

FIG. 1A**SEQ ID NO: 1**>1901Ab1 Heavy Chain

EVQLLESGGGLVQPGGSLRLSCAASGFTFSFAMTWVRQAPGKGLEWVSSLSGSGRS
TYYAASMKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCAKSLSYHHYYFDYWGQ
GTLVTVTSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKT
HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVSVSLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI
SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 2>1901Ab1 and 1901Ab2 Light Chain

DIQLTQSPSFLSASVGDRVPITCRASQGISNFLAWYQQKPGKAPELLIHSASTLQSGVP
SRFSGSGSGTEFTLTISNLQPDFATYYCQQVNSYPLTFGGGTKVEIKRTVAAPSVFIF
PPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS
LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 3>1901Ab2 Heavy Chain

EVQLLESGGGLVQPGGSLRLSCAASGFTFSFAMTWVRQAPGKGLEWVSSLSGSGRS
TYYAASMKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCAKSLSYHHYYFDYWGQ
GTLVTVTSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKT
HTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVSVSLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI
SKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGGGG
SGGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHWVRQAPG
KCLEWVAIIWYDGINKYYADSVKGRFTISRDNSKNTLYLQMNSLKAEDTAVYY
CARDQDYDILTGYYKEDYFDFWGQTLVTVSSGGGGSGGGGSGGGGSGGGGSSY
ELTQPPSVSVSPGQTARITCSGDALPKKYAYWYQQKSGQAPVLVIYEDSKRPSGIPER
FSGSSSGTMATLTISGAQVEDEADYYCYSTDSSGNRVFGCGTKLTVL

FIG. 1A (continued)**SEQ ID NO: 4** >1901Ab3 Heavy Chain

EVQLLESGGGLVQPGGSLRLSCAASGFTFSFAMTWVRQAPGKGLEWVSSLSGSGRS
TYYAASMKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCAKSLSYHYHYFDYWGQ
GTLVTVTSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPTVTSWNSGALTSG
VHTFPAVLQSSGLYSLSSVTVPSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKT
HTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVVSVLTTVLHQDWLNGKEYKCKVSNKALPAPIEKTI
SKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 5 >1901Ab3 Light Chain

DIQLTQSPSFLSASVGDRVPITCRASQGISNFLAWYQQKPGKAPELLIHSASTLQSGVP
SRFSGSGSGTEFTLTISNLQPDFATYYCQOVNSYPLTFGGGTKVEIKRTVAAPSVFIF
PPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS
LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECGGGGSGGGGSGGGGSQ
VQLVESGGGVVQGRSLRLSCAASGFTFSNYGMHWVRQAPGKCLEWVAIIWY
DGINKYYADSVKGRFTISRDNSKNTLYLQMNSLKAEDTAVYYCARDQDYDILTG
YYKEDYFDFWGQGTLVTVSSGGGGSGGGGSGGGGSSYELTQPPSVSVSPG
QTARITCSGDALPKKYAYWYQQKSGQAPVLVIYEDSKRPSGIPERFSGSSSGTM
ATLTISGAQVEDEADYYCYSTDSSGNRVFGCGTKLTVL

SEQ ID NO: 6 >1923Ab4 Heavy Chain

QVQLVESGGGVVQGRSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVAIIWYDG
INKYYADSVKGRFTISRDNSKNTLYLQMNSLKAEDTAVYYCARDQDYDILTGYYKE
DYDFDFWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPTVTSW
NSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSLGKTYTCNVDHKPSNTKVDKRV
ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFN
WYVDGVEVHNAKTKPREEQFNSTYRVVSVLTTVLHQDWLNGKEYKCKVSNKGLPSS
IEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN
NYKTTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSL
GK

SEQ ID NO: 7 >1923Ab4 Light Chain

SYELTQPPSVSVSPGQTARITCSGDALPKKYAYWYQQKSGQAPVLVIYEDSKRPSGIP
ERFSGSSSGTMATLTISGAQVEDEADYYCYSTDSSGNRVFGGGTKLTVLGQPKAAPS
VTLPSPSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTPPSKQSNNNK
YAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

FIG. 1B**SEQ ID NO: 8**>1912Ab1 Heavy Chain

QVQLVQSGAEVKKPGASVKVSCKASGNTFTSYDINWVRQATGQGLEWMGWMNPN
SGNTGYAQKFQGRVTMTRDTSISTAYMELSSLRSEDAVYYCVYYNYVWGSFRFDD
WGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL
TSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD
KHTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK
TISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY
KTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 9>1912 Ab1 1912 Ab3 and 1912Ab5 Light Chain

DIQLTQSPSFLSASVGDRVITICRASQGISSYLAWYQQKPGKAPKLLIYAASTLOSGV
PSRFGSGSGTEFTLAVSSLOPEDFATYYCQQLNSYPYTFGQGTKLEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTY
LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 10>1912Ab2 Heavy Chain

QVQLVESGGGVVQPGRSLRLSCTASGFTFSHYGMHWVRQAPGKGLEWVSFLWFDG
SKDNYADSVKGRFTISRDN SKNMLYLRMDSLRAEDTAVYYCARNGGLTIFDYWGQ
GTLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKT
HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI
SKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 11>1912 Ab2 and 1912Ab4 Light Chain

AIQLTQSPSSLSASVGDRVITICRASQGINSWLAWYQQKPEKAPKSLIYAASSLQSGV
PSRFGSGSGTDFTLTISLQPEDFATYYCQQYNFYPTFGQGTKLEIIRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS
LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIG. 1B (continued)**SEQ ID NO: 12**>1912Ab3 Heavy Chain

QVQLVQSGAEVKKPGASVKVSCKASGNTFTSYDINWVRQATGQGLEWMGWMNP
SGNTGYAQKFQGRVTMTRDTSISTAYMELSSLRSEDTAVYYCVYYNYVWGSFRFDD
WGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL
TSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD
KHTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWY
VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
GGGSGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHWVRQ
APGKCLEWVAIIWYDGINKYYADSVKGRFTISRDNSKNTLYLQMNSLKAEDTAV
YYCARDQDYDILTGYYKEDYFDFWGQGTLVTVSSGGGSGGGSGGGSGGGSGGGG
SYELTQPPSVSVSPGQTARITCSGDALPKKYAYWYQQKSGQAPVLVIYEDSKRPS
GIPERFSGSSSGTMATLTISGAQVEDEADYYCYSTDSSGNRVFGCGTKLTVL

SEQ ID NO: 13>1912Ab4 Heavy Chain

QVQLVESGGGVVQPGRSLRLSCTASGFTFSHYGMHWVRQAPGKGLEWVSFLWFDG
SKDNYADSVKGRFTISRDNSKNMLYLRMDSLRAEDTAVYYCARNGGLTIFDYWGQ
GTLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKT
HTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI
SKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGGGG
SGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHWVRQAPG
KCLEWVAIIWYDGINKYYADSVKGRFTISRDNSKNTLYLQMNSLKAEDTAVYY
CARDQDYDILTGYYKEDYFDFWGQGTLVTVSSGGGSGGGSGGGSGGGSSY
ELTQPPSVSVSPGQTARITCSGDALPKKYAYWYQQKSGQAPVLVIYEDSKRPSGI
PERFSGSSSGTMATLTISGAQVEDEADYYCYSTDSSGNRVFGCGTKLTVL

FIG. 1C**SEQ ID NO: 14**>1925Ab1 Heavy Chain

EVQLVQSGAEVKKPGASVKVSCKASGYTFSTYYIHVVROAPGQRLEWIGWIYPGNV
NTKYTENFKDRATLTADKSASTAYMELSSLRSEDTAVYYCARGLYYFDWVGQGTTL
TVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPC
PAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL
DSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGGGGSGGGG
SGGGGSQVQLVESGGGVVQPGRSRLRSCAASGFTFSNYGMHWVRQAPGKCLE
WVAIIWYDGIKYYADSVKGRFTISRDN SKNTLYLQMNSLKAEDTAVYYCARD
QDYDILTGYKEDYFDWVGQGTTLTVSSGGGGSGGGSGGGSGGGSSYELTQ
PPSVSVSPGQTARITCSGDALPKKYAYWYQQKSGQAPVLVIYEDSKRPSGIPERF
SGSSSGTMTLTISGAQVEDEADYYCYSTDSSGNRVFGCGTKLTVL

SEQ ID NO: 15>1925Ab1 and 1925Ab3 Light Chain

DIQMTQSPSSLSASVGDRVTITCKASQSVNNDVAWYQQKPGKAPKLLIYYASNRDT
GVPSRFGSGSGTDFTLTISSLQPEDFATYYCQQDYSSPYTFGQGTKLEIKRTVAAPSV
FIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDST
YLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 16>1925Ab2 Heavy Chain

EVQLVQSGAEVKKPGASVKVSCKASGYTFSTYYIHVVROAPGQRLEWIGWIYPGNV
NTKYTENFKDRATLTADKSASTAYMELSSLRSEDTAVYYCARGLYYFDWVGQGTTL
TVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPC
PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQ
PREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDS
DGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK

FIG. 1C (continued)**SEQ ID NO: 17** >1925Ab2 Light Chain

DIQMTQSPSSLSASVGDRVTITCKASQSVNNDVAWYQQKPGKAPKLLIYYASNRDT
GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQDYSSPYTFGQGTKLEIKRTVAAPSV
FIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDST
YLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECGGGGSGGGGSGGGG
SQVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHWVRQAPGKCLEWVAIIW
YDGINKYYADSVKGRFTISRDN SKNTLYLQMNSLKAEDTAVYYCARDQDYDILT
GYKEDYFD FWGQGT LVT VSSGGGGSGGGGSGGGGSGGGGSSYELTQPPSVSVSP
GQTARITCSGDALPKKYAYWYQQKSGQAPVLVIYEDSKRPSGIPERFSGSSSGT
MATLTISGAQVEDEADYYCYSTDSSGNRVFGCGTKLTVL

