SEQUENCE LISTING

<110> Ablynx NV

<120> Methods of treating initial episode of TTP with immunoglobulin single variable domains

<130> P18-002-PCT-1

<150> US62/627,082
<151> 2018-02-06

<150> US62/662,381
<151> 2018-04-25

<160> 24

<170> PatentIn version 3.5

<210> 1
<211> 259
<212> PRT
<213> Artificial Sequence

<220>
<223> Nanobody Sequence

<400> 1

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 Arg Thr Phe Ser Tyr Asn
20 25 30

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

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

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

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

Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro
100 105 110

```
Ser Glu Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        115                 120                 125


Ala Ala Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
    130                 135                 140


Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe
145                 150                 155                 160


Ser Tyr Asn Pro Met Gly Trp Phe Arg Gln Ala Pro Gly Lys Gly Arg
                165                 170                 175


Glu Leu Val Ala Ala Ile Ser Arg Thr Gly Gly Ser Thr Tyr Tyr Pro
            180                 185                 190


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


Met Val Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
    210                 215                 220


Tyr Tyr Cys Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg
225                 230                 235                 240


Thr Leu Pro Ser Glu Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr
                245                 250                 255


Val Ser Ser
```

<210>  2
<211>  259
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Nanobody Sequence

<400>  2

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

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

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

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

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

Leu Gln Met Asn Asn Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro
            100                 105                 110

Ser Glu Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        115                 120                 125

Ala Ala Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
    130                 135                 140

Ala Gly Gly Ala Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe
145                 150                 155                 160

Ser Tyr Asn Pro Met Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg
                165                 170                 175

Asp Leu Val Ala Ala Ile Ser Arg Thr Gly Gly Ser Thr Tyr Tyr Pro
            180                 185                 190

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

Met Val Tyr Leu Gln Met Asn Asn Leu Lys Pro Glu Asp Thr Ala Val
    210                 215                 220

Tyr Tyr Cys Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg
225                 230                 235                 240
```

```
Thr Leu Pro Ser Glu Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr
                245                 250                 255


Val Ser Ser



<210>  3
<211>  265
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Nanobody Sequence

<400>  3

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


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


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


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


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


Leu Gln Met Asn Asn Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro
            100                 105                 110


Ser Glu Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        115                 120                 125


Gly Gly Gly Gly Ser Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser
    130                 135                 140
```

```
Gly Gly Gly Leu Val Gln Ala Gly Gly Ala Leu Arg Leu Ser Cys Ala
145                 150                 155                 160


Ala Ser Gly Arg Thr Phe Ser Tyr Asn Pro Met Gly Trp Phe Arg Gln
                165                 170                 175


Ala Pro Gly Lys Glu Arg Asp Leu Val Ala Ala Ile Ser Arg Thr Gly
            180                 185                 190


Gly Ser Thr Tyr Tyr Pro Asp Ser Val Glu Gly Arg Phe Thr Ile Ser
        195                 200                 205


Arg Asp Asn Ala Lys Arg Met Val Tyr Leu Gln Met Asn Asn Leu Lys
    210                 215                 220


Pro Glu Asp Thr Ala Val Tyr Tyr Cys Ala Ala Ala Gly Val Arg Ala
225                 230                 235                 240


Glu Asp Gly Arg Val Arg Thr Leu Pro Ser Glu Tyr Thr Phe Trp Gly
                245                 250                 255


Gln Gly Thr Gln Val Thr Val Ser Ser
            260                 265
```

<210>  4
<211>  286
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Nanobody Sequence

<400>  4

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


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


Pro Met Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg Asp Leu Val
        35                  40                  45
```

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

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

Leu Gln Met Asn Asn Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro
            100                 105                 110

Ser Glu Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val
145                 150                 155                 160

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Ala Gly Gly Ala Leu
                165                 170                 175

Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe Ser Tyr Asn Pro Met
            180                 185                 190

Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg Asp Leu Val Ala Ala
        195                 200                 205

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

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Arg Met Val Tyr Leu Gln
225                 230                 235                 240

Met Asn Asn Leu Lys Pro Glu Gly Thr Ala Val Tyr Tyr Cys Ala Ala
                245                 250                 255

Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro Ser Glu
            260                 265                 270
```

```
Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        275                 280                 285


<210>  5
<211>  247
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Nanobody Sequence

<400>  5

Ala 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 Leu Ala Ser Gly Arg Ile Phe Ser Ile Gly
            20                  25                  30


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


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


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


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


Ala Asn Leu Lys Gln Gly Ser Tyr Gly Tyr Arg Phe Asn Asp Tyr Trp
            100                 105                 110


Gly Gln Gly Thr Gln Val Thr Val Ser Ser Ala Ala Ala Glu Val Gln
        115                 120                 125


Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg
    130                 135                 140


Leu Ser Cys Leu Ala Ser Gly Arg Ile Phe Ser Ile Gly Ala Met Gly
145                 150                 155                 160
```

```
Met Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val Ala Thr Ile
                165                 170                 175


Thr Ser Gly Gly Ser Thr Asn Tyr Ala Asp Pro Val Lys Gly Arg Phe
            180                 185                 190


Thr Ile Ser Arg Asp Gly Pro Lys Asn Thr Val Tyr Leu Gln Met Asn
        195                 200                 205


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


Lys Gln Gly Ser Tyr Gly Tyr Arg Phe Asn Asp Tyr Trp Gly Gln Gly
225                 230                 235                 240


Thr Gln Val Thr Val Ser Ser
                245
```

<210>  6
<211>  253
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Nanobody Sequence

<400>  6

```
Ala 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 Leu Ala Ser Gly Arg Ile Phe Ser Ile Gly
            20                  25                  30


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


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


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


Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys Tyr
```

```
                85                  90                  95

Ala Asn Leu Lys Gln Gly Ser Tyr Gly Tyr Arg Phe Asn Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Gln Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
    130                 135                 140

