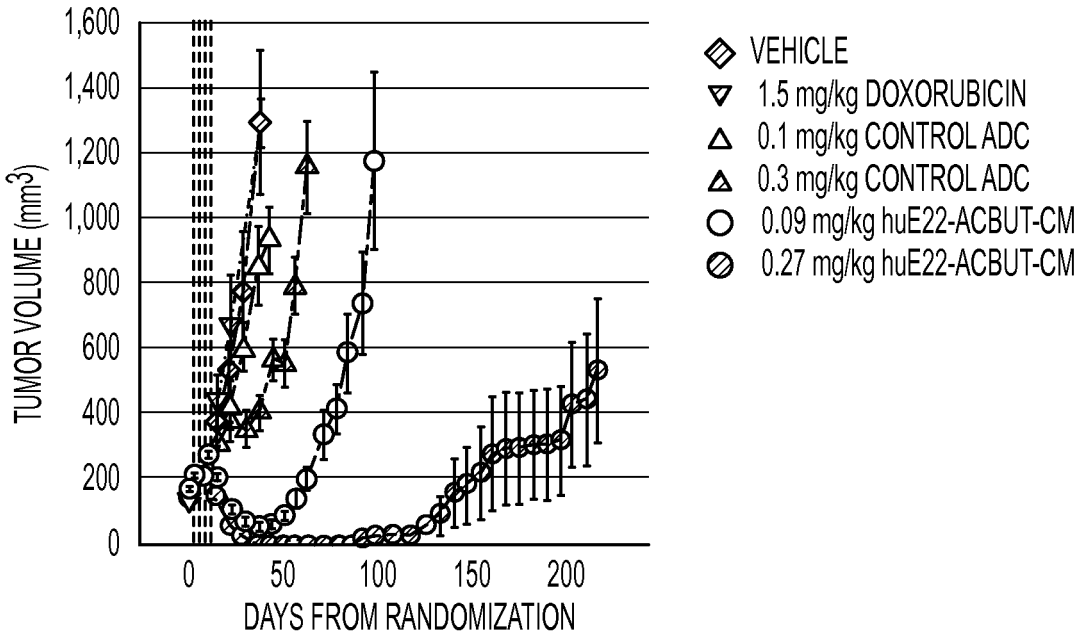

1,600
1,400
1,200
1,000
800
600
400
200
0
TUMOR VOLUME (mm3)
0
50
100
150
200
DAYS FROM RANDOMIZATION
VEHICLE
1.5 mg/kg DOXORUBICIN
0.1 mg/kg CONTROL ADC
0.3 mg/kg CONTROL ADC
0.09 mg/kg huE22-ACBUT-CM
0.27 mg/kg huE22-ACBUT-CM

