

Figure 1A

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

>sp|P29459

MCPARSLLLVATLVLLDHLSSLARNLPVATPDPMFPCLLHHSQNLLRAVSNMLQKARQTLEFYPTCTSEEDHEDITKD
KTSTVEACLPLELTKNESCLNSRETSTITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIF
LDQNMLAVIDELMQALNFNSETVPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

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

>sp|P29459|23-219

RNLPVATPDPMFPCLLHHSQNLLRAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSTITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

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

>sp|P29460

MCHQQLVISWFSVLFLASPLVAIWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTI
QVKEFGDAGQYTCHKGGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTF
SVKSSRGSSDPQGVTCGAATLSAERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRD
IIKPDPPKNLQKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISV
RAQDRYSSSWSEWASVPCS

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

>sp|P29460|23-328

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

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

>sp|P42701

MEPLVTWVPLFLFLLSRQGAACRTSECCFQDPPYPDADSGSASGPRDLRCYRISSDRYECWQYEGPTAGVSHFL
RCCLSSGRCCYFAAGSATRLQFSDQAGVSVLYTTLWVESWARNQTEKSPEVTLQLYNSVKYEPPLGDIKVSCLAGQ
LRMEWETPDNQVGAEVQFRHRTSPSPWKLGDGCGPQDDDESCCLPLEMNVAQEFQLRRRQLGSGSSWSKWSSPVCV
PPENPPQPQVRFVSVEQLGQDGRRLTLKEQPTQLELPEGCQGLAPGTEVTYRLQLHMLSCPCAKATRTLHLGKMPY
LSGAAYNVAVISSNQFGPGLNQTHI PADTHTEPVALNISVGNTGTMYWPARAQSMTYCIEWQPVGQDGGGLATCSL
TAPQDPPDAGMATYSWSRESGAMGQEKYYITIIFASAHPEKLTWSTVLSTYHFGGNASAAGTPHHVSVKNHSLDSV
SVDWAPSLSTCPGVLKEYVVRCDREDSKQVSEHPVQPTETQVTLSSGLRAGVAYTVQVRADTAWLRGVWSQPQRFSI
EVQVSDWLIFFASLGSFLSILLVGVGLGYNRAARHLCPPLTPCASSAIEFPGGKETWQWINPVDFQEEASLQEA
LVVEMSWDKGERTEPLEKTELPEGAPELALDTELSLEDGDRCKAM

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

>sp|P42701|24-545

CRTSECCFQDPPYPDADSGSASGPRDLRCYRISSDRYECWQYEGPTAGVSHFLRCCLSSGRCCYFAAGSATRLQFS
DQAGVSVLYTTLWVESWARNQTEKSPEVTLQLYNSVKYEPPLGDIKVSCLAGQLRMWETPDNQVGAEVQFRHRTP
SSPWKLGDGCGPQDDDESCCLPLEMNVAQEFQLRRRQLGSGSSWSKWSSPVCVPPENPPQPQVRFVSVEQLGQDGR
RLTLKEQPTQLELPEGCQGLAPGTEVTYRLQLHMLSCPCAKATRTLHLGKMPYLSGAAYNVAVISSNQFGPGLNQTHI
PADTHTEPVALNISVGNTGTMYWPARAQSMTYCIEWQPVGQDGGGLATCSLTAPQDPPDAGMATYSWSRESGAM
GQEKYYITIIFASAHPEKLTWSTVLSTYHFGGNASAAGTPHHVSVKNHSLDSVSDWAPSLSTCPGVLKEYVVRCD
REDSKQVSEHPVQPTETQVTLSSGLRAGVAYTVQVRADTAWLRGVWSQPQRFSIEVQVSD

Figure 1B

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

>sp|Q99665

MAHTFRGCSLAFMFIIITWLLIKAKIDACKRGDVTVKPSHVILLGSTVNITCSLKPRQGC FHYSRRNKLILYKFDRRI
NFHHGHSLSNSQVTGLPLGTTLFVCKLACINSDEIQICGAEIFVGVAPEQPQNLS CIQKGEQGT VACTW ERGRDTHLY
TEYTLQLSGPKNLTWQKQCKDIYCDYLD FGINLT PESPE SNFTAKVTAVNSLGSSSSLPSTFTFLDIVRPLPPWDIR
IKFQKASVSRCTLYWRDEGLVLLNRLRYRPSNSRLWNMVNVT KAKGRHDLLDLKPFTEYEFQISSKLHLYKGSWSDW
SESLRAQTPEEEPTGMLDVWYMKRHIDYSRQQISLFWKNLSVSEARGKILHYQVTLQELTG GKAMTQ NITGHTSWTT
VIPRTGNWAVAVSAANSKGSSLPTRINIMNLCEAGLLAPRQVSANSEGMDNILVTWQPPRKDP SAVQEYVVEWRELH
PGGDTQVPLNWLRSRPYNVSALISENIKSYICYEIRVYALSGDQGGCSSILGNSKHKAPLSGPHINAITEEKGSILI
SWNSIPVQE QMGCLLHYRIYWKERDSNSQPQLCEIPYRV SQNSHPINSLQPRVTYVLWMTALTAAGESSHGNEREFC
LQGGANWMAFVAPSICIAIIMVGIFSTHYFQQKVFVLLAALRPQWCSREIPDPANSTCAKKYPIAE EKTQLPLDRLL
IDWPTPEDPEPLVISEVLHQVTPVFRHPPCSNWPQREKGIQGHQASEKDMMHSASSPPPPRALQAESRQLVDLYKVL
ESRGS DPKPENPACPWTVLPAGDLPTH DGYLPSNIDDLPSHEAPLADSL EELEPQHISLSVFPSSSLHPLTFSCGDK
LTLDQLKMRCD SML

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

>sp|Q99665|24-622

KIDACKRGDVTVKPSHVILLGSTVNITCSLKPRQGC FHYSRRNKLILYKFDRRINFHHGHSLSNSQVTGLPLGTTLFV
CKLACINSDEIQICGAEIFVGVAPEQPQNLS CIQKGEQGT VACTW ERGRDTHLYTEYTLQLSGPKNLTWQKQCKDIY
CDYLD FGINLT PESPE SNFTAKVTAVNSLGSSSSLPSTFTFLDIVRPLPPWDIRIKFQKASVSRCTLYWRDEGLVLL
NRLRYRPSNSRLWNMVNVT KAKGRHDLLDLKPFTEYEFQISSKLHLYKGSWSDWSESLRAQTPEEEPTGMLDVWYMK
RHIDYSRQQISLFWKNLSVSEARGKILHYQVTLQELTG GKAMTQ NITGHTSWTTVIPRTGNWAVAVSAANSKGSSLP
TRINIMNLCEAGLLAPRQVSANSEGMDNILVTWQPPRKDP SAVQEYVVEWRELHPGGDTQVPLNWLRSRPYNVSALI
SENIKSYICYEIRVYALSGDQGGCSSILGNSKHKAPLSGPHINAITEEKGSILISWNSIPVQE QMGCLLHYRIYWKE
RDSNSQPQLCEIPYRV SQNSHPINSLQPRVTYVLWMTALTAAGESSHGNEREFC LQGGAN

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>
pI_ISO(-)-Fc only	K274Q/R355Q/N384S/K392N/V397M/Q419E/K447_
pI_(-)_isosteric A-Fc only	Q295E/N384D/Q418E/N421D
pI_(-)_isosteric_B-Fc only	Q295E/Q418E/N421D
pI_ISO(+RR)-Fc only	P217R/P228R/N276K
pI_ISO(+)-Fc only	N276K
pI_(+)_isosteric_A	E269Q/E272Q/E283Q/E357Q
pI_(+)_isosteric_B	E269Q/E272Q/E283Q
pI_(+)_isosteric_E269Q/E272Q	E269Q/E272Q
pI_(+)_isosteric_E269Q/E283Q	E269Q/E283Q
pI_(+)_isosteric_E272Q/E283Q	E272Q/E283Q
pI_(+)_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	247
(GGGGA) ₂	GGGGAAGGGGA	248
(GGGGA) ₃	GGGGAAGGGGAAGGGGA	249
(GGGGA) ₄	GGGGAAGGGGAAGGGGAAGGGGA	250
(GGGGA) ₅	GGGGAAGGGGAAGGGGAAGGGGAAGGGGA	251
(GGGGA) ₆	GGGGAAGGGGAAGGGGAAGGGGAAGGGGAAGGGGA	252
(GGGGA) ₇	GGGGAAGGGGAAGGGGAAGGGGAAGGGGAAGGGGAAGGGGA	253
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
AKTKPREEQYNSTYRVVSVLTVHLQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS
VMHEALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVHLQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSS
VMHEALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVHLQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS
VMHEALHNHYTQKSLSLSPGK

>Backbone monomer 2 (SEQ ID NO:24)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVHLQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSS
VMHEALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVHLQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS
VMHEALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVHLQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCEVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSS
VMHEALHNHYTQKSLSLSPGK

Figure 7B

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS
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
AKTKPREEQYSSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS
VMHEALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYSSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSS
VMHEALHNHYTQKSLSLSPGK

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

ESKYGPPCPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAK
TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEQM
TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFCSSVM
HEALHNHYTQKSLSLGLGK

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

ESKYGPPCPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAK
TKPREEEFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEM
TKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWEQGDVFCSSVM
HEALHNHYTQKSLSLGLGK

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

ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKT
KPREEQFNSTFRVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREQMT
KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPMLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMH
EALHNHYTQKSLSLSPGK

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

ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKT
KPREEEFNSTFRVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMT
KNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPMLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMH
EALHNHYTQKSLSLSPGK

Figure 7D

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

ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVQFNWYVDGVEVHNAKT
KPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREQMT
KNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPMLDSDGSFFLYSKLTVDKSRWQQGNVFSVSMH
EALHNHYTQKSLSLSPGK

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

ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVQFNWYVDGVEVHNAKT
KPREEEFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMT
KNQVSLTCDVSGFYPSDIAVEWESDQGPENNYKTTPMLDSDGSFFLYSKLTVDKSRWEQGDVFSVSMH
EALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFSVCS
VLHEALHSHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCDVSGFYPSDIAVEWESDQGPENNYKTTPVLDSGDSFFLYSKLTVDKSRWEQGDVFSVCS
VLHEALHSHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFSVCS
VMHEALHNHYTQKSLSLSPGK

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFSVCS
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

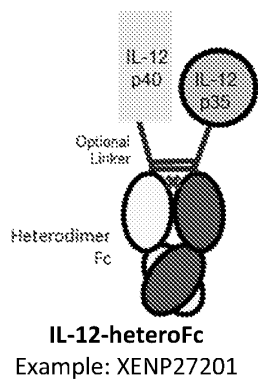


Figure 8B

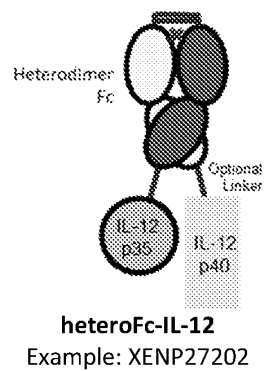


Figure 8C

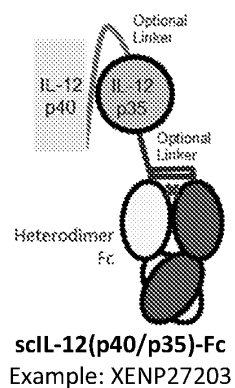


Figure 8D

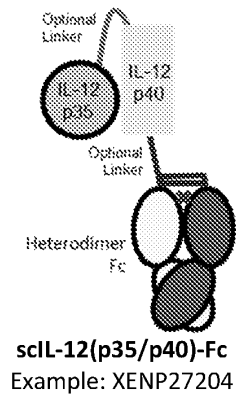


Figure 8E

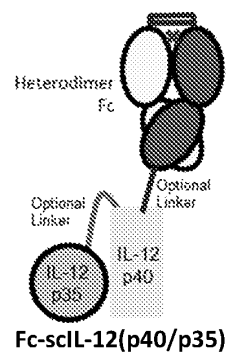


Figure 8F

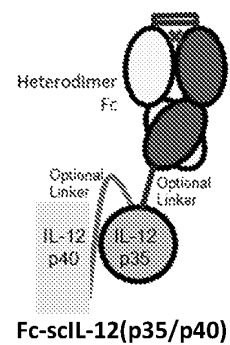


Figure 9

**>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
SLLLLLHKKEDGIWSTDI LKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS /
GGGSGGGGS/ EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO:47)**

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

RNLPVATPDGPMFPCLLHHSQNLRAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS /GGGSGGGGS/ EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVMEALHNHYTQKSLSLSPGK **(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
GFYPSDIAVEWESDGGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYTQKSLSLSPG/
GGGSGGGGS/ IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQY
TCHKGGEVLSHSLLLLLHKKEDGIWSTDI LKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDP
QGVTCGAATLSAERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI 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
GFYPSDIAVEWESNGQPENNYKTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVMEALHNHYTQKSLSLSPG/
GGGSGGGGS/ RNLPVATPDGPMFPCLLHHSQNLRAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPL
ELTKNESCLNSRETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDE
LMQALNFNSETVPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS **(SEQ ID NO:50)**

Chain 1 - human_IL12p40_(GGGGS)5-human_IL12p35_(GGGGS)2_(single-Chain)
) Fc(216) IgG1 pl(-) Isosteric A C220S/PVA /S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIQVKEFGDAGQYTHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQEDSACPAAEESLP I EVMDAVHKLKYENYTSFFIRDI IKPDPKPNLQ LKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS/G
GGGSGGGSGGGSGGGSGGGG/RNLPVATPDPGMFPCILHHSQNLLRAVSNNMLQKARQTLFYPCTSEEDHEDI
 TKDKTSTVEACPLELTKNESCLNSRETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLMDPKR
 QIFLDQNMLAVIDHMLQALNFNSTVPVQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGG
GS/EPKSSDKTHTCPFPAPPVAGPSVFLFPKPKDTLMSIRTEPVTCVVDVKHEDPEVKFNWYVDGVEVHNAKTK
 PREEEYNSYRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYTLPPSRREMTKNQVSLTC
 DVSGFYPSDIAVEWESDGQPENNYKTTPPVLSDSGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNNHYTQKSLSL
 S
 PGK (SEQ ID NO:51)

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

EPKSSDKTHTCTPPCPAPPVAGPSVFLFPPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVTLHQLDNLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVK
GFYPSPDIAVEWESNGQPENNYKTTTPPVLDSGSGFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO:52)

>XENP27204 human IL12p35 (GGGGS)5-human IL12p40 (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_IL12p35_(GGGGS)5-human_IL12p40_(GGGGS)2_(single-Chain)
) Fc(216) IgG1 pl(-) Isosteric A C220S/PVA /S267K/L368D/K370S

RNLVPATPDPMGFCLHHSQNLRLRAVSNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS /GGGGSGGGSGGGSGGGSGGGGS/ IWELKKD
VYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHSLLLLHK
KEDGIWSTDILKDKQKEPKNKTFLRCEAKNYSGRFTCWLLTTITSTDLTFSVKSSRGSSDPQGVTCCAATLSAERVRGD
NKEYEYSVEQEDSACPAAEESLPiEVMVDAVHKLKYENYTSSFFIRDI IKPDPKPNLQLKPLKNSRQVEVSWEYPD
TWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSA TVICRKNASISVRAQDRYYSSSWSEWASVPCS /GGGGSGGG
GS/EPKSSDKTHTCPCPAPPVADGVLFPKPKDKLTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAAKT
PREEEYNSDTPYRVVSLVPLVQLHDWLNKGEYKCKVSNKALPAIEKTI SKAKQGPREPQVYTLPPSR EEMTKNQVSLTC
DVSGFYPSDIAVEWESDGQPENNYKTTPVLDS DGSFFLYSKLTVDKSRWEQGDVFC SVMHEALHNHYTQKSLSL
PGK (SEQ ID NO:53)

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

EPKSSDKTHTCPCPAPPVAGPSVFLFPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVK
GFYPSDIAVEWESNGQPENNYKTTTPPVLDSGGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO:54)

Figure 12A

Purification of
eluate from
Protein A
Chromatography
via Anion
Exchange
Chromatography

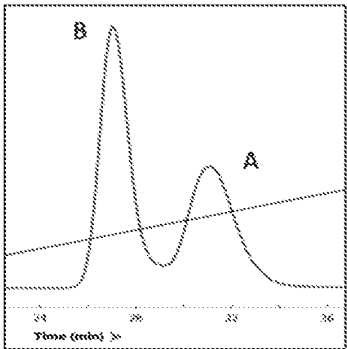


Figure 12B

aSEC-MALS

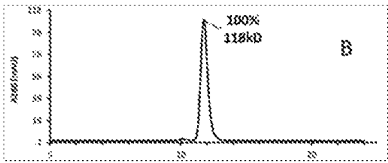
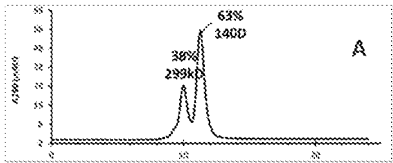


Figure 12C

Analytical
AIEX

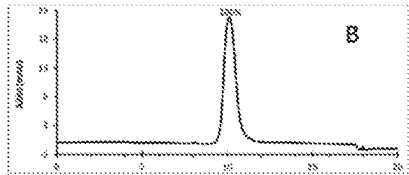
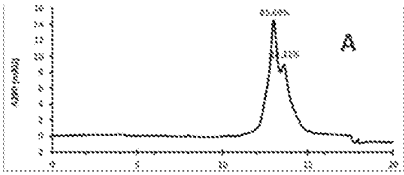


Figure 13A

Purification of
eluate from
Protein A
Chromatography
via Anion
Exchange
Chromatography

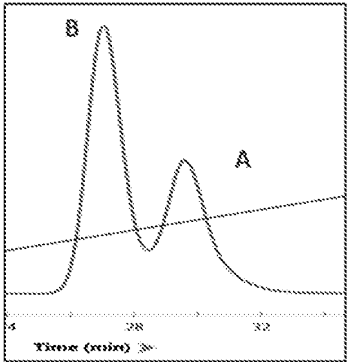


Figure 13B

aSEC-MALS

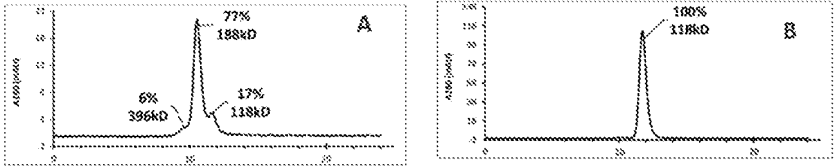


Figure 13C

Analytical
AIEX



Figure 14A

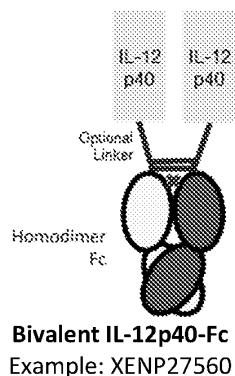


Figure 14B

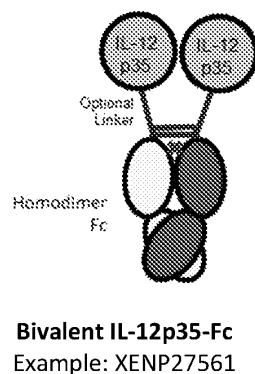


Figure 15

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:55)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSEMMALCLSSIYEDLMKYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:56)

Figure 16A

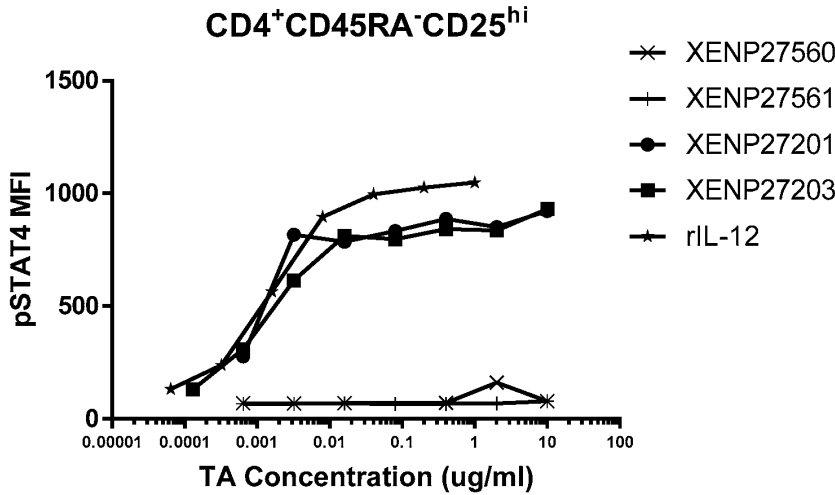


Figure 16B

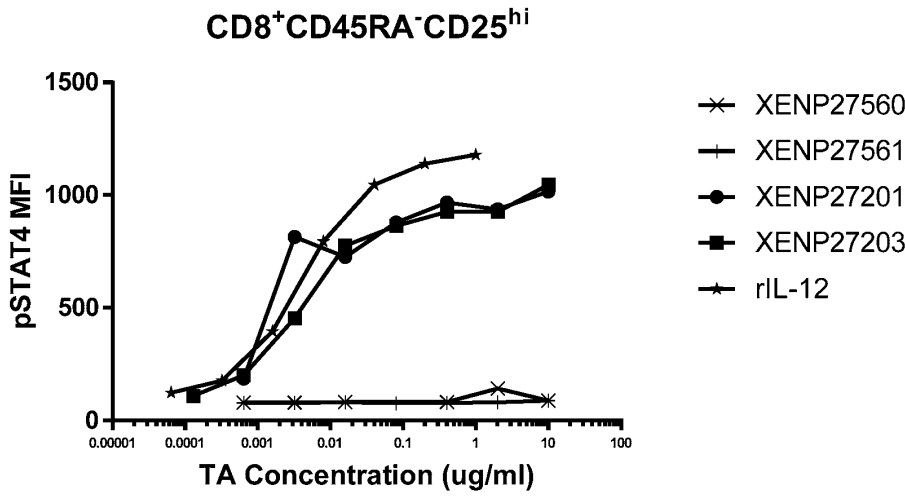


Figure 16C

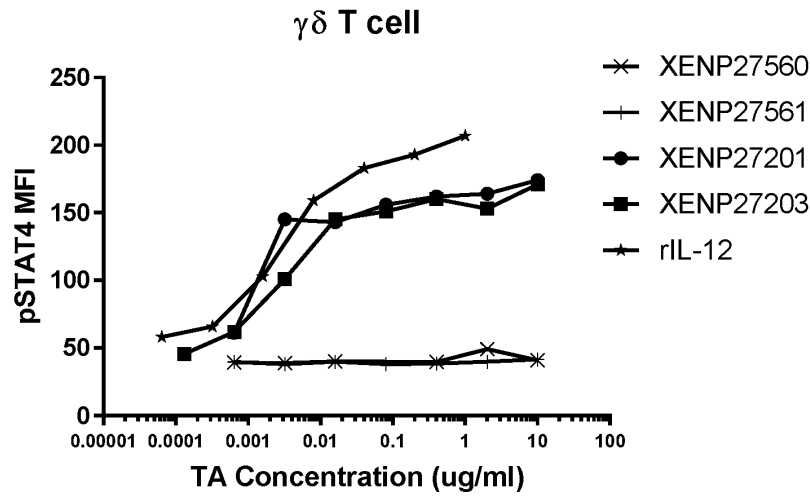


Figure 16D

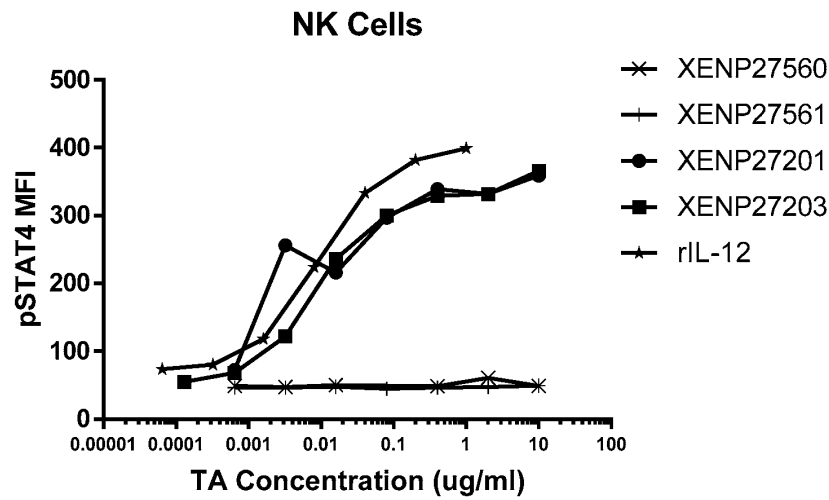


Figure 17

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
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKDYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEDTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKDASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEDTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKDASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDESSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

