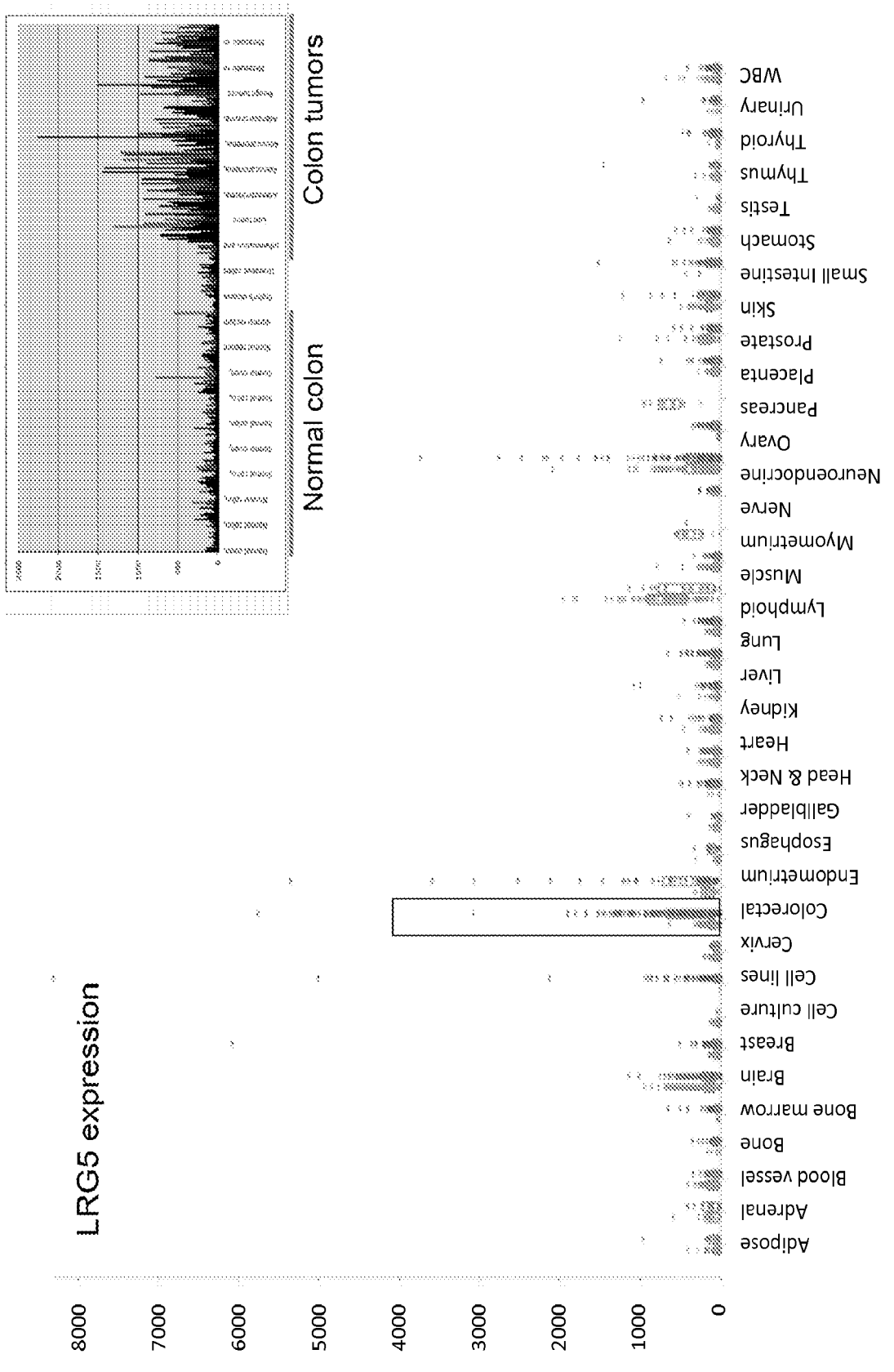

LRG5 expression
8000
7000
6000
5000
4000
3000
2000
1000
0
Adipose
Adrenal
Blood vessel
Bone
Bone marrow
Brain
Breast
Cell culture
Cell lines
Cervix
Colorectal
Endometrium
Esophagus
Gallbladder
Head & Neck
Heart
Kidney
Liver
Lung
Lymphoid
Muscle
Myometrium
Nerve
Neuroendocrine
Ovary
Pancreas
Placenta
Prostate
Skin
Small Intestine
Stomach
Testis
Thymus
Thyroid
Urinary
WBC
Normal colon
Colon tumors

FIG. 1

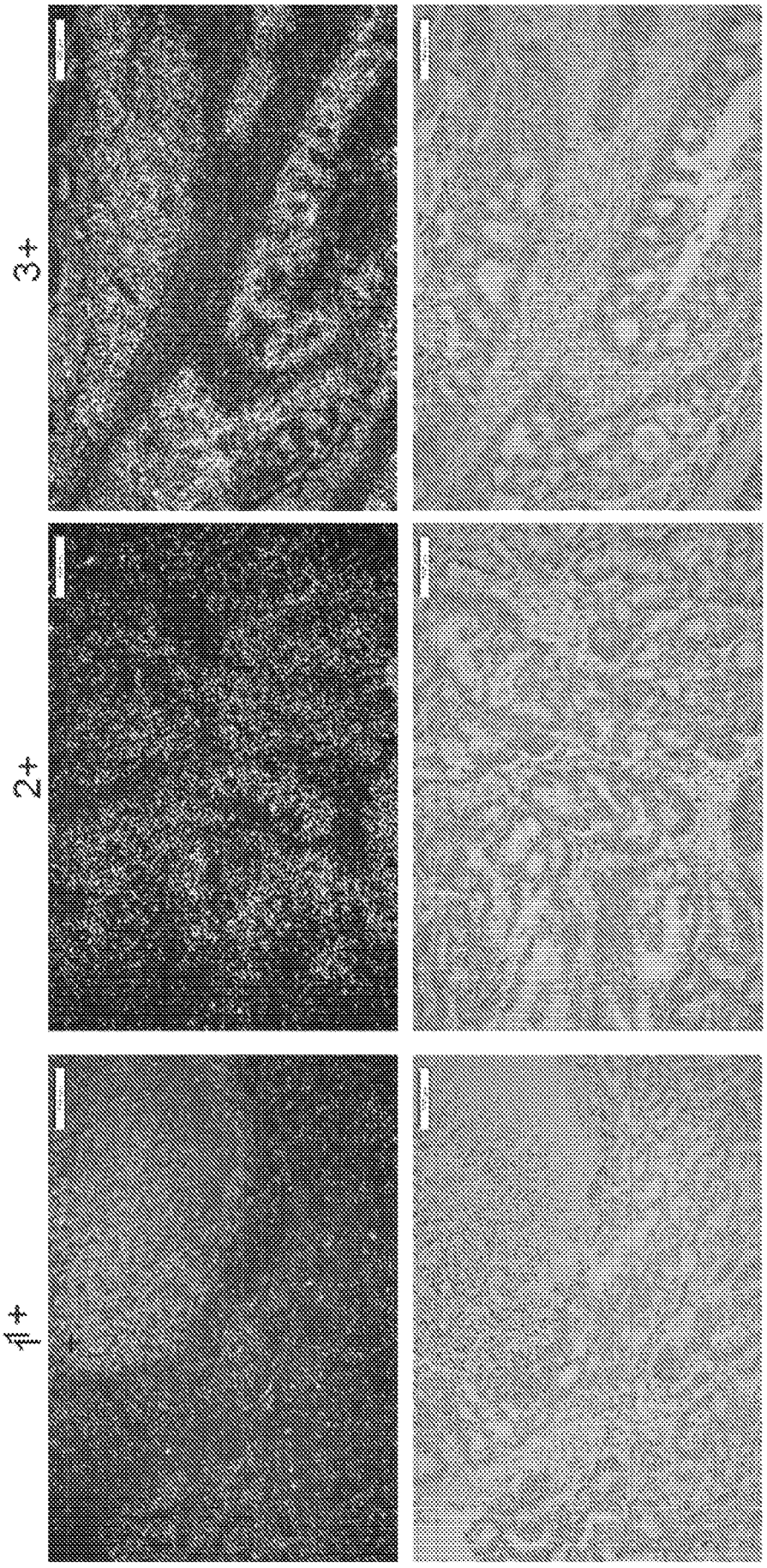


FIG. 2

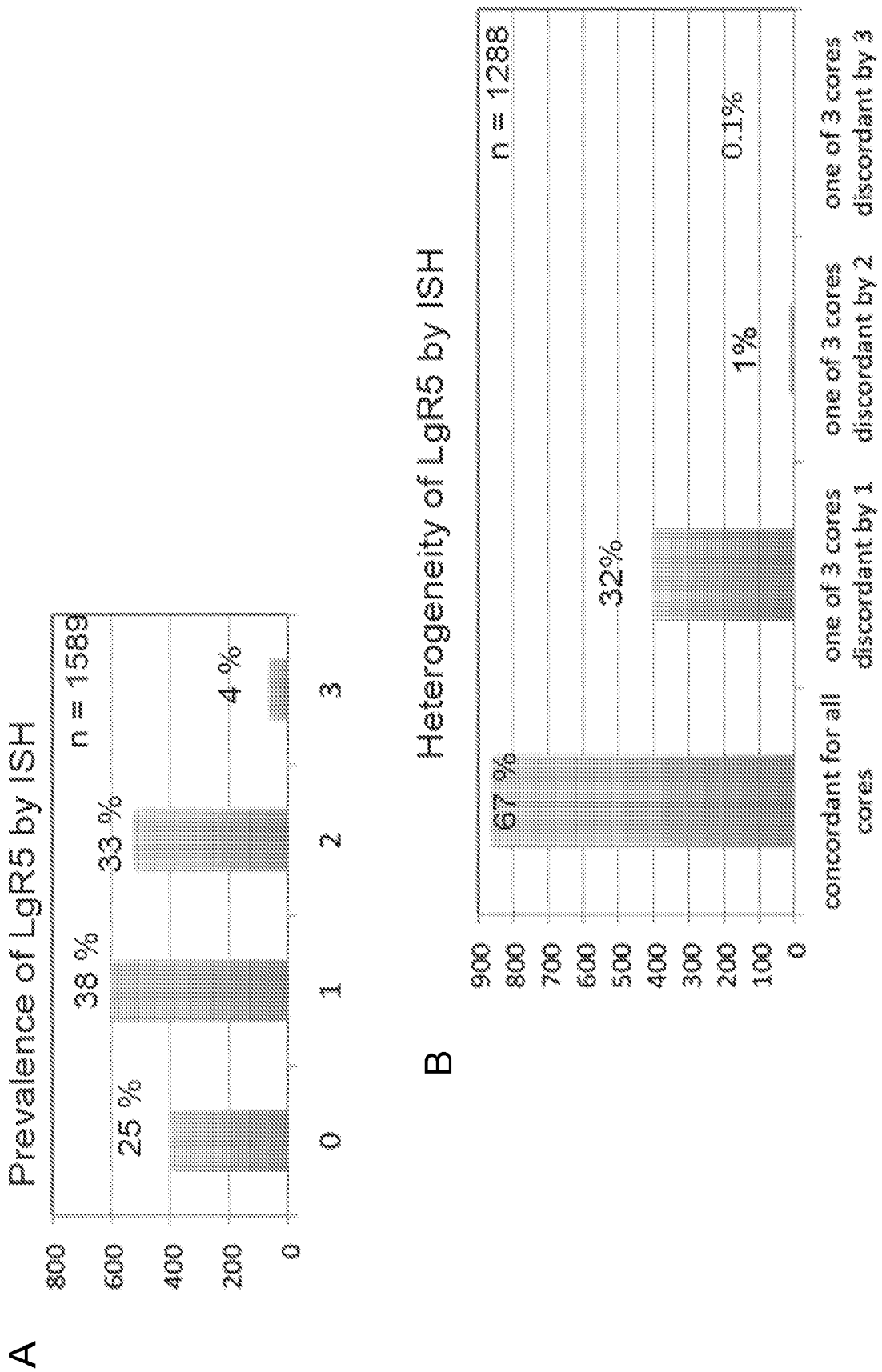

A
Prevalence of LgR5 by ISH
n = 1589
38 %
33 %
25 %
4 %
0
1
2
3
800
600
400
200
0
B
Heterogeneity of LgR5 by ISH
n = 1288
67 %
32%
1%
0.1%
900
800
700
600
500
400
300
200
100
0
concordant for all cores
one of 3 cores discordant by 1
one of 3 cores discordant by 2
one of 3 cores discordant by 3

FIG. 3

Anti-LgR5 Monoclonal Antibodies

Antibody	Epitope Region	FACS				IHC	Western Blot	Affinity (Biacore)	Affinity (Scatchard)
		Human	Cyno	Rat	Mouse				
YW353	22-123	+++	+++	neg	neg	neg	neg	1.6 nM	0.2 nM
ch8E11	22-323	+++	+++	++	+++	neg	neg	2.4 nM	0.4 nM (Hu) 0.2 nM (Mu)
hu8E11.v2	22-323	+++	+++	++	+++	neg	neg	3.1 nM	0.3-0.7 nM (Hu) 0.6-0.6 nM (Mu) 2.4-2.8 nM (Rat)
2H6	324-423	++	n.d.	n.d.	++	NS	+++	208 nM	n.d.
3G12	324-423	+++	n.d.	n.d.	+	NS	+++	72 nM	n.d.

n.d. = not determined
NS = some nonspecific binding

FIG. 4

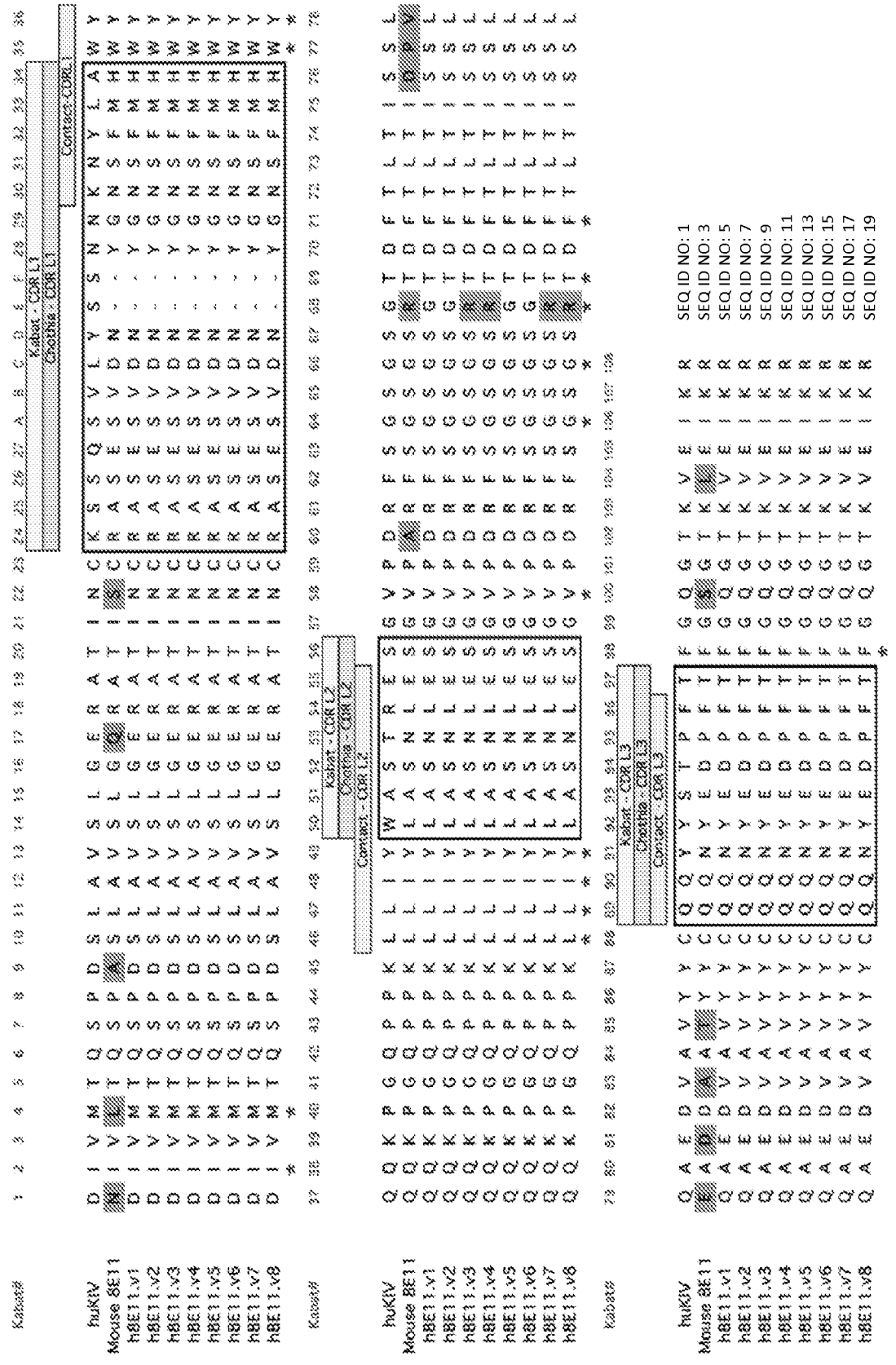

Kabat - CDR L1
Chothia - CDR L1
Contact - CDR L1
Kabat - CDR L2
Chothia - CDR L2
Contact - CDR L2
Kabat - CDR L3
Chothia - CDR L3
Contact - CDR L3
SEQ ID NO: 1
SEQ ID NO: 3
SEQ ID NO: 5
SEQ ID NO: 7
SEQ ID NO: 9
SEQ ID NO: 11
SEQ ID NO: 13
SEQ ID NO: 15
SEQ ID NO: 17
SEQ ID NO: 19

