Fig. 1

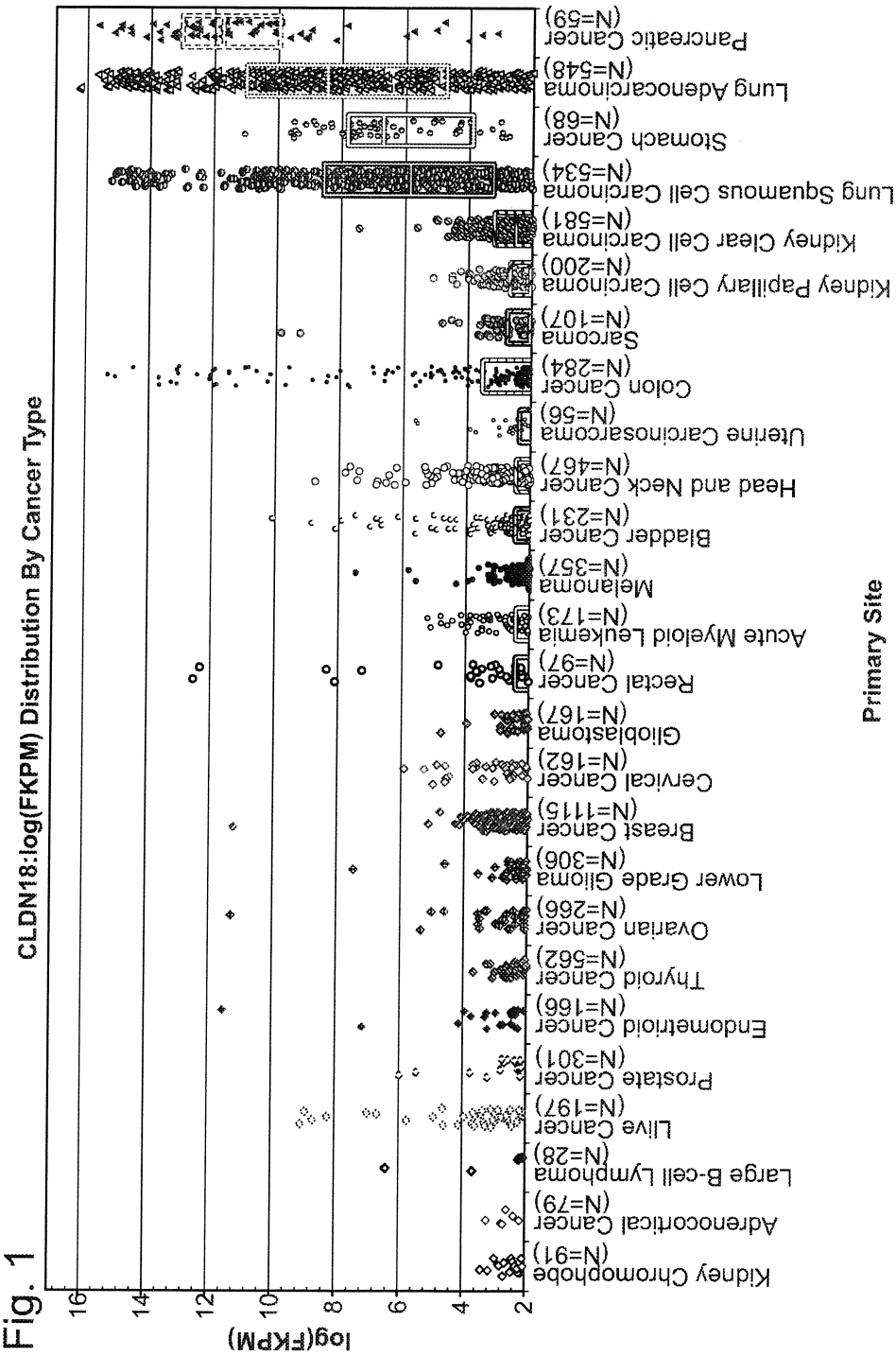
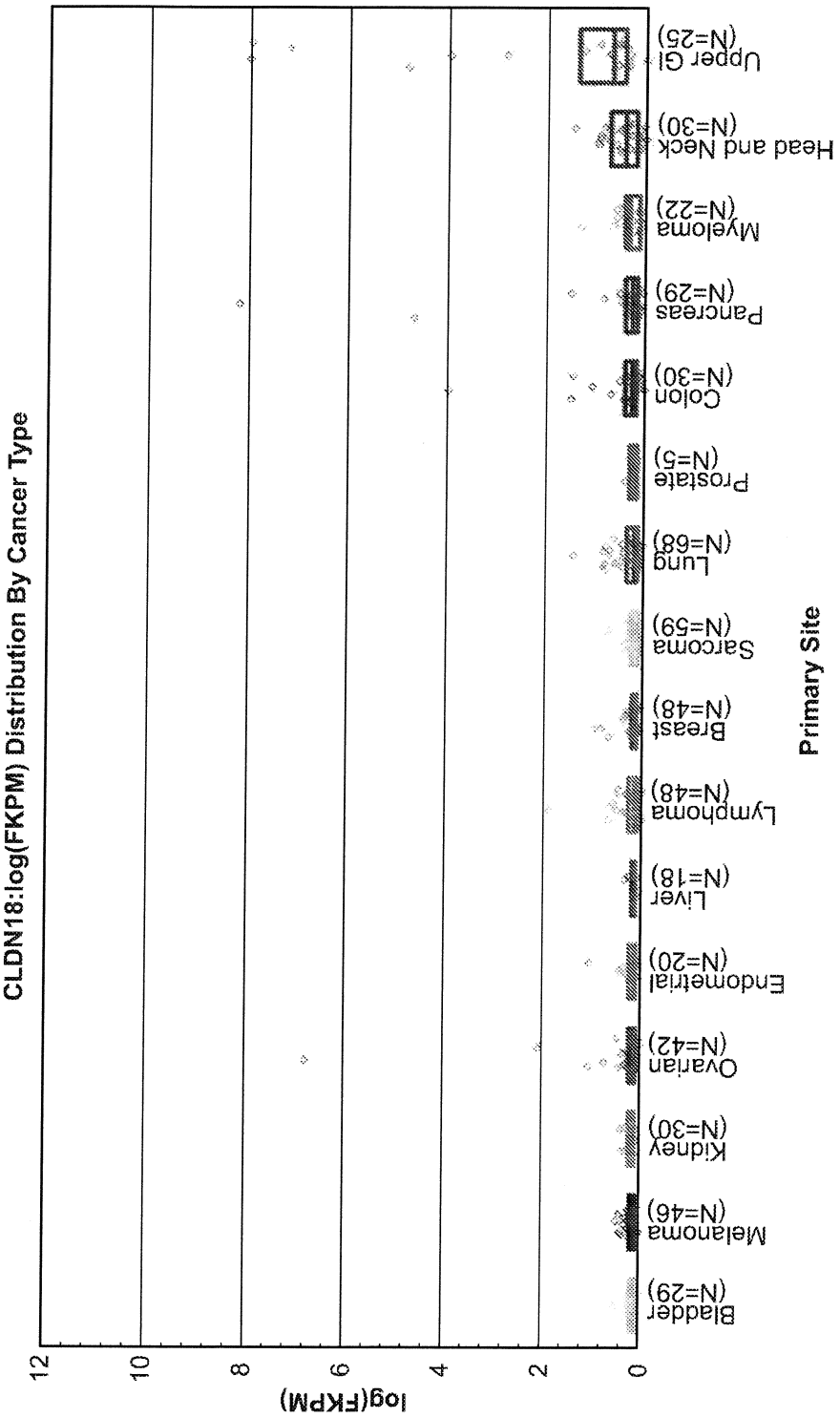

CLDN18:log(FKPM) Distribution By Cancer Type
log(FKPM)
2
4
6
8
10
12
14
16
Primary Site
Kidney Chromophobe (N=91)
Adrenocortical Cancer (N=79)
Large B-cell Lymphoma (N=28)
Live Cancer (N=197)
Prostate Cancer (N=301)
Endometrioid Cancer (N=166)
Thyroid Cancer (N=562)
Ovarian Cancer (N=266)
Lower Grade Glioma (N=306)
Breast Cancer (N=1115)
Cervical Cancer (N=162)
Glioblastoma (N=167)
Rectal Cancer (N=97)
Acute Myeloid Leukemia (N=173)
Melanoma (N=357)
Bladder Cancer (N=231)
Head and Neck Cancer (N=467)
Uterine Carcinosarcoma (N=56)
Colon Cancer (N=284)
Sarcoma (N=107)
Kidney Papillary Cell Carcinoma (N=200)
Kidney Clear Cell Carcinoma (N=581)
Lung Squamous Cell Carcinoma (N=534)
Stomach Cancer (N=68)
Lung Adenocarcinoma (N=548)
Pancreatic Cancer (N=59)

Fig. 2


CLDN18:log(FKPM) Distribution By Cancer Type
log(FKPM)
0
2
4
6
8
10
12
Primary Site
Bladder (N=29)
Melanoma (N=46)
Kidney (N=30)
Ovarian (N=42)
Endometrial (N=20)
Liver (N=18)
Lymphoma (N=48)
Breast (N=48)
Sarcoma (N=59)
Lung (N=68)
Prostate (N=5)
Colon (N=30)
Pancreas (N=29)
Myeloma (N=22)
Head and Neck (N=30)
Upper GI (N=25)

Cell_Line_ID2	Cell_Line_Name	TORClass	CLDN18.2	CLDN18.1
PN022	HUPT4	Pancreas	285.62	2.14
UG002	KATO III	Upper GI	246.53	0
UG023	SNU601	Upper GI	245.64	3.12
UG009	NUGC 4	Upper GI	144.16	0
UG026	SNU620	Upper GI	27.06	0
PN024	PATU 8988S	Pancreas	24.32	0
CL015	SKCO1	Colon	14.48	0
UG027	SNU520	Upper GI	13.16	1.21
OV020	OV-90	Ovarian	6.93	99.53
UG003	OE19	Upper GI	6.02	0
OV032	PEO14	Ovarian	3.18	0
PN023	DAN G	Pancreas	1.82	0
CL002	LOVO	Colon	1.8	0
CL029	SW1116	Colon	1.73	0
HN015	UMSCC-19	Head and Neck	1.68	0
LG013	H810	Lung	1.67	0
UG006	IM95	Upper GI	1.54	0
MM019	MOLP-2	Myeloma	1.48	0
UG008	OE33	Upper GI	1.36	0
CL016	LS513	Colon	1.09	0

Fig. 3

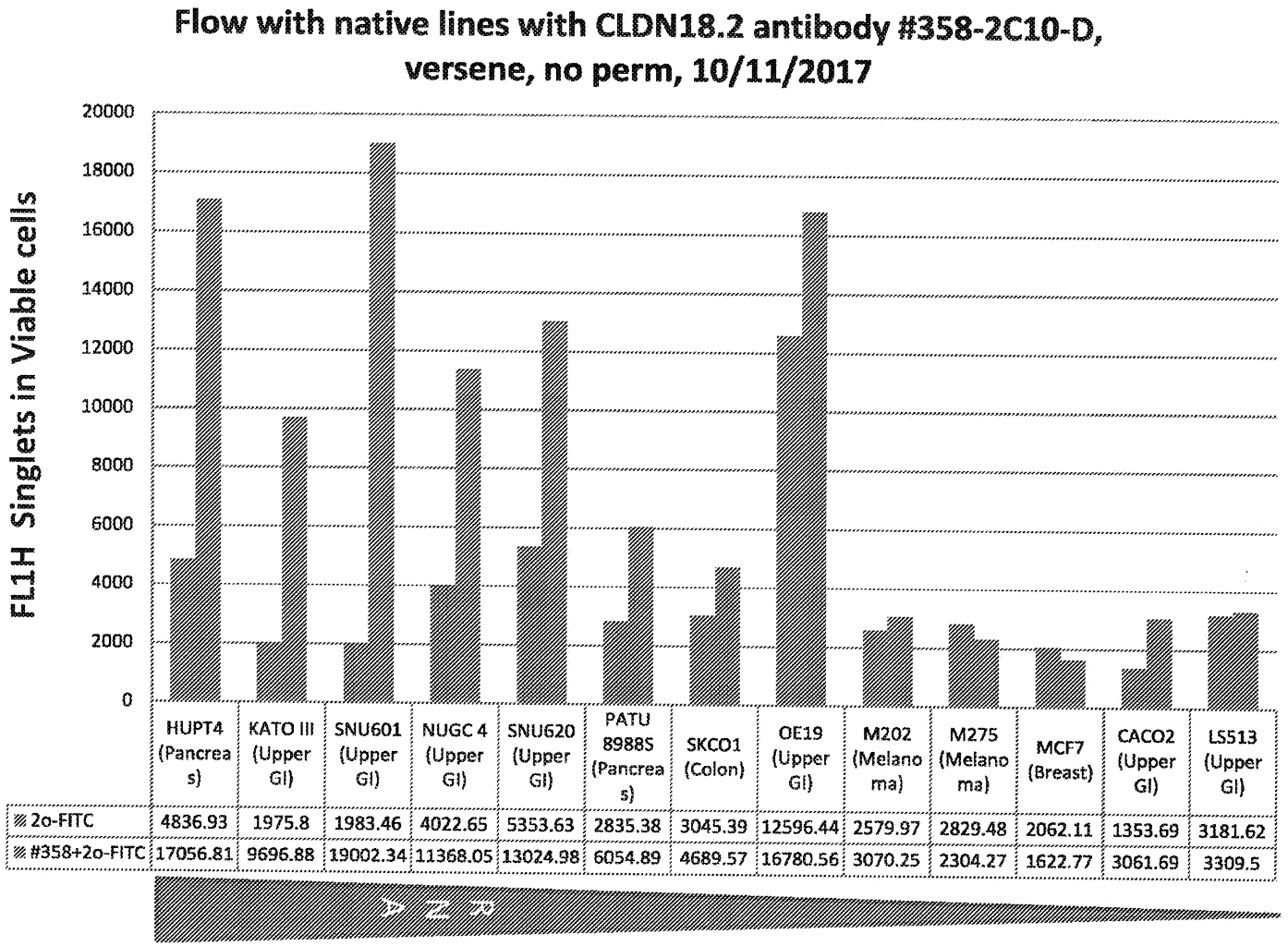

Flow with native lines with CLDN18.2 antibody #358-2C10-D, versene, no perm, 10/11/2017
FL1H Singlets in Viable cells
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
HUPT4 (Pancreas)
KATO III (Upper GI)
SNU601 (Upper GI)
NUGC 4 (Upper GI)
SNU620 (Upper GI)
PATU 8988S (Pancreas)
SKCO1 (Colon)
OE19 (Upper GI)
M202 (Melanoma)
M275 (Melanoma)
MCF7 (Breast)
CACO2 (Upper GI)
LS513 (Upper GI)
% 2o-FITC 4836.93 1975.8 1983.46 4022.65 5353.63 2835.38 3045.39 12596.44 2579.97 2829.48 2062.11 1353.69 3181.62
% #358+2o-FITC 17056.81 9696.88 19002.34 11368.05 13024.98 6054.89 4689.57 16780.56 3070.25 2304.27 1622.77 3061.69 3309.5

Fig. 4

In vivo chimeric antibody screen; SNU601 (UGI) Day 30

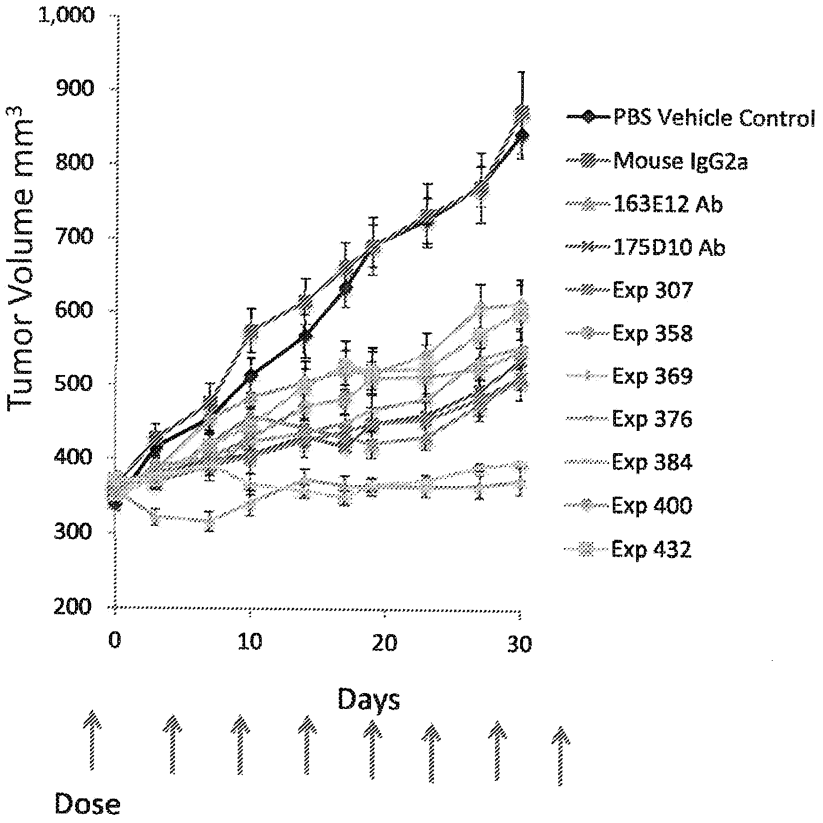


Fig. 5A

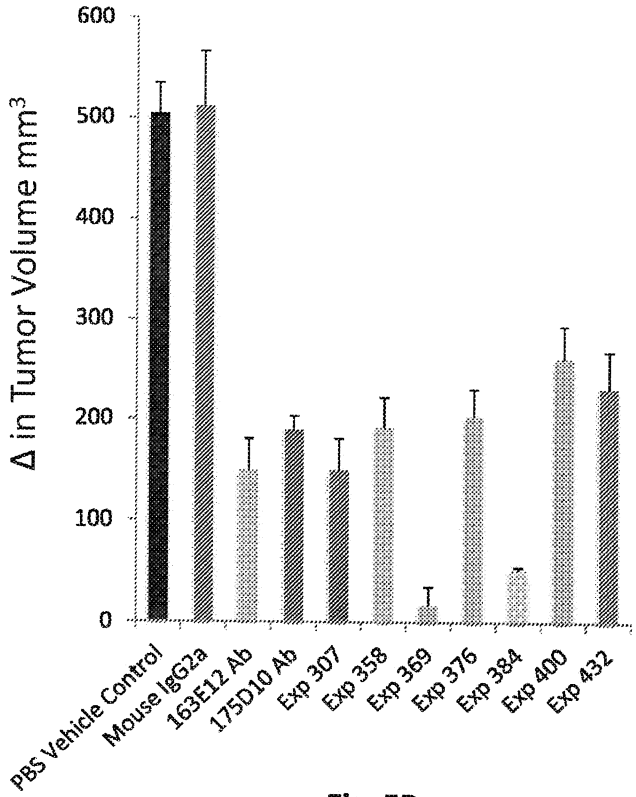


Fig. 5B

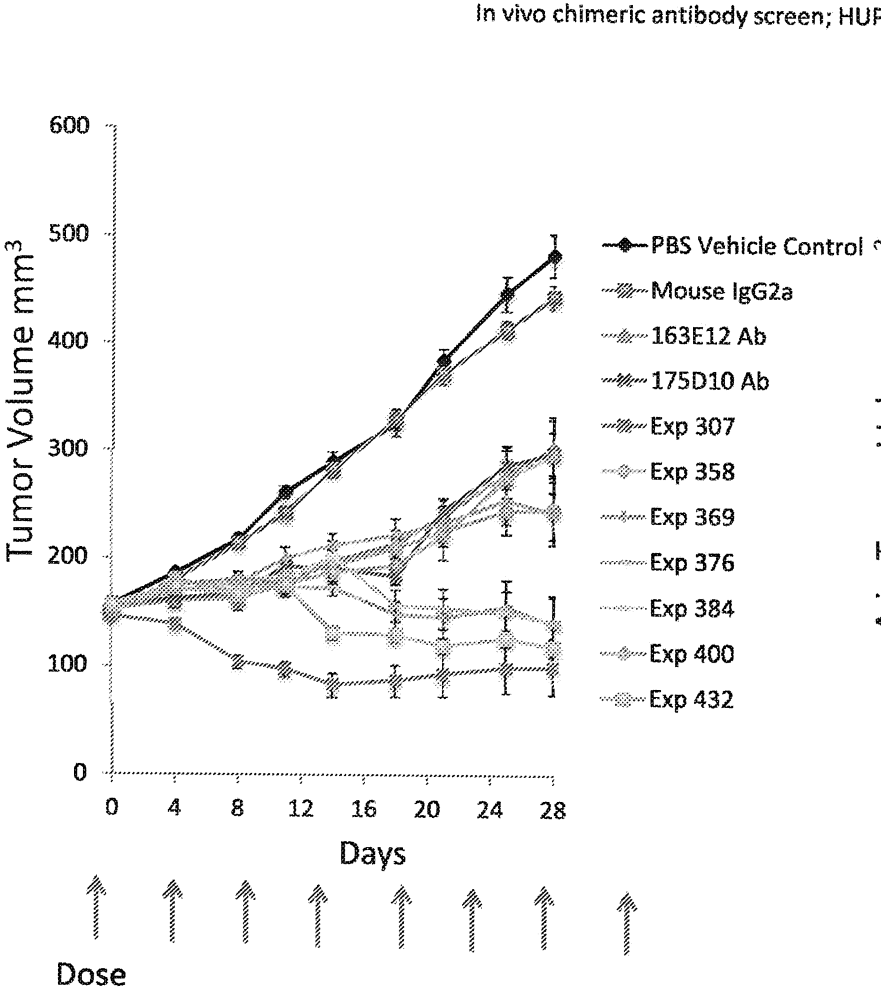

In vivo chimeric antibody screen; HUPT4 (Pancreas) Day 28
Tumor Volume mm3
600
500
400
300
200
100
0
0
4
8
12
16
20
24
28
Days
Dose
PBS Vehicle Control
Mouse IgG2a
163E12 Ab
175D10 Ab
Exp 307
Exp 358
Exp 369
Exp 376
Exp 384
Exp 400
Exp 432