SEQ ID NO: 18 >1925Ab3 Heavy Chain

QVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHWVRQAPGKCLEWVAIIW
YDGINKYYADSVKGRFTISRDN SKNTLYLQMNSLKAEDTAVYYCARDQDYDILT
GYKEDYFD FWGQGT LVT VSSGGGGSGGGGSGGGGSGGGGSSYELTQPPSVSVSP
GQTARITCSGDALPKKYAYWYQQKSGQAPVLVIYEDSKRPSGIPERFSGSSSGT
MATLTISGAQVEDEADYYCYSTDSSGNRVFGCGTKLTVLGGGGSGGGGSGGGGS
GGGGSEVQLVQSGAEVKKPGASVKVSCKASGYTFTTYYIHWVRQAPGORLEWIGWI
YPGNVNTKYTENFKDRATLTADKSASTAYMELSSLRSED TAVYYCARGLYYFD FW
GQGTTLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTS
GVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDK
THTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK
TISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY
KTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 19 >1925Ab4 Heavy Chain

QVQLQQSGPELVKPGASVRISCKASGYTFTTYYIHWVKQRPQGLEWIGWIYPGNV
NTKYTENFKDKATLTADKSSSTAYMQLSSLTSEDSAVYFCARGLYYFD FWGQGTTL
TVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPC
PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQ
PREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSD
DGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

FIG. 1C (continued)**SEQ ID NO: 20**>1925Ab4 Light Chain

SIVMTQTPKFLLVSAGDRVITITCKASQSVNNDVAWYQQKPGQSPKLLIYYASNRDTG
VPDRFTGSGFGTDFTFITISSVQAEDLAVYFCQQDYSSPYTFGGGTKLEIKRTVAAPSV
FIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDST
YLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIG. 1D

SEQ ID NO: 21>1901Ab1_VH

EVQLLESGGGLVQPGGSLRLSCAASGFTFSSFAMTWVRQAPGKGLEWVSSLSGSGRS
TYAAASMKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCAKSLSYHHYYFDYWGQ
GTLVTVTS

SFAMT	SLSGSGRSTYYAASMKG	SLSYYHHYYFDY
SEQ: 33	SEQ: 34	SEQ: 35

SEQ ID NO:22 >1901Ab1 and 1901Ab2_VL

DIQLTQSPSFLSASVGDRVPITCRASQGISNFLAWYQQKPGKAPELLIHSASTLQSGVP
SRFSGSGSGTEFTLTISNLQPQDFATYYCQQVNSYPLTFGGGTKVEIK

RASQGISNFLA	SASTLQS	QQVNSYPLT
SEQ: 36	SEQ: 37	SEQ: 38

SEQ ID NO: 23>1923Ab4_VH

QVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVAIIWYDG
INKYYADSVKGRFTISRDNSKNTLYLQMNSLKAEDTAVYYCARDQDYDILTGYYKEDYFDF
DYFDFWGQGTLVTVSS

NYGMH	IIWYDGINKYYADSVKG	DQDYDILTGYKEDYFDF
SEQ: 39	SEQ: 40	SEQ: 41

SEQ ID NO:24 >1923Ab4_VL

SYELTQPPSVSVSPGQTARITCSGDALPKKYAYWYQQKSGQAPVLVIYEDSKRPSGIP
ERFSGSSSGTMATLTISGAQVEDEADYYCYSTDSSGNRVFGGGTKLTVL

SGDALPKKYAY	EDSKRPS	YSTDSSGNRV
SEQ: 42	SEQ: 43	SEQ: 44

FIG. 1D (continued)

SEQ ID NO: 25>1912Ab1_VH

QVQLVQSGAEVKKPGASVKVSCKASGNTFTSYDINWVRQATGQGLEWMGWMNPNSGNTGYAQKFQGRVTMTRDTSISTAYMELSSLRSEDTAVYYCVYYNYVWGSFRFDDWGQGT

SYDIN	WMNPNSGNTGYAQKFQG	YNYVWGSFRFDD
SEQ: 45	SEQ: 46	SEQ: 47

SEQ ID NO: 26>1912Ab1_VL

DIQLTQSPSFLSASVGDRVITITCRASQGISSYLA^{WY}QKPGKAPKLLIYA^{AASTLQ}SGVPSRFGSGSGTEFTLAVSSLPEDFATYYC^{QQLNSYPYT}FTFGQGTKLEIK

RASQGISSYLA	AASTLQS	QQLNSYPYT
SEQ: 48	SEQ: 49	SEQ: 50

SEQ ID NO: 27>1912Ab2_VH

QVQLVESGGGVVQPGRSLRLSCTASGFTFSHYGMHWVRQAPGKGLEWVSFLWFDGSKDNYADSVKGRFTISRDN^{SKNMLYLRMDSLRAEDTAVYYCARN}GGLTIFDYWGQGT

HYGMH	FLWFDGSKDNYADSVKG	NGGLTIFDY
SEQ: 51	SEQ: 52	SEQ: 53

SEQ ID NO: 28>1912Ab2_VL

AIQLTQSPSSLSASVGDRVITITCRASQGINSWLA^{WY}QKPEKAPKSLIYA^{AASSLQ}SGVPSRFGSGSGTDFTLTIS^{SLQPEDFATYYCQY}NFYPTFTFGQGTKLEIK

RASQGINSWLA	AASSLQS	QYNYFYPT
SEQ: 54	SEQ: 55	SEQ: 56

FIG. 1D (continued)

SEQ ID NO: 29>1925Ab4_VH(Hz)

EVQLVQSGAEVKKPGASVKVSCKASGYTFTTYYIHWVRQAPGQRLEWIGWIYPGNV
NTKYTENFKDRATLTADKSASTAYMELSSLRSEDTAVYYCARGLYYFDFWGQGTTL
TVSS

TYYIH	WIYPGNVNTKYTENFKD	GLYYFDF
SEQ: 57	SEQ: 58	SEQ: 59

SEQ ID NO: 30>1925Ab4_VL(Hz)

DIQMTQSPSSLSASVGDRTITCKASQSVNNDVAWYQQKPGKAPKLLIYYASNRDT
GVPSRFGSGSGTDFTLTISLQPEDFATYYCQQDYSSPYTFGQGTKLEIK

KASQSVNNDVA	YASNRDT	QQDYSSPYT
SEQ: 60	SEQ: 61	SEQ: 62

SEQ ID NO:31 >1925Ab4_VH

QVQLQQSGPELVKPGASVRISCKASGYTFTTYYIHWVKQRPQGQLEWIGWIYPGNV
NTKYTENFKDKATLTADKSSSTAYMQLSSLTSEDSAVYFCARGLYYFDFWGQGTTL
TVSS

TYYIH	WIYPGNVNTKYTENFKD	GLYYFDF
SEQ: 57	SEQ: 58	SEQ: 59

SEQ ID NO:32 >1925Ab4_VL

SIVMTQTPKFLVLSAGDRTITCKASQSVNNDVAWYQQKPGQSPKLLIYYASNRDTG
VPDRFTGSGFGTDFTTISVQAEDLAVYFCQQDYSSPYTFGGGTKLEIK

KASQSVNNDVA	YASNRDT	QQDYSSPYT
SEQ: 60	SEQ: 61	SEQ: 62

FIG. 1D (continued)

SEQ ID NO: 63>Anti-CD137 scFv* with 4x (G4S) linker

QVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHWVRQAPGKCLEWVAIIWYDGI
NKYYADSVKGRFTISRDN SKNTLYLQMNSLKAEDTAVYYCARDQDYDILTGYEYKE
DYFDWVGQGLTVTVSSGGGGSGGGSGGGSGGGSSYELTQPPSVSVSPGQTARIT
CSGDALPKKYAYWYQQKSGQAPVLVIYEDSKRPSGIPERFSGSSSGTMTATLTISGAQ
VEDEADYYCYSTDSSGNRVFGCGTKLTVL

SEQ ID NO: 64>3x (G4S) linker

GGGGSGGGSGGGGS

SEQ ID NO: 65>4x (G4S) linker

GGGGSGGGSGGGSGGGGS

SEQ ID NO: 66> Human IgG1 constant region (allotype)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAP
ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAK
TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPR
EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSD
GSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK

SEQ ID NO: 67> Human IgG1 constant region

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAP
ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAK
TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPR
EPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSD
GSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK

FIG. 1D (continued)

SEQ ID NO: 68> Human IgG1 constant region with LALA no GK

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAP
EAAGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAK
TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPR
EPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDS
DSGFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSP

SEQ ID NO: 69> Human IgG4 constant region with S228P

ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ
SSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVESKYGPPCPPCPAPEFLG
GPSVFLFPPKPKDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKTKPR
EEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVY
TLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFL
YSRLTVDKSRWQEGNVFCFSVMHEALHNHYTQKSLSLSLGLK

SEQ ID NO: 70> Human Kappa constant region

RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVT
EQDSKDSSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 71> Human Lambda constant region

GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTT
PSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