FIG. 5

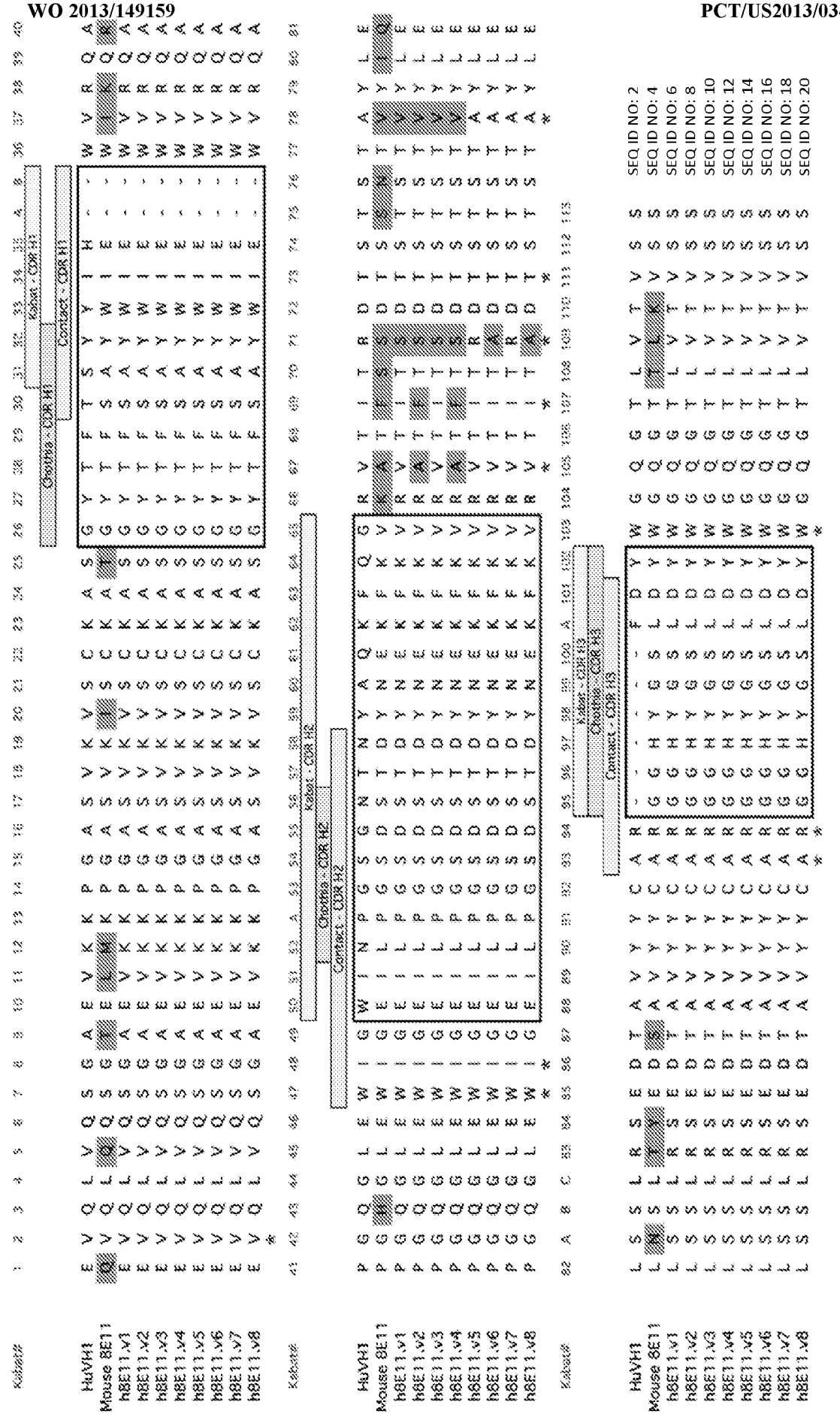

Kabat
HuVH1
Mouse 8E11
h8E11.v1
h8E11.v2
h8E11.v3
h8E11.v4
h8E11.v5
h8E11.v6
h8E11.v7
h8E11.v8
Chothia - CDR H1
Kabat - CDR H1
Contact - CDR H1
Kabat - CDR H2
Chothia - CDR H2
Contact - CDR H2
Kabat - CDR H3
Chothia - CDR H3
Contact - CDR H3
SEQ ID NO: 2
SEQ ID NO: 4
SEQ ID NO: 6
SEQ ID NO: 8
SEQ ID NO: 10
SEQ ID NO: 12
SEQ ID NO: 14
SEQ ID NO: 16
SEQ ID NO: 18
SEQ ID NO: 20

FIG. 6

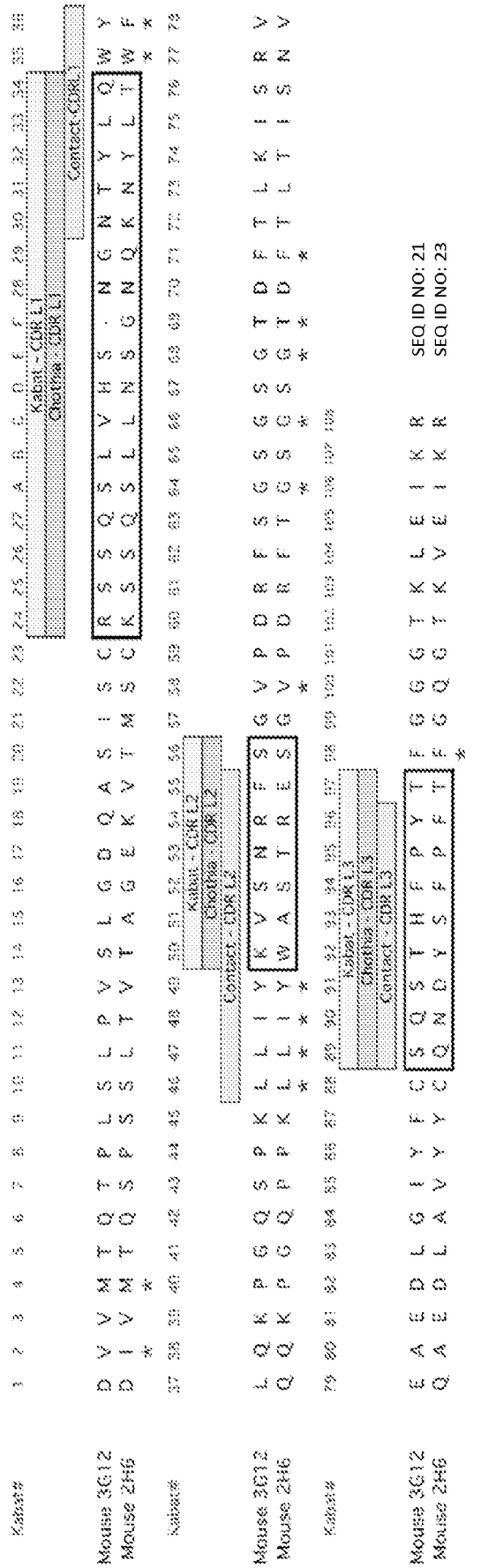

Kabat#
Mouse 3G12
Mouse 2H6
Kabat - CDR L1
Chothia - CDR L1
Contact - CDR L1
Kabat - CDR L2
Chothia - CDR L2
Contact - CDR L2
Kabat - CDR L3
Chothia - CDR L3
Contact - CDR L3
SEQ ID NO: 21
SEQ ID NO: 23

FIG. 7

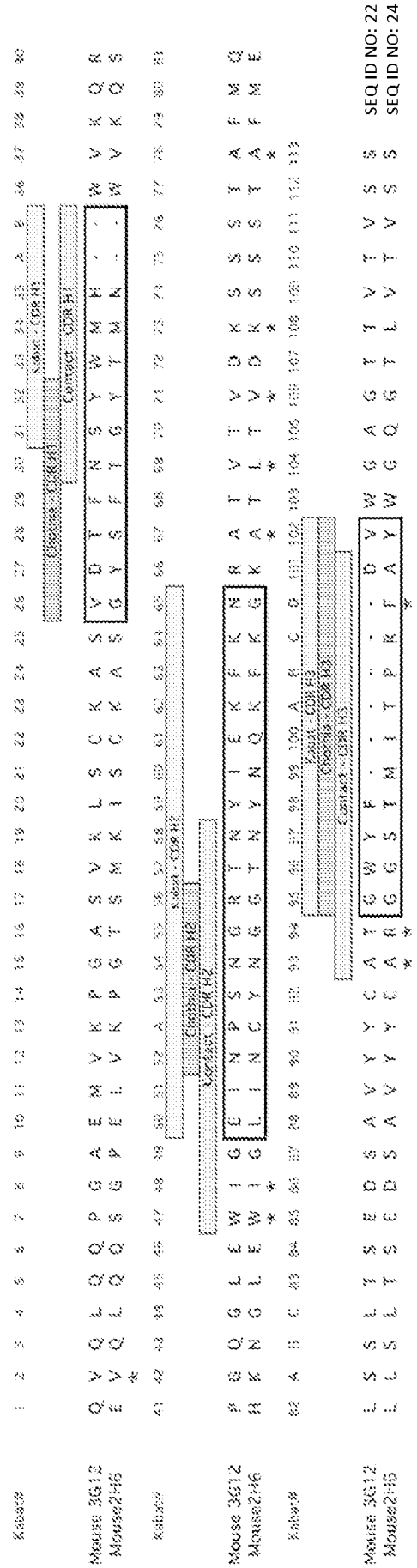


FIG. 8

	VL (KappaIV)	VH (Group I)	Kon($10^5 M^{-1}S^{-1}$)	Koff($10^{-4}S^{-1}$)	KD(nM)
h8E11.v1	CDR graft	CDR graft + 71S/78V	1.53	7.72	5.05
h8E11.v2	CDR graft	CDR graft + 67A/69F/71S/78V	2.79	8.53	3.10
h8E11.v3	CDR graft + 68R	CDR graft + 71S/78V	1.12	5.3	4.73
h8E11.v4	CDR graft + 68R	CDR graft + 67A/69F/71S/78V	2.54	9.22	3.63
h8E11.v5	CDR graft	CDR graft + 71R/78A	0.65	9.33	14.35
h8E11.v6	CDR graft	CDR graft + 71A/78A	1.43	20.2	14.13
h8E11.v7	CDR graft + 68R	CDR graft + 71R/78A	1.17	25.8	22.05
h8E11.v8	CDR graft + 68R	CDR graft + 71A/78A	2.42	21.7	8.97
Chimeric 8E11	Mouse 8E11 VL	Mouse 8E11 VH	2.1	6.4	3.00

FIG. 9

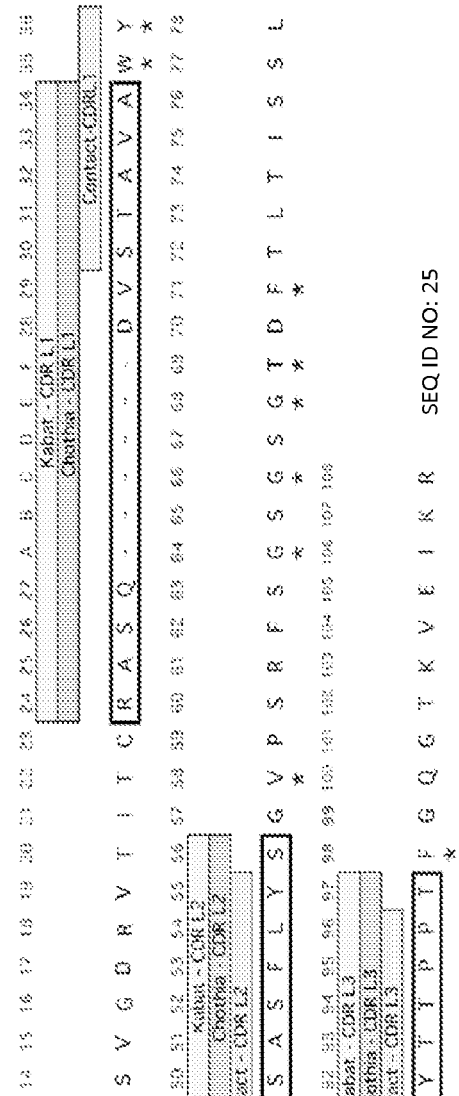

Kabat - CDR L1
Chothia - CDR L1
Contact - CDR L1
Kabat - CDR L2
Chothia - CDR L2
Contact - CDR L2
Kabat - CDR L3
Chothia - CDR L3
Contact - CDR L3
SEQ ID NO: 25

FIG. 10

Kabat - CDR H1
Chothia - CDR H1
Contact - CDR H1
Kabat - CDR H2
Chothia - CDR H2
Contact - CDR H2
Kabat - CDR H3
Chothia - CDR H3
Contact - CDR H3
SEQ ID NO: 26

