

Figure 1A

Human IL-12 subunit alpha (IL-12p35) precursor sequence (SEQ ID NO:1)

>sp | P29459

MCPARSLLLVATLVLLDHLNLARNLPVATPDPGMFCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKD
KTSTVEACLPLELTKNESCLNSRETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIF
LDQNMLAVIDELMQALNFNSETVPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

Human IL-12 subunit alpha (IL-12p35) mature form sequence (SEQ ID NO:2)

>sp | P29459 | 23-219

RNLPVATPDPGMFCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

Human IL-12 subunit beta (IL-12p40) precursor sequence (SEQ ID NO:3)

>sp | P29460

MCHQQLVISWFLSLVFLASPLVAIWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTI
QVKEFGDAGQYTCHKGGEVLSHSLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTF
SVKSSRGSSDPQGVTCGAATLSAERVGRDNKEYEYSVEQEDSACPAAEESLPIEMVDAVHKLKYENYTSSFFIRD
I IKPDPKPNLQKPLKNSRQVEVSWEYPTWTSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISV
RAQDRYSSSWSEWASVPCS

Human IL-12 subunit beta (IL-12p40) mature form sequence (SEQ ID NO:4)

>sp | P29460 | 23-328

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEMVDAVHKLKYENYTSSFFIRD I IKPDPKPNLQKPLKNSRQVE
VSWEYPTWTSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

Human IL-12 receptor subunit beta-1 (IL-12RB1) sequence (SEQ ID NO:5)

>sp | P42701

MEPLVTWVPLFLFLSLRQGAACRTSECCFQDPPYPADSGSASGPRDLRCYRISSDRYECWQYEGPTAGVSHFL
RCCLSSGRCCYFAAGSATRLQFSDQAGVSVLYTTLWVESWARNQTEKSPEVTLQLYNSVKYEPPLGDIKVSKLAGQ
LRMEWETPDNQVGAEVQFRHRTSPSPWKLGDGCPQDDDTESCLCPLMNVAQEFQLRRRQLGSQGSWSKWSPPVCV
PPENPPQPQVRFSVEQLGQDGRRLTLKEQPTQLELPEGCQGLAPGTEVTYRLQLHMLSCPCAKATRTLHLGKMPY
LSGAAYNVAVISSNQFGPGLNQTWHIPADTHTEPVALNISVGTNGTMYWPARAQSMTYCIEWQPVGQDGGGLATCSL
TAPQDPPDAGMATYSWSRESGAMGQEKYYITIFASAHPEKLTWSTVLSTYHFGGNASAAGTPHHVSVKNHSLDSV
SVDWAPSLSTCPGVLKEYVVRCDDESKQVSEHPVQPTETQVTLGLRAGVAYTVQVRADTAWLRGVWSQPQRFISI
EVQVSDWLIFASLGSLFSLILLVGVGLGLNRAARHLCPLPTPCASSAIEFPGGKETWQWINPVDFQEEASLQEA
LVVEMSWDKGERTEPLEKTELPEGAPELALDTELSLEDGDRCKAKM

Human IL-12 receptor subunit beta-1 (IL-12RB1), extracellular domain (SEQ ID NO:6)

>sp | P42701 | 24-545

CRTSECCFQDPPYPADSGSASGPRDLRCYRISSDRYECWQYEGPTAGVSHFLRCCLSSGRCCYFAAGSATRLQFS
DQAGVSVLYTTLWVESWARNQTEKSPEVTLQLYNSVKYEPPLGDIKVSKLAGQLRMEWETPDNQVGAEVQFRHRT
SSPWKLGDGCPQDDDTESCLCPLMNVAQEFQLRRRQLGSQGSWSKWSPPVCVPPENPPQPQVRFSVEQLGQDGR
RLTLKEQPTQLELPEGCQGLAPGTEVTYRLQLHMLSCPCAKATRTLHLGKMPYLSGAAYNVAVISSNQFGPGLNQT
WHIPADTHTEPVALNISVGTNGTMYWPARAQSMTYCIEWQPVGQDGGGLATCSLTAPQDPPDAGMATYSWSRESGAM
GQEKYYITIFASAHPEKLTWSTVLSTYHFGGNASAAGTPHHVSVKNHSLDSVSDWAPSLSTCPGVLKEYVVRCD
DESKQVSEHPVQPTETQVTLGLRAGVAYTVQVRADTAWLRGVWSQPQRFISIEVQVSD

Figure 1B

Human IL-12 receptor subunit beta-2 (IL-12R β 2) sequence (SEQ ID NO:7)

>sp|Q99665

MAHTFRGCSLAFMFIITWLLIKAKIDACKRGDVTVKPSHVILLGSTVNITCSLKPRQGC FHYSRRNKLILYKFDRRI
NFHHGHSLSNSQVTGLPLGTTLFVCKLACINSDEIQICGAEIFVGVAPEQPQNLS CIQKEQGT VACTW ERGRDTHLY
TEYTLQLSGPKNLTWQKQCKDIYCDYLD FGINLTPESPESNFTAKVTAVNSLGSSSSLPSTFTFLDIVRPLPPWDIR
IKFQKASVSRCTLYWRDEGLVLLNRLRYRPSNSRLWNMVNVT KAKGRHDLLDLKPFTEYEFQISSKLHLYKGSWSDW
SESLRAQTPEEEPTGMLDVWYMKRHIDYSRQQISLFWKNLSVSEARGKILHYQVTLQELTG GKAMTQNITGHTSWTT
VIPRTGNWAVAVSAANSKGSSLPTRINIMNLCEAGLLAPRQVSANSEGMDNILVTWQPPRKDPSAVQ EYVVEWRELH
PGGDTQVPLNWLRSRPYNVSALISENIKSYICYEIRVYALSGDQGGCSSILGNSKHKAPLSGPHINAITEEKGSILI
SWNSIPVQEQMGCLLHYRIYWKERDSNSQPQLCEIPYRVSQNSHPINSLQPRVTYVLWMTALTAAGESSHGNEREF C
LQGGANWMAFVAPSICIAIIMVGIFSTHYFQKQVFVLLAALRPQWCSREIPDPANSTCAKKYPIAE EKTQLPLDRLL
IDWPTPEDPEPLVISEVLHQVTPVFRHPPCSNWPQREKGIQGHQASEKDMMHSASSPPPPRALQAESRQLVDLYKVL
ESRGSDPKPENPACPWTVLPAGDLPTHGYLPSNIDDLPSHEAPLADSL EELEPQHISLSVFPSSSLHPLTFSCGDK
LTLDQLKMRCDSLML

Human IL-12 receptor subunit beta-2 (IL-12R β 2), extracellular domain (SEQ ID NO:8)

>sp|Q99665|24-622

KIDACKRGDVTVKPSHVILLGSTVNITCSLKPRQGC FHYSRRNKLILYKFDRRINFHHGHSLSNSQVTGLPLGTTLFV
CKLACINSDEIQICGAEIFVGVAPEQPQNLS CIQKEQGT VACTW ERGRDTHLYTEYTLQLSGPKNLTWQKQCKDIY
CDYLD FGINLTPESPESNFTAKVTAVNSLGSSSSLPSTFTFLDIVRPLPPWDIRIKFQKASVSRCTLYWRDEGLVLL
NRLRYRPSNSRLWNMVNVT KAKGRHDLLDLKPFTEYEFQISSKLHLYKGSWSDWSESLRAQTPEEEPTGMLDVWYMK
RHIDYSRQQISLFWKNLSVSEARGKILHYQVTLQELTG GKAMTQNITGHTSWTTVIPRTGNWAVAVSAANSKGSSLP
TRINIMNLCEAGLLAPRQVSANSEGMDNILVTWQPPRKDPSAVQ EYVVEWRELHPGGDTQVPLNWLRSRPYNVSALI
SENIKSYICYEIRVYALSGDQGGCSSILGNSKHKAPLSGPHINAITEEKGSILISWNSIPVQEQMGCLLHYRIYWK E
RDSNSQPQLCEIPYRVSQNSHPINSLQPRVTYVLWMTALTAAGESSHGNEREFCLQGGAN

Figure 2A

Monomer 1	Monomer 2
F405A	T394F
S364D	Y349K
S364E	L368K
S364E	Y349K
S364F	K370G
S364H	Y349K
S364H	Y349T
S364Y	K370G
T411K	K370E
V397S/F405A	T394F
K370R/T411K	K370E/T411E
L351E/S364D	Y349K/L351K
L351E/S364E	Y349K/L351K
L351E/T366D	L351K/T366K
P395T/V397S/F405A	T394F
S364D/K370G	S364Y/K370R
S364D/T394F	Y349K/F405A
S364E/F405A	Y349K/T394F
S364E/F405S	Y349K/T394Y
S364E/T411E	Y349K/D401K
S364H/D401K	Y349T/T411E
S364H/F405A	Y349T/T394F
S364H/T394F	Y349T/F405A
Y349C/S364E	Y349K/S354C
L351E/S364D/F405A	Y349K/L351K/T394F
L351K/S364H/D401K	Y349T/L351E/T411E
S364E/T411E/F405A	Y349K/T394F/D401K
S364H/D401K/F405A	Y349T/T394F/T411E
S364H/F405A/T411E	Y349T/T394F/D401K

Figure 2B

Monomer 1	Monomer 2
K370E/T411D	T411K
L368E/K409E	L368K
Y349T/T394F/S354C	S364H/F405A/Y349C
T411E	D401K
T411E	D401R/T411R
Q347E/K360E	Q347R
L368E	S364K
L368E/K370S	S364K
L368E/K370T	S364K
L368E/D401R	S364K
L368E/D401N	S364K
L368E	E357S/S364K
L368E	S364K/K409E
L368E	S364K/K409V
L368D	S364K
L368D/K370S	S364K
L368D/K370S	S364K/E357L
L368D/K370S	S364K/E357Q
T411E/K360E/Q362E	D401K
K370S	S364K
L368E/K370S	S364K/E357Q
K370S	S364K/E357Q
T411E/K360D	D401K
T411E/K360E	D401K
T411E/Q362E	D401K
T411E/N390D	D401K
T411E	D401K/Q347K
T411E	D401K/Q347R
T411E/K360D/Q362E	D401K

Figure 2C

Monomer 1	Monomer 2
T411E/K360E/N390D	D401K
T411E/Q362E/N390D	D401K
T411E/Q347R	D401K/K360D
T411E/Q347R	D401K/K360E
T411E/K360	D401K/Q347K
T411E/K360D	D401K/Q347R
T411E/K360E	D401K/Q347K
T411E/K360E	D401K/Q347R
T411E/S364K	D401K/K370S
T411E/K370S	D401K/S364K
Q347E	E357Q
Q347E	E357Q/Q362K
K360D/Q362E	Q347R
K360D/Q362E	D401K
K360D/Q362E	Q347R/D401K
K360E/Q362E	Q347R
K360E/Q362E	D401K
K360E/Q362E	Q347R/D401K
Q362E/N390D	D401K
Q347E/K360D	D401N
K360D	Q347R/N390K
K360D	N390K/D401N
K360E	Y349H
K370S/Q347E	S364K
K370S/E357L	S364K
K370S/E357Q	S364K
K370S/Q347E/E357L	S364K
K370S/Q347E/E357Q	S364K

Figure 2D

Monomer 1	Monomer 2
L368D/K370S/Q347E	S364K
L368D/K370S/E357L	S364K
L368D/K370S/E357Q	S364K
L368D/K370S/Q347E/E357L	S364K
L368D/K370S/Q347E/E357Q	S364K
L368E/K370S/Q347E	S364K
L368E/K370S/E357L	S364K
L368E/K370S/E357Q	S364K
L368E/K370S/Q347E/E357L	S364K
L368E/K370S/Q347E/E357Q	S364K
L368D/K370T/Q347E	S364K
L368D/K370T/E357L	S364K
L368D/K370T/E357Q	S364K
L368D/K370T/Q347E/E357L	S364K
L368D/K370T/Q347E/E357Q	S364K
L368E/K370T/Q347E	S364K
L368E/K370T/E357L	S364K
L368E/K370T/E357Q	S364K
L368E/K370T/Q347E/E357L	S364K
L368E/K370T/Q347E/E357Q	S364K
T411E/Q362E	D401K/T411K
T411E/N390D	D401K/T411K
T411E/Q362E	D401R/T411R
T411E/N390D	D401R/T411R
Y407T	T366Y
F405A	T394W
T366Y/F405A	T394W/Y407T
Y407A	T366W
T366S/L368A/Y407V	T366W
T366S/L368A/Y407V/Y349C	T366W/S354C

Figure 2E

Monomer 1	Monomer 2
K392D/K409D	E356K/D399K
K370D/K392D/K409D	E356K/E357K/D399K
K247Q/R355Q/N384S/K392N/V397M/Q419E/K447_	P217R/P228R/N276K
K247Q/R355Q/N384S/K392N/V397M/Q419E/K447_	N276K
N384S/K392N/V397M/Q419E	N276K
D221E/P228E/L368E	D221R/P228R/K409R
C220E/P228E/L368E	C220R/E224R/P228R/K409R
F405L	K409R
T366I/K392M/T394W	F405A/Y407V
T366V/K409F	L351Y/Y407A
T366A/K392E/K409F/T411E	D399R/S400R/Y407A
L351K	L351E
K247Q/R355Q/Q419E/K447_	P217R/P228R/N276K
K247Q/R355Q/Q419E/K447_	N276K
K274Q/R355Q/N384S/K392N/V397M/Q419E/K447_	
Q295E/N384D/Q418E/N421D	
Q295E/Q418E/N421D	
P217R/P228R/N276K	
N276K	
E269Q/E272Q/E283Q/E357Q	
E269Q/E272Q/E283Q	
E269Q/E272Q	
E269Q/E283Q	
E272Q/E283Q	
E269Q	

Figure 3

<u>Variant constant region</u>	<u>Substitutions</u>
pl_ISO(-)-Fc only	K274Q/R355Q/N384S/K392N/V397M/Q419E/K447_
pl_(-)_isosteric A-Fc only	Q295E/N384D/Q418E/N421D
pl_(-)_isosteric_B-Fc only	Q295E/Q418E/N421D
pl_ISO(+RR)-Fc only	P217R/P228R/N276K
pl_ISO(+)-Fc only	N276K
pl_(+)_isosteric_A	E269Q/E272Q/E283Q/E357Q
pl_(+)_isosteric_B	E269Q/E272Q/E283Q
pl_(+)_isosteric_E269Q/E272Q	E269Q/E272Q
pl_(+)_isosteric_E269Q/E283Q	E269Q/E283Q
pl_(+)_isosteric_E272Q/E283Q	E272Q/E283Q
pl_(+)_isosteric_E269Q	E269Q

Figure 4

Ablation Variants

G236R
S239G
S239K
S239Q
S239R
V266D
S267K
S267R
H268K
E269R
299R
299K
K322A
A327G
A327L
A327N
A327Q
L328E
P329K
A330L
A330S/P331S
I332K
I332R
V266D/A327Q
V266D/P329K
S267R/A327Q
S267R/P329K
G236R/L328R
E233P/L234V/L235A/G236_/S239K
E233P/L234V/L235A/G236_/S267K
E233P/L234V/L235A/G236_/S239K/A327G
E233P/L234V/L235A/G236_/S267K/A327G
E233P/L234V/L235A/G236_
S239K/S267K
267K/P329K

Figure 5

Monomer 1 (-)	Monomer 2 (+)
C220S	C220S
Heterodimer pl variants L368D/K370S	Heterodimer pl variants S364K/E357Q
Isosteric pl substitutions Q295E/N384D/Q418E/N421D	
FcKO E233P/L234V/L235A/G236_/S267K	FcKO E233P/L234V/L235A/G236_/S267K
±M428L/N434S	±M428L/N434S

Figure 6

Name	Sequence	SEQ ID NO:
(GGGGS) ₁ or GGGGS	GGGGS	9
(GGGGS) ₂	GGGGSGGGGS	10
(GGGGS) ₃	GGGGSGGGGSGGGGS	11
(GGGGS) ₄	GGGGSGGGGSGGGGSGGGGS	12
(GGGGS) ₅	GGGGSGGGGSGGGGSGGGGSGGGGS	13
(GGGGS) ₆	GGGGSGGGGSGGGGSGGGGSGGGGSGGGGS	14
(GGGGS) ₇	GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS	15
(GGGGA) ₁ or GGGGA	GGGGA	XXX
(GGGGA) ₂	GGGAGGGGA	XXX
(GGGGA) ₃	GGGAGGGGAGGGGA	XXX
(GGGGA) ₄	GGGAGGGGAGGGGAGGGGA	XXX
(GGGGA) ₅	GGGAGGGGAGGGGAGGGGAGGGGA	XXX
(GGGGA) ₆	GGGAGGGGAGGGGAGGGGAGGGGAGGGGA	XXX
(GGGGA) ₇	GGGAGGGGAGGGGAGGGGAGGGGAGGGGAGGGGA	XXX
30AA-linker	DPALVHQRPAAPPGGGSGGGSGGGSGGG	16
(GKPGS) ₁ or GKPGS	GKPGS	17
(GKPGS) ₅	GKPGSGKPGSGKPGSGKPGSGKPGS	18
(GKPGS) ₆	GKPGSGKPGSGKPGSGKPGSGKPGSGKPGS	19
(GGGES) ₁ or GGGES	GGGES	20

Figure 7A

Backbone 1**>Backbone 1 monomer 1 (SEQ ID NO:21)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CS VMHEALHNHYTQKSLSLSPGK

>Backbone 1 monomer 2 (SEQ ID NO:22)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFS
CS VMHEALHNHYTQKSLSLSPGK

Backbone 2**>Backbone 2 monomer 1 (SEQ ID NO:23)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CS VMHEALHNHYTQKSLSLSPGK

>Backbone monomer 2 (SEQ ID NO:24)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFS
CS VMHEALHNHYTQKSLSLSPGK

Backbone 3**>Backbone 3 monomer 1 (SEQ ID NO:25)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CS VMHEALHNHYTQKSLSLSPGK

>Backbone 3 monomer 2 (SEQ ID NO:26)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCEVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFS
CS VMHEALHNHYTQKSLSLSPGK

Figure 7B

Backbone 4**>Backbone 4 monomer 1 (SEQ ID NO:27)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSEGSFFLYSKLTVDKSRWQQGNVFS
CS VMHEALHNHYTQKSLSLSPGK

>Backbone 4 monomer 2 (SEQ ID NO:28)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTENEVSLTCLVKGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLEVDKSRWEQGDVFS
CS VMHEALHNHYTQKSLSLSPGK

Backbone 5**>Backbone 5 monomer 1 (SEQ ID NO:29)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRD
QLTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CS VMHEALHNHYTQKSLSLSPGK

>Backbone 5 monomer 2 (SEQ ID NO:30)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRD
ELTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFS
CS VMHEALHNHYTQKSLSLSPGK

Backbone 6**>Backbone 6 monomer 1 (SEQ ID NO:31)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CS VMHEALHNHYTQKSLSLSPGK

>Backbone 6 monomer 2 (SEQ ID NO:32)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFS
CS VMHEALHNHYTQKSLSLSPGK

Figure 7C

Backbone 7**>Backbone 7 monomer 1 (SEQ ID NO:33)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYSSYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS
VMHEALHNHYTQKSLSLSPGK

>Backbone 7 monomer 2 (SEQ ID NO:34)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYSSYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDQGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSS
VMHEALHNHYTQKSLSLSPGK

Backbone 8**>Backbone 8 monomer 1 (SEQ ID NO:35)**

ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAK
TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEQM
TKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFCSSVM
HEALHNHYTQKSLSLGLGK

>Backbone 8 monomer 2 (SEQ ID NO:36)

ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAK
TKPREEEFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEM
TKNQVSLTCDVSGFYPSDIAVEWESDQGPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWEEGDVFSCSVM
HEALHNHYTQKSLSLGLGK

Backbone 9**>Backbone 9 monomer 1 (SEQ ID NO:37)**

ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKT
KPREEQFNSTFRVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREQMT
KNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMH
EALHNHYTQKSLSLSPGK

>Backbone 9 monomer 2 (SEQ ID NO:38)

ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKT
KPREEEFNSTFRVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMT
KNQVSLTCDVSGFYPSDIAVEWESDQGPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMH
EALHNHYTQKSLSLSPGK

Figure 7D

Backbone 10**>Backbone 10 monomer 1 (SEQ ID NO:39)**

ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVQFNWYVDGVEVHNAKT
KPREEQFNSTFRVVSFLTVDLHQLDGLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREQMT
KNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSVMH
EALHNHYTQKSLSLSPGK

>Backbone 10 monomer 2 (SEQ ID NO:40)

ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVQFNWYVDGVEVHNAKT
KPREEEFNSTFRVVSFLTVDLHQLDGLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREMT
KNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWEQGDVFSVMH
EALHNHYTQKSLSLSPGK

Backbone 11**>Backbone 11 monomer 1 (SEQ ID NO:41)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSFLTVDLHQLDGLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFS
VLHEALHSHYTQKSLSLSPGK

>Backbone 11 monomer 2 (SEQ ID NO:42)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSFLTVDLHQLDGLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPVLDSGDSFFLYSKLTVDKSRWEQGDVFS
VLHEALHSHYTQKSLSLSPGK

Backbone 12**>Backbone 12 monomer 1 (SEQ ID NO:43)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSFLTVDLHQLDGLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFS
VMHEALHNHYTQKSLSLSPGK

>Backbone 12 monomer 2 (SEQ ID NO:44)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSFLTVDLHQLDGLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFS
VMHEALHNHYTQKSLSLSPGK

Figure 7E

Backbone 13**>Backbone 13 monomer 1 (SEQ ID NO:45)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDFVSCS
VMHEALHNHYTQKSLSLSPGK

>Backbone 13 monomer 2 (SEQ ID NO:46)

ERKSSDKTHTCPRCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFKWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCS
VMHEALHNHYTQKSLSLSPGK

Figure 8A

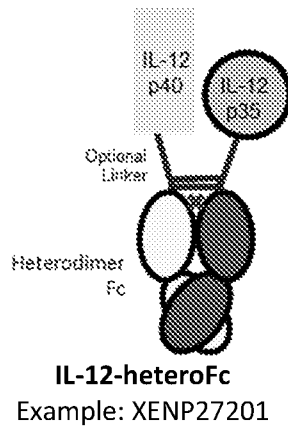


Figure 8B

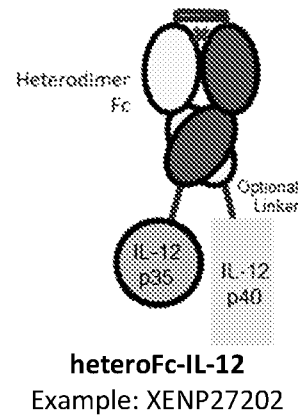


Figure 8C

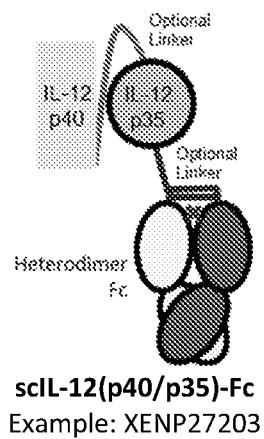


Figure 8D

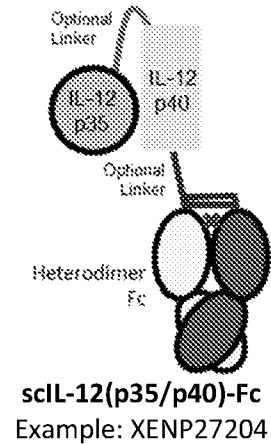


Figure 8E

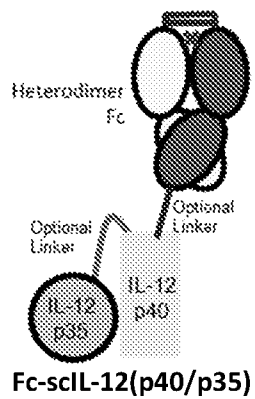


Figure 8F

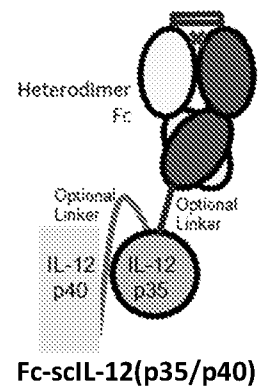


Figure 9

**>XENP27201 human IL12p40 (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

Chain 1 - human_IL12p40_(GGGGS)2_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVSMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:47)**

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLFPVATPDGPMFPCLLHHSQNLLRAVSNNMLQKARQTFEYFCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVSMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:48)**

Figure 10

**>XENP27202 empty-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S (GGGGS)2 human IL12p40-empty-
 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q (GGGGS)2 human IL12p35**

Chain 1 - empty-Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_(GGGGS)2_human_IL12p40

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
 EEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
 GFYPSDIAVEWESDGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVSMHEALHNHYTQKSLSLSPG/
GGGSGGGGS/IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQY
 TCHKGGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDP
 QGVTCGAATLSAERVRGDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQ
 LKPLKNSRQVEVSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSW
 SEWASVPCS **(SEQ ID NO:49)**

Chain 2 - human_IL12p40-empty-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q_(GGGGS)2_human_IL12p35

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
 EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVKLTCLVK
 GFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVSMHEALHNHYTQKSLSLSPG/
GGGSGGGGS/RNLFPVATPDGPMFPCLLHHSQNLLRAVSNNMLQKARQTFEYFCTSEEIDHEDITKDKTSTVEACLPL
 ELTKNESCLNSRETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDE
 LMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS **(SEQ ID NO:50)**

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDITLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVK
GFYPSDIAVEWESNGQPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO:54)

Figure 12A

Purification of
eluate from
Protein A
Chromatography
via Anion
Exchange
Chromatography

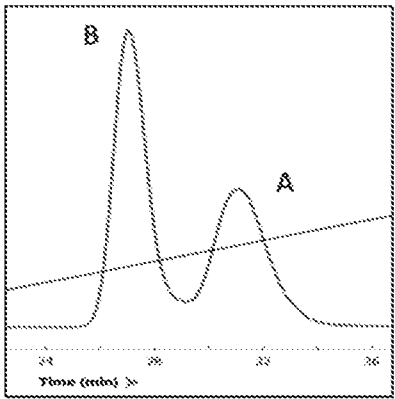


Figure 12B

aSEC-MALS

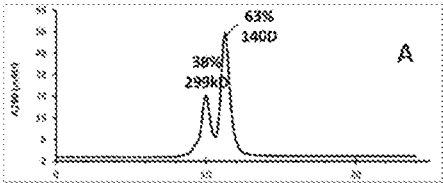
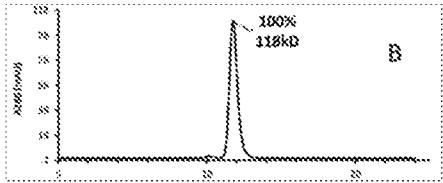


Figure 12C

Analytical
AIEX

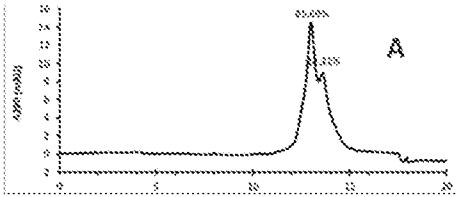
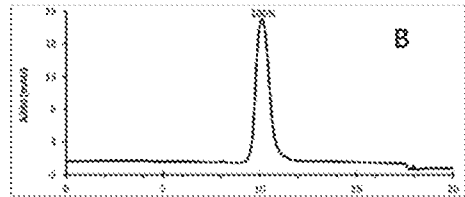


Figure 13A

Purification of
eluate from
Protein A
Chromatography
via Anion
Exchange
Chromatography

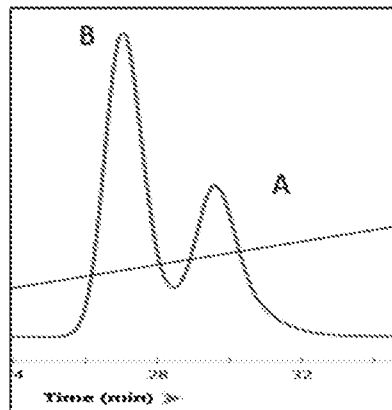


Figure 13B

aSEC-MALS

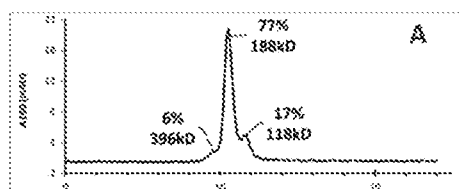
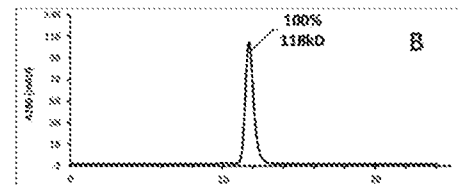


Figure 13C

Analytical
AEX

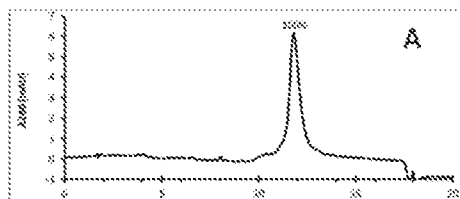
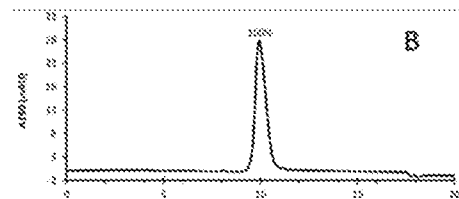