FIG. 14

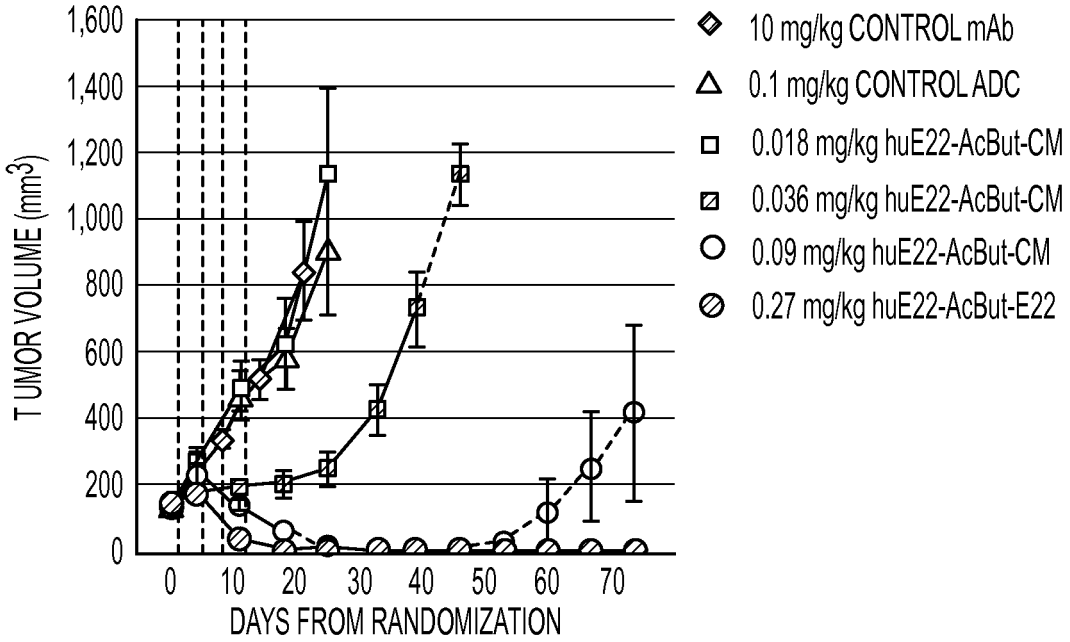

1,600
1,400
1,200
1,000
800
600
400
200
0
TUMOR VOLUME (mm3)
0 10 20 30 40 50 60 70
DAYS FROM RANDOMIZATION
10 mg/kg CONTROL mAb
0.1 mg/kg CONTROL ADC
0.018 mg/kg huE22-AcBut-CM
0.036 mg/kg huE22-AcBut-CM
0.09 mg/kg huE22-AcBut-CM
0.27 mg/kg huE22-AcBut-E22

FIG. 15

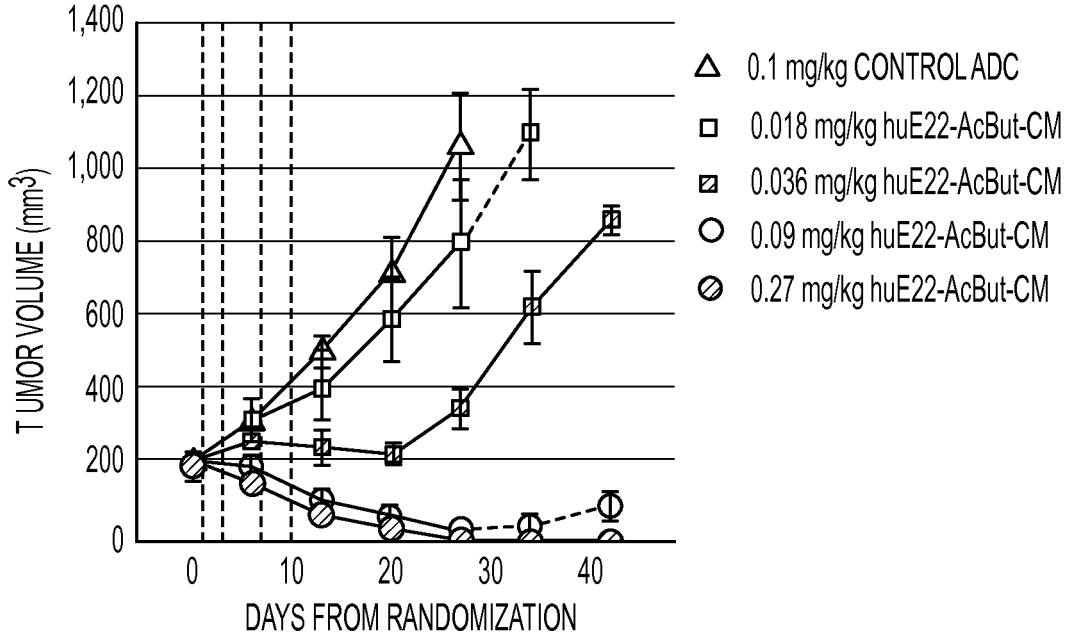

1,400
1,200
1,000
800
600
400
200
0
TUMOR VOLUME (mm3)
0 10 20 30 40
DAYS FROM RANDOMIZATION
0.1 mg/kg CONTROL ADC
0.018 mg/kg huE22-AcBut-CM
0.036 mg/kg huE22-AcBut-CM
0.09 mg/kg huE22-AcBut-CM
0.27 mg/kg huE22-AcBut-CM

