SEQUENCE LISTING

<110> Macrogenics, Inc.
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Lechleider, Robert Joseph
Koenig, Scott
Bonvini, Ezio

<120> Combination Therapy for the Treatment of Cancer

<130> 1301.0120PCT

<150> US 62/175,039
<151> 2015-06-12

<150> US 62/211,109
<151> 2015-08-28

<160> 87

<170> PatentIn version 3.5

<210> 1
<211> 645
<212> DNA
<213> Artificial Sequence

<220>
<223> Polynucleotide Encoding light chain of preferred Variant Chimeric 4D5 Antibodies

<400> 1
gacatcgtga tgacccagtc ccacaagttc atgtccacct ctgtgggcga tagggtcagc 60

atcacctgca aggccagcca ggatgtgaat actgctgtag cctggtatca gcagaaacca 120

ggacattctc ccaaactgct gatttactcc gcatccttcc ggtacactgg agtccctgat 180

cgcttcactg gcagcagatc tgggacagat ttcactttca ccatcagcag tgtgcaggct 240

gaagacctgg cagtttatta ctgtcagcaa cattatacta cacctcccac cttcggaggg 300

ggtaccaagg tggagatcaa acgtacggtg gctgcaccat ctgtcttcat cttcccgcca 360

tctgatgagc agttgaaatc tggaactgcc tctgttgtgt gcctgctgaa taacttctat 420

cccagagagg ccaaagtaca gtggaaggtg gataacgccc tccaatcggg taactcccag 480

gagagtgtca cagagcagga cagcaaggac agcacctaca gcctcagcag caccctgacg 540

ctgagcaaag cagactacga gaaacacaaa gtctacgcct gcgaagtcac ccatcagggc 600

ctgagctcgc ccgtcacaaa gagcttcaac aggggagagt gttag 645

<210> 2
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> light chain of preferred Variant Chimeric 4D5 Antibodies

<400> 2

Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly His Ser Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Phe Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

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

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

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

```
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

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

Phe Asn Arg Gly Glu Cys
    210
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<210> 3
<211> 107
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(107)
<223> Light Chain Variable Domain of Murine 4D5 Antibody

<400> 3

```
Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
1               5                   10                  15

Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala
            20                  25                  30

Val Ala Trp Tyr Gln Gln Lys Pro Gly His Ser Pro Lys Leu Leu Ile
```

35 40 45

Tyr Ser Ala Ser Phe Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

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

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

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 4
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Chimeric 4D5 VL region

<400> 4

Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly His Ser Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Phe Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

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

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

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 5
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Light Chain Variable Domain of Humanized 4D5 Antibody

<400> 5

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

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Phe Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro Pro
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 6

<211> 1353
<212> DNA
<213> Artificial Sequence

<220>
<223> Polynucleotide Encoding Chimeric 4D5 heavy chain having a wild-type Fc Region

<400> 6
caggttcagc tgcagcagtc tggccctgag ctggtgaagc caggggcctc actcaagttg 60

tcctgtacag cttctggctt caacatcaaa gacacctata tccactgggt gaaacagagg 120

cctgaacagg gcctggaatg gattggaagg atttatccta ccaatggcta tactagatat 180

gacccaaagt tccaggacaa ggccactatc acagcagaca catcctccaa cacagcctac 240

ctgcaagtca gccgcctgac atctgaggac actgccgtct attactgctc ccggtgggga 300

ggggacggct tctatgctat ggactactgg ggtcagggag cctccgtgac cgtgagctcc 360

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 420

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 480

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 540

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 600

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagag agttgagccc 660

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 720

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggaccccct 780

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 840

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacaac 900

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 960

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 1020

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggatgag 1080

ctgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 1140

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 1200

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 1260

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 1320

cagaagagcc tctccctgtc tccgggtaaa tga 1353

<210> 7
<211> 450
<212> PRT
<213> Artificial Sequence

<220>
<223> Chimeric 4D5 heavy chain having a wild-type Fc Region

<400> 7

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

Ser Leu Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
20 25 30

Tyr Ile His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
35 40 45

Gly Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Asp Pro Lys Phe
50 55 60

Gln Asp Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
65 70 75 80

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

Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

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

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

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

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

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

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

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

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225                 230                 235                 240

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

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

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

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320
```

```
Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
                325                 330                 335

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

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

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

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly Lys
    450
```