Figure 14A

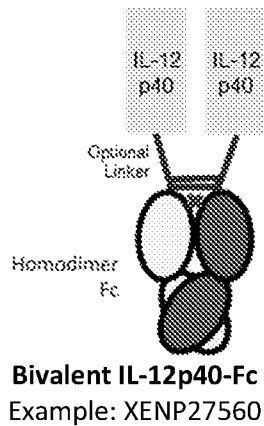


Figure 14B

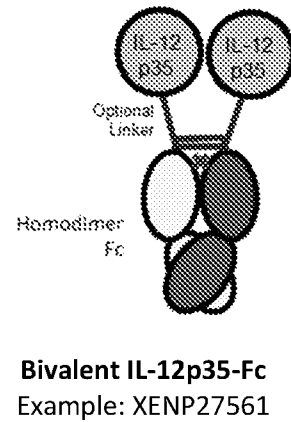


Figure 15

**>XENP27560 human IL12p40 (GGGGS)2-Fc(216) IgG1 pl(-)
Isosteric A C220S/PVA /S267K/L368D/K370S homodimer**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFGFSPDIAVEWESDGPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWEQGDVFSFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:55)**

>XENP27561 human IL12p35 (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q homodimer

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSGDSFFLYSKLTVDKSRWQQGNVFSFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:56)**

Figure 16A

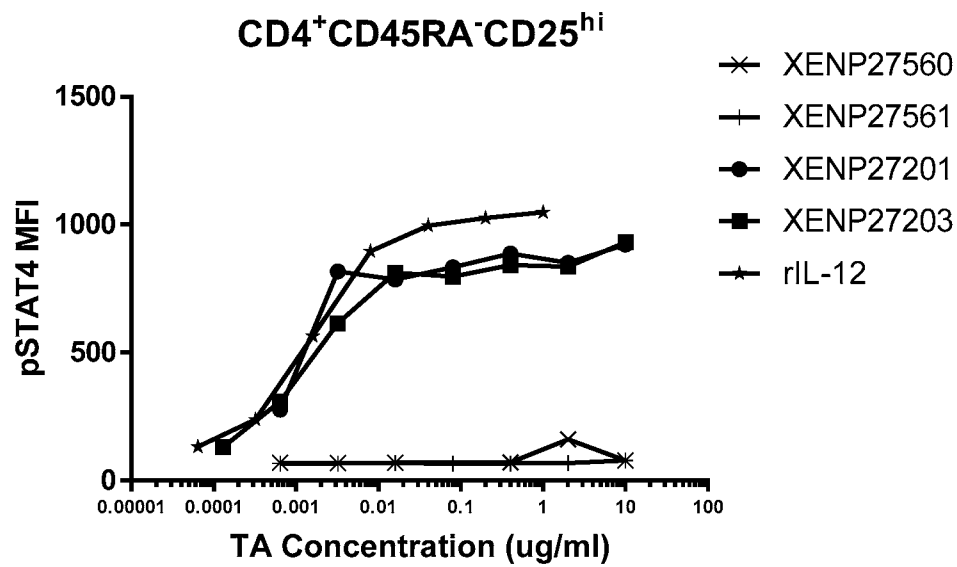


Figure 16B

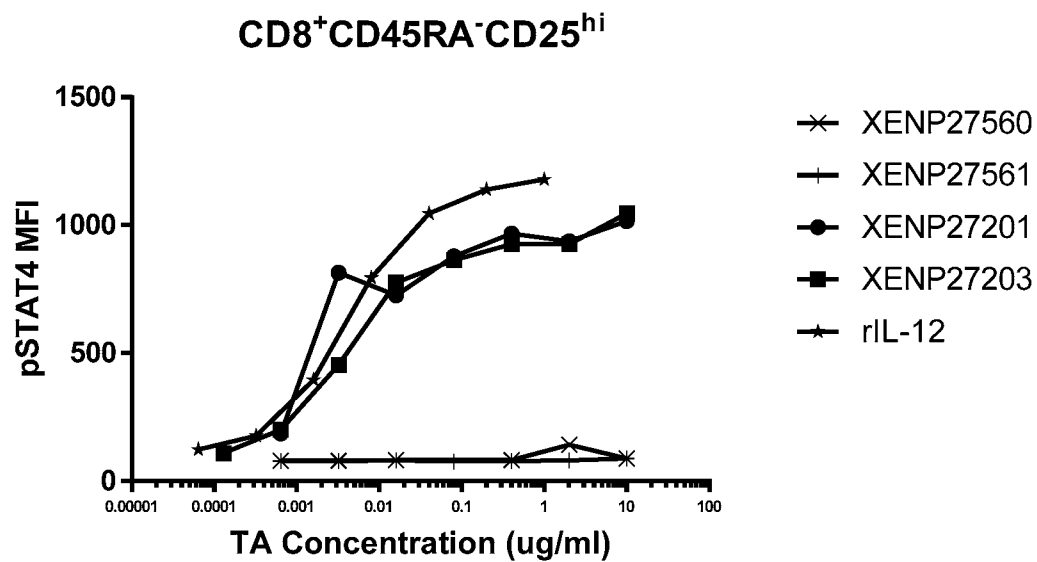


Figure 16C

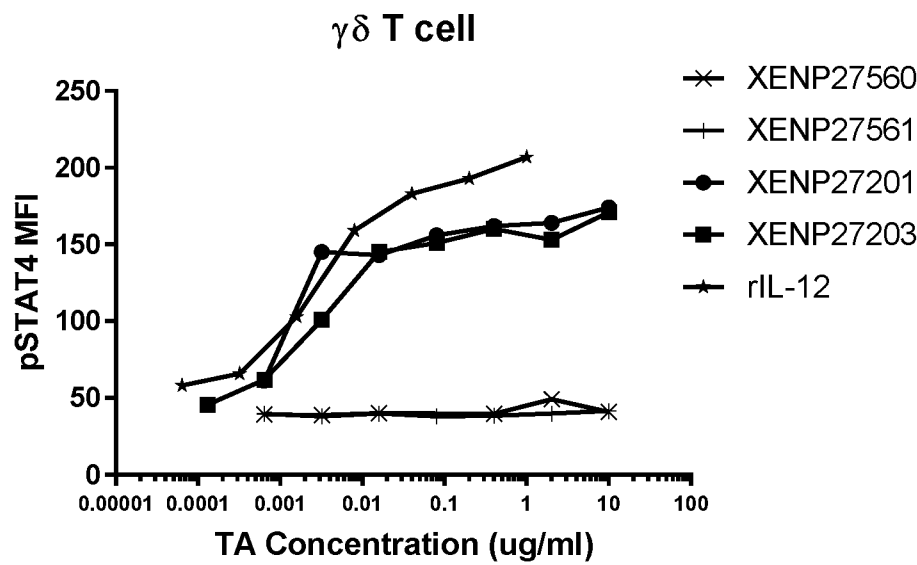


Figure 16D

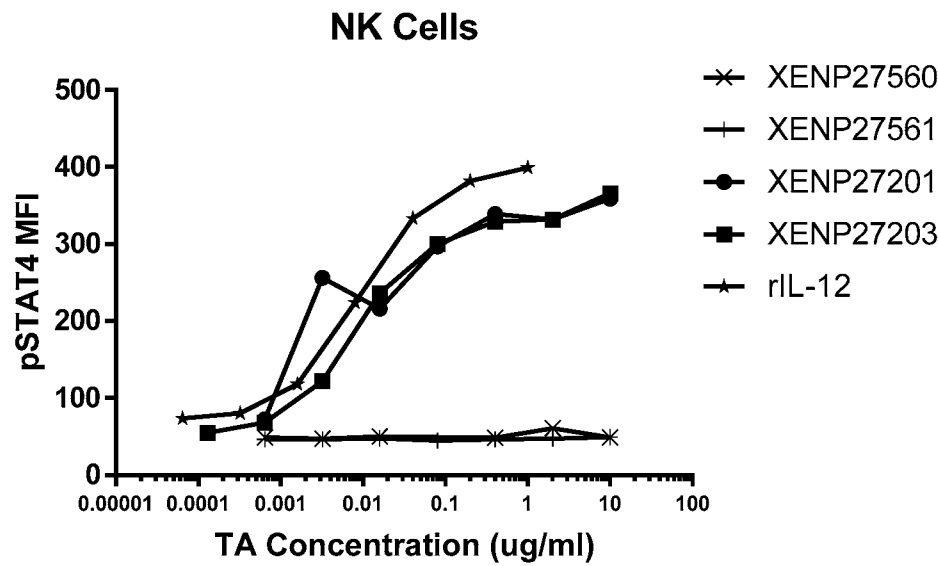


Figure 17

<u>RESIDUE</u>
W15
P17
D18
A19
P20
G21
M23
L40
D41
Q42
S43
E45
L47
T54
I55
Q56
K58
E59
F60
G61
D62
Y66
K84

Figure 18

<u>Residue</u>	<u>ASA</u>	<u>Residue</u>	<u>ASA</u>
E3	85	Q144	150
D7	22	E156	90
E12	72	D161	161
D14	26	N162	62
D18	140	E166	20
E22	50	E170	81
D29	89	Q172	72
E32	80	D174	93
E33	113	E187	63
D41	54	N200	57
Q42	188	D209	73
E45	143	D214	46
Q56	105	N218	67
E59	86	Q220	99
D62	32	N226	134
Q65	75	Q229	114
E73	155	E231	34
E86	88	E235	105
D93	87	Q256	104
D97	22	E262	147
E100	148	D265	60
N103	86	D270	58
E110	41	N281	71
D129	71	Q289	19
D142	69	E299	106

Figure 19

RESIDUE	CONTACT TYPE
D87	DIH
G88	D
I89	D
W90	D
K104	DA
F106	D

Figure 20A

> IL-12p40(N103D) (SEQ ID NO:57)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(N113D) (SEQ ID NO:58)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKDYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(N200D) (SEQ ID NO:59)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYEDTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(N281D) (SEQ ID NO:60)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKDASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(N103D/N113D/N200D/N281D) (SEQ ID NO:61)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYEDTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKDASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(Q42E) (SEQ ID NO:62)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDESSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(E45Q) (SEQ ID NO:63)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

Figure 20B

> IL-12p40(Q56E) (SEQ ID NO:64)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIEVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(E59Q) (SEQ ID NO:65)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(D62N) (SEQ ID NO:66)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(Q42E/E45Q) (SEQ ID NO:67)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDESSQVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(E45Q/Q56E) (SEQ ID NO:68)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIEVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(Q42E/E59Q) (SEQ ID NO:69)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDESSQVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(Q56E/E59Q) (SEQ ID NO:70)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIEVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

Figure 20C

> IL-12p40(Q42E/E45Q/Q56E) (SEQ ID NO:71)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDESSQVLGSGKTLTIEVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(E45Q/Q56E/E59Q) (SEQ ID NO:72)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIEVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(D161N) (SEQ ID NO:73)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGNNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(E73Q) (SEQ ID NO:74)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGQVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(Q144E) (SEQ ID NO:75)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPEGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(E262Q) (SEQ ID NO:76)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKRQKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(E100Q) (SEQ ID NO:77)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

Figure 20D

> IL-12p40(D18N) (SEQ ID NO:78)

IWELKKDVYVVELDWYPNAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(E33Q) (SEQ ID NO:79)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEQDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(Q229E) (SEQ ID NO:80)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSREVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(E235Q) (SEQ ID NO:81)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWQYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(Q256N) (SEQ ID NO:82)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVNGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

> IL-12p40(E299Q) (SEQ ID NO:83)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWQWASVPCS

> IL-12p40(D87N) (SEQ ID NO:84)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKENGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

Figure 20E

> IL-12p40(N103D/N113D) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103D/N200D) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEDTSSFFIRDIIPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103D/N281D) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEDTSSFFIRDIIPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N113D/N200D) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTLRCEAKDYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEDTSSFFIRDIIPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N113D/N281D) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTLRCEAKDYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N200D/N281D) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEDTSSFFIRDIIPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKASISVRAQDRYSSSWSEWASVPCS

Figure 20F

> IL-12p40(N103D/N113D/N200D) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEDYTSSFFIRDIIPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103D/N113D/N281D) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRDASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103D/N200D/N281D) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEDYTSSFFIRDIIPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRDASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N113D/N200D/N281D) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKDYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEDYTSSFFIRDIIPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRDASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103Q) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N113Q) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

Figure 20G

> IL-12p40(N200Q) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N281Q) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRQASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103Q/N113Q) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103Q/N200Q) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103Q/N281Q) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRQASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N113Q/N200Q) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

Figure 20H

> IL-12p40(N113Q/N281Q) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKQYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDKPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N200Q/N281Q) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYQYTSSFFIRDIIPDKPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103Q/N113Q/N200Q) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKQYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYQYTSSFFIRDIIPDKPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103Q/N113Q/N281Q) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKQYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDKPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103Q/N200Q/N281Q) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKNYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYQYTSSFFIRDIIPDKPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N113Q/N200Q/N281Q) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKQYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYQYTSSFFIRDIIPDKPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS

Figure 20I

> IL-12p40(N103Q/N113Q/N200Q/N281Q) (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYYSSSWSEWASVPCS

Figure 21A

**>XenD24752 human IL12p40 N103D (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGS\GGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSGSSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:85)

**>XenD24753 human IL12p40 N113D (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKDYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGS\GGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSGSSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:86)

**>XenD24754 human IL12p40 N200D (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEDYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGS\GGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSGSSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:87)

Figure 21B

>XenD24755 human IL12p40 N281D (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
DASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSGSSFFLYSKLTVDKSRWEQGDVFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:88)

>XenD24756 human IL12p40 N103D/N113D/N200D/N281D (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEDYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
DASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSGSSFFLYSKLTVDKSRWEQGDVFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:89)

>XenD24757 human IL12p40 Q42E (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSESEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSGSSFFLYSKLTVDKSRWEQGDVFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:90)

Figure 21C

**>XenD24758 human IL12p40 E45Q (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGS\GGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:91)

**>XenD24759 human IL12p40 Q56E (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIEVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGS\GGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:92)

**>XenD24760 human IL12p40 E59Q (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGS\GGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:93)

Figure 21D

>XenD24761 human IL12p40 D62N (GGGGS)2-Fc(216) IgG1 pl(-)

) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIQVKEFGNAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDQPE
NNYKTTTPVLDSGSEFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:94)

>XenD24762 human IL12p40 Q42E/E45Q (GGGGS)2-Fc(216) IgG1 pl(-)

) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDQPE
NNYKTTTPVLDSGSEFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:95)

>XenD24763 human IL12p40 E45Q/Q56E (GGGGS)2-Fc(216) IgG1 pl(-)

) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIEVKEFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDQPE
NNYKTTTPVLDSGSEFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:96)

Figure 21E

>XenD24764 human IL12p40 Q42E/E59Q (GGGGS)2-Fc(216) IgG1 pl(-)

) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDDESSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSGSEFFLYSKLTVDKSRWEQGDVFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:97)**

>XenD24765 human IL12p40 Q56E/E59Q (GGGGS)2-Fc(216) IgG1 pl(-)

) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIEVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSGSEFFLYSKLTVDKSRWEQGDVFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:98)**

>XenD24766 human IL12p40 Q42E/E45Q/Q56E (GGGGS)2-Fc(216) IgG1 pl(-)

) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSVLGSGKTLTIEVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSGSEFFLYSKLTVDKSRWEQGDVFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:99)**

Figure 21F

**>XenD24767 human IL12p40 E45Q/Q56E/E59Q (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIEVKQFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID
NO:100)*

**>XenD24768 human IL12p40 D161N (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKFEGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRNNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID
NO:101)*

**>XenD24769 human IL12p40 E73Q (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKFEGDAGQYTCHK
GGQVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID
NO:102)*

Figure 21G

>XenD24770 human IL12p40 Q144E (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPEGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID
NO:103)*

>XenD24771 human IL12p40 E262Q (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKRQKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID
NO:104)*

>XenD24772 human IL12p40 E100Q (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKQPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID
NO:105)*

Figure 21H

**>XenD24773 human IL12p40 D18N (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

*IWELKKDVYVVELDWYPNAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:106)*

**>XenD24774 human IL12p40 E33Q (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEQDGITWTLDQSSEVLGSGKTTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:107)*

**>XenD24775 human IL12p40 Q229E (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSREVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:108)*

Figure 21l

>XenD24776 human IL12p40 E235Q (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWQYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:109)*

>XenD24777 human IL12p40 Q256E (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPTWSTPHSYFSLTFCVQVEGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:110)*

>XenD24778 human IL12p40 E299Q (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSQWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:111)*

Figure 21J

**>XenD24792 human IL12p40 D87N (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLHKKENGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSGSEFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:112)*

Figure 22

<u>Residue</u>	<u>ASA</u>
Q35	134
E38	159
E46	145
D55	159
E67	140
N71	103
N76	119
N85	151
Q135	138
Q146	124
N151	144
E153	189
E162	114
E163	112

Figure 23A

> IL-12p35(N71D)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELT^KDESCLNS
RETSFIT^NGSC^LASR^KTSF^MMALCLSS^IYEDLK^MYQVE^FKTMNA^KLLMD^PKRQ^IFLDQ^NMLAVIDEL^MQALN^FNSET
VPQ^KSSLEED^PFYK^TKIKLCILLHAFRIRAV^TIDRVMSY^LNAS (SEQ ID NO:113)

> IL-12p35(N85D)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELT^KNESCLNS
RETSFIT^NDGSC^LASR^KTSF^MMALCLSS^IYEDLK^MYQVE^FKTMNA^KLLMD^PKRQ^IFLDQ^NMLAVIDEL^MQALN^FNSET
VPQ^KSSLEED^PFYK^TKIKLCILLHAFRIRAV^TIDRVMSY^LNAS (SEQ ID NO:114)

> IL-12p35(N195D)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELT^KNESCLNS
RETSFIT^NGSC^LASR^KTSF^MMALCLSS^IYEDLK^MYQVE^FKTMNA^KLLMD^PKRQ^IFLDQ^NMLAVIDEL^MQALN^FNSET
VPQ^KSSLEED^PFYK^TKIKLCILLHAFRIRAV^TIDRVMSY^LDAS (SEQ ID NO:115)

> IL-12p35(N71D/N85D/N195D)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELT^KDESCLNS
RETSFIT^NDGSC^LASR^KTSF^MMALCLSS^IYEDLK^MYQVE^FKTMNA^KLLMD^PKRQ^IFLDQ^NMLAVIDEL^MQALN^FNSET
VPQ^KSSLEED^PFYK^TKIKLCILLHAFRIRAV^TIDRVMSY^LDAS (SEQ ID NO:116)

> IL-12p35(E153Q)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELT^KNESCLNS
RETSFIT^NGSC^LASR^KTSF^MMALCLSS^IYEDLK^MYQVE^FKTMNA^KLLMD^PKRQ^IFLDQ^NMLAVIDEL^MQALN^FNS^Q_T
VPQ^KSSLEED^PFYK^TKIKLCILLHAFRIRAV^TIDRVMSY^LNAS (SEQ ID NO:117)

> IL-12p35(E38Q)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLQFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELT^KNESCLNS
RETSFIT^NGSC^LASR^KTSF^MMALCLSS^IYEDLK^MYQVE^FKTMNA^KLLMD^PKRQ^IFLDQ^NMLAVIDEL^MQALN^FNSET
VPQ^KSSLEED^PFYK^TKIKLCILLHAFRIRAV^TIDRVMSY^LNAS (SEQ ID NO:118)

> IL-12p35(N151D)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELT^KNESCLNS
RETSFIT^NGSC^LASR^KTSF^MMALCLSS^IYEDLK^MYQVE^FKTMNA^KLLMD^PKRQ^IFLDQ^NMLAVIDEL^MQALN^FDSET
VPQ^KSSLEED^PFYK^TKIKLCILLHAFRIRAV^TIDRVMSY^LNAS (SEQ ID NO:119)

> IL-12p35(Q135E)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELT^KNESCLNS
RETSFIT^NGSC^LASR^KTSF^MMALCLSS^IYEDLK^MYQVE^FKTMNA^KLLMD^PKRQ^IFLDENMLAVIDEL^MQALN^FNSET
VPQ^KSSLEED^PFYK^TKIKLCILLHAFRIRAV^TIDRVMSY^LNAS (SEQ ID NO:120)

Figure 23B

> IL-12p35(Q35D)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELT^KNESCL^NS
RETSFITNGSCLAS^RKTSFMMALCLSS^IYEDLKMYQVEFKTMNAKLLMDPKRQ^IFLDQ^NMLAVIDELMQALN^FNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:121)

> IL-12p35(Q146E)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELT^KNESCL^NS
RETSFITNGSCLAS^RKTSFMMALCLSS^IYEDLKMYQVEFKTMNAKLLMDPKRQ^IFLDQ^NMLAVIDELM^EALN^FNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:122)

> IL-12p35(N76D)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELT^KNESCL^DS
RETSFITNGSCLAS^RKTSFMMALCLSS^IYEDLKMYQVEFKTMNAKLLMDPKRQ^IFLDQ^NMLAVIDELMQALN^FNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:123)

> IL-12p35(E162Q)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELT^KNESCL^NS
RETSFITNGSCLAS^RKTSFMMALCLSS^IYEDLKMYQVEFKTMNAKLLMDPKRQ^IFLDQ^NMLAVIDELMQALN^FNSET
VPQKSSLE^QEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:124)

> IL-12p35(E163Q)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELT^KNESCL^NS
RETSFITNGSCLAS^RKTSFMMALCLSS^IYEDLKMYQVEFKTMNAKLLMDPKRQ^IFLDQ^NMLAVIDELMQALN^FNSET
VPQKSSLE^QPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:125)

> IL-12p35(N71Q)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELT^KQESCL^NS
RETSFITNGSCLAS^RKTSFMMALCLSS^IYEDLKMYQVEFKTMNAKLLMDPKRQ^IFLDQ^NMLAVIDELMQALN^FNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:XXX)

> IL-12p35(N85Q)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELT^KNESCL^NS
RETSFIT^QGSCLAS^RKTSFMMALCLSS^IYEDLKMYQVEFKTMNAKLLMDPKRQ^IFLDQ^NMLAVIDELMQALN^FNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:XXX)

> IL-12p35(N195Q)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELT^KNESCL^NS
RETSFITNGSCLAS^RKTSFMMALCLSS^IYEDLKMYQVEFKTMNAKLLMDPKRQ^IFLDQ^NMLAVIDELMQALN^FNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYL^QAS (SEQ ID NO:XXX)

Figure 23C

> IL-12p35(N71Q/N85Q)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELTK^QESCLNS
RETSFIT^QGSC^LASRKTSF^MMALCLSS^IYEDLKMYQ^VEFKTMNAKLLMDPKRQ^IFLDQ^NNMLAVIDELMQALN^FNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:XXX)

> IL-12p35(N71Q/N195Q)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELTK^QESCLNS
RETSFITNGSCLASRKTSF^MMALCLSS^IYEDLKMYQ^VEFKTMNAKLLMDPKRQ^IFLDQ^NNMLAVIDELMQALN^FNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSY^{LQ}AS (SEQ ID NO:XXX)

> IL-12p35(N85Q/N195Q)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELTK^NESCLNS
RETSFIT^QGSC^LASRKTSF^MMALCLSS^IYEDLKMYQ^VEFKTMNAKLLMDPKRQ^IFLDQ^NNMLAVIDELMQALN^FNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSY^{LQ}AS (SEQ ID NO:XXX)

> IL-12p35(N71Q/N85Q/N195Q)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELTK^QESCLNS
RETSFIT^QGSC^LASRKTSF^MMALCLSS^IYEDLKMYQ^VEFKTMNAKLLMDPKRQ^IFLDQ^NNMLAVIDELMQALN^FNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSY^{LQ}AS (SEQ ID NO:XXX)

> IL-12p35(N71D/N85D)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELTK^DESCLNS
RETSFIT^DGSC^LASRKTSF^MMALCLSS^IYEDLKMYQ^VEFKTMNAKLLMDPKRQ^IFLDQ^NNMLAVIDELMQALN^FNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:XXX)

> IL-12p35(N71D/N195D)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELTK^DESCLNS
RETSFITNGSCLASRKTSF^MMALCLSS^IYEDLKMYQ^VEFKTMNAKLLMDPKRQ^IFLDQ^NNMLAVIDELMQALN^FNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSY^LDAS (SEQ ID NO:XXX)

> IL-12p35(N85D/N195D)

RNLPVATPDPGMFPC^LHHSQNLLRAVS^NMLQKARQ^TLEFY^PCTSEEIDHEDITKD^KTSTVEAC^LPLELTK^NESCLNS
RETSFIT^DGSC^LASRKTSF^MMALCLSS^IYEDLKMYQ^VEFKTMNAKLLMDPKRQ^IFLDQ^NNMLAVIDELMQALN^FNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSY^LDAS (SEQ ID NO:XXX)

Figure 24A

>XenD24779**human IL12p35 N71D (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
DESCLNSRETSFITNGSCLASRKTSFMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:126)

>XenD24780**human IL12p35 N85D (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITDGSCLASRKTSFMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:127)

>XenD24781**human IL12p35 N195D (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLDAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:128)

>XenD24782**human IL12p35 N71D/N85D/N195D (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
DESCLNSRETSFITDGSCLASRKTSFMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLDAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:129)

Figure 24B

>XenD24783**human IL12p35 E153Q (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSQTV P QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS GGGGS\ E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:130)

>XenD24784**human IL12p35 E38Q (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLQFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSQTV P QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS GGGGS\ E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:131)

>XenD24785**human IL12p35 N151D (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFDSETVP QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS GGGGS\ E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:132)

>XenD24786**human IL12p35 Q135E (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDENMLAV
IDELMQALNFNSQTV P QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS GGGGS\ E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:133)

Figure 24C

>XenD24787**human IL12p35 Q35D (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARDTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:134)

>XenD24788**human IL12p35 Q146E (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMEALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:135)

>XenD24789**human IL12p35 N76D (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLDSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:136)

>XenD24790**human IL12p35 E162Q (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:137)

Figure 24D

>XenD24791**human IL12p35 E163Q (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM LAV
IDELMQALNFNSETVPQKSSLEQPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS GGGGS\ E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK **(SEQ ID NO:138)**

Figure 25A

>XENP28820 human IL12p40(N103D/N113D/N200D/N281D) (GGGGS)2-human IL12p35(N71D/N85D/N195D) (GGGGS)2-Fc(216) IgG1 pl(-) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 (XenD24756) - human_IL12p40_N103D/N113D/N200D/N281D_(GGGGS)2-Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYEDYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKDASISVRAQDRYYSSSWSEWASVPCS\G
 GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNATKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVSMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:139)**

Chain 2 (XenD24782) -

human_IL12p35_N71D/N85D/N195D_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLRAVSNNLQKARQTFEYPCTSEEIDHEDITKDKTSTVEACLPLELTKDESCLNS
 RETSFITDGSLASRKTSFMMALCLSSIYEDLQMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLDAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNATKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVSMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:140)**

>XENP28821 human IL12p40(D87N) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 (XenD24792) - human_IL12p40_D87N_(GGGGS)2-Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKENGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS\G
 GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNATKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVSMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:141)**

Figure 25B

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:142)**

**>XENP28822 human_IL12p40(Q42E)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24757) - human_IL12p40_Q42E_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSESEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:143)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:144)**

**>XENP28823 human_IL12p40(E45Q)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24758) - human_IL12p40_E45Q_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:145)**

Figure 25C

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNLMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:146)**

**>XENP28824 human_IL12p40(Q56E)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24759) - human_IL12p40_Q56E_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIEVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
 GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:147)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNLMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:148)**

**>XENP28825 human_IL12p40(E59Q)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24760) - human_IL12p40_E59Q_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
 GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:149)**

Figure 25D

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
 VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:150)**

**>XENP28826 human_IL12p40(D62N)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24761) - human_IL12p40_D62N_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIQVKEFGNAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
 GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:151)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
 VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:152)**

**>XENP28827 human_IL12p40(Q42E/E45Q)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24762) - human_IL12p40_Q42E/E45Q_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
 GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:153)**

Figure 25E

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTFLEFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:154)**

**>XENP28828 human_IL12p40(E45Q/Q56E)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24763) - human_IL12p40_E45Q/Q56E_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIEVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:155)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTFLEFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:156)**

**>XENP28829 human_IL12p40(Q42E/E59Q)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24764) - human_IL12p40_Q42E/E59Q_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSESEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:157)**

Figure 25F

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:158)**

**>XENP28830 human_IL12p40(Q56E/E59Q)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24765) - human_IL12p40_Q56E/E59Q_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIEVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:159)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:160)**

**>XENP28831 human_IL12p40(Q42E/E45Q/Q56E)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24766) - human_IL12p40_Q42E/E45Q/Q56E_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIEVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:161)**

Figure 25G

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNNMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:162)**

**>XENP28832 human_IL12p40(E45Q/Q56E/E59Q)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24767) - human_IL12p40_E45Q/Q56E/E59Q_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIEVKQFGDAGQYTCHKGGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
 GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:163)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNNMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:164)**

**>XENP28833 human_IL12p40(D161N)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24768) - human_IL12p40_D161N_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGNNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
 GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:165)**

Figure 25H

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:166)**

**>XENP28834 human_IL12p40(E73Q)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24769) - human_IL12p40_E73Q_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGQVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:167)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:168)**

**>XENP28835 human_IL12p40(Q144E)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24770) - human_IL12p40_Q144E_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPEGVTGGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:169)**