FIG. 16

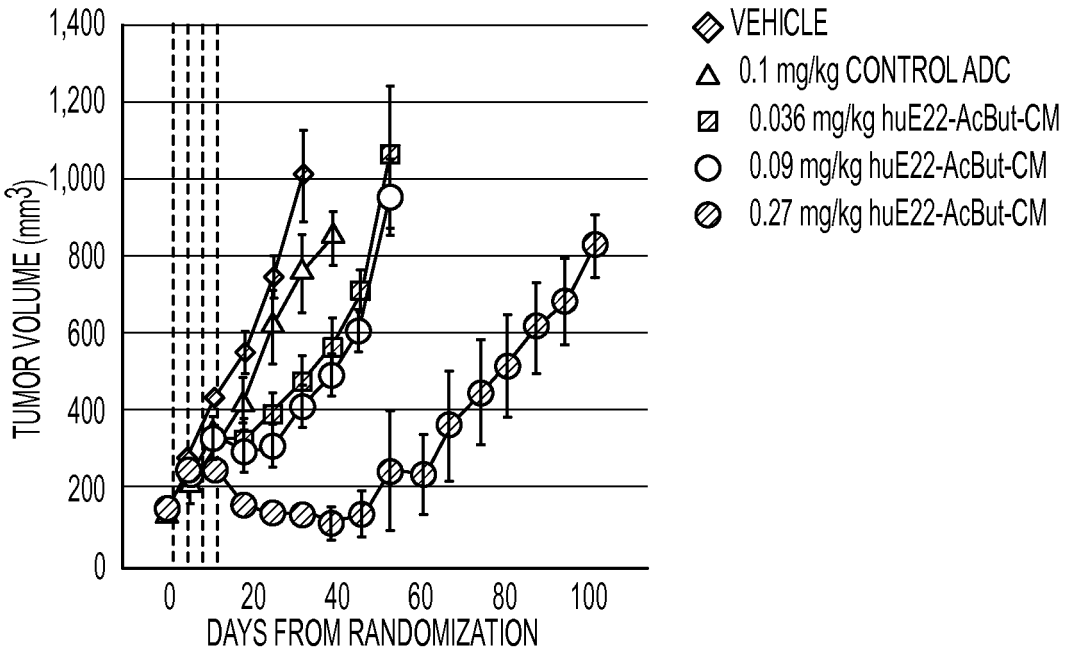

1,400
1,200
1,000
800
600
400
200
0
TUMOR VOLUME (mm3)
0
20
40
60
80
100
DAYS FROM RANDOMIZATION
VEHICLE
0.1 mg/kg CONTROL ADC
0.036 mg/kg huE22-AcBut-CM
0.09 mg/kg huE22-AcBut-CM
0.27 mg/kg huE22-AcBut-CM

