SEQUENCE LISTING

<110> Bioverativ Therapeutics Inc.

<120> Methods of treating hemophilia A

<130> 612297: SA9-461PC

<150> US 62/673,670
<151> 2018-05-18

<150> US 62/712,880
<151> 2018-07-31

<150> US 62/773,785
<151> 2018-11-30

<150> US 62/801,576
<151> 2019-02-05

<160> 218

<170> PatentIn version 3.5

<210> 1
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 1

Thr Gln Ser Phe Asn Asp Phe Thr Arg
1 5

<210> 2
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<400> 2

Pro Arg Ser Phe Ser Gln Asn Gly Thr Ser Glu Ser Ala Thr Pro Glu
1 5 10 15

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
20 25 30

```
Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
        35                  40                  45

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
    50                  55                  60

Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
65                  70                  75                  80

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser
                85                  90                  95

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
            100                 105                 110

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
        115                 120                 125

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly
    130                 135                 140

Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly
145                 150                 155                 160

Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
                165                 170                 175

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser
            180                 185                 190

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
        195                 200                 205

Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
    210                 215                 220

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu
225                 230                 235                 240

Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
                245                 250                 255
```

Ser Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
260 265 270

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
275 280 285

Pro Ser Glu Gly Ser Ala Pro Ala Ser Ser Glu Ile Thr Arg
290 295 300

<210> 3
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 3

Ser Val Ser Gln Thr Ser Lys Leu Thr Arg
1 5 10

<210> 4
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 4

Asp Phe Leu Ala Glu Gly Gly Gly Val Arg
1 5 10

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

<220>
<223> Linker

<400> 5

Thr Thr Lys Ile Lys Pro Arg
1 5

<210> 6
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 6

Leu Val Pro Arg Gly
1   5

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

<220>
<223> Linker

<400> 7

Ala Leu Arg Pro Arg
1   5

<210> 8
<211> 288
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN AE288

<400> 8

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
1   5   10   15

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
            20   25   30

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
        35   40   45

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr
    50   55   60

```
Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr
65                  70                  75                  80

Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
                85                  90                  95

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu
            100                 105                 110

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr
        115                 120                 125

Ser Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
    130                 135                 140

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu
145                 150                 155                 160

Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro
                165                 170                 175

Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
            180                 185                 190

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro
        195                 200                 205

Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr
    210                 215                 220

Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
225                 230                 235                 240

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro
                245                 250                 255

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
            260                 265                 270

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
        275                 280                 285
```

<210> 9
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN AE42

<400> 9

Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
1 5 10 15

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
20 25 30

Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser
35 40

<210> 10
<211> 78
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN AE72

<400> 10

Gly Ala Pro Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
1 5 10 15

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
20 25 30

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
35 40 45

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
50 55 60

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser
65 70 75

<210> 11
<211> 143

<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN AE144

<400> 11

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu
1 5 10 15

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
20 25 30

Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
35 40 45

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro
50 55 60

Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly
65 70 75 80

Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
85 90 95

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu
100 105 110

Ser Ala Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
115 120 125

Glu Thr Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
130 135 140

<210> 12
<211> 56
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN VWF057

<400> 12

Thr Ser Thr Glu Glu Gly Ala Ser Ser Gly Gly Gly Gly Ser Gly Gly

1 5 10 15

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
20 25 30

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Leu Val Pro Arg
35 40 45

Gly Ser Gly Gly Asp Lys Thr His
50 55

<210> 13
<211> 46
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN VWF059

<400> 13

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

Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
20 25 30

Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Asp Lys Thr His
35 40 45

<210> 14
<211> 144
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN AG144

<400> 14

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr
1 5 10 15

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser Thr
20 25 30

```
Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro
        35                  40                  45

Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro
    50                  55                  60

Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
65                  70                  75                  80

Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro
                85                  90                  95

Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Pro
            100                 105                 110

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

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


<210>  15
<211>  864
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  XTEN AE864

<400>  15

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu
1               5                   10                  15

Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu
            20                  25                  30

Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
        35                  40                  45

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
    50                  55                  60

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
```

65 70 75 80

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
85 90 95

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala
100 105 110

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro
115 120 125

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
130 135 140

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala
145 150 155 160

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu
165 170 175

Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
180 185 190

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr
195 200 205

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
210 215 220

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
225 230 235 240

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
245 250 255

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
260 265 270

Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
275 280 285

```
Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu
    290                 295                 300

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
305                 310                 315                 320

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
                325                 330                 335

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
            340                 345                 350

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu
        355                 360                 365

Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
    370                 375                 380

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
385                 390                 395                 400

Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr
                405                 410                 415

Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
            420                 425                 430

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
        435                 440                 445

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
    450                 455                 460

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
465                 470                 475                 480

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr
                485                 490                 495

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
            500                 505                 510
```

```
Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
        515                 520                 525

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala
    530                 535                 540

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro
545                 550                 555                 560

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
                565                 570                 575

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
            580                 585                 590

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
        595                 600                 605

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
    610                 615                 620

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr
625                 630                 635                 640

Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr
                645                 650                 655

Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
            660                 665                 670

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu
        675                 680                 685

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr
    690                 695                 700

Ser Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
705                 710                 715                 720

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu
                725                 730                 735
```

```
Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro
            740                 745                 750


Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
        755                 760                 765


Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro
    770                 775                 780


Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr
785                 790                 795                 800


Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
                805                 810                 815


Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro
            820                 825                 830


Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
        835                 840                 845


Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
    850                 855                 860


<210>  16
<211>  576
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  XTEN AE576

<400>  16

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu
1               5                   10                  15


Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu
            20                  25                  30


Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
        35                  40                  45
```

```
Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
    50                  55                  60

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
65                  70                  75                  80

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
                85                  90                  95

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala
            100                 105                 110

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro
        115                 120                 125

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
    130                 135                 140

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala
145                 150                 155                 160

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu
                165                 170                 175

Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
            180                 185                 190

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr
        195                 200                 205

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
    210                 215                 220

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
225                 230                 235                 240

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
                245                 250                 255

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
            260                 265                 270
```

```
Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
        275                 280                 285

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu
    290                 295                 300

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
305                 310                 315                 320

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
                325                 330                 335

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
            340                 345                 350

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu
        355                 360                 365

Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
    370                 375                 380

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
385                 390                 395                 400

Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr
                405                 410                 415

Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
            420                 425                 430

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
        435                 440                 445

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
    450                 455                 460

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
465                 470                 475                 480

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr
```

```
                485                 490                 495

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
            500                 505                 510

Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
        515                 520                 525

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala
    530                 535                 540

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro
545                 550                 555                 560

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
                565                 570                 575
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<210> 17
<211> 864
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN AG864

<400> 17

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Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Pro
1               5                   10                  15

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser Thr
            20                  25                  30

Gly Thr Gly Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro
        35                  40                  45

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro
    50                  55                  60

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser
65                  70                  75                  80

Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro
                85                  90                  95
```

```
Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Thr Pro Gly
            100                 105                 110

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

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

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

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
                165                 170                 175

Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro
            180                 185                 190

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro
        195                 200                 205

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser Thr
    210                 215                 220

Gly Thr Gly Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro
225                 230                 235                 240

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ala Ser Pro
                245                 250                 255

Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
            260                 265                 270

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
        275                 280                 285

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ala Ser Pro
    290                 295                 300

Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
```

```
305                 310                 315                 320

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
                325                 330                 335

Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Thr Pro Gly
            340                 345                 350

Ser Gly Thr Ala Ser Ser Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
        355                 360                 365

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
    370                 375                 380

Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Thr
385                 390                 395                 400

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
                405                 410                 415

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
            420                 425                 430

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr
        435                 440                 445

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
    450                 455                 460

Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro
465                 470                 475                 480

Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro
                485                 490                 495

Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
            500                 505                 510

Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro
        515                 520                 525
```

```
Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro
    530                 535                 540

Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
545                 550                 555                 560

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
                565                 570                 575

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr
            580                 585                 590

Pro Ser Gly Ala Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala
        595                 600                 605

Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro
    610                 615                 620

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr
625                 630                 635                 640

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
                645                 650                 655

Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro
            660                 665                 670

Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro
        675                 680                 685

Gly Thr Ser Ser Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala
    690                 695                 700

Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro
705                 710                 715                 720

Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro
                725                 730                 735

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser
            740                 745                 750
```

```
Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
        755                 760                 765


Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro
    770                 775                 780


Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser
785                 790                 795                 800


Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro
                805                 810                 815


Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr
            820                 825                 830


Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
        835                 840                 845


Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
    850                 855                 860


<210>  18
<211>  576
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  XTEN AG576

<400>  18

Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser
1               5                   10                  15


Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser
            20                  25                  30


Thr Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly
        35                  40                  45


Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser
    50                  55                  60
```

```
Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser
65                  70                  75                  80


Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser
                85                  90                  95


Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Thr Pro
            100                 105                 110


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


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


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


Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Thr Pro Gly Ser Gly Thr
                165                 170                 175


Ala Ser Ser Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser
            180                 185                 190


Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser
        195                 200                 205


Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly
    210                 215                 220


Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser
225                 230                 235                 240


Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Thr Pro
                245                 250                 255


Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly
            260                 265                 270


Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser
        275                 280                 285
```

```
Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser
    290                 295                 300

Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser
305                 310                 315                 320

Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser
                325                 330                 335

Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ala Ser
            340                 345                 350

Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser
        355                 360                 365

Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser
    370                 375                 380

Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Thr Pro
385                 390                 395                 400

Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly
                405                 410                 415

Ala Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser
            420                 425                 430

Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Thr Pro
        435                 440                 445

Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly
    450                 455                 460

Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser
465                 470                 475                 480

Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser
                485                 490                 495

Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser
            500                 505                 510
```

```
Ser Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser
        515                 520                 525


Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser
    530                 535                 540


Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser
545                 550                 555                 560


Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser
                565                 570                 575


<210>  19
<211>  288
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  XTEN AG288

<400>  19

Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser
1               5                   10                  15


Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr
            20                  25                  30


Ala Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser
        35                  40                  45


Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser
    50                  55                  60


Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr
65                  70                  75                  80


Ala Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser
                85                  90                  95


Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser
            100                 105                 110
```

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

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

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

Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser
165 170 175

Thr Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly
180 185 190

Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser
195 200 205

Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly
210 215 220

Ala Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly
225 230 235 240

Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser
245 250 255

Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Thr Pro Gly Ser Gly Thr
260 265 270

Ala Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser
275 280 285

<210> 20
<211> 8442
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<213> Homo sapiens

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Ser Met Tyr Ser Phe Ala Gly Tyr Cys Ser Tyr Leu Leu Ala Gly Gly
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Cys Gln Lys Arg Ser Phe Ser Ile Ile Gly Asp Phe Gln Asn Gly Lys
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Arg Val Ser Leu Ser Val Tyr Leu Gly Glu Phe Phe Asp Ile His Leu
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Phe Val Asn Gly Thr Val Thr Gln Gly Asp Gln Arg Val Ser Met Pro
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Tyr Ala Ser Lys Gly Leu Tyr Leu Glu Thr Glu Ala Gly Tyr Tyr Lys
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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
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Cys Gln Leu Leu Lys Ser Thr Ser Val Phe Ala Arg Cys His Pro Leu
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Val Asp Pro Glu Pro Phe Val Ala Leu Cys Glu Lys Thr Leu Cys Glu
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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
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Ser Ala Cys Ser Pro Val Cys Pro Ala Gly Met Glu Tyr Arg Gln Cys
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Val Ser Pro Cys Ala Arg Thr Cys Gln Ser Leu His Ile Asn Glu Met
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Cys Gln Glu Arg Cys Val Asp Gly Cys Ser Cys Pro Glu Gly Gln Leu
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Leu Asp Glu Gly Leu Cys Val Glu Ser Thr Glu Cys Pro Cys Val His
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Ser Gly Lys Arg Tyr Pro Pro Gly Thr Ser Leu Ser Arg Asp Cys Asn
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Thr Cys Ile Cys Arg Asn Ser Gln Trp Ile Cys Ser Asn Glu Glu Cys
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Pro Gly Glu Cys Leu Val Thr Gly Gln Ser His Phe Lys Ser Phe Asp
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Asp Cys Gln Asp His Ser Phe Ser Ile Val Ile Glu Thr Val Gln Cys
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Ala Asp Asp Arg Asp Ala Val Cys Thr Arg Ser Val Thr Val Arg Leu
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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
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Asp Leu Gln Met Asp Trp Asp Gly Arg Gly Arg Leu Leu Val Lys Leu
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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
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Thr Arg Phe Ser Glu Glu Ala Cys Ala Val Leu Thr Ser Pro Thr Phe
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Glu Ala Cys His Arg Ala Val Ser Pro Leu Pro Tyr Leu Arg Asn Cys
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Arg Tyr Asp Val Cys Ser Cys Ser Asp Gly Arg Glu Cys Leu Cys Gly
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Ala Leu Ala Ser Tyr Ala Ala Ala Cys Ala Gly Arg Gly Val Arg Val
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Ala Trp Arg Glu Pro Gly Arg Cys Glu Leu Asn Cys Pro Lys Gly Gln
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Val Tyr Leu Gln Cys Gly Thr Pro Cys Asn Leu Thr Cys Arg Ser Leu
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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
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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
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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
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Trp Arg  Tyr Asn Ser Cys Ala  Pro Ala Cys Gln Val  Thr Cys Gln
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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
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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
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Glu Leu  Arg Arg Ile Ala Ser  Gln Val Lys Tyr Ala  Gly Ser Gln
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Val Ala  Ser Thr Ser Glu Val  Leu Lys Tyr Thr Leu  Phe Gln Ile
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Phe Ser  Lys Ile Asp Arg Pro  Glu Ala Ser Arg Ile  Ala Leu Leu
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Leu Met  Ala Ser Gln Glu Pro  Gln Arg Met Ser Arg  Asn Phe Val
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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
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```
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 Asp Met
    1460                1465                1470

Ala Gln  Val Thr Val Gly Pro  Gly Leu Leu Gly Val  Ser Thr Leu
    1475                1480                1485

Gly Pro  Lys Arg Asn Ser Met  Val Leu Asp Val Ala  Phe Val Leu
    1490                1495                1500

Glu Gly  Ser Asp Lys Ile Gly  Glu Ala Asp Phe Asn  Arg Ser Lys
    1505                1510                1515

Glu Phe  Met Glu Glu Val Ile  Gln Arg Met Asp Val  Gly Gln Asp
    1520                1525                1530

Ser Ile  His Val Thr Val Leu  Gln Tyr Ser Tyr Met  Val Thr Val
    1535                1540                1545

Glu Tyr  Pro Phe Ser Glu Ala  Gln Ser Lys Gly Asp  Ile Leu Gln
    1550                1555                1560

Arg Val  Arg Glu Ile Arg Tyr  Gln Gly Gly Asn Arg  Thr Asn Thr
    1565                1570                1575

Gly Leu  Ala Leu Arg Tyr Leu  Ser Asp His Ser Phe  Leu Val Ser
    1580                1585                1590

Gln Gly  Asp Arg Glu Gln Ala  Pro Asn Leu Val Tyr  Met Val Thr
    1595                1600                1605

Gly Asn  Pro Ala Ser Asp Glu  Ile Lys Arg Leu Pro  Gly Asp Ile
    1610                1615                1620

Gln Val  Val Pro Ile Gly Val  Gly Pro Asn Ala Asn  Val Gln Glu
    1625                1630                1635

Leu Glu  Arg Ile Gly Trp Pro  Asn Ala Pro Ile Leu  Ile Gln Asp
    1640                1645                1650
```

```
Phe Glu  Thr Leu Pro Arg Glu  Ala Pro Asp Leu Val  Leu Gln Arg
    1655                1660                1665

Cys Cys  Ser Gly Glu Gly Leu  Gln Ile Pro Thr Leu  Ser Pro Ala
    1670                1675                1680

Pro Asp  Cys Ser Gln Pro Leu  Asp Val Ile Leu Leu  Leu Asp Gly
    1685                1690                1695

Ser Ser  Ser Phe Pro Ala Ser  Tyr Phe Asp Glu Met  Lys Ser Phe
    1700                1705                1710

Ala Lys  Ala Phe Ile Ser Lys  Ala Asn Ile Gly Pro  Arg Leu Thr
    1715                1720                1725

Gln Val  Ser Val Leu Gln Tyr  Gly Ser Ile Thr Thr  Ile Asp Val
    1730                1735                1740

Pro Trp  Asn Val Val Pro Glu  Lys Ala His Leu Leu  Ser Leu Val
    1745                1750                1755

Asp Val  Met Gln Arg Glu Gly  Gly Pro Ser Gln Ile  Gly Asp Ala
    1760                1765                1770

Leu Gly  Phe Ala Val Arg Tyr  Leu Thr Ser Glu Met  His Gly Ala
    1775                1780                1785

Arg Pro  Gly Ala Ser Lys Ala  Val Val Ile Leu Val  Thr Asp Val
    1790                1795                1800

Ser Val  Asp Ser Val Asp Ala  Ala Ala Asp Ala Ala  Arg Ser Asn
    1805                1810                1815

Arg Val  Thr Val Phe Pro Ile  Gly Ile Gly Asp Arg  Tyr Asp Ala
    1820                1825                1830

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

Val Lys  Leu Gln Arg Ile Glu  Asp Leu Pro Thr Met  Val Thr Leu
    1850                1855                1860
```

```
Gly Asn  Ser Phe Leu His Lys  Leu Cys Ser Gly Phe  Val Arg Ile
    1865                 1870                 1875

Cys Met  Asp Glu Asp Gly Asn  Glu Lys Arg Pro Gly  Asp Val Trp
    1880                 1885                 1890

Thr Leu  Pro Asp Gln Cys His  Thr Val Thr Cys Gln  Pro Asp Gly
    1895                 1900                 1905

Gln Thr  Leu Leu Lys Ser His  Arg Val Asn Cys Asp  Arg Gly Leu
    1910                 1915                 1920

Arg Pro  Ser Cys Pro Asn Ser  Gln Ser Pro Val Lys  Val Glu Glu
    1925                 1930                 1935

Thr Cys  Gly Cys Arg Trp Thr  Cys Pro Cys Val Cys  Thr Gly Ser
    1940                 1945                 1950

Ser Thr  Arg His Ile Val Thr  Phe Asp Gly Gln Asn  Phe Lys Leu
    1955                 1960                 1965

Thr Gly  Ser Cys Ser Tyr Val  Leu Phe Gln Asn Lys  Glu Gln Asp
    1970                 1975                 1980

Leu Glu  Val Ile Leu His Asn  Gly Ala Cys Ser Pro  Gly Ala Arg
    1985                 1990                 1995

Gln Gly  Cys Met Lys Ser Ile  Glu Val Lys His Ser  Ala Leu Ser
    2000                 2005                 2010

Val Glu  Xaa His Ser Asp Met  Glu Val Thr Val Asn  Gly Arg Leu
    2015                 2020                 2025

Val Ser  Val Pro Tyr Val Gly  Gly Asn Met Glu Val  Asn Val Tyr
    2030                 2035                 2040

Gly Ala  Ile Met His Glu Val  Arg Phe Asn His Leu  Gly His Ile
    2045                 2050                 2055

Phe Thr  Phe Thr Pro Gln Asn  Asn Glu Phe Gln Leu  Gln Leu Ser
```

```
    2060                2065                2070

Pro Lys  Thr Phe Ala Ser Lys  Thr Tyr Gly Leu Cys  Gly Ile Cys
    2075                2080                2085

Asp Glu  Asn Gly Ala Asn Asp  Phe Met Leu Arg Asp  Gly Thr Val
    2090                2095                2100

Thr Thr  Asp Trp Lys Thr Leu  Val Gln Glu Trp Thr  Val Gln Arg
    2105                2110                2115

Pro Gly  Gln Thr Cys Gln Pro  Ile Leu Glu Glu Gln  Cys Leu Val
    2120                2125                2130

Pro Asp  Ser Ser His Cys Gln  Val Leu Leu Leu Pro  Leu Phe Ala
    2135                2140                2145

Glu Cys  His Lys Val Leu Ala  Pro Ala Thr Phe Tyr  Ala Ile Cys
    2150                2155                2160

Gln Gln  Asp Ser Cys His Gln  Glu Gln Val Cys Glu  Val Ile Ala
    2165                2170                2175

Ser Tyr  Ala His Leu Cys Arg  Thr Asn Gly Val Cys  Val Asp Trp
    2180                2185                2190

Arg Thr  Pro Asp Phe Cys Ala  Met Ser Cys Pro Pro  Ser Leu Val
    2195                2200                2205

Tyr Asn  His Cys Glu His Gly  Cys Pro Arg His Cys  Asp Gly Asn
    2210                2215                2220

Val Ser  Ser Cys Gly Asp His  Pro Ser Glu Gly Cys  Phe Cys Pro
    2225                2230                2235

Pro Asp  Lys Val Met Leu Glu  Gly Ser Cys Val Pro  Glu Glu Ala
    2240                2245                2250

Cys Thr  Gln Cys Ile Gly Glu  Asp Gly Val Gln His  Gln Phe Leu
    2255                2260                2265
```

```
Glu Ala  Trp Val Pro Asp His  Gln Pro Cys Gln Ile  Cys Thr Cys
    2270                 2275                 2280

Leu Ser  Gly Arg Lys Val Asn  Cys Thr Thr Gln Pro  Cys Pro Thr
    2285                 2290                 2295

Ala Lys  Ala Pro Thr Cys Gly  Leu Cys Glu Val Ala  Arg Leu Arg
    2300                 2305                 2310

Gln Asn  Ala Asp Gln Cys Cys  Pro Glu Tyr Glu Cys  Val Cys Asp
    2315                 2320                 2325

Pro Val  Ser Cys Asp Leu Pro  Pro Val Pro His Cys  Glu Arg Gly
    2330                 2335                 2340

Leu Gln  Pro Thr Leu Thr Asn  Pro Gly Glu Cys Arg  Pro Asn Phe
    2345                 2350                 2355

Thr Cys  Ala Cys Arg Lys Glu  Glu Cys Lys Arg Val  Ser Pro Pro
    2360                 2365                 2370

Ser Cys  Pro Pro His Arg Leu  Pro Thr Leu Arg Lys  Thr Gln Cys
    2375                 2380                 2385

Cys Asp  Glu Tyr Glu Cys Ala  Cys Asn Cys Val Asn  Ser Thr Val
    2390                 2395                 2400

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

Gly Cys  Thr Thr Thr Thr Cys  Leu Pro Asp Lys Val  Cys Val His
    2420                 2425                 2430

Arg Ser  Thr Ile Tyr Pro Val  Gly Gln Phe Trp Glu  Glu Gly Cys
    2435                 2440                 2445

Asp Val  Cys Thr Cys Thr Asp  Met Glu Asp Ala Val  Met Gly Leu
    2450                 2455                 2460

Arg Val  Ala Gln Cys Ser Gln  Lys Pro Cys Glu Asp  Ser Cys Arg
    2465                 2470                 2475
```

```
Ser Gly  Phe Thr Tyr Val Leu  His Glu Gly Glu Cys  Cys Gly Arg
    2480                2485                2490

Cys Leu  Pro Ser Ala Cys Glu  Val Val Thr Gly Ser  Pro Arg Gly
    2495                2500                2505

Asp Ser  Gln Ser Ser Trp Lys  Ser Val Gly Ser Gln  Trp Ala Ser
    2510                2515                2520

Pro Glu  Asn Pro Cys Leu Ile  Asn Glu Cys Val Arg  Val Lys Glu
    2525                2530                2535

Glu Val  Phe Ile Gln Gln Arg  Asn Val Ser Cys Pro  Gln Leu Glu
    2540                2545                2550

Val Pro  Val Cys Pro Ser Gly  Phe Gln Leu Ser Cys  Lys Thr Ser
    2555                2560                2565

Ala Cys  Cys Pro Ser Cys Arg  Cys Glu Arg Met Glu  Ala Cys Met
    2570                2575                2580

Leu Asn  Gly Thr Val Ile Gly  Pro Gly Lys Thr Val  Met Ile Asp
    2585                2590                2595

Val Cys  Thr Thr Cys Arg Cys  Met Val Gln Val Gly  Val Ile Ser
    2600                2605                2610

Gly Phe  Lys Leu Glu Cys Arg  Lys Thr Thr Cys Asn  Pro Cys Pro
    2615                2620                2625

Leu Gly  Tyr Lys Glu Glu Asn  Asn Thr Gly Glu Cys  Cys Gly Arg
    2630                2635                2640

Cys Leu  Pro Thr Ala Cys Thr  Ile Gln Leu Arg Gly  Gly Gln Ile
    2645                2650                2655

Met Thr  Leu Lys Arg Asp Glu  Thr Leu Gln Asp Gly  Cys Asp Thr
    2660                2665                2670

His Phe  Cys Lys Val Asn Glu  Arg Gly Glu Tyr Phe  Trp Glu Lys
    2675                2680                2685
```

```
Arg Val  Thr Gly Cys Pro Pro  Phe Asp Glu His Lys  Cys Leu Ala
    2690                2695                2700


Glu Gly  Gly Lys Ile Met Lys  Ile Pro Gly Thr Cys  Cys Asp Thr
    2705                2710                2715


Cys Glu  Glu Pro Glu Cys Asn  Asp Ile Thr Ala Arg  Leu Gln Tyr
    2720                2725                2730


Val Lys  Val Gly Ser Cys Lys  Ser Glu Val Glu Val  Asp Ile His
    2735                2740                2745


Tyr Cys  Gln Gly Lys Cys Ala  Ser Lys Ala Met Tyr  Ser Ile Asp
    2750                2755                2760


Ile Asn  Asp Val Gln Asp Gln  Cys Ser Cys Cys Ser  Pro Thr Arg
    2765                2770                2775


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


Val Tyr  His Glu Val Leu Asn  Ala Met Glu Cys Lys  Cys Ser Pro
    2795                2800                2805


Arg Lys  Cys Ser Lys
    2810


<210>  22
<211>  45
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  pSYN VWF059A

<400>  22

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


Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn
            20                  25                  30
```

Asn Ala Ile Glu Pro Arg Ser Phe Ser Asp Lys Thr His
        35   40   45

<210> 23
<211> 54
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN VWF073

<400> 23

Thr Ser Thr Glu Glu Gly Ala Ser Ser Gly Gly Gly Gly Ser Gly Gly
1   5   10   15

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
            20   25   30

Gly Ser Gly Gly Gly Gly Ser Ile Glu Pro Arg Ser Phe Ser Gly Ser
        35   40   45

Gly Gly Asp Lys Thr His
    50

<210> 24
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Family AD

<400> 24

Gly Glu Ser Pro Gly Gly Ser Ser Gly Ser Glu Ser
1   5   10

<210> 25
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Family AD

<400> 25

Gly Ser Glu Gly Ser Ser Gly Pro Gly Glu Ser Ser
1   5   10

<210> 26
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Family AD

<400> 26

Gly Ser Ser Glu Ser Gly Ser Ser Glu Gly Gly Pro
1   5   10

<210> 27
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Family AD

<400> 27

Gly Ser Gly Gly Glu Pro Ser Glu Ser Gly Ser Ser
1   5   10

<210> 28
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Families AE, AM

<400> 28

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
1   5   10

<210> 29
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Families AE, AM, AQ

<400> 29

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
1   5   10

<210> 30
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Families AE, AM, AQ

<400> 30

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
1   5   10

<210> 31
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Families AE, AM, AQ

<400> 31

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
1   5   10

<210> 32
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Families AF, AM

<400> 32

Gly Ser Thr Ser Glu Ser Pro Ser Gly Thr Ala Pro
1   5   10

<210> 33
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Families AF, AM

<400> 33

Gly Thr Ser Thr Pro Glu Ser Gly Ser Ala Ser Pro
1 5 10

<210> 34
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> AF, AM

<400> 34

Gly Thr Ser Pro Ser Gly Glu Ser Ser Thr Ala Pro
1 5 10

<210> 35
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Families AF, AM

<400> 35

Gly Ser Thr Ser Ser Thr Ala Glu Ser Pro Gly Pro
1 5 10

<210> 36
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Families AG, AM

<400> 36

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro
1 5 10

<210> 37
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Families AG, AM

<400> 37

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro
1   5   10

<210> 38
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Families AG, AM

<400> 38

Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro
1   5   10

<210> 39
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Families AG, AM

<400> 39

Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
1   5   10

<210> 40
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Family AQ

<400> 40

Gly Glu Pro Ala Gly Ser Pro Thr Ser Thr Ser Glu
1   5   10

<210> 41
<211> 12
<212> PRT
<213> Artificial Sequence

<220>

<223> XTEN Motif Family AQ

<400> 41

Gly Thr Gly Glu Pro Ser Ser Thr Pro Ala Ser Glu
1   5   10

<210> 42
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Family AQ

<400> 42

Gly Ser Gly Pro Ser Thr Glu Ser Ala Pro Thr Glu
1   5   10

<210> 43
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Family AQ

<400> 43

Gly Ser Glu Thr Pro Ser Gly Pro Ser Glu Thr Ala
1   5   10

<210> 44
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Family AQ

<400> 44

Gly Pro Ser Glu Thr Ser Thr Ser Glu Pro Gly Ala
1   5   10

<210> 45
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Family AQ

<400> 45

Gly Ser Pro Ser Glu Pro Thr Glu Gly Thr Ser Ala
1   5   10

<210> 46
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Family BC

<400> 46

Gly Ser Gly Ala Ser Glu Pro Thr Ser Thr Glu Pro
1   5   10

<210> 47
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Family BC

<400> 47

Gly Ser Glu Pro Ala Thr Ser Gly Thr Glu Pro Ser
1   5   10

<210> 48
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Family BC

<400> 48

Gly Thr Ser Glu Pro Ser Thr Ser Glu Pro Gly Ala
1   5   10

<210> 49
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Family Motif BC

<400> 49

Gly Thr Ser Thr Glu Pro Ser Glu Pro Gly Ser Ala
1   5   10

<210> 50
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Family BD

<400> 50

Gly Ser Thr Ala Gly Ser Glu Thr Ser Thr Glu Ala
1   5   10

<210> 51
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Family BD

<400> 51

Gly Ser Glu Thr Ala Thr Ser Gly Ser Glu Thr Ala
1   5   10

<210> 52
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN Motif Family BD

<400> 52

Gly Thr Ser Glu Ser Ala Thr Ser Glu Ser Gly Ala
1   5   10

<210> 53
<211> 12
<212> PRT

<213> Artificial Sequence

<220>
<223> XTEN Motif Family BD

<400> 53

Gly Thr Ser Thr Glu Ala Ser Glu Gly Ser Ala Ser
1 5 10

<210> 54
<211> 288
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN AE288_2

<400> 54

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu
1 5 10 15

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
20 25 30

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
35 40 45

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
50 55 60

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu
65 70 75 80

Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
85 90 95

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
100 105 110

Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr
115 120 125

Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
130 135 140

```
Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
145                 150                 155                 160


Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
                165                 170                 175


Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
            180                 185                 190


Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr
        195                 200                 205


Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
    210                 215                 220


Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
225                 230                 235                 240


Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala
                245                 250                 255


Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro
            260                 265                 270


Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
        275                 280                 285


<210>  55
<211>  143
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  XTEN AE144_2A

<400>  55

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser
1               5                   10                  15


Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
            20                  25                  30
```

```
Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr
        35                  40                  45

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro
    50                  55                  60

Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
65                  70                  75                  80

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr
                85                  90                  95

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro
            100                 105                 110

Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
        115                 120                 125

Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
    130                 135                 140


<210>  56
<211>  144
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  XTEN AE144_3B

<400>  56

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser
1               5                   10                  15

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
            20                  25                  30

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
        35                  40                  45

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu
    50                  55                  60
```

```
Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
65                  70                  75                  80


Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
                85                  90                  95


Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu
            100                 105                 110


Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
        115                 120                 125


Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
    130                 135                 140


<210>  57
<211>  144
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  XTEN AE144_4A

<400>  57

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
1               5                   10                  15


Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
            20                  25                  30


Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
        35                  40                  45


Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
    50                  55                  60


Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
65                  70                  75                  80


Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
                85                  90                  95


Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly
```

```
            100                 105                 110

Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu
        115                 120                 125

Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
    130                 135                 140
```

<210> 58
<211> 144
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN AE144_5A

<400> 58

```
Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
1               5                   10                  15

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
            20                  25                  30

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
        35                  40                  45

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
    50                  55                  60

Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
65                  70                  75                  80

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
                85                  90                  95

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
            100                 105                 110

Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
        115                 120                 125

Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
    130                 135                 140
```

<210> 59
<211> 144
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN AE144_6B

<400> 59

```
Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser
1               5                   10                  15


Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
            20                  25                  30


Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
        35                  40                  45


Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala
    50                  55                  60


Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
65                  70                  75                  80


Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
                85                  90                  95


Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro Ala
            100                 105                 110


Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
        115                 120                 125


Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
    130                 135                 140
```

<210> 60
<211> 144
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN AG144_A

<400> 60

Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Pro
1 5 10 15

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser Thr
20 25 30

Gly Thr Gly Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro
35 40 45

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro
50 55 60

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser
65 70 75 80

Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro
85 90 95

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Thr Pro Gly
100 105 110

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

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

<210> 61
<211> 144
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN AG144_B

<400> 61

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr
1 5 10 15

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
20 25 30

```
Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro
        35                  40                  45


Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro
    50                  55                  60


Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser Thr
65                  70                  75                  80


Gly Thr Gly Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro
                85                  90                  95


Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ala Ser Pro
            100                 105                 110


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


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


<210>  62
<211>  144
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  XTEN AG144_C

<400>  62

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ala Ser Pro
1               5                   10                  15


Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
            20                  25                  30


Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
        35                  40                  45


Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Thr Pro Gly
    50                  55                  60
```

```
Ser Gly Thr Ala Ser Ser Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
65                  70                  75                  80


Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
                85                  90                  95


Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Thr
            100                 105                 110


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


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


<210>  63
<211>  144
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  AG144_F

<400>  63

Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro
1               5                   10                  15


Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser
            20                  25                  30


Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
        35                  40                  45


Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro
    50                  55                  60


Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser
65                  70                  75                  80


Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro
                85                  90                  95
```

```
Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr
            100                 105                 110


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


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


<210>  64
<211>  19
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  FVIII Signal Peptide

<400>  64

Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
1               5                   10                  15


Cys Phe Ser



<210>  65
<211>  2332
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Mature Factor VIII

<400>  65

Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser Trp Asp Tyr
1               5                   10                  15


Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro
            20                  25                  30


Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys
        35                  40                  45


Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys Pro
    50                  55                  60
```

```
Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val
65                  70                  75                  80

Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val
                85                  90                  95

Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala
            100                 105                 110

Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val
        115                 120                 125

Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn
    130                 135                 140

Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser
145                 150                 155                 160

His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu
                165                 170                 175

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

His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp
        195                 200                 205

His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser
    210                 215                 220

Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg
225                 230                 235                 240

Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His
                245                 250                 255

Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu
            260                 265                 270

Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile
        275                 280                 285
```

```
Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly
    290                 295                 300

Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met
305                 310                 315                 320

Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg
                325                 330                 335

Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp
            340                 345                 350

Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro Ser Phe
        355                 360                 365

Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His
    370                 375                 380

Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu
385                 390                 395                 400

Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro
                405                 410                 415

Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr
            420                 425                 430

Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile
        435                 440                 445

Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile
    450                 455                 460

Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile
465                 470                 475                 480

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

His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys
```

```
            500                 505                 510

Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys
        515                 520                 525

Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala
    530                 535                 540

Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp
545                 550                 555                 560

Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe
                565                 570                 575

Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln
            580                 585                 590

Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe
        595                 600                 605

Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser
    610                 615                 620

Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu
625                 630                 635                 640

Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr
                645                 650                 655

Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro
            660                 665                 670

Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp
        675                 680                 685

Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr Ala
    690                 695                 700

Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu
705                 710                 715                 720
```

```
Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala
                725                 730                 735

Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Pro Ser Thr Arg
            740                 745                 750

Gln Lys Gln Phe Asn Ala Thr Thr Ile Pro Glu Asn Asp Ile Glu Lys
        755                 760                 765

Thr Asp Pro Trp Phe Ala His Arg Thr Pro Met Pro Lys Ile Gln Asn
    770                 775                 780

Val Ser Ser Ser Asp Leu Leu Met Leu Leu Arg Gln Ser Pro Thr Pro
785                 790                 795                 800

His Gly Leu Ser Leu Ser Asp Leu Gln Glu Ala Lys Tyr Glu Thr Phe
                805                 810                 815

Ser Asp Asp Pro Ser Pro Gly Ala Ile Asp Ser Asn Asn Ser Leu Ser
            820                 825                 830

Glu Met Thr His Phe Arg Pro Gln Leu His His Ser Gly Asp Met Val
        835                 840                 845

Phe Thr Pro Glu Ser Gly Leu Gln Leu Arg Leu Asn Glu Lys Leu Gly
    850                 855                 860

Thr Thr Ala Ala Thr Glu Leu Lys Lys Leu Asp Phe Lys Val Ser Ser
865                 870                 875                 880

Thr Ser Asn Asn Leu Ile Ser Thr Ile Pro Ser Asp Asn Leu Ala Ala
                885                 890                 895

Gly Thr Asp Asn Thr Ser Ser Leu Gly Pro Pro Ser Met Pro Val His
            900                 905                 910

Tyr Asp Ser Gln Leu Asp Thr Thr Leu Phe Gly Lys Lys Ser Ser Pro
        915                 920                 925

Leu Thr Glu Ser Gly Gly Pro Leu Ser Leu Ser Glu Glu Asn Asn Asp
    930                 935                 940
```

```
Ser Lys Leu Leu Glu Ser Gly Leu Met Asn Ser Gln Glu Ser Ser Trp
945                 950                 955                 960


Gly Lys Asn Val Ser Ser Thr Glu Ser Gly Arg Leu Phe Lys Gly Lys
                965                 970                 975


Arg Ala His Gly Pro Ala Leu Leu Thr Lys Asp Asn Ala Leu Phe Lys
            980                 985                 990


Val Ser Ile Ser Leu Leu Lys Thr  Asn Lys Thr Ser Asn  Asn Ser Ala
        995                 1000                1005


Thr Asn  Arg Lys Thr His Ile  Asp Gly Pro Ser Leu  Leu Ile Glu
    1010                1015                1020


Asn Ser  Pro Ser Val Trp Gln  Asn Ile Leu Glu Ser  Asp Thr Glu
    1025                1030                1035


Phe Lys  Lys Val Thr Pro Leu  Ile His Asp Arg Met  Leu Met Asp
    1040                1045                1050


Lys Asn  Ala Thr Ala Leu Arg  Leu Asn His Met Ser  Asn Lys Thr
    1055                1060                1065


Thr Ser  Ser Lys Asn Met Glu  Met Val Gln Gln Lys  Lys Glu Gly
    1070                1075                1080


Pro Ile  Pro Pro Asp Ala Gln  Asn Pro Asp Met Ser  Phe Phe Lys
    1085                1090                1095


Met Leu  Phe Leu Pro Glu Ser  Ala Arg Trp Ile Gln  Arg Thr His
    1100                1105                1110


Gly Lys  Asn Ser Leu Asn Ser  Gly Gln Gly Pro Ser  Pro Lys Gln
    1115                1120                1125


Leu Val  Ser Leu Gly Pro Glu  Lys Ser Val Glu Gly  Gln Asn Phe
    1130                1135                1140


Leu Ser  Glu Lys Asn Lys Val  Val Val Gly Lys Gly  Glu Phe Thr
    1145                1150                1155
```

```
Lys Asp  Val Gly Leu Lys Glu  Met Val Phe Pro Ser  Ser Arg Asn
    1160                1165                1170

Leu Phe  Leu Thr Asn Leu Asp  Asn Leu His Glu Asn  Asn Thr His
    1175                1180                1185

Asn Gln  Glu Lys Lys Ile Gln  Glu Glu Ile Glu Lys  Lys Glu Thr
    1190                1195                1200

Leu Ile  Gln Glu Asn Val Val  Leu Pro Gln Ile His  Thr Val Thr
    1205                1210                1215

Gly Thr  Lys Asn Phe Met Lys  Asn Leu Phe Leu Leu  Ser Thr Arg
    1220                1225                1230

Gln Asn  Val Glu Gly Ser Tyr  Asp Gly Ala Tyr Ala  Pro Val Leu
    1235                1240                1245

Gln Asp  Phe Arg Ser Leu Asn  Asp Ser Thr Asn Arg  Thr Lys Lys
    1250                1255                1260

His Thr  Ala His Phe Ser Lys  Lys Gly Glu Glu Glu  Asn Leu Glu
    1265                1270                1275

Gly Leu  Gly Asn Gln Thr Lys  Gln Ile Val Glu Lys  Tyr Ala Cys
    1280                1285                1290

Thr Thr  Arg Ile Ser Pro Asn  Thr Ser Gln Gln Asn  Phe Val Thr
    1295                1300                1305

Gln Arg  Ser Lys Arg Ala Leu  Lys Gln Phe Arg Leu  Pro Leu Glu
    1310                1315                1320

Glu Thr  Glu Leu Glu Lys Arg  Ile Ile Val Asp Asp  Thr Ser Thr
    1325                1330                1335

Gln Trp  Ser Lys Asn Met Lys  His Leu Thr Pro Ser  Thr Leu Thr
    1340                1345                1350

Gln Ile  Asp Tyr Asn Glu Lys  Glu Lys Gly Ala Ile  Thr Gln Ser
```

```
    1355                1360                1365

Pro Leu  Ser Asp Cys Leu Thr  Arg Ser His Ser Ile  Pro Gln Ala
    1370                1375                1380

Asn Arg  Ser Pro Leu Pro Ile  Ala Lys Val Ser Ser  Phe Pro Ser
    1385                1390                1395

Ile Arg  Pro Ile Tyr Leu Thr  Arg Val Leu Phe Gln  Asp Asn Ser
    1400                1405                1410

Ser His  Leu Pro Ala Ala Ser  Tyr Arg Lys Lys Asp  Ser Gly Val
    1415                1420                1425

Gln Glu  Ser Ser His Phe Leu  Gln Gly Ala Lys Lys  Asn Asn Leu
    1430                1435                1440

Ser Leu  Ala Ile Leu Thr Leu  Glu Met Thr Gly Asp  Gln Arg Glu
    1445                1450                1455

Val Gly  Ser Leu Gly Thr Ser  Ala Thr Asn Ser Val  Thr Tyr Lys
    1460                1465                1470

Lys Val  Glu Asn Thr Val Leu  Pro Lys Pro Asp Leu  Pro Lys Thr
    1475                1480                1485

Ser Gly  Lys Val Glu Leu Leu  Pro Lys Val His Ile  Tyr Gln Lys
    1490                1495                1500

Asp Leu  Phe Pro Thr Glu Thr  Ser Asn Gly Ser Pro  Gly His Leu
    1505                1510                1515

Asp Leu  Val Glu Gly Ser Leu  Leu Gln Gly Thr Glu  Gly Ala Ile
    1520                1525                1530

Lys Trp  Asn Glu Ala Asn Arg  Pro Gly Lys Val Pro  Phe Leu Arg
    1535                1540                1545

Val Ala  Thr Glu Ser Ser Ala  Lys Thr Pro Ser Lys  Leu Leu Asp
    1550                1555                1560
```

```
Pro Leu  Ala Trp Asp Asn His  Tyr Gly Thr Gln Ile  Pro Lys Glu
    1565                1570                1575

Glu Trp  Lys Ser Gln Glu Lys  Ser Pro Glu Lys Thr  Ala Phe Lys
    1580                1585                1590

Lys Lys  Asp Thr Ile Leu Ser  Leu Asn Ala Cys Glu  Ser Asn His
    1595                1600                1605

Ala Ile  Ala Ala Ile Asn Glu  Gly Gln Asn Lys Pro  Glu Ile Glu
    1610                1615                1620

Val Thr  Trp Ala Lys Gln Gly  Arg Thr Glu Arg Leu  Cys Ser Gln
    1625                1630                1635

Asn Pro  Pro Val Leu Lys Arg  His Gln Arg Glu Ile  Thr Arg Thr
    1640                1645                1650

Thr Leu  Gln Ser Asp Gln Glu  Glu Ile Asp Tyr Asp  Asp Thr Ile
    1655                1660                1665

Ser Val  Glu Met Lys Lys Glu  Asp Phe Asp Ile Tyr  Asp Glu Asp
    1670                1675                1680

Glu Asn  Gln Ser Pro Arg Ser  Phe Gln Lys Lys Thr  Arg His Tyr
    1685                1690                1695

Phe Ile  Ala Ala Val Glu Arg  Leu Trp Asp Tyr Gly  Met Ser Ser
    1700                1705                1710

Ser Pro  His Val Leu Arg Asn  Arg Ala Gln Ser Gly  Ser Val Pro
    1715                1720                1725

Gln Phe  Lys Lys Val Val Phe  Gln Glu Phe Thr Asp  Gly Ser Phe
    1730                1735                1740

Thr Gln  Pro Leu Tyr Arg Gly  Glu Leu Asn Glu His  Leu Gly Leu
    1745                1750                1755

Leu Gly  Pro Tyr Ile Arg Ala  Glu Val Glu Asp Asn  Ile Met Val
    1760                1765                1770
```

```
Thr Phe  Arg Asn Gln Ala Ser  Arg Pro Tyr Ser Phe  Tyr Ser Ser
    1775                1780                1785

Leu Ile  Ser Tyr Glu Glu Asp  Gln Arg Gln Gly Ala  Glu Pro Arg
    1790                1795                1800

Lys Asn  Phe Val Lys Pro Asn  Glu Thr Lys Thr Tyr  Phe Trp Lys
    1805                1810                1815

Val Gln  His His Met Ala Pro  Thr Lys Asp Glu Phe  Asp Cys Lys
    1820                1825                1830

Ala Trp  Ala Tyr Phe Ser Asp  Val Asp Leu Glu Lys  Asp Val His
    1835                1840                1845

Ser Gly  Leu Ile Gly Pro Leu  Leu Val Cys His Thr  Asn Thr Leu
    1850                1855                1860

Asn Pro  Ala His Gly Arg Gln  Val Thr Val Gln Glu  Phe Ala Leu
    1865                1870                1875

Phe Phe  Thr Ile Phe Asp Glu  Thr Lys Ser Trp Tyr  Phe Thr Glu
    1880                1885                1890

Asn Met  Glu Arg Asn Cys Arg  Ala Pro Cys Asn Ile  Gln Met Glu
    1895                1900                1905

Asp Pro  Thr Phe Lys Glu Asn  Tyr Arg Phe His Ala  Ile Asn Gly
    1910                1915                1920

Tyr Ile  Met Asp Thr Leu Pro  Gly Leu Val Met Ala  Gln Asp Gln
    1925                1930                1935

Arg Ile  Arg Trp Tyr Leu Leu  Ser Met Gly Ser Asn  Glu Asn Ile
    1940                1945                1950

His Ser  Ile His Phe Ser Gly  His Val Phe Thr Val  Arg Lys Lys
    1955                1960                1965

Glu Glu  Tyr Lys Met Ala Leu  Tyr Asn Leu Tyr Pro  Gly Val Phe
    1970                1975                1980
```

```
Glu Thr  Val Glu Met Leu Pro  Ser Lys Ala Gly Ile  Trp Arg Val
    1985                 1990                 1995

Glu Cys  Leu Ile Gly Glu His  Leu His Ala Gly Met  Ser Thr Leu
    2000                 2005                 2010

Phe Leu  Val Tyr Ser Asn Lys  Cys Gln Thr Pro Leu  Gly Met Ala
    2015                 2020                 2025

Ser Gly  His Ile Arg Asp Phe  Gln Ile Thr Ala Ser  Gly Gln Tyr
    2030                 2035                 2040

Gly Gln  Trp Ala Pro Lys Leu  Ala Arg Leu His Tyr  Ser Gly Ser
    2045                 2050                 2055

Ile Asn  Ala Trp Ser Thr Lys  Glu Pro Phe Ser Trp  Ile Lys Val
    2060                 2065                 2070

Asp Leu  Leu Ala Pro Met Ile  Ile His Gly Ile Lys  Thr Gln Gly
    2075                 2080                 2085

Ala Arg  Gln Lys Phe Ser Ser  Leu Tyr Ile Ser Gln  Phe Ile Ile
    2090                 2095                 2100

Met Tyr  Ser Leu Asp Gly Lys  Lys Trp Gln Thr Tyr  Arg Gly Asn
    2105                 2110                 2115

Ser Thr  Gly Thr Leu Met Val  Phe Phe Gly Asn Val  Asp Ser Ser
    2120                 2125                 2130

Gly Ile  Lys His Asn Ile Phe  Asn Pro Pro Ile Ile  Ala Arg Tyr
    2135                 2140                 2145

Ile Arg  Leu His Pro Thr His  Tyr Ser Ile Arg Ser  Thr Leu Arg
    2150                 2155                 2160

Met Glu  Leu Met Gly Cys Asp  Leu Asn Ser Cys Ser  Met Pro Leu
    2165                 2170                 2175

Gly Met  Glu Ser Lys Ala Ile  Ser Asp Ala Gln Ile  Thr Ala Ser
```

2180 2185 2190

Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala
2195 2200 2205

Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val
2210 2215 2220

Asn Asn Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met
2225 2230 2235

Lys Val Thr Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr
2240 2245 2250

Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly
2255 2260 2265

His Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys Val Lys Val Phe
2270 2275 2280

Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val Asn Ser Leu Asp
2285 2290 2295

Pro Pro Leu Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ser Trp
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Val His Gln Ile Ala Leu Arg Met Glu Val Leu Gly Cys Glu Ala
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gaaacattaa tccaagagaa tgtagttttg cctcagatac atacagtgac tggcactaag 3720

aatttcatga agaacctttt cttactgagc actaggcaaa atgtagaagg ttcatatgac 3780

ggggcatatg ctccagtact tcaagatttt aggtcattaa atgattcaac aaatagaaca 3840

aagaaacaca cagctcattt ctcaaaaaaa ggggaggaag aaaacttgga aggcttggga 3900

aatcaaacca agcaaattgt agagaaatat gcatgcacca caaggatatc tcctaataca 3960

agccagcaga attttgtcac gcaacgtagt aagagagctt tgaaacaatt cagactccca 4020

ctagaagaaa cagaacttga aaaaaggata attgtggatg acacctcaac ccagtggtcc 4080

aaaaacatga aacatttgac cccgagcacc ctcacacaga tagactacaa tgagaaggag 4140

aaaggggcca ttactcagtc tcccttatca gattgcctta cgaggagtca tagcatccct 4200

caagcaaata gatctccatt acccattgca aaggtatcat catttccatc tattagacct 4260

atatatctga ccagggtcct attccaagac aactcttctc atcttccagc agcatcttat 4320

agaaagaaag attctggggt ccaagaaagc agtcatttct tacaaggagc caaaaaaaat 4380

aacctttctt tagccattct aaccttggag atgactggtg atcaaagaga ggttggctcc 4440

ctggggacaa gtgccacaaa ttcagtcaca tacaagaaag ttgagaacac tgttctcccg 4500

aaaccagact tgcccaaaac atctggcaaa gttgaattgc ttccaaaagt tcacatttat 4560

cagaaggacc tattccctac ggaaactagc aatgggtctc ctggccatct ggatctcgtg 4620

gaagggagcc ttcttcaggg aacagaggga gcgattaagt ggaatgaagc aaacagacct 4680

ggaaaagttc cctttctgag agtagcaaca gaaagctctg caaagactcc ctccaagcta 4740

ttggatcctc ttgcttggga taaccactat ggtactcaga taccaaaaga agagtggaaa 4800

tcccaagaga agtcaccaga aaaaacagct tttaagaaaa aggataccat tttgtccctg 4860

aacgcttgtg aaagcaatca tgcaatagca gcaataaatg agggacaaaa taagcccgaa 4920

atagaagtca cctgggcaaa gcaaggtagg actgaaaggc tgtgctctca aaacccacca 4980

gtcttgaaac gccatcaacg ggaaataact cgtactactc ttcagtcaga tcaagaggaa 5040

attgactatg atgataccat atcagttgaa atgaagaagg aagattttga catttatgat 5100

gaggatgaaa atcagagccc ccgcagcttt caaaagaaaa cacgacacta ttttattgct 5160

gcagtggaga ggctctggga ttatgggatg agtagctccc cacatgttct aagaaacagg 5220

gctcagagtg gcagtgtccc tcagttcaag aaagttgttt tccaggaatt tactgatggc 5280

tcctttactc agcccttata ccgtggagaa ctaaatgaac atttgggact cctggggcca 5340

tatataagag cagaagttga agataatatc atggtaactt tcagaaatca ggcctctcgt 5400

ccctattcct tctattctag ccttatttct tatgaggaag atcagaggca aggagcagaa 5460

cctagaaaaa actttgtcaa gcctaatgaa accaaaactt acttttggaa agtgcaacat 5520

catatggcac ccactaaaga tgagtttgac tgcaaagcct gggcttattt ctctgatgtt 5580

gacctggaaa aagatgtgca ctcaggcctg attggacccc ttctggtctg ccacactaac 5640

acactgaacc ctgctcatgg gagacaagtg acagtacagg aatttgctct gtttttcacc 5700

atctttgatg agaccaaaag ctggtacttc actgaaaata tggaaagaaa ctgcagggct 5760

ccctgcaata tccagatgga agatcccact tttaaagaga attatcgctt ccatgcaatc 5820

aatggctaca taatggatac actacctggc ttagtaatgg ctcaggatca aaggattcga 5880

tggtatctgc tcagcatggg cagcaatgaa aacatccatt ctattcattt cagtggacat 5940

gtgttcactg tacgaaaaaa agaggagtat aaaatggcac tgtacaatct ctatccaggt 6000

gtttttgaga cagtggaaat gttaccatcc aaagctggaa tttggcgggt ggaatgcctt 6060

attggcgagc atctacatgc tgggatgagc acacttttc tggtgtacag caataagtgt 6120

cagactcccc tgggaatggc ttctggacac attagagatt ttcagattac agcttcagga 6180

caatatggac agtgggcccc aaagctggcc agacttcatt attccggatc aatcaatgcc 6240

tggagcacca aggagccctt ttcttggatc aaggtggatc tgttggcacc aatgattatt 6300

cacggcatca agacccaggg tgcccgtcag aagttctcca gcctctacat ctctcagttt 6360

atcatcatgt atagtcttga tgggaagaag tggcagactt atcgaggaaa ttccactgga 6420

accttaatgg tcttctttgg caatgtggat tcatctggga taaaacacaa tatttttaac 6480

cctccaatta ttgctcgata catccgtttg cacccaactc attatagcat tcgcagcact 6540

cttcgcatgg agttgatggg ctgtgattta aatagttgca gcatgccatt gggaatggag 6600

agtaaagcaa tatcagatgc acagattact gcttcatcct actttaccaa tatgtttgcc 6660

acctggtctc cttcaaaagc tcgacttcac ctccaaggga ggagtaatgc ctggagacct 6720

caggtgaata atccaaaaga gtggctgcaa gtggacttcc agaagacaat gaaagtcaca 6780

ggagtaacta ctcagggagt aaaatctctg cttaccagca tgtatgtgaa ggagttcctc 6840

atctccagca gtcaagatgg ccatcagtgg actctctttt ttcagaatgg caaagtaaag 6900

gtttttcagg gaaatcaaga ctccttcaca cctgtggtga actctctaga cccaccgtta 6960

ctgactcgct accttcgaat tcacccccag agttgggtgc accagattgc cctgaggatg 7020

gaggttctgg gctgcgaggc acaggacctc tac 7053

<210> 67
<211> 1438
<212> PRT
<213> Artificial Sequence

<220>
<223> BDD FVIII

<400> 67

Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser Trp Asp Tyr
1 5 10 15

Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro
20 25 30

Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys
35 40 45

Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys Pro
50 55 60

Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val
65 70 75 80

Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val
85 90 95

Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala
100 105 110

Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val
115 120 125

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Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn
    130                 135                 140

Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser
145                 150                 155                 160

His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu
                165                 170                 175

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

His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp
        195                 200                 205

His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser
    210                 215                 220

Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg
225                 230                 235                 240

Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His
                245                 250                 255

Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu
            260                 265                 270

Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile
        275                 280                 285

Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly
    290                 295                 300

Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met
305                 310                 315                 320

Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg
                325                 330                 335

Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp
            340                 345                 350
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```
Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro Ser Phe
        355                 360                 365

Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His
    370                 375                 380

Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu
385                 390                 395                 400

Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro
                405                 410                 415

Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr
            420                 425                 430

Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile
        435                 440                 445

Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile
    450                 455                 460

Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile
465                 470                 475                 480

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

His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys
            500                 505                 510

Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys
        515                 520                 525

Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala
    530                 535                 540

Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp
545                 550                 555                 560

Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe
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                565                 570                 575

Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln
            580                 585                 590

Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe
        595                 600                 605

Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser
    610                 615                 620

Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu
625                 630                 635                 640

Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr
                645                 650                 655

Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro
            660                 665                 670

Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp
        675                 680                 685

Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr Ala
    690                 695                 700

Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu
705                 710                 715                 720

Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala
                725                 730                 735

Ile Glu Pro Arg Ser Phe Ser Gln Asn Pro Pro Val Leu Lys Arg His
            740                 745                 750

Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile
        755                 760                 765

Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe Asp
    770                 775                 780
```

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Ile Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe Gln Lys Lys
785                 790                 795                 800


Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr Gly
                805                 810                 815


Met Ser Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser Gly Ser
            820                 825                 830


Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly Ser
        835                 840                 845


Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly Leu
    850                 855                 860


Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr
865                 870                 875                 880


Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile
                885                 890                 895


Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg Lys Asn Phe
            900                 905                 910


Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val Gln His His
        915                 920                 925


Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe
    930                 935                 940


Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro
945                 950                 955                 960


Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His Gly Arg Gln
                965                 970                 975


Val Thr Val Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr
            980                 985                 990


Lys Ser Trp Tyr Phe Thr Glu Asn  Met Glu Arg Asn Cys  Arg Ala Pro
        995                 1000                1005
```

```
Cys Asn  Ile Gln Met Glu Asp  Pro Thr Phe Lys Glu  Asn Tyr Arg
    1010                1015                1020

Phe His  Ala Ile Asn Gly Tyr  Ile Met Asp Thr Leu  Pro Gly Leu
    1025                1030                1035

Val Met  Ala Gln Asp Gln Arg  Ile Arg Trp Tyr Leu  Leu Ser Met
    1040                1045                1050

Gly Ser  Asn Glu Asn Ile His  Ser Ile His Phe Ser  Gly His Val
    1055                1060                1065

Phe Thr  Val Arg Lys Lys Glu  Glu Tyr Lys Met Ala  Leu Tyr Asn
    1070                1075                1080

Leu Tyr  Pro Gly Val Phe Glu  Thr Val Glu Met Leu  Pro Ser Lys
    1085                1090                1095

Ala Gly  Ile Trp Arg Val Glu  Cys Leu Ile Gly Glu  His Leu His
    1100                1105                1110

Ala Gly  Met Ser Thr Leu Phe  Leu Val Tyr Ser Asn  Lys Cys Gln
    1115                1120                1125

Thr Pro  Leu Gly Met Ala Ser  Gly His Ile Arg Asp  Phe Gln Ile
    1130                1135                1140

Thr Ala  Ser Gly Gln Tyr Gly  Gln Trp Ala Pro Lys  Leu Ala Arg
    1145                1150                1155

Leu His  Tyr Ser Gly Ser Ile  Asn Ala Trp Ser Thr  Lys Glu Pro
    1160                1165                1170

Phe Ser  Trp Ile Lys Val Asp  Leu Leu Ala Pro Met  Ile Ile His
    1175                1180                1185

Gly Ile  Lys Thr Gln Gly Ala  Arg Gln Lys Phe Ser  Ser Leu Tyr
    1190                1195                1200

Ile Ser  Gln Phe Ile Ile Met  Tyr Ser Leu Asp Gly  Lys Lys Trp
    1205                1210                1215
```

```
Gln Thr  Tyr Arg Gly Asn Ser  Thr Gly Thr Leu Met  Val Phe Phe
    1220                1225                1230

Gly Asn  Val Asp Ser Ser Gly  Ile Lys His Asn Ile  Phe Asn Pro
    1235                1240                1245

Pro Ile  Ile Ala Arg Tyr Ile  Arg Leu His Pro Thr  His Tyr Ser
    1250                1255                1260

Ile Arg  Ser Thr Leu Arg Met  Glu Leu Met Gly Cys  Asp Leu Asn
    1265                1270                1275

Ser Cys  Ser Met Pro Leu Gly  Met Glu Ser Lys Ala  Ile Ser Asp
    1280                1285                1290

Ala Gln  Ile Thr Ala Ser Ser  Tyr Phe Thr Asn Met  Phe Ala Thr
    1295                1300                1305

Trp Ser  Pro Ser Lys Ala Arg  Leu His Leu Gln Gly  Arg Ser Asn
    1310                1315                1320

Ala Trp  Arg Pro Gln Val Asn  Asn Pro Lys Glu Trp  Leu Gln Val
    1325                1330                1335

Asp Phe  Gln Lys Thr Met Lys  Val Thr Gly Val Thr  Thr Gln Gly
    1340                1345                1350

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

Ser Ser  Ser Gln Asp Gly His  Gln Trp Thr Leu Phe  Phe Gln Asn
    1370                1375                1380

Gly Lys  Val Lys Val Phe Gln  Gly Asn Gln Asp Ser  Phe Thr Pro
    1385                1390                1395

Val Val  Asn Ser Leu Asp Pro  Pro Leu Leu Thr Arg  Tyr Leu Arg
    1400                1405                1410

Ile His  Pro Gln Ser Trp Val  His Gln Ile Ala Leu  Arg Met Glu
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1415 1420 1425

Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr
1430 1435

<210> 68
<211> 1429
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino Acid Sequence of B-domain Deleted Factor VIII (B-domain deletion except 5 amino acid residues

<400> 68

Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser Trp Asp Tyr
1 5 10 15

Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro
20 25 30

Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys
35 40 45

Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys Pro
50 55 60

Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val
65 70 75 80

Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val
85 90 95

Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala
100 105 110

Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val
115 120 125

Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn
130 135 140

Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser

```
145                 150                 155                 160

His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu
                165                 170                 175

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

His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp
        195                 200                 205

His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser
    210                 215                 220

Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg
225                 230                 235                 240

Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His
                245                 250                 255

Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu
            260                 265                 270

Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile
        275                 280                 285

Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly
    290                 295                 300

Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met
305                 310                 315                 320

Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg
                325                 330                 335

Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp
            340                 345                 350

Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro Ser Phe
        355                 360                 365
```

```
Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His
    370                 375                 380

Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu
385                 390                 395                 400

Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro
                405                 410                 415

Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr
            420                 425                 430

Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile
        435                 440                 445

Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile
    450                 455                 460

Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile
465                 470                 475                 480

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

His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys
            500                 505                 510

Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys
        515                 520                 525

Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala
    530                 535                 540

Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp
545                 550                 555                 560

Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe
                565                 570                 575

Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln
            580                 585                 590
```

```
Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe
        595                 600                 605

Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser
    610                 615                 620

Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu
625                 630                 635                 640

Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr
                645                 650                 655

Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro
            660                 665                 670

Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp
        675                 680                 685

Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr Ala
    690                 695                 700

Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu
705                 710                 715                 720

Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala
                725                 730                 735

Ile Glu Pro Arg Ser Phe Ser Gln Asn Glu Ile Thr Arg Thr Thr Leu
            740                 745                 750

Gln Ser Asp Gln Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu
        755                 760                 765

Met Lys Lys Glu Asp Phe Asp Ile Tyr Asp Glu Asp Glu Asn Gln Ser
    770                 775                 780

Pro Arg Ser Phe Gln Lys Lys Thr Arg His Tyr Phe Ile Ala Ala Val
785                 790                 795                 800

Glu Arg Leu Trp Asp Tyr Gly Met Ser Ser Ser Pro His Val Leu Arg
                805                 810                 815
```

```
Asn Arg Ala Gln Ser Gly Ser Val Pro Gln Phe Lys Lys Val Val Phe
            820                 825                 830

Gln Glu Phe Thr Asp Gly Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu
        835                 840                 845

Leu Asn Glu His Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val
    850                 855                 860

Glu Asp Asn Ile Met Val Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr
865                 870                 875                 880

Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly
                885                 890                 895

Ala Glu Pro Arg Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr
            900                 905                 910

Phe Trp Lys Val Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp
        915                 920                 925

Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val
    930                 935                 940

His Ser Gly Leu Ile Gly Pro Leu Leu Val Cys His Thr Asn Thr Leu
945                 950                 955                 960

Asn Pro Ala His Gly Arg Gln Val Thr Val Gln Glu Phe Ala Leu Phe
                965                 970                 975

Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu Asn Met
            980                 985                 990

Glu Arg Asn Cys Arg Ala Pro Cys  Asn Ile Gln Met Glu  Asp Pro Thr
        995                 1000                1005

Phe Lys  Glu Asn Tyr Arg Phe  His Ala Ile Asn Gly  Tyr Ile Met
    1010                1015                1020

Asp Thr  Leu Pro Gly Leu Val  Met Ala Gln Asp Gln  Arg Ile Arg
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    1025                1030                1035

Trp Tyr  Leu Leu Ser Met Gly  Ser Asn Glu Asn Ile  His Ser Ile
    1040                1045                1050

His Phe  Ser Gly His Val Phe  Thr Val Arg Lys Lys  Glu Glu Tyr
    1055                1060                1065

Lys Met  Ala Leu Tyr Asn Leu  Tyr Pro Gly Val Phe  Glu Thr Val
    1070                1075                1080

Glu Met  Leu Pro Ser Lys Ala  Gly Ile Trp Arg Val  Glu Cys Leu
    1085                1090                1095

Ile Gly  Glu His Leu His Ala  Gly Met Ser Thr Leu  Phe Leu Val
    1100                1105                1110

Tyr Ser  Asn Lys Cys Gln Thr  Pro Leu Gly Met Ala  Ser Gly His
    1115                1120                1125

Ile Arg  Asp Phe Gln Ile Thr  Ala Ser Gly Gln Tyr  Gly Gln Trp
    1130                1135                1140

Ala Pro  Lys Leu Ala Arg Leu  His Tyr Ser Gly Ser  Ile Asn Ala
    1145                1150                1155

Trp Ser  Thr Lys Glu Pro Phe  Ser Trp Ile Lys Val  Asp Leu Leu
    1160                1165                1170

Ala Pro  Met Ile Ile His Gly  Ile Lys Thr Gln Gly  Ala Arg Gln
    1175                1180                1185

Lys Phe  Ser Ser Leu Tyr Ile  Ser Gln Phe Ile Ile  Met Tyr Ser
    1190                1195                1200

Leu Asp  Gly Lys Lys Trp Gln  Thr Tyr Arg Gly Asn  Ser Thr Gly
    1205                1210                1215

Thr Leu  Met Val Phe Phe Gly  Asn Val Asp Ser Ser  Gly Ile Lys
    1220                1225                1230
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```
His Asn  Ile Phe Asn Pro Pro  Ile Ile Ala Arg Tyr  Ile Arg Leu
    1235                1240                1245

His Pro  Thr His Tyr Ser Ile  Arg Ser Thr Leu Arg  Met Glu Leu
    1250                1255                1260

Met Gly  Cys Asp Leu Asn Ser  Cys Ser Met Pro Leu  Gly Met Glu
    1265                1270                1275

Ser Lys  Ala Ile Ser Asp Ala  Gln Ile Thr Ala Ser  Ser Tyr Phe
    1280                1285                1290

Thr Asn  Met Phe Ala Thr Trp  Ser Pro Ser Lys Ala  Arg Leu His
    1295                1300                1305

Leu Gln  Gly Arg Ser Asn Ala  Trp Arg Pro Gln Val  Asn Asn Pro
    1310                1315                1320

Lys Glu  Trp Leu Gln Val Asp  Phe Gln Lys Thr Met  Lys Val Thr
    1325                1330                1335

Gly Val  Thr Thr Gln Gly Val  Lys Ser Leu Leu Thr  Ser Met Tyr
    1340                1345                1350

Val Lys  Glu Phe Leu Ile Ser  Ser Ser Gln Asp Gly  His Gln Trp
    1355                1360                1365

Thr Leu  Phe Phe Gln Asn Gly  Lys Val Lys Val Phe  Gln Gly Asn
    1370                1375                1380

Gln Asp  Ser Phe Thr Pro Val  Val Asn Ser Leu Asp  Pro Pro Leu
    1385                1390                1395

Leu Thr  Arg Tyr Leu Arg Ile  His Pro Gln Ser Trp  Val His Gln
    1400                1405                1410

Ile Ala  Leu Arg Met Glu Val  Leu Gly Cys Glu Ala  Gln Asp Leu
    1415                1420                1425

Tyr
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<210> 69
<211> 2754
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN-FVIII-161

<400> 69

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Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
1               5                  10                  15


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


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


Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val
    50                  55                  60


Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile
65                  70                  75                  80


Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln
                85                  90                  95


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


His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser
        115                 120                 125


Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp
    130                 135                 140


Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu
145                 150                 155                 160


Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser
                165                 170                 175
```

```
Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile
            180                 185                 190

Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr
        195                 200                 205

Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly
    210                 215                 220

Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp
225                 230                 235                 240

Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr
                245                 250                 255

Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val
            260                 265                 270

Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile
        275                 280                 285

Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser
    290                 295                 300

Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met
305                 310                 315                 320

Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His
                325                 330                 335

Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro
            340                 345                 350

Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp
        355                 360                 365

Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser
    370                 375                 380

Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
385                 390                 395                 400
```

```
Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro
                405                 410                 415

Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
            420                 425                 430

Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met
        435                 440                 445

Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu
    450                 455                 460

Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
465                 470                 475                 480

Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro
                485                 490                 495

His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys
            500                 505                 510

Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe
        515                 520                 525

Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp
    530                 535                 540

Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg
545                 550                 555                 560

Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu
                565                 570                 575

Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val
            580                 585                 590

Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu
        595                 600                 605

Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp
    610                 615                 620
```

```
Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
625                 630                 635                 640

Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp
                645                 650                 655

Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe
            660                 665                 670

Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
        675                 680                 685

Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro
    690                 695                 700

Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly
705                 710                 715                 720

Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp
                725                 730                 735

Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
            740                 745                 750

Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Pro Pro Val Leu
        755                 760                 765

Lys Arg His Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln
    770                 775                 780

Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu
785                 790                 795                 800

Asp Phe Asp Ile Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe
                805                 810                 815

Gln Lys Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp
            820                 825                 830

Asp Tyr Gly Met Ser Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln
```

```
        835                 840                 845

Ser Gly Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr
    850                 855                 860

Asp Gly Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His
865                 870                 875                 880

Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile
                885                 890                 895

Met Val Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser
            900                 905                 910

Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg
        915                 920                 925

Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val
    930                 935                 940

Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp
945                 950                 955                 960

Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu
                965                 970                 975

Ile Gly Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His
            980                 985                 990

Gly Arg Gln Val Thr Val Gln Glu  Phe Ala Leu Phe Phe  Thr Ile Phe
        995                 1000                1005

Asp Glu  Thr Lys Ser Trp Tyr  Phe Thr Glu Asn Met  Glu Arg Asn
    1010                1015                1020

Cys Arg  Ala Pro Cys Asn Ile  Gln Met Glu Asp Pro  Thr Phe Lys
    1025                1030                1035

Glu Asn  Tyr Arg Phe His Ala  Ile Asn Gly Tyr Ile  Met Asp Thr
    1040                1045                1050
```

```
Leu Pro  Gly Leu Val Met Ala  Gln Asp Gln Arg Ile  Arg Trp Tyr
    1055                1060                1065

Leu Leu  Ser Met Gly Ser Asn  Glu Asn Ile His Ser  Ile His Phe
    1070                1075                1080

Ser Gly  His Val Phe Thr Val  Arg Lys Lys Glu Glu  Tyr Lys Met
    1085                1090                1095

Ala Leu  Tyr Asn Leu Tyr Pro  Gly Val Phe Glu Thr  Val Glu Met
    1100                1105                1110

Leu Pro  Ser Lys Ala Gly Ile  Trp Arg Val Glu Cys  Leu Ile Gly
    1115                1120                1125

Glu His  Leu His Ala Gly Met  Ser Thr Leu Phe Leu  Val Tyr Ser
    1130                1135                1140

Asn Lys  Cys Gln Thr Pro Leu  Gly Met Ala Ser Gly  His Ile Arg
    1145                1150                1155

Asp Phe  Gln Ile Thr Ala Ser  Gly Gln Tyr Gly Gln  Trp Ala Pro
    1160                1165                1170

Lys Leu  Ala Arg Leu His Tyr  Ser Gly Ser Ile Asn  Ala Trp Ser
    1175                1180                1185

Thr Lys  Glu Pro Phe Ser Trp  Ile Lys Val Asp Leu  Leu Ala Pro
    1190                1195                1200

Met Ile  Ile His Gly Ile Lys  Thr Gln Gly Ala Arg  Gln Lys Phe
    1205                1210                1215

Ser Ser  Leu Tyr Ile Ser Gln  Phe Ile Ile Met Tyr  Ser Leu Asp
    1220                1225                1230

Gly Lys  Lys Trp Gln Thr Tyr  Arg Gly Asn Ser Thr  Gly Thr Leu
    1235                1240                1245

Met Val  Phe Phe Gly Asn Val  Asp Ser Ser Gly Ile  Lys His Asn
    1250                1255                1260
```

```
Ile Phe  Asn Pro Pro Ile Ile  Ala Arg Tyr Ile Arg  Leu His Pro
    1265                1270                1275

Thr His  Tyr Ser Ile Arg Ser  Thr Leu Arg Met Glu  Leu Met Gly
    1280                1285                1290

Cys Asp  Leu Asn Ser Cys Ser  Met Pro Leu Gly Met  Glu Ser Lys
    1295                1300                1305

Ala Ile  Ser Asp Ala Gln Ile  Thr Ala Ser Ser Tyr  Phe Thr Asn
    1310                1315                1320

Met Phe  Ala Thr Trp Ser Pro  Ser Lys Ala Arg Leu  His Leu Gln
    1325                1330                1335

Gly Arg  Ser Asn Ala Trp Arg  Pro Gln Val Asn Asn  Pro Lys Glu
    1340                1345                1350

Trp Leu  Gln Val Asp Phe Gln  Lys Thr Met Lys Val  Thr Gly Val
    1355                1360                1365

Thr Thr  Gln Gly Val Lys Ser  Leu Leu Thr Ser Met  Tyr Val Lys
    1370                1375                1380

Glu Phe  Leu Ile Ser Ser Ser  Gln Asp Gly His Gln  Trp Thr Leu
    1385                1390                1395

Phe Phe  Gln Asn Gly Lys Val  Lys Val Phe Gln Gly  Asn Gln Asp
    1400                1405                1410

Ser Phe  Thr Pro Val Val Asn  Ser Leu Asp Pro Pro  Leu Leu Thr
    1415                1420                1425

Arg Tyr  Leu Arg Ile His Pro  Gln Ser Trp Val His  Gln Ile Ala
    1430                1435                1440

Leu Arg  Met Glu Val Leu Gly  Cys Glu Ala Gln Asp  Leu Tyr Asp
    1445                1450                1455

Lys Thr  His Thr Cys Pro Pro  Cys Pro Ala Pro Glu  Leu Leu Gly
    1460                1465                1470
```

```
Gly Pro  Ser Val Phe Leu Phe  Pro Pro Lys Pro Lys  Asp Thr Leu
    1475                 1480                 1485

Met Ile  Ser Arg Thr Pro Glu  Val Thr Cys Val Val  Val Asp Val
    1490                 1495                 1500

Ser His  Glu Asp Pro Glu Val  Lys Phe Asn Trp Tyr  Val Asp Gly
    1505                 1510                 1515

Val Glu  Val His Asn Ala Lys  Thr Lys Pro Arg Glu  Glu Gln Tyr
    1520                 1525                 1530

Asn Ser  Thr Tyr Arg Val Val  Ser Val Leu Thr Val  Leu His Gln
    1535                 1540                 1545

Asp Trp  Leu Asn Gly Lys Glu  Tyr Lys Cys Lys Val  Ser Asn Lys
    1550                 1555                 1560

Ala Leu  Pro Ala Pro Ile Glu  Lys Thr Ile Ser Lys  Ala Lys Gly
    1565                 1570                 1575

Gln Pro  Arg Glu Pro Gln Val  Tyr Thr Leu Pro Pro  Ser Arg Asp
    1580                 1585                 1590

Glu Leu  Thr Lys Asn Gln Val  Ser Leu Thr Cys Leu  Val Lys Gly
    1595                 1600                 1605

Phe Tyr  Pro Ser Asp Ile Ala  Val Glu Trp Glu Ser  Asn Gly Gln
    1610                 1615                 1620

Pro Glu  Asn Asn Tyr Lys Thr  Thr Pro Pro Val Leu  Asp Ser Asp
    1625                 1630                 1635

Gly Ser  Phe Phe Leu Tyr Ser  Lys Leu Thr Val Asp  Lys Ser Arg
    1640                 1645                 1650

Trp Gln  Gln Gly Asn Val Phe  Ser Cys Ser Val Met  His Glu Ala
    1655                 1660                 1665

Leu His  Asn His Tyr Thr Gln  Lys Ser Leu Ser Leu  Ser Pro Gly
```

```
    1670                1675                1680

Lys Arg  Arg Arg Arg Ser Gly  Gly Gly Gly Ser Gly  Gly Gly Gly
    1685                1690                1695

Ser Gly  Gly Gly Gly Ser Gly  Gly Gly Gly Ser Gly  Gly Gly Gly
    1700                1705                1710

Ser Gly  Gly Gly Gly Ser Arg  Lys Arg Arg Lys Arg  Ser Leu Ser
    1715                1720                1725

Cys Arg  Pro Pro Met Val Lys  Leu Val Cys Pro Ala  Asp Asn Leu
    1730                1735                1740

Arg Ala  Glu Gly Leu Glu Cys  Thr Lys Thr Cys Gln  Asn Tyr Asp
    1745                1750                1755

Leu Glu  Cys Met Ser Met Gly  Cys Val Ser Gly Cys  Leu Cys Pro
    1760                1765                1770

Pro Gly  Met Val Arg His Glu  Asn Arg Cys Val Ala  Leu Glu Arg
    1775                1780                1785

Cys Pro  Cys Phe His Gln Gly  Lys Glu Tyr Ala Pro  Gly Glu Thr
    1790                1795                1800

Val Lys  Ile Gly Cys Asn Thr  Cys Val Cys Arg Asp  Arg Lys Trp
    1805                1810                1815

Asn Cys  Thr Asp His Val Cys  Asp Ala Thr Cys Ser  Thr Ile Gly
    1820                1825                1830

Met Ala  His Tyr Leu Thr Phe  Asp Gly Leu Lys Tyr  Leu Phe Pro
    1835                1840                1845

Gly Glu  Cys Gln Tyr Val Leu  Val Gln Asp Tyr Cys  Gly Ser Asn
    1850                1855                1860

Pro Gly  Thr Phe Arg Ile Leu  Val Gly Asn Lys Gly  Cys Ser His
    1865                1870                1875
```

```
Pro Ser  Val Lys Cys Lys Lys  Arg Val Thr Ile Leu  Val Glu Gly
    1880                1885                1890

Gly Glu  Ile Glu Leu Phe Asp  Gly Glu Val Asn Val  Lys Arg Pro
    1895                1900                1905

Met Lys  Asp Glu Thr His Phe  Glu Val Val Glu Ser  Gly Arg Tyr
    1910                1915                1920

Ile Ile  Leu Leu Leu Gly Lys  Ala Leu Ser Val Val  Trp Asp Arg
    1925                1930                1935

His Leu  Ser Ile Ser Val Val  Leu Lys Gln Thr Tyr  Gln Glu Lys
    1940                1945                1950

Val Cys  Gly Leu Cys Gly Asn  Phe Asp Gly Ile Gln  Asn Asn Asp
    1955                1960                1965

Leu Thr  Ser Ser Asn Leu Gln  Val Glu Glu Asp Pro  Val Asp Phe
    1970                1975                1980

Gly Asn  Ser Trp Lys Val Ser  Ser Gln Cys Ala Asp  Thr Arg Lys
    1985                1990                1995

Val Pro  Leu Asp Ser Ser Pro  Ala Thr Cys His Asn  Asn Ile Met
    2000                2005                2010

Lys Gln  Thr Met Val Asp Ser  Ser Cys Arg Ile Leu  Thr Ser Asp
    2015                2020                2025

Val Phe  Gln Asp Cys Asn Lys  Leu Val Asp Pro Glu  Pro Tyr Leu
    2030                2035                2040

Asp Val  Cys Ile Tyr Asp Thr  Cys Ser Cys Glu Ser  Ile Gly Asp
    2045                2050                2055

Cys Ala  Ala Phe Cys Asp Thr  Ile Ala Ala Tyr Ala  His Val Cys
    2060                2065                2070

Ala Gln  His Gly Lys Val Val  Thr Trp Arg Thr Ala  Thr Leu Cys
    2075                2080                2085
```

```
Pro Gln  Ser Cys Glu Glu Arg  Asn Leu Arg Glu Asn  Gly Tyr Glu
    2090                2095                2100

Ala Glu  Trp Arg Tyr Asn Ser  Cys Ala Pro Ala Cys  Gln Val Thr
    2105                2110                2115

Cys Gln  His Pro Glu Pro Leu  Ala Cys Pro Val Gln  Cys Val Glu
    2120                2125                2130

Gly Cys  His Ala His Cys Pro  Pro Gly Lys Ile Leu  Asp Glu Leu
    2135                2140                2145

Leu Gln  Thr Cys Val Asp Pro  Glu Asp Cys Pro Val  Cys Glu Val
    2150                2155                2160

Ala Gly  Arg Arg Phe Ala Ser  Gly Lys Lys Val Thr  Leu Asn Pro
    2165                2170                2175

Ser Asp  Pro Glu His Cys Gln  Ile Cys His Cys Asp  Val Val Asn
    2180                2185                2190

Leu Thr  Cys Glu Ala Cys Gln  Glu Pro Ile Ser Gly  Thr Ser Glu
    2195                2200                2205

Ser Ala  Thr Pro Glu Ser Gly  Pro Gly Ser Glu Pro  Ala Thr Ser
    2210                2215                2220

Gly Ser  Glu Thr Pro Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser
    2225                2230                2235

Gly Pro  Gly Ser Glu Pro Ala  Thr Ser Gly Ser Glu  Thr Pro Gly
    2240                2245                2250

Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly Pro Gly  Thr Ser Thr
    2255                2260                2265

Glu Pro  Ser Glu Gly Ser Ala  Pro Gly Ser Pro Ala  Gly Ser Pro
    2270                2275                2280

Thr Ser  Thr Glu Glu Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser
    2285                2290                2295
```

```
Gly Pro  Gly Ser Glu Pro Ala  Thr Ser Gly Ser Glu  Thr Pro Gly
    2300                 2305                 2310

Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly Pro Gly  Ser Pro Ala
    2315                 2320                 2325

Gly Ser  Pro Thr Ser Thr Glu  Glu Gly Ser Pro Ala  Gly Ser Pro
    2330                 2335                 2340

Thr Ser  Thr Glu Glu Gly Thr  Ser Thr Glu Pro Ser  Glu Gly Ser
    2345                 2350                 2355

Ala Pro  Gly Thr Ser Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly
    2360                 2365                 2370

Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly Pro Gly  Thr Ser Glu
    2375                 2380                 2385

Ser Ala  Thr Pro Glu Ser Gly  Pro Gly Ser Glu Pro  Ala Thr Ser
    2390                 2395                 2400

Gly Ser  Glu Thr Pro Gly Ser  Glu Pro Ala Thr Ser  Gly Ser Glu
    2405                 2410                 2415

Thr Pro  Gly Ser Pro Ala Gly  Ser Pro Thr Ser Thr  Glu Glu Gly
    2420                 2425                 2430

Thr Ser  Thr Glu Pro Ser Glu  Gly Ser Ala Pro Gly  Thr Ser Thr
    2435                 2440                 2445

Glu Pro  Ser Glu Gly Ser Ala  Pro Gly Ser Glu Pro  Ala Thr Ser
    2450                 2455                 2460

Gly Ser  Glu Thr Pro Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser
    2465                 2470                 2475

Gly Pro  Gly Thr Ser Thr Glu  Pro Ser Glu Gly Ser  Ala Pro Asp
    2480                 2485                 2490

Ser Gly  Gly Gly Gly Ser Gly  Gly Gly Gly Ser Gly  Gly Gly Gly
```

```
    2495                2500                2505

Ser Gly  Gly Gly Gly Ser Gly  Gly Gly Gly Ser Leu  Val Pro Arg
    2510                2515                2520

Gly Ser  Gly Gly Asp Lys Thr  His Thr Cys Pro Pro  Cys Pro Ala
    2525                2530                2535

Pro Glu  Leu Leu Gly Gly Pro  Ser Val Phe Leu Phe  Pro Pro Lys
    2540                2545                2550

Pro Lys  Asp Thr Leu Met Ile  Ser Arg Thr Pro Glu  Val Thr Cys
    2555                2560                2565

Val Val  Val Asp Val Ser His  Glu Asp Pro Glu Val  Lys Phe Asn
    2570                2575                2580

Trp Tyr  Val Asp Gly Val Glu  Val His Asn Ala Lys  Thr Lys Pro
    2585                2590                2595

Arg Glu  Glu Gln Tyr Asn Ser  Thr Tyr Arg Val Val  Ser Val Leu
    2600                2605                2610

Thr Val  Leu His Gln Asp Trp  Leu Asn Gly Lys Glu  Tyr Lys Cys
    2615                2620                2625

Lys Val  Ser Asn Lys Ala Leu  Pro Ala Pro Ile Glu  Lys Thr Ile
    2630                2635                2640

Ser Lys  Ala Lys Gly Gln Pro  Arg Glu Pro Gln Val  Tyr Thr Leu
    2645                2650                2655

Pro Pro  Ser Arg Asp Glu Leu  Thr Lys Asn Gln Val  Ser Leu Thr
    2660                2665                2670

Cys Leu  Val Lys Gly Phe Tyr  Pro Ser Asp Ile Ala  Val Glu Trp
    2675                2680                2685

Glu Ser  Asn Gly Gln Pro Glu  Asn Asn Tyr Lys Thr  Thr Pro Pro
    2690                2695                2700
```

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
    2705   2710   2715

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
    2720   2725   2730

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
    2735   2740   2745

Ser Leu Ser Pro Gly Lys
    2750

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Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
1   5   10   15

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

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

Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val
    50   55   60

Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile
65   70   75   80

Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln
                85   90   95

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

His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser

```
        115                 120                 125

Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp
    130                 135                 140

Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu
145                 150                 155                 160

Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser
                165                 170                 175

Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile
            180                 185                 190

Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr
        195                 200                 205

Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly
    210                 215                 220

Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp
225                 230                 235                 240

Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr
                245                 250                 255

Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val
            260                 265                 270

Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile
        275                 280                 285

Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser
    290                 295                 300

Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met
305                 310                 315                 320

Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His
                325                 330                 335
```

```
Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro
            340                 345                 350

Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp
        355                 360                 365

Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser
    370                 375                 380

Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
385                 390                 395                 400

Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro
                405                 410                 415

Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
            420                 425                 430

Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met
        435                 440                 445

Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu
    450                 455                 460

Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
465                 470                 475                 480

Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro
                485                 490                 495

His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys
            500                 505                 510

Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe
        515                 520                 525

Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp
    530                 535                 540

Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg
545                 550                 555                 560
```

```
Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu
                565                 570                 575

Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val
            580                 585                 590

Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu
        595                 600                 605

Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp
    610                 615                 620

Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
625                 630                 635                 640

Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp
                645                 650                 655

Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe
            660                 665                 670

Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
        675                 680                 685

Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro
    690                 695                 700

Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly
705                 710                 715                 720

Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp
                725                 730                 735

Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
            740                 745                 750

Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Gly Ala Pro Gly
        755                 760                 765

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
    770                 775                 780
```

```
Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
785                 790                 795                 800


Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
                805                 810                 815


Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
            820                 825                 830


Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
        835                 840                 845


Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
    850                 855                 860


Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
865                 870                 875                 880


Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
                885                 890                 895


Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
            900                 905                 910


Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser
        915                 920                 925


Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
    930                 935                 940


Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
945                 950                 955                 960


Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala
                965                 970                 975


Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
            980                 985                 990


Thr Glu Glu Gly Thr Ser Thr Glu  Pro Ser Glu Gly Ser  Ala Pro Gly
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995 1000 1005

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro
1010 1015 1020

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr
1025 1030 1035

Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
1040 1045 1050

Ala Pro Ala Ser Ser Pro Pro Val Leu Lys Arg His Gln Ala Glu
1055 1060 1065

Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr
1070 1075 1080

Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe Asp Ile
1085 1090 1095

Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe Gln Lys Lys
1100 1105 1110

Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr
1115 1120 1125

Gly Met Ser Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser
1130 1135 1140

Gly Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr
1145 1150 1155

Asp Gly Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu
1160 1165 1170

His Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp
1175 1180 1185

Asn Ile Met Val Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser
1190 1195 1200

```
Phe Tyr  Ser Ser Leu Ile Ser  Tyr Glu Glu Asp Gln  Arg Gln Gly
    1205                 1210                 1215

Ala Glu  Pro Arg Lys Asn Phe  Val Lys Pro Asn Glu  Thr Lys Thr
    1220                 1225                 1230

Tyr Phe  Trp Lys Val Gln His  His Met Ala Pro Thr  Lys Asp Glu
    1235                 1240                 1245

Phe Asp  Cys Lys Ala Trp Ala  Tyr Phe Ser Asp Val  Asp Leu Glu
    1250                 1255                 1260

Lys Asp  Val His Ser Gly Leu  Ile Gly Pro Leu Leu  Val Cys His
    1265                 1270                 1275

Thr Asn  Thr Leu Asn Pro Ala  His Gly Arg Gln Val  Thr Val Gln
    1280                 1285                 1290

Glu Phe  Ala Leu Phe Phe Thr  Ile Phe Asp Glu Thr  Lys Ser Trp
    1295                 1300                 1305

Tyr Phe  Thr Glu Asn Met Glu  Arg Asn Cys Arg Ala  Pro Cys Asn
    1310                 1315                 1320

Ile Gln  Met Glu Asp Pro Thr  Phe Lys Glu Asn Tyr  Arg Phe His
    1325                 1330                 1335

Ala Ile  Asn Gly Tyr Ile Met  Asp Thr Leu Pro Gly  Leu Val Met
    1340                 1345                 1350

Ala Gln  Asp Gln Arg Ile Arg  Trp Tyr Leu Leu Ser  Met Gly Ser
    1355                 1360                 1365

Asn Glu  Asn Ile His Ser Ile  His Phe Ser Gly His  Val Phe Thr
    1370                 1375                 1380

Val Arg  Lys Lys Glu Glu Tyr  Lys Met Ala Leu Tyr  Asn Leu Tyr
    1385                 1390                 1395

Pro Gly  Val Phe Glu Thr Val  Glu Met Leu Pro Ser  Lys Ala Gly
    1400                 1405                 1410
```

```
Ile Trp  Arg Val Glu Cys Leu  Ile Gly Glu His Leu  His Ala Gly
    1415                 1420                 1425

Met Ser  Thr Leu Phe Leu Val  Tyr Ser Asn Lys Cys  Gln Thr Pro
    1430                 1435                 1440

Leu Gly  Met Ala Ser Gly His  Ile Arg Asp Phe Gln  Ile Thr Ala
    1445                 1450                 1455

Ser Gly  Gln Tyr Gly Gln Trp  Ala Pro Lys Leu Ala  Arg Leu His
    1460                 1465                 1470

Tyr Ser  Gly Ser Ile Asn Ala  Trp Ser Thr Lys Glu  Pro Phe Ser
    1475                 1480                 1485

Trp Ile  Lys Val Asp Leu Leu  Ala Pro Met Ile Ile  His Gly Ile
    1490                 1495                 1500

Lys Thr  Gln Gly Ala Arg Gln  Lys Phe Ser Ser Leu  Tyr Ile Ser
    1505                 1510                 1515

Gln Phe  Ile Ile Met Tyr Ser  Leu Asp Gly Lys Lys  Trp Gln Thr
    1520                 1525                 1530

Tyr Arg  Gly Asn Ser Thr Gly  Thr Leu Met Val Phe  Phe Gly Asn
    1535                 1540                 1545

Val Asp  Ser Ser Gly Ile Lys  His Asn Ile Phe Asn  Pro Pro Ile
    1550                 1555                 1560

Ile Ala  Arg Tyr Ile Arg Leu  His Pro Thr His Tyr  Ser Ile Arg
    1565                 1570                 1575

Ser Thr  Leu Arg Met Glu Leu  Met Gly Cys Asp Leu  Asn Ser Cys
    1580                 1585                 1590

Ser Met  Pro Leu Gly Met Glu  Ser Lys Ala Ile Ser  Asp Ala Gln
    1595                 1600                 1605

Ile Thr  Ala Ser Ser Tyr Phe  Thr Asn Met Phe Ala  Thr Trp Ser
    1610                 1615                 1620
```

```
Pro Ser  Lys Ala Arg Leu His  Leu Gln Gly Arg Ser  Asn Ala Trp
    1625                1630                1635

Arg Pro  Gln Val Asn Asn Pro  Lys Glu Trp Leu Gln  Val Asp Phe
    1640                1645                1650

Gln Lys  Thr Met Lys Val Thr  Gly Val Thr Thr Gln  Gly Val Lys
    1655                1660                1665

Ser Leu  Leu Thr Ser Met Tyr  Val Lys Glu Phe Leu  Ile Ser Ser
    1670                1675                1680

Ser Gln  Asp Gly His Gln Trp  Thr Leu Phe Phe Gln  Asn Gly Lys
    1685                1690                1695

Val Lys  Val Phe Gln Gly Asn  Gln Asp Ser Phe Thr  Pro Val Val
    1700                1705                1710

Asn Ser  Leu Asp Pro Pro Leu  Leu Thr Arg Tyr Leu  Arg Ile His
    1715                1720                1725

Pro Gln  Ser Trp Val His Gln  Ile Ala Leu Arg Met  Glu Val Leu
    1730                1735                1740

Gly Cys  Glu Ala Gln Asp Leu  Tyr Asp Lys Thr His  Thr Cys Pro
    1745                1750                1755

Pro Cys  Pro Ala Pro Glu Leu  Leu Gly Gly Pro Ser  Val Phe Leu
    1760                1765                1770

Phe Pro  Pro Lys Pro Lys Asp  Thr Leu Met Ile Ser  Arg Thr Pro
    1775                1780                1785

Glu Val  Thr Cys Val Val Val  Asp Val Ser His Glu  Asp Pro Glu
    1790                1795                1800

Val Lys  Phe Asn Trp Tyr Val  Asp Gly Val Glu Val  His Asn Ala
    1805                1810                1815

Lys Thr  Lys Pro Arg Glu Glu  Gln Tyr Asn Ser Thr  Tyr Arg Val
```

1820 1825 1830

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
1835 1840 1845

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
1850 1855 1860

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
1865 1870 1875

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
1880 1885 1890

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
1895 1900 1905

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
1910 1915 1920

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
1925 1930 1935

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
1940 1945 1950

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
1955 1960 1965

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
1970 1975

<210> 71
<211> 2242
<212> PRT
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Ser Leu Ser Cys Arg Pro Pro Met Val Lys Leu Val Cys Pro Ala Asp
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Asn Leu Arg Ala Glu Gly Leu Glu Cys Thr Lys Thr Cys Gln Asn Tyr
            20                  25                  30

Asp Leu Glu Cys Met Ser Met Gly Cys Val Ser Gly Cys Leu Cys Pro
        35                  40                  45

Pro Gly Met Val Arg His Glu Asn Arg Cys Val Ala Leu Glu Arg Cys
    50                  55                  60

Pro Cys Phe His Gln Gly Lys Glu Tyr Ala Pro Gly Glu Thr Val Lys
65                  70                  75                  80

Ile Gly Cys Asn Thr Cys Val Cys Arg Asp Arg Lys Trp Asn Cys Thr
                85                  90                  95

Asp His Val Cys Asp Ala Thr Cys Ser Thr Ile Gly Met Ala His Tyr
            100                 105                 110

Leu Thr Phe Asp Gly Leu Lys Tyr Leu Phe Pro Gly Glu Cys Gln Tyr
        115                 120                 125

Val Leu Val Gln Asp Tyr Cys Gly Ser Asn Pro Gly Thr Phe Arg Ile
    130                 135                 140

Leu Val Gly Asn Lys Gly Cys Ser His Pro Ser Val Lys Cys Lys Lys
145                 150                 155                 160

Arg Val Thr Ile Leu Val Glu Gly Gly Glu Ile Glu Leu Phe Asp Gly
                165                 170                 175

Glu Val Asn Val Lys Arg Pro Met Lys Asp Glu Thr His Phe Glu Val
            180                 185                 190

Val Glu Ser Gly Arg Tyr Ile Ile Leu Leu Leu Gly Lys Ala Leu Ser
        195                 200                 205

Val Val Trp Asp Arg His Leu Ser Ile Ser Val Val Leu Lys Gln Thr
    210                 215                 220

Tyr Gln Glu Lys Val Cys Gly Leu Cys Gly Asn Phe Asp Gly Ile Gln
```

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225                 230                 235                 240

Asn Asn Asp Leu Thr Ser Ser Asn Leu Gln Val Glu Glu Asp Pro Val
                245                 250                 255

Asp Phe Gly Asn Ser Trp Lys Val Ser Ser Gln Cys Ala Asp Thr Arg
            260                 265                 270

Lys Val Pro Leu Asp Ser Ser Pro Ala Thr Cys His Asn Asn Ile Met
        275                 280                 285

Lys Gln Thr Met Val Asp Ser Ser Cys Arg Ile Leu Thr Ser Asp Val
    290                 295                 300

Phe Gln Asp Cys Asn Lys Leu Val Asp Pro Glu Pro Tyr Leu Asp Val
305                 310                 315                 320

Cys Ile Tyr Asp Thr Cys Ser Cys Glu Ser Ile Gly Asp Cys Ala Ala
                325                 330                 335

Phe Cys Asp Thr Ile Ala Ala Tyr Ala His Val Cys Ala Gln His Gly
            340                 345                 350

Lys Val Val Thr Trp Arg Thr Ala Thr Leu Cys Pro Gln Ser Cys Glu
        355                 360                 365

Glu Arg Asn Leu Arg Glu Asn Gly Tyr Glu Ala Glu Trp Arg Tyr Asn
    370                 375                 380

Ser Cys Ala Pro Ala Cys Gln Val Thr Cys Gln His Pro Glu Pro Leu
385                 390                 395                 400

Ala Cys Pro Val Gln Cys Val Glu Gly Cys His Ala His Cys Pro Pro
                405                 410                 415

Gly Lys Ile Leu Asp Glu Leu Leu Gln Thr Cys Val Asp Pro Glu Asp
            420                 425                 430

Cys Pro Val Cys Glu Val Ala Gly Arg Arg Phe Ala Ser Gly Lys Lys
        435                 440                 445
```

```
Val Thr Leu Asn Pro Ser Asp Pro Glu His Cys Gln Ile Cys His Cys
    450                 455                 460

Asp Val Val Asn Leu Thr Cys Glu Ala Cys Gln Glu Pro Ile Ser Gly
465                 470                 475                 480

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
                485                 490                 495

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
            500                 505                 510

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
        515                 520                 525

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
    530                 535                 540

Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
545                 550                 555                 560

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
                565                 570                 575

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
            580                 585                 590

Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
        595                 600                 605

Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
    610                 615                 620

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser
625                 630                 635                 640

Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
                645                 650                 655

Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
            660                 665                 670
```

```
Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala
        675                 680                 685

Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
    690                 695                 700

Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
705                 710                 715                 720

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro Ala
                725                 730                 735

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
            740                 745                 750

Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Asp
        755                 760                 765

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
    770                 775                 780

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Leu Val Pro Arg Gly Ser
785                 790                 795                 800

Gly Gly Ala Ser Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu
                805                 810                 815

Ser Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala
            820                 825                 830

Arg Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val
        835                 840                 845

Val Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn
    850                 855                 860

Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
865                 870                 875                 880

Gln Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala
                885                 890                 895
```

```
Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala
            900                 905                 910

Ser Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu
        915                 920                 925

Asp Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val
    930                 935                 940

Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr
945                 950                 955                 960

Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu
                965                 970                 975

Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys
            980                 985                 990

Thr Gln Thr Leu His Lys Phe Ile  Leu Leu Phe Ala Val  Phe Asp Glu
        995                 1000                1005

Gly Lys  Ser Trp His Ser Glu  Thr Lys Asn Ser Leu  Met Gln Asp
    1010                1015                1020

Arg Asp  Ala Ala Ser Ala Arg  Ala Trp Pro Lys Met  His Thr Val
    1025                1030                1035

Asn Gly  Tyr Val Asn Arg Ser  Leu Pro Gly Leu Ile  Gly Cys His
    1040                1045                1050

Arg Lys  Ser Val Tyr Trp His  Val Ile Gly Met Gly  Thr Thr Pro
    1055                1060                1065

Glu Val  His Ser Ile Phe Leu  Glu Gly His Thr Phe  Leu Val Arg
    1070                1075                1080

Asn His  Arg Gln Ala Ser Leu  Glu Ile Ser Pro Ile  Thr Phe Leu
    1085                1090                1095

Thr Ala  Gln Thr Leu Leu Met  Asp Leu Gly Gln Phe  Leu Leu Phe
```

```
    1100                1105                1110

Cys His  Ile Ser Ser His Gln  His Asp Gly Met Glu  Ala Tyr Val
    1115                1120                1125

Lys Val  Asp Ser Cys Pro Glu  Glu Pro Gln Leu Arg  Met Lys Asn
    1130                1135                1140

Asn Glu  Glu Ala Glu Asp Tyr  Asp Asp Asp Leu Thr  Asp Ser Glu
    1145                1150                1155

Met Asp  Val Val Arg Phe Asp  Asp Asp Asn Ser Pro  Ser Phe Ile
    1160                1165                1170

Gln Ile  Arg Ser Val Ala Lys  Lys His Pro Lys Thr  Trp Val His
    1175                1180                1185

Tyr Ile  Ala Ala Glu Glu Glu  Asp Trp Asp Tyr Ala  Pro Leu Val
    1190                1195                1200

Leu Ala  Pro Asp Asp Arg Ser  Tyr Lys Ser Gln Tyr  Leu Asn Asn
    1205                1210                1215

Gly Pro  Gln Arg Ile Gly Arg  Lys Tyr Lys Lys Val  Arg Phe Met
    1220                1225                1230

Ala Tyr  Thr Asp Glu Thr Phe  Lys Thr Arg Glu Ala  Ile Gln His
    1235                1240                1245

Glu Ser  Gly Ile Leu Gly Pro  Leu Leu Tyr Gly Glu  Val Gly Asp
    1250                1255                1260

Thr Leu  Leu Ile Ile Phe Lys  Asn Gln Ala Ser Arg  Pro Tyr Asn
    1265                1270                1275

Ile Tyr  Pro His Gly Ile Thr  Asp Val Arg Pro Leu  Tyr Ser Arg
    1280                1285                1290

Arg Leu  Pro Lys Gly Val Lys  His Leu Lys Asp Phe  Pro Ile Leu
    1295                1300                1305
```

```
Pro Gly  Glu Ile Phe Lys Tyr  Lys Trp Thr Val Thr  Val Glu Asp
    1310                1315                1320

Gly Pro  Thr Lys Ser Asp Pro  Arg Cys Leu Thr Arg  Tyr Tyr Ser
    1325                1330                1335

Ser Phe  Val Asn Met Glu Arg  Asp Leu Ala Ser Gly  Leu Ile Gly
    1340                1345                1350

Pro Leu  Leu Ile Cys Tyr Lys  Glu Ser Val Asp Gln  Arg Gly Asn
    1355                1360                1365

Gln Ile  Met Ser Asp Lys Arg  Asn Val Ile Leu Phe  Ser Val Phe
    1370                1375                1380

Asp Glu  Asn Arg Ser Trp Tyr  Leu Thr Glu Asn Ile  Gln Arg Phe
    1385                1390                1395

Leu Pro  Asn Pro Ala Gly Val  Gln Leu Glu Asp Pro  Glu Phe Gln
    1400                1405                1410

Ala Ser  Asn Ile Met His Ser  Ile Asn Gly Tyr Val  Phe Asp Ser
    1415                1420                1425

Leu Gln  Leu Ser Val Cys Leu  His Glu Val Ala Tyr  Trp Tyr Ile
    1430                1435                1440

Leu Ser  Ile Gly Ala Gln Thr  Asp Phe Leu Ser Val  Phe Phe Ser
    1445                1450                1455

Gly Tyr  Thr Phe Lys His Lys  Met Val Tyr Glu Asp  Thr Leu Thr
    1460                1465                1470

Leu Phe  Pro Phe Ser Gly Glu  Thr Val Phe Met Ser  Met Glu Asn
    1475                1480                1485

Pro Gly  Leu Trp Ile Leu Gly  Cys His Asn Ser Asp  Phe Arg Asn
    1490                1495                1500

Arg Gly  Met Thr Ala Leu Leu  Lys Val Ser Ser Cys  Asp Lys Asn
    1505                1510                1515
```

```
Thr Gly  Asp Tyr Tyr Glu Asp  Ser Tyr Glu Asp Ile  Ser Ala Tyr
    1520                1525                1530

Leu Leu  Ser Lys Asn Asn Ala  Ile Glu Pro Arg Ser  Phe Ser Gln
    1535                1540                1545

Asn Pro  Pro Val Leu Lys Arg  His Gln Arg Glu Ile  Thr Arg Thr
    1550                1555                1560

Thr Leu  Gln Ser Asp Gln Glu  Glu Ile Asp Tyr Asp  Asp Thr Ile
    1565                1570                1575

Ser Val  Glu Met Lys Lys Glu  Asp Phe Asp Ile Tyr  Asp Glu Asp
    1580                1585                1590

Glu Asn  Gln Ser Pro Arg Ser  Phe Gln Lys Lys Thr  Arg His Tyr
    1595                1600                1605

Phe Ile  Ala Ala Val Glu Arg  Leu Trp Asp Tyr Gly  Met Ser Ser
    1610                1615                1620

Ser Pro  His Val Leu Arg Asn  Arg Ala Gln Ser Gly  Ser Val Pro
    1625                1630                1635

Gln Phe  Lys Lys Val Val Phe  Gln Glu Phe Thr Asp  Gly Ser Phe
    1640                1645                1650

Thr Gln  Pro Leu Tyr Arg Gly  Glu Leu Asn Glu His  Leu Gly Leu
    1655                1660                1665

Leu Gly  Pro Tyr Ile Arg Ala  Glu Val Glu Asp Asn  Ile Met Val
    1670                1675                1680

Thr Phe  Arg Asn Gln Ala Ser  Arg Pro Tyr Ser Phe  Tyr Ser Ser
    1685                1690                1695

Leu Ile  Ser Tyr Glu Glu Asp  Gln Arg Gln Gly Ala  Glu Pro Arg
    1700                1705                1710

Lys Asn  Phe Val Lys Pro Asn  Glu Thr Lys Thr Tyr  Phe Trp Lys
    1715                1720                1725
```

```
Val Gln  His His Met Ala Pro  Thr Lys Asp Glu Phe  Asp Cys Lys
    1730                1735                1740

Ala Trp  Ala Tyr Phe Ser Asp  Val Asp Leu Glu Lys  Asp Val His
    1745                1750                1755

Ser Gly  Leu Ile Gly Pro Leu  Leu Val Cys His Thr  Asn Thr Leu
    1760                1765                1770

Asn Pro  Ala His Gly Arg Gln  Val Thr Val Gln Glu  Phe Ala Leu
    1775                1780                1785

Phe Phe  Thr Ile Phe Asp Glu  Thr Lys Ser Trp Tyr  Phe Thr Glu
    1790                1795                1800

Asn Met  Glu Arg Asn Cys Arg  Ala Pro Cys Asn Ile  Gln Met Glu
    1805                1810                1815

Asp Pro  Thr Phe Lys Glu Asn  Tyr Arg Phe His Ala  Ile Asn Gly
    1820                1825                1830

Tyr Ile  Met Asp Thr Leu Pro  Gly Leu Val Met Ala  Gln Asp Gln
    1835                1840                1845

Arg Ile  Arg Trp Tyr Leu Leu  Ser Met Gly Ser Asn  Glu Asn Ile
    1850                1855                1860

His Ser  Ile His Phe Ser Gly  His Val Phe Thr Val  Arg Lys Lys
    1865                1870                1875

Glu Glu  Tyr Lys Met Ala Leu  Tyr Asn Leu Tyr Pro  Gly Val Phe
    1880                1885                1890

Glu Thr  Val Glu Met Leu Pro  Ser Lys Ala Gly Ile  Trp Arg Val
    1895                1900                1905

Glu Cys  Leu Ile Gly Glu His  Leu His Ala Gly Met  Ser Thr Leu
    1910                1915                1920

Phe Leu  Val Tyr Ser Asn Lys  Cys Gln Thr Pro Leu  Gly Met Ala
```

```
    1925                1930                1935

Ser Gly  His Ile Arg Asp Phe  Gln Ile Thr Ala Ser  Gly Gln Tyr
    1940                1945                1950

Gly Gln  Trp Ala Pro Lys Leu  Ala Arg Leu His Tyr  Ser Gly Ser
    1955                1960                1965

Ile Asn  Ala Trp Ser Thr Lys  Glu Pro Phe Ser Trp  Ile Lys Val
    1970                1975                1980

Asp Leu  Leu Ala Pro Met Ile  Ile His Gly Ile Lys  Thr Gln Gly
    1985                1990                1995

Ala Arg  Gln Lys Phe Ser Ser  Leu Tyr Ile Ser Gln  Phe Ile Ile
    2000                2005                2010

Met Tyr  Ser Leu Asp Gly Lys  Lys Trp Gln Thr Tyr  Arg Gly Asn
    2015                2020                2025

Ser Thr  Gly Thr Leu Met Val  Phe Phe Gly Asn Val  Asp Ser Ser
    2030                2035                2040

Gly Ile  Lys His Asn Ile Phe  Asn Pro Pro Ile Ile  Ala Arg Tyr
    2045                2050                2055

Ile Arg  Leu His Pro Thr His  Tyr Ser Ile Arg Ser  Thr Leu Arg
    2060                2065                2070

Met Glu  Leu Met Gly Cys Asp  Leu Asn Ser Cys Ser  Met Pro Leu
    2075                2080                2085

Gly Met  Glu Ser Lys Ala Ile  Ser Asp Ala Gln Ile  Thr Ala Ser
    2090                2095                2100

Ser Tyr  Phe Thr Asn Met Phe  Ala Thr Trp Ser Pro  Ser Lys Ala
    2105                2110                2115

Arg Leu  His Leu Gln Gly Arg  Ser Asn Ala Trp Arg  Pro Gln Val
    2120                2125                2130
```

```
Asn Asn  Pro Lys Glu Trp Leu  Gln Val Asp Phe Gln  Lys Thr Met
    2135                2140                2145


Lys Val  Thr Gly Val Thr Thr  Gln Gly Val Lys Ser  Leu Leu Thr
    2150                2155                2160


Ser Met  Tyr Val Lys Glu Phe  Leu Ile Ser Ser Ser  Gln Asp Gly
    2165                2170                2175


His Gln  Trp Thr Leu Phe Phe  Gln Asn Gly Lys Val  Lys Val Phe
    2180                2185                2190


Gln Gly  Asn Gln Asp Ser Phe  Thr Pro Val Val Asn  Ser Leu Asp
    2195                2200                2205


Pro Pro  Leu Leu Thr Arg Tyr  Leu Arg Ile His Pro  Gln Ser Trp
    2210                2215                2220


Val His  Gln Ile Ala Leu Arg  Met Glu Val Leu Gly  Cys Glu Ala
    2225                2230                2235


Gln Asp  Leu Tyr
    2240
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<211> 1959
<212> PRT
<213> Artificial Sequence

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<223> pSYN-FVIII-173

<400> 72

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Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro
            20                  25                  30


Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys
        35                  40                  45


Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys Pro
```

```
    50                  55                  60

Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val
65                  70                  75                  80

Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val
                85                  90                  95

Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala
            100                 105                 110

Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val
        115                 120                 125

Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn
    130                 135                 140

Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser
145                 150                 155                 160

His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu
                165                 170                 175

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

His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp
        195                 200                 205

His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser
    210                 215                 220

Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg
225                 230                 235                 240

Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His
                245                 250                 255

Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu
            260                 265                 270
```

```
Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile
        275                 280                 285

Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly
    290                 295                 300

Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met
305                 310                 315                 320

Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg
                325                 330                 335

Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp
            340                 345                 350

Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro Ser Phe
        355                 360                 365

Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His
    370                 375                 380

Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu
385                 390                 395                 400

Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro
                405                 410                 415

Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr
            420                 425                 430

Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile
        435                 440                 445

Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile
    450                 455                 460

Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile
465                 470                 475                 480