Figure 25I

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:170)**

**>XENP28836 human_IL12p40(E262Q)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24771) - human_IL12p40_E262Q_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKRQKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:171)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:172)**

**>XENP28837 human_IL12p40(E100Q)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24772) - human_IL12p40_E100Q_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKQPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:173)**

Figure 25J

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDGPMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:174)**

**>XENP28838 human_IL12p40(D18N)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24773) - human_IL12p40_D18N_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPNAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:175)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDGPMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:176)**

**>XENP28839 human_IL12p40(E33Q)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24774) - human_IL12p40_E33Q_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEQDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:177)**

Figure 25K

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:178)**

**>XENP28840 human_IL12p40(Q229E)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24775) - human_IL12p40_Q229E_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSREVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:179)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:180)**

**>XENP28841 human_IL12p40(E235Q)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24776) - human_IL12p40_E235Q_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWQYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:181)**

Figure 25L

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:182)**

**>XENP28842 human_IL12p40(Q256E)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24777) - human_IL12p40_Q256E_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVEGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:183)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:184)**

**>XENP28843 human_IL12p40(E299Q)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD24778) - human_IL12p40_E299Q_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSQWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:185)**

Figure 25M

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:186)**

**>XENP28844 human_IL12p40_(GGGGS)2-human_IL12p35(E153Q)_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:187)**

Chain 2 (XenD24783) - human_IL12p35_E153Q_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNNMLAVIDELMQALNFNSQT
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:188)**

**>XENP28845 human_IL12p40_(GGGGS)2-human_IL12p35(E38Q)_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:189)**

Figure 25N

Chain 2 (XenD24784) - human_IL12p35_E38Q_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLQFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:190)**

**>XENP28846 human_IL12p40_(GGGGS)2-human_IL12p35(N151D)_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:191)**

Chain 2 (XenD24785) - human_IL12p35_N151D_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLQFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFDSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:192)**

**>XENP28847 human_IL12p40_(GGGGS)2-human_IL12p35(Q135E)_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:193)**

Figure 250

Chain 2 (XenD24786) - human_IL12p35_Q135E_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDENMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:194)**

**>XENP28848 human_IL12p40_(GGGGS)2-human_IL12p35(Q35D)_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
 GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:195)**

Chain 2 (XenD24787) - human_IL12p35_Q35D_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARDTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNNMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:196)**

**>XENP28849 human_IL12p40_(GGGGS)2-human_IL12p35(Q146E)_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
 GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:197)**

Figure 25P

Chain 2 (XenD24788) - human_IL12p35_Q146E_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMEALNFNSET
VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:198)**

**>XENP28850 human_IL12p40_(GGGGS)2-human_IL12p35(N76D)_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:199)**

Chain 2 (XenD24789) - human_IL12p35_N76D_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLDS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:200)**

**>XENP28851 human_IL12p40_(GGGGS)2-human_IL12p35(E162Q)_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:201)**

Figure 25Q

Chain 2 (XenD24790) - human_IL12p35_E162Q_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEQPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:202)**

**>XENP28852 human_IL12p40_(GGGGS)2-human_IL12p35(E163Q)_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:203)**

Chain 2 (XenD24791) - human_IL12p35_E163Q_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEQPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:204)**

Figure 26A

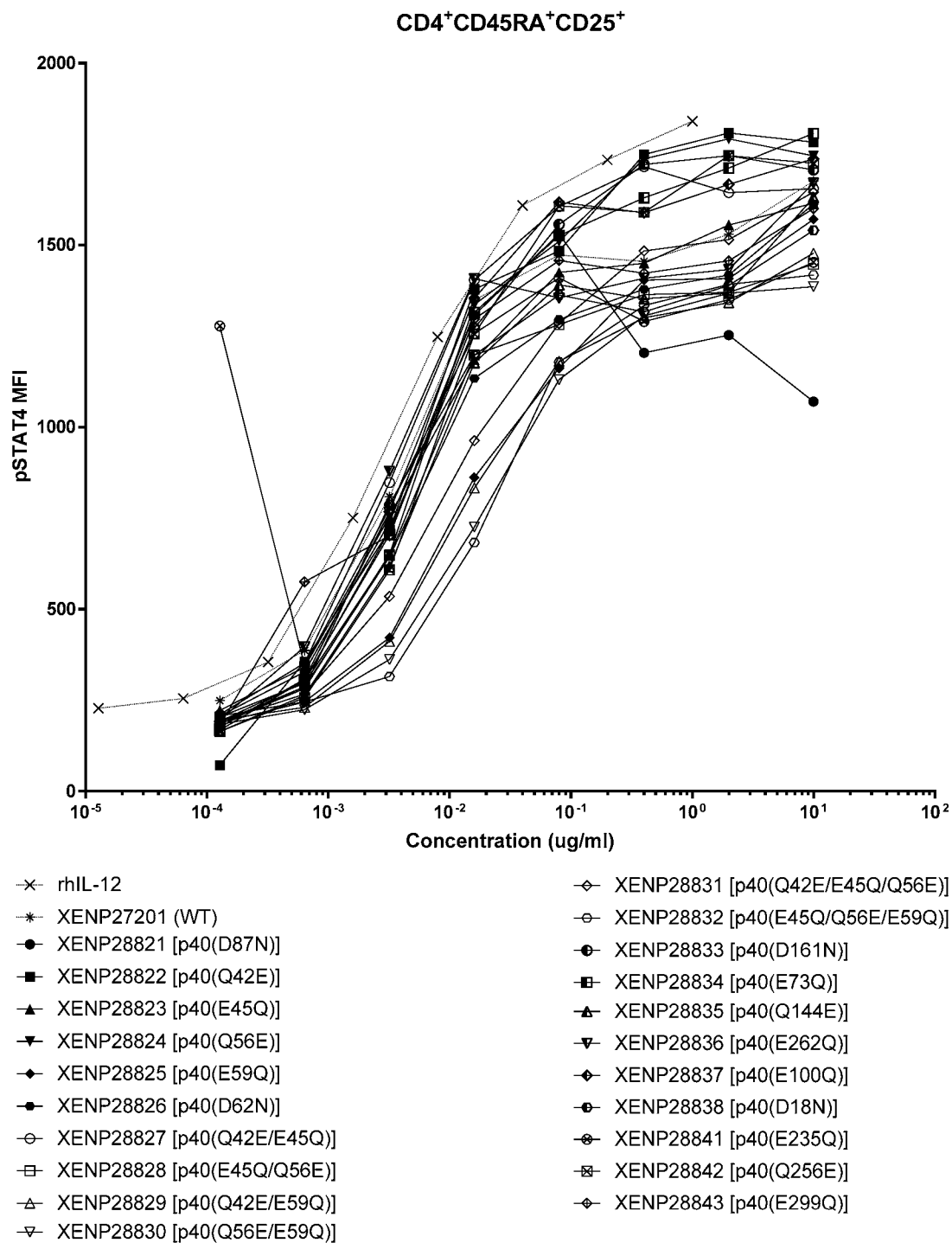


Figure 26B

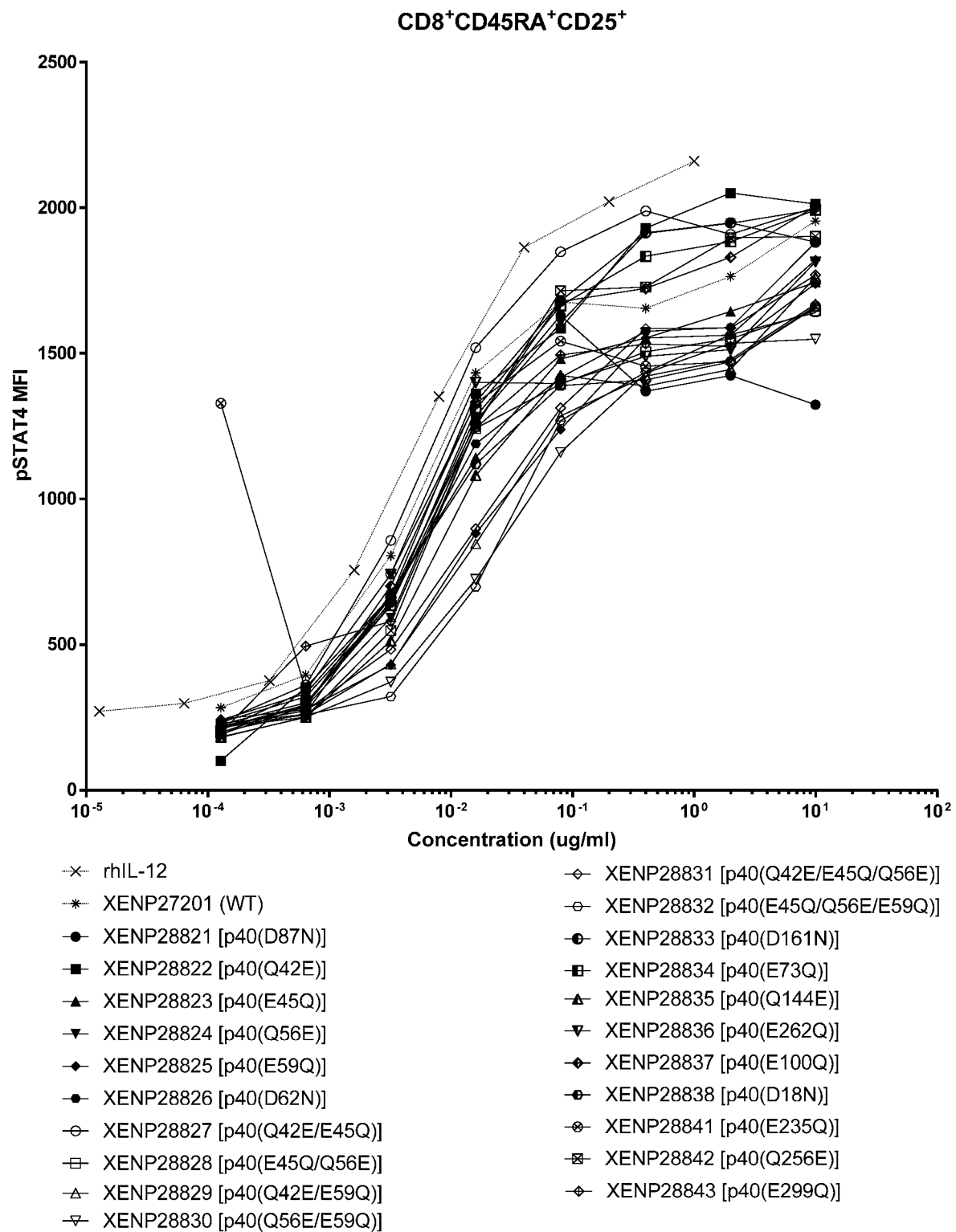


Figure 27A

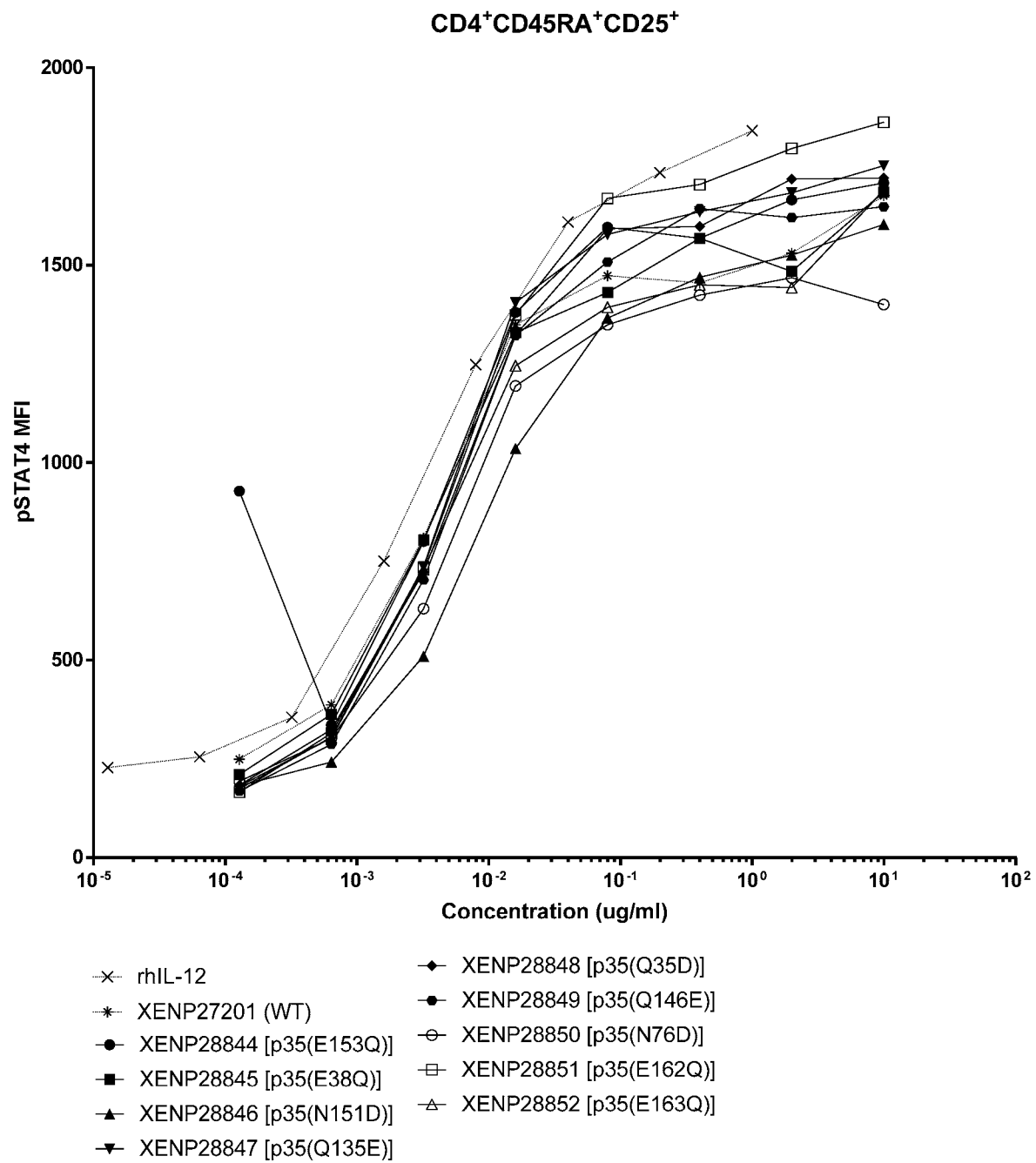


Figure 27B

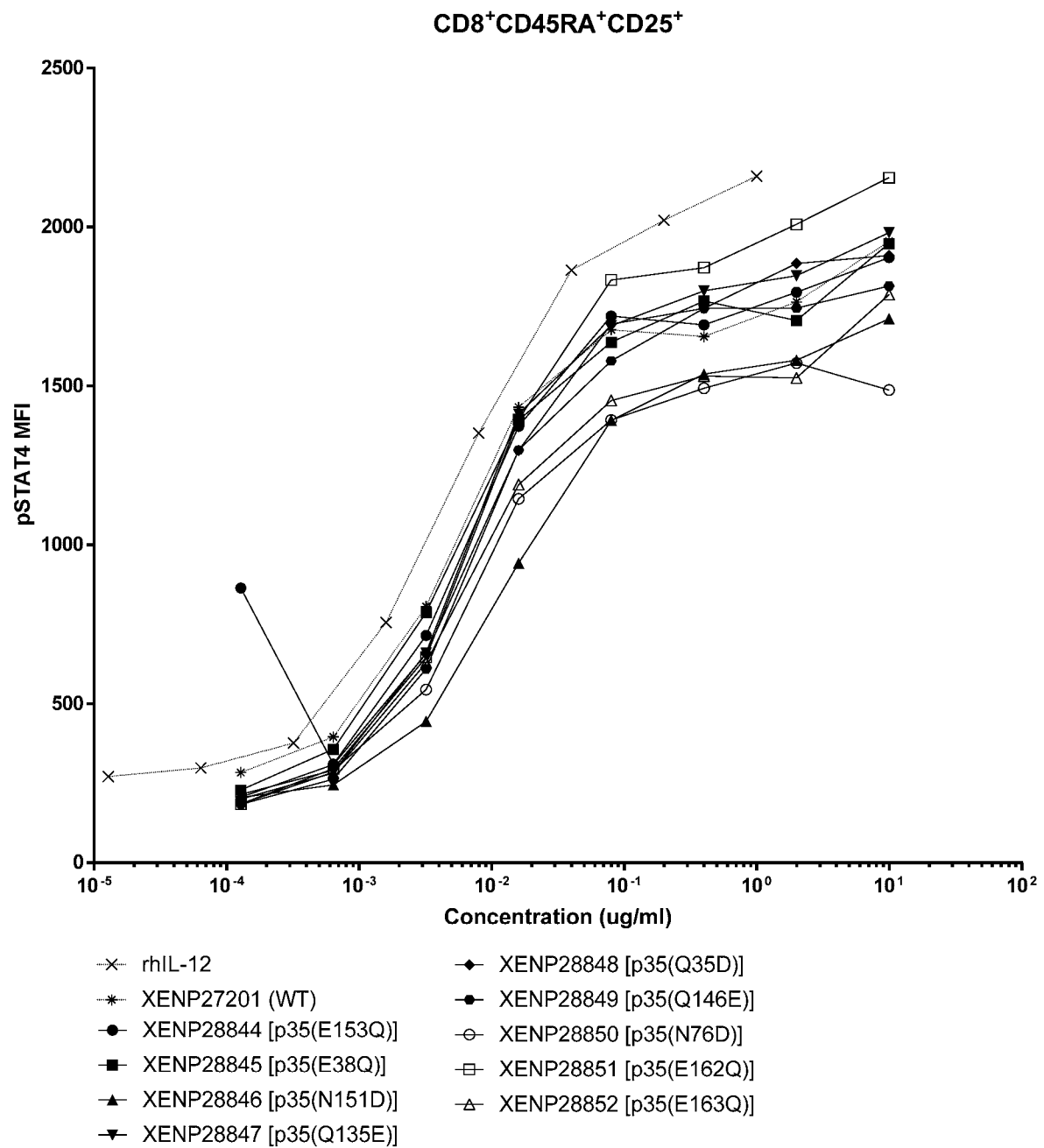


Figure 28

XENP	IL-12p40 Variant	IL-12p35 Variant	PSTAT4 EC50		FOLD DECREASE IN EC50	
			CD4+ CD45RA+ CD25+	CD8+ CD45RA+ CD25+	CD4+ CD45RA+ CD25+	CD8+ CD45RA+ CD25+
27201-1	WT	WT	0.003708	0.005468		
27201-2	WT	WT	0.003182	0.004785		
28821	D87N	WT	0.002181	0.004005	0.63	0.78
28822	Q42E	WT	0.005075	0.008822	1.47	1.72
28823	E45Q	WT	0.005	0.008541	1.45	1.67
28824	Q56E	WT	0.006622	0.01139	1.92	2.22
28825	E59Q	WT	0.01716	0.02519	4.98	4.91
28826	D62N	WT	0.005682	0.008183	1.65	1.60
28827	Q42E/E45Q	WT	0.003749	0.005398	1.09	1.05
28828	E45Q/Q56E	WT	0.004335	0.006014	1.26	1.17
28829	Q42E/E59Q	WT	0.01448	0.01896	4.20	3.70
28830	Q56E/E59Q	WT	0.01949	0.02855	5.66	5.57
28831	Q42E/E45Q/Q56E	WT	0.01266	0.02008	3.67	3.92
28832	E45Q/Q56E/E59Q	WT	0.02254	0.02873	6.54	5.60
28833	D161N	WT	0.006258	0.009723	1.82	1.90
28834	E73Q	WT	0.005763	0.009079	1.67	1.77
28835	Q144E	WT	0.00509	0.008766	1.48	1.71
28836	E262Q	WT	0.00241	0.004113	0.70	0.80
28837	E100Q	WT	0.004449	0.007287	1.29	1.42
28838	D18N	WT	0.003218	0.006053	0.93	1.18
28841	E235Q	WT	0.01259	0.01474	3.65	2.88
28842	Q256E	WT	0.006819	0.009489	1.98	1.85
28843	E299Q	WT	0.004098	0.007258	1.19	1.42
28844	WT	E153Q	0.009734	0.01212	2.83	2.36
28845	WT	E38Q	0.003759	0.005643	1.09	1.10
28846	WT	N151D	0.009653	0.01517	2.80	2.96
28847	WT	Q135E	0.00457	0.006908	1.33	1.35
28848	WT	Q35D	0.005247	0.00824	1.52	1.61
28849	WT	Q146E	0.004868	0.007417	1.41	1.45
28850	WT	N76D	0.004796	0.007424	1.39	1.45
28851	WT	E162Q	0.005616	0.008755	1.63	1.71
28852	WT	E163Q	0.004334	0.007082	1.26	1.38

Figure 29A

>IL12p40(E59K) (SEQ ID NO:205)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

>IL12p40(E32Q/E59Q) (SEQ ID NO:206)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEQEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

>IL12p40(D34N/E59Q) (SEQ ID NO:207)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

>IL12p40(E59Q/E187Q) (SEQ ID NO:208)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIQVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

>IL12p40(S43E/E59Q) (SEQ ID NO:209)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQESEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

Figure 29B

>IL12p40(S43K/E59Q) (SEQ ID NO:210)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQKSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

>IL12p40(E59Q/K163E) (SEQ ID NO:211)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNEEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

>IL12p40(E59Q/K99E) (SEQ ID NO:212)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

>IL12p40(E59Q/K258E) (SEQ ID NO:213)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGESKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

>IL12p40(E59Q/K260E) (SEQ ID NO:214)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGSEREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

Figure 30A

**>XenD25922 human IL12p40 E59K (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:215)*

**>XenD25923 human IL12p40 E32Q/E59Q (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:216)*

**>XenD25924 human IL12p40 D34N/E59Q (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:217)*

Figure 30B

**>XenD25925 human IL12p40 E59Q/E187Q (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIQVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID
NO:218)*

**>XenD25926 human IL12p40 S43E/E59Q (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSESEVLGSGKTTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID
NO:219)*

**>XenD25927 human IL12p40 S43K/E59Q (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQKSEVLGSGKTTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID
NO:220)*

Figure 30C

**>XenD25928 human IL12p40 E59Q/K163E (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRGDNEEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQVGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID
NO:221)*

**>XenD25929 human IL12p40 E59Q/K99E (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRGDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQVGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID
NO:222)*

**>XenD25930 human IL12p40 E59Q/K258E (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRGDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGESKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID
NO:223)*

Figure 30D

**>XenD25931 human IL12p40 E59Q/K260E (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSEREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSGSEFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:224)*

Figure 31A

>IL12p35(N151D/E153Q) (SEQ ID NO:225)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFDSQTVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

>IL12p35(E153K) (SEQ ID NO:226)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSKTVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

>IL12p35(N151K) (SEQ ID NO:227)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFKSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

>IL12p35(N151D/D165N) (SEQ ID NO:228)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFDSETVPQKSSLEEPNFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

>IL12p35(Q130E/N151D) (SEQ ID NO:229)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKREIFLDQNMLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

>IL12p35(N151D/K158E) (SEQ ID NO:230)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFDSETVPQESSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

>IL12p35(E79Q/N151D) (SEQ ID NO:231)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRQTSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

>IL12p35(D55Q/N151D) (SEQ ID NO:232)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKQKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

Figure 31B

>IL12p35(N136D/N151D) (SEQ ID NO:233)

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQDM LAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

>IL12p35(N21D/N151D) (SEQ ID NO:234)

RNLPVATPDPGMFPC LHHSQDLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

>IL12p35(E143Q/N151D) (SEQ ID NO:235)

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDQLMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

Figure 32A

>XenD25911**human IL12p35 N151D/E153Q (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFDSQTV P QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:236)

>XenD25912**human IL12p35 E153K (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSKTVP QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:237)

>XenD25913**human IL12p35 N151K (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFKSETVP QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:238)

>XenD25914**human IL12p35 N151D/D165N (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFDSETVP QKSSLEEPNFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:239)

Figure 32B

>XenD25915**human IL12p35 Q130E/N151D (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKREIFLDQNMLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS GGGGS\E
PKSSDKTHTCPCPAPPVAGPSVFLFPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:240)

>XenD25916**human IL12p35 N151D/K158E (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFDSETVPQESSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS GGGGS\E
PKSSDKTHTCPCPAPPVAGPSVFLFPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:241)

>XenD25917**human IL12p35 E79Q/N151D (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRQTSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS GGGGS\E
PKSSDKTHTCPCPAPPVAGPSVFLFPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:242)

>XenD25918**human IL12p35 D55Q/N151D (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKQKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS GGGGS\E
PKSSDKTHTCPCPAPPVAGPSVFLFPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:243)

Figure 32C

>XenD25919**human IL12p35 N136D/N151D (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQDMLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHA FRIRAVTIDRVMSYLNAS\GGGGS GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:244)

>XenD25920**human IL12p35 N21D/N151D (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQDLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQDMLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHA FRIRAVTIDRVMSYLNAS\GGGGS GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:245)

>XenD25921**human IL12p35 E143Q/N151D (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pTT5**

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQDMLAV
IDQIMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHA FRIRAVTIDRVMSYLNAS\GGGGS GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:246)

Figure 33A

**>XENP29949 human IL12p40(E59Q) (GGGGS)2-human IL12p35(N151D) (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD24760) - human_IL12p40(E59Q)_(GGGGS)2_Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNATKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGQDVFSCSVMEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: 93)**

Chain 2 (XenD24785) - human_IL12p35(N151D)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPLHHSQNLLRAVSNNLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLARKTSFMMALCLSSIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFDSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNATKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: 132)**

**>XENP29950 human IL12p40(Q56E/E59Q) (GGGGS)2-human IL12p35(N151D) (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD24765) - human_IL12p40(Q56E/E59Q)_(GGGGS)2_Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIEVKQFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNATKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGQDVFSCSVMEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: 98)**

Figure 33B

Chain 2 (XenD24785) - human_IL12p35(N151D)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNL PVATPDPGMF PCLHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFDSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV MHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 132)**

**>XENP29951 human IL12p40(E59K) (GGGGS)2-human IL12p35(N151D) (GGGGS)2-Fc(216) IgG1 pl(-)
)_Isosteric A C220S/PVA_/S267K/L368D/K370S Fc(216) IgG1 C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD25922) - human_IL12p40(E59K)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS SDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDV FSCSV MHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: 215)**

Chain 2 (XenD24785) - human_IL12p35(N151D)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNL PVATPDPGMF PCLHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFDSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV MHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 132)**

Figure 33C

**>XENP29952 human IL12p40(E59K) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD25922) - human_IL12p40(E59K)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSSEWASVPCS/_G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVSMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 215)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/_GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTCLVKGFYPSDIAVEWESNGQPENNYK
TTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVSMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

**>XENP29953 human IL12p40(E32Q/E59Q) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD25923) - human_IL12p40(E32Q/E59Q)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSSEWASVPCS/_G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVSMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 216)**

Figure 33D

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

**>XENP29954 human_IL12p40(D34N/E59Q)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD25924) - human_IL12p40(D34N/E59Q)_(GGGGS)2_Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEENGITWTLDQSSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGGEVLSH
LLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 217)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 33E

**>XENP29955 human IL12p40(E59Q/E187Q) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD25925) - human_IL12p40(E59Q/E187Q)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTLRCEAKNYSGRFTCWLLTTISTDLTF SVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECQEDSACPAAEESLPQVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 218)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLMYQVEFKTMNAKLLMDPKRQIFLDQNM LAVIDELMQALNFNSET
VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

**>XENP29956 human IL12p40(S43E/E59Q) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD25926) - human_IL12p40(S43E/E59Q)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTLRCEAKNYSGRFTCWLLTTISTDLTF SVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECQEDSACPAAEESLPQVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 219)**

Figure 33F

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

**>XENP29957 human_IL12p40(S43K/E59Q)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD25927) - human_IL12p40(S43K/E59Q)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQKSEVLGSGKTLTIQVKQFGDAGQYTCHKGGGEVLSH
LLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 220)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 33G

**>XENP29958 human IL12p40(E59Q/K163E) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
)_ Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD25928) - human_IL12p40(E59Q/K163E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_ Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNEEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGQDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 221)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMVQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

**>XENP29959 human IL12p40(E59Q/K99E) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
)_ Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD25929) - human_IL12p40(E59Q/K99E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_ Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGQDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 222)**

Figure 33H

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

**>XENP29960 human_IL12p40(E59Q/K258E)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD25930) - human_IL12p40(E59Q/K258E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGGEVLSH
LLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGESKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 223)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 33I

**>XENP29961 human IL12p40(E59Q/K260E) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD25931) - human_IL12p40(E59Q/K260E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 224)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

**>XENP29962 human IL12p40 (GGGGS)2-human IL12p35(N151D/E153Q) (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 33J

Chain 2 (XenD25911) -**human_IL12p35(N151D/E153Q)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFDSQT
 VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 236)**

**>XENP29963 human_IL12p40 (GGGGS)2-human_IL12p35(E153K) (GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2_Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGGEVLSH
 SLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD25912) - human_IL12p35(E153K)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSKT
 VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 237)**

Figure 33K

**>XENP29964 human IL12p40 (GGGGS)2-human IL12p35(N151K) (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVSMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD25913) - human_IL12p35(N151K)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLRLAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLQMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFKSET
VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG
KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVSMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 238)**