Pro Gly Gly Ser Leu Arg Leu Ser Cys Leu Ala Ser Gly Arg Ile Phe
145                 150                 155                 160

Ser Ile Gly Ala Met Gly Met Tyr Arg Gln Ala Pro Gly Lys Gln Arg
                165                 170                 175

Glu Leu Val Ala Thr Ile Thr Ser Gly Gly Ser Thr Asn Tyr Ala Asp
            180                 185                 190

Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Gly Pro Lys Asn Thr
        195                 200                 205

Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr
    210                 215                 220

Tyr Cys Tyr Ala Asn Leu Lys Gln Gly Ser Tyr Gly Tyr Arg Phe Asn
225                 230                 235                 240

Asp Tyr Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
                245                 250


<210>  7
<211>  274
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Nanobody Sequence

<400>  7

Ala 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 Leu Ala Ser Gly Arg Ile Phe Ser Ile Gly
            20                  25                  30

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

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

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

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

Ala Asn Leu Lys Gln Gly Ser Tyr Gly Tyr Arg Phe Asn Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Gln Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly
145                 150                 155                 160

Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Leu Ala
                165                 170                 175

Ser Gly Arg Ile Phe Ser Ile Gly Ala Met Gly Met Tyr Arg Gln Ala
            180                 185                 190

Pro Gly Lys Gln Arg Glu Leu Val Ala Thr Ile Thr Ser Gly Gly Ser
        195                 200                 205

Thr Asn Tyr Ala Asp Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp
    210                 215                 220

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

225 230 235 240

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

Gly Tyr Arg Phe Asn Asp Tyr Trp Gly Gln Gly Thr Gln Val Thr Val
260 265 270

Ser Ser

<210> 8
<211> 259
<212> PRT
<213> Artificial Sequence

<220>
<223> Nanobody Sequence

<400> 8

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

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

Pro Met Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg Asp Val Val
35 40 45

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

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

Leu Gln Met Asn Ala Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro
100 105 110

Ser Glu Tyr Asn Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
115 120 125

```
Ala Ala Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
    130                 135                 140

Ala Gly Gly Ala Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe
145                 150                 155                 160

Ser Tyr Asn Pro Met Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg
                165                 170                 175

Asp Val Val Ala Ala Ile Ser Arg Thr Gly Gly Ser Thr Tyr Tyr Ala
            180                 185                 190

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

Met Val Tyr Leu Gln Met Asn Ala Leu Lys Pro Glu Asp Thr Ala Val
    210                 215                 220

Tyr Tyr Cys Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg
225                 230                 235                 240

Thr Leu Pro Ser Glu Tyr Asn Phe Trp Gly Gln Gly Thr Gln Val Thr
                245                 250                 255

Val Ser Ser
```

<210> 9
<211> 265
<212> PRT
<213> Artificial Sequence

<220>
<223> Nanobody Sequence

<400> 9

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

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

```
Pro Met Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg Asp Val Val
        35                  40                  45

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

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

Leu Gln Met Asn Ala Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro
            100                 105                 110

Ser Glu Tyr Asn Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser
    130                 135                 140

Gly Gly Gly Leu Val Gln Ala Gly Gly Ala Leu Arg Leu Ser Cys Ala
145                 150                 155                 160

Ala Ser Gly Arg Thr Phe Ser Tyr Asn Pro Met Gly Trp Phe Arg Gln
                165                 170                 175

Ala Pro Gly Lys Glu Arg Asp Val Val Ala Ala Ile Ser Arg Thr Gly
            180                 185                 190

Gly Ser Thr Tyr Tyr Ala Arg Ser Val Glu Gly Arg Phe Thr Ile Ser
        195                 200                 205

Arg Asp Asn Ala Lys Arg Met Val Tyr Leu Gln Met Asn Ala Leu Lys
    210                 215                 220

Pro Glu Asp Thr Ala Val Tyr Tyr Cys Ala Ala Ala Gly Val Arg Ala
225                 230                 235                 240

Glu Asp Gly Arg Val Arg Thr Leu Pro Ser Glu Tyr Asn Phe Trp Gly
                245                 250                 255
```

```
Gln Gly Thr Gln Val Thr Val Ser Ser
            260                 265


<210>  10
<211>  286
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Nanobody Sequence

<400>  10

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


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


Pro Met Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg Asp Val Val
        35                  40                  45


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


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


Leu Gln Met Asn Ala Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro
            100                 105                 110


Ser Glu Tyr Asn Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        115                 120                 125


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140


Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val
145                 150                 155                 160
```

```
Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Ala Gly Gly Ala Leu
                165                 170                 175


Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe Ser Tyr Asn Pro Met
            180                 185                 190


Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg Asp Val Val Ala Ala
        195                 200                 205


Ile Ser Arg Thr Gly Gly Ser Thr Tyr Tyr Ala Arg Ser Val Glu Gly
    210                 215                 220


Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Arg Met Val Tyr Leu Gln
225                 230                 235                 240


Met Asn Ala Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys Ala Ala
                245                 250                 255


Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro Ser Glu
            260                 265                 270


Tyr Asn Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        275                 280                 285


<210>  11
<211>  259
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Nanobody Sequence

<400>  11

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 Arg Thr Phe Ser Tyr Asn
            20                  25                  30


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

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

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

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

Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro
            100                 105                 110

Ser Glu Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        115                 120                 125

Ala Ala Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
    130                 135                 140

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe
145                 150                 155                 160

Ser Tyr Asn Pro Met Gly Trp Phe Arg Gln Ala Pro Gly Lys Gly Arg
                165                 170                 175

Glu Leu Val Ala Ala Ile Ser Arg Thr Gly Gly Ser Thr Tyr Tyr Pro
            180                 185                 190

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

Ser Val Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
    210                 215                 220

Tyr Tyr Cys Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg
225                 230                 235                 240

Thr Leu Pro Ser Glu Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr
                245                 250                 255

Val Ser Ser
```