Figure 20B

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIEVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGNAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDESSQVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSVLGSGKTLTIEVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDESSQVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIEVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

Figure 20C

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDESSQVLGSGKTLTIEVK_QFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERV_RGDNKEYEYSVECCQEDSACPAAEESLPIEVM_DAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDQSSQVLGSGKTLTIEVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERV_RGDNKEYEYSVECCQEDSACPAAEESLPIEVM_DAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERV_RGNKEYEYSVECCQEDSACPAAEESLPIEVM_DAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGQVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERV_RGDNKEYEYSVECCQEDSACPAAEESLPIEVM_DAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPEGVTCGAATLS
AERV_RGDNKEYEYSVECCQEDSACPAAEESLPIEVM_DAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERV_RGDNKEYEYSVECCQEDSACPAAEESLPIEVM_DAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKRQKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTWLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKQPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERV_RGDNKEYEYSVECCQEDSACPAAEESLPIEVM_DAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

Figure 20D

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

IWELKKDVYVVELDWYPNAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEQDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSREVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWQYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVNGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSQWASVPCS

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKENGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS

Figure 20E

> IL-12p40(N103D/N113D) (SEQ ID NO: 254)

IWELKKDVYVVELDWYPDAPGEMMVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103D/N200D) (SEQ ID NO: 255)

IWELKKDVYVVELDWYPDAPGEMMVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKNYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYE^DYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103D/N281D) (SEQ ID NO: 256)

IWELKKDVYVVELDWYPDAPGEMMVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKNYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK^DASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N113D/N200D) (SEQ ID NO: 257)

IWELKKDVYVVELDWYPDAPGEMMVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKDYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYE^DYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N113D/N281D) (SEQ ID NO: 258)

IWELKKDVYVVELDWYPDAPGEMMVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKDYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK^DASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N200D/N281D) (SEQ ID NO: 259)

IWELKKDVYVVELDWYPDAPGEMMVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYE^DYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK^DASISVRAQDRYSSSWSEWASVPCS

Figure 20F

> IL-12p40(N103D/N113D/N200D) (SEQ ID NO: 260)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYE~~D~~YTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103D/N113D/N281D) (SEQ ID NO: 261)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKN~~D~~ASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103D/N200D/N281D) (SEQ ID NO: 262)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKNYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYE~~D~~YTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKN~~D~~ASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N113D/N200D/N281D) (SEQ ID NO: 263)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKDYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
GDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYE~~D~~YTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKN~~D~~ASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103Q) (SEQ ID NO: 264)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKNYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N113Q) (SEQ ID NO: 265)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKQYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

Figure 20G

> IL-12p40(N200Q) (**SEQ ID NO: 266**)

IWELKKDVYVVELDWYPDAPGEMMVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYE**Q**YTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N281Q) (**SEQ ID NO: 267**)

IWELKKDVYVVELDWYPDAPGEMMVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICR**Q**ASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103Q/N113Q) (**SEQ ID NO: 268**)

IWELKKDVYVVELDWYPDAPGEMMVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPK**Q**KTFLRCEAK**Q**YSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103Q/N200Q) (**SEQ ID NO: 269**)

IWELKKDVYVVELDWYPDAPGEMMVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPK**Q**KTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYE**Q**YTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103Q/N281Q) (**SEQ ID NO: 270**)

IWELKKDVYVVELDWYPDAPGEMMVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPK**Q**KTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICR**Q**ASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N113Q/N200Q) (**SEQ ID NO: 271**)

IWELKKDVYVVELDWYPDAPGEMMVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAK**Q**YSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYE**Q**YTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

Figure 20H

> IL-12p40(N113Q/N281Q) (SEQ ID NO: 272)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKQYSGRFTCWWTITSTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N200Q/N281Q) (SEQ ID NO: 273)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWTITSTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103Q/N113Q/N200Q) (SEQ ID NO: 274)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKQYSGRFTCWWTITSTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103Q/N113Q/N281Q) (SEQ ID NO: 275)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKQYSGRFTCWWTITSTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N103Q/N200Q/N281Q) (SEQ ID NO: 276)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKQKTFLRCEAKNYSGRFTCWWTITSTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS

> IL-12p40(N113Q/N200Q/N281Q) (SEQ ID NO: 277)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKQYSGRFTCWWTITSTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS

Figure 20I

> IL-12p40(N103Q/N113Q/N200Q/N281Q) (**SEQ ID NO: 278**)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPK**Q**KTFLRCEAK**Q**YSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYE**Q**YTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK**Q**ASISVRAQDRYSSSWSEWASVPCS

Figure 21A

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGS\GGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:85)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKDYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGS\GGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:86)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEDYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGS\GGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:87)

Figure 21B

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
DASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:88)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYEDYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
DASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:89)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDESSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:90)

Figure 21C

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:91)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIEVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:92)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:93)

Figure 21D

>XenD24761 human IL12p40 D62N (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S pTT5

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIQVKEFGNAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
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
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
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
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSESEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:97)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIEVKQFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:98)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSESSQVLGSGKTLTIEVKEFGDAGQYTCHK
GGEVLSHSLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYTQKSLSLSPGK (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
GGEVLSSHLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID**
NO:100)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSSHLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID**
NO:101)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGQVLSSHLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYTQKSLSLSPGK **(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
GGEVLSSHLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPEGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:103)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKRQKKDRVFTDKTSATVICRK
NASISVRAQDRYYSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:104)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQKQPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (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
GGEVLSSHLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK **(SEQ ID**
NO:106)

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

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

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

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

Figure 21l

>XenD24776 human IL12p40 E235Q (GGGGS)2-Fc(216) IgG1 pl(-

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWQYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGPPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID

NO:109)

>XenD24777 human IL12p40 Q256E (GGGGS)2-Fc(216) IgG1 pl(-

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPTWSTPHSYFSLTFCVQVEGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGPPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID

NO:110)

>XenD24778 human IL12p40 E299Q (GGGGS)2-Fc(216) IgG1 pl(-

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYSSSWSQWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGPPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (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
GGEVLSHSLLLLHKKENGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGS\GGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYTQKSLSLSPGK (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)

RNLPVATPDPGMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKDESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:113)

> IL-12p35(N85D)

RNLPVATPDPGMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITDGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:114)

> IL-12p35(N195D)

RNLPVATPDPGMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:115)

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

RNLPVATPDPGMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKDESCLNS
RETSFITDGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:116)

> IL-12p35(E153Q)

RNLPVATPDPGMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSQT
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:117)

> IL-12p35(E38Q)

RNLPVATPDPGMFPCLLHHSQNLLRAVSNNMLQKARQTQFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:118)

> IL-12p35(N151D)

RNLPVATPDPGMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFDSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:119)

> IL-12p35(Q135E)

RNLPVATPDPGMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDENMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:120)

Figure 23B

> IL-12p35(Q35D)

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQDTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:121)

> IL-12p35(Q146E)

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQDTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMEALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:122)

> IL-12p35(N76D)

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQDTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLDS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:123)

> IL-12p35(E162Q)

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQDTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEQEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:124)

> IL-12p35(E163Q)

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQDTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEQEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:125)

> IL-12p35(N71Q)

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQDTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKQESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:XXX)

> IL-12p35(N85Q)

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQDTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITQGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO:XXX)

> IL-12p35(N195Q)

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQDTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLQAS (SEQ ID NO:XXX)

Figure 23C

> IL-12p35(N71Q/N85Q)

RNLPVATPDPGMFPC~~L~~HHSQNLLRAVS~~N~~MLQKARQTLEFYPC~~T~~SEEIDHEDITKDKTSTVEAC~~L~~PLELT~~K~~QESCLNS
RETSFIT~~Q~~GSC~~L~~ASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO: 282)

> IL-12p35(N71Q/N195Q)

RNLPVATPDPGMFPC~~L~~HHSQNLLRAVS~~N~~MLQKARQTLEFYPC~~T~~SEEIDHEDITKDKTSTVEAC~~L~~PLELT~~K~~QESCLNS
RETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSY~~L~~QAS (SEQ ID NO: 283)

> IL-12p35(N85Q/N195Q)

RNLPVATPDPGMFPC~~L~~HHSQNLLRAVS~~N~~MLQKARQTLEFYPC~~T~~SEEIDHEDITKDKTSTVEAC~~L~~PLELT~~K~~NESCLNS
RETSFIT~~Q~~GSC~~L~~ASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSY~~L~~QAS (SEQ ID NO: 284)

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

RNLPVATPDPGMFPC~~L~~HHSQNLLRAVS~~N~~MLQKARQTLEFYPC~~T~~SEEIDHEDITKDKTSTVEAC~~L~~PLELT~~K~~QESCLNS
RETSFIT~~Q~~GSC~~L~~ASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSY~~L~~QAS (SEQ ID NO: 285)

> IL-12p35(N71D/N85D)

RNLPVATPDPGMFPC~~L~~HHSQNLLRAVS~~N~~MLQKARQTLEFYPC~~T~~SEEIDHEDITKDKTSTVEAC~~L~~PLELT~~K~~D~~E~~SCCLNS
RETSFIT~~D~~GSC~~L~~ASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS (SEQ ID NO: 286)

> IL-12p35(N71D/N195D)

RNLPVATPDPGMFPC~~L~~HHSQNLLRAVS~~N~~MLQKARQTLEFYPC~~T~~SEEIDHEDITKDKTSTVEAC~~L~~PLELT~~K~~D~~E~~SCCLNS
RETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSY~~L~~DAS (SEQ ID NO: 287)

> IL-12p35(N85D/N195D)

RNLPVATPDPGMFPC~~L~~HHSQNLLRAVS~~N~~MLQKARQTLEFYPC~~T~~SEEIDHEDITKDKTSTVEAC~~L~~PLELT~~K~~NESCLNS
RETSFIT~~D~~GSC~~L~~ASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSY~~L~~DAS (SEQ ID NO: 288)

Figure 24A

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
DESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM LAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV 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 IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM LAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV 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 IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM LAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLDAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV 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 IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM LAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLDAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV 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~~HHSQNL~~L~~RAVS~~N~~MLQKARQ~~T~~LEFY~~P~~CT~~S~~EEID~~H~~EDIT~~K~~DKT~~S~~TVEAC~~L~~PLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQ~~N~~MLAV
IDELMQALNFNSQTVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS~~S~~GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK~~T~~ISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK~~T~~TPPVLDSDGSFFLYSKLTVDKSRWQQGNV~~F~~S~~C~~SV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:130)

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

RNLPVATPDPGMFPC~~L~~HHSQNL~~L~~RAVS~~N~~MLQKARQ~~T~~LQFY~~P~~CT~~S~~EEID~~H~~EDIT~~K~~DKT~~S~~TVEAC~~L~~PLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQ~~N~~MLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS~~S~~GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK~~T~~ISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK~~T~~TPPVLDSDGSFFLYSKLTVDKSRWQQGNV~~F~~S~~C~~SV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:131)

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

RNLPVATPDPGMFPC~~L~~HHSQNL~~L~~RAVS~~N~~MLQKARQ~~T~~LEFY~~P~~CT~~S~~EEID~~H~~EDIT~~K~~DKT~~S~~TVEAC~~L~~PLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQ~~N~~MLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS~~S~~GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK~~T~~ISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK~~T~~TPPVLDSDGSFFLYSKLTVDKSRWQQGNV~~F~~S~~C~~SV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:132)

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

RNLPVATPDPGMFPC~~L~~HHSQNL~~L~~RAVS~~N~~MLQKARQ~~T~~LEFY~~P~~CT~~S~~EEID~~H~~EDIT~~K~~DKT~~S~~TVEAC~~L~~PLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDENMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS~~S~~GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK~~T~~ISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK~~T~~TPPVLDSDGSFFLYSKLTVDKSRWQQGNV~~F~~S~~C~~SV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:133)

Figure 24C

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARDTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM LAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:134)

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM LAV
IDELMEALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:135)

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLDSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM LAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:136)

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM LAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:137)

Figure 24D

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEQPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV 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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKDKTFLRCEAKDYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLYEDYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKDASISVRAQDRYSSSWSEWASVPCS\G
 GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:139)**

Chain 2 (XenD24782) - human_IL12p35_N71D/N85D/N195D_(GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPCLLHHSQNLRLRAVSNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKDESCLNS
 RETSFITDGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
 VPQKSSLEEDFYKTKIKLCILHAFRIRAVTIDRVMSYLDAS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO:140)**

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

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKENGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
 GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:141)**

Figure 25B

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:143)

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:145)

Figure 25C

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

RNLPVATPDPMFPCLHHSQNLRLAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIEVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWTITISDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPKPNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:147)

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

RNLPVATPDPMFPCLHHSQNLRLAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWTITISDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPKPNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:149)

Figure 25D

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

RNLPVATPDPMFPCLHHSQNLRLAVSNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:150)

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

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIQVKEFGNAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPKPNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
 GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:151)

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

RNLPVATPDPMFPCLHHSQNLRLAVSNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPKPNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
 GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO:153)

Figure 25E

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:154)

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

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSQVLGSGKTLTIEVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWTITISDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:155)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:156)

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

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSESEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWTITISDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:157)

Figure 25F

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:158)

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

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIEVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:159)

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIEVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:161)

Figure 25G

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNNHYT
QKSLSLSPGK (SEQ ID NO:163)

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNNHYT
QKSLSLSPGK (SEQ ID NO:165)

Figure 25H

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:167)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFVKSSRGSSDEGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:169)

Figure 25I

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKRQKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:171)

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (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
SLLLLHKKEDGIWSTDILKDQKQPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:173)

Figure 25J

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGSGGGGS\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
SLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWTITISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:175)

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGSGGGGS\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
SLLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWTITISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:177)

Figure 25K

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

RNLPVATPDPMFPCLLHHSQNLLRAVSNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWTITISDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPKPNLQLKPLKNSREVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:179)

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

RNLPVATPDPMFPCLLHHSQNLLRAVSNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWTITISDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPKPNLQLKPLKNSRQVE
VSWQYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:181)

RNLVPVATPDPGMFCLHHSQNLRLAVSNMLQKARQTFLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLMKYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPKPKDITLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLCTLVKGFPSPDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:182)

Chain 1 (XenD24777) - human_IL12p40_Q256E_(GGGGS)2-Fc(216)_IgG1_pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVLTCDTPEEDGITWTLQDSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQSACPAEESLPIEVMDAVHKLKYENYTSFFFIRDIKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVEGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:183)**

RNLVPVATPDPGMFCLHHSQNLRLAVSNMLQKARQTFLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYPEFKTMNAKLLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPKPKDITLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCFVSHEALHNHYTQKSLSLSPGK (SEQ ID NO:184)

Chain 1 (XenD24778) - human_IL12p40_E299Q_(GGGGS)2-Fc(216)_IgG1_pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S

IWELKKDVYVVELDWYPDAPGEMVLTCDTPEEDGITWTLDDQSSEVLGSGKTLTIQVKEFGDAGQYTCCHKGGEVLSH
 SLLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVECEQEDSACPAEESLPIEVMDAVHKLKYENYTSFFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSQWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCAPPVAGSPVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDQGPFENNYKTTTPVLDSDSGFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO:185)**

Figure 25M

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGSGGGGS\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**

IWELKKDVYVVELDWYPDAPGEMVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWTITISDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSQT
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGSGGGGS\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**

IWELKKDVYVVELDWYPDAPGEMVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWTITISDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\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\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWTITISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
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\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWTITISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:193)

Figure 250

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDENMLAVIDELMQALNFNSET
VPQKSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (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**

IWELKKDVYVVELDWYPDAPGEMVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWTITISDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:195)

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARDTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (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**

IWELKKDVYVVELDWYPDAPGEMVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWTITISDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:197)

Figure 25P

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMEALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:198)

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

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWTITISDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGVDFSCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:199)

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLDS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:200)

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

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWTITISDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSWSEWASVPCS\G
GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGVDFSCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO:201)

Figure 25Q

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

RNLPVATPDPMFPCLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS SDPQGVTCGAATLS
AERVRGDNKEYEYSVECEQEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
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

RNLPVATPDPMFPCLHHSQNLRLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEQPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:204)