FIG. 11

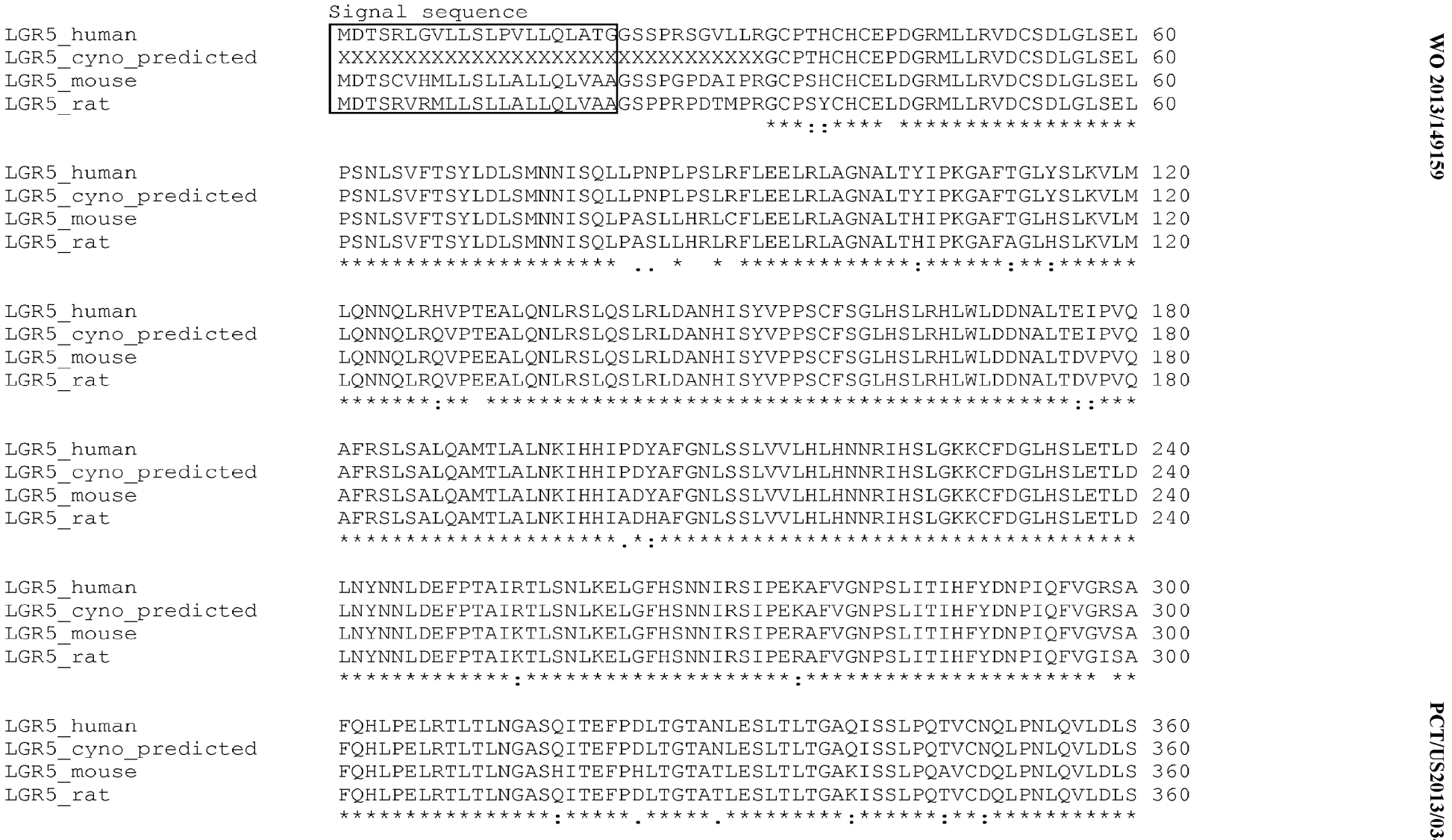

Signal sequence
LGR5_human MDTSRLGVLLSLPVLLQLATGGSSPRSGVLLRGCPTHCHCEPDGRMLLRVDCSDLGLSEL 60
LGR5_cyno_predicted XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXGCPTHCHCEPDGRMLLRVDCSDLGLSEL 60
LGR5_mouse MDTSCVHMLLSLLALLQLVAAGSSPGPDAIPRGCPSHCHCELDGRMLLRVDCSDLGLSEL 60
LGR5_rat MDTSRVRMLLSLLALLQLVAAGSPPRPDTMPRGCPSYCHCELDGRMLLRVDCSDLGLSEL 60
LGR5_human PSNLSVFTSYLDLSMNNISQLLPNPLPSLRFLEELRLAGNALTYIPKGAFTGLYSLKVLM 120
LGR5_cyno_predicted PSNLSVFTSYLDLSMNNISQLLPNPLPSLRFLEELRLAGNALTYIPKGAFTGLYSLKVLM 120
LGR5_mouse PSNLSVFTSYLDLSMNNISQLPASLLHRLCFLEELRLAGNALTHIPKGAFTGLHSLKVLM 120
LGR5_rat PSNLSVFTSYLDLSMNNISQLPASLLHRLRFLEELRLAGNALTHIPKGAFAGLHSLKVLM 120
LGR5_human LQNNQLRHVPTEALQNLRSLQSLRLDANHISYVPPSCFSGLHSLRHLWLDDNALTEIPVQ 180
LGR5_cyno_predicted LQNNQLRQVPTEALQNLRSLQSLRLDANHISYVPPSCFSGLHSLRHLWLDDNALTEIPVQ 180
LGR5_mouse LQNNQLRQVPEEALQNLRSLQSLRLDANHISYVPPSCFSGLHSLRHLWLDDNALTDVPVQ 180
LGR5_rat LQNNQLRQVPEEALQNLRSLQSLRLDANHISYVPPSCFSGLHSLRHLWLDDNALTDVPVQ 180
LGR5_human AFRSLSALQAMTLALNKIHHIPDYAFGNLSSLVVLHLHNNRIHSLGKKCFDGLHSLETLD 240
LGR5_cyno_predicted AFRSLSALQAMTLALNKIHHIPDYAFGNLSSLVVLHLHNNRIHSLGKKCFDGLHSLETLD 240
LGR5_mouse AFRSLSALQAMTLALNKIHHIADYAFGNLSSLVVLHLHNNRIHSLGKKCFDGLHSLETLD 240
LGR5_rat AFRSLSALQAMTLALNKIHHIADHAFGNLSSLVVLHLHNNRIHSLGKKCFDGLHSLETLD 240
LGR5_human LNYNNLDEFPTAIRTLSNLKELGFHSNNIRSIPEKAFVGNPSLITIHFYDNPIQFVGRSA 300
LGR5_cyno_predicted LNYNNLDEFPTAIRTLSNLKELGFHSNNIRSIPEKAFVGNPSLITIHFYDNPIQFVGRSA 300
LGR5_mouse LNYNNLDEFPTAIKTLSNLKELGFHSNNIRSIPERAFVGNPSLITIHFYDNPIQFVGVSA 300
LGR5_rat LNYNNLDEFPTAIKTLSNLKELGFHSNNIRSIPERAFVGNPSLITIHFYDNPIQFVGISA 300
LGR5_human FQHLPELRTLTLNGASQITEFPDLTGTANLESLTLTGAQISSLPQTVCNQLPNLQVLDLS 360
LGR5_cyno_predicted FQHLPELRTLTLNGASQITEFPDLTGTANLESLTLTGAQISSLPQTVCNQLPNLQVLDLS 360
LGR5_mouse FQHLPELRTLTLNGASHITEFPHLTGTATLESLTLTGAKISSLPQAVCDQLPNLQVLDLS 360
LGR5_rat FQHLPELRTLTLNGASQITEFPDLTGTATLESLTLTGAKISSLPQTVCDQLPNLQVLDLS 360

FIG. 12A

```
LGR5_human      YNLLEDLPSFSVCQKLQKIDLRHNEIYEIKVDTFQQLLSLRSLNLAWNKIAIIHPNAFST 420
LGR5_cyno_predicted YNLLEDLPSFSVCQKLQKIDLRHNEIYEIKVDTFQQLLSLRSLNLAWNKIAIIHPNAFST 420
LGR5_mouse      YNLLEDLPSLSGCQKLQKIDLRHNEIYEIKGSTFQQLFNLRSLNLAWNKIAIIHPNAFST 420
LGR5_rat        YNLLEDLPSLSGCQKLQKIDLRHNEIYEIKGGTFQQLFNLRSLNLARNKIAIIHPNAFST 420
                ********:* ********************  .*****:.******* ************

LGR5_human      LPSLIKLDLSSNLLSSFPITGLHGLTHLKLTGNHALQSLISSENFPELKVIEMPYAYQCC 480
LGR5_cyno_predicted LPSLIKLDLSSNLLSSFPVTGLHGLTHLKLTGNHALQSLISSENFPELKIIEMPYAYQCC 480
LGR5_mouse      LPSLIKLDLSSNLLSSFPVTGLHGLTHLKLTGNRALQSLIPSANFPELKIIEMPSAYQCC 480
LGR5_rat        LPSLIKLDLSSNLLSSFPVTGLHGLTHLKLTGNRALQSLIPSANFPELKIIEMPYAYQCC 480
                ********************:**********.* *******:**** *****

LGR5_human      AFGVCENAYKISNQWNKGDNSSMDDLHKKDAGMFQAQDERDLEDFLLDFEEDLKALHSVQ 540
LGR5_cyno_predicted AFGVCENAYKISNQWNKGDNSSMDDLHKKDAGMFQVQDERDLEDFLLDFEEDLKALHSVQ 540
LGR5_mouse      AFGGCENVYKISNQWNKDDGNSVDDLHKKDAGLFQVQDERDLEDFLLDFEEDLKALHSVQ 540
LGR5_rat        AFGGCENVYKIPNQWNKDDSSSVDDLRKKDAGLFQVQDERDLEDFLLDFEEDLKVLHSVQ 540
                *** *** .*** .***** .*..*:*** :***** :** .********************. *****

LGR5_human      CSPSPGPFKPCEHLLDGWLIRIGVWTIAVLALTCNALVTSTVFRSPLYISPIKLLIGVIA 600
LGR5_cyno_predicted CSPSPGPFKPCEHLLDGWLIRIGVWTIAVLALTCNALVTSTVFRSPLYISPIKLLIGVIA 600
LGR5_mouse      CSPSPGPFKPCEHLFGSWLIRIGVWTTAVLALSCNALVALTVFRTPLYISSIKLLIGVIA 600
LGR5_rat        CSPPPGPFKPCEHLFGSWLIRIGVWTTAVLALSCNALVAFTVFRTPLYISSIKLLIGVIA 600
                ***.**************:..********** ********:******: ****:******.**********

LGR5_human      AVNMLTGVSSAVLAGVDAFTFGSFARHGAWWENGVGCHVIGFLSIFASESSVFLLTLAAL 660
LGR5_cyno_predicted VVNMLTGVSSAVLAGVDAFTFGSFARHGAWWENGVGCQVIGFLSIFASESSVFLLTLAAL 660
LGR5_mouse      VVDILMGVSSAVLAAVDAFTFGRFAQHGAWWEDGIGCQIVGFLSIFASESSIFLLTLAAL 660
LGR5_rat        VVDILMGVSSAILAVVDTFTFGSFAQHGAWWEGGIGCQIVGFLSIFASESSVFLLTLAAL 660
                .*::*  ******:** **:**** **:*******.*:**::*********:********

LGR5_human      ERGFSVKYSAKFETKAPFSSLKVIILLCALLALTMAAVPLLGGSKYGASPLCLPLPFGEP 720
LGR5_cyno_predicted ERGFSVKCSAKFETKAPFSSLKVIILLCALLALTMAAVPLLGGSEYGASPLCLPLPFGEP 720
LGR5_mouse      ERGFSVKCSSKFEVKAPLFSLRAIVLLCVLLALTIATIPLLGGSKYNASPLCLPLPFGEP 720
LGR5_rat        ERGFSVKCSSKFEMKAPLSSLKAIILLCVLLALTIATVPLLGGSEYNASPLCLPLPFGEP 720
                ******* *:**** ****: **:.*:****.******:**::********:*.********************
```

FIG. 12B

```
LGR5_human      STMGYMVALLILLNSLCFLMMTIAYTKLYCNLDKGDLENIWDCSMVKHIALLLFTNCILNC 780
LGR5_cyno_predicted STTGYMVALLILLNSLCFLMMTIAYTKLYCNLDKGDLENIWDCSMVKHIALLLFTNCILYC 780
LGR5_mouse      STTGYMVALVLLNSLCFLIMTIAYTKLYCSLEKGELENLWDCSMVKHIALLLFANCILYC 780
LGR5_rat        STTGYMVALVLLNSLCFLIMTIAYTRLYCSLEKGELENLWDCSMVKHTALLLFTNCILYC 780
                ** ********:**********:*****.*:***:***:********** *****:***** *

LGR5_human      PVAFLSFSSLINLTFISPEVIKFILLVVVPLPACLNPLLYIILFNPHFKEDLVSLRKQTYV 840
LGR5_cyno_predicted PVAFLSFSSLLNLTFISPEVIKFILLVIVPLPACLNPLLYIILFNPHFKEDLVSLGKQTYF 840
LGR5_mouse      PVAFLSFSSLLNLTFISPDVIKFILLVIVPLPSCLNPLLYIVFNPHFKEDMGSLGKHTRF 840
LGR5_rat        PVAFLSFSSLLNLTFISPEVIKFILLVIVPLPACLNPLLYIVFNPHFKEDMGSLGKQTRF 840
                ************:*********:*****:**********:********** ** *:*  .

LGR5_human      WTRSKHPSLMSINSDDVEKQSCDSTQALVTFTSSSITYDLPPSSVPSPAYPVTESCHLSS 900
LGR5_cyno_predicted WTRSKHPSLMSINSDDVEKQSCDSTQALVTFTSSSIAYDLPPSSVPSPAYPVTESCHLSS 900
LGR5_mouse      WMRSKHASLLSINSDDVEKRSCESTQALVSFTHASIAYDLPSTSGASPAYPMTESCHLSS 900
LGR5_rat        WTRAKHPSLLSINSDDVEKRSCDSTQALVSFTHASIAYDLPSDSGSSPAYPMTESCHLSS 900
                * *:**.**:**********:**:*******:**  :**:*****.  * .******:********

LGR5_human      VAFVPCL 907   SEQ ID NO: 67
LGR5_cyno_predicted VAFVPCL 907   SEQ ID NO: 69
LGR5_mouse      VAFVPCL 907   SEQ ID NO: 72
LGR5_rat        VAFVPCL 907   SEQ ID NO: 70
                *******
```

FIG. 12C

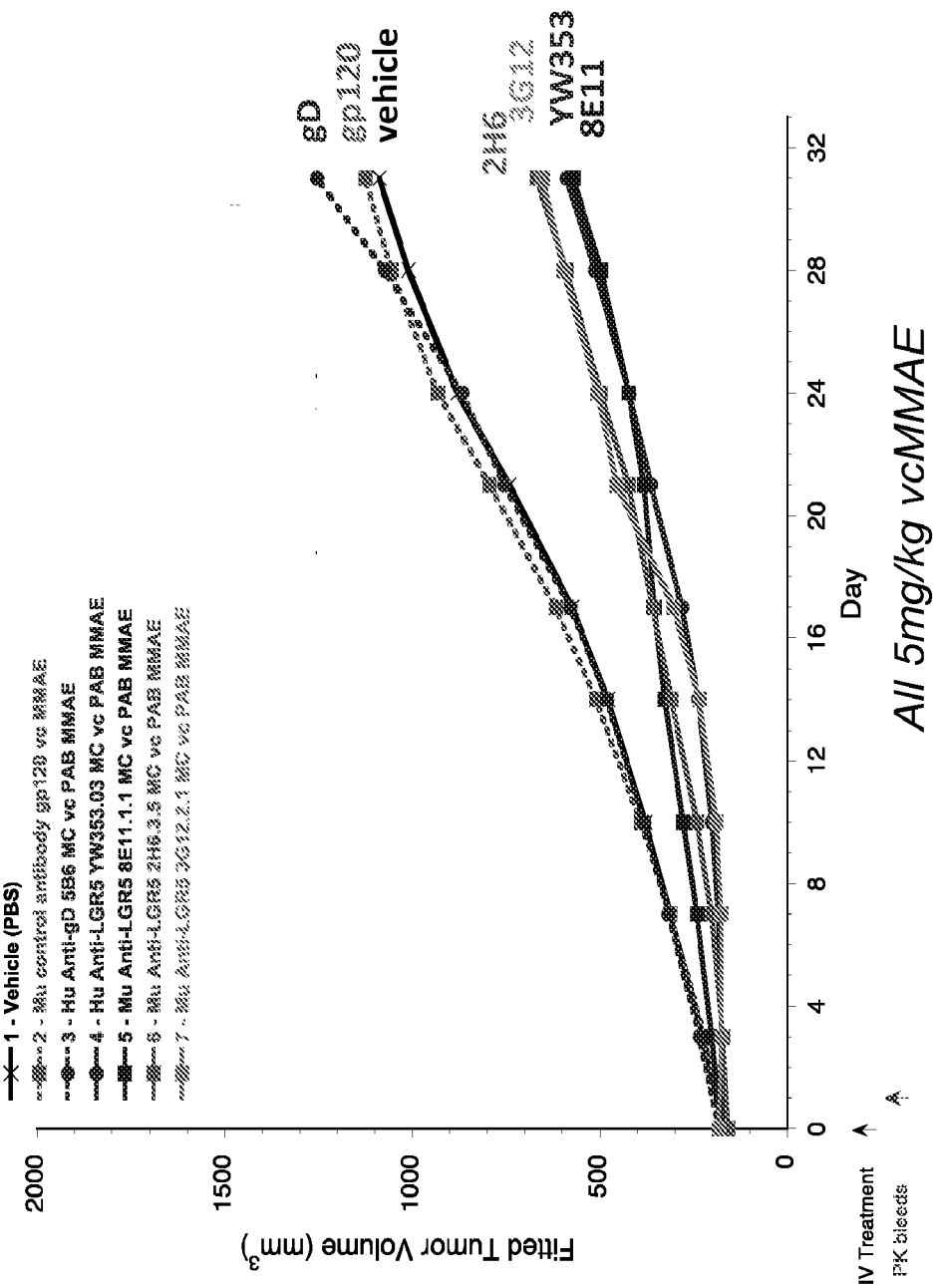

1 - Vehicle (PBS)
2 - Mu control antibody gp120 vc MMAE
3 - Hu Anti-gD 5B6 MC vc PAB MMAE
4 - Hu Anti-LGR5 YW353.03 MC vc PAB MMAE
5 - Mu Anti-LGR5 8E11.1.1 MC vc PAB MMAE
6 - Mu Anti-LGR5 2H6.3.3 MC vc PAB MMAE
7 - Mu Anti-LGR5 3G12.2.1 MC vc PAB MMAE
Fitted Tumor Volume (mm3)
2000
1500
1000
500
0
0
4
8
12
16
20
24
28
32
Day
IV Treatment
PK bleeds
gD
gp120
vehicle
2H6
3G12
YW353
8E11
All 5mg/kg vcMMAE