Fig. 6A

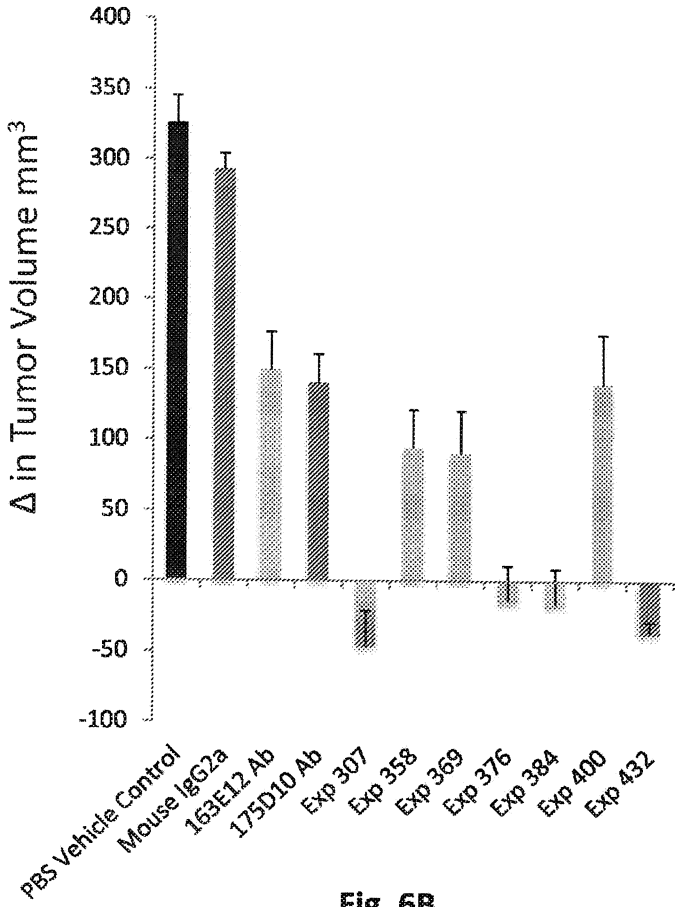

Δ in Tumor Volume mm3
400
350
300
250
200
150
100
50
0
-50
-100
PBS Vehicle Control
Mouse IgG2a
163E12 Ab
175D10 Ab
Exp 307
Exp 358
Exp 369
Exp 376
Exp 384
Exp 400
Exp 432

Fig. 6B

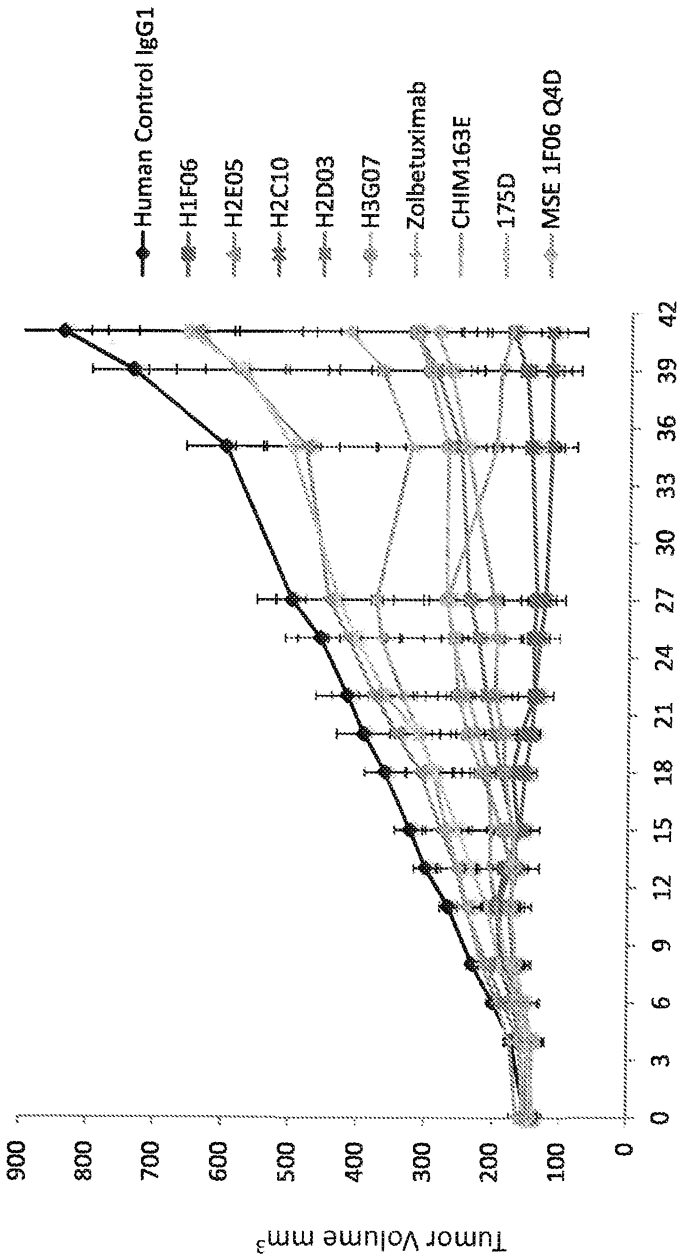


Fig. 7A *In vivo* humanized antibody screen; HUPT4 Day 42

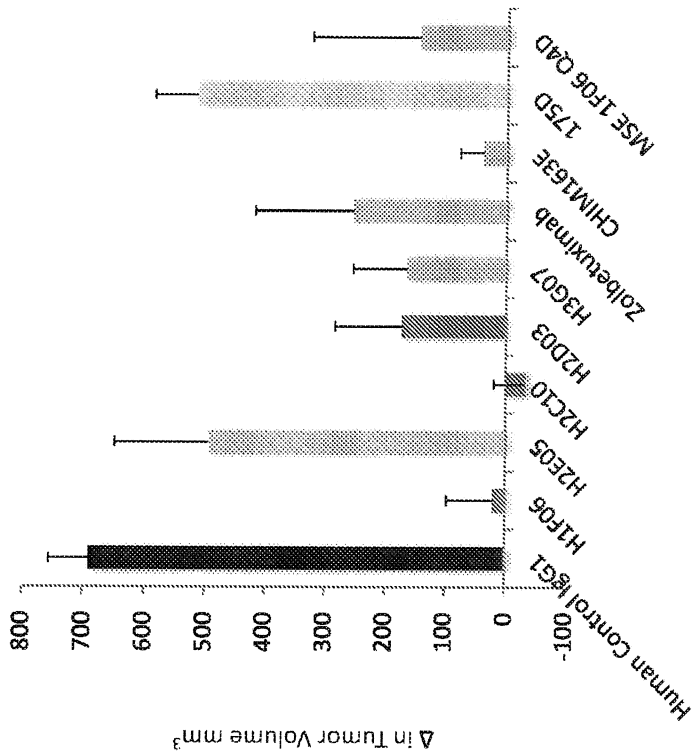


Fig. 7B *In vivo* humanized antibody screen; HUPT4 Day 42

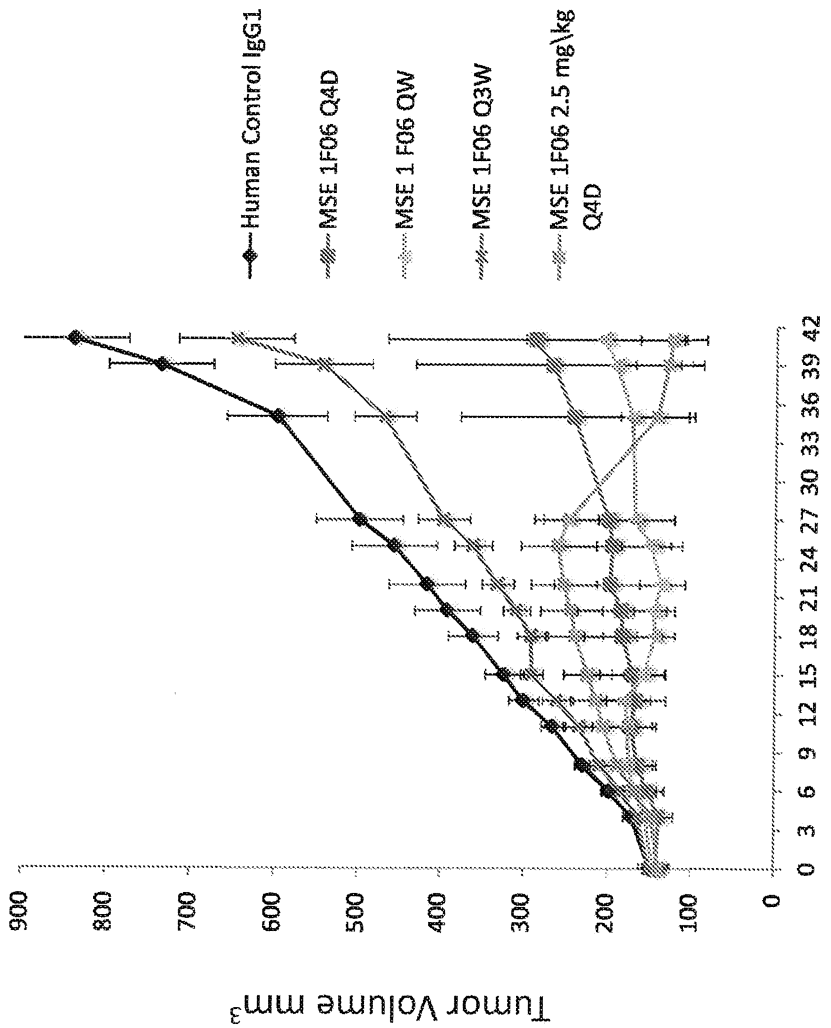


Fig. 8A Dose Scheduling; HUPT4 Day 42

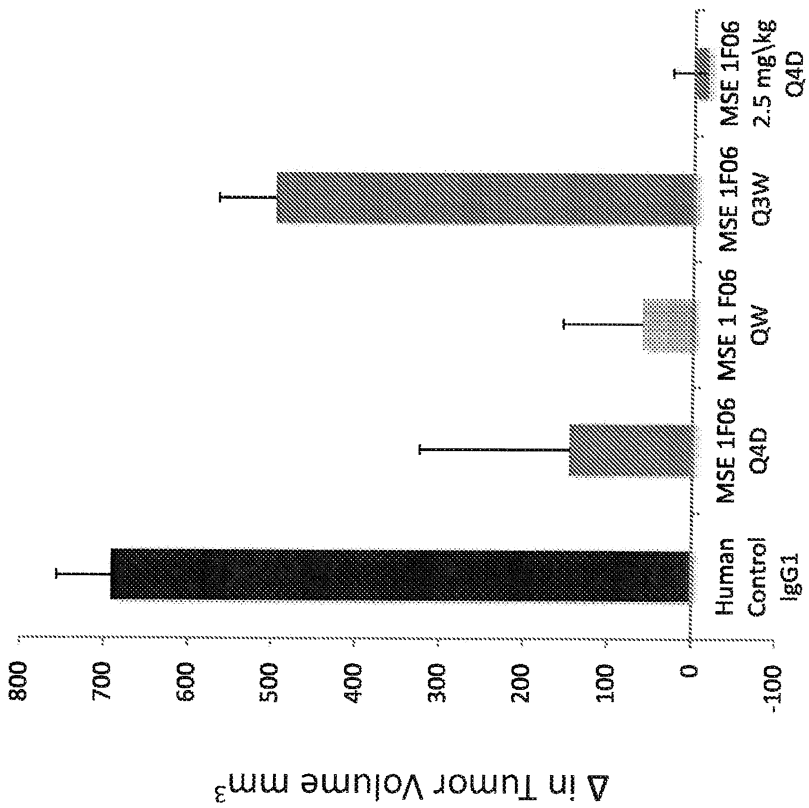


Fig. 8B Dose Scheduling; HUPT4 Day 42

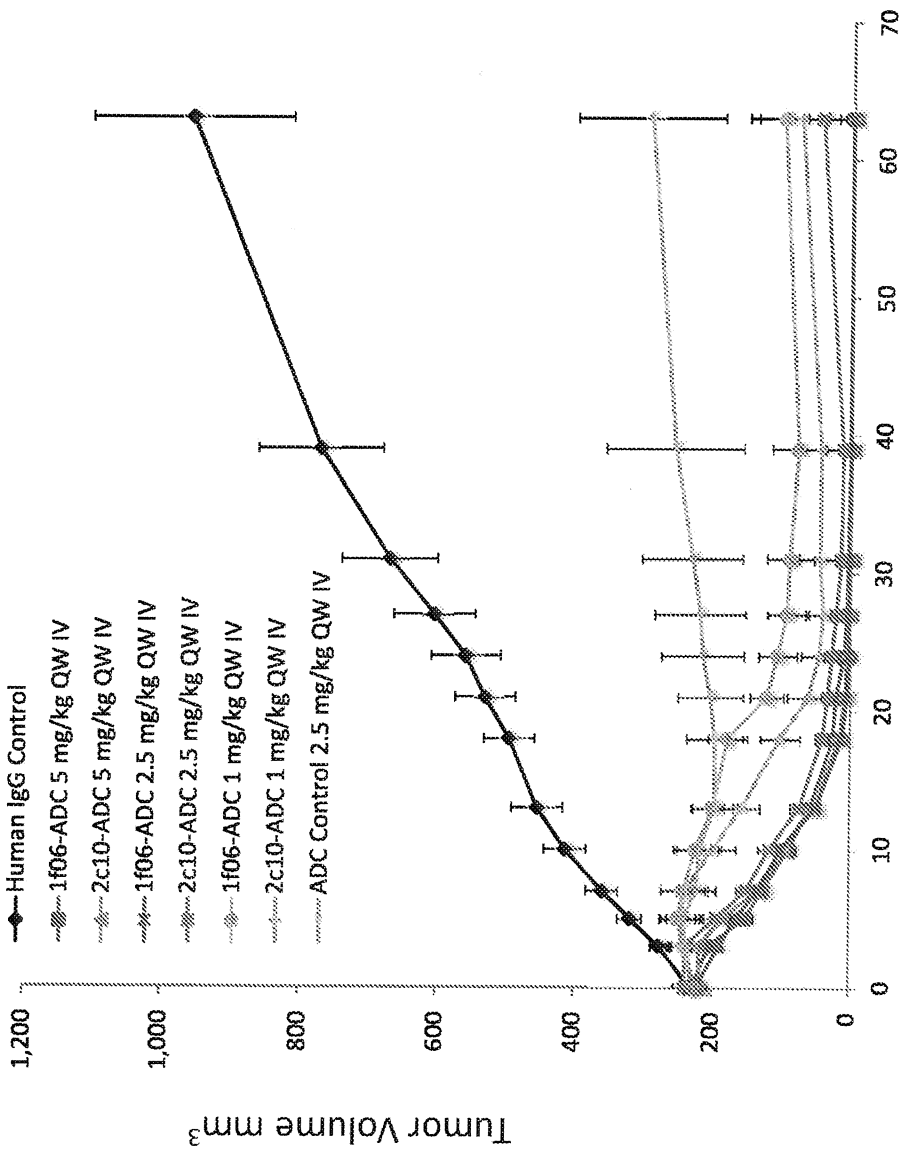


Fig. 9A CLDN18.2 ADC HUPT4 Pancreas

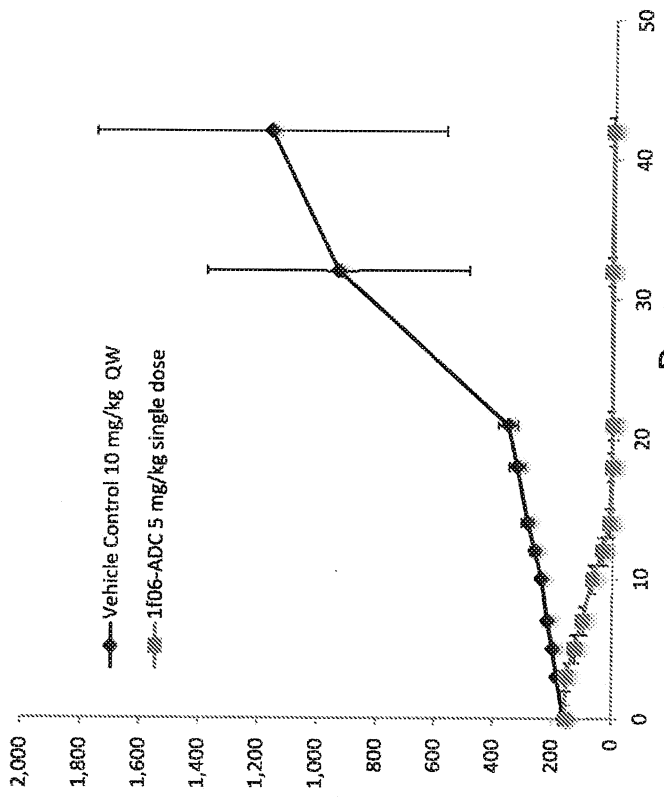


Fig. 9B CLDN18.2 ADC HUPT4 Pancreas

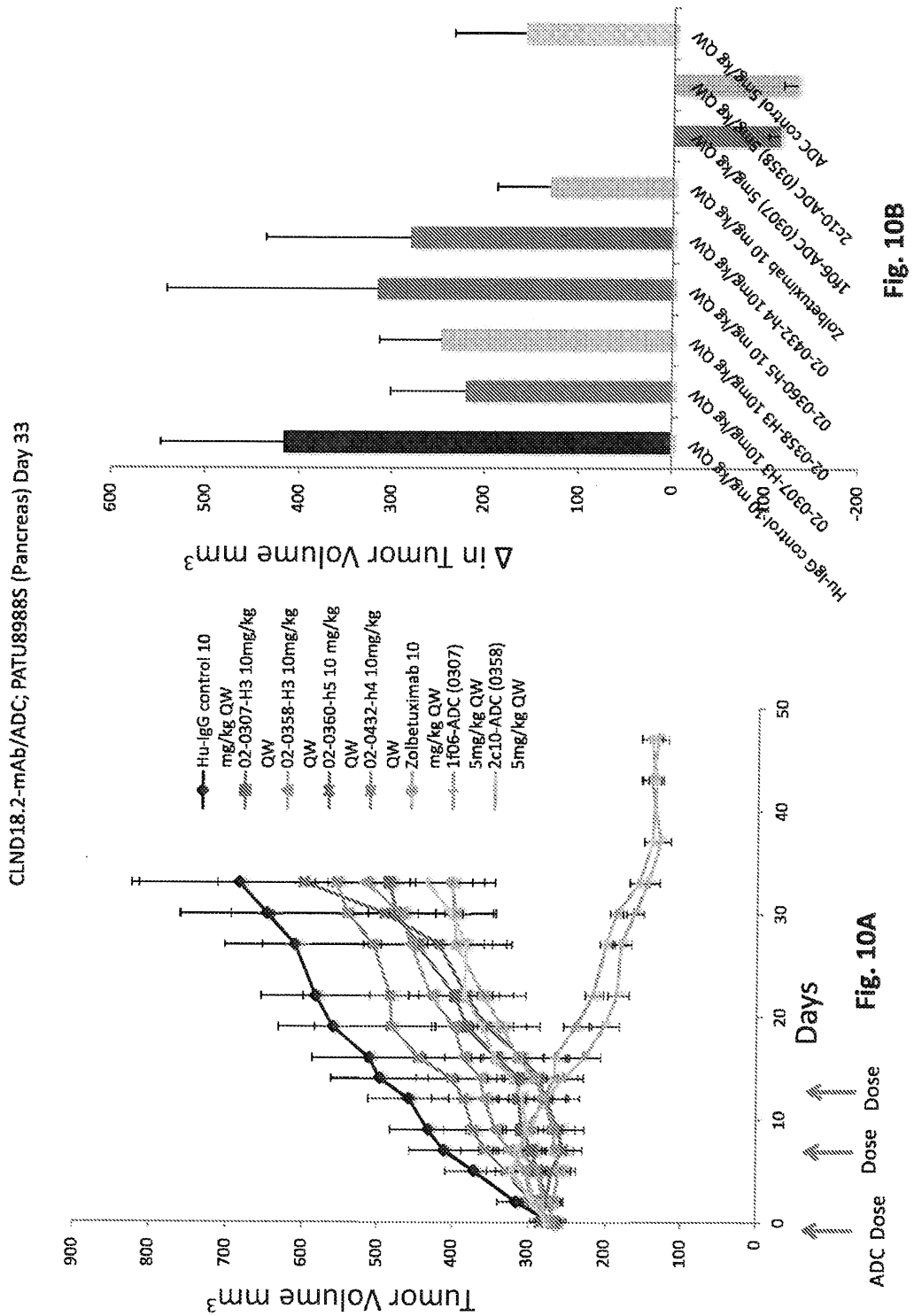


Fig. 10A

Fig. 10B

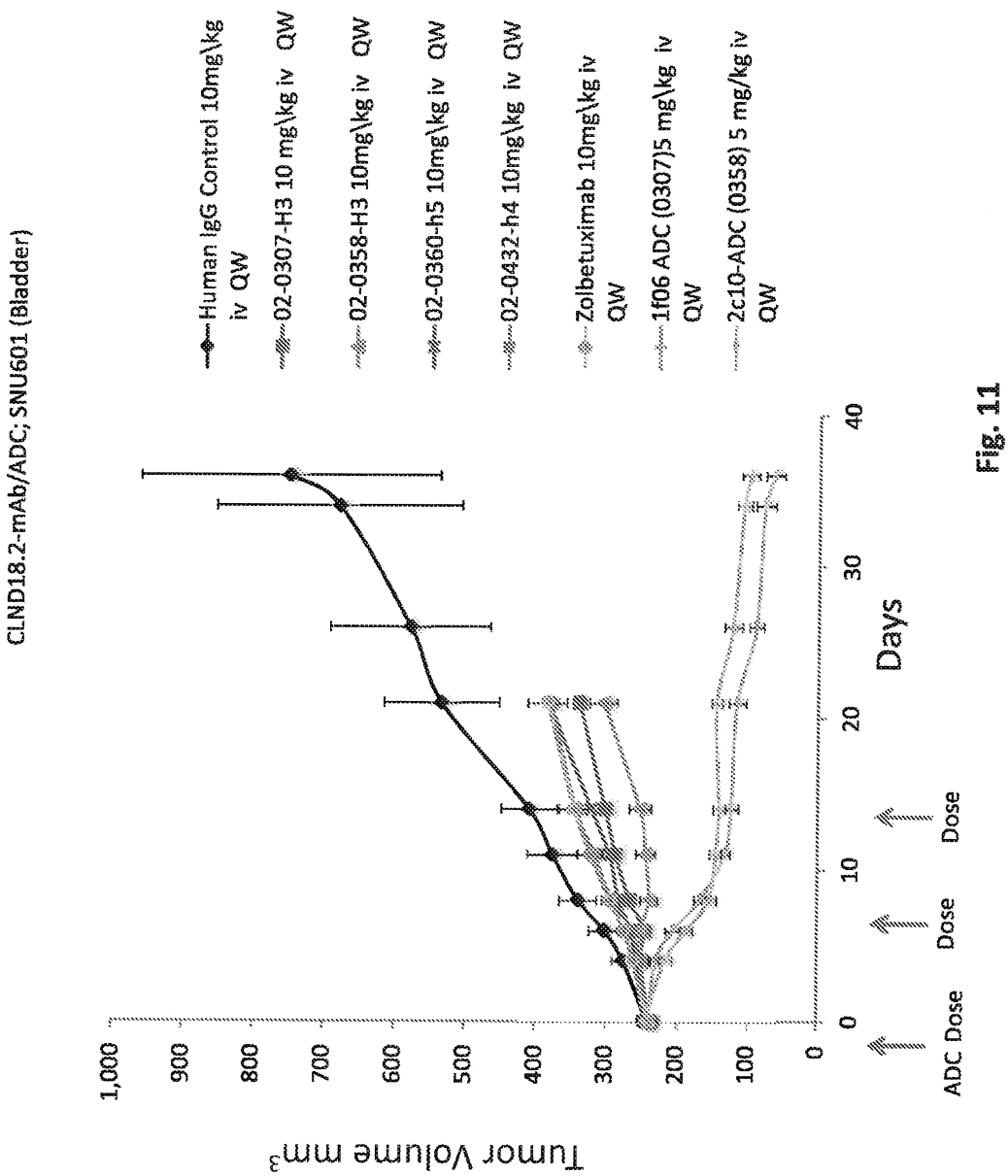

CLND18.2-mAb/ADC; SNU601 (Bladder)
Tumor Volume mm3
1,000
900
800
700
600
500
400
300
200
100
0
0
10
20
30
40
Days
ADC Dose
Dose
Dose
Human IgG Control 10mg\kg iv QW
02-0307-H3 10 mg\kg iv QW
02-0358-H3 10mg\kg iv QW
02-0360-h5 10mg\kg iv QW
02-0432-h4 10mg\kg iv QW
Zolbetuximab 10mg\kg iv QW
1f06 ADC (0307)5 mg\kg iv QW
2c10-ADC (0358) 5 mg/kg iv QW

