

P 09_068 sequence listing_ST25.txt
SEQUENCE LISTING

<110> Merck Serono S.A.

<120> Humanized antibodies against human IL-22RA

<130> P 09/068 WO/PCT

<150> EP 09176525.5

<151> 2009-11-19

<150> US 61/262,998

<151> 2009-11-20

<160> 34

<170> PatentIn version 3.5

<210> 1

<211> 5

<212> PRT

<213> Artificial

<220>

<223> H-CDR1

<400> 1

Ala Glu Tyr Met Asn
1 5

<210> 2

<211> 17

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<223> H-CDR2

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Glu Ile Asn Pro Ser Thr Gly Thr Thr Thr Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 3

<211> 7

<212> PRT

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<220>

<223> H-CDR3

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Phe Asp Ala Tyr Phe Asp Tyr
1 5

P 09_068 sequence listing_ST25.txt

<210> 4
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 <212> PRT
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<220>
 <223> L-CDR1

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Lys Ser Ser Gln Ser Leu Leu Tyr Ser Ser Asn Gln Lys Asn Thr Leu
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Ala

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 <223> L-CDR2

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Trp Ala Ser Ser Arg Glu Ser
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<210> 6
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 <223> L-CDR3

<400> 6

Gln Gln Tyr Tyr Ser Tyr Pro Phe Thr
 1 5

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 <223> Alternative L-CDR3

<400> 7

Gln Gln Tyr Phe Ser Tyr Pro Phe Thr
 1 5

<210> 8
 <211> 30

P 09_068 sequence listing_ST25.txt

<212> PRT
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<220>
<223> H-FR1

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Ser Ile Thr
20 25 30

<210> 9
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<220>
<223> H-FR2

<400> 9

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> 10
<211> 32
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<223> H-FR3

<400> 10

Arg Phe Thr Ile Ser Val Asp Gln Ser Lys Asn Thr Ala Tyr Leu Gln
1 5 10 15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20 25 30

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<212> PRT
<213> Artificial

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<223> H-FR4

<400> 11

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> 12

P 09_068 sequence listing_ST25.txt

<211> 23
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<220>
 <223> L-FR1

<400> 12

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Glu Arg Ala Thr Ile Asn Cys
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<210> 13
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<220>
 <223> L-FR2

<400> 13

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
 1 5 10 15

<210> 14
 <211> 32
 <212> PRT
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 <223> L-FR3

<400> 14

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 1 5 10 15

Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys
 20 25 30

<210> 15
 <211> 11
 <212> PRT
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<220>
 <223> L-FR4

<400> 15

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
 1 5 10

P 09_068 sequence listing_ST25.txt

<210> 16
<211> 116
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<213> Artificial

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<223> Final humanized VH (280.VH3-66-46)

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<223> H-CDR1 (i.e. SEQ ID NO: 1)

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<222> (50)..(66)
<223> H-CDR2 (i.e. SEQ ID NO: 2)

<220>
<221> BINDING
<222> (99)..(105)
<223> H-CDR3 (i.e. SEQ ID NO: 3)

<400> 16

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Ser Ile Thr Ala Glu
20 25 30

Tyr Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asn Pro Ser Thr Gly Thr Thr Thr Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Arg Phe Thr Ile Ser Val Asp Gln Ser Lys Asn Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Phe Asp Ala Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 17
<211> 114
<212> PRT
<213> Artificial

P 09_068 sequence listing_ST25.txt

<220>

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<220>

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<222> (24)..(40)

<223> L-CDR1 (i.e. SEQ ID NO: 4)

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<221> BINDING

<222> (56)..(62)

<223> L-CDR2 (i.e. SEQ ID NO: 5)

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<221> BINDING

<222> (95)..(103)

<223> L-CDR2 (i.e. SEQ ID NO: 6)

<400> 17

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser
20 25 30

Ser Asn Gln Lys Asn Thr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Ser Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln
85 90 95