FIG. 13

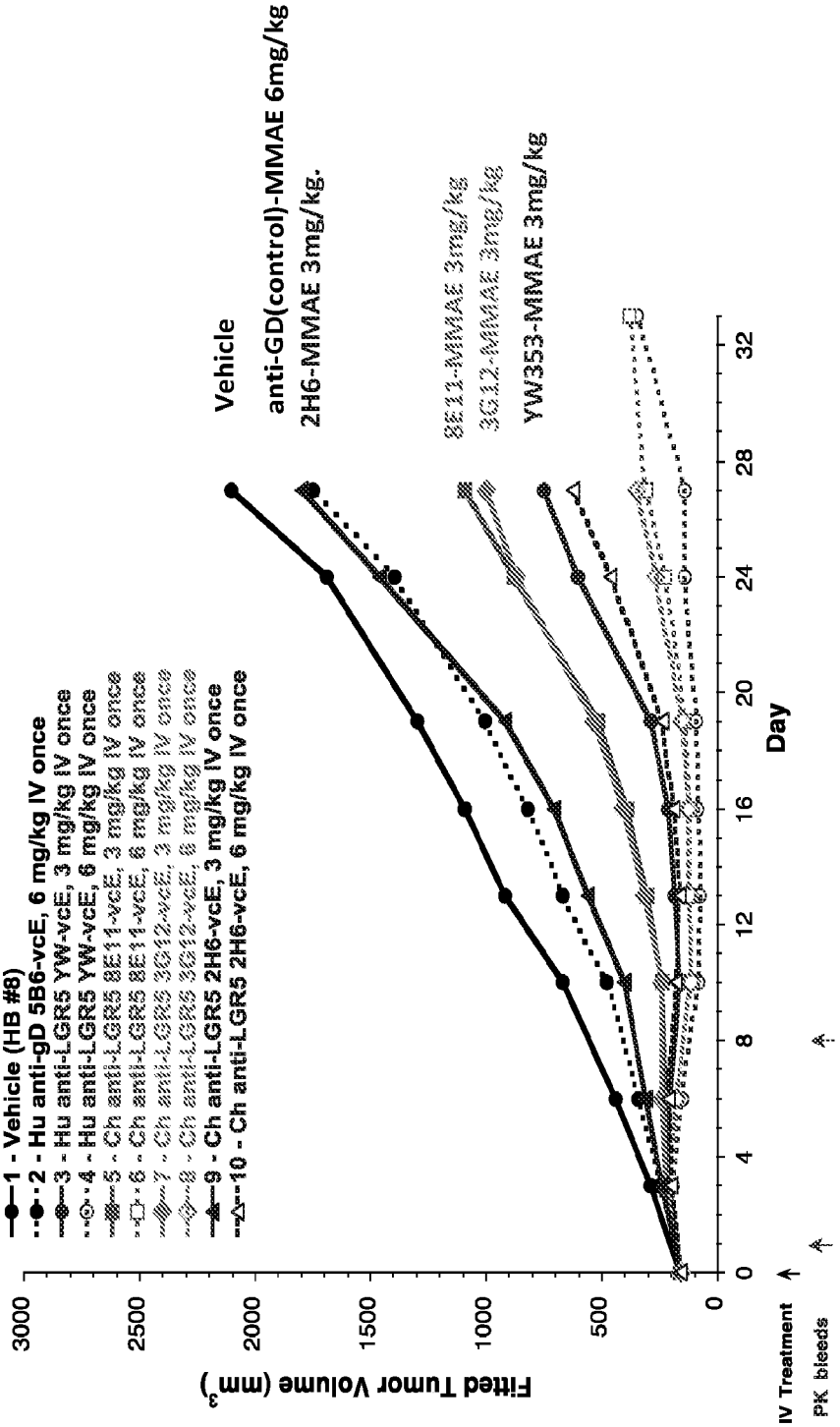

1 - Vehicle (HB #8)
2 - Hu anti-gD 5B6-vcE, 6 mg/kg IV once
3 - Hu anti-LGR5 YW-vcE, 3 mg/kg IV once
4 - Hu anti-LGR5 YW-vcE, 6 mg/kg IV once
5 - Ch anti-LGR5 8E11-vcE, 3 mg/kg IV once
6 - Ch anti-LGR5 8E11-vcE, 6 mg/kg IV once
7 - Ch anti-LGR5 3G12-vcE, 3 mg/kg IV once
8 - Ch anti-LGR5 3G12-vcE, 6 mg/kg IV once
9 - Ch anti-LGR5 2H6-vcE, 3 mg/kg IV once
10 - Ch anti-LGR5 2H6-vcE, 6 mg/kg IV once
Vehicle
anti-GD(control)-MMAE 6mg/kg
2H6-MMAE 3mg/kg.
8E11-MMAE 3mg/kg
3G12-MMAE 3mg/kg
YW353-MMAE 3mg/kg
Fitted Tumor Volume (mm3)
Day
IV Treatment
PK bleeds

FIG. 14

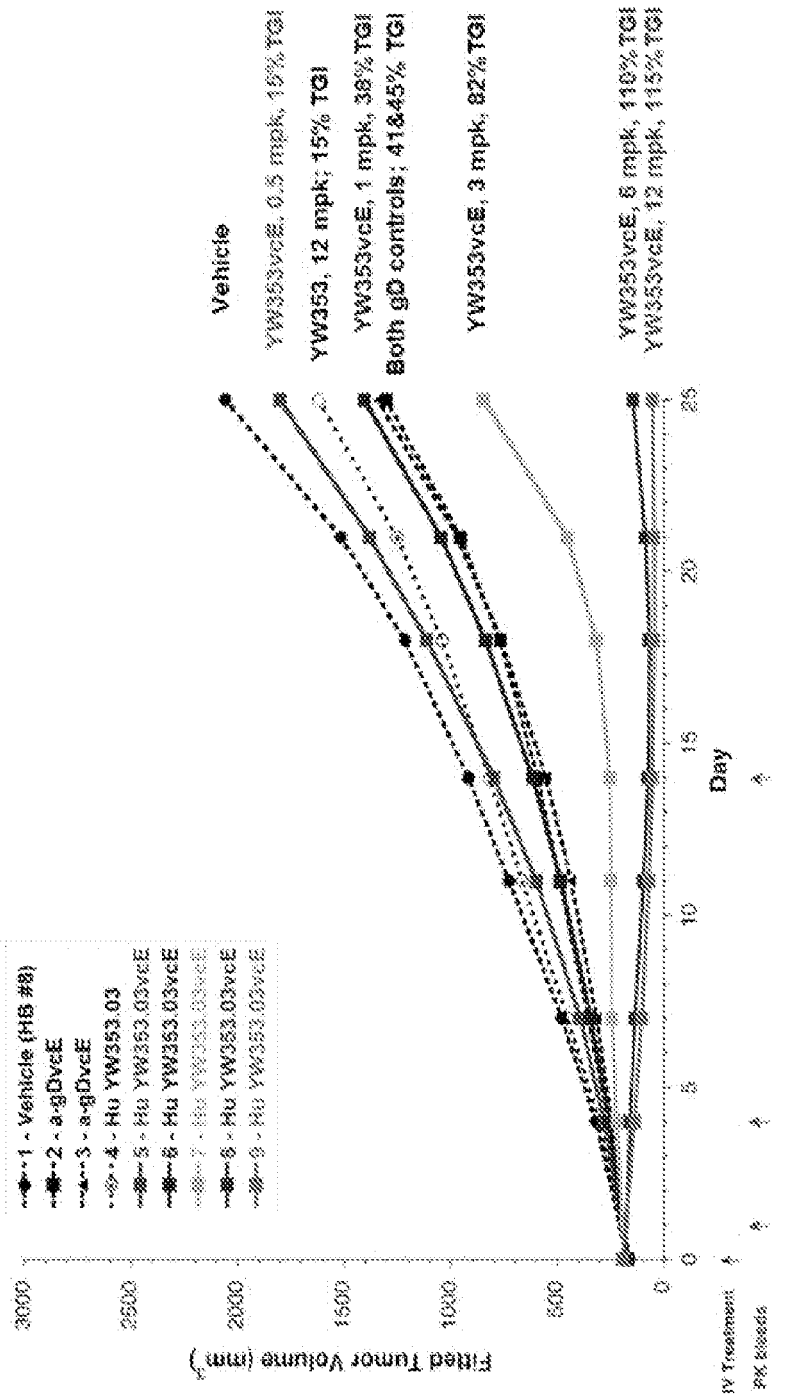

Vehicle
YW353vcE, 0.5 mpk, 15% TGI
YW353, 12 mpk; 15% TGI
YW353vcE, 1 mpk, 38% TGI
Both gD controls; 41&45% TGI
YW353vcE, 3 mpk, 82% TGI
YW353vcE, 8 mpk, 110% TGI
YW353vcE, 12 mpk, 115% TGI
1 - Vehicle (HB #8)
2 - a-gDvcE
3 - a-gDvcE
4 - Hu YW353.03
5 - Hu YW353.03vcE
6 - Hu YW353.03vcE
8 - Hu YW353.03vcE
9 - Hu YW353.03vcE
Filled Tumor Volume (mm³)
3000
2500
2000
1500
1000
500
0
0
5
10
15
20
25
Day
IV Treatment
PK Bleeds

FIG. 15

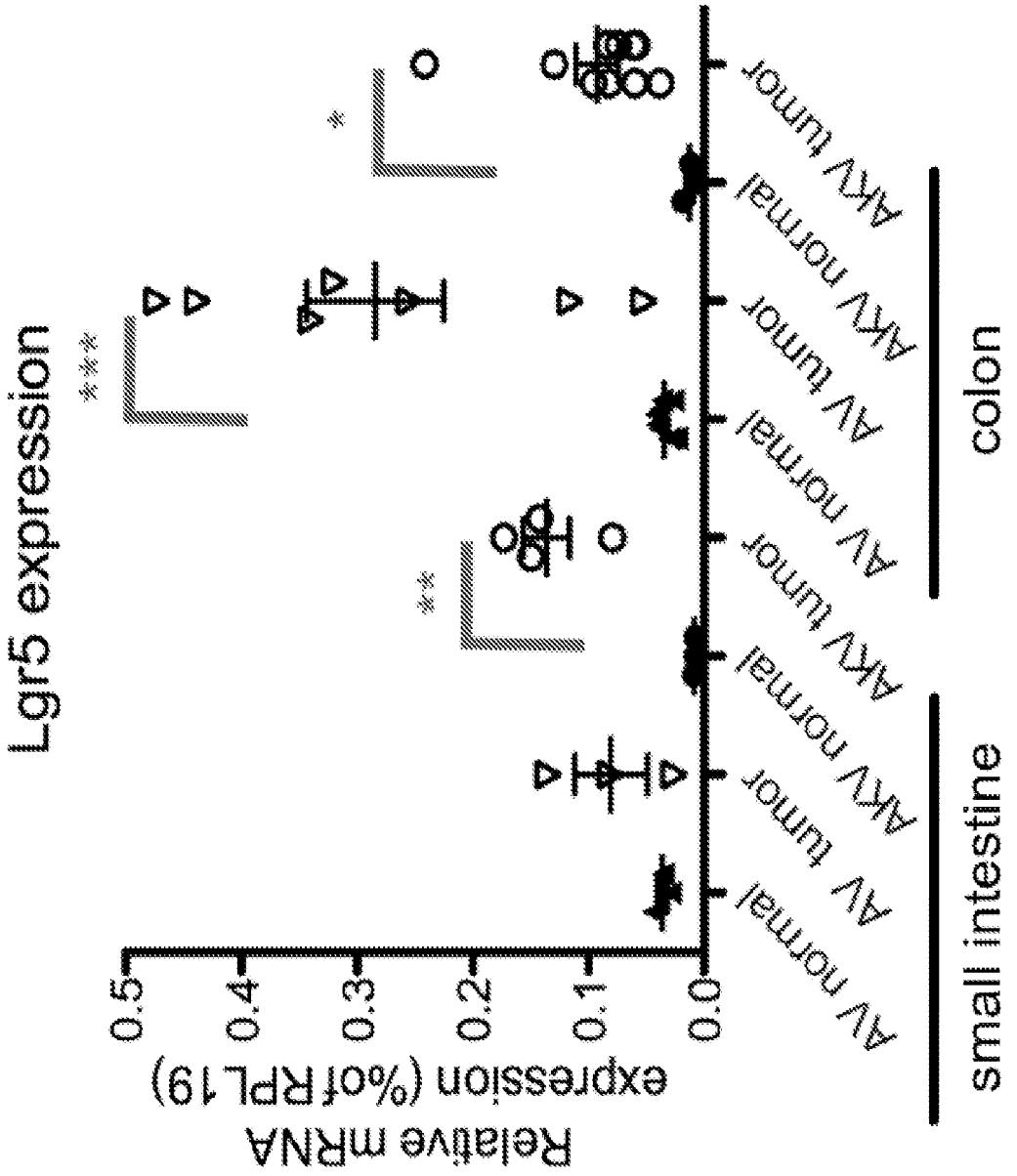

Lgr5 expression
Relative mRNA expression (%of RPL19)
0.0
0.1
0.2
0.3
0.4
0.5
***
**
*
AV normal
AV tumor
AKV normal
AKV tumor
small intestine
colon

FIG. 16

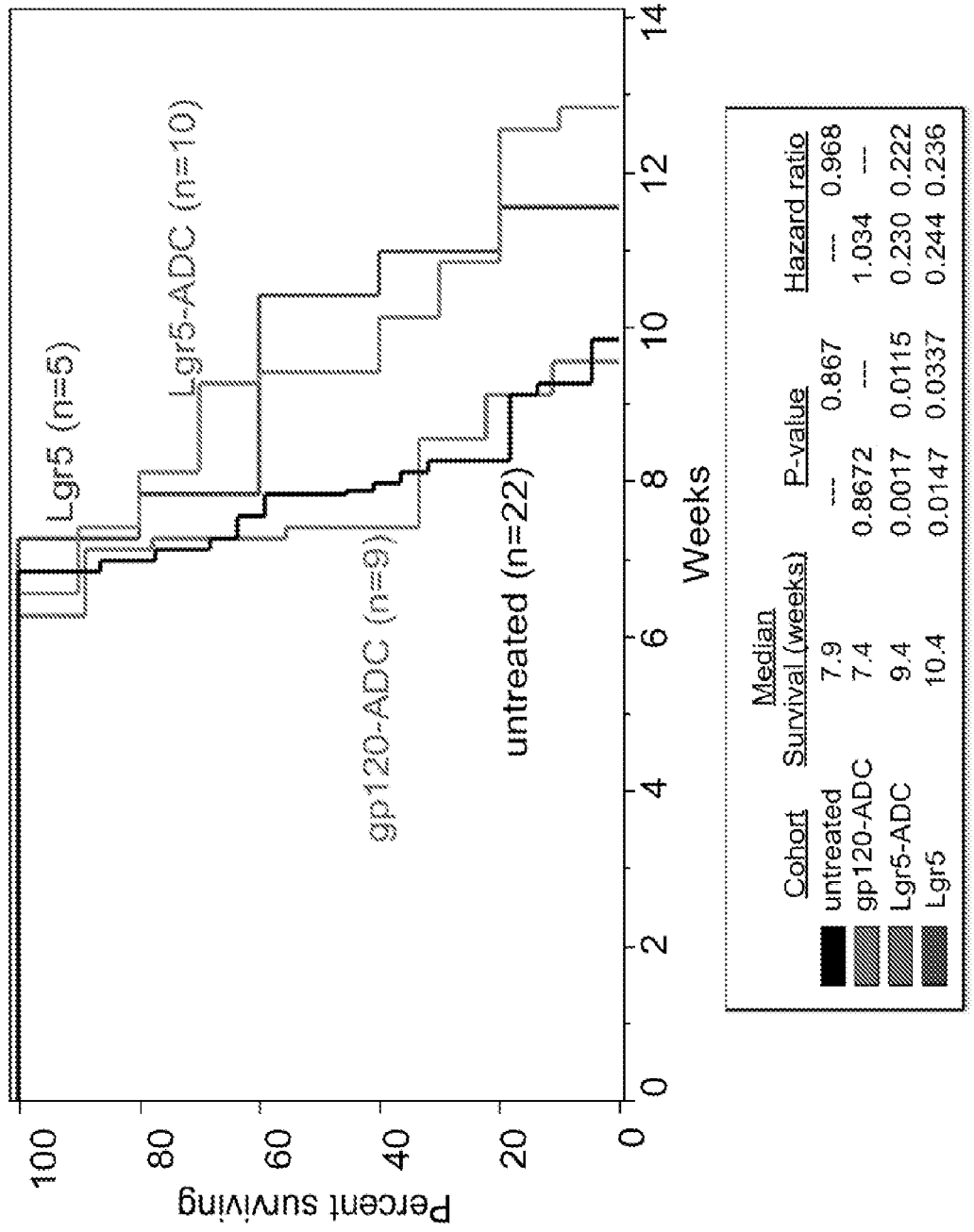

Percent surviving
100
80
60
40
20
0
0
2
4
6
8
10
12
14
Weeks
Lgr5 (n=5)
Lgr5-ADC (n=10)
gp120-ADC (n=9)
untreated (n=22)
Cohort
Median Survival (weeks)
P-value
Hazard ratio
untreated 7.9 --- 0.867 --- 0.968
gp120-ADC 7.4 0.8672 --- 1.034 ---
Lgr5-ADC 9.4 0.0017 0.0115 0.230 0.222
Lgr5 10.4 0.0147 0.0337 0.244 0.236