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

```
His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys
            500                 505                 510

Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys
        515                 520                 525

Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala
    530                 535                 540

Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp
545                 550                 555                 560

Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe
                565                 570                 575

Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln
            580                 585                 590

Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe
        595                 600                 605

Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser
    610                 615                 620

Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu
625                 630                 635                 640

Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr
                645                 650                 655

Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro
            660                 665                 670

Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp
        675                 680                 685

Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr Ala
    690                 695                 700

Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu
705                 710                 715                 720
```

```
Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala
                725                 730                 735

Ile Glu Pro Arg Ser Phe Ser Gln Asn Gly Ala Pro Gly Thr Ser Glu
            740                 745                 750

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
        755                 760                 765

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
    770                 775                 780

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu
785                 790                 795                 800

Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu
                805                 810                 815

Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
            820                 825                 830

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
        835                 840                 845

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
    850                 855                 860

Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
865                 870                 875                 880

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr
                885                 890                 895

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
            900                 905                 910

Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
        915                 920                 925

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
```

```
    930                 935                 940

Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly
945                 950                 955                 960

Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
                965                 970                 975

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
            980                 985                 990

Glu Pro Ser Glu Gly Ser Ala Pro  Gly Ser Glu Pro Ala  Thr Ser Gly
        995                 1000                1005

Ser Glu  Thr Pro Gly Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly
    1010                1015                1020

Pro Gly  Thr Ser Thr Glu Pro  Ser Glu Gly Ser Ala  Pro Ala Ser
    1025                1030                1035

Ser Pro  Pro Val Leu Lys Arg  His Gln Arg Glu Ile  Thr Arg Thr
    1040                1045                1050

Thr Leu  Gln Ser Asp Gln Glu  Glu Ile Asp Tyr Asp  Asp Thr Ile
    1055                1060                1065

Ser Val  Glu Met Lys Lys Glu  Asp Phe Asp Ile Tyr  Asp Glu Asp
    1070                1075                1080

Glu Asn  Gln Ser Pro Arg Ser  Phe Gln Lys Lys Thr  Arg His Tyr
    1085                1090                1095

Phe Ile  Ala Ala Val Glu Arg  Leu Trp Asp Tyr Gly  Met Ser Ser
    1100                1105                1110

Ser Pro  His Val Leu Arg Asn  Arg Ala Gln Ser Gly  Ser Val Pro
    1115                1120                1125

Gln Phe  Lys Lys Val Val Phe  Gln Glu Phe Thr Asp  Gly Ser Phe
    1130                1135                1140
```

```
Thr Gln  Pro Leu Tyr Arg Gly  Glu Leu Asn Glu His  Leu Gly Leu
    1145                1150                1155

Leu Gly  Pro Tyr Ile Arg Ala  Glu Val Glu Asp Asn  Ile Met Val
    1160                1165                1170

Thr Phe  Arg Asn Gln Ala Ser  Arg Pro Tyr Ser Phe  Tyr Ser Ser
    1175                1180                1185

Leu Ile  Ser Tyr Glu Glu Asp  Gln Arg Gln Gly Ala  Glu Pro Arg
    1190                1195                1200

Lys Asn  Phe Val Lys Pro Asn  Glu Thr Lys Thr Tyr  Phe Trp Lys
    1205                1210                1215

Val Gln  His His Met Ala Pro  Thr Lys Asp Glu Phe  Asp Cys Lys
    1220                1225                1230

Ala Trp  Ala Tyr Phe Ser Asp  Val Asp Leu Glu Lys  Asp Val His
    1235                1240                1245

Ser Gly  Leu Ile Gly Pro Leu  Leu Val Cys His Thr  Asn Thr Leu
    1250                1255                1260

Asn Pro  Ala His Gly Arg Gln  Val Thr Val Gln Glu  Phe Ala Leu
    1265                1270                1275

Phe Phe  Thr Ile Phe Asp Glu  Thr Lys Ser Trp Tyr  Phe Thr Glu
    1280                1285                1290

Asn Met  Glu Arg Asn Cys Arg  Ala Pro Cys Asn Ile  Gln Met Glu
    1295                1300                1305

Asp Pro  Thr Phe Lys Glu Asn  Tyr Arg Phe His Ala  Ile Asn Gly
    1310                1315                1320

Tyr Ile  Met Asp Thr Leu Pro  Gly Leu Val Met Ala  Gln Asp Gln
    1325                1330                1335

Arg Ile  Arg Trp Tyr Leu Leu  Ser Met Gly Ser Asn  Glu Asn Ile
    1340                1345                1350
```

```
His Ser  Ile His Phe Ser Gly  His Val Phe Thr Val  Arg Lys Lys
    1355                1360                1365

Glu Glu  Tyr Lys Met Ala Leu  Tyr Asn Leu Tyr Pro  Gly Val Phe
    1370                1375                1380

Glu Thr  Val Glu Met Leu Pro  Ser Lys Ala Gly Ile  Trp Arg Val
    1385                1390                1395

Glu Cys  Leu Ile Gly Glu His  Leu His Ala Gly Met  Ser Thr Leu
    1400                1405                1410

Phe Leu  Val Tyr Ser Asn Lys  Cys Gln Thr Pro Leu  Gly Met Ala
    1415                1420                1425

Ser Gly  His Ile Arg Asp Phe  Gln Ile Thr Ala Ser  Gly Gln Tyr
    1430                1435                1440

Gly Gln  Trp Ala Pro Lys Leu  Ala Arg Leu His Tyr  Ser Gly Ser
    1445                1450                1455

Ile Asn  Ala Trp Ser Thr Lys  Glu Pro Phe Ser Trp  Ile Lys Val
    1460                1465                1470

Asp Leu  Leu Ala Pro Met Ile  Ile His Gly Ile Lys  Thr Gln Gly
    1475                1480                1485

Ala Arg  Gln Lys Phe Ser Ser  Leu Tyr Ile Ser Gln  Phe Ile Ile
    1490                1495                1500

Met Tyr  Ser Leu Asp Gly Lys  Lys Trp Gln Thr Tyr  Arg Gly Asn
    1505                1510                1515

Ser Thr  Gly Thr Leu Met Val  Phe Phe Gly Asn Val  Asp Ser Ser
    1520                1525                1530

Gly Ile  Lys His Asn Ile Phe  Asn Pro Pro Ile Ile  Ala Arg Tyr
    1535                1540                1545

Ile Arg  Leu His Pro Thr His  Tyr Ser Ile Arg Ser  Thr Leu Arg
    1550                1555                1560
```

```
Met Glu  Leu Met Gly Cys Asp  Leu Asn Ser Cys Ser  Met Pro Leu
    1565                 1570                 1575

Gly Met  Glu Ser Lys Ala Ile  Ser Asp Ala Gln Ile  Thr Ala Ser
    1580                 1585                 1590

Ser Tyr  Phe Thr Asn Met Phe  Ala Thr Trp Ser Pro  Ser Lys Ala
    1595                 1600                 1605

Arg Leu  His Leu Gln Gly Arg  Ser Asn Ala Trp Arg  Pro Gln Val
    1610                 1615                 1620

Asn Asn  Pro Lys Glu Trp Leu  Gln Val Asp Phe Gln  Lys Thr Met
    1625                 1630                 1635

Lys Val  Thr Gly Val Thr Thr  Gln Gly Val Lys Ser  Leu Leu Thr
    1640                 1645                 1650

Ser Met  Tyr Val Lys Glu Phe  Leu Ile Ser Ser Ser  Gln Asp Gly
    1655                 1660                 1665

His Gln  Trp Thr Leu Phe Phe  Gln Asn Gly Lys Val  Lys Val Phe
    1670                 1675                 1680

Gln Gly  Asn Gln Asp Ser Phe  Thr Pro Val Val Asn  Ser Leu Asp
    1685                 1690                 1695

Pro Pro  Leu Leu Thr Arg Tyr  Leu Arg Ile His Pro  Gln Ser Trp
    1700                 1705                 1710

Val His  Gln Ile Ala Leu Arg  Met Glu Val Leu Gly  Cys Glu Ala
    1715                 1720                 1725

Gln Asp  Leu Tyr Asp Lys Thr  His Thr Cys Pro Pro  Cys Pro Ala
    1730                 1735                 1740

Pro Glu  Leu Leu Gly Gly Pro  Ser Val Phe Leu Phe  Pro Pro Lys
    1745                 1750                 1755

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

```
    1760                1765                1770

Val Val  Val Asp Val Ser His  Glu Asp Pro Glu Val  Lys Phe Asn
    1775                1780                1785

Trp Tyr  Val Asp Gly Val Glu  Val His Asn Ala Lys  Thr Lys Pro
    1790                1795                1800

Arg Glu  Glu Gln Tyr Asn Ser  Thr Tyr Arg Val Val  Ser Val Leu
    1805                1810                1815

Thr Val  Leu His Gln Asp Trp  Leu Asn Gly Lys Glu  Tyr Lys Cys
    1820                1825                1830

Lys Val  Ser Asn Lys Ala Leu  Pro Ala Pro Ile Glu  Lys Thr Ile
    1835                1840                1845

Ser Lys  Ala Lys Gly Gln Pro  Arg Glu Pro Gln Val  Tyr Thr Leu
    1850                1855                1860

Pro Pro  Ser Arg Asp Glu Leu  Thr Lys Asn Gln Val  Ser Leu Thr
    1865                1870                1875

Cys Leu  Val Lys Gly Phe Tyr  Pro Ser Asp Ile Ala  Val Glu Trp
    1880                1885                1890

Glu Ser  Asn Gly Gln Pro Glu  Asn Asn Tyr Lys Thr  Thr Pro Pro
    1895                1900                1905

Val Leu  Asp Ser Asp Gly Ser  Phe Phe Leu Tyr Ser  Lys Leu Thr
    1910                1915                1920

Val Asp  Lys Ser Arg Trp Gln  Gln Gly Asn Val Phe  Ser Cys Ser
    1925                1930                1935

Val Met  His Glu Ala Leu His  Asn His Tyr Thr Gln  Lys Ser Leu
    1940                1945                1950

Ser Leu  Ser Pro Gly Lys
    1955
```

<210> 73
<211> 1984
<212> PRT
<213> Artificial Sequence

<220>
<223> FVIII 195 (dual chain FVIIIFc with two 144 AE XTENs at amino acid 1656 and 1900)

<400> 73

Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
1 5 10 15

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

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

Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val
50 55 60

Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile
65 70 75 80

Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln
85 90 95

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

His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser
115 120 125

Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp
130 135 140

Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu
145 150 155 160

Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser
165 170 175

```
Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile
            180                 185                 190

Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr
        195                 200                 205

Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly
    210                 215                 220

Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp
225                 230                 235                 240

Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr
                245                 250                 255

Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val
            260                 265                 270

Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile
        275                 280                 285

Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser
    290                 295                 300

Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met
305                 310                 315                 320

Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His
                325                 330                 335

Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro
            340                 345                 350

Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp
        355                 360                 365

Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser
    370                 375                 380

Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
385                 390                 395                 400
```

```
Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro
                405                 410                 415

Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
            420                 425                 430

Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met
        435                 440                 445

Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu
    450                 455                 460

Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
465                 470                 475                 480

Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro
                485                 490                 495

His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys
            500                 505                 510

Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe
        515                 520                 525

Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp
    530                 535                 540

Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg
545                 550                 555                 560

Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu
                565                 570                 575

Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val
            580                 585                 590

Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu
        595                 600                 605

Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp
    610                 615                 620
```

```
Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
625                 630                 635                 640


Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp
                645                 650                 655


Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe
            660                 665                 670


Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
        675                 680                 685


Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro
    690                 695                 700


Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly
705                 710                 715                 720


Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp
                725                 730                 735


Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
            740                 745                 750


Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Pro Pro Val Leu
        755                 760                 765


Lys Arg His Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Gly Ala Pro
    770                 775                 780


Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ala Ser Pro
785                 790                 795                 800


Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
                805                 810                 815


Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
            820                 825                 830


Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Thr Pro Gly
```

```
        835                 840                 845

Ser Gly Thr Ala Ser Ser Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
    850                 855                 860

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
865                 870                 875                 880

Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Thr
                885                 890                 895

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
            900                 905                 910

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
        915                 920                 925

Ala Ser Ser Ser Asp Gln Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser
    930                 935                 940

Val Glu Met Lys Lys Glu Asp Phe Asp Ile Tyr Asp Glu Asp Glu Asn
945                 950                 955                 960

Gln Ser Pro Arg Ser Phe Gln Lys Lys Thr Arg His Tyr Phe Ile Ala
                965                 970                 975

Ala Val Glu Arg Leu Trp Asp Tyr Gly Met Ser Ser Ser Pro His Val
            980                 985                 990

Leu Arg Asn Arg Ala Gln Ser Gly  Ser Val Pro Gln Phe  Lys Lys Val
        995                 1000                1005

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

Arg Gly  Glu Leu Asn Glu His  Leu Gly Leu Leu Gly  Pro Tyr Ile
    1025                1030                1035

Arg Ala  Glu Val Glu Asp Asn  Ile Met Val Thr Phe  Arg Asn Gln
    1040                1045                1050
```

```
Ala Ser  Arg Pro Tyr Ser Phe  Tyr Ser Ser Leu Ile  Ser Tyr Glu
    1055                1060                1065

Glu Asp  Gln Arg Gln Gly Ala  Glu Pro Arg Lys Asn  Phe Val Lys
    1070                1075                1080

Pro Asn  Glu Thr Lys Thr Tyr  Phe Trp Lys Val Gln  His His Met
    1085                1090                1095

Ala Pro  Thr Lys Asp Glu Phe  Asp Cys Lys Ala Trp  Ala Tyr Phe
    1100                1105                1110

Ser Asp  Val Asp Leu Glu Lys  Asp Val His Ser Gly  Leu Ile Gly
    1115                1120                1125

Pro Leu  Leu Val Cys His Thr  Asn Thr Leu Asn Pro  Ala His Gly
    1130                1135                1140

Arg Gln  Val Thr Val Gln Glu  Phe Ala Leu Phe Phe  Thr Ile Phe
    1145                1150                1155

Asp Glu  Thr Lys Ser Trp Tyr  Phe Thr Glu Asn Met  Glu Arg Asn
    1160                1165                1170

Cys Arg  Gly Ala Pro Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly
    1175                1180                1185

Pro Gly  Ser Glu Pro Ala Thr  Ser Gly Ser Glu Thr  Pro Gly Thr
    1190                1195                1200

Ser Glu  Ser Ala Thr Pro Glu  Ser Gly Pro Gly Ser  Glu Pro Ala
    1205                1210                1215

Thr Ser  Gly Ser Glu Thr Pro  Gly Thr Ser Glu Ser  Ala Thr Pro
    1220                1225                1230

Glu Ser  Gly Pro Gly Thr Ser  Thr Glu Pro Ser Glu  Gly Ser Ala
    1235                1240                1245

Pro Gly  Thr Ser Glu Ser Ala  Thr Pro Glu Ser Gly  Pro Gly Ser
    1250                1255                1260
```

```
Pro Ala  Gly Ser Pro Thr Ser  Thr Glu Glu Gly Ser  Pro Ala Gly
    1265                1270                1275

Ser Pro  Thr Ser Thr Glu Glu  Gly Ser Pro Ala Gly  Ser Pro Thr
    1280                1285                1290

Ser Thr  Glu Glu Gly Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly
    1295                1300                1305

Pro Gly  Thr Ser Thr Glu Pro  Ser Glu Gly Ser Ala  Pro Gly Ala
    1310                1315                1320

Ser Ser  Ala Pro Cys Asn Ile  Gln Met Glu Asp Pro  Thr Phe Lys
    1325                1330                1335

Glu Asn  Tyr Arg Phe His Ala  Ile Asn Gly Tyr Ile  Met Asp Thr
    1340                1345                1350

Leu Pro  Gly Leu Val Met Ala  Gln Asp Gln Arg Ile  Arg Trp Tyr
    1355                1360                1365

Leu Leu  Ser Met Gly Ser Asn  Glu Asn Ile His Ser  Ile His Phe
    1370                1375                1380

Ser Gly  His Val Phe Thr Val  Arg Lys Lys Glu Glu  Tyr Lys Met
    1385                1390                1395

Ala Leu  Tyr Asn Leu Tyr Pro  Gly Val Phe Glu Thr  Val Glu Met
    1400                1405                1410

Leu Pro  Ser Lys Ala Gly Ile  Trp Arg Val Glu Cys  Leu Ile Gly
    1415                1420                1425

Glu His  Leu His Ala Gly Met  Ser Thr Leu Phe Leu  Val Tyr Ser
    1430                1435                1440

Asn Lys  Cys Gln Thr Pro Leu  Gly Met Ala Ser Gly  His Ile Arg
    1445                1450                1455

Asp Phe  Gln Ile Thr Ala Ser  Gly Gln Tyr Gly Gln  Trp Ala Pro
    1460                1465                1470
```

```
Lys Leu  Ala Arg Leu His Tyr  Ser Gly Ser Ile Asn  Ala Trp Ser
    1475                 1480                 1485

Thr Lys  Glu Pro Phe Ser Trp  Ile Lys Val Asp Leu  Leu Ala Pro
    1490                 1495                 1500

Met Ile  Ile His Gly Ile Lys  Thr Gln Gly Ala Arg  Gln Lys Phe
    1505                 1510                 1515

Ser Ser  Leu Tyr Ile Ser Gln  Phe Ile Ile Met Tyr  Ser Leu Asp
    1520                 1525                 1530

Gly Lys  Lys Trp Gln Thr Tyr  Arg Gly Asn Ser Thr  Gly Thr Leu
    1535                 1540                 1545

Met Val  Phe Phe Gly Asn Val  Asp Ser Ser Gly Ile  Lys His Asn
    1550                 1555                 1560

Ile Phe  Asn Pro Pro Ile Ile  Ala Arg Tyr Ile Arg  Leu His Pro
    1565                 1570                 1575

Thr His  Tyr Ser Ile Arg Ser  Thr Leu Arg Met Glu  Leu Met Gly
    1580                 1585                 1590

Cys Asp  Leu Asn Ser Cys Ser  Met Pro Leu Gly Met  Glu Ser Lys
    1595                 1600                 1605

Ala Ile  Ser Asp Ala Gln Ile  Thr Ala Ser Ser Tyr  Phe Thr Asn
    1610                 1615                 1620

Met Phe  Ala Thr Trp Ser Pro  Ser Lys Ala Arg Leu  His Leu Gln
    1625                 1630                 1635

Gly Arg  Ser Asn Ala Trp Arg  Pro Gln Val Asn Asn  Pro Lys Glu
    1640                 1645                 1650

Trp Leu  Gln Val Asp Phe Gln  Lys Thr Met Lys Val  Thr Gly Val
    1655                 1660                 1665

Thr Thr  Gln Gly Val Lys Ser  Leu Leu Thr Ser Met  Tyr Val Lys
```

```
    1670                1675                1680

Glu Phe  Leu Ile Ser Ser Ser  Gln Asp Gly His Gln  Trp Thr Leu
    1685                1690                1695

Phe Phe  Gln Asn Gly Lys Val  Lys Val Phe Gln Gly  Asn Gln Asp
    1700                1705                1710

Ser Phe  Thr Pro Val Val Asn  Ser Leu Asp Pro Pro  Leu Leu Thr
    1715                1720                1725

Arg Tyr  Leu Arg Ile His Pro  Gln Ser Trp Val His  Gln Ile Ala
    1730                1735                1740

Leu Arg  Met Glu Val Leu Gly  Cys Glu Ala Gln Asp  Leu Tyr Asp
    1745                1750                1755

Lys Thr  His Thr Cys Pro Pro  Cys Pro Ala Pro Glu  Leu Leu Gly
    1760                1765                1770

Gly Pro  Ser Val Phe Leu Phe  Pro Pro Lys Pro Lys  Asp Thr Leu
    1775                1780                1785

Met Ile  Ser Arg Thr Pro Glu  Val Thr Cys Val Val  Val Asp Val
    1790                1795                1800

Ser His  Glu Asp Pro Glu Val  Lys Phe Asn Trp Tyr  Val Asp Gly
    1805                1810                1815

Val Glu  Val His Asn Ala Lys  Thr Lys Pro Arg Glu  Glu Gln Tyr
    1820                1825                1830

Asn Ser  Thr Tyr Arg Val Val  Ser Val Leu Thr Val  Leu His Gln
    1835                1840                1845

Asp Trp  Leu Asn Gly Lys Glu  Tyr Lys Cys Lys Val  Ser Asn Lys
    1850                1855                1860

Ala Leu  Pro Ala Pro Ile Glu  Lys Thr Ile Ser Lys  Ala Lys Gly
    1865                1870                1875
```

```
Gln Pro  Arg Glu Pro Gln Val  Tyr Thr Leu Pro Pro  Ser Arg Asp
    1880                1885                1890


Glu Leu  Thr Lys Asn Gln Val  Ser Leu Thr Cys Leu  Val Lys Gly
    1895                1900                1905


Phe Tyr  Pro Ser Asp Ile Ala  Val Glu Trp Glu Ser  Asn Gly Gln
    1910                1915                1920


Pro Glu  Asn Asn Tyr Lys Thr  Thr Pro Pro Val Leu  Asp Ser Asp
    1925                1930                1935


Gly Ser  Phe Phe Leu Tyr Ser  Lys Leu Thr Val Asp  Lys Ser Arg
    1940                1945                1950


Trp Gln  Gln Gly Asn Val Phe  Ser Cys Ser Val Met  His Glu Ala
    1955                1960                1965


Leu His  Asn His Tyr Thr Gln  Lys Ser Leu Ser Leu  Ser Pro Gly
    1970                1975                1980


Lys
```

<210> 74
<211> 2134
<212> PRT
<213> Artificial Sequence

<220>
<223> FVIII 196 (dual chain FVIIIFc with three 144 AE XTENs at amino acid 26, 1656 and 1900)

<400> 74

```
Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
1               5                  10                  15


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


Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro Val Gly Ala Pro
        35                  40                  45
```

```
Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro
    50                  55                  60

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser
65                  70                  75                  80

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
                85                  90                  95

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro
            100                 105                 110

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

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

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

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
                165                 170                 175

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
            180                 185                 190

Ala Ser Ser Asp Ala Arg Phe Pro Pro Arg Val Pro Lys Ser Phe Pro
        195                 200                 205

Phe Asn Thr Ser Val Val Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr
    210                 215                 220

Asp His Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu
225                 230                 235                 240

Leu Gly Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr Val Val Ile Thr
                245                 250                 255

Leu Lys Asn Met Ala Ser His Pro Val Ser Leu His Ala Val Gly Val
            260                 265                 270
```

```
Ser Tyr Trp Lys Ala Ser Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser
        275                 280                 285

Gln Arg Glu Lys Glu Asp Asp Lys Val Phe Pro Gly Gly Ser His Thr
    290                 295                 300

Tyr Val Trp Gln Val Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro
305                 310                 315                 320

Leu Cys Leu Thr Tyr Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp
                325                 330                 335

Leu Asn Ser Gly Leu Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser
            340                 345                 350

Leu Ala Lys Glu Lys Thr Gln Thr Leu His Lys Phe Ile Leu Leu Phe
        355                 360                 365

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

Leu Met Gln Asp Arg Asp Ala Ala Ser Ala Arg Ala Trp Pro Lys Met
385                 390                 395                 400

His Thr Val Asn Gly Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly
                405                 410                 415

Cys His Arg Lys Ser Val Tyr Trp His Val Ile Gly Met Gly Thr Thr
            420                 425                 430

Pro Glu Val His Ser Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg
        435                 440                 445

Asn His Arg Gln Ala Ser Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr
    450                 455                 460

Ala Gln Thr Leu Leu Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His
465                 470                 475                 480

Ile Ser Ser His Gln His Asp Gly Met Glu Ala Tyr Val Lys Val Asp
                485                 490                 495
```

```
Ser Cys Pro Glu Glu Pro Gln Leu Arg Met Lys Asn Asn Glu Glu Ala
            500                 505                 510

Glu Asp Tyr Asp Asp Asp Leu Thr Asp Ser Glu Met Asp Val Val Arg
        515                 520                 525

Phe Asp Asp Asp Asn Ser Pro Ser Phe Ile Gln Ile Arg Ser Val Ala
    530                 535                 540

Lys Lys His Pro Lys Thr Trp Val His Tyr Ile Ala Ala Glu Glu Glu
545                 550                 555                 560

Asp Trp Asp Tyr Ala Pro Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr
                565                 570                 575

Lys Ser Gln Tyr Leu Asn Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr
            580                 585                 590

Lys Lys Val Arg Phe Met Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg
        595                 600                 605

Glu Ala Ile Gln His Glu Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly
    610                 615                 620

Glu Val Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg
625                 630                 635                 640

Pro Tyr Asn Ile Tyr Pro His Gly Ile Thr Asp Val Arg Pro Leu Tyr
                645                 650                 655

Ser Arg Arg Leu Pro Lys Gly Val Lys His Leu Lys Asp Phe Pro Ile
            660                 665                 670

Leu Pro Gly Glu Ile Phe Lys Tyr Lys Trp Thr Val Thr Val Glu Asp
        675                 680                 685

Gly Pro Thr Lys Ser Asp Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser
    690                 695                 700

Phe Val Asn Met Glu Arg Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu
```

```
705                 710                 715                 720

Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly Asn Gln Ile Met
                725                 730                 735

Ser Asp Lys Arg Asn Val Ile Leu Phe Ser Val Phe Asp Glu Asn Arg
            740                 745                 750

Ser Trp Tyr Leu Thr Glu Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala
        755                 760                 765

Gly Val Gln Leu Glu Asp Pro Glu Phe Gln Ala Ser Asn Ile Met His
    770                 775                 780

Ser Ile Asn Gly Tyr Val Phe Asp Ser Leu Gln Leu Ser Val Cys Leu
785                 790                 795                 800

His Glu Val Ala Tyr Trp Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp
                805                 810                 815

Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys His Lys Met Val
            820                 825                 830

Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly Glu Thr Val Phe
        835                 840                 845

Met Ser Met Glu Asn Pro Gly Leu Trp Ile Leu Gly Cys His Asn Ser
    850                 855                 860

Asp Phe Arg Asn Arg Gly Met Thr Ala Leu Leu Lys Val Ser Ser Cys
865                 870                 875                 880

Asp Lys Asn Thr Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser
                885                 890                 895

Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
            900                 905                 910

Gln Asn Pro Pro Val Leu Lys Arg His Gln Arg Glu Ile Thr Arg Thr
        915                 920                 925
```

```
Thr Leu Gln Gly Ala Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser
    930                 935                 940

Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala
945                 950                 955                 960

Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr
                965                 970                 975

Ser Ser Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr
            980                 985                 990

Gly Pro Gly Thr Pro Gly Ser Gly  Thr Ala Ser Ser Ser  Pro Gly Ala
        995                 1000                1005

Ser Pro  Gly Thr Ser Ser Thr  Gly Ser Pro Gly Ala  Ser Pro Gly
    1010                1015                1020

Thr Ser  Ser Thr Gly Ser Pro  Gly Ala Ser Pro Gly  Thr Ser Ser
    1025                1030                1035

Thr Gly  Ser Pro Gly Ser Ser  Thr Pro Ser Gly Ala  Thr Gly Ser
    1040                1045                1050

Pro Gly  Ser Ser Thr Pro Ser  Gly Ala Thr Gly Ser  Pro Gly Ala
    1055                1060                1065

Ser Pro  Gly Thr Ser Ser Thr  Gly Ser Pro Ala Ser  Ser Ser Asp
    1070                1075                1080

Gln Glu  Glu Ile Asp Tyr Asp  Asp Thr Ile Ser Val  Glu Met Lys
    1085                1090                1095

Lys Glu  Asp Phe Asp Ile Tyr  Asp Glu Asp Glu Asn  Gln Ser Pro
    1100                1105                1110

Arg Ser  Phe Gln Lys Lys Thr  Arg His Tyr Phe Ile  Ala Ala Val
    1115                1120                1125

Glu Arg  Leu Trp Asp Tyr Gly  Met Ser Ser Ser Pro  His Val Leu
    1130                1135                1140
```

```
Arg Asn  Arg Ala Gln Ser Gly  Ser Val Pro Gln Phe  Lys Lys Val
    1145                1150                1155

Val Phe  Gln Glu Phe Thr Asp  Gly Ser Phe Thr Gln  Pro Leu Tyr
    1160                1165                1170

Arg Gly  Glu Leu Asn Glu His  Leu Gly Leu Leu Gly  Pro Tyr Ile
    1175                1180                1185

Arg Ala  Glu Val Glu Asp Asn  Ile Met Val Thr Phe  Arg Asn Gln
    1190                1195                1200

Ala Ser  Arg Pro Tyr Ser Phe  Tyr Ser Ser Leu Ile  Ser Tyr Glu
    1205                1210                1215

Glu Asp  Gln Arg Gln Gly Ala  Glu Pro Arg Lys Asn  Phe Val Lys
    1220                1225                1230

Pro Asn  Glu Thr Lys Thr Tyr  Phe Trp Lys Val Gln  His His Met
    1235                1240                1245

Ala Pro  Thr Lys Asp Glu Phe  Asp Cys Lys Ala Trp  Ala Tyr Phe
    1250                1255                1260

Ser Asp  Val Asp Leu Glu Lys  Asp Val His Ser Gly  Leu Ile Gly
    1265                1270                1275

Pro Leu  Leu Val Cys His Thr  Asn Thr Leu Asn Pro  Ala His Gly
    1280                1285                1290

Arg Gln  Val Thr Val Gln Glu  Phe Ala Leu Phe Phe  Thr Ile Phe
    1295                1300                1305

Asp Glu  Thr Lys Ser Trp Tyr  Phe Thr Glu Asn Met  Glu Arg Asn
    1310                1315                1320

Cys Arg  Gly Ala Pro Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly
    1325                1330                1335

Pro Gly  Ser Glu Pro Ala Thr  Ser Gly Ser Glu Thr  Pro Gly Thr
    1340                1345                1350
```

```
Ser Glu  Ser Ala Thr Pro Glu  Ser Gly Pro Gly Ser  Glu Pro Ala
    1355                1360                1365

Thr Ser  Gly Ser Glu Thr Pro  Gly Thr Ser Glu Ser  Ala Thr Pro
    1370                1375                1380

Glu Ser  Gly Pro Gly Thr Ser  Thr Glu Pro Ser Glu  Gly Ser Ala
    1385                1390                1395

Pro Gly  Thr Ser Glu Ser Ala  Thr Pro Glu Ser Gly  Pro Gly Ser
    1400                1405                1410

Pro Ala  Gly Ser Pro Thr Ser  Thr Glu Glu Gly Ser  Pro Ala Gly
    1415                1420                1425

Ser Pro  Thr Ser Thr Glu Glu  Gly Ser Pro Ala Gly  Ser Pro Thr
    1430                1435                1440

Ser Thr  Glu Glu Gly Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly
    1445                1450                1455

Pro Gly  Thr Ser Thr Glu Pro  Ser Glu Gly Ser Ala  Pro Gly Ala
    1460                1465                1470

Ser Ser  Ala Pro Cys Asn Ile  Gln Met Glu Asp Pro  Thr Phe Lys
    1475                1480                1485

Glu Asn  Tyr Arg Phe His Ala  Ile Asn Gly Tyr Ile  Met Asp Thr
    1490                1495                1500

Leu Pro  Gly Leu Val Met Ala  Gln Asp Gln Arg Ile  Arg Trp Tyr
    1505                1510                1515

Leu Leu  Ser Met Gly Ser Asn  Glu Asn Ile His Ser  Ile His Phe
    1520                1525                1530

Ser Gly  His Val Phe Thr Val  Arg Lys Lys Glu Glu  Tyr Lys Met
    1535                1540                1545

Ala Leu  Tyr Asn Leu Tyr Pro  Gly Val Phe Glu Thr  Val Glu Met
```

```
    1550                1555                1560

Leu Pro  Ser Lys Ala Gly Ile  Trp Arg Val Glu Cys  Leu Ile Gly
    1565                1570                1575

Glu His  Leu His Ala Gly Met  Ser Thr Leu Phe Leu  Val Tyr Ser
    1580                1585                1590

Asn Lys  Cys Gln Thr Pro Leu  Gly Met Ala Ser Gly  His Ile Arg
    1595                1600                1605

Asp Phe  Gln Ile Thr Ala Ser  Gly Gln Tyr Gly Gln  Trp Ala Pro
    1610                1615                1620

Lys Leu  Ala Arg Leu His Tyr  Ser Gly Ser Ile Asn  Ala Trp Ser
    1625                1630                1635

Thr Lys  Glu Pro Phe Ser Trp  Ile Lys Val Asp Leu  Leu Ala Pro
    1640                1645                1650

Met Ile  Ile His Gly Ile Lys  Thr Gln Gly Ala Arg  Gln Lys Phe
    1655                1660                1665

Ser Ser  Leu Tyr Ile Ser Gln  Phe Ile Ile Met Tyr  Ser Leu Asp
    1670                1675                1680

Gly Lys  Lys Trp Gln Thr Tyr  Arg Gly Asn Ser Thr  Gly Thr Leu
    1685                1690                1695

Met Val  Phe Phe Gly Asn Val  Asp Ser Ser Gly Ile  Lys His Asn
    1700                1705                1710

Ile Phe  Asn Pro Pro Ile Ile  Ala Arg Tyr Ile Arg  Leu His Pro
    1715                1720                1725

Thr His  Tyr Ser Ile Arg Ser  Thr Leu Arg Met Glu  Leu Met Gly
    1730                1735                1740

Cys Asp  Leu Asn Ser Cys Ser  Met Pro Leu Gly Met  Glu Ser Lys
    1745                1750                1755
```

```
Ala Ile  Ser Asp Ala Gln Ile  Thr Ala Ser Ser Tyr  Phe Thr Asn
    1760                1765                1770

Met Phe  Ala Thr Trp Ser Pro  Ser Lys Ala Arg Leu  His Leu Gln
    1775                1780                1785

Gly Arg  Ser Asn Ala Trp Arg  Pro Gln Val Asn Asn  Pro Lys Glu
    1790                1795                1800

Trp Leu  Gln Val Asp Phe Gln  Lys Thr Met Lys Val  Thr Gly Val
    1805                1810                1815

Thr Thr  Gln Gly Val Lys Ser  Leu Leu Thr Ser Met  Tyr Val Lys
    1820                1825                1830

Glu Phe  Leu Ile Ser Ser Ser  Gln Asp Gly His Gln  Trp Thr Leu
    1835                1840                1845

Phe Phe  Gln Asn Gly Lys Val  Lys Val Phe Gln Gly  Asn Gln Asp
    1850                1855                1860

Ser Phe  Thr Pro Val Val Asn  Ser Leu Asp Pro Pro  Leu Leu Thr
    1865                1870                1875

Arg Tyr  Leu Arg Ile His Pro  Gln Ser Trp Val His  Gln Ile Ala
    1880                1885                1890

Leu Arg  Met Glu Val Leu Gly  Cys Glu Ala Gln Asp  Leu Tyr Asp
    1895                1900                1905

Lys Thr  His Thr Cys Pro Pro  Cys Pro Ala Pro Glu  Leu Leu Gly
    1910                1915                1920

Gly Pro  Ser Val Phe Leu Phe  Pro Pro Lys Pro Lys  Asp Thr Leu
    1925                1930                1935

Met Ile  Ser Arg Thr Pro Glu  Val Thr Cys Val Val  Val Asp Val
    1940                1945                1950

Ser His  Glu Asp Pro Glu Val  Lys Phe Asn Trp Tyr  Val Asp Gly
    1955                1960                1965
```

```
Val Glu  Val His Asn Ala Lys  Thr Lys Pro Arg Glu  Glu Gln Tyr
    1970                1975                1980

Asn Ser  Thr Tyr Arg Val Val  Ser Val Leu Thr Val  Leu His Gln
    1985                1990                1995

Asp Trp  Leu Asn Gly Lys Glu  Tyr Lys Cys Lys Val  Ser Asn Lys
    2000                2005                2010

Ala Leu  Pro Ala Pro Ile Glu  Lys Thr Ile Ser Lys  Ala Lys Gly
    2015                2020                2025

Gln Pro  Arg Glu Pro Gln Val  Tyr Thr Leu Pro Pro  Ser Arg Asp
    2030                2035                2040

Glu Leu  Thr Lys Asn Gln Val  Ser Leu Thr Cys Leu  Val Lys Gly
    2045                2050                2055

Phe Tyr  Pro Ser Asp Ile Ala  Val Glu Trp Glu Ser  Asn Gly Gln
    2060                2065                2070

Pro Glu  Asn Asn Tyr Lys Thr  Thr Pro Pro Val Leu  Asp Ser Asp
    2075                2080                2085

Gly Ser  Phe Phe Leu Tyr Ser  Lys Leu Thr Val Asp  Lys Ser Arg
    2090                2095                2100

Trp Gln  Gln Gly Asn Val Phe  Ser Cys Ser Val Met  His Glu Ala
    2105                2110                2115

Leu His  Asn His Tyr Thr Gln  Lys Ser Leu Ser Leu  Ser Pro Gly
    2120                2125                2130

Lys
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<210> 75
<211> 1984
<212> PRT
<213> Artificial Sequence

<220>

<223> FVIII 199 (single chain FVIIIFc with three 144 AE XTENs at amino acid 1656 and 1900)

<400> 75

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Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
1               5                  10                  15


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


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


Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val
    50                  55                  60


Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile
65                  70                  75                  80


Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln
                85                  90                  95


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


His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser
        115                 120                 125


Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp
    130                 135                 140


Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu
145                 150                 155                 160


Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser
                165                 170                 175


Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile
            180                 185                 190


Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr
        195                 200                 205
```

```
Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly
    210                 215                 220

Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp
225                 230                 235                 240

Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr
                245                 250                 255

Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val
            260                 265                 270

Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile
        275                 280                 285

Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser
    290                 295                 300

Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met
305                 310                 315                 320

Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His
                325                 330                 335

Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro
            340                 345                 350

Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp
        355                 360                 365

Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser
    370                 375                 380

Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
385                 390                 395                 400

Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro
                405                 410                 415

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

```
            420                 425                 430

Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met
        435                 440                 445

Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu
    450                 455                 460

Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
465                 470                 475                 480

Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro
                485                 490                 495

His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys
            500                 505                 510

Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe
        515                 520                 525

Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp
    530                 535                 540

Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg
545                 550                 555                 560

Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu
                565                 570                 575

Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val
            580                 585                 590

Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu
        595                 600                 605

Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp
    610                 615                 620

Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
625                 630                 635                 640
```

```
Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp
                645                 650                 655

Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe
            660                 665                 670

Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
        675                 680                 685

Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro
    690                 695                 700

Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly
705                 710                 715                 720

Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp
                725                 730                 735

Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
            740                 745                 750

Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Pro Pro Val Leu
        755                 760                 765

Lys Arg His Gln Ala Glu Ile Thr Arg Thr Thr Leu Gln Gly Ala Pro
    770                 775                 780

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ala Ser Pro
785                 790                 795                 800

Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
                805                 810                 815

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
            820                 825                 830

Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Thr Pro Gly
        835                 840                 845

Ser Gly Thr Ala Ser Ser Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
    850                 855                 860
```

```
Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
865                 870                 875                 880


Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Thr
                885                 890                 895


Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
            900                 905                 910


Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
        915                 920                 925


Ala Ser Ser Ser Asp Gln Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser
    930                 935                 940


Val Glu Met Lys Lys Glu Asp Phe Asp Ile Tyr Asp Glu Asp Glu Asn
945                 950                 955                 960


Gln Ser Pro Arg Ser Phe Gln Lys Lys Thr Arg His Tyr Phe Ile Ala
                965                 970                 975


Ala Val Glu Arg Leu Trp Asp Tyr Gly Met Ser Ser Ser Pro His Val
            980                 985                 990


Leu Arg Asn Arg Ala Gln Ser Gly  Ser Val Pro Gln Phe  Lys Lys Val
        995                 1000                1005


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


Arg Gly  Glu Leu Asn Glu His  Leu Gly Leu Leu Gly  Pro Tyr Ile
    1025                1030                1035


Arg Ala  Glu Val Glu Asp Asn  Ile Met Val Thr Phe  Arg Asn Gln
    1040                1045                1050


Ala Ser  Arg Pro Tyr Ser Phe  Tyr Ser Ser Leu Ile  Ser Tyr Glu
    1055                1060                1065


Glu Asp  Gln Arg Gln Gly Ala  Glu Pro Arg Lys Asn  Phe Val Lys
    1070                1075                1080
```

```
Pro Asn  Glu Thr Lys Thr Tyr  Phe Trp Lys Val Gln  His His Met
    1085                1090                1095

Ala Pro  Thr Lys Asp Glu Phe  Asp Cys Lys Ala Trp  Ala Tyr Phe
    1100                1105                1110

Ser Asp  Val Asp Leu Glu Lys  Asp Val His Ser Gly  Leu Ile Gly
    1115                1120                1125

Pro Leu  Leu Val Cys His Thr  Asn Thr Leu Asn Pro  Ala His Gly
    1130                1135                1140

Arg Gln  Val Thr Val Gln Glu  Phe Ala Leu Phe Phe  Thr Ile Phe
    1145                1150                1155

Asp Glu  Thr Lys Ser Trp Tyr  Phe Thr Glu Asn Met  Glu Arg Asn
    1160                1165                1170

Cys Arg  Gly Ala Pro Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly
    1175                1180                1185

Pro Gly  Ser Glu Pro Ala Thr  Ser Gly Ser Glu Thr  Pro Gly Thr
    1190                1195                1200

Ser Glu  Ser Ala Thr Pro Glu  Ser Gly Pro Gly Ser  Glu Pro Ala
    1205                1210                1215

Thr Ser  Gly Ser Glu Thr Pro  Gly Thr Ser Glu Ser  Ala Thr Pro
    1220                1225                1230

Glu Ser  Gly Pro Gly Thr Ser  Thr Glu Pro Ser Glu  Gly Ser Ala
    1235                1240                1245

Pro Gly  Thr Ser Glu Ser Ala  Thr Pro Glu Ser Gly  Pro Gly Ser
    1250                1255                1260

Pro Ala  Gly Ser Pro Thr Ser  Thr Glu Glu Gly Ser  Pro Ala Gly
    1265                1270                1275

Ser Pro  Thr Ser Thr Glu Glu  Gly Ser Pro Ala Gly  Ser Pro Thr
```

```
    1280                1285                1290

Ser Thr  Glu Glu Gly Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly
    1295                1300                1305

Pro Gly  Thr Ser Thr Glu Pro  Ser Glu Gly Ser Ala  Pro Gly Ala
    1310                1315                1320

Ser Ser  Ala Pro Cys Asn Ile  Gln Met Glu Asp Pro  Thr Phe Lys
    1325                1330                1335

Glu Asn  Tyr Arg Phe His Ala  Ile Asn Gly Tyr Ile  Met Asp Thr
    1340                1345                1350

Leu Pro  Gly Leu Val Met Ala  Gln Asp Gln Arg Ile  Arg Trp Tyr
    1355                1360                1365

Leu Leu  Ser Met Gly Ser Asn  Glu Asn Ile His Ser  Ile His Phe
    1370                1375                1380

Ser Gly  His Val Phe Thr Val  Arg Lys Lys Glu Glu  Tyr Lys Met
    1385                1390                1395

Ala Leu  Tyr Asn Leu Tyr Pro  Gly Val Phe Glu Thr  Val Glu Met
    1400                1405                1410

Leu Pro  Ser Lys Ala Gly Ile  Trp Arg Val Glu Cys  Leu Ile Gly
    1415                1420                1425

Glu His  Leu His Ala Gly Met  Ser Thr Leu Phe Leu  Val Tyr Ser
    1430                1435                1440

Asn Lys  Cys Gln Thr Pro Leu  Gly Met Ala Ser Gly  His Ile Arg
    1445                1450                1455

Asp Phe  Gln Ile Thr Ala Ser  Gly Gln Tyr Gly Gln  Trp Ala Pro
    1460                1465                1470

Lys Leu  Ala Arg Leu His Tyr  Ser Gly Ser Ile Asn  Ala Trp Ser
    1475                1480                1485
```

```
Thr Lys  Glu Pro Phe Ser Trp  Ile Lys Val Asp Leu  Leu Ala Pro
    1490                1495                1500

Met Ile  Ile His Gly Ile Lys  Thr Gln Gly Ala Arg  Gln Lys Phe
    1505                1510                1515

Ser Ser  Leu Tyr Ile Ser Gln  Phe Ile Ile Met Tyr  Ser Leu Asp
    1520                1525                1530

Gly Lys  Lys Trp Gln Thr Tyr  Arg Gly Asn Ser Thr  Gly Thr Leu
    1535                1540                1545

Met Val  Phe Phe Gly Asn Val  Asp Ser Ser Gly Ile  Lys His Asn
    1550                1555                1560

Ile Phe  Asn Pro Pro Ile Ile  Ala Arg Tyr Ile Arg  Leu His Pro
    1565                1570                1575

Thr His  Tyr Ser Ile Arg Ser  Thr Leu Arg Met Glu  Leu Met Gly
    1580                1585                1590

Cys Asp  Leu Asn Ser Cys Ser  Met Pro Leu Gly Met  Glu Ser Lys
    1595                1600                1605

Ala Ile  Ser Asp Ala Gln Ile  Thr Ala Ser Ser Tyr  Phe Thr Asn
    1610                1615                1620

Met Phe  Ala Thr Trp Ser Pro  Ser Lys Ala Arg Leu  His Leu Gln
    1625                1630                1635

Gly Arg  Ser Asn Ala Trp Arg  Pro Gln Val Asn Asn  Pro Lys Glu
    1640                1645                1650

Trp Leu  Gln Val Asp Phe Gln  Lys Thr Met Lys Val  Thr Gly Val
    1655                1660                1665

Thr Thr  Gln Gly Val Lys Ser  Leu Leu Thr Ser Met  Tyr Val Lys
    1670                1675                1680

Glu Phe  Leu Ile Ser Ser Ser  Gln Asp Gly His Gln  Trp Thr Leu
    1685                1690                1695
```

```
Phe Phe  Gln Asn Gly Lys Val  Lys Val Phe Gln Gly  Asn Gln Asp
    1700                1705                1710

Ser Phe  Thr Pro Val Val Asn  Ser Leu Asp Pro Pro  Leu Leu Thr
    1715                1720                1725

Arg Tyr  Leu Arg Ile His Pro  Gln Ser Trp Val His  Gln Ile Ala
    1730                1735                1740

Leu Arg  Met Glu Val Leu Gly  Cys Glu Ala Gln Asp  Leu Tyr Asp
    1745                1750                1755

Lys Thr  His Thr Cys Pro Pro  Cys Pro Ala Pro Glu  Leu Leu Gly
    1760                1765                1770

Gly Pro  Ser Val Phe Leu Phe  Pro Pro Lys Pro Lys  Asp Thr Leu
    1775                1780                1785

Met Ile  Ser Arg Thr Pro Glu  Val Thr Cys Val Val  Val Asp Val
    1790                1795                1800

Ser His  Glu Asp Pro Glu Val  Lys Phe Asn Trp Tyr  Val Asp Gly
    1805                1810                1815

Val Glu  Val His Asn Ala Lys  Thr Lys Pro Arg Glu  Glu Gln Tyr
    1820                1825                1830

Asn Ser  Thr Tyr Arg Val Val  Ser Val Leu Thr Val  Leu His Gln
    1835                1840                1845

Asp Trp  Leu Asn Gly Lys Glu  Tyr Lys Cys Lys Val  Ser Asn Lys
    1850                1855                1860

Ala Leu  Pro Ala Pro Ile Glu  Lys Thr Ile Ser Lys  Ala Lys Gly
    1865                1870                1875

Gln Pro  Arg Glu Pro Gln Val  Tyr Thr Leu Pro Pro  Ser Arg Asp
    1880                1885                1890

Glu Leu  Thr Lys Asn Gln Val  Ser Leu Thr Cys Leu  Val Lys Gly
    1895                1900                1905
```

```
Phe Tyr  Pro Ser Asp Ile Ala  Val Glu Trp Glu Ser  Asn Gly Gln
    1910                1915                1920


Pro Glu  Asn Asn Tyr Lys Thr  Thr Pro Pro Val Leu  Asp Ser Asp
    1925                1930                1935


Gly Ser  Phe Phe Leu Tyr Ser  Lys Leu Thr Val Asp  Lys Ser Arg
    1940                1945                1950


Trp Gln  Gln Gly Asn Val Phe  Ser Cys Ser Val Met  His Glu Ala
    1955                1960                1965


Leu His  Asn His Tyr Thr Gln  Lys Ser Leu Ser Leu  Ser Pro Gly
    1970                1975                1980


Lys
```

<210> 76
<211> 2134
<212> PRT
<213> Artificial Sequence

<220>
<223> FVIII 201 (single chain FVIIIFc with three 144 AE XTENs at amino acid 26, 1656 &1900)

<400> 76

```
Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
1               5                   10                  15


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


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


Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro
    50                  55                  60


Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser
65                  70                  75                  80
```

```
Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
                85                  90                  95

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro
            100                 105                 110

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

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

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

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
                165                 170                 175

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
            180                 185                 190

Ala Ser Ser Asp Ala Arg Phe Pro Pro Arg Val Pro Lys Ser Phe Pro
        195                 200                 205

Phe Asn Thr Ser Val Val Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr
    210                 215                 220

Asp His Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu
225                 230                 235                 240

Leu Gly Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr Val Val Ile Thr
                245                 250                 255

Leu Lys Asn Met Ala Ser His Pro Val Ser Leu His Ala Val Gly Val
            260                 265                 270

Ser Tyr Trp Lys Ala Ser Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser
        275                 280                 285

Gln Arg Glu Lys Glu Asp Asp Lys Val Phe Pro Gly Gly Ser His Thr
```

```
    290                 295                 300

Tyr Val Trp Gln Val Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro
305                 310                 315                 320

Leu Cys Leu Thr Tyr Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp
                325                 330                 335

Leu Asn Ser Gly Leu Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser
            340                 345                 350

Leu Ala Lys Glu Lys Thr Gln Thr Leu His Lys Phe Ile Leu Leu Phe
        355                 360                 365

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

Leu Met Gln Asp Arg Asp Ala Ala Ser Ala Arg Ala Trp Pro Lys Met
385                 390                 395                 400

His Thr Val Asn Gly Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly
                405                 410                 415

Cys His Arg Lys Ser Val Tyr Trp His Val Ile Gly Met Gly Thr Thr
            420                 425                 430

Pro Glu Val His Ser Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg
        435                 440                 445

Asn His Arg Gln Ala Ser Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr
    450                 455                 460

Ala Gln Thr Leu Leu Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His
465                 470                 475                 480

Ile Ser Ser His Gln His Asp Gly Met Glu Ala Tyr Val Lys Val Asp
                485                 490                 495

Ser Cys Pro Glu Glu Pro Gln Leu Arg Met Lys Asn Asn Glu Glu Ala
            500                 505                 510
```

```
Glu Asp Tyr Asp Asp Asp Leu Thr Asp Ser Glu Met Asp Val Val Arg
        515                 520                 525

Phe Asp Asp Asp Asn Ser Pro Ser Phe Ile Gln Ile Arg Ser Val Ala
    530                 535                 540

Lys Lys His Pro Lys Thr Trp Val His Tyr Ile Ala Ala Glu Glu Glu
545                 550                 555                 560

Asp Trp Asp Tyr Ala Pro Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr
                565                 570                 575

Lys Ser Gln Tyr Leu Asn Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr
            580                 585                 590

Lys Lys Val Arg Phe Met Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg
        595                 600                 605

Glu Ala Ile Gln His Glu Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly
    610                 615                 620

Glu Val Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg
625                 630                 635                 640

Pro Tyr Asn Ile Tyr Pro His Gly Ile Thr Asp Val Arg Pro Leu Tyr
                645                 650                 655

Ser Arg Arg Leu Pro Lys Gly Val Lys His Leu Lys Asp Phe Pro Ile
            660                 665                 670

Leu Pro Gly Glu Ile Phe Lys Tyr Lys Trp Thr Val Thr Val Glu Asp
        675                 680                 685

Gly Pro Thr Lys Ser Asp Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser
    690                 695                 700

Phe Val Asn Met Glu Arg Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu
705                 710                 715                 720

Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly Asn Gln Ile Met
                725                 730                 735
```

```
Ser Asp Lys Arg Asn Val Ile Leu Phe Ser Val Phe Asp Glu Asn Arg
            740                 745                 750

Ser Trp Tyr Leu Thr Glu Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala
        755                 760                 765

Gly Val Gln Leu Glu Asp Pro Glu Phe Gln Ala Ser Asn Ile Met His
    770                 775                 780

Ser Ile Asn Gly Tyr Val Phe Asp Ser Leu Gln Leu Ser Val Cys Leu
785                 790                 795                 800

His Glu Val Ala Tyr Trp Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp
                805                 810                 815

Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys His Lys Met Val
            820                 825                 830

Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly Glu Thr Val Phe
        835                 840                 845

Met Ser Met Glu Asn Pro Gly Leu Trp Ile Leu Gly Cys His Asn Ser
    850                 855                 860

Asp Phe Arg Asn Arg Gly Met Thr Ala Leu Leu Lys Val Ser Ser Cys
865                 870                 875                 880

Asp Lys Asn Thr Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser
                885                 890                 895

Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
            900                 905                 910

Gln Asn Pro Pro Val Leu Lys Arg His Gln Ala Glu Ile Thr Arg Thr
        915                 920                 925

Thr Leu Gln Gly Ala Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser
    930                 935                 940

Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala
945                 950                 955                 960
```

```
Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr
                965                 970                 975


Ser Ser Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr
            980                 985                 990


Gly Pro Gly Thr Pro Gly Ser Gly  Thr Ala Ser Ser Ser  Pro Gly Ala
        995                 1000                1005


Ser Pro  Gly Thr Ser Ser Thr  Gly Ser Pro Gly Ala  Ser Pro Gly
    1010                1015                1020


Thr Ser  Ser Thr Gly Ser Pro  Gly Ala Ser Pro Gly  Thr Ser Ser
    1025                1030                1035


Thr Gly  Ser Pro Gly Ser Ser  Thr Pro Ser Gly Ala  Thr Gly Ser
    1040                1045                1050


Pro Gly  Ser Ser Thr Pro Ser  Gly Ala Thr Gly Ser  Pro Gly Ala
    1055                1060                1065


Ser Pro  Gly Thr Ser Ser Thr  Gly Ser Pro Ala Ser  Ser Ser Asp
    1070                1075                1080


Gln Glu  Glu Ile Asp Tyr Asp  Asp Thr Ile Ser Val  Glu Met Lys
    1085                1090                1095


Lys Glu  Asp Phe Asp Ile Tyr  Asp Glu Asp Glu Asn  Gln Ser Pro
    1100                1105                1110


Arg Ser  Phe Gln Lys Lys Thr  Arg His Tyr Phe Ile  Ala Ala Val
    1115                1120                1125


Glu Arg  Leu Trp Asp Tyr Gly  Met Ser Ser Ser Pro  His Val Leu
    1130                1135                1140


Arg Asn  Arg Ala Gln Ser Gly  Ser Val Pro Gln Phe  Lys Lys Val
    1145                1150                1155


Val Phe  Gln Glu Phe Thr Asp  Gly Ser Phe Thr Gln  Pro Leu Tyr
```

```
    1160                1165                1170

Arg Gly  Glu Leu Asn Glu His  Leu Gly Leu Leu Gly  Pro Tyr Ile
    1175                1180                1185

Arg Ala  Glu Val Glu Asp Asn  Ile Met Val Thr Phe  Arg Asn Gln
    1190                1195                1200

Ala Ser  Arg Pro Tyr Ser Phe  Tyr Ser Ser Leu Ile  Ser Tyr Glu
    1205                1210                1215

Glu Asp  Gln Arg Gln Gly Ala  Glu Pro Arg Lys Asn  Phe Val Lys
    1220                1225                1230

Pro Asn  Glu Thr Lys Thr Tyr  Phe Trp Lys Val Gln  His His Met
    1235                1240                1245

Ala Pro  Thr Lys Asp Glu Phe  Asp Cys Lys Ala Trp  Ala Tyr Phe
    1250                1255                1260

Ser Asp  Val Asp Leu Glu Lys  Asp Val His Ser Gly  Leu Ile Gly
    1265                1270                1275

Pro Leu  Leu Val Cys His Thr  Asn Thr Leu Asn Pro  Ala His Gly
    1280                1285                1290

Arg Gln  Val Thr Val Gln Glu  Phe Ala Leu Phe Phe  Thr Ile Phe
    1295                1300                1305

Asp Glu  Thr Lys Ser Trp Tyr  Phe Thr Glu Asn Met  Glu Arg Asn
    1310                1315                1320

Cys Arg  Gly Ala Pro Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly
    1325                1330                1335

Pro Gly  Ser Glu Pro Ala Thr  Ser Gly Ser Glu Thr  Pro Gly Thr
    1340                1345                1350

Ser Glu  Ser Ala Thr Pro Glu  Ser Gly Pro Gly Ser  Glu Pro Ala
    1355                1360                1365
```

```
Thr Ser  Gly Ser Glu Thr Pro  Gly Thr Ser Glu Ser  Ala Thr Pro
    1370                 1375                 1380

Glu Ser  Gly Pro Gly Thr Ser  Thr Glu Pro Ser Glu  Gly Ser Ala
    1385                 1390                 1395

Pro Gly  Thr Ser Glu Ser Ala  Thr Pro Glu Ser Gly  Pro Gly Ser
    1400                 1405                 1410

Pro Ala  Gly Ser Pro Thr Ser  Thr Glu Glu Gly Ser  Pro Ala Gly
    1415                 1420                 1425

Ser Pro  Thr Ser Thr Glu Glu  Gly Ser Pro Ala Gly  Ser Pro Thr
    1430                 1435                 1440

Ser Thr  Glu Glu Gly Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly
    1445                 1450                 1455

Pro Gly  Thr Ser Thr Glu Pro  Ser Glu Gly Ser Ala  Pro Gly Ala
    1460                 1465                 1470

Ser Ser  Ala Pro Cys Asn Ile  Gln Met Glu Asp Pro  Thr Phe Lys
    1475                 1480                 1485

Glu Asn  Tyr Arg Phe His Ala  Ile Asn Gly Tyr Ile  Met Asp Thr
    1490                 1495                 1500

Leu Pro  Gly Leu Val Met Ala  Gln Asp Gln Arg Ile  Arg Trp Tyr
    1505                 1510                 1515

Leu Leu  Ser Met Gly Ser Asn  Glu Asn Ile His Ser  Ile His Phe
    1520                 1525                 1530

Ser Gly  His Val Phe Thr Val  Arg Lys Lys Glu Glu  Tyr Lys Met
    1535                 1540                 1545

Ala Leu  Tyr Asn Leu Tyr Pro  Gly Val Phe Glu Thr  Val Glu Met
    1550                 1555                 1560

Leu Pro  Ser Lys Ala Gly Ile  Trp Arg Val Glu Cys  Leu Ile Gly
    1565                 1570                 1575
```

```
Glu His  Leu His Ala Gly Met  Ser Thr Leu Phe Leu  Val Tyr Ser
    1580                1585                1590

Asn Lys  Cys Gln Thr Pro Leu  Gly Met Ala Ser Gly  His Ile Arg
    1595                1600                1605

Asp Phe  Gln Ile Thr Ala Ser  Gly Gln Tyr Gly Gln  Trp Ala Pro
    1610                1615                1620

Lys Leu  Ala Arg Leu His Tyr  Ser Gly Ser Ile Asn  Ala Trp Ser
    1625                1630                1635

Thr Lys  Glu Pro Phe Ser Trp  Ile Lys Val Asp Leu  Leu Ala Pro
    1640                1645                1650

Met Ile  Ile His Gly Ile Lys  Thr Gln Gly Ala Arg  Gln Lys Phe
    1655                1660                1665

Ser Ser  Leu Tyr Ile Ser Gln  Phe Ile Ile Met Tyr  Ser Leu Asp
    1670                1675                1680

Gly Lys  Lys Trp Gln Thr Tyr  Arg Gly Asn Ser Thr  Gly Thr Leu
    1685                1690                1695

Met Val  Phe Phe Gly Asn Val  Asp Ser Ser Gly Ile  Lys His Asn
    1700                1705                1710

Ile Phe  Asn Pro Pro Ile Ile  Ala Arg Tyr Ile Arg  Leu His Pro
    1715                1720                1725

Thr His  Tyr Ser Ile Arg Ser  Thr Leu Arg Met Glu  Leu Met Gly
    1730                1735                1740

Cys Asp  Leu Asn Ser Cys Ser  Met Pro Leu Gly Met  Glu Ser Lys
    1745                1750                1755

Ala Ile  Ser Asp Ala Gln Ile  Thr Ala Ser Ser Tyr  Phe Thr Asn
    1760                1765                1770

Met Phe  Ala Thr Trp Ser Pro  Ser Lys Ala Arg Leu  His Leu Gln
    1775                1780                1785
```

```
Gly Arg  Ser Asn Ala Trp Arg  Pro Gln Val Asn Asn  Pro Lys Glu
    1790                1795                1800

Trp Leu  Gln Val Asp Phe Gln  Lys Thr Met Lys Val  Thr Gly Val
    1805                1810                1815

Thr Thr  Gln Gly Val Lys Ser  Leu Leu Thr Ser Met  Tyr Val Lys
    1820                1825                1830

Glu Phe  Leu Ile Ser Ser Ser  Gln Asp Gly His Gln  Trp Thr Leu
    1835                1840                1845

Phe Phe  Gln Asn Gly Lys Val  Lys Val Phe Gln Gly  Asn Gln Asp
    1850                1855                1860

Ser Phe  Thr Pro Val Val Asn  Ser Leu Asp Pro Pro  Leu Leu Thr
    1865                1870                1875

Arg Tyr  Leu Arg Ile His Pro  Gln Ser Trp Val His  Gln Ile Ala
    1880                1885                1890

Leu Arg  Met Glu Val Leu Gly  Cys Glu Ala Gln Asp  Leu Tyr Asp
    1895                1900                1905

Lys Thr  His Thr Cys Pro Pro  Cys Pro Ala Pro Glu  Leu Leu Gly
    1910                1915                1920

Gly Pro  Ser Val Phe Leu Phe  Pro Pro Lys Pro Lys  Asp Thr Leu
    1925                1930                1935

Met Ile  Ser Arg Thr Pro Glu  Val Thr Cys Val Val  Val Asp Val
    1940                1945                1950

Ser His  Glu Asp Pro Glu Val  Lys Phe Asn Trp Tyr  Val Asp Gly
    1955                1960                1965

Val Glu  Val His Asn Ala Lys  Thr Lys Pro Arg Glu  Glu Gln Tyr
    1970                1975                1980

Asn Ser  Thr Tyr Arg Val Val  Ser Val Leu Thr Val  Leu His Gln
```

