

Figure 1A

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

>sp|P29459

MCPARSLLVATLVLLDHLNLPVATPDPMFCLHHSQNLLRAVSNMLQKARQTLEFYPTCTSEEDHEDITKD
KTSTVEACLPLELTKNESCLNSRETSFITNGSCLASRKTSMFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIF
LDQNMLAVIDELMQALNFNSETVPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

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

>sp|P29459|23-219

RNLPVATPDPMFCLHHSQNLLRAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSMFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

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

>sp|P29460

MCHQQQLVISWFSVLFLASPLVAIWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTI
QVKEFGDAGQYTCHKGGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTF
SVKSSRGSSDPQGVTCGAATLSAERVRGDNKEYEYSVECCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSFFIRD
IIKPDPPKNLQKPLKNSRQVEVSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISV
RAQDRYSSSWSEWASVPCS

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

>sp|P29460|23-328

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVECCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSFFIRDIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

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

>sp|P42701

MEPLVTWVPLFLFLLSRQGAACRTSECCFQDPYPADSGSASGPRDLRCYRISSDRYECWSQYEGPTAGVSHFL
RCCLSSGRCCYFAAGSATRLQFSDQAGVSVLYTVTLWVESWARNQTEKSPEVTLQLYNSVKYEPPLGDIKVSCLAGQ
LRMEWETPDNQVGAEVQFRHRTSPSPWKLGDGCGPQDDDTESCLCLEMNVAQEFQLRRRQLGSQGSWSKWSPPVCV
PPENPPQPQVRFSVEQLGQDGRRLTLKEQPTQLELPEGCQGLAPGTEVTYRLQLHMLSCPCAKATRTHLHGKMPY
LSGAAYNAVIVSSNQFGPGLNQTHI PADTHTEPVALNISVGNTGTMYPARAQSMYTCIEWQPVGQDGLATCSL
TAPQDPDPAGMATYSWSRESGAMQGEKCYIITIFASAHPEKLTWSTVLSTYHFGGNASAAAGTPHHVSVKNHSLDSV
SVDWAPSLSTCPGVLKEYVVRCDDEDSKQVSEHPVQPTETQVTLSSGLRAGVAYTVQVRADTAWLRGVWSQPQRFSI
EVQVSDWLIFFASLGSFLSILLVGVGLGYNRAARHLCPPLTPCASSAIEFPGGKETWQWINPVDFQEEASLQEA
LVVEMSWDKGERTEPLEKTELPEGAPELALDTELSLEDGDRCKAM

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

>sp|P42701|24-545

CRTSECCFQDPYPADSGSASGPRDLRCYRISSDRYECWSQYEGPTAGVSHFLRCCLSSGRCCYFAAGSATRLQFSD
DQAGVSVLYTVTLWVESWARNQTEKSPEVTLQLYNSVKYEPPLGDIKVSCLAGQLRMEWETPDNQVGAEVQFRHRT
SPWKLGDGCGPQDDDTESCLCLEMNVAQEFQLRRRQLGSQGSWSKWSPPVCVPPENPPQPQVRFSVEQLGQDGR
RLTLKEQPTQLELPEGCQGLAPGTEVTYRLQLHMLSCPCAKATRTHLHGKMPYLSGAAYNAVIVSSNQFGPGLNQ
THI PADTHTEPVALNISVGNTGTMYPARAQSMYTCIEWQPVGQDGLATCSLTAPQDPDPAGMATYSWSRESGAM
QGEKCYIITIFASAHPEKLTWSTVLSTYHFGGNASAAAGTPHHVSVKNHSLDSVVDWAPSLSTCPGVLKEYVVR
CDDEDSKQVSEHPVQPTETQVTLSSGLRAGVAYTVQVRADTAWLRGVWSQPQRFSIEVQVSD

Figure 1B

Human IL-12 receptor subunit beta-2 (IL-12RB2) sequence (SEQ ID NO:7)

>sp|Q99665

MAHTFRGCSLAFMFIIITWLLIKAKIDACKRGDVTVKPSHVILLGSTVNITCSLKPRQGC FHYSRNKLILYKFDRRI
NFHHGHSLSNSQVTGLPLGTTLFVCKLACINSDEIQICGAEIFVGVAPEQPQNLSCIQKGEQGT VACTWGERGRDTHLY
TEYTLQLSGPKNLTWQKQCKDIYCDYLD FGINLTPESPESNFTAKVTAVNSLGSSSSLPSTFTFLDIVRPLPPWDIR
IKFQKASVSRCTLYWRDEGLVLLNRLRYRPSNSRLWNMVNVTAKGRHDLLDLKPFTEYEFQISSKLHLYKGSWSDW
SESLRAQTPEEEPTGMLDVWYMKRHIDYSRQQISLFWKNLSVSEARGKILHYQVTLQELTG GKAMTQNTGHTSWTT
VIPRTGNWAVAVSAANSKGSSLPTRINIMNLCEAGLLAPRQVSANSEGMDNILVTWQPPRKDP SAVQEYVVEWRELH
PGGDTQVPLNWLRSRPYNVSALISENIKSYICYEIRVYALSGDQGGCSSILGNSKHKAPLSGPHINAITEEKGSILI
SWNSIPVQEOMGCLLHYRIYWKERDSNSQPQLCEIPYRVSQNSHPINSLQPRVTYVLWMTALTAAGESSHGNEREFC
LQGGANWMAFVAPSICIAIIMVGIFSTHYFQQKFVLLAALRPQWCSREIPDPANSTCAKKYPIAEKTKQLPLDRLL
IDWPTPEDPEPLVISEVLHQVTPVFRHPPCSNWPQREKGIQGHQASEKDMMHSASSPPPPRALQAESRQLVDLYKVL
ESRGSDBPKPENPACPWTVLPAGDLPTHGDLPSNIDDLPSHEAPLADSLLEELEPQHISLSVFPSSSLHPLTFSCGDK
LTLDQLKMRCDLSML

Human IL-12 receptor subunit beta-2 (IL-12RB2), extracellular domain (SEQ ID NO:8)

>sp|Q99665|24-622

KIDACKRGDVTVKPSHVILLGSTVNITCSLKPRQGC FHYSRNKLILYKFDRRINFHHGHSLSNSQVTGLPLGTTLFV
CKLACINSDEIQICGAEIFVGVAPEQPQNLSCIQKGEQGT VACTWGERGRDTHLYTEYTLQLSGPKNLTWQKQCKDIY
CDYLD FGINLTPESPESNFTAKVTAVNSLGSSSSLPSTFTFLDIVRPLPPWDIRIKFQKASVSRCTLYWRDEGLVLL
NRLRYRPSNSRLWNMVNVTAKGRHDLLDLKPFTEYEFQISSKLHLYKGSWSDWSESLRAQTPEEEPTGMLDVWYMK
RHIDYSRQQISLFWKNLSVSEARGKILHYQVTLQELTG GKAMTQNTGHTSWTTVIPRTGNWAVAVSAANSKGSSLP
TRINIMNLCEAGLLAPRQVSANSEGMDNILVTWQPPRKDP SAVQEYVVEWRELHPGGDTQVPLNWLRSRPYNVSALI
SENIKSYICYEIRVYALSGDQGGCSSILGNSKHKAPLSGPHINAITEEKGSILISWNSIPVQEOMGCLLHYRIYWKE
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	GGGGAGGGGA	XXX
(GGGGA) ₃	GGGGAGGGGAGGGGA	XXX
(GGGGA) ₄	GGGGAGGGGAGGGGAGGGGA	XXX
(GGGGA) ₅	GGGGAGGGGAGGGGAGGGGAGGGGA	XXX
(GGGGA) ₆	GGGGAGGGGAGGGGAGGGGAGGGGAGGGGA	XXX
(GGGGA) ₇	GGGGAGGGGAGGGGAGGGGAGGGGAGGGGAGGGGA	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
QMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CS VMHEALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFS
CS VMHEALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CS VMHEALHNHYTQKSLSLSPGK

>Backbone monomer 2 (SEQ ID NO:24)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFS
CS VMHEALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CS VMHEALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCEVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFS
CS VMHEALHNHYTQKSLSLSPGK

Figure 7B

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSKGSFFLYSKLTVDKSRWQQGNVFCSS
VMHEALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTENEVSLTCLVKGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLEVDKSRWEQGDFVFCSS
VMHEALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRD
QLTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS
VMHEALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRD
ELTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDFVFCSS
VMHEALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS
VMHEALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDFVFCSS
VMHEALHNHYTQKSLSLSPGK

Figure 7C

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYSSSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS
VMHEALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYSSSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFPYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSS
VMHEALHNHYTQKSLSLSPGK

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

ESKYGPPCPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAK
TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEQM
TKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFCSSVM
HEALHNHYTQKSLSLSLGK

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

ESKYGPPCPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAK
TKPREEEFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEM
TKNQVSLTCDVSGFPYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWEQGDVFCSSVM
HEALHNHYTQKSLSLSLGK

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

ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKT
KPREEQFNSTFRVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREQMT
KNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMH
EALHNHYTQKSLSLSPGK

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

ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKT
KPREEEFNSTFRVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMT
KNQVSLTCDVSGFPYPSDIAVEWESDGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMH
EALHNHYTQKSLSLSPGK

Figure 7D

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

ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVQFNWYVDGVEVHNAKT
KPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREQMT
KNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPMLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMH
EALHNHYTQKSLSLSPGK

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

ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVQFNWYVDGVEVHNAKT
KPREEEFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMT
KNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPMLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMH
EALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCFS
VLHEALHSHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPVLDSGDSFFLYSKLTVDKSRWEQGDVFCFS
VLHEALHSHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCFS
VMHEALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCFS
VMHEALHNHYTQKSLSLSPGK

Figure 7E

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCS
VMHEALHNHYTQKSLSLSPGK

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

ERKSSDKTHTCPRCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFKWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSPGK

Figure 8A

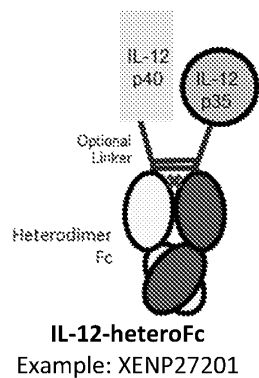


Figure 8B

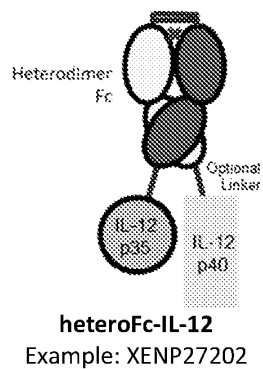


Figure 8C

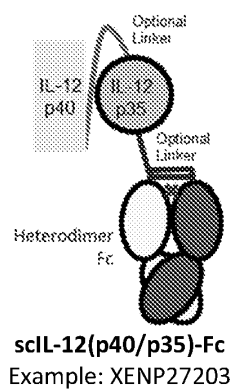


Figure 8D

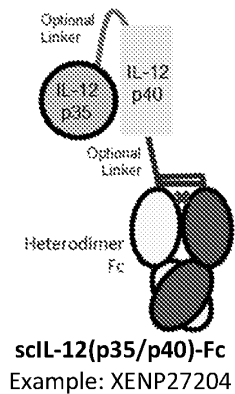


Figure 8E

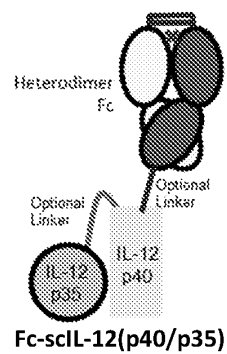


Figure 8F

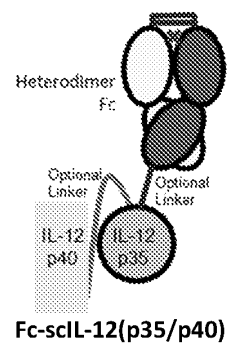


Figure 9

**>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
SLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO:47)**

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

RNLPVATPDGPMFPCLLHHSQNLRAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNLAVIDEMLQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(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
EEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVS
GFYPSDIAVEWESDGPENNYKTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYTQKSLSLSPG/
GGGSGGGGS/ IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQY
TCHKGGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDP
QGVTCGAATLSAERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSFFIRDI IKPDPPKNLQ
LKPLKNSRQVEVSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSW
SEWASVPCS **(SEQ ID NO:49)**

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVK
GFYPSDIAVEWESNGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPG/
GGGSGGGGS/ RNLPVATPDGPMFPCLLHHSQNLRAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPL
ELTKNESCLNSRETSFITNGSCLASRKTSFMMALCLSSIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNLAVIDE
LMQALNFNSETVPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS **(SEQ ID NO:50)**

EPKSSDKTHTCPCPPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVK
GFYPSDIAVEWESNGQPENNYKTTTPPVLDSGSGFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO:54)

(SEQ ID NO:54)

Figure 12A

Purification of
eluate from
Protein A
Chromatography
via Anion
Exchange
Chromatography

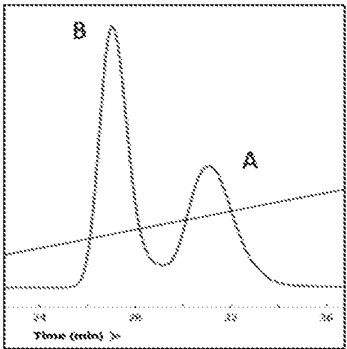


Figure 12B

aSEC-MALS

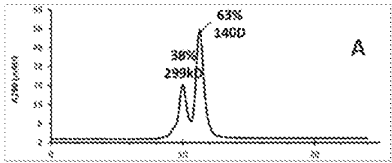
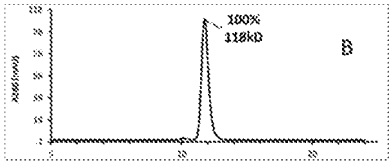


Figure 12C

Analytical
AIEX

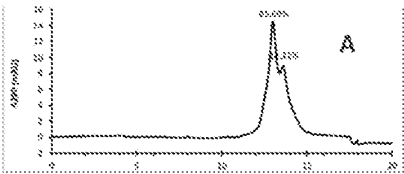
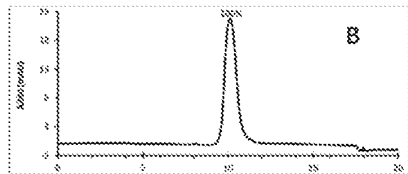


Figure 13A

Purification of
eluate from
Protein A
Chromatography
via Anion
Exchange
Chromatography

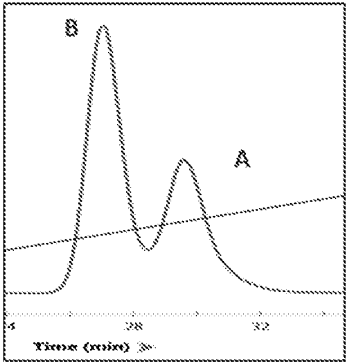


Figure 13B

aSEC-MALS

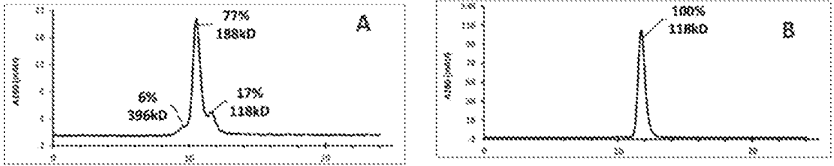


Figure 13C

Analytical
AIEX



Figure 14A

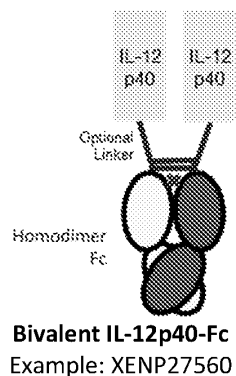


Figure 14B

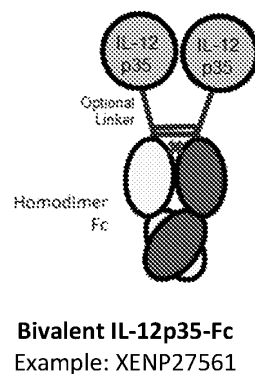


Figure 15

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAEEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:55)**

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSEMMALCLSSIYEDLMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
VPQKSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:56)**

Figure 16A

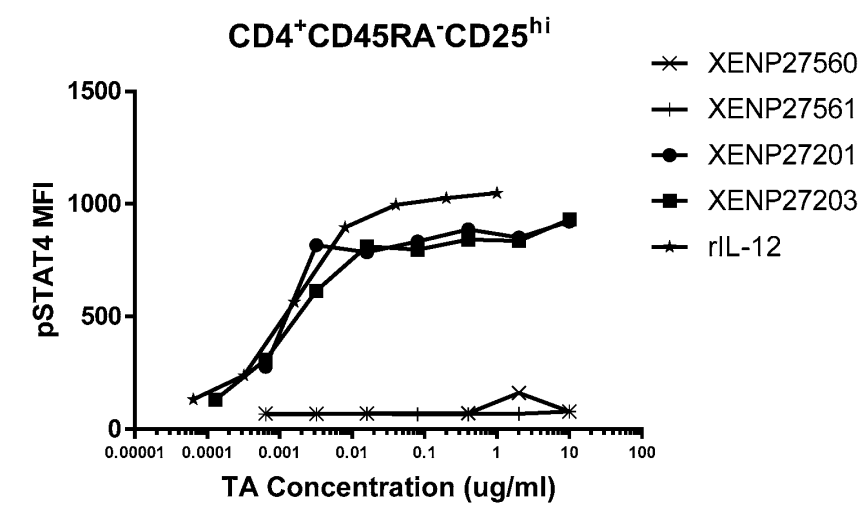


Figure 16B

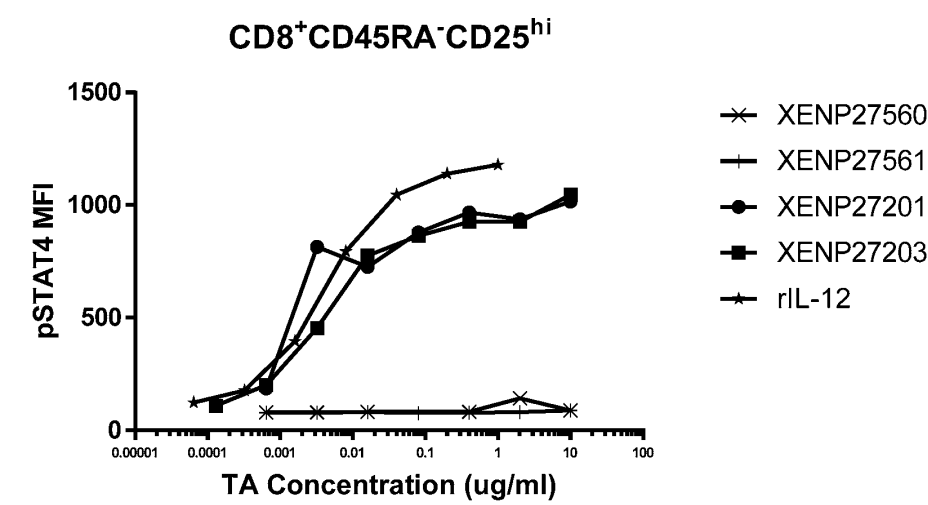


Figure 16C

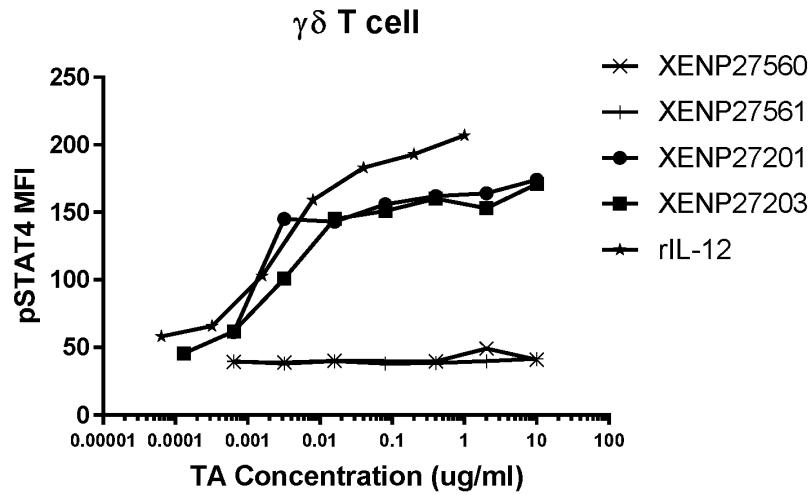


Figure 16D

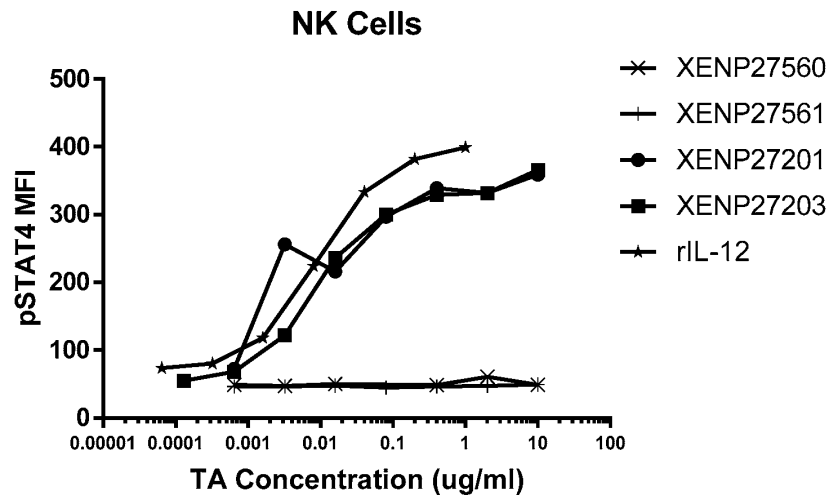


Figure 17

RESIDUE

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
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKDYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYEDTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKDASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYEDTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKDASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDESSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