FIG. 17

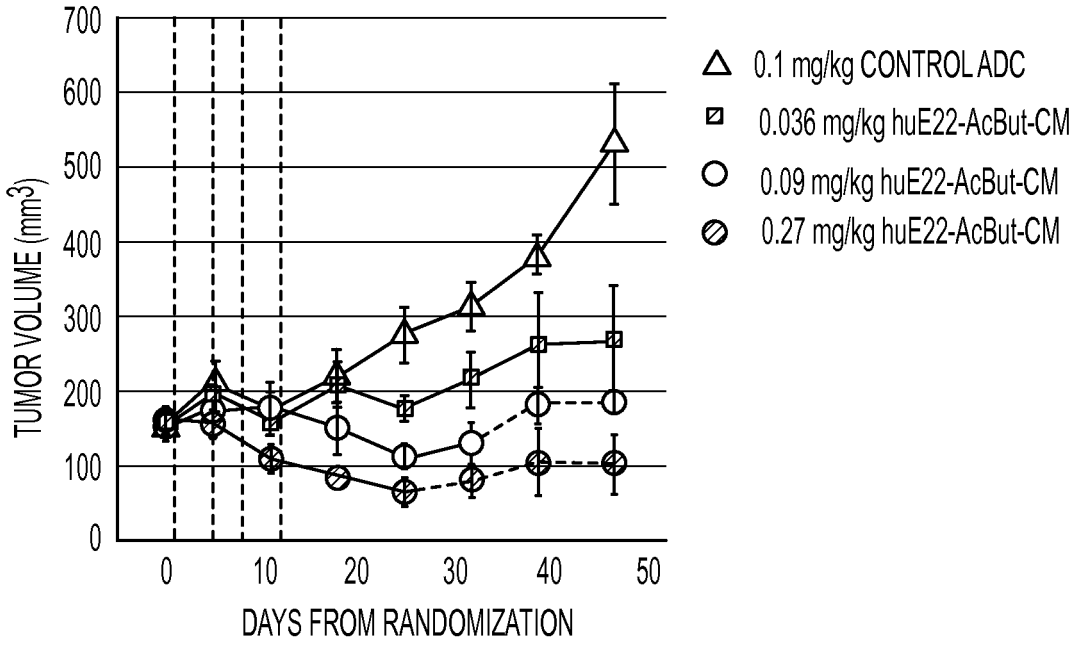

700
600
500
400
300
200
100
0
TUMOR VOLUME (mm3)
0
10
20
30
40
50
DAYS FROM RANDOMIZATION
0.1 mg/kg CONTROL ADC
0.036 mg/kg huE22-AcBut-CM
0.09 mg/kg huE22-AcBut-CM
0.27 mg/kg huE22-AcBut-CM

FIG. 18

EFFICACY OF VARIOUS ANTI-EFNA4-MTIs IN BR22 TNBC PDX

DAY	VEHICLE	3 mg/kg huE15-vc0101	10 mg/kg huE15-mc8261	3 mg/kg huE22-vc0101	10 mg/kg huE22-mc8261	3 mg/kg huE47-vc0101	10 mg/kg huE47-mc8261
0	195 ± 17	198 ± 16	198 ± 22	184 ± 24	184 ± 24	172 ± 17	184 ± 15
7	376 ± 43	313 ± 17	329 ± 52	317 ± 37	339 ± 36	259 ±33	288 ± 21
14	564 ± 54	354 ± 39	664 ± 65	558 ± 83	781 ± 98	547 ± 56	735 ± 101
21	819 ± 97	299 ±59	1061 ± 69	901 ± 175	1377± 125	839 ± 110	1270 ± 125
28	GT	478 ± 113	1739 ± 110	1537 ± 321	2257 ± 173	1618 ± 221	2442 ± 344
35	GT	1032 ± 216	2935 ± 341	2617 ± 414	3284 ± 261	2468 ± 271	3190 ± 265

FIG. 19

EFFICACY OF VARIOUS ANTI-EFNA4-MTIs IN BR31 TNBC PDX

DAY	VEHICLE	3 mg/kg CONTROL-AcBut-CM	3 mg/kg huE22-vc0101	3 mg/kg huE47-vc0101	3 mg/kg huE15-vc0101
0	159 ± 10	148 ± 12	151 ± 13	142 ± 11	167 ± 17
7	269 ± 17	227 ± 23	188 ± 17	176 ± 18	174 ± 18
14	425 ± 32	133 ± 10	80 ± 8	84 ± 8	99 ± 10
21	668 ± 50	101 ± 21	67 ± 6	58 ± 10	44 ± 11
28	1088 ± 93	70 ± 17	44 ± 10	60 ± 13	33 ± 10
36	GT	105 ± 28	57 ± 13	79 ± 17	41 ± 13
44	GT	214 ± 76	87 ± 28	146 ± 32	91 ± 30
49	GT	234 ± 83	111 ± 37	205 ± 43	119 ± 36
56	GT	393 ± 103	151 ± 55	285 ± 57	169 ± 44
63	GT	680 ± 181	454 ± 138	637 ± 140	376 ± 98
71	GT	1169 ± 300	680 ± 206	857 ± 176	641± 178
78	GT	1300 ± 331	949 ± 215	1005 ± 256	837 ± 271
85	GT	GT	1005 ± 201	GT	1129 ± 374

FIG. 20

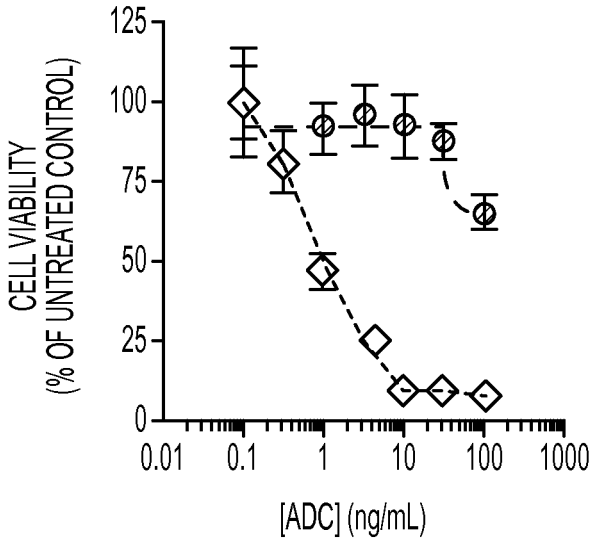

CELL VIABILITY
(% OF UNTREATED CONTROL)
125
100
75
50
25
0
0.01
0.1
1
10
100
1000
[ADC] (ng/mL)