Fig. 11

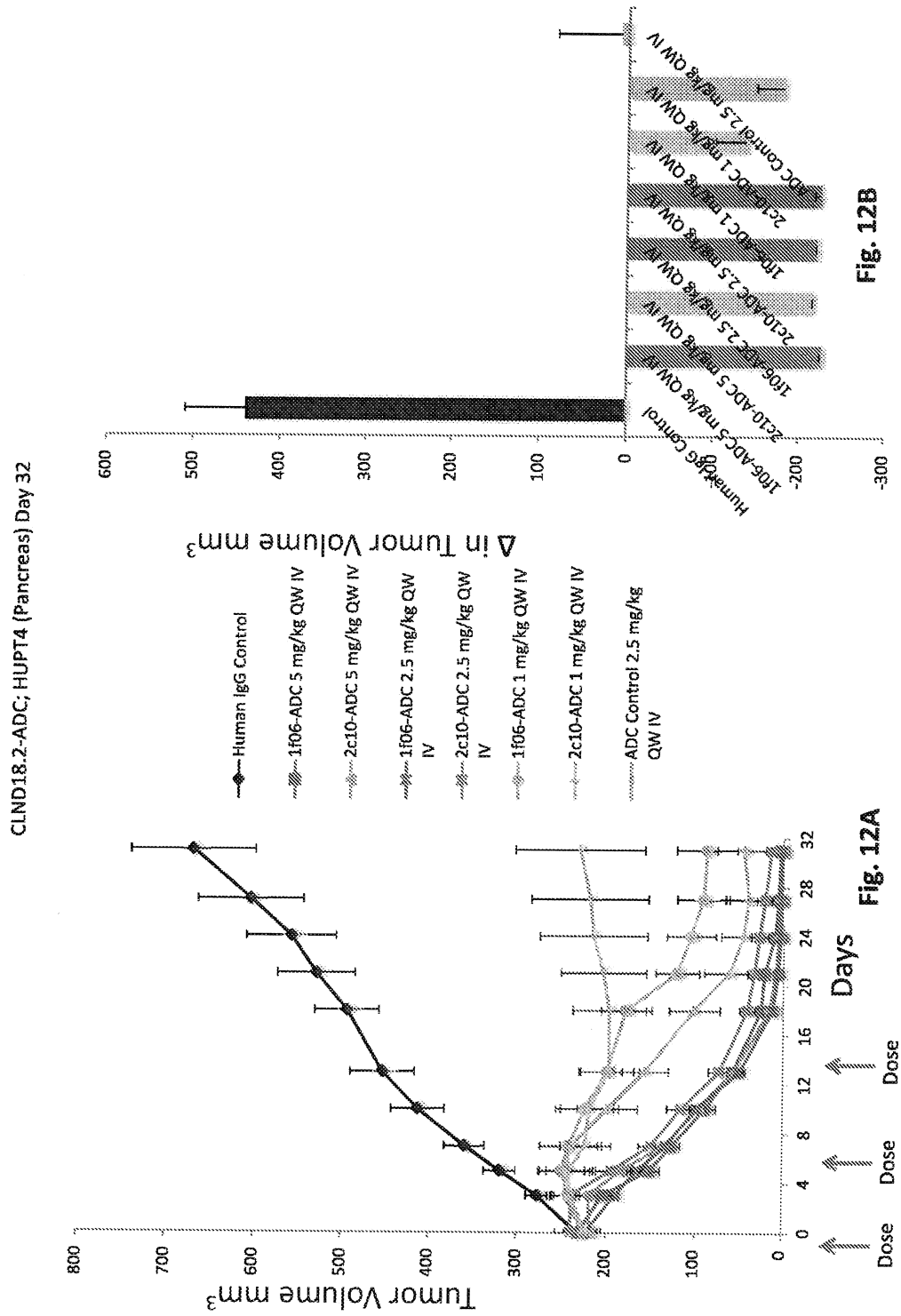

CLND18.2-ADC; HUPT4 (Pancreas) Day 32
Tumor Volume mm3
Days
Dose
Dose
Dose
Human IgG Control
1f06-ADC 5 mg/kg QW IV
2c10-ADC 5 mg/kg QW IV
1f06-ADC 2.5 mg/kg QW IV
2c10-ADC 2.5 mg/kg QW IV
1f06-ADC 1 mg/kg QW IV
2c10-ADC 1 mg/kg QW IV
ADC Control 2.5 mg/kg QW IV
Fig. 12A
Δ in Tumor Volume mm3
Human IgG Control
1f06-ADC 5 mg/kg QW IV
2c10-ADC 5 mg/kg QW IV
1f06-ADC 2.5 mg/kg QW IV
2c10-ADC 2.5 mg/kg QW IV
1f06-ADC 1 mg/kg QW IV
2c10-ADC 1 mg/kg QW IV
ADC Control 2.5 mg/kg QW IV
Fig. 12B

Fig. 13

SEQ ID NO:	Ab Clone	Amino Acid Sequence
		Light Chain Variable Region
11	307	DIVMTQSPSSLTVTTGEKVTMSCKSSQSLLNSGNQKNYLSWYQQIPGQPPKLLFYWASTRESGVPDRFTGSGS GTDFTLTISNVQAEDLAVYYCQNDYSYPFTFGAGTKLELR
13	369	DILMTQSPSSLTVTAGEKVTMTCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASSRESGVPDRFTGSGS GTDFTLTISSVQAEDLAVYYCQNDYSYPFTFGAGTKLELK
15	376	DIVMTQSPSSLTVTAGEKVTMSCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFTGSGS GTGFTLTISSVQAEDLAVYYCQNDYSYPFTFGAGTKLELK
17	358	DIVMTQSPSSLTVTAGEKVTMSCKSSQSLFNSGNQRNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFTGSGS GTGFTLTISSVQAEDLAFYYCQNVYIYPLTFGLGTKLELR
19	384	DIVMTQSPSSLTVTAGEKVTMSCKSSQSLLNSGNQKNYLTWYQQRPGQPPKLLIYWASTRESGVPDRFTGSGS GTDFTLTISSVQAEDLAVYCCQNNYYYPFTFGGGTKLGIK
21	360	DIVMTQSPSSLAVTAGEQVTMSCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASIRQSGVPDRFTGSGS GTDFTLTISSVQAEDLAVYYCLNDYGFPLTFGAGTKLELK
23	432	DIVMTQSPSSLTVTAREKVTMNCKSTQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFTGSGS GTDFTLTISSVQAEDLAVYYCQNAYYYPFTFGGGTKLEIK
25	400	DVVMTQSPSSLTVTAGEKVTMNCKSSQSLLNSGNQRSYLTWYQQKPGQPPKLLIYWASTRESGAPDRFTGSGS GADFTLTISSVQAEDLAIYYCQNNYNYPFTFGSGTKLEIK
27	331	DIVMTQSPSSLTVTAGEKVTMSCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLFYWASTKKSGVPDRFTGSGS RTDFTLTISSVQAEDLAVYYCLNDYSFPLTFGAGTKLELK
29	347	DIVMTQSPSSLTVTAGEKVTMSCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTRQSGVPDRFTGSGS GTDFTLTISSVQAEDLTVYYCLNDYSFPLTFGAGTKLELK
31	339	DIVMTQSPSSLTVTAGEKVTMTCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTGASGVPDRFTGSGS GTDFTLTISSAQAADLAVYYCLNDYSFPLTFGAGTKLELK
33	301	DIVMTQSPSSLAVTTGEQVTMNCKSSQSLLNSGNQKNYLTWYQQKTGQSPKLLIYWASTRQSGVPDRFTGSGS GTDFTLTISSVQAEDLAVYYCLNDYGFPLTFGAGTKLELK
35	392	DIVMTQSPSSLTVTTGEKVTMDCKSSQSLLNSGNQKNYLTWYQQKSGQPPKLLIYWASIRKSGVPDRFTGSGS GTDFTLTISSVQAEDLAVYYCLNDYSFPLTFGAGTKLELK
37	416	QIVLTQSPAIMSASPGQKVTITCSASSTINYMHWYQQKLGSSPKLWIYDTSKLAPGVPARFSGSGSGTSYSLT ISSMEAEDAASYFCHQWSSYPPTFGSGTKLELK
39	409	DIQMTQTTSSLSASLGDRVTISCRASQDISNYLNWYQQKPDGTVKLLIYYTSRLHSGVPSRFSGSGSGTDYSL TISNLEPEDIATYYCQHYSKLPPTFGSGTKLEIK
41	424	DIVITQDELSNPVTSGESVSISCRSSKSLLYKDGKTYLNWFLQRPGQSPQLLVYWMSTRASGVSDRFSGSGSG TDFTLEISRVKAEDVGVYYCQQVVYYPYTFGSGTKLEIK
58	Benchmark 1-175D10	DIVMTQSPSSLTVTAGEKVTMSCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFTGSGS GTDFTLTISSVQAEDLAVYYCQNDYSYPFTFGSGTKLEIK

Fig. 13, cont.

SEQ ID NO:	Ab Clone	Amino Acid Sequence
60	Benchmark 2-163E12	DIVMTQSPSSLTVTAGEKVTMSCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFTGSGS GTDFTLTISSVQAEDLAVYYCQNDYSYPLTFGAGTKLELK
62	Benchmark 3-zoletuximab	DIVMTQSPSSLTVTAGEKVTMSCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFTGSGS GTDFTLTISSVQAEDLAVYYCQNDYSYPFTFGSGTKLEIK
		Heavy Chain Variable Region
10	307	DVKLVESGGGLVKPGGSLKLSCAASGFTFSSYTMSWVRQTPEKRLEWVATIIIGGSYTYYPDSVKGRFTISRD NAKNTLYLQMSSLKSEDTAMYYCTRLVKGNAMDYWGQGTSVAVSS
12	369	DVKLVESGGGLVKPGGSLKLSCAASGFTFTSYTMSWVRQTPEKRLEWVATIIIGGSYTYYPDSVKGRFTISRD NAKNTLYLQMSSLKSEDTAMYYCTRLVKGNAMDYWGQGTSVTVSS
14	376	DVKLVESGGGLVKPGGSLKLSCAASGFTFSSYTMSWVRQTPEKRLYWVATISSGVSYTYYPDSVKGRFTISRD NAKNTLYLQMSSLKSEDTAMYYCTRLTKGNAMDYWGQGTSVTVSS
16	358	VVQLVESGGDFVQPGGSRKLSCAVSGFTFSSFGMHWVRQAPEKGLEWVAYISSGTTNIYYADTVKGRFTVSRD NPKNSLFLHMTSLRSEDTAMYYCVRSGYYGNSLDYWGQGTPLTVSS
18	384	QVQLQQSGAELARPGASVKLSCKASDYTFTSYVISWVKQRTGQGLEWIGEIYPRNGNTYYNEKFKGKATLTAD KSSSTAYMELRSLTSEDSAVYFCARSYYGNSFAYWGQGTLVTVSA
20	360	VVQLQQSGPELVKPGASVKMSCKASGYTFTSYLMHWVRQKPGLGLDWIGYINPYNDGTNYNAKFIDKATLTSD KTSSTAYMELSSLTSEDSAIYYCTRGDYWGQGTSVTVSS
22	432	QIQLQQSGAELARPRASVKLSCKASGYTFTSDVISWVKQRPGQGLEWIGESYLRNGNTYYNENFKGKATLTAD KSSSTAYMELRSLTSEDSAVYFCARSYYGNSFAYWGQGTLVTVSA
24	400	QVQLKESGPGLVAPSQSLSITCTVSGFSLNSYGVSWVRQPPGKGLEWLGVIWGDGSTNYHSALKSRLNINKDK SKSQVFLKLNSLQTDDTATYYCARPTRGNAMDYWGQGTSVTVSS
26	331	EVQLQQSGPELVKPGASVRMSCKASGYTFTSYIMHWVKQKPGQGPEWMGYINPYNDGTNYNEKFKDKATLTSD KSSSTAYMDLSSLTSEDSAVYYCTRGDYWGQGTSVTVSS
28	347	EVQLQQSGPELVKPGASVKMSCKASGYTFTSYLIHWVKQKPGQGLEWIGYINPYNDATYYNEKFKAKATLTSD KSSSTAYMELSSLTSEDTAIYYCTRGDYWSQGTSVTVSS
30	339	EVQLQQSGPELVKPGASVKMSCKASGYTFTSYVMHWVKQKPGQGLEWIGYFNPYNDDTKYNEKFKGKATLTSD KSSSTAYMDLSSLTSEDSAVYXCTRGDYWGQGTSVTVSS
32	301	VVQLQQSGPELVKPGASVKMSCKASGYTFTSFLIHWVRQKPGLGLEWIGYINPYDYGINYNVKFMDKVTLTSD KTSSTAYMELSSLTSADSAIYYCTRGDYWGQGTSVIVSS
34	392	EVQLQQSGPELVKPGASVKMSCKASGFTFTSYVMHWVKQKSGQGLEWIGYINPYNDDIKYNAKFEDKATLTSD RSSSTAYMELSSLTSDDSAVYFCTRGDYWGQGTTLTVSS
36	416	EFQLQQSGPELVKPGASVKISCKASVYSFTGYNMNWVKQSNGKSLEWIGVINPNYGNTNYNQRFKGKATLTVD QSSSTAYMQLNSLTSEDSAVYYCARSEDYYNIRGASWGQGTLVTVSA
38	409	QVQLQQSGAELARPGASVKLSCKASGYTFTSYGISWVKQRTGQGLEWIGEISPRSGNTYYNEKFKGKATLTAD KSSSTAYMELRSLTSEDSAVYFCATGVITTVIPTDWYFDVWGTGTTVTVSS

Fig. 13, cont.

SEQ ID NO:	Ab Clone	Amino Acid Sequence
40	424	EVQLQQSGPELVKPGASVKISCKASGYSFTVYYMNWVKQSPEKSLEWIGEINPSTGGTTYNPKFKAKATLTVD KSSSTAYMQLKSLTSEDSAIYFCVRWADYWGQGTTLTVSS
59	Benchmark 1	QVQLQQPGAELVRPGASVKLSCKASGYTFTSYWINWVKQRPGQGLEWIGNIYPSDSYTNYNQKFKDKATLTVD KSSSTAYMQLSSPTSEDSAVYYCTRSWRGNSFDYWGQGTTLTVSS
61	Benchmark 2	QVQLQQSGAELARPGASVKLSCKASGYTFTDYYINWVKQRTGQGLEWIGEIYPGSGNTYYNEKFKGKATLTAD KSSSTAYMQLSSLTSEDSAVYFCARSYGAFDYWGQGTTLTVSS
148	Benchmark 2-1	QIQLVQSGPELKKPGETVKISCKASGYTFTNYGMNWVKQAPGKGLKWMGWINTNTGEPTYAEEFKGRFAFSLE TSASTAYLQINNLKNEDTATYFCARLGFGNAMDYWGQGTSVTVSS
63	Benchmark 3-zoletuximab	QVQLQQPGAELVRPGASVKLSCKASGYTFTSYWINWVKQRPGQGLEWIGNIYPSDSYTNYNQKFKDKATLTVD KSSSTAYMQLSSPTSEDSAVYYCTRSWRGNSFDYWGQGTTLTVSS
		Humanized Light Chain Variable Region
43	HuAb307-1 (L1)	DIVMTQSP**D**SL**A**V**S**LGE**R**A**T**I**N**CKSSQSLLNSGNQKNYLSWYQQ**K**PGQPPKLL**I**YWASTRESGVPDRF**S**GSGS GTDFTLTI**SS**LQAED**V**AVYYCQNDYSYPFTFG**Q**GTKLE**IK**
44	HuAb307-2 (L2)	DIVMTQSP**D**SL**A**V**S**LGE**R**A**T**I**N**CKSSQSLLNSGNQKNYLSWYQQKPGQPPKLLFYWASTRESGVPDRF**S**GSGS GTDFTLTI**SS**LQAED**V**AVYYCQNDYSYPFTFG**Q**GTKLE**IK**
45	HuAb307-3 (L3)	DIVMTQSP**D**SL**A**V**S**LGE**R**V**T**M**N**CKSSQSLLNSGNQKNYLSWYQQKPGQPPKLLFYWASTRES**G**VPDRF**S**GSGS GTDFTLTI**S**VQAED**V**AVYYCQNDYSYPFTFG**Q**GTKLE**IK**
47	HuAb376-1 (L1)	DIVMTQSP**D**SL**A**V**S**LGE**R**A**T**I**N**CKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRF**S**GSGS GT**D**FTLTISS**L**QAED**V**AVYYCQNDYSYPFTFG**Q**GTKLEIK
48	HuAb376-2 (L2)	DIVMTQSP**D**SL**A**V**S**LGE**R**VTMNCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRF**S**GSGS GT**D**FTLTISSVQAED**V**AVYYCQNDYSYPFTFGQGTKLEIK
149	HuAb358-1 (L1)	DIVMTQSP**D**SL**A**V**S**LGE**R**A**T**I**N**CKSSQSLFNSGNQRNYLTWYQQKPGQPPKLLIYWASTRESGVPDRF**S**GSGS GT**D**FTLTISS**L**QAED**VAV**YYCQNVYIYPLTFGQGTKLE**IK**
150	HuAb358-2 (L2)	DIVMTQSP**D**SL**A**V**S**LGE**R**VTM**N**CKSSQSLFNSGNQRNYLTWYQQKPGQPPKLLIYWASTRESGVPDRF**S**GSGS GT**D**FTLTISSVQAED**VAV**YYCQNVYIYPLTFGQGTKLEI**K**
53	HuAb360-1 (L1)	DIVMTQSP**D**SLAV**S**LGE**R**A**T**I**N**CKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASIRQSGVPDRF**S**GSGS GTDFTLTISS**L**QAED**V**AVYYCLNDYGFPLTFG**Q**GTKLE**I**K
54	HuAb360-2 (L2)	DIVMTQSP**D**SLAV**S**LGE**R**VTM**N**CKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASIRQSGVPDRFSGSGS GTDFTLTISSVQAED**V**AVYYCLNDYGFPLTFG**Q**GTKLE**I**K
53	HuAb360-3 (L1)	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASIRQSGVPDRFSGSGS GTDFTLTISSLQAEDVAVYYCLNDYGFPLTFGQGTKLEIK
54	HuAb360-4 (L2)	DIVMTQSPDSLAVSLGERVTMNCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASIRQSGVPDRFSGSGS GTDFTLTISSVQAEDVAVYYCLNDYGFPLTFGQGTKLEIK
53	HuAb360-5 (L1)	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASIRQSGVPDRFSGSGS GTDFTLTISSLQAEDVAVYYCLNDYGFPLTFGQGTKLEIK

Fig. 13, cont.