Figure 20B

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIEVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGNAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDESSQVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSVLGSGKTLTIEVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDESSQVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIEVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

Figure 20C

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDESSQVLGSGKTLTIEVK~~Q~~FGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERV~~R~~GDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQ~~L~~KPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDQSSQVLGSGKTLTIEVK~~Q~~FGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERV~~R~~GDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQ~~L~~KPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGQVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERV~~R~~GDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQ~~L~~KPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGQVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERV~~R~~GDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQ~~L~~KPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGQVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPEGVTCGAATLS
AERV~~R~~GDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQ~~L~~KPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERV~~R~~GDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQ~~L~~KPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKRQKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKQPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERV~~R~~GDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQ~~L~~KPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

Figure 20D

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

IWELKKDVYVVELDWYPNAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPSC

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEQDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPSC

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSREVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPSC

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWQYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPSC

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVNGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPSC

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSQWASVPSC

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKENGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPSC

Figure 20E

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKNYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEDYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKNYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKDASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKDYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEDYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKDYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKDASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEDYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKDASISVRAQDRYYSSSWSEWASVPCS

Figure 20F

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEDYTSSFFIRDIIPDPKPNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKDASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKNYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEDYTSSFFIRDIIPDPKPNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKDASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKDYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEDYTSSFFIRDIIPDPKPNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKDASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKNYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKQYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

Figure 20G

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEQTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKQYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKNYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEQTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKNYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKQYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEQTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

Figure 20H

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKQYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKQYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKQYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKNYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKQYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYYSSSWSEWASVPCS

Figure 20I

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYYSSSWSEWASVPCS

Figure 21A

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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:85)**

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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKDYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:86)**

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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEDYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:87)**

Figure 21B

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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
DASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEDYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
DASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:89)

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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDESSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:90)

Figure 21C

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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:91)

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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIEVKEFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:92)

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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (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
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:94)

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

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:95)

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

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIEVKEFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (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**

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSESEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGS\GGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:97)

**>XenD24765 human IL12p40 Q56E/E59Q (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIEVKQFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGS\GGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:98)

**>XenD24766 human IL12p40 Q42E/E45Q/Q56E (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5**

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDESSQVLGSGKTLTIEVKEFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGS\GGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (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
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID
NO:100)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRNKNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID
NO:101)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGQVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID
NO:102)

Figure 21G

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPEGVTGGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK **(SEQ ID**
NO:103)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKRQKKDRVFTDKTSATVICRK
NASISVRAQDRYYSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK **(SEQ ID**
NO:104)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKQPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK **(SEQ ID**
NO:105)

Figure 21H

>XenD24773 human IL12p40 D18N (GGGGS)2-Fc(216) IgG1 pl(-)

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

IWELKKDVYVVELDWYPNAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK **(SEQ ID**
NO:106)

>XenD24774 human IL12p40 E33Q (GGGGS)2-Fc(216) IgG1 pl(-)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEQDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK **(SEQ ID**
NO:107)

>XenD24775 human IL12p40 Q229E (GGGGS)2-Fc(216) IgG1 pl(-)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSREVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK **(SEQ ID**
NO:108)

Figure 21l

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWQYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK **(SEQ ID**
NO:109)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVEGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK **(SEQ ID**
NO:110)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSQWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK **(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
GGEVLSHSLLLLHKKENGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGS\GGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYTQKSLSLSPGK (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)

RNLPVATPDGPMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKDESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:113)

> IL-12p35(N85D)

RNLPVATPDGPMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITDGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:114)

> IL-12p35(N195D)

RNLPVATPDGPMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLDAS (SEQ ID NO:115)

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

RNLPVATPDGPMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKDESCLNS
RETSFITDGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLDAS (SEQ ID NO:116)

> IL-12p35(E153Q)

RNLPVATPDGPMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSQT
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:117)

> IL-12p35(E38Q)

RNLPVATPDGPMFPCLLHHSQNLRLRAVSNNMLQKARQTLQFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:118)

> IL-12p35(N151D)

RNLPVATPDGPMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNDSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:119)

> IL-12p35(Q135E)

RNLPVATPDGPMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDENMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:120)

Figure 23B

> IL-12p35(Q35D)

RNLPVATPDGMPFCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:121)

> IL-12p35(Q146E)

RNLPVATPDGMPFCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:122)

> IL-12p35(N76D)

RNLPVATPDGMPFCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:123)

> IL-12p35(E162Q)

RNLPVATPDGMPFCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:124)

> IL-12p35(E163Q)

RNLPVATPDGMPFCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:125)

> IL-12p35(N71Q)

RNLPVATPDGMPFCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:XXX)

> IL-12p35(N85Q)

RNLPVATPDGMPFCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:XXX)

> IL-12p35(N195Q)

RNLPVATPDGMPFCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:XXX)

Figure 23C

> IL-12p35(N71Q/N85Q)

RNLPVATPDGMPFCLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEIDHEDITKDKTSTVEACLPLELTKQESCLNS
RETSFITQGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:XXX)

> IL-12p35(N71Q/N195Q)

RNLPVATPDGMPFCLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEIDHEDITKDKTSTVEACLPLELTKQESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:XXX)

> IL-12p35(N85Q/N195Q)

RNLPVATPDGMPFCLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITQGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:XXX)

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

RNLPVATPDGMPFCLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEIDHEDITKDKTSTVEACLPLELTKQESCLNS
RETSFITQGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:XXX)

> IL-12p35(N71D/N85D)

RNLPVATPDGMPFCLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEIDHEDITKDKTSTVEACLPLELTKDESCLNS
RETSFITDGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:XXX)

> IL-12p35(N71D/N195D)

RNLPVATPDGMPFCLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEIDHEDITKDKTSTVEACLPLELTKDESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLDAS (SEQ ID NO:XXX)

> IL-12p35(N85D/N195D)

RNLPVATPDGMPFCLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITDGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLDAS (SEQ ID NO:XXX)

Figure 24A

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
DESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:126)

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITDGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:127)

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLDAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:128)

>XenD24782**human IL12p35 N71D/N85D/N195D (GGGGS)2 Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q pT
T5**

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
DESCLNSRETSFITDGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLDAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:129)

Figure 24B

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

RNLPVATPDPGMFPC~~L~~HHSQNLLRAVS~~N~~MLQKARQTLEFY~~P~~CTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQ~~N~~MLAV
IDELMQALN~~F~~NSQTVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS~~S~~GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTKAKAGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV~~F~~SCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:130)

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

RNLPVATPDPGMFPC~~L~~HHSQNLLRAVS~~N~~MLQKARQTLQFY~~P~~CTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQ~~N~~MLAV
IDELMQALN~~F~~NSQ~~T~~VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS~~S~~GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTKAKAGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV~~F~~SCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:131)

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

RNLPVATPDPGMFPC~~L~~HHSQNLLRAVS~~N~~MLQKARQTLEFY~~P~~CTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQ~~N~~MLAV
IDELMQALN~~F~~NDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS~~S~~GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTKAKAGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV~~F~~SCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:132)

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

RNLPVATPDPGMFPC~~L~~HHSQNLLRAVS~~N~~MLQKARQTLEFY~~P~~CTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDENMLAV
IDELMQALN~~F~~NSQ~~T~~VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS~~S~~GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTKAKAGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV~~F~~SCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:133)

Figure 24C

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

RNLPVATPDPGMFPC~~L~~HHSQNL~~L~~RAVS~~N~~MLQKARD~~T~~LEFY~~P~~CTSE~~E~~IDHEDITKDKTSTVEAC~~L~~PLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQ~~N~~MLAV
IDELMQALN~~F~~NSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS~~S~~GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK~~T~~ISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK~~T~~TPPVLDSDGSFFLYSKLTVDKSRWQQGNV~~F~~SCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:134)

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

RNLPVATPDPGMFPC~~L~~HHSQNL~~L~~RAVS~~N~~MLQKARQ~~T~~LEFY~~P~~CTSE~~E~~IDHEDITKDKTSTVEAC~~L~~PLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQ~~N~~MLAV
IDELMEALN~~F~~NSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS~~S~~GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK~~T~~ISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK~~T~~TPPVLDSDGSFFLYSKLTVDKSRWQQGNV~~F~~SCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:135)

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

RNLPVATPDPGMFPC~~L~~HHSQNL~~L~~RAVS~~N~~MLQKARQ~~T~~LEFY~~P~~CTSE~~E~~IDHEDITKDKTSTVEAC~~L~~PLELTK
NESCLDSRETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQ~~N~~MLAV
IDELMQALN~~F~~NSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS~~S~~GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK~~T~~ISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK~~T~~TPPVLDSDGSFFLYSKLTVDKSRWQQGNV~~F~~SCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:136)

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

RNLPVATPDPGMFPC~~L~~HHSQNL~~L~~RAVS~~N~~MLQKARQ~~T~~LEFY~~P~~CTSE~~E~~IDHEDITKDKTSTVEAC~~L~~PLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQ~~N~~MLAV
IDELMQALN~~F~~NSETVPQKSS~~L~~QEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS~~S~~GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK~~T~~ISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK~~T~~TPPVLDSDGSFFLYSKLTVDKSRWQQGNV~~F~~SCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:137)

Figure 24D

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM LAV
IDELMQALNFNSETVPQKSSLEQPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS GGGGS\ E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
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

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWNLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMVDAVHKLKYEDYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKDASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:139)**

Chain 2 (XenD24782) -

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

RNLVPATPDPGMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKDESCLNS
RETSFITDGSCLASRKTSFMMALCLSSIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLDAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGGEVLSH
SLLLLHKKENGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:141)**

Figure 25B

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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
SLLLLLHKKEGDIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:143)

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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
SLLLLLHKKEGDIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:145)

Figure 25C

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

RNLPVATPDPMFPCLHHSQNLLRAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIEVKEFGDAGQYTCHKGGGEVLSH
SLLLLLHKKEGDIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:147)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGGEVLSH
SLLLLLHKKEGDIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:149)

Figure 25D

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIQVKEFGNAGQYTCHKGGSEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:151)

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGSEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:153)

Figure 25E

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

RNLPVATPDPMFPCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLARKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKSLSLSPGK (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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIEVKEFGDAGQYTCHKGGGEVLSH
SLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNNHYT
QKSLSLSPGK (SEQ ID NO:155)

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

RNLPVATPDPMFPCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLARKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKSLSLSPGK (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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSESEVLGSGKTLTIQVKQFGDAGQYTCHKGGGEVLSH
SLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNNHYT
QKSLSLSPGK (SEQ ID NO:157)

Figure 25F

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKSLSLSPGK (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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIEVKQFGDAGQYTCHKGGGEVLSH
SLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNNHYT
QKSLSLSPGK (SEQ ID NO:159)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKSLSLSPGK (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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDESSQVLGSGKTLTIEVKEFGDAGQYTCHKGGGEVLSH
SLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNNHYT
QKSLSLSPGK (SEQ ID NO:161)

Figure 25G

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKSLSLSPGK (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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIEVKQFGDAGQYTCHKGGEVLSH
SLLLLLHKKEGDIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNNHYT
QKSLSLSPGK (SEQ ID NO:163)

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKSLSLSPGK (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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLLHKKEGDIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRNNKEYEYSVECEQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNNHYT
QKSLSLSPGK (SEQ ID NO:165)

Figure 25H

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

RNLPVATPDPMFPCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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
SLLLLLHKKEGDIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:167)

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

RNLPVATPDPMFPCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGQVLSH
SLLLLLHKKEGDIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:169)

Figure 25I

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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
SLLLLLHKKEGDIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKRQKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:171)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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
SLLLLLHKKEGDIWSTDILKDQKQPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:173)

Figure 25J

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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**

IWELKKDVYVVELDWYPNAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLLHKKEGDIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:175)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEQDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLLHKKEGDIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:177)

Figure 25K

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSREVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:179)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWQYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:181)

Figure 25L

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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
SLLLLLHKKEGDIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQEGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:183)

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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
SLLLLLHKKEGDIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWQWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:185)

Figure 25M

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

RNLPVATPDPMFPCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGSEVLSH
SLLLLLHKKEGDIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:187)

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

RNLPVATPDPMFPCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSQT
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGSEVLSH
SLLLLLHKKEGDIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:189)

Figure 25N

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLQFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGSEVLSH
SLLLLLHKKEGDIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:191)

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLQFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFDSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGSEVLSH
SLLLLLHKKEGDIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:193)

Figure 250

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

RNLPVATPDPMFPCLHHSQNLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDENMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGSEVLSH
SLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:195)

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

RNLPVATPDPMFPCLHHSQNLRAVSNNMLQKARDTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGSEVLSH
SLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
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

RNLPVATPDPMFPCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMEALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGSEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:199)

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

RNLPVATPDPMFPCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLDS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGSEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:201)

Figure 25Q

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

RNLPVATPDPMFPCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSEMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEQPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSDDPQGVTCGAATLS
AERVRGDNKEYEYSVECEQEDSACPAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:203)

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

RNLPVATPDPMFPCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSEMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEQPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:204)