<210> 8
<211> 1353
<212> DNA
<213> Artificial Sequence

<220>
<223> Polynucleotide Encoding heavy chain of a Variant Chimeric 4D5 Antibody having the FcMT1 variant Fc Region

<400> 8

caggttcagc tgcagcagtc tggccctgag ctggtgaagc caggggcctc actcaagttg 60

tcctgtacag cttctggctt caacatcaaa gacacctata tccactgggt gaaacagagg 120

cctgaacagg gcctggaatg gattggaagg atttatccta ccaatggcta tactagatat 180

gacccaaagt tccaggacaa ggccactatc acagcagaca catcctccaa cacagcctac 240

ctgcaagtca gccgcctgac atctgaggac actgccgtct attactgctc ccggtgggga 300

ggggacggct tctatgctat ggactactgg ggtcagggag cctccgtgac cgtgagctcc 360

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 420

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 480

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 540

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 600

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagag agttgagccc 660

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 720

ccgtcagtct tcctcttacc cccaaaaccc aaggacaccc tcatgatctc ccggaccccct 780

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 840

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgccggagga gcagtacaac 900

agcacgctcc gtgtggtcag catcctcacc gtcctgcacc aggactggct gaatggcaag 960

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 1020

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggatgag 1080

ctgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 1140

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctctcgtg 1200

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 1260

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 1320

cagaagagcc tctccctgtc tccgggtaaa tga 1353

<210> 9

<211> 450
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain of a Variant Chimeric 4D5 Antibody having the FcMT1 variant Fc Region

<400> 9

```
Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1               5                   10                  15


Ser Leu Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
            20                  25                  30


Tyr Ile His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
        35                  40                  45


Gly Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Asp Pro Lys Phe
    50                  55                  60


Gln Asp Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
65                  70                  75                  80


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


Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln
            100                 105                 110


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


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


Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160
```

```
Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

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

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

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

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225                 230                 235                 240

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

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

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

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

Val Val Ser Ile Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

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

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

```
Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

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

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly Lys
    450
```

<210> 10
<211> 1353
<212> DNA
<213> Artificial Sequence

<220>
<223> Polynucleotide Encoding heavy chain of a Variant Chimeric 4D5 Antibody having the FcMT2 variant Fc Region

<400> 10

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caggttcagc tgcagcagtc tggccctgag ctggtgaagc caggggcctc actcaagttg       60

tcctgtacag cttctggctt caacatcaaa gacacctata tccactgggt gaaacagagg      120

cctgaacagg gcctggaatg gattggaagg atttatccta ccaatggcta tactagatat      180

gacccaaagt tccaggacaa ggccactatc acagcagaca catcctccaa cacagcctac      240
```

ctgcaagtca gccgcctgac atctgaggac actgccgtct attactgctc ccggtgggga 300

ggggacggct tctatgctat ggactactgg ggtcagggag cctccgtgac cgtgagctcc 360

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 420

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 480

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 540

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 600

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagag agttgagccc 660

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cgtgggggga 720

ccgtcagtct tcctcttacc cccaaaaccc aaggacaccc tcatgatctc ccggaccccct 780

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 840

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgccggagga gcagtacaac 900

agcacgctcc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 960

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 1020

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggatgag 1080

ctgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 1140

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctctcgtg 1200

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 1260

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 1320

cagaagagcc tctccctgtc tccgggtaaa tga 1353

<210> 11
<211> 450
<212> PRT
<213> Artificial Sequence

<220>
<223> heavy chain of a Variant Chimeric 4D5 Antibody having the FcMT2 variant Fc Region

<400> 11

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

Ser Leu Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
            20                  25                  30

Tyr Ile His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Asp Pro Lys Phe
    50                  55                  60

Gln Asp Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
65                  70                  75                  80

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

Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln
            100                 105                 110

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

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

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

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

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

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

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

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Val Gly Gly
225                 230                 235                 240

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

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

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

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

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

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

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

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380
```

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


Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415


Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430


Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445


Gly Lys
    450
```

<210> 12
<211> 1353
<212> DNA
<213> Artificial Sequence

<220>
<223> Polynucleotide Encoding Variant Chimeric 4D5 Antibody having the FcMT3 variant Fc Region