FIG. 17

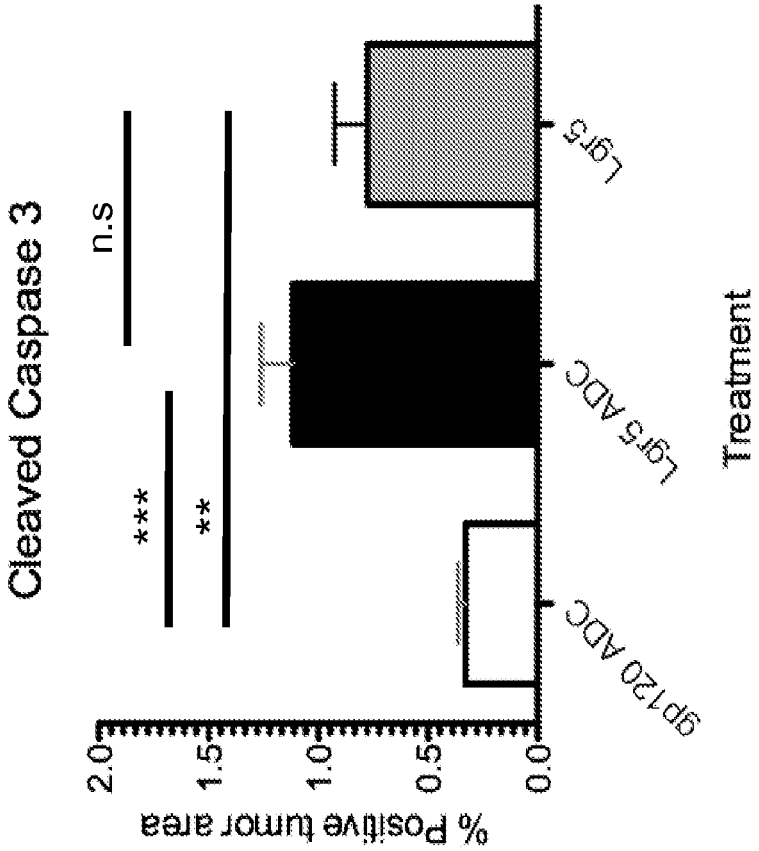

Cleaved Caspase 3
n.s
***
**
% Positive tumor area
2.0
1.5
1.0
0.5
0.0
gp120 ADC
Lgr5 ADC
Lgr5
Treatment

FIG. 18

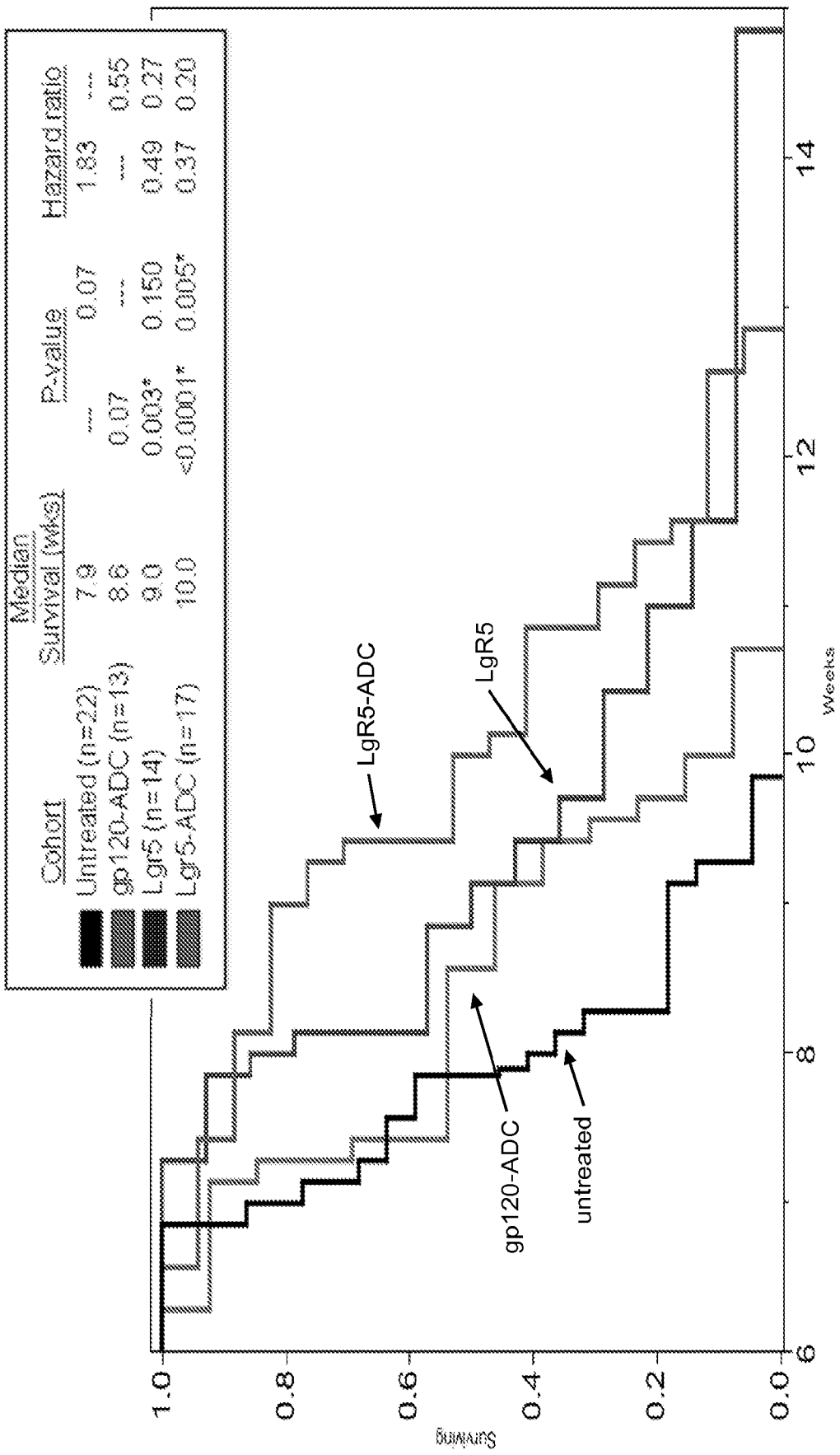

Cohort
Median Survival (wks)
P-value
Hazard ratio
Untreated (n=22) 7.9 --- 0.07 1.83 ---
gp120-ADC (n=13) 8.6 0.07 --- --- 0.55
Lgr5 (n=14) 9.0 0.003* 0.150 0.49 0.27
Lgr5-ADC (n=17) 10.0 <0.0001* 0.005* 0.37 0.20
LgR5-ADC
LgR5
gp120-ADC
untreated
Surviving
Weeks
1.0
0.8
0.6
0.4
0.2
0.0
6
8
10
12
14

FIG. 19

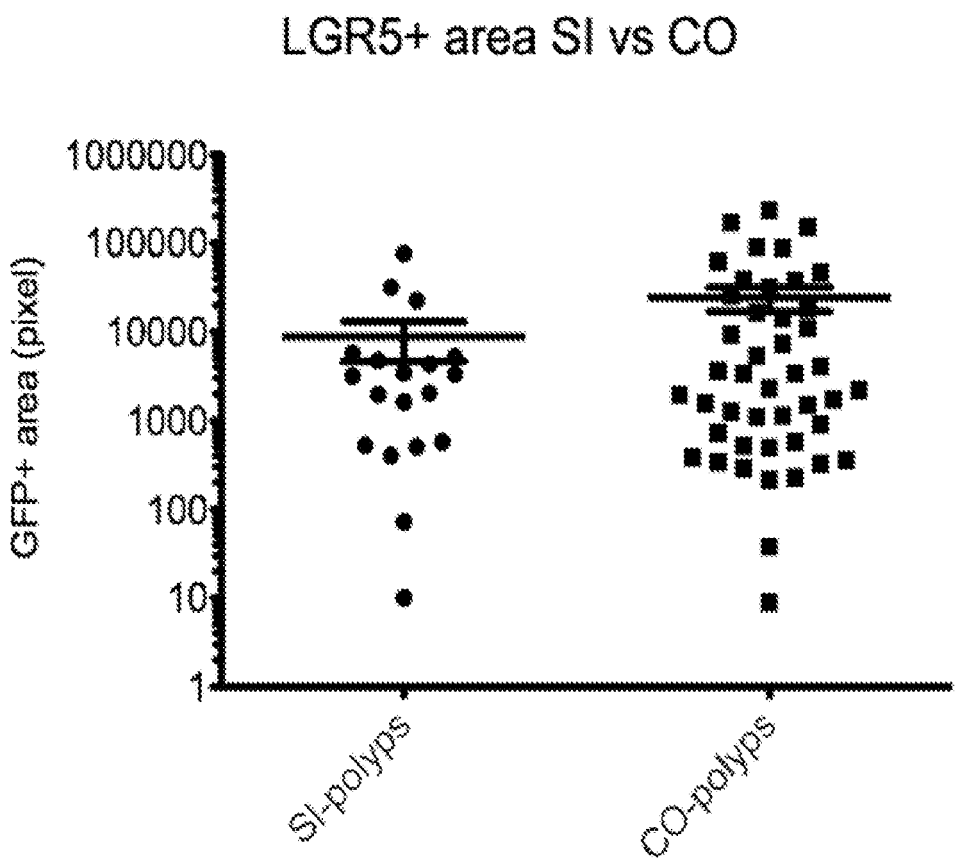

LGR5+ area SI vs CO
GFP+ area (pixel)
1000000
100000
10000
1000
100
10
1
SI-polyps
CO-polyps

FIG. 20

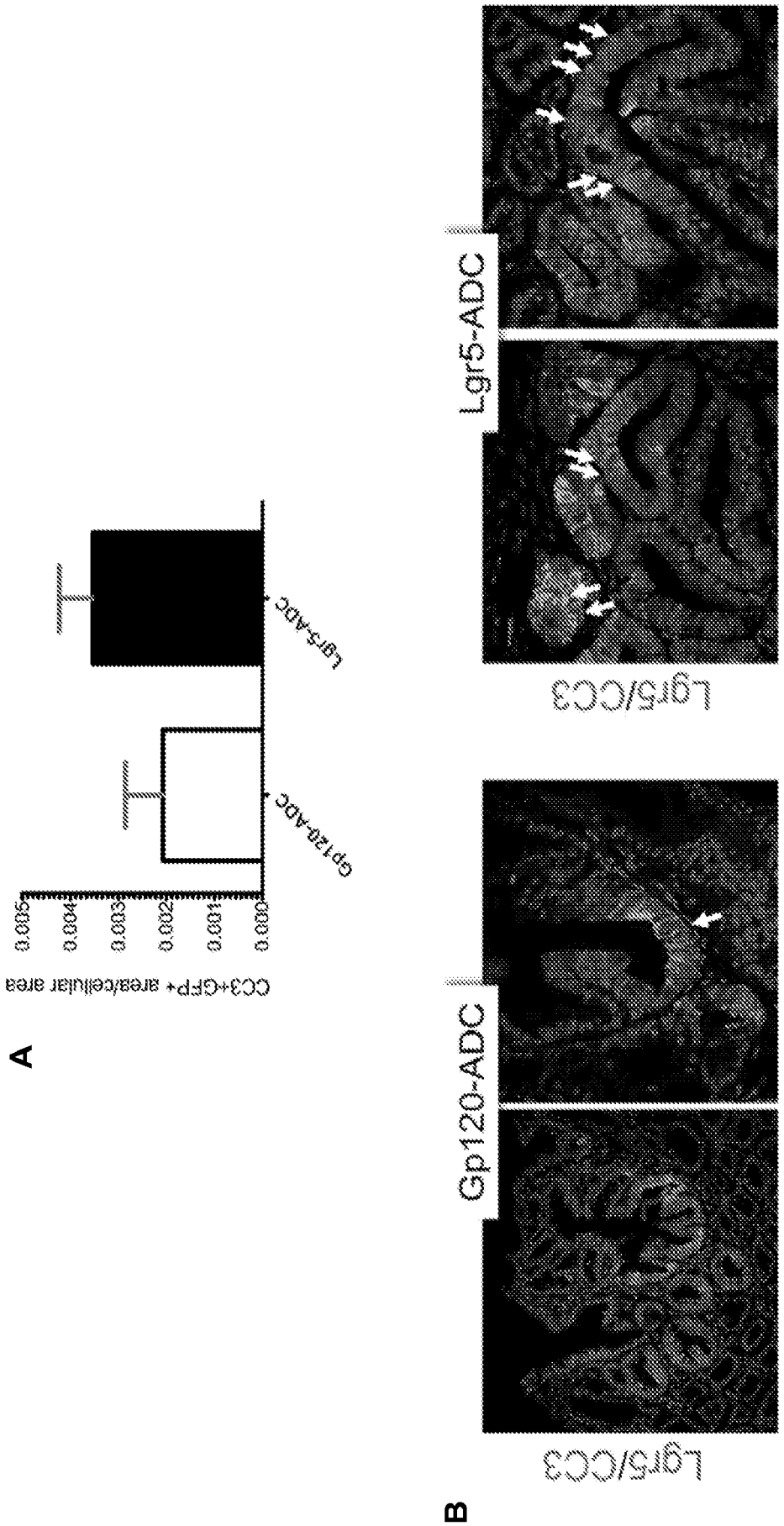

A
CC3+GFP+ area/cellular area
0.005
0.004
0.003
0.002
0.001
0.000
Gp120-ADC
Lgr5-ADC
B
Gp120-ADC
Lgr5/CC3
Lgr5-ADC
Lgr5/CC3

FIG. 21

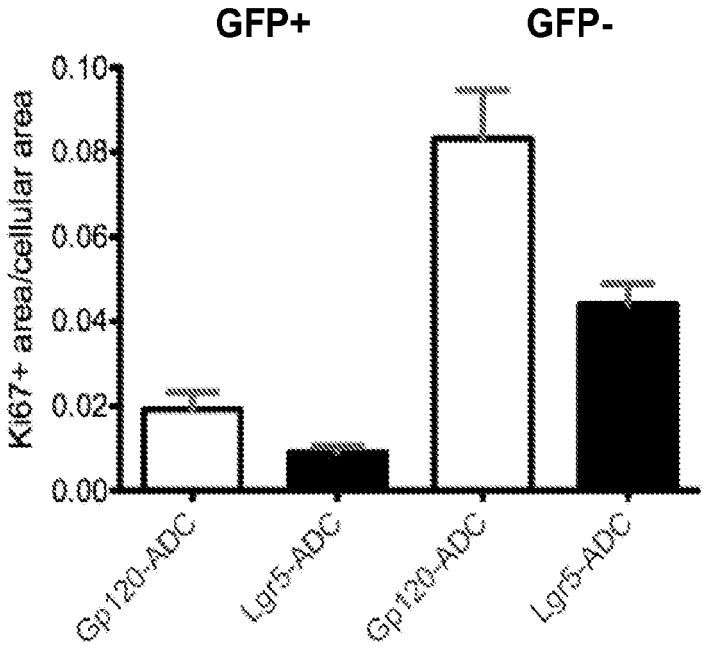

GFP+
GFP-
Ki67+ area/cellular area
0.10
0.08
0.06
0.04
0.02
0.00
Gp120-ADC
Lgr5-ADC
Gp120-ADC
Lgr5-ADC

