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<110> Mitsubishi Tanabe Pharma Corporation

<120> A Therapeutic Agent for Endometriosis comprising IL-33 Antagonist

<130> P180453

<150> US 62/552,594
<151> 2017-08-31

<160> 16

<170> PatentIn version 3.5

<210> 1
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Gln Gln Lys Ala Lys Glu Val Cys Pro Met Tyr Phe Met Lys Leu Arg
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Ser Gly Leu Met Ile Lys Lys Glu Ala Cys Tyr Phe Arg Arg Glu Thr
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Thr Lys Arg Pro Ser Leu Lys Thr Gly Arg Lys His Lys Arg His Leu
65                  70                  75                  80

Val Leu Ala Ala Cys Gln Gln Gln Ser Thr Val Glu Cys Phe Ala Phe
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Gly Ile Ser Gly Val Gln Lys Tyr Thr Arg Ala Leu His Asp Ser Ser
            100                 105                 110
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Ile Thr Gly Ile Ser Pro Ile Thr Glu Tyr Leu Ala Ser Leu Ser Thr
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Tyr Asn Asp Gln Ser Ile Thr Phe Ala Leu Glu Asp Glu Ser Tyr Glu
130 135 140

Ile Tyr Val Glu Asp Leu Lys Lys Asp Glu Lys Lys Asp Lys Val Leu
145 150 155 160

Leu Ser Tyr Tyr Glu Ser Gln His Pro Ser Asn Glu Ser Gly Asp Gly
165 170 175

Val Asp Gly Lys Met Leu Met Val Thr Leu Ser Pro Thr Lys Asp Phe
180 185 190

Trp Leu His Ala Asn Asn Lys Glu His Ser Val Glu Leu His Lys Cys
195 200 205

Glu Lys Pro Leu Pro Asp Gln Ala Phe Phe Val Leu His Asn Met His
210 215 220

Ser Asn Cys Val Ser Phe Glu Cys Lys Thr Asp Pro Gly Val Phe Ile
225 230 235 240

Gly Val Lys Asp Asn His Leu Ala Leu Ile Lys Val Asp Ser Ser Glu
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Asn Leu Cys Thr Glu Asn Ile Leu Phe Lys Leu Ser Glu Thr
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caaagccuug uguuucaagc ugggaaaauc ccaacagaag gccaaagaag uuugccccau 180

guacuuuaug aagcuccgcu cuggccuuau gauaaaaaag gaggccuguu acuuuaggag 240

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gaaauauacu agagcacuuc augauucaag uaucacagga auuucaccua uuacagagua 420

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gaugccaaaa cguuuauucu gcuuugucug uuguagaauu uuagauaaag cuauuaaugg 2160

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gagaccuauu agauguaagu gcuaguagaa uauaagauaa aagaggcuga gaauuaccau 2460

acaaggguau uacaacugua aaacaauuua ucuuuguuuc auuguucugu caauaauugu 2520

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auuguuuaua uuauugaaua aaguauauuu uccaaaaaaa aaaaaaaaa 2689

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<212> PRT
<213> Homo sapiens

<400> 3

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Ile Val Arg Cys Pro Arg Gln Gly Lys Pro Ser Tyr Thr Val Asp Trp
35 40 45

