

1 / 20

CD40 Receptor (SEQ ID NO:40) (from EMBO J, 8(5), 1403-1410 (1989))

10	20	30	40	50
MVRLPLQCVL	WGCLLTAVHP	EPPTACREKQ	YLINSQCCSL	CQPGQKLVSD
60	70	80	90	100
CTEFTETECL	PCGESEFLDT	WNRETHCHQH	KYCDPNLGLR	VQQKGTSETD
110	120	130	140	150
TICTCEEGWH	CTSEACESCV	LHRSCSPGFG	VKQIATGVSD	TICEPCPVGF
160	170	180	190	200
FSNVSSAFEK	CHPWTSCETK	DLVVQQAGTN	KTDVVCGPQD	RLRALVVIPI
210	220	230	240	250
IFGILFAILL	VLVFIKKVAK	KPTNKAPHPK	QEPQEINFPD	DLPGSNTAAP
260	270			
VQETLHGCQP	VTQEDGKESR	ISVQERQ		

CD40 Ligand (SEQ ID NO:41) (from FEBS Letters, 315 (3), 259-266 (1993))

10	20	30	40	50
MIETYNQTSP	RSAATGLPIS	MKIFMYLLTV	FLITQMIGSA	LFAYVLHRRRL
60	70	80	90	100
DKIEDERNLH	EDFVFMKTIQ	RCNTGERSLS	LLNCEEIKSQ	FEGFVKDIML
110	120	130	140	150
NKEETKKENS	FEMQKGDQNP	QIAAHVISEA	SSKTTSVLQW	AEKGYTMSN
160	170	180	190	200
NLVTLENGKQ	LTVKRQGLYY	IYAQVTFCNS	REASSQAPFI	ASLCLKSPGR
210	220	230	240	250
FERILLRAAN	THSSAKPCGQ	QSIHLGGVFE	LQPGASVFN	VTDPVSQVSHG
260				
TGFTSFGLLK	L			

FIG. 1

2 / 20

Mouse anti-human CD40 Antibody DomainsVariable domains (CDRs in **bold**)muAb1 V_H (SEQ ID NO: 101)

QVQLQQPGAELVKPGASVKMSCKASGYTFTSYWITWVKORPGQGLEWIG**INPGSGS**
TNYNEKFKSKATLTVDTSSSTAYMQLSSLTSEDSAVYYCARN**RGTDGYWGQGTTLTVSS**

muAb1 V_L (SEQ ID NO: 151)

DVVMQTPLSLPVSLGDAQASISCR**SSQSLVHSYGN**TYLHWYLOKPGQSPKFLY**KVSNR**
ISGVPDRLSGSGGTDFTLKISRVEPEDLGVYFC**SQSTHVPYTFGGG**TKLEIK

muAb2 V_H (SEQ ID NO: 102)

QVQLQQSGAELMKPGASAKLSCKATGYTFTGYWQWVKORPGHGLEWIG**ILPGGD**
HTKYNEKFRGKATFTSDTSSNTVMQLSSLTTEDSAIYYCAR**VGGDYGQGTTLTVSS**

muAb2 V_L (SEQ ID NO: 152)

DVVMQTPLSLPVSLGDAQASISCR**SSQSLVNSN**ENTYLHWYLOKPGQSPKLLY**KVFNR**
YSGVPDRFSGSGGTDFTLKISRVEAEDLGVYFC**FQSTHVPWTFGGG**TKLEIK

muAb3 V_H (SEQ ID NO: 103)

EVQLQQSGPELVKPGASVKISCKASGYTFTDYMMNWVKQSHGKSLEWIG**INPNNGG**
TSYNQKFKGKATLTVDKSSSTAYMELRSLTSEDSAVYYCAR**RGGGRGTYALDYWGQGT**SVTVSS

muAb3 V_L (SEQ ID NO: 153)

DIQMTQTSSLSASLGDRVTISCRASQDISNYLNWYQQKPDGTVKPLIY**TSRLHLGVP**
 SRFSGSGGTDSLTSISLEQEDIA**TYFCQQGNTLPLTFGAG**TKLEIK

FIG. 2A

3 / 20

Mouse anti-human CD40 Antibody DomainsVariable domains (CDRs in **bold**)muAb4 V_H (SEQ ID NO: 104)LVQPGGSLSLSCAAS**GGFTFSDYMS**WVRQPPGKALEWLGFI**RNKANGY**TTEFSASVK
GRFTISRDN**SO**SILYLQMNALRAEDSATY**CARYGGLRQGWY**FDVWGTGTTVTVSSmuAb4 V_L (SEQ ID NO: 154)DIQMTQTSSLSASLGDRVTISCRAS**QDIR**NYLNWYQQKPDGTVKLLI**YTSRLH**SGVP
SRFSGSGGTDYSLTISNLEQEDIA**TYFCQQGK**TLPWTFGGGSKLEMKmuAb5 V_H (SEQ ID NO: 105)DVQLQESGPGLVPEPSQSLFLTC**SVTGYSIT**NYNWNWIRQFPGNKLEWMGY**IRHD**GTN
NYNPSLKNRISIRDTPKNQFFLKLNSVT**TTEDTA**IFCTRLDYWGQGT**SV**TVSSmuAb5 V_L (SEQ ID NO: 155)DAVMTQTPLSPVSLGDQASISCR**SSQS**LENSYGN**TFL**NWFLQRPQSPQ**LLI**RVSNR
FCGVPDRFSGSGGTDFTLKISRVEAEDLG**IFY**CLQV**TH**VPYTFGGG**TK**LEIKmuAb6 V_H (SEQ ID NO: 106)QVQLQQPGAEIVRPGSSVKLSCKASGY**TF**TSYWMHWVKQRP**IQGLEW**IGNID**PS**NGE
THYNQKFKDKATLTVDKSSSTAYMQLSSLTSEDSAVY**CARER**IYSGSTYDGYFDVWGTGTTVTVSSmuAb6 V_L (SEQ ID NO: 156)QIVLTQSPAIMSASPGEKVTMTCS**ASS**LSYMHWYQQKSGTSPKRW**YD**TSKLASGVPA
RFSGSGGTSYSLTISSEAEADAATY**CQQWSS**NPWTFGGG**TK**LEIKmuAb7 V_L (SEQ ID NO: 157)QIVLTQSPAIMSASPGEKVTMTCS**ASS**LSYMHWYQQKSGTSPKRW**YD**TSKLASGVPA
RFSGSGGTSYSLTISSEMEGEDGATY**CQQWSS**NPWTFGGG**TK**LEIK**FIG. 2B**

4 / 20

Mouse anti-human CD40 Antibody DomainsVariable domains (CDRs in **bold**)muAb8 V_H (SEQ ID NO: 107)

QVQLQQSGPELVKSGASVKISKASGY**TFDYYIN**WVKQRPQGQLEWIG**WIFPGSGSV**
YCNEQFKGQATLTVDRSSSTAYMLLSLTSEDSAVYFCASS**LGKFAY**WGQGTLLVTVSA

muAb8 V_L (SEQ ID NO: 158)