SEQ ID NO: 72> 1912Ab5 Heavy Chain

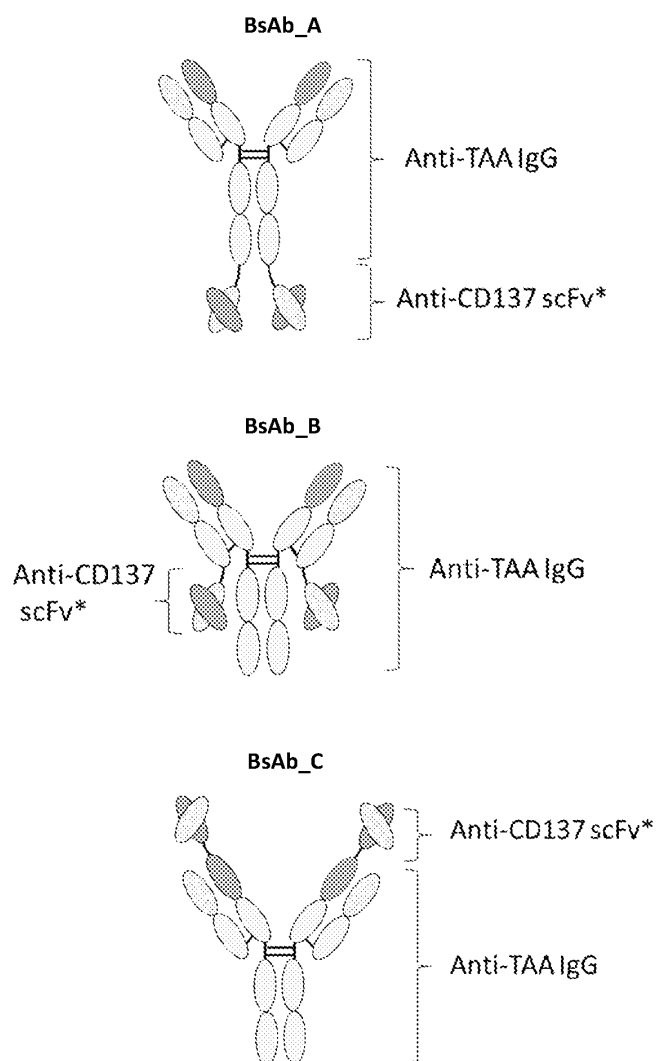
QVQLVQSGAEVKKPGASVKVSCKASGNTFTSYDINWVRQATGQGLEWMGWMNPN
SGNTGYAQKFQGRVTMTRDTSISTAYMELSSLRSEDAVYYCVYYNYVWGSFRFDD
WGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL
TSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD
KTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWY
VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIE
KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN
YKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPG
GGGSGGGSGGGGSQVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHWVRQ
APGKCLEWVAIIWYDGINKYYADSVKGRFTISRDNSKNTLYLQMNSLKAEDTAV
YYCARDQDYDILTGYYKEDYFDFWGQGLTVTVSSGGGSGGGSGGGSGGGGS
SYELTQPPSVSVSPGQTARITCSGDALPKKYAYWYQQKSGQAPVLVIYEDSKRPS
GIPERFSGSSSGTMTLTISGAQVEDEADYYCYSTDSSGNRVFGCGTKLTVL

FIG. 1D (continued)

SEQ ID NO: 73> Human IgG1 constant region with LALAPA no GK

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAP
EAAGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAK
TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPR
EPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSD
GSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSP

FIG. 2



*: scFv is stabilized by disulfide bond

FIG. 3**Bispecific** (* introduced disulfide bond to stabilize scFv, Hz, humanized)

Proteinaceous Molecule	Heavy chain (HC)	Light chain (LC)
1901Ab1	1901Ab1 VH-hIgG1	1901Ab1 VL-hKappa
1901Ab2	1901 Ab1 VH-hIgG1 LALA-3x(G4S)-1923Ab4 VH*-4x(G4S)-1923Ab4 VL*	1901Ab1 VL-hKappa
1901Ab3	1901Ab1 VH-hIgG1 LALA	1901Ab1 VL-hKappa-3x(G4S)-1923Ab4 VH*-4x(G4S)-1923Ab4 VL*
1923Ab4	1923Ab4 VH-hIgG4 S228P	1923Ab4 VL-hLambda
1912Ab1	1912Ab1 VH-hIgG1	1912Ab1 VL-hKappa
1912Ab2	1912Ab2 VH-hIgG1	1912Ab2 VL-hKappa
1912Ab3	1912Ab1 VH- hIgG1 LALA-3x(G4S)-1923Ab4 VH*-4x(G4S)-1923Ab4 VL*	1912Ab1 VL-hKappa
1912Ab4	1912Ab2 VH- hIgG1 LALA-3x(G4S)-1923Ab4 VH*-4x(G4S)-1923Ab4 VL*	1912Ab2 VL-hKappa
1912Ab5	1912Ab1 VH- hIgG1 LALAPA-3x(G4S)-1923Ab4 VH*-4x(G4S)-1923Ab4 VL*	1912Ab1 VL-hKappa
1925Ab1	1925Ab4 VH(Hz)- hIgG1 LALA-3x(G4S)-1923Ab4 VH*-4x(G4S)-1923Ab4 VL*	1925Ab4 VL(Hz)-hKappa
1925Ab2	1925Ab4 VH(Hz)- hIgG1	1925Ab4 VL(Hz)-hKappa-3x(G4S)-1923Ab4 VH*-4x(G4S)-1923Ab4 VL*
1925Ab3	1923Ab4 VH*-4x(G4S)-1923Ab4 VL*-4x(G4S)-1925Ab4 VH(Hz)-IgG1 LALA	1925Av4 VL(Hz)-hKappa
1925Ab4	1925Ab4 VH-hIgG1	1925Ab4 VL-hKappa

FIG. 4

Ab	Configuration	Antibody Scaffold Module 1 (IgG)		Binding Module (scFv)				
		Target	Fc	Fusion location to IgG	Fusion Linker	Target	scFv format	Stabilized
1901Ab1	mAb	Claudin 18.2	hIgG1					
1901Ab2	BsAb_A	Claudin 18.2	hIgG1 LALA	HC C-terminus	3x (G4S)	CD137	VH-4x(G4S)-VL	Yes
1901Ab3	BsAb_B	Claudin 18.2	hIgG1 LALA	LC C-terminus	3x (G4S)	CD137	VH-4x(G4S)-VL	Yes
1923Ab4	mAb	CD137	hIgG4 S228P					
1912Ab1	mAb	Claudin 6	hIgG1					
1912Ab2	mAb	Claudin 6	hIgG1					
1912Ab3	BsAb_A	Claudin 6	hIgG1 LALA	HC C-terminus	3x (G4S)	CD137	VH-4x(G4S)-VL	Yes
1912Ab4	BsAb_A	Claudin 6	hIgG1 LALA	HC C-terminus	3x (G4S)	CD137	VH-4x(G4S)-VL	Yes
1912Ab5	BsAb_A	Claudin 6	hIgG1 LALAPA	HC C-terminus	3x (G4S)	CD137	VH-4x(G4S)-VL	Yes
1925Ab1	BsAb_A	Nectin-4	hIgG1 LALA	HC C-terminus	3x (G4S)	CD137	VH-4x(G4S)-VL	Yes
1925Ab2	BsAb_B	Nectin-4	hIgG1	LC C-terminus	3x (G4S)	CD137	VH-4x(G4S)-VL	Yes
1925Ab3	BsAb_C	Nectin-4	hIgG1 LALA	HC N-terminus	4x (G4S)	CD137	VH-4x(G4S)-VL	Yes
1925Ab4	mAb	Nectin-4	hIgG1					

FIG. 5

Antibody	Heavy chain	Light chain
1901Ab1	SEQ ID NO: 1	SEQ ID NO: 2
1901Ab2	SEQ ID NO: 3	SEQ ID NO: 2
1901Ab3	SEQ ID NO: 4	SEQ ID NO: 5
1923Ab4	SEQ ID NO: 6	SEQ ID NO: 7
1912Ab1	SEQ ID NO: 8	SEQ ID NO: 9
1912Ab2	SEQ ID NO: 10	SEQ ID NO:11
1912Ab3	SEQ ID NO: 12	SEQ ID NO:9
1912Ab4	SEQ ID NO: 13	SEQ ID NO:11
1912Ab5	SEQ ID NO: 72	SEQ ID NO:9
1925Ab1	SEQ ID NO: 14	SEQ ID NO:15
1925Ab2	SEQ ID NO: 16	SEQ ID NO:17
1925Ab3	SEQ ID NO: 18	SEQ ID NO:15
1925Ab4	SEQ ID NO: 19	SEQ ID NO:20

FIG. 6A

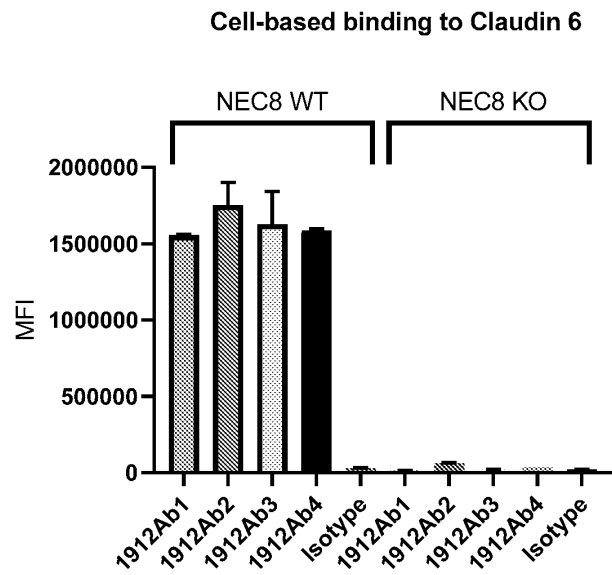


FIG. 6B

Cell-based binding of Claudin6-CD137 bispecific to Nec8 cells

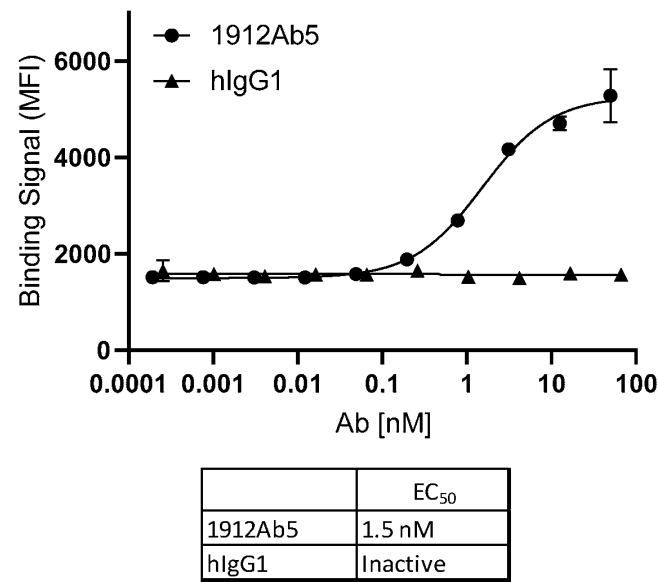
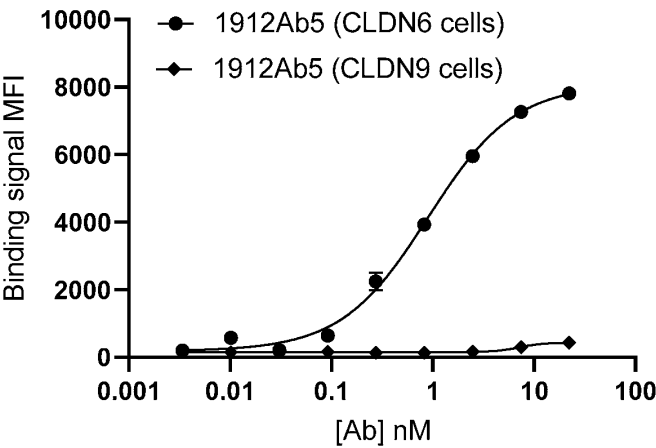