FIG. 21

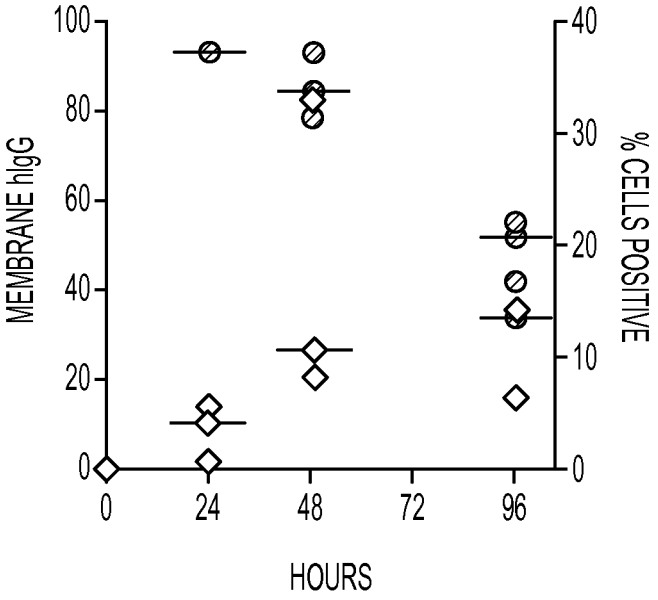

MEMBRANE hIgG
100
80
60
40
20
0
% CELLS POSITIVE
40
30
20
10
0
0
24
48
72
96
HOURS

FIG. 22

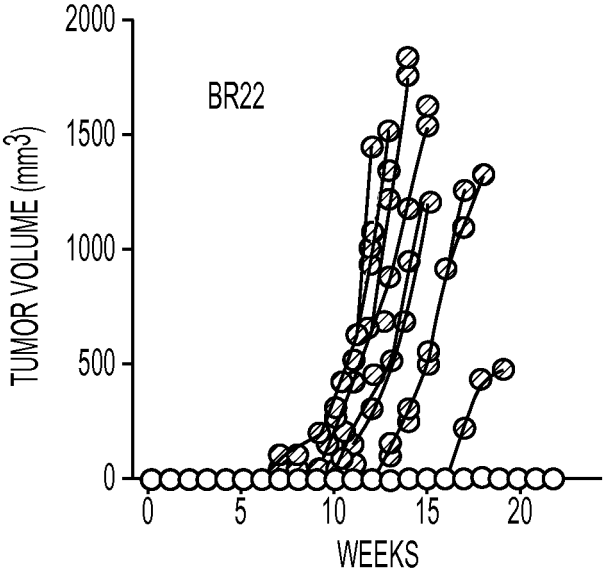

BR22
TUMOR VOLUME (mm3)
2000
1500
1000
500
0
0
5
10
15
20
WEEKS

FIG. 23

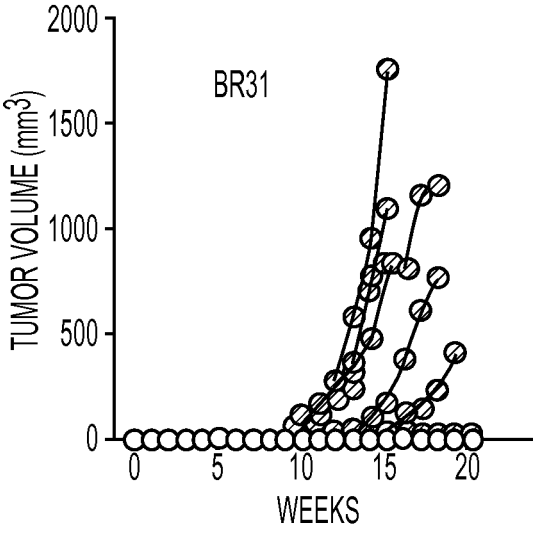

BR31
TUMOR VOLUME (mm3)
2000
1500
1000
500
0
0
5
10
15
20
WEEKS

FIG. 24

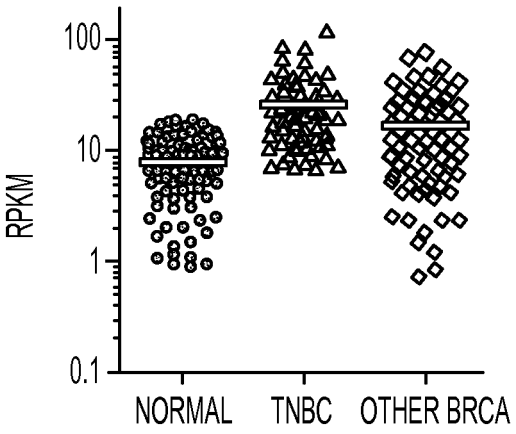

100
10
1
0.1
RPKM
NORMAL