Tyr Tyr Ser Tyr Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
100 105 110

Lys Arg

<210> 18

<211> 329

<212> PRT

<213> Artificial

<220>

<223> Heavy chain constant region of a particular 280.346.TSY

<400> 18

P 09_068 sequence listing_ST25.txt

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
115 120 125

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
130 135 140

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
145 150 155 160

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
165 170 175

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
180 185 190

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
195 200 205

Ala Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
210 215 220

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
225 230 235 240

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
245 250 255

P 09_068 sequence listing_ST25.txt

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
260 265 270

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
275 280 285

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
290 295 300

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
305 310 315 320

Lys Ser Leu Ser Leu Ser Pro Gly Lys
325

<210> 19
<211> 106
<212> PRT
<213> Artificial

<220>
<223> Light chain constant domain of a particular 280.346.TSY
<400> 19

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> 20
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P 09_068 sequence listing_ST25.txt

<220>

<223> Heavy chain of a particular 280.346.TSY

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<222> (1)..(116)

<223> Heavy chain variable domain (i.e. SEQ ID NO: 16)

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<221> MISC_FEATURE

<222> (117)..(445)

<223> Heavy chain constant region (i.e. SEQ ID NO: 18)

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Ser Ile Thr Ala Glu
20 25 30

Tyr Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asn Pro Ser Thr Gly Thr Thr Thr Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Arg Phe Thr Ile Ser Val Asp Gln Ser Lys Asn Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Phe Asp Ala Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

P 09_068 sequence listing_ST25.txt

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
195 200 205

Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
210 215 220

Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu
225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
325 330 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
340 345 350

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385 390 395 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
405 410 415

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

435

440

445

<210> 21
<211> 220
<212> PRT
<213> Artificial

<220>
<223> Light chain of a particular 280.346.TSY

<220>
<221> DOMAIN
<222> (1)..(114)
<223> Light chain variable domain (i.e. SEQ ID NO: 17)

<220>
<221> DOMAIN
<222> (115)..(220)
<223> Light chain constant domain (i.e. SEQ ID NO: 19)

<400> 21

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser
20 25 30

Ser Asn Gln Lys Asn Thr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Ser Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln
85 90 95

Tyr Tyr Ser Tyr Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
100 105 110

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
115 120 125

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
130 135 140

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
145 150 155 160

P 09_068 sequence listing_ST25.txt

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
165 170 175

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
180 185 190

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
195 200 205

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215 220

<210> 22
<211> 1335
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<213> Artificial

<220>
<223> cDNA encoding the heavy chain of a particular 280.346.TSY

<400> 22
gaggtgcagc tggctgagag cggcggaggg ctggtgcagc caggcggag cttgaggctg 60
tcctgcgccg ccagcggcta cagcatcacc gccgagtaca tgaactgggt gcggcaggcc 120
ccaggcaagg gcctggaatg gatcggcgag atcaaccca gcaccggcac caccacctac 180
aaccagaagt tcaagggcag gttcaccatc agcgtggacc agagcaagaa caccgcctac 240
ctgcagatga acagcctgag ggccgaggac accgccgtgt actactgcgc cagattcgac 300
gcctacttcg actactgggg acagggcacc ctggtgaccg tgagcagcgc tagcaccaag 360
ggccccagcg tgttccccct ggccccagc agcaagtcca caagcggagg aacagccgcc 420
ctgggctgcc tgggtgaagga ctacttcccc gagcccgtga cctgttcctg gaacagcgga 480
gccctgacct ccggcgtgca caccttcccc gccgtgctgc agagcagcgg cctgtacagc 540
ctgagcagcg tgggtgacagt gccaagcagc agcctgggaa cccagaccta catctgcaac 600
gtgaaccaca agcccagcaa caccaagggt gacaagagag tggagcccaa gagctgcgac 660
aagaccata cctgtccacc ctgcccagcc cccccagtgg ccggaccctc cgtgttcctg 720
ttcccccca agccaagga caccctgatg atcagcagga cccccgaggt gacctgcgtg 780
gtggtggacg tgagccacga ggaccagag gtgaagtca attggtatgt ggacggcgtg 840
gaggtgcaca acgccaagac caagcccaga gaggaacagt acaacagcac ctacagggtg 900
gtgtccgtgc tgaccgtgct gcaccaggac tggctgaacg gcaaggaata caagtgaag 960
gtctccaaca aggccctgcc ctccagcatc gagaaaacca tcagcaaggc caagggccag 1020
ccacgggagc cccaggtgta cactctgccc ccatctcggg aagaaatgac caagaaccag 1080
gtgtccctga cctgtctggt gaagggttt tacccagcg acatcgccgt ggagtgggag 1140