1985 1990 1995

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
2000 2005 2010

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
2015 2020 2025

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp
2030 2035 2040

Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
2045 2050 2055

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
2060 2065 2070

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
2075 2080 2085

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
2090 2095 2100

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
2105 2110 2115

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
2120 2125 2130

Lys

<210> 77
<211> 2128
<212> PRT
<213> Artificial Sequence

<220>
<223> FVIII 203 (single chain FVIIIFc with two AE XTENs, one 288AE XTEN in B-domain and one 144 AE XTEN at amino acid 1900)

<400> 77

Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe

```
1               5                   10                  15

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

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

Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val
    50                  55                  60

Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile
65                  70                  75                  80

Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln
                85                  90                  95

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

His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser
        115                 120                 125

Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp
    130                 135                 140

Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu
145                 150                 155                 160

Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser
                165                 170                 175

Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile
            180                 185                 190

Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr
        195                 200                 205

Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly
    210                 215                 220
```

```
Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp
225                 230                 235                 240

Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr
                245                 250                 255

Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val
            260                 265                 270

Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile
        275                 280                 285

Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser
    290                 295                 300

Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met
305                 310                 315                 320

Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His
                325                 330                 335

Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro
            340                 345                 350

Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp
        355                 360                 365

Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser
    370                 375                 380

Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
385                 390                 395                 400

Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro
                405                 410                 415

Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
            420                 425                 430

Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met
        435                 440                 445
```

```
Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu
    450                 455                 460

Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
465                 470                 475                 480

Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro
                485                 490                 495

His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys
            500                 505                 510

Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe
        515                 520                 525

Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp
    530                 535                 540

Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg
545                 550                 555                 560

Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu
                565                 570                 575

Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val
            580                 585                 590

Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu
        595                 600                 605

Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp
    610                 615                 620

Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
625                 630                 635                 640

Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp
                645                 650                 655

Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe
            660                 665                 670
```

```
Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
        675                 680                 685

Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro
    690                 695                 700

Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly
705                 710                 715                 720

Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp
                725                 730                 735

Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
            740                 745                 750

Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Gly Ala Pro Gly
        755                 760                 765

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
    770                 775                 780

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
785                 790                 795                 800

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
                805                 810                 815

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
            820                 825                 830

Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
        835                 840                 845

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
    850                 855                 860

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
865                 870                 875                 880

Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
```

```
               885                 890                 895

Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
            900                 905                 910

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser
        915                 920                 925

Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
    930                 935                 940

Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
945                 950                 955                 960

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala
                965                 970                 975

Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
            980                 985                 990

Thr Glu Glu Gly Thr Ser Thr Glu  Pro Ser Glu Gly Ser  Ala Pro Gly
        995                 1000                1005

Thr Ser  Thr Glu Pro Ser Glu  Gly Ser Ala Pro Gly  Ser Glu Pro
    1010                1015                1020

Ala Thr  Ser Gly Ser Glu Thr  Pro Gly Thr Ser Glu  Ser Ala Thr
    1025                1030                1035

Pro Glu  Ser Gly Pro Gly Thr  Ser Thr Glu Pro Ser  Glu Gly Ser
    1040                1045                1050

Ala Pro  Ala Ser Ser Pro Pro  Val Leu Lys Arg His  Gln Ala Glu
    1055                1060                1065

Ile Thr  Arg Thr Thr Leu Gln  Ser Asp Gln Glu Glu  Ile Asp Tyr
    1070                1075                1080

Asp Asp  Thr Ile Ser Val Glu  Met Lys Lys Glu Asp  Phe Asp Ile
    1085                1090                1095
```

```
Tyr Asp  Glu Asp Glu Asn Gln  Ser Pro Arg Ser Phe  Gln Lys Lys
    1100                1105                1110

Thr Arg  His Tyr Phe Ile Ala  Ala Val Glu Arg Leu  Trp Asp Tyr
    1115                1120                1125

Gly Met  Ser Ser Ser Pro His  Val Leu Arg Asn Arg  Ala Gln Ser
    1130                1135                1140

Gly Ser  Val Pro Gln Phe Lys  Lys Val Val Phe Gln  Glu Phe Thr
    1145                1150                1155

Asp Gly  Ser Phe Thr Gln Pro  Leu Tyr Arg Gly Glu  Leu Asn Glu
    1160                1165                1170

His Leu  Gly Leu Leu Gly Pro  Tyr Ile Arg Ala Glu  Val Glu Asp
    1175                1180                1185

Asn Ile  Met Val Thr Phe Arg  Asn Gln Ala Ser Arg  Pro Tyr Ser
    1190                1195                1200

Phe Tyr  Ser Ser Leu Ile Ser  Tyr Glu Glu Asp Gln  Arg Gln Gly
    1205                1210                1215

Ala Glu  Pro Arg Lys Asn Phe  Val Lys Pro Asn Glu  Thr Lys Thr
    1220                1225                1230

Tyr Phe  Trp Lys Val Gln His  His Met Ala Pro Thr  Lys Asp Glu
    1235                1240                1245

Phe Asp  Cys Lys Ala Trp Ala  Tyr Phe Ser Asp Val  Asp Leu Glu
    1250                1255                1260

Lys Asp  Val His Ser Gly Leu  Ile Gly Pro Leu Leu  Val Cys His
    1265                1270                1275

Thr Asn  Thr Leu Asn Pro Ala  His Gly Arg Gln Val  Thr Val Gln
    1280                1285                1290

Glu Phe  Ala Leu Phe Phe Thr  Ile Phe Asp Glu Thr  Lys Ser Trp
    1295                1300                1305
```

```
Tyr Phe  Thr Glu Asn Met Glu  Arg Asn Cys Arg Gly  Ala Pro Thr
    1310                 1315                 1320

Ser Glu  Ser Ala Thr Pro Glu  Ser Gly Pro Gly Ser  Glu Pro Ala
    1325                 1330                 1335

Thr Ser  Gly Ser Glu Thr Pro  Gly Thr Ser Glu Ser  Ala Thr Pro
    1340                 1345                 1350

Glu Ser  Gly Pro Gly Ser Glu  Pro Ala Thr Ser Gly  Ser Glu Thr
    1355                 1360                 1365

Pro Gly  Thr Ser Glu Ser Ala  Thr Pro Glu Ser Gly  Pro Gly Thr
    1370                 1375                 1380

Ser Thr  Glu Pro Ser Glu Gly  Ser Ala Pro Gly Thr  Ser Glu Ser
    1385                 1390                 1395

Ala Thr  Pro Glu Ser Gly Pro  Gly Ser Pro Ala Gly  Ser Pro Thr
    1400                 1405                 1410

Ser Thr  Glu Glu Gly Ser Pro  Ala Gly Ser Pro Thr  Ser Thr Glu
    1415                 1420                 1425

Glu Gly  Ser Pro Ala Gly Ser  Pro Thr Ser Thr Glu  Glu Gly Thr
    1430                 1435                 1440

Ser Glu  Ser Ala Thr Pro Glu  Ser Gly Pro Gly Thr  Ser Thr Glu
    1445                 1450                 1455

Pro Ser  Glu Gly Ser Ala Pro  Gly Ala Ser Ser Ala  Pro Cys Asn
    1460                 1465                 1470

Ile Gln  Met Glu Asp Pro Thr  Phe Lys Glu Asn Tyr  Arg Phe His
    1475                 1480                 1485

Ala Ile  Asn Gly Tyr Ile Met  Asp Thr Leu Pro Gly  Leu Val Met
    1490                 1495                 1500

Ala Gln  Asp Gln Arg Ile Arg  Trp Tyr Leu Leu Ser  Met Gly Ser
    1505                 1510                 1515
```

```
Asn Glu  Asn Ile His Ser Ile  His Phe Ser Gly His  Val Phe Thr
    1520                1525                1530

Val Arg  Lys Lys Glu Glu Tyr  Lys Met Ala Leu Tyr  Asn Leu Tyr
    1535                1540                1545

Pro Gly  Val Phe Glu Thr Val  Glu Met Leu Pro Ser  Lys Ala Gly
    1550                1555                1560

Ile Trp  Arg Val Glu Cys Leu  Ile Gly Glu His Leu  His Ala Gly
    1565                1570                1575

Met Ser  Thr Leu Phe Leu Val  Tyr Ser Asn Lys Cys  Gln Thr Pro
    1580                1585                1590

Leu Gly  Met Ala Ser Gly His  Ile Arg Asp Phe Gln  Ile Thr Ala
    1595                1600                1605

Ser Gly  Gln Tyr Gly Gln Trp  Ala Pro Lys Leu Ala  Arg Leu His
    1610                1615                1620

Tyr Ser  Gly Ser Ile Asn Ala  Trp Ser Thr Lys Glu  Pro Phe Ser
    1625                1630                1635

Trp Ile  Lys Val Asp Leu Leu  Ala Pro Met Ile Ile  His Gly Ile
    1640                1645                1650

Lys Thr  Gln Gly Ala Arg Gln  Lys Phe Ser Ser Leu  Tyr Ile Ser
    1655                1660                1665

Gln Phe  Ile Ile Met Tyr Ser  Leu Asp Gly Lys Lys  Trp Gln Thr
    1670                1675                1680

Tyr Arg  Gly Asn Ser Thr Gly  Thr Leu Met Val Phe  Phe Gly Asn
    1685                1690                1695

Val Asp  Ser Ser Gly Ile Lys  His Asn Ile Phe Asn  Pro Pro Ile
    1700                1705                1710

Ile Ala  Arg Tyr Ile Arg Leu  His Pro Thr His Tyr  Ser Ile Arg
```

```
    1715                1720                1725

Ser Thr  Leu Arg Met Glu Leu  Met Gly Cys Asp Leu  Asn Ser Cys
    1730                1735                1740

Ser Met  Pro Leu Gly Met Glu  Ser Lys Ala Ile Ser  Asp Ala Gln
    1745                1750                1755

Ile Thr  Ala Ser Ser Tyr Phe  Thr Asn Met Phe Ala  Thr Trp Ser
    1760                1765                1770

Pro Ser  Lys Ala Arg Leu His  Leu Gln Gly Arg Ser  Asn Ala Trp
    1775                1780                1785

Arg Pro  Gln Val Asn Asn Pro  Lys Glu Trp Leu Gln  Val Asp Phe
    1790                1795                1800

Gln Lys  Thr Met Lys Val Thr  Gly Val Thr Thr Gln  Gly Val Lys
    1805                1810                1815

Ser Leu  Leu Thr Ser Met Tyr  Val Lys Glu Phe Leu  Ile Ser Ser
    1820                1825                1830

Ser Gln  Asp Gly His Gln Trp  Thr Leu Phe Phe Gln  Asn Gly Lys
    1835                1840                1845

Val Lys  Val Phe Gln Gly Asn  Gln Asp Ser Phe Thr  Pro Val Val
    1850                1855                1860

Asn Ser  Leu Asp Pro Pro Leu  Leu Thr Arg Tyr Leu  Arg Ile His
    1865                1870                1875

Pro Gln  Ser Trp Val His Gln  Ile Ala Leu Arg Met  Glu Val Leu
    1880                1885                1890

Gly Cys  Glu Ala Gln Asp Leu  Tyr Asp Lys Thr His  Thr Cys Pro
    1895                1900                1905

Pro Cys  Pro Ala Pro Glu Leu  Leu Gly Gly Pro Ser  Val Phe Leu
    1910                1915                1920
```

```
Phe Pro  Pro Lys Pro Lys Asp  Thr Leu Met Ile Ser  Arg Thr Pro
    1925                1930                1935

Glu Val  Thr Cys Val Val Val  Asp Val Ser His Glu  Asp Pro Glu
    1940                1945                1950

Val Lys  Phe Asn Trp Tyr Val  Asp Gly Val Glu Val  His Asn Ala
    1955                1960                1965

Lys Thr  Lys Pro Arg Glu Glu  Gln Tyr Asn Ser Thr  Tyr Arg Val
    1970                1975                1980

Val Ser  Val Leu Thr Val Leu  His Gln Asp Trp Leu  Asn Gly Lys
    1985                1990                1995

Glu Tyr  Lys Cys Lys Val Ser  Asn Lys Ala Leu Pro  Ala Pro Ile
    2000                2005                2010

Glu Lys  Thr Ile Ser Lys Ala  Lys Gly Gln Pro Arg  Glu Pro Gln
    2015                2020                2025

Val Tyr  Thr Leu Pro Pro Ser  Arg Asp Glu Leu Thr  Lys Asn Gln
    2030                2035                2040

Val Ser  Leu Thr Cys Leu Val  Lys Gly Phe Tyr Pro  Ser Asp Ile
    2045                2050                2055

Ala Val  Glu Trp Glu Ser Asn  Gly Gln Pro Glu Asn  Asn Tyr Lys
    2060                2065                2070

Thr Thr  Pro Pro Val Leu Asp  Ser Asp Gly Ser Phe  Phe Leu Tyr
    2075                2080                2085

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

Phe Ser  Cys Ser Val Met His  Glu Ala Leu His Asn  His Tyr Thr
    2105                2110                2115

Gln Lys  Ser Leu Ser Leu Ser  Pro Gly Lys
    2120                2125
```

<210> 78
<211> 2128
<212> PRT
<213> Artificial Sequence

<220>
<223> FVIII 204 (single chain FVIIIFc with two AE XTENs, one 288AE XTEN in B-domain and one 144 AE XTEN at amino acid 403)

<400> 78

Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
1 5 10 15

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

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

Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val
50 55 60

Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile
65 70 75 80

Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln
85 90 95

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

His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser
115 120 125

Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp
130 135 140

Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu
145 150 155 160

Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser
165 170 175

```
Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile
            180                 185                 190

Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr
        195                 200                 205

Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly
    210                 215                 220

Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp
225                 230                 235                 240

Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr
                245                 250                 255

Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val
            260                 265                 270

Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile
        275                 280                 285

Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser
    290                 295                 300

Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met
305                 310                 315                 320

Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His
                325                 330                 335

Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro
            340                 345                 350

Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp
        355                 360                 365

Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser
    370                 375                 380

Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
385                 390                 395                 400
```

```
Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro
                405                 410                 415

Leu Val Leu Ala Pro Asp Gly Ala Pro Thr Ser Thr Glu Pro Ser Glu
            420                 425                 430

Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
        435                 440                 445

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
    450                 455                 460

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
465                 470                 475                 480

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
                485                 490                 495

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
            500                 505                 510

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Thr Glu Pro Ser Glu
        515                 520                 525

Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
    530                 535                 540

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu
545                 550                 555                 560

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ala Ser Ser Asp Arg Ser Tyr
                565                 570                 575

Lys Ser Gln Tyr Leu Asn Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr
            580                 585                 590

Lys Lys Val Arg Phe Met Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg
        595                 600                 605

Glu Ala Ile Gln His Glu Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly
```

610 615 620

Glu Val Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg
625 630 635 640

Pro Tyr Asn Ile Tyr Pro His Gly Ile Thr Asp Val Arg Pro Leu Tyr
645 650 655

Ser Arg Arg Leu Pro Lys Gly Val Lys His Leu Lys Asp Phe Pro Ile
660 665 670

Leu Pro Gly Glu Ile Phe Lys Tyr Lys Trp Thr Val Thr Val Glu Asp
675 680 685

Gly Pro Thr Lys Ser Asp Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser
690 695 700

Phe Val Asn Met Glu Arg Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu
705 710 715 720

Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly Asn Gln Ile Met
725 730 735

Ser Asp Lys Arg Asn Val Ile Leu Phe Ser Val Phe Asp Glu Asn Arg
740 745 750

Ser Trp Tyr Leu Thr Glu Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala
755 760 765

Gly Val Gln Leu Glu Asp Pro Glu Phe Gln Ala Ser Asn Ile Met His
770 775 780

Ser Ile Asn Gly Tyr Val Phe Asp Ser Leu Gln Leu Ser Val Cys Leu
785 790 795 800

His Glu Val Ala Tyr Trp Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp
805 810 815

Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys His Lys Met Val
820 825 830

```
Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly Glu Thr Val Phe
        835                 840                 845

Met Ser Met Glu Asn Pro Gly Leu Trp Ile Leu Gly Cys His Asn Ser
    850                 855                 860

Asp Phe Arg Asn Arg Gly Met Thr Ala Leu Leu Lys Val Ser Ser Cys
865                 870                 875                 880

Asp Lys Asn Thr Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser
                885                 890                 895

Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
            900                 905                 910

Gln Asn Gly Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
        915                 920                 925

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser
    930                 935                 940

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
945                 950                 955                 960

Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
                965                 970                 975

Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro
            980                 985                 990

Ala Gly Ser Pro Thr Ser Thr Glu  Glu Gly Thr Ser Glu  Ser Ala Thr
        995                 1000                1005

Pro Glu  Ser Gly Pro Gly Ser  Glu Pro Ala Thr Ser  Gly Ser Glu
    1010                1015                1020

Thr Pro  Gly Thr Ser Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly
    1025                1030                1035

Ser Pro  Ala Gly Ser Pro Thr  Ser Thr Glu Glu Gly  Ser Pro Ala
    1040                1045                1050
```

```
Gly Ser  Pro Thr Ser Thr Glu  Glu Gly Thr Ser Thr  Glu Pro Ser
    1055                1060                1065

Glu Gly  Ser Ala Pro Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser
    1070                1075                1080

Gly Pro  Gly Thr Ser Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly
    1085                1090                1095

Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly Pro Gly  Ser Glu Pro
    1100                1105                1110

Ala Thr  Ser Gly Ser Glu Thr  Pro Gly Ser Glu Pro  Ala Thr Ser
    1115                1120                1125

Gly Ser  Glu Thr Pro Gly Ser  Pro Ala Gly Ser Pro  Thr Ser Thr
    1130                1135                1140

Glu Glu  Gly Thr Ser Thr Glu  Pro Ser Glu Gly Ser  Ala Pro Gly
    1145                1150                1155

Thr Ser  Thr Glu Pro Ser Glu  Gly Ser Ala Pro Gly  Ser Glu Pro
    1160                1165                1170

Ala Thr  Ser Gly Ser Glu Thr  Pro Gly Thr Ser Glu  Ser Ala Thr
    1175                1180                1185

Pro Glu  Ser Gly Pro Gly Thr  Ser Thr Glu Pro Ser  Glu Gly Ser
    1190                1195                1200

Ala Pro  Ala Ser Ser Pro Pro  Val Leu Lys Arg His  Gln Ala Glu
    1205                1210                1215

Ile Thr  Arg Thr Thr Leu Gln  Ser Asp Gln Glu Glu  Ile Asp Tyr
    1220                1225                1230

Asp Asp  Thr Ile Ser Val Glu  Met Lys Lys Glu Asp  Phe Asp Ile
    1235                1240                1245

Tyr Asp  Glu Asp Glu Asn Gln  Ser Pro Arg Ser Phe  Gln Lys Lys
    1250                1255                1260
```

```
Thr Arg  His Tyr Phe Ile Ala  Ala Val Glu Arg Leu  Trp Asp Tyr
    1265                1270                1275

Gly Met  Ser Ser Ser Pro His  Val Leu Arg Asn Arg  Ala Gln Ser
    1280                1285                1290

Gly Ser  Val Pro Gln Phe Lys  Lys Val Val Phe Gln  Glu Phe Thr
    1295                1300                1305

Asp Gly  Ser Phe Thr Gln Pro  Leu Tyr Arg Gly Glu  Leu Asn Glu
    1310                1315                1320

His Leu  Gly Leu Leu Gly Pro  Tyr Ile Arg Ala Glu  Val Glu Asp
    1325                1330                1335

Asn Ile  Met Val Thr Phe Arg  Asn Gln Ala Ser Arg  Pro Tyr Ser
    1340                1345                1350

Phe Tyr  Ser Ser Leu Ile Ser  Tyr Glu Glu Asp Gln  Arg Gln Gly
    1355                1360                1365

Ala Glu  Pro Arg Lys Asn Phe  Val Lys Pro Asn Glu  Thr Lys Thr
    1370                1375                1380

Tyr Phe  Trp Lys Val Gln His  His Met Ala Pro Thr  Lys Asp Glu
    1385                1390                1395

Phe Asp  Cys Lys Ala Trp Ala  Tyr Phe Ser Asp Val  Asp Leu Glu
    1400                1405                1410

Lys Asp  Val His Ser Gly Leu  Ile Gly Pro Leu Leu  Val Cys His
    1415                1420                1425

Thr Asn  Thr Leu Asn Pro Ala  His Gly Arg Gln Val  Thr Val Gln
    1430                1435                1440

Glu Phe  Ala Leu Phe Phe Thr  Ile Phe Asp Glu Thr  Lys Ser Trp
    1445                1450                1455

Tyr Phe  Thr Glu Asn Met Glu  Arg Asn Cys Arg Ala  Pro Cys Asn
```

```
    1460                1465                1470

Ile Gln  Met Glu Asp Pro Thr  Phe Lys Glu Asn Tyr  Arg Phe His
    1475                1480                1485

Ala Ile  Asn Gly Tyr Ile Met  Asp Thr Leu Pro Gly  Leu Val Met
    1490                1495                1500

Ala Gln  Asp Gln Arg Ile Arg  Trp Tyr Leu Leu Ser  Met Gly Ser
    1505                1510                1515

Asn Glu  Asn Ile His Ser Ile  His Phe Ser Gly His  Val Phe Thr
    1520                1525                1530

Val Arg  Lys Lys Glu Glu Tyr  Lys Met Ala Leu Tyr  Asn Leu Tyr
    1535                1540                1545

Pro Gly  Val Phe Glu Thr Val  Glu Met Leu Pro Ser  Lys Ala Gly
    1550                1555                1560

Ile Trp  Arg Val Glu Cys Leu  Ile Gly Glu His Leu  His Ala Gly
    1565                1570                1575

Met Ser  Thr Leu Phe Leu Val  Tyr Ser Asn Lys Cys  Gln Thr Pro
    1580                1585                1590

Leu Gly  Met Ala Ser Gly His  Ile Arg Asp Phe Gln  Ile Thr Ala
    1595                1600                1605

Ser Gly  Gln Tyr Gly Gln Trp  Ala Pro Lys Leu Ala  Arg Leu His
    1610                1615                1620

Tyr Ser  Gly Ser Ile Asn Ala  Trp Ser Thr Lys Glu  Pro Phe Ser
    1625                1630                1635

Trp Ile  Lys Val Asp Leu Leu  Ala Pro Met Ile Ile  His Gly Ile
    1640                1645                1650

Lys Thr  Gln Gly Ala Arg Gln  Lys Phe Ser Ser Leu  Tyr Ile Ser
    1655                1660                1665
```

```
Gln Phe  Ile Ile Met Tyr Ser  Leu Asp Gly Lys Lys  Trp Gln Thr
    1670                1675                1680

Tyr Arg  Gly Asn Ser Thr Gly  Thr Leu Met Val Phe  Phe Gly Asn
    1685                1690                1695

Val Asp  Ser Ser Gly Ile Lys  His Asn Ile Phe Asn  Pro Pro Ile
    1700                1705                1710

Ile Ala  Arg Tyr Ile Arg Leu  His Pro Thr His Tyr  Ser Ile Arg
    1715                1720                1725

Ser Thr  Leu Arg Met Glu Leu  Met Gly Cys Asp Leu  Asn Ser Cys
    1730                1735                1740

Ser Met  Pro Leu Gly Met Glu  Ser Lys Ala Ile Ser  Asp Ala Gln
    1745                1750                1755

Ile Thr  Ala Ser Ser Tyr Phe  Thr Asn Met Phe Ala  Thr Trp Ser
    1760                1765                1770

Pro Ser  Lys Ala Arg Leu His  Leu Gln Gly Arg Ser  Asn Ala Trp
    1775                1780                1785

Arg Pro  Gln Val Asn Asn Pro  Lys Glu Trp Leu Gln  Val Asp Phe
    1790                1795                1800

Gln Lys  Thr Met Lys Val Thr  Gly Val Thr Thr Gln  Gly Val Lys
    1805                1810                1815

Ser Leu  Leu Thr Ser Met Tyr  Val Lys Glu Phe Leu  Ile Ser Ser
    1820                1825                1830

Ser Gln  Asp Gly His Gln Trp  Thr Leu Phe Phe Gln  Asn Gly Lys
    1835                1840                1845

Val Lys  Val Phe Gln Gly Asn  Gln Asp Ser Phe Thr  Pro Val Val
    1850                1855                1860

Asn Ser  Leu Asp Pro Pro Leu  Leu Thr Arg Tyr Leu  Arg Ile His
    1865                1870                1875
```

```
Pro Gln  Ser Trp Val His Gln  Ile Ala Leu Arg Met  Glu Val Leu
    1880                1885                1890

Gly Cys  Glu Ala Gln Asp Leu  Tyr Asp Lys Thr His  Thr Cys Pro
    1895                1900                1905

Pro Cys  Pro Ala Pro Glu Leu  Leu Gly Gly Pro Ser  Val Phe Leu
    1910                1915                1920

Phe Pro  Pro Lys Pro Lys Asp  Thr Leu Met Ile Ser  Arg Thr Pro
    1925                1930                1935

Glu Val  Thr Cys Val Val Val  Asp Val Ser His Glu  Asp Pro Glu
    1940                1945                1950

Val Lys  Phe Asn Trp Tyr Val  Asp Gly Val Glu Val  His Asn Ala
    1955                1960                1965

Lys Thr  Lys Pro Arg Glu Glu  Gln Tyr Asn Ser Thr  Tyr Arg Val
    1970                1975                1980

Val Ser  Val Leu Thr Val Leu  His Gln Asp Trp Leu  Asn Gly Lys
    1985                1990                1995

Glu Tyr  Lys Cys Lys Val Ser  Asn Lys Ala Leu Pro  Ala Pro Ile
    2000                2005                2010

Glu Lys  Thr Ile Ser Lys Ala  Lys Gly Gln Pro Arg  Glu Pro Gln
    2015                2020                2025

Val Tyr  Thr Leu Pro Pro Ser  Arg Asp Glu Leu Thr  Lys Asn Gln
    2030                2035                2040

Val Ser  Leu Thr Cys Leu Val  Lys Gly Phe Tyr Pro  Ser Asp Ile
    2045                2050                2055

Ala Val  Glu Trp Glu Ser Asn  Gly Gln Pro Glu Asn  Asn Tyr Lys
    2060                2065                2070

Thr Thr  Pro Pro Val Leu Asp  Ser Asp Gly Ser Phe  Phe Leu Tyr
    2075                2080                2085
```

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

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
    2105   2110   2115

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    2120   2125

<210> 79
<211> 2128
<212> PRT
<213> Artificial Sequence

<220>
<223> FVIII 205 (single chain FVIIIFc with two AE XTEN, one 288AE XTEN
       in B-domain and one 144 AE XTEN at amino acid 18)

<400> 79

Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
1   5   10   15

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

Trp Asp Tyr Met Gln Gly Ala Pro Thr Ser Glu Ser Ala Thr Pro Glu
        35   40   45

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
    50   55   60

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
65   70   75   80

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
                85   90   95

Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
            100   105   110

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser
        115   120   125

```
Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
    130                 135                 140

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
145                 150                 155                 160

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly
                165                 170                 175

Ser Pro Thr Ser Thr Glu Glu Gly Ala Ser Ser Ser Asp Leu Gly Glu
            180                 185                 190

Leu Pro Val Asp Ala Arg Phe Pro Pro Arg Val Pro Lys Ser Phe Pro
        195                 200                 205

Phe Asn Thr Ser Val Val Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr
    210                 215                 220

Asp His Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu
225                 230                 235                 240

Leu Gly Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr Val Val Ile Thr
                245                 250                 255

Leu Lys Asn Met Ala Ser His Pro Val Ser Leu His Ala Val Gly Val
            260                 265                 270

Ser Tyr Trp Lys Ala Ser Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser
        275                 280                 285

Gln Arg Glu Lys Glu Asp Asp Lys Val Phe Pro Gly Gly Ser His Thr
    290                 295                 300

Tyr Val Trp Gln Val Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro
305                 310                 315                 320

Leu Cys Leu Thr Tyr Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp
                325                 330                 335

Leu Asn Ser Gly Leu Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser
```

```
            340                 345                 350

Leu Ala Lys Glu Lys Thr Gln Thr Leu His Lys Phe Ile Leu Leu Phe
        355                 360                 365

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

Leu Met Gln Asp Arg Asp Ala Ala Ser Ala Arg Ala Trp Pro Lys Met
385                 390                 395                 400

His Thr Val Asn Gly Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly
                405                 410                 415

Cys His Arg Lys Ser Val Tyr Trp His Val Ile Gly Met Gly Thr Thr
            420                 425                 430

Pro Glu Val His Ser Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg
        435                 440                 445

Asn His Arg Gln Ala Ser Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr
    450                 455                 460

Ala Gln Thr Leu Leu Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His
465                 470                 475                 480

Ile Ser Ser His Gln His Asp Gly Met Glu Ala Tyr Val Lys Val Asp
                485                 490                 495

Ser Cys Pro Glu Glu Pro Gln Leu Arg Met Lys Asn Asn Glu Glu Ala
            500                 505                 510

Glu Asp Tyr Asp Asp Asp Leu Thr Asp Ser Glu Met Asp Val Val Arg
        515                 520                 525

Phe Asp Asp Asp Asn Ser Pro Ser Phe Ile Gln Ile Arg Ser Val Ala
    530                 535                 540

Lys Lys His Pro Lys Thr Trp Val His Tyr Ile Ala Ala Glu Glu Glu
545                 550                 555                 560
```

```
Asp Trp Asp Tyr Ala Pro Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr
                565                 570                 575

Lys Ser Gln Tyr Leu Asn Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr
            580                 585                 590

Lys Lys Val Arg Phe Met Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg
        595                 600                 605

Glu Ala Ile Gln His Glu Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly
    610                 615                 620

Glu Val Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg
625                 630                 635                 640

Pro Tyr Asn Ile Tyr Pro His Gly Ile Thr Asp Val Arg Pro Leu Tyr
                645                 650                 655

Ser Arg Arg Leu Pro Lys Gly Val Lys His Leu Lys Asp Phe Pro Ile
            660                 665                 670

Leu Pro Gly Glu Ile Phe Lys Tyr Lys Trp Thr Val Thr Val Glu Asp
        675                 680                 685

Gly Pro Thr Lys Ser Asp Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser
    690                 695                 700

Phe Val Asn Met Glu Arg Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu
705                 710                 715                 720

Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly Asn Gln Ile Met
                725                 730                 735

Ser Asp Lys Arg Asn Val Ile Leu Phe Ser Val Phe Asp Glu Asn Arg
            740                 745                 750

Ser Trp Tyr Leu Thr Glu Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala
        755                 760                 765

Gly Val Gln Leu Glu Asp Pro Glu Phe Gln Ala Ser Asn Ile Met His
    770                 775                 780
```

```
Ser Ile Asn Gly Tyr Val Phe Asp Ser Leu Gln Leu Ser Val Cys Leu
785                 790                 795                 800


His Glu Val Ala Tyr Trp Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp
                805                 810                 815


Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys His Lys Met Val
            820                 825                 830


Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly Glu Thr Val Phe
        835                 840                 845


Met Ser Met Glu Asn Pro Gly Leu Trp Ile Leu Gly Cys His Asn Ser
    850                 855                 860


Asp Phe Arg Asn Arg Gly Met Thr Ala Leu Leu Lys Val Ser Ser Cys
865                 870                 875                 880


Asp Lys Asn Thr Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser
                885                 890                 895


Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
            900                 905                 910


Gln Asn Gly Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
        915                 920                 925


Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser
    930                 935                 940


Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
945                 950                 955                 960


Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
                965                 970                 975


Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro
            980                 985                 990


Ala Gly Ser Pro Thr Ser Thr Glu  Glu Gly Thr Ser Glu  Ser Ala Thr
        995                 1000                1005
```

```
Pro Glu  Ser Gly Pro Gly Ser  Glu Pro Ala Thr Ser  Gly Ser Glu
    1010                1015                1020

Thr Pro  Gly Thr Ser Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly
    1025                1030                1035

Ser Pro  Ala Gly Ser Pro Thr  Ser Thr Glu Glu Gly  Ser Pro Ala
    1040                1045                1050

Gly Ser  Pro Thr Ser Thr Glu  Glu Gly Thr Ser Thr  Glu Pro Ser
    1055                1060                1065

Glu Gly  Ser Ala Pro Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser
    1070                1075                1080

Gly Pro  Gly Thr Ser Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly
    1085                1090                1095

Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly Pro Gly  Ser Glu Pro
    1100                1105                1110

Ala Thr  Ser Gly Ser Glu Thr  Pro Gly Ser Glu Pro  Ala Thr Ser
    1115                1120                1125

Gly Ser  Glu Thr Pro Gly Ser  Pro Ala Gly Ser Pro  Thr Ser Thr
    1130                1135                1140

Glu Glu  Gly Thr Ser Thr Glu  Pro Ser Glu Gly Ser  Ala Pro Gly
    1145                1150                1155

Thr Ser  Thr Glu Pro Ser Glu  Gly Ser Ala Pro Gly  Ser Glu Pro
    1160                1165                1170

Ala Thr  Ser Gly Ser Glu Thr  Pro Gly Thr Ser Glu  Ser Ala Thr
    1175                1180                1185

Pro Glu  Ser Gly Pro Gly Thr  Ser Thr Glu Pro Ser  Glu Gly Ser
    1190                1195                1200

Ala Pro  Ala Ser Ser Pro Pro  Val Leu Lys Arg His  Gln Ala Glu
```

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    1205                1210                1215

Ile Thr  Arg Thr Thr Leu Gln  Ser Asp Gln Glu Glu  Ile Asp Tyr
    1220                1225                1230

Asp Asp  Thr Ile Ser Val Glu  Met Lys Lys Glu Asp  Phe Asp Ile
    1235                1240                1245

Tyr Asp  Glu Asp Glu Asn Gln  Ser Pro Arg Ser Phe  Gln Lys Lys
    1250                1255                1260

Thr Arg  His Tyr Phe Ile Ala  Ala Val Glu Arg Leu  Trp Asp Tyr
    1265                1270                1275

Gly Met  Ser Ser Ser Pro His  Val Leu Arg Asn Arg  Ala Gln Ser
    1280                1285                1290

Gly Ser  Val Pro Gln Phe Lys  Lys Val Val Phe Gln  Glu Phe Thr
    1295                1300                1305

Asp Gly  Ser Phe Thr Gln Pro  Leu Tyr Arg Gly Glu  Leu Asn Glu
    1310                1315                1320

His Leu  Gly Leu Leu Gly Pro  Tyr Ile Arg Ala Glu  Val Glu Asp
    1325                1330                1335

Asn Ile  Met Val Thr Phe Arg  Asn Gln Ala Ser Arg  Pro Tyr Ser
    1340                1345                1350

Phe Tyr  Ser Ser Leu Ile Ser  Tyr Glu Glu Asp Gln  Arg Gln Gly
    1355                1360                1365

Ala Glu  Pro Arg Lys Asn Phe  Val Lys Pro Asn Glu  Thr Lys Thr
    1370                1375                1380

Tyr Phe  Trp Lys Val Gln His  His Met Ala Pro Thr  Lys Asp Glu
    1385                1390                1395

Phe Asp  Cys Lys Ala Trp Ala  Tyr Phe Ser Asp Val  Asp Leu Glu
    1400                1405                1410
```

```
Lys Asp  Val His Ser Gly Leu  Ile Gly Pro Leu Leu  Val Cys His
    1415                 1420                 1425

Thr Asn  Thr Leu Asn Pro Ala  His Gly Arg Gln Val  Thr Val Gln
    1430                 1435                 1440

Glu Phe  Ala Leu Phe Phe Thr  Ile Phe Asp Glu Thr  Lys Ser Trp
    1445                 1450                 1455

Tyr Phe  Thr Glu Asn Met Glu  Arg Asn Cys Arg Ala  Pro Cys Asn
    1460                 1465                 1470

Ile Gln  Met Glu Asp Pro Thr  Phe Lys Glu Asn Tyr  Arg Phe His
    1475                 1480                 1485

Ala Ile  Asn Gly Tyr Ile Met  Asp Thr Leu Pro Gly  Leu Val Met
    1490                 1495                 1500

Ala Gln  Asp Gln Arg Ile Arg  Trp Tyr Leu Leu Ser  Met Gly Ser
    1505                 1510                 1515

Asn Glu  Asn Ile His Ser Ile  His Phe Ser Gly His  Val Phe Thr
    1520                 1525                 1530

Val Arg  Lys Lys Glu Glu Tyr  Lys Met Ala Leu Tyr  Asn Leu Tyr
    1535                 1540                 1545

Pro Gly  Val Phe Glu Thr Val  Glu Met Leu Pro Ser  Lys Ala Gly
    1550                 1555                 1560

Ile Trp  Arg Val Glu Cys Leu  Ile Gly Glu His Leu  His Ala Gly
    1565                 1570                 1575

Met Ser  Thr Leu Phe Leu Val  Tyr Ser Asn Lys Cys  Gln Thr Pro
    1580                 1585                 1590

Leu Gly  Met Ala Ser Gly His  Ile Arg Asp Phe Gln  Ile Thr Ala
    1595                 1600                 1605

Ser Gly  Gln Tyr Gly Gln Trp  Ala Pro Lys Leu Ala  Arg Leu His
    1610                 1615                 1620
```

```
Tyr Ser  Gly Ser Ile Asn Ala  Trp Ser Thr Lys Glu  Pro Phe Ser
    1625                1630                1635

Trp Ile  Lys Val Asp Leu Leu  Ala Pro Met Ile Ile  His Gly Ile
    1640                1645                1650

Lys Thr  Gln Gly Ala Arg Gln  Lys Phe Ser Ser Leu  Tyr Ile Ser
    1655                1660                1665

Gln Phe  Ile Ile Met Tyr Ser  Leu Asp Gly Lys Lys  Trp Gln Thr
    1670                1675                1680

Tyr Arg  Gly Asn Ser Thr Gly  Thr Leu Met Val Phe  Phe Gly Asn
    1685                1690                1695

Val Asp  Ser Ser Gly Ile Lys  His Asn Ile Phe Asn  Pro Pro Ile
    1700                1705                1710

Ile Ala  Arg Tyr Ile Arg Leu  His Pro Thr His Tyr  Ser Ile Arg
    1715                1720                1725

Ser Thr  Leu Arg Met Glu Leu  Met Gly Cys Asp Leu  Asn Ser Cys
    1730                1735                1740

Ser Met  Pro Leu Gly Met Glu  Ser Lys Ala Ile Ser  Asp Ala Gln
    1745                1750                1755

Ile Thr  Ala Ser Ser Tyr Phe  Thr Asn Met Phe Ala  Thr Trp Ser
    1760                1765                1770

Pro Ser  Lys Ala Arg Leu His  Leu Gln Gly Arg Ser  Asn Ala Trp
    1775                1780                1785

Arg Pro  Gln Val Asn Asn Pro  Lys Glu Trp Leu Gln  Val Asp Phe
    1790                1795                1800

Gln Lys  Thr Met Lys Val Thr  Gly Val Thr Thr Gln  Gly Val Lys
    1805                1810                1815

Ser Leu  Leu Thr Ser Met Tyr  Val Lys Glu Phe Leu  Ile Ser Ser
    1820                1825                1830
```

```
Ser Gln  Asp Gly His Gln Trp  Thr Leu Phe Phe Gln  Asn Gly Lys
    1835                 1840                 1845

Val Lys  Val Phe Gln Gly Asn  Gln Asp Ser Phe Thr  Pro Val Val
    1850                 1855                 1860

Asn Ser  Leu Asp Pro Pro Leu  Leu Thr Arg Tyr Leu  Arg Ile His
    1865                 1870                 1875

Pro Gln  Ser Trp Val His Gln  Ile Ala Leu Arg Met  Glu Val Leu
    1880                 1885                 1890

Gly Cys  Glu Ala Gln Asp Leu  Tyr Asp Lys Thr His  Thr Cys Pro
    1895                 1900                 1905

Pro Cys  Pro Ala Pro Glu Leu  Leu Gly Gly Pro Ser  Val Phe Leu
    1910                 1915                 1920

Phe Pro  Pro Lys Pro Lys Asp  Thr Leu Met Ile Ser  Arg Thr Pro
    1925                 1930                 1935

Glu Val  Thr Cys Val Val Val  Asp Val Ser His Glu  Asp Pro Glu
    1940                 1945                 1950

Val Lys  Phe Asn Trp Tyr Val  Asp Gly Val Glu Val  His Asn Ala
    1955                 1960                 1965

Lys Thr  Lys Pro Arg Glu Glu  Gln Tyr Asn Ser Thr  Tyr Arg Val
    1970                 1975                 1980

Val Ser  Val Leu Thr Val Leu  His Gln Asp Trp Leu  Asn Gly Lys
    1985                 1990                 1995

Glu Tyr  Lys Cys Lys Val Ser  Asn Lys Ala Leu Pro  Ala Pro Ile
    2000                 2005                 2010

Glu Lys  Thr Ile Ser Lys Ala  Lys Gly Gln Pro Arg  Glu Pro Gln
    2015                 2020                 2025

Val Tyr  Thr Leu Pro Pro Ser  Arg Asp Glu Leu Thr  Lys Asn Gln
```

```
    2030                2035                2040


Val Ser  Leu Thr Cys Leu Val  Lys Gly Phe Tyr Pro  Ser Asp Ile
    2045                2050                2055


Ala Val  Glu Trp Glu Ser Asn  Gly Gln Pro Glu Asn  Asn Tyr Lys
    2060                2065                2070


Thr Thr  Pro Pro Val Leu Asp  Ser Asp Gly Ser Phe  Phe Leu Tyr
    2075                2080                2085


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


Phe Ser  Cys Ser Val Met His  Glu Ala Leu His Asn  His Tyr Thr
    2105                2110                2115


Gln Lys  Ser Leu Ser Leu Ser  Pro Gly Lys
    2120                2125


<210>  80
<211>  2020
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  pSYN FVIII 266  (FVIII Fc with 42 AE-XTEN at amino acid 18 and
       288 AE XTEN in B-domain)

<400>  80

Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
1               5                   10                  15


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


Trp Asp Tyr Met Gln Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr
        35                  40                  45


Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
    50                  55                  60


Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Ser
```

```
65                  70                  75                  80

Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro Arg Val Pro
                85                  90                  95

Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys Thr Leu Phe
            100                 105                 110

Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro
        115                 120                 125

Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr
    130                 135                 140

Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val Ser Leu His
145                 150                 155                 160

Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala Glu Tyr Asp
                165                 170                 175

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

Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn Gly Pro Met
        195                 200                 205

Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser His Val Asp
    210                 215                 220

Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu Leu Val Cys
225                 230                 235                 240

Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr Gln Thr Leu His Lys Phe
                245                 250                 255

Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp His Ser Glu
            260                 265                 270

Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser Ala Arg Ala
        275                 280                 285
```

```
Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg Ser Leu Pro
    290                 295                 300

Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His Val Ile Gly
305                 310                 315                 320

Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu Gly His Thr
                325                 330                 335

Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile Ser Pro Ile
            340                 345                 350

Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly Gln Phe Leu
        355                 360                 365

Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met Glu Ala Tyr
    370                 375                 380

Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg Met Lys Asn
385                 390                 395                 400

Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp Ser Glu Met
                405                 410                 415

Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro Ser Phe Ile Gln Ile
            420                 425                 430

Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His Tyr Ile Ala
        435                 440                 445

Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu Ala Pro Asp
    450                 455                 460

Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro Gln Arg Ile
465                 470                 475                 480

Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr Asp Glu Thr
                485                 490                 495

Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile Leu Gly Pro
            500                 505                 510
```

```
Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn
        515                 520                 525

Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile Thr Asp Val
    530                 535                 540

Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys Gly Val Lys His Leu Lys
545                 550                 555                 560

Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys Trp Thr Val
                565                 570                 575

Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys Leu Thr Arg
            580                 585                 590

Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala Ser Gly Leu
        595                 600                 605

Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly
    610                 615                 620

Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe Ser Val Phe
625                 630                 635                 640

Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln Arg Phe Leu
                645                 650                 655

Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe Gln Ala Ser
            660                 665                 670

Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser Leu Gln Leu
        675                 680                 685

Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu Ser Ile Gly
    690                 695                 700

Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys
705                 710                 715                 720

His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly
                725                 730                 735
```

```
Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp Ile Leu Gly
            740                 745                 750

Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr Ala Leu Leu Lys
        755                 760                 765

Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu Asp Ser Tyr
    770                 775                 780

Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro
785                 790                 795                 800

Arg Ser Phe Ser Gln Asn Gly Ala Pro Gly Thr Ser Glu Ser Ala Thr
                805                 810                 815

Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr
            820                 825                 830

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu
        835                 840                 845

Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr
    850                 855                 860

Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
865                 870                 875                 880

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser
                885                 890                 895

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
            900                 905                 910

Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
        915                 920                 925

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro
    930                 935                 940

Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser
```

```
945                 950                 955                 960

Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
                965                 970                 975

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser
            980                 985                 990

Glu Ser Ala Thr Pro Glu Ser Gly  Pro Gly Ser Glu Pro  Ala Thr Ser
        995                 1000                1005

Gly Ser  Glu Thr Pro Gly Ser  Glu Pro Ala Thr Ser  Gly Ser Glu
    1010                1015                1020

Thr Pro  Gly Ser Pro Ala Gly  Ser Pro Thr Ser Thr  Glu Glu Gly
    1025                1030                1035

Thr Ser  Thr Glu Pro Ser Glu  Gly Ser Ala Pro Gly  Thr Ser Thr
    1040                1045                1050

Glu Pro  Ser Glu Gly Ser Ala  Pro Gly Ser Glu Pro  Ala Thr Ser
    1055                1060                1065

Gly Ser  Glu Thr Pro Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser
    1070                1075                1080

Gly Pro  Gly Thr Ser Thr Glu  Pro Ser Glu Gly Ser  Ala Pro Ala
    1085                1090                1095

Ser Ser  Pro Pro Val Leu Lys  Arg His Gln Ala Glu  Ile Thr Arg
    1100                1105                1110

Thr Thr  Leu Gln Ser Asp Gln  Glu Glu Ile Asp Tyr  Asp Asp Thr
    1115                1120                1125

Ile Ser  Val Glu Met Lys Lys  Glu Asp Phe Asp Ile  Tyr Asp Glu
    1130                1135                1140

Asp Glu  Asn Gln Ser Pro Arg  Ser Phe Gln Lys Lys  Thr Arg His
    1145                1150                1155
```

```
Tyr Phe  Ile Ala Ala Val Glu  Arg Leu Trp Asp Tyr  Gly Met Ser
    1160                1165                1170

Ser Ser  Pro His Val Leu Arg  Asn Arg Ala Gln Ser  Gly Ser Val
    1175                1180                1185

Pro Gln  Phe Lys Lys Val Val  Phe Gln Glu Phe Thr  Asp Gly Ser
    1190                1195                1200

Phe Thr  Gln Pro Leu Tyr Arg  Gly Glu Leu Asn Glu  His Leu Gly
    1205                1210                1215

Leu Leu  Gly Pro Tyr Ile Arg  Ala Glu Val Glu Asp  Asn Ile Met
    1220                1225                1230

Val Thr  Phe Arg Asn Gln Ala  Ser Arg Pro Tyr Ser  Phe Tyr Ser
    1235                1240                1245

Ser Leu  Ile Ser Tyr Glu Glu  Asp Gln Arg Gln Gly  Ala Glu Pro
    1250                1255                1260

Arg Lys  Asn Phe Val Lys Pro  Asn Glu Thr Lys Thr  Tyr Phe Trp
    1265                1270                1275

Lys Val  Gln His His Met Ala  Pro Thr Lys Asp Glu  Phe Asp Cys
    1280                1285                1290

Lys Ala  Trp Ala Tyr Phe Ser  Asp Val Asp Leu Glu  Lys Asp Val
    1295                1300                1305

His Ser  Gly Leu Ile Gly Pro  Leu Leu Val Cys His  Thr Asn Thr
    1310                1315                1320

Leu Asn  Pro Ala His Gly Arg  Gln Val Thr Val Gln  Glu Phe Ala
    1325                1330                1335

Leu Phe  Phe Thr Ile Phe Asp  Glu Thr Lys Ser Trp  Tyr Phe Thr
    1340                1345                1350

Glu Asn  Met Glu Arg Asn Cys  Arg Ala Pro Cys Asn  Ile Gln Met
    1355                1360                1365
```

```
Glu Asp  Pro Thr Phe Lys Glu  Asn Tyr Arg Phe His  Ala Ile Asn
    1370                1375                1380

Gly Tyr  Ile Met Asp Thr Leu  Pro Gly Leu Val Met  Ala Gln Asp
    1385                1390                1395

Gln Arg  Ile Arg Trp Tyr Leu  Leu Ser Met Gly Ser  Asn Glu Asn
    1400                1405                1410

Ile His  Ser Ile His Phe Ser  Gly His Val Phe Thr  Val Arg Lys
    1415                1420                1425

Lys Glu  Glu Tyr Lys Met Ala  Leu Tyr Asn Leu Tyr  Pro Gly Val
    1430                1435                1440

Phe Glu  Thr Val Glu Met Leu  Pro Ser Lys Ala Gly  Ile Trp Arg
    1445                1450                1455

Val Glu  Cys Leu Ile Gly Glu  His Leu His Ala Gly  Met Ser Thr
    1460                1465                1470

Leu Phe  Leu Val Tyr Ser Asn  Lys Cys Gln Thr Pro  Leu Gly Met
    1475                1480                1485

Ala Ser  Gly His Ile Arg Asp  Phe Gln Ile Thr Ala  Ser Gly Gln
    1490                1495                1500

Tyr Gly  Gln Trp Ala Pro Lys  Leu Ala Arg Leu His  Tyr Ser Gly
    1505                1510                1515

Ser Ile  Asn Ala Trp Ser Thr  Lys Glu Pro Phe Ser  Trp Ile Lys
    1520                1525                1530

Val Asp  Leu Leu Ala Pro Met  Ile Ile His Gly Ile  Lys Thr Gln
    1535                1540                1545

Gly Ala  Arg Gln Lys Phe Ser  Ser Leu Tyr Ile Ser  Gln Phe Ile
    1550                1555                1560

Ile Met  Tyr Ser Leu Asp Gly  Lys Lys Trp Gln Thr  Tyr Arg Gly
    1565                1570                1575
```

```
Asn Ser  Thr Gly Thr Leu Met  Val Phe Phe Gly Asn  Val Asp Ser
    1580                1585                1590

Ser Gly  Ile Lys His Asn Ile  Phe Asn Pro Pro Ile  Ile Ala Arg
    1595                1600                1605

Tyr Ile  Arg Leu His Pro Thr  His Tyr Ser Ile Arg  Ser Thr Leu
    1610                1615                1620

Arg Met  Glu Leu Met Gly Cys  Asp Leu Asn Ser Cys  Ser Met Pro
    1625                1630                1635

Leu Gly  Met Glu Ser Lys Ala  Ile Ser Asp Ala Gln  Ile Thr Ala
    1640                1645                1650

Ser Ser  Tyr Phe Thr Asn Met  Phe Ala Thr Trp Ser  Pro Ser Lys
    1655                1660                1665

Ala Arg  Leu His Leu Gln Gly  Arg Ser Asn Ala Trp  Arg Pro Gln
    1670                1675                1680

Val Asn  Asn Pro Lys Glu Trp  Leu Gln Val Asp Phe  Gln Lys Thr
    1685                1690                1695

Met Lys  Val Thr Gly Val Thr  Thr Gln Gly Val Lys  Ser Leu Leu
    1700                1705                1710

Thr Ser  Met Tyr Val Lys Glu  Phe Leu Ile Ser Ser  Ser Gln Asp
    1715                1720                1725

Gly His  Gln Trp Thr Leu Phe  Phe Gln Asn Gly Lys  Val Lys Val
    1730                1735                1740

Phe Gln  Gly Asn Gln Asp Ser  Phe Thr Pro Val Val  Asn Ser Leu
    1745                1750                1755

Asp Pro  Pro Leu Leu Thr Arg  Tyr Leu Arg Ile His  Pro Gln Ser
    1760                1765                1770

Trp Val  His Gln Ile Ala Leu  Arg Met Glu Val Leu  Gly Cys Glu
```

```
    1775                1780                1785

Ala Gln  Asp Leu Tyr Asp Lys  Thr His Thr Cys Pro  Pro Cys Pro
    1790                1795                1800

Ala Pro  Glu Leu Leu Gly Gly  Pro Ser Val Phe Leu  Phe Pro Pro
    1805                1810                1815

Lys Pro  Lys Asp Thr Leu Met  Ile Ser Arg Thr Pro  Glu Val Thr
    1820                1825                1830

Cys Val  Val Val Asp Val Ser  His Glu Asp Pro Glu  Val Lys Phe
    1835                1840                1845

Asn Trp  Tyr Val Asp Gly Val  Glu Val His Asn Ala  Lys Thr Lys
    1850                1855                1860

Pro Arg  Glu Glu Gln Tyr Asn  Ser Thr Tyr Arg Val  Val Ser Val
    1865                1870                1875

Leu Thr  Val Leu His Gln Asp  Trp Leu Asn Gly Lys  Glu Tyr Lys
    1880                1885                1890

Cys Lys  Val Ser Asn Lys Ala  Leu Pro Ala Pro Ile  Glu Lys Thr
    1895                1900                1905

Ile Ser  Lys Ala Lys Gly Gln  Pro Arg Glu Pro Gln  Val Tyr Thr
    1910                1915                1920

Leu Pro  Pro Ser Arg Asp Glu  Leu Thr Lys Asn Gln  Val Ser Leu
    1925                1930                1935

Thr Cys  Leu Val Lys Gly Phe  Tyr Pro Ser Asp Ile  Ala Val Glu
    1940                1945                1950

Trp Glu  Ser Asn Gly Gln Pro  Glu Asn Asn Tyr Lys  Thr Thr Pro
    1955                1960                1965