Figure 26A

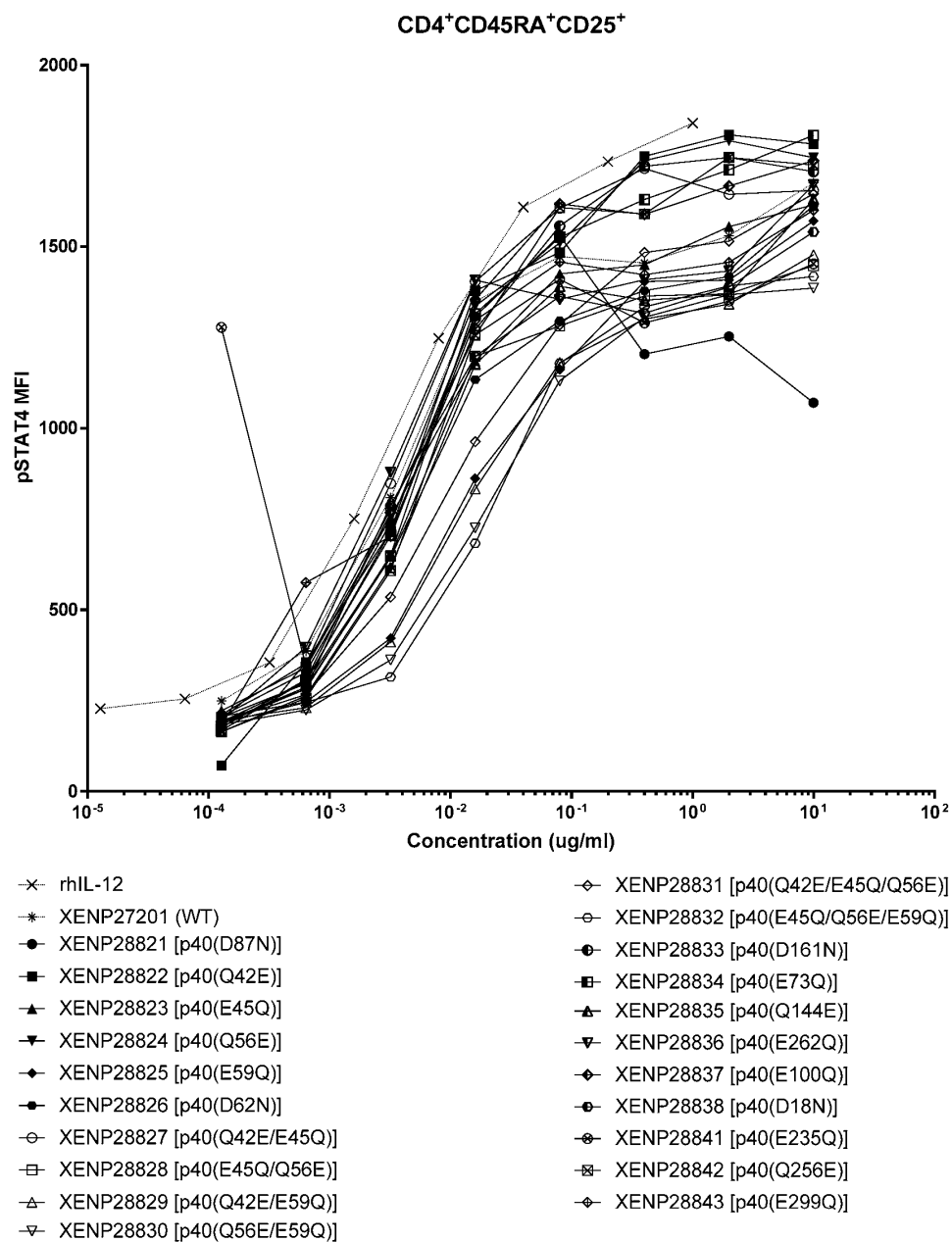


Figure 26B

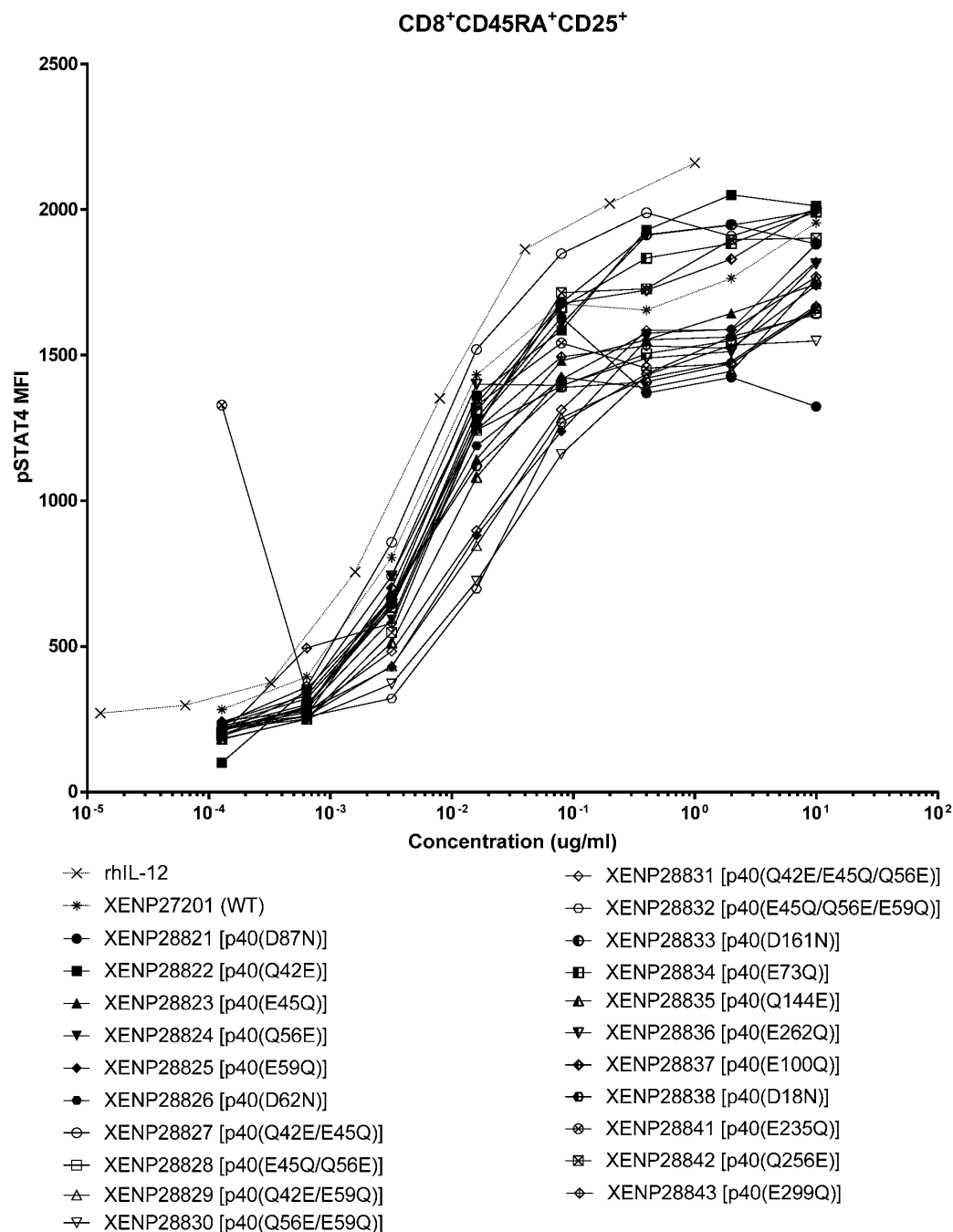


Figure 27A

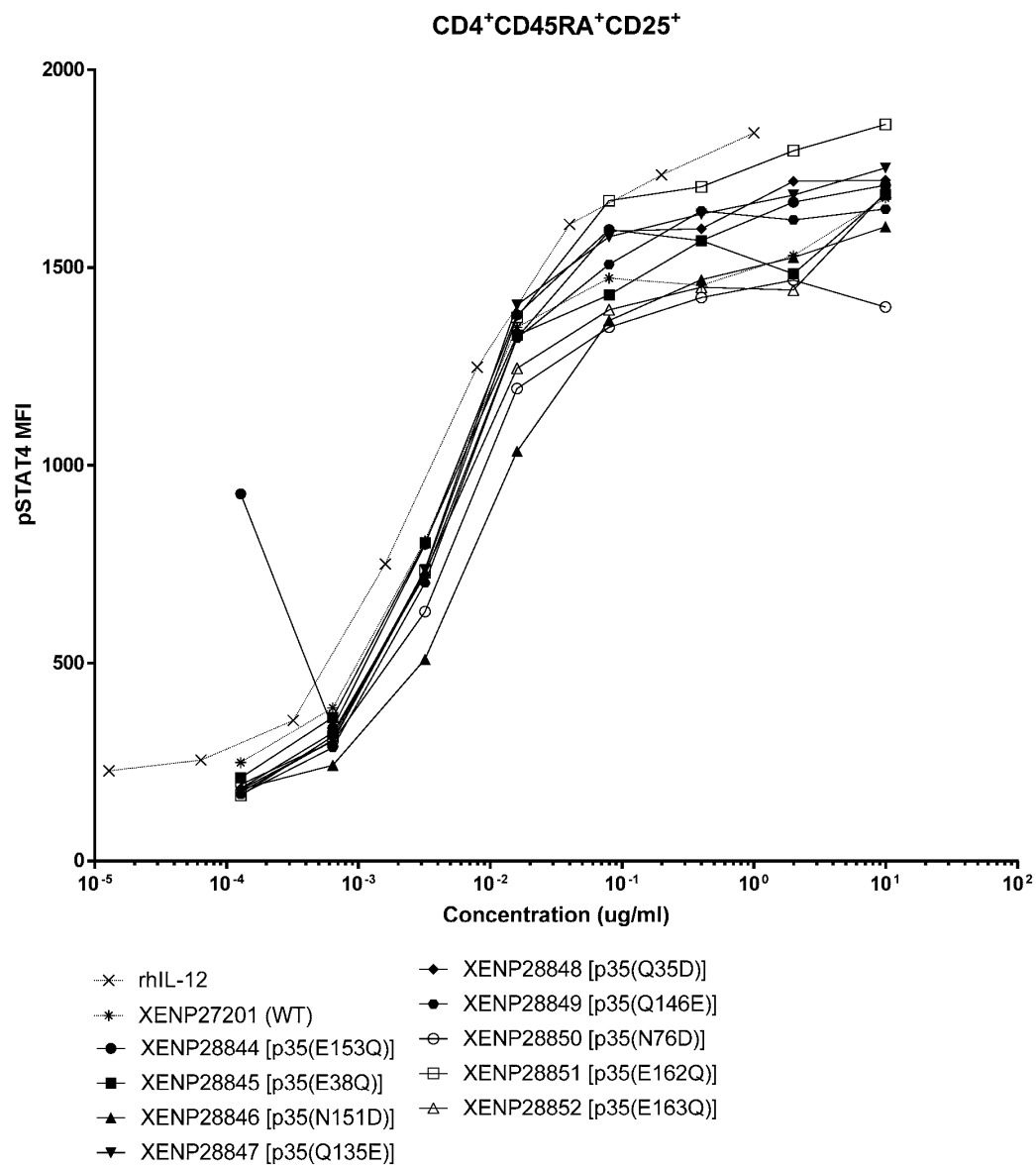


Figure 27B

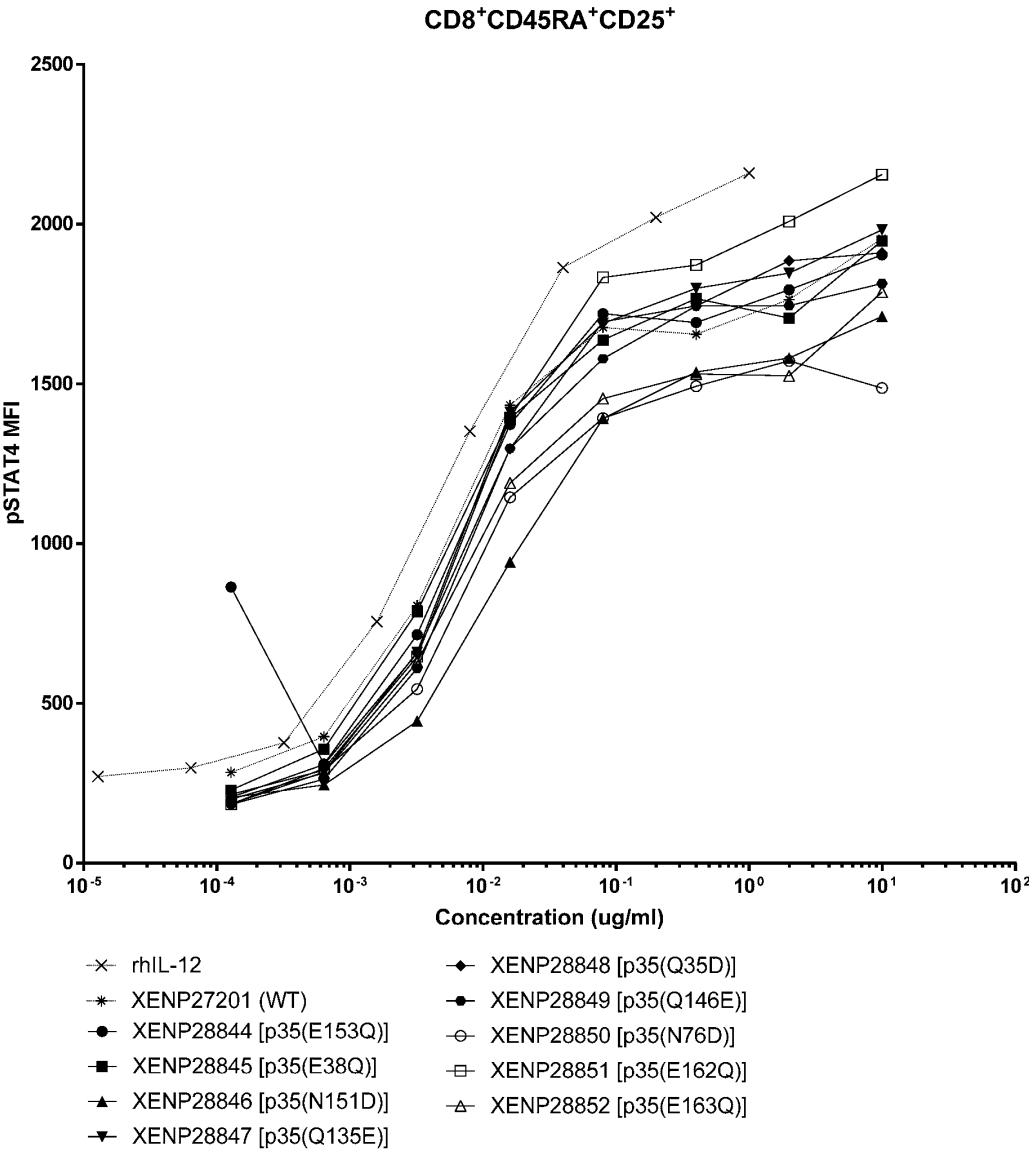


Figure 28

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)**

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVK**K**FGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPE**Q**EDGITWTLDQSSEVLGSGKTLTIQVK**Q**FGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEE**N**GITWTLDQSSEVLGSGKTLTIQVK**Q**FGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVK**Q**FGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPI**Q**VMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQ**E**SEVLGSGKTLTIQVK**Q**FGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

Figure 29B

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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQKSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNEEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGESKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGSEREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS

Figure 30A

>XenD25922 human IL12p40 E59K (GGGGS)2-Fc(216) IgG1 pl(-)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK **(SEQ ID**
NO:215)

>XenD25923 human IL12p40 E32Q/E59Q (GGGGS)2-Fc(216) IgG1 pl(-)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK **(SEQ ID**
NO:216)

>XenD25924 human IL12p40 D34N/E59Q (GGGGS)2-Fc(216) IgG1 pl(-)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK **(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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIQVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID**
NO:218)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIQVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID**
NO:219)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQKSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIQVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYTQKSLSLSPGK **(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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRGDNEEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK **(SEQ ID**
NO:221)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK **(SEQ ID**
NO:222)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGESKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK **(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
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSEREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGS\GGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID
NO:224)**

Figure 31A

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

RNLFPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSF ITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFD SQTVPQKSSLEEPDFYKTKIKLCILHAFRIRAVTIDRVMSYLNAS

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

RNLFPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSF ITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFN SKTVPQKSSLEEPDFYKTKIKLCILHAFRIRAVTIDRVMSYLNAS

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

RNLFPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSF ITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFD KSETVPQKSSLEEPDFYKTKIKLCILHAFRIRAVTIDRVMSYLNAS

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

RNLFPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSF ITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFD DSETVPQKSSLEEP NFYKTKIKLCILHAFRIRAVTIDRVMSYLNAS

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

RNLFPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSF ITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKR EIFLDQNMLAV
IDELMQALNFD DSETVPQKSSLEEPDFYKTKIKLCILHAFRIRAVTIDRVMSYLNAS

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

RNLFPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSF ITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFD DSETVPQ ESSLEEPDFYKTKIKLCILHAFRIRAVTIDRVMSYLNAS

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

RNLFPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSR QTSF ITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFD DSETVPQKSSLEEPDFYKTKIKLCILHAFRIRAVTIDRVMSYLNAS

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

RNLFPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITK QKTSTVEACLPLELTK
NESCLNSRETSF ITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFD DSETVPQKSSLEEPDFYKTKIKLCILHAFRIRAVTIDRVMSYLNAS

Figure 31B

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQDM LAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

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

RNLPVATPDPGMFPC LHHSQDLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDQLMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

Figure 32A

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALV
IDELMQALNFDSTVTPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:236)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALV
IDELMQALNFDSTVTPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:237)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALV
IDELMQALNFDSETVTPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:238)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMALV
IDELMQALNFDSETVTPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:239)

Figure 32B

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKREIFLDQNMMLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:240)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAV
IDELMQALNFDSETVPQESSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:241)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRQTSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:242)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTSEEIDHEDITKQKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:243)

Figure 32C

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

RNLPVATPDPMFPCLHHSQNLLRAVSNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQDMLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:244)

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

RNLPVATPDPMFPCLHHSQDLLRAVSNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQDMLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:245)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQDMLAV
IDQLMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSV
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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 93)**

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTFEYFCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLARKTSEMMALCLSSIYEDLMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFDSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 98)**

Figure 33B

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFDSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNYTQKSLSLSPGK **(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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSDDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNYT
QKSLSLSPGK **(SEQ ID NO: 215)**

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFDSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNYTQKSLSLSPGK **(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

IWELKKDVYVVELDWYDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFSCSMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 215)**

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSEMMALCLSSYIEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNNVFSCSMHEALHNHYTQKSLSLSPGK **(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

IWELKKDVYVVELDWYDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFSCSMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 216)**

Figure 33D

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEPPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWYDPAPGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVECEQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: 217)**

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEPPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIQVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 218)**

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

RNLVPATPDPMFPCLLHHSQNLRLAVSNMLQKARQTFEYFCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLARKTSEMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSGGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 219)**

Figure 33F

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEPPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQKSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVETDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 220)**

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEPPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 221)**

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTFEYFCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSEMMALCLSSYEDLKMVQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 222)**

Figure 33H

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

RNLPVATPDPMFPCLLHHSQNLRAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGESKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 223)**

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

RNLPVATPDPMFPCLLHHSQNLRAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 224)**

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLARKTSEMMALCLSSYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 33J

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFDST
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWYDPAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVETDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFSKT
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKSLSLSPGK **(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
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTFEYFCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLARKTSEMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFKSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSGGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 33L

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFDSET
 VPQKSLEEPPNFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFPSPDI AVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWYDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFVCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKREIFLDQNMLAVIDELMQALNFDSET
 VPQKSLEEPPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFPSPDI AVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSVHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLARKTSEMMALCLSSIYEDLMYQVEFKTMNAKLLMDPKRQIFLDQNNMLAVIDELMQALNFDSET
 VPQESSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSVHEALHNHYTQKSLSLSPGK **(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
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSVHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 33N

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RQTSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFDSET
VPQKSLEEPPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWYDPAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKQKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFDSET
VPQKSLEEPPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLARKTSEMMALCLSSIYEDLMYQVEFKTMNAKLLMDPKRQIFLDQDMLAVIDELMQALNFDSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVMEALHNHYTQKSLSLSPGK **(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
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 33P

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

RNLPVATPDPMFPCLLHHSQDLLRAVSNNMLQKARQTLEFYPCCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFDSET
 VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/ EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 245)**

**>XENP29972 human_IL12p40_(GGGGS)2-human_IL12p35(E143Q/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
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/ EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLEFYPCCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDQLMQALNFDSET
 VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/ EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 246)**