TNBC
OTHER BRCA

FIG. 25

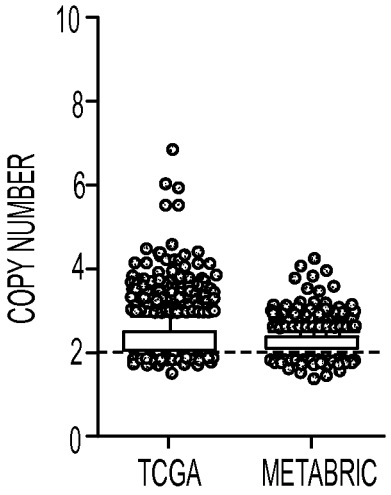

10
8
6
4
2
0
COPY NUMBER
TCGA
METABRIC

FIG. 26

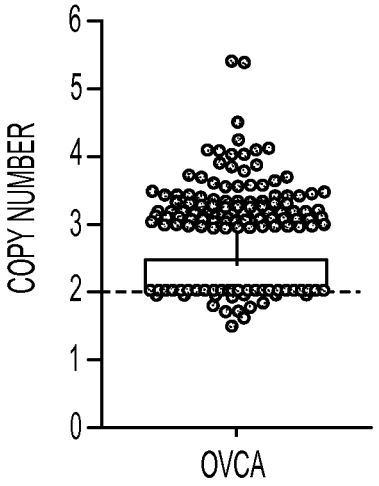

COPY NUMBER
6
5
4
3
2
1
0
OVCA

FIG. 27

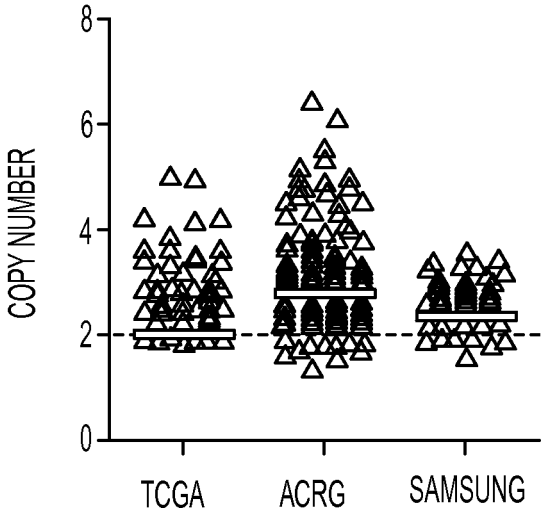

COPY NUMBER
8
6
4
2
0
TCGA
ACRG
SAMSUNG

FIG. 28

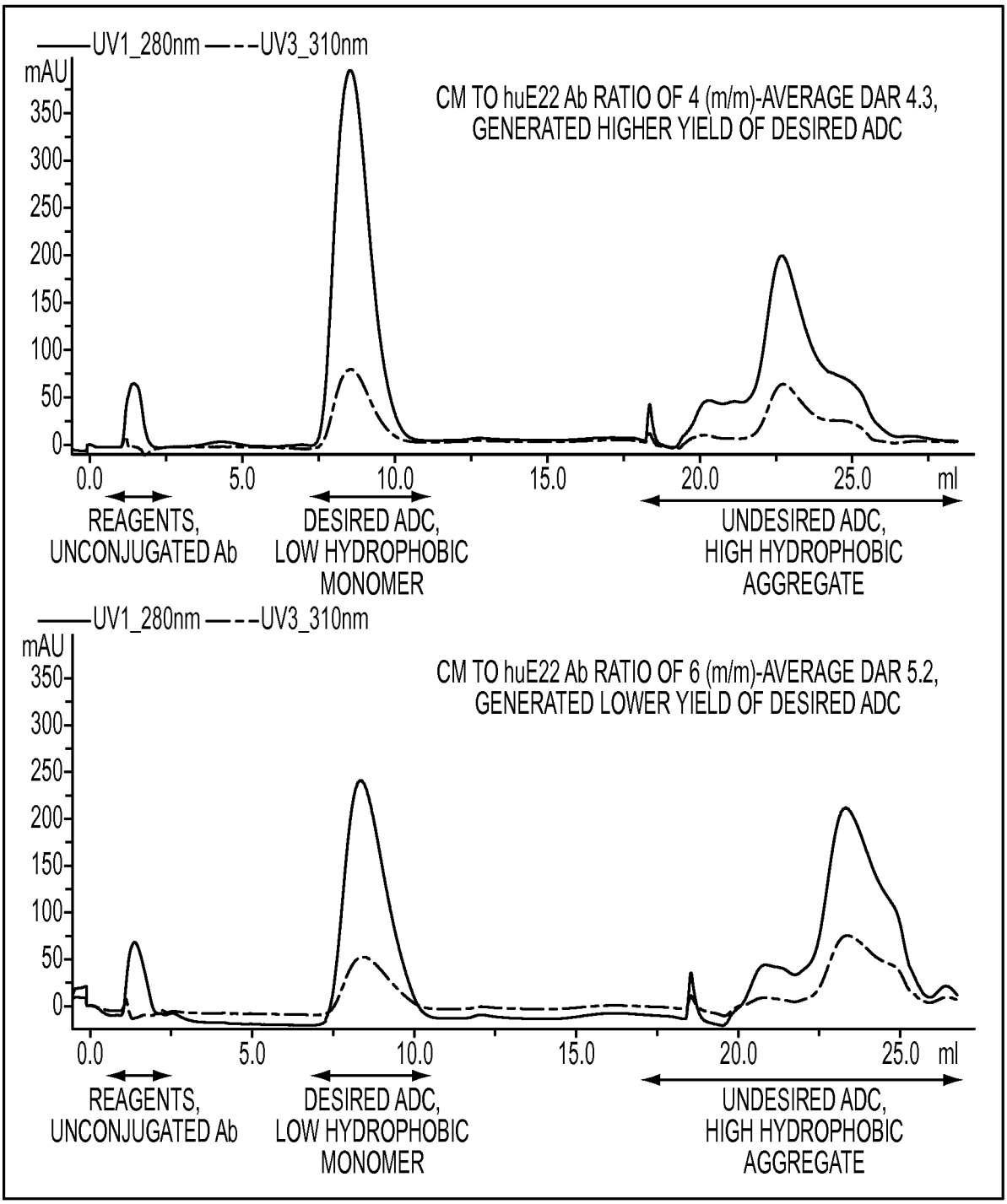

UV1_280nm
UV3_310nm
mAU
350
300
250
200
150
100
50
0
CM TO huE22 Ab RATIO OF 4 (m/m)-AVERAGE DAR 4.3,
GENERATED HIGHER YIELD OF DESIRED ADC
0.0
5.0
10.0
15.0
20.0
25.0
ml
REAGENTS,
UNCONJUGATED Ab
DESIRED ADC,
LOW HYDROPHOBIC
MONOMER
UNDESIRED ADC,
HIGH HYDROPHOBIC
AGGREGATE
UV1_280nm
UV3_310nm
mAU
350
300
250
200
150
100
50
0
CM TO huE22 Ab RATIO OF 6 (m/m)-AVERAGE DAR 5.2,
GENERATED LOWER YIELD OF DESIRED ADC
0.0
5.0
10.0
15.0
20.0
25.0
ml
REAGENTS,
UNCONJUGATED Ab
DESIRED ADC,
LOW HYDROPHOBIC
MONOMER
UNDESIRED ADC,
HIGH HYDROPHOBIC
AGGREGATE