FIG. 6C

Cell-based binding of Claudin6-CD137 bispecific to CHO cells overexpressing Claudin6 or Claudin9



	EC ₅₀
CHO-CLDN6	0.9 nM
CHO-CLDN9	Inactive

FIG. 7A

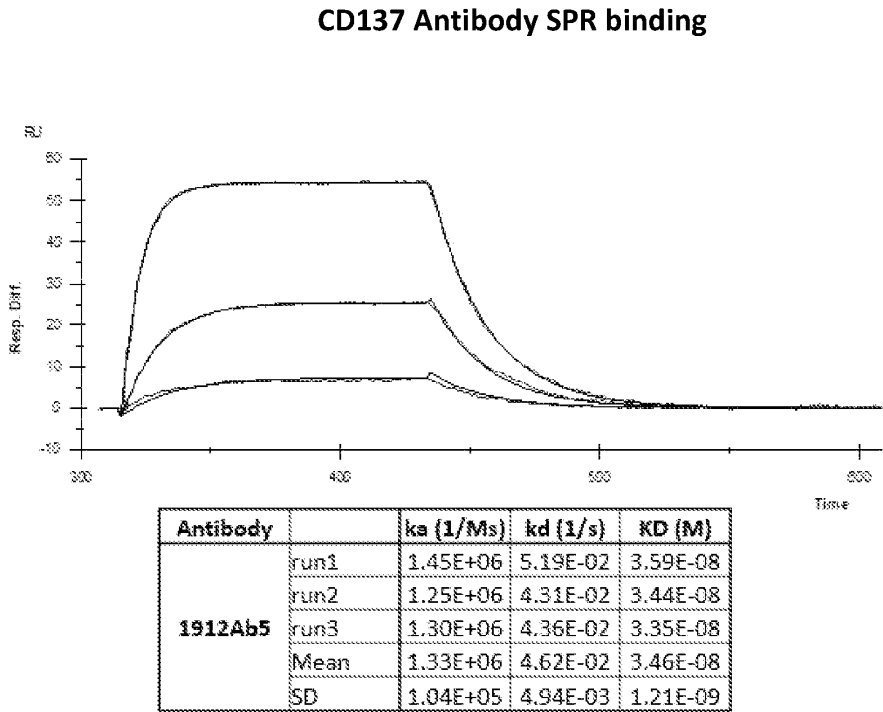


FIG. 7B

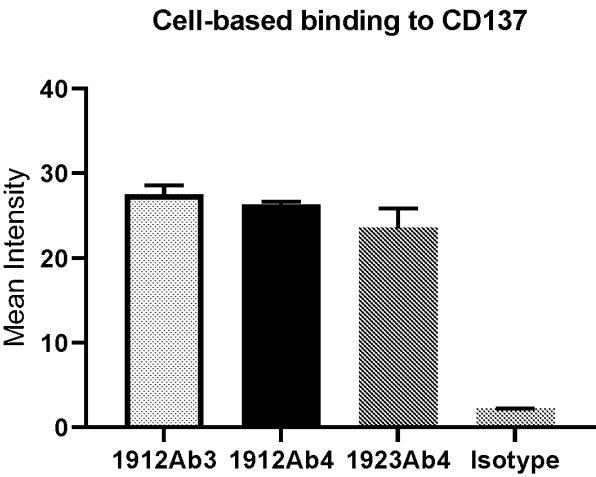
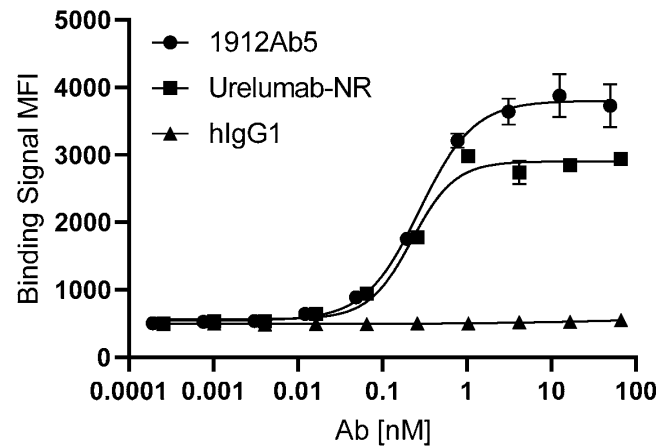


