SEQUENCE LISTING

<110> AKREVIA THERAPEUTICS INC.
KAROW, Margaret

<120> ANTI-CTLA4 ANTIBODIES AND METHODS OF USE
THEREOF

<130> 73776-20025.40

<140> Not yet assigned
<141> Concurrently herewith

<150> US 62/785,111
<151> 2018-12-26

<160> 39

<170> FastSEQ for Windows Version 4.0

<210> 1
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-L1 Antibody 1

<400> 1
Gln Ser Leu Leu Asn Ser Asp Gly Asn Thr Tyr
1 5 10

<210> 2
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-L2 Antibody 1

<400> 2
Leu Val Ser
1

<210> 3
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-L3 Antibody 1

<400> 3
Val Gln Gly Thr His Asp Pro
 1   5

<210> 4
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-H1 Antibody 1

<400> 4
Tyr His Thr Ile Thr Ser Gly Tyr
 1   5

<210> 5
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-H2 Antibody 1

<400> 5
Ile Ser Tyr Ser Gly Asn Thr
 1   5

<210> 6
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-H3 Antibody 1

<400> 6
Ala Ser Met Met Val Pro His Tyr Tyr Val Met Asp Ala
 1   5   10

<210> 7
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-L1 (Kabat) Antibody 1

<400> 7

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

<210> 8
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-L2 (Kabat) Antibody 1

<400> 8
Leu Val Ser Lys Leu Gly Ser
 1   5

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

<220>
<223> CDR-L3 (Kabat) Antibody 1

<400> 9
Val Gln Gly Thr His Asp Pro Trp Thr
 1   5

<210> 10
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-H1 (Kabat) Antibody 1

<400> 10
Ser Gly Tyr Asp Trp Thr
 1   5

<210> 11
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-H2 (Kabat) Antibody 1

<400> 11
Tyr Ile Ser Tyr Ser Gly Asn Thr Asn Tyr Asn Pro Ser Leu Lys Ser
 1   5   10   15

<210> 12
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-H3(Kabat) Antibody 1

<400> 12
Met Met Val Pro His Tyr Tyr Val Met Asp Ala
 1   5   10

<210> 13
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-L1 Antibody 2

<400> 13
Ser Ala Leu Ser Tyr Met
 1   5

<210> 14
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-L2 Antibody 2

<400> 14
Gly Thr Ser
 1

<210> 15
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-L3 Antibody 2

<400> 15
His His Trp Ser Asn Thr Gln
 1   5

<210> 16
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-H1 Antibody 2

<400> 16
Gly Tyr Thr Phe Thr Asn Tyr Phe
 1   5

<210> 17
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-H2 Antibody 2

<400> 17
Val Asp Pro Glu Gln Gly Arg Ala Asp
 1   5

<210> 18
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-H3 Antibody 2

<400> 18
Arg Arg Ala Met Asp Asn Tyr Gly Phe Ala Tyr
 1   5   10

<210> 19
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-L1 (Kabat) Antibody 2

<400> 19
Ser Ala Asn Ser Ala Leu Ser Tyr Met Tyr
 1   5   10

<210> 20

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

<220>
<223> CDR-L2 (Kabat) Antibody 2

<400> 20
Gly Thr Ser Asn Leu Ala Ser
 1   5

<210> 21
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-L3 (Kabat) Antibody 2

<400> 21
His His Trp Ser Asn Thr Gln Trp Thr
 1   5

<210> 22
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-H1 (Kabat) Antibody 2

<400> 22
Asn Tyr Phe Met Asn
 1   5

<210> 23
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR-H2 (Kabat) Antibody 2

<400> 23
Arg Val Asp Pro Glu Gln Gly Arg Ala Asp Tyr Ala Glu Lys Phe Lys
 1   5   10   15
Lys

<210> 24

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

<220>
<223> CDR-H3 (Kabat) Antibody 2

<400> 24
Arg Ala Met Asp Asn Tyr Gly Phe Ala Tyr
 1   5   10

<210> 25
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<223> VL domain
      (Antibody 1)

<400> 25
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
 1   5   10   15
Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Asn Ser
            20   25   30
Asp Gly Asn Thr Tyr Leu Tyr Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35   40   45
Pro Gln Leu Leu Ile Tyr Leu Val Ser Lys Leu Gly Ser Gly Val Pro
    50   55   60
Asn 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 Val Gln Gly
                85   90   95
Thr His Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105   110
Arg

<210> 26
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> VH domain
      (Antibody 1)

<400> 26
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
 1   5   10   15

```
Thr Leu Ser Leu Thr Cys Ser Val Thr Tyr His Thr Ile Thr Ser Gly
            20                  25                  30
Tyr Asp Trp Thr Trp Ile Arg Lys Pro Pro Gly Lys Gly Met Glu Trp
        35                  40                  45
Ile Gly Tyr Ile Ser Tyr Ser Gly Asn Thr Asn Tyr Asn Pro Ser Leu
    50                  55                  60
Lys Ser Arg Val Thr Ile Ser Arg Asp Thr Ser Lys Asn Gln Phe Phe
65                  70                  75                  80
Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Ser Met Met Val Pro His Tyr Tyr Val Met Asp Ala Trp Gly Gln
            100                 105                 110
Gly Thr Leu Val Thr Val Ser Ser Ala
        115                 120
```