Figure 34A

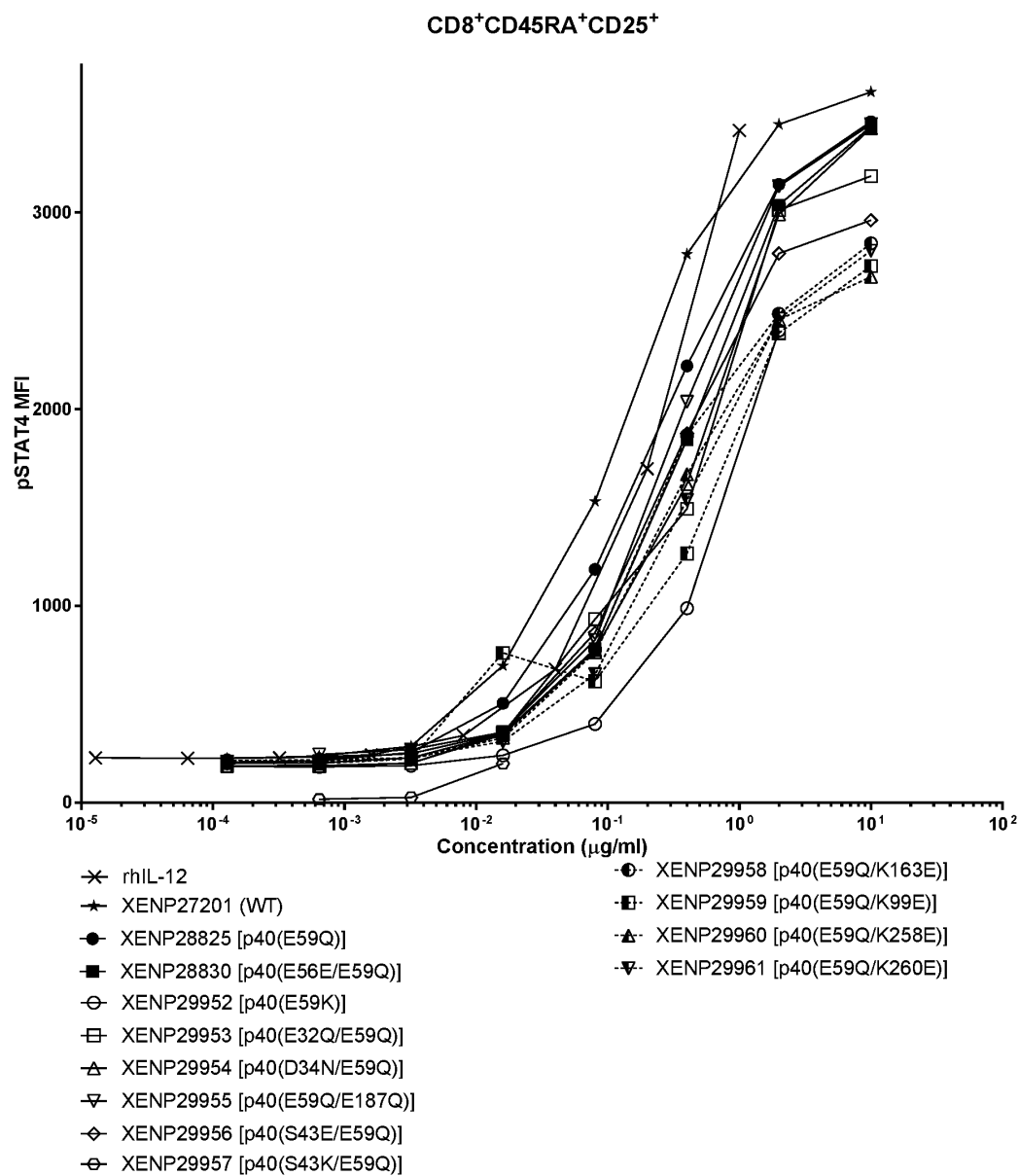


Figure 34B

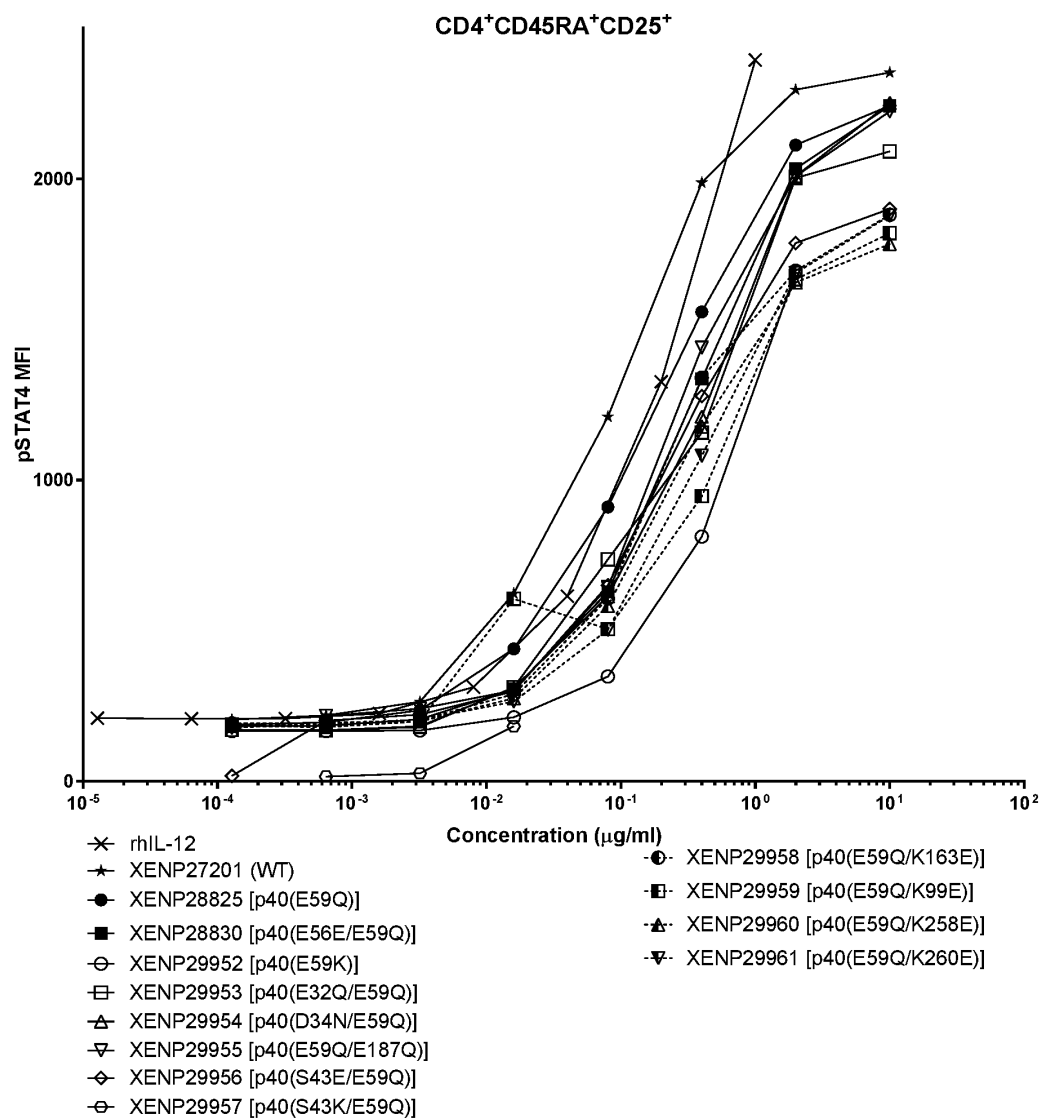


Figure 35A

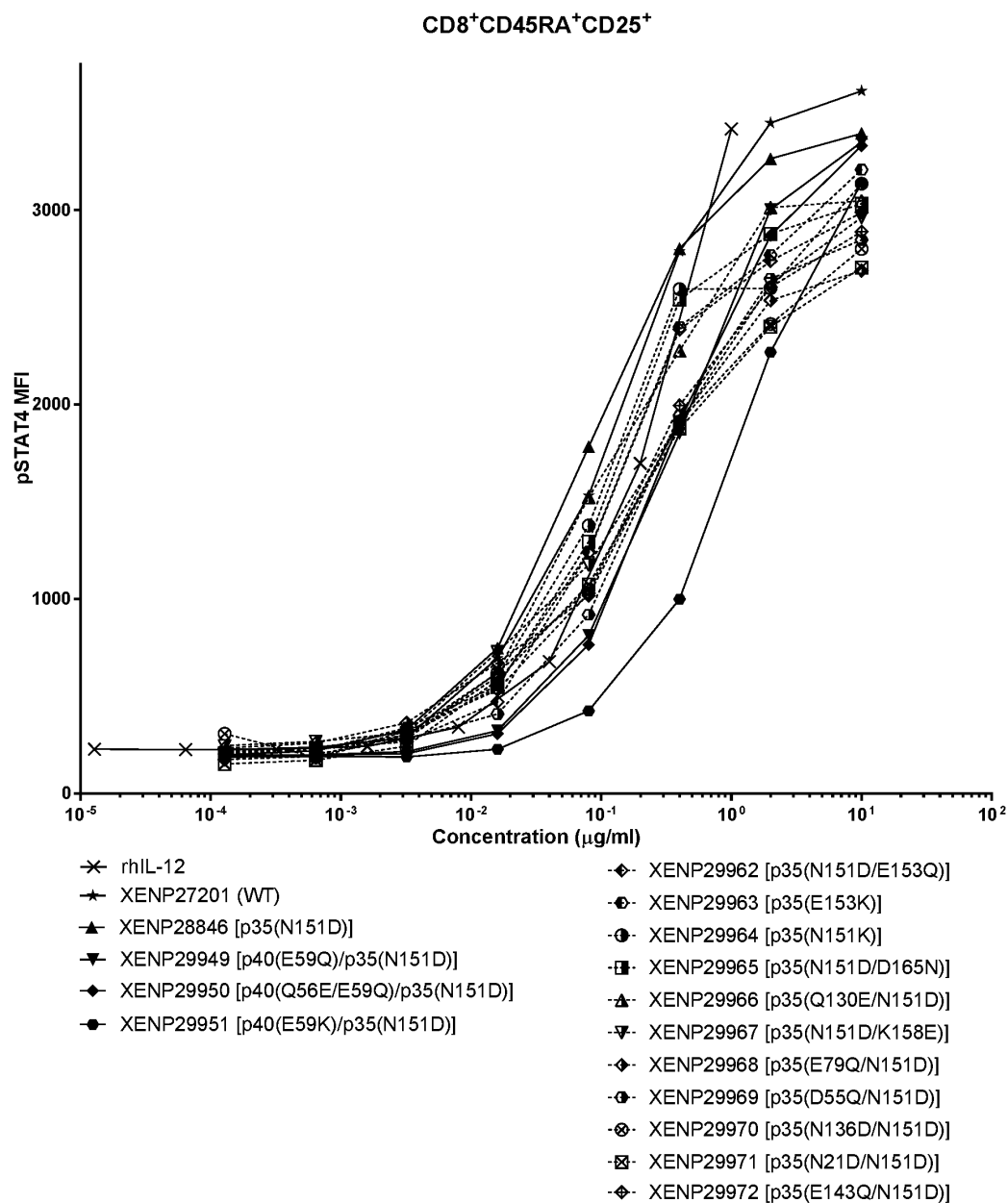


Figure 35B

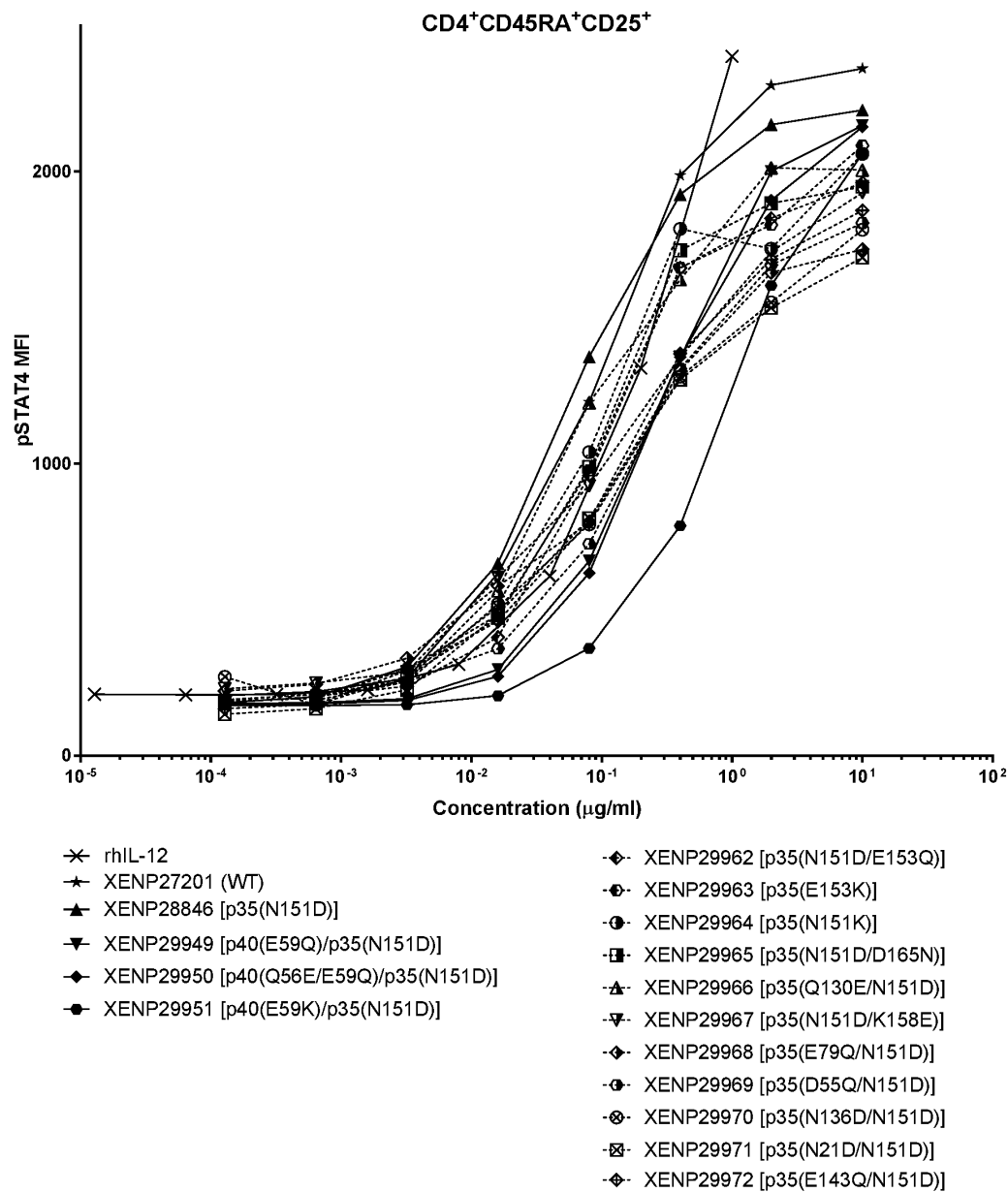


Figure 36

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
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTF_{FLR}CEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(D34N/E59K)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTF_{FLR}CEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(D34N/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTF_{FLR}CEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(D34K/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEKGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTF_{FLR}CEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(E32Q/D34N/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEQNGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTF_{FLR}CEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

Figure 37B

>IL12p40(E32Q/D34K/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPTQEKGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(E32K/D34N/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPTKENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(E32K/D34K/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPTKEKGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

Figure 38

>IL12p35(D55Q)

RNLPVATPDPGMFCLHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKQKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCIL LHAFRIRAVTIDRVMSYLNAS **(SEQ ID NO: XXX)**

>IL12p35(D55K)

RNLPVATPDPGMFCLHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKKKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCIL LHAFRIRAVTIDRVMSYLNAS **(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
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTFEYFPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTVLKGFPYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 39B

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEPPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVETDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEPPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTFLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLARKTSEMMALCLSSYIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(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
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 39D

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEPPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEKGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVEQEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEPPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNYTQKSLSLSPGK **(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

IWELKKDVYVVELDWYPDAPGEMVVLTC DTPKENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

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

RNLPVATPDPMFPCLHHSQNLRLAVSNMLQKARQTFEYFPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLARKTSEMMALCLSSIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(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

IWELKKDVYVVELDWYPDAPGEMVVLTC DTPKEKGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 39F

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEQNGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: XXX)**

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKQKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO: XXX)

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTFEYFCTSEEDHEDITKQKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVSMHEALHNHYTQKSLSLSPGK (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
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO: XXX)

Figure 39H

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKQKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLARKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEKKGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVEQCEDSACPAEESLPIEVMVDAVHKLKYENYTSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFQVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKQKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLARKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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 DTPKEKGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTF LRCEAKNYSGRFTCWNLTTISTDLTF SVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECDQEDSACPAAEESLP I EVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

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

RNLPVATPDPMFPCLHHSQNLRLRAVS NMLQKARQTLEFYPTCTSEEDHEDITKKKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLARKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCVKGIFYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

Figure 40A

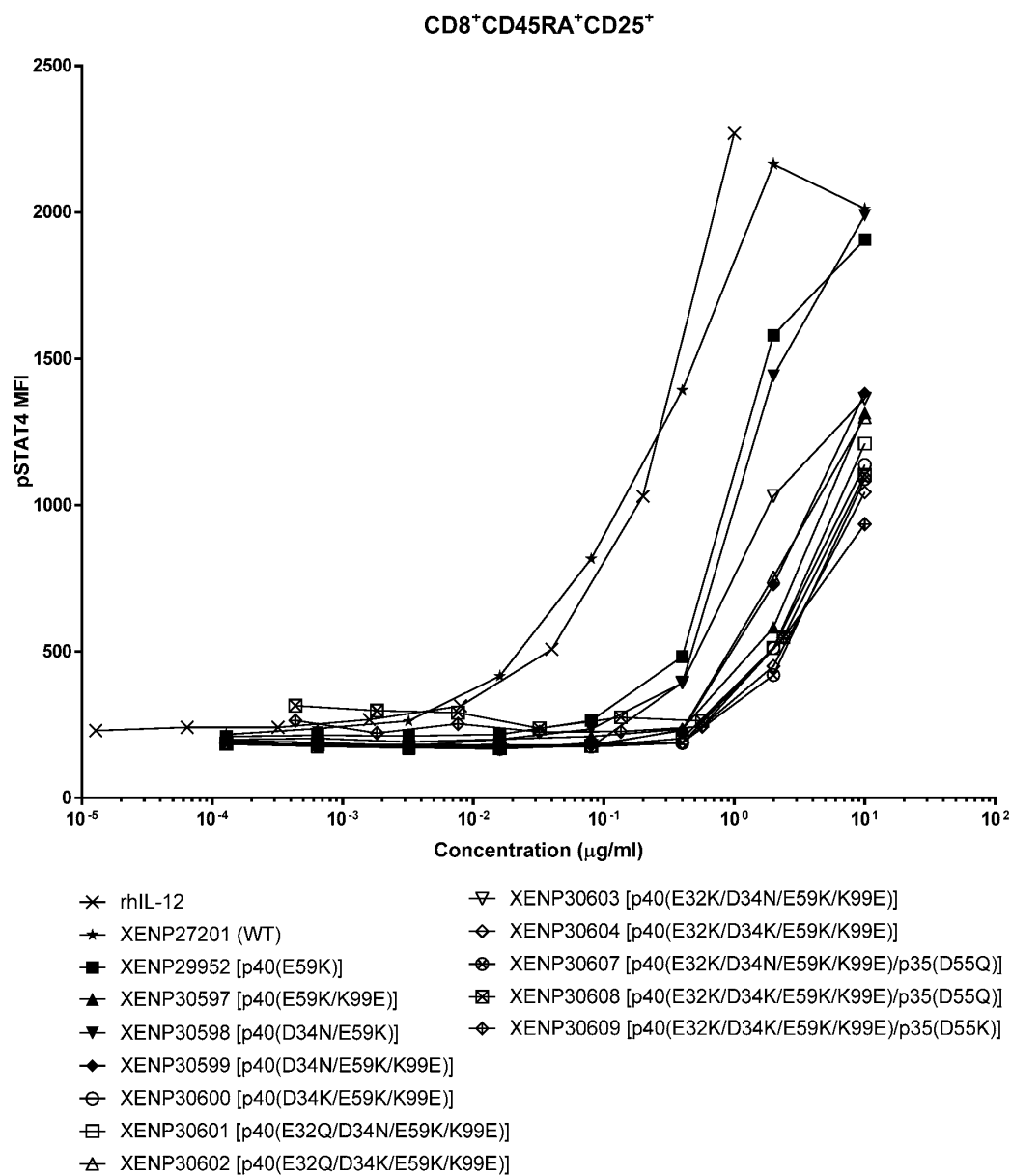


Figure 40B

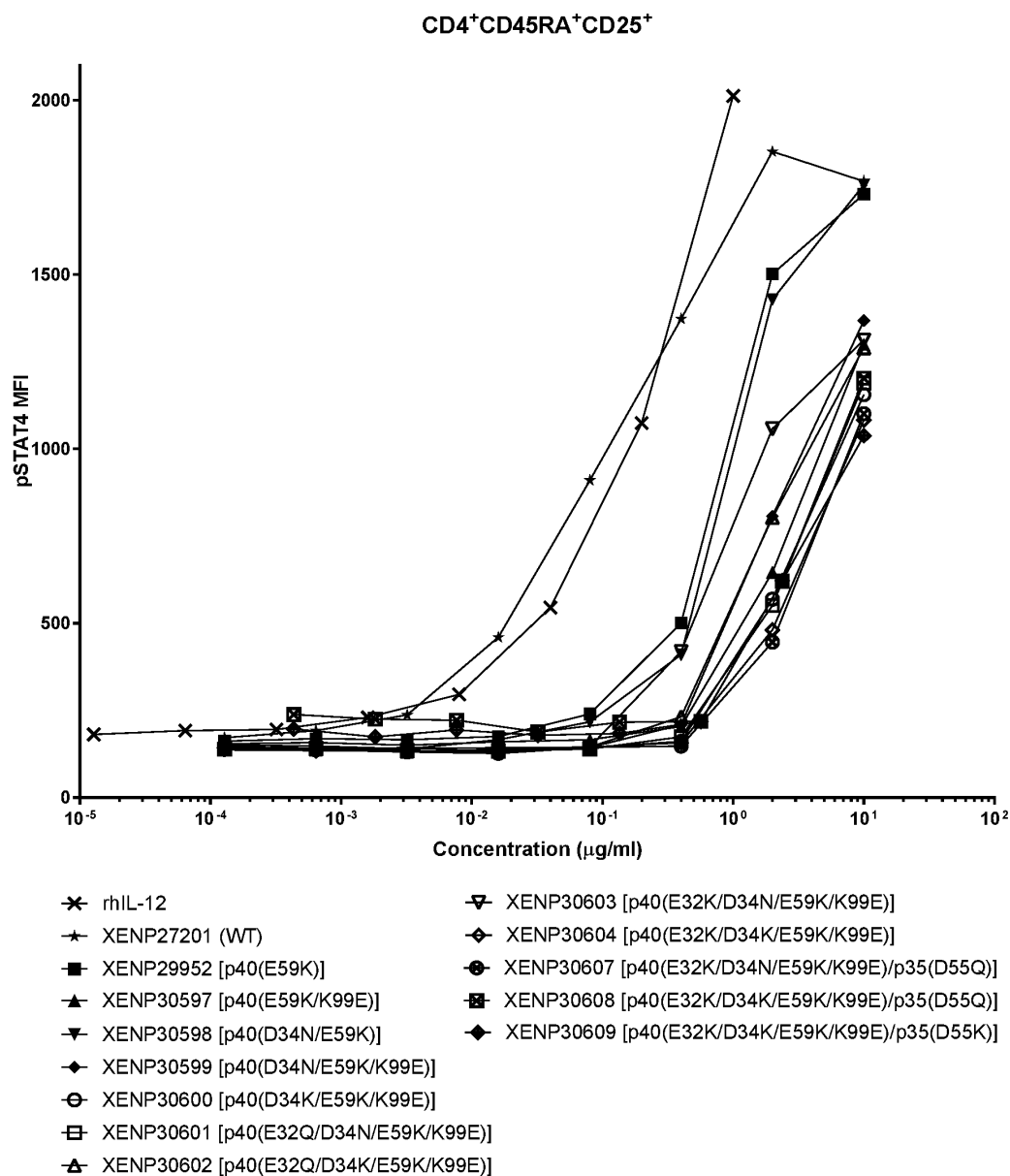


Figure 41

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)

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVK~~Y~~FGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQ~~E~~EPKNKTF~~L~~RCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(E59K/K99Y)

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVK~~K~~FGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQ~~Y~~EPKNKTF~~L~~RCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(E59Y/K99Y)

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVK~~Y~~FGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQ~~Y~~EPKNKTF~~L~~RCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(E45K/E59K/K99E)

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSS~~K~~VLGSGKTLTIQVK~~K~~FGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQ~~E~~EPKNKTF~~L~~RCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(D18K/E59K/K99E)

IWELKKDVYVVVELDWY~~P~~~~K~~APGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVK~~K~~FGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQ~~E~~EPKNKTF~~L~~RCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

Figure 42B

>IL12p40(E59K/K99E/Q144E)

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPEGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(E59K/K99E/Q144K)

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPKGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(E59K/K99E/R159E)

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVEGDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(E59K/K99E/K264E)

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKEDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

>IL12p40(D18K/E59K/K99E/K264E)

IWELKKDVYVVVELDWYPKAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKEDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: XXX)

Figure 43

>IL12p35(F96A)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTS AMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETV P QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO: XXX)

>IL12p35(M97A)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSF AMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETV P QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO: XXX)

>IL12p35(L89A)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTS AMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETV P QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO: XXX)

>IL12p35(L124A)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKL AMDPKRQIFLDQNMLAV
IDELMQALNFNSETV P QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO: XXX)

>IL12p35(M125A)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLL ADPKRQIFLDQNMLAV
IDELMQALNFNSETV P QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO: XXX)

>IL12p35(L75A)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESC ANSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETV P QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO: XXX)

>IL12p35(I171A)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETV P QKSSLEEPDFYKTK AKLCILLHAFRIRAVTIDRVMSYLNAS (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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKYFGDAGQYTCHKGGEVLSHSLLLHKKED
GIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWTITSTDLTFSVKSSRGSSDPQGVTCGAATLSAERVGRDNKEYEYSVEQEDS
ACPAEESLPIEVMVDVAHVHLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPTWSTPHSYFSLTFCVQVQGKSKREKK
DRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDT
LMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIS
KAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVF
SCSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

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

RNLPVATPDPMFPCLHHSQNLRLAVSNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNSRETSFITNGSCL
ASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSETVPQKSSLEEDFYKTKIKLCILL
HAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQM
TKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSHSLLLHKKED
GIWSTDILKDQYEPKNKTLRCEAKNYSGRFTCWWTITSTDLTFSVKSSRGSSDPQGVTCGAATLSAERVGRDNKEYEYSVEQEDS
ACPAEESLPIEVMVDVAHVHLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPTWSTPHSYFSLTFCVQVQGKSKREKK
DRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDT
LMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIS
KAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVF
SCSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:XXX)**

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

RNLPVATPDPMFPCLHHSQNLRLAVSNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNSRETSFITNGSCL
ASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSETVPQKSSLEEDFYKTKIKLCILL
HAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQM
TKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKYFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQYEPKNTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTGGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVSMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)

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

RNLPVATPDPGMFPCLLHHSQNLRLRAVSNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVSMHEALHNHYTQKSLSLSPGK (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
SLLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTGGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVSMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)

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

RNLPVATPDPGMFPCLLHHSQNLRLRAVSNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVSMHEALHNHYTQKSLSLSPGK (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
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVECEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)

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

RNLPAVATPDPMFPCLLHHSQNLLRAVSNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (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
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVECEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)

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

RNLPAVATPDPMFPCLLHHSQNLLRAVSNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

Figure 44D

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPCCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFVMSHEALHNHYTQKSLSLSPGK **(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
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPKGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:XXX)**

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

RNLPVATPDPMFPCLLHHSQNLRAVSNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLARKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
 VPQKSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVEGRDNKEYEYSVECEQEDSACPAEESLPIEVMMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:XXX)**

Figure 44F

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

RNLPVATPDPGMFPCLLHHSQNLRLAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWYDPAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRSGSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQEDSACPAEESLPIEVMVDVHKLKYENYTSSFFIRDIKPDPPKNLQKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
 NQVSLTCDVSGFYPYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:XXX)**

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

RNLPVATPDPGMFPCLLHHSQNLRLAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:XXX)**

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

RNLPVATPDPMFPCLHHSQNLRLAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSAMMALCLSSIYEDLMYQVEFKTMNAKLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:XXX)**