FIG. 7C

Cell-based binding of Claudin6-CD137 bispecific to CD137



	EC ₅₀
1912Ab5	0.28 nM
Urelumab-NR	0.22 nM
hIgG1	Inactive

FIG. 8A

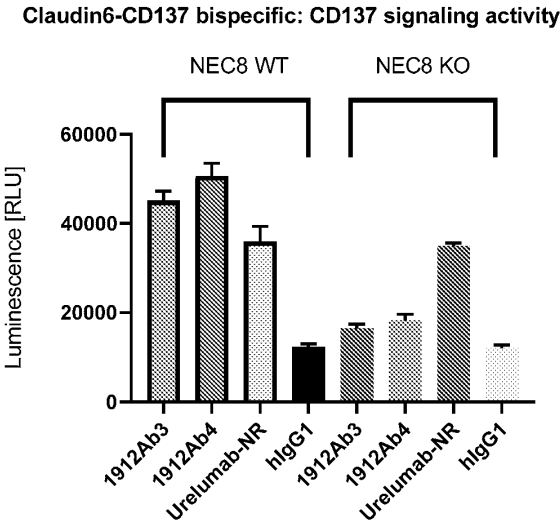


FIG. 8B

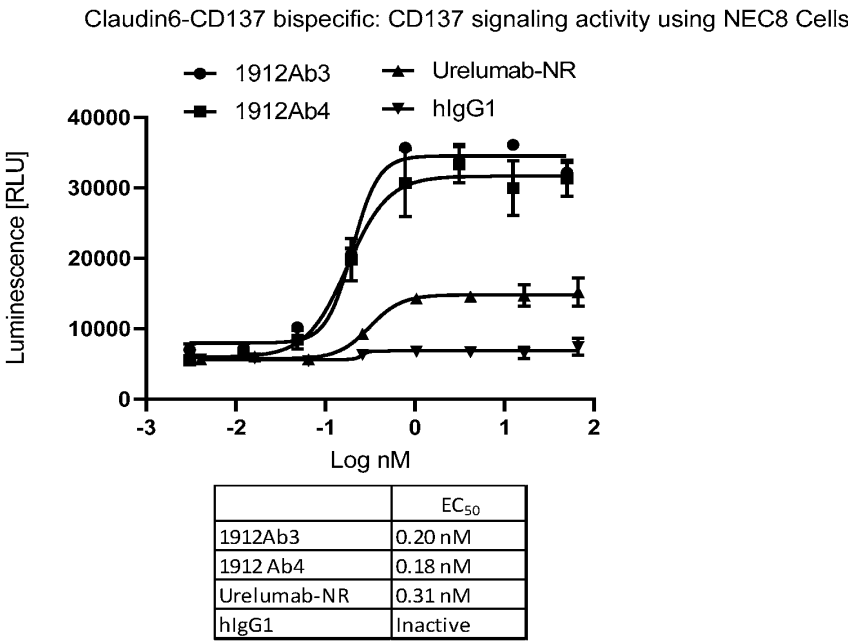


FIG. 8C

Claudin6-CD137 bispecific: CD137 signaling activity using NEC8 cells

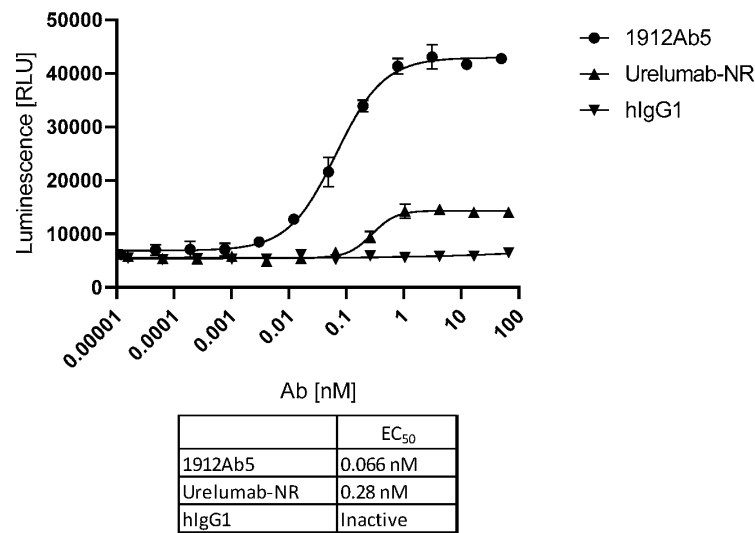


FIG. 8D

Claudin6-CD137 bispecific: CD137 signaling activity using OV90 cells

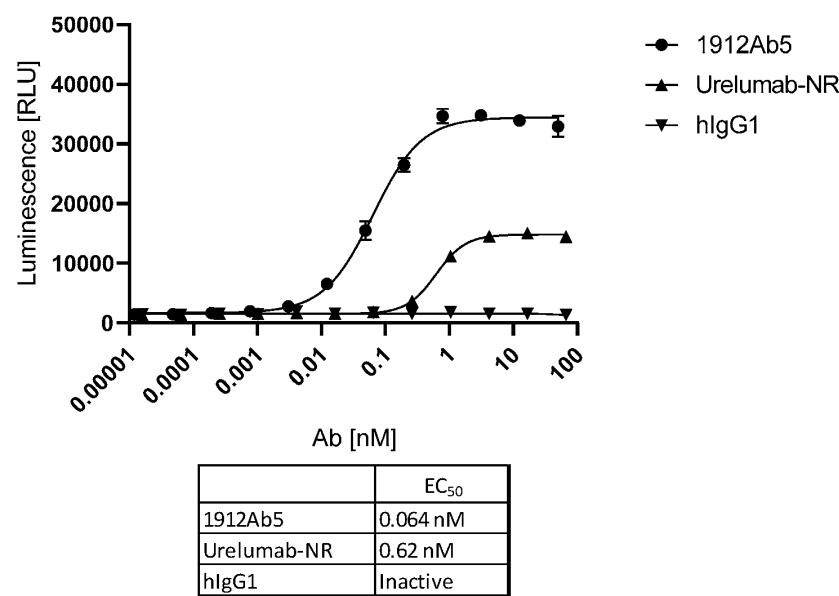


FIG. 9A

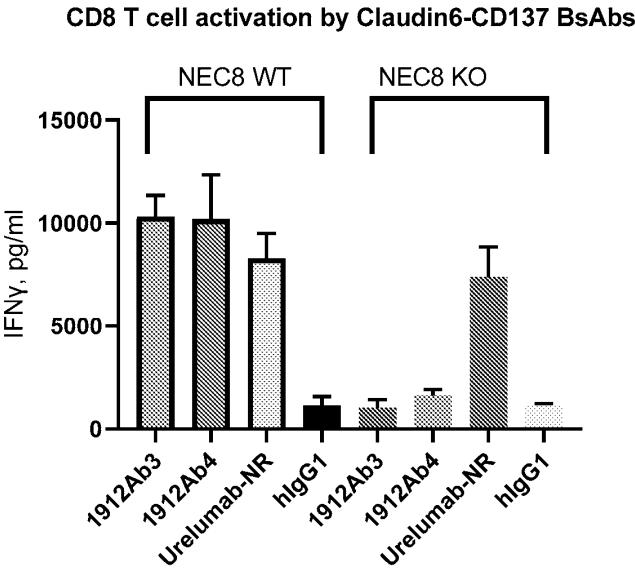


FIG. 9B

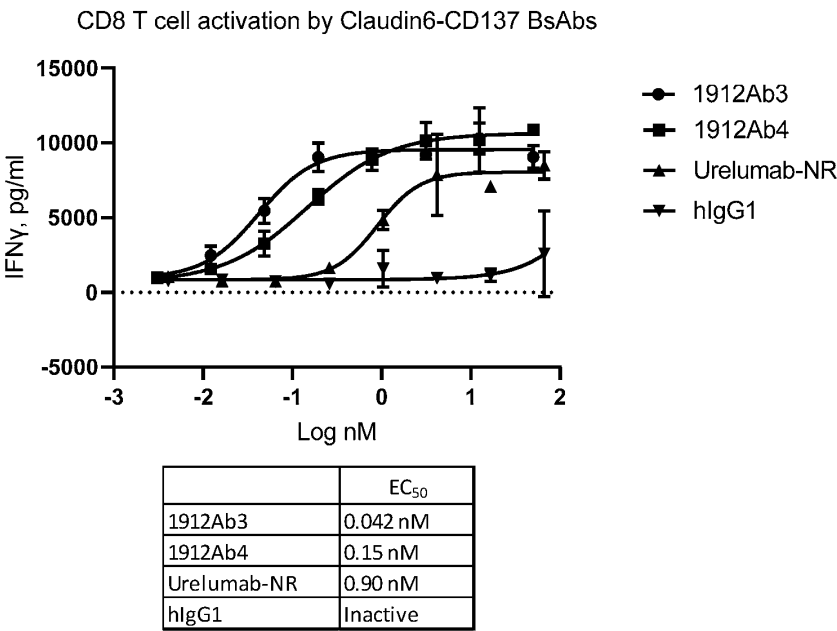


FIG. 9C

CD8 T cell activation by Claudin6-CD137 BsAb using NEC8 cells

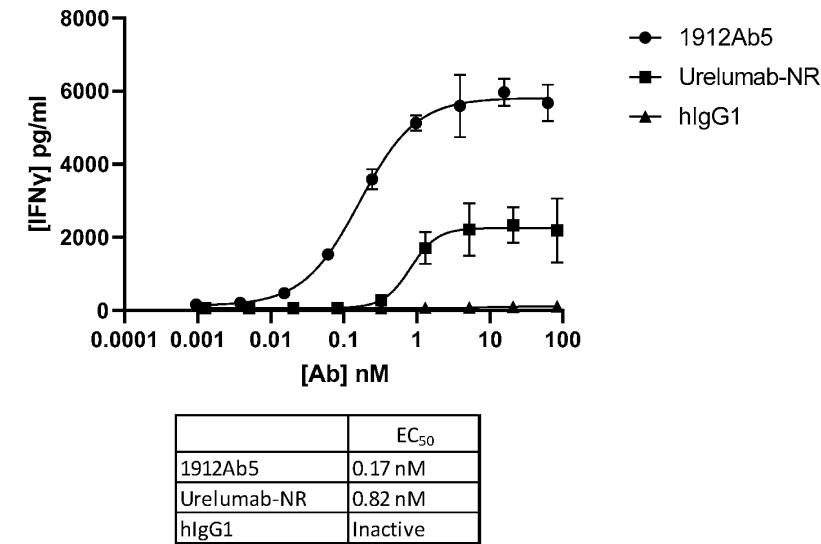


FIG. 9D

CD8 T cell activation by Claudin6-CD137 BsAb using NEC8 KO cells