SEQ ID NO:	Ab Clone	Amino Acid Sequence
54	HuAb360-6 (L2)	DIVMTQSPDSLAVSLGERVTMNCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASIRQSGVPDRFSGSGS GTDFTLTISSVQAEDVAVYYCLNDYGFPLTFGQGTKLEIK
50	HuAb432-1 (L1)	DIVMTQSPDSLAVSLGERATINCKSTQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGS GTDFTLTISSLQAEDVAVYYCQNAYYYPFTFGQGTKLEIK
51	HuAb432-2 (L2)	DIVMTQSPDSLAVSLGERVTMNCKSTQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGS GTDFTLTISSVQAEDVAVYYCQNAYYYPFTFGQGTKLEIK
50	HuAb432-3 (L1)	DIVMTQSPDSLAVSLGERATINCKSTQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGS GTDFTLTISSLQAEDVAVYYCQNAYYYPFTFGQGTKLEIK
51	HuAb432-4 (L2)	DIVMTQSPDSLAVSLGERVTMNCKSTQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGS GTDFTLTISSVQAEDVAVYYCQNAYYYPFTFGQGTKLEIK
		Humanized Heavy Chain Variable Region
42	HuAb307-1 (H2)	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYTMSWVRQAPGKGLEWVATIIIGGSYTYYADSVKGRFTISRD NSKNTLYLQMNSLRAEDTAVYYCTRLVKGNAMDYWGQGTLVTVSS
42	HuAb307-2 (H2)	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYTMSWVRQAPGKGLEWVATIIIGGSYTYYADSVKGRFTISRD NSKNTLYLQMNSLRAEDTAVYYCTRLVKGNAMDYWGQGTLVTVSS
42	HuAb307-3 (H2)	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYTMSWVRQAPGKGLEWVATIIIGGSYTYYADSVKGRFTISRD NSKNTLYLQMNSLRAEDTAVYYCTRLVKGNAMDYWGQGTLVTVSS
46	HuAb376-1 (H2)	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYTMSWVRQAPGKGLEWVATISSGVSYTYYADSVKGRFTISRD NSKNTLYLQMNSLRAEDTAVYYCTRLTKGNAMDYWGQGTLVTVSS
46	HuAb376-2 (H2)	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYTMSWVRQAPGKGLEWVATISSGVSYTYYADSVKGRFTISRD NSKNTLYLQMNSLRAEDTAVYYCTRLTKGNAMDYWGQGTLVTVSS
131	HuAb358-1 (H2)	EVQLVESGGGLVQPGGSLRLSCAVSGFTFSSFGMHWVRQAPGKGLEWVAYISSGTTNIYYADSVKGRFTVSRD NAKNSLYLQMNSLRAEDTAVYYCVRSGYYGNSLDYWGQGTLVTVSS
131	HuAb358-2 (H2)	EVQLVESGGGLVQPGGSLRLSCAVSGFTFSSFGMHWVRQAPGKGLEWVAYISSGTTNIYYADSVKGRFTVSRD NAKNSLYLQMNSLRAEDTAVYYCVRSGYYGNSLDYWGQGTLVTVSS
52	HuAb360-1 (H2)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYLMHWVRQAPGQGLEWIGYINPYNDGTNYAQKFQGRVTMTSD TSTSTVYMELSSLRSEDTAVYYCTRGDYWGQGTLVTVSS
52	HuAb360-2 (H2)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYLMHWVRQAPGQGLEWIGYINPYNDGTNYAQKFQGRVTMTSD TSTSTVYMELSSLRSEDTAVYYCTRGDYWGQGTLVTVSS
55	HuAb360-3 (H3)	QVQLVQSGAEVKKPGASVKMSCKASGYTFTSYLMHWVRQAPGQGLEWIGYINPYNDGTNYAQKFQGRATLTSD TSTSTAYMELSSLRSEDTAVYYCTRGDYWGQGTLVTVSS
55	HuAb360-4 (H3)	QVQLVQSGAEVKKPGASVKMSCKASGYTFTSYLMHWVRQAPGQGLEWIGYINPYNDGTNYAQKFQGRATLTSD TSTSTAYMELSSLRSEDTAVYYCTRGDYWGQGTLVTVSS
56	HuAb360-5 (H4)	QVQLVQSGAEVKKPGASVKMSCKASGYTFTSYLMHWVRQAPGQGLEWIGYINPYNDGTNYAQKFQGRATLTSD KSTSTAYMELSSLRSEDTAVYYCTRGDYWGQGTLVTVSS

Fig. 13, cont.

SEQ ID NO:	Ab Clone	Amino Acid Sequence
56	HuAb360-6 (H4)	QVQLVQSGAEVKKPGASVKMSCKASGYTFTSYLMHWVRQAPGQGLEWIGYINPYNDGTNYAQKFQGRATLTSD KSTSTAYMELSSLRSEDTAVYYCTRGDYWGQGTLVTVSS
57	HuAb432-1 (H1)	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSDVISWVRQAPGQGLEWMGESYLRNGNTYYAQKFQGRVTITAD KSTSTAYMELSSLRSEDTAVYYCARSYYGNSFAYWGQGTLVTVSS
57	HuAb432-2 (H1)	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSDVISWVRQAPGQGLEWMGESYLRNGNTYYAQKFQGRVTITAD KSTSTAYMELSSLRSEDTAVYYCARSYYGNSFAYWGQGTLVTVSS
49	HuAb432-3 (H2)	QVQLVQSGAEVKKPGSSVKLSCKASGYTFTSDVISWVRQAPGQGLEWIGESYLRNGNTYYAQKFQGRATLTAD KSTSTAYMELSSLRSEDTAVYYCARSYYGNSFAYWGQGTLVTVSS
49	HuAb432-4 (H2)	QVQLVQSGAEVKKPGSSVKLSCKASGYTFTSDVISWVRQAPGQGLEWIGESYLRNGNTYYAQKFQGRATLTAD KSTSTAYMELSSLRSEDTAVYYCARSYYGNSFAYWGQGTLVTVSS

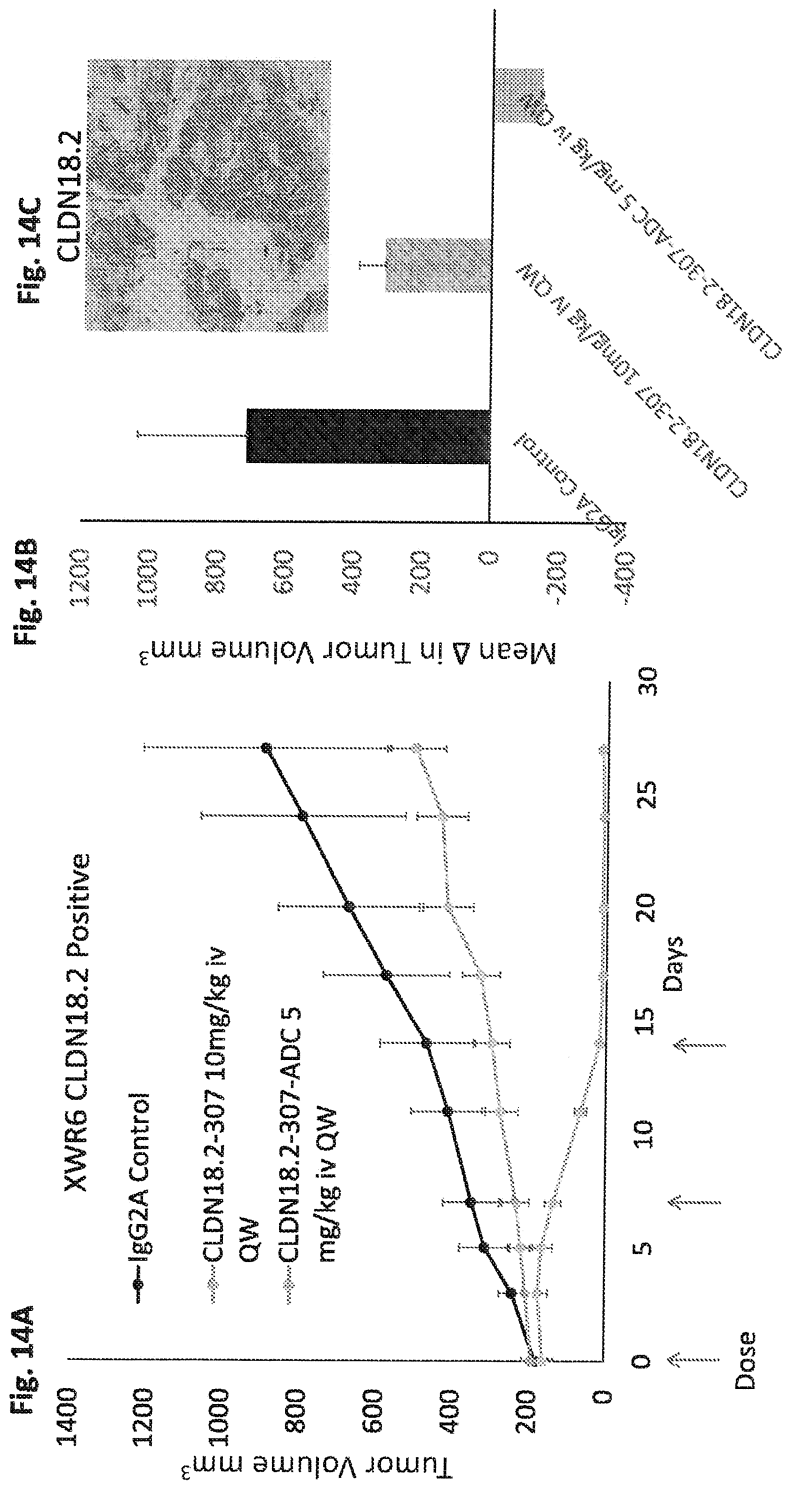


Fig. 14A
XWR6 CLDN18.2 Positive
IgG2A Control
CLDN18.2-307 10mg/kg iv QW
CLDN18.2-307-ADC 5 mg/kg iv QW
Tumor Volume mm3
1400
1200
1000
800
600
400
200
0
0
5
10
15
20
25
30
Days
Dose
Fig. 14B
Mean Δ in Tumor Volume mm3
1200
1000
800
600
400
200
0
-200
-400
IgG2A Control
CLDN18.2-307 10mg/kg iv QW
CLDN18.2-307-ADC 5 mg/kg iv QW
Fig. 14C
CLDN18.2

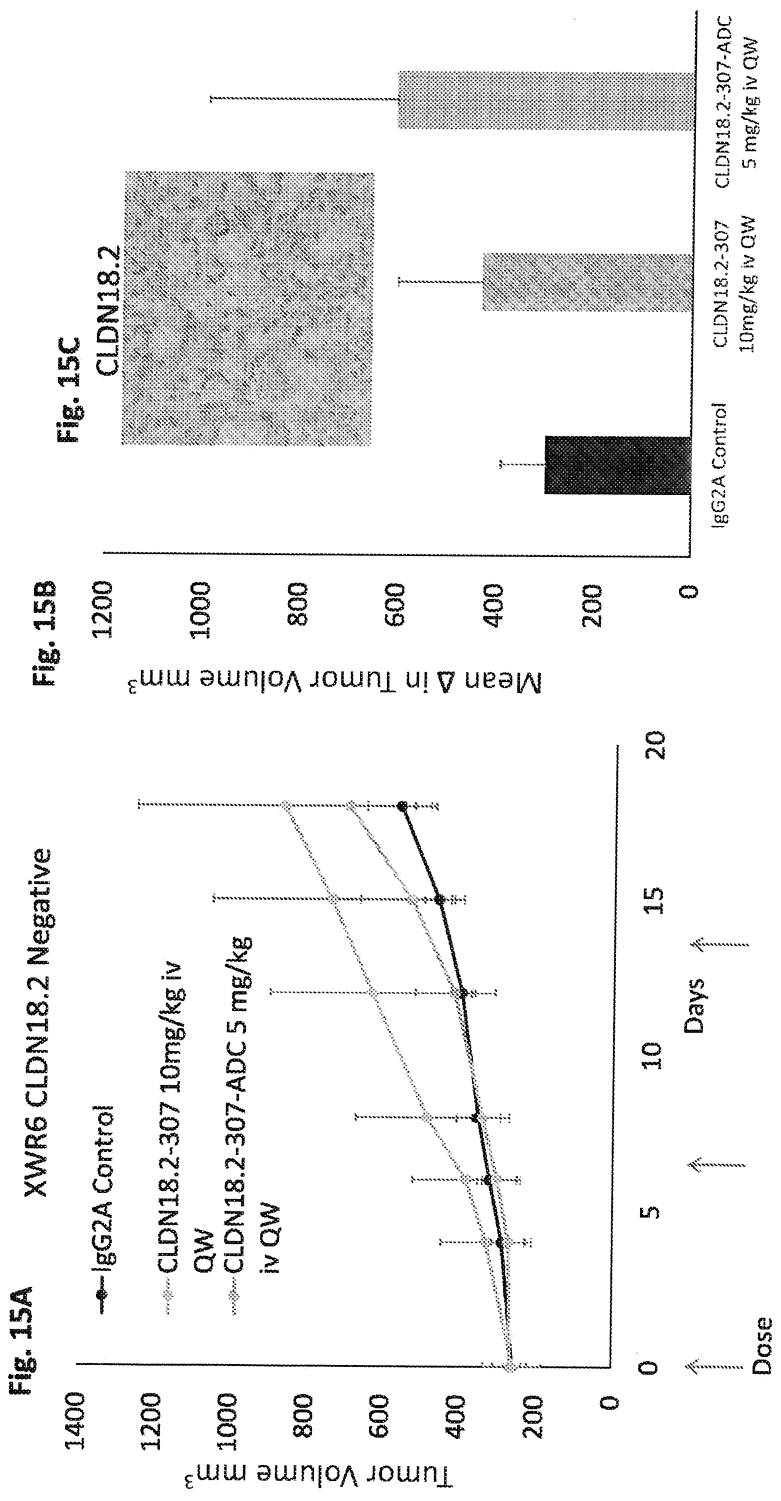


Fig. 15A
XWR6 CLDN18.2 Negative
IgG2A Control
CLDN18.2-307 10mg/kg iv QW
CLDN18.2-307-ADC 5 mg/kg iv QW
Tumor Volume mm3
1400
1200
1000
800
600
400
200
0
0
5
10
15
20
Days
Dose
Fig. 15B
Mean Δ in Tumor Volume mm3
1200
1000
800
600
400
200
0
IgG2A Control
CLDN18.2-307 10mg/kg iv QW
CLDN18.2-307-ADC 5 mg/kg iv QW
Fig. 15C
CLDN18.2

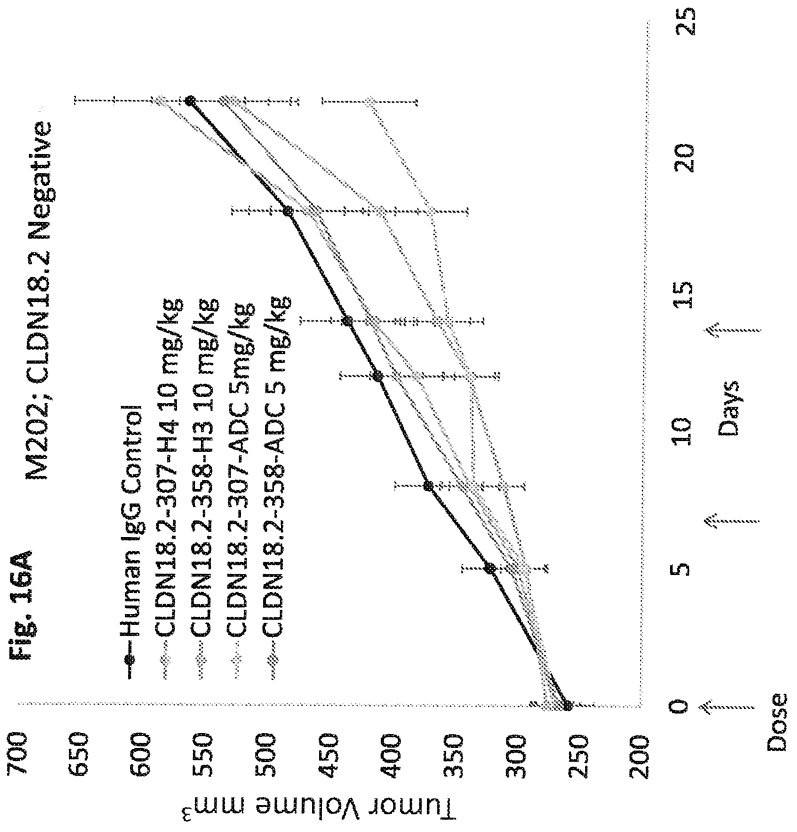


Fig. 16A
M202; CLDN18.2 Negative
Tumor Volume mm3
700
650
600
550
500
450
400
350
300
250
200
Human IgG Control
CLDN18.2-307-H4 10 mg/kg
CLDN18.2-358-H3 10 mg/kg
CLDN18.2-307-ADC 5mg/kg
CLDN18.2-358-ADC 5 mg/kg
0
5
10
15
20
25
Dose
Days

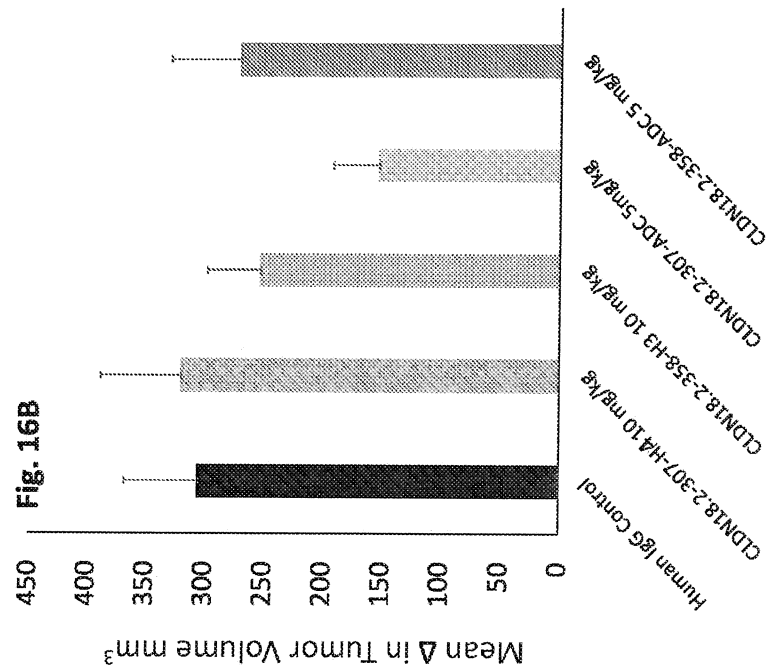


Fig. 16B
Mean Δ in Tumor Volume mm3
450
400
350
300
250
200
150
100
50
0
Human IgG Control
CLDN18.2-307-H4 10 mg/kg
CLDN18.2-358-H3 10 mg/kg
CLDN18.2-307-ADC 5mg/kg
CLDN18.2-358-ADC 5 mg/kg