FIG. 29

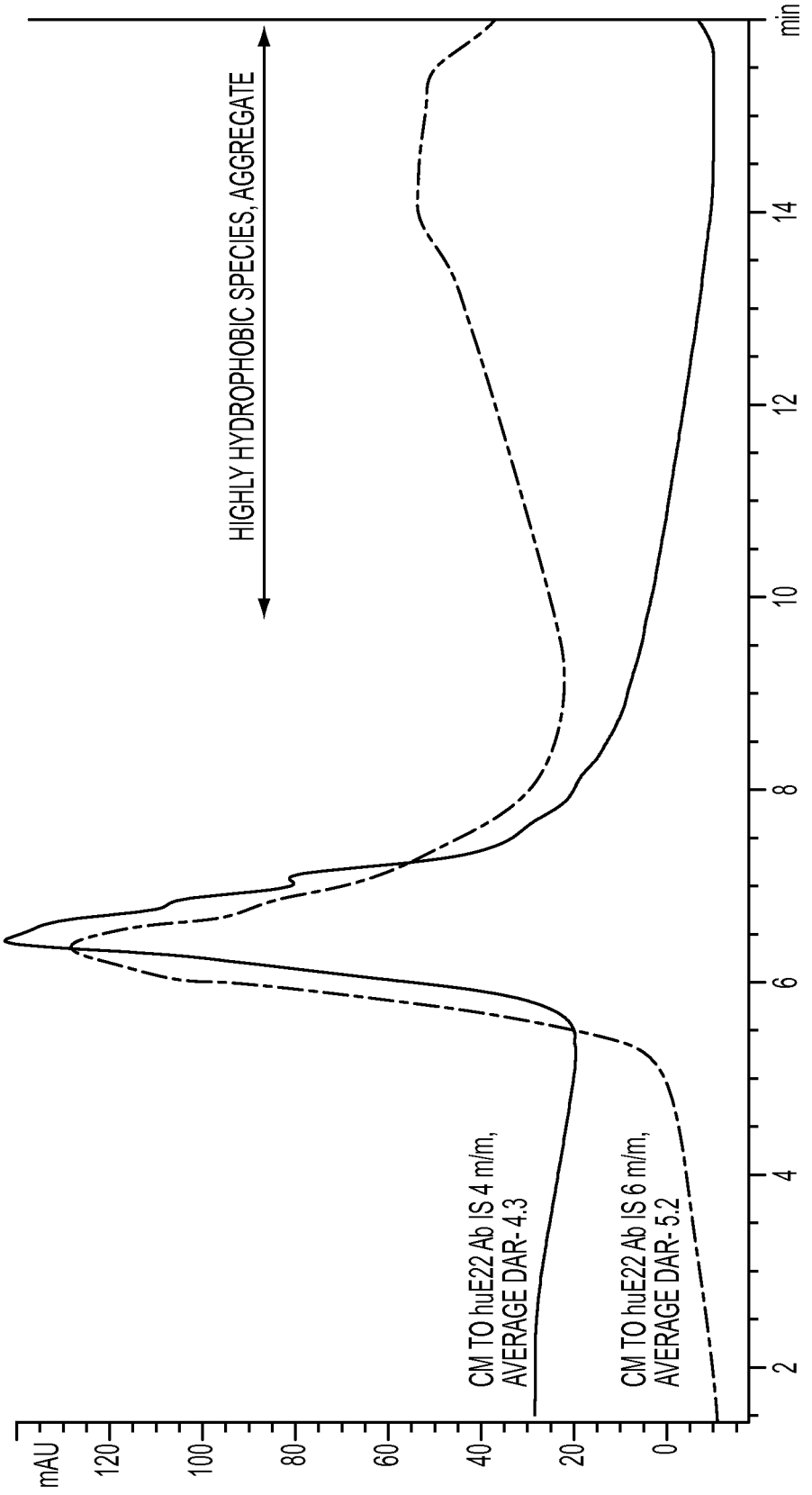

HIGHLY HYDROPHOBIC SPECIES, AGGREGATE
CM TO huE22 Ab IS 4 m/m, AVERAGE DAR- 4.3
CM TO huE22 Ab IS 6 m/m, AVERAGE DAR- 5.2
mAU
120
100
80
60
40
20
0
2
4
6
8
10
12
14
min

FIG. 30