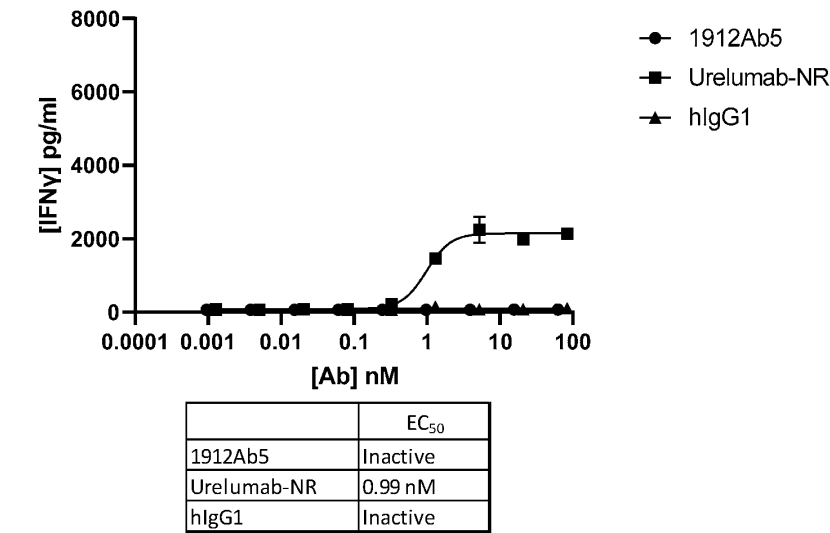


FIG. 10A

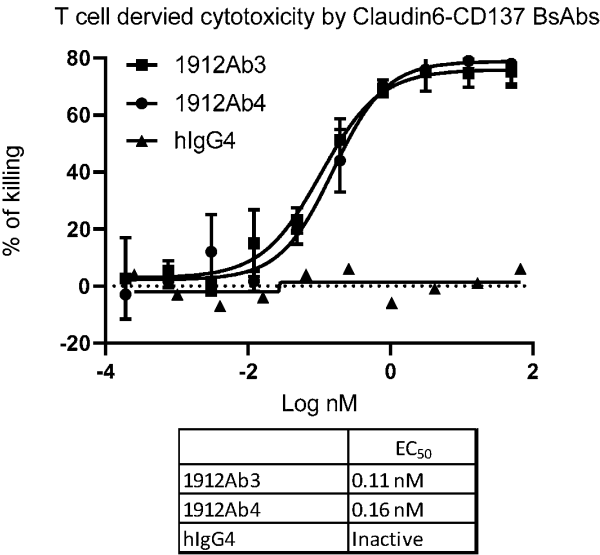


FIG. 10B

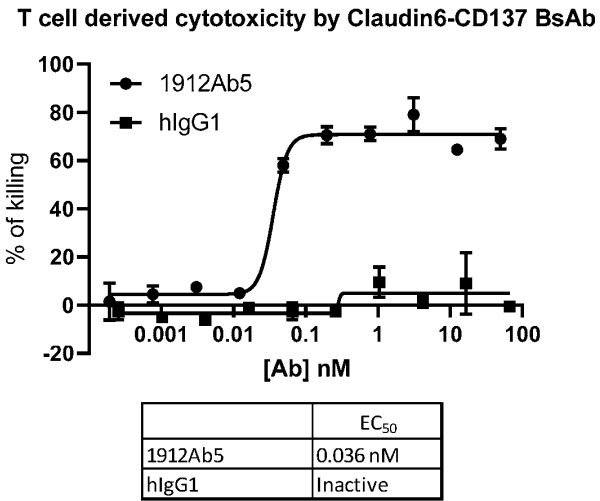


FIG. 11A

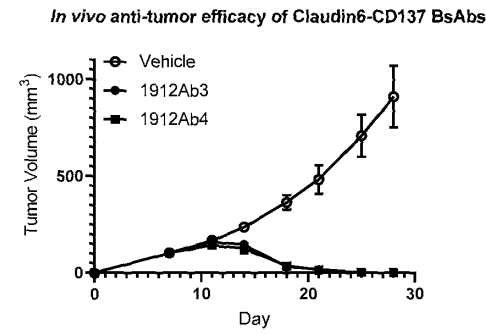


FIG. 11B

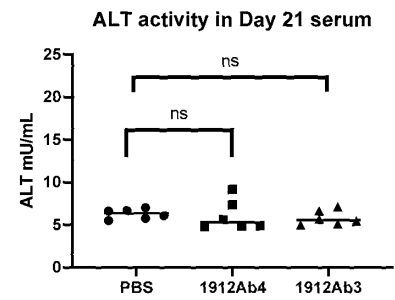


FIG. 11C

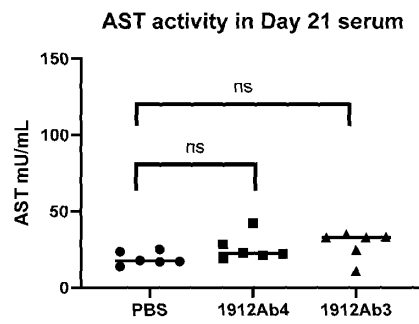


FIG. 11D

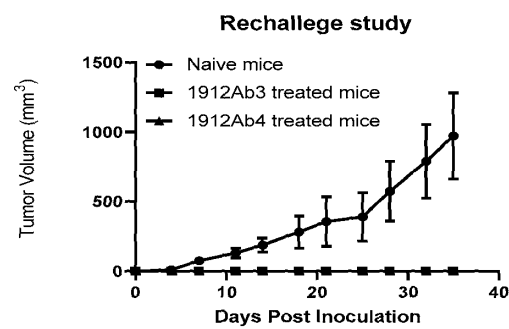


FIG. 12

In vivo anti-tumor efficacy of Claudin6-CD137 BsAb
in MC38 tumor model

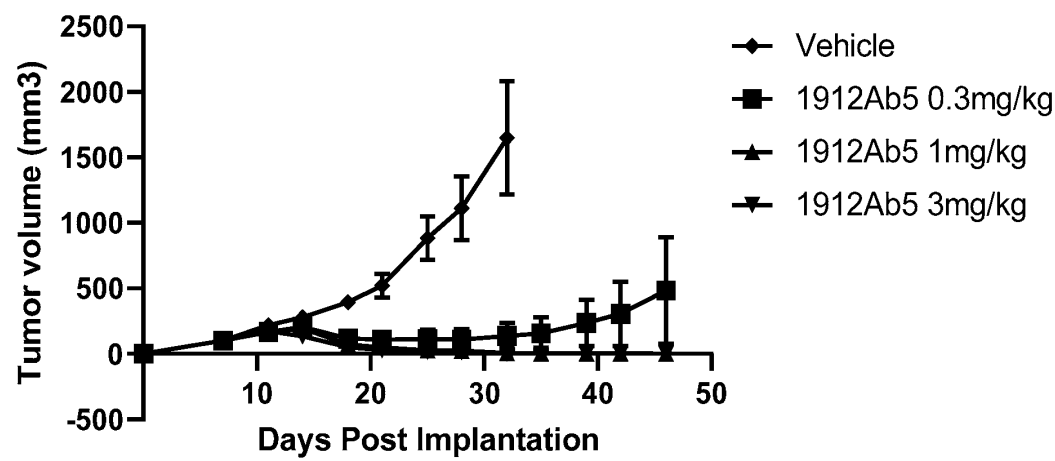


FIG. 13

***In vivo* anti-tumor efficacy of low dose Claudin6-CD137 BsAb and Urelumab in MC38 tumor model**

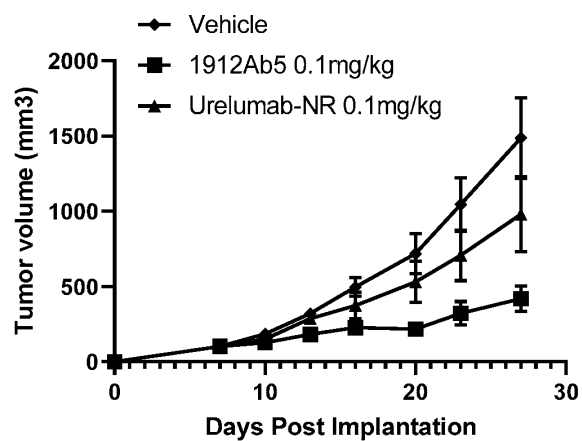


FIG. 14

In vivo anti-tumor efficacy of Claudin6-CD137 BsAb
in the established large tumor