Fig. 17

SEQ ID NO	Name	Description	Sequence
131	02-0358-4h_VH	02-0358-4h antibody	EVQLVESGGGLVQPGGSLRLSCAVSGFTFSSFGMHWVRQAPGKGLEWVAYISSGTTNIYYADSVKGRFTVSRDNAKNSLYLQMNSLRAEDTAVYYCVRSGYYGNSLDYWGQGTLVTVSS
135	02-0358-4h_VL	02-0358-4h antibody	DIVMTQSPDSLAVSLGERVTMNCKSSQSLFQSGNQRNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSVQAEDVAVYYCQNVYIYPLTFGQGTKLEIK
131	02-0358-5h_VH	02-0358-5h antibody	EVQLVESGGGLVQPGGSLRLSCAVSGFTFSSFGMHWVRQAPGKGLEWVAYISSGTTNIYYADSVKGRFTVSRDNAKNSLYLQMNSLRAEDTAVYYCVRSGYYGNSLDYWGQGTLVTVSS
138	02-0358-5h_VL	02-0358-5h antibody	DIVMTQSPDSLAVSLGERVTMNCKSSQSLFSSGNQRNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSVQAEDVAVYYCQNVYIYPLTFGQGTKLEIK
133	02-0358-6h_VH	02-0358-6h antibody	EVQLVESGGGLVQPGGSLRLSCAVSGFTFSSFGMHWVRQAPGKGLEWVAYISSGTTNIYYADSVKGRFTVSRDNAKNSLYLQMNSLRAEDTAVYYCVRSGYYGQSLDYWGQGTLVTVSS
137	02-0358-6h_VL	02-0358-6h antibody	DIVMTQSPDSLAVSLGERVTMNCKSSQSLFNSGNQRNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSVQAEDVAVYYCQNVYIYPLTFGQGTKLEIK
134	02-0358-7h_VH	02-0358-7h antibody	EVQLVESGGGLVQPGGSLRLSCAVSGFTFSSFGMHWVRQAPGKGLEWVAYISSGTTNIYYADSVKGRFTVSRDNAKNSLYLQMNSLRAEDTAVYYCVRSGYYGSSLDYWGQGTLVTVSS
137	02-0358-7h_VL	02-0358-7h antibody	DIVMTQSPDSLAVSLGERVTMNCKSSQSLFNSGNQRNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSVQAEDVAVYYCQNVYIYPLTFGQGTKLEIK
133	02-0358-8h_VH	02-0358-8h antibody	EVQLVESGGGLVQPGGSLRLSCAVSGFTFSSFGMHWVRQAPGKGLEWVAYISSGTTNIYYADSVKGRFTVSRDNAKNSLYLQMNSLRAEDTAVYYCVRSGYYGQSLDYWGQGTLVTVSS
135	02-0358-8h_VL	02-0358-8h antibody	DIVMTQSPDSLAVSLGERVTMNCKSSQSLFQSGNQRNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSVQAEDVAVYYCQNVYIYPLTFGQGTKLEIK
133	02-0358-9h_VH	02-0358-9h antibody	EVQLVESGGGLVQPGGSLRLSCAVSGFTFSSFGMHWVRQAPGKGLEWVAYISSGTTNIYYADSVKGRFTVSRDNAKNSLYLQMNSLRAEDTAVYYCVRSGYYGQSLDYWGQGTLVTVSS
136	02-0358-9h_VL	02-0358-9h antibody	DIVMTQSPDSLAVSLGERVTMNCKSSQSLFSSGNQRNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSVQAEDVAVYYCQNVYIYPLTFGQGTKLEIK
134	02-0358-10h_VH	02-0358-10h antibody	EVQLVESGGGLVQPGGSLRLSCAVSGFTFSSFGMHWVRQAPGKGLEWVAYISSGTTNIYYADSVKGRFTVSRDNAKNSLYLQMNSLRAEDTAVYYCVRSGYYGSSLDYWGQGTLVTVSS
135	02-0358-10h_VL	02-0358-10h antibody	DIVMTQSPDSLAVSLGERVTMNCKSSQSLFQSGNQRNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSVQAEDVAVYYCQNVYIYPLTFGQGTKLEIK
134	02-0358-11h_VH	02-0358-11h antibody	EVQLVESGGGLVQPGGSLRLSCAVSGFTFSSFGMHWVRQAPGKGLEWVAYISSGTTNIYYADSVKGRFTVSRDNAKNSLYLQMNSLRAEDTAVYYCVRSGYYGSSLDYWGQGTLVTVSS
136	02-0358-11h_VL	02-0358-11h antibody	DIVMTQSPDSLAVSLGERVTMNCKSSQSLFSSGNQRNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSVQAEDVAVYYCQNVYIYPLTFGQGTKLEIK
42	02-h1F06-5h_VH	02-0307-5h antibody	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYTMSWVRQAPGKGLEWVATIIGGSYTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCTRLVKGNAMDYWGQGTLVTVSS
140	02-h1F06-5h_VL	02-0307-5h antibody	DIVMTQSPDSLAVSLGERVTMNCKSSQSLLQSGNQKNYLSWYQQKPGQPPKLLFYWASTRESGVPDRFSGSGSGTDFTLTISSVQAEDVAVYYCQNDYSYPFTFGQGTKLEIK
42	02-h1F06-6h_VH	02-0307-6h antibody	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYTMSWVRQAPGKGLEWVATIIGGSYTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCTRLVKGNAMDYWGQGTLVTVSS
141	02-h1F06-6h_VL	02-0307-6h antibody	DIVMTQSPDSLAVSLGERVTMNCKSSQSLLSSGNQKNYLSWYQQKPGQPPKLLFYWASTRESGVPDRFSGSGSGTDFTLTISSVQAEDVAVYYCQNDYSYPFTFGQGTKLEIK
138	02-h1F06-7h_VH	02-0307-7h antibody	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYTMSWVRQAPGKGLEWVATIIGGSYTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCTRLVKGQAMDYWGQGTLVTVSS
142	02-h1F06-7h_VL	02-0307-7h antibody	DIVMTQSPDSLAVSLGERVTMNCKSSQSLLNSGNQKNYLSWYQQKPGQPPKLLFYWASTRESGVPDRFSGSGSGTDFTLTISSVQAEDVAVYYCQNDYSYPFTFGQGTKLEIK
138	02-h1F06-8h_VH	02-0307-8h antibody	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYTMSWVRQAPGKGLEWVATIIGGSYTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCTRLVKGQAMDYWGQGTLVTVSS
140	02-h1F06-8h_VL	02-0307-8h antibody	DIVMTQSPDSLAVSLGERVTMNCKSSQSLLQSGNQKNYLSWYQQKPGQPPKLLFYWASTRESGVPDRFSGSGSGTDFTLTISSVQAEDVAVYYCQNDYSYPFTFGQGTKLEIK
138	02-h1F06-9h_VH	02-0307-9h antibody	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYTMSWVRQAPGKGLEWVATIIGGSYTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCTRLVKGQAMDYWGQGTLVTVSS
141	02-h1F06-9h_VL	02-0307-9h antibody	DIVMTQSPDSLAVSLGERVTMNCKSSQSLLSSGNQKNYLSWYQQKPGQPPKLLFYWASTRESGVPDRFSGSGSGTDFTLTISSVQAEDVAVYYCQNDYSYPFTFGQGTKLEIK
139	02-h1F06-10h_VH	02-0307-10h antibody	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYTMSWVRQAPGKGLEWVATIIGGSYTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCTRLVKGQAMDYWGQGTLVTVSS
142	02-h1F06-10h_VL	02-0307-10h antibody	DIVMTQSPDSLAVSLGERVTMNCKSSQSLLNSGNQKNYLSWYQQKPGQPPKLLFYWASTRESGVPDRFSGSGSGTDFTLTISSVQAEDVAVYYCQNDYSYPFTFGQGTKLEIK
139	02-h1F06-11h_VH	02-0307-11h antibody	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYTMSWVRQAPGKGLEWVATIIGGSYTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCTRLVKGSAMDYWGQGTLVTVSS
140	02-h1F06-11h_VL	02-0307-11h antibody	DIVMTQSPDSLAVSLGERVTMNCKSSQSLLQSGNQKNYLSWYQQKPGQPPKLLFYWASTRESGVPDRFSGSGSGTDFTLTISSVQAEDVAVYYCQNDYSYPFTFGQGTKLEIK
139	02-h1F06-12h_VH	02-0307-12h antibody	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYTMSWVRQAPGKGLEWVATIIGGSYTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCTRLVKGSAMDYWGQGTLVTVSS
141	02-h1F06-12h_VL	02-0307-12h antibody	DIVMTQSPDSLAVSLGERVTMNCKSSQSLLSSGNQKNYLSWYQQKPGQPPKLLFYWASTRESGVPDRFSGSGSGTDFTLTISSVQAEDVAVYYCQNDYSYPFTFGQGTKLEIK

Fig. 18

Order ID	Name	HER2BET parental 1ug	HER2BET parental 0.2ug	HER2BET parental 0.04ug	HER2BET cLDN18.2 1ug	HER2BET cLDN18.2 0.2ug	HER2BET cLDN18.2 0.04ug	M2G2 1ug	M2G2 0.2ug	M2G2 0.04ug	HUPT4 1ug	HUPT4 0.2ug	HUPT4 0.04ug	ratio OE	ratio native
	358 Jun 10162018	8,323.00	8,164.00	9,679.00	7,207,652.0	7,445,933.0	3,663,369.0	8,851.0	9,954.5	8,714.0	1,538,407.0	1,483,036.0	655,824.5	700.03	133.62
U2761EH060-1	02-0358-4h	9,743.00	9,875.00	9,163.00	7,989,737.0	6,273,300.5	2,280,899.0	15,099.5	10,721.5	11,716.0	1,634,110.0	1,459,323.0	433,762.0	574.82	93.97
U2761EH060-2	02-0358-5h	9,627.00	8,763.00	9,020.00	7,694,093.5	5,837,613.5	2,198,515.5	12,521.0	10,424.0	10,962.5	1,643,079.0	1,607,770.0	512,437.0	573.89	110.99
U2761EH060-3	02-0358-6h	9,256.00	9,969.00	8,441.00	7,722,012.5	4,113,183.0	691,375.0	12,774.0	10,568.0	10,456.0	1,437,921.0	1,041,623.0	222,124.0	434.71	79.94
U2761EH060-4	02-0358-7h	13,061.00	10,058.00	8,687.00	7,454,133.0	5,618,634.0	1,207,647.0	13,544.5	9,470.0	9,566.0	1,486,990.0	1,324,881.0	252,917.5	448.98	94.07
U2761EH060-5	02-0358-8h	11,052.00	11,712.50	8,051.50	3,926,428.0	2,659,513.0	463,876.0	12,614.0	8,445.0	8,869.0	888,216.0	649,161.0	193,841.0	228.71	57.85
U2761EH060-6	02-0358-9h	8,931.00	8,258.00	8,188.00	6,033,871.0	4,696,716.0	755,247.5	9,069.0	7,454.5	9,414.5	1,464,129.0	924,009.5	33,989.0	452.61	93.38
U340LEH060-1	02-0358-10h	9,988.50	9,849.50	7,017.00	4,372,013.0	2,545,571.5	447,864.0	8,366.0	8,391.0	8,197.5	782,883.0	539,386.0	27,118.0	274.27	54.07
U340LEH060-2	02-0358-11h	9,060.50	9,481.50	8,169.00	6,120,827.0	5,617,706.0	448,173.0	10,883.5	8,545.0	8,995.0	1,355,931.5	1,077,192.5	90,925.0	456.24	88.80
	307 Jun 07022018	10,207.00	7,785.00	10,070.00	6,442,704.5	6,151,103.0	882,289.0	10,194.5	10,266.0	9,137.0	1,668,181.0	1,518,551.0	357,802.0	480.23	119.76
U505BEH130-2	02-h1F06-5h	7,865.00	10,928.00	9,805.00	5,481,294.0	5,720,888.0	469,344.0	10,221.5	8,942.5	11,408.0	1,665,867.0	1,606,587.0	437,194.5	408.12	121.34
U505BEH130-3	02-h1F06-6h	8,109.00	10,555.00	8,628.00	5,506,377.0	6,545,772.0	1,101,019.5	8,874.0	8,055.0	10,555.0	1,645,893.5	1,693,376.5	412,621.0	481.94	136.51
U505BEH130-4	02-h1F06-7h	8,392.00	11,628.00	7,914.00	4,703,051.0	3,286,723.0	1,106,724.0	8,991.0	8,895.0	10,695.0	373,477.5	213,932.0	55,716.0	325.64	22.50
U505BEH130-5	02-h1F06-8h	11,460.50	10,362.00	8,408.00	2,741,802.0	1,690,797.5	574,195.5	10,637.5	7,571.0	9,893.0	217,507.0	91,583.0	33,043.0	165.62	12.17
U519NEH130-1	02-h1F06-9h	8,538.50	10,288.00	8,196.50	3,845,698.0	2,446,037.0	1,088,188.0	7,685.0	7,225.5	10,005.0	576,193.0	359,285.0	188,556.5	273.10	45.11
U519NEH130-2	02-h1F06-10h	13,151.50	9,047.50	7,776.50	2,973,269.5	2,509,094.0	566,415.0	10,404.5	7,012.0	8,390.0	101,787.0	42,834.5	20,990.0	201.79	6.42
U519NEH130-3	02-h1F06-11h	8,251.00	9,627.00	7,177.00	658,134.5	295,746.5	48,044.0	7,569.5	7,203.5	8,228.0	16,637.0	11,092.0	7,142.5	39.99	1.52
U519NEH130-4	02-h1F06-12h	8,384.00	9,948.50	8,416.00	2,442,569.5	2,024,693.0	437,912.0	7,197.0	7,266.0	9,325.0	154,905.0	63,210.5	17,154.5	183.38	9.89

Fig. 19

Cell Line	02-0307-h4-AF647 10ug	02-0307-h4-AF647 1ug	02-0307-h4-AF647 0.1ug	02-0358-h3-AF647 10ug	02-0358-h3-AF647 1ug	02-0358-h3-AF647 0.1ug	02-0307-h6-AF647 10ug	02-0307-h6-AF647 1ug	02-0307-h6-AF647 0.1ug	02-0358-h5-AF647 10ug	02-0358-h5-AF647 1ug	02-0358-h5-AF647 0.1ug
HEK293T parental	12,759.00	5,328.00	3,276.00	16,812.50	4,198.00	3,268.00	22,390.50	9,051.00	2,726.00	29,683.50	8,287.00	3,589.50
HEK293T human CLDN18.2 mGFP clone C12	5,670,306.00	4,311,651.00	578,978.00	3,920,860.00	2,704,978.00	542,378.00	7,156,050.50	7,325,915.00	4,029,889.00	7,049,930.50	6,956,214.00	3,801,790.00
HEK293T human CLDN18.1 mGFP 2B14	76,882.00	54,053.50	52,064.00	99,053.00	55,250.00	50,394.00	155,836.00	68,751.00	53,053.50	140,467.00	64,830.00	52,692.00
HEK293T mouse CLDN18.2 mGFP mass pop	6,924,857.00	4,027,795.50	472,034.50	5,528,398.00	2,287,345.50	285,031.00	9,668,013.00	9,479,164.00	2,845,982.00	9,496,337.00	8,763,309.00	2,517,805.00
HEK293T dogCLDN18 moxGFP mass pop	10,150.00	6,025.50	3,862.00	11,728.50	4,232.00	3,705.00	21,807.00	9,480.00	3,691.00	20,562.00	8,759.00	4,696.00
HEK293T rat CLDN18 moxGFP Clone5	13,790.00	7,323.00	3,807.50	16,723.50	5,067.00	3,715.50	30,657.50	10,860.00	3,601.00	31,180.00	12,384.00	4,580.00

Fig. 20

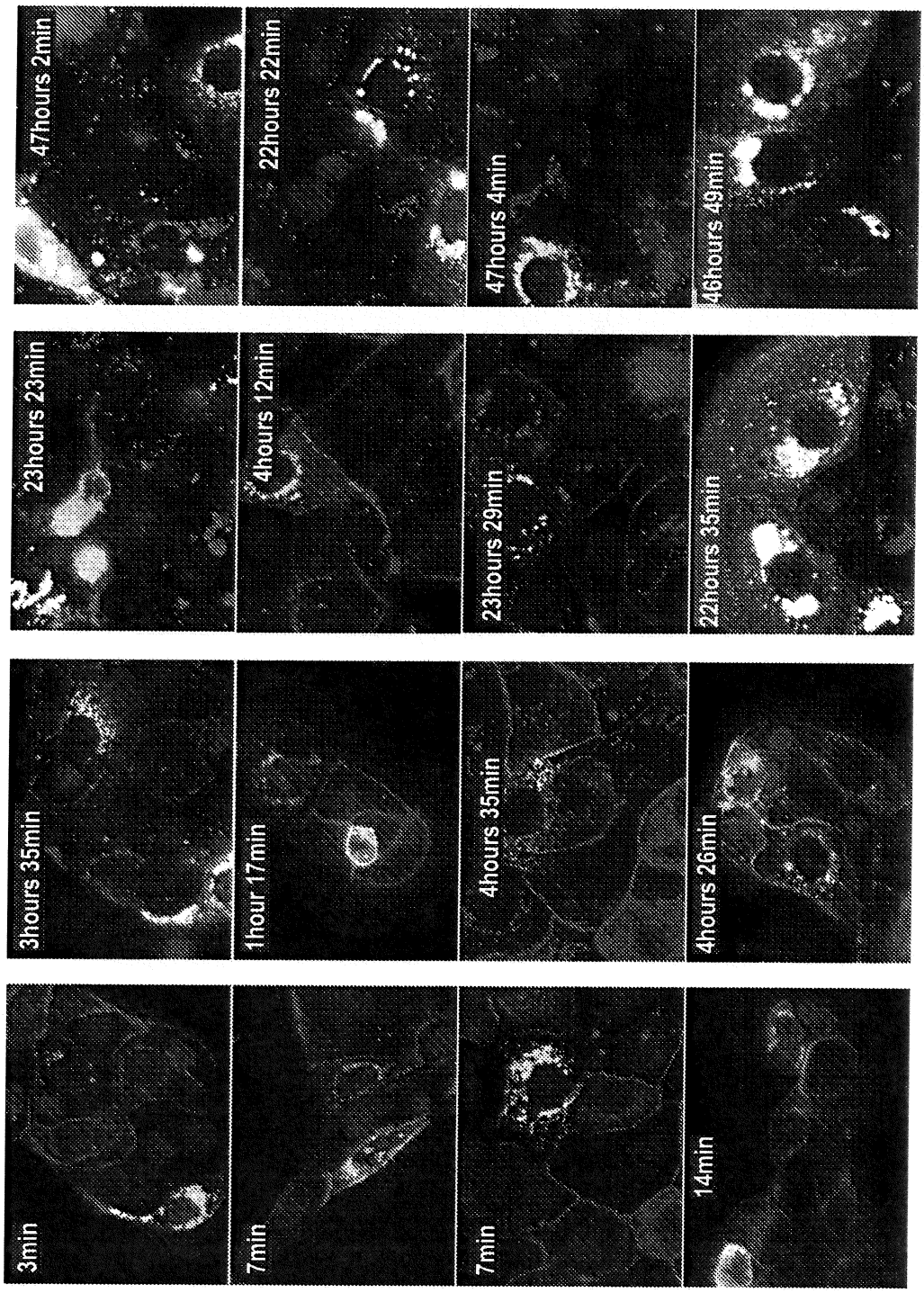

3min
7min
14min
3hours 35min
1hour 17min
4hours 35min
4hours 26min
23hours 23min
4hours 12min
23hours 29min
22hours 35min
47hours 2min
22hours 22min
47hours 4min
46hours 49min
02-0307-h4
02-0307-h6
02-0358-h3
02-0358-h5

Fig. 21A

CLDN18.2 hAb	KD			Expression Level		Equilibrium Curves	Cell Model	Detached by
	KD	Error%	95% Confidence Interval (CI)	Expression Level	95% Confidence Interval (CI)			
pNK-307-h1F06-4	3.65nM	2.35	2.12nM - 6.47nM	2.085E+06	1.498E+06 - 3.195E+06	500pM, 2nM, 10nM	HEK293T-CLDN18.2-mGFP C12	Versene
pNK-358-h2C10-3	3.00nM	1.84	2.03nM - 4.44nM	4.983E+06	3.869E+06 - 6.623E+06	500pM, 2nM, 10nM	HEK293T-CLDN18.2-mGFP C12	Versene
#307-6h	1.42nM	7.72	0.18nM - 11.91nM	3.024E+06	1.642E+06 - 1.474E+07	500pM and 10nM	HEK293T-CLDN18.2-mGFP C12	Versene
#358-5h	1.81nM	7.19	0.43nM - 6.90nM	2.922E+06	1.561E+06 - 7.021E+06	500pM and 10nM	HEK293T-CLDN18.2-mGFP C12	Versene
pNK-307-h1F06-4	0.69nM	3.57	0.31nM - 1.34nM	3.313E+05	2.558E+05 - 4.458E+05	1nM, 20nM	HUPT4	Versene
pNK-358-h2C10-3	1.70nM	3.73	0.87nM - 3.23nM	4.085E+05	2.934E+05 - 6.197E+05	1nM, 20nM	HUPT4	Versene
#307-6h	0.93nM	2.72	0.58nM - 1.43nM	3.454E+05	2.760E+05 - 4.410E+05	1nM, 20nM	HUPT4	Versene
#358-5h	0.67nM	3.90	0.28nM - 1.32nM	3.059E+05	2.212E+05 - 4.487E+05	1nM, 20nM	HUPT4	Versene

Fig. 21B

Cell Line Name		Histology	KinExA 4000			Quantum Flow
			Average Expression Level (EL)	95% Confidence Interval (CI)		Average ABC (Bivalent Binding) (ABC Monovalent x2)
				EL Low	EL High	
Artificial Overexpressing Line	293T-CLDN18.2-mGFP C12	Artificial	3,338,000	2,683,500	4,909,000	1,664,366
CLDN18.2 Positive Native Cell Lines	HUPT4	Pancreas	460,700	361,850	599,200	188,201
	NUGC4	Upper GI	452,950	288,550	823,350	212,069
	KATOIII	Upper GI	514,350	293,450	845,400	161,738
	PATU8988S	Pancreas	394,800	216,650	606,250	102,503

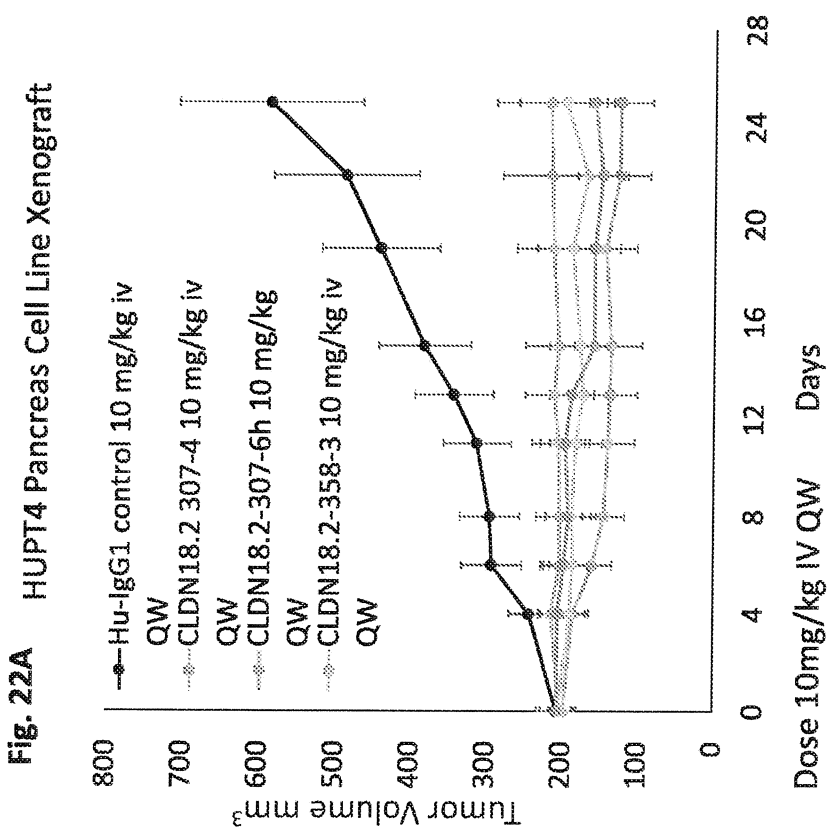


Fig. 22A
HUPT4 Pancreas Cell Line Xenograft
Hu-IgG1 control 10 mg/kg iv QW
CLDN18.2 307-4 10 mg/kg iv QW
CLDN18.2-307-6h 10 mg/kg QW
CLDN18.2-358-3 10 mg/kg iv QW
Tumor Volume mm3
800
700
600
500
400
300
200
100
0
0
4
8
12
16
20
24
28
Dose 10mg/kg IV QW
Days