FIG. 22

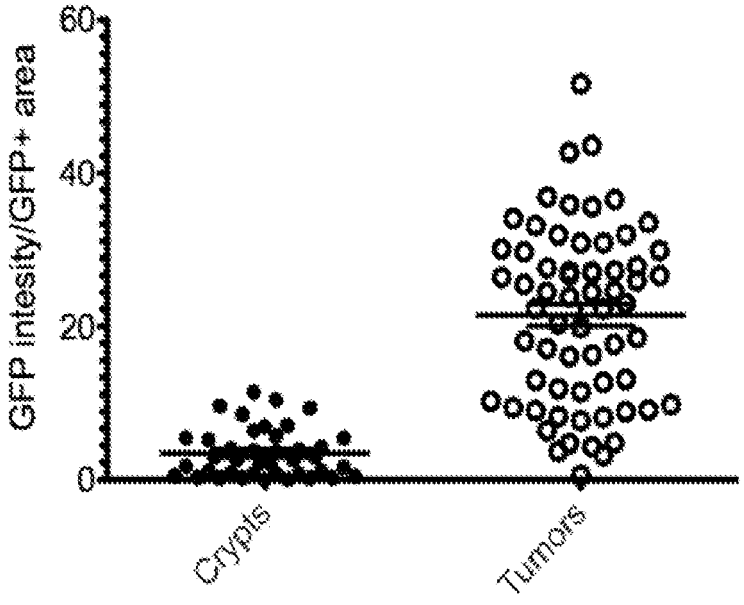

GFP intesity/GFP+ area
60
40
20
0
Crypts
Tumors

FIG. 23

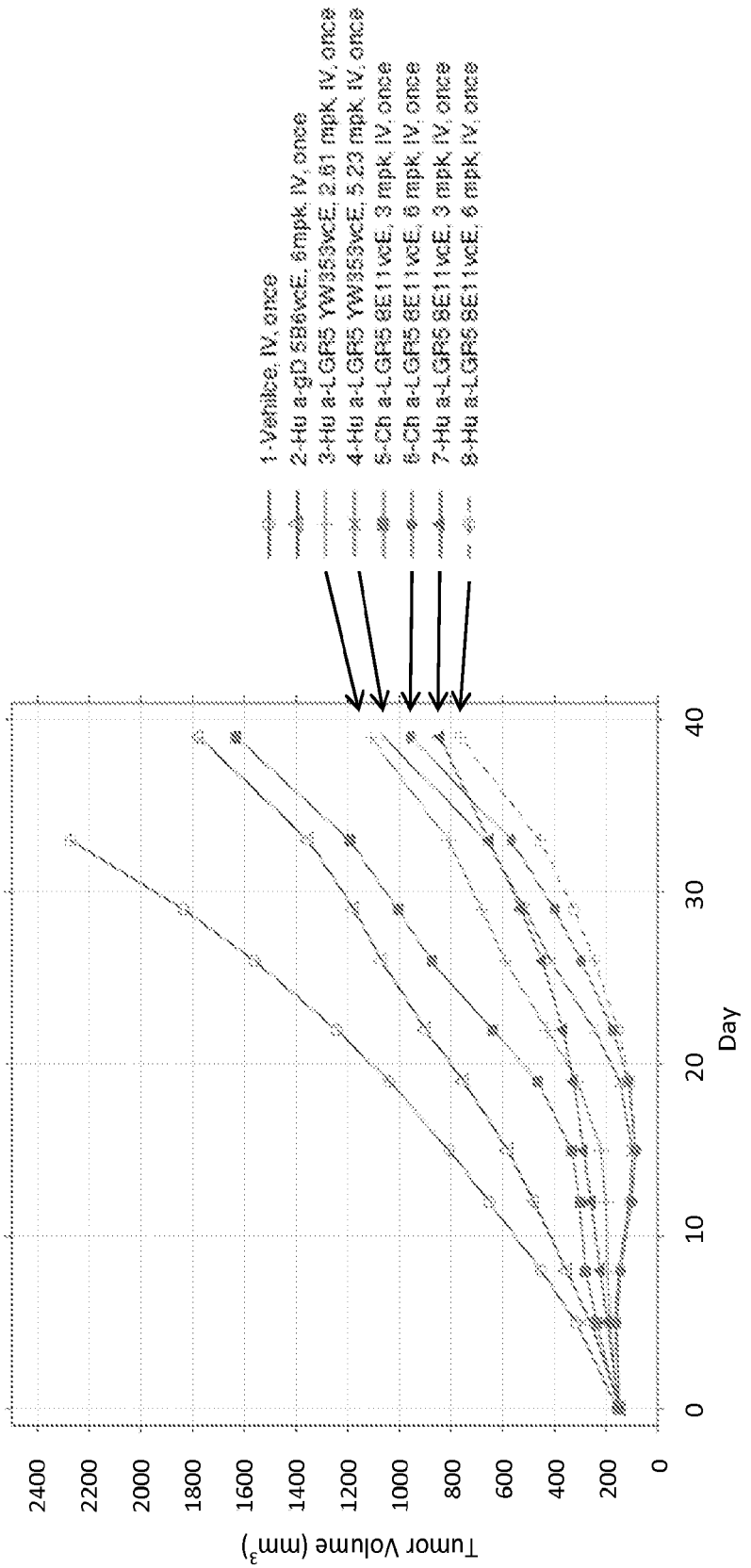

1-Vehicle, IV, once
2-Hu a-gD 5B6vcE, 6mpk, IV, once
3-Hu a-LGR5 YW353vcE, 2.61 mpk, IV, once
4-Hu a-LGR5 YW353vcE, 5.23 mpk, IV, once
5-Ch a-LGR5 6E11vcE, 3 mpk, IV, once
6-Ch a-LGR5 6E11vcE, 6 mpk, IV, once
7-Hu a-LGR5 8E11vcE, 3 mpk, IV, once
8-Hu a-LGR5 8E11vcE, 6 mpk, IV, once
Tumor Volume (mm3)
0
200
400
600
800
1000
1200
1400
1600
1800
2000
2200
2400
0
10
20
30
40
Day

FIG. 24

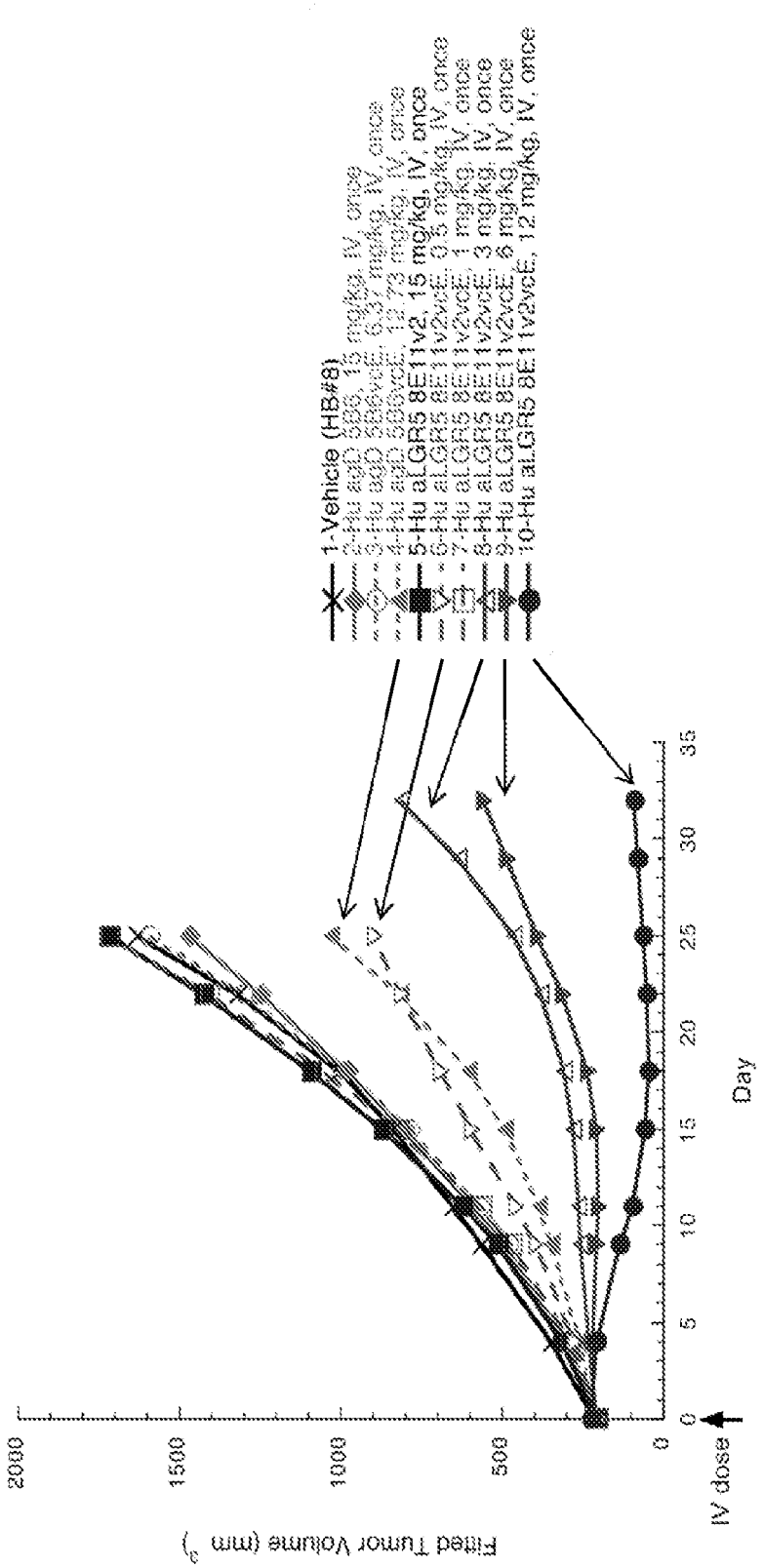

1-Vehicle (HB#8)
2-Hu aD 586_15 mg/kg, IV, once
3-Hu aD 586vcE, 6.37 mg/kg, IV, once
4-Hu aD 586vcE, 12.73 mg/kg, IV, once
5-Hu aLGR5 8E11v2_15 mg/kg, IV, once
6-Hu aLGR5 8E11v2vcE, 0.5 mg/kg, IV, once
7-Hu aLGR5 8E11v2vcE, 1 mg/kg, IV, once
8-Hu aLGR5 8E11v2vcE, 3 mg/kg, IV, once
9-Hu aLGR5 8E11v2vcE, 6 mg/kg, IV, once
10-Hu aLGR5 8E11v2vcE, 12 mg/kg, IV, once
Fitted Tumor Volume (mm 3)
2000
1500
1000
500
0
0
5
10
15
20
25
30
35
Day
IV dose

FIG. 25

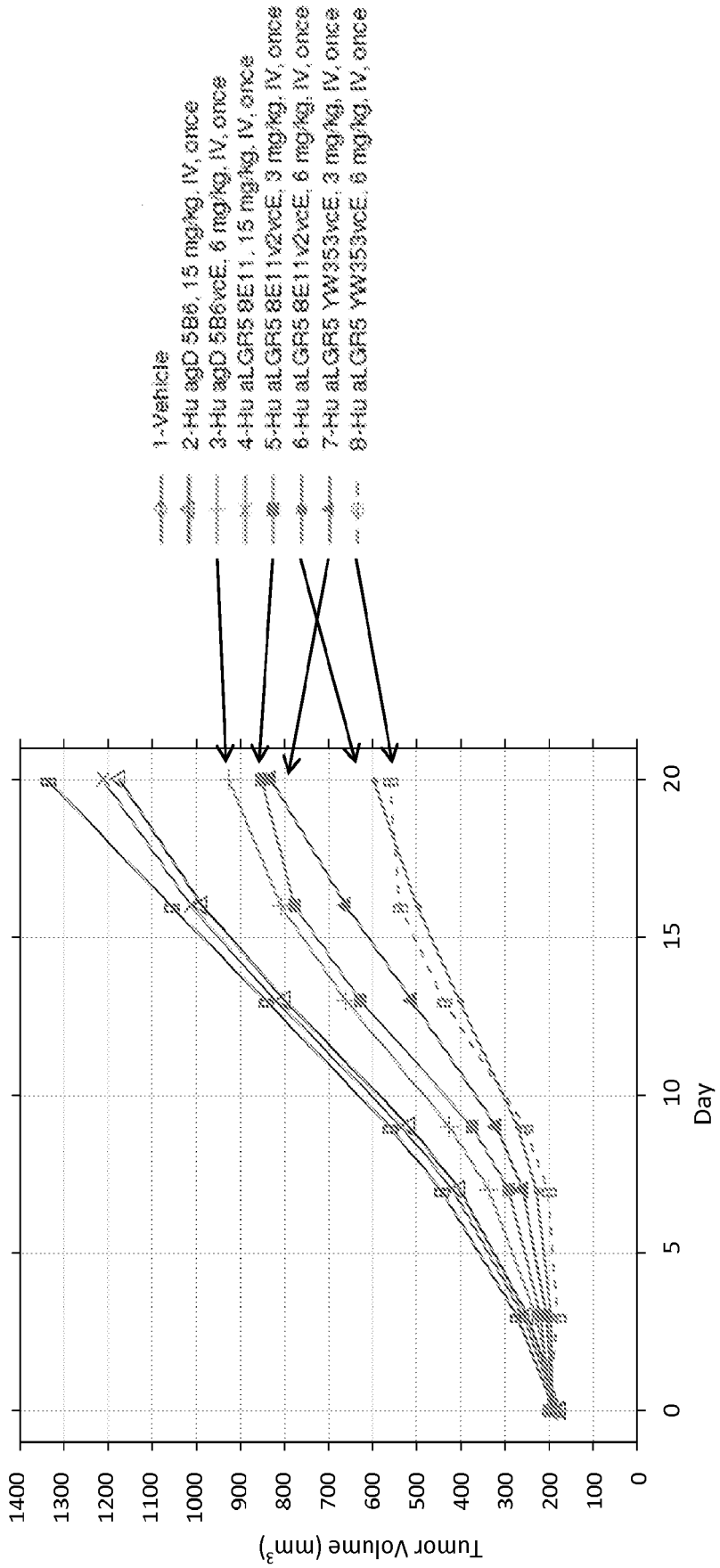

1-Vehicle
2-Hu agD 5B6, 15 mg/kg, IV, once
3-Hu agD 5B6xcE, 6 mg/kg, IV, once
4-Hu aLGR5 8E11, 15 mg/kg, IV, once
5-Hu aLGR5 8E11v2xcE, 3 mg/kg, IV, once
6-Hu aLGR5 8E11v2xcE, 6 mg/kg, IV, once
7-Hu aLGR5 YW353xcE, 3 mg/kg, IV, once
8-Hu aLGR5 YW353xcE, 6 mg/kg, IV, once
Tumor Volume (mm3)
0
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
Day
0
5
10
15
20

FIG. 26

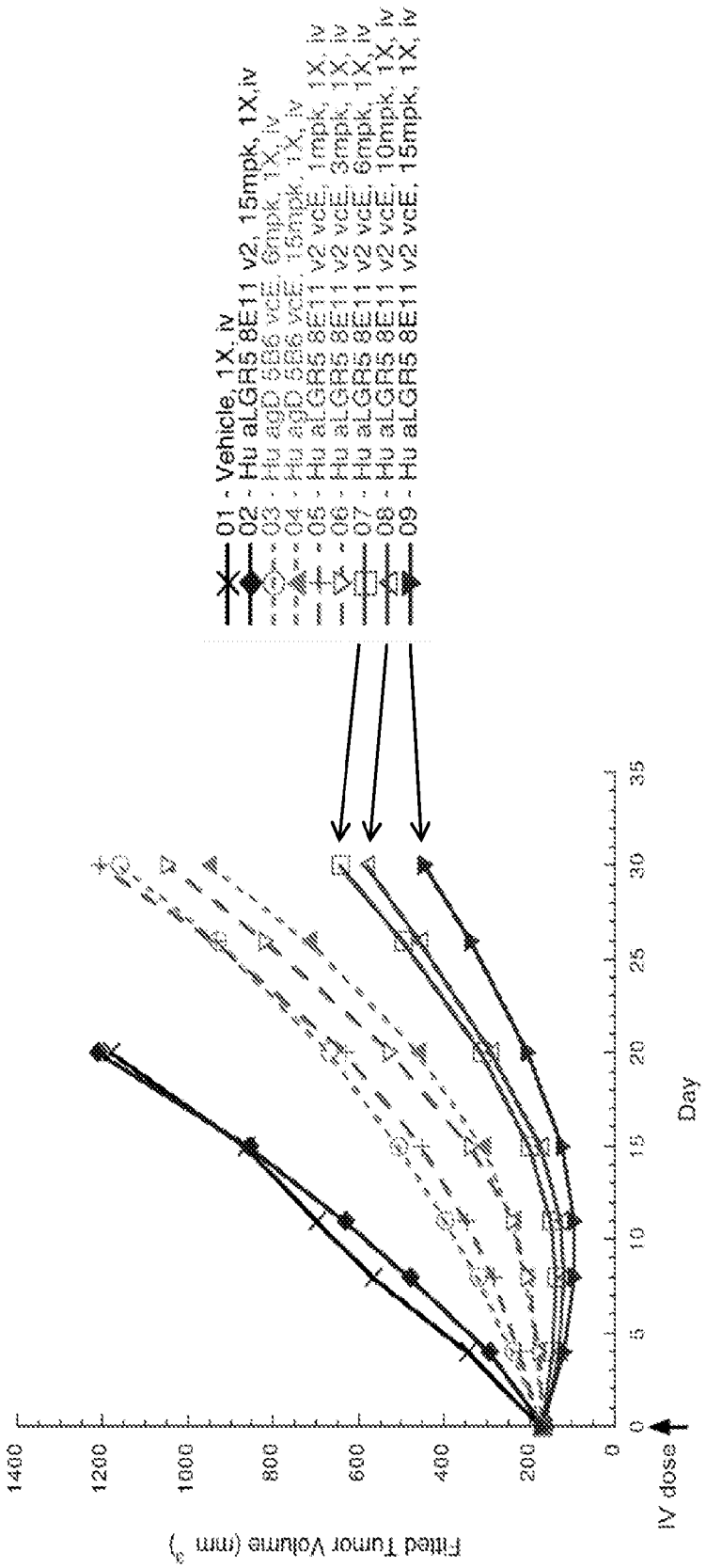

01 - Vehicle, 1X, iv
02 - Hu aLGR5 8E11 v2, 15mpk, 1X,iv
03 - Hu agD 586 vcE, 6mpk, 1X, iv
04 - Hu agD 586 vcE, 15mpk, 1X, iv
05 - Hu aLGR5 8E11 v2 vcE, 1mpk, 1X, iv
06 - Hu aLGR5 8E11 v2 vcE, 3mpk, 1X, iv
07 - Hu aLGR5 8E11 v2 vcE, 6mpk, 1X, iv
08 - Hu aLGR5 8E11 v2 vcE, 10mpk, 1X, iv
09 - Hu aLGR5 8E11 v2 vcE, 15mpk, 1X, iv
Tumor Volume (mm3)
1400
1200
1000
800
600
400
200
0
0
5
10
15
20
25
30
35
Day
IV dose