Pro Val  Leu Asp Ser Asp Gly  Ser Phe Phe Leu Tyr  Ser Lys Leu
    1970                1975                1980
```

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
1985 1990 1995

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
2000 2005 2010

Leu Ser Leu Ser Pro Gly Lys
2015 2020

<210> 81
<211> 2056
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN FVIII 267 (FVIII Fc with 72 AE-XTEN at amino acid 18 and 288 AE XTEN in B-domain)

<400> 81

Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
1 5 10 15

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

Trp Asp Tyr Met Gln Gly Ala Pro Thr Ser Glu Ser Ala Thr Pro Glu
35 40 45

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
50 55 60

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
65 70 75 80

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
85 90 95

Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
100 105 110

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

```
Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys
    130                 135                 140

Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys
145                 150                 155                 160

Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu
                165                 170                 175

Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro
            180                 185                 190

Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly
        195                 200                 205

Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys
    210                 215                 220

Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu
225                 230                 235                 240

Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu
                245                 250                 255

Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala
            260                 265                 270

Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr Gln Thr
        275                 280                 285

Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser
    290                 295                 300

Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala
305                 310                 315                 320

Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn
                325                 330                 335

Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp
            340                 345                 350
```

```
His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu
        355                 360                 365

Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu
    370                 375                 380

Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu
385                 390                 395                 400

Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly
                405                 410                 415

Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu
            420                 425                 430

Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr
        435                 440                 445

Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro Ser
    450                 455                 460

Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val
465                 470                 475                 480

His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val
                485                 490                 495

Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly
            500                 505                 510

Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr
        515                 520                 525

Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly
    530                 535                 540

Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile
545                 550                 555                 560

Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly
                565                 570                 575
```

```
Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys Gly Val
            580                 585                 590

Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr
        595                 600                 605

Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg
    610                 615                 620

Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu
625                 630                 635                 640

Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val
                645                 650                 655

Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu
            660                 665                 670

Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile
        675                 680                 685

Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu
    690                 695                 700

Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp
705                 710                 715                 720

Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile
                725                 730                 735

Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly
            740                 745                 750

Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe
        755                 760                 765

Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu
    770                 775                 780

Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr
```

785 790 795 800

Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr
805 810 815

Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn
820 825 830

Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Gly Ala Pro Gly Thr Ser
835 840 845

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
850 855 860

Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
865 870 875 880

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser
885 890 895

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser
900 905 910

Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu
915 920 925

Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu
930 935 940

Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr
945 950 955 960

Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu
965 970 975

Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser
980 985 990

Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr
995 1000 1005

```
Pro Glu  Ser Gly Pro Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser
    1010                1015                1020

Gly Pro  Gly Thr Ser Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly
    1025                1030                1035

Ser Glu  Pro Ala Thr Ser Gly  Ser Glu Thr Pro Gly  Ser Glu Pro
    1040                1045                1050

Ala Thr  Ser Gly Ser Glu Thr  Pro Gly Ser Pro Ala  Gly Ser Pro
    1055                1060                1065

Thr Ser  Thr Glu Glu Gly Thr  Ser Thr Glu Pro Ser  Glu Gly Ser
    1070                1075                1080

Ala Pro  Gly Thr Ser Thr Glu  Pro Ser Glu Gly Ser  Ala Pro Gly
    1085                1090                1095

Ser Glu  Pro Ala Thr Ser Gly  Ser Glu Thr Pro Gly  Thr Ser Glu
    1100                1105                1110

Ser Ala  Thr Pro Glu Ser Gly  Pro Gly Thr Ser Thr  Glu Pro Ser
    1115                1120                1125

Glu Gly  Ser Ala Pro Ala Ser  Ser Pro Pro Val Leu  Lys Arg His
    1130                1135                1140

Gln Ala  Glu Ile Thr Arg Thr  Thr Leu Gln Ser Asp  Gln Glu Glu
    1145                1150                1155

Ile Asp  Tyr Asp Asp Thr Ile  Ser Val Glu Met Lys  Lys Glu Asp
    1160                1165                1170

Phe Asp  Ile Tyr Asp Glu Asp  Glu Asn Gln Ser Pro  Arg Ser Phe
    1175                1180                1185

Gln Lys  Lys Thr Arg His Tyr  Phe Ile Ala Ala Val  Glu Arg Leu
    1190                1195                1200

Trp Asp  Tyr Gly Met Ser Ser  Ser Pro His Val Leu  Arg Asn Arg
    1205                1210                1215
```

```
Ala Gln  Ser Gly Ser Val Pro  Gln Phe Lys Lys Val  Val Phe Gln
    1220                 1225                 1230

Glu Phe  Thr Asp Gly Ser Phe  Thr Gln Pro Leu Tyr  Arg Gly Glu
    1235                 1240                 1245

Leu Asn  Glu His Leu Gly Leu  Leu Gly Pro Tyr Ile  Arg Ala Glu
    1250                 1255                 1260

Val Glu  Asp Asn Ile Met Val  Thr Phe Arg Asn Gln  Ala Ser Arg
    1265                 1270                 1275

Pro Tyr  Ser Phe Tyr Ser Ser  Leu Ile Ser Tyr Glu  Glu Asp Gln
    1280                 1285                 1290

Arg Gln  Gly Ala Glu Pro Arg  Lys Asn Phe Val Lys  Pro Asn Glu
    1295                 1300                 1305

Thr Lys  Thr Tyr Phe Trp Lys  Val Gln His His Met  Ala Pro Thr
    1310                 1315                 1320

Lys Asp  Glu Phe Asp Cys Lys  Ala Trp Ala Tyr Phe  Ser Asp Val
    1325                 1330                 1335

Asp Leu  Glu Lys Asp Val His  Ser Gly Leu Ile Gly  Pro Leu Leu
    1340                 1345                 1350

Val Cys  His Thr Asn Thr Leu  Asn Pro Ala His Gly  Arg Gln Val
    1355                 1360                 1365

Thr Val  Gln Glu Phe Ala Leu  Phe Phe Thr Ile Phe  Asp Glu Thr
    1370                 1375                 1380

Lys Ser  Trp Tyr Phe Thr Glu  Asn Met Glu Arg Asn  Cys Arg Ala
    1385                 1390                 1395

Pro Cys  Asn Ile Gln Met Glu  Asp Pro Thr Phe Lys  Glu Asn Tyr
    1400                 1405                 1410

Arg Phe  His Ala Ile Asn Gly  Tyr Ile Met Asp Thr  Leu Pro Gly
    1415                 1420                 1425
```

```
Leu Val  Met Ala Gln Asp Gln  Arg Ile Arg Trp Tyr  Leu Leu Ser
    1430                1435                1440

Met Gly  Ser Asn Glu Asn Ile  His Ser Ile His Phe  Ser Gly His
    1445                1450                1455

Val Phe  Thr Val Arg Lys Lys  Glu Glu Tyr Lys Met  Ala Leu Tyr
    1460                1465                1470

Asn Leu  Tyr Pro Gly Val Phe  Glu Thr Val Glu Met  Leu Pro Ser
    1475                1480                1485

Lys Ala  Gly Ile Trp Arg Val  Glu Cys Leu Ile Gly  Glu His Leu
    1490                1495                1500

His Ala  Gly Met Ser Thr Leu  Phe Leu Val Tyr Ser  Asn Lys Cys
    1505                1510                1515

Gln Thr  Pro Leu Gly Met Ala  Ser Gly His Ile Arg  Asp Phe Gln
    1520                1525                1530

Ile Thr  Ala Ser Gly Gln Tyr  Gly Gln Trp Ala Pro  Lys Leu Ala
    1535                1540                1545

Arg Leu  His Tyr Ser Gly Ser  Ile Asn Ala Trp Ser  Thr Lys Glu
    1550                1555                1560

Pro Phe  Ser Trp Ile Lys Val  Asp Leu Leu Ala Pro  Met Ile Ile
    1565                1570                1575

His Gly  Ile Lys Thr Gln Gly  Ala Arg Gln Lys Phe  Ser Ser Leu
    1580                1585                1590

Tyr Ile  Ser Gln Phe Ile Ile  Met Tyr Ser Leu Asp  Gly Lys Lys
    1595                1600                1605

Trp Gln  Thr Tyr Arg Gly Asn  Ser Thr Gly Thr Leu  Met Val Phe
    1610                1615                1620

Phe Gly  Asn Val Asp Ser Ser  Gly Ile Lys His Asn  Ile Phe Asn
```

```
    1625                1630                1635

Pro Pro  Ile Ile Ala Arg Tyr  Ile Arg Leu His Pro  Thr His Tyr
    1640                1645                1650

Ser Ile  Arg Ser Thr Leu Arg  Met Glu Leu Met Gly  Cys Asp Leu
    1655                1660                1665

Asn Ser  Cys Ser Met Pro Leu  Gly Met Glu Ser Lys  Ala Ile Ser
    1670                1675                1680

Asp Ala  Gln Ile Thr Ala Ser  Ser Tyr Phe Thr Asn  Met Phe Ala
    1685                1690                1695

Thr Trp  Ser Pro Ser Lys Ala  Arg Leu His Leu Gln  Gly Arg Ser
    1700                1705                1710

Asn Ala  Trp Arg Pro Gln Val  Asn Asn Pro Lys Glu  Trp Leu Gln
    1715                1720                1725

Val Asp  Phe Gln Lys Thr Met  Lys Val Thr Gly Val  Thr Thr Gln
    1730                1735                1740

Gly Val  Lys Ser Leu Leu Thr  Ser Met Tyr Val Lys  Glu Phe Leu
    1745                1750                1755

Ile Ser  Ser Ser Gln Asp Gly  His Gln Trp Thr Leu  Phe Phe Gln
    1760                1765                1770

Asn Gly  Lys Val Lys Val Phe  Gln Gly Asn Gln Asp  Ser Phe Thr
    1775                1780                1785

Pro Val  Val Asn Ser Leu Asp  Pro Pro Leu Leu Thr  Arg Tyr Leu
    1790                1795                1800

Arg Ile  His Pro Gln Ser Trp  Val His Gln Ile Ala  Leu Arg Met
    1805                1810                1815

Glu Val  Leu Gly Cys Glu Ala  Gln Asp Leu Tyr Asp  Lys Thr His
    1820                1825                1830
```

```
Thr Cys  Pro Pro Cys Pro Ala  Pro Glu Leu Leu Gly  Gly Pro Ser
    1835                 1840                 1845

Val Phe  Leu Phe Pro Pro Lys  Pro Lys Asp Thr Leu  Met Ile Ser
    1850                 1855                 1860

Arg Thr  Pro Glu Val Thr Cys  Val Val Val Asp Val  Ser His Glu
    1865                 1870                 1875

Asp Pro  Glu Val Lys Phe Asn  Trp Tyr Val Asp Gly  Val Glu Val
    1880                 1885                 1890

His Asn  Ala Lys Thr Lys Pro  Arg Glu Glu Gln Tyr  Asn Ser Thr
    1895                 1900                 1905

Tyr Arg  Val Val Ser Val Leu  Thr Val Leu His Gln  Asp Trp Leu
    1910                 1915                 1920

Asn Gly  Lys Glu Tyr Lys Cys  Lys Val Ser Asn Lys  Ala Leu Pro
    1925                 1930                 1935

Ala Pro  Ile Glu Lys Thr Ile  Ser Lys Ala Lys Gly  Gln Pro Arg
    1940                 1945                 1950

Glu Pro  Gln Val Tyr Thr Leu  Pro Pro Ser Arg Asp  Glu Leu Thr
    1955                 1960                 1965

Lys Asn  Gln Val Ser Leu Thr  Cys Leu Val Lys Gly  Phe Tyr Pro
    1970                 1975                 1980

Ser Asp  Ile Ala Val Glu Trp  Glu Ser Asn Gly Gln  Pro Glu Asn
    1985                 1990                 1995

Asn Tyr  Lys Thr Thr Pro Pro  Val Leu Asp Ser Asp  Gly Ser Phe
    2000                 2005                 2010

Phe Leu  Tyr Ser Lys Leu Thr  Val Asp Lys Ser Arg  Trp Gln Gln
    2015                 2020                 2025

Gly Asn  Val Phe Ser Cys Ser  Val Met His Glu Ala  Leu His Asn
    2030                 2035                 2040
```

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    2045   2050   2055

<210> 82
<211> 1834
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN FVIII 268 (FVIII Fc with 144 AE-XTEN at amino acid 18)

<400> 82

Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
1   5   10   15

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

Trp Asp Tyr Met Gln Gly Ala Pro Thr Ser Glu Ser Ala Thr Pro Glu
        35   40   45

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
    50   55   60

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
65   70   75   80

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
                85   90   95

Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
            100   105   110

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser
        115   120   125

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
    130   135   140

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
145   150   155   160

```
Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly
                165                 170                 175

Ser Pro Thr Ser Thr Glu Glu Gly Ala Ser Ser Ser Asp Leu Gly Glu
            180                 185                 190

Leu Pro Val Asp Ala Arg Phe Pro Pro Arg Val Pro Lys Ser Phe Pro
        195                 200                 205

Phe Asn Thr Ser Val Val Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr
    210                 215                 220

Asp His Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu
225                 230                 235                 240

Leu Gly Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr Val Val Ile Thr
                245                 250                 255

Leu Lys Asn Met Ala Ser His Pro Val Ser Leu His Ala Val Gly Val
            260                 265                 270

Ser Tyr Trp Lys Ala Ser Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser
        275                 280                 285

Gln Arg Glu Lys Glu Asp Asp Lys Val Phe Pro Gly Gly Ser His Thr
    290                 295                 300

Tyr Val Trp Gln Val Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro
305                 310                 315                 320

Leu Cys Leu Thr Tyr Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp
                325                 330                 335

Leu Asn Ser Gly Leu Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser
            340                 345                 350

Leu Ala Lys Glu Lys Thr Gln Thr Leu His Lys Phe Ile Leu Leu Phe
        355                 360                 365

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

```
Leu Met Gln Asp Arg Asp Ala Ala Ser Ala Arg Ala Trp Pro Lys Met
385                 390                 395                 400

His Thr Val Asn Gly Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly
                405                 410                 415

Cys His Arg Lys Ser Val Tyr Trp His Val Ile Gly Met Gly Thr Thr
            420                 425                 430

Pro Glu Val His Ser Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg
        435                 440                 445

Asn His Arg Gln Ala Ser Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr
    450                 455                 460

Ala Gln Thr Leu Leu Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His
465                 470                 475                 480

Ile Ser Ser His Gln His Asp Gly Met Glu Ala Tyr Val Lys Val Asp
                485                 490                 495

Ser Cys Pro Glu Glu Pro Gln Leu Arg Met Lys Asn Asn Glu Glu Ala
            500                 505                 510

Glu Asp Tyr Asp Asp Asp Leu Thr Asp Ser Glu Met Asp Val Val Arg
        515                 520                 525

Phe Asp Asp Asp Asn Ser Pro Ser Phe Ile Gln Ile Arg Ser Val Ala
    530                 535                 540

Lys Lys His Pro Lys Thr Trp Val His Tyr Ile Ala Ala Glu Glu Glu
545                 550                 555                 560

Asp Trp Asp Tyr Ala Pro Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr
                565                 570                 575

Lys Ser Gln Tyr Leu Asn Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr
            580                 585                 590

Lys Lys Val Arg Phe Met Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg
        595                 600                 605
```

```
Glu Ala Ile Gln His Glu Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly
    610                 615                 620

Glu Val Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg
625                 630                 635                 640

Pro Tyr Asn Ile Tyr Pro His Gly Ile Thr Asp Val Arg Pro Leu Tyr
                645                 650                 655

Ser Arg Arg Leu Pro Lys Gly Val Lys His Leu Lys Asp Phe Pro Ile
            660                 665                 670

Leu Pro Gly Glu Ile Phe Lys Tyr Lys Trp Thr Val Thr Val Glu Asp
        675                 680                 685

Gly Pro Thr Lys Ser Asp Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser
    690                 695                 700

Phe Val Asn Met Glu Arg Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu
705                 710                 715                 720

Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly Asn Gln Ile Met
                725                 730                 735

Ser Asp Lys Arg Asn Val Ile Leu Phe Ser Val Phe Asp Glu Asn Arg
            740                 745                 750

Ser Trp Tyr Leu Thr Glu Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala
        755                 760                 765

Gly Val Gln Leu Glu Asp Pro Glu Phe Gln Ala Ser Asn Ile Met His
    770                 775                 780

Ser Ile Asn Gly Tyr Val Phe Asp Ser Leu Gln Leu Ser Val Cys Leu
785                 790                 795                 800

His Glu Val Ala Tyr Trp Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp
                805                 810                 815

Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys His Lys Met Val
```

```
            820                 825                 830

Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly Glu Thr Val Phe
        835                 840                 845

Met Ser Met Glu Asn Pro Gly Leu Trp Ile Leu Gly Cys His Asn Ser
    850                 855                 860

Asp Phe Arg Asn Arg Gly Met Thr Ala Leu Leu Lys Val Ser Ser Cys
865                 870                 875                 880

Asp Lys Asn Thr Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser
                885                 890                 895

Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
            900                 905                 910

Gln Asn Pro Pro Val Leu Lys Arg His Gln Ala Glu Ile Thr Arg Thr
        915                 920                 925

Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser
    930                 935                 940

Val Glu Met Lys Lys Glu Asp Phe Asp Ile Tyr Asp Glu Asp Glu Asn
945                 950                 955                 960

Gln Ser Pro Arg Ser Phe Gln Lys Lys Thr Arg His Tyr Phe Ile Ala
                965                 970                 975

Ala Val Glu Arg Leu Trp Asp Tyr Gly Met Ser Ser Ser Pro His Val
            980                 985                 990

Leu Arg Asn Arg Ala Gln Ser Gly  Ser Val Pro Gln Phe  Lys Lys Val
        995                 1000                1005

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

Arg Gly  Glu Leu Asn Glu His  Leu Gly Leu Leu Gly  Pro Tyr Ile
    1025                1030                1035
```

```
Arg Ala  Glu Val Glu Asp Asn  Ile Met Val Thr Phe  Arg Asn Gln
    1040                1045                1050

Ala Ser  Arg Pro Tyr Ser Phe  Tyr Ser Ser Leu Ile  Ser Tyr Glu
    1055                1060                1065

Glu Asp  Gln Arg Gln Gly Ala  Glu Pro Arg Lys Asn  Phe Val Lys
    1070                1075                1080

Pro Asn  Glu Thr Lys Thr Tyr  Phe Trp Lys Val Gln  His His Met
    1085                1090                1095

Ala Pro  Thr Lys Asp Glu Phe  Asp Cys Lys Ala Trp  Ala Tyr Phe
    1100                1105                1110

Ser Asp  Val Asp Leu Glu Lys  Asp Val His Ser Gly  Leu Ile Gly
    1115                1120                1125

Pro Leu  Leu Val Cys His Thr  Asn Thr Leu Asn Pro  Ala His Gly
    1130                1135                1140

Arg Gln  Val Thr Val Gln Glu  Phe Ala Leu Phe Phe  Thr Ile Phe
    1145                1150                1155

Asp Glu  Thr Lys Ser Trp Tyr  Phe Thr Glu Asn Met  Glu Arg Asn
    1160                1165                1170

Cys Arg  Ala Pro Cys Asn Ile  Gln Met Glu Asp Pro  Thr Phe Lys
    1175                1180                1185

Glu Asn  Tyr Arg Phe His Ala  Ile Asn Gly Tyr Ile  Met Asp Thr
    1190                1195                1200

Leu Pro  Gly Leu Val Met Ala  Gln Asp Gln Arg Ile  Arg Trp Tyr
    1205                1210                1215

Leu Leu  Ser Met Gly Ser Asn  Glu Asn Ile His Ser  Ile His Phe
    1220                1225                1230

Ser Gly  His Val Phe Thr Val  Arg Lys Lys Glu Glu  Tyr Lys Met
    1235                1240                1245
```

```
Ala Leu  Tyr Asn Leu Tyr Pro  Gly Val Phe Glu Thr  Val Glu Met
    1250                 1255                 1260

Leu Pro  Ser Lys Ala Gly Ile  Trp Arg Val Glu Cys  Leu Ile Gly
    1265                 1270                 1275

Glu His  Leu His Ala Gly Met  Ser Thr Leu Phe Leu  Val Tyr Ser
    1280                 1285                 1290

Asn Lys  Cys Gln Thr Pro Leu  Gly Met Ala Ser Gly  His Ile Arg
    1295                 1300                 1305

Asp Phe  Gln Ile Thr Ala Ser  Gly Gln Tyr Gly Gln  Trp Ala Pro
    1310                 1315                 1320

Lys Leu  Ala Arg Leu His Tyr  Ser Gly Ser Ile Asn  Ala Trp Ser
    1325                 1330                 1335

Thr Lys  Glu Pro Phe Ser Trp  Ile Lys Val Asp Leu  Leu Ala Pro
    1340                 1345                 1350

Met Ile  Ile His Gly Ile Lys  Thr Gln Gly Ala Arg  Gln Lys Phe
    1355                 1360                 1365

Ser Ser  Leu Tyr Ile Ser Gln  Phe Ile Ile Met Tyr  Ser Leu Asp
    1370                 1375                 1380

Gly Lys  Lys Trp Gln Thr Tyr  Arg Gly Asn Ser Thr  Gly Thr Leu
    1385                 1390                 1395

Met Val  Phe Phe Gly Asn Val  Asp Ser Ser Gly Ile  Lys His Asn
    1400                 1405                 1410

Ile Phe  Asn Pro Pro Ile Ile  Ala Arg Tyr Ile Arg  Leu His Pro
    1415                 1420                 1425

Thr His  Tyr Ser Ile Arg Ser  Thr Leu Arg Met Glu  Leu Met Gly
    1430                 1435                 1440

Cys Asp  Leu Asn Ser Cys Ser  Met Pro Leu Gly Met  Glu Ser Lys
    1445                 1450                 1455
```

```
Ala Ile  Ser Asp Ala Gln Ile  Thr Ala Ser Ser Tyr  Phe Thr Asn
    1460                1465                1470

Met Phe  Ala Thr Trp Ser Pro  Ser Lys Ala Arg Leu  His Leu Gln
    1475                1480                1485

Gly Arg  Ser Asn Ala Trp Arg  Pro Gln Val Asn Asn  Pro Lys Glu
    1490                1495                1500

Trp Leu  Gln Val Asp Phe Gln  Lys Thr Met Lys Val  Thr Gly Val
    1505                1510                1515

Thr Thr  Gln Gly Val Lys Ser  Leu Leu Thr Ser Met  Tyr Val Lys
    1520                1525                1530

Glu Phe  Leu Ile Ser Ser Ser  Gln Asp Gly His Gln  Trp Thr Leu
    1535                1540                1545

Phe Phe  Gln Asn Gly Lys Val  Lys Val Phe Gln Gly  Asn Gln Asp
    1550                1555                1560

Ser Phe  Thr Pro Val Val Asn  Ser Leu Asp Pro Pro  Leu Leu Thr
    1565                1570                1575

Arg Tyr  Leu Arg Ile His Pro  Gln Ser Trp Val His  Gln Ile Ala
    1580                1585                1590

Leu Arg  Met Glu Val Leu Gly  Cys Glu Ala Gln Asp  Leu Tyr Asp
    1595                1600                1605

Lys Thr  His Thr Cys Pro Pro  Cys Pro Ala Pro Glu  Leu Leu Gly
    1610                1615                1620

Gly Pro  Ser Val Phe Leu Phe  Pro Pro Lys Pro Lys  Asp Thr Leu
    1625                1630                1635

Met Ile  Ser Arg Thr Pro Glu  Val Thr Cys Val Val  Val Asp Val
    1640                1645                1650

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

1655 1660 1665

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
1670 1675 1680

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
1685 1690 1695

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
1700 1705 1710

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
1715 1720 1725

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp
1730 1735 1740

Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
1745 1750 1755

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
1760 1765 1770

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
1775 1780 1785

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
1790 1795 1800

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
1805 1810 1815

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
1820 1825 1830

Lys

<210> 83
<211> 1762
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN FVIII 269 (FVIII Fc with 72 AE-XTEN at amino acid 18)

<400> 83

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Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
1               5                   10                  15


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


Trp Asp Tyr Met Gln Gly Ala Pro Thr Ser Glu Ser Ala Thr Pro Glu
        35                  40                  45


Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
    50                  55                  60


Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
65                  70                  75                  80


Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
                85                  90                  95


Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
            100                 105                 110


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


Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys
    130                 135                 140


Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys
145                 150                 155                 160


Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu
                165                 170                 175


Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro
            180                 185                 190


Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly
```

```
        195                 200                 205

Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys
    210                 215                 220

Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu
225                 230                 235                 240

Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu
                245                 250                 255

Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala
            260                 265                 270

Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr Gln Thr
        275                 280                 285

Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser
    290                 295                 300

Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala
305                 310                 315                 320

Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn
                325                 330                 335

Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp
            340                 345                 350

His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu
        355                 360                 365

Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu
    370                 375                 380

Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu
385                 390                 395                 400

Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly
                405                 410                 415
```

```
Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu
            420                 425                 430

Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr
        435                 440                 445

Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro Ser
    450                 455                 460

Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val
465                 470                 475                 480

His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val
                485                 490                 495

Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly
            500                 505                 510

Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr
        515                 520                 525

Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly
    530                 535                 540

Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile
545                 550                 555                 560

Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly
                565                 570                 575

Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys Gly Val
            580                 585                 590

Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr
        595                 600                 605

Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg
    610                 615                 620

Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu
625                 630                 635                 640
```

```
Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val
                645                 650                 655

Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu
            660                 665                 670

Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile
        675                 680                 685

Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu
    690                 695                 700

Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp
705                 710                 715                 720

Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile
                725                 730                 735

Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly
            740                 745                 750

Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe
        755                 760                 765

Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu
    770                 775                 780

Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr
785                 790                 795                 800

Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr
                805                 810                 815

Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn
            820                 825                 830

Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Pro Pro Val Leu Lys Arg
        835                 840                 845

His Gln Ala Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu
    850                 855                 860
```

```
Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe
865                 870                 875                 880


Asp Ile Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe Gln Lys
                885                 890                 895


Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr
            900                 905                 910


Gly Met Ser Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser Gly
        915                 920                 925


Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly
    930                 935                 940


Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly
945                 950                 955                 960


Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val
                965                 970                 975


Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu
            980                 985                 990


Ile Ser Tyr Glu Glu Asp Gln Arg  Gln Gly Ala Glu Pro  Arg Lys Asn
        995                 1000                1005


Phe Val  Lys Pro Asn Glu Thr  Lys Thr Tyr Phe Trp  Lys Val Gln
    1010                1015                1020


His His  Met Ala Pro Thr Lys  Asp Glu Phe Asp Cys  Lys Ala Trp
    1025                1030                1035


Ala Tyr  Phe Ser Asp Val Asp  Leu Glu Lys Asp Val  His Ser Gly
    1040                1045                1050


Leu Ile  Gly Pro Leu Leu Val  Cys His Thr Asn Thr  Leu Asn Pro
    1055                1060                1065


Ala His  Gly Arg Gln Val Thr  Val Gln Glu Phe Ala  Leu Phe Phe
```

```
    1070                1075                1080

Thr Ile  Phe Asp Glu Thr Lys  Ser Trp Tyr Phe Thr  Glu Asn Met
    1085                1090                1095

Glu Arg  Asn Cys Arg Ala Pro  Cys Asn Ile Gln Met  Glu Asp Pro
    1100                1105                1110

Thr Phe  Lys Glu Asn Tyr Arg  Phe His Ala Ile Asn  Gly Tyr Ile
    1115                1120                1125

Met Asp  Thr Leu Pro Gly Leu  Val Met Ala Gln Asp  Gln Arg Ile
    1130                1135                1140

Arg Trp  Tyr Leu Leu Ser Met  Gly Ser Asn Glu Asn  Ile His Ser
    1145                1150                1155

Ile His  Phe Ser Gly His Val  Phe Thr Val Arg Lys  Lys Glu Glu
    1160                1165                1170

Tyr Lys  Met Ala Leu Tyr Asn  Leu Tyr Pro Gly Val  Phe Glu Thr
    1175                1180                1185

Val Glu  Met Leu Pro Ser Lys  Ala Gly Ile Trp Arg  Val Glu Cys
    1190                1195                1200

Leu Ile  Gly Glu His Leu His  Ala Gly Met Ser Thr  Leu Phe Leu
    1205                1210                1215

Val Tyr  Ser Asn Lys Cys Gln  Thr Pro Leu Gly Met  Ala Ser Gly
    1220                1225                1230

His Ile  Arg Asp Phe Gln Ile  Thr Ala Ser Gly Gln  Tyr Gly Gln
    1235                1240                1245

Trp Ala  Pro Lys Leu Ala Arg  Leu His Tyr Ser Gly  Ser Ile Asn
    1250                1255                1260

Ala Trp  Ser Thr Lys Glu Pro  Phe Ser Trp Ile Lys  Val Asp Leu
    1265                1270                1275
```

```
Leu Ala  Pro Met Ile Ile His  Gly Ile Lys Thr Gln  Gly Ala Arg
    1280                1285                1290

Gln Lys  Phe Ser Ser Leu Tyr  Ile Ser Gln Phe Ile  Ile Met Tyr
    1295                1300                1305

Ser Leu  Asp Gly Lys Lys Trp  Gln Thr Tyr Arg Gly  Asn Ser Thr
    1310                1315                1320

Gly Thr  Leu Met Val Phe Phe  Gly Asn Val Asp Ser  Ser Gly Ile
    1325                1330                1335

Lys His  Asn Ile Phe Asn Pro  Pro Ile Ile Ala Arg  Tyr Ile Arg
    1340                1345                1350

Leu His  Pro Thr His Tyr Ser  Ile Arg Ser Thr Leu  Arg Met Glu
    1355                1360                1365

Leu Met  Gly Cys Asp Leu Asn  Ser Cys Ser Met Pro  Leu Gly Met
    1370                1375                1380

Glu Ser  Lys Ala Ile Ser Asp  Ala Gln Ile Thr Ala  Ser Ser Tyr
    1385                1390                1395

Phe Thr  Asn Met Phe Ala Thr  Trp Ser Pro Ser Lys  Ala Arg Leu
    1400                1405                1410

His Leu  Gln Gly Arg Ser Asn  Ala Trp Arg Pro Gln  Val Asn Asn
    1415                1420                1425

Pro Lys  Glu Trp Leu Gln Val  Asp Phe Gln Lys Thr  Met Lys Val
    1430                1435                1440

Thr Gly  Val Thr Thr Gln Gly  Val Lys Ser Leu Leu  Thr Ser Met
    1445                1450                1455

Tyr Val  Lys Glu Phe Leu Ile  Ser Ser Ser Gln Asp  Gly His Gln
    1460                1465                1470

Trp Thr  Leu Phe Phe Gln Asn  Gly Lys Val Lys Val  Phe Gln Gly
    1475                1480                1485
```

```
Asn Gln  Asp Ser Phe Thr Pro  Val Val Asn Ser Leu  Asp Pro Pro
    1490                 1495                 1500

Leu Leu  Thr Arg Tyr Leu Arg  Ile His Pro Gln Ser  Trp Val His
    1505                 1510                 1515

Gln Ile  Ala Leu Arg Met Glu  Val Leu Gly Cys Glu  Ala Gln Asp
    1520                 1525                 1530

Leu Tyr  Asp Lys Thr His Thr  Cys Pro Pro Cys Pro  Ala Pro Glu
    1535                 1540                 1545

Leu Leu  Gly Gly Pro Ser Val  Phe Leu Phe Pro Pro  Lys Pro Lys
    1550                 1555                 1560

Asp Thr  Leu Met Ile Ser Arg  Thr Pro Glu Val Thr  Cys Val Val
    1565                 1570                 1575

Val Asp  Val Ser His Glu Asp  Pro Glu Val Lys Phe  Asn Trp Tyr
    1580                 1585                 1590

Val Asp  Gly Val Glu Val His  Asn Ala Lys Thr Lys  Pro Arg Glu
    1595                 1600                 1605

Glu Gln  Tyr Asn Ser Thr Tyr  Arg Val Val Ser Val  Leu Thr Val
    1610                 1615                 1620

Leu His  Gln Asp Trp Leu Asn  Gly Lys Glu Tyr Lys  Cys Lys Val
    1625                 1630                 1635

Ser Asn  Lys Ala Leu Pro Ala  Pro Ile Glu Lys Thr  Ile Ser Lys
    1640                 1645                 1650

Ala Lys  Gly Gln Pro Arg Glu  Pro Gln Val Tyr Thr  Leu Pro Pro
    1655                 1660                 1665

Ser Arg  Asp Glu Leu Thr Lys  Asn Gln Val Ser Leu  Thr Cys Leu
    1670                 1675                 1680

Val Lys  Gly Phe Tyr Pro Ser  Asp Ile Ala Val Glu  Trp Glu Ser
    1685                 1690                 1695
```

```
Asn Gly  Gln Pro Glu Asn Asn  Tyr Lys Thr Thr Pro  Pro Val Leu
    1700                1705                1710


Asp Ser  Asp Gly Ser Phe Phe  Leu Tyr Ser Lys Leu  Thr Val Asp
    1715                1720                1725


Lys Ser  Arg Trp Gln Gln Gly  Asn Val Phe Ser Cys  Ser Val Met
    1730                1735                1740


His Glu  Ala Leu His Asn His  Tyr Thr Gln Lys Ser  Leu Ser Leu
    1745                1750                1755


Ser Pro  Gly Lys
    1760
```

<210> 84
<211> 1726
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYNFVIII 271 (FVIII Fc with 42 AE-XTEN at amino acid 18)

<400> 84

```
Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
1               5                   10                  15


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


Trp Asp Tyr Met Gln Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr
        35                  40                  45


Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
    50                  55                  60


Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Ser
65                  70                  75                  80


Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro Arg Val Pro
                85                  90                  95
```

```
Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys Thr Leu Phe
            100                 105                 110

Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro
        115                 120                 125

Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr
    130                 135                 140

Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val Ser Leu His
145                 150                 155                 160

Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala Glu Tyr Asp
                165                 170                 175

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

Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn Gly Pro Met
        195                 200                 205

Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser His Val Asp
    210                 215                 220

Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu Leu Val Cys
225                 230                 235                 240

Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr Gln Thr Leu His Lys Phe
                245                 250                 255

Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp His Ser Glu
            260                 265                 270

Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser Ala Arg Ala
        275                 280                 285

Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg Ser Leu Pro
    290                 295                 300

Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His Val Ile Gly
305                 310                 315                 320
```

```
Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu Gly His Thr
                325                 330                 335

Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile Ser Pro Ile
            340                 345                 350

Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly Gln Phe Leu
        355                 360                 365

Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met Glu Ala Tyr
    370                 375                 380

Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg Met Lys Asn
385                 390                 395                 400

Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp Ser Glu Met
                405                 410                 415

Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro Ser Phe Ile Gln Ile
            420                 425                 430

Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His Tyr Ile Ala
        435                 440                 445

Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu Ala Pro Asp
    450                 455                 460

Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro Gln Arg Ile
465                 470                 475                 480

Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr Asp Glu Thr
                485                 490                 495

Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile Leu Gly Pro
            500                 505                 510

Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn
        515                 520                 525

Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile Thr Asp Val
```

```
    530                 535                 540

Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys Gly Val Lys His Leu Lys
545                 550                 555                 560

Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys Trp Thr Val
                565                 570                 575

Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys Leu Thr Arg
            580                 585                 590

Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala Ser Gly Leu
        595                 600                 605

Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly
    610                 615                 620

Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe Ser Val Phe
625                 630                 635                 640

Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln Arg Phe Leu
                645                 650                 655

Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe Gln Ala Ser
            660                 665                 670

Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser Leu Gln Leu
        675                 680                 685

Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu Ser Ile Gly
    690                 695                 700

Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys
705                 710                 715                 720

His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly
                725                 730                 735

Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp Ile Leu Gly
            740                 745                 750
```

```
Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr Ala Leu Leu Lys
        755                 760                 765

Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu Asp Ser Tyr
    770                 775                 780

Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro
785                 790                 795                 800

Arg Ser Phe Ser Gln Asn Pro Pro Val Leu Lys Arg His Gln Ala Glu
                805                 810                 815

Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr Asp
            820                 825                 830

Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe Asp Ile Tyr Asp
        835                 840                 845

Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe Gln Lys Lys Thr Arg His
    850                 855                 860

Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr Gly Met Ser Ser
865                 870                 875                 880

Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser Gly Ser Val Pro Gln
                885                 890                 895

Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly Ser Phe Thr Gln
            900                 905                 910

Pro Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly Leu Leu Gly Pro
        915                 920                 925

Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Arg Asn
    930                 935                 940

Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Glu
945                 950                 955                 960

Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg Lys Asn Phe Val Lys Pro
                965                 970                 975
```

```
Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro
            980                 985                 990

Thr Lys Asp Glu Phe Asp Cys Lys  Ala Trp Ala Tyr Phe  Ser Asp Val
        995                 1000                1005

Asp Leu  Glu Lys Asp Val His  Ser Gly Leu Ile Gly  Pro Leu Leu
    1010                1015                1020

Val Cys  His Thr Asn Thr Leu  Asn Pro Ala His Gly  Arg Gln Val
    1025                1030                1035

Thr Val  Gln Glu Phe Ala Leu  Phe Phe Thr Ile Phe  Asp Glu Thr
    1040                1045                1050

Lys Ser  Trp Tyr Phe Thr Glu  Asn Met Glu Arg Asn  Cys Arg Ala
    1055                1060                1065

Pro Cys  Asn Ile Gln Met Glu  Asp Pro Thr Phe Lys  Glu Asn Tyr
    1070                1075                1080

Arg Phe  His Ala Ile Asn Gly  Tyr Ile Met Asp Thr  Leu Pro Gly
    1085                1090                1095

Leu Val  Met Ala Gln Asp Gln  Arg Ile Arg Trp Tyr  Leu Leu Ser
    1100                1105                1110

Met Gly  Ser Asn Glu Asn Ile  His Ser Ile His Phe  Ser Gly His
    1115                1120                1125

Val Phe  Thr Val Arg Lys Lys  Glu Glu Tyr Lys Met  Ala Leu Tyr
    1130                1135                1140

Asn Leu  Tyr Pro Gly Val Phe  Glu Thr Val Glu Met  Leu Pro Ser
    1145                1150                1155

Lys Ala  Gly Ile Trp Arg Val  Glu Cys Leu Ile Gly  Glu His Leu
    1160                1165                1170

His Ala  Gly Met Ser Thr Leu  Phe Leu Val Tyr Ser  Asn Lys Cys
    1175                1180                1185
```

```
Gln Thr  Pro Leu Gly Met Ala  Ser Gly His Ile Arg  Asp Phe Gln
    1190                 1195                 1200

Ile Thr  Ala Ser Gly Gln Tyr  Gly Gln Trp Ala Pro  Lys Leu Ala
    1205                 1210                 1215

Arg Leu  His Tyr Ser Gly Ser  Ile Asn Ala Trp Ser  Thr Lys Glu
    1220                 1225                 1230

Pro Phe  Ser Trp Ile Lys Val  Asp Leu Leu Ala Pro  Met Ile Ile
    1235                 1240                 1245

His Gly  Ile Lys Thr Gln Gly  Ala Arg Gln Lys Phe  Ser Ser Leu
    1250                 1255                 1260

Tyr Ile  Ser Gln Phe Ile Ile  Met Tyr Ser Leu Asp  Gly Lys Lys
    1265                 1270                 1275

Trp Gln  Thr Tyr Arg Gly Asn  Ser Thr Gly Thr Leu  Met Val Phe
    1280                 1285                 1290

Phe Gly  Asn Val Asp Ser Ser  Gly Ile Lys His Asn  Ile Phe Asn
    1295                 1300                 1305

Pro Pro  Ile Ile Ala Arg Tyr  Ile Arg Leu His Pro  Thr His Tyr
    1310                 1315                 1320

Ser Ile  Arg Ser Thr Leu Arg  Met Glu Leu Met Gly  Cys Asp Leu
    1325                 1330                 1335

Asn Ser  Cys Ser Met Pro Leu  Gly Met Glu Ser Lys  Ala Ile Ser
    1340                 1345                 1350

Asp Ala  Gln Ile Thr Ala Ser  Ser Tyr Phe Thr Asn  Met Phe Ala
    1355                 1360                 1365

Thr Trp  Ser Pro Ser Lys Ala  Arg Leu His Leu Gln  Gly Arg Ser
    1370                 1375                 1380

Asn Ala  Trp Arg Pro Gln Val  Asn Asn Pro Lys Glu  Trp Leu Gln
```

```
    1385                1390                1395

Val Asp  Phe Gln Lys Thr Met  Lys Val Thr Gly Val  Thr Thr Gln
    1400                1405                1410

Gly Val  Lys Ser Leu Leu Thr  Ser Met Tyr Val Lys  Glu Phe Leu
    1415                1420                1425

Ile Ser  Ser Ser Gln Asp Gly  His Gln Trp Thr Leu  Phe Phe Gln
    1430                1435                1440

Asn Gly  Lys Val Lys Val Phe  Gln Gly Asn Gln Asp  Ser Phe Thr
    1445                1450                1455

Pro Val  Val Asn Ser Leu Asp  Pro Pro Leu Leu Thr  Arg Tyr Leu
    1460                1465                1470

Arg Ile  His Pro Gln Ser Trp  Val His Gln Ile Ala  Leu Arg Met
    1475                1480                1485

Glu Val  Leu Gly Cys Glu Ala  Gln Asp Leu Tyr Asp  Lys Thr His
    1490                1495                1500

Thr Cys  Pro Pro Cys Pro Ala  Pro Glu Leu Leu Gly  Gly Pro Ser
    1505                1510                1515

Val Phe  Leu Phe Pro Pro Lys  Pro Lys Asp Thr Leu  Met Ile Ser
    1520                1525                1530

Arg Thr  Pro Glu Val Thr Cys  Val Val Val Asp Val  Ser His Glu
    1535                1540                1545

Asp Pro  Glu Val Lys Phe Asn  Trp Tyr Val Asp Gly  Val Glu Val
    1550                1555                1560

His Asn  Ala Lys Thr Lys Pro  Arg Glu Glu Gln Tyr  Asn Ser Thr
    1565                1570                1575

Tyr Arg  Val Val Ser Val Leu  Thr Val Leu His Gln  Asp Trp Leu
    1580                1585                1590
```

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
    1595   1600   1605

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
    1610   1615   1620

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
    1625   1630   1635

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    1640   1645   1650

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
    1655   1660   1665

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
    1670   1675   1680

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
    1685   1690   1695

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
    1700   1705   1710

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    1715   1720   1725

<210> 85
<211> 1901
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN FVIII 272 (FVIII with 144 AE XTEN at amino acid 18 and 244
       AE XTEN in B-domain- no Fc)

<400> 85

Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
1   5   10   15

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

```
Trp Asp Tyr Met Gln Gly Ala Pro Thr Ser Glu Ser Ala Thr Pro Glu
        35                  40                  45

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
    50                  55                  60

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
65                  70                  75                  80

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
                85                  90                  95

Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
            100                 105                 110

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser
        115                 120                 125

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
    130                 135                 140

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
145                 150                 155                 160

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly
                165                 170                 175

Ser Pro Thr Ser Thr Glu Glu Gly Ala Ser Ser Ser Asp Leu Gly Glu
            180                 185                 190

Leu Pro Val Asp Ala Arg Phe Pro Pro Arg Val Pro Lys Ser Phe Pro
        195                 200                 205

Phe Asn Thr Ser Val Val Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr
    210                 215                 220

Asp His Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu
225                 230                 235                 240

Leu Gly Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr Val Val Ile Thr
                245                 250                 255
```

```
Leu Lys Asn Met Ala Ser His Pro Val Ser Leu His Ala Val Gly Val
            260                 265                 270

Ser Tyr Trp Lys Ala Ser Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser
        275                 280                 285

Gln Arg Glu Lys Glu Asp Asp Lys Val Phe Pro Gly Gly Ser His Thr
    290                 295                 300

Tyr Val Trp Gln Val Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro
305                 310                 315                 320

Leu Cys Leu Thr Tyr Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp
                325                 330                 335

Leu Asn Ser Gly Leu Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser
            340                 345                 350

Leu Ala Lys Glu Lys Thr Gln Thr Leu His Lys Phe Ile Leu Leu Phe
        355                 360                 365

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

Leu Met Gln Asp Arg Asp Ala Ala Ser Ala Arg Ala Trp Pro Lys Met
385                 390                 395                 400

His Thr Val Asn Gly Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly
                405                 410                 415

Cys His Arg Lys Ser Val Tyr Trp His Val Ile Gly Met Gly Thr Thr
            420                 425                 430

Pro Glu Val His Ser Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg
        435                 440                 445

Asn His Arg Gln Ala Ser Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr
    450                 455                 460

Ala Gln Thr Leu Leu Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His
465                 470                 475                 480
```

```
Ile Ser Ser His Gln His Asp Gly Met Glu Ala Tyr Val Lys Val Asp
                485                 490                 495

Ser Cys Pro Glu Glu Pro Gln Leu Arg Met Lys Asn Asn Glu Glu Ala
            500                 505                 510

Glu Asp Tyr Asp Asp Asp Leu Thr Asp Ser Glu Met Asp Val Val Arg
        515                 520                 525

Phe Asp Asp Asp Asn Ser Pro Ser Phe Ile Gln Ile Arg Ser Val Ala
    530                 535                 540

Lys Lys His Pro Lys Thr Trp Val His Tyr Ile Ala Ala Glu Glu Glu
545                 550                 555                 560

Asp Trp Asp Tyr Ala Pro Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr
                565                 570                 575

Lys Ser Gln Tyr Leu Asn Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr
            580                 585                 590

Lys Lys Val Arg Phe Met Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg
        595                 600                 605

Glu Ala Ile Gln His Glu Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly
    610                 615                 620

Glu Val Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg
625                 630                 635                 640

Pro Tyr Asn Ile Tyr Pro His Gly Ile Thr Asp Val Arg Pro Leu Tyr
                645                 650                 655

Ser Arg Arg Leu Pro Lys Gly Val Lys His Leu Lys Asp Phe Pro Ile
            660                 665                 670

Leu Pro Gly Glu Ile Phe Lys Tyr Lys Trp Thr Val Thr Val Glu Asp
        675                 680                 685

Gly Pro Thr Lys Ser Asp Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser
```

```
    690                 695                 700

Phe Val Asn Met Glu Arg Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu
705                 710                 715                 720

Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly Asn Gln Ile Met
                725                 730                 735

Ser Asp Lys Arg Asn Val Ile Leu Phe Ser Val Phe Asp Glu Asn Arg
            740                 745                 750

Ser Trp Tyr Leu Thr Glu Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala
        755                 760                 765

Gly Val Gln Leu Glu Asp Pro Glu Phe Gln Ala Ser Asn Ile Met His
    770                 775                 780

Ser Ile Asn Gly Tyr Val Phe Asp Ser Leu Gln Leu Ser Val Cys Leu
785                 790                 795                 800

His Glu Val Ala Tyr Trp Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp
                805                 810                 815

Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys His Lys Met Val
            820                 825                 830

Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly Glu Thr Val Phe
        835                 840                 845

Met Ser Met Glu Asn Pro Gly Leu Trp Ile Leu Gly Cys His Asn Ser
    850                 855                 860

Asp Phe Arg Asn Arg Gly Met Thr Ala Leu Leu Lys Val Ser Ser Cys
865                 870                 875                 880

Asp Lys Asn Thr Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser
                885                 890                 895

Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
            900                 905                 910
```

```
Gln Asn Gly Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
        915                 920                 925


Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser
    930                 935                 940


Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
945                 950                 955                 960


Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
                965                 970                 975


Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro
            980                 985                 990


Ala Gly Ser Pro Thr Ser Thr Glu  Glu Gly Thr Ser Glu  Ser Ala Thr
        995                 1000                1005


Pro Glu  Ser Gly Pro Gly Ser  Glu Pro Ala Thr Ser  Gly Ser Glu
    1010                1015                1020


Thr Pro  Gly Thr Ser Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly
    1025                1030                1035


Ser Pro  Ala Gly Ser Pro Thr  Ser Thr Glu Glu Gly  Ser Pro Ala
    1040                1045                1050


Gly Ser  Pro Thr Ser Thr Glu  Glu Gly Thr Ser Thr  Glu Pro Ser
    1055                1060                1065


Glu Gly  Ser Ala Pro Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser
    1070                1075                1080


Gly Pro  Gly Thr Ser Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly
    1085                1090                1095


Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly Pro Gly  Ser Glu Pro
    1100                1105                1110


Ala Thr  Ser Gly Ser Glu Thr  Pro Gly Ser Glu Pro  Ala Thr Ser
    1115                1120                1125
```

```
Gly Ser  Glu Thr Pro Gly Ser  Pro Ala Gly Ser Pro  Thr Ser Thr
    1130                1135                1140

Glu Glu  Gly Thr Ser Thr Glu  Pro Ser Glu Gly Ser  Ala Pro Gly
    1145                1150                1155

Thr Ser  Thr Glu Pro Ser Glu  Gly Ser Ala Pro Gly  Ser Glu Pro
    1160                1165                1170

Ala Thr  Ser Gly Ser Glu Thr  Pro Gly Thr Ser Glu  Ser Ala Thr
    1175                1180                1185

Pro Glu  Ser Gly Pro Gly Thr  Ser Thr Glu Pro Ser  Glu Gly Ser
    1190                1195                1200

Ala Pro  Ala Ser Ser Pro Pro  Val Leu Lys Arg His  Gln Ala Glu
    1205                1210                1215

Ile Thr  Arg Thr Thr Leu Gln  Ser Asp Gln Glu Glu  Ile Asp Tyr
    1220                1225                1230

Asp Asp  Thr Ile Ser Val Glu  Met Lys Lys Glu Asp  Phe Asp Ile
    1235                1240                1245

Tyr Asp  Glu Asp Glu Asn Gln  Ser Pro Arg Ser Phe  Gln Lys Lys
    1250                1255                1260

Thr Arg  His Tyr Phe Ile Ala  Ala Val Glu Arg Leu  Trp Asp Tyr
    1265                1270                1275

Gly Met  Ser Ser Ser Pro His  Val Leu Arg Asn Arg  Ala Gln Ser
    1280                1285                1290

Gly Ser  Val Pro Gln Phe Lys  Lys Val Val Phe Gln  Glu Phe Thr
    1295                1300                1305

Asp Gly  Ser Phe Thr Gln Pro  Leu Tyr Arg Gly Glu  Leu Asn Glu
    1310                1315                1320

His Leu  Gly Leu Leu Gly Pro  Tyr Ile Arg Ala Glu  Val Glu Asp
    1325                1330                1335
```

```
Asn Ile  Met Val Thr Phe Arg  Asn Gln Ala Ser Arg  Pro Tyr Ser
    1340                1345                1350

Phe Tyr  Ser Ser Leu Ile Ser  Tyr Glu Glu Asp Gln  Arg Gln Gly
    1355                1360                1365

Ala Glu  Pro Arg Lys Asn Phe  Val Lys Pro Asn Glu  Thr Lys Thr
    1370                1375                1380

Tyr Phe  Trp Lys Val Gln His  His Met Ala Pro Thr  Lys Asp Glu
    1385                1390                1395

Phe Asp  Cys Lys Ala Trp Ala  Tyr Phe Ser Asp Val  Asp Leu Glu
    1400                1405                1410

Lys Asp  Val His Ser Gly Leu  Ile Gly Pro Leu Leu  Val Cys His
    1415                1420                1425

Thr Asn  Thr Leu Asn Pro Ala  His Gly Arg Gln Val  Thr Val Gln
    1430                1435                1440

Glu Phe  Ala Leu Phe Phe Thr  Ile Phe Asp Glu Thr  Lys Ser Trp
    1445                1450                1455

Tyr Phe  Thr Glu Asn Met Glu  Arg Asn Cys Arg Ala  Pro Cys Asn
    1460                1465                1470

Ile Gln  Met Glu Asp Pro Thr  Phe Lys Glu Asn Tyr  Arg Phe His
    1475                1480                1485

Ala Ile  Asn Gly Tyr Ile Met  Asp Thr Leu Pro Gly  Leu Val Met
    1490                1495                1500

Ala Gln  Asp Gln Arg Ile Arg  Trp Tyr Leu Leu Ser  Met Gly Ser
    1505                1510                1515

Asn Glu  Asn Ile His Ser Ile  His Phe Ser Gly His  Val Phe Thr
    1520                1525                1530

Val Arg  Lys Lys Glu Glu Tyr  Lys Met Ala Leu Tyr  Asn Leu Tyr
```

```
    1535                1540                1545

Pro Gly  Val Phe Glu Thr Val  Glu Met Leu Pro Ser  Lys Ala Gly
    1550                1555                1560

Ile Trp  Arg Val Glu Cys Leu  Ile Gly Glu His Leu  His Ala Gly
    1565                1570                1575

Met Ser  Thr Leu Phe Leu Val  Tyr Ser Asn Lys Cys  Gln Thr Pro
    1580                1585                1590

Leu Gly  Met Ala Ser Gly His  Ile Arg Asp Phe Gln  Ile Thr Ala
    1595                1600                1605

Ser Gly  Gln Tyr Gly Gln Trp  Ala Pro Lys Leu Ala  Arg Leu His
    1610                1615                1620

Tyr Ser  Gly Ser Ile Asn Ala  Trp Ser Thr Lys Glu  Pro Phe Ser
    1625                1630                1635

Trp Ile  Lys Val Asp Leu Leu  Ala Pro Met Ile Ile  His Gly Ile
    1640                1645                1650

Lys Thr  Gln Gly Ala Arg Gln  Lys Phe Ser Ser Leu  Tyr Ile Ser
    1655                1660                1665

Gln Phe  Ile Ile Met Tyr Ser  Leu Asp Gly Lys Lys  Trp Gln Thr
    1670                1675                1680

Tyr Arg  Gly Asn Ser Thr Gly  Thr Leu Met Val Phe  Phe Gly Asn
    1685                1690                1695

Val Asp  Ser Ser Gly Ile Lys  His Asn Ile Phe Asn  Pro Pro Ile
    1700                1705                1710

Ile Ala  Arg Tyr Ile Arg Leu  His Pro Thr His Tyr  Ser Ile Arg
    1715                1720                1725

Ser Thr  Leu Arg Met Glu Leu  Met Gly Cys Asp Leu  Asn Ser Cys
    1730                1735                1740
```

```
Ser Met  Pro Leu Gly Met Glu  Ser Lys Ala Ile Ser  Asp Ala Gln
    1745                1750                1755

Ile Thr  Ala Ser Ser Tyr Phe  Thr Asn Met Phe Ala  Thr Trp Ser
    1760                1765                1770

Pro Ser  Lys Ala Arg Leu His  Leu Gln Gly Arg Ser  Asn Ala Trp
    1775                1780                1785

Arg Pro  Gln Val Asn Asn Pro  Lys Glu Trp Leu Gln  Val Asp Phe
    1790                1795                1800

Gln Lys  Thr Met Lys Val Thr  Gly Val Thr Thr Gln  Gly Val Lys
    1805                1810                1815

Ser Leu  Leu Thr Ser Met Tyr  Val Lys Glu Phe Leu  Ile Ser Ser
    1820                1825                1830

Ser Gln  Asp Gly His Gln Trp  Thr Leu Phe Phe Gln  Asn Gly Lys
    1835                1840                1845

Val Lys  Val Phe Gln Gly Asn  Gln Asp Ser Phe Thr  Pro Val Val
    1850                1855                1860

Asn Ser  Leu Asp Pro Pro Leu  Leu Thr Arg Tyr Leu  Arg Ile His
    1865                1870                1875

Pro Gln  Ser Trp Val His Gln  Ile Ala Leu Arg Met  Glu Val Leu
    1880                1885                1890

Gly Cys  Glu Ala Gln Asp Leu  Tyr
    1895                1900
```

<210> 86
<211> 1515
<212> PRT
<213> Artificial Sequence

<220>
<223> VWF031

<400> 86

```
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
```

```
Ala 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 Ala 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  Ile Ser Gly Gly Gly  Gly Ser Gly
    1235                1240                1245

Gly Gly  Gly Ser Gly Gly Gly  Gly Ser Gly Gly Gly  Gly Ser Gly
    1250                1255                1260

Gly Gly  Gly Ser Gly Gly Gly  Gly Ser Leu Val Pro  Arg Gly Ser
    1265                1270                1275

Gly Gly  Gly Gly Ser Gly Gly  Gly Gly Ser Asp Lys  Thr His Thr
    1280                1285                1290

Cys Pro  Pro Cys Pro Ala Pro  Glu Leu Leu Gly Gly  Pro Ser Val
    1295                1300                1305
```

```
Phe Leu  Phe Pro Pro Lys Pro  Lys Asp Thr Leu Met  Ile Ser Arg
    1310                1315                1320

Thr Pro  Glu Val Thr Cys Val  Val Val Asp Val Ser  His Glu Asp
    1325                1330                1335

Pro Glu  Val Lys Phe Asn Trp  Tyr Val Asp Gly Val  Glu Val His
    1340                1345                1350

Asn Ala  Lys Thr Lys Pro Arg  Glu Glu Gln Tyr Asn  Ser Thr Tyr
    1355                1360                1365

Arg Val  Val Ser Val Leu Thr  Val Leu His Gln Asp  Trp Leu Asn
    1370                1375                1380

Gly Lys  Glu Tyr Lys Cys Lys  Val Ser Asn Lys Ala  Leu Pro Ala
    1385                1390                1395

Pro Ile  Glu Lys Thr Ile Ser  Lys Ala Lys Gly Gln  Pro Arg Glu
    1400                1405                1410

Pro Gln  Val Tyr Thr Leu Pro  Pro Ser Arg Asp Glu  Leu Thr Lys
    1415                1420                1425

Asn Gln  Val Ser Leu Thr Cys  Leu Val Lys Gly Phe  Tyr Pro Ser
    1430                1435                1440

Asp Ile  Ala Val Glu Trp Glu  Ser Asn Gly Gln Pro  Glu Asn Asn
    1445                1450                1455

Tyr Lys  Thr Thr Pro Pro Val  Leu Asp Ser Asp Gly  Ser Phe Phe
    1460                1465                1470

Leu Tyr  Ser Lys Leu Thr Val  Asp Lys Ser Arg Trp  Gln Gln Gly
    1475                1480                1485

Asn Val  Phe Ser Cys Ser Val  Met His Glu Ala Leu  His Asn His
    1490                1495                1500

Tyr Thr  Gln Lys Ser Leu Ser  Leu Ser Pro Gly Lys
    1505                1510                1515
```