DIVMTQSQKFMSTTVGDRV**SITCKASQSV**TAVAWYQQKPGQSPKLLIY**SASNRY**TGV
 PDRFTGSGSGTDFAL**TIRTMQ**SEDLADYFCQ**QYSSYP**TFEGG**G**TKLEIK

muAb9 V_H (SEQ ID NO: 108)

DVQLQESGPGLVKPSQSL**SLTCSVTGY**SITSNYYWNWIRQFPGNKLEWMGY**IRYDGSN**
NYNPSLKNRISITRDTSKNQFFLKLNSVT**TDATY**CARLDYWGGGTT**LVSS**

muAb9 V_L (SEQ ID NO: 159)

DAVMTQTPLSLPVSLG**DQASISCRSSQ**SL**ENTNG**N**TFL**NWFLQKPGQSPQLLIY**RVSNR**
FSGVPDRFSGSGGTDFTLKISRVEAEDLG**VYFCLQV**TH**VP**TFGSGTKLEIK

muAb10 V_H (SEQ ID NO: 109)

DVQLQESGPGLVKPSQSL**SLTCSVTGY**SITSNYYWNWIRQFPGNKLEWMGY**IRYDGSN**
NYNPSLKNRISITRDTSKNQFFLRLNSVT**TDATY**CTRLDYWGQGT**TLVSS**

muAb10 V_L (SEQ ID NO: 160)

DAVMTQTPLSLPVSLG**DQASISCRSSQ**SL**ENSGN**T**FL**NWFLQKPGQSPQLLIY**RISNRF**
SGVPDRFSGSGGTDFTLKISRVEAEDLG**VYFCLQV**TH**VP**TFGSGTKLEIK

FIG. 2C

5 / 20

Humanized anti-human CD40 Antibody Domains

Variable domains (CDRs in **bold**)huAb6-1 V_H (SEQ ID NO: 110)EVQLVQSGAEVKKPGSSVKVCKASGYFTSYWMHWVRQAPGQGLEWIGNIDPSNGETHY**NQ**
KFKDRATLTVDKSTSTAYMELSSLRSEDTAVYCARERIYSGSTYDGYFDVWGQGTTVTVSShuAb6-1 V_L (SEQ ID NO: 161)DIQLTQSPSFLSASVGDRVTITCS**ASSSL**SYMHWYQQKPKSPKRWYDTSKL**ASG**VPSPRFSGSGS
GTEYTLTISSLPEDFATY**CCQWSSNP**WTFGGGTKVEIKhuAb6-2 V_H (SEQ ID NO: 111)EVQLVQSGAEVKKPGSSVKVCKASGYFTSYWMHWVRQAPGQGLEWIGNIDPSNGETHY**NQ**
KFKDRVITITVDKSTSTAYMELSSLRSEDTAVYCARERIYSGSTYDGYFDVWGQGTTVTVSShuAb6-3 V_H (SEQ ID NO: 112)EVQLVQSGAEVKKPGSSVKVCKASGYFTSYWMHWVRQAPGQGLEWIGNIDPSNGETHY**AAQ**
KFQGRVITITVDKSTSTAYMELSSLRSEDTAVYCARERIYSGSTYDGYFDVWGQGTTVTVSShuAb8-1 V_H (SEQ ID NO: 113)EVQLVQSGAEVKKPGSSVKVCKASGYFTDYYINWVRQAPGQGLEWIGWIFPGSGSVYC**NEQF**
KGRATLTVDRSTSTAYMELSSLRSEDTAVYFCASS**LGKF**AYWGQGLTVTVSShuAb8-1 V_L (SEQ ID NO: 162)DIQMTQSPSSLSASVGDRVTITCK**ASQSWT**AVAWYQQKPKSPKLLIY**SASN**RYTGVPSPRFSGSGS
GTDFTLTISLQPEDFATY**FCQQYSSYP**TFFGGGTKVEIKhuAb8-2 V_H (SEQ ID NO: 114)EVQLVQSGAEVKKPGSSVKVCKASGYFTDYYINWVRQAPGQGLEWIGWIFPGSGSVYS**NEQF**
KGRATLTVDRSTSTAYMELSSLRSEDTAVYFCASS**LGKF**AYWGQGLTVTVSS**FIG. 2D**

6 / 20

Humanized anti-human CD40 Antibody Domains

Variable domains (CDRs in **bold**)huAb8-3 V_H (SEQ ID NO: 115)

EVQLVQSGAEVKKPGSSVKVSKKASGYTFTDYINWVRQAPGQGLEWIGWIFPGSGSVYCNEQF
KGRVTITVDKSTSTAYMELSSLRSEDTAVYCA**SSLGKFAYWGQ**GLTVTVSS

huAb9-1 V_H (SEQ ID NO: 116)

EVQLQESGPGGLVKPSETLSLTCTVSGYSITSNYYWNWIRPPGKGLEWMGYIRYDGSNNYNPSL
KNRITISRDTSKNQFSLKLSSVTAADTAVYCA**RLDYWGGQ**TTTVTVSS

huAb9-1 V_L (SEQ ID NO: 163)

DAVMTQTPLSLSVTPGQPASISCRSSQSLENTNGNTFLNWFLQPGQSPQLLIYRVSNRFSGVPD
 RFSGSGSGTDFTLKISRVEAEDVGVYFCLQVTHVPFTFGQGTKLEIK

huAb9-2 V_H (SEQ ID NO: 117)

EVQLQESGPGGLVKPSETLSLTCTVSGYSITSNYYWNWIRPPGKGLEWMGYIRYDGSNNYNPSL
KNRVTISRDTSKNQFSLKLSSVTAADTAVYCA**RLDYWGGQ**TTTVTVSS

huAb9-3 V_H (SEQ ID NO: 118)

EVQLQESGPGGLVKPSETLSLTCTVSGYSISSNYYWNWIRPPGKGLEWMGYIRYDGSNNYNPSL
KSRVTISRDTSKNQFSLKLSSVTAADTAVYCA**RLDYWGGQ**TTTVTVSS

huAb9-4 V_L (SEQ ID NO: 164)

DAVMTQTPLSLSVTPGQPASISCRSSQSLENTNGNTFLNWYLOKPGQSPQLLIYRVSNRFSGVPD
 RFSGSGSGTDFTLKISRVEAEDVGVYCLQVTHVPFTFGQGTKLEIK

FIG. 2E

Humanized anti-human CD40 Antibody Domains
Variable domains (CDRs in **bold**)

huAb9-7 V_H (SEQ ID NO: 119)

EVQLVESGGGLVKPGETLSLTCTV**SGYSITS**NYWNWIRQPPGKGLEWMGYIRYDGSNNYNPSL
KGRVTISRDTSKNQFYLLKSSVTAADTAVYYCARLDYWGGGTLTVSS

huAb9-8 V_H (SEQ ID NO: 120)

EVQLVESGGGLVQPGGSLRLSCAAS**GY**SITSNYWNWIRQPPGKGLEWMGYIRYDGSNNYNPS
LKGRVTISRDTSKNQFYLLKSSVTAADTAVYYCARLDYWGGGTLTVSS

huAb9-9 V_H (SEQ ID NO: 121)

EVQLVESGGGLVKPGETLILCTV**SGYDITS**NYWNWIRQPPGKGLEWMGYIRYDGSNNYNPSL
KGRVTISRDTSKNQFYLLKSSVTAADTAVYYCARLDYWGGGTLTVSS

huAb9 rehu V_{H4} V_H (SEQ ID NO: 122)