**>XENP29965 human IL12p40 (GGGGS)2-human IL12p35(N151D/D165N) (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVSMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 33L

Chain 2 (XenD25914) -**human_IL12p35(N151D/D165N)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNNMLAVIDELMQALNFDSET
 VPQKSSLEEPNFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 239)**

**>XENP29966 human_IL12p40 (GGGGS)2-human_IL12p35(Q130E/N151D) (GGGGS)2-Fc(216)_IgG1 pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGGEVLSH
 SLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQKPLKNSRQVE
 VSWEPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD25915) -**human_IL12p35(Q130E/N151D)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKREIFLDQNNMLAVIDELMQALNFDSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 240)**

Figure 33M

**>XENP29967 human IL12p40 (GGGGS)2-human IL12p35(N151D/K158E) (GGGGS)2-Fc(216) IgG1 pl(-)
Isosteric A C220S/PVA/S267K/L368D/K370S Fc(216) IgG1 C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

**Chain 2 (XenD25916) -
human_IL12p35(N151D/K158E)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

RNLPVATPDPGMFCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLQMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFDSET
VPQESSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTTPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: 241)**

**>XENP29968 human IL12p40 (GGGGS)2-human IL12p35(E79Q/N151D) (GGGGS)2-Fc(216) IgG1 pl(-)
Isosteric A C220S/PVA/S267K/L368D/K370S Fc(216) IgG1 C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 33N

Chain 2 (XenD25917) -**human_IL12p35(E79Q/N151D)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RQTSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFDSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 242)**

**>XENP29969 human_IL12p40 (GGGGS)2-human_IL12p35(D55Q/N151D) (GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2_Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD25918) -**human_IL12p35(D55Q/N151D)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKQKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFDSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 243)**

Figure 330

**>XENP29970 human IL12p40 (GGGGS)2-human IL12p35(N136D/N151D) (GGGGS)2-Fc(216) IgG1 pl(-)
)_Isosteric A C220S/PVA_/S267K/L368D/K370S Fc(216) IgG1 C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFSVSMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)***

**Chain 2 (XenD25919) -
 human_IL12p35(N136D/N151D)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

*RNLPVATPDPMFPCLLHHSQNLRAVSNNLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIYEDLQMYQVEFKTMNAKLLMDPKRQIFLDQDMLAVIDELMQALNFDSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSGGSFFLYSKLTVDKSRWQQGNVFSVSMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 244)***

**>XENP29971 human IL12p40 (GGGGS)2-human IL12p35(N21D/N151D) (GGGGS)2-Fc(216) IgG1 pl(-)
)_Isosteric A C220S/PVA_/S267K/L368D/K370S Fc(216) IgG1 C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFSVSMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)***

Figure 33P

Chain 2 (XenD25920) -**human_IL12p35(N21D/N151D)_(GGGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

RNLPVATPDPGMFCLHHSQDLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNNMLAVIDELMQALNFDSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 245)**

**>XENP29972 human_IL12p40 (GGGGGS)2-human_IL12p35(E143Q/N151D) (GGGGGS)2-Fc(216)_IgG1 pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD22914) - human_IL12p40_(GGGGGS)2_Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQKLPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD25921) -**human_IL12p35(E143Q/N151D)_(GGGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

RNLPVATPDPGMFCLHHSQNNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNNMLAVIDQLMQALNFDSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 246)**

Figure 34A

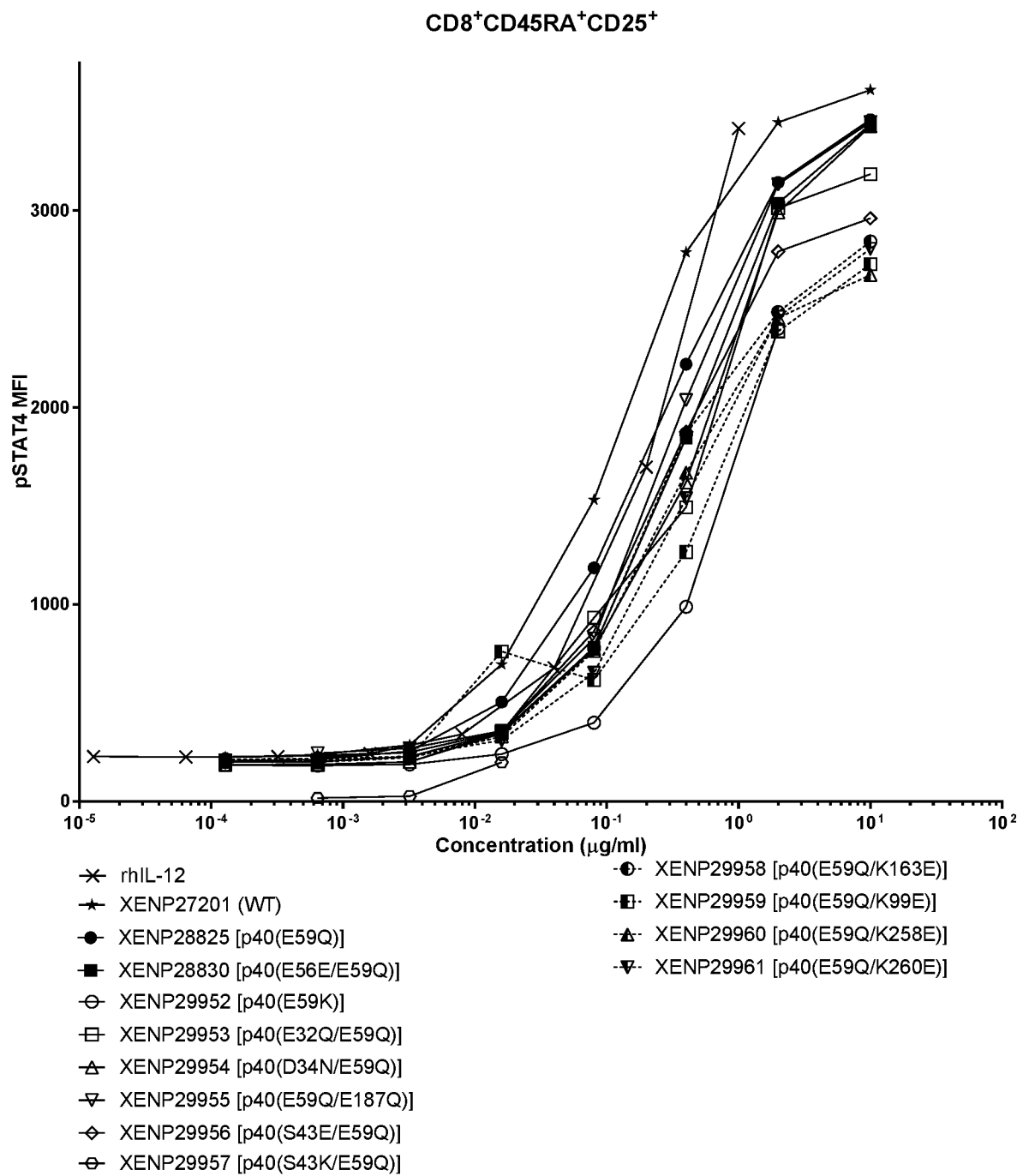


Figure 34B

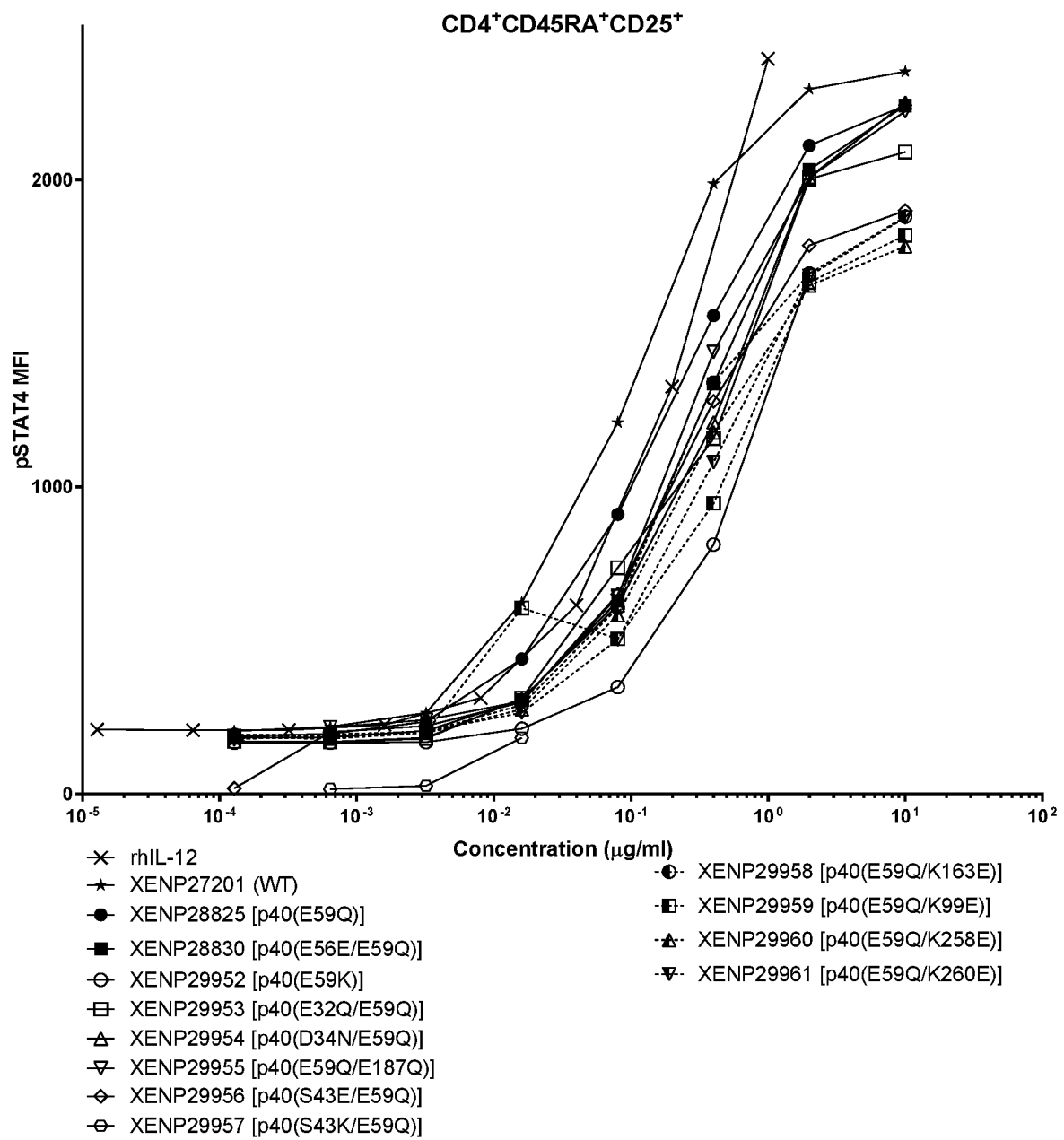


Figure 35A

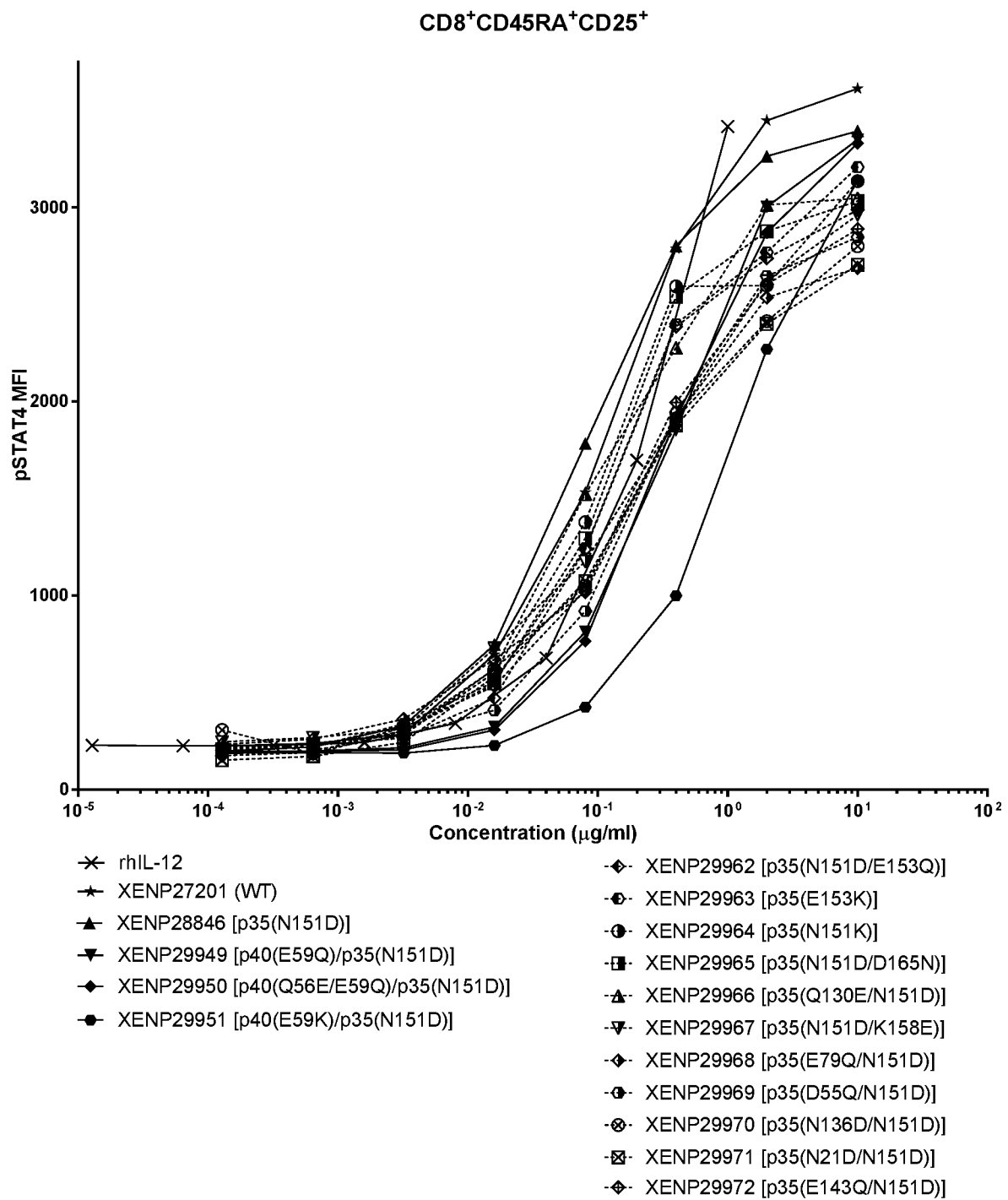


Figure 35B

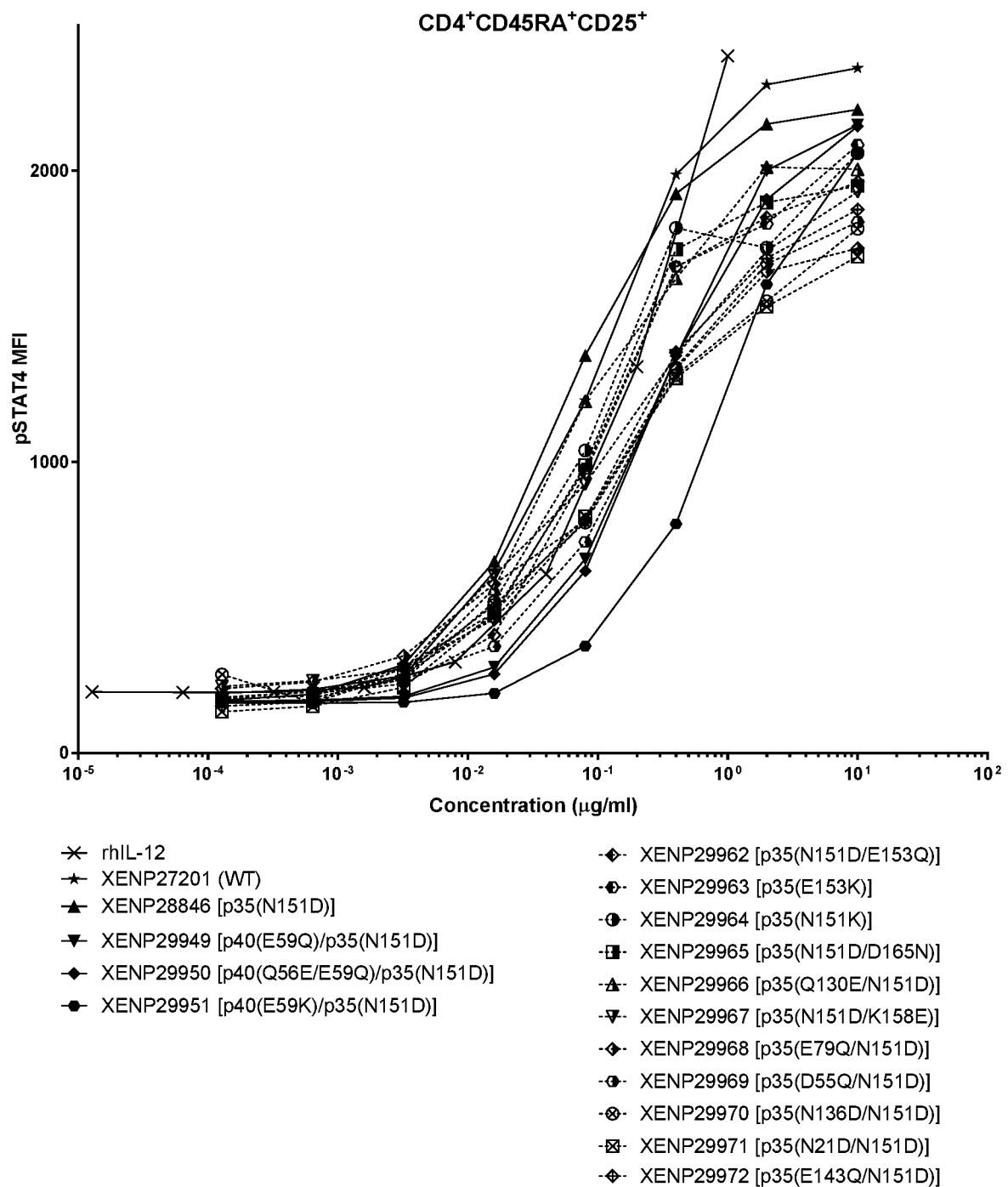


Figure 36

XENP	IL-12p40 Variant	IL-12p35 Variant	<u>PSTAT4 EC50</u>		<u>FOLD DECREASE IN EC50</u>	
			CD4+ CD45RA+ CD25+	CD8+ CD45RA+ CD25+	CD4+ CD45RA+ CD25+	CD8+ CD45RA+ CD25+
27201	WT	WT	0.08704	0.1286		
28825	E59Q	WT	0.1737	0.2259	2.00	1.76
28830	Q56E/E59Q	WT	0.3278	0.41	3.77	3.19
28846	WT	N151D	0.05648	0.08265	0.65	0.64
29949	E59Q	N151D	0.2748	0.3765	3.16	2.93
29950	Q56E/E59Q	N151D	0.2794	0.3592	3.21	2.79
29951	E59K	N151D	0.9019	1.195	10.36	9.29
29952	E59K	WT	1.012	1.547	11.63	12.03
29953	E32Q/E59Q	WT	0.3248	0.4581	3.73	3.56
29954	D34N/E59Q	WT	0.4004	0.5114	4.60	3.98
29955	E59Q/E187Q	WT	0.2823	0.3446	3.24	2.68
29956	S43E/E59Q	WT	0.2149	0.2776	2.47	2.16
29957	S43K/E59Q	WT	N/A	N/A	N/A	N/A
29958	E59Q/K163E	WT	0.2182	0.2643	2.51	2.06
29959	E59Q/K99E	WT	0.4892	0.6045	5.62	4.70
29960	E59Q/K258E	WT	0.2553	0.2885	2.93	2.24
29961	E59Q/K260E	WT	0.3782	0.4094	4.35	3.18
29962	WT	N151D/E153Q	0.09898	0.128	1.14	1.00
29963	WT	E153K	0.1044	0.1458	1.20	1.13
29964	WT	N151K	0.07835	0.1011	0.90	0.79
29965	WT	N151D/D165N	0.08989	0.118	1.03	0.92
29966	WT	Q130E/N151D	0.06791	0.1092	0.78	0.85
29967	WT	N151D/K158E	0.1255	0.1984	1.44	1.54
29968	WT	E79Q/N151D	0.1367	0.1862	1.57	1.45
29969	WT	D55Q/N151D	0.1769	0.2245	2.03	1.75
29970	WT	N136D/N151D	0.145	0.188	1.67	1.46
29971	WT	N21D/N151D	0.1043	0.1561	1.20	1.21
29972	WT	E143Q/N151D	0.1426	0.1919	1.64	1.49

Figure 37A

>IL12p40(E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYISSSSWSEWASVPCS **(SEQ ID NO: XXX)**

>IL12p40(D34N/E59K)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYISSSSWSEWASVPCS **(SEQ ID NO: XXX)**

>IL12p40(D34N/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYISSSSWSEWASVPCS **(SEQ ID NO: XXX)**

>IL12p40(D34K/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEKGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYISSSSWSEWASVPCS **(SEQ ID NO: XXX)**

>IL12p40(E32Q/D34N/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEQENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYISSSSWSEWASVPCS **(SEQ ID NO: XXX)**

Figure 37B

>IL12p40(E32Q/D34K/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDT**PQEK**GITWTLDQSSEVLGSGKTLTIQVK**K**FGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQ**E**EPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS **(SEQ ID NO: XXX)**

>IL12p40(E32K/D34N/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDT**PKEN**GITWTLDQSSEVLGSGKTLTIQVK**K**FGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQ**E**EPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS **(SEQ ID NO: XXX)**

>IL12p40(E32K/D34K/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDT**PKEK**GITWTLDQSSEVLGSGKTLTIQVK**K**FGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQ**E**EPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS **(SEQ ID NO: XXX)**

Figure 38

>IL12p35(D55Q)

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKQKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS **(SEQ ID NO: XXX)**

>IL12p35(D55K)

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKKKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS **(SEQ ID NO: XXX)**

Figure 39A

**>XENP30597 human IL12p40 E59K/K99E (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
)_ Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD26411) - human_IL12p40_E59K/K99E_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_ Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/_G
GGGSGGGGS/_EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)***

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

*RNLPVATPDPMFPLHHSQNLLRAVSNNLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/_GGGSGGGGS/_EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)***

**>XENP30598 human IL12p40 D34N/E59K (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
)_ Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD26412) - human_IL12p40_D34N/E59K_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_ Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/_G
GGGSGGGGS/_EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)***

Figure 39B

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

**>XENP30599 human_IL12p40_D34N/E59K/K99E_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD26413) - human_IL12p40_D34N/E59K/K99E_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 39C

**>XENP30600 human IL12p40 D34K/E59K/K99E (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD26414) - human_IL12p40_D34K/E59K/K99E_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEKGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLARKTSFMMALCLSSIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

**>XENP30601 human IL12p40 E32Q/D34N/E59K/K99E (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD26415) - human_IL12p40_E32Q/D34N/E59K/K99E_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 39D

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

**>XENP30602 human_IL12p40_E32Q/D34K/E59K/K99E_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD26416) - human_IL12p40_E32Q/D34K/E59K/K99E_(GGGGS)2_Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEKGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 39E

**>XENP30603 human IL12p40 E32K/D34N/E59K/K99E (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
)_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD26417) - human_IL12p40_E32K/D34N/E59K/K99E_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPKENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)***

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

*RNLPVATPDPMFPLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)***

**>XENP30604 human IL12p40 E32K/D34K/E59K/K99E (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
)_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD26418) - human_IL12p40_E32K/D34K/E59K/K99E_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPKKEGKITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)***

Figure 39F

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNNMLAVIDELMQALNFNSET
 VPQKSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

**>XENP30605 human_IL12p40_E32Q/D34N/E59K/K99E_(GGGGS)2-human_IL12p35_D55Q_(GGGGS)2-
 Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD26415) - human_IL12p40_E32Q/D34N/E59K/K99E_(GGGGS)2_Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPTQENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD26427) - human_IL12p35_D55Q_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKQKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNNMLAVIDELMQALNFNSET
 VPQKSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 39G

>XENP30606 human IL12p40 E32Q/D34K/E59K/K99E (GGGGS)2-human IL12p35 D55Q (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 (XenD26416) - human_IL12p40_E32Q/D34K/E59K/K99E_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEKGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWEQGDVVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD26427) - human_IL12p35_D55Q_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLRAVSNNLQKARQTFEYFCTSEEIDHEDITKQKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLARKTSFMMALCLSSIYEDLMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

>XENP30607 human IL12p40 E32K/D34N/E59K/K99E (GGGGS)2-human IL12p35 D55Q (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 (XenD26417) - human_IL12p40_E32K/D34N/E59K/K99E_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEKNGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWEQGDVVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 39H

Chain 2 (XenD26427) - human_IL12p35_D55Q_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKQKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS /EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

**>XENP30608 human_IL12p40_E32K/D34K/E59K/K99E_(GGGGS)2-human_IL12p35_D55Q_(GGGGS)2-
 Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD26418) - human_IL12p40_E32K/D34K/E59K/K99E_(GGGGS)2_Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCCTPKEGKITWTLTDSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSSEWASVPCS/G
GGGSGGGGS /EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD26427) - human_IL12p35_D55Q_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKQKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS /EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 39I

>XENP30609 human IL12p40_E32K/D34K/E59K/K99E_(GGGGS)2-human IL12p35_D55K_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 (XenD26418) - human_IL12p40_E32K/D34K/E59K/K99E_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

*IWELKKDVYVVELDWYPDAPGEMVVLTC DTPKEKGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWEQGDVFSFSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)***

Chain 2 (XenD26428) - human_IL12p35_D55K_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

*RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKKKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSGDSFFLYSKLTVDKSRWQQGNVFSFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)***