Figure 44H

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLARKTSFAMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVECEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO:XXX)**

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCAARKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK **(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
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)

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

RNLPVATPDPMFPCLHHSQNLRLRAVSNNMLQKARQTFLEFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLMYQVEFKTMNAKLAMPKRQIFLDQNMMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (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
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)

Figure 44J

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

RNLPVATPDPMFCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLADPKRQIFLDQNMMLAVIDELMQALNFNSET
VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK (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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSDDPQGVTCGAATLS
AERVRGDNKEYEYSVECEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)

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

RNLPVATPDPMFCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCAN
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK (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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK (SEQ ID NO: XXX)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSEMMALCLSSYIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKAKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMEALHNHYTQKSLSLSPGK (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

IWELKKDVYVVELDWYPKAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSEMMALCLSSYIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMEALHNHYTQKSLSLSPGK (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
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYT
 QKSLSLSPGK (SEQ ID NO: XXX)

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

RNLPVATPDPMFCLHHSQNLLRAVSNNMLQKARQTFEYFCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLARKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVLHEALHSHYTQKSLSLSPGK (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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYT
 QKSLSLSPGK (SEQ ID NO: XXX)

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

RNLPVATPDPMFCLHHSQNLLRAVSNNMLQKARQTFEYFCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLARKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVLHEALHSHYTQKSLSLSPGK (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

IWELKKDVYVVELDWYPDAPGEMVVLTC DTPKENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTF LRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVECEQEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYT
QKSLSLSPGK (SEQ ID NO: XXX)

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

RNLPVATPDPMFPC LHHSONLLRAVSNMLQKARQTLEFYPC TSEEIDHEDITKQKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVLHEALHSHYTQKSLSLSPGK (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

IWELKKDVYVVELDWYPDAPGEMVVLTC DTPKEKGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTF LRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVECEQEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYT
QKSLSLSPGK (SEQ ID NO: XXX)

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

RNLPVATPDPMFPC LHHSONLLRAVSNMLQKARQTLEFYPC TSEEIDHEDITKQKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVLHEALHSHYTQKSLSLSPGK (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
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFVSKSSRGSSDPQGVTCTGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEEQGDVFSCSVLHEALHSHYT
QKSLSLSPGK (SEQ ID NO: XXX)*

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

*RNLVPATPDPMFPCLLHHSQNLRLRAVSNMLQKARQTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLARKTSFMMALCLSSYIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKSLSLSPGK (SEQ ID NO: XXX)*

Figure 46A

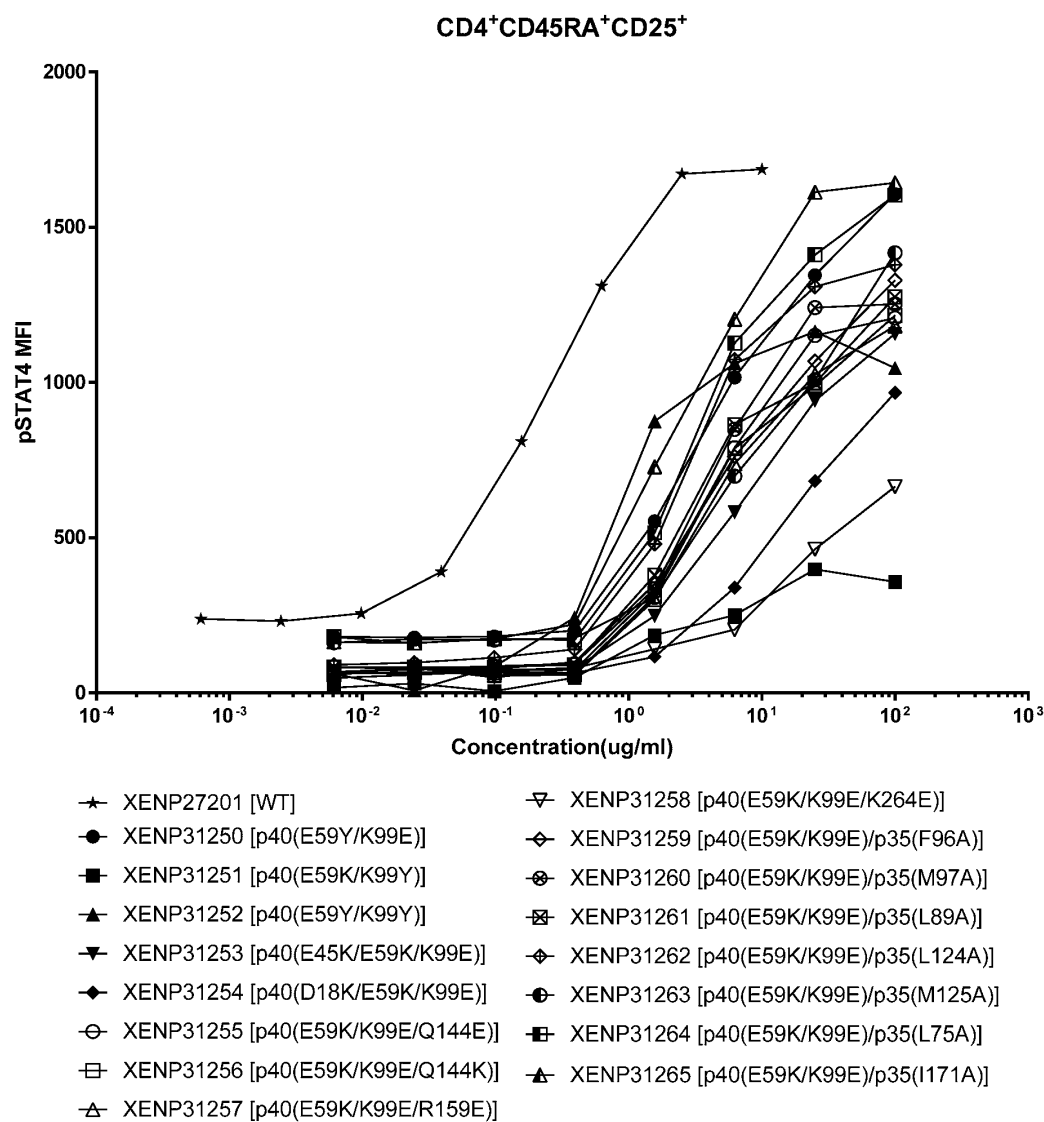


Figure 46B

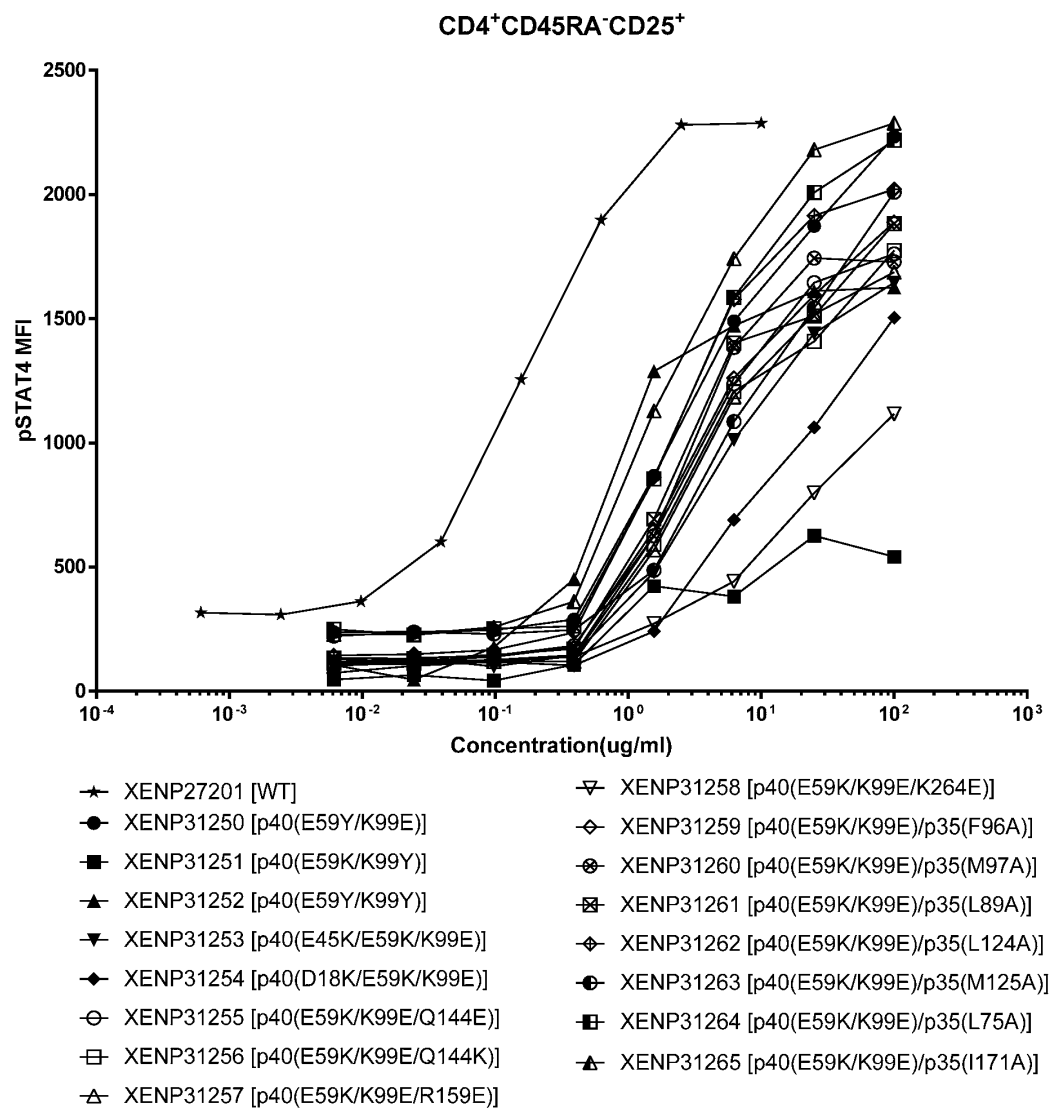


Figure 46C

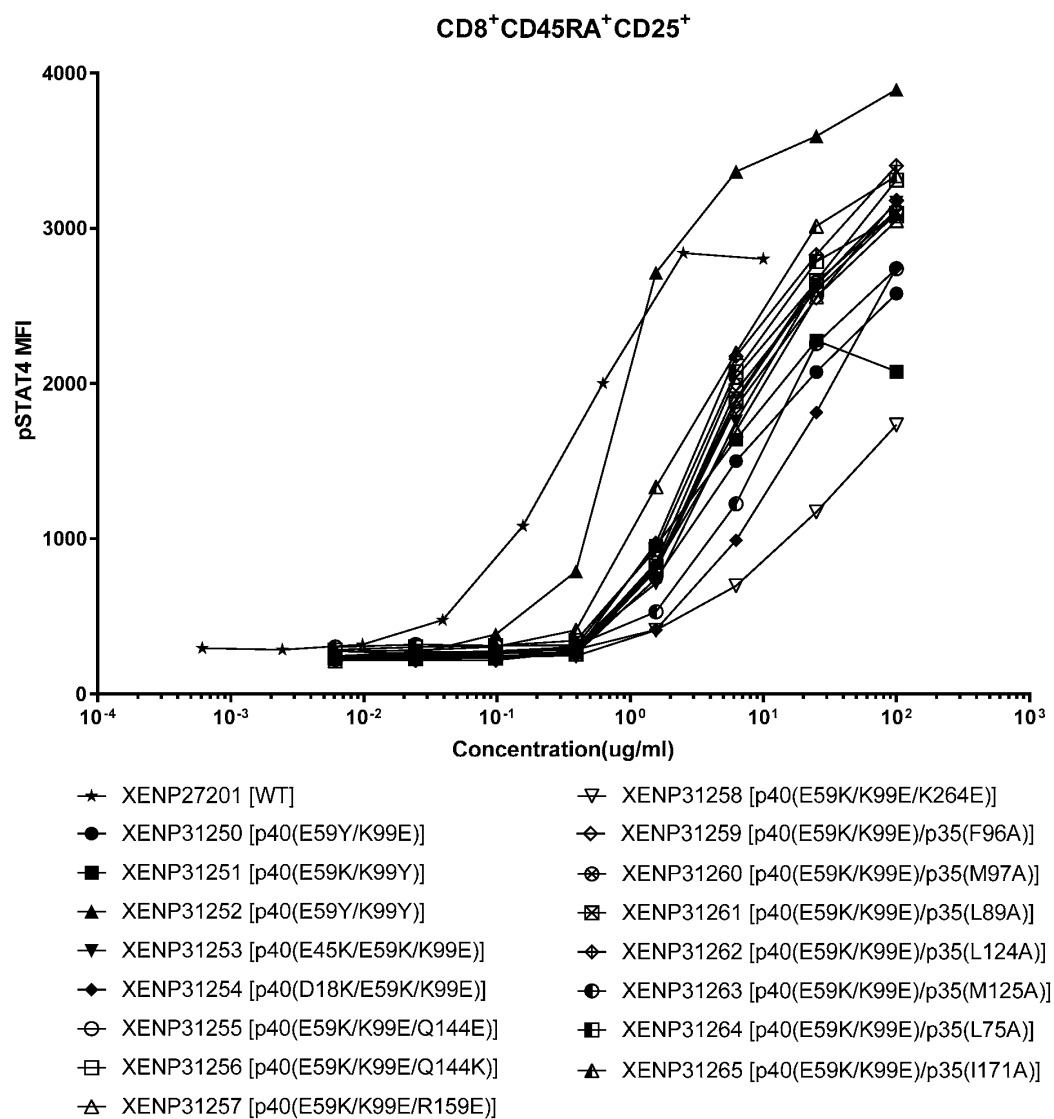


Figure 46D

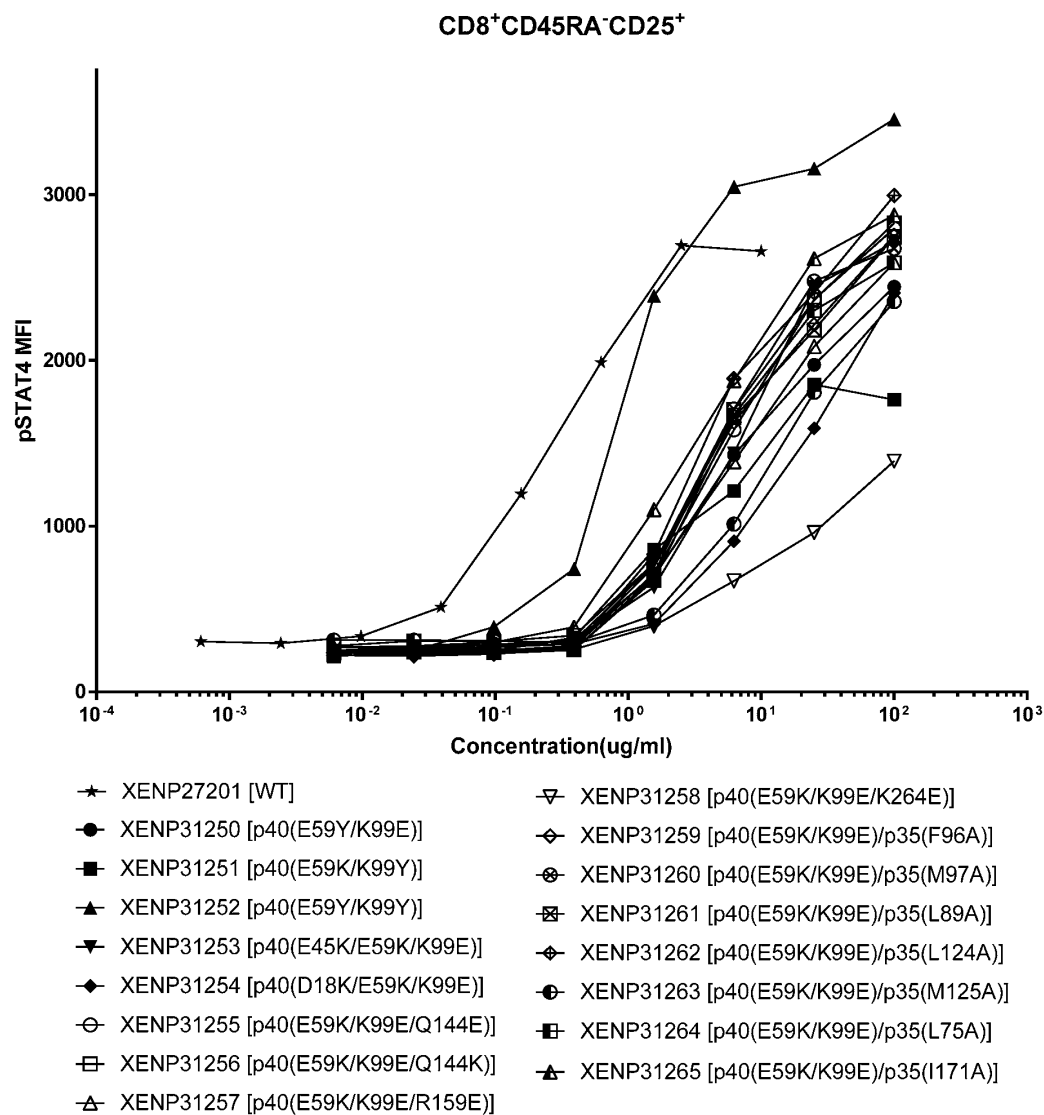
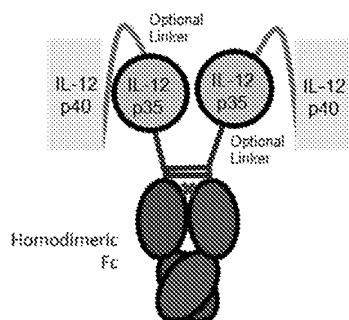


Figure 47

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)

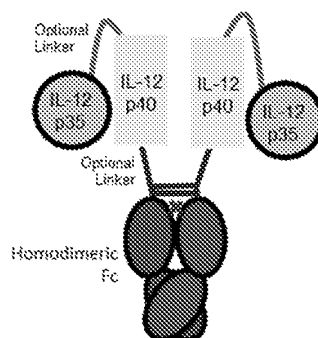
**(scIL-12(p35/p40))₂-Fc**

Figure 48C

C)

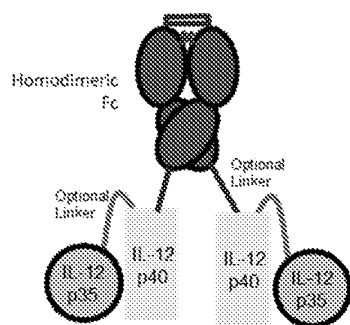
**Fc-(scIL-12(p40/p35))₂**

Figure 48D

D)

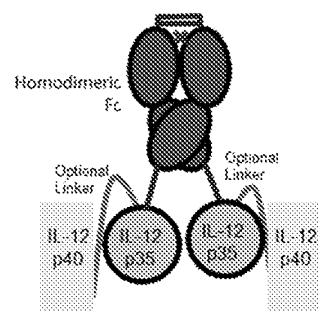
**Fc-(scIL-12(p35/p40))₂**

Figure 49

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTLRCEAKNYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/GGGGSGGGGS
GGGGSGGGGSGGGGS/RNLPVATPDPGMFPCLLHHSQNLRAVSNMLQKARQTLEFYPCTSEEIDHEDITKDKTSTVEA
CLPLELTKNESCLNSRETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVID
ELMQALNFNSETVPQKSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPC
PAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGP
ENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDFVSCSVMEALHNHYTQKSLSLSPGK (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
LLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/GGGGSGGGGS
GGGGSGGGGSGGGGS/RNLPVATPDPGMFPCLLHHSQNLRAVSNMLQKARQTLEFYPCTSEEIDHEDITKDKTSTVEA
CLPLELTKNESCLNSRETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVID
ELMQALNFNSETVPQKSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPC
PAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGP
ENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDFVSCSVMEALHNHYTQKSLSLSPGK (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

IWELKKDYYVVELDWYPDAPGEMVVLTCDTPEEDGITWLTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSHS
 LLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWTITSTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
 GDNKEYEYSVEQCEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
 WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/GGGGSGGGGS
GGGGSGGGGSGGGGS/RNLVPATPDPGMFCLHHSQNLRAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEA
 CLPLELTKNESCLNSRETSFITNGSCLSRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVID
 ELMQALNFNSETVPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCP
 PAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEYNSTYRVVSVLTVL
 HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGGP
 ENNYKTTTPVLDSGDSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: XXX)**