Figure 26A

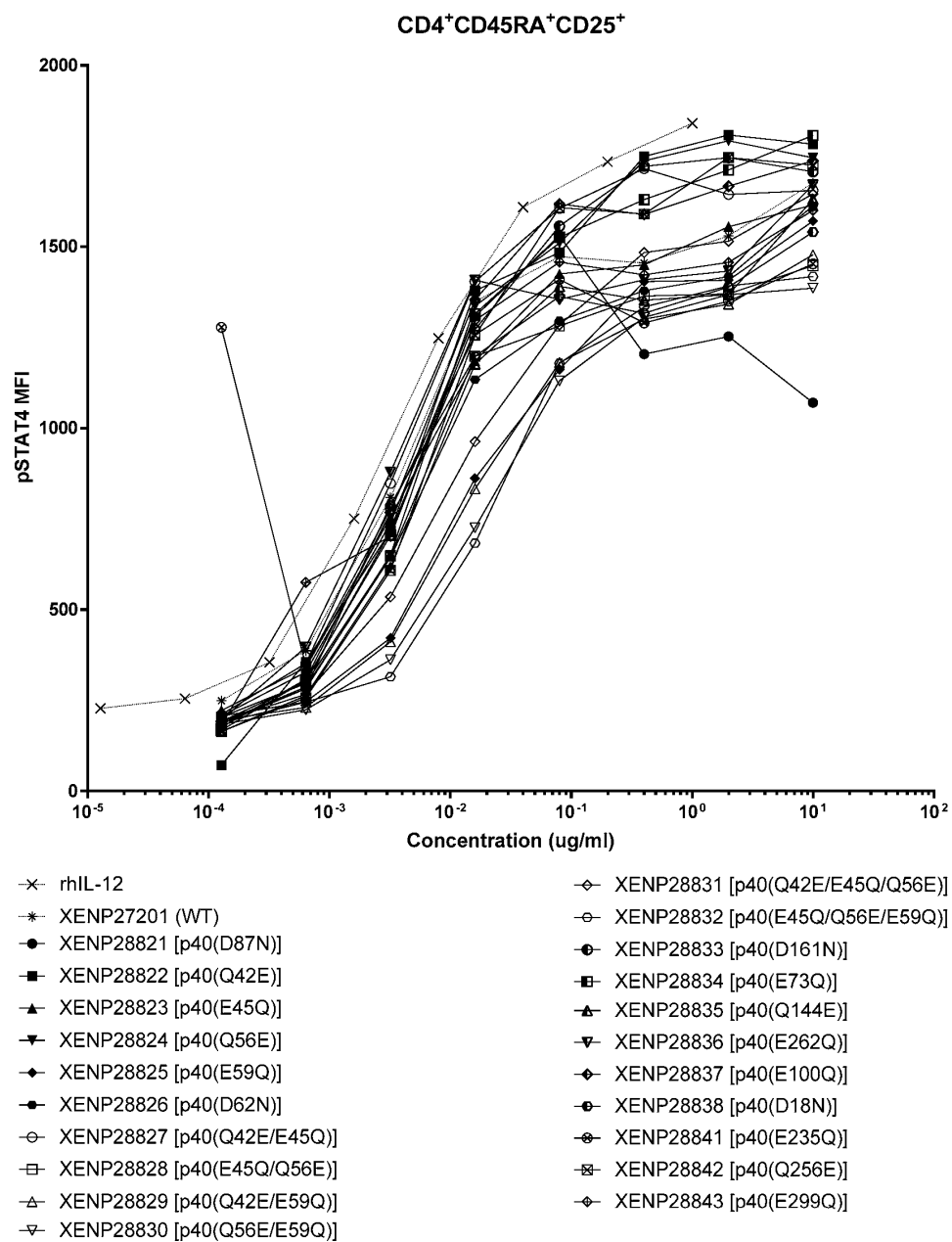


Figure 26B

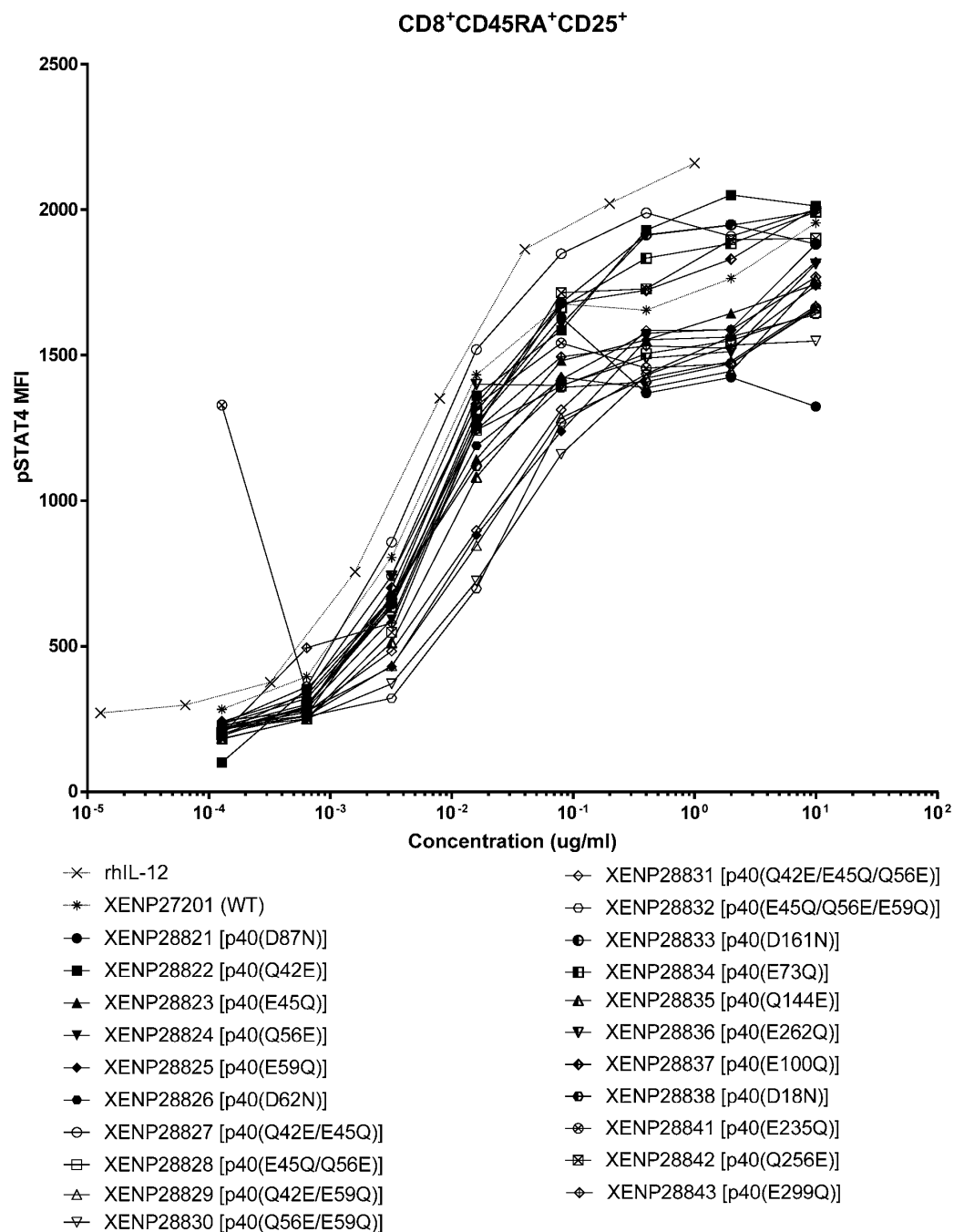


Figure 27A

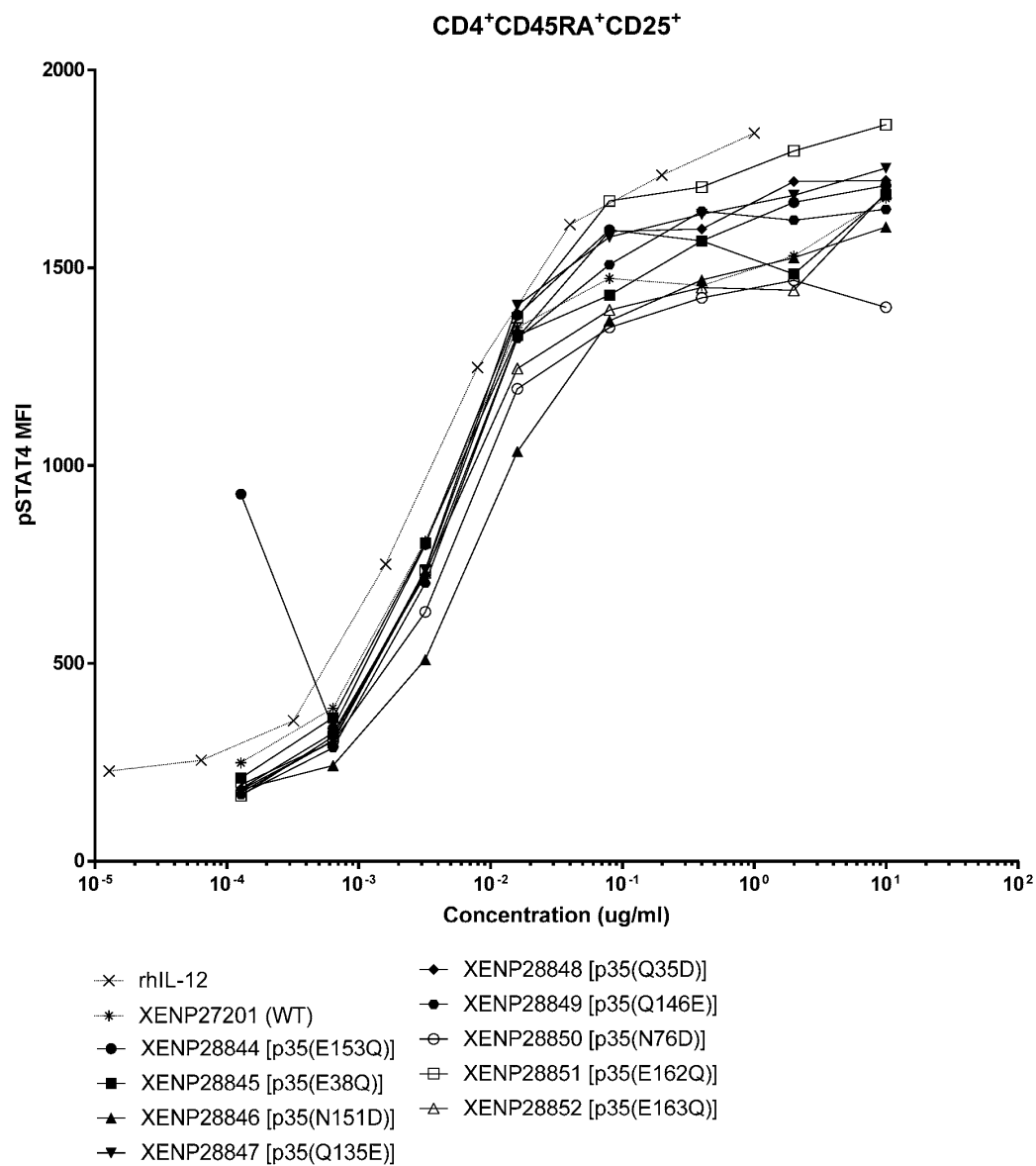


Figure 27B

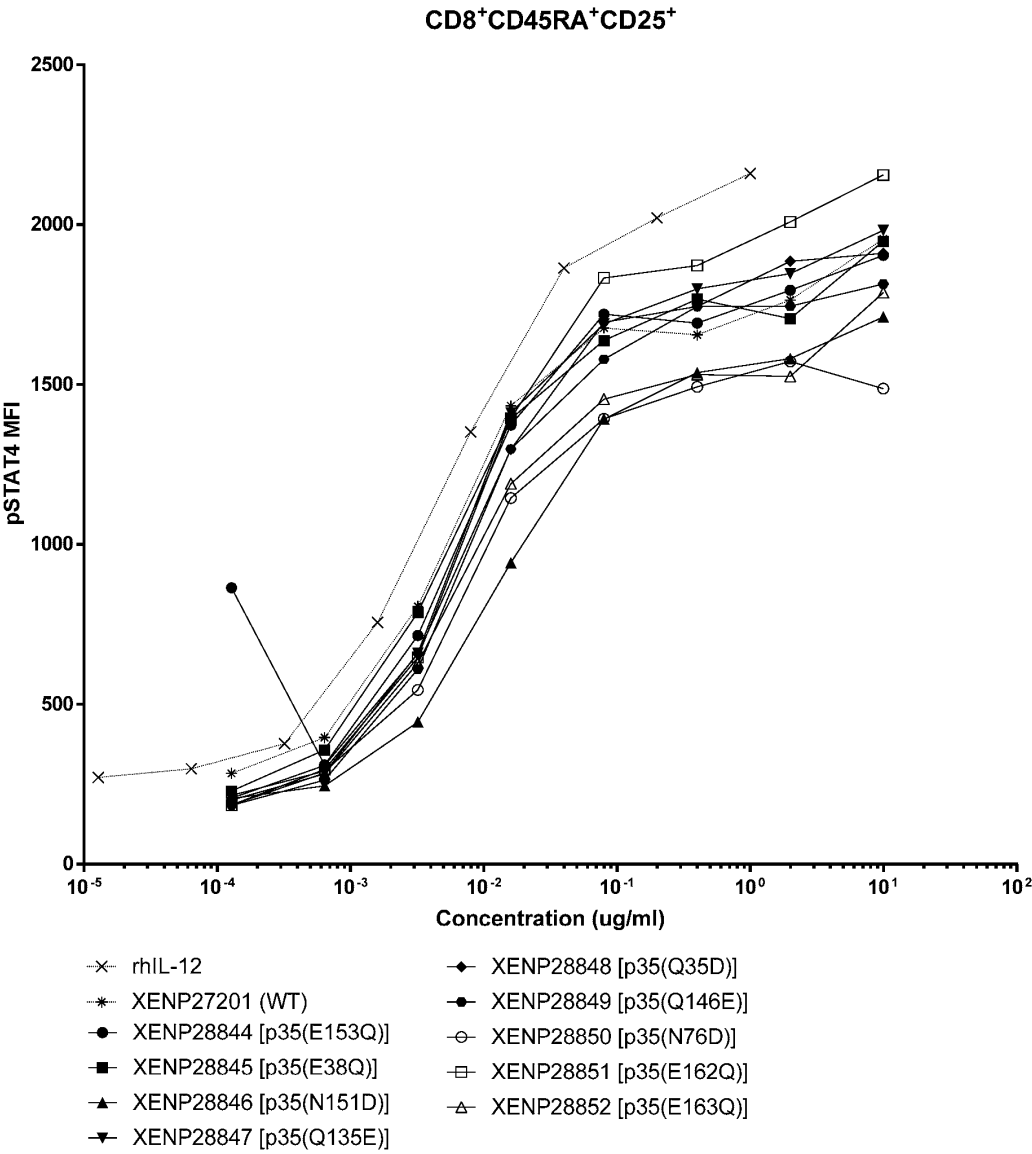


Figure 28

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)**

IWELKKDVYVVVELDWYPDAPGEMVVLTCDTPE**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
GGEVLSSHLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:215)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:216)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIQVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGPPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:218)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIQVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGPPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:219)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQKSEVLGSGKTLTIQVKQFGDAGQYTCHK
GGEVLSSHLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIQVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGPPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (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
NASISVRAQDRYYSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (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
NASISVRAQDRYYSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (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
NASISVRAQDRYYSWSEWASVPCS\GGGSGGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (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
GGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSEREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS\GGGGS\GGGGS\EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYTQKSLSLSPGK (SEQ ID*

NO:224

Figure 31A

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

RNLFPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSF ITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFD SQTVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

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

RNLFPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSF ITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFN SKTVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

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

RNLFPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSF ITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNF KSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

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

RNLFPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSF ITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFD SETVPQKSSLEEP NFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

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

RNLFPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSF ITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKR EIFLDQNMLAV
IDELMQALNFD SETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

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

RNLFPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSF ITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFD SETVPQ ESSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

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

RNLFPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSR QTSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFD SETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

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

RNLFPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITK QKTSTVEACLPLELTK
NESCLNSRETSF ITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFD SETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

Figure 31B

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

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQDM LAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

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

RNLPVATPDPGMFPC LHHSQDLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM LAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

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

RNLPVATPDPGMFPC LHHSQNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM LAV
IDQLMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS

Figure 32A

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

RNLPVATPDPGMFPC~~L~~HHSQNL~~L~~RAVS~~N~~MLQKARQTLEFY~~P~~CTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM~~L~~AV
IDELMQALNFD~~S~~QTV~~P~~QKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS~~S~~GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK **(SEQ ID NO:236)**

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

RNLPVATPDPGMFPC~~L~~HHSQNL~~L~~RAVS~~N~~MLQKARQTLEFY~~P~~CTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM~~L~~AV
IDELMQALN~~F~~NSKTVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS~~S~~GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK **(SEQ ID NO:237)**

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

RNLPVATPDPGMFPC~~L~~HHSQNL~~L~~RAVS~~N~~MLQKARQTLEFY~~P~~CTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM~~L~~AV
IDELMQALN~~F~~FKSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS~~S~~GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK **(SEQ ID NO:238)**

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

RNLPVATPDPGMFPC~~L~~HHSQNL~~L~~RAVS~~N~~MLQKARQTLEFY~~P~~CTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS~~I~~YEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM~~L~~AV
IDELMQALNFD~~S~~ETVPQKSSLEEPN~~F~~YKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGGS~~S~~GGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK **(SEQ ID NO:239)**

Figure 32B

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKREIFLDQNM LAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:240)

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM LAV
IDELMQALNFDSETVPQESSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:241)

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRQTSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM LAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:242)

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKQKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNM LAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:243)

Figure 32C

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQDMLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:244)

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

RNLPVATPDPGMFPC LHHSQDLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQDMLAV
IDELMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
MHEALHNHYTQKSLSLSPGK (SEQ ID NO:245)

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQDMLAV
IDQLMQALNFDSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS\GGGSGGGGS\E
PKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQ
MTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV
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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 93)**

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

RNLPVATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLARKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFDSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVMEALHNHYTQKSLSLSPGK **(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
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWNLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 98)**

Figure 33B

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFDSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKSLSLSPGK **(SEQ ID NO: 132)**

**>XENP29951 human_IL12p40(E59K)_(GGGGG)2-human_IL12p35(N151D)_(GGGGG)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)_(GGGGG)2_Fc(216)_IgG1_pl(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSDDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFVCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/G
____GGGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNNHYT
QKSLSLSPGK **(SEQ ID NO: 215)**

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

RNLPVATPDPMFPCLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFDSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/____GGGGSGGGGS____/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKSLSLSPGK **(SEQ ID NO: 132)**

Figure 33C

**>XENP29952 human_IL12p40(E59K)_(GGGGG)2-human_IL12p35_(GGGGG)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)_(GGGGG)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWTITISDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 215)**

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

RNLVPATPDPMFCLHHSQNLRAVSNMLQKARQTLEFYPCSTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 433)**

**>XENP29953 human_IL12p40(E32Q/E59Q)_(GGGGG)2-human_IL12p35_(GGGGG)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)_(GGGGG)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWTITISDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 216)**

Figure 33D

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

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 434)**

**>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**

IWELKKDVYVELDWYFDAPGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKFLRCEAKNYSGRFTCWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 217)**

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

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 435)**

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

IWELKKDVYVVELDWNYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIQVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 218)**

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

RNLPVATPDPMFCLHHSQNLRAVSNNLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVQLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: 436)**

>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

IWELKKDVYVVELDWNYPDAPGEMVVLTCDTPEEDGITWTLDQSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDVAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 219)**

Figure 33F

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

RNL PVATPD PGMF PCLHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHA FRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: 437)**

**>XENP29957 human_IL12p40(S43K/E59Q)_(GGGGS)2-human_IL12p35_(GGGGS)2-Fc(216)_IgG1_pi(-
)_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_pi(-
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTL DQKSEVLGSGKTLTIQVKQFGDAGQY TCHKGGEVL SH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERV RGDNKEYEYSVECEDSACPAAEESLP I EVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEY PDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: 220)**

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

RNL PVATPD PGMF PCLHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHA FRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: 438)**

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**

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 221)**

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

RNLVPATPDPMFPCLLHHSQNLRLRAVS NMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 439)**

**>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**

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 222)**

Figure 33H

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

RNLPVATPDPGMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 440)**

**>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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTLRCEAKNYSGRFTCWWTITISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGESKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 223)**

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

RNLPVATPDPGMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 441)**

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**

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKQFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPKPNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSEREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 224)**

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

RNLPVATPDPGMFCLHHSQNLRAVSNMLQKARQTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMVQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEPDPFYKTIKLCILHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
NKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 442)**

**>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**

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPKPNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 47)**

Figure 33J

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

RNL PVATPD PGMF PCLHHS QNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFDST
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPPKNLQKPLKNSRQVE
VSWEYPD TWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 47)**

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

RNL PVATPD PGMF PCLHHS QNLLRAVSNMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFSKT
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWNYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 47)**

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

RNLVPATPDPMFPCLLHHSQNLRAVSNMLQKARQTFEYFCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFKSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVQLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVMEALHNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWNYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 47)**

Figure 33L

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

RNL PVATPD PGMF PCLHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFDSET
 VPQSSLEEPNIFYTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWYFDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDV FSCSVMEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: 47)**

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

RNL PVATPD PGMF PCLHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKREIFLDQNMLAVIDELMQALNFDSET
 VPQSSLEEPDFYTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWNYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 47)**

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

RNLVPATPDPMFCLHHSQNLRAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFDSET
VPQESSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWNYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 47)**

Figure 33N

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

RNL PVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RQTSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFDSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTKLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQVMHEALHNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIPDPPKNLQKPLKNSRQVE
VSWEYPDWTSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 47)**

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

RNL PVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPCCTSEEIDHEDITKQKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFDSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTKLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQVMHEALHNHYTQKSLSLSPGK **(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

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMIISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: 47)**

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

RNLPVATPDPGMFCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMVQVEFKTMNAKLMDPKRQIFLDQDMLAVIDELMQALNFDSET
 VPQSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMIISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(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

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMIISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: 47)**

Figure 33P

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

RNL PVATPDPGMF PCLHHSQDLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFDSET
VPQKSSLEEPDFYKTKIKLCILHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK **(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**

IWELKKDVYVVELDWYFDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTF LRCEAKNYSGRFTCWLTITISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWEQGDV FSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 47)**

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

RNL PVATPDPGMF PCLHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFDSET
VPQKSSLEEPDFYKTKIKLCILHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: 246)**