P 09_068 sequence listing_ST25.txt

agcaacggcc agcccgagaa caactacaag accaccccc ctgtgctgga cagcgacggc	1200
agcttcttcc tgtacagcaa gctgaccgtg gacaagtcca ggtggcagca gggcaacgtg	1260
ttcagctgca gcgtgatgca cgaggccctg cacaaccact acacacagaa gagcctgagc	1320
ctgtcccccg gcaag	1335

<210> 23
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 <212> DNA
 <213> Artificial

<220>
 <223> cDNA encoding the light chain of a particular 280.346.TSY

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atcaactgca agagcagcca gagcctgctg tattcctcca accagaagaa caccctggcc	120
tggtatcagc agaagcccgg ccagccccc aagctgctga tctactgggc cagcagccgg	180
gagagcggcg tgcccgacag gttcagcggc agcggctccg gcaccgactt caccctgacc	240
atcagcagcc tgcaggccga ggacgtggcc gtgtactact gccagcagta ctacagctac	300
cccttcacct tcggccaggg caccaaggtg gagatcaaga ggaccgtggc cgcccccagc	360
gtgttcattt tccccccag cgacgagcag ctgaagagcg gcaccgccag cgtggtgtgc	420
ctgctgaaca actttttacc ccgggaggcc aaggtgcagt ggaagggtgga caacgccctg	480
cagagcggca acagccagga aagcgtcacc gagcaggaca gcaaggactc cacctacagc	540
ctgagcagca ccctgaccct gagcaaggcc gactacgaga agcacaaggt gtacgcctgc	600
gaggtgaccc accagggcct gtccagcccc gtgaccaaga gcttcaacag gggcgagtgc	660