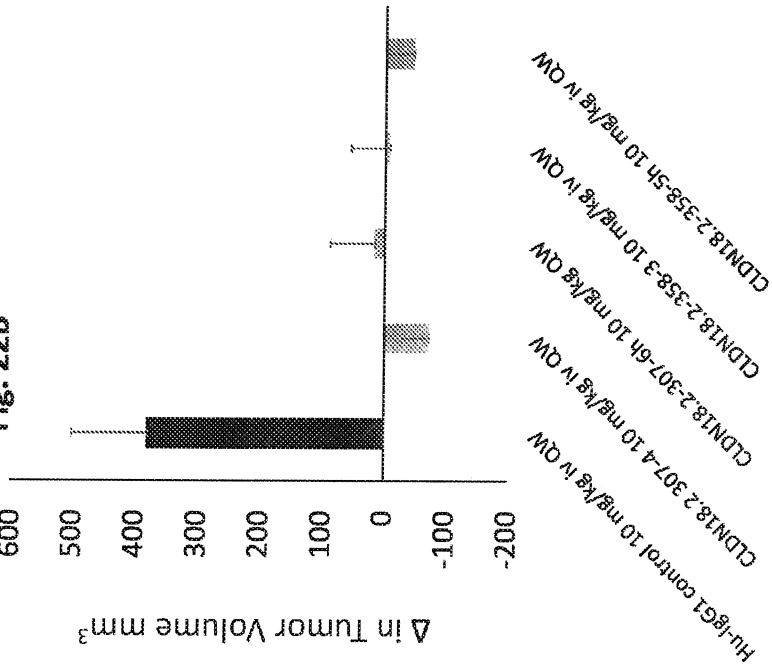
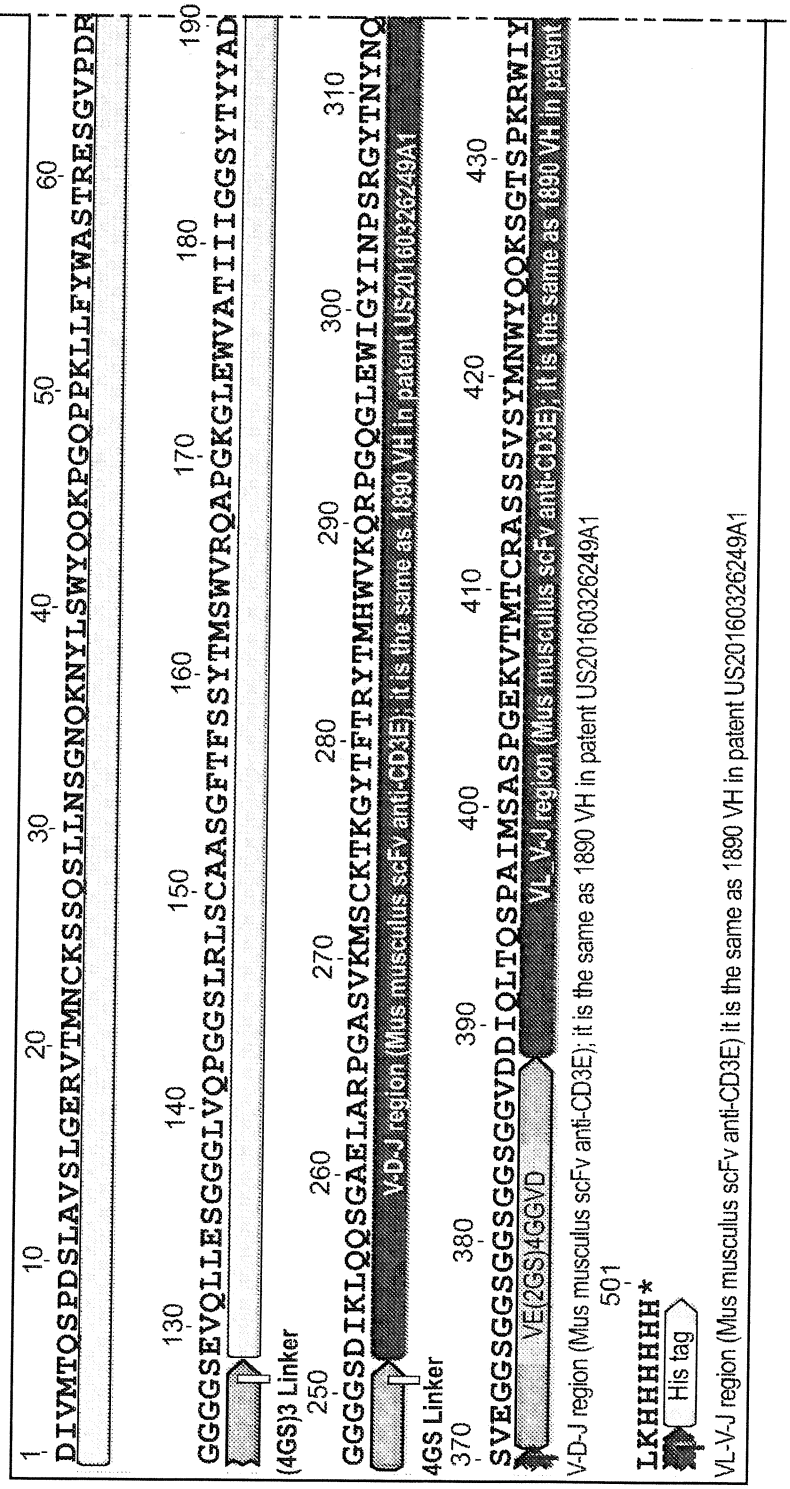


Fig. 22B
Δ in Tumor Volume mm3
600
500
400
300
200
100
0
-100
-200
Hu-IgG1 control 10 mg/kg iv QW
CLDN18.2 307-4 10 mg/kg iv QW
CLDN18.2-307-6h 10 mg/kg QW
CLDN18.2-358-3 10 mg/kg iv QW
CLDN18.2-358-5h 10 mg/kg iv QW

Fig. 23A


02-0307-h4-Bs (SEQ ID NO: 143)
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30
40
50
60
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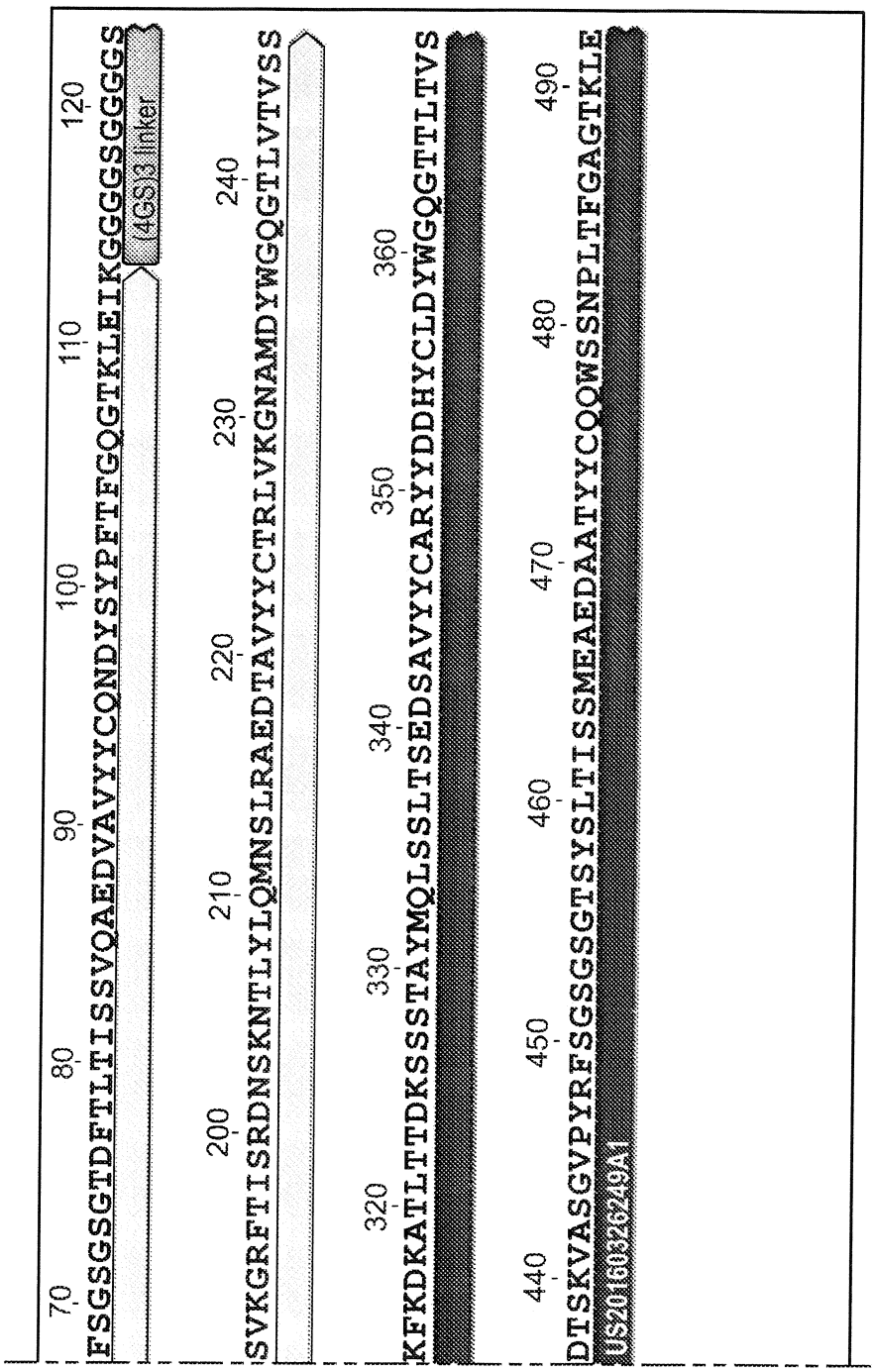
130
140
150
160
170
180
190
GGGGSEVQLLESGGGLVQPGGSLRLSCAASGFTFSSYTMSWVRQAPGKGLEWVATIIIGGSYTYYAD
(4GS)3 Linker
250
260
270
280
290
300
310
GGGGSDIKLQQSGAELARPGASVKMSCKTKGYTFTRYTMHWVKQRPGQGLEWIGYINPSRGYTNYNQ
VH-J region (Mus musculus scFv anti-CD3E); it is the same as 1890 VH in patent US20160326249A1
4GS Linker
370
380
390
400
410
420
430
SVEGGSGGGSGGGSGGGVDDIQLTQSPAIMSASPGEKVTMTCRASSSVSYMNWYQQKSGTSPKRWIY
VE(2GS)4GGVD
VL-VJ region (Mus musculus scFv anti-CD3E); it is the same as 1890 VH in patent
501
LKHHHHHH*
His tag
V-D-J region (Mus musculus scFv anti-CD3E); it is the same as 1890 VH in patent US20160326249A1
VL-V-J region (Mus musculus scFv anti-CD3E) it is the same as 1890 VH in patent US20160326249A1

Fig. 23A (cont.)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80
90
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110
120
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(4GS)3 linker
200
210
220
230
240
SVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCTRLVKGNAMDYWGQGTLVTVSS
320
330
340
350
360
KFKDKATLTTDKSSSTAYMQLSSLTSEDSAVYYCARYYDDHYCLDYWGQGTTLTVS
440
450
460
470
480
490
DTSKVASGVPYRFSGSGSGTSYSLTISSMEAEDAATYYCQQWSSNPLTFGAGTKLE
US20160362249A1

Fig. 23B

02-0307-h4-CD16A_His (SEQ ID NO: 144)

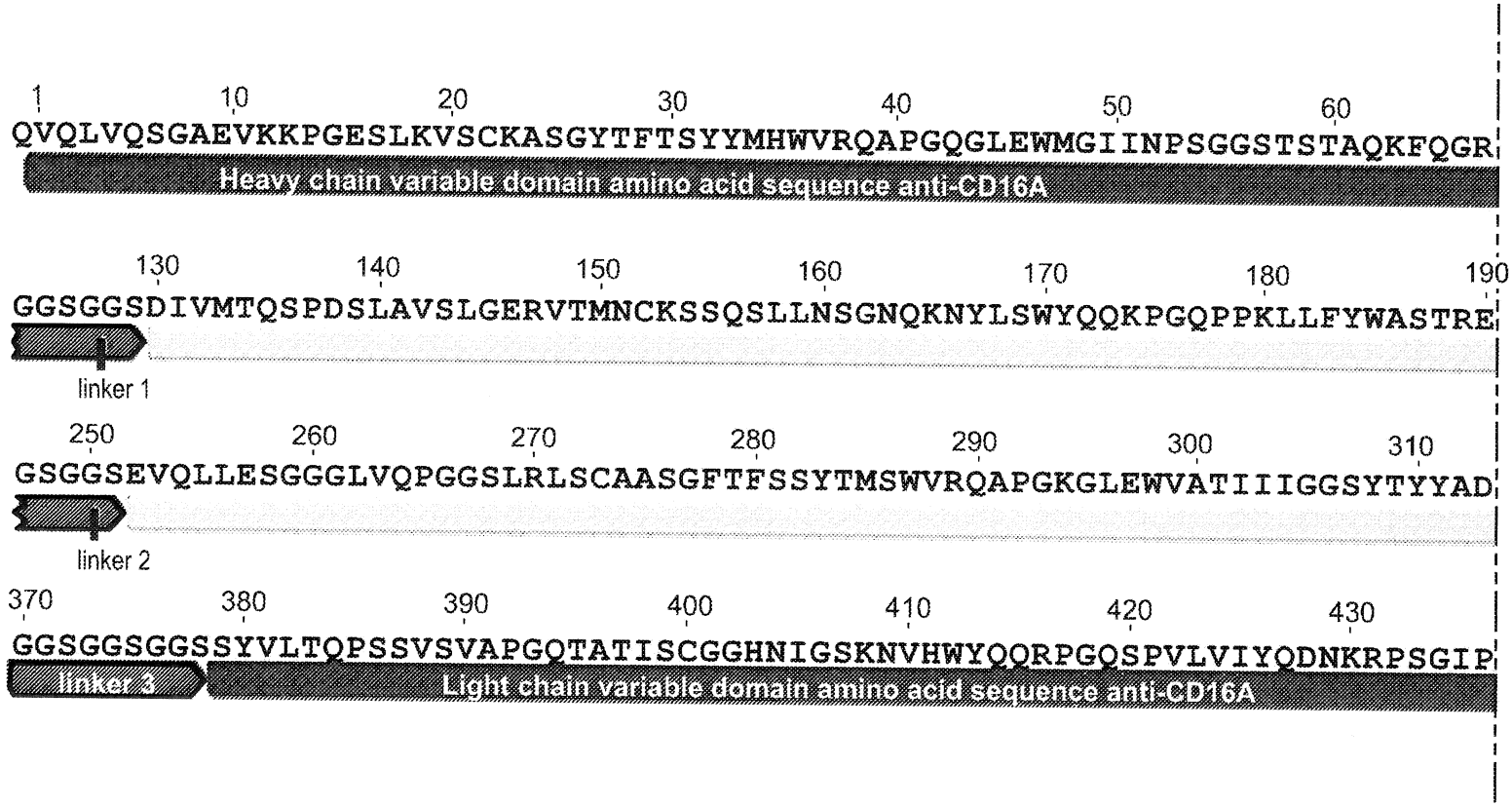
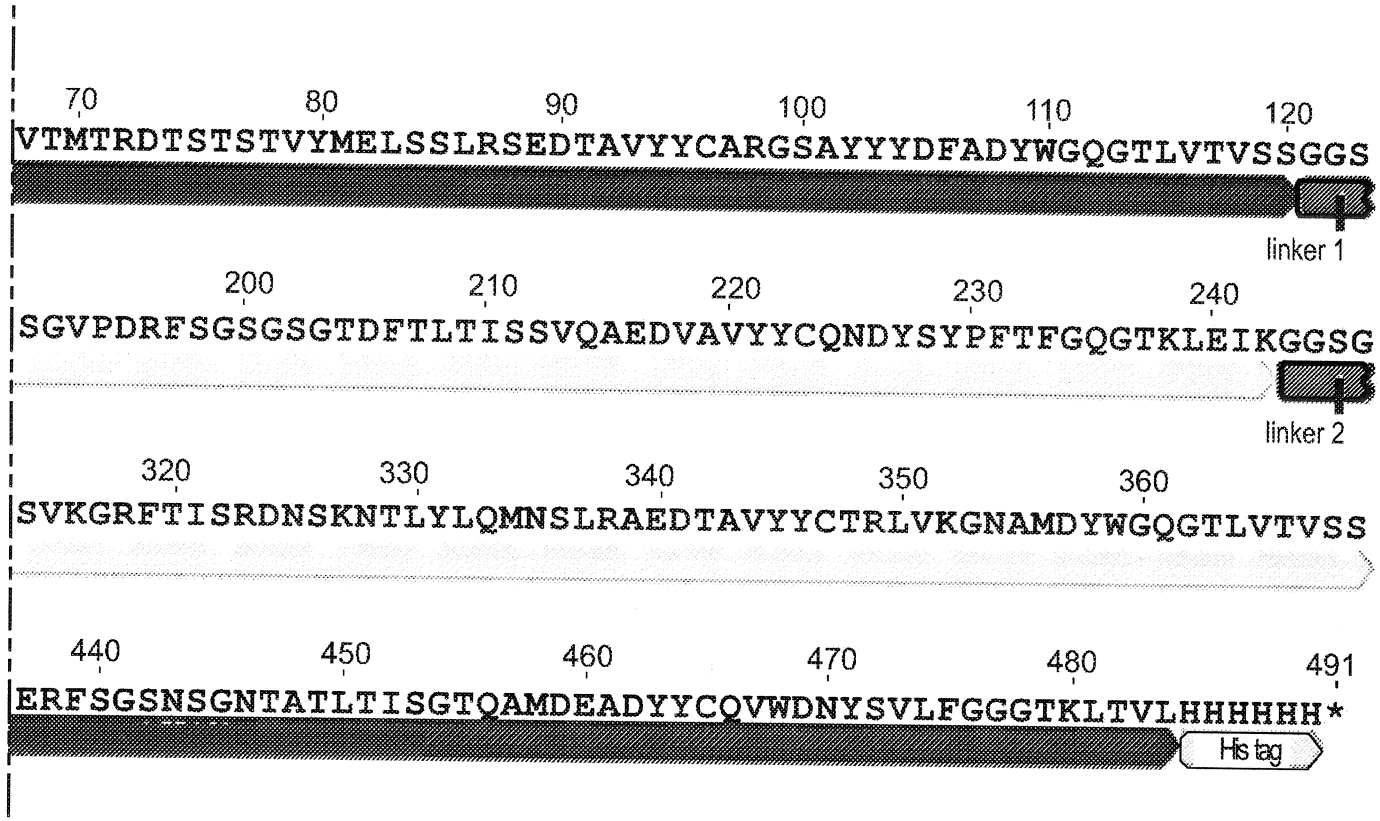


Fig. 23B (cont.)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80
90
100
110
120
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linker 1
200
210
220
230
240
SGVPDRFSGSGSGTDFTLTISSVQAEDVAVYYCQNDYSYPFTFGQGTKLEIKGGSG
linker 2
320
330
340
350
360
SVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCTRLVKGNAMDYWGQGTLVTVSS
440
450
460
470
480
491
ERFSGSNSGNTATLTISGTQAMDEADYYCQVWDNYSVLFGGGTKLTVLHHHHHH*
His tag

Fig. 23C

Name	Description	Sequence
02-0307-h4-Bs SEQ ID NO: 143	CLDN18.2 - CD3E BiTE (Bispecific T cell engager)	DIVMTQSPDSLAVSLGERVTMNCKSSQSLLNSGNQKNYLSWYQQKPGQPPKLLFYWASTRESGVPDRF SGSGSGTDFTLTISSVQAEDVAVYYCQNDYSYPFTFGQGTKLEIKGGGGSGGGGSGGGGSEVQLLESGGG LVQPGGSLRLSCAASGFTFSSYTMSWVRQAPGKGLEWVATIIIGGSYTYYADSVKGRFTISRDNSKNTLYL QMNSLRAEDTAVYYCTRLVKGNAMDYWGQGTLVTVSSGGGGSDIKLQQSGAELARPGASVKMSCKTS GYTFTRYTMHWVKQRPGQGLEWIGYINPSRGYTNYNQKFKDKATLTTDKSSSTAYMQLSSLTSEDSAVY YCARYYDDHYCLDYWGQGTTLTVSSVEGGSGGSGGSGGSGGVDDIQLTQSPAIMSASPGEKVTMTCRA SSSVSYMNWYQQKSGTSPKRWIYDTSKVASGVPYRFSGSGSGTSYSLTISSMEAEDAATYYCQQWSSNP LTFGAGTKLELKHHHHHH*
02-0307-h4-CD16A_His SEQ ID NO: 144	CLDN18.2 - CD16A TandAb	QVQLVQSGAEVKKPGESLKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINPSGGSTSYAQKFQGR VTMTRDTSTSTVYMELSSLRSEDTAVYYCARGSAYYYDFADYWGQGTLVTVSSGGSGGSGGSDIVMTQS PDSLAVSLGERVTMNCKSSQSLLNSGNQKNYLSWYQQKPGQPPKLLFYWASTRESGVPDRFSGSGSGT DFTLTISSVQAEDVAVYYCQNDYSYPFTFGQGTKLEIKGGSGGSGGSEVQLLESGGGLVQPGGSLRLSCAA SGFTFSSYTMSWVRQAPGKGLEWVATIIIGGSYTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVY YCTRLVKGNAMDYWGQGTLVTVSSGGSGGSGGSSYVLTQPSSVSVAPGQTATISCGGHNIGSKNVHW YQQRPGQSPVLVIYQDNKRPSGIPERFSGSNSGNTATLTISGTQAMDEADYYCQVWDNYSVLFGGGTKL TVLHHHHHH*

Fig. 23C (cont.)