FIG. 27

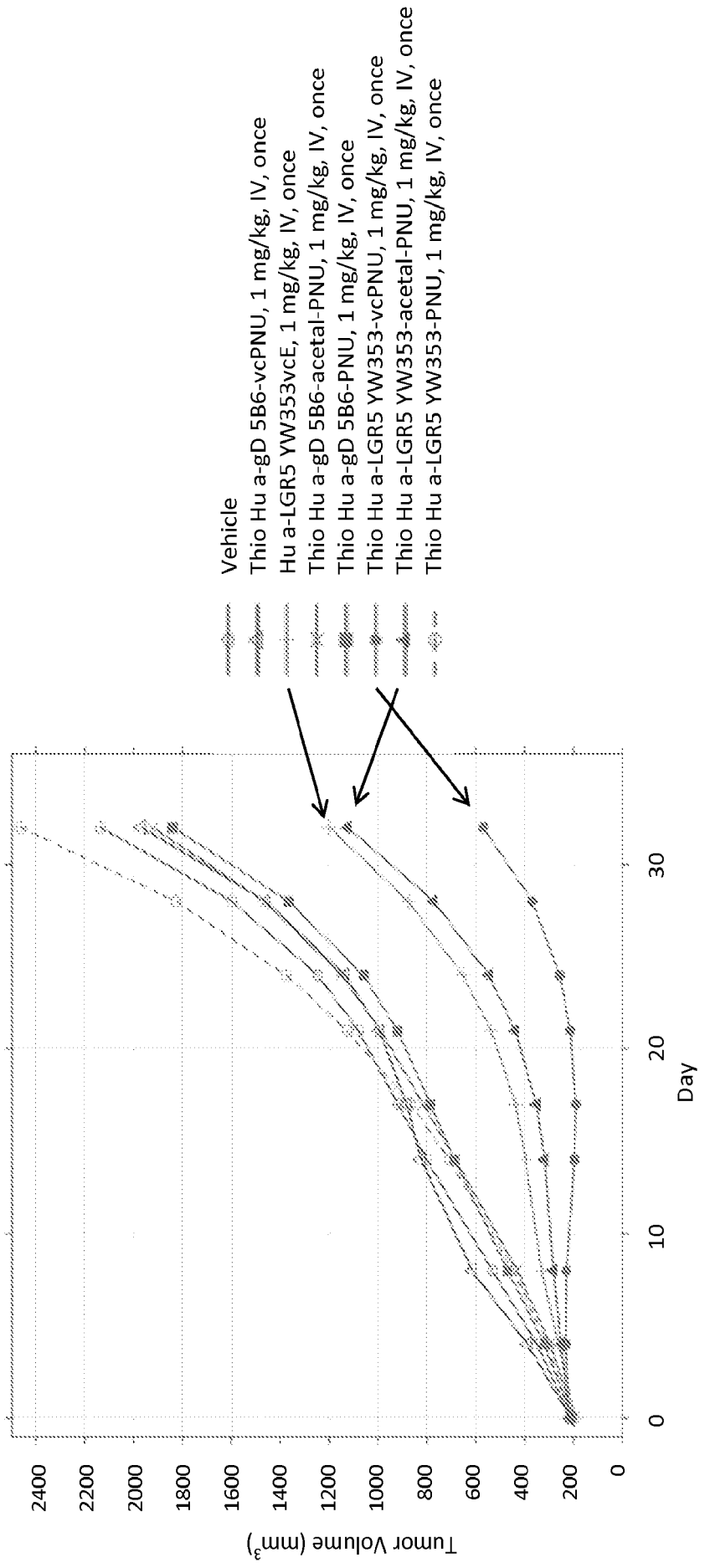

Vehicle
Thio Hu a-gD 5B6-vcPNU, 1 mg/kg, IV, once
Hu a-LGR5 YW353vcE, 1 mg/kg, IV, once
Thio Hu a-gD 5B6-acetal-PNU, 1 mg/kg, IV, once
Thio Hu a-gD 5B6-PNU, 1 mg/kg, IV, once
Thio Hu a-LGR5 YW353-vcPNU, 1 mg/kg, IV, once
Thio Hu a-LGR5 YW353-acetal-PNU, 1 mg/kg, IV, once
Thio Hu a-LGR5 YW353-PNU, 1 mg/kg, IV, once
Tumor Volume (mm3)
0
200
400
600
800
1000
1200
1400
1600
1800
2000
2200
2400
0
10
20
30
Day

FIG. 28

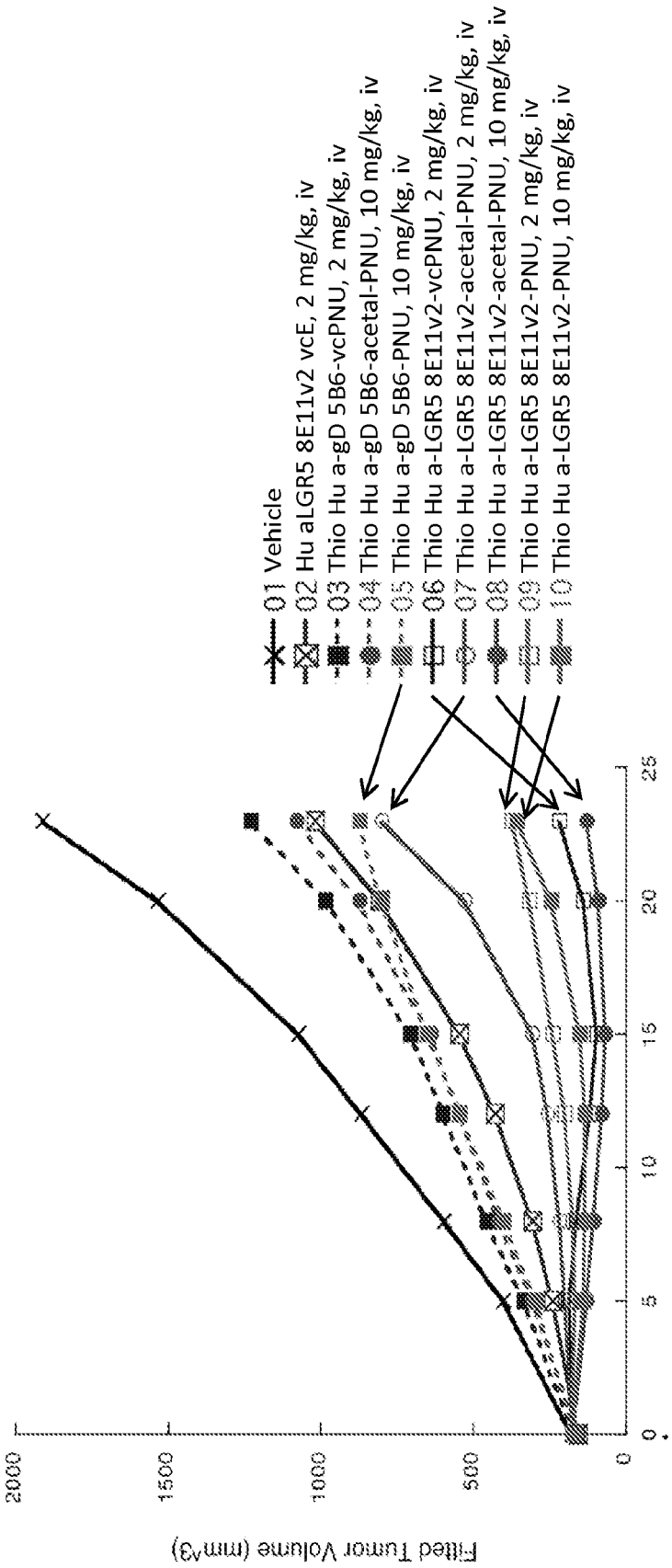

01 Vehicle
02 Hu aLGR5 8E11v2 vcE, 2 mg/kg, iv
03 Thio Hu a-gD 5B6-vcPNU, 2 mg/kg, iv
04 Thio Hu a-gD 5B6-acetal-PNU, 10 mg/kg, iv
05 Thio Hu a-gD 5B6-PNU, 10 mg/kg, iv
06 Thio Hu a-LGR5 8E11v2-vcPNU, 2 mg/kg, iv
07 Thio Hu a-LGR5 8E11v2-acetal-PNU, 2 mg/kg, iv
08 Thio Hu a-LGR5 8E11v2-acetal-PNU, 10 mg/kg, iv
09 Thio Hu a-LGR5 8E11v2-PNU, 2 mg/kg, iv
10 Thio Hu a-LGR5 8E11v2-PNU, 10 mg/kg, iv
Filled Tumor Volume (mm^3)
2000
1500
1000
500
0
0
5
10
15
20
25

FIG. 29

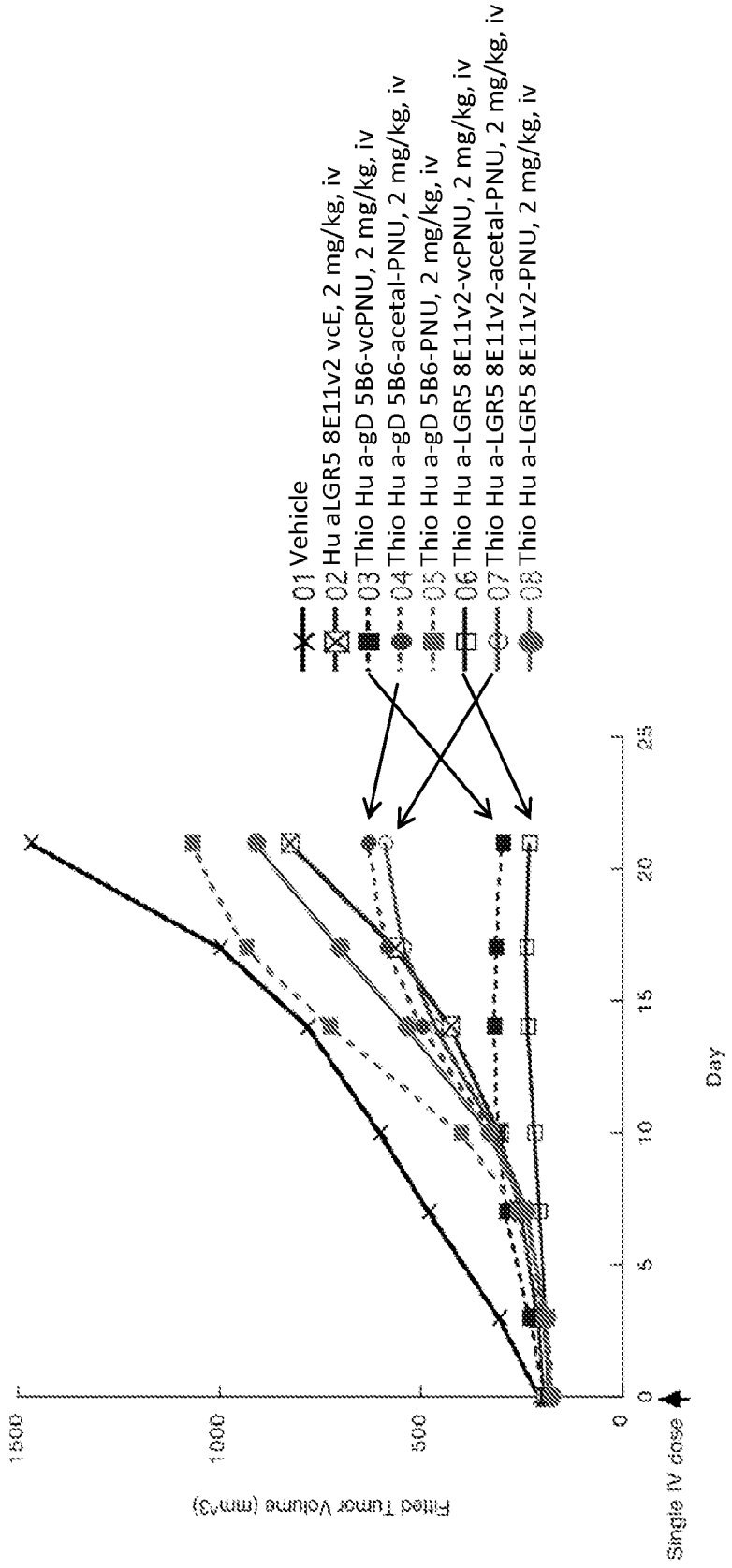

01 Vehicle
02 Hu aLGR5 8E11v2 vcE, 2 mg/kg, iv
03 Thio Hu a-gD 5B6-vcPNU, 2 mg/kg, iv
04 Thio Hu a-gD 5B6-acetal-PNU, 2 mg/kg, iv
05 Thio Hu a-gD 5B6-PNU, 2 mg/kg, iv
06 Thio Hu a-LGR5 8E11v2-vcPNU, 2 mg/kg, iv
07 Thio Hu a-LGR5 8E11v2-acetal-PNU, 2 mg/kg, iv
08 Thio Hu a-LGR5 8E11v2-PNU, 2 mg/kg, iv
Filed Tumor Volume (mm^3)
1500
1000
500
0
0
5
10
15
20
25
Day
Single IV dose

FIG. 30

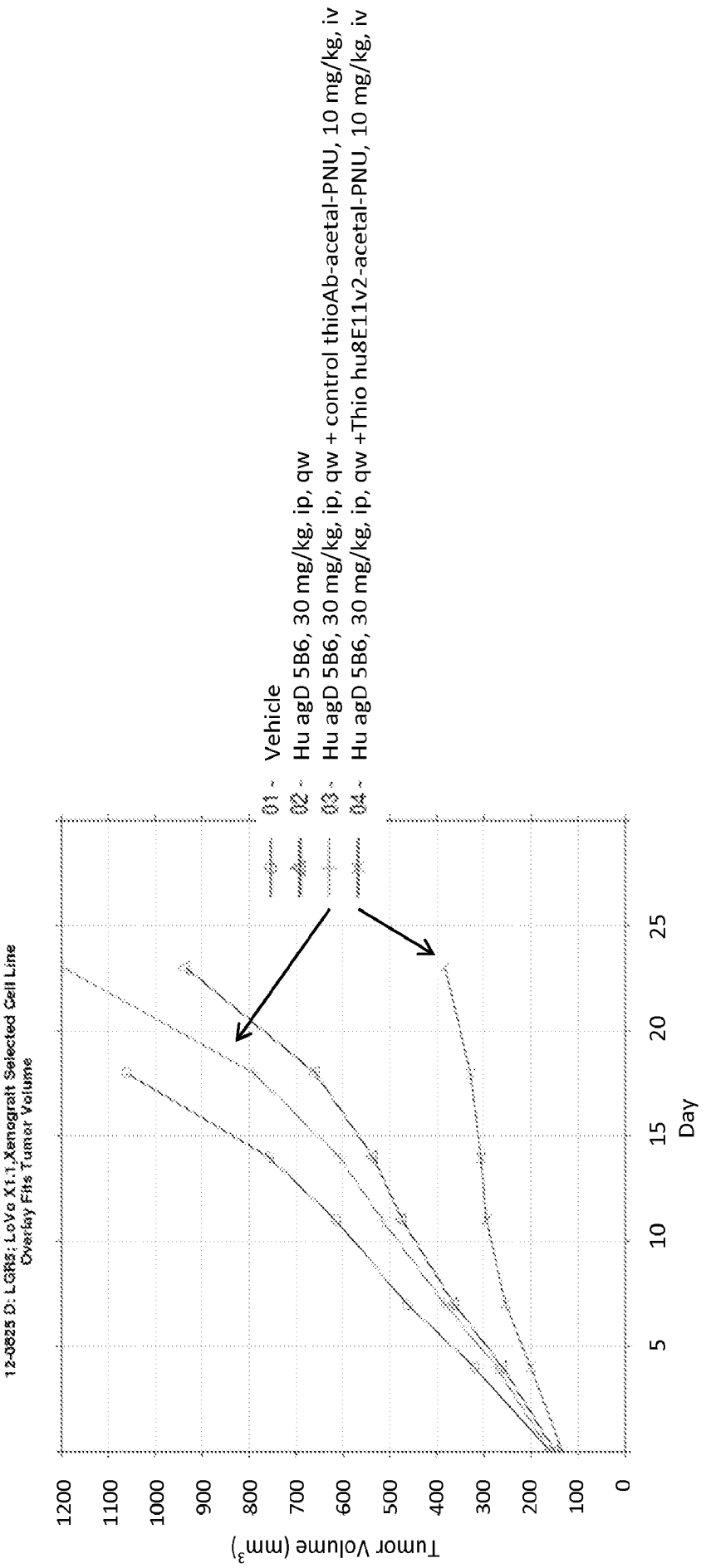

12-0825 D: LGR5; LoVo X1.1 Xenograft Selected Cell Line
Overlay Fits Tumor Volume
01 - Vehicle
02 - Hu agD 5B6, 30 mg/kg, ip, qw
03 - Hu agD 5B6, 30 mg/kg, ip, qw + control thioAb-acetal-PNU, 10 mg/kg, iv
04 - Hu agD 5B6, 30 mg/kg, ip, qw +Thio hu8E11v2-acetal-PNU, 10 mg/kg, iv
Tumor Volume (mm3)
0
100
200
300
400
500
600
700
800
900
1000
1100
1200
Day
5
10
15
20
25