<400> 12
caggttcagc tgcagcagtc tggccctgag ctggtgaagc caggggcctc actcaagttg 60

tcctgtacag cttctggctt caacatcaaa gacacctata tccactgggt gaaacagagg 120

cctgaacagg gcctggaatg gattggaagg atttatccta ccaatggcta tactagatat 180

gacccaaagt tccaggacaa ggccactatc acagcagaca catcctccaa cacagcctac 240

ctgcaagtca gccgcctgac atctgaggac actgccgtct attactgctc ccggtgggga 300

ggggacggct tctatgctat ggactactgg ggtcagggag cctccgtgac cgtgagctcc 360

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 420

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 480

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 540

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 600

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagag agttgagccc 660

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 720

ccgtcagtct tcctcttacc cccaaaaccc aaggacaccc tcatgatctc ccggaccct 780

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 840

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgccggagga gcagtacaac 900

agcacgctcc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 960

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 1020

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggatgag 1080

ctgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 1140

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 1200

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 1260

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 1320

cagaagagcc tctccctgtc tccgggtaaa tga 1353

<210> 13
<211> 450
<212> PRT
<213> Artificial Sequence

<220>
<223> Variant Chimeric 4D5 Antibody having the FcMT3 variant Fc Region

<220>
<221> MISC_FEATURE
<222> (1)..(450)
<223> Variant Chimeric 4D5 Antibody having the FcMT3 variant Fc Region

<400> 13

Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala

```
1               5                  10                  15

Ser Leu Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
            20                  25                  30

Tyr Ile His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Asp Pro Lys Phe
    50                  55                  60

Gln Asp Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
65                  70                  75                  80

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

Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln
            100                 105                 110

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

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

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

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

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

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
```

195 200 205

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

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

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

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

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

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

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

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

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

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

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

385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 14
<211> 288
<212> PRT
<213> Homo sapiens

<220>
<221> MISC_FEATURE
<222> (1)..(288)
<223> Human PD-1

<400> 14

Met Gln Ile Pro Gln Ala Pro Trp Pro Val Val Trp Ala Val Leu Gln
1 5 10 15

Leu Gly Trp Arg Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp
20 25 30

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

Asn Ala Thr Phe Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val
50 55 60

```
Leu Asn Trp Tyr Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala
65                  70                  75                  80

Ala Phe Pro Glu Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg
                85                  90                  95

Val Thr Gln Leu Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg
            100                 105                 110

Ala Arg Arg Asn Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu
        115                 120                 125

Ala Pro Lys Ala Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val
    130                 135                 140

Thr Glu Arg Arg Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro
145                 150                 155                 160

Arg Pro Ala Gly Gln Phe Gln Thr Leu Val Val Gly Val Val Gly Gly
                165                 170                 175

Leu Leu Gly Ser Leu Val Leu Leu Val Trp Val Leu Ala Val Ile Cys
            180                 185                 190

Ser Arg Ala Ala Arg Gly Thr Ile Gly Ala Arg Arg Thr Gly Gln Pro
        195                 200                 205

Leu Lys Glu Asp Pro Ser Ala Val Pro Val Phe Ser Val Asp Tyr Gly
    210                 215                 220

Glu Leu Asp Phe Gln Trp Arg Glu Lys Thr Pro Glu Pro Pro Val Pro
225                 230                 235                 240

Cys Val Pro Glu Gln Thr Glu Tyr Ala Thr Ile Val Phe Pro Ser Gly
                245                 250                 255
```

Met Gly Thr Ser Ser Pro Ala Arg Arg Gly Ser Ala Asp Gly Pro Arg
260 265 270

Ser Ala Gln Pro Leu Arg Pro Glu Asp Gly His Cys Ser Trp Pro Leu
275 280 285

<210> 15
<211> 113
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(113)
<223> heavy chain variable domain of PD-1 mAb 1

<400> 15

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

Ser Leu Arg Leu Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser Asn Ser
20 25 30

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

Ala Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val
50 55 60

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

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

Ala Thr Asn Asp Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
100 105 110

Ser

<210> 16
<211> 5
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(5)
<223> CDRH1 of PD-1 mAb 1

