SEQUENCE LISTING

<110> United Biomedical, Inc.
Wang, Chang-Yi

<120> TREATMENT AND FUNCTIONAL CURE OF HIV INFECTION BY MONOCLONAL ANTIBODIES TO CD4 MEDIATING COMPETITIVE HIV ENTRY INHIBITION

<130> 1004263.213WO (2034WO)

<150> US 62/051,200
<151> 2014-09-16

<160> 14

<170> PatentIn version 3.5

<210> 1
<211> 5
<212> PRT
<213> Murine anibody

<220>
<221> DOMAIN
<222> (1)..(5)
<223> CDR1 of heavy chain of murine antibody B4

<400> 1

Asp Tyr Val Ile His
1 5

<210> 2
<211> 17
<212> PRT
<213> Murine antibody

<220>
<221> DOMAIN
<222> (1)..(17)
<223> CDR2 of heavy chain of murine antibody B4

<400> 2

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

Asp

<210> 3
<211> 9
<212> PRT
<213> Murine antibody

<220>
<221> DOMAIN

<222> (1)..(9)
<223> CDR3 of heavy chain of murie antibody B4

<400> 3

Arg Gly Asn Gly Thr Gly Phe Ala Tyr
1   5

<210> 4
<211> 15
<212> PRT
<213> Murine antibody

<220>
<221> DOMAIN
<222> (1)..(15)
<223> CDR1 of light chain of murine antibody B4

<400> 4

Lys Ala Gly Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Met Asn
1   5   10   15

<210> 5
<211> 7
<212> PRT
<213> Murine antibody

<220>
<221> DOMAIN
<222> (1)..(7)
<223> CDR2 of light chain of murine antibody B4

<400> 5

Val Ala Ser Asn Leu Glu Ser
1   5

<210> 6
<211> 9
<212> PRT
<213> Murine antibody

<220>
<221> DOMAIN
<222> (1)..(9)
<223> CDR3 of light chain of murine antibody B4

<400> 6

Gln Gln Ser Tyr Lys Asp Pro Leu Thr
1   5

<210> 7
<211> 448
<212> PRT

<213> Murine antibody

<220>
<221> DOMAIN
<222> (1)..(448)
<223> Heavy Chain of deimmunized human antibody B4 [UB421] with identical CDRs1, 2 and 3 derived from the corresponding CDRs1, 2 and 3 from the heavy chain sequence of the parental murine B4 antibody

<400> 7

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

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

Val Ile His Trp Val Lys Gln Ala Thr Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

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

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

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

Ala Arg Arg Gly Asn Gly Thr Gly Phe Ala Tyr Trp Gly Gln Gly Thr
            100                 105                 110

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

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

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

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

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

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
        195                 200                 205
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Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
    210                 215                 220

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

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

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

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

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

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

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

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

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

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

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

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

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

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445
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<210> 8

<211> 218
<212> PRT
<213> Murine antibody

<220>
<221> DOMAIN
<222> (1)..(218)
<223> Light Chain of deimmuized human antibody B4 [UB421] with identical CDRs1, 2 and 3 derived from the corresponding CDRs1, 2,and 3 from the light chain sequence of the parental murine B4 antibody

<400> 8

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

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

Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
        35                  40                  45

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

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

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
        115                 120                 125

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

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

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

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
            180                 185                 190
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His Lys Leu Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
        195                 200                 205


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


<210>  9
<211>  448
<212>  PRT
<213>  Murine antibody


<220>
<221>  DOMAIN
<222>  (1)..(448)
<223>  Heavy Chain of the deimmunized human antibody B4 [UB421] with
       M253Y/S255T/T257E substitutions

<400>  9

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


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


Val Ile His Trp Val Lys Gln Ala Thr Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45


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


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


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


Ala Arg Arg Gly Asn Gly Thr Gly Phe Ala Tyr Trp Gly Gln Gly Thr
            100                 105                 110


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


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


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


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

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

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

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

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

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Tyr Ile Thr Arg
                245                 250                 255

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

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

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

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

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

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

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

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

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

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415
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Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
420 425 430

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

<210> 10
<211> 448
<212> PRT
<213> Humanized anibody

<220>
<221> MISC_FEATURE
<222> (253)..(253)
<223> M or Y

<220>
<221> MISC_FEATURE
<222> (255)..(255)
<223> S or T

<220>
<221> MISC_FEATURE
<222> (257)..(257)
<223> T or E

<220>
<221> MISC_FEATURE
<222> (298)..(298)
<223> N or H

<400> 10

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

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

Val Ile His Trp Val Lys Gln Ala Thr Gly Gln Gly Leu Glu Trp Ile
35 40 45

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

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

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

Ala Arg Arg Gly Asn Gly Thr Gly Phe Ala Tyr Trp Gly Gln Gly Thr
100 105 110

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

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

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

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

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

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

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

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

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Xaa Ile Xaa Arg
                245                 250                 255

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

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

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

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

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

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

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

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

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

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

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

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


<210>  11
<211>  118
<212>  PRT
<213>  Murine antibody

<400>  11

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

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

Val Ile His Trp Val Lys Gln Ala Thr Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

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

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

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

Ala Arg Arg Gly Asn Gly Thr Gly Phe Ala Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser
        115


<210>  12
<211>  330
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<212> PRT
<213> Human antibody

<220>
<221> MISC_FEATURE
<222> (135)..(135)
<223> M or Y

<220>
<221> MISC_FEATURE
<222> (137)..(137)
<223> S or T

<220>
<221> MISC_FEATURE
<222> (139)..(139)
<223> T or E

<220>
<221> MISC_FEATURE
<222> (180)..(180)
<223> N or H

<400> 12

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


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


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


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


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


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


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


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


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


Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
```

145 150 155 160

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

Glu Gln Tyr Xaa Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

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

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

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

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

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

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

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

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

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> 13
<211> 111
<212> PRT
<213> Murine antibody

<400> 13

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

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

Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro

35 40 45

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

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

<210> 14
<211> 107
<212> PRT
<213> Human antibody

<400> 14

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 Leu 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