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

Val Phe Ala Ser Gly Gln Leu Leu Lys Phe Leu Pro Ala Ala Val Ala
65 70 75 80

Asp Ser Gly Ile Tyr Thr Cys Ile Val Arg Ser Pro Thr Phe Asn Arg
85 90 95

Thr Gly Tyr Ala Asn Val Thr Ile Tyr Lys Lys Gln Ser Asp Cys Asn
100 105 110

Val Pro Asp Tyr Leu Met Tyr Ser Thr Val Ser Gly Ser Glu Lys Asn
115 120 125

Ser Lys Ile Tyr Cys Pro Thr Ile Asp Leu Tyr Asn Trp Thr Ala Pro
130 135 140

Leu Glu Trp Phe Lys Asn Cys Gln Ala Leu Gln Gly Ser Arg Tyr Arg
145 150 155 160

Ala His Lys Ser Phe Leu Val Ile Asp Asn Val Met Thr Glu Asp Ala
165 170 175

Gly Asp Tyr Thr Cys Lys Phe Ile His Asn Glu Asn Gly Ala Asn Tyr
180 185 190

Ser Val Thr Ala Thr Arg Ser Phe Thr Val Lys Asp Glu Gln Gly Phe
195 200 205

Ser Leu Phe Pro Val Ile Gly Ala Pro Ala Gln Asn Glu Ile Lys Glu
210 215 220

Val Glu Ile Gly Lys Asn Ala Asn Leu Thr Cys Ser Ala Cys Phe Gly
225 230 235 240

Lys Gly Thr Gln Phe Leu Ala Ala Val Leu Trp Gln Leu Asn Gly Thr
245 250 255

Lys Ile Thr Asp Phe Gly Glu Pro Arg Ile Gln Gln Glu Glu Gly Gln
260 265 270

Asn Gln Ser Phe Ser Asn Gly Leu Ala Cys Leu Asp Met Val Leu Arg
275 280 285

Ile Ala Asp Val Lys Glu Glu Asp Leu Leu Leu Gln Tyr Asp Cys Leu
290 295 300

Ala Leu Asn Leu His Gly Leu Arg Arg His Thr Val Arg Leu Ser Arg
305 310 315 320

Lys Asn Pro Ile Asp His His Ser Ile Tyr Cys Ile Ile Ala Val Cys
325 330 335

Ser Val Phe Leu Met Leu Ile Asn Val Leu Val Ile Ile Leu Lys Met
340 345 350

Phe Trp Ile Glu Ala Thr Leu Leu Trp Arg Asp Ile Ala Lys Pro Tyr
355 360 365

Lys Thr Arg Asn Asp Gly Lys Leu Tyr Asp Ala Tyr Val Val Tyr Pro
370 375 380

Arg Asn Tyr Lys Ser Ser Thr Asp Gly Ala Ser Arg Val Glu His Phe
385 390 395 400

Val His Gln Ile Leu Pro Asp Val Leu Glu Asn Lys Cys Gly Tyr Thr
405 410 415

Leu Cys Ile Tyr Gly Arg Asp Met Leu Pro Gly Glu Asp Val Val Thr
420 425 430

Ala Val Glu Thr Asn Ile Arg Lys Ser Arg Arg His Ile Phe Ile Leu
435 440 445

Thr Pro Gln Ile Thr His Asn Lys Glu Phe Ala Tyr Glu Gln Glu Val
450 455 460

Ala Leu His Cys Ala Leu Ile Gln Asn Asp Ala Lys Val Ile Leu Ile
465 470 475 480

Glu Met Glu Ala Leu Ser Glu Leu Asp Met Leu Gln Ala Glu Ala Leu
485 490 495

Gln Asp Ser Leu Gln His Leu Met Lys Val Gln Gly Thr Ile Lys Trp
500 505 510

Arg Glu Asp His Ile Ala Asn Lys Arg Ser Leu Asn Ser Lys Phe Trp
515 520 525

Lys His Val Arg Tyr Gln Met Pro Val Pro Ser Lys Ile Pro Arg Lys
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545 550 555

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caugggccu ggaaaaugag gcuuuaauug uaagaugucc uagacaagga aaaccuaguu 360

acaccgugga uugguauuac ucacaaacaa acaaaaguau ucccacucag gaaagaaauc 420

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cauuuuuggu cauugauaau gugaugacug aggacgcagg ugauuacacc uguaaauuua 780

uacacaauga aaauggagcc aauuauagug ugacggcgac cagguccuuc acggucaagg 840

augagcaagg cuuuucucug uuuccaguaa ucggagcccc ugcacaaaau gaaauaaagg 900

aaguggaaau uggaaaaaac gcaaaccuaa cuugcucugc uuguuuugga aaaggcacuc 960

aguucuuggc ugccguccug uggcagcuua auggaacaaa aauuacagac uuuggugaac 1020

caagaauuca acaagaggaa gggcaaaauc aaaguuucag caaugggcug gcuugucuag 1080

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guaaggagug uuucugagac uuugaucacc ugaacuuucu cuagcaagug uaagcagaau 1260