<400> 16

Asn Ser Gly Met His
1 5

<210> 17
<211> 17
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(17)
<223> CDRH2 of PD-1 mAb 1

<400> 17

Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 18
<211> 4
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(4)
<223> CDRH3 of PD-1 mAb 1

<400> 18

Asn Asp Asp Tyr
1

<210> 19
<211> 107
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(107)
<223> light chain variable domain of PD-1 mAb 1

<400> 19

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

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

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65   70   75   80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Ser Asn Trp Pro Arg
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 20
<211> 11
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(11)
<223> CDRL1 of PD-1 mAb 1

<400> 20

Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
1 5 10

<210> 21
<211> 7
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(7)
<223> CDRL2 of PD-1 mAb 1

<400> 21

Asp Ala Ser Asn Arg Ala Thr
1 5

<210> 22
<211> 9
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(9)

<223> CDRL3 of PD-1 mAb 1

<400> 22

Gln Gln Ser Ser Asn Trp Pro Arg Thr
1 5

<210> 23
<211> 120
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(120)
<223> heavy chain variable domain of PD-1 mAb 2

<400> 23

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

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

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

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

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

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

Ala Arg Arg Asp Tyr Arg Phe Asp Met Gly Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 24
<211> 5
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(5)
<223> heavy chain variable domain of PD-1 mAb 2 CDR1

<400> 24

Asn Tyr Tyr Met Tyr
1 5

<210> 25
<211> 17
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(17)
<223> heavy chain variable domain of PD-1 mAb 2 CDR2

<400> 25

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

Asn

<210> 26
<211> 11
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(11)
<223> heavy chain variable domain of PD-1 mAb 2 CDR3

<400> 26

Arg Asp Tyr Arg Phe Asp Met Gly Phe Asp Tyr
1 5 10

<210> 27
<211> 111
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(111)
<223> light chain variable domain of PD-1 mAb 2

<400> 27

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

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Gly Val Ser Thr Ser
20 25 30

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

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

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

Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Ser Arg
85 90 95

Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 28
<211> 15
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(15)
<223> light chain variable domain of PD-1 mAb 2 CDR1

<400> 28

Arg Ala Ser Lys Gly Val Ser Thr Ser Gly Tyr Ser Tyr Leu His
1 5 10 15

<210> 29
<211> 7
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(7)
<223> light chain variable domain of PD-1 mAb 2 CDR2

<400> 29

Leu Ala Ser Tyr Leu Glu Ser
1 5

<210> 30
<211> 9
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(9)

<223> light chain variable domain of PD-1 mAb 2 CDR3

<400> 30

Gln His Ser Arg Asp Leu Pro Leu Thr
1 5

<210> 31
<211> 121
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(121)
<223> heavy chain variable domain of PD-1 mAb 3

<400> 31

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

Ser Val Gln Met Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Ser Ser
20 25 30

Trp Ile His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

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

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

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

Ala Arg Trp Arg Asp Ser Ser Gly Tyr His Ala Met Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Ser Val Thr Val Ser Ser
        115   120

<210> 32
<211> 5
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(5)
<223> heavy chain variable domain of PD-1 mAb 3 CDR1

<400> 32

Ser Ser Trp Ile His
1   5

<210> 33
<211> 17
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(17)
<223> heavy chain variable domain of PD-1 mAb 3 CDR2

<400> 33

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

Asp

<210> 34
<211> 13
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(13)
<223> heavy chain variable domain of PD-1 mAb 3 CDR3

<400> 34

Arg Trp Arg Asp Ser Ser Gly Tyr His Ala Met Asp Tyr
1 5 10

<210> 35
<211> 111
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(111)
<223> light chain variable domain of PD-1 mAb 3

<400> 35

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

Gln Arg Ala Thr Ile Ser Cys Arg Ala Ser Gln Ser Val Ser Thr Ser
20 25 30

Gly Tyr Ser Tyr Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Lys Phe Gly Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

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

Pro Val Glu Glu Glu Asp Thr Ala Thr Tyr Tyr Cys Gln His Ser Trp
85 90 95

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

<210> 36
<211> 15
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(15)
<223> light chain variable domain of PD-1 mAb 3 CDR1

<400> 36

Arg Ala Ser Gln Ser Val Ser Thr Ser Gly Tyr Ser Tyr Met His
1 5 10 15

<210> 37
<211> 7
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(7)
<223> light chain variable domain of PD-1 mAb 3 CDR2