QVQLQESGPGLVKPSSETLSLTCTV**SGYSITS**NYWNWIRQPPGKGLEWMGYIRYDGSNNYNPSL
KNRITISRDTSKNQFSLKSSVTAADTAVYYCARLDYWGGGTLTVSS

huAb9 rehu V_{H3} V_H (SEQ ID NO: 123)

EVQLVESGGGLVQPGGSLRLSCAAS**GY**SITSNYWNWVRQAPGKGLEWMGYIRYDGSNNYNPS
LKNRITISRDTSKNTFYLMNSLRAEDTAVYYCARLDYWGGGTLTVSS

FIG. 2F

Humanized anti-human CD40 Antibody Domains

Variable domains (CDRs in **bold**)

huAb9-7 V_L (SEQ ID NO: 165)

DAVMTQTPLSLVTEGQPASISCR**SSQ**SLNTNGNTFLNWYLQKPGQSPQLLIYRVSNRFSGVDP
RFGSGSGTDFTLKISRVEAEDVGVYCLQVTHVPFTFGQGTKLEIK

huAb9-9 V_L (SEQ ID NO: 166)

DAVMTQTPLSLVLPQQPASISCR**SSQ**SLNTNGNTFLNWYLQKPGQSPQLLIYRVSNRFSGVDP
RFGSGSGTDFTLKISRVEAEDVGVYCLQVTHVPFTFGQGTKLEIK

huAb9 VK1 V_L (SEQ ID NO: 167)

DIQMTQSPSSLSASVGDRTITCR**SSQ**SLNTNGNTFLNWYQQKPGKAPKLLIYRVSNRFSGVPS
RFGSGSGTDFTLTISLQPEDFATYICLVTHVPFTFGQGTKVEIK

huAb9 rehu VK2 V_L (SEQ ID NO: 168)

DAVMTQSPSLPVTILGEPASISCR**SSQ**SLNTNGNTFLNWYQQKPGQSPRLLIYRVSNRFSGVDP
RFGSGSGTDFTLKISRVEAEDVGVYCLQVTHVPFTFGQGTKLEIK

huAb9 rehu VK1 V_L (SEQ ID NO: 169)

DAQMTQSPSSLSASVGDRTITCR**SSQ**SLNTNGNTFLNWYQQKPGKAPKLLIYRVSNRFSGVPS
RFGSGSGTDFTLTISLQPEDFATYICLVTHVPFTFGQGTKLEIK

huAb9 A2I V_L (SEQ ID NO: 170)

DIVMTQTPLSLVTPGQPASISCR**SSQ**SLNTNGNTFLNWYLQKPGQSPQLLIYRVSNRFSGVDPDR
FSGSGSGTDFTLKISRVEAEDVGVYCLQVTHVPFTFGQGTKLEIK

huAb9 A2V V_L (SEQ ID NO: 171)