<210> 12
<211> 259
<212> PRT
<213> Artificial Sequence

<220>
<223> Nanobody Sequence

<400> 12

```
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 Arg Thr Phe Ser Tyr Asn
            20                  25                  30


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


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


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


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


Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro
            100                 105                 110


Ser Glu Tyr Asn Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        115                 120                 125


Ala Ala Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
    130                 135                 140


Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe
145                 150                 155                 160


Ser Tyr Asn Pro Met Gly Trp Phe Arg Gln Ala Pro Gly Lys Gly Arg
                165                 170                 175
```

```
Glu Val Val Ala Ala Ile Ser Arg Thr Gly Gly Ser Thr Tyr Tyr Ala
            180                 185                 190

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

Met Val Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
    210                 215                 220

Tyr Tyr Cys Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg
225                 230                 235                 240

Thr Leu Pro Ser Glu Tyr Asn Phe Trp Gly Gln Gly Thr Gln Val Thr
                245                 250                 255

Val Ser Ser
```

<210> 13
<211> 265
<212> PRT
<213> Artificial Sequence

<220>
<223> Nanobody Sequence

<400> 13

```
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 Arg Thr Phe Ser Tyr Asn
            20                  25                  30

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

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

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

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
```

```
                85                  90                  95

Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro
            100                 105                 110

Ser Glu Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser
    130                 135                 140

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala
145                 150                 155                 160

Ala Ser Gly Arg Thr Phe Ser Tyr Asn Pro Met Gly Trp Phe Arg Gln
                165                 170                 175

Ala Pro Gly Lys Gly Arg Glu Leu Val Ala Ala Ile Ser Arg Thr Gly
            180                 185                 190

Gly Ser Thr Tyr Tyr Pro Asp Ser Val Glu Gly Arg Phe Thr Ile Ser
        195                 200                 205

Arg Asp Asn Ala Lys Arg Met Val Tyr Leu Gln Met Asn Ser Leu Arg
    210                 215                 220

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Ala Ala Gly Val Arg Ala
225                 230                 235                 240

Glu Asp Gly Arg Val Arg Thr Leu Pro Ser Glu Tyr Thr Phe Trp Gly
                245                 250                 255

Gln Gly Thr Gln Val Thr Val Ser Ser
            260                 265
```

<210> 14
<211> 265
<212> PRT
<213> Artificial Sequence

<220>
<223> Nanobody Sequence

<400> 14

```
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 Arg Thr Phe Ser Tyr Asn
            20                  25                  30

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

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

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

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

Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro
            100                 105                 110

Ser Glu Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser
    130                 135                 140

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala
145                 150                 155                 160

Ala Ser Gly Arg Thr Phe Ser Tyr Asn Pro Met Gly Trp Phe Arg Gln
                165                 170                 175

Ala Pro Gly Lys Gly Arg Glu Leu Val Ala Ala Ile Ser Arg Thr Gly
            180                 185                 190

Gly Ser Thr Tyr Tyr Pro Asp Ser Val Glu Gly Arg Phe Thr Ile Ser
        195                 200                 205

Arg Asp Asn Ala Lys Arg Ser Val Tyr Leu Gln Met Asn Ser Leu Arg
```

```
    210                 215                 220

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Ala Ala Gly Val Arg Ala
225                 230                 235                 240

Glu Asp Gly Arg Val Arg Thr Leu Pro Ser Glu Tyr Thr Phe Trp Gly
                245                 250                 255

Gln Gly Thr Gln Val Thr Val Ser Ser
            260                 265
```

<210> 15
<211> 265
<212> PRT
<213> Artificial Sequence

<220>
<223> Nanobody Sequence

<400> 15

```
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 Arg Thr Phe Ser Tyr Asn
            20                  25                  30

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

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

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

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

Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro
            100                 105                 110

Ser Glu Tyr Asn Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        115                 120                 125
```

```
Gly Gly Gly Gly Ser Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser
    130                 135                 140


Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala
145                 150                 155                 160


Ala Ser Gly Arg Thr Phe Ser Tyr Asn Pro Met Gly Trp Phe Arg Gln
                165                 170                 175


Ala Pro Gly Lys Gly Arg Glu Val Val Ala Ala Ile Ser Arg Thr Gly
            180                 185                 190


Gly Ser Thr Tyr Tyr Ala Arg Ser Val Glu Gly Arg Phe Thr Ile Ser
        195                 200                 205


Arg Asp Asn Ala Lys Arg Met Val Tyr Leu Gln Met Asn Ser Leu Arg
    210                 215                 220


Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Ala Ala Gly Val Arg Ala
225                 230                 235                 240


Glu Asp Gly Arg Val Arg Thr Leu Pro Ser Glu Tyr Asn Phe Trp Gly
                245                 250                 255


Gln Gly Thr Gln Val Thr Val Ser Ser
            260                 265


<210>  16
<211>  286
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Nanobody Sequence

<400>  16

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


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

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

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

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

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

Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro
            100                 105                 110

Ser Glu Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val
145                 150                 155                 160

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
                165                 170                 175

Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe Ser Tyr Asn Pro Met
            180                 185                 190

Gly Trp Phe Arg Gln Ala Pro Gly Lys Gly Arg Glu Leu Val Ala Ala
        195                 200                 205

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

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Arg Met Val Tyr Leu Gln
225                 230                 235                 240

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Ala
                245                 250                 255
```

```
Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro Ser Glu
            260                 265                 270


Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        275                 280                 285


<210>  17
<211>  286
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Nanobody Sequence

<400>  17

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 Arg Thr Phe Ser Tyr Asn
            20                  25                  30


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


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


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


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


Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro
            100                 105                 110


Ser Glu Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        115                 120                 125


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140
```

```
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val
145                 150                 155                 160


Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
                165                 170                 175


Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe Ser Tyr Asn Pro Met
            180                 185                 190


Gly Trp Phe Arg Gln Ala Pro Gly Lys Gly Arg Glu Leu Val Ala Ala
        195                 200                 205


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


Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Arg Ser Val Tyr Leu Gln
225                 230                 235                 240


Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Ala
                245                 250                 255


Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro Ser Glu
            260                 265                 270


Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        275                 280                 285


<210>  18
<211>  286
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Nanobody Sequence

<400>  18

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 Arg Thr Phe Ser Tyr Asn
            20                  25                  30
```

```
Pro Met Gly Trp Phe Arg Gln Ala Pro Gly Lys Gly Arg Glu Val Val
        35                  40                  45

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

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

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

Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro
            100                 105                 110

Ser Glu Tyr Asn Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val
145                 150                 155                 160

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
                165                 170                 175

Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe Ser Tyr Asn Pro Met
            180                 185                 190

Gly Trp Phe Arg Gln Ala Pro Gly Lys Gly Arg Glu Val Val Ala Ala
        195                 200                 205

Ile Ser Arg Thr Gly Gly Ser Thr Tyr Tyr Ala Arg Ser Val Glu Gly
    210                 215                 220

Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Arg Met Val Tyr Leu Gln
225                 230                 235                 240

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Ala
                245                 250                 255
```

```
Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro Ser Glu
            260                 265                 270


Tyr Asn Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        275                 280                 285


<210>  19
<211>  128
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Nanobody Sequence

<400>  19

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 Arg Thr Phe Ser Tyr Asn
            20                  25                  30


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


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


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


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


Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro
            100                 105                 110


Ser Glu Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        115                 120                 125


<210>  20
<211>  2804
<212>  PRT
<213>  Homo sapiens
```