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

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

Figure 51A

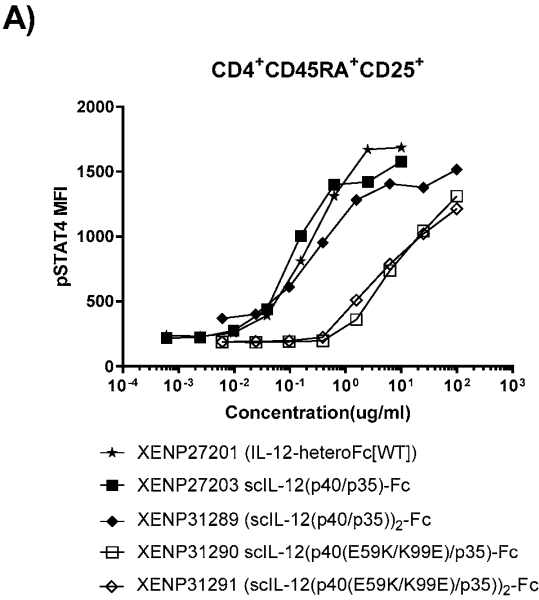


Figure 51B

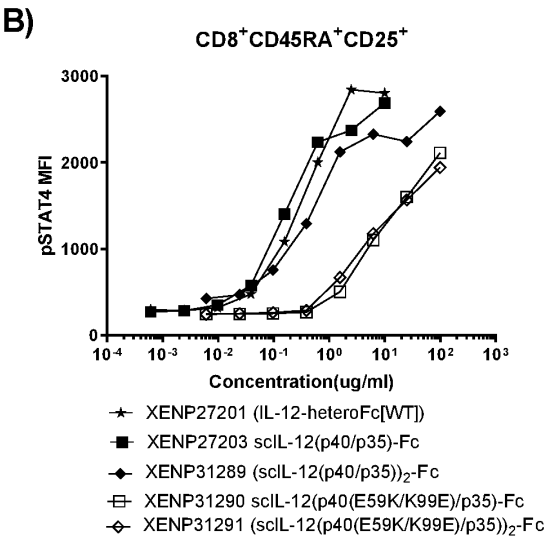


Figure 51C

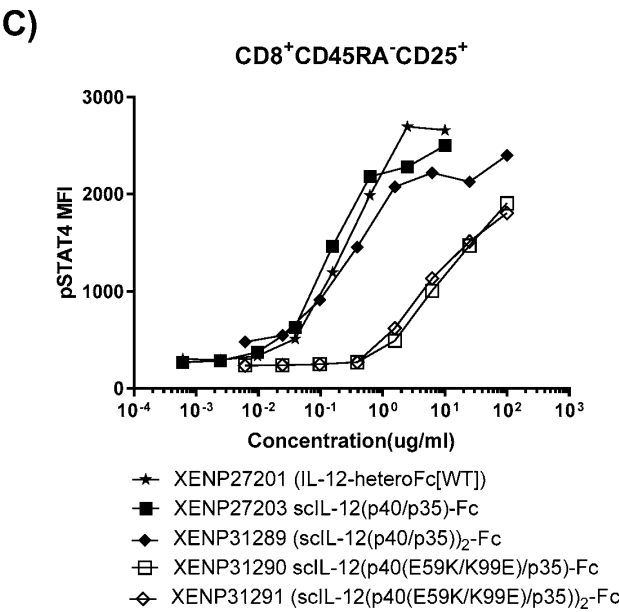


Figure 51D

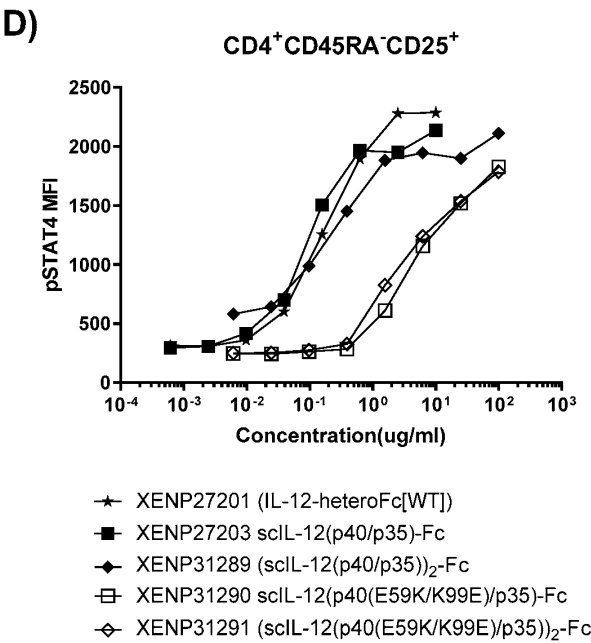


Figure 52

XENP	Format	IL-12p40 Variant	IL-12p30 Variant	pSTAT4 EC50 (μg/ml)	
				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

QVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAVIWYDGSKRYYADSVKGRFTISRDN
NTLFLQMNSLRAEDTAVYYCATNDDYWGQGLTVVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTP
PVLDSGGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: XXX)

XENP016432 Nivolumab_H0L0_IgG1_PVA_/S267K Light Chain

EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLT
FAVYYCQQSSNWPRTFGQGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: XXX)