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agcuucucug cugcuuaaau uguucguccu cccccacucc cuccuaucgu ugguuugucu 1440

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uuggcucaca guucugcagg cuguauggga agcauggcgg caucugcuuc uggggacacc 1860

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ccaaucaccu cccaccaggc uccaccucga auacugggga uuaccauuca gcaugagauu 2100

ugggcaggaa cacagaccca aaccauacca cacacauuau cauuguuaaa cuuuguaaag 2160

uauuuaaggu acauggaaca cacgggaagu cugguagcuc agcccauuuc uuuauugcau 2220

cuguuauuca ccauguaauu cagguaccac guauuccagg gagccuuucu uggcccucag 2280

uuugcaguau acacacuuuc caaguacucu uguagcaucc uguuuguauc auagcacugg 2340

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Ser Gln Thr Asn Lys Ser Ile Pro Thr Gln Glu Arg Asn Arg Val Phe
35 40 45

Ala Ser Gly Gln Leu Leu Lys Phe Leu Pro Ala Ala Val Ala Asp Ser

50 55 60

Gly Ile Tyr Thr Cys Ile Val Arg Ser Pro Thr Phe Asn Arg Thr Gly
65 70 75 80

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

Asp Tyr Leu Met Tyr Ser Thr Val Ser Gly Ser Glu Lys Asn Ser Lys
100 105 110

Ile Tyr Cys Pro Thr Ile Asp Leu Tyr Asn Trp Thr Ala Pro Leu Glu
115 120 125

Trp Phe Lys Asn Cys Gln Ala Leu Gln Gly Ser Arg Tyr Arg Ala His
130 135 140

Lys Ser Phe Leu Val Ile Asp Asn Val Met Thr Glu Asp Ala Gly Asp
145 150 155 160

Tyr Thr Cys Lys Phe Ile His Asn Glu Asn Gly Ala Asn Tyr Ser Val
165 170 175

Thr Ala Thr Arg Ser Phe Thr Val Lys Asp Glu Gln Gly Phe Ser Leu
180 185 190

Phe Pro Val Ile Gly Ala Pro Ala Gln Asn Glu Ile Lys Glu Val Glu
195 200 205

Ile Gly Lys Asn Ala Asn Leu Thr Cys Ser Ala Cys Phe Gly Lys Gly
210 215 220

Thr Gln Phe Leu Ala Ala Val Leu Trp Gln Leu Asn Gly Thr Lys Ile
225 230 235 240

Thr Asp Phe Gly Glu Pro Arg Ile Gln Gln Glu Glu Gly Gln Asn Gln
245 250 255

Ser Phe Ser Asn Gly Leu Ala Cys Leu Asp Met Val Leu Arg Ile Ala
260 265 270

Asp Val Lys Glu Glu Asp Leu Leu Leu Gln Tyr Asp Cys Leu Ala Leu
275 280 285

Asn Leu His Gly Leu Arg Arg His Thr Val Arg Leu Ser Arg Lys Asn
290 295 300

Pro Ile Asp His His Ser Pro Lys Ser Cys Asp Lys Thr His Thr Cys
305 310 315 320

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
325 330 335

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
340 345 350

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
355 360 365

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
370 375 380

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
385 390 395 400

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
405 410 415

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
420 425 430

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
435 440 445

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys

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    450                 455                 460

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
465                 470                 475                 480

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
                485                 490                 495

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
            500                 505                 510