<400> 37

Phe Gly Ser Asn Leu Glu Ser
1 5

<210> 38
<211> 9
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(9)

<223> light chain variable domain of PD-1 mAb 3 CDR3

<400> 38

Gln His Ser Trp Glu Ile Pro Tyr Thr
1 5

<210> 39
<211> 117
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(117)
<223> heavy chain variable domain of PD-1 mAb 4

<400> 39

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

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

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Gln Trp Met
35 40 45

Gly Trp Ile Asn Thr Asp Ser Gly Glu Ser Thr Tyr Ala Glu Glu Phe
50 55 60

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

Leu Gln Ile Thr Ser Leu Thr Ala Glu Asp Thr Gly Met Tyr Phe Cys
85 90 95

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

Val Thr Val Ser Ser
        115

<210> 40
<211> 5
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(5)
<223> heavy chain variable domain of PD-1 mAb 4 CDR1

<400> 40

Asn Tyr Gly Met Asn
1   5

<210> 41
<211> 16
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(16)
<223> heavy chain variable domain of PD-1 mAb 4 CDR2

<400> 41

Trp Ile Asn Thr Asp Ser Gly Glu Ser Thr Tyr Ala Glu Glu Phe Lys
1   5   10   15

<210> 42
<211> 8
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(8)

<223> heavy chain variable domain of PD-1 mAb 4 CDR3

<400> 42

Val Gly Tyr Asp Ala Leu Asp Tyr
1 5

<210> 43
<211> 106
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(106)
<223> light chain variable domain of PD-1 mAb 4

<400> 43

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

Asp Arg Val Thr Ile Thr Cys Ser Ala Arg Ser Ser Val Ser Tyr Met
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp Ile Tyr
35 40 45

Arg Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Cys Leu Thr Ile Asn Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Ser Phe Pro Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 44
<211> 10
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(10)
<223> light chain variable domain of PD-1 mAb 4 CDR1

<400> 44

Ser Ala Arg Ser Ser Val Ser Tyr Met His
1 5 10

<210> 45
<211> 7
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(7)
<223> light chain variable domain of PD-1 mAb 4 CDR2

<400> 45

Arg Thr Ser Asn Leu Ala Ser
1 5

<210> 46
<211> 9
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(9)
<223> light chain variable domain of PD-1 mAb 4 CDR3

<400> 46

Gln Gln Arg Ser Ser Phe Pro Leu Thr
1 5

<210> 47
<211> 120
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(120)
<223> Heavy Chain Variable Domain of Murine 4D5 Antibody

<400> 47

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

Ser Leu Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
20 25 30

Tyr Ile His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
35 40 45

Gly Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Asp Pro Lys Phe
50 55 60

Gln Asp Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
65 70 75 80

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

Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Ala Ser Val Thr Val Ser Ser
115 120

<210> 48
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> Heavy Chain Variable Domain of Humanized 4D5 Antibody

<400> 48

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 Asn Ile Lys Asp Thr
20 25 30

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

Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr 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

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

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 49
<211> 217
<212> PRT
<213> Homo sapiens

<220>
<221> MISC_FEATURE
<222> (1)..(217)
<223> IgG1 Fc Region

<220>
<221> MISC_FEATURE
<222> (217)..(217)
<223> wherein, X is a lysine (K) or is absent

<400> 49

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


Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
            20                  25                  30


Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
        35                  40                  45


Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    50                  55                  60


Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65                  70                  75                  80


Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                85                  90                  95


Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
            100                 105                 110


Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
        115                 120                 125


Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    130                 135                 140
```

```
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
145                 150                 155                 160


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


Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
            180                 185                 190


Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
        195                 200                 205


Lys Ser Leu Ser Leu Ser Pro Gly Xaa
    210                 215


<210>  50
<211>  216
<212>  PRT
<213>  Homo sapiens


<220>
<221>  MISC_FEATURE
<222>  (1)..(216)
<223>  CH2-CH3 domain of an exemplary human IgG2

<220>
<221>  MISC_FEATURE
<222>  (216)..(216)
<223>  wherein, X is a lysine (K) or is absent

<400>  50

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


Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
            20                  25                  30