Figure 34A

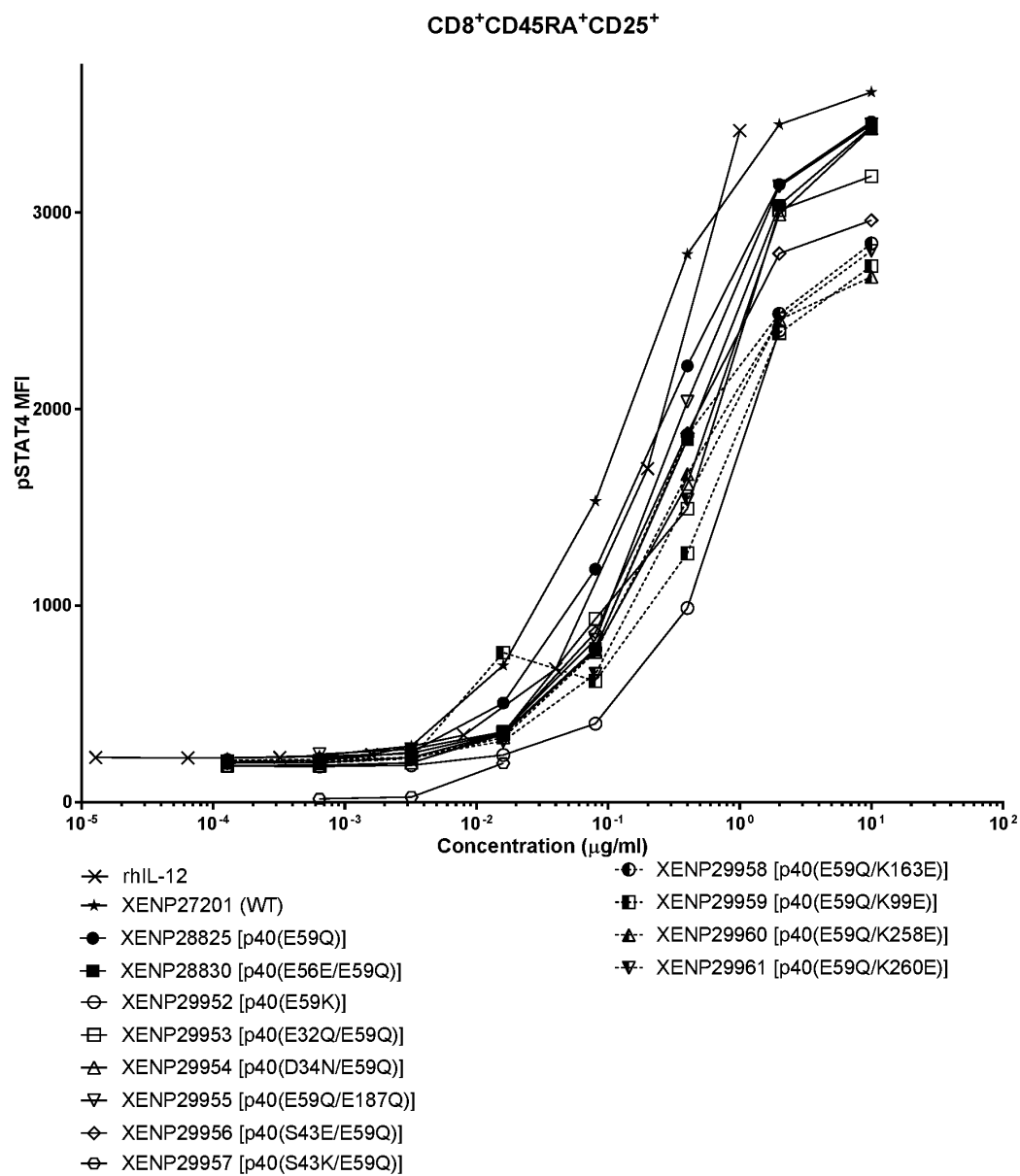


Figure 34B

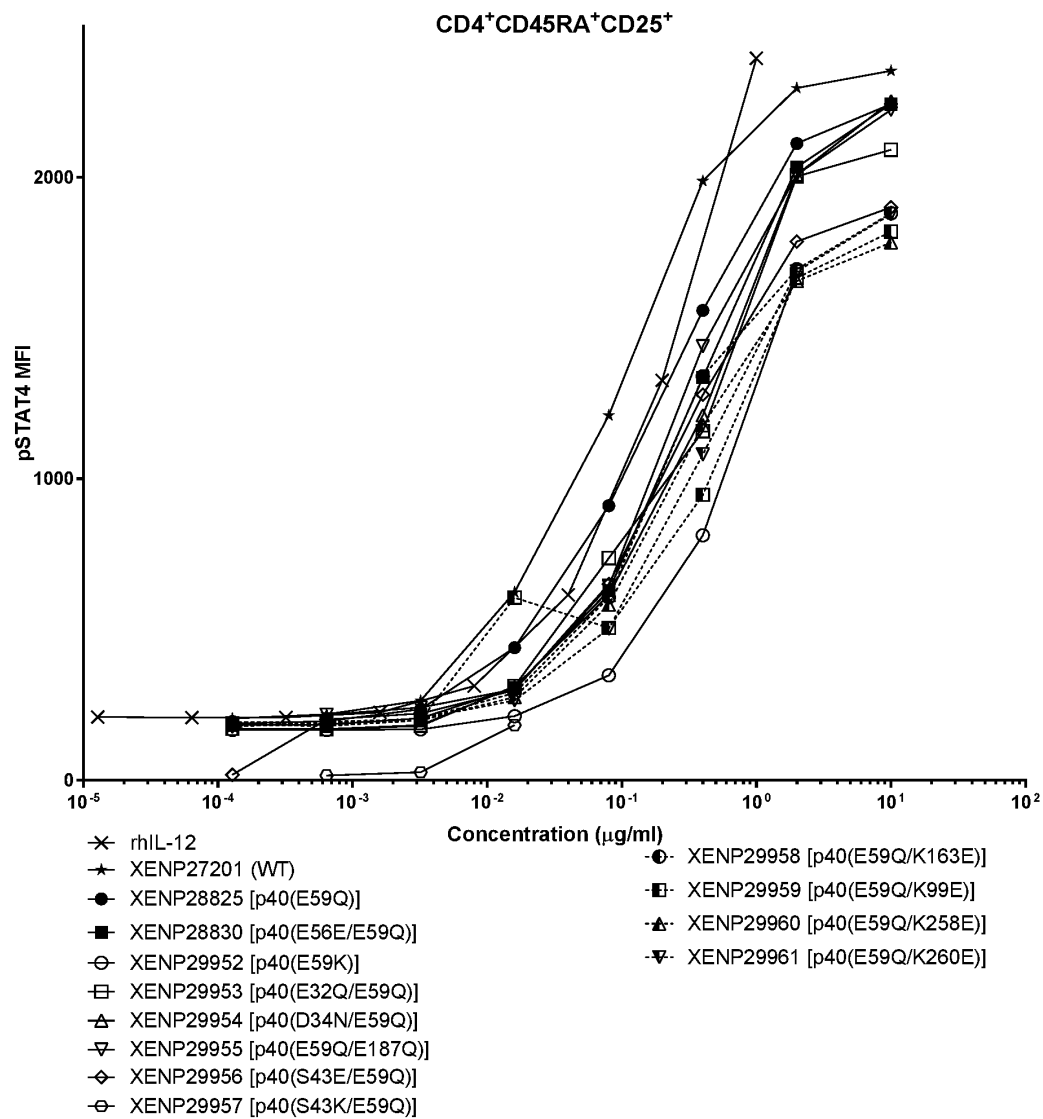


Figure 35A

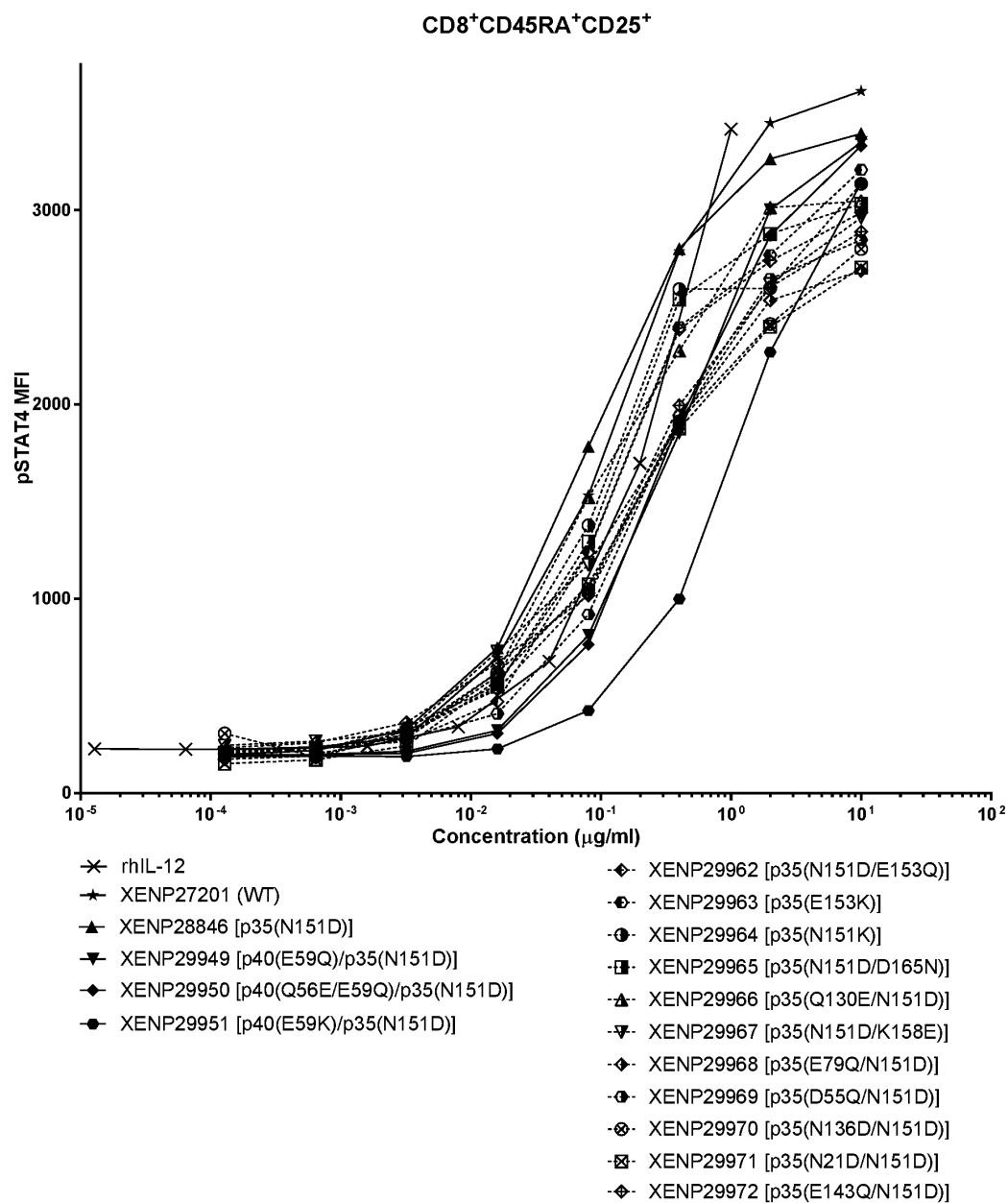


Figure 35B

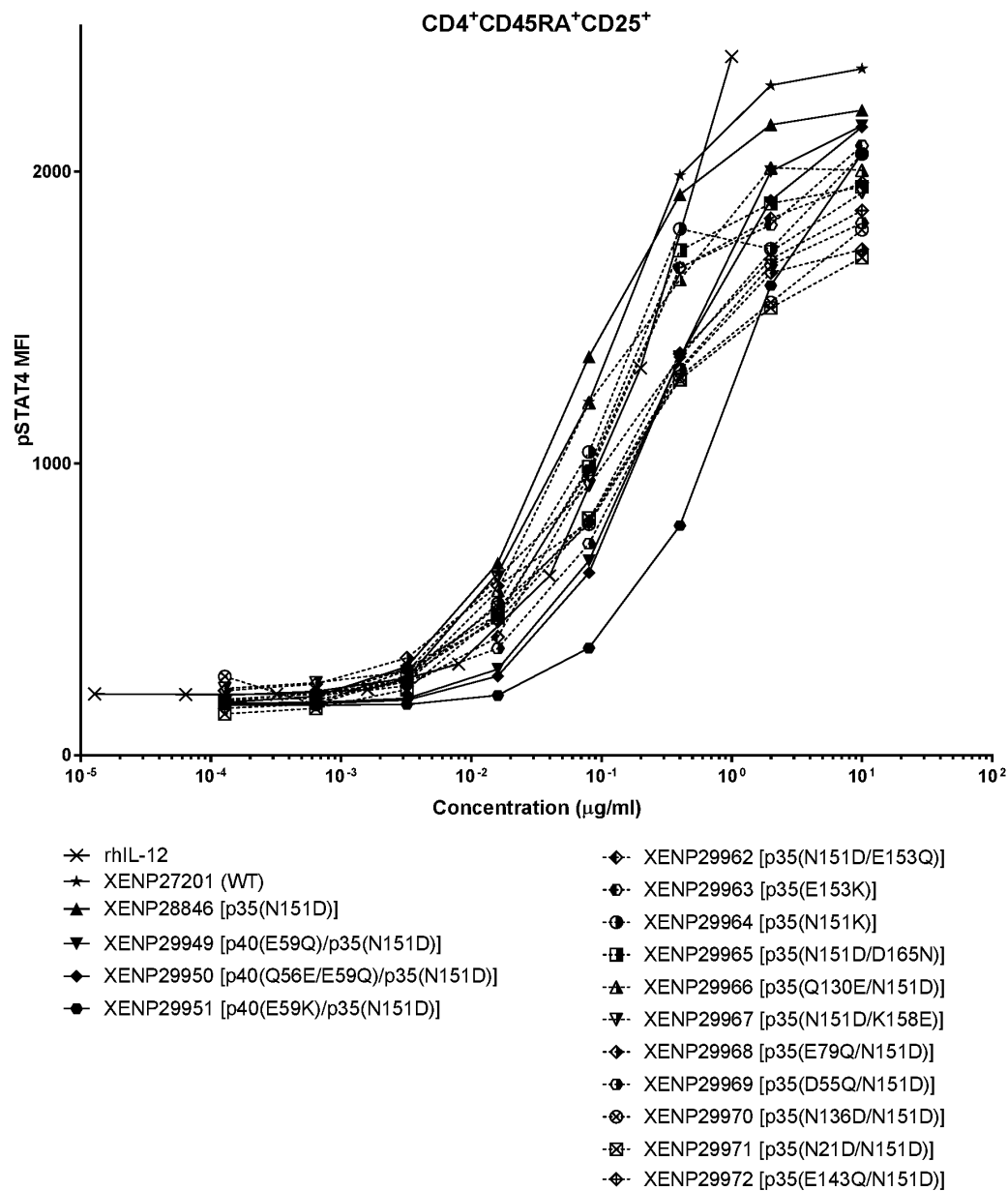


Figure 36

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)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: 325)

>IL12p40(D34N/E59K)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEENNGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: 326)

>IL12p40(D34N/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEENNGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: 327)

>IL12p40(D34K/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEKKGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: 328)

>IL12p40(E32Q/D34N/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEQENNGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: 329)

Figure 37B

>IL12p40(E32Q/D34K/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEKNGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: 330)

>IL12p40(E32K/D34N/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEKNGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: 331)

>IL12p40(E32K/D34K/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEKNGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: 332)

Figure 38

>IL12p35(D55Q)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITK QKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS **(SEQ ID NO: 333)**

>IL12p35(D55K)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITK KKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS **(SEQ ID NO: 334)**

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**

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEPKNTFLRCEAKNYSGRFTCWWLTTISTDLTFVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 291)**

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

RNLVPATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: 443)**

**>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**

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEPKNTFLRCEAKNYSGRFTCWWLTTISTDLTFVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 292)**

Figure 39B

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPCCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS / EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 444)**

**>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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYCHKGGEVLSH
SLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIIPDPKPNLQKPLKNSRQVE
VSWEYPDWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS / EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 293)**

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLEFYPCCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS / EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 445)**

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**

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEKGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 294)**

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

RNLVPATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTIKILCLLHAFIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: 446)**

**>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**

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 295)**

Figure 39D

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

RNL PVATPD PGMF PCLHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: 447)**

**>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**

IWELKKDVYVVELDWYPDAPGEMVVLTC DTPQEKGITWTL DQSSEVLGSGKTLTIQVKKFGDAGQY TCHKGGEVL SH
SLLLLHKKEDGIWSTDILKDQEEPKNKTF LRCEAKNYSGRFTCW LTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERV RGDNKEYEYSVE CQEDSACPAAEESLP I EVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEY PDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 296)**

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

RNL PVATPD PGMF PCLHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: 448)**

Figure 39E

**>XENP30603 human_IL12p40_E32K/D34N/E59K/K99E_(GGGGG)2-human_IL12p35_(GGGGG)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_(GGGGG)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWPDPAGEMVVLTCDTPKENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGG/EPKSSDKTHTCPPCPAPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 297)**

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

RNLVPATPDPMFPCLLHHSQNLRLAVSNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGG/EPKSSDKTHTCPPCPAPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 449)**

**>XENP30604 human_IL12p40_E32K/D34K/E59K/K99E_(GGGGG)2-human_IL12p35_(GGGGG)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_(GGGGG)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEKENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGG/EPKSSDKTHTCPPCPAPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 298)**

Figure 39F

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

RNL PVATPD PGMF PCLHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: 450)**

**>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**

IWELKKDVYVVELDWYPDAPGEMVVLTC DTPQENGITWTL DQSSEVLGSGKTLTIQVKKFGDAGQY TCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTF SVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVECEQSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDV FSCSVMEALHNHYT
 QKSLSLSPGK **(SEQ ID NO: 295)**

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

RNL PVATPD PGMF PCLHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKQKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: 299)**

Figure 39G

>XENP30606 human IL12p40 E32Q/D34K/E59K/K99E (GGGGG)2-human IL12p35 D55Q (GGGGG)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_(GGGGG)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEKGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEPKNTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGG/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 296)

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

RNLVPATPDPMFPLHHSQNLLRAVSNNLQKARQTFEYFPTCTSEEIDHEDITKQKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGG/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 299)

>XENP30607 human IL12p40 E32K/D34N/E59K/K99E (GGGGG)2-human IL12p35 D55Q (GGGGG)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_(GGGGG)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEKNGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEPKNTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGG/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 297)

Figure 39H

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKQKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS /EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 299)**

**>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**

IWELKKDVYVVELDWYPDAPGEMVVLTCPTPEKGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWTITISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIEMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS /EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 298)**

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKQKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS /EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 299)**

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
 SLLLLHKKEDGIWSTDILKDQEPKNTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
 VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
 QKSLSLSPGK (SEQ ID NO: 298)

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

RNLPVATPDPMFPCLHHSQNLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKKKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVQLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO: 300)

Figure 40A

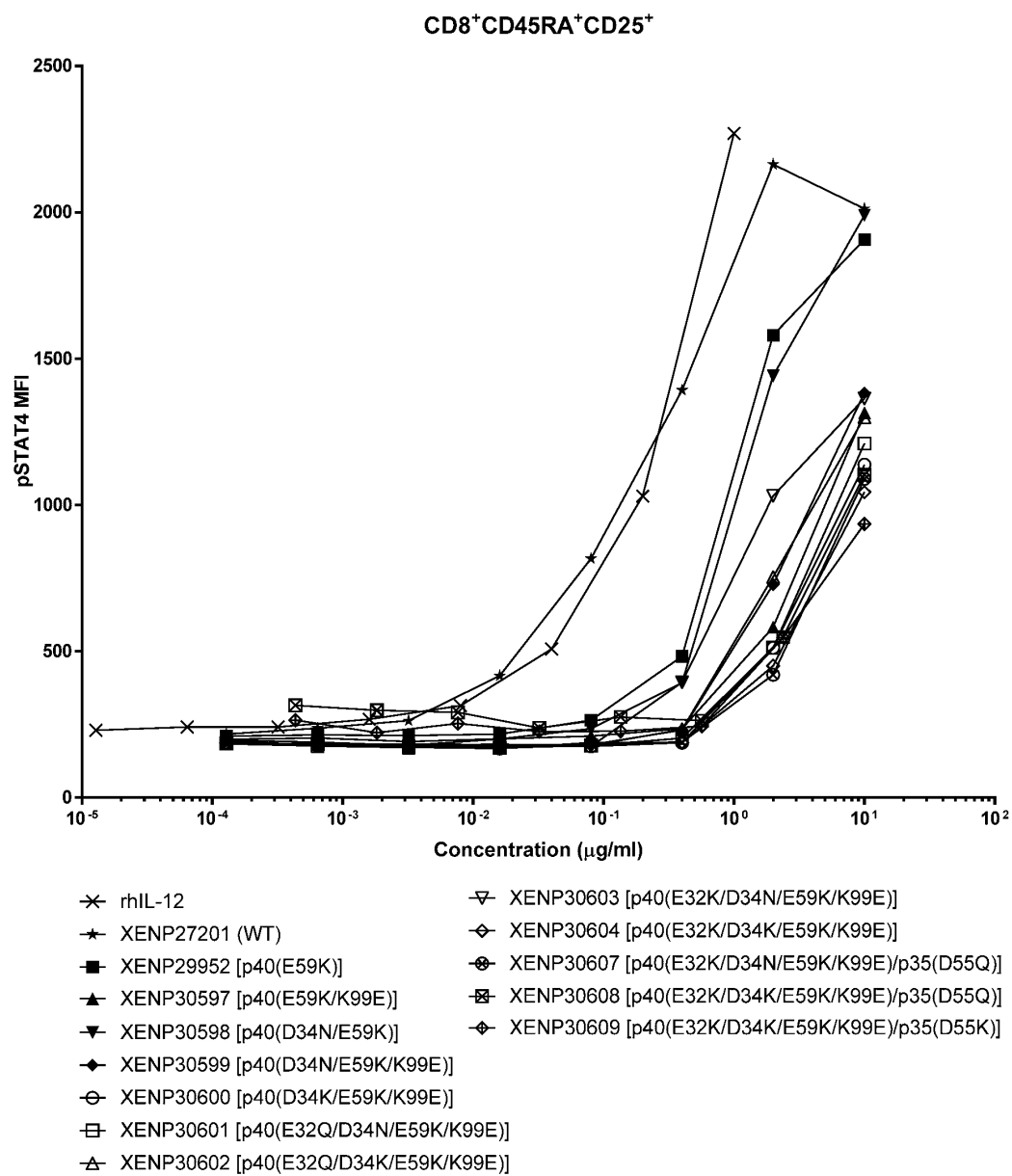


Figure 40B

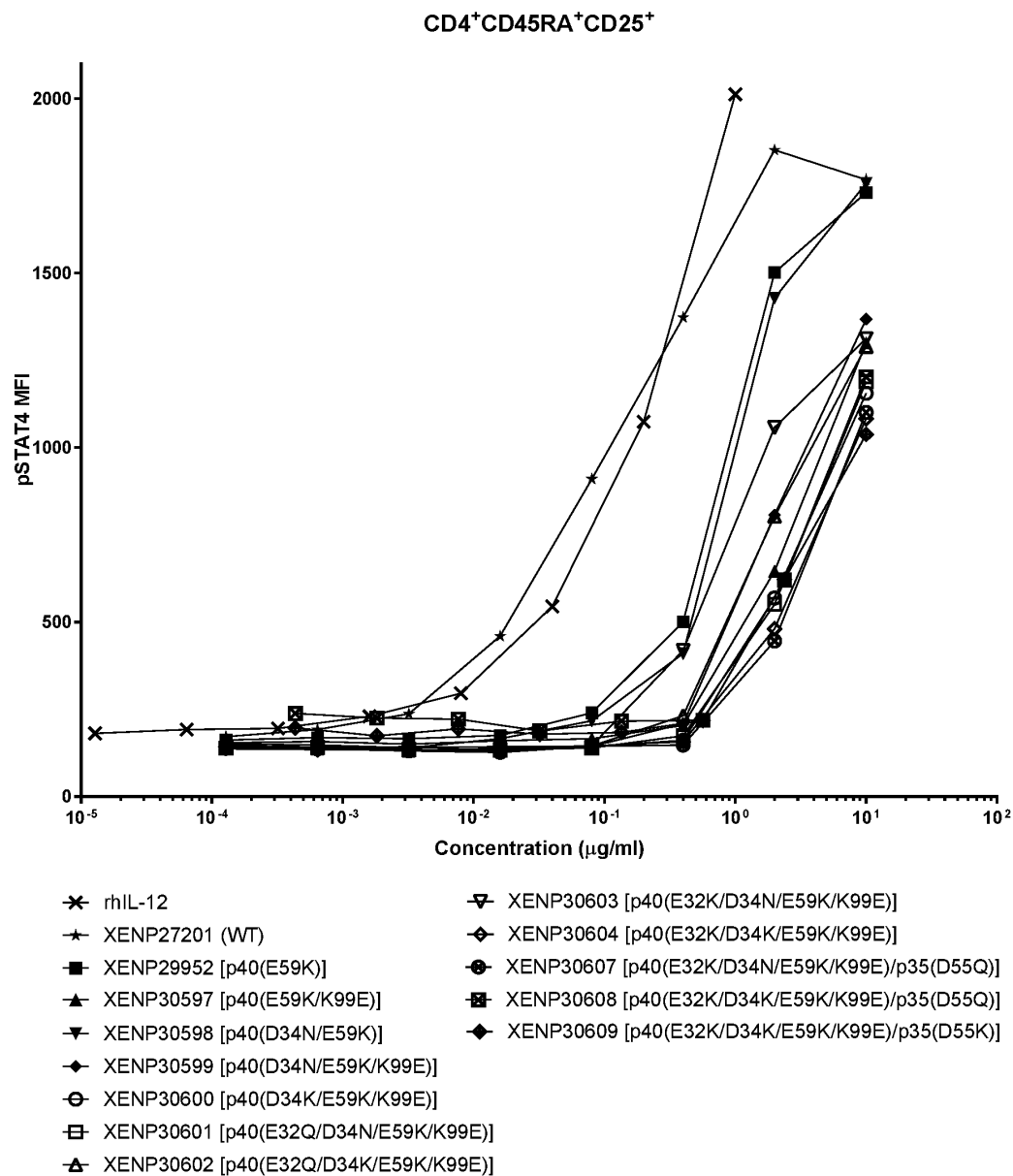


Figure 41

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

Figure 42A

>IL12p40(E59Y/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKYFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYSSSWSEWASVPCS (SEQ ID NO: 335)

>IL12p40(E59K/K99Y)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQYEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYSSSWSEWASVPCS (SEQ ID NO: 336)

>IL12p40(E59Y/K99Y)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKYFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQYEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYSSSWSEWASVPCS (SEQ ID NO: 337)

>IL12p40(E45K/E59K/K99E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSKVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYSSSWSEWASVPCS (SEQ ID NO: 338)

>IL12p40(D18K/E59K/K99E)

IWELKKDVYVVELDWYPKAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYSSSWSEWASVPCS (SEQ ID NO: 339)

Figure 42B

>IL12p40(E59K/K99E/Q144E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPEGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: 340)

>IL12p40(E59K/K99E/Q144K)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPKGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: 341)

>IL12p40(E59K/K99E/R159E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVEGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: 342)

>IL12p40(E59K/K99E/K264E)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKEDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: 343)

>IL12p40(D18K/E59K/K99E/K264E)

IWELKKDVYVVELDWYPKAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHK
GGEVLSHSLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGS
SDPQGVTCGAATLSAERVRGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI
IKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKEDRVFTDKTSATVICRK
NASISVRAQDRYYSSSWSEWASVPCS (SEQ ID NO: 344)

Figure 43

>IL12p35(F96A)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTS AMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS **(SEQ ID NO: 345)**

>IL12p35(M97A)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSF AMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS **(SEQ ID NO: 346)**

>IL12p35(L89A)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCL ASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS **(SEQ ID NO: 347)**

>IL12p35(L124A)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLL AMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS **(SEQ ID NO: 348)**

>IL12p35(M125A)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLL ADPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS **(SEQ ID NO: 349)**

>IL12p35(L75A)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESC ANSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS **(SEQ ID NO: 350)**

>IL12p35(I171A)

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTK
NESCLNSRETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV
IDELMQALNFNSETVPQKSSLEEPDFYKTK AKLCILLHAFRIRAVTIDRVMSYLNAS **(SEQ ID NO: 351)**