FIG. 31

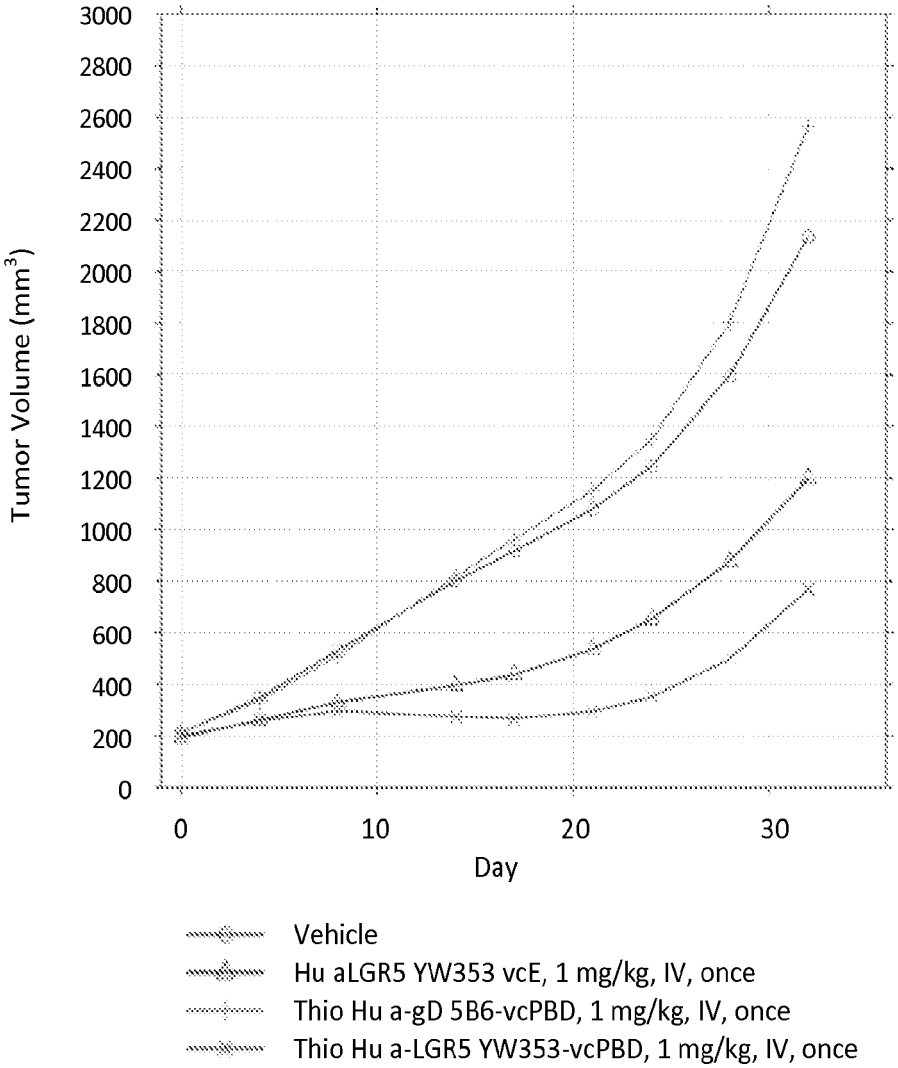

3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
Tumor Volume (mm3)
0
10
20
30
Day
Vehicle
Hu aLGR5 YW353 vcE, 1 mg/kg, IV, once
Thio Hu a-gD 5B6-vcPBD, 1 mg/kg, IV, once
Thio Hu a-LGR5 YW353-vcPBD, 1 mg/kg, IV, once

FIG. 32

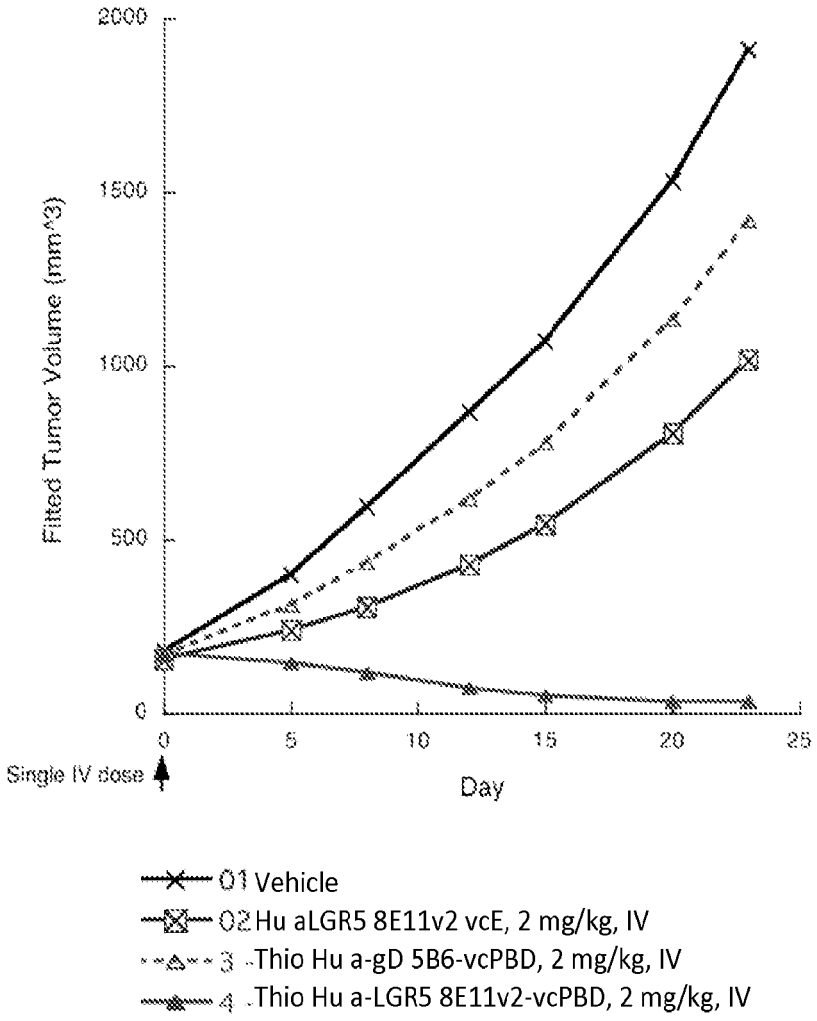

2000
1500
1000
500
0
Fitted Tumor Volume (mm^3)
0
5
10
15
20
25
Day
Single IV dose
01 Vehicle
02 Hu aLGR5 8E11v2 vcE, 2 mg/kg, IV
3 Thio Hu a-gD 5B6-vcPBD, 2 mg/kg, IV
4 Thio Hu a-LGR5 8E11v2-vcPBD, 2 mg/kg, IV

FIG. 33

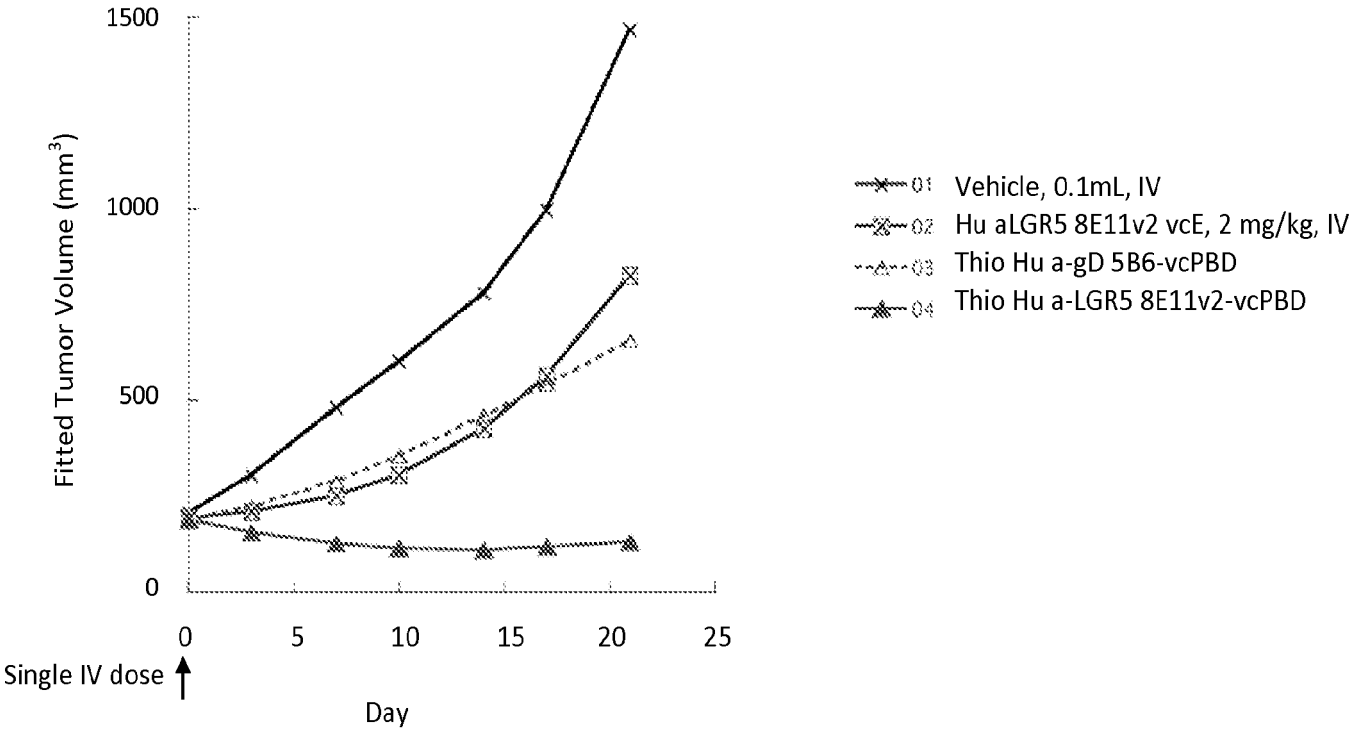
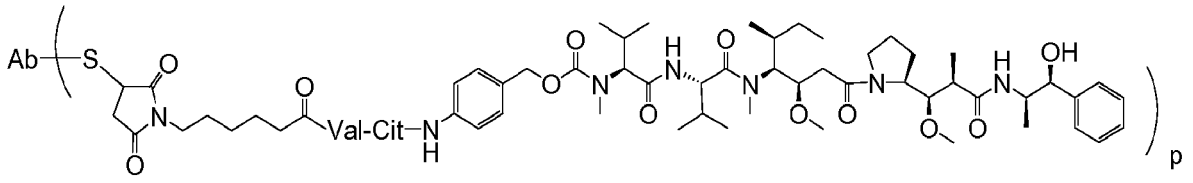
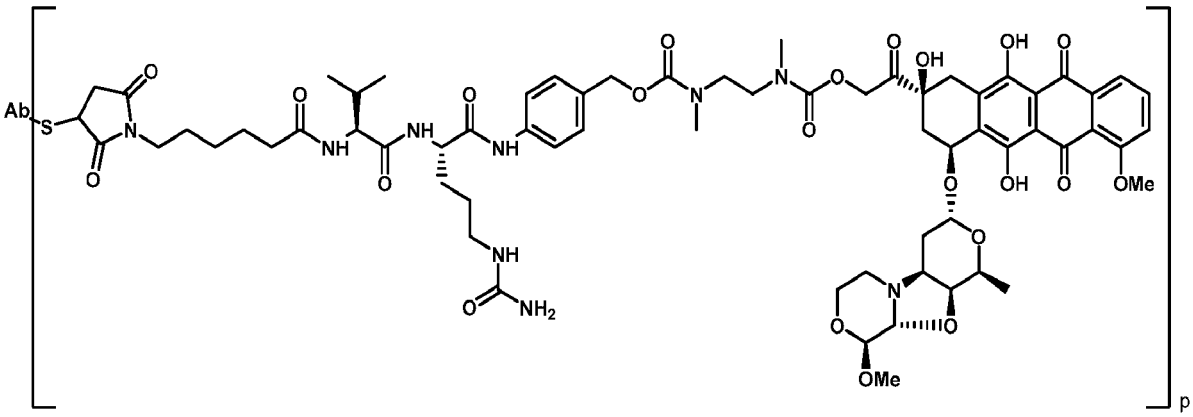

1500
1000
500
0
Fitted Tumor Volume (mm3)
0
5
10
15
20
25
Day
Single IV dose
01 Vehicle, 0.1mL, IV
02 Hu aLGR5 8E11v2 vcE, 2 mg/kg, IV
03 Thio Hu a-gD 5B6-vcPBD
04 Thio Hu a-LGR5 8E11v2-vcPBD

FIG. 34

A


Ab
S
O
N
O
O
Val-Cit
N
H
O
N
H
O
N
H
O
N
O
O
N
O
O
N
H
OH
p

B


Ab
S
O
N
O
O
NH
NH
NH
O
O
O
N
N
O
O
OH
OH
OH
O
O
OMe
NH
O
NH2
N
O
O
O
OMe
p

C

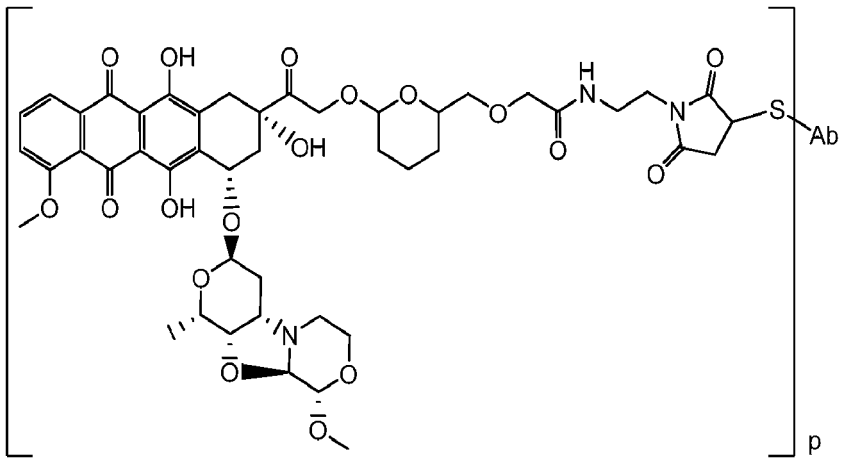
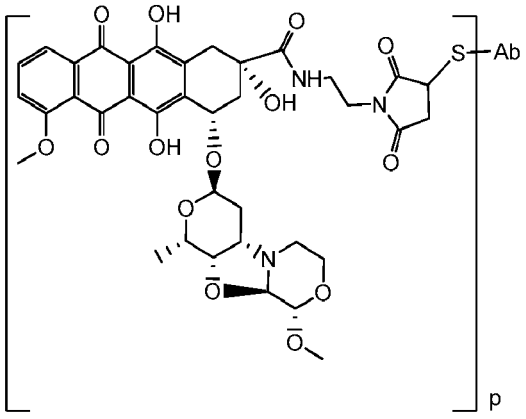

O
OH
O
O
O
O
H
N
O
N
S
Ab
O
O
OH
OH
O
O
O
N
O
O
O
p

FIG. 35

D



E

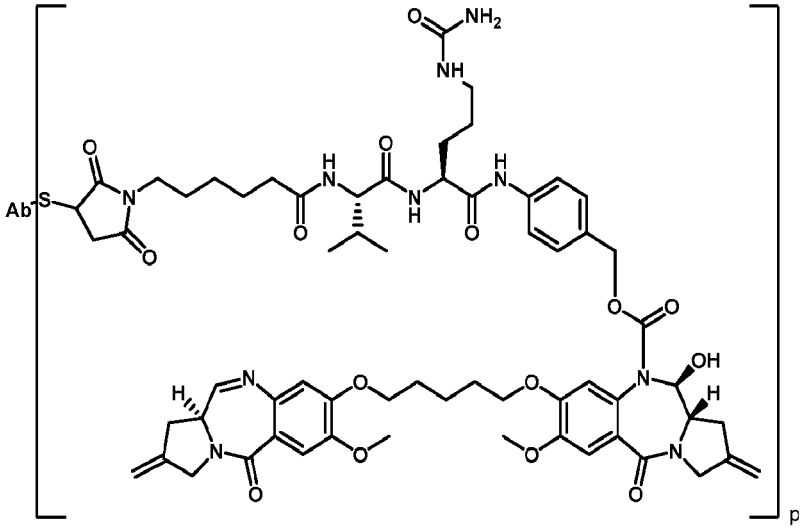


FIG. 35 (cont.)