DVVMQTPLSLVTPGQPASISCR**SSQ**SLNTNGNTFLNWYLQKPGQSPQLLIYRVSNRFSGVDP
RFGSGSGTDFTLKISRVEAEDVGVYCLQVTHVPFTFGQGTKLEIK

FIG. 2G

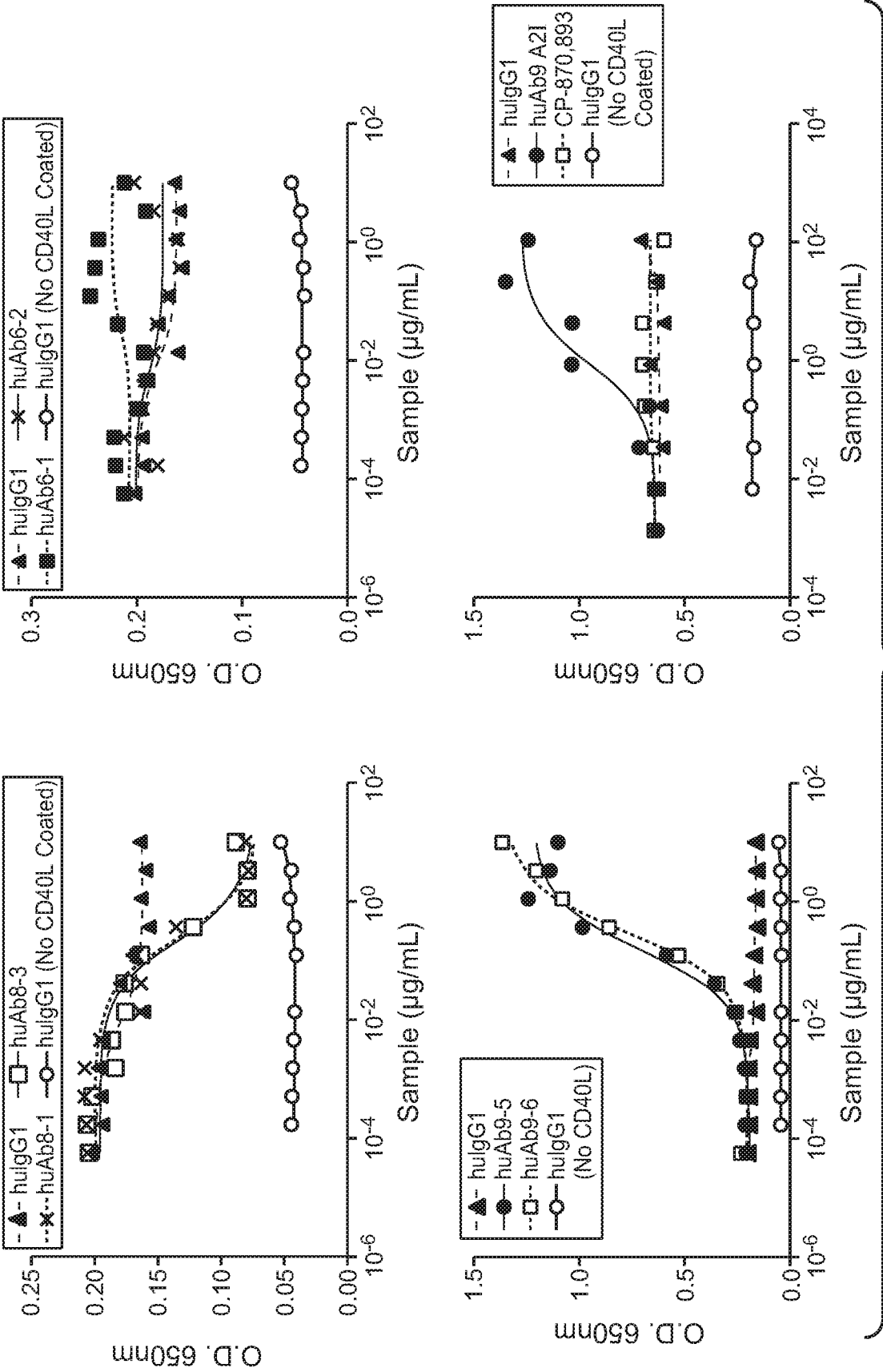


FIG. 3

10 / 20

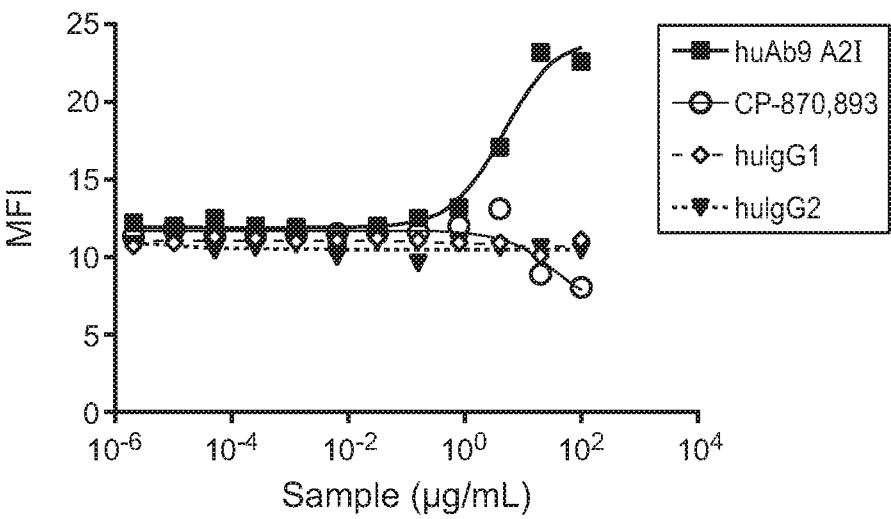


FIG. 4

11 / 20