<210> 87
<211> 1778
<212> PRT
<213> Artificial Sequence

<220>
<223> VWF034

<400> 87

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

Ala 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 Ala 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  Ile Ser Gly Thr Ser  Glu Ser Ala
    1235                1240                1245

Thr Pro  Glu Ser Gly Pro Gly  Ser Glu Pro Ala Thr  Ser Gly Ser
    1250                1255                1260
```

```
Glu Thr  Pro Gly Thr Ser Glu  Ser Ala Thr Pro Glu  Ser Gly Pro
    1265                1270                1275

Gly Ser  Glu Pro Ala Thr Ser  Gly Ser Glu Thr Pro  Gly Thr Ser
    1280                1285                1290

Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly Thr Ser  Thr Glu Pro
    1295                1300                1305

Ser Glu  Gly Ser Ala Pro Gly  Ser Pro Ala Gly Ser  Pro Thr Ser
    1310                1315                1320

Thr Glu  Glu Gly Thr Ser Glu  Ser Ala Thr Pro Glu  Ser Gly Pro
    1325                1330                1335

Gly Ser  Glu Pro Ala Thr Ser  Gly Ser Glu Thr Pro  Gly Thr Ser
    1340                1345                1350

Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly Ser Pro  Ala Gly Ser
    1355                1360                1365

Pro Thr  Ser Thr Glu Glu Gly  Ser Pro Ala Gly Ser  Pro Thr Ser
    1370                1375                1380

Thr Glu  Glu Gly Thr Ser Thr  Glu Pro Ser Glu Gly  Ser Ala Pro
    1385                1390                1395

Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser Gly Pro  Gly Thr Ser
    1400                1405                1410

Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly Thr Ser  Glu Ser Ala
    1415                1420                1425

Thr Pro  Glu Ser Gly Pro Gly  Ser Glu Pro Ala Thr  Ser Gly Ser
    1430                1435                1440

Glu Thr  Pro Gly Ser Glu Pro  Ala Thr Ser Gly Ser  Glu Thr Pro
    1445                1450                1455

Gly Ser  Pro Ala Gly Ser Pro  Thr Ser Thr Glu Glu  Gly Thr Ser
```

```
    1460                1465                1470

Thr Glu  Pro Ser Glu Gly Ser  Ala Pro Gly Thr Ser  Thr Glu Pro
    1475                1480                1485

Ser Glu  Gly Ser Ala Pro Gly  Ser Glu Pro Ala Thr  Ser Gly Ser
    1490                1495                1500

Glu Thr  Pro Gly Thr Ser Glu  Ser Ala Thr Pro Glu  Ser Gly Pro
    1505                1510                1515

Gly Thr  Ser Thr Glu Pro Ser  Glu Gly Ser Ala Pro  Asp Ile Gly
    1520                1525                1530

Gly Gly  Gly Gly Ser Gly Gly  Gly Gly Ser Leu Val  Pro Arg Gly
    1535                1540                1545

Ser Gly  Gly Asp Lys Thr His  Thr Cys Pro Pro Cys  Pro Ala Pro
    1550                1555                1560

Glu Leu  Leu Gly Gly Pro Ser  Val Phe Leu Phe Pro  Pro Lys Pro
    1565                1570                1575

Lys Asp  Thr Leu Met Ile Ser  Arg Thr Pro Glu Val  Thr Cys Val
    1580                1585                1590

Val Val  Asp Val Ser His Glu  Asp Pro Glu Val Lys  Phe Asn Trp
    1595                1600                1605

Tyr Val  Asp Gly Val Glu Val  His Asn Ala Lys Thr  Lys Pro Arg
    1610                1615                1620

Glu Glu  Gln Tyr Asn Ser Thr  Tyr Arg Val Val Ser  Val Leu Thr
    1625                1630                1635

Val Leu  His Gln Asp Trp Leu  Asn Gly Lys Glu Tyr  Lys Cys Lys
    1640                1645                1650

Val Ser  Asn Lys Ala Leu Pro  Ala Pro Ile Glu Lys  Thr Ile Ser
    1655                1660                1665
```

```
Lys Ala  Lys Gly Gln Pro Arg  Glu Pro Gln Val Tyr  Thr Leu Pro
    1670                1675                1680


Pro Ser  Arg Asp Glu Leu Thr  Lys Asn Gln Val Ser  Leu Thr Cys
    1685                1690                1695


Leu Val  Lys Gly Phe Tyr Pro  Ser Asp Ile Ala Val  Glu Trp Glu
    1700                1705                1710


Ser Asn  Gly Gln Pro Glu Asn  Asn Tyr Lys Thr Thr  Pro Pro Val
    1715                1720                1725


Leu Asp  Ser Asp Gly Ser Phe  Phe Leu Tyr Ser Lys  Leu Thr Val
    1730                1735                1740


Asp Lys  Ser Arg Trp Gln Gln  Gly Asn Val Phe Ser  Cys Ser Val
    1745                1750                1755


Met His  Glu Ala Leu His Asn  His Tyr Thr Gln Lys  Ser Leu Ser
    1760                1765                1770


Leu Ser  Pro Gly Lys
    1775


<210>  88
<211>  32
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Cleavable linker

<400>  88

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


Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
            20                  25                  30


<210>  89
<211>  11
<212>  PRT
<213>  Artificial Sequence
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<220>
<223> Ig constant region portion

<400> 89

Pro Lys Asn Ser Ser Met Ile Ser Asn Thr Pro
1   5   10

<210> 90
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Ig constant region portion

<400> 90

His Gln Ser Leu Gly Thr Gln
1   5

<210> 91
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Ig constant region portion

<400> 91

His Gln Asn Leu Ser Asp Gly Lys
1   5

<210> 92
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Ig constant region portion

<400> 92

His Gln Asn Ile Ser Asp Gly Lys
1   5

<210> 93
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Ig constant region portion

<400> 93

Val Ile Ser Ser His Leu Gly Gln
1   5

<210> 94
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker, where the sequence can repeated between 1-20 times

<400> 94

Gly Gly Gly Gly Ser
1   5

<210> 95
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker, where the sequence can be repeated between 1-100 times or
       1-20 times

<400> 95

Gly Gly Ser Gly Gly Gly Gly Ser
1   5

<210> 96
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 96

Ser Gly Gly Ser Gly Gly Ser
1   5

<210> 97
<211> 15

<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 97

Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Gly
1 5 10 15

<210> 98
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 98

Gly Gly Ser Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 99
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 99

Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly
1 5 10 15

Gly Ser

<210> 100
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 100

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser

1 5 10 15

<210> 101
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker, where the sequence can be repeated between 1-00 times or 1-20 times

<400> 101

Gly Gly Gly Ser
1

<210> 102
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavage site

<400> 102

Arg Arg Arg Arg
1

<210> 103
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavage site

<400> 103

Arg Lys Arg Arg Lys Arg
1 5

<210> 104
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavage site

<400> 104

Arg Arg Arg Arg Ser
1 5

<210> 105
<211> 4
<212> PRT
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<220>
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<220>
<221> misc_feature
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<223> Xaa is an aliphatic amino acid

<400> 105

Xaa Val Pro Arg
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<210> 106
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 106

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

Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser
20 25 30

Phe Ser

<210> 107
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 107

Ile Ser Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu
1 5 10 15

Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro
20 25 30

Ser Phe Ile Gln Ile Arg Ser Val
35 40

<210> 108
<211> 46
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 108

Ile Ser Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile
1 5 10 15

Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe Asp
20 25 30

Ile Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe Gln
35 40 45

<210> 109
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> PAR1 exosite interaction motif

<400> 109

Ser Phe Leu Leu Arg Asn
1 5

<210> 110
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> PAR1 exosite interaction motif

<400> 110

Pro Asn Asp Lys
1

<210> 111
<211> 5
<212> PRT
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<220>
<223> PAR1 exosite interaction motif

<400> 111

Pro Asn Asp Lys Tyr
1   5

<210> 112
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> PAR1 exosite interaction motif

<400> 112

Pro Asn Asp Lys Tyr Glu
1   5

<210> 113
<211> 7
<212> PRT
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<220>
<223> PAR1 exosite interaction motif

<400> 113

Pro Asn Asp Lys Tyr Glu Pro
1   5

<210> 114
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> PAR1 exosite interaction motif

<400> 114

Pro Asn Asp Lys Tyr Glu Pro Phe
1   5

<210> 115
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> PAR1 exosite interaction motif

<400> 115

Pro Asn Asp Lys Tyr Glu Pro Phe Trp
1   5

<210> 116
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> PAR1 exosite interaction motif

<400> 116

Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu
1   5   10

<210> 117
<211> 11
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<220>
<223> PAR1 exosite interaction motif

<400> 117

Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp
1   5   10

<210> 118
<211> 12
<212> PRT

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<220>
<223> PAR1 exosite interaction motif

<400> 118

Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu
1 5 10

<210> 119
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<400> 119

Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu
1 5 10

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<220>
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<400> 120

Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu Ser
1 5 10

<210> 121
<211> 7
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<220>
<223> FXIa cleavage site

<400> 121

Lys Leu Thr Arg Ala Glu Thr
1 5

<210> 122
<211> 7

<212> PRT
<213> Artificial Sequence

<220>
<223> FXIa cleavage site

<400> 122

Asp Phe Thr Arg Val Val Gly
1 5

<210> 123
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<212> PRT
<213> Artificial Sequence

<220>
<223> FXIIa cleavage site

<400> 123

Thr Met Thr Arg Ile Val Gly Gly
1 5

<210> 124
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Kallikrein cleavage site

<400> 124

Ser Pro Phe Arg Ser Thr Gly Gly
1 5

<210> 125
<211> 8
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<220>
<223> FVIIa cleavage site

<400> 125

Leu Gln Val Arg Ile Val Gly Gly
1 5

<210> 126

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

<220>
<223> FIXa cleavage site

<400> 126

Pro Leu Gly Arg Ile Val Gly Gly
1 5

<210> 127
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<212> PRT
<213> Artificial Sequence

<220>
<223> FXa cleavage site

<400> 127

Ile Glu Gly Arg Thr Val Gly Gly
1 5

<210> 128
<211> 8
<212> PRT
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<220>
<223> FIIa (thrombin) cleavage site

<400> 128

Leu Thr Pro Arg Ser Leu Leu Val
1 5

<210> 129
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Elastase-2 cleavage site

<400> 129

Leu Gly Pro Val Ser Gly Val Pro
1 5

<210> 130
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Granzyme-B cleavage

<400> 130

Val Ala Gly Asp Ser Leu Glu Glu
1 5

<210> 131
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> MMP-12 cleavage site

<400> 131

Gly Pro Ala Gly Leu Gly Gly Ala
1 5

<210> 132
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> MMP-13 cleavage site

<400> 132

Gly Pro Ala Gly Leu Arg Gly Ala
1 5

<210> 133
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> MMP-17 cleavage site

<400> 133

Ala Pro Leu Gly Leu Arg Leu Arg
1 5

<210> 134
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> MMP-20 cleavage site

<400> 134

Pro Ala Leu Pro Leu Val Ala Gln
1   5

<210> 135
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> TEV cleavage site

<400> 135

Glu Asn Leu Tyr Phe Gln Gly
1   5

<210> 136
<211> 8
<212> PRT
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<220>
<223> Enterokinase cleavage site

<400> 136

Asp Asp Asp Lys Ile Val Gly Gly
1   5

<210> 137
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Protease 3C (PRESCISSION) cleavage site

<400> 137

Leu Glu Val Leu Phe Gln Gly Pro
1   5

<210> 138
<211> 8
<212> PRT
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<220>
<223> Sortase A cleavage site

<400> 138

Leu Pro Lys Thr Gly Ser Glu Ser
1 5

<210> 139
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 139

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

Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
20 25 30

<210> 140
<211> 30
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<220>
<223> Cleavable linker

<400> 140

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

Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
20 25 30

<210> 141
<211> 29
<212> PRT

<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 141

Thr Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu
1 5 10 15

Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
20 25

<210> 142
<211> 28
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 142

Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu
1 5 10 15

Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
20 25

<210> 143
<211> 27
<212> PRT
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<220>
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<400> 143

Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser
1 5 10 15

Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
20 25

<210> 144
<211> 26
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 144

Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
1   5   10   15

Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
            20   25

<210> 145
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Thrombin cleavage site

<400> 145

Ala Leu Arg Pro Arg Val Val Gly Gly Ala
1   5   10

<210> 146
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 146

Thr Leu Asp Pro Arg Ser Phe Leu Leu Arg Asn Pro Asn Asp Lys Tyr
1   5   10   15

Glu Pro Phe Trp Glu Asp Glu Glu Lys
            20   25

<210> 147
<211> 4548
<212> DNA
<213> Artificial Sequence

<220>
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<400> 147

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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
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Leu Cys Gly Asn Phe Asn Ile Phe Ala Glu Asp Asp Phe Met Thr Gln
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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
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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
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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
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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
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Pro Gly Glu Cys Leu Val Thr Gly Gln Ser His Phe Lys Ser Phe Asp
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Asn Arg Tyr Phe Thr Phe Ser Gly Ile Cys Gln Tyr Leu Leu Ala Arg
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Asp Cys Gln Asp His Ser Phe Ser Ile Val Ile Glu Thr Val Gln Cys
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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
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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
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Asp Leu Gln Met Asp Trp Asp Gly Arg Gly Arg Leu Leu Val Lys Leu
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Ser Pro Val Tyr Ala Gly Lys Thr Cys Gly Leu Cys Gly Asn Tyr Asn
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Gly Asn Gln Gly Asp Asp Phe Leu Thr Pro Ser Gly Leu Ala Glu Pro
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Arg Val Glu Asp Phe Gly Asn Ala Trp Lys Leu His Gly Asp Cys Gln
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Asp Leu Gln Lys Gln His Ser Asp Pro Cys Ala Leu Asn Pro Arg Met
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Thr Arg Phe Ser Glu Glu Ala Cys Ala Val Leu Thr Ser Pro Thr Phe
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Ala Trp Arg Glu Pro Gly Arg Cys Glu Leu Asn Cys Pro Lys Gly Gln
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Val Tyr Leu Gln Cys Gly Thr Pro Cys Asn Leu Thr Cys Arg Ser Leu
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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
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Ala Gln Cys Pro Cys Tyr Tyr Asp Gly Glu Ile Phe Gln Pro Glu Asp
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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
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Gly Leu Glu Cys Thr Lys Thr Cys Gln Asn Tyr Asp Leu Glu Cys Met
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His Glu Asn Arg Cys Val Ala Leu Glu Arg Cys Pro Cys Phe His Gln
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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
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Arg Pro Met Lys Asp Glu Thr His Phe Glu Val Val Glu Ser Gly Arg
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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

Ala 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 Ala 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  Ile Ser Gly Gly Gly  Gly Ser Gly
    1235                1240                1245

Gly Gly  Gly Ser Gly Gly Gly  Gly Ser Gly Gly Gly  Gly Ser Gly
    1250                1255                1260

Gly Gly  Gly Ser Gly Gly Gly  Gly Ser Leu Val Pro  Arg Gly Ser
    1265                1270                1275

Gly Gly  Gly Gly Ser Gly Gly  Gly Gly Ser Asp Lys  Thr His Thr
    1280                1285                1290

Cys Pro  Pro Cys Pro Ala Pro  Glu Leu Leu Gly Gly  Pro Ser Val
    1295                1300                1305

Phe Leu  Phe Pro Pro Lys Pro  Lys Asp Thr Leu Met  Ala Ser Arg
    1310                1315                1320

Thr Pro  Glu Val Thr Cys Val  Val Val Asp Val Ser  His Glu Asp
    1325                1330                1335

Pro Glu  Val Lys Phe Asn Trp  Tyr Val Asp Gly Val  Glu Val His
    1340                1345                1350

Asn Ala  Lys Thr Lys Pro Arg  Glu Glu Gln Tyr Asn  Ser Thr Tyr
    1355                1360                1365

Arg Val  Val Ser Val Leu Thr  Val Leu Ala Gln Asp  Trp Leu Asn
    1370                1375                1380

Gly Lys  Glu Tyr Lys Cys Lys  Val Ser Asn Lys Ala  Leu Pro Ala
    1385                1390                1395

Pro Ile  Glu Lys Thr Ile Ser  Lys Ala Lys Gly Gln  Pro Arg Glu
    1400                1405                1410

Pro Gln  Val Tyr Thr Leu Pro  Pro Ser Arg Asp Glu  Leu Thr Lys
    1415                1420                1425

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

```
    1430                1435                1440

Asp Ile  Ala Val Glu Trp Glu  Ser Asn Gly Gln Pro  Glu Asn Asn
    1445                1450                1455

Tyr Lys  Thr Thr Pro Pro Val  Leu Asp Ser Asp Gly  Ser Phe Phe
    1460                1465                1470

Leu Tyr  Ser Lys Leu Thr Val  Asp Lys Ser Arg Trp  Gln Gln Gly
    1475                1480                1485

Asn Val  Phe Ser Cys Ser Val  Met His Glu Ala Leu  His Asn Ala
    1490                1495                1500

Tyr Thr  Gln Lys Ser Leu Ser  Leu Ser Pro Gly Lys
    1505                1510                1515
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<210> 151
<211> 4959
<212> DNA
<213> Artificial Sequence

<220>
<223> VWF057

<400> 151

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gacttcgtca acacctttga tgggagcatg tacagctttg cgggatactg cagttacctc      180

ctggcagggg gctgccagaa acgctccttc tcgattattg gggacttcca gaatggcaag      240

agagtgagcc tctccgtgta tcttggggaa ttttttgaca tccatttgtt tgtcaatggt      300

accgtgacac agggggacca aagagtctcc atgccctatg cctccaaagg gctgtatcta      360

gaaactgagg ctgggtacta caagctgtcc ggtgaggcct atggctttgt ggccaggatc      420

gatggcagcg gcaactttca agtcctgctg tcagacagat acttcaacaa gacctgcggg      480

ctgtgtggca actttaacat ctttgctgaa gatgacttta tgacccaaga agggaccttg      540

acctcggacc cttatgactt tgccaactca tgggctctga gcagtggaga acagtggtgt      600

gaacgggcat ctcctcccag cagctcatgc aacatctcct ctggggaaat gcagaagggc      660

ctgtgggagc agtgccagct tctgaagagc acctcggtgt ttgcccgctg ccaccctctg      720
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gtgctgtacg gctggaccga ccacagcgcg tgcagcccag tgtgccctgc tggtatggag 900

tataggcagt gtgtgtcccc ttgcgccagg acctgccaga gcctgcacat caatgaaatg 960

tgtcaggagc gatgcgtgga tggctgcagc tgccctgagg gacagctcct ggatgaaggc 1020

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aatgaagaat gtccagggga gtgccttgtc actggtcaat cccacttcaa gagctttgac 1200

aacagatact tcaccttcag tgggatctgc cagtacctgc tggcccggga ttgccaggac 1260

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cgcatccagc atacagtgac ggcctccgtg cgcctcagct acggggagga cctgcagatg 1500

gactgggatg gccgcgggag gctgctggtg aagctgtccc ccgtctatgc cgggaagacc 1560

tgcggcctgt gtgggaatta caatggcaac cagggcgacg acttccttac cccctctggg 1620

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tgcgggaccc cctgcaacct gacctgccgc tctctctctt acccggatga ggaatgcaat 2040

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agtggagtcc ccggaagctt gctgcctgac gctgtcctca gcagtcccct gtctcatcgc 2280

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<210> 152
<211> 1652
<212> PRT
<213> Artificial Sequence

<220>
<223> VWF057

<400> 152

Met Ile Pro Ala Arg Phe Ala Gly Val Leu Leu Ala Leu Ala Leu Ile
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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

Ala 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 Ala Glu
    1130                1135                1140
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```
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  Ile Ser Gly Ala Pro  Thr Ser Glu
    1235                1240                1245

Ser Ala  Thr Pro Glu Ser Gly  Pro Gly Ser Glu Pro  Ala Thr Ser
    1250                1255                1260

Gly Ser  Glu Thr Pro Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser
    1265                1270                1275

Gly Pro  Gly Ser Glu Pro Ala  Thr Ser Gly Ser Glu  Thr Pro Gly
    1280                1285                1290

Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly Pro Gly  Thr Ser Thr
    1295                1300                1305

Glu Pro  Ser Glu Gly Ser Ala  Pro Gly Ser Pro Ala  Gly Ser Pro
    1310                1315                1320

Thr Ser  Thr Glu Glu Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser
    1325                1330                1335

Gly Pro  Gly Ser Glu Pro Ala  Thr Ser Gly Ser Glu  Thr Pro Gly
```

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    1340                1345                1350

Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly Pro Gly  Ser Pro Ala
    1355                1360                1365

Gly Ser  Pro Thr Ser Thr Glu  Glu Gly Ser Pro Ala  Gly Ser Pro
    1370                1375                1380

Thr Ser  Thr Glu Glu Gly Ala  Ser Ser Gly Gly Gly  Gly Ser Gly
    1385                1390                1395

Gly Gly  Gly Ser Gly Gly Gly  Gly Ser Gly Gly Gly  Gly Ser Gly
    1400                1405                1410

Gly Gly  Gly Ser Leu Val Pro  Arg Gly Ser Gly Gly  Asp Lys Thr
    1415                1420                1425

His Thr  Cys Pro Pro Cys Pro  Ala Pro Glu Leu Leu  Gly Gly Pro
    1430                1435                1440

Ser Val  Phe Leu Phe Pro Pro  Lys Pro Lys Asp Thr  Leu Met Ile
    1445                1450                1455

Ser Arg  Thr Pro Glu Val Thr  Cys Val Val Val Asp  Val Ser His
    1460                1465                1470

Glu Asp  Pro Glu Val Lys Phe  Asn Trp Tyr Val Asp  Gly Val Glu
    1475                1480                1485

Val His  Asn Ala Lys Thr Lys  Pro Arg Glu Glu Gln  Tyr Asn Ser
    1490                1495                1500

Thr Tyr  Arg Val Val Ser Val  Leu Thr Val Leu His  Gln Asp Trp
    1505                1510                1515

Leu Asn  Gly Lys Glu Tyr Lys  Cys Lys Val Ser Asn  Lys Ala Leu
    1520                1525                1530

Pro Ala  Pro Ile Glu Lys Thr  Ile Ser Lys Ala Lys  Gly Gln Pro
    1535                1540                1545
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Arg Glu  Pro Gln Val Tyr Thr  Leu Pro Pro Ser Arg  Asp Glu Leu
    1550                1555                1560

Thr Lys  Asn Gln Val Ser Leu  Thr Cys Leu Val Lys  Gly Phe Tyr
    1565                1570                1575

Pro Ser  Asp Ile Ala Val Glu  Trp Glu Ser Asn Gly  Gln Pro Glu
    1580                1585                1590

Asn Asn  Tyr Lys Thr Thr Pro  Pro Val Leu Asp Ser  Asp Gly Ser
    1595                1600                1605

Phe Phe  Leu Tyr Ser Lys Leu  Thr Val Asp Lys Ser  Arg Trp Gln
    1610                1615                1620

Gln Gly  Asn Val Phe Ser Cys  Ser Val Met His Glu  Ala Leu His
    1625                1630                1635

Asn His  Tyr Thr Gln Lys Ser  Leu Ser Leu Ser Pro  Gly Lys
    1640                1645                1650
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<210> 153
<211> 5379
<212> DNA
<213> Artificial Sequence

<220>
<223> VWF058 (VWF034 with IHH mutation)

<400> 153

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gacttcgtca acacctttga tgggagcatg tacagctttg cgggatactg cagttacctc      180

ctggcagggg gctgccagaa acgctccttc tcgattattg gggacttcca gaatggcaag      240

agagtgagcc tctccgtgta tcttggggaa ttttttgaca tccatttgtt tgtcaatggt      300

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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
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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
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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
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Ala Trp Arg Glu Pro Gly Arg Cys Glu Leu Asn Cys Pro Lys Gly Gln
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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
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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

Ala 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 Ala 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
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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  Ile Ser Gly Thr Ser  Glu Ser Ala
    1235                1240                1245

Thr Pro  Glu Ser Gly Pro Gly  Ser Glu Pro Ala Thr  Ser Gly Ser
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Glu Thr  Pro Gly Thr Ser Glu  Ser Ala Thr Pro Glu  Ser Gly Pro
    1265                1270                1275
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Gly Ser  Glu Pro Ala Thr Ser  Gly Ser Glu Thr Pro  Gly Thr Ser
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Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly Thr Ser  Thr Glu Pro
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Ser Glu  Gly Ser Ala Pro Gly  Ser Pro Ala Gly Ser  Pro Thr Ser
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Thr Glu  Glu Gly Thr Ser Glu  Ser Ala Thr Pro Glu  Ser Gly Pro
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Gly Ser  Glu Pro Ala Thr Ser  Gly Ser Glu Thr Pro  Gly Thr Ser
    1340                 1345                 1350

Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly Ser Pro  Ala Gly Ser
    1355                 1360                 1365

Pro Thr  Ser Thr Glu Glu Gly  Ser Pro Ala Gly Ser  Pro Thr Ser
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Thr Glu  Glu Gly Thr Ser Thr  Glu Pro Ser Glu Gly  Ser Ala Pro
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Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser Gly Pro  Gly Thr Ser
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Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly Thr Ser  Glu Ser Ala
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Thr Pro  Glu Ser Gly Pro Gly  Ser Glu Pro Ala Thr  Ser Gly Ser
    1430                 1435                 1440

Glu Thr  Pro Gly Ser Glu Pro  Ala Thr Ser Gly Ser  Glu Thr Pro
    1445                 1450                 1455

Gly Ser  Pro Ala Gly Ser Pro  Thr Ser Thr Glu Glu  Gly Thr Ser
    1460                 1465                 1470

Thr Glu  Pro Ser Glu Gly Ser  Ala Pro Gly Thr Ser  Thr Glu Pro
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Ser Glu  Gly Ser Ala Pro Gly  Ser Glu Pro Ala Thr  Ser Gly Ser
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Gly Thr  Ser Thr Glu Pro Ser  Glu Gly Ser Ala Pro  Asp Ser Gly
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Gly Gly  Gly Ser Gly Gly Gly  Gly Ser Gly Gly Gly  Gly Ser Gly
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Gly Gly  Gly Ser Gly Gly Gly  Gly Ser Leu Val Pro  Arg Gly Ser
    1550                1555                1560

Gly Gly  Asp Lys Thr His Thr  Cys Pro Pro Cys Pro  Ala Pro Glu
    1565                1570                1575

Leu Leu  Gly Gly Pro Ser Val  Phe Leu Phe Pro Pro  Lys Pro Lys
    1580                1585                1590

Asp Thr  Leu Met Ala Ser Arg  Thr Pro Glu Val Thr  Cys Val Val
    1595                1600                1605

Val Asp  Val Ser His Glu Asp  Pro Glu Val Lys Phe  Asn Trp Tyr
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Val Asp  Gly Val Glu Val His  Asn Ala Lys Thr Lys  Pro Arg Glu
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Glu Gln  Tyr Asn Ser Thr Tyr  Arg Val Val Ser Val  Leu Thr Val
    1640                1645                1650

Leu Ala  Gln Asp Trp Leu Asn  Gly Lys Glu Tyr Lys  Cys Lys Val
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Ser Asn  Lys Ala Leu Pro Ala  Pro Ile Glu Lys Thr  Ile Ser Lys
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Ala Lys  Gly Gln Pro Arg Glu  Pro Gln Val Tyr Thr  Leu Pro Pro
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Ser Arg  Asp Glu Leu Thr Lys  Asn Gln Val Ser Leu  Thr Cys Leu
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Val Lys  Gly Phe Tyr Pro Ser  Asp Ile Ala Val Glu  Trp Glu Ser
    1715                1720                1725


Asn Gly  Gln Pro Glu Asn Asn  Tyr Lys Thr Thr Pro  Pro Val Leu
    1730                1735                1740


Asp Ser  Asp Gly Ser Phe Phe  Leu Tyr Ser Lys Leu  Thr Val Asp
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Lys Ser  Arg Trp Gln Gln Gly  Asn Val Phe Ser Cys  Ser Val Met
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Ser Pro  Gly Lys
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<400> 157

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Trp Asp Tyr Met Gln Gly Ala Pro Thr Ser Glu Ser Ala Thr Pro Glu
35 40 45

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
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Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
65 70 75 80

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu

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Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
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Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser
        115                 120                 125

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
    130                 135                 140

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
145                 150                 155                 160

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly
                165                 170                 175

Ser Pro Thr Ser Thr Glu Glu Gly Ala Ser Ser Ser Asp Leu Gly Glu
            180                 185                 190

Leu Pro Val Asp Ala Arg Phe Pro Pro Arg Val Pro Lys Ser Phe Pro
        195                 200                 205

Phe Asn Thr Ser Val Val Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr
    210                 215                 220

Asp His Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu
225                 230                 235                 240

Leu Gly Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr Val Val Ile Thr
                245                 250                 255

Leu Lys Asn Met Ala Ser His Pro Val Ser Leu His Ala Val Gly Val
            260                 265                 270

Ser Tyr Trp Lys Ala Ser Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser
        275                 280                 285

Gln Arg Glu Lys Glu Asp Asp Lys Val Phe Pro Gly Gly Ser His Thr
    290                 295                 300
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Tyr Val Trp Gln Val Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro
305                 310                 315                 320

Leu Cys Leu Thr Tyr Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp
                325                 330                 335

Leu Asn Ser Gly Leu Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser
            340                 345                 350

Leu Ala Lys Glu Lys Thr Gln Thr Leu His Lys Phe Ile Leu Leu Phe
        355                 360                 365

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

Leu Met Gln Asp Arg Asp Ala Ala Ser Ala Arg Ala Trp Pro Lys Met
385                 390                 395                 400

His Thr Val Asn Gly Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly
                405                 410                 415

Cys His Arg Lys Ser Val Tyr Trp His Val Ile Gly Met Gly Thr Thr
            420                 425                 430

Pro Glu Val His Ser Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg
        435                 440                 445

Asn His Arg Gln Ala Ser Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr
    450                 455                 460

Ala Gln Thr Leu Leu Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His
465                 470                 475                 480

Ile Ser Ser His Gln His Asp Gly Met Glu Ala Tyr Val Lys Val Asp
                485                 490                 495

Ser Cys Pro Glu Glu Pro Gln Leu Arg Met Lys Asn Asn Glu Glu Ala
            500                 505                 510

Glu Asp Tyr Asp Asp Asp Leu Thr Asp Ser Glu Met Asp Val Val Arg
        515                 520                 525
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Phe Asp Asp Asp Asn Ser Pro Ser Phe Ile Gln Ile Arg Ser Val Ala
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Lys Lys His Pro Lys Thr Trp Val His Tyr Ile Ala Ala Glu Glu Glu
545                 550                 555                 560

Asp Trp Asp Tyr Ala Pro Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr
                565                 570                 575

Lys Ser Gln Tyr Leu Asn Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr
            580                 585                 590

Lys Lys Val Arg Phe Met Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg
        595                 600                 605

Glu Ala Ile Gln His Glu Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly
    610                 615                 620

Glu Val Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg
625                 630                 635                 640

Pro Tyr Asn Ile Tyr Pro His Gly Ile Thr Asp Val Arg Pro Leu Tyr
                645                 650                 655

Ser Arg Arg Leu Pro Lys Gly Val Lys His Leu Lys Asp Phe Pro Ile
            660                 665                 670

Leu Pro Gly Glu Ile Phe Lys Tyr Lys Trp Thr Val Thr Val Glu Asp
        675                 680                 685

Gly Pro Thr Lys Ser Asp Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser
    690                 695                 700

Phe Val Asn Met Glu Arg Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu
705                 710                 715                 720

Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly Asn Gln Ile Met
                725                 730                 735

Ser Asp Lys Arg Asn Val Ile Leu Phe Ser Val Phe Asp Glu Asn Arg
            740                 745                 750
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Ser Trp Tyr Leu Thr Glu Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala
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Gly Val Gln Leu Glu Asp Pro Glu Phe Gln Ala Ser Asn Ile Met His
    770                 775                 780

Ser Ile Asn Gly Tyr Val Phe Asp Ser Leu Gln Leu Ser Val Cys Leu
785                 790                 795                 800

His Glu Val Ala Tyr Trp Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp
                805                 810                 815

Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys His Lys Met Val
            820                 825                 830

Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly Glu Thr Val Phe
        835                 840                 845

Met Ser Met Glu Asn Pro Gly Leu Trp Ile Leu Gly Cys His Asn Ser
    850                 855                 860

Asp Phe Arg Asn Arg Gly Met Thr Ala Leu Leu Lys Val Ser Ser Cys
865                 870                 875                 880

Asp Lys Asn Thr Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser
                885                 890                 895

Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
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Gln Asn Gly Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
        915                 920                 925

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser
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Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
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Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
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Pro Glu  Ser Gly Pro Gly Ser  Glu Pro Ala Thr Ser  Gly Ser Glu
    1010                1015                1020

Thr Pro  Gly Thr Ser Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly
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Ser Pro  Ala Gly Ser Pro Thr  Ser Thr Glu Glu Gly  Ser Pro Ala
    1040                1045                1050

Gly Ser  Pro Thr Ser Thr Glu  Glu Gly Thr Ser Thr  Glu Pro Ser
    1055                1060                1065

Glu Gly  Ser Ala Pro Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser
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Gly Pro  Gly Thr Ser Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly
    1085                1090                1095

Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly Pro Gly  Ser Glu Pro
    1100                1105                1110

Ala Thr  Ser Gly Ser Glu Thr  Pro Gly Ser Glu Pro  Ala Thr Ser
    1115                1120                1125

Gly Ser  Glu Thr Pro Gly Ser  Pro Ala Gly Ser Pro  Thr Ser Thr
    1130                1135                1140

Glu Glu  Gly Thr Ser Thr Glu  Pro Ser Glu Gly Ser  Ala Pro Gly
    1145                1150                1155

Thr Ser  Thr Glu Pro Ser Glu  Gly Ser Ala Pro Gly  Ser Glu Pro
    1160                1165                1170
```

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Ala Thr  Ser Gly Ser Glu Thr  Pro Gly Thr Ser Glu  Ser Ala Thr
    1175                1180                1185

Pro Glu  Ser Gly Pro Gly Thr  Ser Thr Glu Pro Ser  Glu Gly Ser
    1190                1195                1200

Ala Pro  Ala Ser Ser Pro Pro  Val Leu Lys Arg His  Gln Ala Glu
    1205                1210                1215

Ile Thr  Arg Thr Thr Leu Gln  Ser Asp Gln Glu Glu  Ile Asp Tyr
    1220                1225                1230

Asp Asp  Thr Ile Ser Val Glu  Met Lys Lys Glu Asp  Phe Asp Ile
    1235                1240                1245

Tyr Asp  Glu Asp Glu Asn Gln  Ser Pro Arg Ser Phe  Gln Lys Lys
    1250                1255                1260

Thr Arg  His Tyr Phe Ile Ala  Ala Val Glu Arg Leu  Trp Asp Tyr
    1265                1270                1275

Gly Met  Ser Ser Ser Pro His  Val Leu Arg Asn Arg  Ala Gln Ser
    1280                1285                1290

Gly Ser  Val Pro Gln Phe Lys  Lys Val Val Phe Gln  Glu Phe Thr
    1295                1300                1305

Asp Gly  Ser Phe Thr Gln Pro  Leu Tyr Arg Gly Glu  Leu Asn Glu
    1310                1315                1320

His Leu  Gly Leu Leu Gly Pro  Tyr Ile Arg Ala Glu  Val Glu Asp
    1325                1330                1335

Asn Ile  Met Val Thr Phe Arg  Asn Gln Ala Ser Arg  Pro Tyr Ser
    1340                1345                1350

Phe Tyr  Ser Ser Leu Ile Ser  Tyr Glu Glu Asp Gln  Arg Gln Gly
    1355                1360                1365

Ala Glu  Pro Arg Lys Asn Phe  Val Lys Pro Asn Glu  Thr Lys Thr
    1370                1375                1380
```

```
Tyr Phe  Trp Lys Val Gln His  His Met Ala Pro Thr  Lys Asp Glu
    1385                1390                1395

Phe Asp  Cys Lys Ala Trp Ala  Tyr Phe Ser Asp Val  Asp Leu Glu
    1400                1405                1410

Lys Asp  Val His Ser Gly Leu  Ile Gly Pro Leu Leu  Val Cys His
    1415                1420                1425

Thr Asn  Thr Leu Asn Pro Ala  His Gly Arg Gln Val  Thr Val Gln
    1430                1435                1440

Glu Phe  Ala Leu Phe Phe Thr  Ile Phe Asp Glu Thr  Lys Ser Trp
    1445                1450                1455

Tyr Phe  Thr Glu Asn Met Glu  Arg Asn Cys Arg Ala  Pro Cys Asn
    1460                1465                1470

Ile Gln  Met Glu Asp Pro Thr  Phe Lys Glu Asn Tyr  Arg Phe His
    1475                1480                1485

Ala Ile  Asn Gly Tyr Ile Met  Asp Thr Leu Pro Gly  Leu Val Met
    1490                1495                1500

Ala Gln  Asp Gln Arg Ile Arg  Trp Tyr Leu Leu Ser  Met Gly Ser
    1505                1510                1515

Asn Glu  Asn Ile His Ser Ile  His Phe Ser Gly His  Val Phe Thr
    1520                1525                1530

Val Arg  Lys Lys Glu Glu Tyr  Lys Met Ala Leu Tyr  Asn Leu Tyr
    1535                1540                1545

Pro Gly  Val Phe Glu Thr Val  Glu Met Leu Pro Ser  Lys Ala Gly
    1550                1555                1560

Ile Trp  Arg Val Glu Cys Leu  Ile Gly Glu His Leu  His Ala Gly
    1565                1570                1575

Met Ser  Thr Leu Phe Leu Val  Tyr Ser Asn Lys Cys  Gln Thr Pro
    1580                1585                1590
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```
Leu Gly  Met Ala Ser Gly His  Ile Arg Asp Phe Gln  Ile Thr Ala
    1595                 1600                 1605

Ser Gly  Gln Tyr Gly Gln Trp  Ala Pro Lys Leu Ala  Arg Leu His
    1610                 1615                 1620

Tyr Ser  Gly Ser Ile Asn Ala  Trp Ser Thr Lys Glu  Pro Phe Ser
    1625                 1630                 1635

Trp Ile  Lys Val Asp Leu Leu  Ala Pro Met Ile Ile  His Gly Ile
    1640                 1645                 1650

Lys Thr  Gln Gly Ala Arg Gln  Lys Phe Ser Ser Leu  Tyr Ile Ser
    1655                 1660                 1665

Gln Phe  Ile Ile Met Tyr Ser  Leu Asp Gly Lys Lys  Trp Gln Thr
    1670                 1675                 1680

Tyr Arg  Gly Asn Ser Thr Gly  Thr Leu Met Val Phe  Phe Gly Asn
    1685                 1690                 1695

Val Asp  Ser Ser Gly Ile Lys  His Asn Ile Phe Asn  Pro Pro Ile
    1700                 1705                 1710

Ile Ala  Arg Tyr Ile Arg Leu  His Pro Thr His Tyr  Ser Ile Arg
    1715                 1720                 1725

Ser Thr  Leu Arg Met Glu Leu  Met Gly Cys Asp Leu  Asn Ser Cys
    1730                 1735                 1740

Ser Met  Pro Leu Gly Met Glu  Ser Lys Ala Ile Ser  Asp Ala Gln
    1745                 1750                 1755

Ile Thr  Ala Ser Ser Tyr Phe  Thr Asn Met Phe Ala  Thr Trp Ser
    1760                 1765                 1770

Pro Ser  Lys Ala Arg Leu His  Leu Gln Gly Arg Ser  Asn Ala Trp
    1775                 1780                 1785

Arg Pro  Gln Val Asn Asn Pro  Lys Glu Trp Leu Gln  Val Asp Phe
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    1790                1795                1800

Gln Lys  Thr Met Lys Val Thr  Gly Val Thr Thr Gln  Gly Val Lys
    1805                1810                1815

Ser Leu  Leu Thr Ser Met Tyr  Val Lys Glu Phe Leu  Ile Ser Ser
    1820                1825                1830

Ser Gln  Asp Gly His Gln Trp  Thr Leu Phe Phe Gln  Asn Gly Lys
    1835                1840                1845

Val Lys  Val Phe Gln Gly Asn  Gln Asp Ser Phe Thr  Pro Val Val
    1850                1855                1860

Asn Ser  Leu Asp Pro Pro Leu  Leu Thr Arg Tyr Leu  Arg Ile His
    1865                1870                1875

Pro Gln  Ser Trp Val His Gln  Ile Ala Leu Arg Met  Glu Val Leu
    1880                1885                1890

Gly Cys  Glu Ala Gln Asp Leu  Tyr Asp Lys Thr His  Thr Cys Pro
    1895                1900                1905

Pro Cys  Pro Ala Pro Glu Leu  Leu Gly Gly Pro Ser  Val Phe Leu
    1910                1915                1920

Phe Pro  Pro Lys Pro Lys Asp  Thr Leu Met Ala Ser  Arg Thr Pro
    1925                1930                1935

Glu Val  Thr Cys Val Val Val  Asp Val Ser His Glu  Asp Pro Glu
    1940                1945                1950

Val Lys  Phe Asn Trp Tyr Val  Asp Gly Val Glu Val  His Asn Ala
    1955                1960                1965

Lys Thr  Lys Pro Arg Glu Glu  Gln Tyr Asn Ser Thr  Tyr Arg Val
    1970                1975                1980

Val Ser  Val Leu Thr Val Leu  Ala Gln Asp Trp Leu  Asn Gly Lys
    1985                1990                1995
```

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Glu Tyr  Lys Cys Lys Val Ser  Asn Lys Ala Leu Pro  Ala Pro Ile
    2000                2005                2010

Glu Lys  Thr Ile Ser Lys Ala  Lys Gly Gln Pro Arg  Glu Pro Gln
    2015                2020                2025

Val Tyr  Thr Leu Pro Pro Ser  Arg Asp Glu Leu Thr  Lys Asn Gln
    2030                2035                2040

Val Ser  Leu Thr Cys Leu Val  Lys Gly Phe Tyr Pro  Ser Asp Ile
    2045                2050                2055

Ala Val  Glu Trp Glu Ser Asn  Gly Gln Pro Glu Asn  Asn Tyr Lys
    2060                2065                2070

Thr Thr  Pro Pro Val Leu Asp  Ser Asp Gly Ser Phe  Phe Leu Tyr
    2075                2080                2085

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

Phe Ser  Cys Ser Val Met His  Glu Ala Leu His Asn  Ala Tyr Thr
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Gln Lys  Ser Leu Ser Leu Ser  Pro Gly Lys
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Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg
35 40 45

Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val
50 55 60

Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile
65 70 75 80

Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln
85 90 95

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

His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser
115 120 125

Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp
130 135 140

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Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu
145                 150                 155                 160

Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser
                165                 170                 175

Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile
            180                 185                 190

Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr
        195                 200                 205

Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly
    210                 215                 220

Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp
225                 230                 235                 240

Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr
                245                 250                 255

Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val
            260                 265                 270

Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile
        275                 280                 285

Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser
    290                 295                 300

Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met
305                 310                 315                 320

Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His
                325                 330                 335

Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro
            340                 345                 350

Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp
        355                 360                 365
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Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser
    370                 375                 380

Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
385                 390                 395                 400

Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro
                405                 410                 415

Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
            420                 425                 430

Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met
        435                 440                 445

Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu
    450                 455                 460

Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
465                 470                 475                 480

Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro
                485                 490                 495

His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys
            500                 505                 510

Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe
        515                 520                 525

Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp
    530                 535                 540

Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg
545                 550                 555                 560

Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu
                565                 570                 575

Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val
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            580                 585                 590

Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu
        595                 600                 605

Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp
    610                 615                 620

Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
625                 630                 635                 640

Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp
                645                 650                 655

Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe
            660                 665                 670

Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
        675                 680                 685

Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro
    690                 695                 700

Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly
705                 710                 715                 720

Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp
                725                 730                 735

Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
            740                 745                 750

Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Gly Ala Pro Thr
        755                 760                 765

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr
    770                 775                 780

Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
785                 790                 795                 800
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Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro
            820                 825                 830

Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr
        835                 840                 845

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
    850                 855                 860

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
865                 870                 875                 880

Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr
                885                 890                 895

Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ala
            900                 905                 910

Ser Ser Pro Pro Val Leu Lys Arg His Gln Ala Glu Ile Thr Arg Thr
        915                 920                 925

Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser
    930                 935                 940

Val Glu Met Lys Lys Glu Asp Phe Asp Ile Tyr Asp Glu Asp Glu Asn
945                 950                 955                 960

Gln Ser Pro Arg Ser Phe Gln Lys Lys Thr Arg His Tyr Phe Ile Ala
                965                 970                 975

Ala Val Glu Arg Leu Trp Asp Tyr Gly Met Ser Ser Ser Pro His Val
            980                 985                 990

Leu Arg Asn Arg Ala Gln Ser Gly  Ser Val Pro Gln Phe  Lys Lys Val
        995                 1000                1005

Val Phe  Gln Glu Phe Thr Asp  Gly Ser Phe Thr Gln  Pro Leu Tyr
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Arg Ala  Glu Val Glu Asp Asn  Ile Met Val Thr Phe  Arg Asn Gln
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Ala Ser  Arg Pro Tyr Ser Phe  Tyr Ser Ser Leu Ile  Ser Tyr Glu
    1055                1060                1065

Glu Asp  Gln Arg Gln Gly Ala  Glu Pro Arg Lys Asn  Phe Val Lys
    1070                1075                1080

Pro Asn  Glu Thr Lys Thr Tyr  Phe Trp Lys Val Gln  His His Met
    1085                1090                1095

Ala Pro  Thr Lys Asp Glu Phe  Asp Cys Lys Ala Trp  Ala Tyr Phe
    1100                1105                1110

Ser Asp  Val Asp Leu Glu Lys  Asp Val His Ser Gly  Leu Ile Gly
    1115                1120                1125

Pro Leu  Leu Val Cys His Thr  Asn Thr Leu Asn Pro  Ala His Gly
    1130                1135                1140

Arg Gln  Val Thr Val Gln Glu  Phe Ala Leu Phe Phe  Thr Ile Phe
    1145                1150                1155

Asp Glu  Thr Lys Ser Trp Tyr  Phe Thr Glu Asn Met  Glu Arg Asn
    1160                1165                1170

Cys Arg  Ala Pro Cys Asn Ile  Gln Met Glu Asp Pro  Thr Phe Lys
    1175                1180                1185

Glu Asn  Tyr Arg Phe His Ala  Ile Asn Gly Tyr Ile  Met Asp Thr
    1190                1195                1200

Leu Pro  Gly Leu Val Met Ala  Gln Asp Gln Arg Ile  Arg Trp Tyr
    1205                1210                1215

Leu Leu  Ser Met Gly Ser Asn  Glu Asn Ile His Ser  Ile His Phe
    1220                1225                1230
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```
Ser Gly  His Val Phe Thr Val  Arg Lys Lys Glu Glu  Tyr Lys Met
    1235                1240                1245

Ala Leu  Tyr Asn Leu Tyr Pro  Gly Val Phe Glu Thr  Val Glu Met
    1250                1255                1260

Leu Pro  Ser Lys Ala Gly Ile  Trp Arg Val Glu Cys  Leu Ile Gly
    1265                1270                1275

Glu His  Leu His Ala Gly Met  Ser Thr Leu Phe Leu  Val Tyr Ser
    1280                1285                1290

Asn Lys  Cys Gln Thr Pro Leu  Gly Met Ala Ser Gly  His Ile Arg
    1295                1300                1305

Asp Phe  Gln Ile Thr Ala Ser  Gly Gln Tyr Gly Gln  Trp Ala Pro
    1310                1315                1320

Lys Leu  Ala Arg Leu His Tyr  Ser Gly Ser Ile Asn  Ala Trp Ser
    1325                1330                1335

Thr Lys  Glu Pro Phe Ser Trp  Ile Lys Val Asp Leu  Leu Ala Pro
    1340                1345                1350

Met Ile  Ile His Gly Ile Lys  Thr Gln Gly Ala Arg  Gln Lys Phe
    1355                1360                1365

Ser Ser  Leu Tyr Ile Ser Gln  Phe Ile Ile Met Tyr  Ser Leu Asp
    1370                1375                1380

Gly Lys  Lys Trp Gln Thr Tyr  Arg Gly Asn Ser Thr  Gly Thr Leu
    1385                1390                1395

Met Val  Phe Phe Gly Asn Val  Asp Ser Ser Gly Ile  Lys His Asn
    1400                1405                1410

Ile Phe  Asn Pro Pro Ile Ile  Ala Arg Tyr Ile Arg  Leu His Pro
    1415                1420                1425

Thr His  Tyr Ser Ile Arg Ser  Thr Leu Arg Met Glu  Leu Met Gly
```

```
    1430                1435                1440

Cys Asp  Leu Asn Ser Cys Ser  Met Pro Leu Gly Met  Glu Ser Lys
    1445                1450                1455

Ala Ile  Ser Asp Ala Gln Ile  Thr Ala Ser Ser Tyr  Phe Thr Asn
    1460                1465                1470

Met Phe  Ala Thr Trp Ser Pro  Ser Lys Ala Arg Leu  His Leu Gln
    1475                1480                1485

Gly Arg  Ser Asn Ala Trp Arg  Pro Gln Val Asn Asn  Pro Lys Glu
    1490                1495                1500

Trp Leu  Gln Val Asp Phe Gln  Lys Thr Met Lys Val  Thr Gly Val
    1505                1510                1515

Thr Thr  Gln Gly Val Lys Ser  Leu Leu Thr Ser Met  Tyr Val Lys
    1520                1525                1530

Glu Phe  Leu Ile Ser Ser Ser  Gln Asp Gly His Gln  Trp Thr Leu
    1535                1540                1545

Phe Phe  Gln Asn Gly Lys Val  Lys Val Phe Gln Gly  Asn Gln Asp
    1550                1555                1560

Ser Phe  Thr Pro Val Val Asn  Ser Leu Asp Pro Pro  Leu Leu Thr
    1565                1570                1575

Arg Tyr  Leu Arg Ile His Pro  Gln Ser Trp Val His  Gln Ile Ala
    1580                1585                1590

Leu Arg  Met Glu Val Leu Gly  Cys Glu Ala Gln Asp  Leu Tyr Asp
    1595                1600                1605

Lys Thr  His Thr Cys Pro Pro  Cys Pro Ala Pro Glu  Leu Leu Gly
    1610                1615                1620

Gly Pro  Ser Val Phe Leu Phe  Pro Pro Lys Pro Lys  Asp Thr Leu
    1625                1630                1635
```

```
Met Ile  Ser Arg Thr Pro Glu  Val Thr Cys Val Val  Val Asp Val
    1640                1645                1650

Ser His  Glu Asp Pro Glu Val  Lys Phe Asn Trp Tyr  Val Asp Gly
    1655                1660                1665

Val Glu  Val His Asn Ala Lys  Thr Lys Pro Arg Glu  Glu Gln Tyr
    1670                1675                1680

Asn Ser  Thr Tyr Arg Val Val  Ser Val Leu Thr Val  Leu His Gln
    1685                1690                1695

Asp Trp  Leu Asn Gly Lys Glu  Tyr Lys Cys Lys Val  Ser Asn Lys
    1700                1705                1710

Ala Leu  Pro Ala Pro Ile Glu  Lys Thr Ile Ser Lys  Ala Lys Gly
    1715                1720                1725

Gln Pro  Arg Glu Pro Gln Val  Tyr Thr Leu Pro Pro  Ser Arg Asp
    1730                1735                1740

Glu Leu  Thr Lys Asn Gln Val  Ser Leu Thr Cys Leu  Val Lys Gly
    1745                1750                1755

Phe Tyr  Pro Ser Asp Ile Ala  Val Glu Trp Glu Ser  Asn Gly Gln
    1760                1765                1770

Pro Glu  Asn Asn Tyr Lys Thr  Thr Pro Pro Val Leu  Asp Ser Asp
    1775                1780                1785

Gly Ser  Phe Phe Leu Tyr Ser  Lys Leu Thr Val Asp  Lys Ser Arg
    1790                1795                1800

Trp Gln  Gln Gly Asn Val Phe  Ser Cys Ser Val Met  His Glu Ala
    1805                1810                1815

Leu His  Asn His Tyr Thr Gln  Lys Ser Leu Ser Leu  Ser Pro Gly
    1820                1825                1830

Lys
```

<210> 160
<211> 5937
<212> DNA
<213> Artificial Sequence

<220>
<223> FVIII 283 (FVIII 169 with IHH triple mutation)

<400> 160
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ggtgagctgc ctgtggacgc aagatttcct cctagagtgc caaaatcttt tccattcaac 180

acctcagtcg tgtacaaaaa gactctgttt gtagaattca cggatcacct tttcaacatc 240

gctaagccaa ggccaccctg gatgggtctg ctaggtccta ccatccaggc tgaggtttat 300

gatacagtgg tcattacact taagaacatg gcttcccatc ctgtcagtct tcatgctgtt 360

ggtgtatcct actggaaagc ttctgaggga gctgaatatg atgatcagac cagtcaaagg 420

gagaaagaag atgataaagt cttccctggt ggaagccata catatgtctg gcaggtcctg 480

aaagagaatg gtccaatggc ctctgaccca ctgtgcctta cctactcata tctttctcat 540

gtggacctgg taaaagactt gaattcaggc ctcattggag ccctactagt atgtagagaa 600

gggagtctgg ccaaggaaaa gacacagacc ttgcacaaat ttatactact ttttgctgta 660

tttgatgaag ggaaaagttg gcactcagaa acaaagaact ccttgatgca ggatagggat 720

gctgcatctg ctcgggcctg gcctaaaatg cacacagtca atggttatgt aaacaggtct 780

ctgccaggtc tgattggatg ccacaggaaa tcagtctatt ggcatgtgat tggaatgggc 840

accactcctg aagtgcactc aatattcctc gaaggtcaca catttcttgt gaggaaccat 900

cgccaggcta gcttggaaat ctcgccaata actttcctta ctgctcaaac actcttgatg 960

gaccttggac agtttctact gttttgtcat atctcttccc accaacatga tggcatggaa 1020

gcttatgtca aagtagacag ctgtccagag gaaccccaac tacgaatgaa aaataatgaa 1080

gaagcggaag actatgatga tgatcttact gattctgaaa tggatgtggt caggtttgat 1140

gatgacaact ctccttcctt tatccaaatt cgctcagttg ccaagaagca tcctaaaact 1200

tgggtacatt acattgctgc tgaagaggag gactgggact atgctccctt agtcctcgcc 1260

cccgatgaca gaagttataa aagtcaatat ttgaacaatg gccctcagcg gattggtagg 1320

aagtacaaaa aagtccgatt tatggcatac acagatgaaa cctttaagac tcgtgaagct 1380

attcagcatg aatcaggaat cttgggacct ttactttatg gggaagttgg agacacactg 1440

ttgattatat ttaagaatca agcaagcaga ccatataaca tctaccctca cggaatcact 1500

gatgtccgtc ctttgtattc aaggagatta ccaaaaggtg taaaacattt gaaggatttt 1560

ccaattctgc caggagaaat attcaaatat aaatggacag tgactgtaga agatgggcca 1620

actaaatcag atcctcggtg cctgacccgc tattactcta gtttcgttaa tatggagaga 1680

gatctagctt caggactcat tggccctctc ctcatctgct acaaagaatc tgtagatcaa 1740

agaggaaacc agataatgtc agacaagagg aatgtcatcc tgttttctgt atttgatgag 1800

aaccgaagct ggtacctcac agagaatata caacgctttc tccccaatcc agctggagtg 1860

cagcttgagg atccagagtt ccaagcctcc aacatcatgc acagcatcaa tggctatgtt 1920

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tccggacccg ggtccgagcc cgccacttcc ggctccgaaa ctcccggcac aagcgagagc 2460

gctaccccag agtcaggacc aggaacatct acagagccct ctgaaggctc cgctccaggg 2520

tccccagccg gcagtcccac tagcaccgag gagggaacct ctgaaagcgc cacacccgaa 2580

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ccaagcgagg gctccgcacc cggaacaagc actgaaccca gtgagggttc agcacccggc 3060

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gctcagagtg gcagtgtccc tcagttcaag aaagttgttt tccaggaatt tactgatggc 3480

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tggagcacca aggagccctt ttcttggatc aaggtggatc tgttggcacc aatgattatt 4500

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acctggtctc cttcaaaagc tcgacttcac ctccaaggga ggagtaatgc ctggagacct 4920

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gtttttcagg gaaatcaaga ctccttcaca cctgtggtga actctctaga cccaccgtta 5160

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gaccctgagg tcaagttcaa ctggtacgtg gacggcgtgg aggtgcataa tgccaagaca 5460

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gcccaggact ggctgaatgg caaggagtac aagtgcaagg tctccaacaa agccctccca 5580

gcccccatcg agaaaaccat ctccaaagcc aaagggcagc cccgagaacc acaggtgtac 5640

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aaaggcttct atcccagcga catcgccgtg gagtgggaga gcaatgggca gccggagaac 5760

aactacaaga ccacgcctcc cgtgttggac tccgacggct ccttcttcct ctacagcaag 5820

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<210> 161
<211> 1978
<212> PRT
<213> Artificial Sequence

<220>
<223> FVIII 283 (FVIII 169 with IHH triple mutation)

<400> 161

Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe

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

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

Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val
    50                  55                  60

Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile
65                  70                  75                  80

Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln
                85                  90                  95

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

His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser
        115                 120                 125

Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp
    130                 135                 140

Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu
145                 150                 155                 160

Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser
                165                 170                 175

Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile
            180                 185                 190

Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr
        195                 200                 205

Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly
    210                 215                 220
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Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp
225                 230                 235                 240

Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr
                245                 250                 255

Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val
            260                 265                 270

Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile
        275                 280                 285

Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser
    290                 295                 300

Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met
305                 310                 315                 320

Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His
                325                 330                 335

Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro
            340                 345                 350

Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp
        355                 360                 365

Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser
    370                 375                 380

Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
385                 390                 395                 400

Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro
                405                 410                 415

Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
            420                 425                 430

Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met
        435                 440                 445
```

```
Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu
    450                 455                 460

Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
465                 470                 475                 480

Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro
                485                 490                 495

His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys
            500                 505                 510

Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe
        515                 520                 525

Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp
    530                 535                 540

Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg
545                 550                 555                 560

Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu
                565                 570                 575

Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val
            580                 585                 590

Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu
        595                 600                 605

Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp
    610                 615                 620

Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
625                 630                 635                 640

Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp
                645                 650                 655

Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe
            660                 665                 670
```