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
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His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    530                 535                 540
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            20                  25                  30

Thr Asn Glu Ser Ile Pro Thr Gln Lys Arg Asn Arg Ile Phe Val Ser
        35                  40                  45

Arg Asp Arg Leu Lys Phe Leu Pro Ala Arg Val Glu Asp Ser Gly Ile
    50                  55                  60

Tyr Ala Cys Val Ile Arg Ser Pro Asn Leu Asn Lys Thr Gly Tyr Leu
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65 70 75 80

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

Leu Met Tyr Ser Thr Val Arg Gly Ser Asp Lys Asn Phe Lys Ile Thr
100 105 110

Cys Pro Thr Ile Asp Leu Tyr Asn Trp Thr Ala Pro Val Gln Trp Phe
115 120 125

Lys Asn Cys Lys Ala Leu Gln Glu Pro Arg Phe Arg Ala His Arg Ser
130 135 140

Tyr Leu Phe Ile Asp Asn Val Thr His Asp Asp Glu Gly Asp Tyr Thr
145 150 155 160

Cys Gln Phe Thr His Ala Glu Asn Gly Thr Asn Tyr Ile Val Thr Ala
165 170 175

Thr Arg Ser Phe Thr Val Glu Glu Lys Gly Phe Ser Met Phe Pro Val
180 185 190

Ile Thr Asn Pro Pro Tyr Asn His Thr Met Glu Val Glu Ile Gly Lys
195 200 205

Pro Ala Ser Ile Ala Cys Ser Ala Cys Phe Gly Lys Gly Ser His Phe
210 215 220

Leu Ala Asp Val Leu Trp Gln Ile Asn Lys Thr Val Val Gly Asn Phe
225 230 235 240

Gly Glu Ala Arg Ile Gln Glu Glu Glu Gly Arg Asn Glu Ser Ser Ser
245 250 255

Asn Asp Met Asp Cys Leu Thr Ser Val Leu Arg Ile Thr Gly Val Thr
260 265 270

Glu Lys Asp Leu Ser Leu Glu Tyr Asp Cys Leu Ala Leu Asn Leu His
275 280 285

Gly Met Ile Arg His Thr Ile Arg Leu Arg Arg Lys Gln Pro Ile Asp
290 295 300

His Arg Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
305 310 315 320

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
325 330 335

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
340 345 350

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
355 360 365

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
370 375 380

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
385 390 395 400

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
405 410 415

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
420 425 430

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
435 440 445

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
450 455 460

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn

465 470 475 480

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
485 490 495

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
500 505 510

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
515 520 525

Lys Ser Leu Ser Leu Ser Pro Gly Lys
530 535

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<211> 234
<212> PRT
<213> Artificial Sequence

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Ser Trp Ala Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr
20 25 30

Pro Gly Gln Arg Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile
35 40 45

Gly Ala Val Tyr Asp Val His Trp Tyr Gln Gln Leu Pro Gly Thr Ala
50 55 60

Pro Lys Leu Leu Ile Tyr Arg Asn Asn Gln Arg Pro Ser Gly Val Pro
65 70 75 80

Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile

85 90 95

Ser Gly Leu Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Thr Tyr
100 105 110

Asp Ser Ser Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
115 120 125

Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser
130 135 140

Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp
145 150 155 160

Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro
165 170 175

Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn
180 185 190

Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys
195 200 205

Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val
210 215 220

Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
225 230

<210> 8
<211> 465
<212> PRT
<213> Artificial Sequence

<220>
<223> Heavy Chain of Antibody

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Met Glu Phe Gly Leu Ser Trp Leu Phe Leu Val Ala Ile Leu Lys Gly

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20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Asp Tyr Tyr Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ser Ser Ile Ser Arg Tyr Ser Ser Tyr Ile Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Asp Ile Gly Gly Met Asp Val Trp Gly Gln Gly
115 120 125

Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
130 135 140

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
145 150 155 160

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
165 170 175

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
180 185 190

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
195 200 205

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
210 215 220

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
225 230 235 240

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
245 250 255

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
260 265 270

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
275 280 285

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
290 295 300

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
305 310 315 320

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
325 330 335

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
340 345 350

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
355 360 365

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
370 375 380

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
385 390 395 400

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu

405 410 415

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
420 425 430

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
435 440 445

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
450 455 460

Lys
465

<210> 9
<211> 235
<212> PRT
<213> Artificial Sequence

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<223> Light Chain of Antibody

<400> 9

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Ser Trp Ala Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr
20 25 30

Pro Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile
35 40 45

Gly Asn Asn Ala Val Ser Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro
50 55 60

Lys Leu Leu Ile Tyr Ala Ser Asn Met Arg Val Ile Gly Val Pro Asp
65 70 75 80

Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser

20

85 90 95

Gly Leu Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Gly Ala Trp Asp
100 105 110

Asp Ser Gln Lys Ala Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val
115 120 125

Leu Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser
130 135 140

Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser
145 150 155 160

Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser
165 170 175

Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn
180 185 190

Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp
195 200 205

Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr
210 215 220

Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
225 230 235

<210> 10
<211> 468
<212> PRT
<213> Artificial Sequence

<220>
<223> Heavy Chain of Antibody

<400> 10

Met Glu Phe Gly Leu Ser Trp Leu Phe Leu Val Ala Ile Leu Lys Gly

1 5 10 15

Val Gln Cys Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Asn Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ser Ser Ile Ser Ala Arg Ser Arg Tyr His Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Leu Ala Thr Arg His Asn Ala Phe Asp Ile Trp
115 120 125

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
130 135 140

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
145 150 155 160

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
165 170 175

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
180 185 190

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
195 200 205

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
210 215 220

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
225 230 235 240

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
245 250 255

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
260 265 270

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
275 280 285

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
290 295 300

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
305 310 315 320

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
325 330 335

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
340 345 350

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
355 360 365

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
370 375 380

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
385 390 395 400

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro

405 410 415

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
420 425 430

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
435 440 445

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
450 455 460

Ser Pro Gly Lys
465

<210> 11
<211> 235
<212> PRT
<213> Artificial Sequence

<220>
<223> Light Chain of Antibody

<400> 11

Met Ala Gly Phe Pro Leu Leu Leu Thr Leu Leu Thr His Cys Ala Gly
1 5 10 15

Ser Trp Ala Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr
20 25 30

Pro Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile
35 40 45

Gly Arg Asn Ala Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro
50 55 60

Lys Leu Leu Ile Tyr Ala Ser Asn Met Arg Val Ser Gly Val Pro Asp
65 70 75 80

Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser

85 90 95

Gly Leu Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Trp Ala Trp Asp
100 105 110

Asp Ser Gln Lys Val Gly Val Phe Gly Gly Gly Thr Lys Leu Thr Val
115 120 125

Leu Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser
130 135 140

Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser
145 150 155 160

Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser
165 170 175

Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn
180 185 190

Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp
195 200 205

Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr
210 215 220

Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
225 230 235

<210> 12
<211> 468
<212> PRT
<213> Artificial Sequence

<220>
<223> Heavy Chain of Antibody

<400> 12

Met Glu Phe Gly Leu Ser Trp Leu Phe Leu Val Ala Ile Leu Lys Gly

25

1 5 10 15

Val Gln Cys Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Asn Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ser Ser Ile Ser Ala Arg Ser Ser Tyr Ile Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Leu Ala Thr Arg Asn Asn Ala Phe Asp Ile Trp
115 120 125