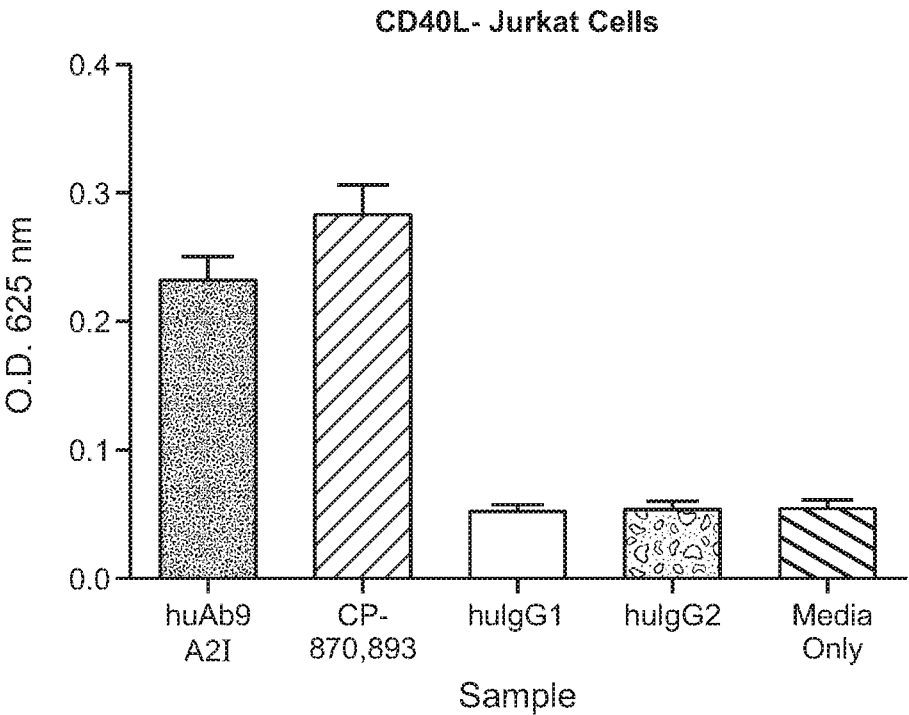


FIG. 5A

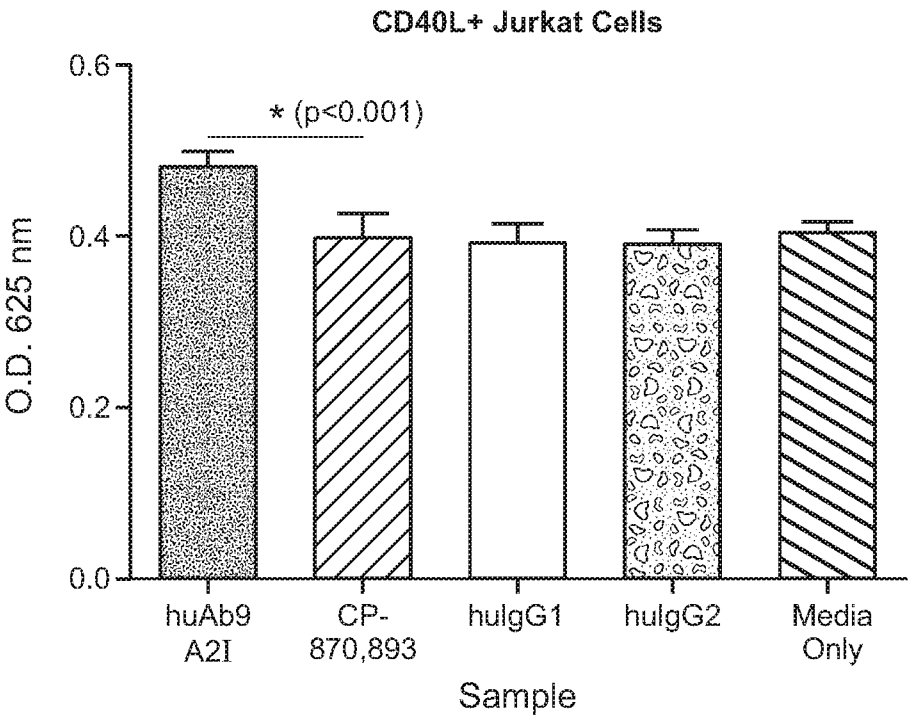


FIG. 5B

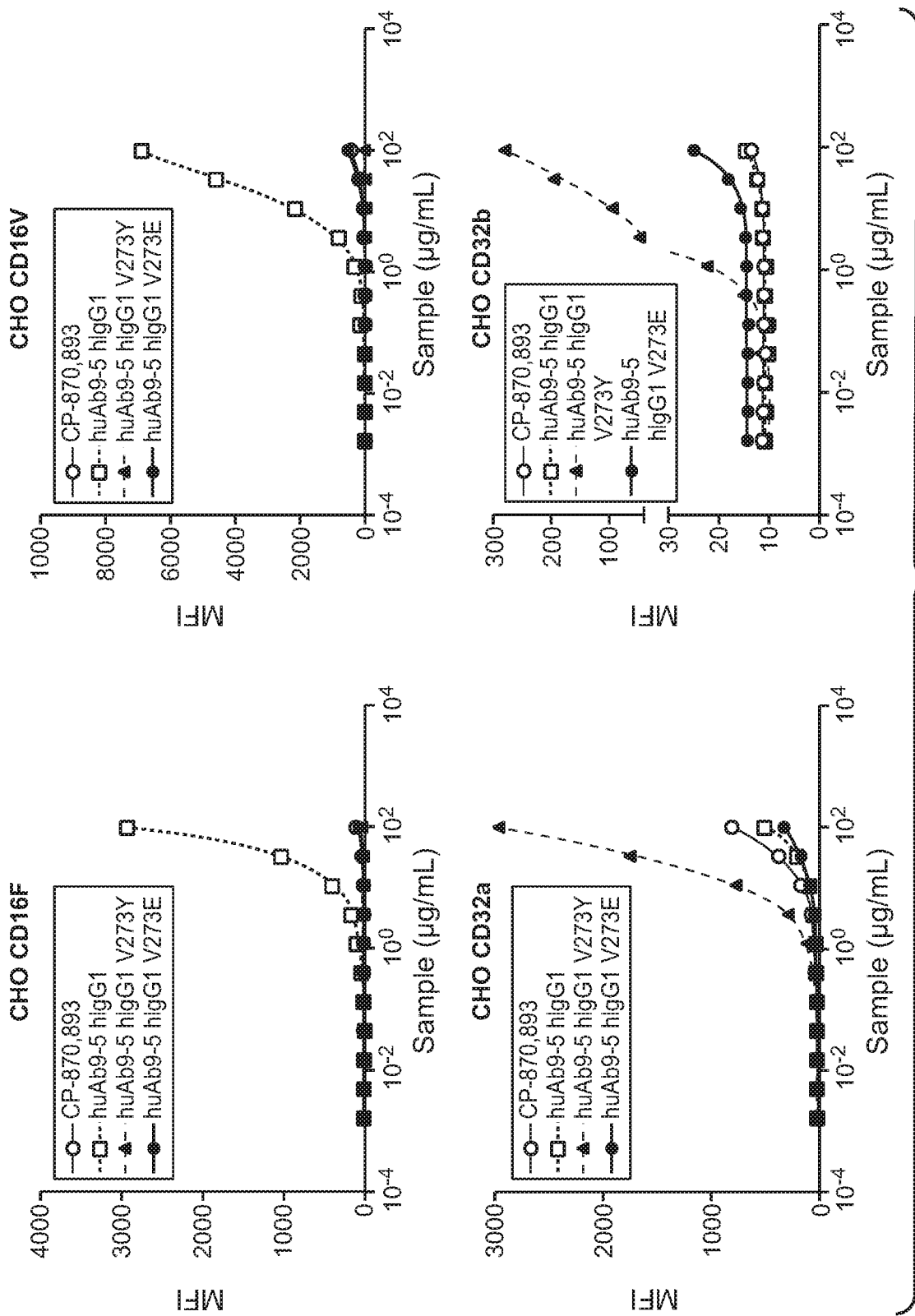
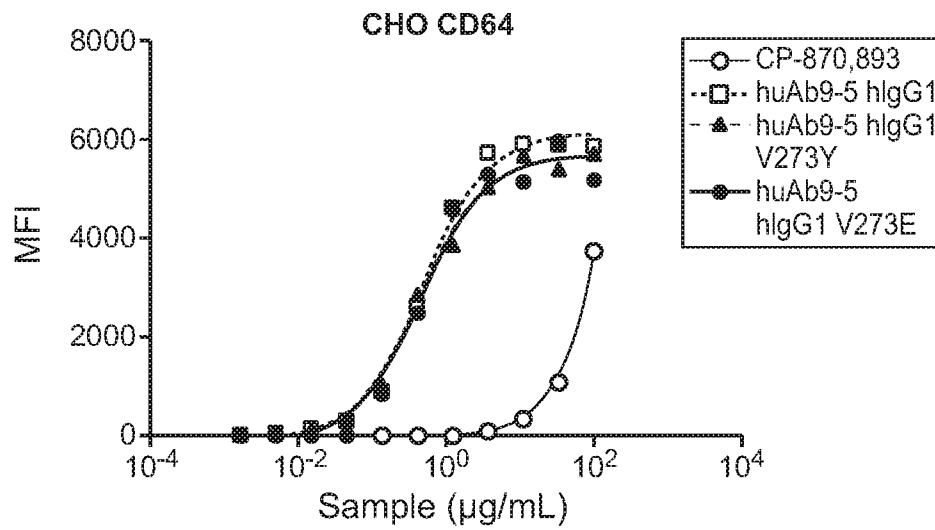
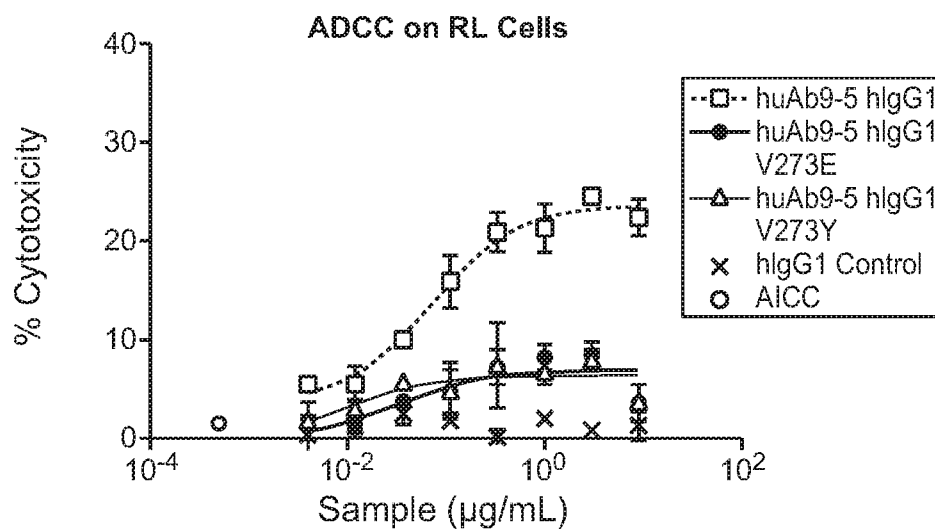
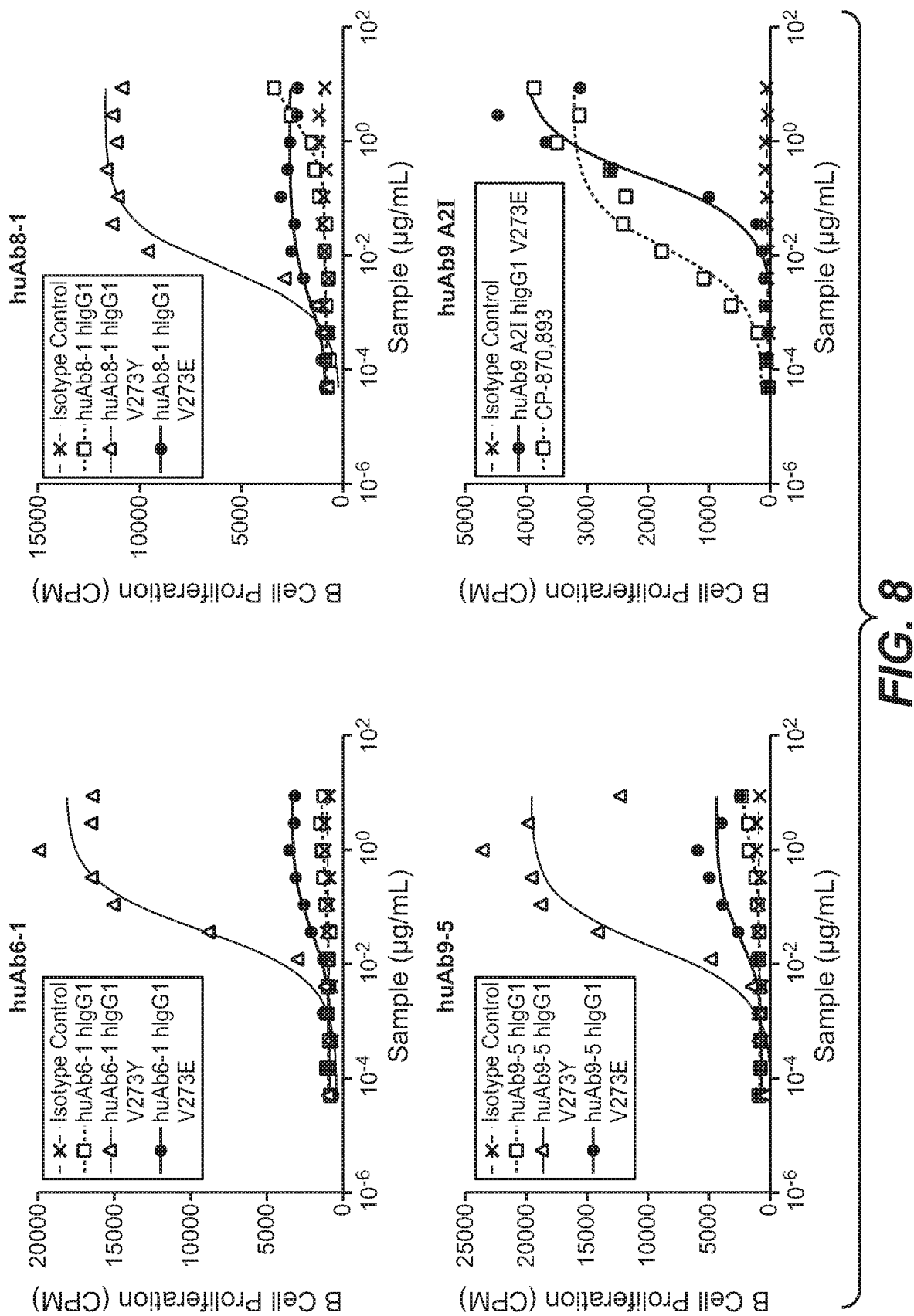