Figure 54A

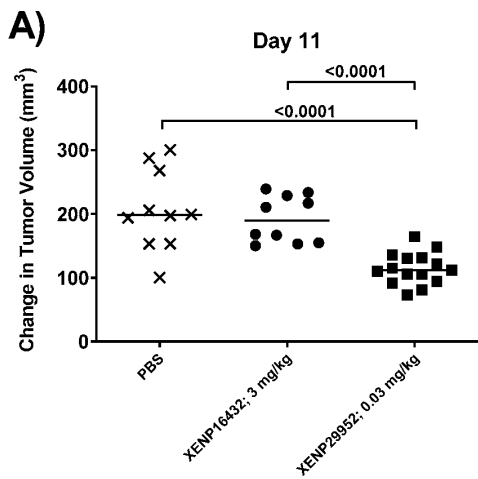


Figure 54B

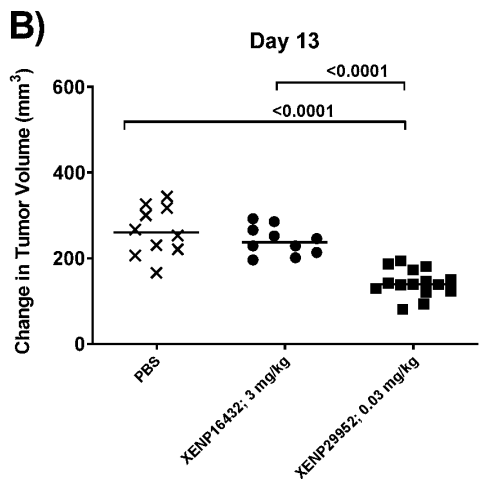


Figure 54C

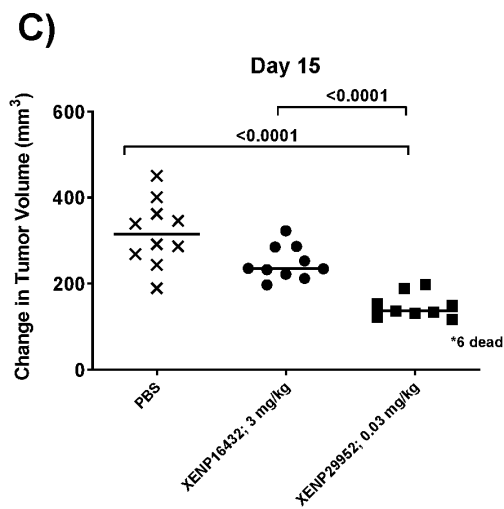


Figure 54D

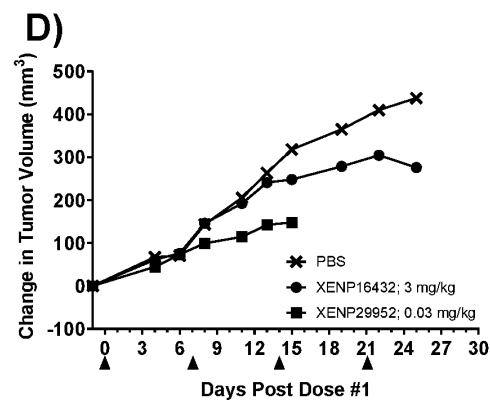


Figure 55A

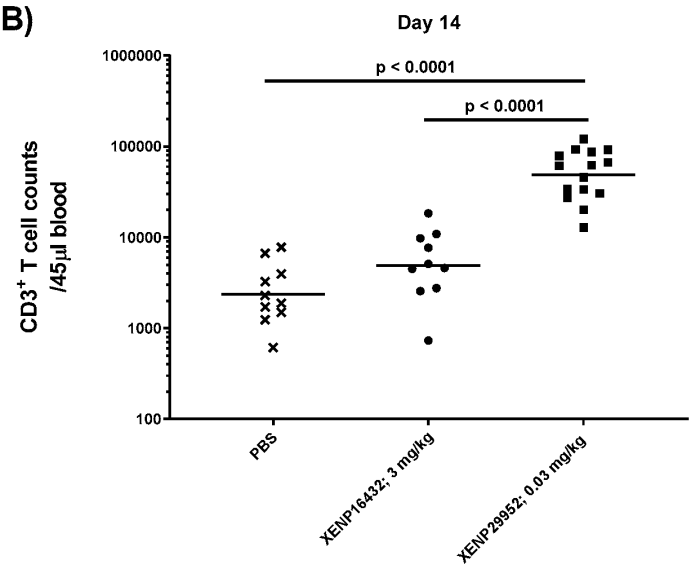


Figure 55B

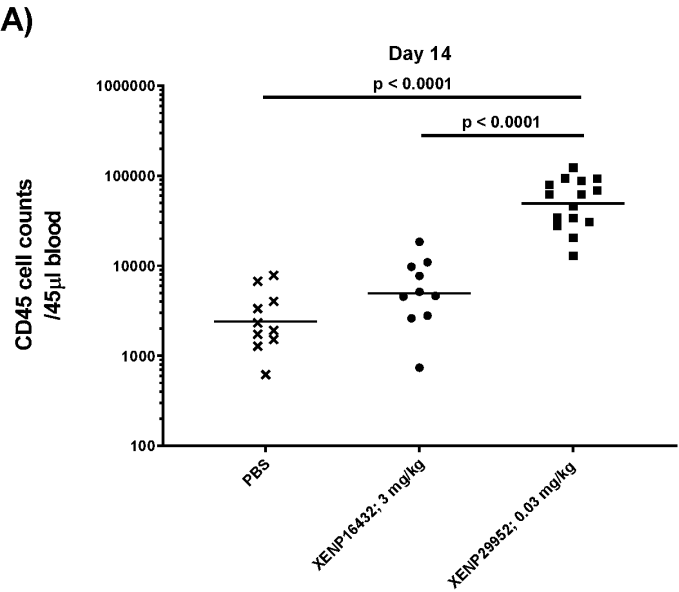


Figure 55C

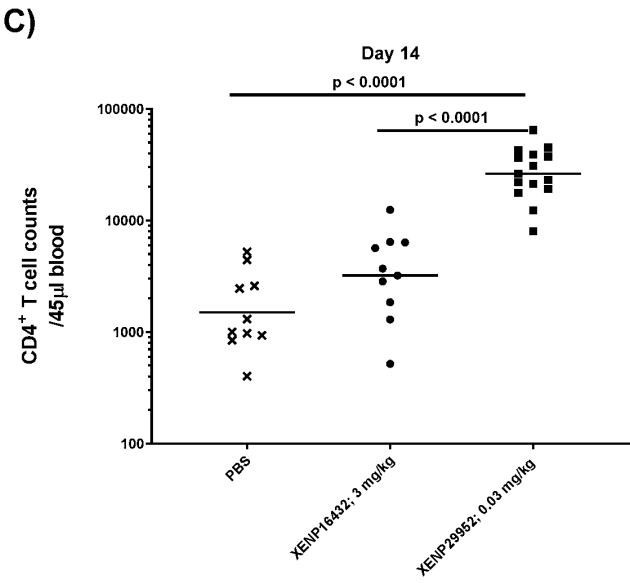


Figure 55D

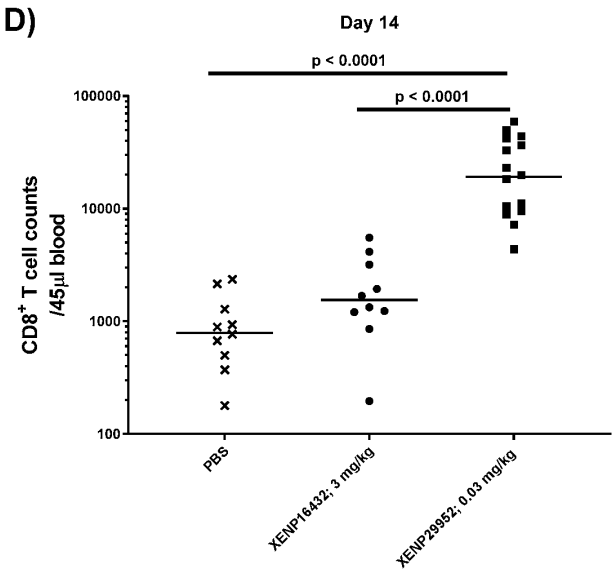


Figure 55E

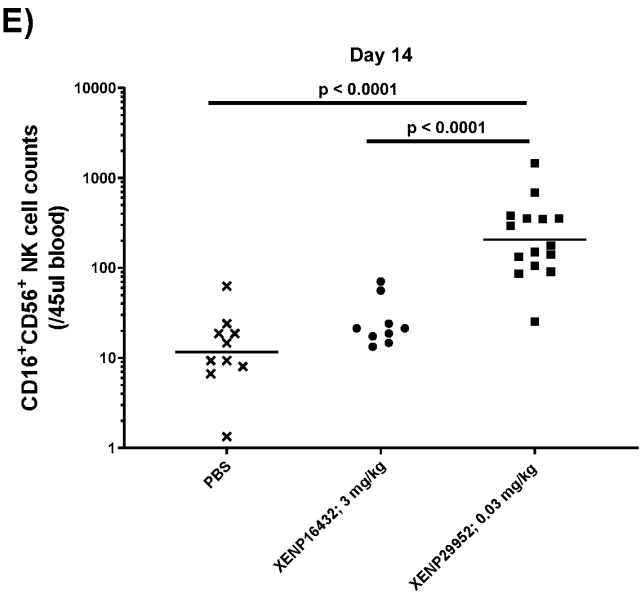


Figure 55F

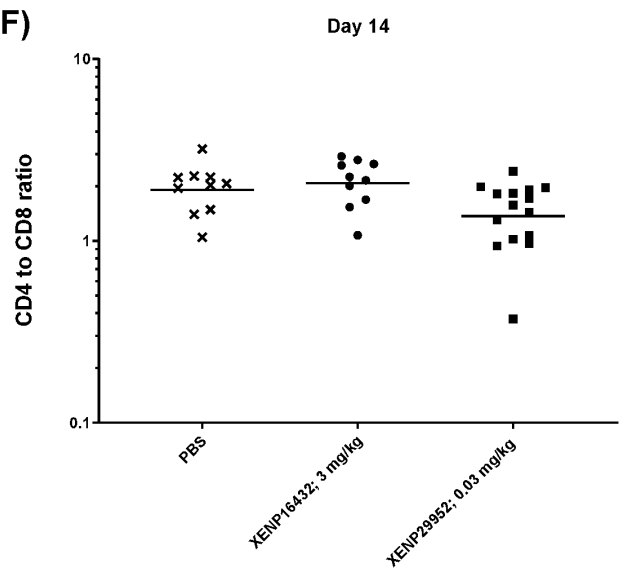


Figure 56A

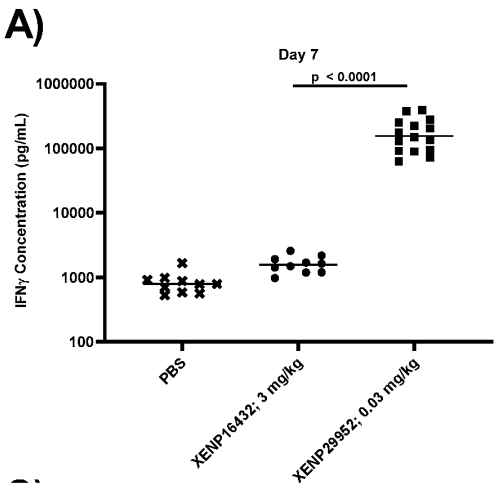


Figure 56B

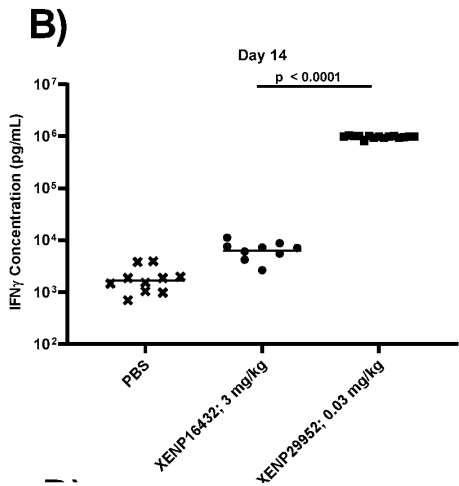


Figure 56C

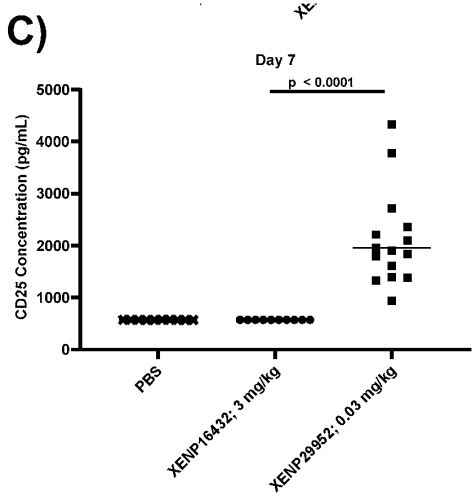


Figure 56D

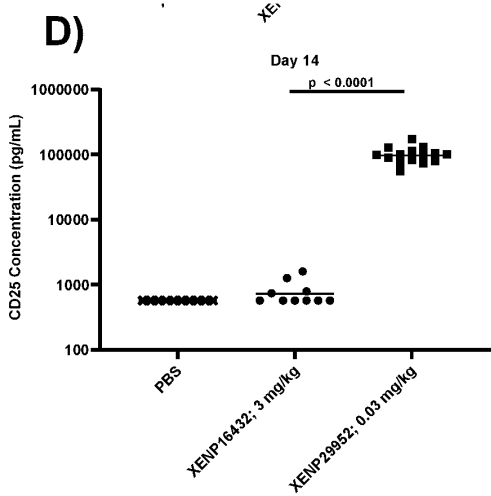


Figure 57A

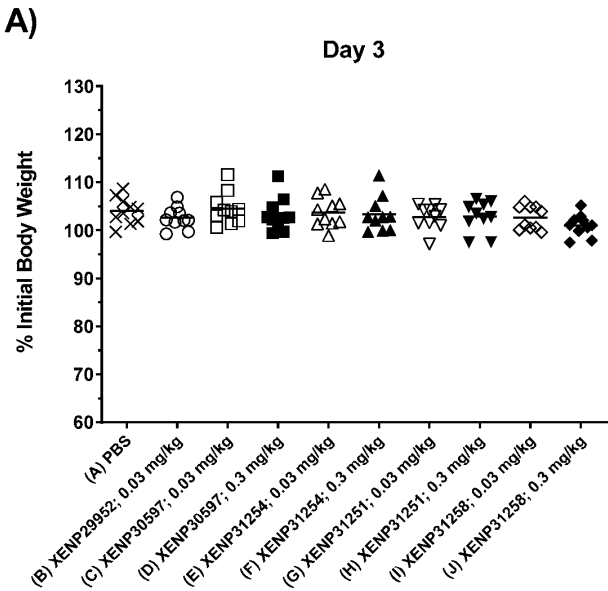


Figure 57B

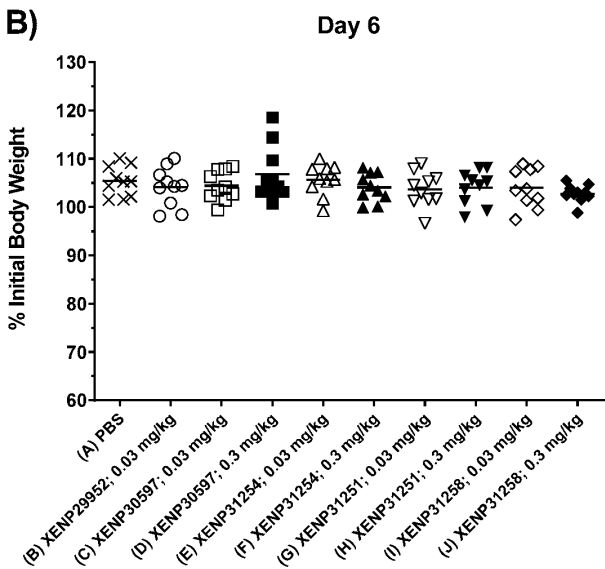


Figure 57C

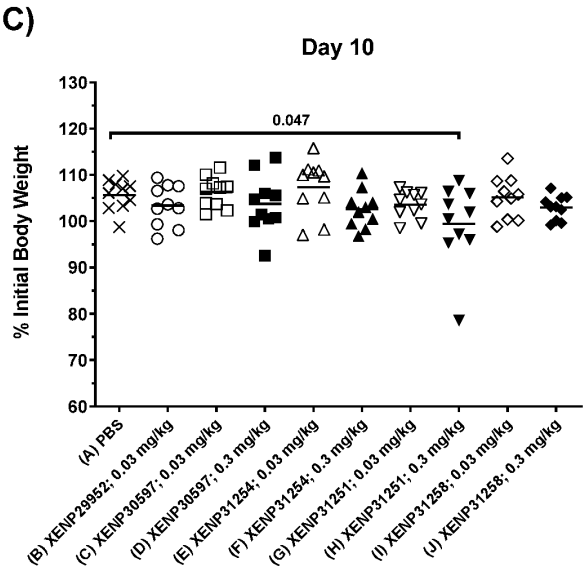


Figure 57D

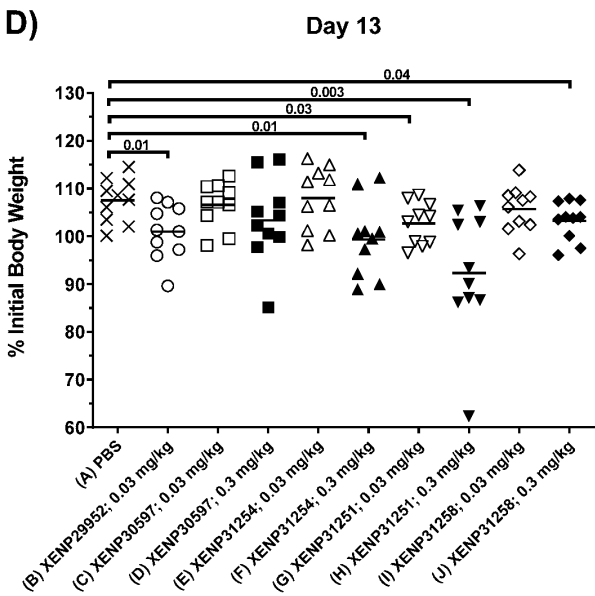


Figure 57E

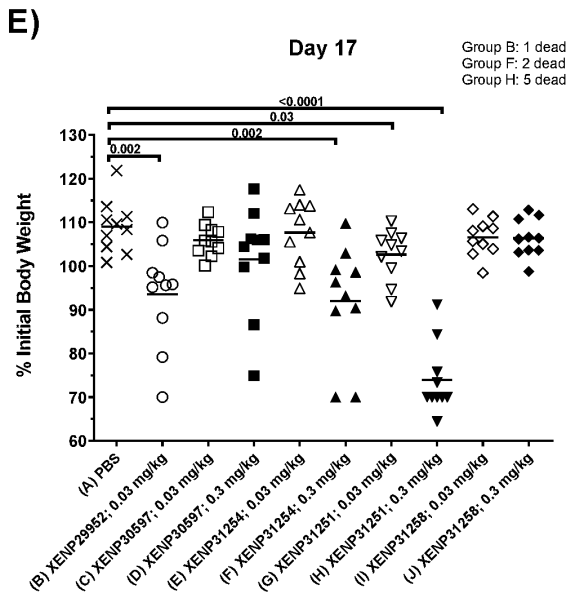


Figure 57F

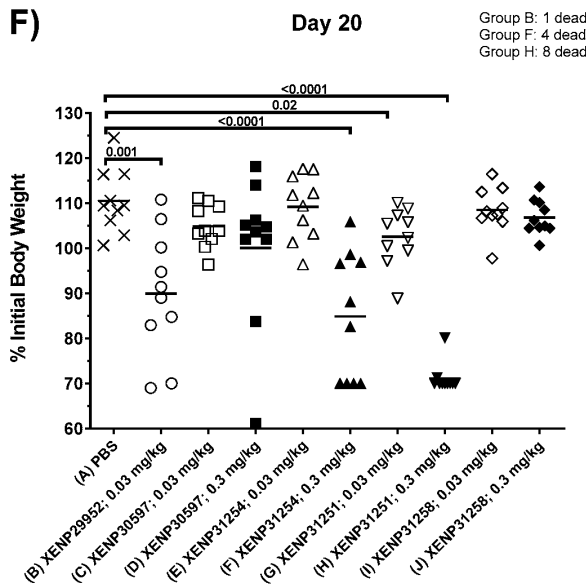


Figure 57G

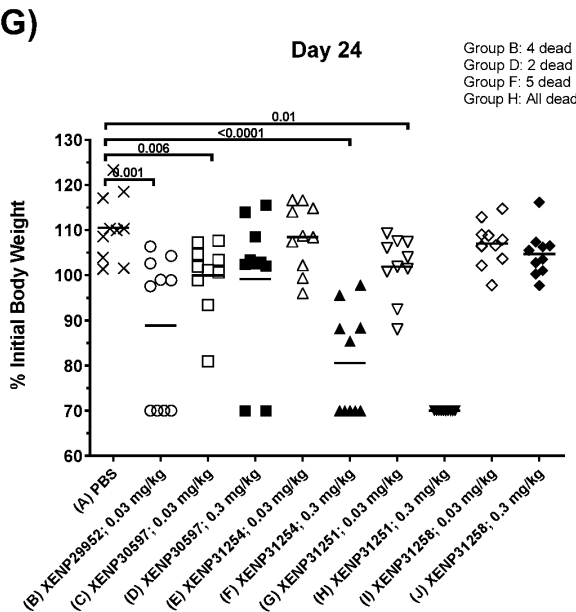
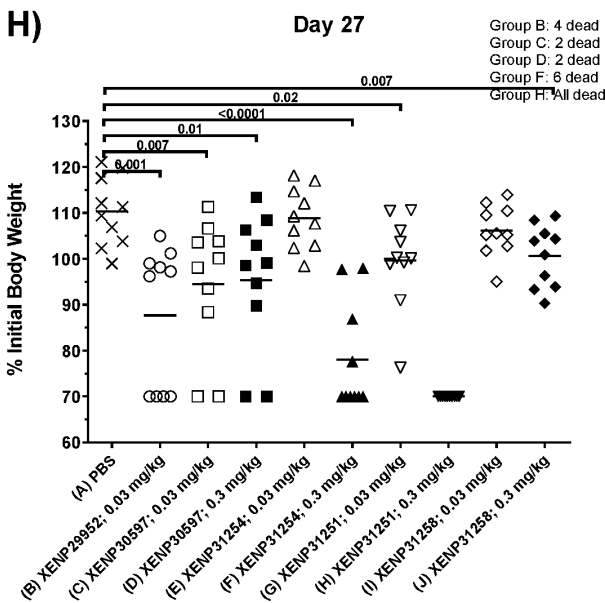


Figure 57H



1)

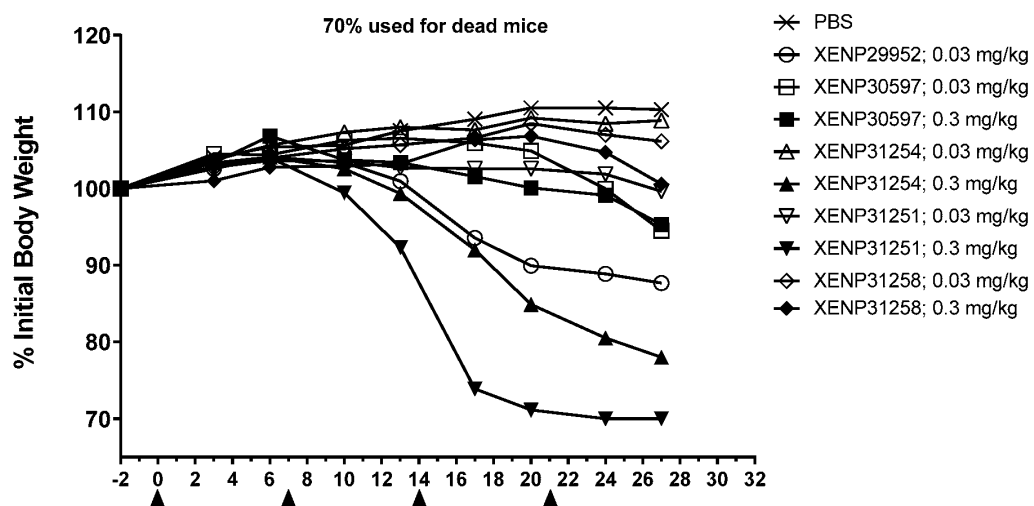


Figure 58A

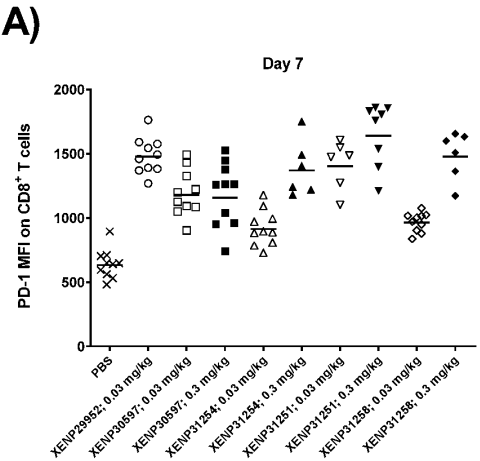


Figure 58B

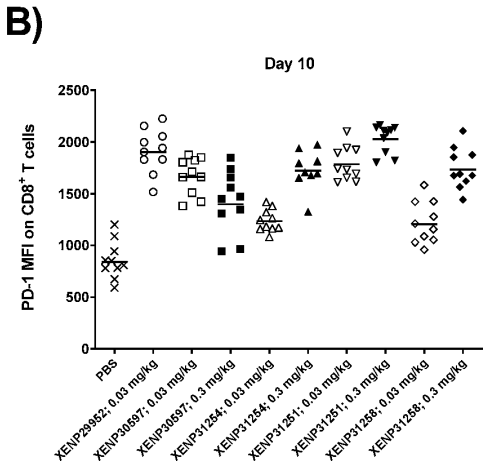


Figure 58C

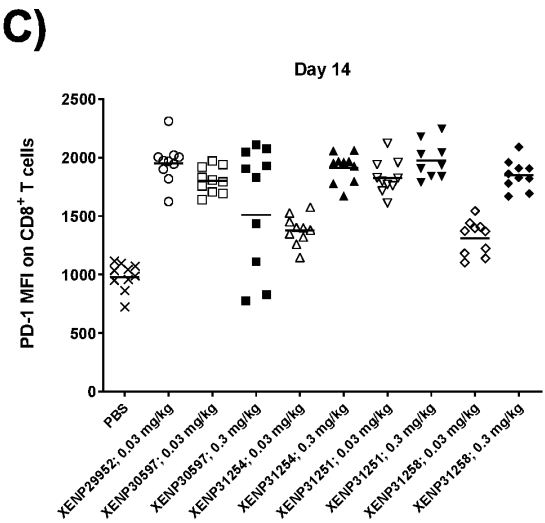


Figure 59A

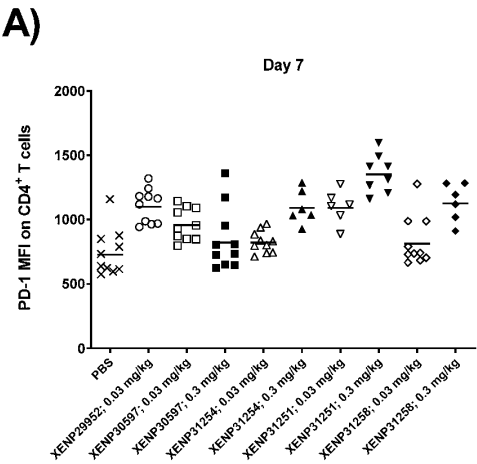


Figure 59B

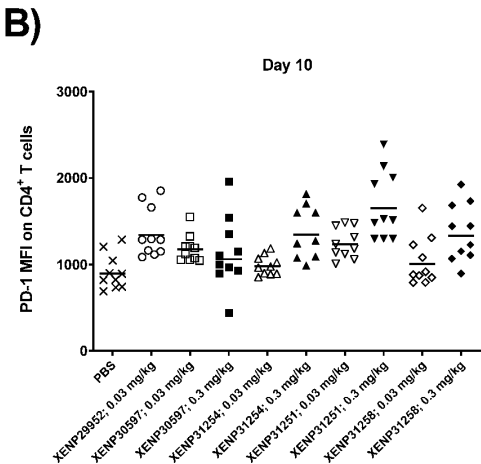


Figure 59C

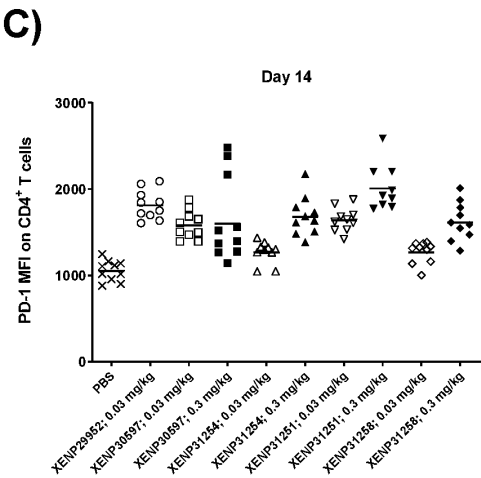


Figure 60A

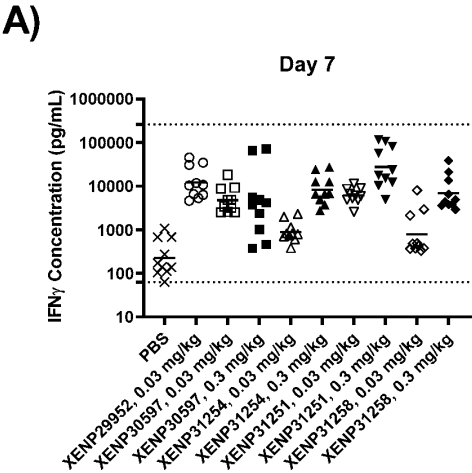


Figure 60B

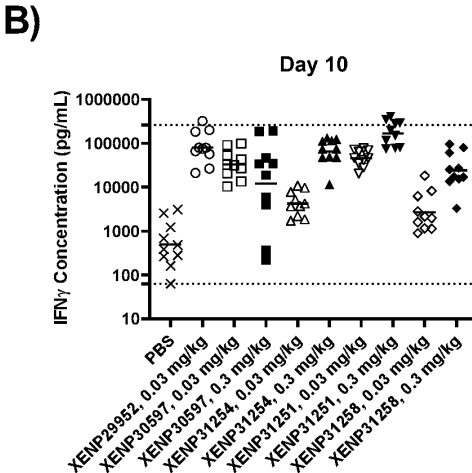


Figure 60C

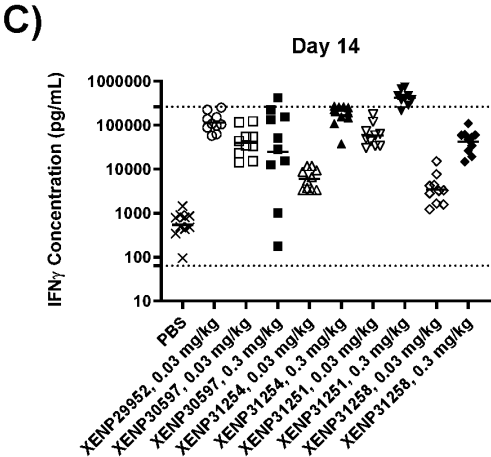


Figure 60D

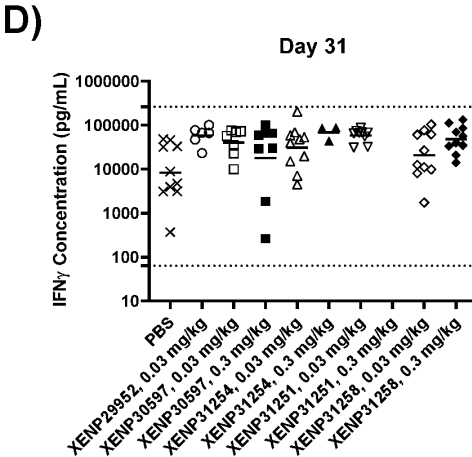


Figure 61A

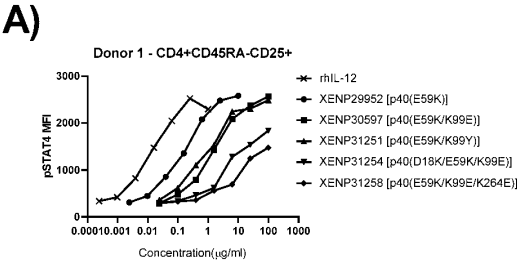


Figure 61C

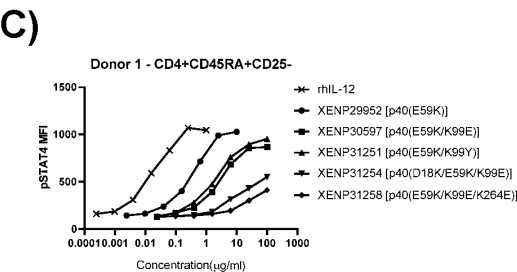


Figure 61E

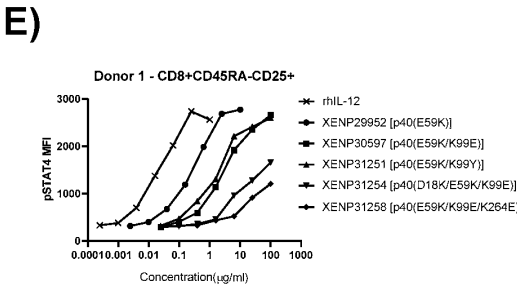


Figure 61B

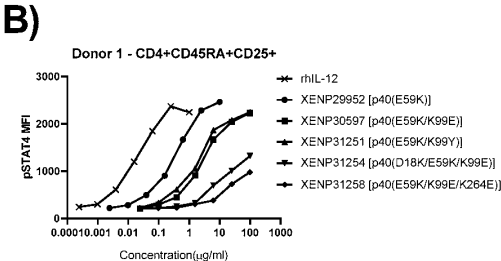


Figure 61D

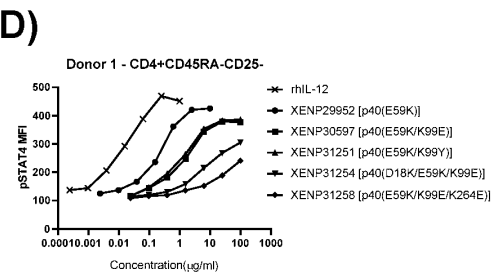


Figure 61F

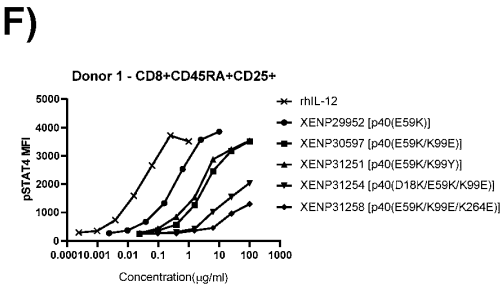


Figure 61G

G)

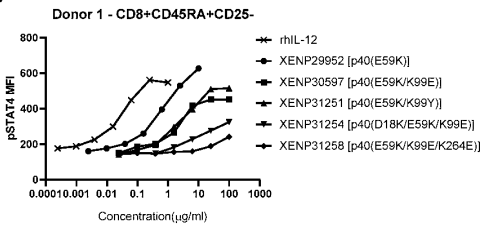


Figure 61I

I)

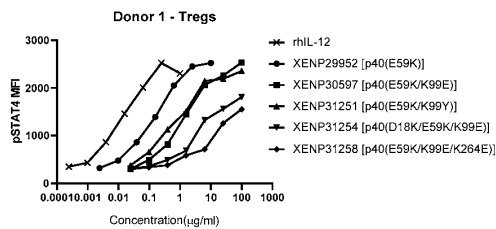


Figure 61K

K)

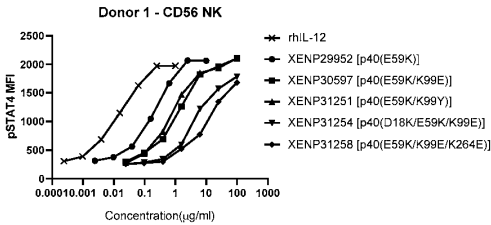


Figure 61H

H)

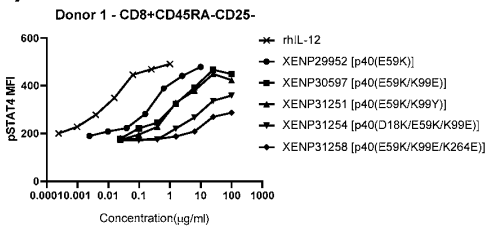


Figure 61J

J)