Val Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val
```

```
        35                  40                  45

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
    50                  55                  60

Phe Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val His Gln
65                  70                  75                  80

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly
                85                  90                  95

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro
            100                 105                 110

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
        115                 120                 125

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
    130                 135                 140

Asp Ile Ser Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
145                 150                 155                 160

Lys Thr Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
                165                 170                 175

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
            180                 185                 190

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

Ser Leu Ser Leu Ser Pro Gly Xaa
    210                 215
```

<210> 51

<211> 217
<212> PRT
<213> Homo sapiens

<220>
<221> MISC_FEATURE
<222> (1)..(217)
<223> CH2-CH3 Domain of an exemplary human IgG3

<220>
<221> MISC_FEATURE
<222> (217)..(217)
<223> wherein, X is a lysine (K) or is absent

<400> 51

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


Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
            20                  25                  30


Val Val Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Lys Trp Tyr
        35                  40                  45


Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    50                  55                  60


Gln Tyr Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Leu His
65                  70                  75                  80


Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                85                  90                  95


Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln
            100                 105                 110


Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
        115                 120                 125
```

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
130 135 140

Ser Asp Ile Ala Val Glu Trp Glu Ser Ser Gly Gln Pro Glu Asn Asn
145 150 155 160

Tyr Asn Thr Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu
165 170 175

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Ile
180 185 190

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn Arg Phe Thr Gln
195 200 205

Lys Ser Leu Ser Leu Ser Pro Gly Xaa
210 215

<210> 52
<211> 217
<212> PRT
<213> Homo sapiens

<220>
<221> MISC_FEATURE
<222> (1)..(217)
<223> CH2-CH3 domain of an exemplary human IgG4

<220>
<221> MISC_FEATURE
<222> (217)..(217)
<223> wherein, X is a lysine (K) or is absent

<400> 52

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

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

```
            20                  25                  30

Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr
        35                  40                  45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    50                  55                  60

Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65                  70                  75                  80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                85                  90                  95

Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
            100                 105                 110

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met
        115                 120                 125

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    130                 135                 140

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
145                 150                 155                 160

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

Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val
            180                 185                 190

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
        195                 200                 205

Lys Ser Leu Ser Leu Ser Leu Gly Xaa
```

210 215

<210> 53
<211> 116
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(116)
<223> heavy chain variable domain of PD-1 mAb 5

<400> 53

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 Val Phe Ser Ser Phe
20 25 30

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

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

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

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

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

Thr Val Ser Ser
115

<210> 54
<211> 5
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(5)
<223> heavy chain variable domain of PD-1 mAb 5 CDR1

<400> 54

Ser Phe Gly Met His
1 5

<210> 55
<211> 17
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(17)
<223> heavy chain variable domain of PD-1 mAb 5 CDR2

<400> 55

Tyr Ile Ser Ser Gly Ser Met Ser Ile Ser Tyr Ala Asp Thr Val Lys
1 5 10 15

Gly

<210> 56
<211> 7
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(7)
<223> heavy chain variable domain of PD-1 mAb 5 CDR3

<400> 56

Leu Ser Asp Tyr Phe Asp Tyr
1 5

<210> 57
<211> 112
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(112)
<223> light chain variable domain of PD-1 mAb 5

<400> 57

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

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

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

Pro Gln Leu Leu Ile Tyr Arg Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

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

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

Thr His Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 58
<211> 16
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(16)
<223> light chain variable domain of PD-1 mAb 5 CDR1

<400> 58

Arg Ser Ser Gln Ser Leu Val His Ser Thr Gly Asn Thr Tyr Leu His
1 5 10 15

<210> 59
<211> 7
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(7)
<223> light chain variable domain of PD-1 mAb 5 CDR2

<400> 59

Arg Val Ser Asn Arg Phe Ser
1 5

<210> 60
<211> 9
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(9)
<223> light chain variable domain of PD-1 mAb 5 CDR3

<400> 60

Ser Gln Thr Thr His Val Pro Trp Thr

1 5

<210> 61
<211> 119
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(119)
<223> heavy chain variable domain of PD-1 mAb 6

<400> 61

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

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

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Xaa
35 40 45

Gly Val Ile His Pro Ser Asp Ser Glu Thr Trp Leu Asp Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Glu His Tyr Gly Thr Ser Pro Phe Ala Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 62
<211> 5
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(5)
<223> heavy chain variable domain of PD-1 mAb 6 CDR1