Figure 40A

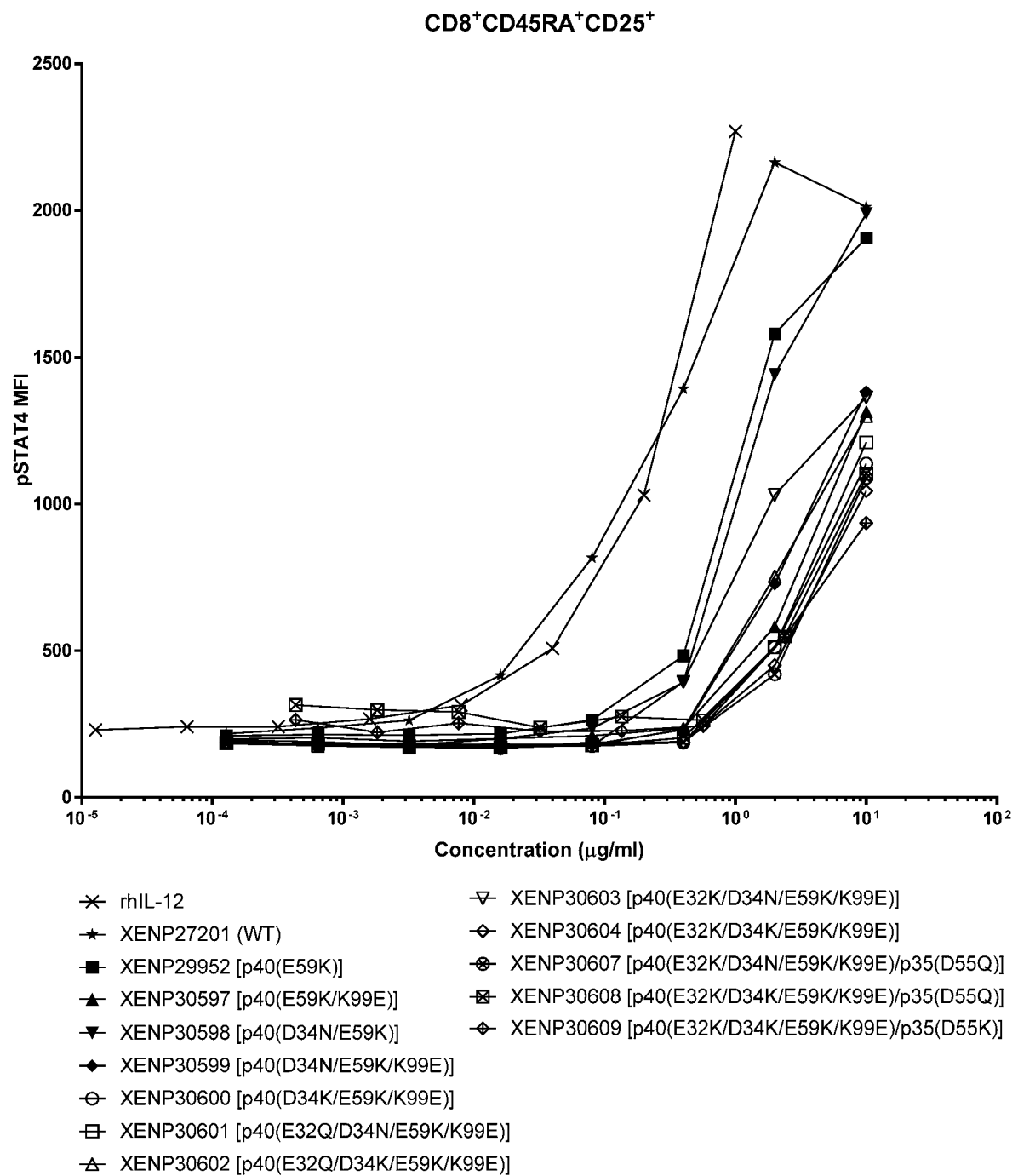


Figure 40B

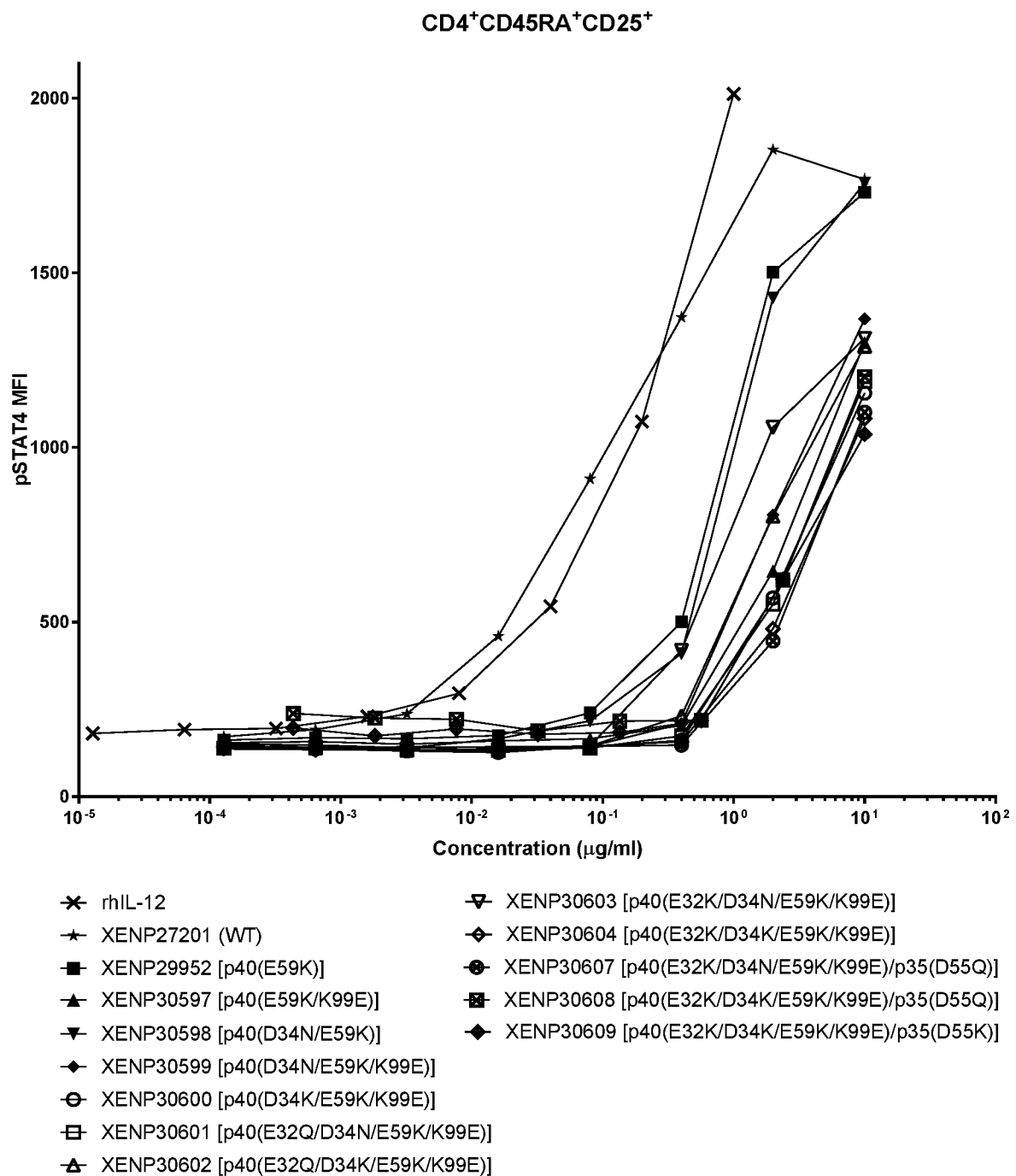


Figure 41

XENP	IL-12p40 Variant	IL-12p35 Variant	<u>PSTAT4 EC50</u>		<u>FOLD DECREASE IN EC50</u>	
			CD4+ CD45RA+ CD25+	CD8+ CD45RA+ CD25+	CD4+ CD45RA+ CD25+	CD8+ CD45RA+ CD25+
27201	WT	WT	0.1101	0.2097		
29952	E59K	WT	1.056	1.287	9.59	6.14
30597	E59K/K99E	WT	5.507	9.768	50.02	46.58
30598	D34N/E59K	WT	1.308	1.806	11.88	8.61
30599	D34N/E59K/K99E	WT	3.23	4.839	29.34	23.08
30600	D34K/E59K/K99E	WT	5.929	9.898	53.85	47.20
30601	E32Q/D34N/E59K/K99E	WT	6.804	11.71	61.80	55.84
30602	E32Q/D34K/E59K/K99E	WT	2.714	3.645	24.65	17.38
30603	E32K/D34N/E59K/K99E	WT	1.13	1.482	10.26	7.07
30604	E32K/D34K/E59K/K99E	WT	8.44	12.98	76.66	61.90
30607	E32K/D34N/E59K/K99E	D55Q	12.1	24.31	109.90	115.93
30608	E32K/D34K/E59K/K99E	D55Q	10.25	25.27	93.10	120.51
30609	E32K/D34K/E59K/K99E	D55K	5.426	8.258	49.28	39.38

Figure 42A

>IL12p40(E59Y/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKYFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS **(SEQ ID NO: XXX)**

>IL12p40(E59K/K99Y)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQYEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS **(SEQ ID NO: XXX)**

>IL12p40(E59Y/K99Y)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKYFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQYEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS **(SEQ ID NO: XXX)**

>IL12p40(E45K/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSKVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS **(SEQ ID NO: XXX)**

>IL12p40(D18K/E59K/K99E)

IWELKKDVYVVELDWYPKAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS **(SEQ ID NO: XXX)**

Figure 42B

>IL12p40(E59K/K99E/Q144E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKKFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPEGVTCGAATLSAERVVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYISSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(E59K/K99E/Q144K)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKKFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPKGVTCGAATLSAERVVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYISSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(E59K/K99E/R159E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKKFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVEGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYISSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(E59K/K99E/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKKFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKEDRVFTDKTSATVICRK
NASISVRAQDRYISSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(D18K/E59K/K99E/K264E)

IWELKKDVYVVELDWYPKAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTTLTIQVKKFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKEDRVFTDKTSATVICRK
NASISVRAQDRYISSSWSEWASVPCS (SEQ ID NO: XXX)

Figure 43

>IL12p35(F96A)

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTS~~A~~MMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETV P QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO: XXX)

>IL12p35(M97A)

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSF~~A~~MMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETV P QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO: XXX)

>IL12p35(L89A)

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSC~~A~~ASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETV P QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO: XXX)

>IL12p35(L124A)

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLL~~A~~MDPKRQIFLDQNMLAV
IDELMQALNFNSETV P QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO: XXX)

>IL12p35(M125A)

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLL~~A~~DPKRQIFLDQNMLAV
IDELMQALNFNSETV P QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO: XXX)

>IL12p35(L75A)

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESC~~A~~NSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETV P QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO: XXX)

>IL12p35(I171A)

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETV P QKSSLEEPDFYKTK~~A~~KLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO: XXX)

Figure 44A

**>XENP31250 human IL12p40(E59Y/K99E) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD27070) - human_IL12p40(E59Y/K99E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IEWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKYFGDAGQYTCHKGGEVLSHSLLLHKKED
GIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVGRDNKEYEYSVECCQEDS
ACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPTWSTPHSYFSLTFCVQVQGKSKREKK
DRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDT
LMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIS
KAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVF
SCSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLVPVATPDPGMFPCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNSRETSFITNGSCL
ASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSETVPQKSSLEEDFYKTKIKLCILL
HAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQM
TKNQVQLTCLVKGFPYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
PGK **(SEQ ID NO: XXX)**

**>XENP31251 human IL12p40(E59K/K99Y) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD27071) - human_IL12p40(E59K/K99Y)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IEWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSHSLLLHKKED
GIWSTDILKDQYEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVGRDNKEYEYSVECCQEDS
ACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPTWSTPHSYFSLTFCVQVQGKSKREKK
DRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDT
LMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIS
KAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVF
SCSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:XXX)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLVPVATPDPGMFPCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNSRETSFITNGSCL
ASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSETVPQKSSLEEDFYKTKIKLCILL
HAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQM
TKNQVQLTCLVKGFPYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
PGK **(SEQ ID NO:XXX)**

Figure 44B

**>XENP31252 human IL12p40(E59Y/K99Y) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
_ Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD27072) - human_IL12p40(E59Y/K99Y)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_ Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIQVKYFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQYEPKNTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEEQGDVFSVMSHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:XXX)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPCPLHHSQNLLRAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSHEALHNHYTQKSLSLSPGK **(SEQ ID NO:XXX)**

**>XENP31253 human IL12p40(E45K/E59K/K99E) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
_ Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD27073) - human_IL12p40(E45K/E59K/K99E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_ Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSKVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEEQGDVFSVMSHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:XXX)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPCPLHHSQNLLRAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSHEALHNHYTQKSLSLSPGK **(SEQ ID NO:XXX)**

Figure 44C

**>XENP31254 human IL12p40(D18K/E59K/K99E) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
)_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD27074) - human_IL12p40(D18K/E59K/K99E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

*IWELKKDVYVVELDWYPKAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVVFSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:XXX)***

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

*RNLPVATPDPMFPCPLHHSQNLLRAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:XXX)***

**>XENP31255 human IL12p40(E59K/K99E/Q144E) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
)_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD27075) - human_IL12p40(E59K/K99E/Q144E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPEGVTCTGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVVFSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:XXX)***

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

*RNLPVATPDPMFPCPLHHSQNLLRAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:XXX)***

Figure 44D

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

*RNLPVATPDPGMFCLHHSQNLLRAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMFLAVIDELMQALNFNSET
VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:XXX)***

Figure 44E

**>XENP31256 human IL12p40(E59K/K99E/Q144K) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD27076) - human_IL12p40(E59K/K99E/Q144K)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPKGVTCGAATLS
AERVRGDNKEYEYSVECDQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/_G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFSVSMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:XXX)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLRAVSNNMLQKARQTFEYFCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/_GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSGGSFFLYSKLTVDKSRWQQGNVFSVSMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:XXX)**

**>XENP31257 human IL12p40(E59K/K99E/R159E) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD27077) - human_IL12p40(E59K/K99E/R159E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVEGDNKEYEYSVECDQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/_G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFSVSMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:XXX)**

Figure 44F

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:XXX)**

**>XENP31258 human_IL12p40(E59K/K99E/K264E)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD27078) - human_IL12p40(E59K/K99E/K264E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
LLLLLHKKEDGIWSTDILKDQEEPKNKTLFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:XXX)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:XXX)**

Figure 44G

**>XENP31259 human IL12p40(E59K/K99E) (GGGGS)2-human IL12p35(F96A) (GGGGS)2-Fc(216) IgG1 pl(-)
)_Isosteric A C220S/PVA_/S267K/L368D/K370S Fc(216) IgG1 C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD26411) - human_IL12p40(E59K/K99E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
LLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:XXX)***

Chain 2 (XenD27088) - human_IL12p35(F96A)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

*RNLPVATPDPGMFPLHHSQNLLRAVSNNLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSAMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:XXX)***

**>XENP31260 human IL12p40(E59K/K99E) (GGGGS)2-human IL12p35(M97A) (GGGGS)2-Fc(216) IgG1 pl(-)
)_Isosteric A C220S/PVA_/S267K/L368D/K370S Fc(216) IgG1 C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD26411) - human_IL12p40(E59K/K99E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
LLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:XXX)***

Figure 44H

Chain 2 (XenD27089) - human_IL12p35(M97A)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFAMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

**>XENP31261 human_IL12p40(E59K/K99E)_(GGGGS)2-human_IL12p35(L89A)_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD26411) - human_IL12p40(E59K/K99E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/_G
 GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 (XenD27090) - human_IL12p35(L89A)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCAASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

Figure 44I

**>XENP31262 human IL12p40(E59K/K99E) (GGGGS)2-human IL12p35(L124A) (GGGGS)2-Fc(216) IgG1 pl(-)
Isosteric A C220S/PVA/S267K/L368D/K370S Fc(216) IgG1 C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD26411) - human_IL12p40(E59K/K99E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
LLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:XXX)**

Chain 2 (XenD27091) - human_IL12p35(L124A)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMVQVEFKTMNAKLAMD PKRQIFLDQNM LAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:XXX)**

**>XENP31263 human IL12p40(E59K/K99E) (GGGGS)2-human IL12p35(M125A) (GGGGS)2-Fc(216) IgG1 pl(-)
Isosteric A C220S/PVA/S267K/L368D/K370S Fc(216) IgG1 C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD26411) - human_IL12p40(E59K/K99E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
LLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:XXX)**

Figure 44J

Chain 2 (XenD27092) - human_IL12p35(M125A)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLADPKRQIFLDQNMALVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVSMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

**>XENP31264 human_IL12p40(E59K/K99E)_(GGGGS)2-human_IL12p35(L75A)_(GGGGS)2-Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 (XenD26411) - human_IL12p40(E59K/K99E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/_G
 GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVSMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 (XenD27093) - human_IL12p35(L57A)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVSMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

Figure 44K

**>XENP31265 human IL12p40(E59K/K99E) (GGGGS)2-human IL12p35(I171A) (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD26411) - human_IL12p40(E59K/K99E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD27094) - human_IL12p35(I171A)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKAKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO:XXX)**

**>XENP32186 human IL12p40(D18K/E59K/K99E/K264E) (GGGGS)2-human IL12p35 (GGGGS)2-
Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 (XenD28173) - human_IL12p40(D18K/E59K/K99E/K264E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPKAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO:XXX)**

Chain 2 (XenD22915) - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 45A

**>XENP31142 human IL12p40 (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S/M428L/N434S-IgG1 PVA /S267K/S364K/E357Q/M428L/N434S**

**Chain 1 (XenD24876) - human_IL12p40_(GGGGS)2_Fc(216)_IgG1_pl(-)
) Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCSVLHEALHSHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD24877) - human_IL12p35_(GGGGS)2_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

RNLPVATPDPGMFCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCSVLHEALHSHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

**>XENP31143 human IL12p40 E32Q/D34N/E59K/K99E (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S/M428L/N434S-IgG1 PVA /S267K/S364K/E357Q/M428L/N434S**

**Chain 1 (XenD27162) - human_IL12p40_E32Q/D34N/E59K/K99E_(GGGGS)2_Fc(216)_IgG1_pl(-)
) Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCSVLHEALHSHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD24877) - human_IL12p35_(GGGGS)2_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

RNLPVATPDPGMFCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCSVLHEALHSHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 45B

>XENP31144 human IL12p40 E32K/D34N/E59K/K99E (GGGGS)2-human IL12p35 D55Q (GGGGS)2-Fc(216) IgG1 pl(-) Isosteric A C220S/PVA /S267K/L368D/K370S/M428L/N434S-IgG1 PVA /S267K/S364K/E357Q/M428L/N434S

Chain 1 (XenD27163) - human_IL12p40_E32K/D34N/E59K/K99E_(GGGGS)2_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S

IWELKKDVYVVELDWYPDAPGEMVVLTCDDPKENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGGEVLSH
 SLLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNATKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCSVLHEALHSHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD27166) - human_IL12p35_D55Q_(GGGGS)2_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

RNLPVATPDGPMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKQKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNATKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCSVLHEALHSHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

>XENP31145 human IL12p40 E32K/D34K/E59K/K99E (GGGGS)2-human IL12p35 D55Q (GGGGS)2-Fc(216) IgG1 pl(-) Isosteric A C220S/PVA /S267K/L368D/K370S/M428L/N434S-IgG1 PVA /S267K/S364K/E357Q/M428L/N434S

Chain 1 (XenD27164) - human_IL12p40_E32K/D34K/E59K/K99E_(GGGGS)2_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S

IWELKKDVYVVELDWYPDAPGEMVVLTCDDPKENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGGEVLSH
 SLLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNATKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCSVLHEALHSHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD27166) - human_IL12p35_D55Q_(GGGGS)2_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

RNLPVATPDGPMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKQKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNATKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCSVLHEALHSHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 45C

**>XENP31146 human IL12p40 E59K/K99E (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
)_Isosteric A C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1 PVA_/S267K/S364K/E357Q/M428L/N434S**

**Chain 1 (XenD27165) - human_IL12p40_E59K/K99E_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/_G
GGGSGGGGS/_EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDFVSCSVLHEALHSHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 (XenD24877) - human_IL12p35_(GGGGS)2_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

RNLPVATPDPGMFCLHHSQNLLRAVSNNLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/_GGGSGGGGS/_EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 46A

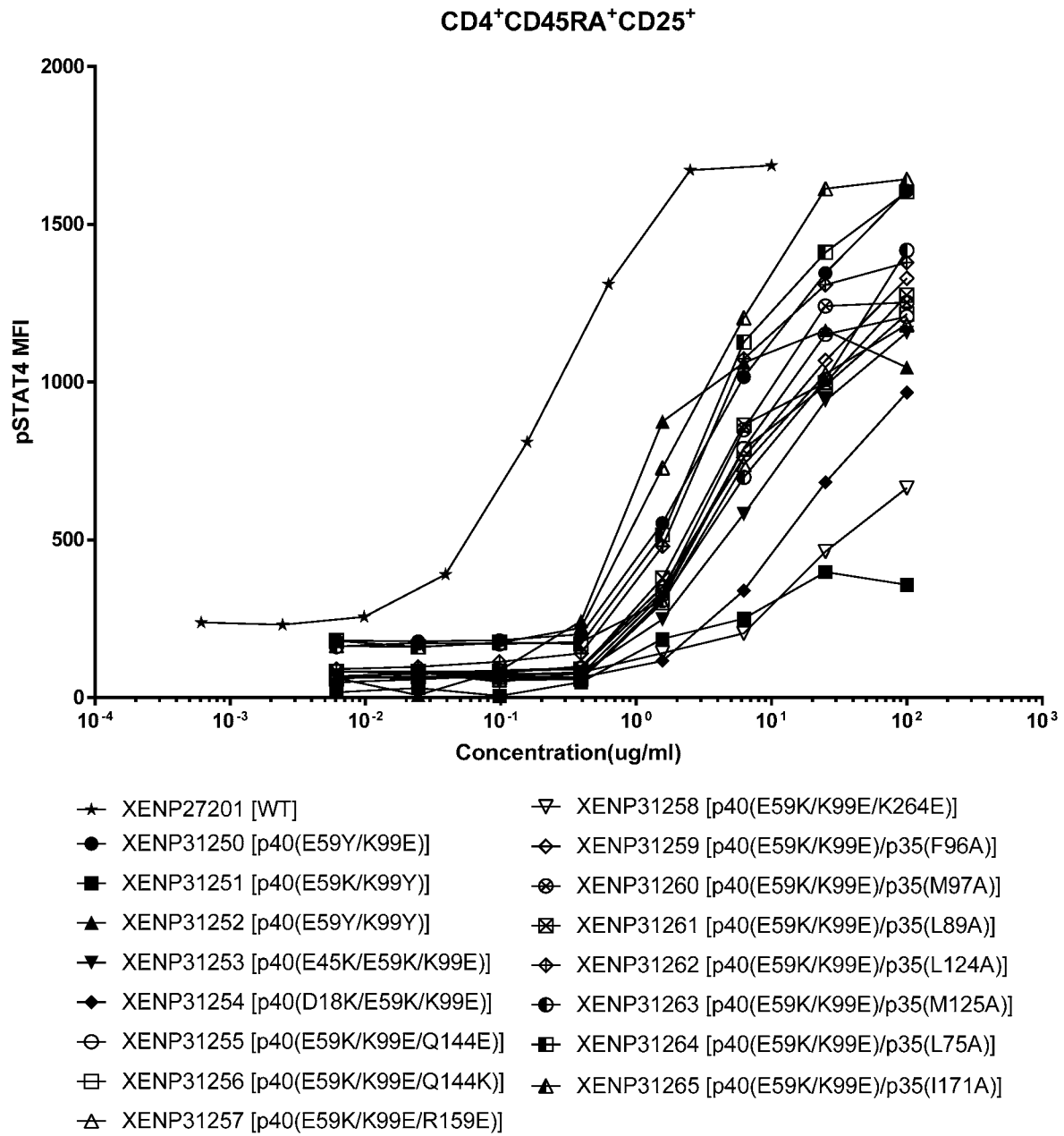


Figure 46B

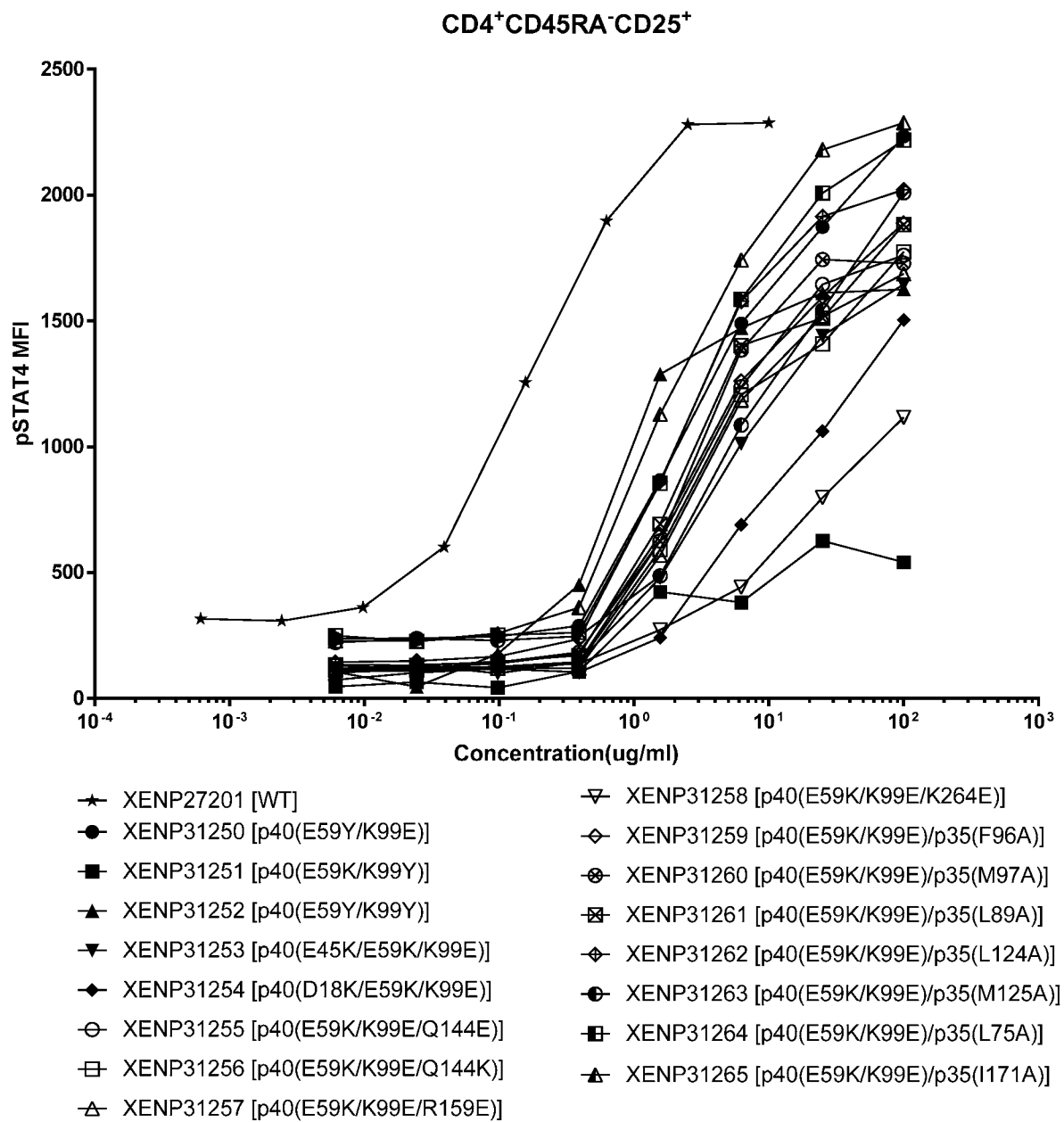


Figure 46C

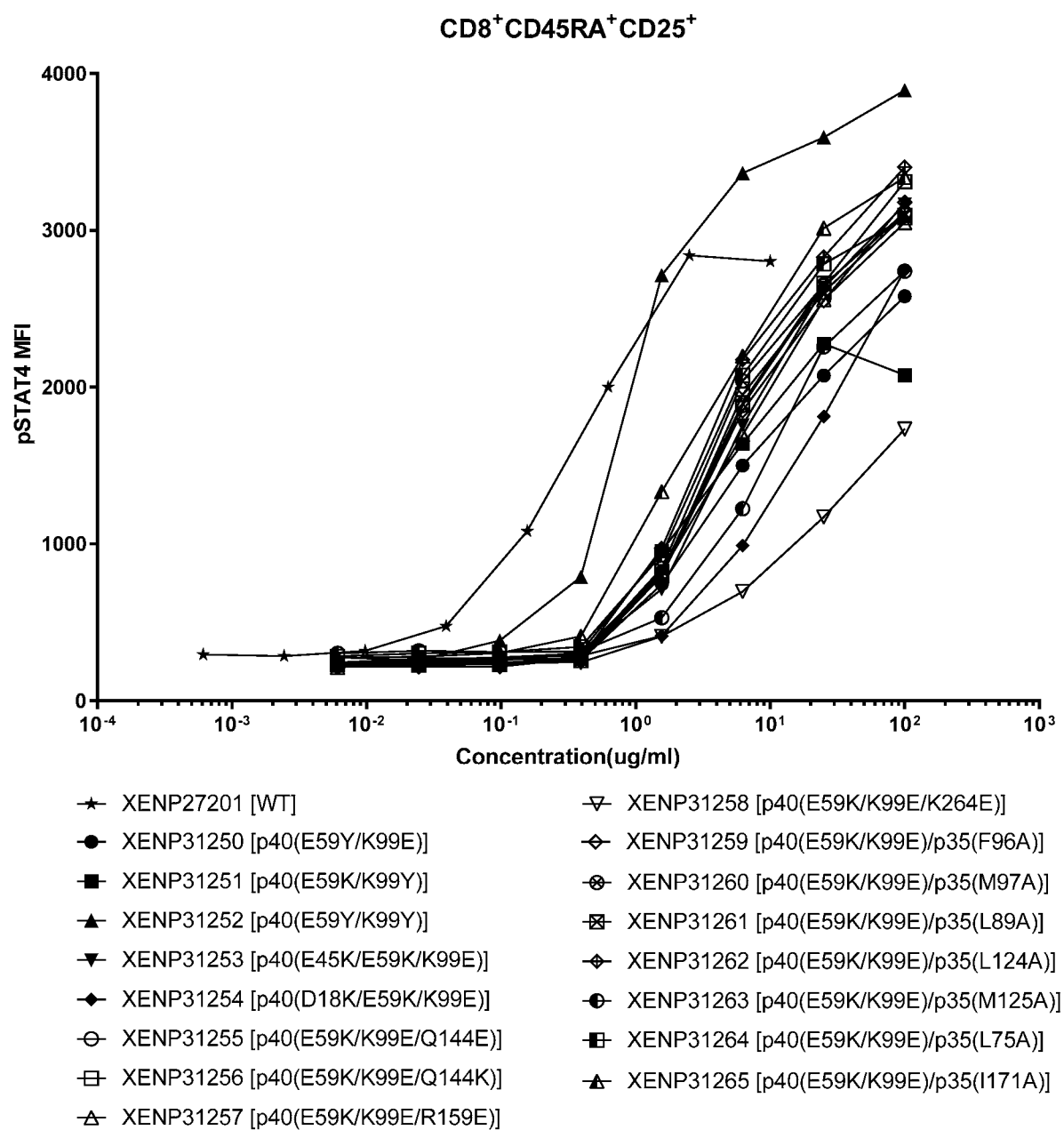


Figure 46D

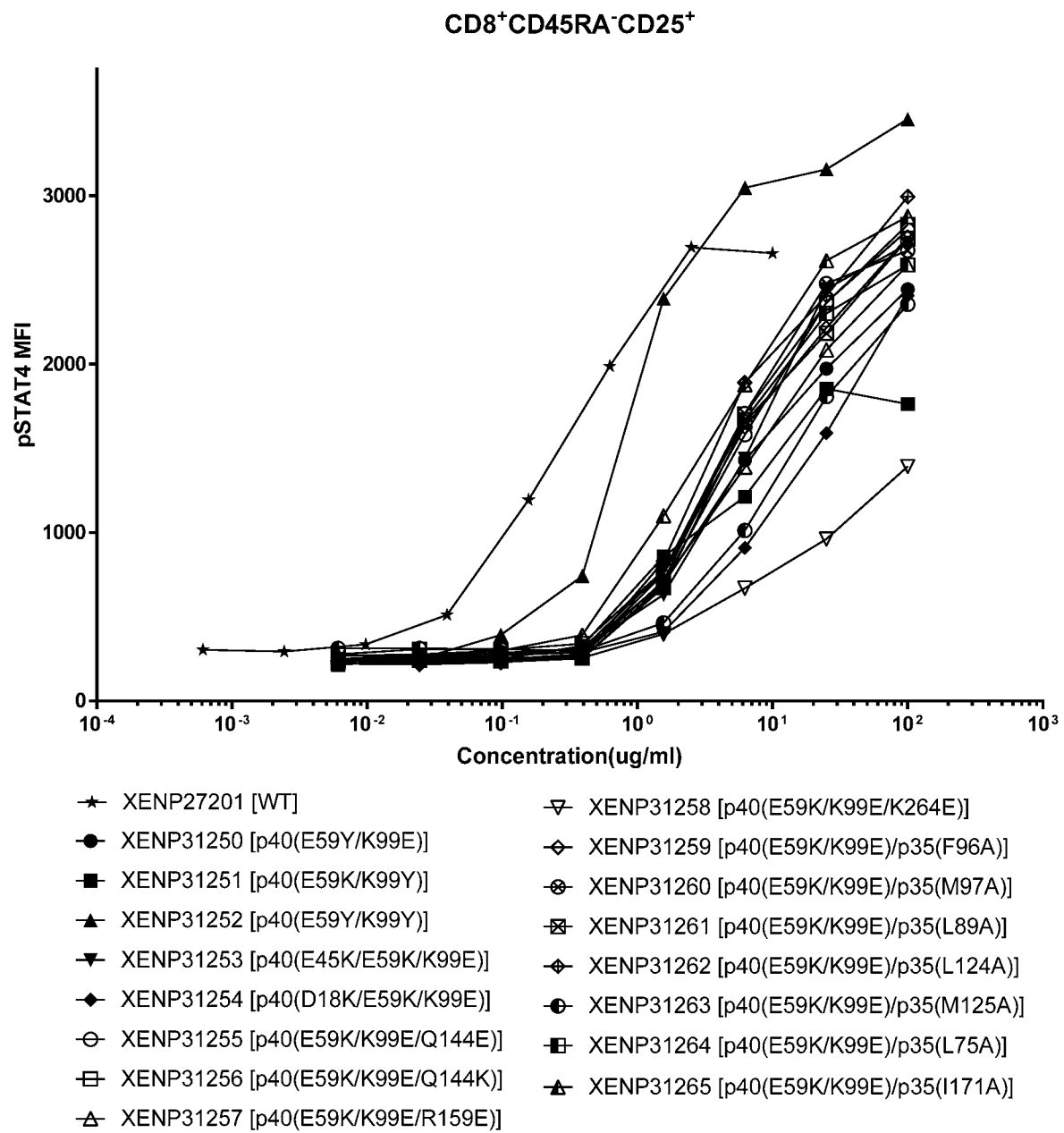
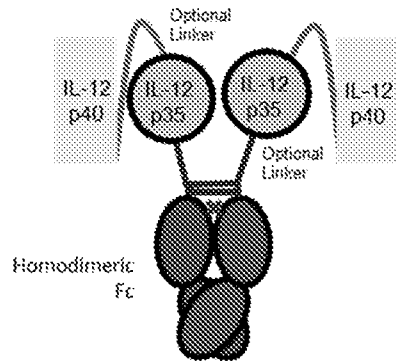