<210> 24
 <211> 574
 <212> PRT
 <213> Homo sapiens

<400> 24

Met Arg Thr Leu Leu Thr Ile Leu Thr Val Gly Ser Leu Ala Ala His	
1 5 10 15	

Ala Pro Glu Asp Pro Ser Asp Leu Leu Gln His Val Lys Phe Gln Ser	
20 25 30	

Ser Asn Phe Glu Asn Ile Leu Thr Trp Asp Ser Gly Pro Glu Gly Thr	
35 40 45	

Pro Asp Thr Val Tyr Ser Ile Glu Tyr Lys Thr Tyr Gly Glu Arg Asp	
50 55 60	

P 09_068 sequence listing_ST25.txt

Trp Val Ala Lys Lys Gly Cys Gln Arg Ile Thr Arg Lys Ser Cys Asn
65 70 75 80

Leu Thr Val Glu Thr Gly Asn Leu Thr Glu Leu Tyr Tyr Ala Arg Val
85 90 95

Thr Ala Val Ser Ala Gly Gly Arg Ser Ala Thr Lys Met Thr Asp Arg
100 105 110

Phe Ser Ser Leu Gln His Thr Thr Leu Lys Pro Pro Asp Val Thr Cys
115 120 125

Ile Ser Lys Val Arg Ser Ile Gln Met Ile Val His Pro Thr Pro Thr
130 135 140

Pro Ile Arg Ala Gly Asp Gly His Arg Leu Thr Leu Glu Asp Ile Phe
145 150 155 160

His Asp Leu Phe Tyr His Leu Glu Leu Gln Val Asn Arg Thr Tyr Gln
165 170 175

Met His Leu Gly Gly Lys Gln Arg Glu Tyr Glu Phe Phe Gly Leu Thr
180 185 190

Pro Asp Thr Glu Phe Leu Gly Thr Ile Met Ile Cys Val Pro Thr Trp
195 200 205

Ala Lys Glu Ser Ala Pro Tyr Met Cys Arg Val Lys Thr Leu Pro Asp
210 215 220

Arg Thr Trp Thr Tyr Ser Phe Ser Gly Ala Phe Leu Phe Ser Met Gly
225 230 235 240

Phe Leu Val Ala Val Leu Cys Tyr Leu Ser Tyr Arg Tyr Val Thr Lys
245 250 255

Pro Pro Ala Pro Pro Asn Ser Leu Asn Val Gln Arg Val Leu Thr Phe
260 265 270

Gln Pro Leu Arg Phe Ile Gln Glu His Val Leu Ile Pro Val Phe Asp
275 280 285

Leu Ser Gly Pro Ser Ser Leu Ala Gln Pro Val Gln Tyr Ser Gln Ile
290 295 300

Arg Val Ser Gly Pro Arg Glu Pro Ala Gly Ala Pro Gln Arg His Ser

P 09_068 sequence listing_ST25.txt

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305                               310                               315                               320
Leu Ser Glu Ile Thr Tyr Leu Gly Gln Pro Asp Ile Ser Ile Leu Gln
325                               330                               335
Pro Ser Asn Val Pro Pro Pro Gln Ile Leu Ser Pro Leu Ser Tyr Ala
340                               345                               350
Pro Asn Ala Ala Pro Glu Val Gly Pro Pro Ser Tyr Ala Pro Gln Val
355                               360                               365
Thr Pro Glu Ala Gln Phe Pro Phe Tyr Ala Pro Gln Ala Ile Ser Lys
370                               375                               380
Val Gln Pro Ser Ser Tyr Ala Pro Gln Ala Thr Pro Asp Ser Trp Pro
385                               390                               395                               400
Pro Ser Tyr Gly Val Cys Met Glu Gly Ser Gly Lys Asp Ser Pro Thr
405                               410                               415
Gly Thr Leu Ser Ser Pro Lys His Leu Arg Pro Lys Gly Gln Leu Gln
420                               425                               430
Lys Glu Pro Pro Ala Gly Ser Cys Met Leu Gly Gly Leu Ser Leu Gln
435                               440                               445
Glu Val Thr Ser Leu Ala Met Glu Glu Ser Gln Glu Ala Lys Ser Leu
450                               455                               460
His Gln Pro Leu Gly Ile Cys Thr Asp Arg Thr Ser Asp Pro Asn Val
465                               470                               475                               480
Leu His Ser Gly Glu Glu Gly Thr Pro Gln Tyr Leu Lys Gly Gln Leu
485                               490                               495
Pro Leu Leu Ser Ser Val Gln Ile Glu Gly His Pro Met Ser Leu Pro
500                               505                               510
Leu Gln Pro Pro Ser Arg Pro Cys Ser Pro Ser Asp Gln Gly Pro Ser
515                               520                               525
Pro Trp Gly Leu Leu Glu Ser Leu Val Cys Pro Lys Asp Glu Ala Lys
530                               535                               540
Ser Pro Ala Pro Glu Thr Ser Asp Leu Glu Gln Pro Thr Glu Leu Asp
545                               550                               555                               560

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P 09_068 sequence listing_ST25.txt

Ser Leu Phe Arg Gly Leu Ala Leu Thr Val Gln Trp Glu Ser
565 570

<210> 25
<211> 116
<212> PRT
<213> Mus musculus

<400> 25

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Arg Pro Gly Thr
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Leu Thr Ala Asp
20 25 30

Tyr Met Asn Trp Val Lys Gln Ser Pro Glu Glu Ser Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asn Pro Ser Thr Gly Thr Thr Thr Tyr Asn Gln Lys Phe
50 55 60