FIG. 6A

13 / 20

**FIG. 6B****FIG. 7**



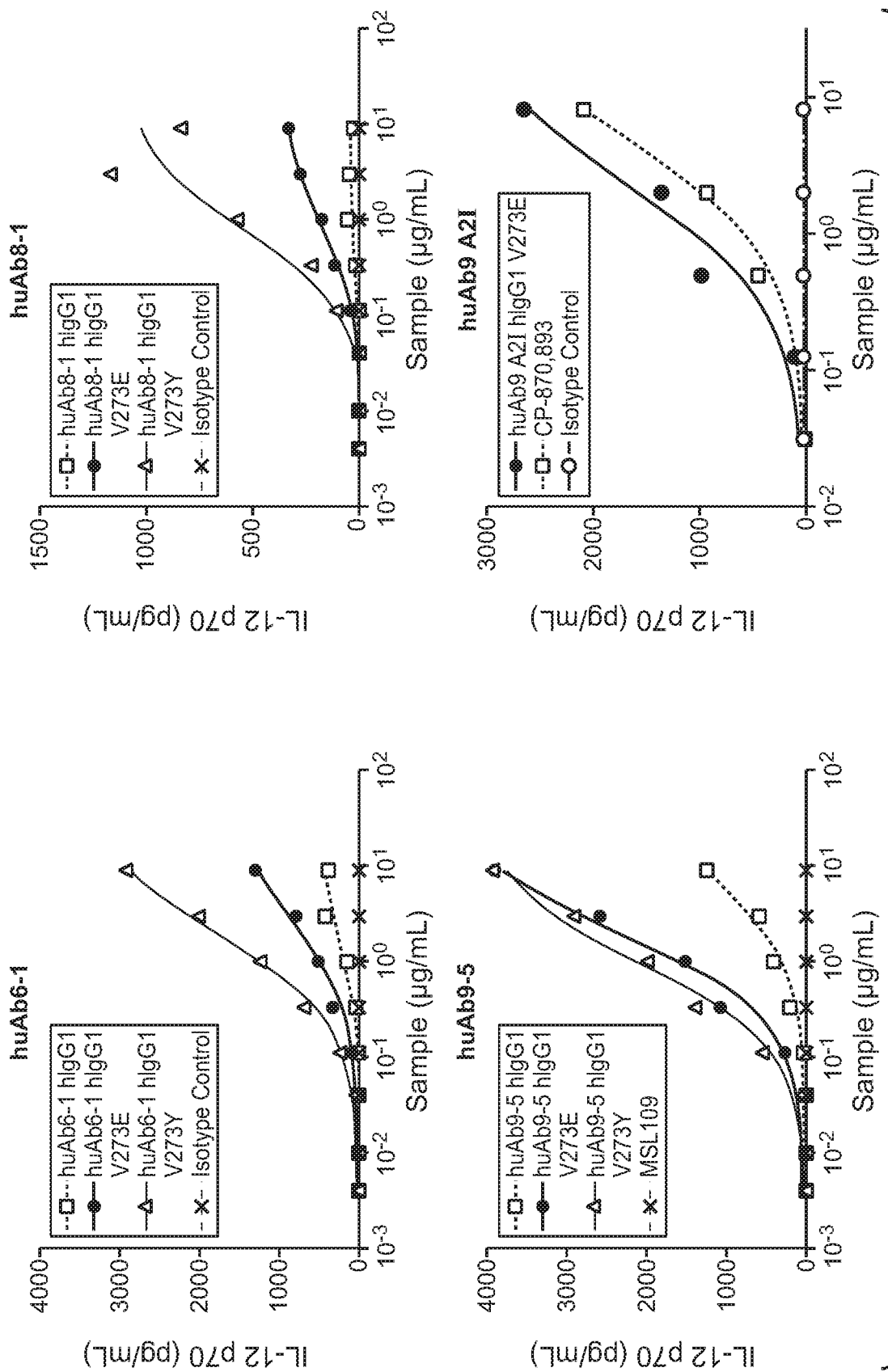


FIG. 9

16 / 20