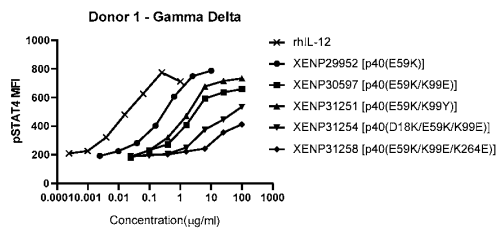


Figure 62A

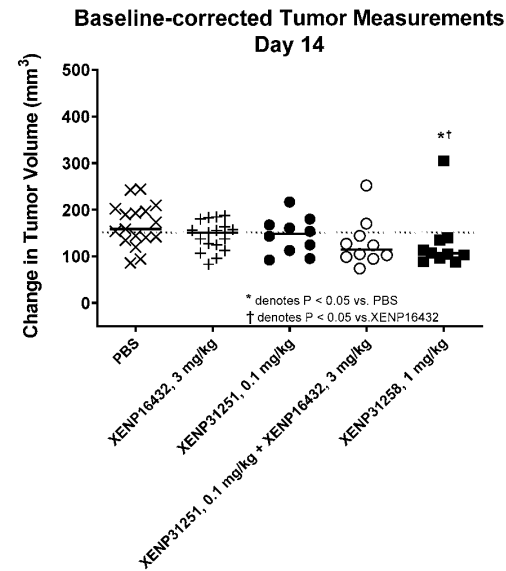


Figure 62B

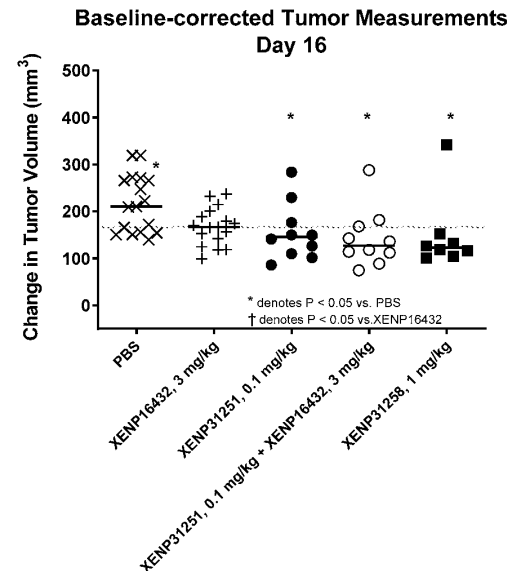


Figure 62C

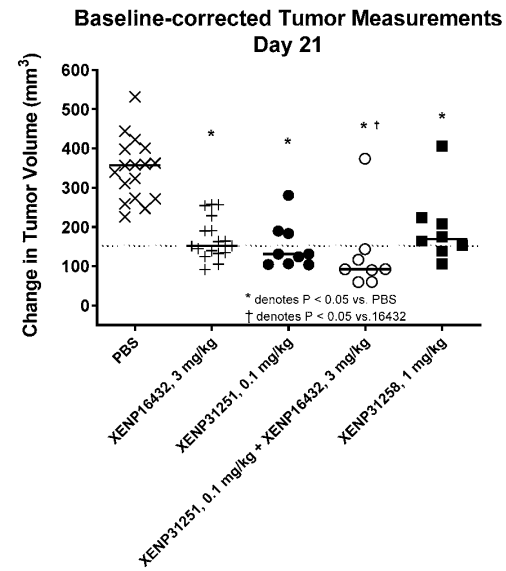


Figure 62D

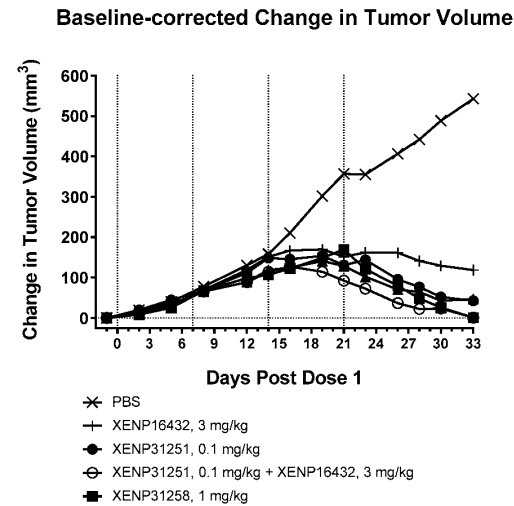


Figure 63A

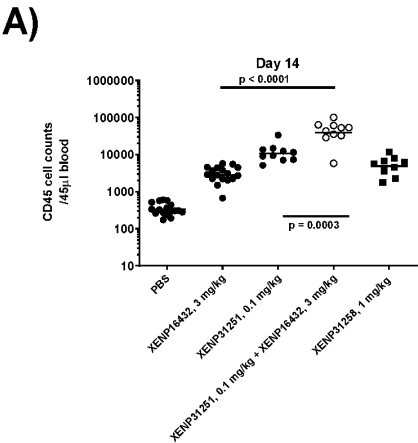


Figure 63B

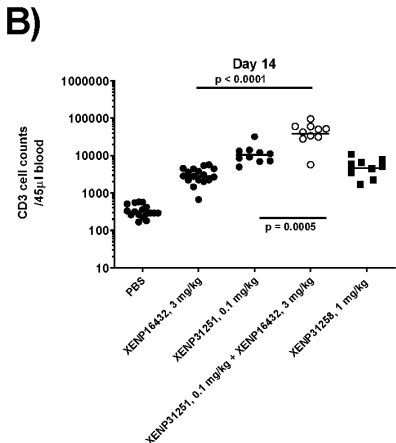


Figure 63C

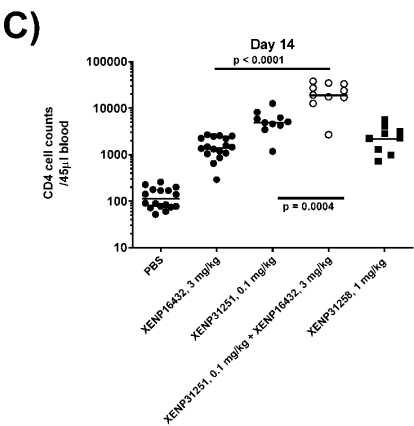


Figure 63D

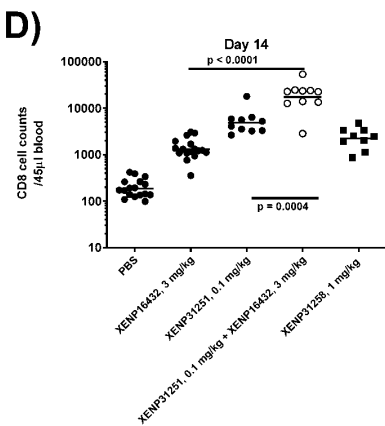


Figure 63E

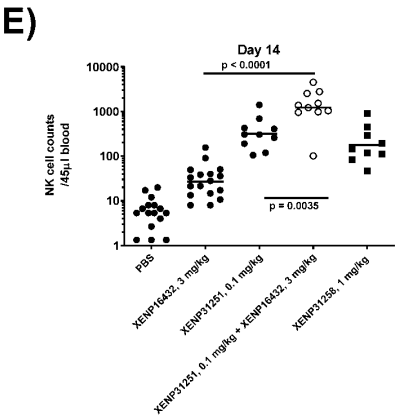


Figure 63F

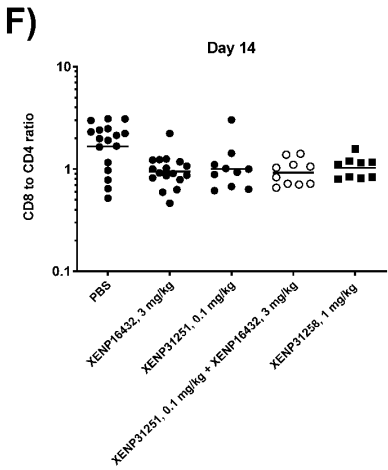


Figure 64A

>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

IWELKKDVVVVELDWYPKAPGEMVVLTCDTPEEDGITWTLTDSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/GGGGSGGGGS/
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEE
YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
DIAVEWESDGGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK (SEQ ID
NO: XXX)

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

RNLPVATPDPGMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNSRET
SFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSETVPQK
SSLEEDFYKTIKILCILLHAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
KDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS
NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGS
FFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK (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**

IWELKKDYYVVELDWYPDAPGEMVVLTCDTPEEDGITWLTLDQSSEVLGSGKTLTIQVKKFGDAGQYCHKGGEVLSSH
LLLLHKKEDGIWSTDILKDQYEPKNKTLRCEAKNYSGRFTCWWLTISTDLTFSVKSSRGSSDPQGVTGCAATLSAERV
GDNKEYEYSVEQCEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/GGGGSGGGGS/
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREE
YNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
DIAVEWESDGQPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK (SEQ ID
NO: XXX)

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

RNLPVATPDPMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNSRET
SFITNGSCLASRKTSFMMALCLSIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSETVPQK
SSLEEDFYKTIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPK
KDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVS
NKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTTPVLDSGGS
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

IWELKKDVVVVELDWYPDAPGEMVVLTCDTPEEDGITWTLTDSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSHS
 LLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
 GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
 WSTPHSYFSLTFCVQVQGGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/GGGGSGGGGS/
 EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEE
 YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
 DIAVEWESDGGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK (SEQ ID NO: XXX)

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

RNLPVATPDPMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNSRET
 SFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSETVPQK
 SSLEEDFYKTIKILCILLHAIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
 KDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
 DIAVEWESDGGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVLHEALHSHYTQKSLSLSPGK (SEQ ID NO: XXX)

Figure 65A

> IL-12p40(C252S)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS
(SEQ ID NO: XXX)

> IL-12p40(D18K/E59K/K99E/C252S)

IWELKKDVYVVELDWYPKAPGEMVVLTCDTPEEDGITWTWLDQSSEVLGSGKTLTIQVKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS
(SEQ ID NO: XXX)

> IL-12p40(D18K/E59K/K99E/C252S/K264E)

IWELKKDVYVVELDWYPKAPGEMVVLTCDTPEEDGITWTWLDQSSEVLGSGKTLTIQVKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS
(SEQ ID NO: XXX)

> IL-12p40(E59K/K99Y/C252S)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDQSSEVLGSGKTLTIQVKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQYEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS
(SEQ ID NO: XXX)

> IL-12p40(E59K/K99E/C252S/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDQSSEVLGSGKTLTIQVKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS
(SEQ ID NO: XXX)

> IL-12p40(E59K/K99E/C252S)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDQSSEVLGSGKTLTIQVKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS
(SEQ ID NO: XXX)

Figure 65B

>IL-12p40 (E59K/K99E/N103Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWTSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N113Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWTSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N200Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYEQYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWTSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N281Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWTSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYSSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N103Q/N113Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWTSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N103Q/N200Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYEQYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWTSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N103Q/N281Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWTSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYSSSSWSEWASVPCS

(SEQ ID NO: XXX)

Figure 65C

>IL-12p40 (E59K/K99E/N113Q/N200Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYEQYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWTSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (IL12p40_E59K/K99E/N113Q/N281Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYEYNTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWTSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYSSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N200Q/N281Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYEQYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWTSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYSSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N103Q/N113Q/N200Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYEQYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWTSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N103Q/N200Q/N281Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYEQYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWTSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYSSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N113Q/N200Q/N281Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYEQYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWTSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYSSSSWSEWASVPCS

(SEQ ID NO: XXX)

>IL-12p40 (E59K/K99E/N103Q/N113Q/N200Q/N281Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYEQYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWTSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYSSSSWSEWASVPCS

(SEQ ID NO: XXX)

Figure 66A

>XENP32187 human IL12p40(D18K/E59K/K99E/C252S) (GGGGG)2-human IL12p35 (GGGGG)2-Fc(216) IgG1 pI(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 - human_IL12p40(D18K/E59K/K99E/C252S)_(GGGGGS)2_Fc(216)_IgG1_pl(-)
Isosteric A C220S/PVA /S267K/L368D/K370S

IWELKKDVYVVELDWYFKAPGEMVVLTCDEEDGITWLTLDQSSSEVLGSGKTLTIQVKKFGDAGQYTHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTLFLRCEAKNYSGRFTCWLLTITISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNGKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVLSLTQDSVSGFYNSDIADVVESSDQGEPENNYKTTTPVLDSDSGFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNYT
 QKSLSLSPGK (SEQ ID NO: XXX)

Chain 2 - IL12p35 (GGGGS)₂ Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

RNLVPATPDGGMF PCLHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKM YQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKLCLILLHAFIRAVTIDRVMSYLNAS/ GGGGSGGGGS /EPKSSDKTHTCPPCPAPVPVAGP
SVFLFPKPKDITLMSRTPEVTCVVVDVKHEDPEVKFNWYDGVGVHNAKTLCKPREEQYNSTIRVSVSLTVLHQDWLNL
GKEYKCKNSKALPAPIEKTISKAGKQPREPQVYTLPPSREQMTKNVKTCLVKGVYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFGFLYSKLTVDKSRWQQGNVFCSCVMHEALHNSYTKQSLSLSPGK (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

IWELKKDVYVELDWYPKAPGEMVVLTCDTPEEDGITWLLDQSSEVLGSGKTLTIQVKKFGDAGQYTHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTLFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDVHKLKYENYTSFFIRDIKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSYTRVYVSLTVLHQDWLNGKEYCKVSNKALPAPIEKTI SAKAGQPREPQVYTLPPSREEMTK
 NVQSLTCDVSYGFPSDIAVEWESDQGEPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNYT
 QKSLSLSPGK (SEQ ID NO: XXX)

Chain 2 - IL12p35 (GGGGS)₂ Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

RNLVPVATPDPGMFCLHHSQNLRLAVSNMLQKARQTFLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLMKYQVEFKTMNAKLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEDFDYKTKIKLCILLHAFIRAVTTIDRVMSYLNAS//GGGGSGGGGS//EPKSSDKTHTCPPCPAPVPVAGP
SVFLFPKPKDITLMSIRTPETVCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTIRVVSVLTVLHQDWLN
GKEYKCKSDNGKALPAPIEKTISKAKQGPREPQYVYTLPPSREAHMTKNQVKLTLVKGFPYSIDIAVEWESNGQPENNYK
TTPPVLDKVSNGSFFLYSKLTVDKSRWQOGNVFSCSVMEALHNHYTKQSLSLSPGK (SEQ ID NO: XXX)

Figure 66B

**>XENP32189 human IL12p40(E59K/K99Y/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/K99Y/C252S)_ (GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYDPAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQYEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: XXX)

Chain 2 - IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPCLHHSQNLRLRAVSNNMLQKARQTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: XXX)

**>XENP32190 human IL12p40(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(E59K/K99E/C252S/K264E)_ (GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYDPAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: XXX)

Chain 2 - IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPCLHHSQNLRLRAVSNNMLQKARQTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (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
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSGFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

Chain 2 - IL12p35_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSEMMALCLSSIEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSGFFLYSKLTVDKSRWQQGNVFCSCSVMHEALHNHYTQKSLSLSPGK **(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
 SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSGFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: XXX)**

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSEMMALCLSSIEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPVLDSDGSGFFLYSKLTVDKSRWQQGNVFCSCSVMHEALHNHYTQKSLSLSPGK **(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
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKQYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

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

RNLPVATPDPMFPCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (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
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Figure 66E

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNLN
 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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

> IL-12p40(E59K/K99E/N103Q/N113Q/C252S/K264E_(GGGGGS)2_Fc(216)_IgG1_pl(-
) Isosteric A C220S/PVA /S267K/L368D/K370S

IWELKKDVYVELDWYPDAPGEMVVLTCDTPEEDGITWLTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCCHKGGEVLSH
 SLLLLLHKKEDGIWSTDILKDQEEPQKQTLFLRCEAKQYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVT CGAATLS
 AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLYENYTSSFFIRDIIKDPDPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGSPSVFLFPPKPKDTLMISRTPEVTCVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 OKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 - human IL12p35 (GGGGS)₂ Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

RNLVPVATPDPGMFPCLHHSQNLRLRAVSNMLQKARQTFLEFYPTCTSEEDIHEDITKDKTSTVEACPLPLETKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLMKYQVEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEDFDYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPFPVAGP
SVFLFPKPKDITLMSIRTP EVTCSVVVDVKHEDPEVKFNWYVDGVEVHNAKTCLPREEQYNSTYRVVSVLTVLHQDWLNL
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMKNQVKTCLVKGFPSDIAVEWESNGQPENNYK
TPPVLDSDGSFFLYSKLTVDKSRWOOGNFVSCSVMHAEALHNNHYTKOISLSLSPGK (SEQ ID NO: XXXX)

> IL-12p40(E59K/K99E/N103Q/N200Q/C252S/K264E_(GGGGGS)2_Fc(216)_IgG1_pl(-
) Isosteric A C220S/PVA /S267K/L368D/K370S

IWELKKDVYVELDWYPDAPGEMVVLTCDTPEEDGITWLLDQSSSEVLGSGKTLTIQVKKFGDAQYTHCKGGEVLSH
 SLLLLLHKKEDGIWSTDILKDQEEPQKQTLFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSFFFIRDIKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
 OKSLSLSPGK (SEQ ID NO:XXX)

Figure 66G

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (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
 SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDGNKEYEYSVECEQEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPYPSDIAVEWESDGPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (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
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKQYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)*

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

*RNLPVATPDPGMFPCLLHHSQNLLRAVS NMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQVMHEALHNHYTQKSLSLSPGK (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
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKQYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYEYNTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)*

Figure 66I

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEDIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
 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
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFILRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEDIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
 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
SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKQYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)

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

RNLPVATPDPMFPCLLHHSQNLRLRAVS NMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQVSCVMHEALHNHYTQKSLSLSPGK (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
SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQKASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)

Figure 66K

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

RNLPVATPDPMFCLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
 N 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

IWELKKDVYVVELDWYDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKQYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMDAVHKLKYEQYTSSFFIRDIKPDPPKNLQKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS/_
 GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

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

RNLPVATPDPMFCLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
 N 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
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKQYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTGCAATLS
 AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMVDAVHKLKYEQTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSEMMALCLSSIYEDLMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTVLKGFPYPSDIAVEWESNGQPENNYK
 TTPVLDSGGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (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
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTGCAATLS
 AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMVDAVHKLKYEYNTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Figure 66M

Chain 2 - human_IL12p35(N71Q)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKQESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEPPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTEPVTCTVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
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
SLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQKPLKNSRQVE
VSWEPDTPWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTEPVTCTVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 - human_IL12p35(N85Q)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITQGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEPPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTEPVTCTVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWLLDQSSSEVLGSGKTLTIQVKKFGDAQYTCCHKGGVEVLSH
 SLLLLLHKKEDGIWSTDILKDQEEPKNKTLFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLYENYTSFFFIRDIIKDPDPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
 OKSLSLSPGK (SEQ ID NO:XXX)

Figure 66O

Chain 2 - human_IL12p35(N71Q/N85Q)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKQESCLNS
 RETSFITQGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTEPVTCTVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVCSVMHEALHNHYTQKSLSLSPGK (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**

IWELKKDVYVVELDWYDPAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQKPLKNSRQVE
 VSWEPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTEPVTCTVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVCSVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 - human_IL12p35(N71Q/N195Q)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKQESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLQAS/____GGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTEPVTCTVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVCSVMHEALHNHYTQKSLSLSPGK (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
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Chain 2 - human_IL12p35(N85Q/N195Q)_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPCLHHSQNLLRAVSNMLQKARQTLEFYPCCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITQGSCLASRKTSFMMALCLSSIYEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLOAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
 NKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (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
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:XXX)

Figure 66Q

Chain 2 - human_IL12p35(N71Q/N85Q/N195Q)_(GGGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKQESCLNS
RETSFITQGSCLASRKTSFMMALCLSSYYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLQAS/ GGGGSGGGGS/EPKSSDKTHTCPPCPAPFVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:XXX)

Figure 67A

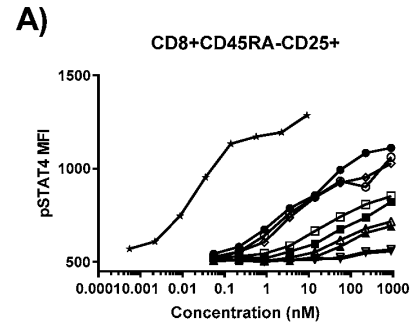


Figure 67B

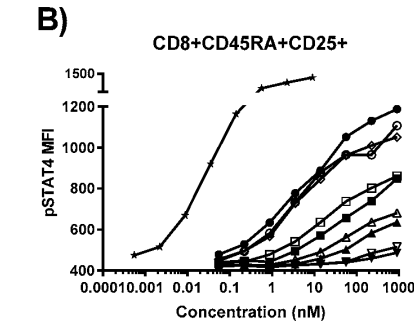


Figure 67C

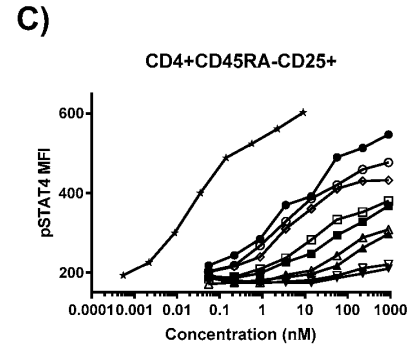


Figure 67C

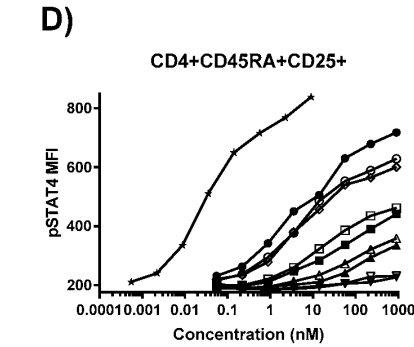


Figure 67D