Figure 47

XENP	IL-12p40 Variant	IL-12p30 Variant	pSTAT4 EC50 (μg/ml)		FOLD DECREASE IN EC50	
			CD4+	CD8+	CD4+	CD8+
			CD45RA+	CD45RA+	CD45RA+	CD45RA+
			CD25+	CD25+	CD25+	CD25+
27201	WT	WT	0.2535	0.3516		
31250	E59Y/K99E	WT	4.767	6.049	18.80	17.20
31251	E59K/K99Y	WT	2.383	2.751	9.40	7.82
31252	E59Y/K99Y	WT	0.8014	1.037	3.16	2.95
31253	E45K/E59K/K99E	WT	8.04	7.157	31.72	20.36
31254	D18K/E59K/K99E	WT	17.75	21.89	70.02	62.26
31255	E59K/K99E/Q144E	WT	4.581	5.638	18.07	16.04
31256	E59K/K99E/Q144K	WT	4.713	6.344	18.59	18.04
31257	E59K/K99E/R159E	WT	5.084	6.481	20.06	18.43
31258	E59K/K99E/K264E	WT	24.15	20.38	95.27	57.96
31259	E59K/K99E	F96A	5.822	6.153	22.97	17.50
31260	E59K/K99E	M97A	4.431	4.729	17.48	13.45
31261	E59K/K99E	L89A	4.067	5.22	16.04	14.85
31262	E59K/K99E	L124A	3.102	4.657	12.24	13.25
31263	E59K/K99E	M125A	11.99	11.7	47.30	33.28
31264	E59K/K99E	L75A	4.112	4.49	16.22	12.77
31265	E59K/K99E	I171A	2.897	3.565	11.43	10.14

Figure 48A

A)

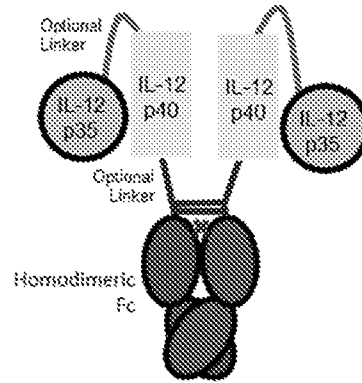


(scIL-12(p40/p35))₂-Fc

Example: XENP31289

Figure 48B

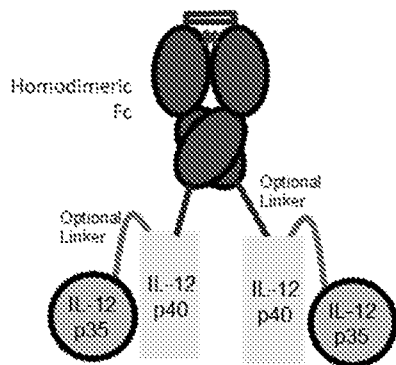
B)



(scIL-12(p35/p40))₂-Fc

Figure 48C

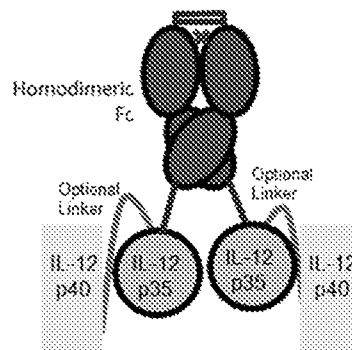
C)



Fc-(scIL-12(p40/p35))₂

Figure 48D

D)



Fc-(scIL-12(p35/p40))₂

Figure 49

**>XENP31289 human IL12p40 (GGGGS)5-human IL12p35 (GGGGS)2 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/GGGGSGGGGS
GGGGSGGGSGGGGS/RNLPVATPDPGMFPCLLHHSQNLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEA
CLPLELTKNESCLNSRETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNNMLAVID
ELMQALNFNSETVPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPC
PAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGGQP
ENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: XXX)

**>XENP31291 human IL12p40(E59K/K99E) (GGGGS)5-human IL12p35 (GGGGS)2 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/GGGGSGGGGS
GGGGSGGGSGGGGS/RNLPVATPDPGMFPCLLHHSQNLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEA
CLPLELTKNESCLNSRETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNNMLAVID
ELMQALNFNSETVPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPC
PAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGGQP
ENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: XXX)

Figure 50

>XENP31290 human IL12p40(E59K/K99E) (GGGGS)5-human IL12p35 (GGGGS)2 (single-chain)-empty-Fc Fc(216) IgG1 pl(-) Isosteric A C220S/PVA /S267K/L368D/K370S-Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 - human_IL12p40(E59K/K99E)_(GGGGS)5-human_IL12p35_(GGGGS)2_(single-chain)_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSHS
 LLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
 GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
 WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/GGGGSGGGGS
GGGGSGGGGS/RNLPVATPDPGMFCLHHSQNLRAVSNNMLQKARQTLEFYPCTSEEIDHEDITKDKTSTVEA
 CLPLELTKNESCLNSRETSFITNGSCLASRKTSFMMALCLSSIEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNNMLAVID
 ELMQALNFNSETVPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPC
 PAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
 HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGGQP
 ENNYKTTTPVLDSGDSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 - empty-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREE
 QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFY
 PSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 51A

A)

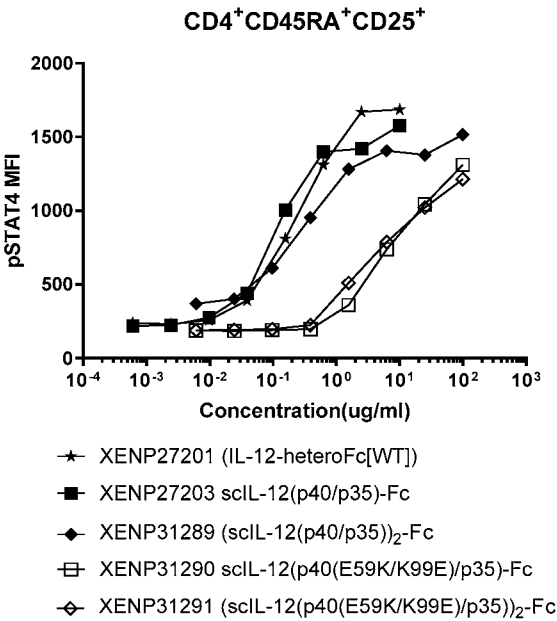


Figure 51B

B)

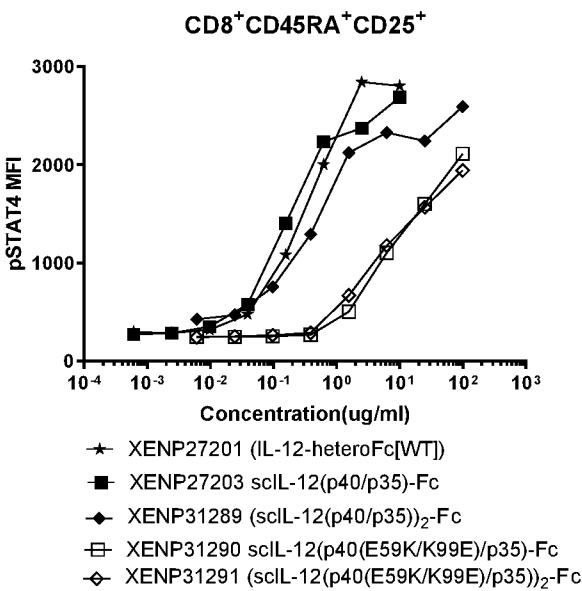


Figure 51C

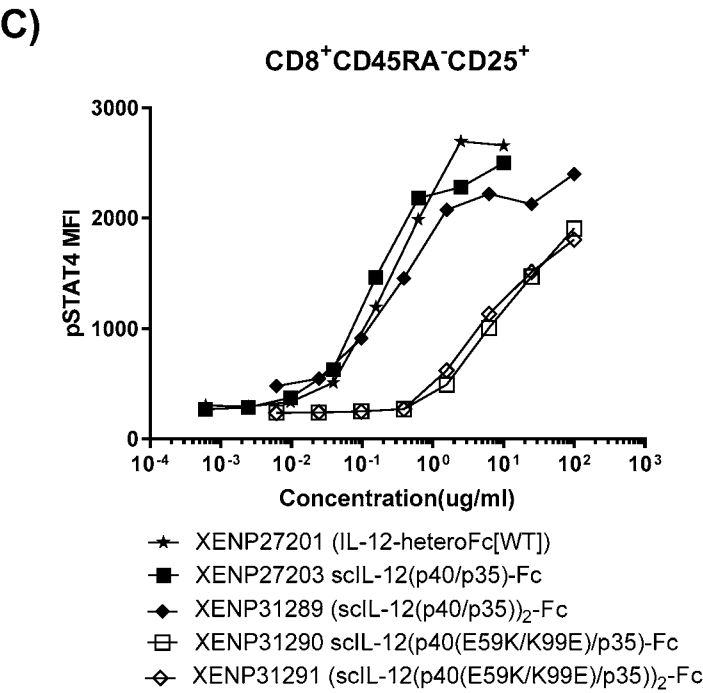


Figure 51D

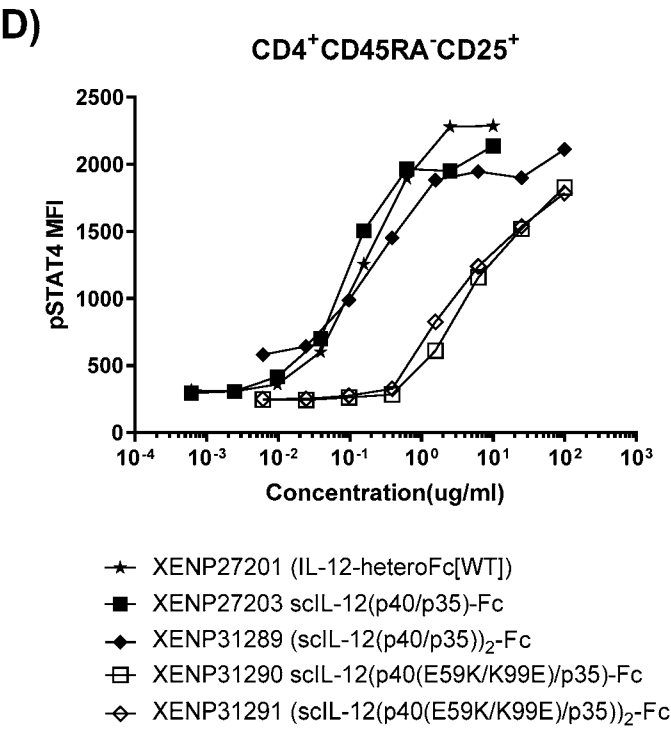


Figure 52

				pSTAT4 EC50 (μg/ml)	
XENP	Format	IL-12p40 Variant	IL-12p30 Variant	CD4+	CD8+
				CD45RA+	CD45RA+
				CD25+	CD25+
27201	IL-12-heteroFc	WT	WT	0.2535	0.3516
27203	scIL-12(p40/p35)-Fc	WT	WT	0.1205	0.1743
31289	(scIL-12(P40/P35))2-Fc	WT	WT	0.3151	0.4397
31290	scIL-12(p40/p35)-Fc	E59K/K99E	WT	8.005	9.459
31291	(scIL-12(P40/P35))2-Fc	E59K/K99E	WT	4.241	5.549

Figure 53

> XENP016432 Nivolumab_H0L0_IgG1_PVA_/S267K

XENP016432 Nivolumab_H0L0_IgG1_PVA_/S267K Heavy Chain

QVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAVIWDGSKRYYADSVKGRFTISRDN
NTLFLQMNSLRAEDTAVYYCATNDDYWGQGLTVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP
VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCP
PCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR
VVSIVLTQVQLDQSLSPGERATLSCASQSVSSYLAWYQQKPGQAPRLIYDASNRATGIPARFSGSGSGTDFTL
TISILEPEDFAVYYCQQSSNWPRTFGQGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPR
EAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
(SEQ ID NO: XXX)

XENP016432 Nivolumab_H0L0_IgG1_PVA_/S267K Light Chain

EIVLTQSPATLSLSPGERATLSCASQSVSSYLAWYQQKPGQAPRLIYDASNRATGIPARFSGSGSGTDFTL
TISILEPEDFAVYYCQQSSNWPRTFGQGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPR
EAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
(SEQ ID NO: XXX)