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Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
        675                 680                 685

Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro
    690                 695                 700

Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly
705                 710                 715                 720

Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp
                725                 730                 735

Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
            740                 745                 750

Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Gly Ala Pro Gly
        755                 760                 765

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
    770                 775                 780

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
785                 790                 795                 800

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
                805                 810                 815

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
            820                 825                 830

Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
        835                 840                 845

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
    850                 855                 860

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
865                 870                 875                 880

Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
```

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                885                 890                 895

Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
            900                 905                 910

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser
        915                 920                 925

Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
    930                 935                 940

Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
945                 950                 955                 960

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala
                965                 970                 975

Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
            980                 985                 990

Thr Glu Glu Gly Thr Ser Thr Glu  Pro Ser Glu Gly Ser  Ala Pro Gly
        995                 1000                1005

Thr Ser  Thr Glu Pro Ser Glu  Gly Ser Ala Pro Gly  Ser Glu Pro
    1010                1015                1020

Ala Thr  Ser Gly Ser Glu Thr  Pro Gly Thr Ser Glu  Ser Ala Thr
    1025                1030                1035

Pro Glu  Ser Gly Pro Gly Thr  Ser Thr Glu Pro Ser  Glu Gly Ser
    1040                1045                1050

Ala Pro  Ala Ser Ser Pro Pro  Val Leu Lys Arg His  Gln Ala Glu
    1055                1060                1065

Ile Thr  Arg Thr Thr Leu Gln  Ser Asp Gln Glu Glu  Ile Asp Tyr
    1070                1075                1080

Asp Asp  Thr Ile Ser Val Glu  Met Lys Lys Glu Asp  Phe Asp Ile
    1085                1090                1095
```

```
Tyr Asp  Glu Asp Glu Asn Gln  Ser Pro Arg Ser Phe  Gln Lys Lys
    1100                1105                1110

Thr Arg  His Tyr Phe Ile Ala  Ala Val Glu Arg Leu  Trp Asp Tyr
    1115                1120                1125

Gly Met  Ser Ser Ser Pro His  Val Leu Arg Asn Arg  Ala Gln Ser
    1130                1135                1140

Gly Ser  Val Pro Gln Phe Lys  Lys Val Val Phe Gln  Glu Phe Thr
    1145                1150                1155

Asp Gly  Ser Phe Thr Gln Pro  Leu Tyr Arg Gly Glu  Leu Asn Glu
    1160                1165                1170

His Leu  Gly Leu Leu Gly Pro  Tyr Ile Arg Ala Glu  Val Glu Asp
    1175                1180                1185

Asn Ile  Met Val Thr Phe Arg  Asn Gln Ala Ser Arg  Pro Tyr Ser
    1190                1195                1200

Phe Tyr  Ser Ser Leu Ile Ser  Tyr Glu Glu Asp Gln  Arg Gln Gly
    1205                1210                1215

Ala Glu  Pro Arg Lys Asn Phe  Val Lys Pro Asn Glu  Thr Lys Thr
    1220                1225                1230

Tyr Phe  Trp Lys Val Gln His  His Met Ala Pro Thr  Lys Asp Glu
    1235                1240                1245

Phe Asp  Cys Lys Ala Trp Ala  Tyr Phe Ser Asp Val  Asp Leu Glu
    1250                1255                1260

Lys Asp  Val His Ser Gly Leu  Ile Gly Pro Leu Leu  Val Cys His
    1265                1270                1275

Thr Asn  Thr Leu Asn Pro Ala  His Gly Arg Gln Val  Thr Val Gln
    1280                1285                1290

Glu Phe  Ala Leu Phe Phe Thr  Ile Phe Asp Glu Thr  Lys Ser Trp
    1295                1300                1305
```

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Tyr Phe  Thr Glu Asn Met Glu  Arg Asn Cys Arg Ala  Pro Cys Asn
    1310                1315                1320

Ile Gln  Met Glu Asp Pro Thr  Phe Lys Glu Asn Tyr  Arg Phe His
    1325                1330                1335

Ala Ile  Asn Gly Tyr Ile Met  Asp Thr Leu Pro Gly  Leu Val Met
    1340                1345                1350

Ala Gln  Asp Gln Arg Ile Arg  Trp Tyr Leu Leu Ser  Met Gly Ser
    1355                1360                1365

Asn Glu  Asn Ile His Ser Ile  His Phe Ser Gly His  Val Phe Thr
    1370                1375                1380

Val Arg  Lys Lys Glu Glu Tyr  Lys Met Ala Leu Tyr  Asn Leu Tyr
    1385                1390                1395

Pro Gly  Val Phe Glu Thr Val  Glu Met Leu Pro Ser  Lys Ala Gly
    1400                1405                1410

Ile Trp  Arg Val Glu Cys Leu  Ile Gly Glu His Leu  His Ala Gly
    1415                1420                1425

Met Ser  Thr Leu Phe Leu Val  Tyr Ser Asn Lys Cys  Gln Thr Pro
    1430                1435                1440

Leu Gly  Met Ala Ser Gly His  Ile Arg Asp Phe Gln  Ile Thr Ala
    1445                1450                1455

Ser Gly  Gln Tyr Gly Gln Trp  Ala Pro Lys Leu Ala  Arg Leu His
    1460                1465                1470

Tyr Ser  Gly Ser Ile Asn Ala  Trp Ser Thr Lys Glu  Pro Phe Ser
    1475                1480                1485

Trp Ile  Lys Val Asp Leu Leu  Ala Pro Met Ile Ile  His Gly Ile
    1490                1495                1500

Lys Thr  Gln Gly Ala Arg Gln  Lys Phe Ser Ser Leu  Tyr Ile Ser
    1505                1510                1515
```

```
Gln Phe  Ile Ile Met Tyr Ser  Leu Asp Gly Lys Lys  Trp Gln Thr
    1520                1525                1530

Tyr Arg  Gly Asn Ser Thr Gly  Thr Leu Met Val Phe  Phe Gly Asn
    1535                1540                1545

Val Asp  Ser Ser Gly Ile Lys  His Asn Ile Phe Asn  Pro Pro Ile
    1550                1555                1560

Ile Ala  Arg Tyr Ile Arg Leu  His Pro Thr His Tyr  Ser Ile Arg
    1565                1570                1575

Ser Thr  Leu Arg Met Glu Leu  Met Gly Cys Asp Leu  Asn Ser Cys
    1580                1585                1590

Ser Met  Pro Leu Gly Met Glu  Ser Lys Ala Ile Ser  Asp Ala Gln
    1595                1600                1605

Ile Thr  Ala Ser Ser Tyr Phe  Thr Asn Met Phe Ala  Thr Trp Ser
    1610                1615                1620

Pro Ser  Lys Ala Arg Leu His  Leu Gln Gly Arg Ser  Asn Ala Trp
    1625                1630                1635

Arg Pro  Gln Val Asn Asn Pro  Lys Glu Trp Leu Gln  Val Asp Phe
    1640                1645                1650

Gln Lys  Thr Met Lys Val Thr  Gly Val Thr Thr Gln  Gly Val Lys
    1655                1660                1665

Ser Leu  Leu Thr Ser Met Tyr  Val Lys Glu Phe Leu  Ile Ser Ser
    1670                1675                1680

Ser Gln  Asp Gly His Gln Trp  Thr Leu Phe Phe Gln  Asn Gly Lys
    1685                1690                1695

Val Lys  Val Phe Gln Gly Asn  Gln Asp Ser Phe Thr  Pro Val Val
    1700                1705                1710

Asn Ser  Leu Asp Pro Pro Leu  Leu Thr Arg Tyr Leu  Arg Ile His
```

```
    1715                1720                1725

Pro Gln  Ser Trp Val His Gln  Ile Ala Leu Arg Met  Glu Val Leu
    1730                1735                1740

Gly Cys  Glu Ala Gln Asp Leu  Tyr Asp Lys Thr His  Thr Cys Pro
    1745                1750                1755

Pro Cys  Pro Ala Pro Glu Leu  Leu Gly Gly Pro Ser  Val Phe Leu
    1760                1765                1770

Phe Pro  Pro Lys Pro Lys Asp  Thr Leu Met Ala Ser  Arg Thr Pro
    1775                1780                1785

Glu Val  Thr Cys Val Val Val  Asp Val Ser His Glu  Asp Pro Glu
    1790                1795                1800

Val Lys  Phe Asn Trp Tyr Val  Asp Gly Val Glu Val  His Asn Ala
    1805                1810                1815

Lys Thr  Lys Pro Arg Glu Glu  Gln Tyr Asn Ser Thr  Tyr Arg Val
    1820                1825                1830

Val Ser  Val Leu Thr Val Leu  Ala Gln Asp Trp Leu  Asn Gly Lys
    1835                1840                1845

Glu Tyr  Lys Cys Lys Val Ser  Asn Lys Ala Leu Pro  Ala Pro Ile
    1850                1855                1860

Glu Lys  Thr Ile Ser Lys Ala  Lys Gly Gln Pro Arg  Glu Pro Gln
    1865                1870                1875

Val Tyr  Thr Leu Pro Pro Ser  Arg Asp Glu Leu Thr  Lys Asn Gln
    1880                1885                1890

Val Ser  Leu Thr Cys Leu Val  Lys Gly Phe Tyr Pro  Ser Asp Ile
    1895                1900                1905

Ala Val  Glu Trp Glu Ser Asn  Gly Gln Pro Glu Asn  Asn Tyr Lys
    1910                1915                1920
```

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
    1925   1930   1935

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    1940   1945   1950

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn Ala Tyr Thr
    1955   1960   1965

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    1970   1975

<210> 162
<211> 5055
<212> DNA
<213> Artificial Sequence

<220>
<223> pSYNFVIII 010 (Dual chain FVIIIFc)

<400> 162
atgcaaatag agctctccac ctgcttcttt ctgtgccttt tgcgattctg ctttagtgcc 60

accagaagat actacctggg tgcagtggaa ctgtcatggg actatatgca aagtgatctc 120

ggtgagctgc ctgtggacgc aagatttcct cctagagtgc caaaatcttt tccattcaac 180

acctcagtcg tgtacaaaaa gactctgttt gtagaattca cggatcacct tttcaacatc 240

gctaagccaa ggccaccctg gatgggtctg ctaggtccta ccatccaggc tgaggtttat 300

gatacagtgg tcattacact taagaacatg gcttcccatc ctgtcagtct tcatgctgtt 360

ggtgtatcct actggaaagc ttctgaggga gctgaatatg atgatcagac cagtcaaagg 420

gagaaagaag atgataaagt cttccctggt ggaagccata catatgtctg gcaggtcctg 480

aaagagaatg gtccaatggc ctctgaccca ctgtgcctta cctactcata tctttctcat 540

gtggacctgg taaaagactt gaattcaggc ctcattggag ccctactagt atgtagagaa 600

gggagtctgg ccaaggaaaa gacacagacc ttgcacaaat ttatactact ttttgctgta 660

tttgatgaag ggaaaagttg gcactcagaa acaaagaact ccttgatgca ggatagggat 720

gctgcatctg ctcgggcctg gcctaaaatg cacacagtca atggttatgt aaacaggtct 780

ctgccaggtc tgattggatg ccacaggaaa tcagtctatt ggcatgtgat tggaatgggc 840

accactcctg aagtgcactc aatattcctc gaaggtcaca catttcttgt gaggaaccat 900

cgccaggcgt ccttggaaat ctcgccaata actttcctta ctgctcaaac actcttgatg 960

gaccttggac agtttctact gttttgtcat atctcttccc accaacatga tggcatggaa 1020

gcttatgtca aagtagacag ctgtccagag gaaccccaac tacgaatgaa aaataatgaa 1080

gaagcggaag actatgatga tgatcttact gattctgaaa tggatgtggt caggtttgat 1140

gatgacaact ctccttcctt tatccaaatt cgctcagttg ccaagaagca tcctaaaact 1200

tgggtacatt acattgctgc tgaagaggag gactgggact atgctccctt agtcctcgcc 1260

cccgatgaca gaagttataa aagtcaatat ttgaacaatg gccctcagcg gattggtagg 1320

aagtacaaaa aagtccgatt tatggcatac acagatgaaa cctttaagac tcgtgaagct 1380

attcagcatg aatcaggaat cttgggacct ttactttatg gggaagttgg agacacactg 1440

ttgattatat ttaagaatca agcaagcaga ccatataaca tctaccctca cggaatcact 1500

gatgtccgtc ctttgtattc aaggagatta ccaaaaggtg taaaacattt gaaggatttt 1560

ccaattctgc caggagaaat attcaaatat aaatggacag tgactgtaga agatgggcca 1620

actaaatcag atcctcggtg cctgacccgc tattactcta gtttcgttaa tatggagaga 1680

gatctagctt caggactcat tggccctctc ctcatctgct acaaagaatc tgtagatcaa 1740

agaggaaacc agataatgtc agacaagagg aatgtcatcc tgttttctgt atttgatgag 1800

aaccgaagct ggtacctcac agagaatata caacgctttc tccccaatcc agctggagtg 1860

cagcttgagg atccagagtt ccaagcctcc aacatcatgc acagcatcaa tggctatgtt 1920

tttgatagtt tgcagttgtc agtttgtttg catgaggtgg catactggta cattctaagc 1980

attggagcac agactgactt cctttctgtc ttcttctctg gatatacctt caaacacaaa 2040

atggtctatg aagacacact caccctattc ccattctcag gagaaactgt cttcatgtcg 2100

atggaaaacc caggtctatg gattctgggg tgccacaact cagactttcg gaacagaggc 2160

atgaccgcct tactgaaggt ttctagttgt gacaagaaca ctggtgatta ttacgaggac 2220

agttatgaag atatttcagc atacttgctg agtaaaaaca atgccattga accaagaagc 2280

ttctctcaaa acccaccagt cttgaaacgc catcaacggg aaataactcg tactactctt 2340

cagtcagatc aagaggaaat tgactatgat gataccatat cagttgaaat gaagaaggaa 2400

gattttgaca tttatgatga ggatgaaaat cagagccccc gcagctttca aaagaaaaca 2460

cgacactatt ttattgctgc agtggagagg ctctgggatt atgggatgag tagctcccca 2520

catgttctaa gaaacagggc tcagagtggc agtgtccctc agttcaagaa agttgttttc 2580

caggaattta ctgatggctc ctttactcag cccttatacc gtggagaact aaatgaacat 2640

ttgggactcc tggggccata tataagagca gaagttgaag ataatatcat ggtaactttc 2700

agaaatcagg cctctcgtcc ctattccttc tattctagcc ttatttctta tgaggaagat 2760

cagaggcaag gagcagaacc tagaaaaaac tttgtcaagc ctaatgaaac caaaacttac 2820

ttttggaaag tgcaacatca tatggcaccc actaaagatg agtttgactg caaagcctgg 2880

gcttatttct ctgatgttga cctggaaaaa gatgtgcact caggcctgat tggacccctt 2940

ctggtctgcc acactaacac actgaaccct gctcatggga gacaagtgac agtacaggaa 3000

tttgctctgt ttttcaccat ctttgatgag accaaaagct ggtacttcac tgaaaatatg 3060

gaaagaaact gcagggctcc ctgcaatatc cagatggaag atcccacttt taaagagaat 3120

tatcgcttcc atgcaatcaa tggctacata atggatacac tacctggctt agtaatggct 3180

caggatcaaa ggattcgatg gtatctgctc agcatgggca gcaatgaaaa catccattct 3240

attcatttca gtggacatgt gttcactgta cgaaaaaaag aggagtataa aatggcactg 3300

tacaatctct atccaggtgt ttttgagaca gtggaaatgt taccatccaa agctggaatt 3360

tggcgggtgg aatgccttat tggcgagcat ctacatgctg ggatgagcac acttttctg 3420

gtgtacagca ataagtgtca gactcccctg ggaatggctt ctggacacat tagagatttt 3480

cagattacag cttcaggaca atatggacag tgggccccaa agctggccag acttcattat 3540

tccggatcaa tcaatgcctg gagcaccaag gagccctttt cttggatcaa ggtggatctg 3600

ttggcaccaa tgattattca cggcatcaag acccagggtg cccgtcagaa gttctccagc 3660

ctctacatct ctcagtttat catcatgtat agtcttgatg ggaagaagtg gcagacttat 3720

cgaggaaatt ccactggaac cttaatggtc ttctttggca atgtggattc atctgggata 3780

aaacacaata tttttaaccc tccaattatt gctcgataca tccgtttgca cccaactcat 3840

tatagcattc gcagcactct tcgcatggag ttgatgggct gtgatttaaa tagttgcagc 3900

atgccattgg gaatggagag taaagcaata tcagatgcac agattactgc ttcatcctac 3960

tttaccaata tgtttgccac ctggtctcct tcaaaagctc gacttcacct ccaagggagg 4020

agtaatgcct ggagacctca ggtgaataat ccaaaagagt ggctgcaagt ggacttccag 4080

aagacaatga aagtcacagg agtaactact cagggagtaa aatctctgct taccagcatg 4140

tatgtgaagg agttcctcat ctccagcagt caagatggcc atcagtggac tctcttttt 4200

cagaatggca aagtaaaggt ttttcaggga aatcaagact ccttcacacc tgtggtgaac 4260

tctctagacc caccgttact gactcgctac cttcgaattc acccccagag ttgggtgcac 4320

cagattgccc tgaggatgga ggttctgggc tgcgaggcac aggacctcta cgacaaaact 4380

cacacatgcc caccgtgccc agctccagaa ctcctgggcg gaccgtcagt cttcctcttc 4440

cccccaaaac ccaaggacac cctcatgatc tcccggaccc ctgaggtcac atgcgtggtg 4500

gtggacgtga gccacgaaga ccctgaggtc aagttcaact ggtacgtgga cggcgtggag 4560

gtgcataatg ccaagacaaa gccgcgggag gagcagtaca acagcacgta ccgtgtggtc 4620

agcgtcctca ccgtcctgca ccaggactgg ctgaatggca aggagtacaa gtgcaaggtc 4680

tccaacaaag ccctcccagc ccccatcgag aaaaccatct ccaaagccaa agggcagccc 4740

cgagaaccac aggtgtacac cctgccccca tcccgggatg agctgaccaa gaaccaggtc 4800

agcctgacct gcctggtcaa aggcttctat cccagcgaca tcgccgtgga gtgggagagc 4860

aatgggcagc cggagaacaa ctacaagacc acgcctcccg tgttggactc cgacggctcc 4920

ttcttcctct acagcaagct caccgtggac aagagcaggt ggcagcaggg gaacgtcttc 4980

tcatgctccg tgatgcatga ggctctgcac aaccactaca cgcagaagag cctctccctg 5040

tctccgggta aatga 5055

<210> 163
<211> 1684
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYNFVIII 010 (Dual chain FVIIIFc)

<400> 163

Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
1 5 10 15

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

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

Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val
50 55 60

```
Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile
65                  70                  75                  80

Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln
                85                  90                  95

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

His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser
        115                 120                 125

Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp
    130                 135                 140

Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu
145                 150                 155                 160

Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser
                165                 170                 175

Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile
            180                 185                 190

Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr
        195                 200                 205

Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly
    210                 215                 220

Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp
225                 230                 235                 240

Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr
                245                 250                 255

Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val
            260                 265                 270

Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile
```

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        275                 280                 285

Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser
    290                 295                 300

Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met
305                 310                 315                 320

Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His
                325                 330                 335

Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro
            340                 345                 350

Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp
        355                 360                 365

Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser
    370                 375                 380

Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
385                 390                 395                 400

Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro
                405                 410                 415

Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
            420                 425                 430

Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met
        435                 440                 445

Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu
    450                 455                 460

Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
465                 470                 475                 480

Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro
                485                 490                 495
```

```
His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys
            500                 505                 510

Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe
        515                 520                 525

Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp
    530                 535                 540

Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg
545                 550                 555                 560

Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu
                565                 570                 575

Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val
            580                 585                 590

Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu
        595                 600                 605

Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp
    610                 615                 620

Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
625                 630                 635                 640

Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp
                645                 650                 655

Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe
            660                 665                 670

Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
        675                 680                 685

Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro
    690                 695                 700

Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly
705                 710                 715                 720
```

```
Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp
                725                 730                 735

Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
            740                 745                 750

Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Pro Pro Val Leu
        755                 760                 765

Lys Arg His Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln
    770                 775                 780

Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu
785                 790                 795                 800

Asp Phe Asp Ile Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe
                805                 810                 815

Gln Lys Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp
            820                 825                 830

Asp Tyr Gly Met Ser Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln
        835                 840                 845

Ser Gly Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr
    850                 855                 860

Asp Gly Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His
865                 870                 875                 880

Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile
                885                 890                 895

Met Val Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser
            900                 905                 910

Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg
        915                 920                 925

Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val
    930                 935                 940
```

```
Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp
945                 950                 955                 960


Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu
                965                 970                 975


Ile Gly Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His
            980                 985                 990


Gly Arg Gln Val Thr Val Gln Glu  Phe Ala Leu Phe Phe  Thr Ile Phe
        995                 1000                1005


Asp Glu  Thr Lys Ser Trp Tyr  Phe Thr Glu Asn Met  Glu Arg Asn
    1010                1015                1020


Cys Arg  Ala Pro Cys Asn Ile  Gln Met Glu Asp Pro  Thr Phe Lys
    1025                1030                1035


Glu Asn  Tyr Arg Phe His Ala  Ile Asn Gly Tyr Ile  Met Asp Thr
    1040                1045                1050


Leu Pro  Gly Leu Val Met Ala  Gln Asp Gln Arg Ile  Arg Trp Tyr
    1055                1060                1065


Leu Leu  Ser Met Gly Ser Asn  Glu Asn Ile His Ser  Ile His Phe
    1070                1075                1080


Ser Gly  His Val Phe Thr Val  Arg Lys Lys Glu Glu  Tyr Lys Met
    1085                1090                1095


Ala Leu  Tyr Asn Leu Tyr Pro  Gly Val Phe Glu Thr  Val Glu Met
    1100                1105                1110


Leu Pro  Ser Lys Ala Gly Ile  Trp Arg Val Glu Cys  Leu Ile Gly
    1115                1120                1125


Glu His  Leu His Ala Gly Met  Ser Thr Leu Phe Leu  Val Tyr Ser
    1130                1135                1140


Asn Lys  Cys Gln Thr Pro Leu  Gly Met Ala Ser Gly  His Ile Arg
```

1145 1150 1155

Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro
1160 1165 1170

Lys Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser
1175 1180 1185

Thr Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro
1190 1195 1200

Met Ile Ile His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe
1205 1210 1215

Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp
1220 1225 1230

Gly Lys Lys Trp Gln Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu
1235 1240 1245

Met Val Phe Phe Gly Asn Val Asp Ser Ser Gly Ile Lys His Asn
1250 1255 1260

Ile Phe Asn Pro Pro Ile Ile Ala Arg Tyr Ile Arg Leu His Pro
1265 1270 1275

Thr His Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly
1280 1285 1290

Cys Asp Leu Asn Ser Cys Ser Met Pro Leu Gly Met Glu Ser Lys
1295 1300 1305

Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser Ser Tyr Phe Thr Asn
1310 1315 1320

Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg Leu His Leu Gln
1325 1330 1335

Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn Pro Lys Glu
1340 1345 1350

```
Trp Leu  Gln Val Asp Phe Gln  Lys Thr Met Lys Val  Thr Gly Val
    1355                1360                1365

Thr Thr  Gln Gly Val Lys Ser  Leu Leu Thr Ser Met  Tyr Val Lys
    1370                1375                1380

Glu Phe  Leu Ile Ser Ser Ser  Gln Asp Gly His Gln  Trp Thr Leu
    1385                1390                1395

Phe Phe  Gln Asn Gly Lys Val  Lys Val Phe Gln Gly  Asn Gln Asp
    1400                1405                1410

Ser Phe  Thr Pro Val Val Asn  Ser Leu Asp Pro Pro  Leu Leu Thr
    1415                1420                1425

Arg Tyr  Leu Arg Ile His Pro  Gln Ser Trp Val His  Gln Ile Ala
    1430                1435                1440

Leu Arg  Met Glu Val Leu Gly  Cys Glu Ala Gln Asp  Leu Tyr Asp
    1445                1450                1455

Lys Thr  His Thr Cys Pro Pro  Cys Pro Ala Pro Glu  Leu Leu Gly
    1460                1465                1470

Gly Pro  Ser Val Phe Leu Phe  Pro Pro Lys Pro Lys  Asp Thr Leu
    1475                1480                1485

Met Ile  Ser Arg Thr Pro Glu  Val Thr Cys Val Val  Val Asp Val
    1490                1495                1500

Ser His  Glu Asp Pro Glu Val  Lys Phe Asn Trp Tyr  Val Asp Gly
    1505                1510                1515

Val Glu  Val His Asn Ala Lys  Thr Lys Pro Arg Glu  Glu Gln Tyr
    1520                1525                1530

Asn Ser  Thr Tyr Arg Val Val  Ser Val Leu Thr Val  Leu His Gln
    1535                1540                1545

Asp Trp  Leu Asn Gly Lys Glu  Tyr Lys Cys Lys Val  Ser Asn Lys
    1550                1555                1560
```

```
Ala Leu  Pro Ala Pro Ile Glu  Lys Thr Ile Ser Lys  Ala Lys Gly
    1565                1570                1575


Gln Pro  Arg Glu Pro Gln Val  Tyr Thr Leu Pro Pro  Ser Arg Asp
    1580                1585                1590


Glu Leu  Thr Lys Asn Gln Val  Ser Leu Thr Cys Leu  Val Lys Gly
    1595                1600                1605


Phe Tyr  Pro Ser Asp Ile Ala  Val Glu Trp Glu Ser  Asn Gly Gln
    1610                1615                1620


Pro Glu  Asn Asn Tyr Lys Thr  Thr Pro Pro Val Leu  Asp Ser Asp
    1625                1630                1635


Gly Ser  Phe Phe Leu Tyr Ser  Lys Leu Thr Val Asp  Lys Ser Arg
    1640                1645                1650


Trp Gln  Gln Gly Asn Val Phe  Ser Cys Ser Val Met  His Glu Ala
    1655                1660                1665


Leu His  Asn His Tyr Thr Gln  Lys Ser Leu Ser Leu  Ser Pro Gly
    1670                1675                1680


Lys
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<210> 164
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker, where the sequence can be repeated betweeen 1-10 times

<400> 164

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Ser Gly Gly Gly Gly Ser
1               5
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<210> 165
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 165

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser
            20

<210> 166
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 166

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1   5   10   15

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Leu Val Pro Arg Gly Ser
            20   25   30

Gly Gly

<210> 167
<211> 314
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN FVIII 169

<400> 167

Pro Arg Ser Phe Ser Gln Asn Gly Ala Pro Gly Thr Ser Glu Ser Ala
1   5   10   15

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
            20   25   30

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser

```
        35                  40                  45

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
    50                  55                  60

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
65                  70                  75                  80

Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr
                85                  90                  95

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr
            100                 105                 110

Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
        115                 120                 125

Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser
    130                 135                 140

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro
145                 150                 155                 160

Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
                165                 170                 175

Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
            180                 185                 190

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr
        195                 200                 205

Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
    210                 215                 220

Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr
225                 230                 235                 240

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro
                245                 250                 255
```

Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
            260   265   270

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
        275   280   285

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Ala Ser Ser Pro Pro Val
    290   295   300

Leu Lys Arg His Gln Ala Glu Ile Thr Arg
305   310

<210> 168
<211> 302
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN FVIII 310

<400> 168

Pro Arg Ser Phe Gly Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
1   5   10   15

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
            20   25   30

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
        35   40   45

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
    50   55   60

Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
65   70   75   80

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser
                85   90   95

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
            100   105   110

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly

```
        115                 120                 125

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly
    130                 135                 140

Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly
145                 150                 155                 160

Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
                165                 170                 175

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser
            180                 185                 190

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
        195                 200                 205

Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
    210                 215                 220

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu
225                 230                 235                 240

Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
                245                 250                 255

Ser Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
            260                 265                 270

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
        275                 280                 285

Pro Ser Glu Gly Ser Ala Pro Ala Ser Ser Glu Ile Thr Arg
    290                 295                 300


<210>  169
<211>  305
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  pSYN FVIII 312
```

<400> 169

```
Pro Arg Ser Phe Ser Gln Asn Gly Ala Pro Gly Thr Ser Glu Ser Ala
1               5                   10                  15

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
            20                  25                  30

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
        35                  40                  45

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
    50                  55                  60

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
65                  70                  75                  80

Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr
                85                  90                  95

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr
            100                 105                 110

Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
        115                 120                 125

Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser
    130                 135                 140

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro
145                 150                 155                 160

Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
                165                 170                 175

Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
            180                 185                 190

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr
        195                 200                 205

Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
```

```
    210                 215                 220

Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr
225                 230                 235                 240

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro
                245                 250                 255

Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
            260                 265                 270

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
        275                 280                 285

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Ala Ser Ser Glu Ile Thr
    290                 295                 300

Arg
305
```

<210> 170
<211> 5892
<212> DNA
<213> Artificial Sequence

<220>
<223> pSYN FVIII 310 (encoding FVIII with complete B-domain deletion except 2 amino acid residues and 288 AE-XTEN inserted after aa 742)

<400> 170
atgcaaatag agctctccac ctgcttcttt ctgtgccttt tgcgattctg ctttagtgcc 60

accagaagat actacctggg tgcagtggaa ctgtcatggg actatatgca aagtgatctc 120

ggtgagctgc ctgtggacgc aagatttcct cctagagtgc caaaatcttt tccattcaac 180

acctcagtcg tgtacaaaaa gactctgttt gtagaattca cggatcacct tttcaacatc 240

gctaagccaa ggccaccctg gatgggtctg ctaggtccta ccatccaggc tgaggtttat 300

gatacagtgg tcattacact taagaacatg gcttcccatc ctgtcagtct tcatgctgtt 360

ggtgtatcct actggaaagc ttctgaggga gctgaatatg atgatcagac cagtcaaagg 420

gagaaagaag atgataaagt cttccctggt ggaagccata catatgtctg gcaggtcctg 480

aaagagaatg gtccaatggc ctctgaccca ctgtgcctta cctactcata tctttctcat 540

gtggacctgg taaaagactt gaattcaggc ctcattggag ccctactagt atgtagagaa 600

gggagtctgg ccaaggaaaa gacacagacc ttgcacaaat ttatactact ttttgctgta 660

tttgatgaag ggaaaagttg gcactcagaa acaaagaact ccttgatgca ggatagggat 720

gctgcatctg ctcgggcctg gcctaaaatg cacacagtca atggttatgt aaacaggtct 780

ctgccaggtc tgattggatg ccacaggaaa tcagtctatt ggcatgtgat tggaatgggc 840

accactcctg aagtgcactc aatattcctc gaaggtcaca catttcttgt gaggaaccat 900

cgccaggcgt ccttggaaat ctcgccaata actttcctta ctgctcaaac actcttgatg 960

gaccttggac agtttctact gttttgtcat atctcttccc accaacatga tggcatggaa 1020

gcttatgtca aagtagacag ctgtccagag gaaccccaac tacgaatgaa aaataatgaa 1080

gaagcggaag actatgatga tgatcttact gattctgaaa tggatgtggt caggtttgat 1140

gatgacaact ctccttcctt tatccaaatt cgctcagttg ccaagaagca tcctaaaact 1200

tgggtacatt acattgctgc tgaagaggag gactgggact atgctccctt agtcctcgcc 1260

cccgatgaca gaagttataa aagtcaatat ttgaacaatg gccctcagcg gattggtagg 1320

aagtacaaaa aagtccgatt tatggcatac acagatgaaa cctttaagac tcgtgaagct 1380

attcagcatg aatcaggaat cttgggacct ttactttatg gggaagttgg agacacactg 1440

ttgattatat ttaagaatca agcaagcaga ccatataaca tctaccctca cggaatcact 1500

gatgtccgtc ctttgtattc aaggagatta ccaaaaggtg taaaacattt gaaggatttt 1560

ccaattctgc caggagaaat attcaaatat aaatggacag tgactgtaga agatgggcca 1620

actaaatcag atcctcggtg cctgacccgc tattactcta gtttcgttaa tatggagaga 1680

gatctagctt caggactcat tggccctctc ctcatctgct acaaagaatc tgtagatcaa 1740

agaggaaacc agataatgtc agacaagagg aatgtcatcc tgttttctgt atttgatgag 1800

aaccgaagct ggtacctcac agagaatata caacgctttc tccccaatcc agctggagtg 1860

cagcttgagg atccagagtt ccaagcctcc aacatcatgc acagcatcaa tggctatgtt 1920

tttgatagtt tgcagttgtc agtttgtttg catgaggtgg catactggta cattctaagc 1980

attggagcac agactgactt cctttctgtc ttcttctctg gatatacctt caaacacaaa 2040

atggtctatg aagacacact caccctattc ccattctcag gagaaactgt cttcatgtcg 2100

atggaaaacc caggtctatg gattctgggg tgccacaact cagactttcg gaacagaggc 2160

atgaccgcct tactgaaggt ttctagttgt gacaagaaca ctggtgatta ttacgaggac 2220

agttatgaag atatttcagc atacttgctg agtaaaaaca atgccattga accaagaagc 2280

ttcggtacct cagagtctgc tacccccgag tcagggccag gatcagagcc agccacctcc 2340

gggtctgaga cacccgggac ttccgagagt gccacccctg agtccggacc cgggtccgag 2400

cccgccactt ccggctccga aactcccggc acaagcgaga gcgctacccc agagtcagga 2460

ccaggaacat ctacagagcc ctctgaaggc tccgctccag ggtccccagc cggcagtccc 2520

actagcaccg aggagggaac ctctgaaagc gccacacccg aatcagggcc agggtctgag 2580

cctgctacca gcggcagcga gacaccaggc acctctgagt ccgccacacc agagtccgga 2640

cccggatctc ccgctgggag ccccacctcc actgaggagg gatctcctgc tggctctcca 2700

acatctactg aggaaggtac ctcaaccgag ccatccgagg gatcagctcc cggcacctca 2760

gagtcggcaa ccccggagtc tggacccgga acttccgaaa gtgccacacc agagtccggt 2820

cccgggactt cagaatcagc aacacccgag tccggccctg ggtctgaacc cgccacaagt 2880

ggtagtgaga caccaggatc agaacctgct acctcagggt cagagacacc cggatctccg 2940

gcaggctcac caacctccac tgaggagggc accagcacag aaccaagcga gggctccgca 3000

cccggaacaa gcactgaacc cagtgagggt tcagcacccg gctctgagcc ggccacaagt 3060

ggcagtgaga cacccggcac ttcagagagt gccacccccg agagtggccc aggcactagt 3120

accgagccct ctgaaggcag tgcgccagcc tcgagcgaaa taactcgtac tactcttcag 3180

tcagatcaag aggaaatcga ttatgatgat accatatcag ttgaaatgaa gaaggaagat 3240

tttgacattt atgatgagga tgaaaatcag agcccccgca gctttcaaaa gaaaacacga 3300

cactatttta ttgctgcagt ggagaggctc tgggattatg ggatgagtag ctccccacat 3360

gttctaagaa acagggctca gagtggcagt gtccctcagt tcaagaaagt tgttttccag 3420

gaatttactg atggctcctt tactcagccc ttataccgtg gagaactaaa tgaacatttg 3480

ggactcctgg ggccatatat aagagcagaa gttgaagata atatcatggt aactttcaga 3540

aatcaggcct ctcgtcccta ttccttctat tctagcctta tttcttatga ggaagatcag 3600

aggcaaggag cagaacctag aaaaaacttt gtcaagccta atgaaaccaa aacttacttt 3660

tggaaagtgc aacatcatat ggcacccact aaagatgagt ttgactgcaa agcctgggct 3720

tatttctctg atgttgacct ggaaaaagat gtgcactcag gcctgattgg acccttctg 3780

gtctgccaca ctaacacact gaaccctgct catgggagac aagtgacagt acaggaattt 3840

gctctgtttt tcaccatctt tgatgagacc aaaagctggt acttcactga aaatatggaa 3900

agaaactgca gggctccctg caatatccag atggaagatc ccacttttaa agagaattat 3960

cgcttccatg caatcaatgg ctacataatg gatacactac ctggcttagt aatggctcag 4020

gatcaaagga ttcgatggta tctgctcagc atgggcagca atgaaaacat ccattctatt 4080

catttcagtg gacatgtgtt cactgtacga aaaaaagagg agtataaaat ggcactgtac 4140

aatctctatc caggtgtttt tgagacagtg gaaatgttac catccaaagc tggaatttgg 4200

cgggtggaat gccttattgg cgagcatcta catgctggga tgagcacact ttttctggtg 4260

tacagcaata agtgtcagac tcccctggga atggcttctg gacacattag agattttcag 4320

attacagctt caggacaata tggacagtgg gccccaaagc tggccagact tcattattcc 4380

ggatcaatca atgcctggag caccaaggag ccctttttctt ggatcaaggt ggatctgttg 4440

gcaccaatga ttattcacgg catcaagacc cagggtgccc gtcagaagtt ctccagcctc 4500

tacatctctc agtttatcat catgtatagt cttgatggga agaagtggca gacttatcga 4560

ggaaattcca ctggaacctt aatggtcttc tttggcaatg tggattcatc tgggataaaa 4620

cacaatattt ttaaccctcc aattattgct cgatacatcc gtttgcaccc aactcattat 4680

agcattcgca gcactcttcg catggagttg atgggctgtg atttaaatag ttgcagcatg 4740

ccattgggaa tggagagtaa agcaatatca gatgcacaga ttactgcttc atcctacttt 4800

accaatatgt ttgccacctg gtctccttca aaagctcgac ttcacctcca agggaggagt 4860

aatgcctgga gacctcaggt gaataatcca aaagagtggc tgcaagtgga cttccagaag 4920

acaatgaaag tcacaggagt aactactcag ggagtaaaat ctctgcttac cagcatgtat 4980

gtgaaggagt tcctcatctc cagcagtcaa gatggccatc agtggactct ctttttcag 5040

aatggcaaag taaaggtttt tcagggaaat caagactcct tcacacctgt ggtgaactct 5100

ctagacccac cgttactgac tcgctacctt cgaattcacc cccagagttg ggtgcaccag 5160

attgccctga ggatggaggt tctgggctgc gaggcacagg acctctacga caaaactcac 5220

acatgcccac cgtgcccagc tccagaactc ctgggcggac cgtcagtctt cctcttcccc 5280

ccaaaaccca aggacaccct catgatctcc cggacccctg aggtcacatg cgtggtggtg 5340

gacgtgagcc acgaagaccc tgaggtcaag ttcaactggt acgtggacgg cgtggaggtg 5400

cataatgcca agacaaagcc gcgggaggag cagtacaaca gcacgtaccg tgtggtcagc 5460

gtcctcaccg tcctgcacca ggactggctg aatggcaagg agtacaagtg caaggtctcc 5520

aacaaagccc tcccagcccc catcgagaaa accatctcca aagccaaagg gcagccccga 5580

gaaccacagg tgtacaccct gcccccatcc cgggatgagc tgaccaagaa ccaggtcagc 5640

ctgacctgcc tggtcaaagg cttctatccc agcgacatcg ccgtggagtg ggagagcaat 5700

gggcagccgg agaacaacta caagaccacg cctcccgtgt tggactccga cggctccttc 5760

ttcctctaca gcaagctcac cgtggacaag agcaggtggc agcaggggaa cgtcttctca 5820

tgctccgtga tgcatgaggc tctgcacaac cactacacgc agaagagcct ctccctgtct 5880

ccgggtaaat ga 5892

<210> 171
<211> 1944
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN FVIII 310 (FVIII with complete B-domain deletion except 2 amino acid residues and 288 AE-XTEN inserted after aa 742)

<400> 171

Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser Trp Asp Tyr
1 5 10 15

Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro
20 25 30

Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys
35 40 45

Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys Pro
50 55 60

Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val
65 70 75 80

Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val
85 90 95

Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala
100 105 110

```
Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val
        115                 120                 125

Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn
    130                 135                 140

Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser
145                 150                 155                 160

His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu
                165                 170                 175

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

His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp
        195                 200                 205

His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser
    210                 215                 220

Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg
225                 230                 235                 240

Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His
                245                 250                 255

Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu
            260                 265                 270

Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile
        275                 280                 285

Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly
    290                 295                 300

Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met
305                 310                 315                 320

Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg
                325                 330                 335
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Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp
            340                 345                 350

Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro Ser Phe
        355                 360                 365

Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His
    370                 375                 380

Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu
385                 390                 395                 400

Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro
                405                 410                 415

Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr
            420                 425                 430

Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile
        435                 440                 445

Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile
    450                 455                 460

Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile
465                 470                 475                 480

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

His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys
            500                 505                 510

Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys
        515                 520                 525

Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala
    530                 535                 540

Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp
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545                 550                 555                 560

Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe
                565                 570                 575

Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln
            580                 585                 590

Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe
        595                 600                 605

Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser
    610                 615                 620

Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu
625                 630                 635                 640

Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr
                645                 650                 655

Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro
            660                 665                 670

Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp
        675                 680                 685

Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr Ala
    690                 695                 700

Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu
705                 710                 715                 720

Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala
                725                 730                 735

Ile Glu Pro Arg Ser Phe Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
            740                 745                 750

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr
        755                 760                 765
```

```
Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr
    770                 775                 780

Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
785                 790                 795                 800

Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser
                805                 810                 815

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala
            820                 825                 830

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
        835                 840                 845

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
    850                 855                 860

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly Ser
865                 870                 875                 880

Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
                885                 890                 895

Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
            900                 905                 910

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala
        915                 920                 925

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
    930                 935                 940

Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser
945                 950                 955                 960

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro
                965                 970                 975

Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
            980                 985                 990
```

```
Ala Pro Gly Ser Glu Pro Ala Thr  Ser Gly Ser Glu Thr  Pro Gly Thr
        995                 1000                1005


Ser Glu  Ser Ala Thr Pro Glu  Ser Gly Pro Gly Thr  Ser Thr Glu
    1010                1015                1020


Pro Ser  Glu Gly Ser Ala Pro  Ala Ser Ser Glu Ile  Thr Arg Thr
    1025                1030                1035


Thr Leu  Gln Ser Asp Gln Glu  Glu Ile Asp Tyr Asp  Asp Thr Ile
    1040                1045                1050


Ser Val  Glu Met Lys Lys Glu  Asp Phe Asp Ile Tyr  Asp Glu Asp
    1055                1060                1065


Glu Asn  Gln Ser Pro Arg Ser  Phe Gln Lys Lys Thr  Arg His Tyr
    1070                1075                1080


Phe Ile  Ala Ala Val Glu Arg  Leu Trp Asp Tyr Gly  Met Ser Ser
    1085                1090                1095


Ser Pro  His Val Leu Arg Asn  Arg Ala Gln Ser Gly  Ser Val Pro
    1100                1105                1110


Gln Phe  Lys Lys Val Val Phe  Gln Glu Phe Thr Asp  Gly Ser Phe
    1115                1120                1125


Thr Gln  Pro Leu Tyr Arg Gly  Glu Leu Asn Glu His  Leu Gly Leu
    1130                1135                1140


Leu Gly  Pro Tyr Ile Arg Ala  Glu Val Glu Asp Asn  Ile Met Val
    1145                1150                1155


Thr Phe  Arg Asn Gln Ala Ser  Arg Pro Tyr Ser Phe  Tyr Ser Ser
    1160                1165                1170


Leu Ile  Ser Tyr Glu Glu Asp  Gln Arg Gln Gly Ala  Glu Pro Arg
    1175                1180                1185


Lys Asn  Phe Val Lys Pro Asn  Glu Thr Lys Thr Tyr  Phe Trp Lys
    1190                1195                1200
```

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Val Gln  His His Met Ala Pro  Thr Lys Asp Glu Phe  Asp Cys Lys
    1205                 1210                 1215

Ala Trp  Ala Tyr Phe Ser Asp  Val Asp Leu Glu Lys  Asp Val His
    1220                 1225                 1230

Ser Gly  Leu Ile Gly Pro Leu  Leu Val Cys His Thr  Asn Thr Leu
    1235                 1240                 1245

Asn Pro  Ala His Gly Arg Gln  Val Thr Val Gln Glu  Phe Ala Leu
    1250                 1255                 1260

Phe Phe  Thr Ile Phe Asp Glu  Thr Lys Ser Trp Tyr  Phe Thr Glu
    1265                 1270                 1275

Asn Met  Glu Arg Asn Cys Arg  Ala Pro Cys Asn Ile  Gln Met Glu
    1280                 1285                 1290

Asp Pro  Thr Phe Lys Glu Asn  Tyr Arg Phe His Ala  Ile Asn Gly
    1295                 1300                 1305

Tyr Ile  Met Asp Thr Leu Pro  Gly Leu Val Met Ala  Gln Asp Gln
    1310                 1315                 1320

Arg Ile  Arg Trp Tyr Leu Leu  Ser Met Gly Ser Asn  Glu Asn Ile
    1325                 1330                 1335

His Ser  Ile His Phe Ser Gly  His Val Phe Thr Val  Arg Lys Lys
    1340                 1345                 1350

Glu Glu  Tyr Lys Met Ala Leu  Tyr Asn Leu Tyr Pro  Gly Val Phe
    1355                 1360                 1365

Glu Thr  Val Glu Met Leu Pro  Ser Lys Ala Gly Ile  Trp Arg Val
    1370                 1375                 1380

Glu Cys  Leu Ile Gly Glu His  Leu His Ala Gly Met  Ser Thr Leu
    1385                 1390                 1395

Phe Leu  Val Tyr Ser Asn Lys  Cys Gln Thr Pro Leu  Gly Met Ala
```

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    1400                1405                1410

Ser Gly  His Ile Arg Asp Phe  Gln Ile Thr Ala Ser  Gly Gln Tyr
    1415                1420                1425

Gly Gln  Trp Ala Pro Lys Leu  Ala Arg Leu His Tyr  Ser Gly Ser
    1430                1435                1440

Ile Asn  Ala Trp Ser Thr Lys  Glu Pro Phe Ser Trp  Ile Lys Val
    1445                1450                1455

Asp Leu  Leu Ala Pro Met Ile  Ile His Gly Ile Lys  Thr Gln Gly
    1460                1465                1470

Ala Arg  Gln Lys Phe Ser Ser  Leu Tyr Ile Ser Gln  Phe Ile Ile
    1475                1480                1485

Met Tyr  Ser Leu Asp Gly Lys  Lys Trp Gln Thr Tyr  Arg Gly Asn
    1490                1495                1500

Ser Thr  Gly Thr Leu Met Val  Phe Phe Gly Asn Val  Asp Ser Ser
    1505                1510                1515

Gly Ile  Lys His Asn Ile Phe  Asn Pro Pro Ile Ile  Ala Arg Tyr
    1520                1525                1530

Ile Arg  Leu His Pro Thr His  Tyr Ser Ile Arg Ser  Thr Leu Arg
    1535                1540                1545

Met Glu  Leu Met Gly Cys Asp  Leu Asn Ser Cys Ser  Met Pro Leu
    1550                1555                1560

Gly Met  Glu Ser Lys Ala Ile  Ser Asp Ala Gln Ile  Thr Ala Ser
    1565                1570                1575

Ser Tyr  Phe Thr Asn Met Phe  Ala Thr Trp Ser Pro  Ser Lys Ala
    1580                1585                1590

Arg Leu  His Leu Gln Gly Arg  Ser Asn Ala Trp Arg  Pro Gln Val
    1595                1600                1605
```

```
Asn Asn  Pro Lys Glu Trp Leu  Gln Val Asp Phe Gln  Lys Thr Met
    1610                 1615                 1620

Lys Val  Thr Gly Val Thr Thr  Gln Gly Val Lys Ser  Leu Leu Thr
    1625                 1630                 1635

Ser Met  Tyr Val Lys Glu Phe  Leu Ile Ser Ser Ser  Gln Asp Gly
    1640                 1645                 1650

His Gln  Trp Thr Leu Phe Phe  Gln Asn Gly Lys Val  Lys Val Phe
    1655                 1660                 1665

Gln Gly  Asn Gln Asp Ser Phe  Thr Pro Val Val Asn  Ser Leu Asp
    1670                 1675                 1680

Pro Pro  Leu Leu Thr Arg Tyr  Leu Arg Ile His Pro  Gln Ser Trp
    1685                 1690                 1695

Val His  Gln Ile Ala Leu Arg  Met Glu Val Leu Gly  Cys Glu Ala
    1700                 1705                 1710

Gln Asp  Leu Tyr Asp Lys Thr  His Thr Cys Pro Pro  Cys Pro Ala
    1715                 1720                 1725

Pro Glu  Leu Leu Gly Gly Pro  Ser Val Phe Leu Phe  Pro Pro Lys
    1730                 1735                 1740

Pro Lys  Asp Thr Leu Met Ile  Ser Arg Thr Pro Glu  Val Thr Cys
    1745                 1750                 1755

Val Val  Val Asp Val Ser His  Glu Asp Pro Glu Val  Lys Phe Asn
    1760                 1765                 1770

Trp Tyr  Val Asp Gly Val Glu  Val His Asn Ala Lys  Thr Lys Pro
    1775                 1780                 1785

Arg Glu  Glu Gln Tyr Asn Ser  Thr Tyr Arg Val Val  Ser Val Leu
    1790                 1795                 1800

Thr Val  Leu His Gln Asp Trp  Leu Asn Gly Lys Glu  Tyr Lys Cys
    1805                 1810                 1815
```

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
1820 1825 1830

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
1835 1840 1845

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
1850 1855 1860

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
1865 1870 1875

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
1880 1885 1890

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
1895 1900 1905

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
1910 1915 1920

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
1925 1930 1935

Ser Leu Ser Pro Gly Lys
1940

<210> 172
<211> 5900
<212> DNA
<213> Artificial Sequence

<220>
<223> pSYN FVIII 312 (FVIII with complete B-domain deletion except 5 amino acid residues and 288 AE-XTEN inserted after aa 745- FVIII B5 version)

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ggtgagctgc ctgtggacgc aagatttcct cctagagtgc caaaatcttt tccattcaac 180

acctcagtcg tgtacaaaaa gactctgttt gtagaattca cggatcacct tttcaacatc 240

gctaagccaa ggccaccctg gatgggtctg ctaggtccta ccatccaggc tgaggtttat 300

gatacagtgg tcattacact taagaacatg gcttcccatc ctgtcagtct tcatgctgtt 360

ggtgtatcct actggaaagc ttctgaggga gctgaatatg atgatcagac cagtcaaagg 420

gagaaagaag atgataaagt cttccctggt ggaagccata catatgtctg gcaggtcctg 480

aaagagaatg gtccaatggc ctctgaccca ctgtgcctta cctactcata tctttctcat 540

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tttgatgaag ggaaaagttg gcactcagaa acaaagaact ccttgatgca ggatagggat 720

gctgcatctg ctcgggcctg gcctaaaatg cacacagtca atggttatgt aaacaggtct 780

ctgccaggtc tgattggatg ccacaggaaa tcagtctatt ggcatgtgat tggaatgggc 840

accactcctg aagtgcactc aatattcctc gaaggtcaca catttcttgt gaggaaccat 900

cgccaggcgt ccttggaaat ctcgccaata actttcctta ctgctcaaac actcttgatg 960

gaccttggac agtttctact gttttgtcat atctcttccc accaacatga tggcatggaa 1020

gcttatgtca aagtagacag ctgtccagag gaaccccaac tacgaatgaa aaataatgaa 1080

gaagcggaag actatgatga tgatcttact gattctgaaa tggatgtggt caggtttgat 1140

gatgacaact ctccttcctt tatccaaatt cgctcagttg ccaagaagca tcctaaaact 1200

tgggtacatt acattgctgc tgaagaggag gactgggact atgctccctt agtcctcgcc 1260

cccgatgaca gaagttataa aagtcaatat ttgaacaatg gccctcagcg gattggtagg 1320

aagtacaaaa aagtccgatt tatggcatac acagatgaaa cctttaagac tcgtgaagct 1380

attcagcatg aatcaggaat cttgggacct ttactttatg gggaagttgg agacacactg 1440

ttgattatat ttaagaatca agcaagcaga ccatataaca tctaccctca cggaatcact 1500

gatgtccgtc ctttgtattc aaggagatta ccaaaaggtg taaaacattt gaaggatttt 1560

ccaattctgc caggagaaat attcaaatat aaatggacag tgactgtaga agatgggcca 1620

actaaatcag atcctcggtg cctgacccgc tattactcta gtttcgttaa tatggagaga 1680

gatctagctt caggactcat tggccctctc ctcatctgct acaaagaatc tgtagatcaa 1740

agaggaaacc agataatgtc agacaagagg aatgtcatcc tgttttctgt atttgatgag 1800

aaccgaagct ggtacctcac agagaatata caacgctttc tccccaatcc agctggagtg 1860

cagcttgagg atccagagtt ccaagcctcc aacatcatgc acagcatcaa tggctatgtt 1920

tttgatagtt tgcagttgtc agtttgtttg catgaggtgg catactggta cattctaagc 1980

attggagcac agactgactt cctttctgtc ttcttctctg gatatacctt caaacacaaa 2040

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atggaaaacc caggtctatg gattctgggg tgccacaact cagactttcg gaacagaggc 2160

atgaccgcct tactgaaggt ttctagttgt gacaagaaca ctggtgatta ttacgaggac 2220

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ggctccgcac ccggaacaag cactgaaccc agtgagggtt cagcacccgg ctctgagccg 3060

gccacaagtg gcagtgagac acccggcact tcagagagtg ccacccccga gagtggccca 3120

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aaggaagatt ttgacattta tgatgaggat gaaaatcaga gcccccgcag ctttcaaaag 3300

aaaacacgac actattttat tgctgcagtg gagaggctct gggattatgg gatgagtagc 3360

tccccacatg ttctaagaaa cagggctcag agtggcagtg tccctcagtt caagaaagtt 3420

gttttccagg aatttactga tggctccttt actcagccct tataccgtgg agaactaaat 3480

gaacatttgg gactcctggg gccatatata agagcagaag ttgaagataa tatcatggta 3540

actttcagaa atcaggcctc tcgtccctat tccttctatt ctagccttat ttcttatgag 3600

gaagatcaga ggcaaggagc agaacctaga aaaaactttg tcaagcctaa tgaaaccaaa 3660

acttactttt ggaaagtgca acatcatatg gcacccacta aagatgagtt tgactgcaaa 3720

gcctgggctt atttctctga tgttgacctg gaaaaagatg tgcactcagg cctgattgga 3780

ccccttctgg tctgccacac taacacactg aaccctgctc atgggagaca agtgacagta 3840

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gcactgtaca atctctatcc aggtgttttt gagacagtgg aaatgttacc atccaaagct 4200

ggaatttggc gggtggaatg ccttattggc gagcatctac atgctgggat gagcacactt 4260

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gtgaactctc tagacccacc gttactgact cgctaccttc gaattcaccc ccagagttgg 5160

gtgcaccaga ttgccctgag gatggaggtt ctgggctgcg aggcacagga cctctacgac 5220

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gtggtcagcg tcctcaccgt cctgcaccag gactggctga atggcaagga gtacaagtgc 5520

aaggtctcca acaaagccct cccagccccc atcgagaaaa ccatctccaa agccaaaggg 5580

cagccccgag aaccacaggt gtacaccctg cccccatccc gggatgagct gaccaagaac 5640

caggtcagcc tgacctgcct ggtcaaaggc ttctatccca gcgacatcgc cgtggagtgg 5700

gagagcaatg ggcagccgga gaacaactac aagaccacgc ctcccgtgtt ggactccgac 5760

ggctccttct tcctctacag caagctcacc gtggacaaga gcaggtggca gcaggggaac 5820

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<210> 173
<211> 1947
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN FVIII 312 (FVIII with complete B-domain deletion except 5 amino acid residues and 288 AE-XTEN inserted after aa 745- FVIII B5 version)

<400> 173

Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser Trp Asp Tyr
1 5 10 15

Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro
20 25 30

Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys
35 40 45

Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys Pro
50 55 60

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Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val
65                  70                  75                  80

Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val
                85                  90                  95

Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala
            100                 105                 110

Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val
        115                 120                 125

Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn
    130                 135                 140

Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser
145                 150                 155                 160

His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu
                165                 170                 175

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

His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp
        195                 200                 205

His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser
    210                 215                 220

Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg
225                 230                 235                 240

Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His
                245                 250                 255

Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu
            260                 265                 270

Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile
        275                 280                 285
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Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly
    290                 295                 300

Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met
305                 310                 315                 320

Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg
                325                 330                 335

Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp
            340                 345                 350

Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro Ser Phe
        355                 360                 365

Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His
    370                 375                 380

Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu
385                 390                 395                 400

Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro
                405                 410                 415

Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr
            420                 425                 430

Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile
        435                 440                 445

Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile
    450                 455                 460

Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile
465                 470                 475                 480

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

His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys
            500                 505                 510
```

```
Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys
        515                 520                 525

Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala
    530                 535                 540

Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp
545                 550                 555                 560

Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe
                565                 570                 575

Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln
            580                 585                 590

Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe
        595                 600                 605

Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser
    610                 615                 620

Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu
625                 630                 635                 640

Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr
                645                 650                 655

Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro
            660                 665                 670

Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp
        675                 680                 685

Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr Ala
    690                 695                 700

Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu
705                 710                 715                 720

Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala
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                725                 730                 735

Ile Glu Pro Arg Ser Phe Ser Gln Asn Gly Thr Ser Glu Ser Ala Thr
            740                 745                 750

Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr
        755                 760                 765

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu
    770                 775                 780

Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr
785                 790                 795                 800

Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
                805                 810                 815

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser
            820                 825                 830

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
        835                 840                 845

Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
    850                 855                 860

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro
865                 870                 875                 880

Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser
                885                 890                 895

Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
            900                 905                 910

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser
        915                 920                 925

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
    930                 935                 940
```