<210> 27
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<223> Light chain (Antibody 1)

<400> 27

```
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
 1               5                  10                  15
Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Asn Ser
            20                  25                  30
Asp Gly Asn Thr Tyr Leu Tyr Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45
Pro Gln Leu Leu Ile Tyr Leu Val Ser Lys Leu Gly Ser Gly Val Pro
    50                  55                  60
Asn 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 Val Gln Gly
                85                  90                  95
Thr His Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105                 110
Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
        115                 120                 125
Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
    130                 135                 140
Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145                 150                 155                 160
Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
                165                 170                 175
Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
            180                 185                 190
Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
        195                 200                 205
Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215
```

<210> 28
<211> 450
<212> PRT
<213> Artificial Sequence

<220>
<223> Heavy chain
(Antibody 1)

<400> 28
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
 1   5   10   15
Thr Leu Ser Leu Thr Cys Ser Val Thr Tyr His Thr Ile Thr Ser Gly
            20   25   30
Tyr Asp Trp Thr Trp Ile Arg Lys Pro Pro Gly Lys Gly Met Glu Trp
        35   40   45
Ile Gly Tyr Ile Ser Tyr Ser Gly Asn Thr Asn Tyr Asn Pro Ser Leu
    50   55   60
Lys Ser Arg Val Thr Ile Ser Arg Asp Thr Ser Lys Asn Gln Phe Phe
65   70   75   80
Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85   90   95
Ala Ser Met Met Val Pro His Tyr Tyr Val Met Asp Ala Trp Gly Gln
            100   105   110
Gly Thr Leu 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 Lys 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> 29
<211> 450
<212> PRT
<213> Artificial Sequence

<220>
<223> Heavy chain
(Antibody 1-S239D, I332E)

<400> 29

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
 1               5                  10                  15
Thr Leu Ser Leu Thr Cys Ser Val Thr Tyr His Thr Ile Thr Ser Gly
            20                  25                  30
Tyr Asp Trp Thr Trp Ile Arg Lys Pro Pro Gly Lys Gly Met Glu Trp
        35                  40                  45
Ile Gly Tyr Ile Ser Tyr Ser Gly Asn Thr Asn Tyr Asn Pro Ser Leu
    50                  55                  60
Lys Ser Arg Val Thr Ile Ser Arg Asp Thr Ser Lys Asn Gln Phe Phe
65                  70                  75                  80
Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Ser Met Met Val Pro His Tyr Tyr Val Met Asp Ala Trp Gly Gln
            100                 105                 110
Gly Thr Leu 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 Lys 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 Asp 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 Glu 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> 30
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> VL domain
(Antibody 2)

<400> 30

```
Glu Ile Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys
 1               5                  10                  15
Glu Lys Val Thr Ile Thr Cys Ser Ala Asn Ser Ala Leu Ser Tyr Met
            20                  25                  30
Tyr Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Leu Trp Val His
        35                  40                  45
Gly Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
```

```
    50                  55                  60
Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu
65                  70                  75                  80
Asp Ala Ala Thr Tyr Tyr Cys His His Trp Ser Asn Thr Gln Trp Thr
                85                  90                  95
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
```

<210> 31
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> VH domain
(Antibody 2)

<400> 31

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20                  25                  30
Phe Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Arg Val Asp Pro Glu Gln Gly Arg Ala Asp Tyr Ala Glu Lys Phe
    50                  55                  60
Lys Lys Arg Val Thr Ile Thr Ala 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 Arg Ala Met Asp Asn Tyr Gly Phe Ala Tyr Trp Gly Gln Gly
            100                 105                 110
Thr Leu Val Thr Val Ser Ser Ala
        115                 120
```

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

<220>
<223> Light chain
(Antibody 2)

<400> 32

```
Glu Ile Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys
 1               5                  10                  15
Glu Lys Val Thr Ile Thr Cys Ser Ala Asn Ser Ala Leu Ser Tyr Met
            20                  25                  30
Tyr Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Leu Trp Val His
```

```
        35                  40                  45
Gly Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    50                  55                  60
Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu
65                  70                  75                  80
Asp Ala Ala Thr Tyr Tyr Cys His His Trp Ser Asn Thr Gln Trp Thr
                85                  90                  95
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
            100                 105                 110
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
        115                 120                 125
Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
    130                 135                 140
Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145                 150                 155                 160
Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
                165                 170                 175
Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
            180                 185                 190
Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
        195                 200                 205
Asn Arg Gly Glu Cys
    210
```

<210> 33
<211> 449
<212> PRT
<213> Artificial Sequence

<220>
<223> Heavy chain
(Antibody 2)

<400> 33

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20                  25                  30
Phe Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Arg Val Asp Pro Glu Gln Gly Arg Ala Asp Tyr Ala Glu Lys Phe
    50                  55                  60
Lys Lys Arg Val Thr Ile Thr Ala 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 Arg Ala Met Asp Asn Tyr Gly 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 Ser Ser Lys Ser Thr Ser Gly Gly 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
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 Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
        195                 200                 205
Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
    210                 215                 220
Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225                 230                 235                 240
Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
                245                 250                 255
Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
            260                 265                 270
Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
        275                 280                 285
Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
    290                 295                 300
Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305                 310                 315                 320
Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
                325                 330                 335
Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
            340                 345                 350
Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
        355                 360                 365
Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
    370                 375                 380
Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385                 390                 395                 400
Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
                405                 410                 415
Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
            420                 425                 430
Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
        435                 440                 445
Lys
```