Glu Ala Lys Ala Thr Leu Thr Val Asp Gln Ser Ser Asn Thr Ala Tyr
65 70 75 80

Leu Gln Leu Thr Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Phe Asp Ala Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Thr Val
100 105 110

Thr Val Ser Ser
115

<210> 26
<211> 114
<212> PRT
<213> Mus musculus

<400> 26

Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ala Val Ser Val Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser
20 25 30

Ser Asn Gln Lys Asn Cys Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Ser Arg Glu Ser Gly Val
Page 16

50 P 09_068 sequence listing_ST25.txt 60
55

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Lys Thr Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln
85 90 95

Tyr Phe Ser Tyr Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile
100 105 110

Lys Arg

<210> 27
<211> 101
<212> PRT
<213> Artificial

<220>
<223> Immunoglobulin kappa variable 4-1 (IGKV4-1)

<400> 27

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser
20 25 30

Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln
85 90 95

Tyr Tyr Ser Thr Pro
100

<210> 28
<211> 97
<212> PRT
<213> Artificial

<220>

<223> Immunoglobulin heavy variable 3-66 (IGHV3-66)

<400> 28

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Asn
20 25 30

Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg

<210> 29

<211> 113

<212> PRT

<213> Artificial

<220>

<223> First version of humanized 280.46.3.4 VL (280.VK4-1-C)

<400> 29

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser
20 25 30

Ser Asn Gln Lys Asn Cys Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Ser Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln

85

90

95

Tyr Phe Ser Tyr Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
100 105 110

Lys

<210> 30
<211> 116
<212> PRT
<213> Artificial

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<223> First version of humanized 280.46.3.4 VH (280.VH3-66.1)
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Ser Leu Thr Ala Asp
20 25 30

Tyr Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asn Pro Ser Thr Gly Thr Thr Thr Tyr Asn Gln Lys Phe
50 55 60

Glu Ala Arg Ala Thr Leu Thr Val Asp Gln Ser Lys Asn Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Phe Asp Ala Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 31
<211> 113
<212> PRT
<213> Artificial

<220>
<223> Second version of humanized 280.46.3.4 VL (280.VK4-1-S)
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P 09_068 sequence listing_ST25.txt

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
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Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser
20 25 30

Ser Asn Gln Lys Asn Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Ser Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln
85 90 95

Tyr Phe Ser Tyr Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
100 105 110

Lys

<210> 32
<211> 113
<212> PRT
<213> Artificial

<220>
<223> Third version of humanized 280.46.3.4 VL (280.VK4-1-T)

<400> 32

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser
20 25 30

Ser Asn Gln Lys Asn Thr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Ser Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln

85

90

95

Tyr Phe Ser Tyr Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
100 105 110

Lys

<210> 33
<211> 116
<212> PRT
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<223> version 4 of the humanized 280.46.3.4 VH (280.VH3-66-4)
<400> 33

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Ser Leu Thr Ala Asp
20 25 30

Tyr Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asn Pro Ser Thr Gly Thr Thr Thr Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Ser Val Asp Gln Ser Lys Asn Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Phe Asp Ala Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 34
<211> 116
<212> PRT
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<220>
<223> version 18 of the humanized 280.46.3.4 VH (280.VH3-66-18)
<400> 34

P 09_068 sequence listing_ST25.txt

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Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Tyr	Ser	Leu	Thr	Ala	Glu
			20					25					30		
Tyr	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Ile
		35					40					45			
Gly	Glu	Ile	Asn	Pro	Ser	Thr	Gly	Thr	Thr	Thr	Tyr	Asn	Gln	Lys	Phe
	50					55					60				
Lys	Gly	Arg	Ala	Thr	Leu	Ser	Val	Asp	Gln	Ser	Lys	Asn	Thr	Ala	Tyr
65					70					75					80
Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90					95	
Ala	Arg	Phe	Asp	Ala	Tyr	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Leu	Val
			100					105					110		
Thr	Val	Ser	Ser												
		115													