Figure 54A

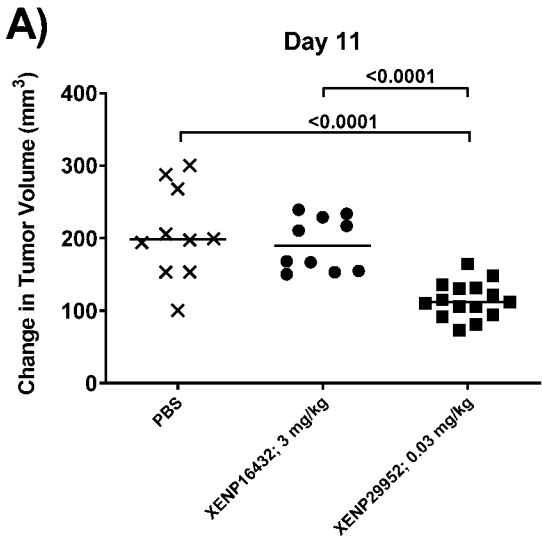


Figure 54B

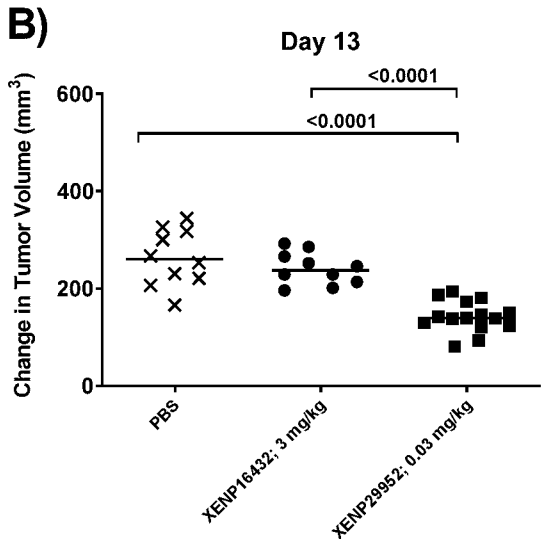


Figure 54C

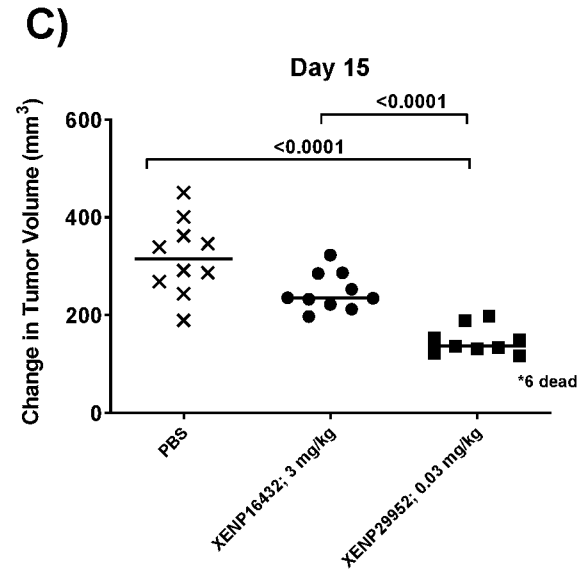


Figure 54D

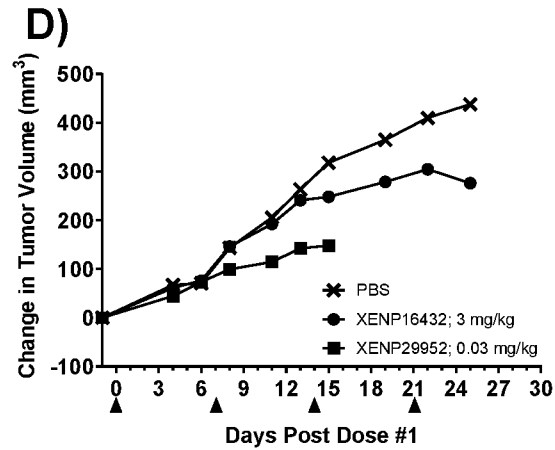


Figure 55A

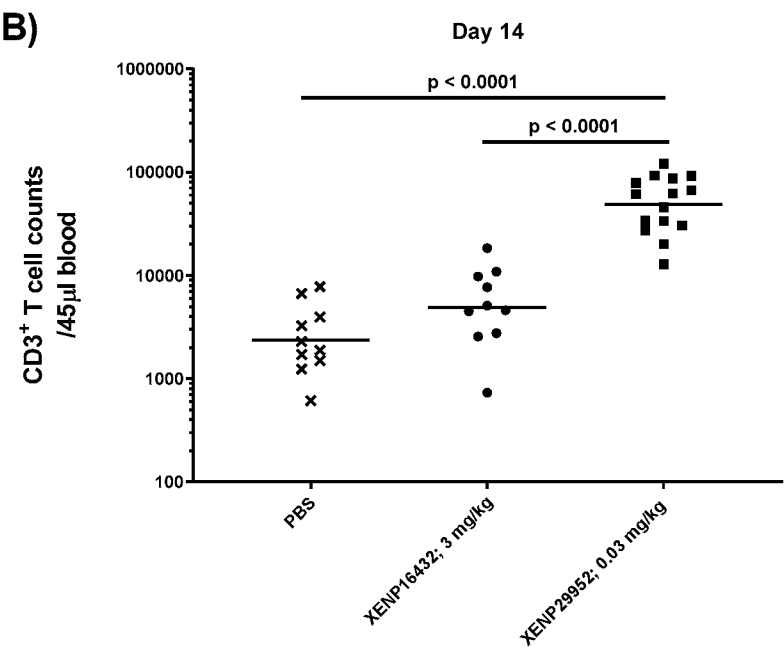


Figure 55B

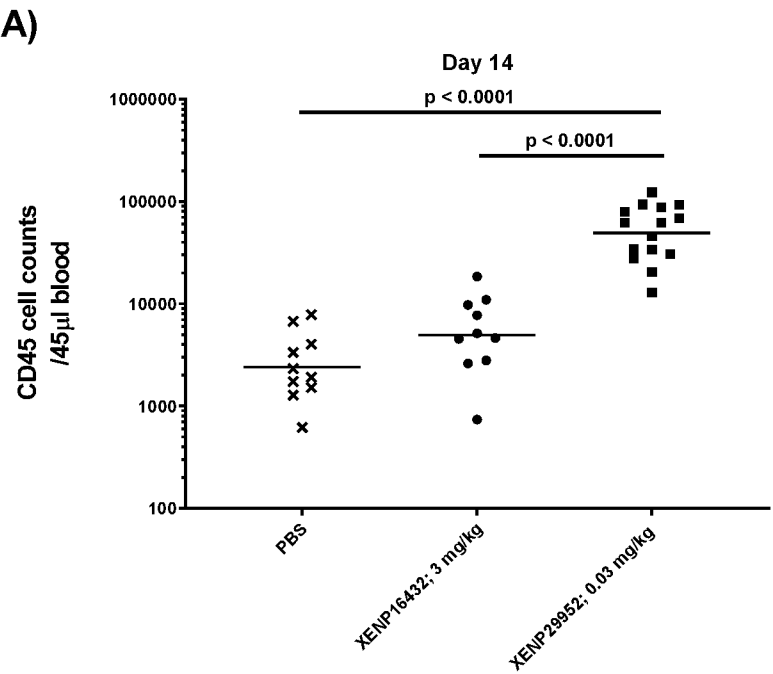


Figure 55C

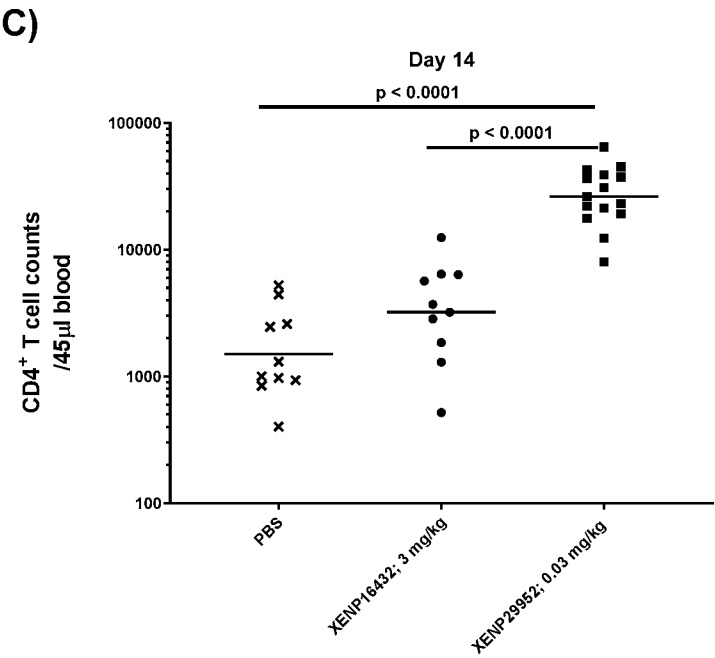


Figure 55D

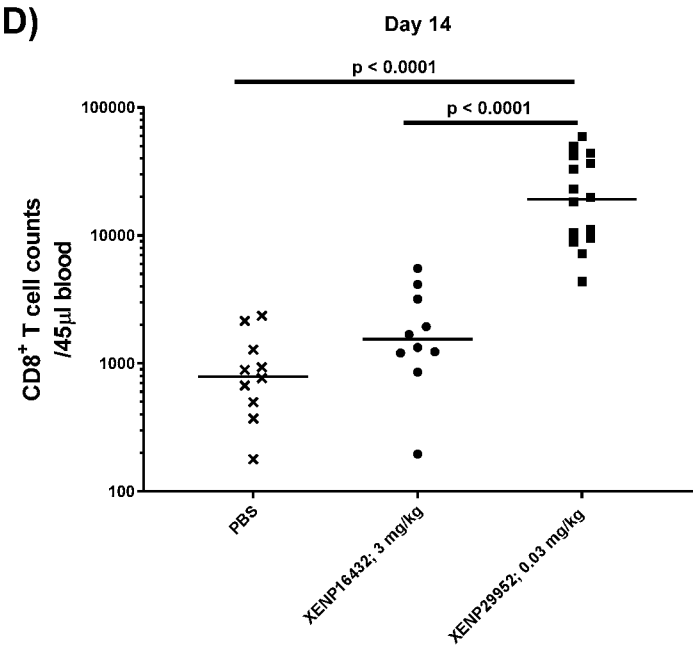


Figure 55E

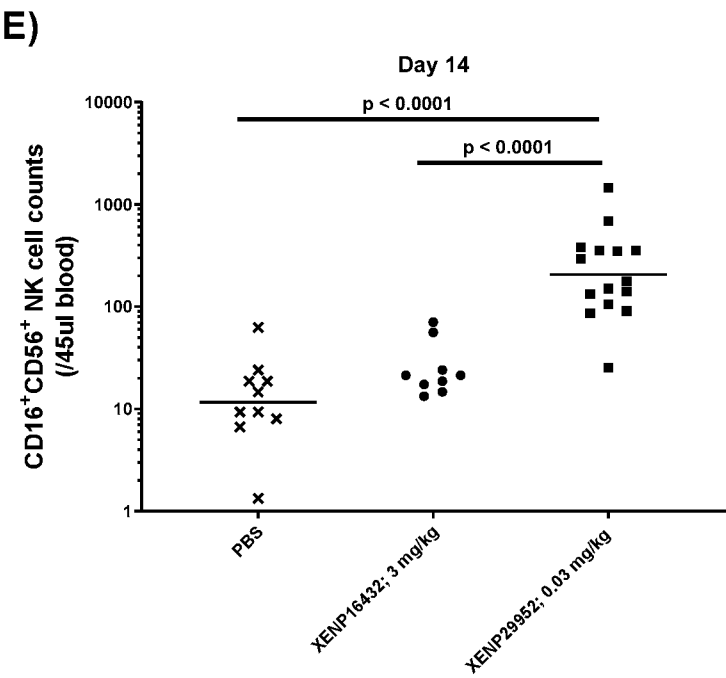


Figure 55F

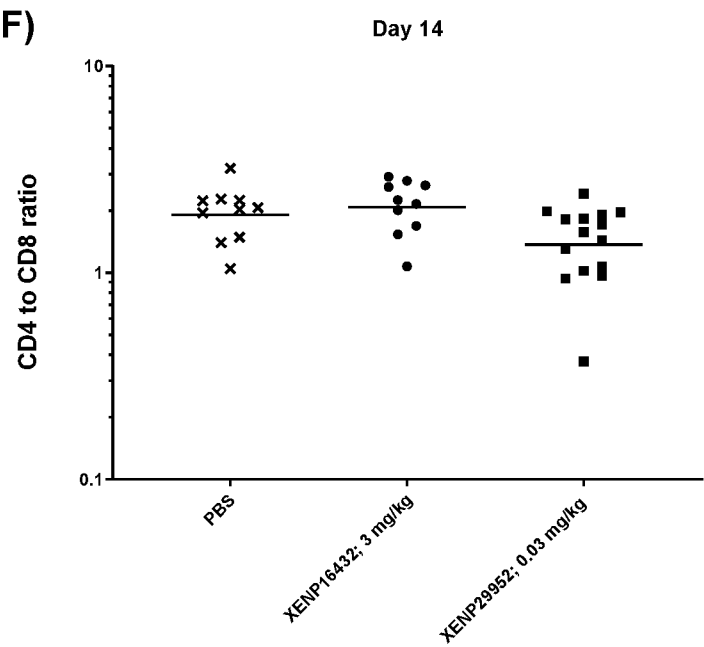


Figure 56A

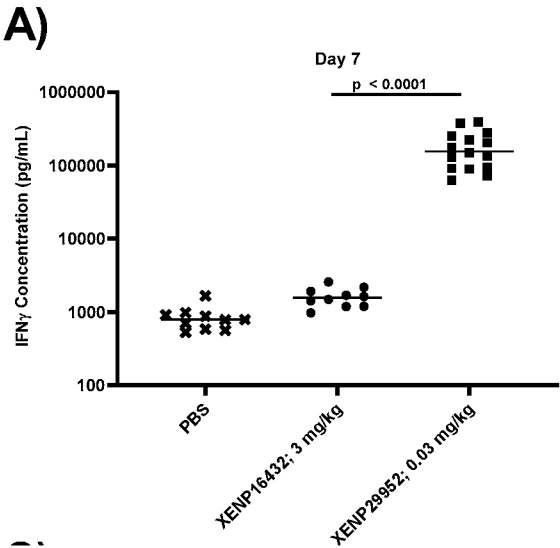


Figure 56B

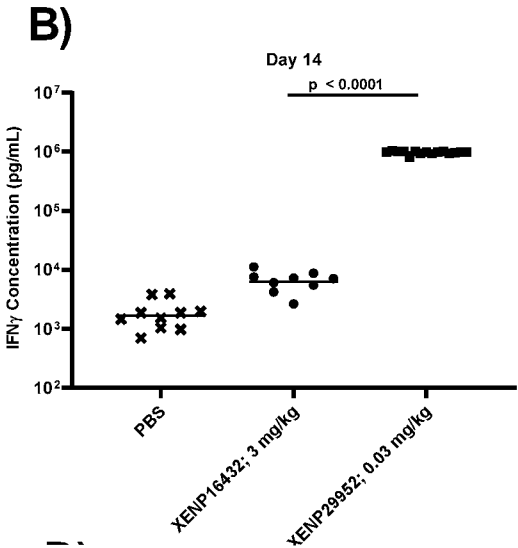


Figure 56C

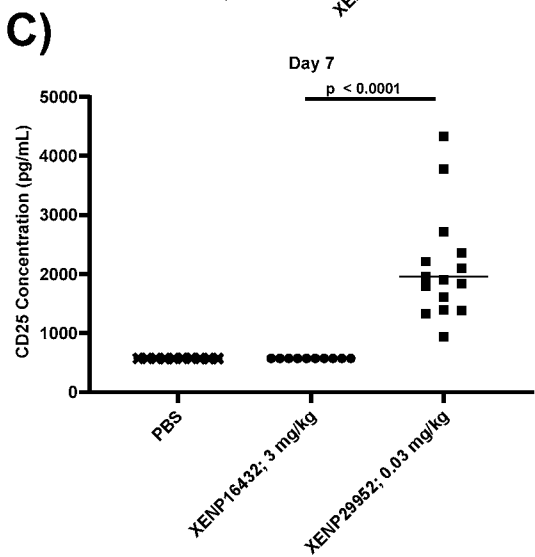


Figure 56D

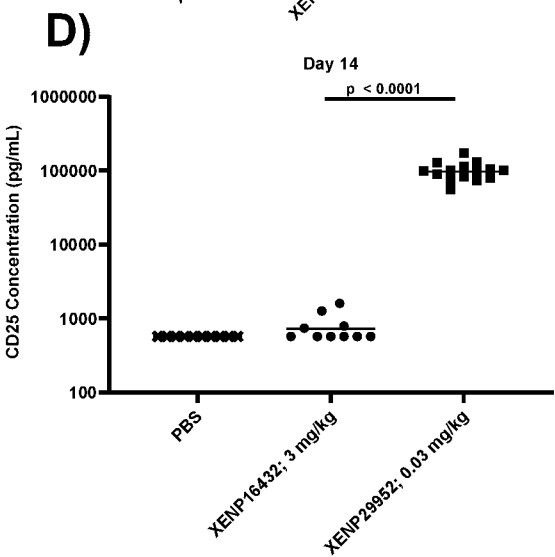


Figure 57A

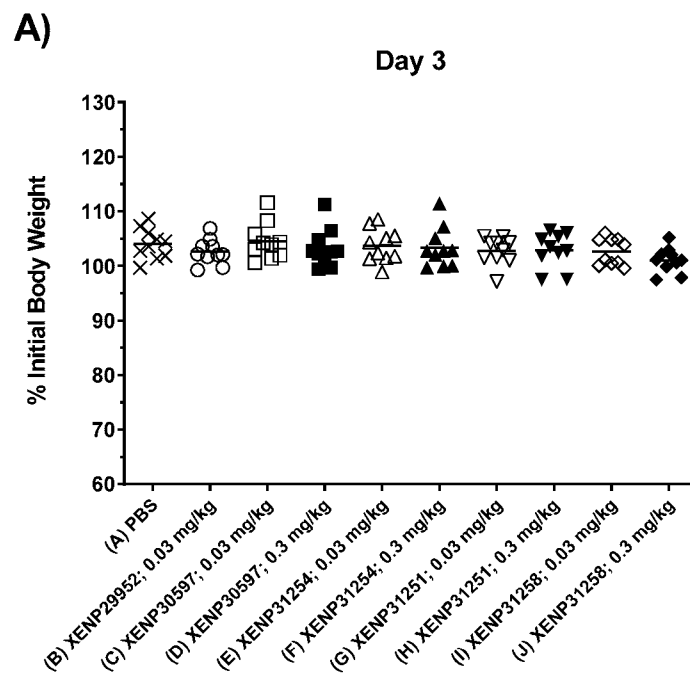


Figure 57B

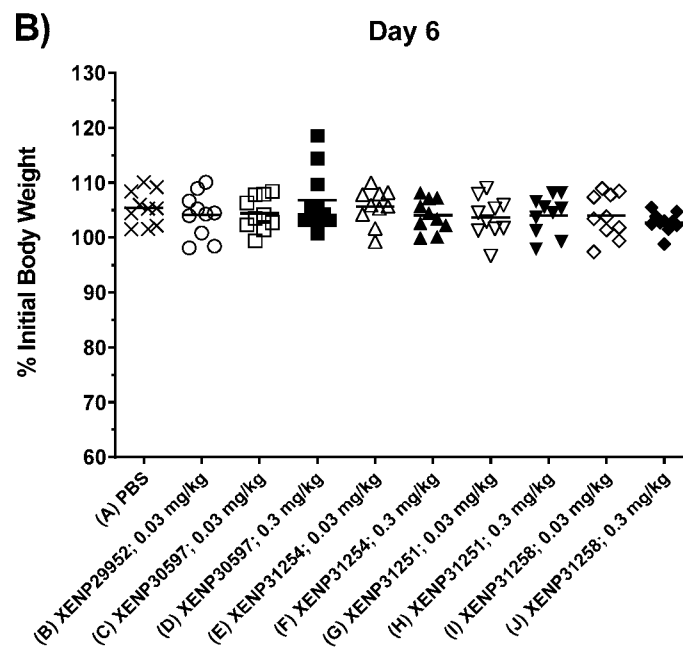


Figure 57C

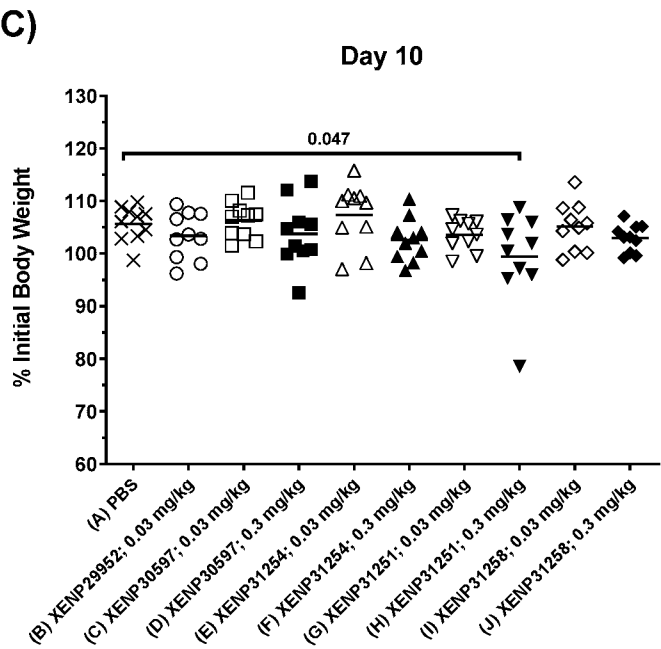


Figure 57D

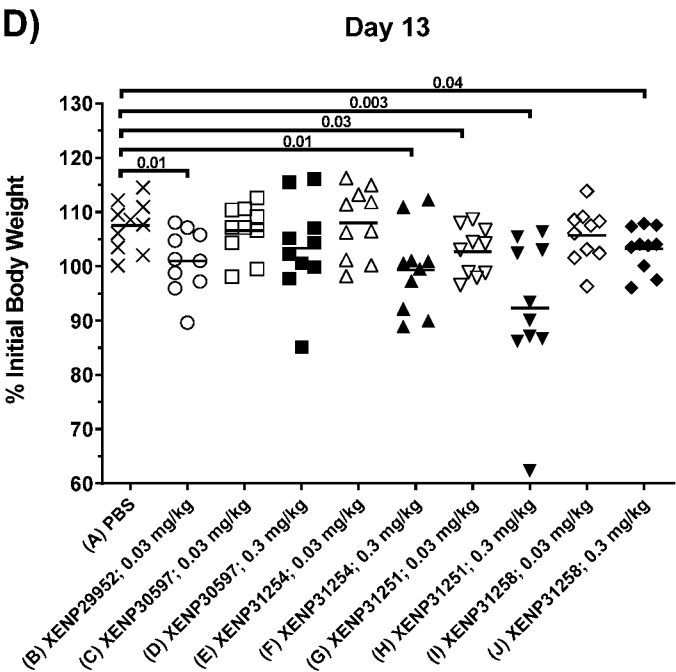


Figure 57E

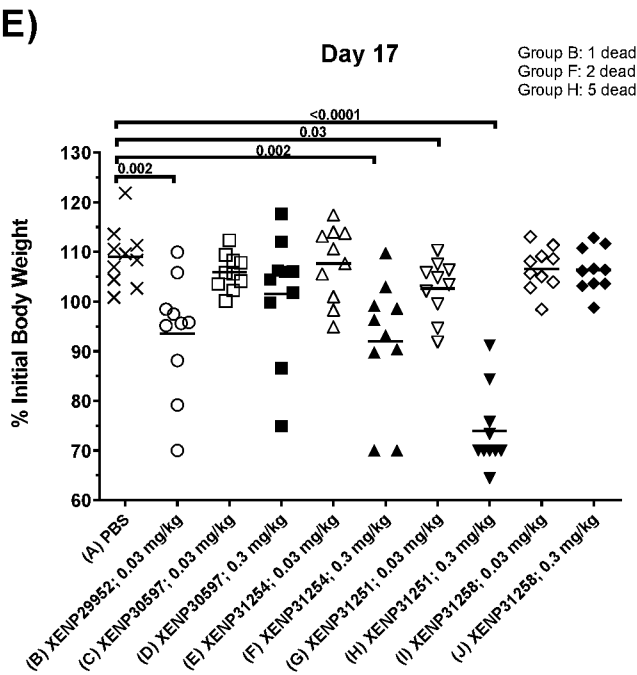


Figure 57F

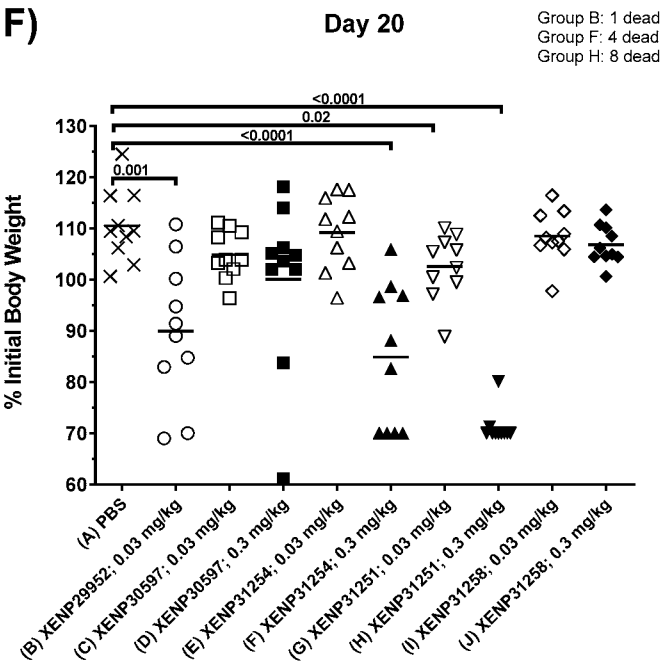


Figure 57G

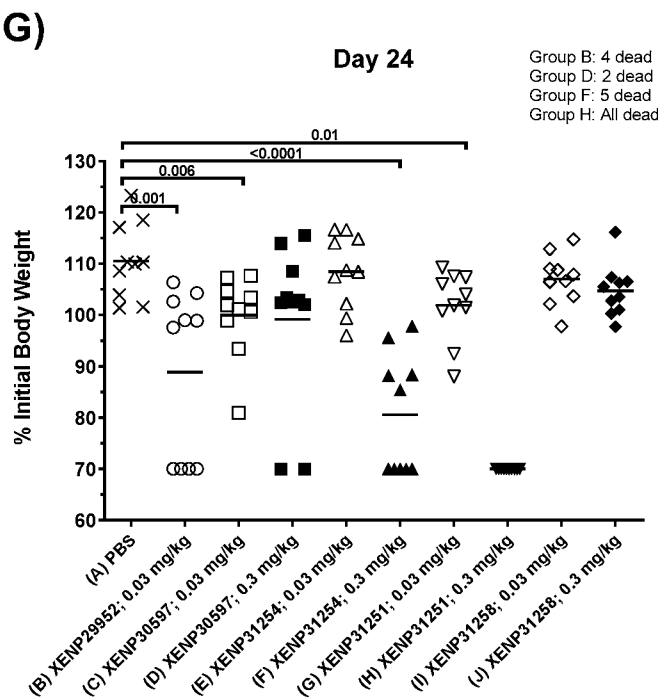


Figure 57H

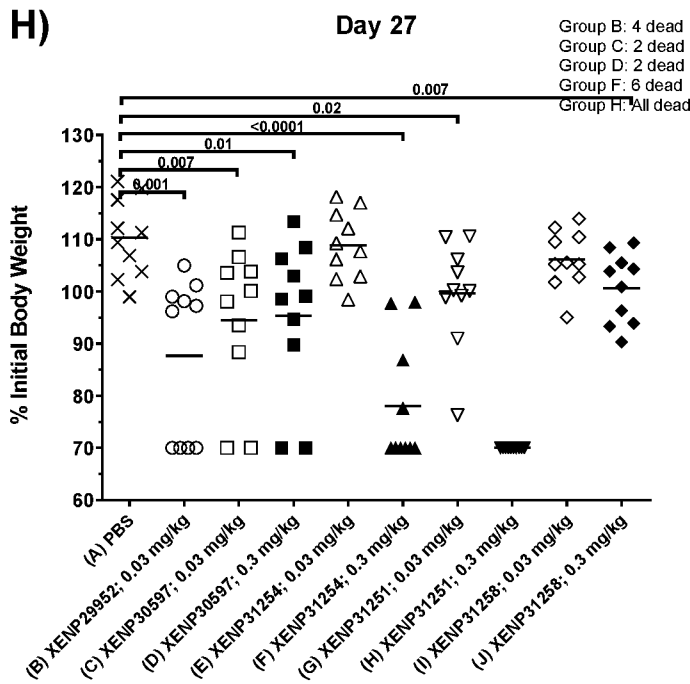


Figure 571

I)

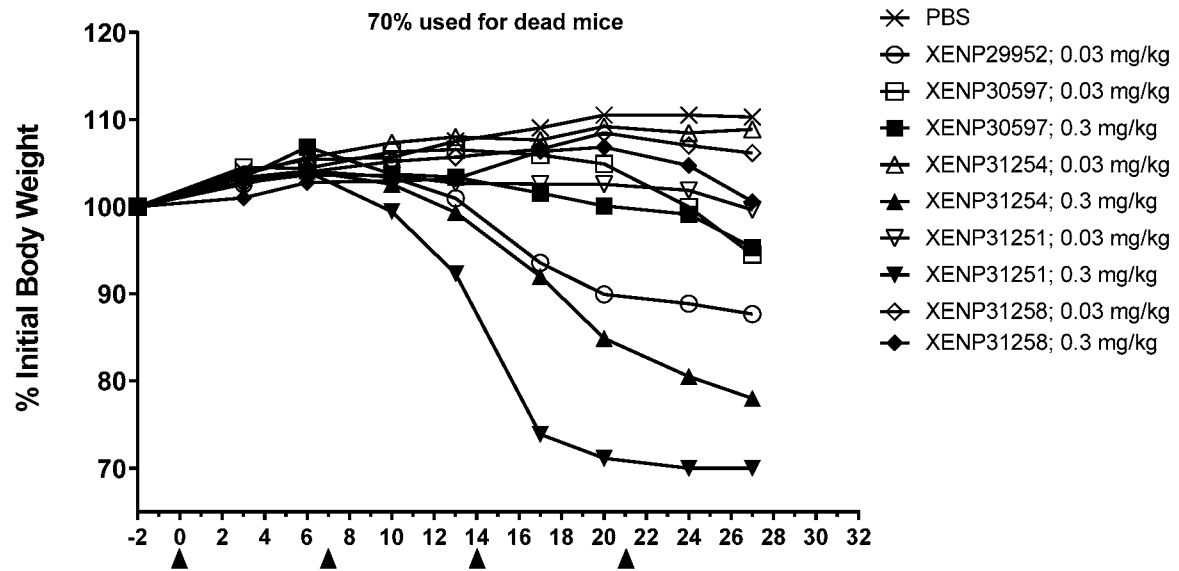


Figure 58A

Figure 58B

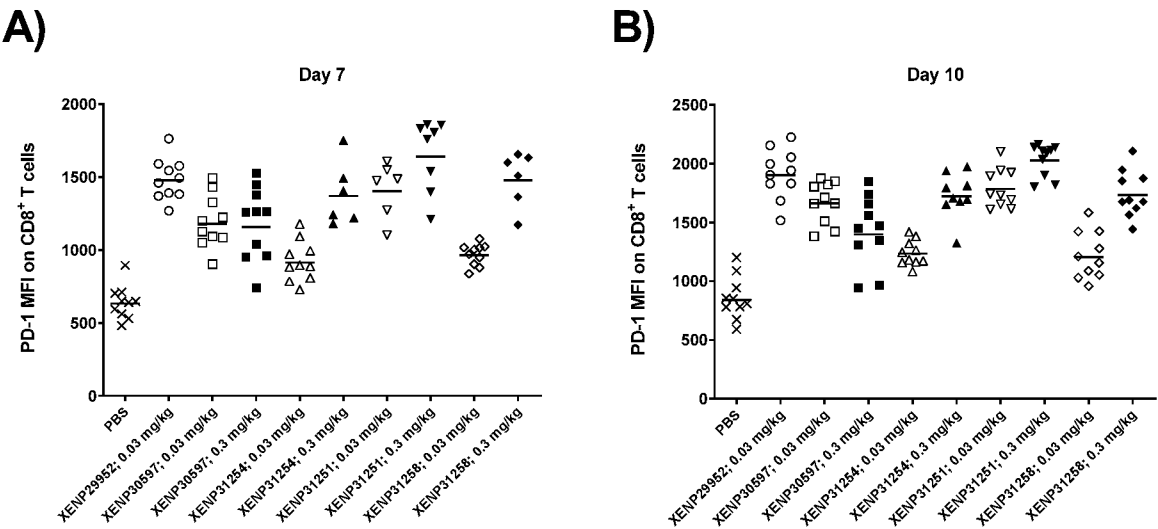


Figure 58C

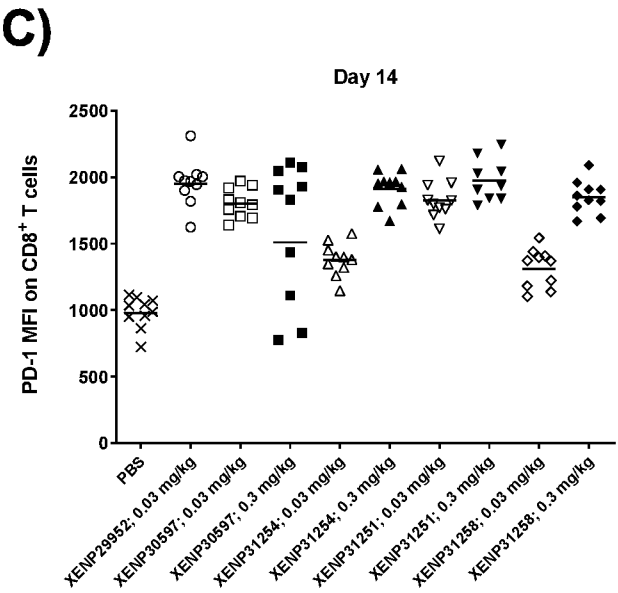


Figure 59A

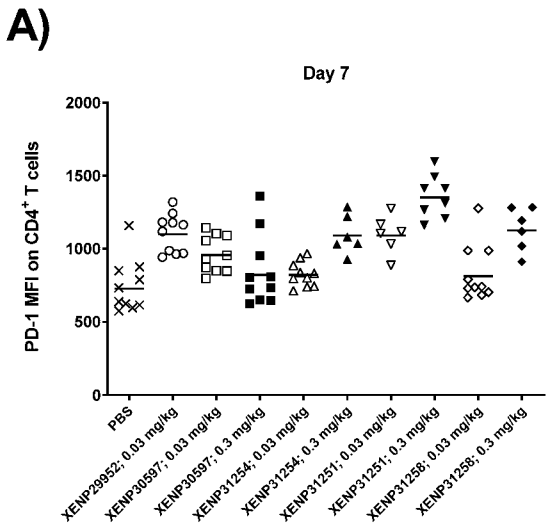


Figure 59B

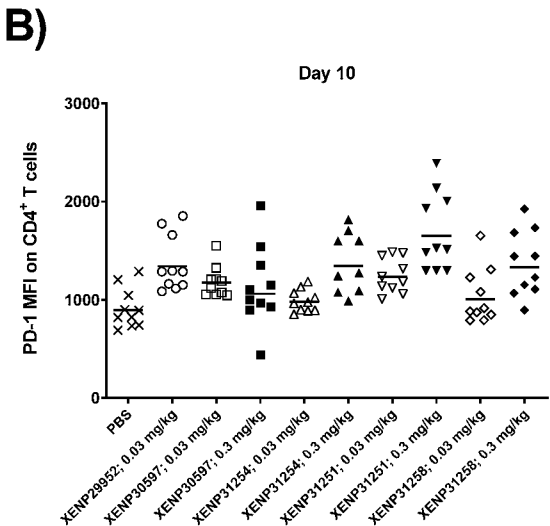


Figure 59C

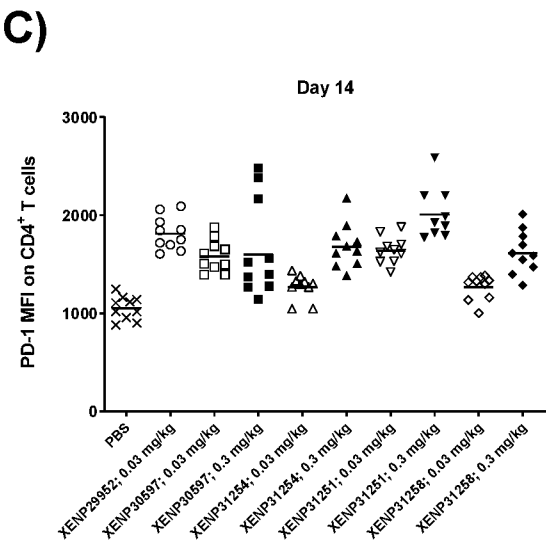


Figure 60A

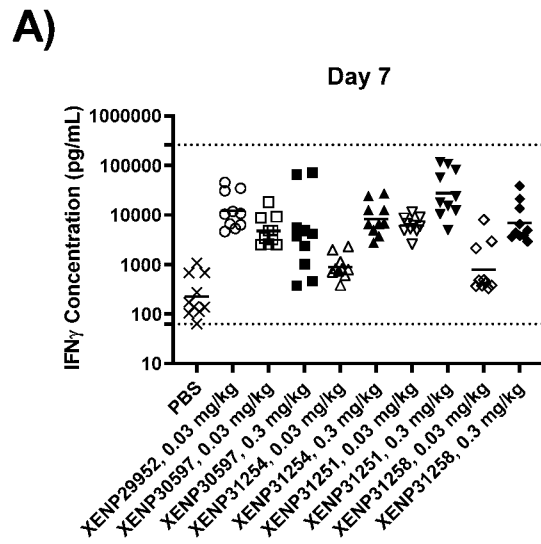


Figure 60B

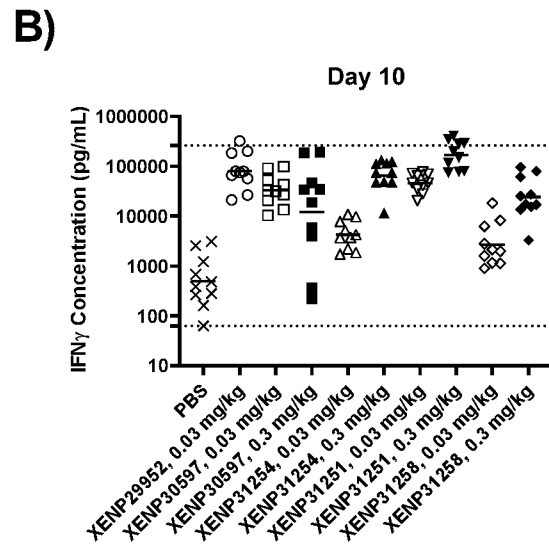


Figure 60C

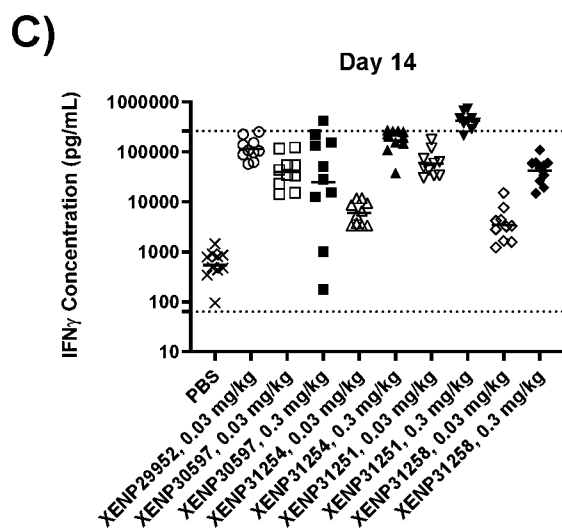


Figure 60D

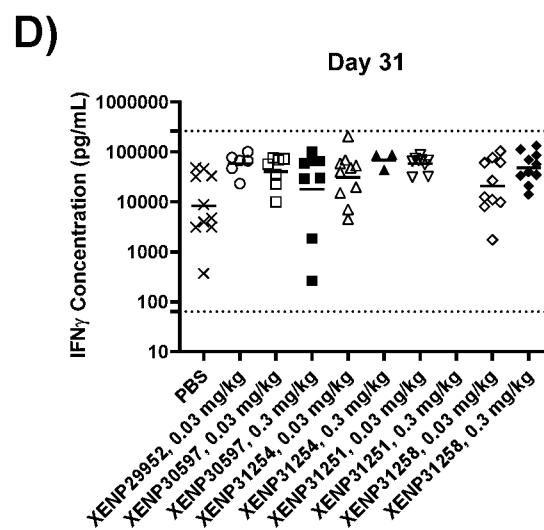


Figure 61A

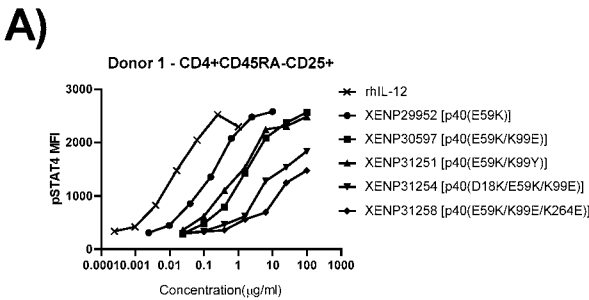


Figure 61C

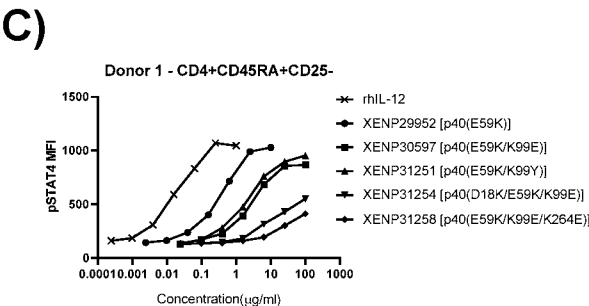


Figure 61E

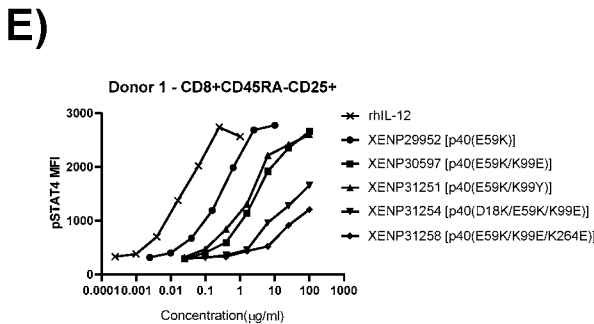


Figure 61B

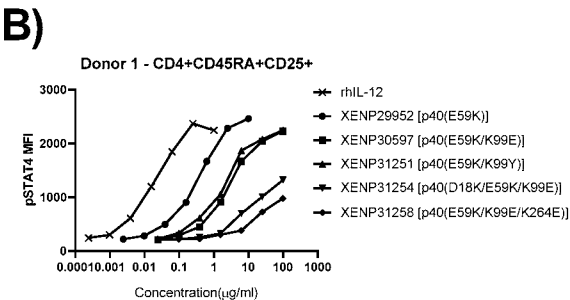


Figure 61D

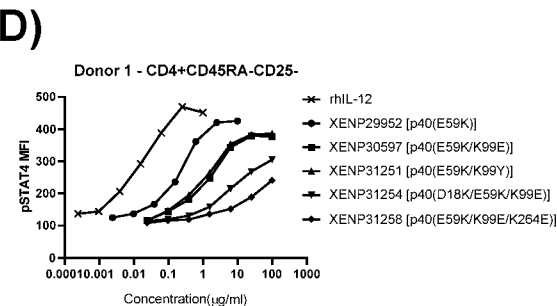


Figure 61F

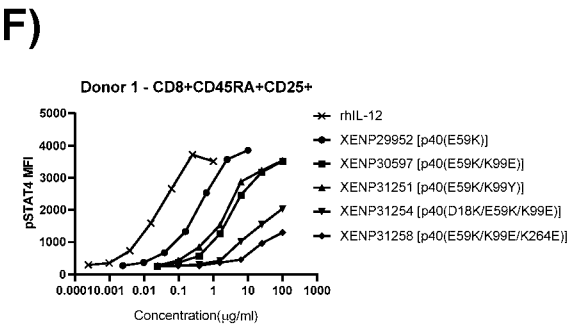
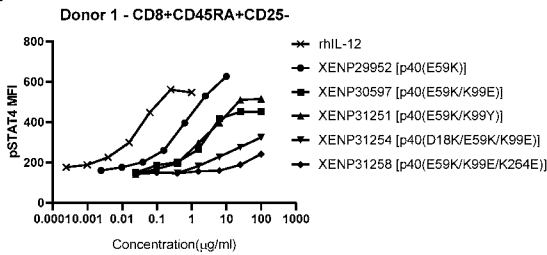