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**

IWELKKDYYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKYFGDAGQYTCHKGGEVLSHSLLLHKKED
GIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWTITSTDLTFSVKSSRGSSDPQGVTCGAATLSAERVGRDNKEYEYSVEQCEDS
ACPAAEESLPIEVMVDVAVHKLKYENYTSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPTDWTSTPHSYFSLTFCVQVQGKSKREKK
DRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDT
LMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIS
KAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVF
SCSVMHSEALHNHYTQKSLSLSPGK **(SEQ ID NO: 301)**

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

RNLPVATPDGPMFPCLLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNSRETSFITNGSCL
ASRKTSFMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSETVPQKSLEEDFYKTIKLCILL
HAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQM
TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHSEALHNHYTQKSLSL
PGK **(SEQ ID NO: 451)**

**>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**

IWELKKDYYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSHSLLLHKKED
GIWSTDILKDQYEPKNKTLRCEAKNYSGRFTCWWTITSTDLTFSVKSSRGSSDPQGVTCGAATLSAERVGRDNKEYEYSVEQCEDS
ACPAAEESLPIEVMVDVAVHKLKYENYTSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPTDWTSTPHSYFSLTFCVQVQGKSKREKK
DRVFTDKTSATVICRKNASISVRAQDRYSSSSWSEWASVPCS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDT
LMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIS
KAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVF
SCSVMHSEALHNHYTQKSLSLSPGK **(SEQ ID NO: 302)**

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

RNLPVATPDGPMFPCLLHHSQNLLRAVSNNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEACLPLELTKNESCLNSRETSFITNGSCL
ASRKTSFMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSETVPQKSLEEDFYKTIKLCILL
HAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQM
TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHSEALHNHYTQKSLSL
PGK **(SEQ ID NO: 452)**

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**

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIQVKYFGDAGQYTCHKGGEVLISH
SLLLLLHKKEDGIWSTDILKDQYEPKNKTLFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQKLPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 303)

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

RNLPVATPDPMFPCPLHHSQNLRLRAVSNNLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMVQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 453)

**>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**

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSKVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLISH
SLLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQKLPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 304)

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

RNLPVATPDPMFPCPLHHSQNLRLRAVSNNLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMVQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 454)

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
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 305)

Chain 2 (XenD22915) - human_IL12p35 (GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPCLLHHSQNLRAVSNNLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVQLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 455)

**>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
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSVMSHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 306)

Chain 2 (XenD22915) - human_IL12p35 (GGGGS)2_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFPCLLHHSQNLRAVSNNLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVQLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 456)

Figure 44D

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

RNL PVATPDPGMFCLHHSQNLRAVSNMLQKARQTLEFYPC TSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCP P P P VAGP
SVFLFPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFPSPDI AVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV MHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 457)**

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**

IWELKKDVYVVELDWYPDAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPKGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 307)**

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

RNLPVATPDPMFCLHHSQNLLRAVSNNLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMVQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 458)**

**>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**

IWELKKDVYVVELDWYPDAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVEGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 308)**

Figure 44F

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

RNL PVATPD PGMF PCLHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO: 459)

**>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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCCHKGGEVLSH
 SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPD TWSTPHSYFSLTFCVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDQGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDV FSCSVMEALHNHYT
 QKSLSLSPGK (SEQ ID NO: 309)

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

RNL PVATPD PGMF PCLHHSQNLLRAVS NMLQKARQTLEFY PCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO: 460)

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
SLLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 291)**

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSAMMALCLSSIIYEDLKMVQVEFKTMNAKLMDPKRQIFLDQNMALVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: 310)**

>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
SLLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 291)**

Figure 44H

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

RNL PVATPDPGMF PCLHHSQNLLRAVSNMLQKARQTLEFYPC TSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFAMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL N
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: 311)**

**>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
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPD TWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDV FSCSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 291)**

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

RNL PVATPDPGMF PCLHHSQNLLRAVSNMLQKARQTLEFYPC TSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCAASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL N
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: 312)**

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
SLLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 291)**

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLAMDPKRQIFLDQNNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQVMSVMEALHNHYTQKSLSLSPGK **(SEQ ID NO: 313)**

**>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
SLLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSQVMSVMEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 291)**

Figure 44J

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

RNL PVATPD PGMF PCLHHSQNLLRAVSNMLQKARQTLEFYPC TSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLADPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
N GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO: 314)

**>XENP31264 human_IL12p40(E59K/K99E)_(GGGGG)2-human_IL12p35(L75A)_(GGGGG)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)_(GGGGG)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPD TWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDV FSCSVMEALHNHYT
QKSLSLSPGK (SEQ ID NO: 291)

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

RNL PVATPD PGMF PCLHHSQNLLRAVSNMLQKARQTLEFYPC TSEEIDHEDITKDKTSTVEACLPLELTKNESCAN
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPKPKD TLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL
N GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO: 315)

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**

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 291)**

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

RNLPVATPDPMFPCLLHHSQNLRLRAVS NMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKAKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 316)**

**>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**

IWELKKDVYVVELDWPDPKAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 317)**

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

RNLPVATPDPMFPCLLHHSQNLRLRAVS NMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVCLTVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 461)**

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**

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVLHEALHSHYT
QKSLSLSPGK (SEQ ID NO: 318)

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

RNLVPATPDPMFPCPLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCLLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVLHEALHSHYTQKSLSLSPGK (SEQ ID NO: 319)

**>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**

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVLHEALHSHYT
QKSLSLSPGK (SEQ ID NO: 320)

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

RNLVPATPDPMFPCPLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEDHEDITKDKTSVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCLLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVLHEALHSHYTQKSLSLSPGK (SEQ ID NO: 319)

Figure 45B

>XENP31144 human IL12p40 E32K/D34N/E59K/K99E (GGGGG)2-human IL12p35 D55Q (GGGGG)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_(GGGGG)2_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S

IWELKKDVYVVELDWNYPDAPGEMVVLTC DTPKENGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEGQDVFSCSVLHEALHSHYT
QKSLSLSPGK (SEQ ID NO: 321)

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

RNLVPATPDPMFPCLLHHSQNLLRAVS NMLQKARQTLEFYPTCTSEEDHEDITKQKTSVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVLHEALHSHYTQKSLSLSPGK (SEQ ID NO: 322)

>XENP31145 human IL12p40 E32K/D34K/E59K/K99E (GGGGG)2-human IL12p35 D55Q (GGGGG)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_(GGGGG)2_Fc(216)_IgG1_pl(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S

IWELKKDVYVVELDWNYPDAPGEMVVLTC DTPKEGKITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEGQDVFSCSVLHEALHSHYT
QKSLSLSPGK (SEQ ID NO: 323)

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

RNLVPATPDPMFPCLLHHSQNLLRAVS NMLQKARQTLEFYPTCTSEEDHEDITKQKTSVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVLHEALHSHYTQKSLSLSPGK (SEQ ID NO: 322)

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
SLLLLHKKEDGIWSTDILKDQEPKNTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYT
QKSLSLSPGK **(SEQ ID NO: 324)**

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

RNLPVATPDPGMFPCLLHHSQNLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVLHEALHSHYTQKSLSLSPGK **(SEQ ID NO: 319)**

Figure 46A

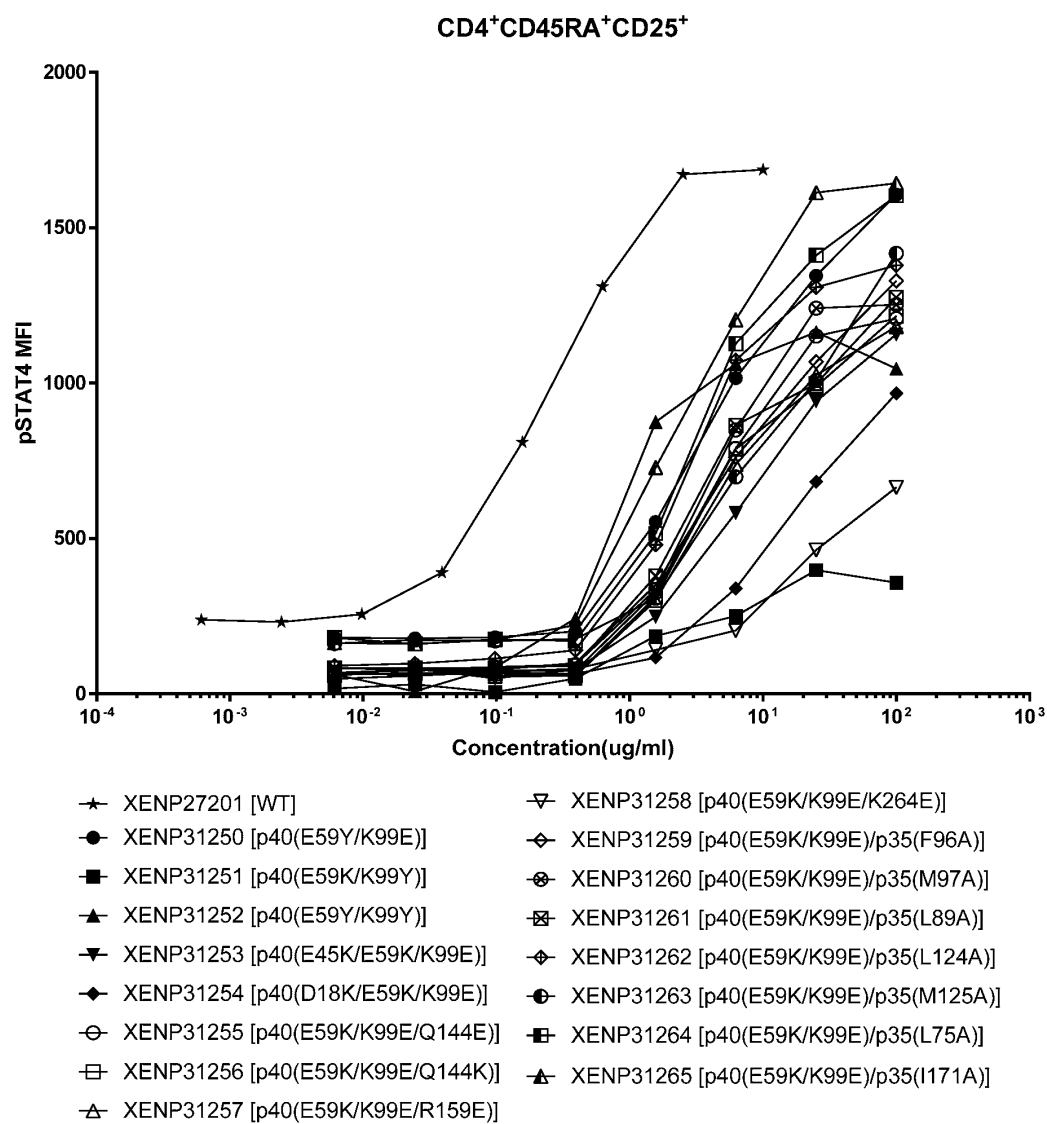


Figure 46B

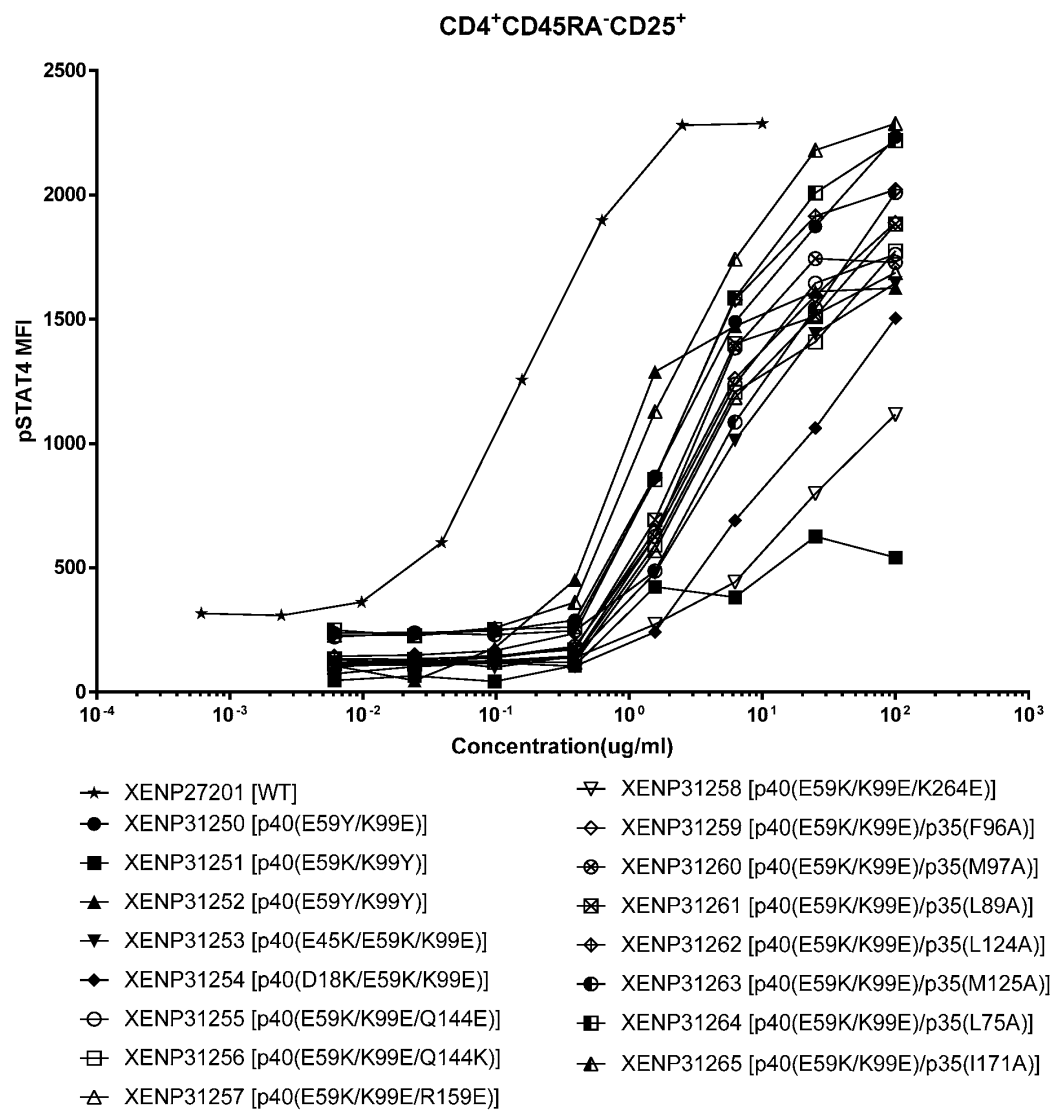


Figure 46C

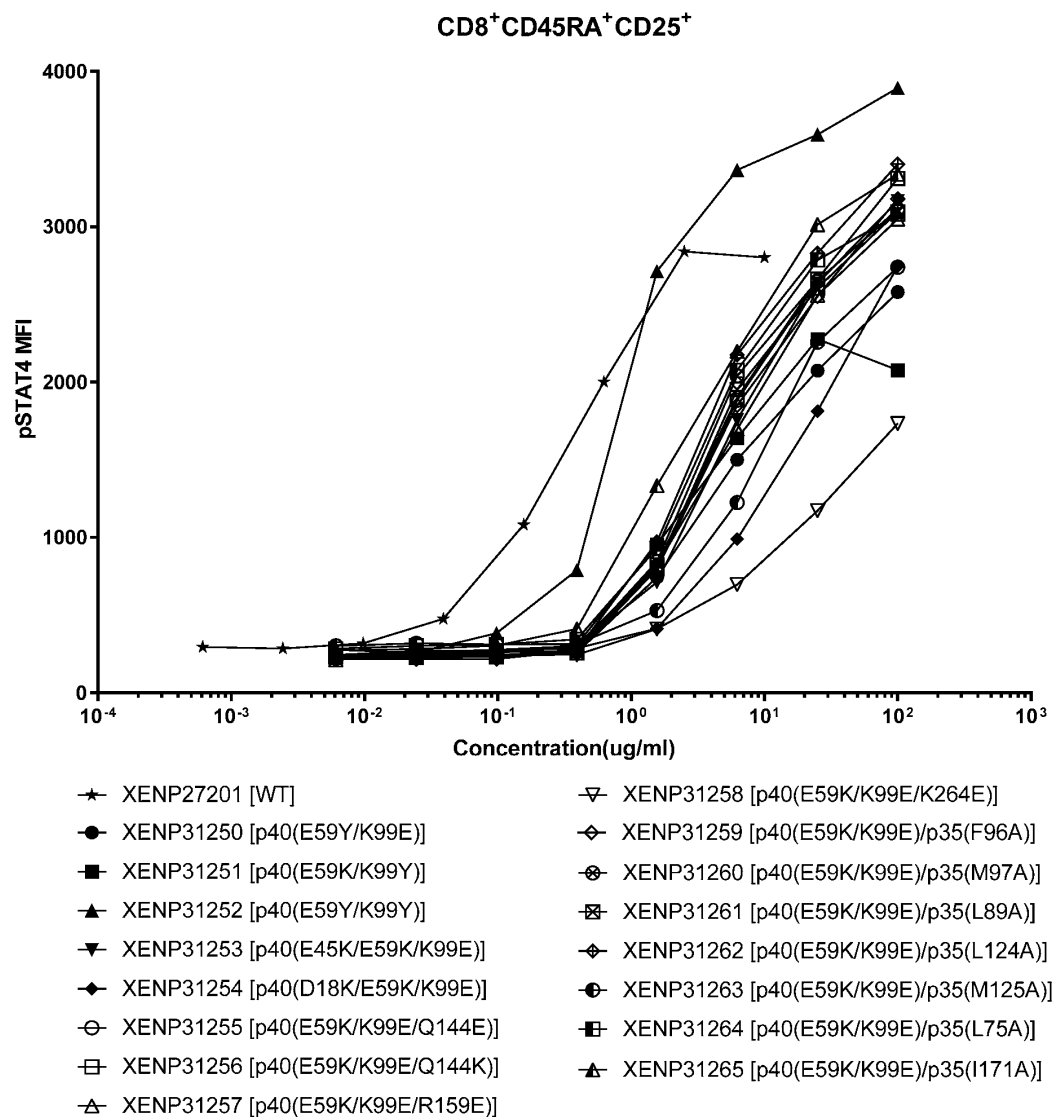


Figure 46D

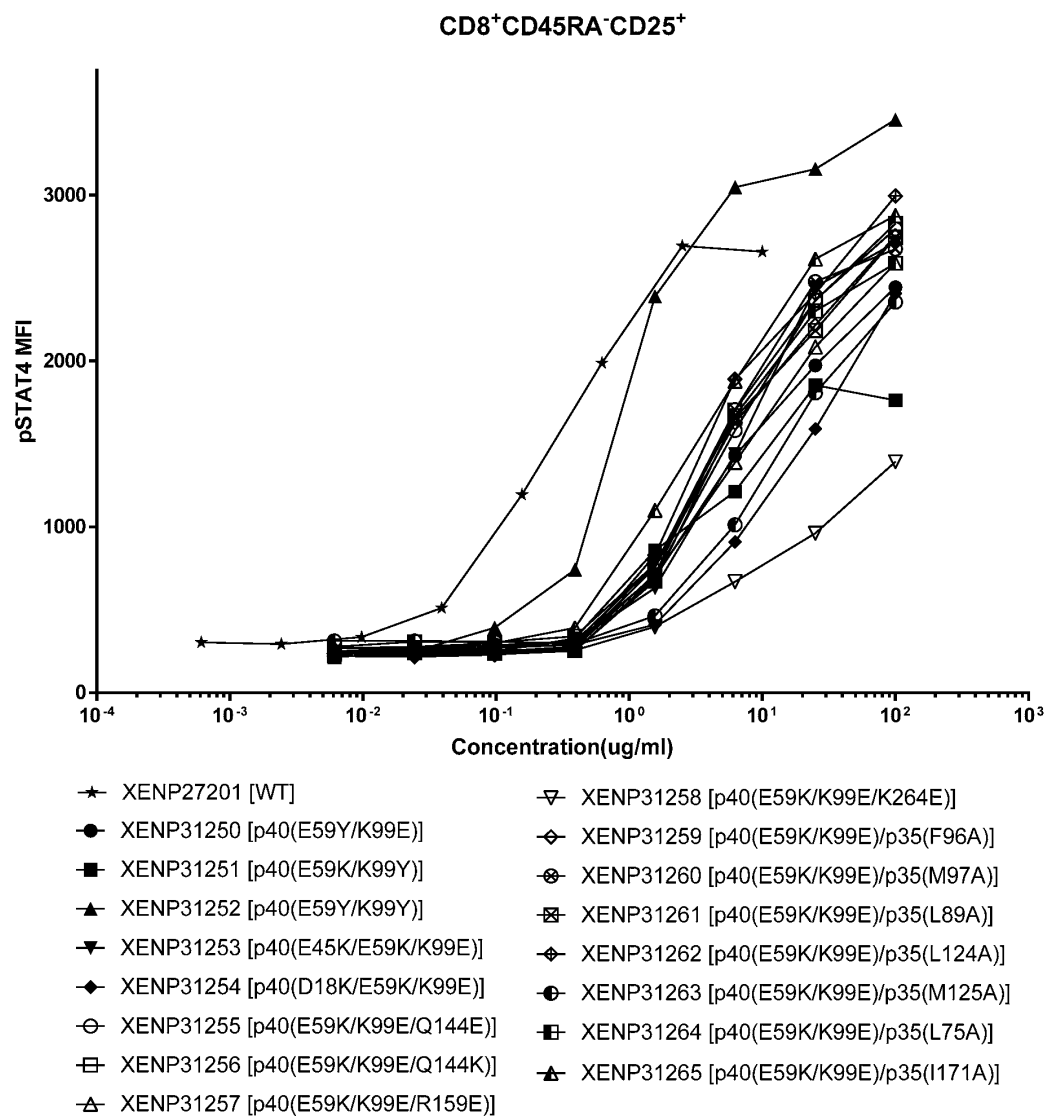
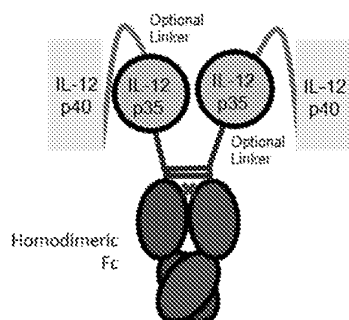


Figure 47

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)

 $(\text{scIL-12(p40/p35)})_2\text{-Fc}$

Example: XENP31289

Figure 48B

B)

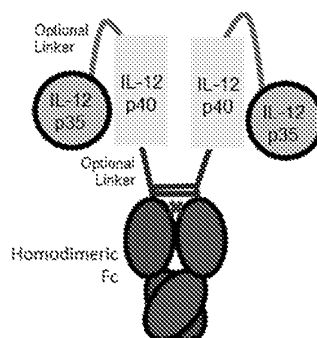
 $(\text{scIL-12(p35/p40)})_2\text{-Fc}$

Figure 48C

C)