<400> 62

Ser Tyr Trp Met Asn
1 5

<210> 63
<211> 17
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(17)
<223> heavy chain variable domain of PD-1 mAb 6 CDR2

<400> 63

Val Ile His Pro Ser Asp Ser Glu Thr Trp Leu Asp Gln Lys Phe Lys
1 5 10 15

Asp

<210> 64
<211> 10
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(10)
<223> heavy chain variable domain of PD-1 mAb 6 CDR3

<400> 64

Glu His Tyr Gly Thr Ser Pro Phe Ala Tyr
1 5 10

<210> 65
<211> 111
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(111)
<223> light chain variable domain of PD-1 mAb 6

<400> 65

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

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

Gly Met Ser Phe Met Asn Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile His Ala Ala Ser Asn Xaa Gly Ser Gly Val Pro Ser
50 55 60

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

Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Ser Lys
85 90 95

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

<210> 66
<211> 15
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(15)
<223> light chain variable domain of PD-1 mAb 6 CDR1

<400> 66

Arg Ala Xaa Glu Ser Val Asp Asn Tyr Gly Met Ser Phe Met Asn
1 5 10 15

<210> 67
<211> 7
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(7)
<223> light chain variable domain of PD-1 mAb 6 CDR2

<220>
<221> MISC_FEATURE
<222> (5)..(5)
<223> wherein X1 is N or S and X2 is Q or R; or X1 is N and X2 is Q;
or X1 is S and X2 is Q; or X1 is S and X2 is R

<400> 67

Ala Ala Ser Asn Xaa Gly Ser
1 5

<210> 68
<211> 9
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE

<222> (1)..(9)
<223> light chain variable domain of PD-1 mAb 6 CDR3

<220>
<221> MISC_FEATURE
<222> (1)..(9)
<223> wherein X1 is N or S and X2 is Q or R; or X1 is N and X2 is Q; or X1 is S and X2 is Q; or X1 is S and X2 is R

<400> 68

Gln Gln Ser Lys Glu Val Pro Tyr Thr
1 5

<210> 69
<211> 119
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(119)
<223> heavy chain variable domain of PD-1 mAb 7

<220>
<221> MISC_FEATURE
<222> (1)..(119)
<223> wherein X1 is V or A; X2 is S or G; X3 is V or T; X4 is L or A; X1 is V, X2 is S, X3 is V, and X4 is L; or X1 is A, X2 is G, X3 is T, and X4 is A

<400> 69

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

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

Leu Val Xaa Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Xaa
35 40 45

Ala Thr Ile Ser Gly Gly Gly Gly Asn Thr Tyr Tyr Ser Asp Ser Val

50 55 60

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

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

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

Thr Leu Val Thr Val Ser Ser
115

<210> 70
<211> 5
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(5)
<223> heavy chain variable domain of PD-1 mAb 7 CDR1

<220>
<221> MISC_FEATURE
<222> (1)..(5)
<223> wherein X1 is V or A; X2 is S or G; X3 is V or T; X4 is L or A; X1 is V, X2 is S, X3 is V, and X4 is L; or X1 is A, X2 is G, X3 is T, and X4 is A

<400> 70

Ser Tyr Leu Val Xaa
1 5

<210> 71
<211> 17
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(17)
<223> heavy chain variable domain of PD-1 mAb 7 CDR2

<220>
<221> MISC_FEATURE
<222> (1)..(17)
<223> wherein X1 is V or A; X2 is S or G; X3 is V or T; X4 is L or A; X1 is V, X2 is S, X3 is V, and X4 is L; or X1 is A, X2 is G, X3 is T, and X4 is A

<400> 71

Thr Ile Ser Gly Gly Gly Gly Asn Thr Tyr Tyr Ser Asp Ser Val Lys
1 5 10 15

Gly

<210> 72
<211> 10
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(10)
<223> heavy chain variable domain of PD-1 mAb 7 CDR3

<220>
<221> MISC_FEATURE
<222> (1)..(10)
<223> wherein X1 is V or A; X2 is S or G; X3 is V or T; X4 is L or A; X1 is V, X2 is S, X3 is V, and X4 is L; or X1 is A, X2 is G, X3 is T, and X4 is A