Figure 61G

Figure 61H

G)



H)

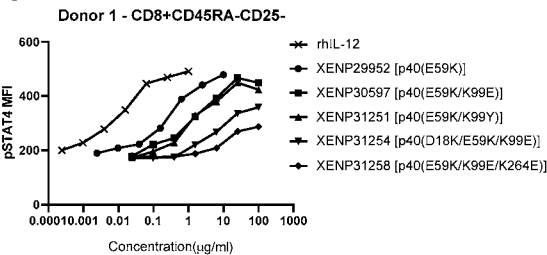
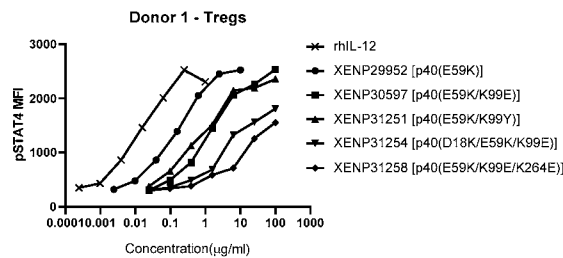


Figure 61I

Figure 61J

I)



J)

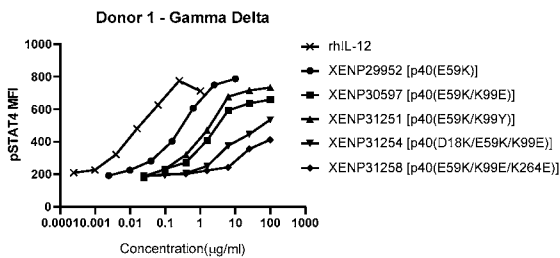


Figure 61K

K)

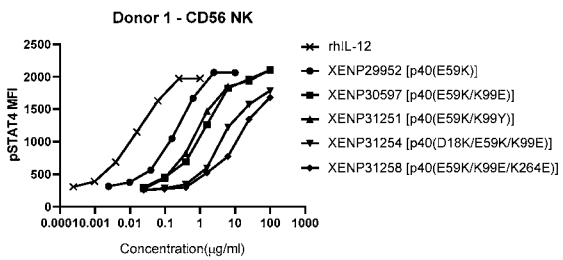


Figure 62A

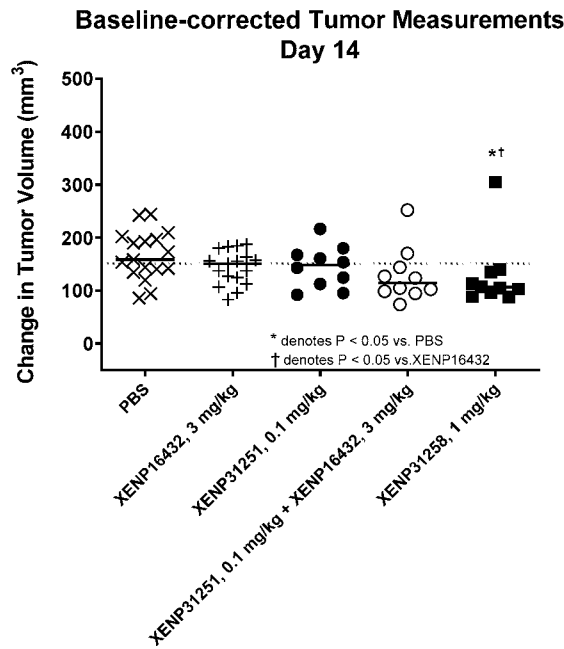


Figure 62B

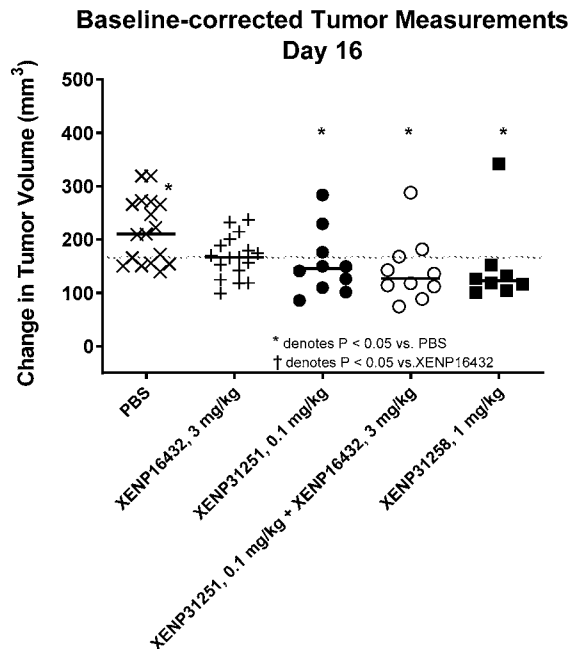


Figure 62C

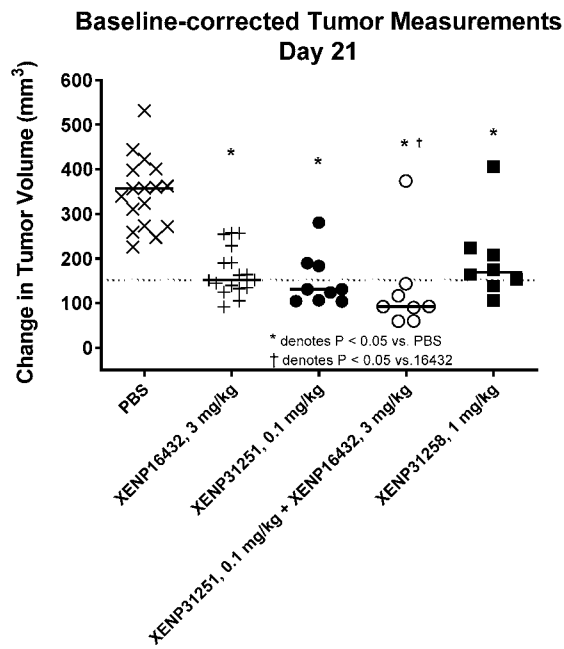


Figure 62D

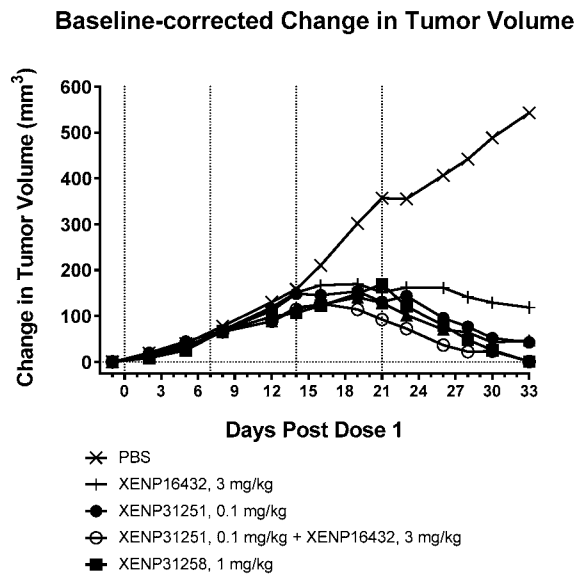


Figure 63A

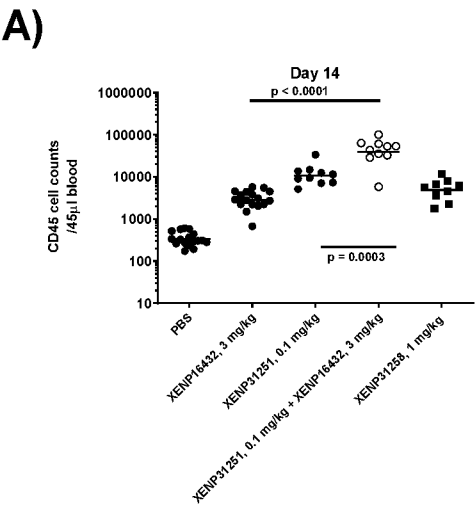


Figure 63B

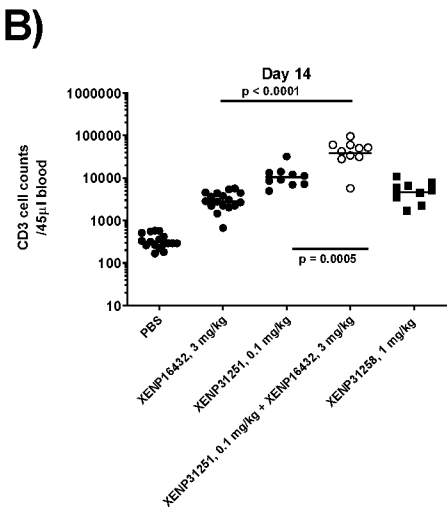


Figure 63C

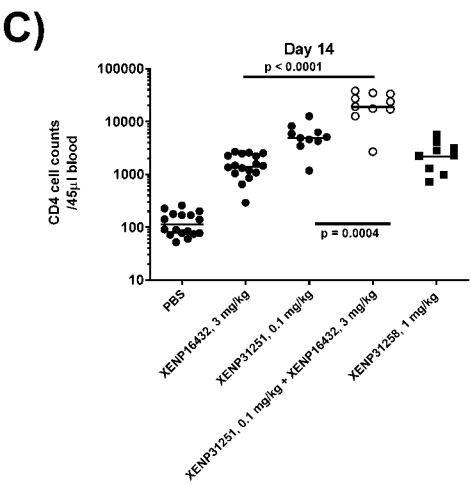


Figure 63D

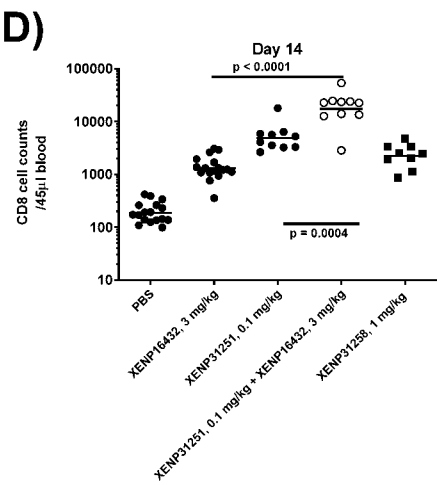


Figure 63E

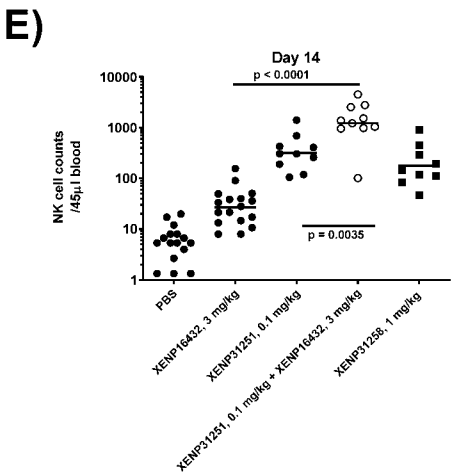


Figure 63F

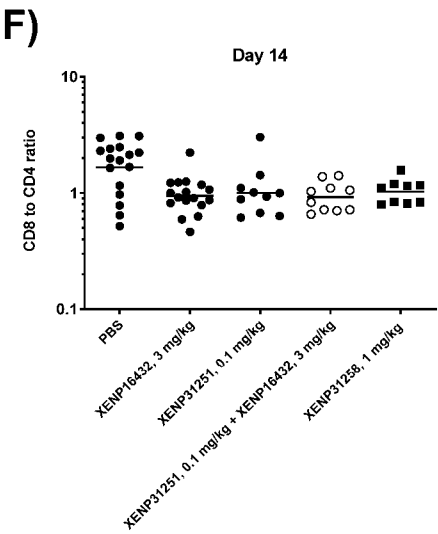


Figure 64A

>XENP31582 human IL12p40(D18K/E59K/K99E) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S/M428L/N434S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL12p40(D18K/E59K/K99E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S

IWELKKDVYVVELDWYPKAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/GGGGSGGGGS/
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEE
YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
DIAVEWESDGGQPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK (SEQ ID
NO: XXX)

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q/M428L/N434S

RNLPVATPDPMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNSRET
SFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSETVPQK
SSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPK
KDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS
NKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGGS
FFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK (SEQ ID NO: XXX)

Figure 64B

>XENP31583 human IL12p40(E59K/K99Y) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S Fc(216) IgG1_C220S/PVA_/S267K/S3
64K/E357Q/M428L/N434S

Chain 1 - human_IL12p40(E59K/K99Y)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQYEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
GDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/GGGGSGGGGS/
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEE
YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
DIAVEWESDGGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSVLHEALHSHYTQKSLSLSPGK (SEQ ID
NO: XXX)

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q/M428L/N434S

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNSRET
SFITNGSCLASRKTSFMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM LAVIDELMQALNFNSETVPQK
SSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPK
KDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS
NKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGS
FFLYSKLTVDKSRWQQGNVFCSVLHEALHSHYTQKSLSLSPGK (SEQ ID NO: XXX)

Figure 64C

>XENP31584 human IL12p40(E59K/K99E/K264E) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S/M428L/N434S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL12p40(E59K/K99E/K264E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/GGGGS/EPKSSDKTHTCP
PCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLT
VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTTPVLDSGSGFFLYSKLTVDKSRWEQGDVFCVSVLHEALHSHYTQKSLSLSPGK (SEQ ID NO: XXX)

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q/M428L/N434S

RNLPVATPDPMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNSRET
SFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSETVPQK
SSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRT
PEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKT
ISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGSGFFLYSKLTVDK
SRWQQGNVFCVSVLHEALHSHYTQKSLSLSPGK (SEQ ID NO: XXX)

Figure 65A

> IL-12p40(C252S)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS
(SEQ ID NO: XXX)

> IL-12p40(D18K/E59K/K99E/C252S)

IWELKKDVYVVELDWYPKAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS
(SEQ ID NO: XXX)

> IL-12p40(D18K/E59K/K99E/C252S/K264E)

IWELKKDVYVVELDWYPKAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS
(SEQ ID NO: XXX)

> IL-12p40(E59K/K99Y/C252S)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQYEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS
(SEQ ID NO: XXX)

> IL-12p40(E59K/K99E/C252S/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS
(SEQ ID NO: XXX)

> IL-12p40(E59K/K99E/C252S)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS
(SEQ ID NO: XXX)

Figure 65B

>IL-12p40 (E59K/K99E/N103Q/C252S/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQTLFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N113Q/C252S/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTLFLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N200Q/C252S/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTLFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N281Q/C252S/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTLFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N103Q/N113Q/C252S/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQTLFLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N103Q/N200Q/C252S/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQTLFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N103Q/N281Q/C252S/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQTLFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: XXX)

Figure 65C

>IL-12p40 (E59K/K99E/N113Q/N200Q/C252S/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKQYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (IL12p40_E59K/K99E/N113Q/N281Q/C252S/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKQYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N200Q/N281Q/C252S/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N103Q/N113Q/N200Q/C252S/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKQYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N103Q/N200Q/N281Q/C252S/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N113Q/N200Q/N281Q/C252S/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKQYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N103Q/N113Q/N200Q/N281Q/C252S/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKQYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: XXX)

Figure 66A

**>XENP32187 human IL12p40(D18K/E59K/K99E/C252S) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 - human_IL12p40(D18K/E59K/K99E/C252S)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPKAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 - IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPLHHSQNLLRAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

**>XENP32188 human IL12p40(D18K/E59K/K99E/C252S/K264E) (GGGGS)2-human IL12p35 (GGGGS)2-
Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 - human_IL12p40(D18K/E59K/K99E/C252S/K264E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPKAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 - IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPLHHSQNLLRAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 66B

**>XENP32189 human IL12p40(E59K/K99Y/C252S) (GGGGGS)2-human IL12p35 (GGGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 - human_IL12p40(E59K/K99Y/C252S)_(GGGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGGEVLSH
 SLLLLHKKEDGIWSTDILKDQYEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVECDQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/_G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCSVMEALHNHYT
 QKSLSLSPGK (SEQ ID NO: XXX)*

Chain 2 - IL12p35_(GGGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

*RNLPVATPDPMFPCPLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/_GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO: XXX)*

**>XENP32190 human IL12p40(E59K/K99E/C252S/K264E) (GGGGGS)2-human IL12p35 (GGGGGS)2-
 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 - human_IL12p40(E59K/K99E/C252S/K264E)_(GGGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

*IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVECDQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/_G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCSVMEALHNHYT
 QKSLSLSPGK (SEQ ID NO: XXX)*

Chain 2 - IL12p35_(GGGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

*RNLPVATPDPMFPCPLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/_GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO: XXX)*

Figure 66C

**>XENP32191 human IL12p40(E59K/K99E/C252S) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 - human_IL12p40(E59K/K99E/C252S)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVECDQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWEQGDVDFSCSVMEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 - IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSGDSFFLYSKLTVDKSRWQQGNVDFSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

**>XENP32991 human IL12p40 E59K/K99E/N103Q/C252S/K264E (GGGGS)2-human IL12p35 (GGGGS)2-
 Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**> IL-12p40(E59K/K99E/N103Q/C252S/K264E_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVECDQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWEQGDVDFSCSVMEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSGDSFFLYSKLTVDKSRWQQGNVDFSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 66D

>XENP32992 human IL12p40 E59K/K99E/N113Q/C252S/K264E (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-

) _Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

> IL-12p40(E59K/K99E/N113Q/C252S/K264E_(GGGGS)2_Fc(216)_IgG1_pl(-

)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKQYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/_G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCSVMEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPLHHSQNLLRAVSNNLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNM LAVIDELMQALNFNSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/_GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVDFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

>XENP32993 human IL12p40 E59K/K99E/N200Q/C252S/K264E (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-

) _Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

> IL-12p40(E59K/K99E/N200Q/C252S/K264E_(GGGGS)2_Fc(216)_IgG1_pl(-

)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYEYQYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/_G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVDFSCSVMEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Figure 66E

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

**>XENP32994 human IL12p40 E59K/K99E/N281Q/C252S/K264E (GGGGS)2-human IL12p35 (GGGGS)2-
 Fc(216) IgG1 pl(-
)_Isosteric A C220S/PVA_/S267K/L368D/K370S Fc(216) IgG1 C220S/PVA_/S267K/S364K/E357Q**

**> IL-12p40(E59K/K99E/N281Q/C252S/K264E_(GGGGS)2_Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDQVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRGDNKEYEYSVEQCEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYSSSSWSEWASVPCS/_G
 GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

Figure 66F

>XENP32995 human IL12p40 E59K/K99E/N103Q/N113Q/C252S/K264E (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

> IL-12p40(E59K/K99E/N103Q/N113Q/C252S/K264E_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKQYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVVFSCSVMEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
 NKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

>XENP32996 human IL12p40 E59K/K99E/N103Q/N200Q/C252S/K264E (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

> IL-12p40(E59K/K99E/N103Q/N200Q/C252S/K264E_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVVFSCSVMEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Figure 66G

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

**>XENP32997 human IL12p40 E59K/K99E/N103Q/N281Q/C252S/K264E (GGGGS)2-human IL12p35 (GGGGS)2-
 Fc(216) IgG1 pl(-**

)_Isosteric A C220S/PVA_/S267K/L368D/K370S Fc(216) IgG1 C220S/PVA_/S267K/S364K/E357Q

> IL-12p40(E59K/K99E/N103Q/N281Q/C252S/K264E_(GGGGS)2_Fc(216)_IgG1_pl(-

)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYSSSSWSEWASVPCS/G
 _____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

Figure 66H

>XENP32998 human IL12p40 E59K/K99E/N113Q/N200Q/C252S/K264E (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

> IL-12p40(E59K/K99E/N113Q/N200Q/C252S/K264E_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKQYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYEQYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLARKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

>XENP32999 human IL12p40 E59K/K99E/N113Q/N281Q/C252S/K264E (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

> IL-12p40(E59K/K99E/N113Q/N281Q/C252S/K264E_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKQYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYEYNTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Figure 66l

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

**>XENP33000 human IL12p40 E59K/K99E/N200Q/N281Q/C252S/K264E (GGGGS)2-human IL12p35 (GGGGS)2-
 Fc(216) IgG1 pl(-**

) Isosteric A C220S/PVA_/S267K/L368D/K370S Fc(216) IgG1 C220S/PVA_/S267K/S364K/E357Q

> IL-12p40(E59K/K99E/N200Q/N281Q/C252S/K264E_(GGGGS)2_Fc(216)_IgG1_pl(-

) Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYEQYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

Figure 66J

**>XENP33001 human IL12p40 E59K/K99E/N103Q/N113Q/N200Q/C252S/K264E (GGGGS)2-
human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**> IL-12p40(E59K/K99E/N103Q/N113Q/N200Q/C252S/K264E_(GGGGS)2_Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKQYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPVEMVDAVHKLKYEQYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSHEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

**>XENP33002 human IL12p40 E59K/K99E/N103Q/N200Q/N281Q/C252S/K264E (GGGGS)2-
human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**> IL-12p40(E59K/K99E/N103Q/N200Q/N281Q/C252S/K264E_(GGGGS)2_Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPVEMVDAVHKLKYEQYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSHEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)

Figure 66K

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

**>XENP33003 human IL12p40 E59K/K99E/N113Q/N200Q/N281Q/C252S/K264E (GGGGS)2-
human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-
) Isosteric A C220S/PVA_/S267K/L368D/K370S Fc(216) IgG1 C220S/PVA_/S267K/S364K/E357Q**

**> IL-12p40(E59K/K99E/N113Q/N200Q/N281Q/C252S/K264E_(GGGGS)2_Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKQYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYSSSWSEWASVPCS/_G
____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

Figure 66L

**>XENP33004 human IL12p40 E59K/K99E/N103Q/N113Q/N200Q/N281Q/C252S/K264E (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**> IL-12p40(E59K/K99E/N103Q/N113Q/N200Q/N281Q/C252S/K264E_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQKTLRCEAKQYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVCSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 - human_IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG
KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

**>XENP33005 human IL12p40(E59K/K99E/C252S/K264E) (GGGGS)2-human IL12p35(N71Q) (GGGGS)2-
Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 - human_IL12p40(E59K/K99E/C252S/K264E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEYNTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVCSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)

Figure 66M

Chain 2 - human_IL12p35(N71Q)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKQESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNNMLAVIDELMQALNFNSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

**>XENP33006 human_IL12p40(E59K/K99E/C252S/K264E)_(GGGGS)2-human_IL12p35(N85Q)_(GGGGS)2-
 Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 - human_IL12p40(E59K/K99E/C252S/K264E)_(GGGGS)2_Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWWTITISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
 _____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 - human_IL12p35(N85Q)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITQGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNNMLAVIDELMQALNFNSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

Figure 66N

>XENP33007 human IL12p40(E59K/K99E/C252S/K264E) (GGGGS)2-human IL12p35(N195Q) (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 - human_IL12p40(E59K/K99E/C252S/K264E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVECDQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVSMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 - human_IL12p35(N195Q)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLQAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
 NKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVSMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

>XENP33008 human IL12p40(E59K/K99E/C252S/K264E) (GGGGS)2-human IL12p35(N71Q/N85Q) (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 - human_IL12p40(E59K/K99E/C252S/K264E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVECDQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVSMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Figure 66O

Chain 2 - human_IL12p35(N71Q/N85Q)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKQESCLNS
 RETSFITQGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

**>XENP33009 human_IL12p40(E59K/K99E/C252S/K264E)_(GGGGS)2-human_IL12p35(N71Q/N195Q)_(GGGGS)2-
 Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q**

**Chain 1 - human_IL12p40(E59K/K99E/C252S/K264E)_(GGGGS)2_Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDQVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
 GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 - human_IL12p35(N71Q/N195Q)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKQESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLQAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

Figure 66P

>XENP33010 human IL12p40(E59K/K99E/C252S/K264E) (GGGGS)2-human IL12p35(N85Q/N195Q) (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 - human_IL12p40(E59K/K99E/C252S/K264E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECDQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSVHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 - human_IL12p35(N85Q/N195Q)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITQGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLQAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG
 KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSVHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

>XENP33011 human IL12p40(E59K/K99E/C252S/K264E) (GGGGS)2-
human IL12p35(N71Q/N85Q/N195Q) (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 - human_IL12p40(E59K/K99E/C252S/K264E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECDQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSVHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Figure 66Q

Chain 2 - human_IL12p35(N71Q/N85Q/N195Q)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKQESCLNS
RETSFITQGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLQAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

Figure 67A

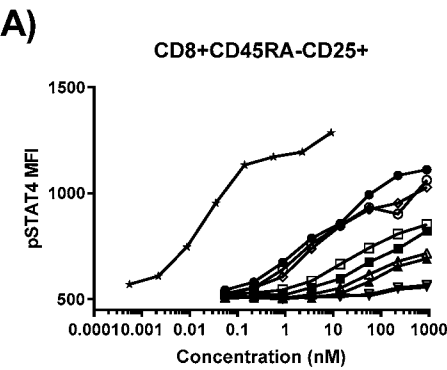


Figure 67B

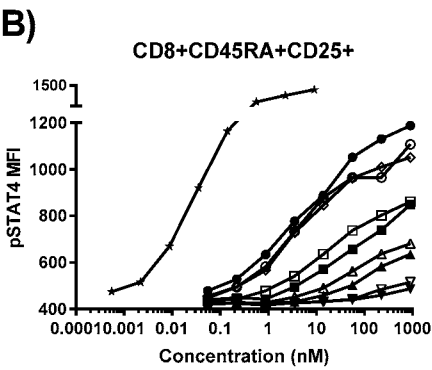


Figure 67C

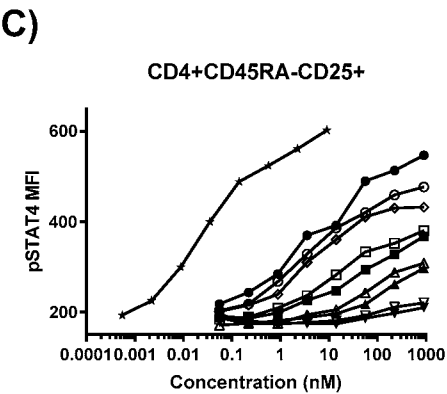


Figure 67C

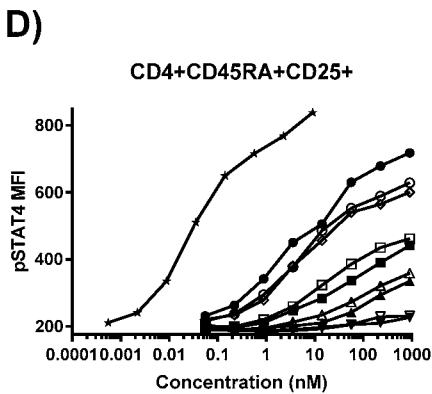
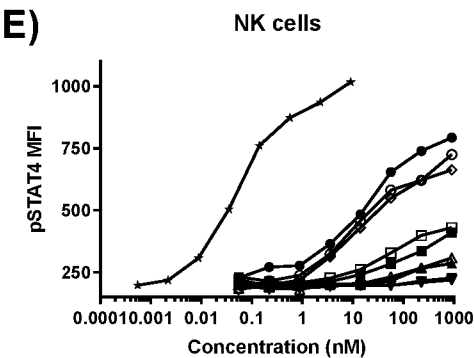


Figure 67D



Open symbols: C252S

- XENP27201 [WT]
- XENP31251 [p40(E59K/K99Y)]
- XENP31254 [p40(D18K/E59K/K99E)]
- XENP31258 [p40(E59K/K99E/K264E)]
- XENP32186 [p40(D18K/E59K/K99E/K264E)]
- XENP32187 [p40(D18K/E59K/K99E/C252S)]
- XENP32188 [p40(D18K/E59K/K99E/C252S/K264E)]
- XENP32189 [p40(E59K/K99Y/C252S)]
- XENP32190 [p40(E59K/K99E/C252S/K264E)]
- XENP32191 [p40(E59K/K99E/C252S)]