<210> 34
<211> 449
<212> PRT
<213> Artificial Sequence

<220>
<223> Heavy chain
(Antibody 2-S239D, I332E)

<400> 34
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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
```

```
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20                  25                  30
Phe Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Arg Val Asp Pro Glu Gln Gly Arg Ala Asp Tyr Ala Glu Lys Phe
    50                  55                  60
Lys Lys Arg Val Thr Ile Thr Ala 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 Arg Ala Met Asp Asn Tyr Gly 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 Ser Ser Lys Ser Thr Ser Gly Gly 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
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 Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
        195                 200                 205
Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
    210                 215                 220
Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225                 230                 235                 240
Asp Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
                245                 250                 255
Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
            260                 265                 270
Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
        275                 280                 285
Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
    290                 295                 300
Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305                 310                 315                 320
Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Glu Glu Lys
                325                 330                 335
Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
            340                 345                 350
Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
        355                 360                 365
Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
    370                 375                 380
Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385                 390                 395                 400
Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
                405                 410                 415
Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
            420                 425                 430
Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
```

```
        435                 440                 445
Lys



<210> 35
<211> 329
<212> PRT
<213> Artificial Sequence

<220>
<223> Heavy Chain Constant Domain

<400> 35
Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
 1               5                  10                  15
Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
            20                  25                  30
Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
        35                  40                  45
Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
    50                  55                  60
Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
65                  70                  75                  80
Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys
                85                  90                  95
Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
            100                 105                 110
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        115                 120                 125
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    130                 135                 140
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
145                 150                 155                 160
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                165                 170                 175
Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            180                 185                 190
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        195                 200                 205
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    210                 215                 220
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
225                 230                 235                 240
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
                245                 250                 255
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            260                 265                 270
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        275                 280                 285
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    290                 295                 300
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
305                 310                 315                 320
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Lys Ser Leu Ser Leu Ser Pro Gly Lys
325

<210> 36
<211> 329
<212> PRT
<213> Artificial Sequence

<220>
<223> Heavy Chain Constant Domain S239D

<400> 36
Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
1 5 10 15
Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
20 25 30
Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
35 40 45
Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
50 55 60
Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
65 70 75 80
Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys
85 90 95
Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
100 105 110
Ala Pro Glu Leu Leu Gly Gly Pro Asp Val Phe Leu Phe Pro Pro Lys
115 120 125
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
130 135 140
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
145 150 155 160
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
165 170 175
Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
180 185 190
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
195 200 205
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
210 215 220
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
225 230 235 240
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
245 250 255
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
260 265 270
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
275 280 285
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
290 295 300
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
305 310 315 320
Lys Ser Leu Ser Leu Ser Pro Gly Lys

325

<210> 37
<211> 329
<212> PRT
<213> Artificial Sequence

<220>
<223> Heavy Chain Constant Domain
I332E

<400> 37
Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
1 5 10 15
Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
20 25 30
Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
35 40 45
Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
50 55 60
Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
65 70 75 80
Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys
85 90 95
Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
100 105 110
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
115 120 125
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
130 135 140
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
145 150 155 160
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
165 170 175
Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
180 185 190
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
195 200 205
Ala Leu Pro Ala Pro Glu Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
210 215 220
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
225 230 235 240
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
245 250 255
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
260 265 270
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
275 280 285
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
290 295 300
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
305 310 315 320

Lys Ser Leu Ser Leu Ser Pro Gly Lys
325

<210> 38
<211> 329
<212> PRT
<213> Artificial Sequence

<220>
<223> Heavy Chain Constant Domain
S239D, I332E

<400> 38
Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
1 5 10 15
Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
20 25 30
Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
35 40 45
Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
50 55 60
Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
65 70 75 80
Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys
85 90 95
Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
100 105 110
Ala Pro Glu Leu Leu Gly Gly Pro Asp Val Phe Leu Phe Pro Pro Lys
115 120 125
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
130 135 140
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
145 150 155 160
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
165 170 175
Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
180 185 190
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
195 200 205
Ala Leu Pro Ala Pro Glu Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
210 215 220
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
225 230 235 240
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
245 250 255
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
260 265 270
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
275 280 285
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
290 295 300
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln

305 310 315 320
Lys Ser Leu Ser Leu Ser Pro Gly Lys
325

<210> 39
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Light chain Constant Domain

<400> 39
Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15
Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30
Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45
Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60
Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80
His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95
Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105