<400> 20

```
Met Ile Pro Ala Arg Phe Ala Gly Val Leu Leu Ala Leu Ala Leu Ile
1               5                   10                  15

Leu Pro Gly Thr Leu Cys Ala Glu Gly Thr Arg Gly Arg Ser Ser Thr
            20                  25                  30

Ala Arg Cys Ser Leu Phe Gly Ser Asp Phe Val Asn Thr Phe Asp Gly
        35                  40                  45

Ser Met Tyr Ser Phe Ala Gly Tyr Cys Ser Tyr Leu Leu Ala Gly Gly
    50                  55                  60

Cys Gln Lys Arg Ser Phe Ser Ile Ile Gly Asp Phe Gln Asn Gly Lys
65                  70                  75                  80

Arg Val Ser Leu Ser Val Tyr Leu Gly Glu Phe Phe Asp Ile His Leu
                85                  90                  95

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

Tyr Ala Ser Lys Gly Leu Tyr Leu Glu Thr Glu Ala Gly Tyr Tyr Lys
        115                 120                 125

Leu Ser Gly Glu Ala Tyr Gly Phe Val Ala Arg Ile Asp Gly Ser Gly
    130                 135                 140

Asn Phe Gln Val Leu Leu Ser Asp Arg Tyr Phe Asn Lys Thr Cys Gly
145                 150                 155                 160

Leu Cys Gly Asn Phe Asn Ile Phe Ala Glu Asp Asp Phe Met Thr Gln
                165                 170                 175

Glu Gly Thr Leu Thr Ser Asp Pro Tyr Asp Phe Ala Asn Ser Trp Ala
            180                 185                 190

Leu Ser Ser Gly Glu Gln Trp Cys Glu Arg Ala Ser Pro Pro Ser Ser
        195                 200                 205
```

```
Ser Cys Asn Ile Ser Ser Gly Glu Met Gln Lys Gly Leu Trp Glu Gln
    210                 215                 220

Cys Gln Leu Leu Lys Ser Thr Ser Val Phe Ala Arg Cys His Pro Leu
225                 230                 235                 240

Val Asp Pro Glu Pro Phe Val Ala Leu Cys Glu Lys Thr Leu Cys Glu
                245                 250                 255

Cys Ala Gly Gly Leu Glu Cys Ala Cys Pro Ala Leu Leu Glu Tyr Ala
            260                 265                 270

Arg Thr Cys Ala Gln Glu Gly Met Val Leu Tyr Gly Trp Thr Asp His
        275                 280                 285

Ser Ala Cys Ser Pro Val Cys Pro Ala Gly Met Glu Tyr Arg Gln Cys
    290                 295                 300

Val Ser Pro Cys Ala Arg Thr Cys Gln Ser Leu His Ile Asn Glu Met
305                 310                 315                 320

Cys Gln Glu Arg Cys Val Asp Gly Cys Ser Cys Pro Glu Gly Gln Leu
                325                 330                 335

Leu Asp Glu Gly Leu Cys Val Glu Ser Thr Glu Cys Pro Cys Val His
            340                 345                 350

Ser Gly Lys Arg Tyr Pro Pro Gly Thr Ser Leu Ser Arg Asp Cys Asn
        355                 360                 365

Thr Cys Ile Cys Arg Asn Ser Gln Trp Ile Cys Ser Asn Glu Glu Cys
    370                 375                 380

Pro Gly Glu Cys Leu Val Thr Gly Gln Ser His Phe Lys Ser Phe Asp
385                 390                 395                 400

Asn Arg Tyr Phe Thr Phe Ser Gly Ile Cys Gln Tyr Leu Leu Ala Arg
                405                 410                 415

Asp Cys Gln Asp His Ser Phe Ser Ile Val Ile Glu Thr Val Gln Cys
            420                 425                 430
```

```
Ala Asp Asp Arg Asp Ala Val Cys Thr Arg Ser Val Thr Val Arg Leu
        435                 440                 445

Pro Gly Leu His Asn Ser Leu Val Lys Leu Lys His Gly Ala Gly Val
    450                 455                 460

Ala Met Asp Gly Gln Asp Ile Gln Leu Pro Leu Leu Lys Gly Asp Leu
465                 470                 475                 480

Arg Ile Gln His Thr Val Thr Ala Ser Val Arg Leu Ser Tyr Gly Glu
                485                 490                 495

Asp Leu Gln Met Asp Trp Asp Gly Arg Gly Arg Leu Leu Val Lys Leu
            500                 505                 510

Ser Pro Val Tyr Ala Gly Lys Thr Cys Gly Leu Cys Gly Asn Tyr Asn
        515                 520                 525

Gly Asn Gln Gly Asp Asp Phe Leu Thr Pro Ser Gly Leu Ala Glu Pro
    530                 535                 540

Arg Val Glu Asp Phe Gly Asn Ala Trp Lys Leu His Gly Asp Cys Gln
545                 550                 555                 560

Asp Leu Gln Lys Gln His Ser Asp Pro Cys Ala Leu Asn Pro Arg Met
                565                 570                 575

Thr Arg Phe Ser Glu Glu Ala Cys Ala Val Leu Thr Ser Pro Thr Phe
            580                 585                 590

Glu Ala Cys His Arg Ala Val Ser Pro Leu Pro Tyr Leu Arg Asn Cys
        595                 600                 605

Arg Tyr Asp Val Cys Ser Cys Ser Asp Gly Arg Glu Cys Leu Cys Gly