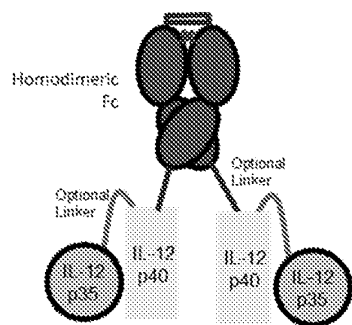
 $\text{Fc-(scIL-12(p40/p35))}_2$

Figure 48D

D)

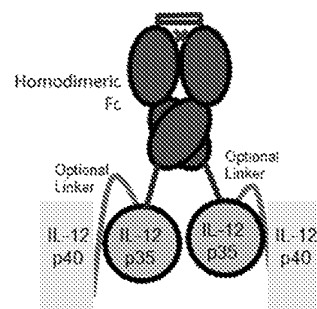
 $\text{Fc-(scIL-12(p35/p40))}_2$

Figure 49

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWTITSTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
RGDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDVAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/GGGGSGGGGS
GGGGSGGGGSGGGGS/RNLPVATPDPGMFPCLHHSQNLRAVSNNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEA
CLPLELTKNESCLNSRETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVID
ELMQALNFNSETVPQKSSLEEDFYKTIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPC
PAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGGP
ENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 51)**

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSHS
LLLLHKKEDGIWSTDILKDQKEPKNKTFRLCEAKNYSGRFTCWWTITSTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
GDNKEYEYSVEQCQEDSACPAAEESLPIEVMVDVAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/GGGGSGGGGS
GGGGSGGGGSGGGGS/RNLPVATPDPGMFPCLHHSQNLRAVSNNMLQKARQTLFYPCTSEEDHEDITKDKTSTVEA
CLPLELTKNESCLNSRETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVID
ELMQALNFNSETVPQKSSLEEDFYKTIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPC
PAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGGP
ENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 353)**

Figure 50

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

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSHS
 LLLHHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVR
 GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
 WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/GGGGSGGGGS
GGGGSGGGGSGGGGS/RNLPVATPDPGMFCLHHSQNLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEA
 CLPLELTKNESCLNSRETSFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVID
 ELMQALNFNSETVPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPC
 PAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEYNSTYRVVSVLTVL
 HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQP
 ENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 424)

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

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREE
 QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFY
 PSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ
 ID NO: 467)

Figure 51A

A)

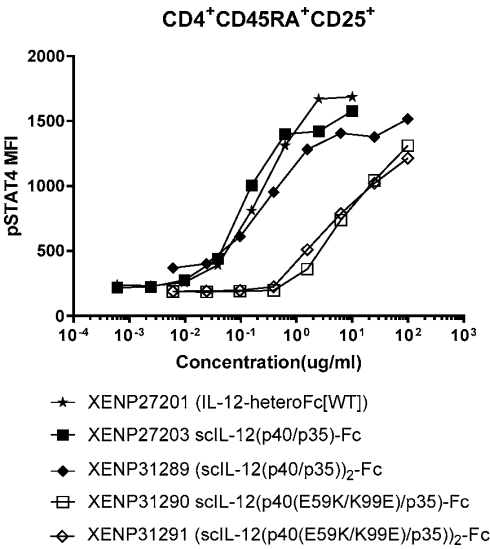


Figure 51B

B)

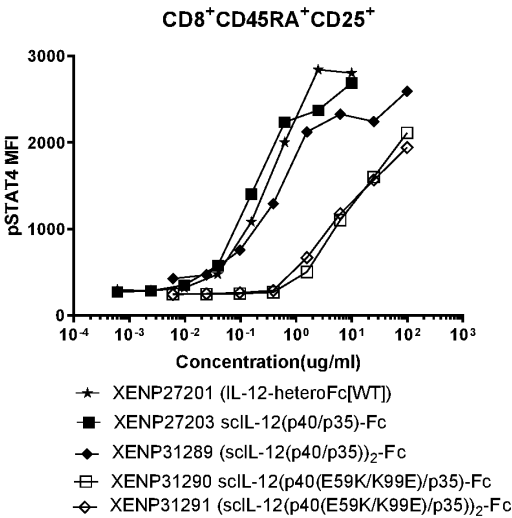


Figure 51C

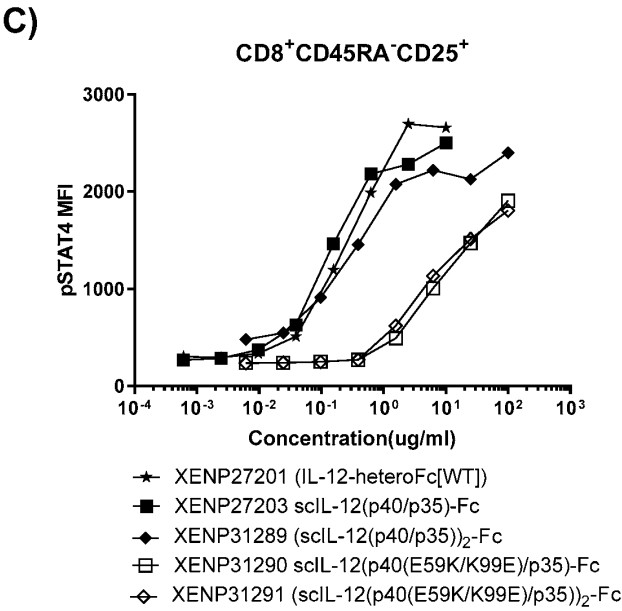


Figure 51D

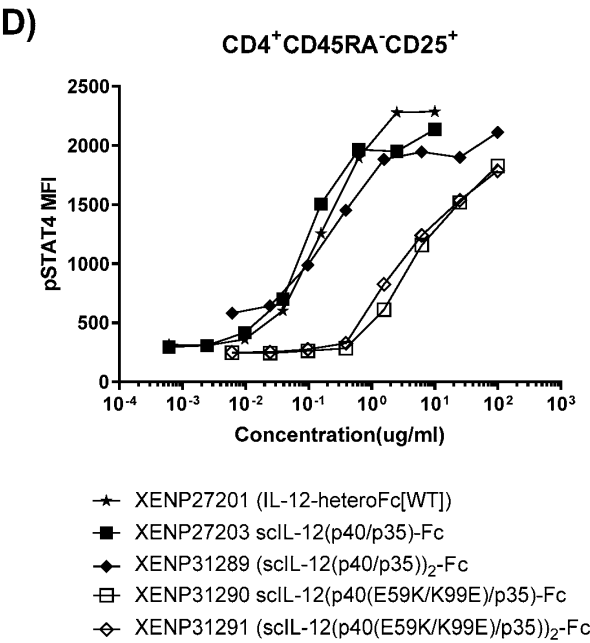


Figure 52

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**

QVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAVIWIYDGSKRYYADSVKGRFTISRDNK
NTLFLQMNSLRAEDTAVYYCATNDDYWGQGLTVVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTP
PVLDSDSGFFLYSKLTVDKSRWQQGNVFCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 355)

XENP016432 Nivolumab_H0L0_IgG1_PVA_/S267K Light Chain

EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSEPED
FAVYYCQSSNWPRTFGQGTKEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSSTLSSTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 356)