02-0358-h3-Bs SEQ ID NO: 145	CLDN18.2 - CD3E BiTE	DIVMTQSPDSLAVSLGERVTMNCKSSQSLFNSGNQRNYLTWYQQKPGQPPKLLIYWASTRESGVPDRF SGSGSGTDFTLTISSVQAEDVAVYYCQNVYIYPLTFGQGTKLEIKGGGGSGGGGSGGGGSEVQLVESGGG LVQPGGSLRLSCAVSGFTFSSFGMHWVRQAPGKGLEWVAYISSGTTNIYYADSVKGRFTVSRDNAKNSL YLQMNSLRAEDTAVYYCVRSGYYGNSLDYWGQGTLVTVSSGGGGSDIKLQQSGAELARPGASVKMSCK TSGYTFTRYTMHWVKQRPGQGLEWIGYINPSRGYTNYNQKFKDKATLTTDKSSSTAYMQLSSLTSEDSA VYYCARYYDDHYCLDYWGQGTTLTVSSVEGGSGGSGGSGGSGGVDDIQLTQSPAIMSASPGEKVTMTC RASSSVSYMNWYQQKSGTSPKRWIYDTSKVASGVPYRFSGSGSGTSYSLTISSMEAEDAATYYCQQWSS NPLTFGAGTKLELKHHHHHH*
02-0358-h3-CD16A-His SEQ ID NO: 146	CLDN18.2 - CD16A TandAb	QVQLVQSGAEVKKPGESLKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINPSGGSTSYAQKFQGR VTMTRDTSTSTVYMELSSLRSEDTAVYYCARGSAYYYDFADYWGQGTLVTVSSGGSGGSGGSDIVMTQS PDSLAVSLGERVTMNCKSSQSLFNSGNQRNYLTWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGT DFTLTISSVQAEDVAVYYCQNVYIYPLTFGQGTKLEIKGGSGGSGGSEVQLVESGGGLVQPGGSLRLSCAV SGFTFSSFGMHWVRQAPGKGLEWVAYISSGTTNIYYADSVKGRFTVSRDNAKNSLYLQMNSLRAEDTA VYYCVRSGYYGNSLDYWGQGTLVTVSSGGSGGSGGSSYVLTQPSSVSVAPGQTATISCGGHNIGSKNVH WYQQRPGQSPVLVIYQDNKRPSGIPERFSGSNSGNTATLTISGTQAMDEADYYCQVWDNYSVLFGGGT KLTVLHHHHHH*

Fig. 24A

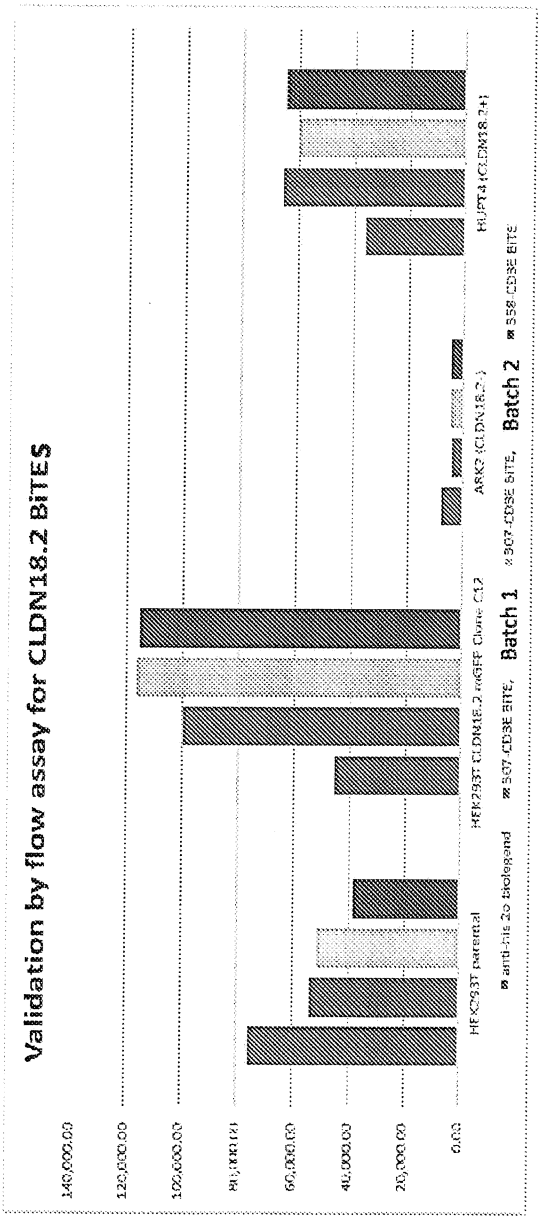


Fig. 24B

FL4H/AF647 signal	anti-his 2o biolegend	307-CD3E BiTE, Batch 1	307-CD3E BiTE, Batch 2	358-CD3E BiTE
HEK293T parental	75,686.40	53,898.98	51,368.41	38,348.49
HEK293T CLDN18.2 mGFP Clone C12	45,137.33	99,526.45	116,087.32	115,349.70
ARK2 (CLDN18.2-)	7,347.16	3,808.00	4,277.47	4,363.59
HUPT4 (CLDN18.2+)	35,983.32	65,621.23	60,123.18	64,647.73

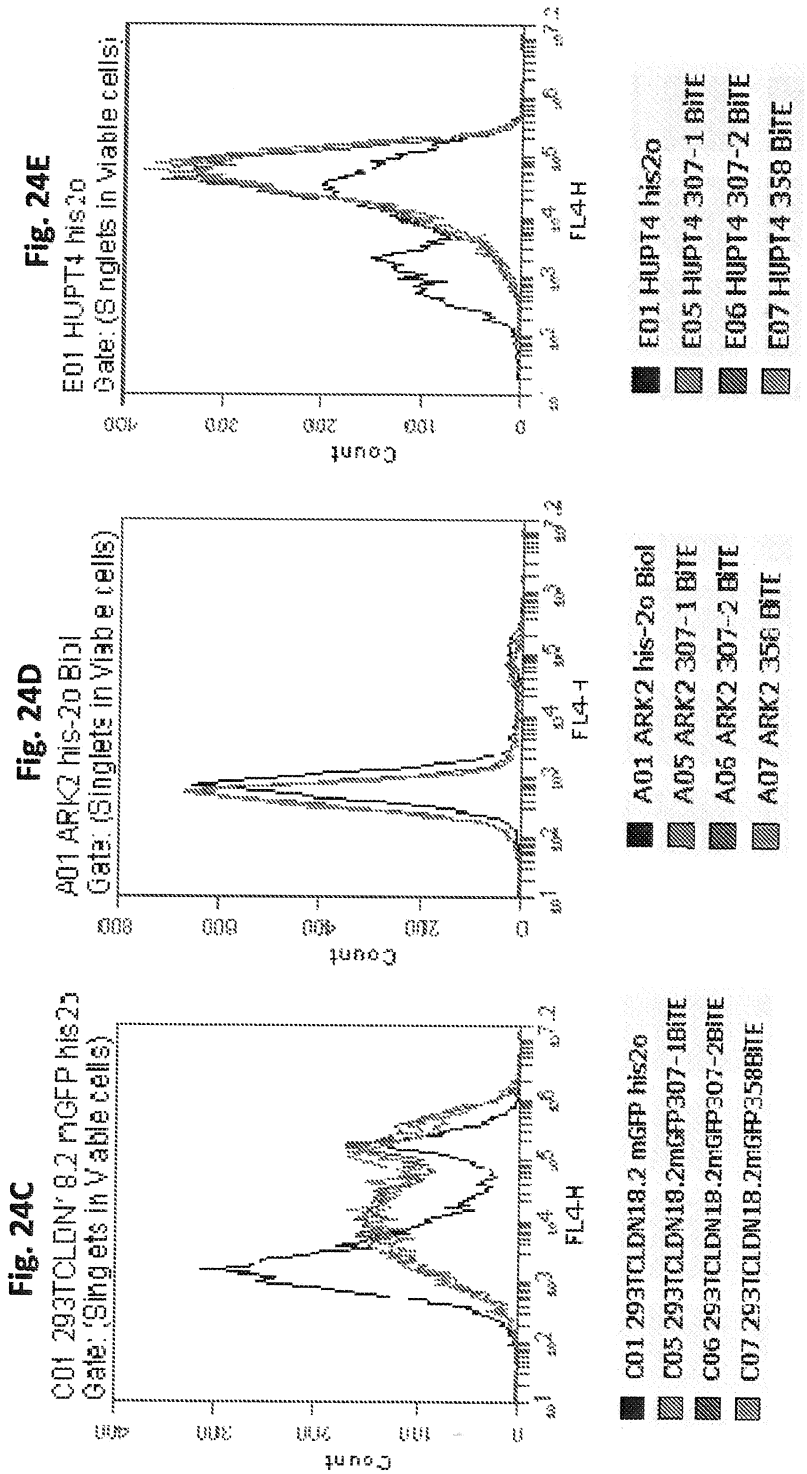


Fig. 24C
C01 293TCLDN18.2 mGFP his2o
Gate: (Singlets in Viable cells)
Count
FL4-H
C01 293TCLDN18.2 mGFP his2o
C05 293TCLDN18.2mGFP307-1BiTE
C06 293TCLDN18.2mGFP307-2BiTE
C07 293TCLDN18.2mGFP358BiTE
Fig. 24D
A01 ARK2 his-2o Biol
Gate: (Singlets in Viable cells)
Count
FL4-H
A01 ARK2 his-2o Biol
A05 ARK2 307-1 BiTE
A06 ARK2 307-2 BiTE
A07 ARK2 356 BiTE
Fig. 24E
E01 HUPT4 his2o
Gate: (Singlets in Viable cells)
Count
FL4-H
E01 HUPT4 his2o
E05 HUPT4 307-1 BiTE
E06 HUPT4 307-2 BiTE
E07 HUPT4 358 BiTE

Fig. 25A **Flow Assay of Purifed BiTE diabody (2ug/reaction) flow assay, trypsin to detach cells**

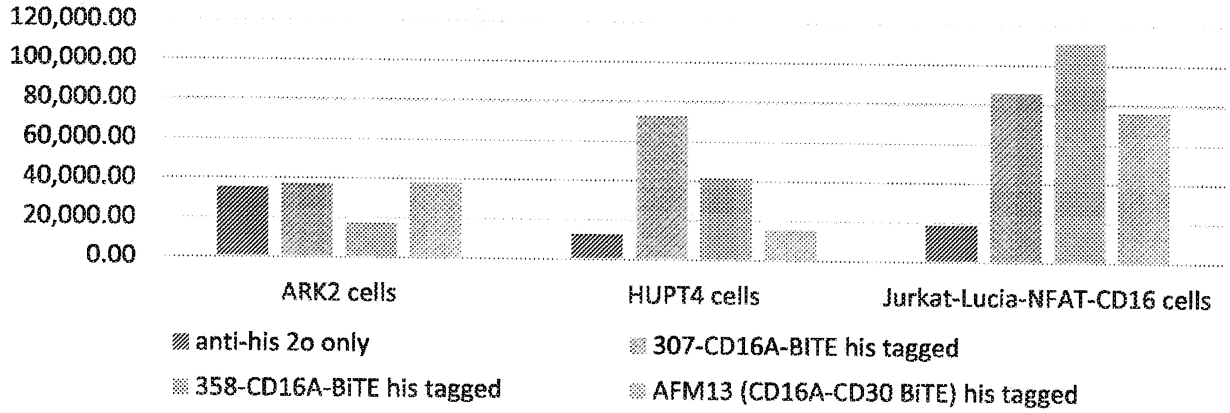


Fig. 25B

	anti-his 2o only	307-CD16A-BITE his tagged	358-CD16A-BiTE his tagged	AFM13 (CD16A-CD30 BiTE) his tagged
ARK2 cells	35,124.48	37,108.71	17,564.03	37,777.38
HUPT4 cells	12,730.43	72,589.71	41,612.48	15,728.04
Jurkat-Lucia-NFAT-CD16 cells	18,863.83	85,725.83	111,262.28	76,513.58

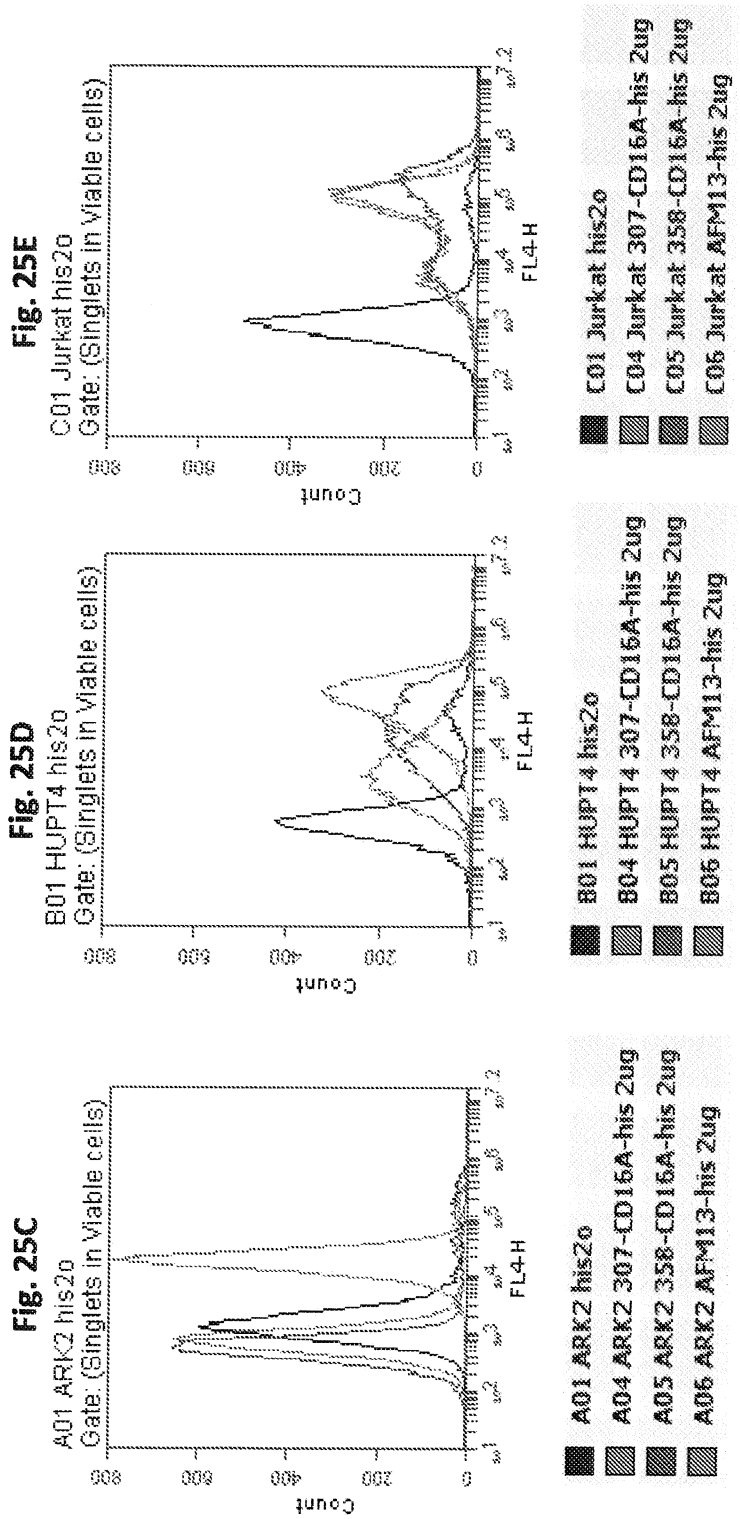


Fig. 25C
A01 ARK2 his2o
Gate: (Singlets in Viable cells)
Count
FL4-H
A01 ARK2 his2o
A04 ARK2 307-CD16A-his 2ug
A05 ARK2 358-CD16A-his 2ug
A06 ARK2 AFM13-his 2ug
Fig. 25D
B01 HUPT4 his2o
Gate: (Singlets in Viable cells)
Count
FL4-H
B01 HUPT4 his2o
B04 HUPT4 307-CD16A-his 2ug
B05 HUPT4 358-CD16A-his 2ug
B06 HUPT4 AFM13-his 2ug
Fig. 25E
C01 Jurkat his2o
Gate: (Singlets in Viable cells)
Count
FL4-H
C01 Jurkat his2o
C04 Jurkat 307-CD16A-his 2ug
C05 Jurkat 358-CD16A-his 2ug
C06 Jurkat AFM13-his 2ug

Fig. 26A **Flow assay for Tandab 307-CD16A and Tandab 358-CD16A 09/18/2019**

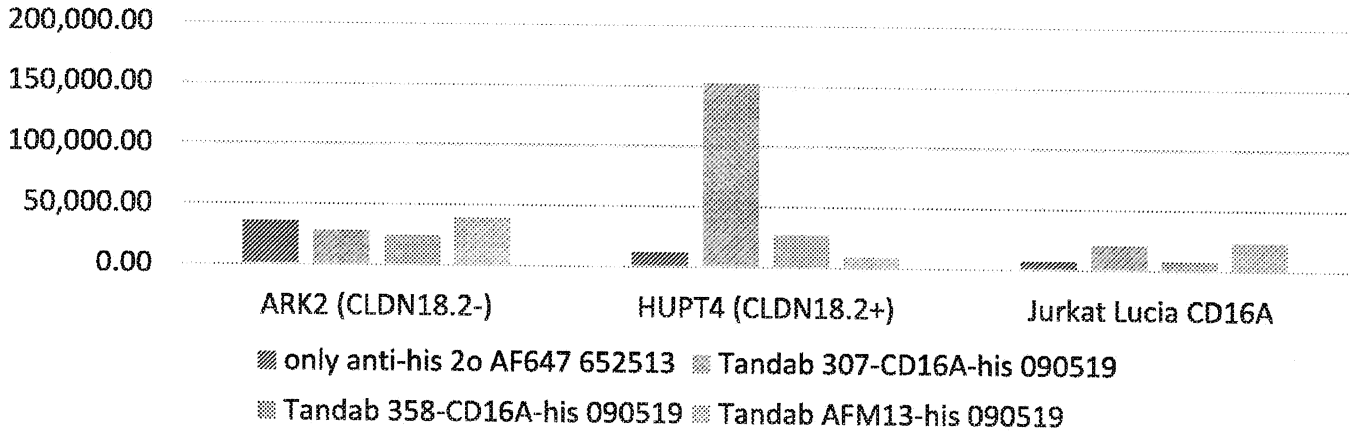
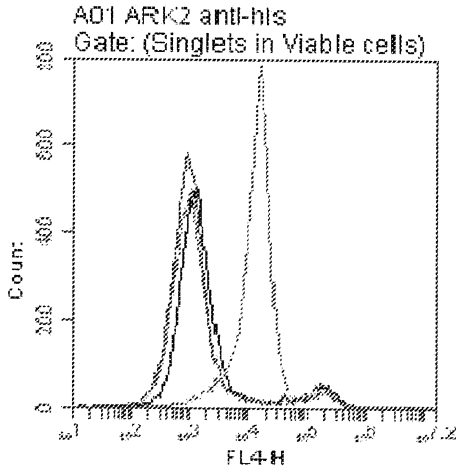


Fig. 26B

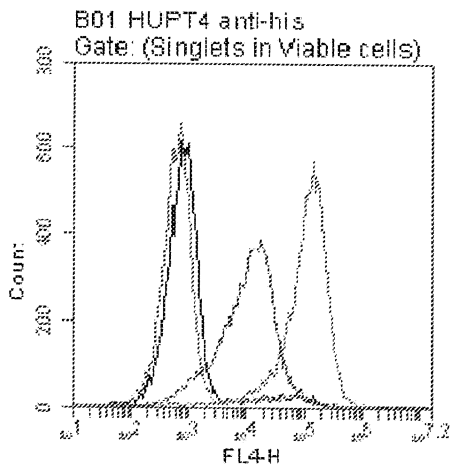
	only anti-his 2o AF647 652513	Tandab 307-CD16A-his 090519	Tandab 358-CD16A-his 090519	Tandab AFM13-his 090519
ARK2 (CLDN18.2-)	36,416.11	28,480.06	25,080.61	39,787.16
HUPT4 (CLDN18.2+)	12,046.33	152,355.14	27,623.41	8,939.97
Jurkat Lucia CD16A	7,290.88	21,167.48	8,175.19	23,503.69

Fig. 26C



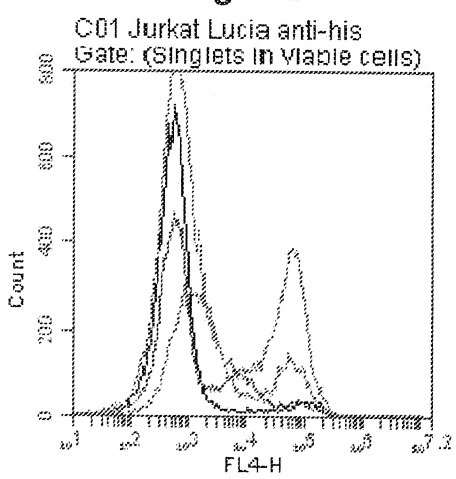
A01 ARK2 anti-his
A04 ARK2 Tandab-307-his
A05 ARK2 Tandab-358-his
A06 ARK2 Tandab-AFM13-his

Fig. 26D



B01 HUPT4 anti-his
B04 HUPT4 Tandab-307-his
B05 HUPT4 Tandab-358-his
B06 HUPT4 Tandab-AFM13-his

Fig. 26E



C01 Jurkat Lucia anti-his
C04 JurkatLucia Tandab307-his
C05 JurkatLucia Tandab358-his
C06 JurkatLuc TandabAFM13-his