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
130 135 140

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
145 150 155 160

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
165 170 175

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
180 185 190

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
195 200 205

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
210 215 220

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
225 230 235 240

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
245 250 255

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
260 265 270

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
275 280 285

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
290 295 300

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
305 310 315 320

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
325 330 335

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
340 345 350

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
355 360 365

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
370 375 380

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
385 390 395 400

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro

405 410 415

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
420 425 430

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
435 440 445

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
450 455 460

Ser Pro Gly Lys
465

<210> 13
<211> 235
<212> PRT
<213> Artificial Sequence

<220>
<223> Light Chain of Antibody

<400> 13

Met Ala Gly Phe Pro Leu Leu Leu Thr Leu Leu Thr His Cys Ala Gly
1 5 10 15

Ser Trp Ala Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr
20 25 30

Pro Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile
35 40 45

Gly Arg Asn Ala Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro
50 55 60

Lys Leu Leu Ile Tyr Ala Ser Asn Met Arg Arg Ser Gly Val Pro Asp
65 70 75 80

Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser

85 90 95

Gly Leu Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ala Trp Asp
100 105 110

Asp Ser Gln Lys Val Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val
115 120 125

Leu Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser
130 135 140

Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser
145 150 155 160

Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser
165 170 175

Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn
180 185 190

Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp
195 200 205

Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr
210 215 220

Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
225 230 235

<210> 14
<211> 468
<212> PRT
<213> Artificial Sequence

<220>
<223> Heavy Chain of Antibody

<400> 14

Met Glu Phe Gly Leu Ser Trp Leu Phe Leu Val Ala Ile Leu Lys Gly

1 5 10 15

Val Gln Cys Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Arg Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ser Ser Ile Ser Ala Gln Ser Ser His Ile Tyr Tyr Ala
65 70 75 80

Asp Ser Val Glu Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Leu Ala Thr Arg Gln Asn Ala Phe Asp Ile Trp
115 120 125

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
130 135 140

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
145 150 155 160

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
165 170 175

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
180 185 190

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
195 200 205

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
210 215 220

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
225 230 235 240

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
245 250 255

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
260 265 270

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
275 280 285

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
290 295 300

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
305 310 315 320

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
325 330 335

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
340 345 350

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
355 360 365

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
370 375 380

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
385 390 395 400

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro

405 410 415

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
420 425 430

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
435 440 445

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
450 455 460

Ser Pro Gly Lys
465

<210> 15
<211> 235
<212> PRT
<213> Artificial Sequence

<220>
<223> Light Chain of Antibody

<400> 15

Met Ala Gly Phe Pro Leu Leu Leu Thr Leu Leu Thr His Cys Ala Gly
1 5 10 15

Ser Trp Ala Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr
20 25 30

Pro Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile
35 40 45

Gly Asn Asn Ala Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro
50 55 60

Lys Leu Leu Ile Tyr Ala Ser Asn Met Arg Arg Pro Gly Val Pro Asp
65 70 75 80

Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser

85 90 95

Gly Leu Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Glu Ala Trp Asp
100 105 110

Asp Ser Gln Lys Ala Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val
115 120 125

Leu Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser
130 135 140

Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser
145 150 155 160

Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser
165 170 175

Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn
180 185 190

Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp
195 200 205

Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr
210 215 220

Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
225 230 235

<210> 16
<211> 468
<212> PRT
<213> Artificial Sequence

<220>
<223> Heavy Chain of Antibody

<400> 16

Met Glu Phe Gly Leu Ser Trp Leu Phe Leu Val Ala Ile Leu Lys Gly

1 5 10 15

Val Gln Cys Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Asn Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ser Ser Ile Ser Ala Arg Ser Ser Tyr Leu Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Leu Ala Thr Arg His Val Ala Phe Asp Ile Trp
115 120 125

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
130 135 140

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
145 150 155 160

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
165 170 175

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
180 185 190

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
195 200 205

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
210 215 220

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
225 230 235 240

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
245 250 255

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
260 265 270

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
275 280 285

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
290 295 300

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
305 310 315 320

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
325 330 335

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
340 345 350

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
355 360 365

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
370 375 380

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
385 390 395 400

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro

405 410 415

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
420 425 430

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
435 440 445

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
450 455 460

Ser Pro Gly Lys
465