Figure 54A

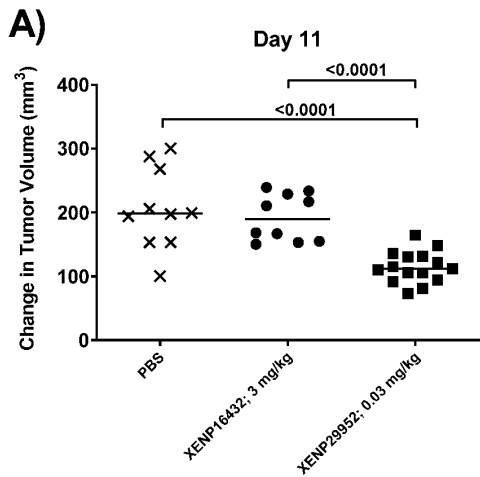


Figure 54B

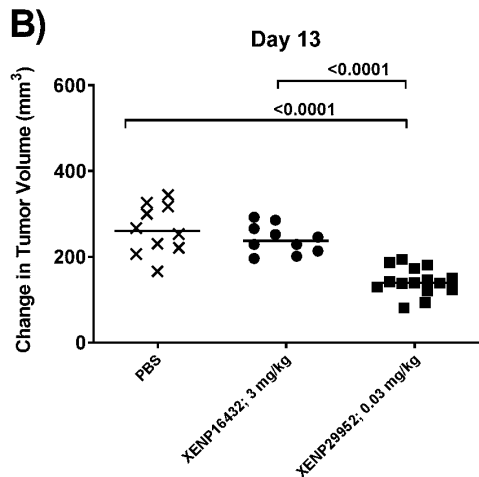


Figure 54C

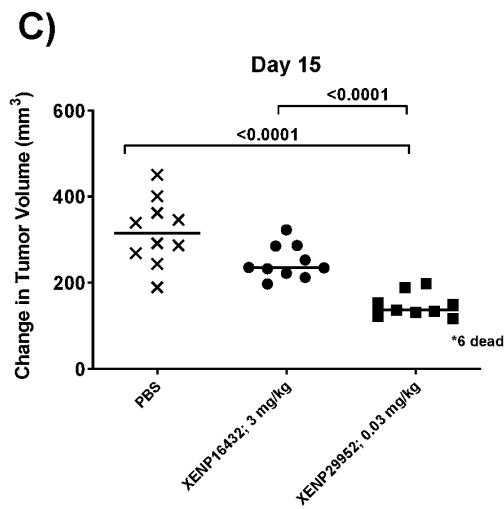


Figure 54D

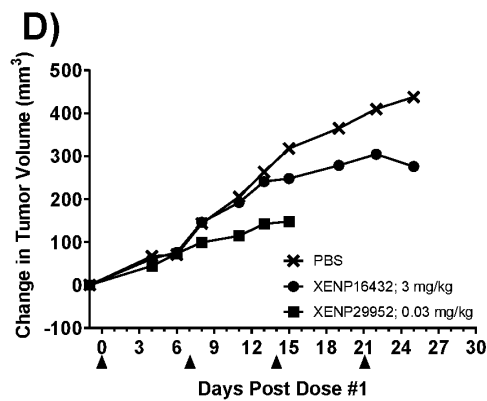


Figure 55A

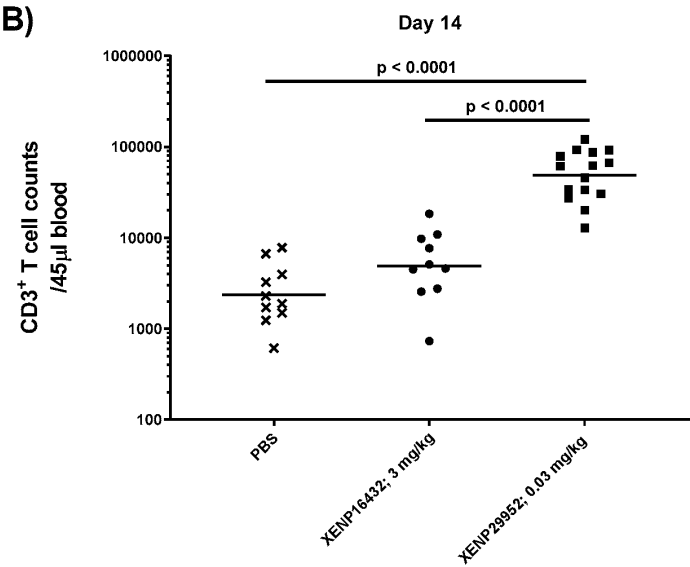


Figure 55B

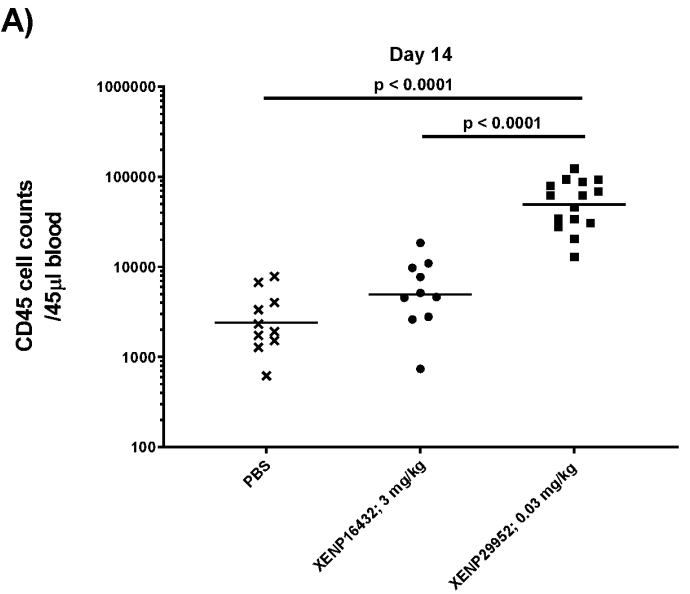


Figure 55C

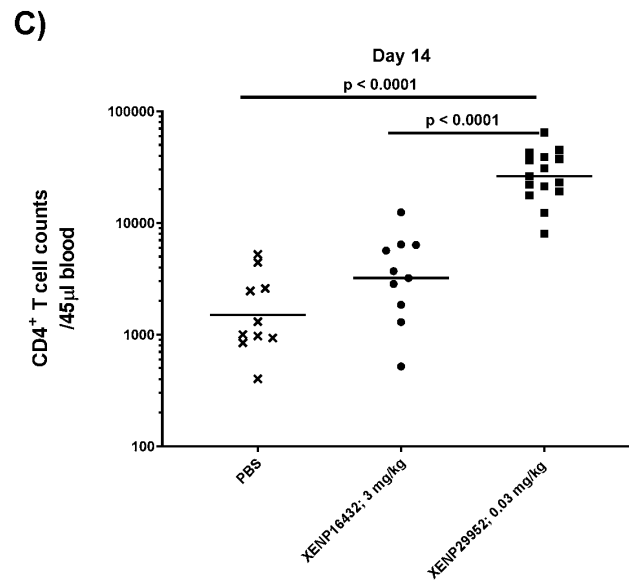


Figure 55D

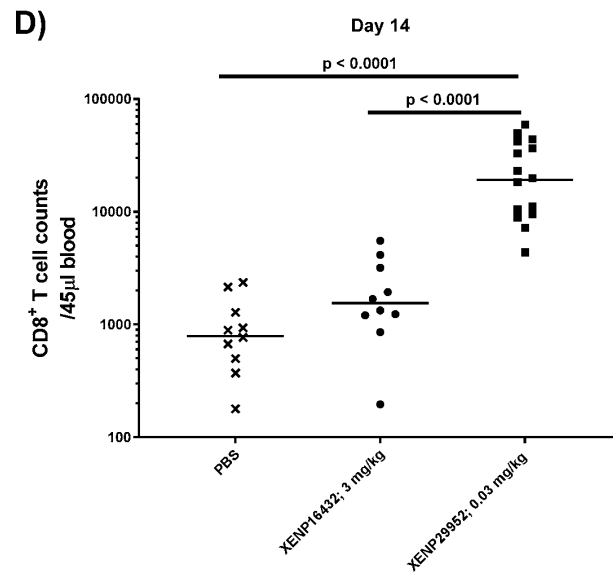


Figure 55E

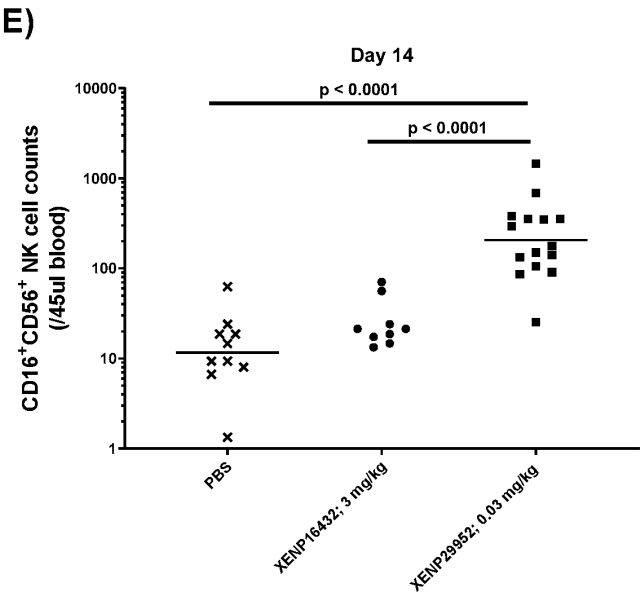


Figure 55F

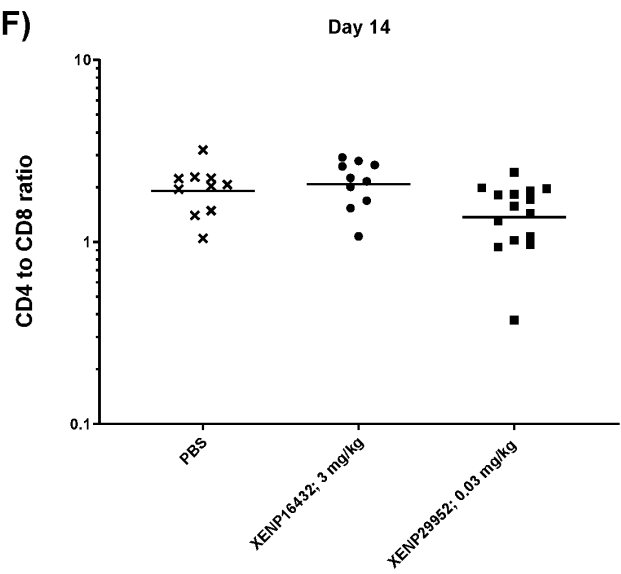


Figure 56A

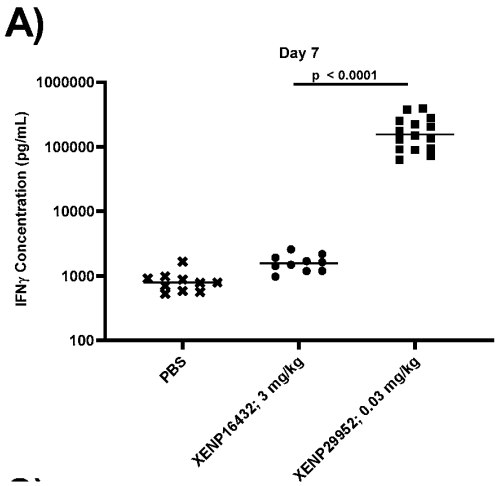


Figure 56B

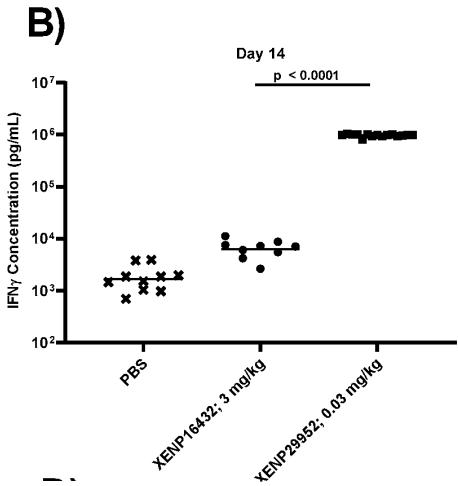


Figure 56C

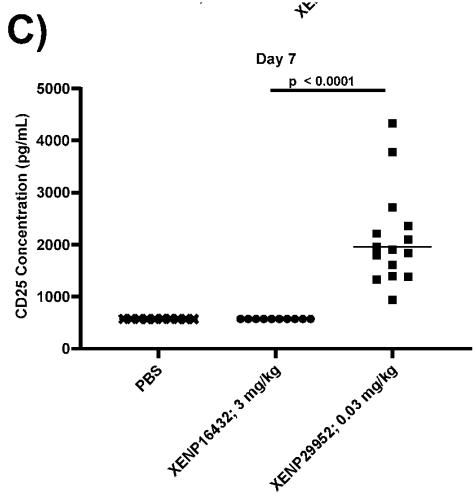


Figure 56D

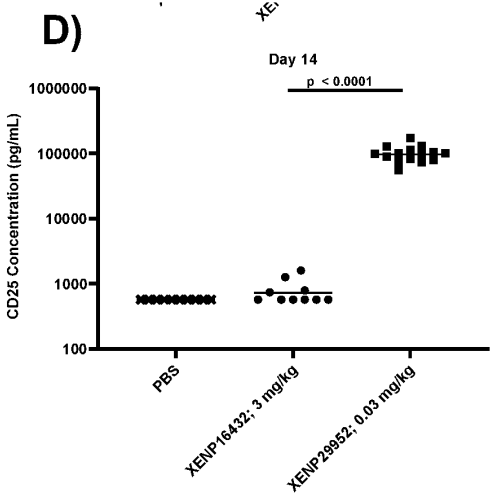


Figure 57A

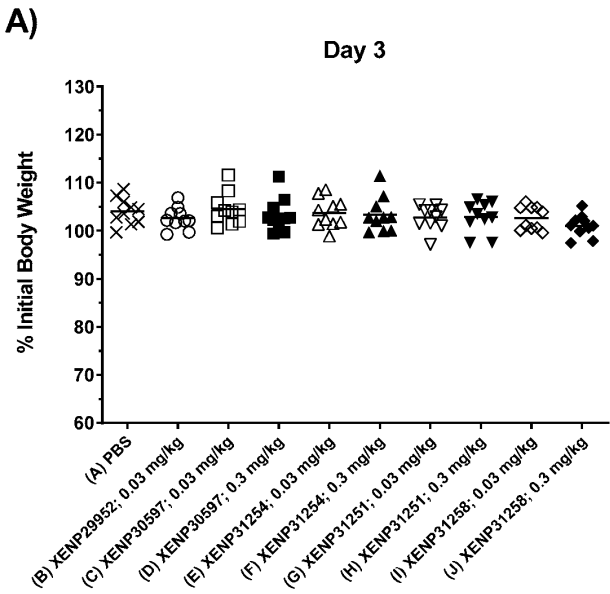


Figure 57B

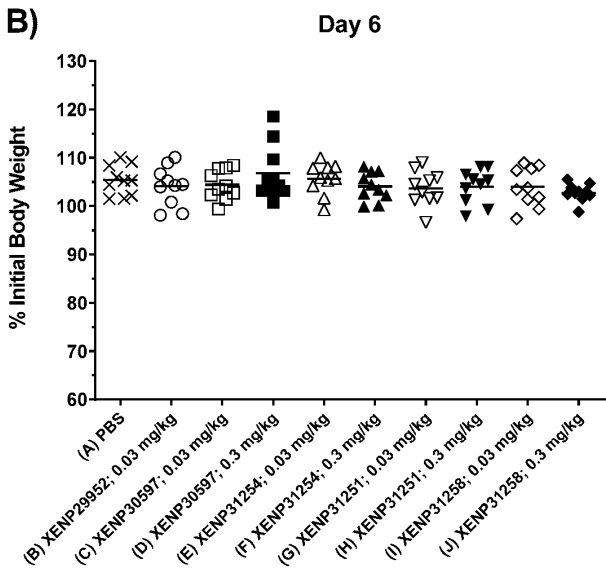


Figure 57C

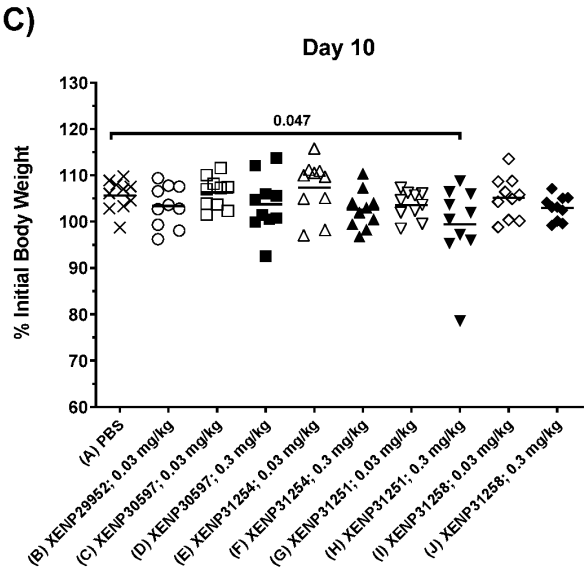


Figure 57D

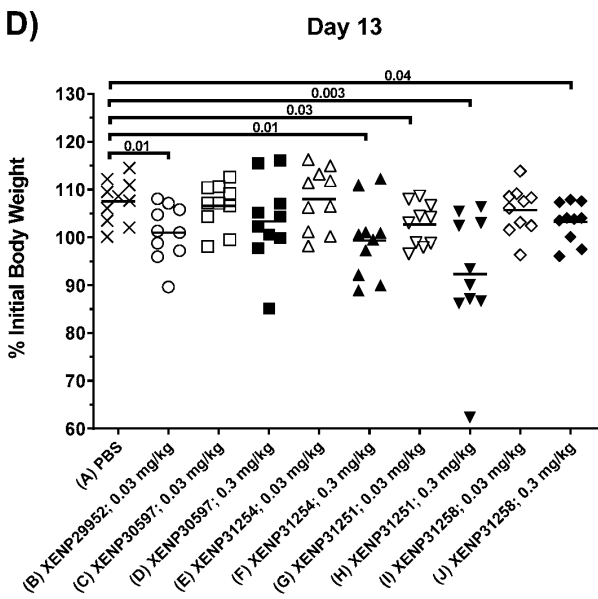


Figure 57E

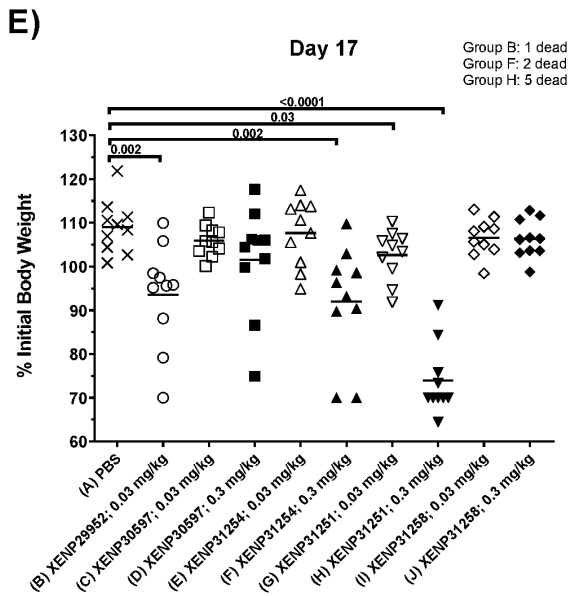


Figure 57F

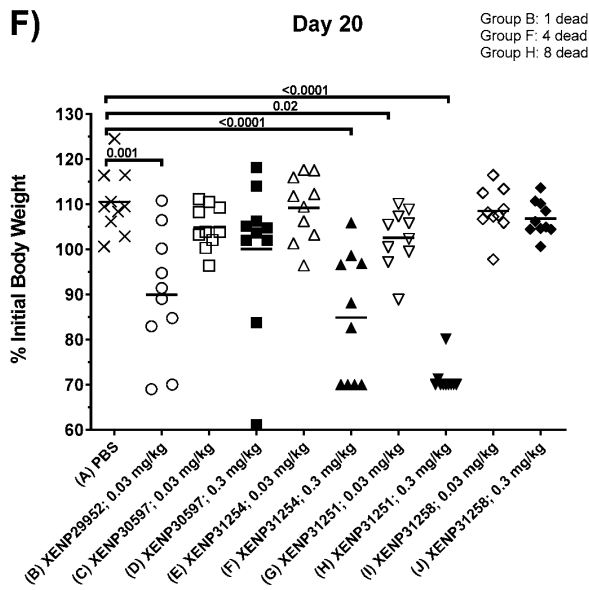


Figure 57G

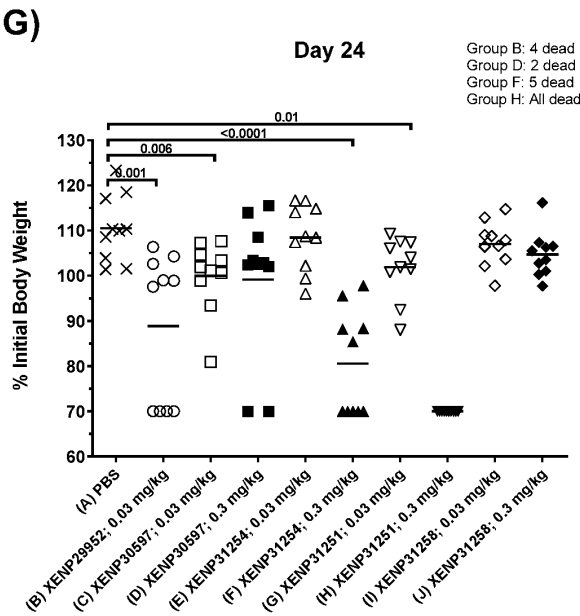


Figure 57H

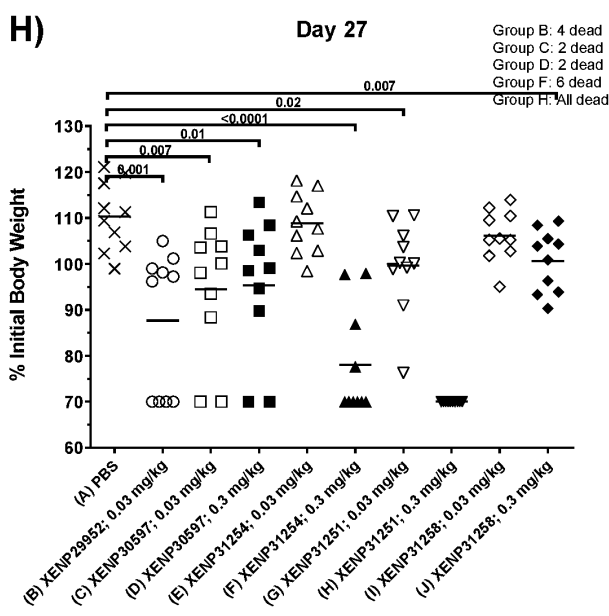


Figure 57I

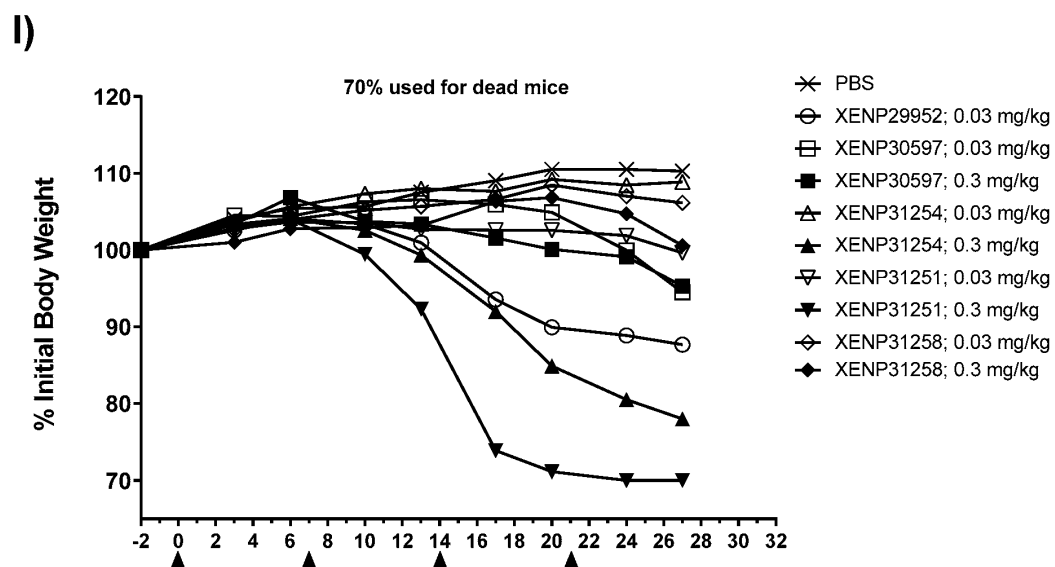


Figure 58A

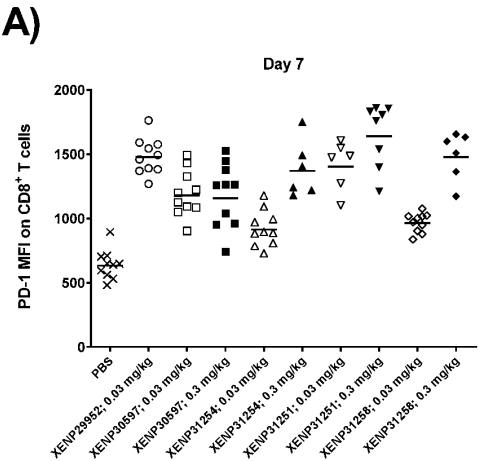


Figure 58B

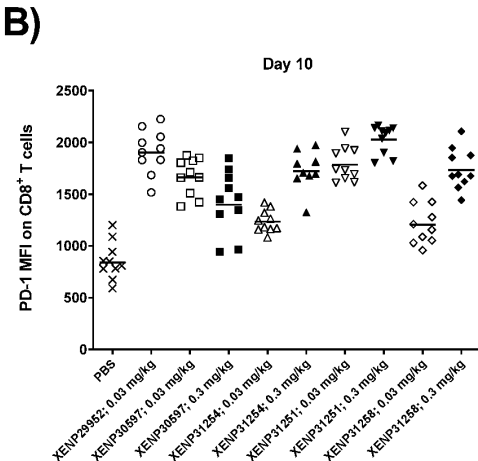


Figure 58C

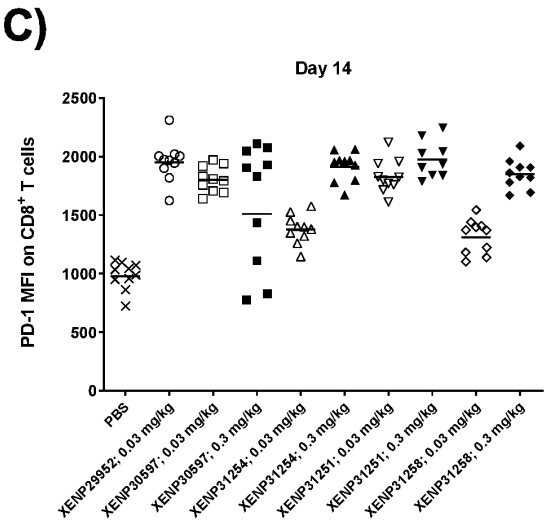


Figure 59A

Figure 59B

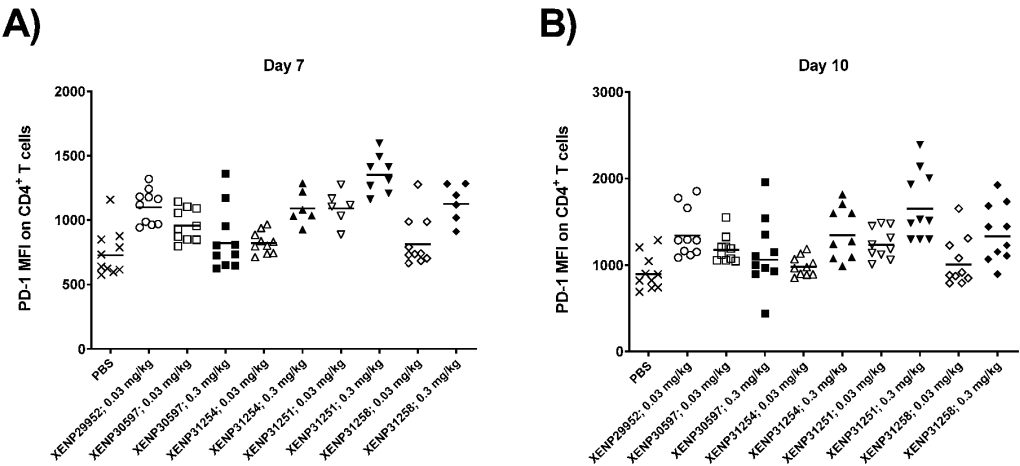


Figure 59C

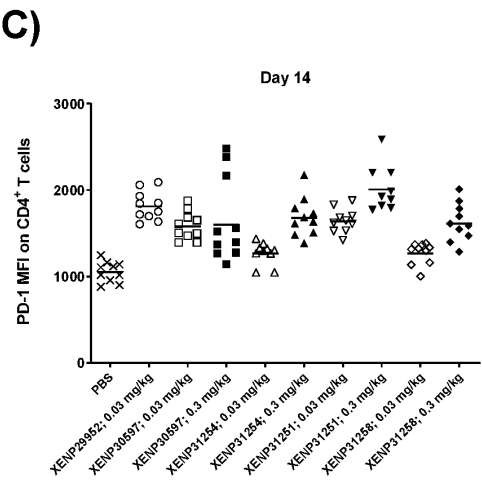


Figure 60A

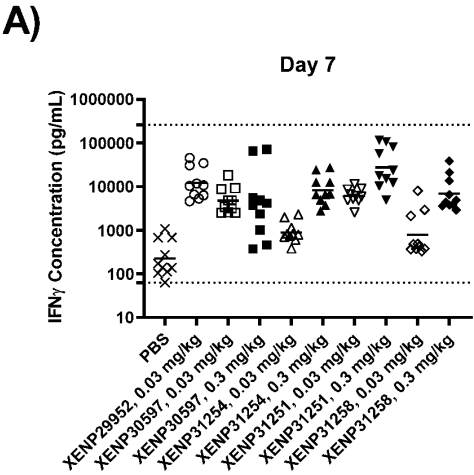


Figure 60B

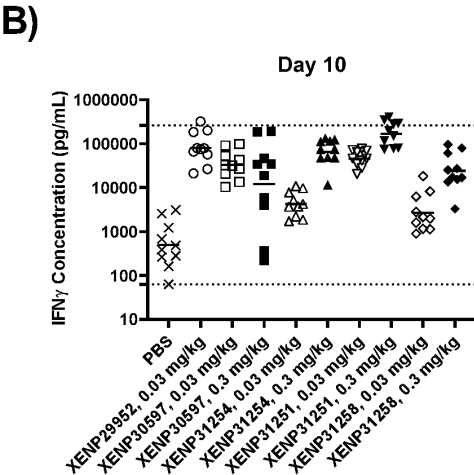


Figure 60C

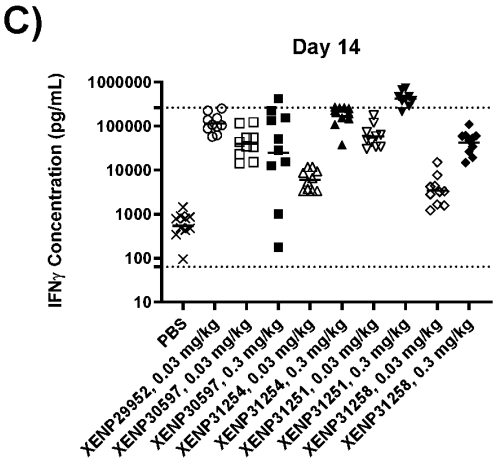


Figure 60D

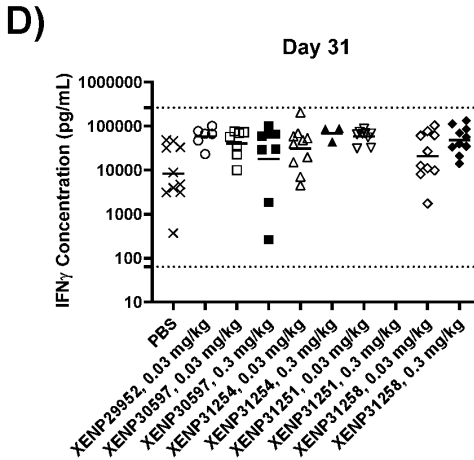


Figure 61A

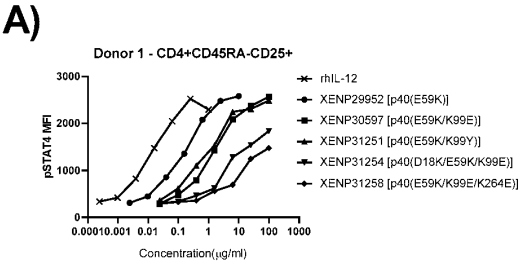


Figure 61B

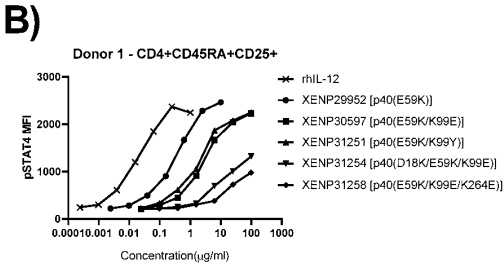


Figure 61C

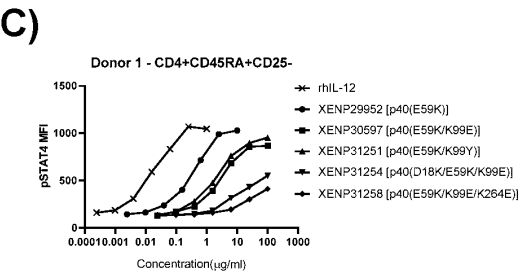


Figure 61D

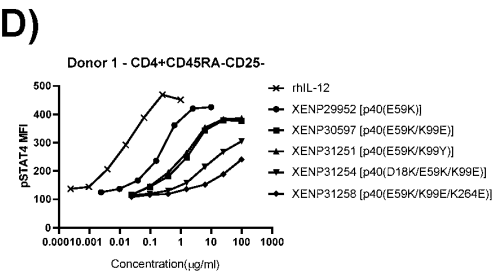


Figure 61E

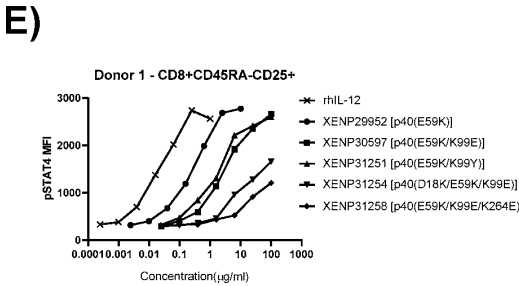


Figure 61F

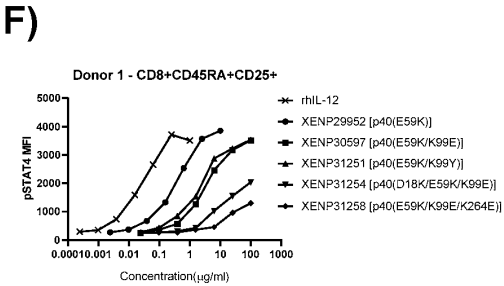


Figure 61G

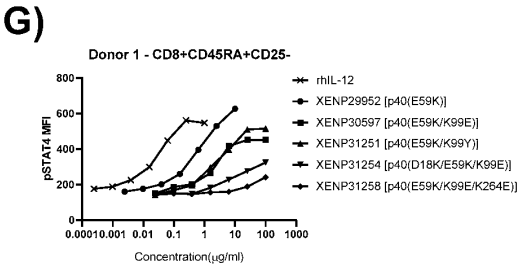


Figure 61I

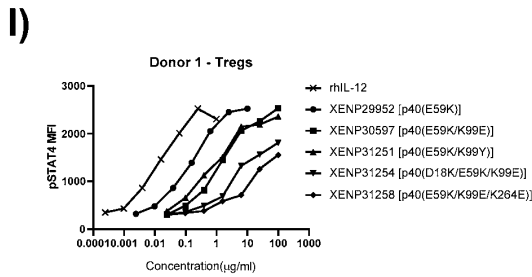


Figure 61K

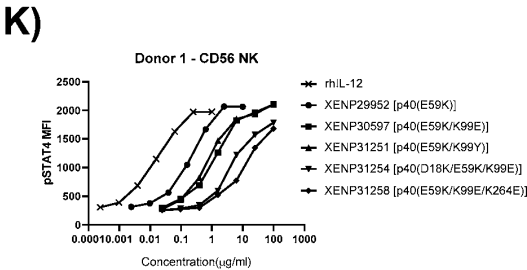


Figure 61H

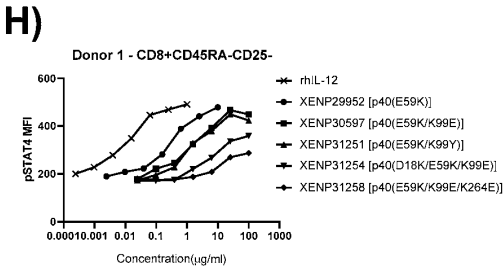


Figure 61J

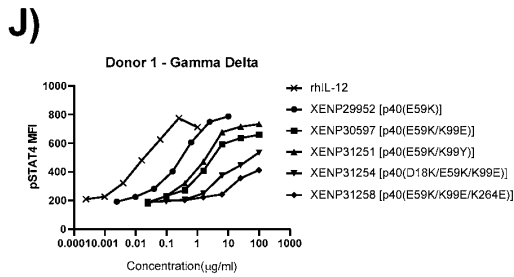


Figure 62A

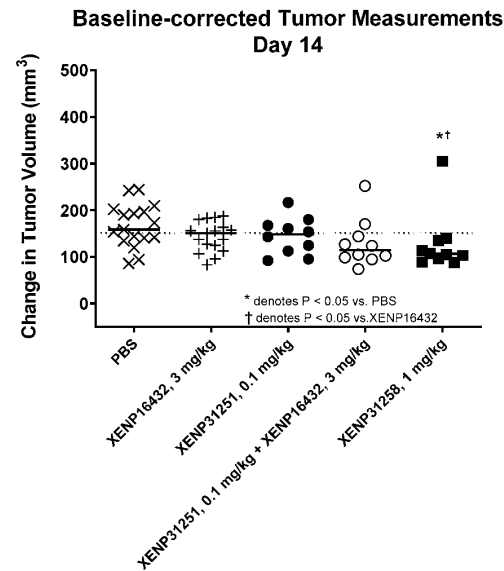


Figure 62B

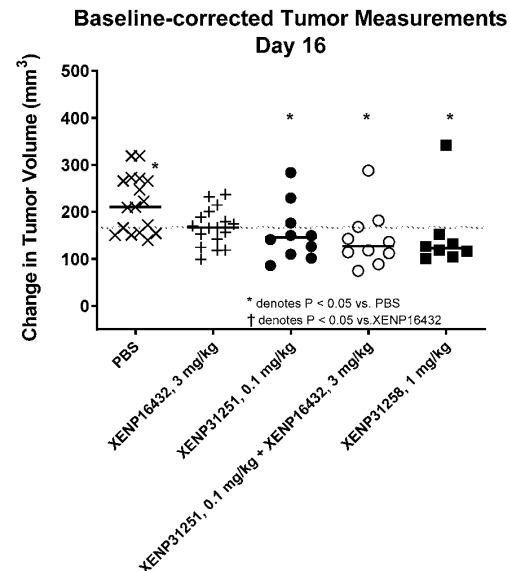


Figure 62C

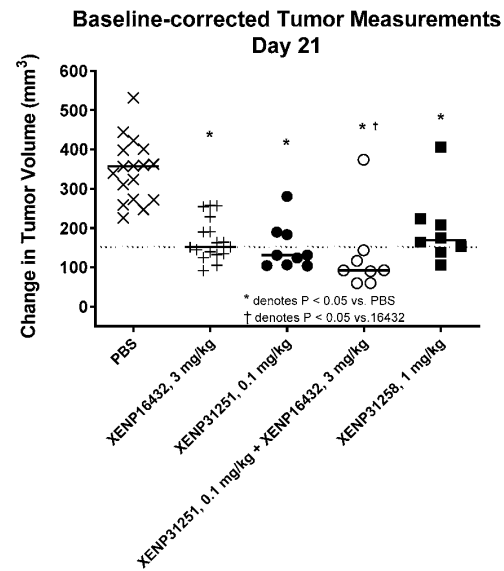


Figure 62D

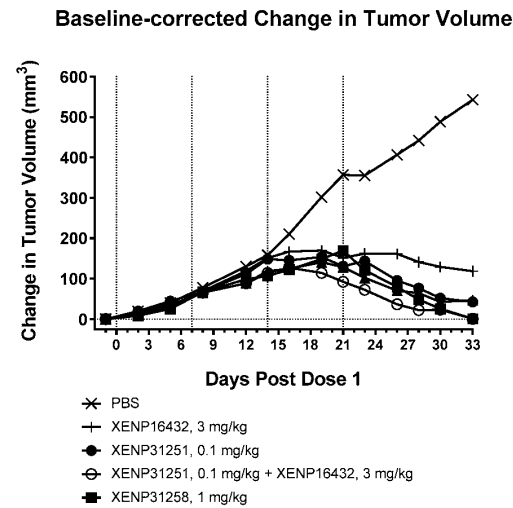


Figure 63A

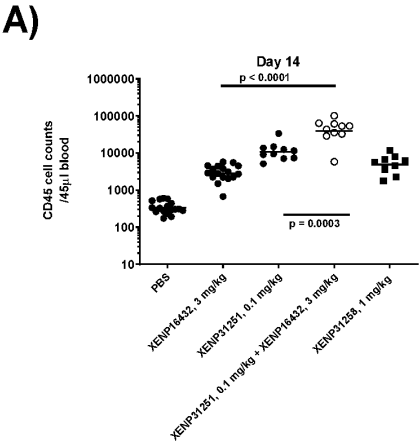


Figure 63B

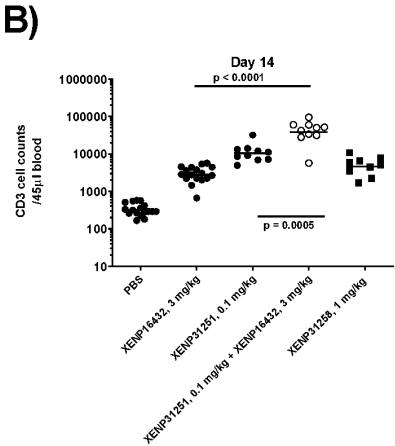


Figure 63C

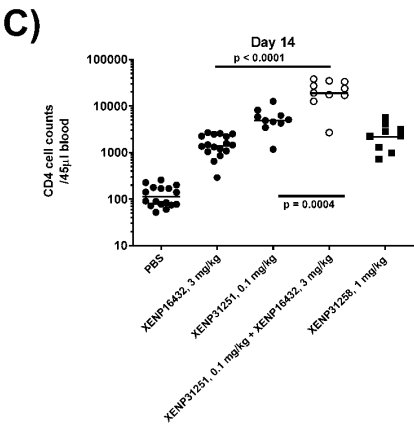


Figure 63D

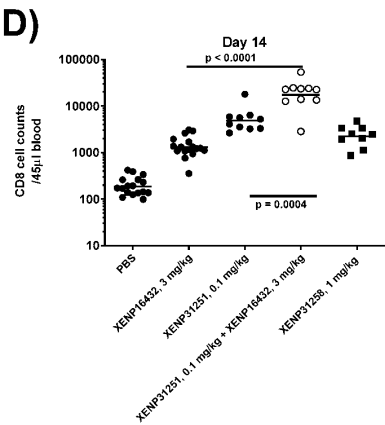


Figure 63E

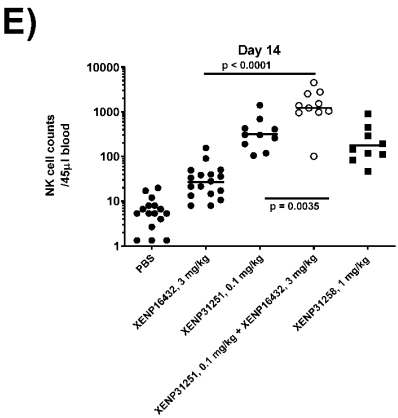


Figure 63F

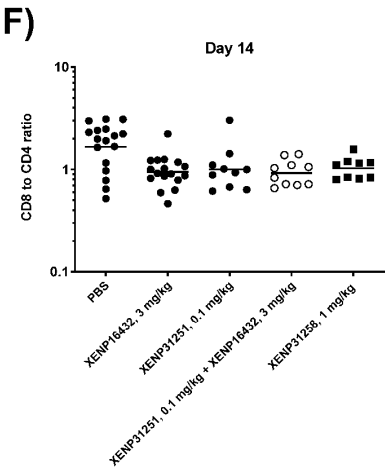


Figure 64A

>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/S3
64K/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

IWELKKDVYVVELDWYPKAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSHS
 LLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
 GDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
 WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/GGGGSGGGGS/
 EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREE
 YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
 DIAVEWESDGGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALSHYTTQKSLSLSPGK **(SEQ ID**
NO: 357)

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

RNLVPATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNSRET
 SFITNGSCLASRKTSFMMALCLSSIEDLKMVQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSETVPQK
 SSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPK
 KDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV
 SNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTPPVLDSDGS
 FFYLSKLTVDKSRWQQGNVFSVCSVLHEALSHYTTQKSLSLSPGK **(SEQ ID NO: 421)**

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

IWELKKD VYVVELDWYPDAPGEMVVLTC DTP EEDGITWTL DQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVL SHS
LLLLHKKEDGIWSTDILKDQYEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
GDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSW EYPDT
WSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/ GGGGS GGGGS /
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREE
YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
DIAVEWESDGGQPENNYKTTTPVLDSG SFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK (SEQ ID
NO: 358)

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

RNLPVATPDPGMFPC LHHSQNLLRAVS NMLQKARQTLEFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNSRET
SFITNGSCLASRKTSFMMALCLSSIEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSETVPQK
SSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGGS GGGGS /EPKSSDKTHTCPPCPAPPVAGPSVFLFPPK
KDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV
SNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFPYPSDIAVEWESNGQPENNYKTTTPVLDSG
SFFLYSKLTVDKSRWQQGNV FSCSVLHEALHSHYTQKSLSLSPGK (SEQ ID NO: 422)

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/S3
64K/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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSHS
 LLLHHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWTISTDLTFSVKSSRGSSDPQGVTCGAATLSAERV
 GDNKEYEYSVEQCEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIKPDPPKNLQLKPLKNSRQVEVSWEYPDT
 WSTPHSYFSLTFCVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/GGGGSGGGGS/
 EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREE
 YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
 DIAVEWESDGGQENNYKTTTPVLDSGSGFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK (SEQ ID
 NO: 359)

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

RNLPVATPDPMFPCLLHHSQNLRAVSNNMLQKARQTLEFYPTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNSRET
 SFITNGSCLASRKTSFMMALCLSSYEDLKMYYQVEFKTMNAKLLMDPKRQIFLDQNMMLAVIDELMQALNFNSETVPQK
 SSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPK
 KDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV
 SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFPYSDIAVEWESNGQENNYKTTTPVLDSGSG
 FFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK (SEQ ID NO: 423)

Figure 65A

> IL-12p40(C252S)

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKF~~K~~FGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQ~~E~~EPKNKTF~~E~~LRCEAKNYSGRFTCW~~E~~WLT~~E~~TI~~E~~STDLTFSVKSSRGSSDPQGVTCGAATLS
AERV~~R~~GD~~N~~KEYEYSVE~~C~~QEDSACPA~~A~~EESLP~~E~~IEVMVDAVHKLKYENYTSSFFIRDI~~I~~KPD~~P~~PKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTF~~S~~VQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS
(SEQ ID NO: 360)

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

IWELKKDVYVVELDWYP~~K~~APGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVK~~K~~FGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQ~~E~~EPKNKTF~~E~~LRCEAKNYSGRFTCW~~E~~WLT~~E~~TI~~E~~STDLTFSVKSSRGSSDPQGVTCGAATLS
AERV~~R~~GD~~N~~KEYEYSVE~~C~~QEDSACPA~~A~~EESLP~~E~~IEVMVDAVHKLKYENYTSSFFIRDI~~I~~KPD~~P~~PKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTF~~S~~VQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS
(SEQ ID NO: 361)

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

IWELKKDVYVVELDWYP~~K~~APGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVK~~K~~FGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQ~~E~~EPKNKTF~~E~~LRCEAKNYSGRFTCW~~E~~WLT~~E~~TI~~E~~STDLTFSVKSSRGSSDPQGVTCGAATLS
AERV~~R~~GD~~N~~KEYEYSVE~~C~~QEDSACPA~~A~~EESLP~~E~~IEVMVDAVHKLKYENYTSSFFIRDI~~I~~KPD~~P~~PKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTF~~S~~VQVQGKSKREK~~E~~DRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS
(SEQ ID NO: 362)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVK~~K~~FGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQ~~E~~EPKNKTF~~E~~LRCEAKNYSGRFTCW~~E~~WLT~~E~~TI~~E~~STDLTFSVKSSRGSSDPQGVTCGAATLS
AERV~~R~~GD~~N~~KEYEYSVE~~C~~QEDSACPA~~A~~EESLP~~E~~IEVMVDAVHKLKYENYTSSFFIRDI~~I~~KPD~~P~~PKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTF~~S~~VQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS
(SEQ ID NO: 363)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVK~~K~~FGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQ~~E~~EPKNKTF~~E~~LRCEAKNYSGRFTCW~~E~~WLT~~E~~TI~~E~~STDLTFSVKSSRGSSDPQGVTCGAATLS
AERV~~R~~GD~~N~~KEYEYSVE~~C~~QEDSACPA~~A~~EESLP~~E~~IEVMVDAVHKLKYENYTSSFFIRDI~~I~~KPD~~P~~PKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTF~~S~~VQVQGKSKREK~~E~~DRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS
(SEQ ID NO: 364)

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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVK~~K~~FGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQ~~E~~EPKNKTF~~E~~LRCEAKNYSGRFTCW~~E~~WLT~~E~~TI~~E~~STDLTFSVKSSRGSSDPQGVTCGAATLS
AERV~~R~~GD~~N~~KEYEYSVE~~C~~QEDSACPA~~A~~EESLP~~E~~IEVMVDAVHKLKYENYTSSFFIRDI~~I~~KPD~~P~~PKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTF~~S~~VQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS
(SEQ ID NO: 365)

Figure 65B

>IL-12p40 (E59K/K99E/N103Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: 366)

>IL-12p40 (E59K/K99E/N113Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: 367)

>IL-12p40 (E59K/K99E/N200Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMMDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: 368)

>IL-12p40 (E59K/K99E/N281Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: 369)

>IL-12p40 (E59K/K99E/N103Q/N113Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKTFLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: 370)

>IL-12p40 (E59K/K99E/N103Q/N200Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMMDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: 371)

>IL-12p40 (E59K/K99E/N103Q/N281Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: 372)

Figure 65C

>IL-12p40 (E59K/K99E/N113Q/N200Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMMDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: 373)

>IL-12p40 (IL12p40_E59K/K99E/N113Q/N281Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMMDAVHKLKYEYNTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: 374)

>IL-12p40 (E59K/K99E/N200Q/N281Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMMDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: 375)

>IL-12p40 (E59K/K99E/N103Q/N113Q/N200Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMMDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: 376)

>IL-12p40 (E59K/K99E/N103Q/N200Q/N281Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMMDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: 377)

>IL-12p40 (E59K/K99E/N113Q/N200Q/N281Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMMDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: 378)

>IL-12p40 (E59K/K99E/N103Q/N113Q/N200Q/N281Q/C252S/K264E)
IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMMDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPDTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYYSSSWSEWASVPCS

(SEQ ID NO: 379)

Figure 66A

**>XENP32187 human IL12p40(D18K/E59K/K99E/C252S) (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
_Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q**

**Chain 1 - human IL12p40(D18K/E59K/K99E/C252S) (GGGGS)2_Fc(216)_IgG1_pl(-)
_Isosteric_A_C220S/PVA_/S267K/L368D/K370S**

IWELKKDVYVVELDWYPKAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLISH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFVSVQVQGKSKREKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK (SEQ ID NO: 380)

Chain 2 - IL12p35 (GGGGS)2_Fc(216)_IgG1 C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFCLHHSQNLRAVSNNLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTVLKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 402)

**>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**

IWELKKDVYVVELDWYPKAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLISH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWWLTTISTDLTFVSKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAAEESLPIEVMMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFVSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMEALHNHYT
QKSLSLSPGK (SEQ ID NO: 381)

Chain 2 - IL12p35 (GGGGS)2_Fc(216)_IgG1 C220S/PVA_/S267K/S364K/E357Q