    610                 615                 620

Ala Leu Ala Ser Tyr Ala Ala Ala Cys Ala Gly Arg Gly Val Arg Val
625                 630                 635                 640

Ala Trp Arg Glu Pro Gly Arg Cys Glu Leu Asn Cys Pro Lys Gly Gln
                645                 650                 655
```

```
Val Tyr Leu Gln Cys Gly Thr Pro Cys Asn Leu Thr Cys Arg Ser Leu
            660                 665                 670

Ser Tyr Pro Asp Glu Glu Cys Asn Glu Ala Cys Leu Glu Gly Cys Phe
        675                 680                 685

Cys Pro Pro Gly Leu Tyr Met Asp Glu Arg Gly Asp Cys Val Pro Lys
    690                 695                 700

Ala Gln Cys Pro Cys Tyr Tyr Asp Gly Glu Ile Phe Gln Pro Glu Asp
705                 710                 715                 720

Ile Phe Ser Asp His His Thr Met Cys Tyr Cys Glu Asp Gly Phe Met
                725                 730                 735

His Cys Thr Met Ser Gly Val Pro Gly Ser Leu Leu Pro Asp Ala Val
            740                 745                 750

Leu Ser Ser Pro Leu Ser His Arg Ser Lys Arg Ser Leu Ser Cys Arg
        755                 760                 765

Pro Pro Met Val Lys Leu Val Cys Pro Ala Asp Asn Leu Arg Ala Glu
    770                 775                 780

Gly Leu Glu Cys Thr Lys Thr Cys Gln Asn Tyr Asp Leu Glu Cys Met
785                 790                 795                 800

Ser Met Gly Cys Val Ser Gly Cys Leu Cys Pro Pro Gly Met Val Arg
                805                 810                 815

His Glu Asn Arg Cys Val Ala Leu Glu Arg Cys Pro Cys Phe His Gln
            820                 825                 830

Gly Lys Glu Tyr Ala Pro Gly Glu Thr Val Lys Ile Gly Cys Asn Thr
        835                 840                 845

Cys Val Cys Arg Asp Arg Lys Trp Asn Cys Thr Asp His Val Cys Asp
    850                 855                 860

Ala Thr Cys Ser Thr Ile Gly Met Ala His Tyr Leu Thr Phe Asp Gly
```

```
865                 870                 875                 880

Leu Lys Tyr Leu Phe Pro Gly Glu Cys Gln Tyr Val Leu Val Gln Asp
                885                 890                 895

Tyr Cys Gly Ser Asn Pro Gly Thr Phe Arg Ile Leu Val Gly Asn Lys
            900                 905                 910

Gly Cys Ser His Pro Ser Val Lys Cys Lys Lys Arg Val Thr Ile Leu
        915                 920                 925

Val Glu Gly Gly Glu Ile Glu Leu Phe Asp Gly Glu Val Asn Val Lys
    930                 935                 940

Arg Pro Met Lys Asp Glu Thr His Phe Glu Val Val Glu Ser Gly Arg
945                 950                 955                 960

Tyr Ile Ile Leu Leu Leu Gly Lys Ala Leu Ser Val Val Trp Asp Arg
                965                 970                 975

His Leu Ser Ile Ser Val Val Leu Lys Gln Thr Tyr Gln Glu Lys Val
            980                 985                 990

Cys Gly Leu Cys Gly Asn Phe Asp  Gly Ile Gln Asn Asn  Asp Leu Thr
        995                 1000                1005

Ser Ser  Asn Leu Gln Val Glu  Glu Asp Pro Val Asp  Phe Gly Asn
    1010                1015                1020

Ser Trp  Lys Val Ser Ser Gln  Cys Ala Asp Thr Arg  Lys Val Pro
    1025                1030                1035

Leu Asp  Ser Ser Pro Ala Thr  Cys His Asn Asn Ile  Met Lys Gln
    1040                1045                1050

Thr Met  Val Asp Ser Ser Cys  Arg Ile Leu Thr Ser  Asp Val Phe
    1055                1060                1065

Gln Asp  Cys Asn Lys Leu Val  Asp Pro Glu Pro Tyr  Leu Asp Val
    1070                1075                1080
```

```
Cys Ile  Tyr Asp Thr Cys Ser  Cys Glu Ser Ile Gly  Asp Cys Ala
    1085                1090                1095

Cys Phe  Cys Asp Thr Ile Ala  Ala Tyr Ala His Val  Cys Ala Gln
    1100                1105                1110

His Gly  Lys Val Val Thr Trp  Arg Thr Ala Thr Leu  Cys Pro Gln
    1115                1120                1125

Ser Cys  Glu Glu Arg Asn Leu  Arg Glu Asn Gly Tyr  Glu Cys Glu
    1130                1135                1140

Trp Arg  Tyr Asn Ser Cys Ala  Pro Ala Cys Gln Val  Thr Cys Gln
    1145                1150                1155

His Pro  Glu Pro Leu Ala Cys  Pro Val Gln Cys Val  Glu Gly Cys
    1160                1165                1170

His Ala  His Cys Pro Pro Gly  Lys Ile Leu Asp Glu  Leu Leu Gln
    1175                1180                1185

Thr Cys  Val Asp Pro Glu Asp  Cys Pro Val Cys Glu  Val Ala Gly
    1190                1195                1200

Arg Arg  Phe Ala Ser Gly Lys  Lys Val Thr Leu Asn  Pro Ser Asp
    1205                1210                1215

Pro Glu  His Cys Gln Ile Cys  His Cys Asp Val Val  Asn Leu Thr