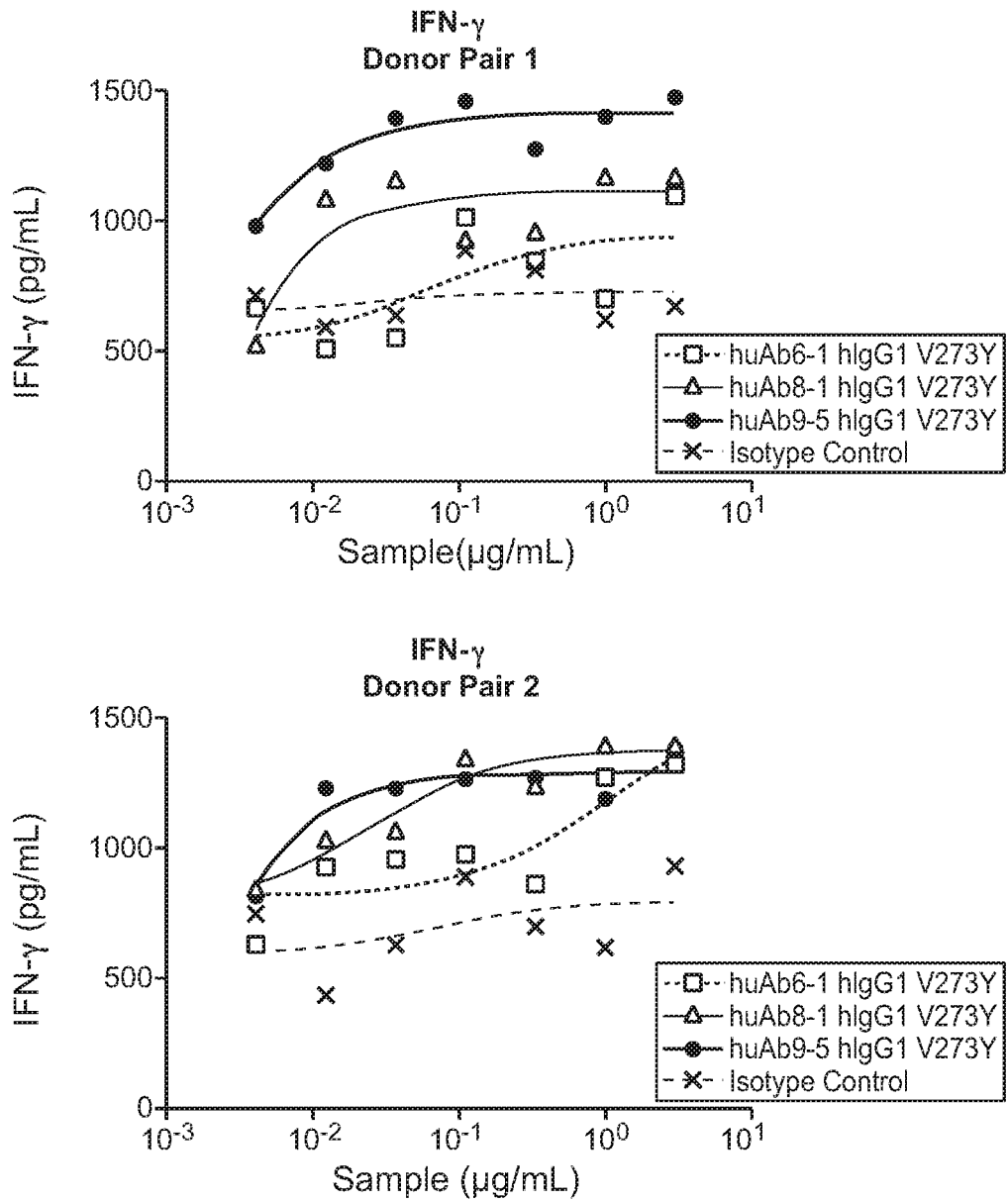
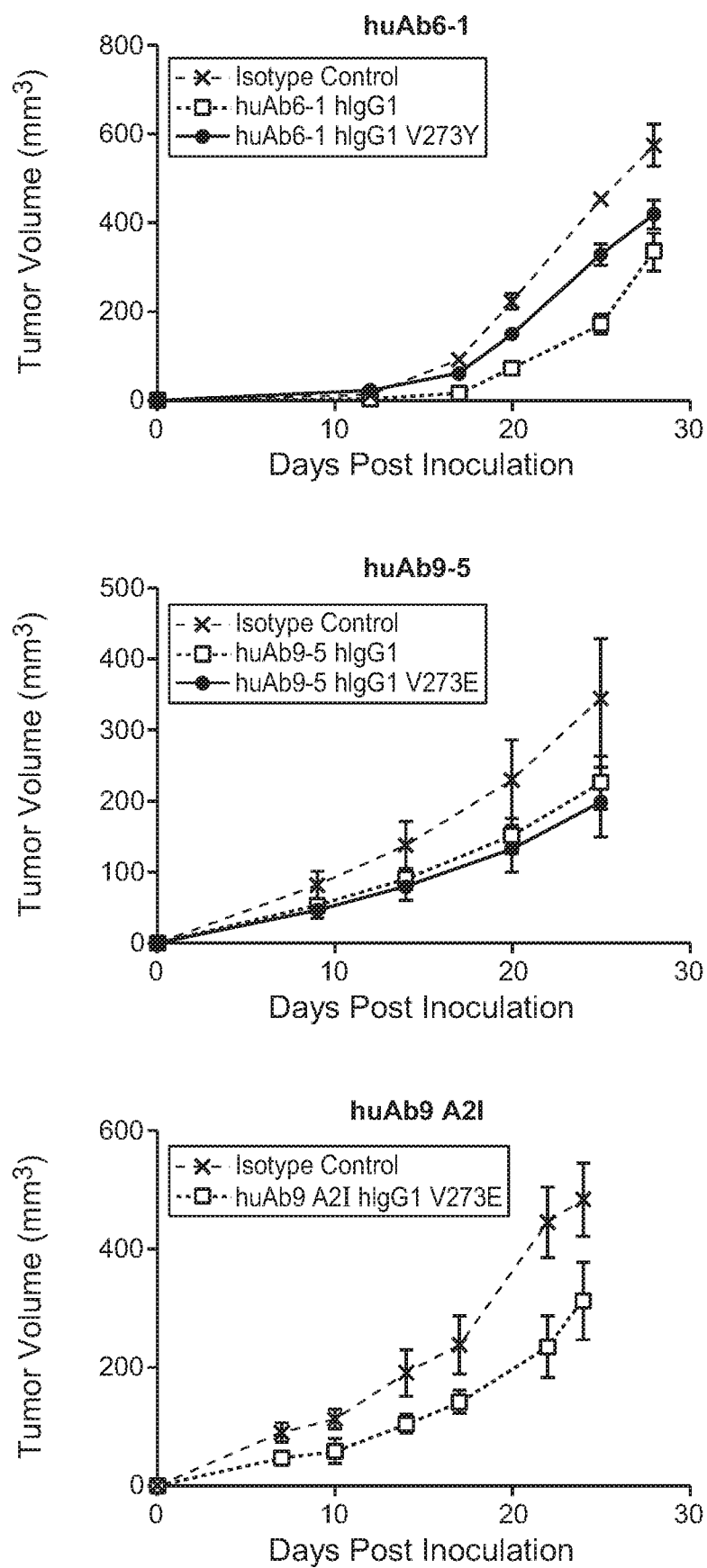
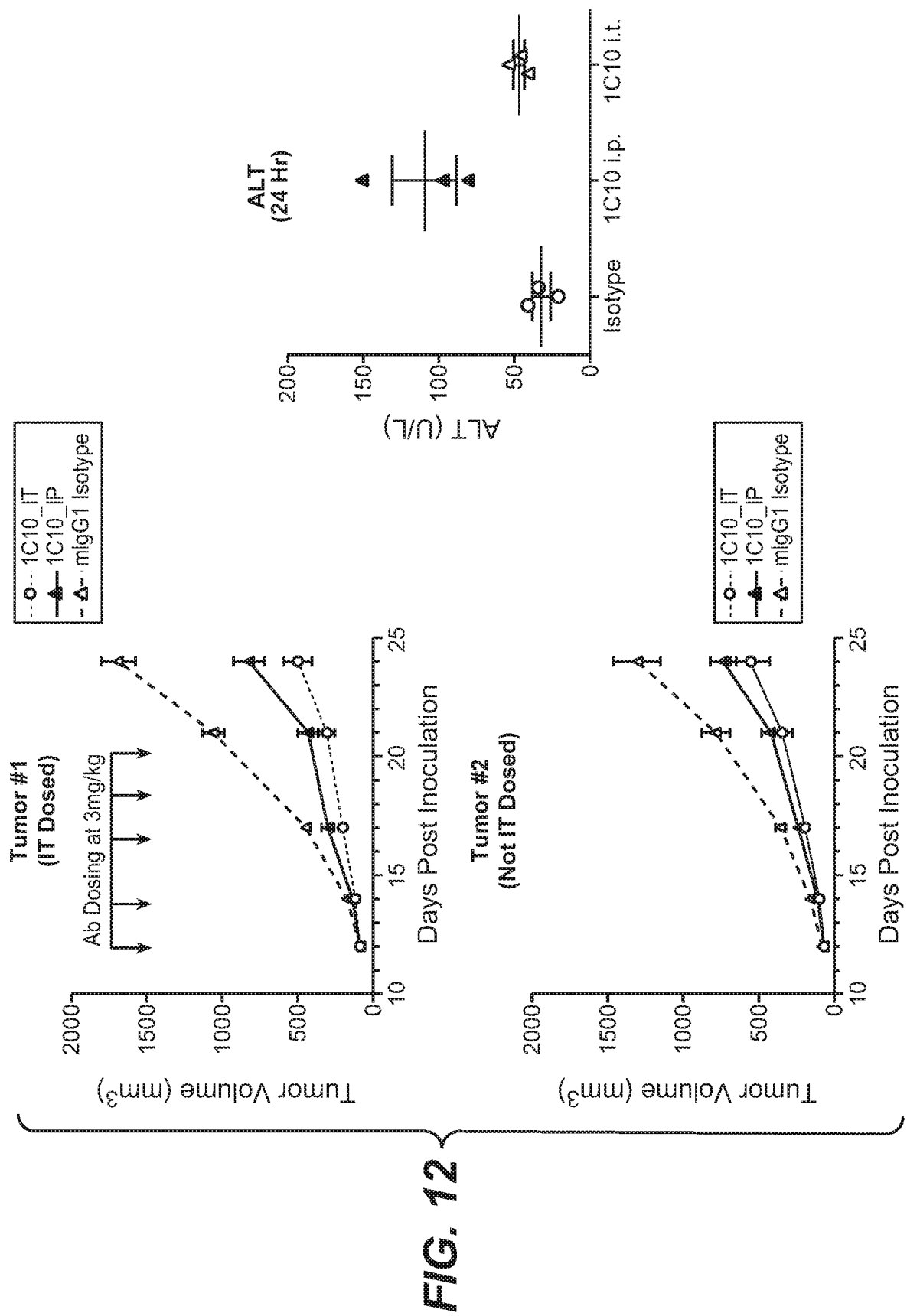