Fig. 27A

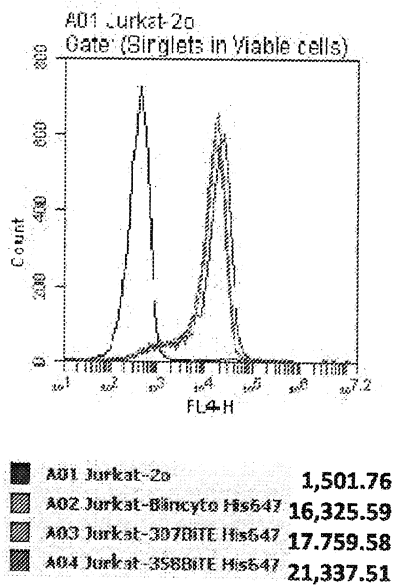
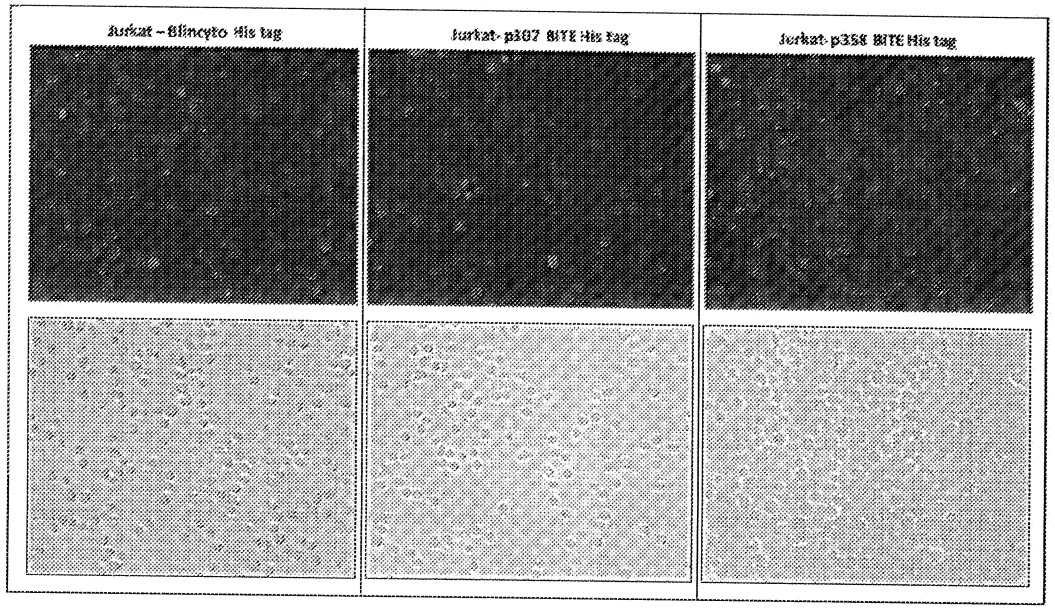
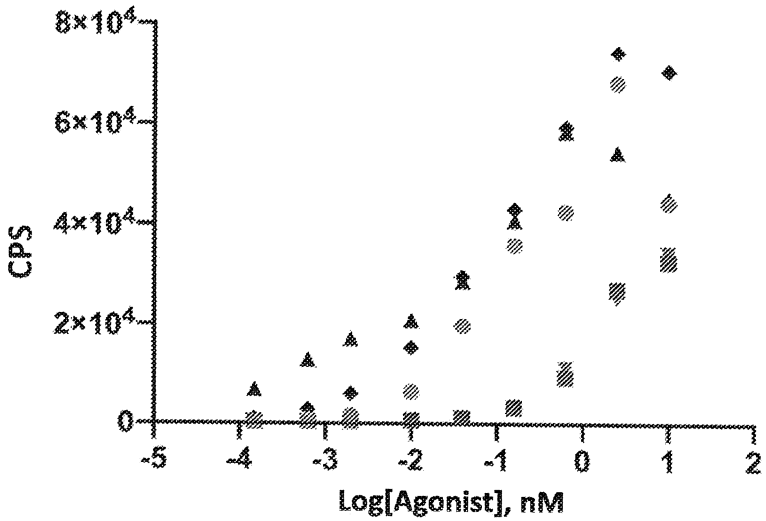


Fig. 27B



40X on Keyence

Fig. 28 CD3-Cldn18.2 BiTE



Bioluminescence assay using CD3⁺ Jurkat T cells modified with luciferase reporter genes on the nuclear factor of activated T cell (NFAT) response element

Activation data indicate target specific activation of T cells (note ▨▽ vs. ▲◆)

▨	OKT3	→ Positive control (anti-CD3 mAb)
▨	Cldn18.2 BiTE	→ BiTE only
▲	Cldn18.2 BiTE+293T Cldn18.2	→ Cldn18.2 overexpressing cell line
▽	Cldn18.2 BiTE+H1819	→ Cldn18.2⁻ cell line
◆	Cldn18.2 BiTE+HUPT4	→ Endogenous Cldn18.2⁺ cell line

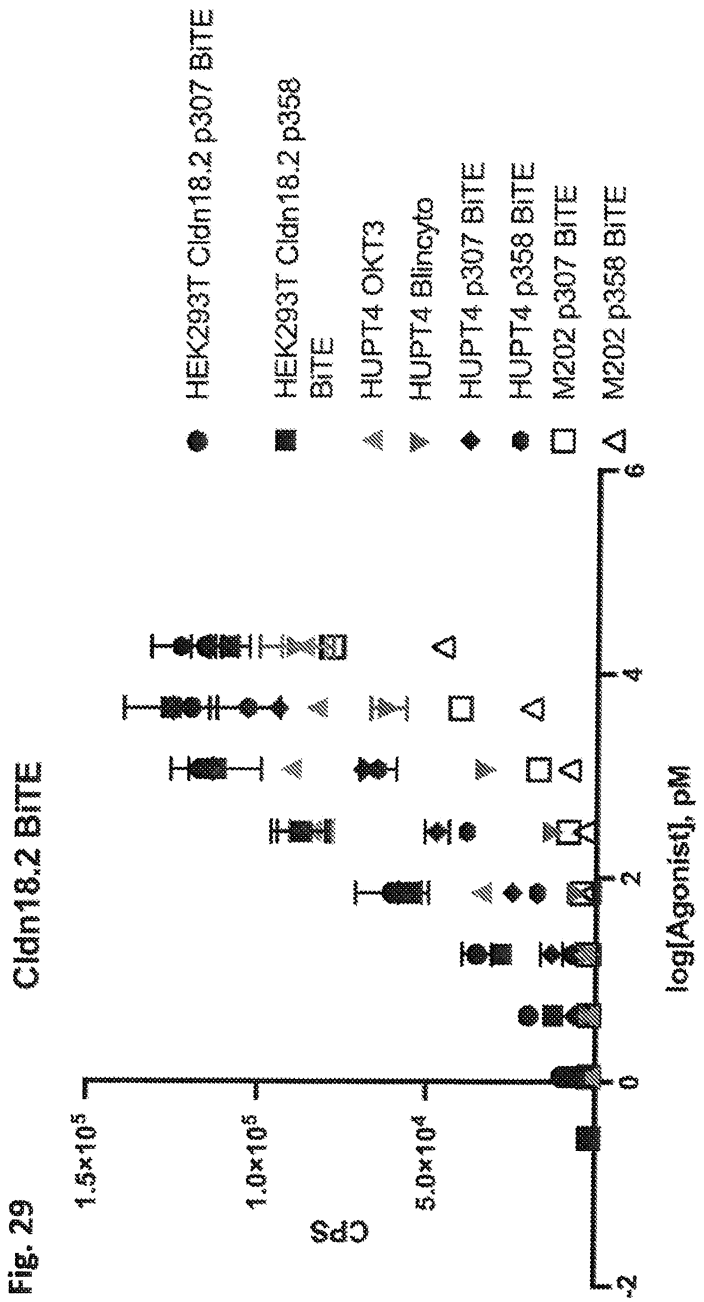

Cldn18.2 BiTE
CPS
1.5×10^5
1.0×10^5
5.0×10^4
0
2
4
6
-2
log[Agonist], pM
HEK293T Cldn18.2 p307 BiTE
HEK293T Cldn18.2 p358 BiTE
HUPT4 OKT3
HUPT4 Blincyto
HUPT4 p307 BiTE
HUPT4 p358 BiTE
M202 p307 BiTE
M202 p358 BiTE

Fig. 29

Fig. 30A 125 ng/mL Blincyto

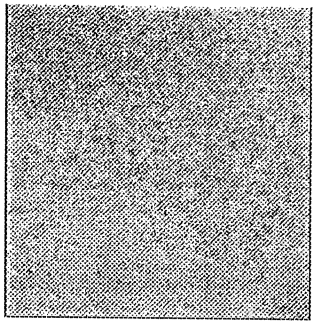


Fig. 30B 12.5 ng/mL Blincyto

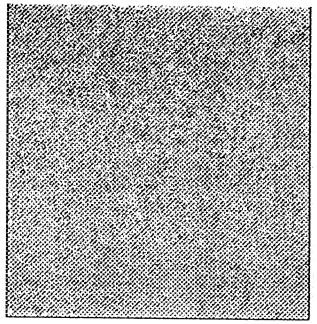


Fig. 30C 1.25 ng/mL Blincyto

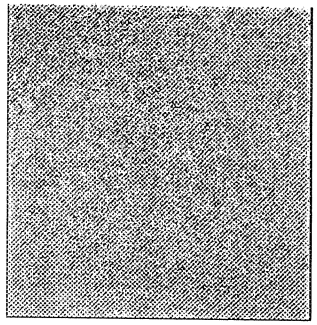


Fig. 30D 125 ng/mL p307 BiTE

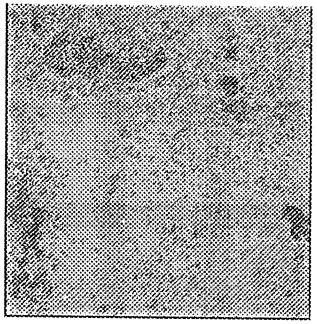


Fig. 30E 12.5 ng/mL p307 BiTE

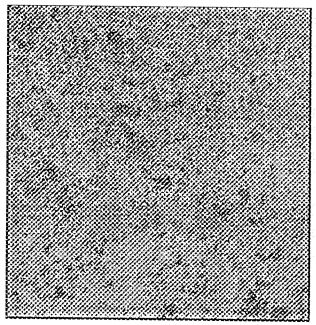


Fig. 30F 1.25 ng/mL p307 BiTE

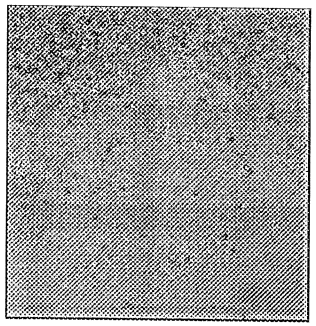


Fig. 31

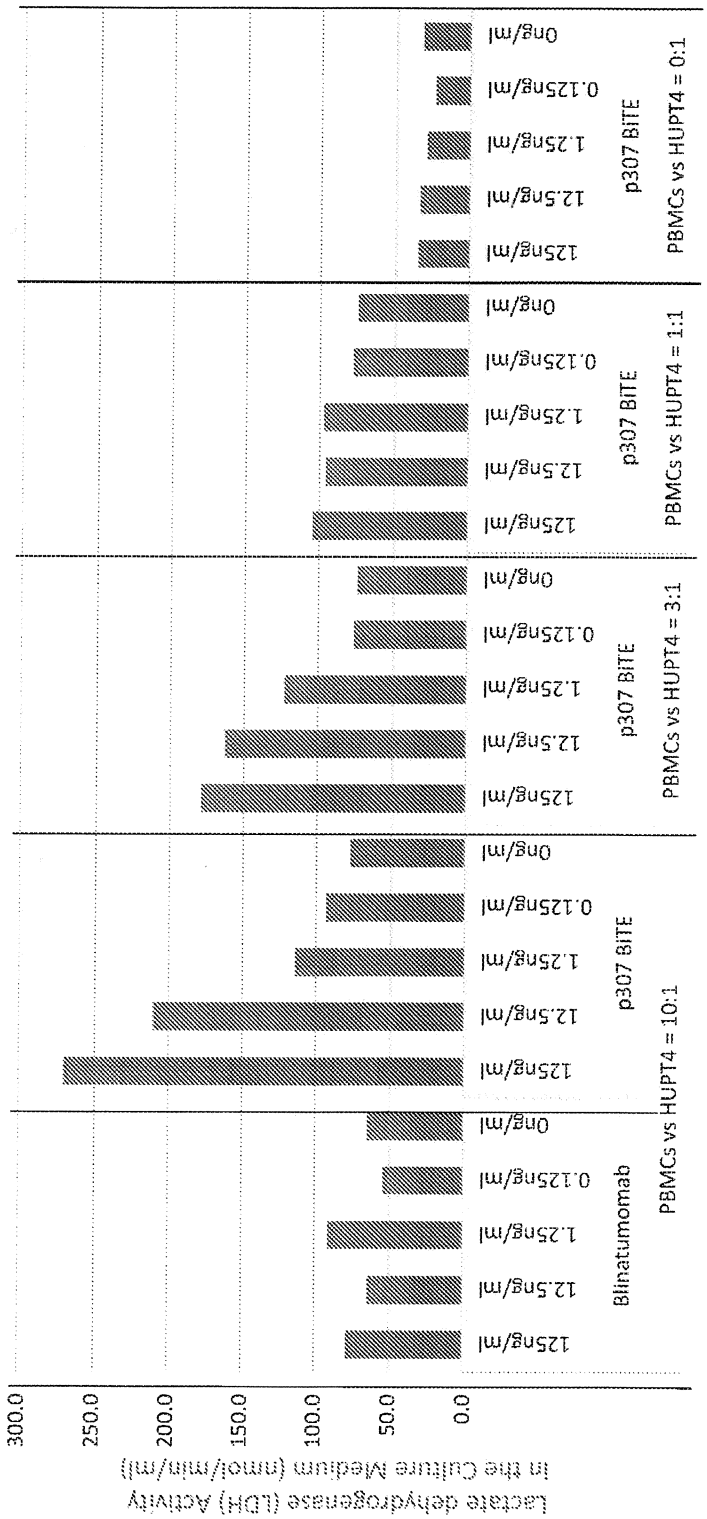
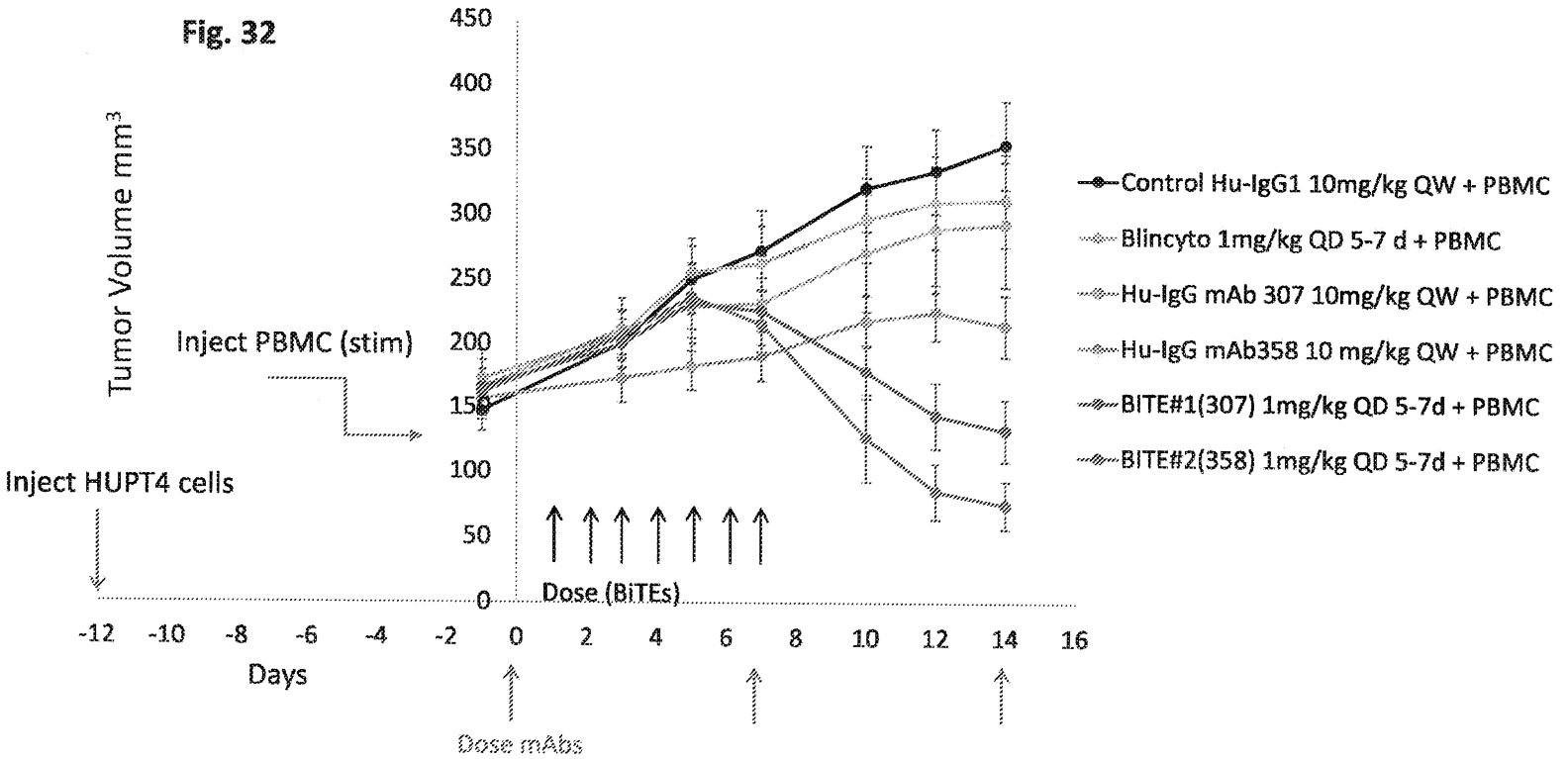

Lactate dehydrogenase (LDH) Activity
in the Culture Medium (mmol/min/ml)
300.0
250.0
200.0
150.0
100.0
50.0
0.0
PBMCs vs HUPT4 = 10:1
PBMCs vs HUPT4 = 3:1
PBMCs vs HUPT4 = 1:1
PBMCs vs HUPT4 = 0:1
Blinatumomab
p307 BiTE
125ng/ml
12.5ng/ml
1.25ng/ml
0.125ng/ml
0ng/ml

Fig. 32


Tumor Volume mm3
450
400
350
300
250
200
150
100
50
0
Inject PBMC (stim)
Inject HUPT4 cells
Dose (BiTEs)
-12
-10
-8
-6
-4
-2
0
2
4
6
8
10
12
14
16
Days
Dose mAbs
Control Hu-IgG1 10mg/kg QW + PBMC
Blincyto 1mg/kg QD 5-7 d + PBMC
Hu-IgG mAb 307 10mg/kg QW + PBMC
Hu-IgG mAb358 10 mg/kg QW + PBMC
BITE#1(307) 1mg/kg QD 5-7d + PBMC
BITE#2(358) 1mg/kg QD 5-7d + PBMC

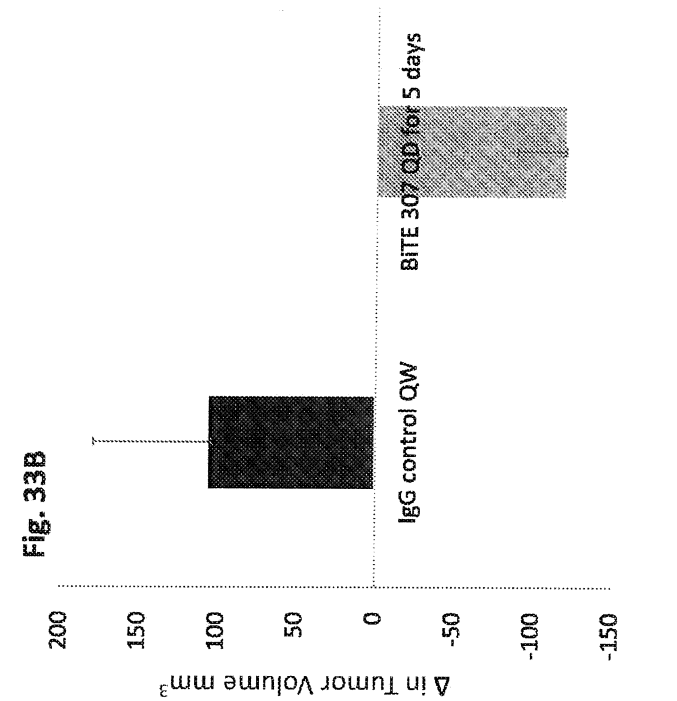


Fig. 33B
Δ in Tumor Volume mm3
200
150
100
50
0
-50
-100
-150
IgG control QW
BiTE 307 QD for 5 days

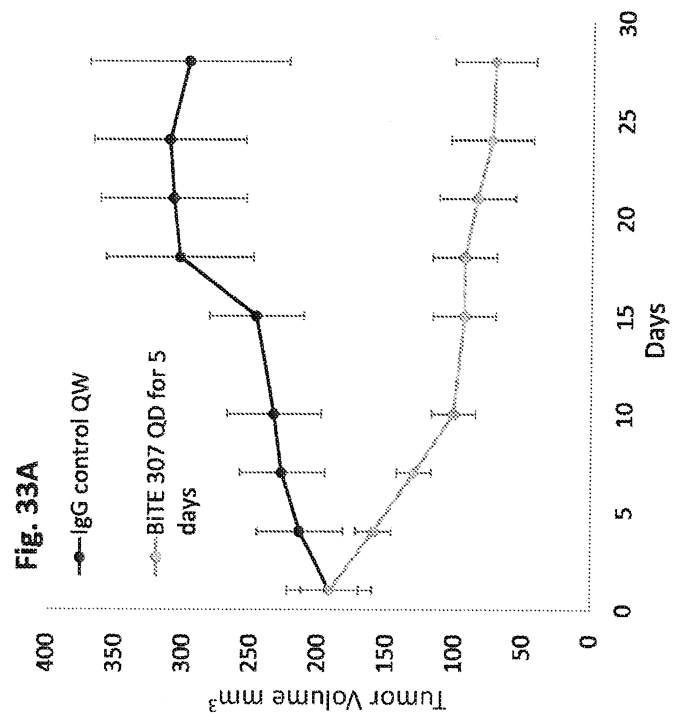


Fig. 33A
IgG control QW
BiTE 307 QD for 5 days
Tumor Volume mm3
400
350
300
250
200
150
100
50
0
0
5
10
15
20
25
30
Days