    1220                1225                1230

Cys Glu  Ala Cys Gln Glu Pro  Gly Gly Leu Val Val  Pro Pro Thr
    1235                1240                1245

Asp Ala  Pro Val Ser Pro Thr  Thr Leu Tyr Val Glu  Asp Ile Ser
    1250                1255                1260

Glu Pro  Pro Leu His Asp Phe  Tyr Cys Ser Arg Leu  Leu Asp Leu
    1265                1270                1275

Val Phe  Leu Leu Asp Gly Ser  Ser Arg Leu Ser Glu  Ala Glu Phe
    1280                1285                1290
```

```
Glu Val  Leu Lys Ala Phe Val  Val Asp Met Met Glu  Arg Leu Arg
    1295                1300                1305

Ile Ser  Gln Lys Trp Val Arg  Val Ala Val Val Glu  Tyr His Asp
    1310                1315                1320

Gly Ser  His Ala Tyr Ile Gly  Leu Lys Asp Arg Lys  Arg Pro Ser
    1325                1330                1335

Glu Leu  Arg Arg Ile Ala Ser  Gln Val Lys Tyr Ala  Gly Ser Gln
    1340                1345                1350

Val Ala  Ser Thr Ser Glu Val  Leu Lys Tyr Thr Leu  Phe Gln Ile
    1355                1360                1365

Phe Ser  Lys Ile Asp Arg Pro  Glu Ala Ser Arg Ile  Ala Leu Leu
    1370                1375                1380

Leu Met  Ala Ser Gln Glu Pro  Gln Arg Met Ser Arg  Asn Phe Val
    1385                1390                1395

Arg Tyr  Val Gln Gly Leu Lys  Lys Lys Lys Val Ile  Val Ile Pro
    1400                1405                1410

Val Gly  Ile Gly Pro His Ala  Asn Leu Lys Gln Ile  Arg Leu Ile
    1415                1420                1425

Glu Lys  Gln Ala Pro Glu Asn  Lys Ala Phe Val Leu  Ser Ser Val
    1430                1435                1440

Asp Glu  Leu Glu Gln Gln Arg  Asp Glu Ile Val Ser  Tyr Leu Cys
    1445                1450                1455

Asp Leu  Ala Pro Glu Ala Pro  Pro Pro Thr Leu Pro  Pro His Met
    1460                1465                1470

Ala Gln  Val Thr Val Gly Pro  Gly Leu Arg Asn Ser  Met Val Leu
    1475                1480                1485

Asp Val  Ala Phe Val Leu Glu  Gly Ser Asp Lys Ile  Gly Glu Ala
    1490                1495                1500
```

```
Asp Phe  Asn Arg Ser Lys Glu  Phe Met Glu Glu Val  Ile Gln Arg
    1505                 1510                 1515

Met Asp  Val Gly Gln Asp Ser  Ile His Val Thr Val  Leu Gln Tyr
    1520                 1525                 1530

Ser Tyr  Met Val Thr Val Glu  Tyr Pro Phe Ser Glu  Ala Gln Ser
    1535                 1540                 1545

Lys Gly  Asp Ile Leu Gln Arg  Val Arg Glu Ile Arg  Tyr Gln Gly
    1550                 1555                 1560

Gly Asn  Arg Thr Asn Thr Gly  Leu Ala Leu Arg Tyr  Leu Ser Asp
    1565                 1570                 1575

His Ser  Phe Leu Val Ser Gln  Gly Asp Arg Glu Gln  Ala Pro Asn
    1580                 1585                 1590

Leu Val  Tyr Met Val Thr Gly  Asn Pro Ala Ser Asp  Glu Ile Lys
    1595                 1600                 1605

Arg Leu  Pro Gly Asp Ile Gln  Val Val Pro Ile Gly  Val Gly Pro
    1610                 1615                 1620

Asn Ala  Asn Val Gln Glu Leu  Glu Arg Ile Gly Trp  Pro Asn Ala
    1625                 1630                 1635

Pro Ile  Leu Ile Gln Asp Phe  Glu Thr Leu Pro Arg  Glu Ala Pro
    1640                 1645                 1650

Asp Leu  Val Leu Gln Arg Cys  Cys Ser Gly Glu Gly  Leu Gln Ile
    1655                 1660                 1665

Pro Thr  Leu Ser Pro Ala Pro  Asp Cys Ser Gln Pro  Leu Asp Val
    1670                 1675                 1680

Ile Leu  Leu Leu Asp Gly Ser  Ser Ser Phe Pro Ala  Ser Tyr Phe
    1685                 1690                 1695

Asp Glu  Met Lys Ser Phe Ala  Lys Ala Phe Ile Ser  Lys Ala Asn
```

```
    1700                1705                1710

Ile Gly  Pro Arg Leu Thr Gln  Val Ser Val Leu Gln  Tyr Gly Ser
    1715                1720                1725

Ile Thr  Thr Ile Asp Val Pro  Trp Asn Val Val Pro  Glu Lys Ala
    1730                1735                1740

His Leu  Leu Ser Leu Val Asp  Val Met Gln Arg Glu  Gly Gly Pro
    1745                1750                1755

Ser Gln  Ile Gly Asp Ala Leu  Gly Phe Ala Val Arg  Tyr Leu Thr
    1760                1765                1770

Ser Glu  Met His Gly Ala Arg  Pro Gly Ala Ser Lys  Ala Val Val
    1775                1780                1785

Ile Leu  Val Thr Asp Val Ser  Val Asp Ser Val Asp  Ala Ala Ala
    1790                1795                1800

Asp Ala  Ala Arg Ser Asn Arg  Val Thr Val Phe Pro  Ile Gly Ile
    1805                1810                1815

Gly Asp  Arg Tyr Asp Ala Ala  Gln Leu Arg Ile Leu  Ala Gly Pro
    1820                1825                1830