RNLPVATPDPMFCLHHSQNLRAVSNNLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTVLKGFPYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 403)

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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQYEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFVSVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 382)

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

RNLVPATPDPGMFCLHHSQNLRAVSNNLQKARQTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCLLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 404)

**>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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCQEDSACPAEESLPIEVMDAVHKLKYENYTSSFFIRDIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFVSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 425)

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

RNLVPATPDPGMFCLHHSQNLRAVSNNLQKARQTLEFYPCCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCLLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 405)

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
SLLLLLHKKEDGIWSTDILKDQEEPKNKTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 384)**

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

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCLLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 406)**

**>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
SLLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK **(SEQ ID NO: 385)**

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

RNLPVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDPFYKTKIKLCLLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK **(SEQ ID NO: 407)**

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
 SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO: 386)

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

RNLPVATPDPMFPCLLHHSQNLRLRAVS NMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMVQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTIKILCLLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNACTKPREEQYNSTYRVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 408)

>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
 SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYEQYTSSFFIRDI IKPDPPKNLQLKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
 GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNACTKPREEEYNSTYRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO: 387)

Figure 66E

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

RNLPVATPDPMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 409)

>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
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVGRDNKEYEYSVECEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQKPLKNSRQVE
 VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO: 388)

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

RNLPVATPDPMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPKPKDITLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 410)

Figure 66F

>XENP32995 human IL12p40 E59K/K99E/N103Q/N113Q/C252S/K264E (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

> IL-12p40(E59K/K99E/N103Q/N113Q/C252S/K264E_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQTLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYENYTSFFIRDIIPDPKPNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 389)

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

RNLPVATPDPMFCLHHSQNLRAVS NMLQKARQTFEYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 411)

>XENP32996 human IL12p40 E59K/K99E/N103Q/N200Q/C252S/K264E (GGGGS)2-human IL12p35 (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

> IL-12p40(E59K/K99E/N103Q/N200Q/C252S/K264E_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWYPDAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIIPDPKPNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 390)

Figure 66G

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

RNLPVATPDPMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTIKILLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFPYSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 412)

>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
SLLLLHKKEDGIWSTDILKDQEEPQKQKTLRCEAKNYSGRFTCWMLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 391)

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

RNLPVATPDPMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTIKILLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFPYSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 413)

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
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKQYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIIPDPPKNLQKPLKNSRQVE
 VSWEPDTPWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO: 392)

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

RNLVPATPDPMFPCLLHHSQNLRLRAVSNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSVEACLPLELTKNESCLNS
 RETSFITNGSCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFNSET
 VPQKSSLEEPDFYTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
 GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
 TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 414)

>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
 SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKQYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
 AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYEYNTSSFFIRDIIPDPPKNLQKPLKNSRQVE
 VSWEPDTPWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
 VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
 NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
 QKSLSLSPGK (SEQ ID NO: 393)

Figure 66l

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 415)

>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
SLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWLLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 394)

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

RNLPVATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 416)

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
SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMDAVHKLKYEQYTSSFFIRDIIPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 395)

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

RNLVPATPDPMFPCLLHHSQNLRLRAVSNNMLQKARQTLFYPCTSEEIDHEDITKDKTSVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMMLAVIDELMQALNFNSET
VPQSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 417)

>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
SLLLLHKKEDGIWSTDILKDQEEPQKQTFRLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVRGDNKEYEYSVEQCEDSACPAAEESLPIEVMDAVHKLKYEQYTSSFFIRDIIPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRQASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCFSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 396)

Figure 66K

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

RNL PVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 418)

>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

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYCHKGGEVLSH
SLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKQYSGRFTCWWTITISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVECEQEDSACPAEESLPIEVMMDAVHKLKYEQYTSSEFFIRDIIPDPKPNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGSKREKEDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 397)

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

RNL PVATPDPGMFCLHHSQNLLRAVSNNMLQKARQTLEFYPCSTSEEDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 419)

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

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPQKQKTLRCEAKQYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYEQYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKQASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 398)

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

RNLPVATPDPGMFCLHHSQNLRAVS NMLQKARQTFEYPC TSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYKTKIKLCLLHAFRIRAVTIDRVMSYLNAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVVKLTCLVKGFPYPSDIAVEWESNGQPENNYK
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 420)

>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

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 426)

Figure 66M

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

RNLPVATPDPMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTQESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 399)

>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
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIPDPKPNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 427)

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

RNLPVATPDPMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITQGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 400)

Figure 66N

>XENP33007 human IL12p40(E59K/K99E/C252S/K264E) (GGGGS)2-human IL12p35(N195Q) (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 - human_IL12p40(E59K/K99E/C252S/K264E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 428)

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

RNLPVATPDPMFCLHHSQNLRAVS NMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITNGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSLEEDFYKTKIKLCILLHAFRIRAVTIDRVMSYLOAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPVLDSDGGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 401)

>XENP33008 human IL12p40(E59K/K99E/C252S/K264E) (GGGGS)2-human IL12p35(N71Q/N85Q) (GGGGS)2-Fc(216) IgG1 pl(-)
) Isosteric A C220S/PVA /S267K/L368D/K370S Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 - human_IL12p40(E59K/K99E/C252S/K264E)_(GGGGS)2_Fc(216)_IgG1_pl(-)
)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 429)

Figure 66O

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

RNLPVATPDPMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTQESCLNS
RETSFITQGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS/ GGGSGGGGS / EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 289)

>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**

IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTFRLCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQCEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIPDPKPNLQLKPLKNSRQVE
VSWEYPDWTSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGSGGGGS / EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSCVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 430)

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

RNLPVATPDPMFPCLLHHSQNLLRAVSNNMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTQESCLNS
RETSFITNGSCLASRKTSFMMALCLSSIIYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLQAS/ GGGSGGGGS / EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 290)

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

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 431)

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

RNLPVATPDPGMFCLHHSQNLRAVS NMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNS
RETSFITQGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQKSSLEEDFYFKTKIKLCILLHAFRIRAVTIDRVMSYLOAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 352)

>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

IWELKKDVYVVELDWPDPAGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVKKFGDAGQYTCHKGGEVLSH
SLLLLHKKEDGIWSTDILKDQEEPKNKTLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGSSDPQGVTCGAATLS
AERVGRDNKEYEYSVEQEDSACPAAEESLPIEVMDAVHKLKYENYTSSFFIRDIIKPDPPKNLQKPLKNSRQVE
VSWEYPTWSTPHSYFSLTFSVQVQGKSKREKEDRVFTDKTSATVICRKNASISVRAQDRYSSSWSEWASVPCS/G
GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVE
VHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFCSSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 383)

Figure 66Q

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

RNLPVATPDPGMFCLHHSQNLRLRAVS NMLQKARQTLEFYPTCTSEEIDHEDITKDKTSTVEACLPLELTKQESCLNS
RETSFITQGSCLASRKTSFMMALCLSS IYEDLKMYQVEFKTMNAKLMDPKRQIFLDQNMLAVIDELMQALNFNSET
VPQSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLQAS/GGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMI SRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 354)

Figure 67A

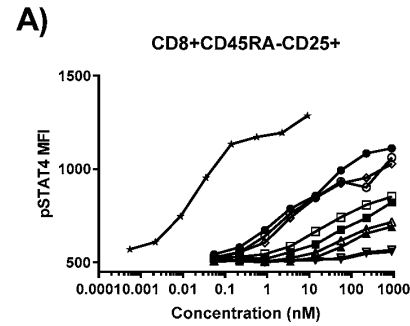


Figure 67B

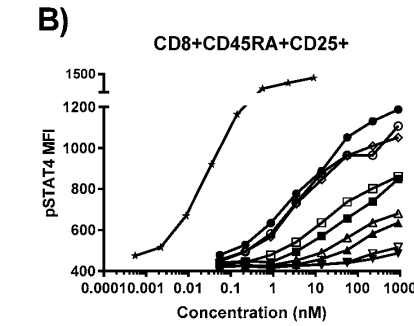


Figure 67C

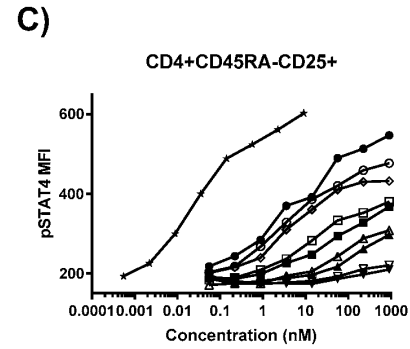


Figure 67C

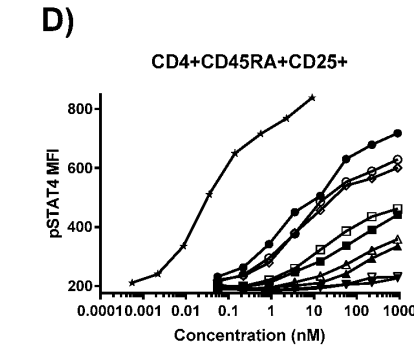


Figure 67D