FIG. 10

17 / 20

FIG. 11



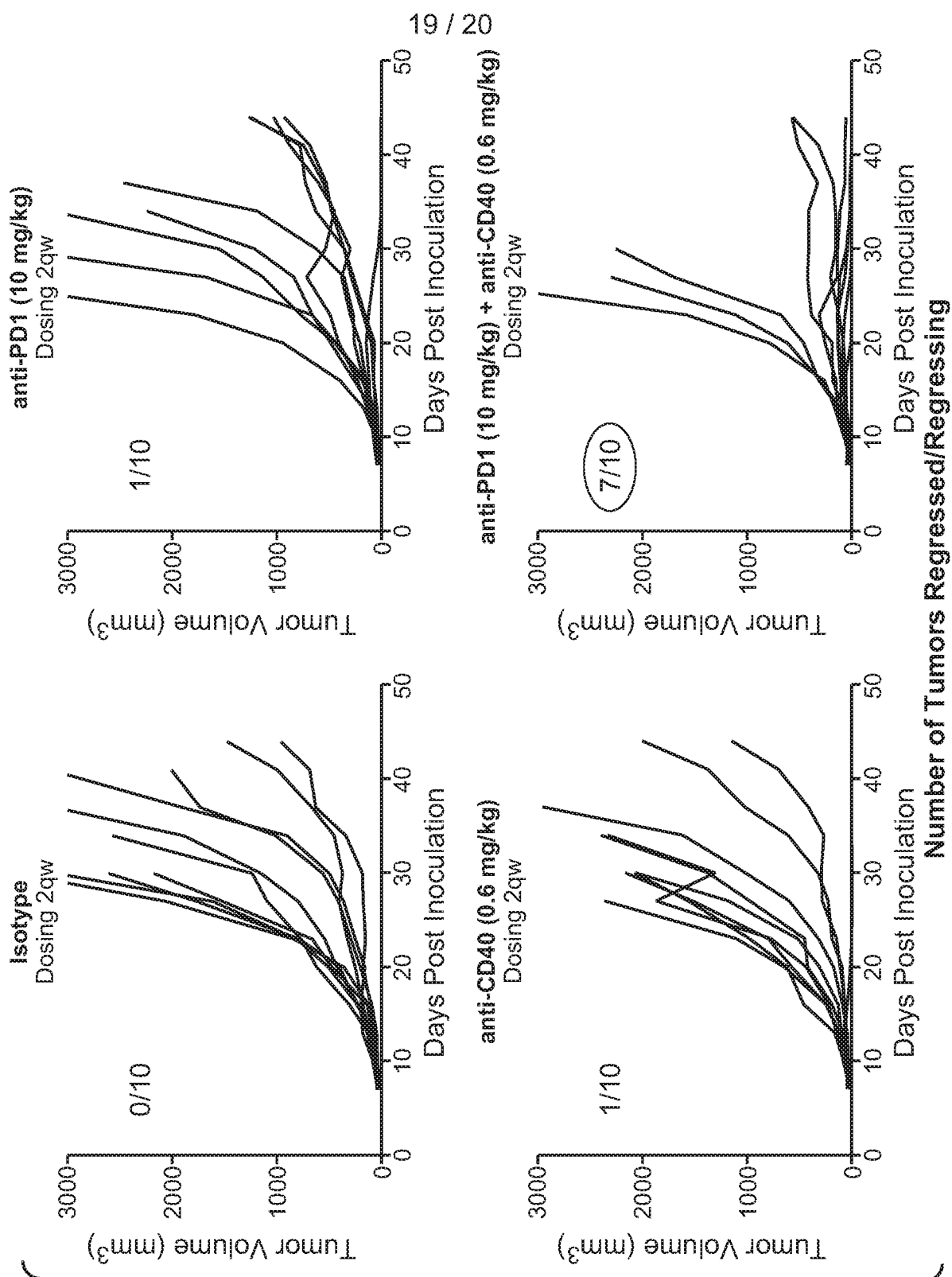


FIG. 13