Ala Gly  Asp Ser Asn Val Val  Lys Leu Gln Arg Ile  Glu Asp Leu
    1835                1840                1845

Pro Thr  Met Val Thr Leu Gly  Asn Ser Phe Leu His  Lys Leu Cys
    1850                1855                1860

Ser Gly  Phe Val Arg Ile Cys  Met Asp Glu Asp Gly  Asn Glu Lys
    1865                1870                1875

Arg Pro  Gly Asp Val Trp Thr  Leu Pro Asp Gln Cys  His Thr Val
    1880                1885                1890

Thr Cys  Gln Pro Asp Gly Gln  Thr Leu Leu Lys Ser  His Arg Val
    1895                1900                1905
```

```
Asn Cys  Asp Arg Gly Leu Arg  Pro Ser Cys Pro Asn  Ser Gln Ser
    1910                1915                1920

Pro Val  Lys Val Glu Glu Thr  Cys Gly Cys Arg Trp  Thr Cys Pro
    1925                1930                1935

Cys Val  Cys Thr Gly Ser Ser  Thr Arg His Ile Val  Thr Phe Asp
    1940                1945                1950

Gly Gln  Asn Phe Lys Leu Thr  Gly Ser Cys Ser Tyr  Val Leu Phe
    1955                1960                1965

Gln Asn  Lys Glu Gln Asp Leu  Glu Val Ile Leu His  Asn Gly Ala
    1970                1975                1980

Cys Ser  Pro Gly Ala Arg Gln  Gly Cys Met Lys Ser  Ile Glu Val
    1985                1990                1995

Lys His  Ser Ala Leu Ser Val  Glu Leu His Ser Asp  Met Glu Val
    2000                2005                2010

Thr Val  Asn Gly Arg Leu Val  Ser Val Pro Tyr Val  Gly Gly Asn
    2015                2020                2025

Met Glu  Val Asn Val Tyr Gly  Ala Ile Met His Glu  Val Arg Phe
    2030                2035                2040

Asn His  Leu Gly His Ile Phe  Thr Phe Thr Pro Gln  Asn Asn Glu
    2045                2050                2055

Phe Gln  Leu Gln Leu Ser Pro  Lys Thr Phe Ala Ser  Lys Thr Tyr
    2060                2065                2070

Gly Leu  Cys Gly Ile Cys Asp  Glu Asn Gly Ala Asn  Asp Phe Met
    2075                2080                2085

Leu Arg  Asp Gly Thr Val Thr  Thr Asp Trp Lys Thr  Leu Val Gln
    2090                2095                2100

Glu Trp  Thr Val Gln Arg Pro  Gly Gln Thr Cys Gln  Pro Ile Leu
    2105                2110                2115
```

```
Glu Glu  Gln Cys Leu Val Pro  Asp Ser Ser His Cys  Gln Val Leu
    2120                2125                2130

Leu Leu  Pro Leu Phe Ala Glu  Cys His Lys Val Leu  Ala Pro Ala
    2135                2140                2145

Thr Phe  Tyr Ala Ile Cys Gln  Gln Asp Ser Cys His  Gln Glu Gln
    2150                2155                2160

Val Cys  Glu Val Ile Ala Ser  Tyr Ala His Leu Cys  Arg Thr Asn
    2165                2170                2175

Gly Val  Cys Val Asp Trp Arg  Thr Pro Asp Phe Cys  Ala Met Ser
    2180                2185                2190

Cys Pro  Pro Ser Leu Val Tyr  Asn His Cys Glu His  Gly Cys Pro
    2195                2200                2205

Arg His  Cys Asp Gly Asn Val  Ser Ser Cys Gly Asp  His Pro Ser
    2210                2215                2220

Glu Gly  Cys Phe Cys Pro Pro  Asp Lys Val Met Leu  Glu Gly Ser
    2225                2230                2235

Cys Val  Pro Glu Glu Ala Cys  Thr Gln Cys Ile Gly  Glu Asp Gly
    2240                2245                2250

Val Gln  His Gln Phe Leu Glu  Ala Trp Val Pro Asp  His Gln Pro
    2255                2260                2265

Cys Gln  Ile Cys Thr Cys Leu  Ser Gly Arg Lys Val  Asn Cys Thr
    2270                2275                2280

Thr Gln  Pro Cys Pro Thr Ala  Lys Ala Pro Thr Cys  Gly Leu Cys
    2285                2290                2295

Glu Val  Ala Arg Leu Arg Gln  Asn Ala Asp Gln Cys  Cys Pro Glu
    2300                2305                2310

Tyr Glu  Cys Val Cys Asp Pro  Val Ser Cys Asp Leu  Pro Pro Val
    2315                2320                2325
```

```
Pro His  Cys Glu Arg Gly Leu  Gln Pro Thr Leu Thr  Asn Pro Gly
    2330                2335                2340

Glu Cys  Arg Pro Asn Phe Thr  Cys Ala Cys Arg Lys  Glu Glu Cys
    2345                2350                2355

Lys Arg  Val Ser Pro Pro Ser  Cys Pro Pro His Arg  Leu Pro Thr
    2360                2365                2370

Leu Arg  Lys Thr Gln Cys Cys  Asp Glu Tyr Glu Cys  Ala Cys Asn
    2375                2380                2385

Cys Val  Asn Ser Thr Val Ser  Cys Pro Leu Gly Tyr  Leu Ala Ser
    2390                2395                2400

Thr Ala  Thr Asn Asp Cys Gly  Cys Thr Thr Thr Thr  Cys Leu Pro
    2405                2410                2415

Asp Lys  Val Cys Val His Arg  Ser Thr Ile Tyr Pro  Val Gly Gln
    2420                2425                2430

Phe Trp  Glu Glu Gly Cys Asp  Val Cys Thr Cys Thr  Asp Met Glu
    2435                2440                2445