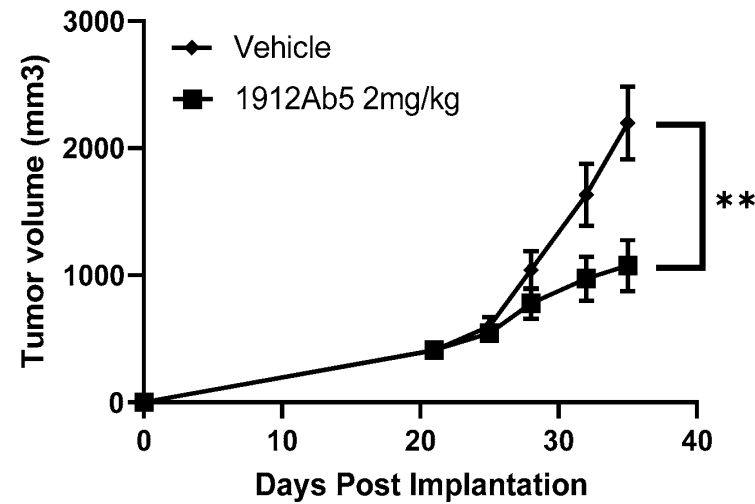


FIG. 15A

Vehicle treated tumor

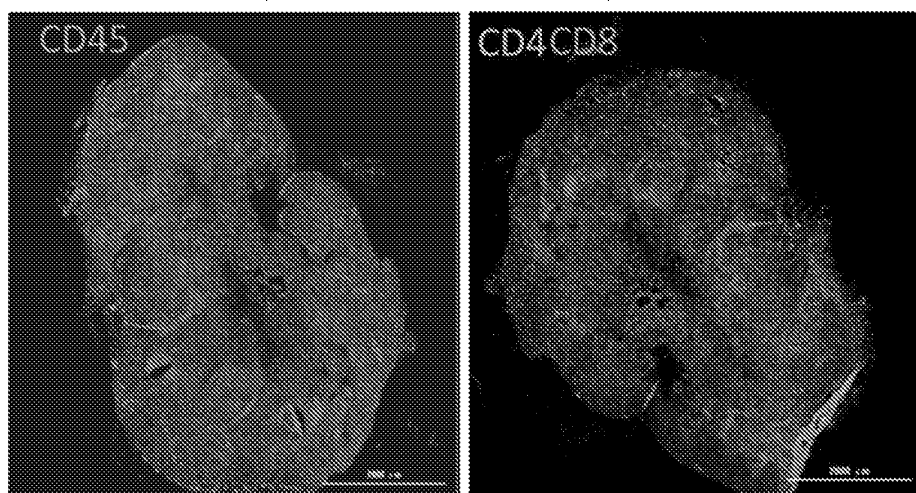


FIG. 15B

1921Ab5 treated tumor

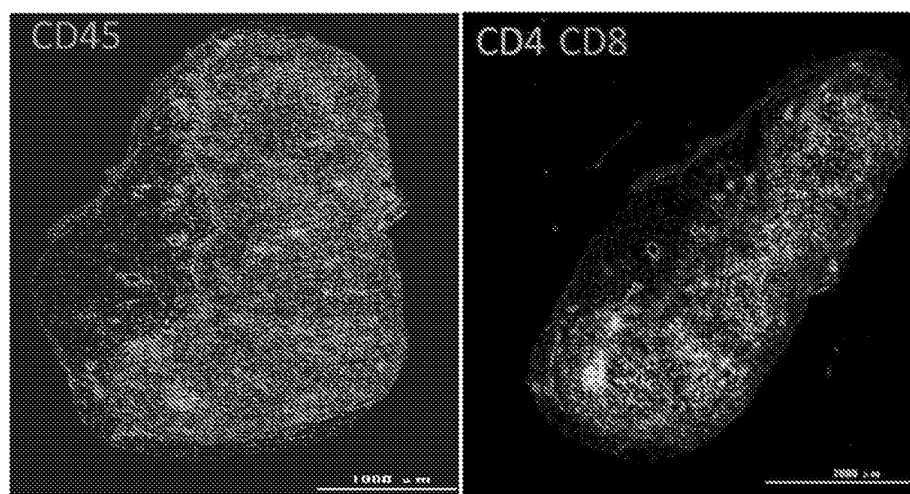


FIG. 16A

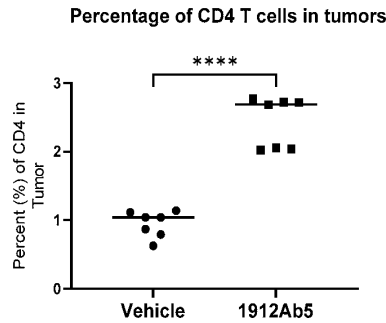


FIG. 16B

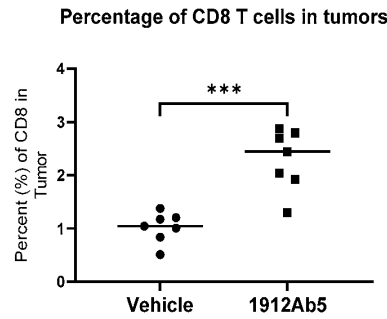


FIG. 16C

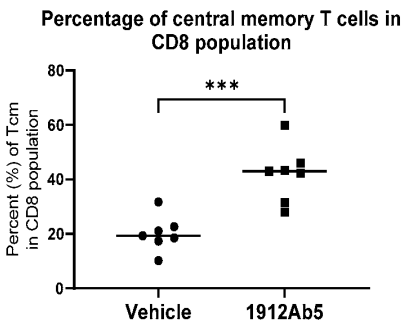


FIG. 16D

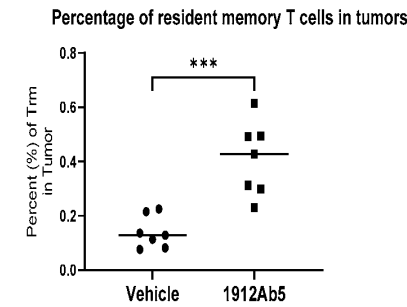


FIG. 16E

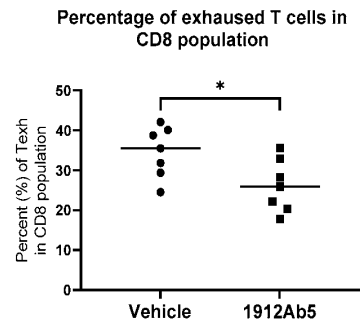


FIG. 16F

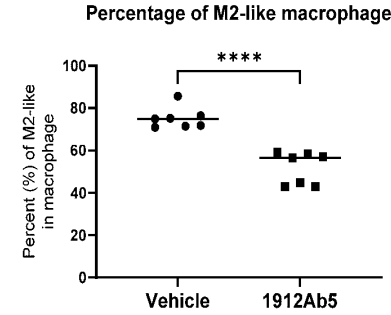


FIG. 17

In vivo anti-tumor efficacy of Claudin6-CD137 BsAb
in B16-F10 tumor model

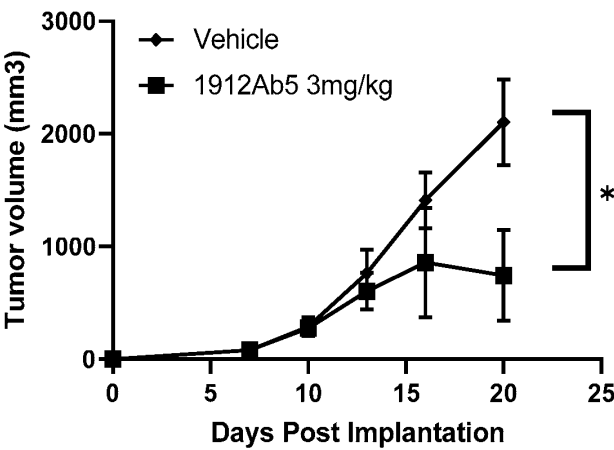


FIG. 18

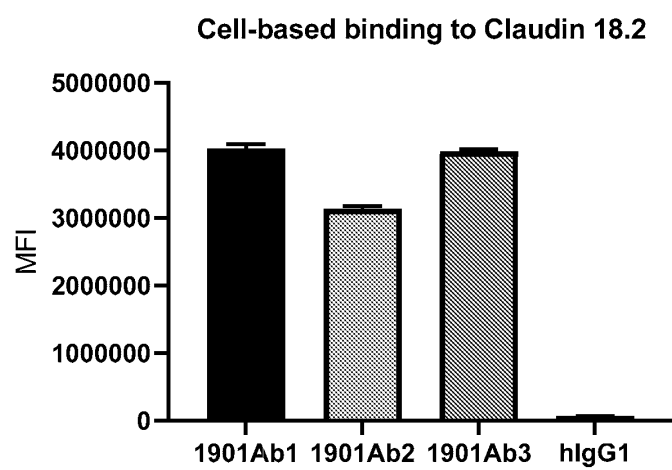


FIG. 19

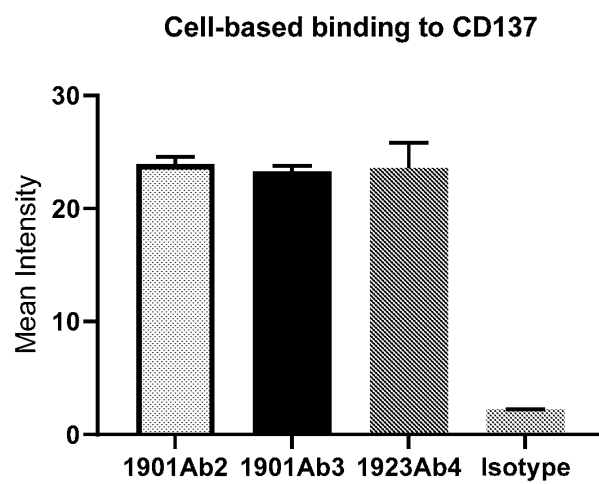


FIG. 20A

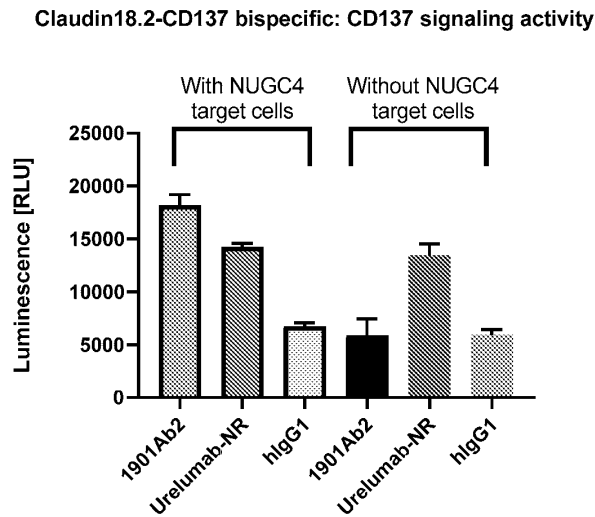


FIG. 20B

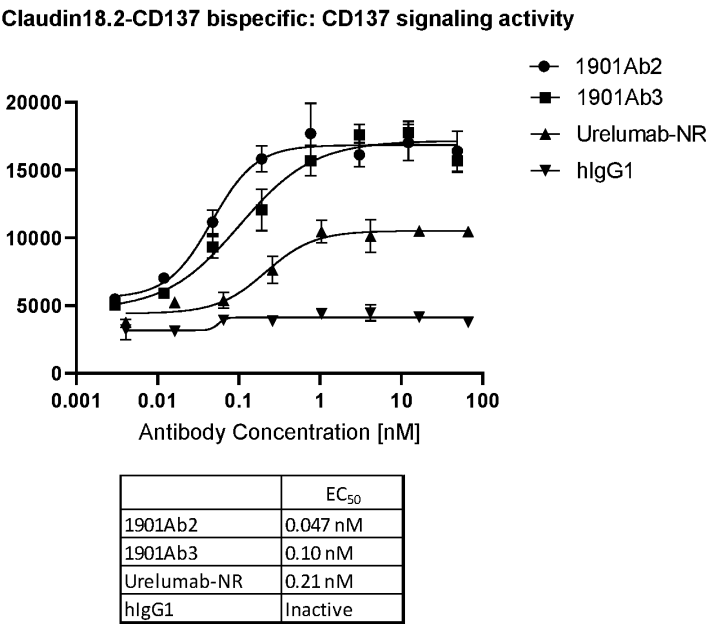
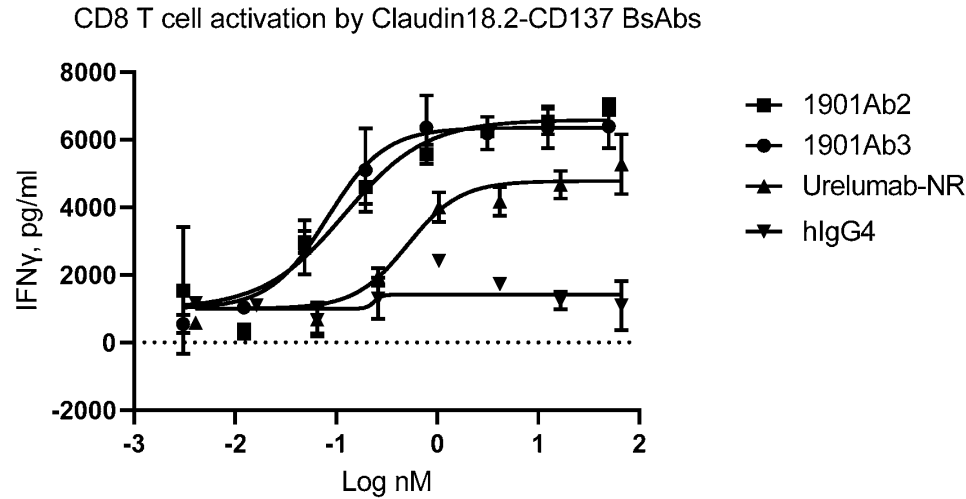