<400> 72

Tyr Gly Phe Asp Gly Ala Trp Phe Ala Tyr
1 5 10

<210> 73

<211> 107
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(107)
<223> light chain variable domain of PD-1 mAb 7

<220>
<221> MISC_FEATURE
<222> (1)..(107)
<223> wherein X1 is N or S and X2 is N or D; X1 is S and X2 is N; or X1 is N and X2 is D

<400> 73

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

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Xaa Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Xaa Ala Lys Thr Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His His Tyr Ala Val Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 74
<211> 11

<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(11)
<223> PD-1 mAb 7 CDRL1

<220>
<221> MISC_FEATURE
<222> (1)..(11)
<223> wherein X1 is N or S and X2 is N or D; X1 is S and X2 is N; or X1 is N and X2 is D

<400> 74

Arg Ala Ser Glu Asn Ile Tyr Xaa Tyr Leu Ala
1 5 10

<210> 75
<211> 7
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(7)
<223> PD-1 mAb 7 CDRL2

<220>
<221> MISC_FEATURE
<222> (1)..(7)
<223> wherein X1 is N or S and X2 is N or D; X1 is S and X2 is N; or X1 is N and X2 is D

<400> 75

Xaa Ala Lys Thr Leu Ala Ala
1 5

<210> 76
<211> 9
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(9)
<223> PD-1 mAb 7 CDRL3

<400> 76

Gln His His Tyr Ala Val Pro Trp Thr
1 5

<210> 77
<211> 117
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(117)
<223> heavy chain variable domain of PD-1 mAb 8

<400> 77

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

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

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

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

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

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

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

Val Thr Val Ser Ser
115

<210> 78
<211> 5
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(5)
<223> PD-1 mAb 8 CDRH1

<400> 78

Ser Tyr Leu Ile Ser
1 5

<210> 79
<211> 17
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(17)
<223> PD-1 mAb 8 CDRH2

<400> 79

Ala Ile Ser Gly Gly Gly Ala Asp Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 80
<211> 8
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(8)
<223> PD-1 mAb 8 CDRH3

<400> 80

Arg Gly Thr Tyr Ala Met Asp Tyr
1 5

<210> 81
<211> 107
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(107)
<223> light chain variable domain of PD-1 mAb 8

<400> 81

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

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

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Asp Ala Lys Thr Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His His Tyr Ala Val Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 82
<211> 11
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(11)
<223> PD-1 mAb 8 CDRL1

<400> 82

Arg Ala Ser Glu Asn Ile Tyr Asn Tyr Leu Ala
1 5 10

<210> 83
<211> 7
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(7)
<223> PD-1 mAb 8 CDRL2

<400> 83

Asp Ala Lys Thr Leu Ala Ala
1 5

<210> 84
<211> 9
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(9)
<223> PD-1 mAb 8 CDRL3

<400> 84

Gln His His Tyr Ala Val Pro Trp Thr
1   5

<210> 85
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> kappa CL Domain

<400> 85

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

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

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

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

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

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

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys

100 105

<210> 86
<211> 110
<212> PRT
<213> Homo sapiens

<220>
<221> MISC_FEATURE
<222> (1)..(110)
<223> IgG4 CH1 Domain and Stabilized Hinge

<400> 86

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

Ser Thr Ser Glu Ser 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 Lys Thr
65 70 75 80

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

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro
100 105 110

<210> 87
<211> 445
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<222> (1)..(445)
<223> complete heavy chain of PD-1 mAb 6-ISQ

<400> 87

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


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


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


Gly Val Ile His Pro Ser Asp Ser Glu Thr Trp Leu Asp Gln Lys Phe
    50                  55                  60


Lys Asp Arg Val Thr Ile Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80


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


Ala Arg Glu His Tyr Gly Thr Ser Pro Phe Ala Tyr Trp Gly Gln Gly
            100                 105                 110


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


Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu
    130                 135                 140


Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145                 150                 155                 160
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Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
                165                 170                 175

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

Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro
        195                 200                 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro
    210                 215                 220

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

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

Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val
            260                 265                 270

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

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

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

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

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
            340                 345                 350
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Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
        355                 360                 365


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


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


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


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


Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
        435                 440                 445
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