Asp Ala  Val Met Gly Leu Arg  Val Ala Gln Cys Ser  Gln Lys Pro
    2450                2455                2460

Cys Glu  Asp Ser Cys Arg Ser  Gly Phe Thr Tyr Val  Leu His Glu
    2465                2470                2475

Gly Glu  Cys Cys Gly Arg Cys  Leu Pro Ser Ala Cys  Glu Val Val
    2480                2485                2490

Thr Gly  Ser Pro Arg Gly Asp  Ser Gln Ser Ser Trp  Lys Ser Val
    2495                2500                2505

Gly Ser  Gln Trp Ala Ser Pro  Glu Asn Pro Cys Leu  Ile Asn Glu
    2510                2515                2520

Cys Val  Arg Val Lys Glu Glu  Val Phe Ile Gln Gln  Arg Asn Val
```

```
    2525                2530                2535

Ser Cys  Pro Gln Leu Glu Val  Pro Val Cys Pro Ser  Gly Phe Gln
    2540                2545                2550

Leu Ser  Cys Lys Thr Ser Ala  Cys Cys Pro Ser Cys  Arg Cys Glu
    2555                2560                2565

Arg Met  Glu Ala Cys Met Leu  Asn Gly Thr Val Ile  Gly Pro Gly
    2570                2575                2580

Lys Thr  Val Met Ile Asp Val  Cys Thr Thr Cys Arg  Cys Met Val
    2585                2590                2595

Gln Val  Gly Val Ile Ser Gly  Phe Lys Leu Glu Cys  Arg Lys Thr
    2600                2605                2610

Thr Cys  Asn Pro Cys Pro Leu  Gly Tyr Lys Glu Glu  Asn Asn Thr
    2615                2620                2625

Gly Glu  Cys Cys Gly Arg Cys  Leu Pro Thr Ala Cys  Thr Ile Gln
    2630                2635                2640

Leu Arg  Gly Gly Gln Ile Met  Thr Leu Lys Arg Asp  Glu Thr Leu
    2645                2650                2655

Gln Asp  Gly Cys Asp Thr His  Phe Cys Lys Val Asn  Glu Arg Gly
    2660                2665                2670

Glu Tyr  Phe Trp Glu Lys Arg  Val Thr Gly Cys Pro  Pro Phe Asp
    2675                2680                2685

Glu His  Lys Cys Leu Ala Glu  Gly Gly Lys Ile Met  Lys Ile Pro
    2690                2695                2700

Gly Thr  Cys Cys Asp Thr Cys  Glu Glu Pro Glu Cys  Asn Asp Ile
    2705                2710                2715

Thr Ala  Arg Leu Gln Tyr Val  Lys Val Gly Ser Cys  Lys Ser Glu
    2720                2725                2730
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Val Glu  Val Asp Ile His Tyr  Cys Gln Gly Lys Cys  Ala Ser Lys
    2735                 2740                 2745

Ala Met  Tyr Ser Ile Asp Ile  Asn Asp Val Gln Asp  Gln Cys Ser
    2750                 2755                 2760

Cys Cys  Ser Pro Thr Arg Thr  Glu Pro Met Gln Val  Ala Leu His
    2765                 2770                 2775

Cys Thr  Asn Gly Ser Val Val  Tyr His Glu Val Leu  Asn Ala Met
    2780                 2785                 2790

Glu Cys  Lys Cys Ser Pro Arg  Lys Cys Ser Lys
    2795                 2800

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<213>  Artificial Sequence

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Gly

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<213> Artificial Sequence

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Tyr Thr Phe

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<212> PRT
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe Ser Tyr Asn
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Pro Met Gly Trp Phe Arg Gln Ala Pro Gly Lys Gly Arg Glu Leu Val
35 40 45

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

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

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

Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg Thr Leu Pro
100 105 110

Ser Glu Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
115 120 125

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Ala Ala Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
    130                 135                 140

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe
145                 150                 155                 160

Ser Tyr Asn Pro Met Gly Trp Phe Arg Gln Ala Pro Gly Lys Gly Arg
                165                 170                 175

Glu Leu Val Ala Ala Ile Ser Arg Thr Gly Gly Ser Thr Tyr Tyr Pro
            180                 185                 190

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

Met Val Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
    210                 215                 220

Tyr Tyr Cys Ala Ala Ala Gly Val Arg Ala Glu Asp Gly Arg Val Arg
225                 230                 235                 240

Thr Leu Pro Ser Glu Tyr Thr Phe Trp Gly Gln Gly Thr Gln Val Thr
                245                 250                 255

Val Ser Ser Ala
            260
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