FIG. 21



	EC ₅₀
1901Ab2	0.12 nM
1901Ab3	0.08 nM
Urelumab-NR	0.51 nM
hIgG4	Inactive

FIG. 22

T cell derived cytotoxicity by Claudin18.2-CD137 BsAbs

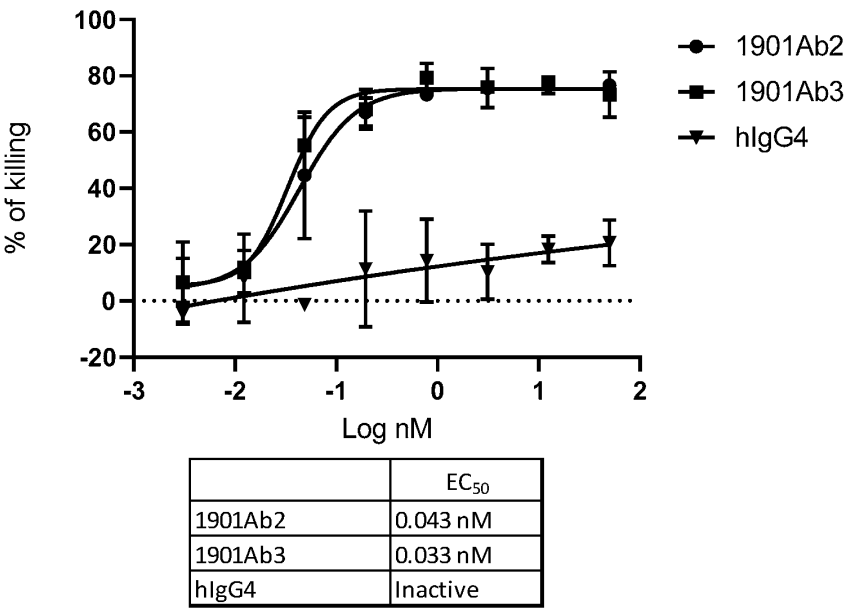


FIG. 23

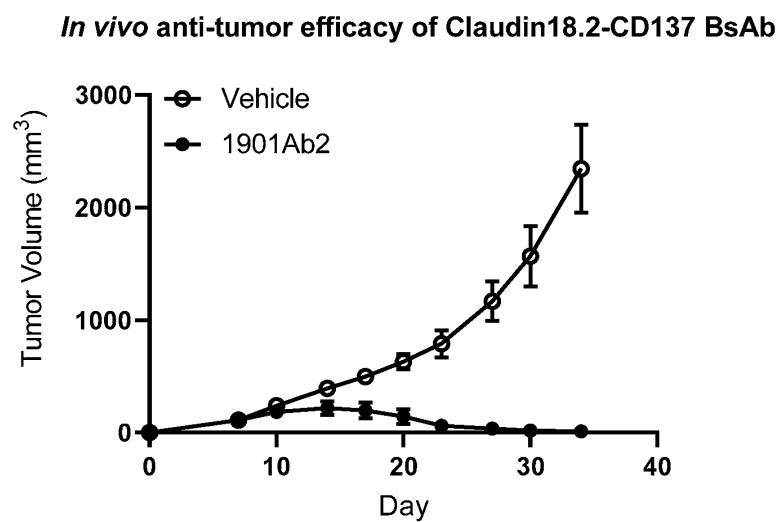


FIG. 24

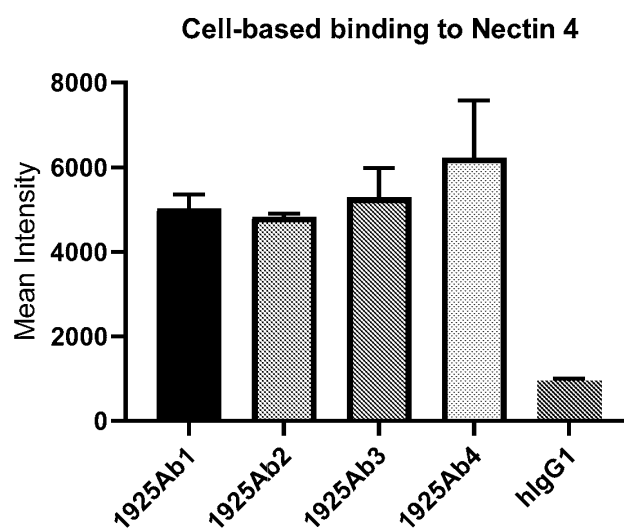


FIG. 25

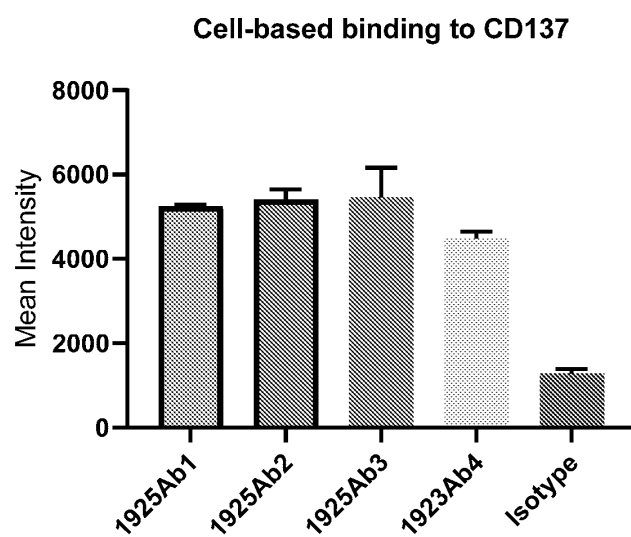


FIG. 26A

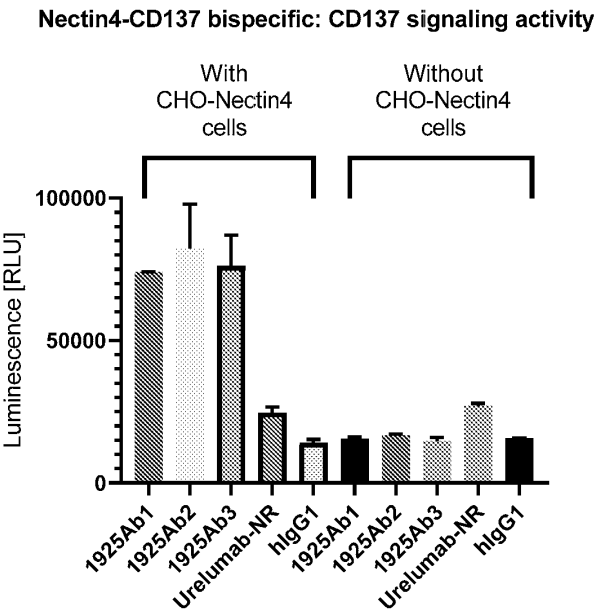


FIG. 26B

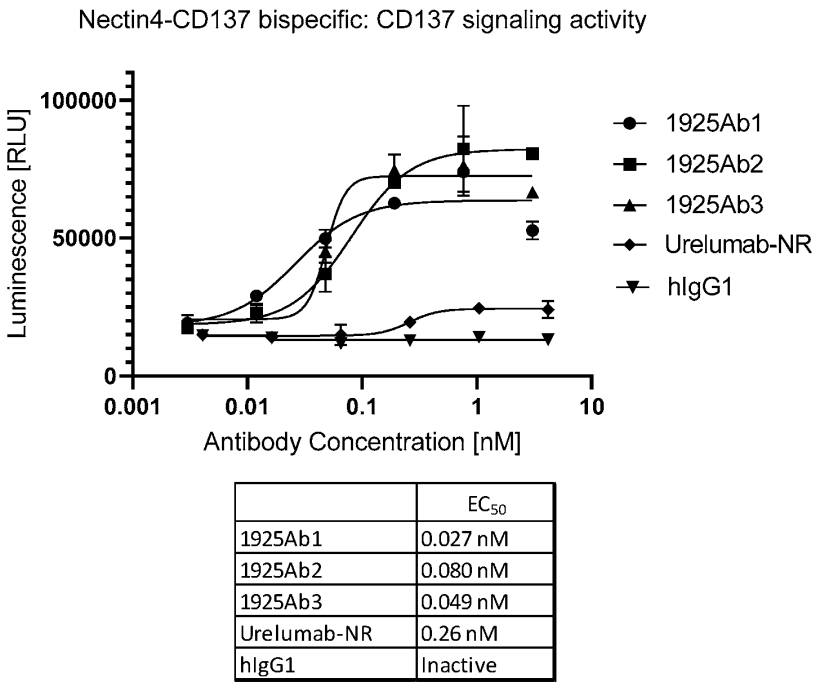


FIG. 27A

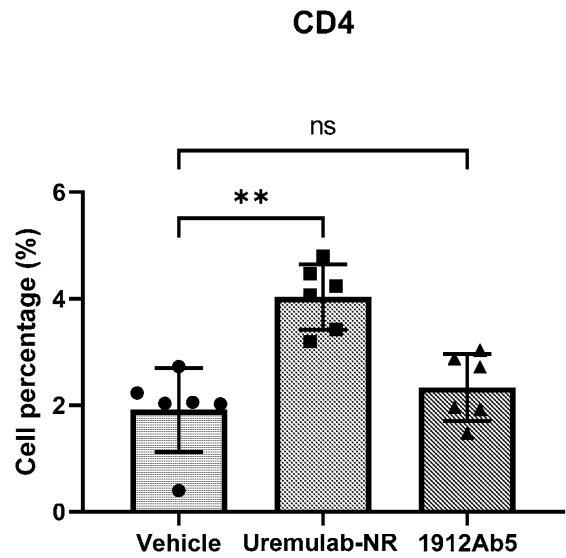


FIG. 27B

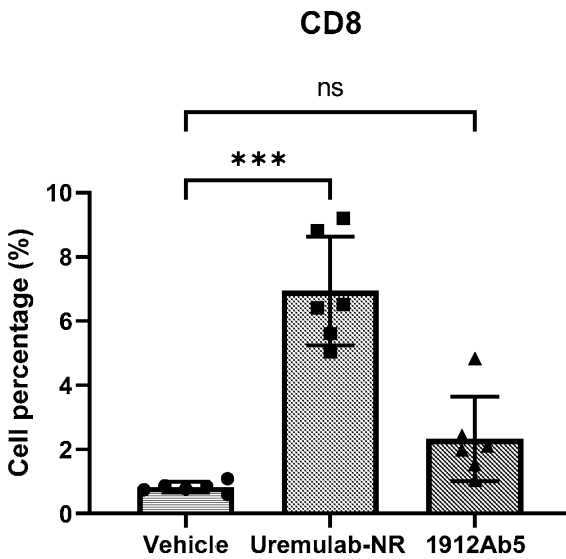


FIG. 27C

F4/80