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Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr
945                 950                 955                 960


Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser
                965                 970                 975


Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser
            980                 985                 990


Glu Gly Ser Ala Pro Gly Ser Glu  Pro Ala Thr Ser Gly  Ser Glu Thr
        995                 1000                1005


Pro Gly  Thr Ser Glu Ser Ala  Thr Pro Glu Ser Gly  Pro Gly Thr
    1010                1015                1020


Ser Thr  Glu Pro Ser Glu Gly  Ser Ala Pro Ala Ser  Ser Glu Ile
    1025                1030                1035


Thr Arg  Thr Thr Leu Gln Ser  Asp Gln Glu Glu Ile  Asp Tyr Asp
    1040                1045                1050


Asp Thr  Ile Ser Val Glu Met  Lys Lys Glu Asp Phe  Asp Ile Tyr
    1055                1060                1065


Asp Glu  Asp Glu Asn Gln Ser  Pro Arg Ser Phe Gln  Lys Lys Thr
    1070                1075                1080


Arg His  Tyr Phe Ile Ala Ala  Val Glu Arg Leu Trp  Asp Tyr Gly
    1085                1090                1095


Met Ser  Ser Ser Pro His Val  Leu Arg Asn Arg Ala  Gln Ser Gly
    1100                1105                1110


Ser Val  Pro Gln Phe Lys Lys  Val Val Phe Gln Glu  Phe Thr Asp
    1115                1120                1125


Gly Ser  Phe Thr Gln Pro Leu  Tyr Arg Gly Glu Leu  Asn Glu His
    1130                1135                1140


Leu Gly  Leu Leu Gly Pro Tyr  Ile Arg Ala Glu Val  Glu Asp Asn
    1145                1150                1155
```

```
Ile Met  Val Thr Phe Arg Asn  Gln Ala Ser Arg Pro  Tyr Ser Phe
    1160                 1165                 1170

Tyr Ser  Ser Leu Ile Ser Tyr  Glu Glu Asp Gln Arg  Gln Gly Ala
    1175                 1180                 1185

Glu Pro  Arg Lys Asn Phe Val  Lys Pro Asn Glu Thr  Lys Thr Tyr
    1190                 1195                 1200

Phe Trp  Lys Val Gln His His  Met Ala Pro Thr Lys  Asp Glu Phe
    1205                 1210                 1215

Asp Cys  Lys Ala Trp Ala Tyr  Phe Ser Asp Val Asp  Leu Glu Lys
    1220                 1225                 1230

Asp Val  His Ser Gly Leu Ile  Gly Pro Leu Leu Val  Cys His Thr
    1235                 1240                 1245

Asn Thr  Leu Asn Pro Ala His  Gly Arg Gln Val Thr  Val Gln Glu
    1250                 1255                 1260

Phe Ala  Leu Phe Phe Thr Ile  Phe Asp Glu Thr Lys  Ser Trp Tyr
    1265                 1270                 1275

Phe Thr  Glu Asn Met Glu Arg  Asn Cys Arg Ala Pro  Cys Asn Ile
    1280                 1285                 1290

Gln Met  Glu Asp Pro Thr Phe  Lys Glu Asn Tyr Arg  Phe His Ala
    1295                 1300                 1305

Ile Asn  Gly Tyr Ile Met Asp  Thr Leu Pro Gly Leu  Val Met Ala
    1310                 1315                 1320

Gln Asp  Gln Arg Ile Arg Trp  Tyr Leu Leu Ser Met  Gly Ser Asn
    1325                 1330                 1335

Glu Asn  Ile His Ser Ile His  Phe Ser Gly His Val  Phe Thr Val
    1340                 1345                 1350

Arg Lys  Lys Glu Glu Tyr Lys  Met Ala Leu Tyr Asn  Leu Tyr Pro
    1355                 1360                 1365
```

```
Gly Val  Phe Glu Thr Val Glu  Met Leu Pro Ser Lys  Ala Gly Ile
    1370                1375                1380

Trp Arg  Val Glu Cys Leu Ile  Gly Glu His Leu His  Ala Gly Met
    1385                1390                1395

Ser Thr  Leu Phe Leu Val Tyr  Ser Asn Lys Cys Gln  Thr Pro Leu
    1400                1405                1410

Gly Met  Ala Ser Gly His Ile  Arg Asp Phe Gln Ile  Thr Ala Ser
    1415                1420                1425

Gly Gln  Tyr Gly Gln Trp Ala  Pro Lys Leu Ala Arg  Leu His Tyr
    1430                1435                1440

Ser Gly  Ser Ile Asn Ala Trp  Ser Thr Lys Glu Pro  Phe Ser Trp
    1445                1450                1455

Ile Lys  Val Asp Leu Leu Ala  Pro Met Ile Ile His  Gly Ile Lys
    1460                1465                1470

Thr Gln  Gly Ala Arg Gln Lys  Phe Ser Ser Leu Tyr  Ile Ser Gln
    1475                1480                1485

Phe Ile  Ile Met Tyr Ser Leu  Asp Gly Lys Lys Trp  Gln Thr Tyr
    1490                1495                1500

Arg Gly  Asn Ser Thr Gly Thr  Leu Met Val Phe Phe  Gly Asn Val
    1505                1510                1515

Asp Ser  Ser Gly Ile Lys His  Asn Ile Phe Asn Pro  Pro Ile Ile
    1520                1525                1530

Ala Arg  Tyr Ile Arg Leu His  Pro Thr His Tyr Ser  Ile Arg Ser
    1535                1540                1545

Thr Leu  Arg Met Glu Leu Met  Gly Cys Asp Leu Asn  Ser Cys Ser
    1550                1555                1560

Met Pro  Leu Gly Met Glu Ser  Lys Ala Ile Ser Asp  Ala Gln Ile
```

```
    1565                1570                1575

Thr Ala  Ser Ser Tyr Phe Thr  Asn Met Phe Ala Thr  Trp Ser Pro
    1580                1585                1590

Ser Lys  Ala Arg Leu His Leu  Gln Gly Arg Ser Asn  Ala Trp Arg
    1595                1600                1605

Pro Gln  Val Asn Asn Pro Lys  Glu Trp Leu Gln Val  Asp Phe Gln
    1610                1615                1620

Lys Thr  Met Lys Val Thr Gly  Val Thr Thr Gln Gly  Val Lys Ser
    1625                1630                1635

Leu Leu  Thr Ser Met Tyr Val  Lys Glu Phe Leu Ile  Ser Ser Ser
    1640                1645                1650

Gln Asp  Gly His Gln Trp Thr  Leu Phe Phe Gln Asn  Gly Lys Val
    1655                1660                1665

Lys Val  Phe Gln Gly Asn Gln  Asp Ser Phe Thr Pro  Val Val Asn
    1670                1675                1680

Ser Leu  Asp Pro Pro Leu Leu  Thr Arg Tyr Leu Arg  Ile His Pro
    1685                1690                1695

Gln Ser  Trp Val His Gln Ile  Ala Leu Arg Met Glu  Val Leu Gly
    1700                1705                1710

Cys Glu  Ala Gln Asp Leu Tyr  Asp Lys Thr His Thr  Cys Pro Pro
    1715                1720                1725

Cys Pro  Ala Pro Glu Leu Leu  Gly Gly Pro Ser Val  Phe Leu Phe
    1730                1735                1740

Pro Pro  Lys Pro Lys Asp Thr  Leu Met Ile Ser Arg  Thr Pro Glu
    1745                1750                1755

Val Thr  Cys Val Val Val Asp  Val Ser His Glu Asp  Pro Glu Val
    1760                1765                1770
```

```
Lys Phe  Asn Trp Tyr Val Asp  Gly Val Glu Val His  Asn Ala Lys
    1775                1780                1785

Thr Lys  Pro Arg Glu Glu Gln  Tyr Asn Ser Thr Tyr  Arg Val Val
    1790                1795                1800

Ser Val  Leu Thr Val Leu His  Gln Asp Trp Leu Asn  Gly Lys Glu
    1805                1810                1815

Tyr Lys  Cys Lys Val Ser Asn  Lys Ala Leu Pro Ala  Pro Ile Glu
    1820                1825                1830

Lys Thr  Ile Ser Lys Ala Lys  Gly Gln Pro Arg Glu  Pro Gln Val
    1835                1840                1845

Tyr Thr  Leu Pro Pro Ser Arg  Asp Glu Leu Thr Lys  Asn Gln Val
    1850                1855                1860

Ser Leu  Thr Cys Leu Val Lys  Gly Phe Tyr Pro Ser  Asp Ile Ala
    1865                1870                1875

Val Glu  Trp Glu Ser Asn Gly  Gln Pro Glu Asn Asn  Tyr Lys Thr
    1880                1885                1890

Thr Pro  Pro Val Leu Asp Ser  Asp Gly Ser Phe Phe  Leu Tyr Ser
    1895                1900                1905

Lys Leu  Thr Val Asp Lys Ser  Arg Trp Gln Gln Gly  Asn Val Phe
    1910                1915                1920

Ser Cys  Ser Val Met His Glu  Ala Leu His Asn His  Tyr Thr Gln
    1925                1930                1935

Lys Ser  Leu Ser Leu Ser Pro  Gly Lys
    1940                1945
```

<210> 174
<211> 4977
<212> DNA
<213> Artificial Sequence

<220>
<223> pSYN VWF073 (VWFD1D2D'D3- 144 AE XTEN- FVIII truncated a2

thrombin site-Fc)

<400> 174
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gacttcgtca acacctttga tgggagcatg tacagctttg cgggatactg cagttacctc 180

ctggcagggg gctgccagaa acgctccttc tcgattattg gggacttcca gaatggcaag 240

agagtgagcc tctccgtgta tcttggggaa ttttttgaca tccatttgtt tgtcaatggt 300

accgtgacac agggggacca aagagtctcc atgccctatg cctccaaagg gctgtatcta 360

gaaactgagg ctgggtacta caagctgtcc ggtgaggcct atggctttgt ggccaggatc 420

gatggcagcg gcaactttca agtcctgctg tcagacagat acttcaacaa gacctgcggg 480

ctgtgtggca actttaacat ctttgctgaa gatgacttta tgacccaaga agggaccttg 540

acctcggacc cttatgactt tgccaactca tgggctctga gcagtggaga acagtggtgt 600

gaacgggcat ctcctcccag cagctcatgc aacatctcct ctggggaaat gcagaagggc 660

ctgtgggagc agtgccagct tctgaagagc acctcggtgt ttgcccgctg ccaccctctg 720

gtggaccccg agccttttgt ggccctgtgt gagaagactt tgtgtgagtg tgctgggggg 780

ctggagtgcg cctgccctgc cctcctggag tacgcccgga cctgtgccca ggagggaatg 840

gtgctgtacg gctggaccga ccacagcgcg tgcagcccag tgtgccctgc tggtatggag 900

tataggcagt gtgtgtcccc ttgcgccagg acctgccaga gcctgcacat caatgaaatg 960

tgtcaggagc gatgcgtgga tggctgcagc tgccctgagg gacagctcct ggatgaaggc 1020

ctctgcgtgg agagcaccga gtgtccctgc gtgcattccg gaaagcgcta ccctcccggc 1080

acctccctct ctcgagactg caacacctgc atttgccgaa acagccagtg gatctgcagc 1140

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cgcatccagc atacagtgac ggcctccgtg cgcctcagct acggggagga cctgcagatg 1500

gactgggatg gccgcgggag gctgctggtg aagctgtccc ccgtctatgc cgggaagacc 1560

tgcggcctgt gtgggaatta caatggcaac cagggcgacg acttccttac cccctctggg 1620

ctggcggagc cccgggtgga ggacttcggg aacgcctgga agctgcacgg ggactgccag 1680

gacctgcaga agcagcacag cgatccctgc gccctcaacc cgcgcatgac caggttctcc 1740

gaggaggcgt gcgcggtcct gacgtccccc acattcgagg cctgccatcg tgccgtcagc 1800

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tgcctgtgcg gcgccctggc cagctatgcc gcggcctgcg cggggagagg cgtgcgcgtc 1920

gcgtggcgcg agccaggccg ctgtgagctg aactgcccga aaggccaggt gtacctgcag 1980

tgcgggaccc cctgcaacct gacctgccgc tctctctctt acccggatga ggaatgcaat 2040

gaggcctgcc tggagggctg cttctgcccc ccagggctct acatggatga gaggggggac 2100

tgcgtgccca aggcccagtg cccctgttac tatgacggtg agatcttcca gccagaagac 2160

atcttctcag accatcacac catgtgctac tgtgaggatg gcttcatgca ctgtaccatg 2220

agtggagtcc ccggaagctt gctgcctgac gctgtcctca gcagtcccct gtctcatcgc 2280

agcaaaagga gcctatcctg tcggcccccc atggtcaagc tggtgtgtcc cgctgacaac 2340

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catgtgtgtg atgccacgtg ctccacgatc ggcatggccc actacctcac cttcgacggg 2640

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aaccctggga cctttcggat cctagtgggg aataagggat gcagccaccc ctcagtgaaa 2760

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gagccactgg cctgccctgt gcagtgtgtg gagggctgcc atgcccactg ccctccaggg 3540

aaaatcctgg atgagctttt gcagacctgc gttgaccctg aagactgtcc agtgtgtgag 3600

gtggctggcc ggcgttttgc ctcaggaaag aaagtcacct tgaatcccag tgaccctgag 3660

cactgccaga tttgccactg tgatgttgtc aacctcacct gtgaagcctg ccaggagccg 3720

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gaacccgcta cctcaggcag tgagacgcca ggaacgagcg agtccgctac accggagagt 4080

gggccaggga gccctgctgg atctcctacg tccactgagg aagggtcacc agcgggctcg 4140

cccaccagca ctgaagaagg tgcctcgagc ggcggtggag gatccggtgg cgggggatcc 4200

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gcccccatcg agaaaaccat ctccaaagcc aaagggcagc cccgagaacc acaggtgtac 4680

accctgcccc catcccggga tgagctgacc aagaaccagg tcagcctgac ctgcctggtc 4740

aaaggcttct atcccagcga catcgccgtg gagtgggaga gcaatgggca gccggagaac 4800

aactacaaga ccacgcctcc cgtgttggac tccgacggct ccttcttcct ctacagcaag 4860

ctcaccgtgg acaagagcag gtggcagcag gggaacgtct tctcatgctc cgtgatgcat 4920

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<210> 175
<211> 1658
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN VWF073 (VWFD1D2D'D3- 144 AE XTEN- truncated a2 thrombin site-Fc)

<400> 175

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

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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
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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
```

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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

Ala 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 Ala 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 Ala Pro Thr Ser  Glu Ser Ala
    1235                1240                1245
```

```
Thr Pro  Glu Ser Gly Pro Gly  Ser Glu Pro Ala Thr  Ser Gly Ser
    1250                 1255                 1260

Glu Thr  Pro Gly Thr Ser Glu  Ser Ala Thr Pro Glu  Ser Gly Pro
    1265                 1270                 1275

Gly Ser  Glu Pro Ala Thr Ser  Gly Ser Glu Thr Pro  Gly Thr Ser
    1280                 1285                 1290

Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly Thr Ser  Thr Glu Pro
    1295                 1300                 1305

Ser Glu  Gly Ser Ala Pro Gly  Ser Pro Ala Gly Ser  Pro Thr Ser
    1310                 1315                 1320

Thr Glu  Glu Gly Thr Ser Glu  Ser Ala Thr Pro Glu  Ser Gly Pro
    1325                 1330                 1335

Gly Ser  Glu Pro Ala Thr Ser  Gly Ser Glu Thr Pro  Gly Thr Ser
    1340                 1345                 1350

Glu Ser  Ala Thr Pro Glu Ser  Gly Pro Gly Ser Pro  Ala Gly Ser
    1355                 1360                 1365

Pro Thr  Ser Thr Glu Glu Gly  Ser Pro Ala Gly Ser  Pro Thr Ser
    1370                 1375                 1380

Thr Glu  Glu Gly Ala Ser Ser  Gly Gly Gly Gly Ser  Gly Gly Gly
    1385                 1390                 1395

Gly Ser  Gly Gly Gly Gly Ser  Gly Gly Gly Gly Ser  Gly Gly Gly
    1400                 1405                 1410

Gly Ser  Gly Gly Gly Gly Ser  Ile Glu Pro Arg Ser  Phe Ser Gly
    1415                 1420                 1425

Ser Gly  Gly Asp Lys Thr His  Thr Cys Pro Pro Cys  Pro Ala Pro
    1430                 1435                 1440

Glu Leu  Leu Gly Gly Pro Ser  Val Phe Leu Phe Pro  Pro Lys Pro
```

```
    1445                1450                1455

Lys Asp  Thr Leu Met Ile Ser  Arg Thr Pro Glu Val  Thr Cys Val
    1460                1465                1470

Val Val  Asp Val Ser His Glu  Asp Pro Glu Val Lys  Phe Asn Trp
    1475                1480                1485

Tyr Val  Asp Gly Val Glu Val  His Asn Ala Lys Thr  Lys Pro Arg
    1490                1495                1500

Glu Glu  Gln Tyr Asn Ser Thr  Tyr Arg Val Val Ser  Val Leu Thr
    1505                1510                1515

Val Leu  His Gln Asp Trp Leu  Asn Gly Lys Glu Tyr  Lys Cys Lys
    1520                1525                1530

Val Ser  Asn Lys Ala Leu Pro  Ala Pro Ile Glu Lys  Thr Ile Ser
    1535                1540                1545

Lys Ala  Lys Gly Gln Pro Arg  Glu Pro Gln Val Tyr  Thr Leu Pro
    1550                1555                1560

Pro Ser  Arg Asp Glu Leu Thr  Lys Asn Gln Val Ser  Leu Thr Cys
    1565                1570                1575

Leu Val  Lys Gly Phe Tyr Pro  Ser Asp Ile Ala Val  Glu Trp Glu
    1580                1585                1590

Ser Asn  Gly Gln Pro Glu Asn  Asn Tyr Lys Thr Thr  Pro Pro Val
    1595                1600                1605

Leu Asp  Ser Asp Gly Ser Phe  Phe Leu Tyr Ser Lys  Leu Thr Val
    1610                1615                1620

Asp Lys  Ser Arg Trp Gln Gln  Gly Asn Val Phe Ser  Cys Ser Val
    1625                1630                1635

Met His  Glu Ala Leu His Asn  His Tyr Thr Gln Lys  Ser Leu Ser
    1640                1645                1650
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Leu Ser Pro Gly Lys
    1655

<210> 176
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 176

Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn
1   5   10   15

Asn Ala Ile Glu Pro Arg Ser Phe Ser
            20   25

<210> 177
<211> 24
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 177

Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn
1   5   10   15

Ala Ile Glu Pro Arg Ser Phe Ser
            20

<210> 178
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 178

Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala
1   5   10   15

Ile Glu Pro Arg Ser Phe Ser

20

<210> 179
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 179

Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile
1 5 10 15

Glu Pro Arg Ser Phe Ser
20

<210> 180
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 180

Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu
1 5 10 15

Pro Arg Ser Phe Ser
20

<210> 181
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 181

Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro
1 5 10 15

Arg Ser Phe Ser
20

<210> 182
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 182

Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg
1   5   10   15

Ser Phe Ser

<210> 183
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 183

Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser
1   5   10   15

Phe Ser

<210> 184
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 184

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

Ser

<210> 185
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 185

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

<210> 186
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 186

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

<210> 187
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 187

Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
1   5   10

<210> 188
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 188

Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
1   5   10

<210> 189
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 189

Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
1 5 10

<210> 190
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 190

Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
1 5 10

<210> 191
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 191

Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser
1 5 10

<210> 192
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 192

Asn Ala Ile Glu Pro Arg Ser Phe Ser

1 5

<210> 193
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 193

Ala Ile Glu Pro Arg Ser Phe Ser
1 5

<210> 194
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 194

Ile Glu Pro Arg Ser Phe Ser
1 5

<210> 195
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 195

Glu Pro Arg Ser Phe Ser
1 5

<210> 196
<211> 4959
<212> DNA
<213> Artificial Sequence

<220>
<223> pSYN VWF059 (VWF D'D3-Fc with acidic region 2 (a2) thrombin site in the linker)

<400> 196

atgattcctg ccagatttgc cggggtgctg cttgctctgg ccctcatttt gccagggacc 60

ctttgtgcag aaggaactcg cggcaggtca tccacggccc gatgcagcct tttcggaagt 120

gacttcgtca acacctttga tgggagcatg tacagctttg cgggatactg cagttacctc 180

ctggcagggg gctgccagaa acgctccttc tcgattattg gggacttcca gaatggcaag 240

agagtgagcc tctccgtgta tcttggggaa ttttttgaca tccatttgtt tgtcaatggt 300

accgtgacac agggggacca aagagtctcc atgccctatg cctccaaagg gctgtatcta 360

gaaactgagg ctgggtacta caagctgtcc ggtgaggcct atggctttgt ggccaggatc 420

gatggcagcg gcaactttca agtcctgctg tcagacagat acttcaacaa gacctgcggg 480

ctgtgtggca actttaacat ctttgctgaa gatgacttta tgacccaaga agggaccttg 540

acctcggacc cttatgactt tgccaactca tgggctctga gcagtggaga acagtggtgt 600

gaacgggcat ctcctcccag cagctcatgc aacatctcct ctggggaaat gcagaagggc 660

ctgtgggagc agtgccagct tctgaagagc acctcggtgt ttgcccgctg ccaccctctg 720

gtggaccccg agccttttgt ggccctgtgt gagaagactt tgtgtgagtg tgctgggggg 780

ctggagtgcg cctgccctgc cctcctggag tacgcccgga cctgtgccca ggagggaatg 840

gtgctgtacg gctggaccga ccacagcgcg tgcagcccag tgtgccctgc tggtatggag 900

tataggcagt gtgtgtcccc ttgcgccagg acctgccaga gcctgcacat caatgaaatg 960

tgtcaggagc gatgcgtgga tggctgcagc tgccctgagg gacagctcct ggatgaaggc 1020

ctctgcgtgg agagcaccga gtgtccctgc gtgcattccg gaaagcgcta ccctcccggc 1080

acctccctct ctcgagactg caacacctgc atttgccgaa acagccagtg gatctgcagc 1140

aatgaagaat gtccagggga gtgccttgtc actggtcaat cccacttcaa gagctttgac 1200

aacagatact tcaccttcag tgggatctgc cagtacctgc tggcccggga ttgccaggac 1260

cactccttct ccattgtcat tgagactgtc cagtgtgctg atgaccgcga cgctgtgtgc 1320

acccgctccg tcaccgtccg gctgcctggc ctgcacaaca gccttgtgaa actgaagcat 1380

ggggcaggag ttgccatgga tggccaggac atccagctcc ccctcctgaa aggtgacctc 1440

cgcatccagc atacagtgac ggcctccgtg cgcctcagct acggggagga cctgcagatg 1500

gactgggatg gccgcgggag gctgctggtg aagctgtccc ccgtctatgc cgggaagacc 1560

tgcggcctgt gtgggaatta caatggcaac cagggcgacg acttccttac cccctctggg 1620

ctggcggagc cccgggtgga ggacttcggg aacgcctgga agctgcacgg ggactgccag 1680

gacctgcaga agcagcacag cgatccctgc gccctcaacc cgcgcatgac caggttctcc 1740

gaggaggcgt gcgcggtcct gacgtccccc acattcgagg cctgccatcg tgccgtcagc 1800

ccgctgccct acctgcggaa ctgccgctac gacgtgtgct cctgctcgga cggccgcgag 1860

tgcctgtgcg gcgccctggc cagctatgcc gcggcctgcg cggggagagg cgtgcgcgtc 1920

gcgtggcgcg agccaggccg ctgtgagctg aactgcccga aaggccaggt gtacctgcag 1980

tgcgggaccc cctgcaacct gacctgccgc tctctctctt acccggatga ggaatgcaat 2040

gaggcctgcc tggagggctg cttctgcccc ccagggctct acatggatga gaggggggac 2100

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atcttctcag accatcacac catgtgctac tgtgaggatg gcttcatgca ctgtaccatg 2220

agtggagtcc ccggaagctt gctgcctgac gctgtcctca gcagtcccct gtctcatcgc 2280

agcaaaagga gcctatcctg tcggcccccc atggtcaagc tggtgtgtcc cgctgacaac 2340

ctgcgggctg aagggctcga gtgtaccaaa acgtgccaga actatgacct ggagtgcatg 2400

agcatgggct gtgtctctgg ctgcctctgc cccccgggca tggtccggca tgagaacaga 2460

tgtgtggccc tggaaaggtg tccctgcttc catcagggca aggagtatgc ccctggagaa 2520

acagtgaaga ttggctgcaa cacttgtgtc tgtcgggacc ggaagtggaa ctgcacagac 2580

catgtgtgtg atgccacgtg ctccacgatc ggcatggccc actacctcac cttcgacggg 2640

ctcaaatacc tgttccccgg ggagtgccag tacgttctgg tgcaggatta ctgcggcagt 2700

aaccctggga cctttcggat cctagtgggg aataagggat gcagccaccc ctcagtgaaa 2760

tgcaagaaac gggtcaccat cctggtggag ggaggagaga ttgagctgtt tgacggggag 2820

gtgaatgtga agaggcccat gaaggatgag actcactttg aggtggtgga gtctggccgg 2880

tacatcattc tgctgctggg caaagccctc tccgtggtct gggaccgcca cctgagcatc 2940

tccgtggtcc tgaagcagac ataccaggag aaagtgtgtg gcctgtgtgg gaattttgat 3000

ggcatccaga acaatgacct caccagcagc aacctccaag tggaggaaga ccctgtggac 3060

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tcatcccctg ccacctgcca taacaacatc atgaagcaga cgatggtgga ttcctcctgt 3180

agaatcctta ccagtgacgt cttccaggac tgcaacaagc tggtggaccc cgagccatat 3240

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aggacggcca cattgtgccc ccagagctgc gaggagagga atctccggga gaacgggtat 3420

gaggctgagt ggcgctataa cagctgtgca cctgcctgtc aagtcacgtg tcagcaccct 3480

gagccactgg cctgccctgt gcagtgtgtg gagggctgcc atgcccactg ccctccaggg 3540

aaaatcctgg atgagctttt gcagacctgc gttgaccctg aagactgtcc agtgtgtgag 3600

gtggctggcc ggcgttttgc ctcaggaaag aaagtcacct tgaatcccag tgaccctgag 3660

cactgccaga tttgccactg tgatgttgtc aacctcacct gtgaagcctg ccaggagccg 3720

atatcgggcg cgccaacatc agagagcgcc acccctgaaa gtggtcccgg gagcgagcca 3780

gccacatctg ggtcggaaac gccaggcaca agtgagtctg caactcccga gtccggacct 3840

ggctccgagc ctgccactag cggctccgag actccgggaa cttccgagag cgctacacca 3900

gaaagcggac ccggaaccag taccgaacct agcgagggct ctgctccggg cagcccagcc 3960

ggctctccta catccacgga ggagggcact tccgaatccg ccaccccgga gtcagggcca 4020

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gagagtgggc cagggagccc tgctggatct cctacgtcca ctgaggaagg gtcaccagcg 4140

ggctcgccca ccagcactga agaaggtgcc tcgatatctg acaagaacac tggtgattat 4200

tacgaggaca gttatgaaga tatttcagca tacttgctga gtaaaaacaa tgccattgaa 4260

ccaagaagct tctctgacaa aactcacaca tgcccaccgt gcccagctcc agaactcctg 4320

ggcggaccgt cagtcttcct cttcccccca aaacccaagg acaccctcat gatctcccgg 4380

acccctgagg tcacatgcgt ggtggtggac gtgagccacg aagaccctga ggtcaagttc 4440

aactggtacg tggacggcgt ggaggtgcat aatgccaaga caaagccgcg ggaggagcag 4500

tacaacagca cgtaccgtgt ggtcagcgtc ctcaccgtcc tgcaccagga ctggctgaat 4560

ggcaaggagt acaagtgcaa ggtctccaac aaagccctcc cagccccat cgagaaaacc 4620

atctccaaag ccaaagggca gccccgagaa ccacaggtgt acaccctgcc cccatcccgg 4680

gatgagctga ccaagaacca ggtcagcctg acctgcctgg tcaaaggctt ctatcccagc 4740

gacatcgccg tggagtggga gagcaatggg cagccggaga acaactacaa gaccacgcct 4800

cccgtgttgg actccgacgg ctccttcttc ctctacagca agctcaccgt ggacaagagc 4860

aggtggcagc aggggaacgt cttctcatgc tccgtgatgc atgaggctct gcacaaccac 4920

tacacgcaga agagcctctc cctgtctccg ggtaaatga 4959

<210> 197
<211> 1652
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN VWF059 (VWF D'D3-Fc with LVPR thrombin site in the linker)

<400> 197

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

Ala 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 Ala 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  Ile Ser Gly Ala Pro  Thr Ser Glu
    1235                1240                1245

Ser Ala  Thr Pro Glu Ser Gly  Pro Gly Ser Glu Pro  Ala Thr Ser
    1250                1255                1260
```

```
Gly Ser  Glu Thr Pro Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser
    1265                1270                1275

Gly Pro  Gly Ser Glu Pro Ala  Thr Ser Gly Ser Glu  Thr Pro Gly
    1280                1285                1290

Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly Pro Gly  Thr Ser Thr
    1295                1300                1305

Glu Pro  Ser Glu Gly Ser Ala  Pro Gly Ser Pro Ala  Gly Ser Pro
    1310                1315                1320

Thr Ser  Thr Glu Glu Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser
    1325                1330                1335

Gly Pro  Gly Ser Glu Pro Ala  Thr Ser Gly Ser Glu  Thr Pro Gly
    1340                1345                1350

Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly Pro Gly  Ser Pro Ala
    1355                1360                1365

Gly Ser  Pro Thr Ser Thr Glu  Glu Gly Ser Pro Ala  Gly Ser Pro
    1370                1375                1380

Thr Ser  Thr Glu Glu Gly Ala  Ser Ile Ser Asp Lys  Asn Thr Gly
    1385                1390                1395

Asp Tyr  Tyr Glu Asp Ser Tyr  Glu Asp Ile Ser Ala  Tyr Leu Leu
    1400                1405                1410

Ser Lys  Asn Asn Ala Ile Glu  Pro Arg Ser Phe Ser  Asp Lys Thr
    1415                1420                1425

His Thr  Cys Pro Pro Cys Pro  Ala Pro Glu Leu Leu  Gly Gly Pro
    1430                1435                1440

Ser Val  Phe Leu Phe Pro Pro  Lys Pro Lys Asp Thr  Leu Met Ile
    1445                1450                1455

Ser Arg  Thr Pro Glu Val Thr  Cys Val Val Val Asp  Val Ser His
```

```
    1460                1465                1470

Glu Asp  Pro Glu Val Lys Phe  Asn Trp Tyr Val Asp  Gly Val Glu
    1475                1480                1485

Val His  Asn Ala Lys Thr Lys  Pro Arg Glu Glu Gln  Tyr Asn Ser
    1490                1495                1500

Thr Tyr  Arg Val Val Ser Val  Leu Thr Val Leu His  Gln Asp Trp
    1505                1510                1515

Leu Asn  Gly Lys Glu Tyr Lys  Cys Lys Val Ser Asn  Lys Ala Leu
    1520                1525                1530

Pro Ala  Pro Ile Glu Lys Thr  Ile Ser Lys Ala Lys  Gly Gln Pro
    1535                1540                1545

Arg Glu  Pro Gln Val Tyr Thr  Leu Pro Pro Ser Arg  Asp Glu Leu
    1550                1555                1560

Thr Lys  Asn Gln Val Ser Leu  Thr Cys Leu Val Lys  Gly Phe Tyr
    1565                1570                1575

Pro Ser  Asp Ile Ala Val Glu  Trp Glu Ser Asn Gly  Gln Pro Glu
    1580                1585                1590

Asn Asn  Tyr Lys Thr Thr Pro  Pro Val Leu Asp Ser  Asp Gly Ser
    1595                1600                1605

Phe Phe  Leu Tyr Ser Lys Leu  Thr Val Asp Lys Ser  Arg Trp Gln
    1610                1615                1620

Gln Gly  Asn Val Phe Ser Cys  Ser Val Met His Glu  Ala Leu His
    1625                1630                1635

Asn His  Tyr Thr Gln Lys Ser  Leu Ser Leu Ser Pro  Gly Lys
    1640                1645                1650
```

<210> 198
<211> 4860
<212> DNA
<213> Artificial Sequence

<220>
<223> pSYN VWF062 (VWF D'D3-Fc with no thrombin site in the linker)

<400> 198
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ctttgtgcag aaggaactcg cggcaggtca tccacggccc gatgcagcct tttcggaagt 120

gacttcgtca acacctttga tgggagcatg tacagctttg cgggatactg cagttacctc 180

ctggcagggg gctgccagaa acgctccttc tcgattattg gggacttcca gaatggcaag 240

agagtgagcc tctccgtgta tcttggggaa ttttttgaca tccatttgtt tgtcaatggt 300

accgtgacac agggggacca aagagtctcc atgccctatg cctccaaagg gctgtatcta 360

gaaactgagg ctgggtacta caagctgtcc ggtgaggcct atggctttgt ggccaggatc 420

gatggcagcg gcaactttca agtcctgctg tcagacagat acttcaacaa gacctgcggg 480

ctgtgtggca actttaacat ctttgctgaa gatgacttta tgacccaaga agggaccttg 540

acctcggacc cttatgactt tgccaactca tgggctctga gcagtggaga acagtggtgt 600

gaacgggcat ctcctcccag cagctcatgc aacatctcct ctggggaaat gcagaagggc 660

ctgtgggagc agtgccagct tctgaagagc acctcggtgt ttgcccgctg ccaccctctg 720

gtggaccccg agccttttgt ggccctgtgt gagaagactt tgtgtgagtg tgctgggggg 780

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tgtcaggagc gatgcgtgga tggctgcagc tgccctgagg gacagctcct ggatgaaggc 1020

ctctgcgtgg agagcaccga gtgtccctgc gtgcattccg gaaagcgcta ccctcccggc 1080

acctccctct ctcgagactg caacacctgc atttgccgaa acagccagtg gatctgcagc 1140

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aacagatact tcaccttcag tgggatctgc cagtacctgc tggcccggga ttgccaggac 1260

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acccgctccg tcaccgtccg gctgcctggc ctgcacaaca gccttgtgaa actgaagcat 1380

ggggcaggag ttgccatgga tggccaggac atccagctcc ccctcctgaa aggtgacctc 1440

cgcatccagc atacagtgac ggcctccgtg cgcctcagct acggggagga cctgcagatg 1500

gactgggatg gccgcgggag gctgctggtg aagctgtccc ccgtctatgc cgggaagacc 1560

tgcggcctgt gtgggaatta caatggcaac cagggcgacg acttccttac cccctctggg 1620

ctggcggagc cccgggtgga ggacttcggg aacgcctgga agctgcacgg ggactgccag 1680

gacctgcaga agcagcacag cgatccctgc gccctcaacc cgcgcatgac caggttctcc 1740

gaggaggcgt gcgcggtcct gacgtccccc acattcgagg cctgccatcg tgccgtcagc 1800

ccgctgccct acctgcggaa ctgccgctac gacgtgtgct cctgctcgga cggccgcgag 1860

tgcctgtgcg gcgccctggc cagctatgcc gcggcctgcg cggggagagg cgtgcgcgtc 1920

gcgtggcgcg agccaggccg ctgtgagctg aactgcccga aaggccaggt gtacctgcag 1980

tgcgggaccc cctgcaacct gacctgccgc tctctctctt acccggatga ggaatgcaat 2040

gaggcctgcc tggagggctg cttctgcccc ccagggctct acatggatga gaggggggac 2100

tgcgtgccca aggcccagtg cccctgttac tatgacggtg agatcttcca gccagaagac 2160

atcttctcag accatcacac catgtgctac tgtgaggatg gcttcatgca ctgtaccatg 2220

agtggagtcc ccggaagctt gctgcctgac gctgtcctca gcagtcccct gtctcatcgc 2280

agcaaaagga gcctatcctg tcggcccccc atggtcaagc tggtgtgtcc cgctgacaac 2340

ctgcgggctg aagggctcga gtgtaccaaa acgtgccaga actatgacct ggagtgcatg 2400

agcatgggct gtgtctctgg ctgcctctgc cccccgggca tggtccggca tgagaacaga 2460

tgtgtggccc tggaaaggtg tccctgcttc catcagggca aggagtatgc ccctggagaa 2520

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catgtgtgtg atgccacgtg ctccacgatc ggcatggccc actacctcac cttcgacggg 2640

ctcaaatacc tgttccccgg ggagtgccag tacgttctgg tgcaggatta ctgcggcagt 2700

aaccctggga cctttcggat cctagtgggg aataagggat gcagccaccc ctcagtgaaa 2760

tgcaagaaac gggtcaccat cctggtggag ggaggagaga ttgagctgtt tgacggggag 2820

gtgaatgtga agaggcccat gaaggatgag actcactttg aggtggtgga gtctggccgg 2880

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tttgggaact cctggaaagt gagctcgcag tgtgctgaca ccagaaaagt gcctctggac 3120

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ctggatgtct gcatttacga cacctgctcc tgtgagtcca ttggggactg cgccgcattc 3300

tgcgacacca ttgctgccta tgcccacgtg tgtgcccagc atggcaaggt ggtgacctgg 3360

aggacggcca cattgtgccc ccagagctgc gaggagagga atctccggga gaacgggtat 3420

gaggctgagt ggcgctataa cagctgtgca cctgcctgtc aagtcacgtg tcagcaccct 3480

gagccactgg cctgccctgt gcagtgtgtg gagggctgcc atgcccactg ccctccaggg 3540

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gtggctggcc ggcgttttgc ctcaggaaag aaagtcacct tgaatcccag tgaccctgag 3660

cactgccaga tttgccactg tgatgttgtc aacctcacct gtgaagcctg ccaggagccg 3720

atatcgggcg cgccaacatc agagagcgcc acccctgaaa gtggtcccgg gagcgagcca 3780

gccacatctg ggtcggaaac gccaggcaca agtgagtctg caactcccga gtccggacct 3840

ggctccgagc ctgccactag cggctccgag actccgggaa cttccgagag cgctacacca 3900

gaaagcggac ccggaaccag taccgaacct agcgagggct ctgctccggg cagcccagcc 3960

ggctctccta catccacgga ggagggcact tccgaatccg ccaccccgga gtcagggcca 4020

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gacaccctca tgatctcccg gacccctgag gtcacatgcg tggtggtgga cgtgagccac 4320

gaagaccctg aggtcaagtt caactggtac gtggacggcg tggaggtgca taatgccaag 4380

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ccagccccca tcgagaaaac catctccaaa gccaaagggc agccccgaga accacaggtg 4560

tacaccctgc ccccatcccg ggatgagctg accaagaacc aggtcagcct gacctgcctg 4620

gtcaaaggct tctatcccag cgacatcgcc gtggagtggg agagcaatgg gcagccggag 4680

aacaactaca agaccacgcc tcccgtgttg gactccgacg gctccttctt cctctacagc 4740

aagctcaccg tggacaagag caggtggcag caggggaacg tcttctcatg ctccgtgatg 4800

catgaggctc tgcacaacca ctacacgcag aagagcctct ccctgtctcc gggtaaatga 4860

<210> 199
<211> 1619
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN VWF062 (VWF D'D3-Fc with no thrombin site in the linker)

<400> 199

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

Ala 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 Ala 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  Ile Ser Gly Ala Pro  Thr Ser Glu
    1235                1240                1245

Ser Ala  Thr Pro Glu Ser Gly  Pro Gly Ser Glu Pro  Ala Thr Ser
```

```
    1250                1255                1260

Gly Ser  Glu Thr Pro Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser
    1265                1270                1275

Gly Pro  Gly Ser Glu Pro Ala  Thr Ser Gly Ser Glu  Thr Pro Gly
    1280                1285                1290

Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly Pro Gly  Thr Ser Thr
    1295                1300                1305

Glu Pro  Ser Glu Gly Ser Ala  Pro Gly Ser Pro Ala  Gly Ser Pro
    1310                1315                1320

Thr Ser  Thr Glu Glu Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser
    1325                1330                1335

Gly Pro  Gly Ser Glu Pro Ala  Thr Ser Gly Ser Glu  Thr Pro Gly
    1340                1345                1350

Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly Pro Gly  Ser Pro Ala
    1355                1360                1365

Gly Ser  Pro Thr Ser Thr Glu  Glu Gly Ser Pro Ala  Gly Ser Pro
    1370                1375                1380

Thr Ser  Thr Glu Glu Gly Ala  Ser Ser Asp Lys Thr  His Thr Cys
    1385                1390                1395

Pro Pro  Cys Pro Ala Pro Glu  Leu Leu Gly Gly Pro  Ser Val Phe
    1400                1405                1410

Leu Phe  Pro Pro Lys Pro Lys  Asp Thr Leu Met Ile  Ser Arg Thr
    1415                1420                1425

Pro Glu  Val Thr Cys Val Val  Val Asp Val Ser His  Glu Asp Pro
    1430                1435                1440

Glu Val  Lys Phe Asn Trp Tyr  Val Asp Gly Val Glu  Val His Asn
    1445                1450                1455
```

```
Ala Lys  Thr Lys Pro Arg Glu  Glu Gln Tyr Asn Ser  Thr Tyr Arg
    1460                1465                1470

Val Val  Ser Val Leu Thr Val  Leu His Gln Asp Trp  Leu Asn Gly
    1475                1480                1485

Lys Glu  Tyr Lys Cys Lys Val  Ser Asn Lys Ala Leu  Pro Ala Pro
    1490                1495                1500

Ile Glu  Lys Thr Ile Ser Lys  Ala Lys Gly Gln Pro  Arg Glu Pro
    1505                1510                1515

Gln Val  Tyr Thr Leu Pro Pro  Ser Arg Asp Glu Leu  Thr Lys Asn
    1520                1525                1530

Gln Val  Ser Leu Thr Cys Leu  Val Lys Gly Phe Tyr  Pro Ser Asp
    1535                1540                1545

Ile Ala  Val Glu Trp Glu Ser  Asn Gly Gln Pro Glu  Asn Asn Tyr
    1550                1555                1560

Lys Thr  Thr Pro Pro Val Leu  Asp Ser Asp Gly Ser  Phe Phe Leu
    1565                1570                1575

Tyr Ser  Lys Leu Thr Val Asp  Lys Ser Arg Trp Gln  Gln Gly Asn
    1580                1585                1590

Val Phe  Ser Cys Ser Val Met  His Glu Ala Leu His  Asn His Tyr
    1595                1600                1605

Thr Gln  Lys Ser Leu Ser Leu  Ser Pro Gly Lys
    1610                1615
```

<210> 200
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Cleavable linker

<400> 200

Ile Glu Pro Arg

1

<210> 201
<211> 1945
<212> PRT
<213> Artificial Sequence

<220>
<223> FVIII(XTEN)-Fc

<400> 201

Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser Trp Asp Tyr Met
1 5 10 15

Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro Arg
20 25 30

Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys Thr
35 40 45

Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys Pro Arg
50 55 60

Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val Tyr
65 70 75 80

Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val Ser
85 90 95

Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala Glu
100 105 110

Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val Phe
115 120 125

Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn Gly
130 135 140

Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser His
145 150 155 160

Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu Leu
165 170 175

```
Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr Gln Thr Leu His
            180                 185                 190

Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp His
        195                 200                 205

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

Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg Ser
225                 230                 235                 240

Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His Val
                245                 250                 255

Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu Gly
            260                 265                 270

His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile Ser
        275                 280                 285

Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly Gln
    290                 295                 300

Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met Glu
305                 310                 315                 320

Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg Met
                325                 330                 335

Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp Ser
            340                 345                 350

Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro Ser Phe Ile
        355                 360                 365

Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His Tyr
    370                 375                 380

Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu Ala
```

385 390 395 400

Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro Gln
405 410 415

Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr Asp
420 425 430

Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile Leu
435 440 445

Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile Phe
450 455 460

Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile Thr
465 470 475 480

Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys Gly Val Lys His
485 490 495

Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys Trp
500 505 510

Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys Leu
515 520 525

Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala Ser
530 535 540

Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln
545 550 555 560

Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe Ser
565 570 575

Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln Arg
580 585 590

Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe Gln
595 600 605

```
Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser Leu
    610                 615                 620

Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu Ser
625                 630                 635                 640

Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr
                645                 650                 655

Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe
            660                 665                 670

Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp Ile
        675                 680                 685

Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr Ala Leu
    690                 695                 700

Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu Asp
705                 710                 715                 720

Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile
                725                 730                 735

Glu Pro Arg Ser Phe Ser Gln Asn Gly Thr Ser Glu Ser Ala Thr Pro
            740                 745                 750

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
        755                 760                 765

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
    770                 775                 780

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
785                 790                 795                 800

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
                805                 810                 815

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu
            820                 825                 830
```

```
Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
        835                 840                 845

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
    850                 855                 860

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala
865                 870                 875                 880

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu
                885                 890                 895

Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
            900                 905                 910

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu
        915                 920                 925

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
    930                 935                 940

Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
945                 950                 955                 960

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr
                965                 970                 975

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu
            980                 985                 990

Gly Ser Ala Pro Gly Ser Glu Pro  Ala Thr Ser Gly Ser  Glu Thr Pro
        995                 1000                1005

Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser Gly Pro  Gly Thr Ser
    1010                1015                1020

Thr Glu  Pro Ser Glu Gly Ser  Ala Pro Ala Ser Ser  Glu Ile Thr
    1025                1030                1035

Arg Thr  Thr Leu Gln Ser Asp  Gln Glu Glu Ile Asp  Tyr Asp Asp
    1040                1045                1050
```

```
Thr Ile  Ser Val Glu Met Lys  Lys Glu Asp Phe Asp  Ile Tyr Asp
    1055                1060                1065

Glu Asp  Glu Asn Gln Ser Pro  Arg Ser Phe Gln Lys  Lys Thr Arg
    1070                1075                1080

His Tyr  Phe Ile Ala Ala Val  Glu Arg Leu Trp Asp  Tyr Gly Met
    1085                1090                1095

Ser Ser  Ser Pro His Val Leu  Arg Asn Arg Ala Gln  Ser Gly Ser
    1100                1105                1110

Val Pro  Gln Phe Lys Lys Val  Val Phe Gln Glu Phe  Thr Asp Gly
    1115                1120                1125

Ser Phe  Thr Gln Pro Leu Tyr  Arg Gly Glu Leu Asn  Glu His Leu
    1130                1135                1140

Gly Leu  Leu Gly Pro Tyr Ile  Arg Ala Glu Val Glu  Asp Asn Ile
    1145                1150                1155

Met Val  Thr Phe Arg Asn Gln  Ala Ser Arg Pro Tyr  Ser Phe Tyr
    1160                1165                1170

Ser Ser  Leu Ile Ser Tyr Glu  Glu Asp Gln Arg Gln  Gly Ala Glu
    1175                1180                1185

Pro Arg  Lys Asn Phe Val Lys  Pro Asn Glu Thr Lys  Thr Tyr Phe
    1190                1195                1200

Trp Lys  Val Gln His His Met  Ala Pro Thr Lys Asp  Glu Phe Asp
    1205                1210                1215

Cys Lys  Ala Trp Ala Tyr Phe  Ser Asp Val Asp Leu  Glu Lys Asp
    1220                1225                1230

Val His  Ser Gly Leu Ile Gly  Pro Leu Leu Val Cys  His Thr Asn
    1235                1240                1245

Thr Leu  Asn Pro Ala His Gly  Arg Gln Val Thr Val  Gln Glu Phe
```

```
    1250                1255                1260

Ala Leu  Phe Phe Thr Ile Phe  Asp Glu Thr Lys Ser  Trp Tyr Phe
    1265                1270                1275

Thr Glu  Asn Met Glu Arg Asn  Cys Arg Ala Pro Cys  Asn Ile Gln
    1280                1285                1290

Met Glu  Asp Pro Thr Phe Lys  Glu Asn Tyr Arg Phe  His Ala Ile
    1295                1300                1305

Asn Gly  Tyr Ile Met Asp Thr  Leu Pro Gly Leu Val  Met Ala Gln
    1310                1315                1320

Asp Gln  Arg Ile Arg Trp Tyr  Leu Leu Ser Met Gly  Ser Asn Glu
    1325                1330                1335

Asn Ile  His Ser Ile His Phe  Ser Gly His Val Phe  Thr Val Arg
    1340                1345                1350

Lys Lys  Glu Glu Tyr Lys Met  Ala Leu Tyr Asn Leu  Tyr Pro Gly
    1355                1360                1365

Val Phe  Glu Thr Val Glu Met  Leu Pro Ser Lys Ala  Gly Ile Trp
    1370                1375                1380

Arg Val  Glu Cys Leu Ile Gly  Glu His Leu His Ala  Gly Met Ser
    1385                1390                1395

Thr Leu  Phe Leu Val Tyr Ser  Asn Lys Cys Gln Thr  Pro Leu Gly
    1400                1405                1410

Met Ala  Ser Gly His Ile Arg  Asp Phe Gln Ile Thr  Ala Ser Gly
    1415                1420                1425

Gln Tyr  Gly Gln Trp Ala Pro  Lys Leu Ala Arg Leu  His Tyr Ser
    1430                1435                1440

Gly Ser  Ile Asn Ala Trp Ser  Thr Lys Glu Pro Phe  Ser Trp Ile
    1445                1450                1455
```

```
Lys Val  Asp Leu Leu Ala Pro  Met Ile Ile His Gly  Ile Lys Thr
    1460                1465                1470

Gln Gly  Ala Arg Gln Lys Phe  Ser Ser Leu Tyr Ile  Ser Gln Phe
    1475                1480                1485

Ile Ile  Met Tyr Ser Leu Asp  Gly Lys Lys Trp Gln  Thr Tyr Arg
    1490                1495                1500

Gly Asn  Ser Thr Gly Thr Leu  Met Val Phe Phe Gly  Asn Val Asp
    1505                1510                1515

Ser Ser  Gly Ile Lys His Asn  Ile Phe Asn Pro Pro  Ile Ile Ala
    1520                1525                1530

Arg Tyr  Ile Arg Leu His Pro  Thr His Tyr Ser Ile  Arg Ser Thr
    1535                1540                1545

Leu Arg  Met Glu Leu Met Gly  Cys Asp Leu Asn Ser  Cys Ser Met
    1550                1555                1560

Pro Leu  Gly Met Glu Ser Lys  Ala Ile Ser Asp Ala  Gln Ile Thr
    1565                1570                1575

Ala Ser  Ser Tyr Phe Thr Asn  Met Phe Ala Thr Trp  Ser Pro Ser
    1580                1585                1590

Lys Ala  Arg Leu His Leu Gln  Gly Arg Ser Asn Ala  Trp Arg Pro
    1595                1600                1605

Gln Val  Asn Asn Pro Lys Glu  Trp Leu Gln Val Asp  Phe Gln Lys
    1610                1615                1620

Thr Met  Lys Val Thr Gly Val  Thr Thr Gln Gly Val  Lys Ser Leu
    1625                1630                1635

Leu Thr  Ser Met Tyr Val Lys  Glu Phe Leu Ile Ser  Ser Ser Gln
    1640                1645                1650

Asp Gly  His Gln Trp Thr Leu  Phe Phe Gln Asn Gly  Lys Val Lys
    1655                1660                1665
```

```
Val Phe  Gln Gly Asn Gln Asp  Ser Phe Thr Pro Val  Val Asn Ser
    1670                1675                1680

Leu Asp  Pro Pro Leu Leu Thr  Arg Tyr Leu Arg Ile  His Pro Gln
    1685                1690                1695

Ser Trp  Val His Gln Ile Ala  Leu Arg Met Glu Val  Leu Gly Cys
    1700                1705                1710

Glu Ala  Gln Asp Leu Tyr Asp  Lys Thr His Thr Cys  Pro Pro Cys
    1715                1720                1725

Pro Ala  Pro Glu Leu Leu Gly  Gly Pro Ser Val Phe  Leu Phe Pro
    1730                1735                1740

Pro Lys  Pro Lys Asp Thr Leu  Met Ile Ser Arg Thr  Pro Glu Val
    1745                1750                1755

Thr Cys  Val Val Val Asp Val  Ser His Glu Asp Pro  Glu Val Lys
    1760                1765                1770

Phe Asn  Trp Tyr Val Asp Gly  Val Glu Val His Asn  Ala Lys Thr
    1775                1780                1785

Lys Pro  Arg Glu Glu Gln Tyr  Asn Ser Thr Tyr Arg  Val Val Ser
    1790                1795                1800

Val Leu  Thr Val Leu His Gln  Asp Trp Leu Asn Gly  Lys Glu Tyr
    1805                1810                1815

Lys Cys  Lys Val Ser Asn Lys  Ala Leu Pro Ala Pro  Ile Glu Lys
    1820                1825                1830

Thr Ile  Ser Lys Ala Lys Gly  Gln Pro Arg Glu Pro  Gln Val Tyr
    1835                1840                1845

Thr Leu  Pro Pro Ser Arg Asp  Glu Leu Thr Lys Asn  Gln Val Ser
    1850                1855                1860

Leu Thr  Cys Leu Val Lys Gly  Phe Tyr Pro Ser Asp  Ile Ala Val
    1865                1870                1875
```

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
    1880   1885   1890

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
    1895   1900   1905

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
    1910   1915   1920

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
    1925   1930   1935

Ser Leu Ser Leu Ser Pro Gly
    1940   1945

<210> 202
<211> 883
<212> PRT
<213> Artificial Sequence

<220>
<223> VWF(D'D3)-XTEN-a2 Linker-Fc

<400> 202

Ser Leu Ser Cys Arg Pro Pro Met Val Lys Leu Val Cys Pro Ala Asp
1   5   10   15

Asn Leu Arg Ala Glu Gly Leu Glu Cys Thr Lys Thr Cys Gln Asn Tyr
            20   25   30

Asp Leu Glu Cys Met Ser Met Gly Cys Val Ser Gly Cys Leu Cys Pro
        35   40   45

Pro Gly Met Val Arg His Glu Asn Arg Cys Val Ala Leu Glu Arg Cys
    50   55   60

Pro Cys Phe His Gln Gly Lys Glu Tyr Ala Pro Gly Glu Thr Val Lys
65   70   75   80

Ile Gly Cys Asn Thr Cys Val Cys Arg Asp Arg Lys Trp Asn Cys Thr
                85   90   95

```
Asp His Val Cys Asp Ala Thr Cys Ser Thr Ile Gly Met Ala His Tyr
            100                 105                 110

Leu Thr Phe Asp Gly Leu Lys Tyr Leu Phe Pro Gly Glu Cys Gln Tyr
        115                 120                 125

Val Leu Val Gln Asp Tyr Cys Gly Ser Asn Pro Gly Thr Phe Arg Ile
    130                 135                 140

Leu Val Gly Asn Lys Gly Cys Ser His Pro Ser Val Lys Cys Lys Lys
145                 150                 155                 160

Arg Val Thr Ile Leu Val Glu Gly Gly Glu Ile Glu Leu Phe Asp Gly
                165                 170                 175

Glu Val Asn Val Lys Arg Pro Met Lys Asp Glu Thr His Phe Glu Val
            180                 185                 190

Val Glu Ser Gly Arg Tyr Ile Ile Leu Leu Leu Gly Lys Ala Leu Ser
        195                 200                 205

Val Val Trp Asp Arg His Leu Ser Ile Ser Val Val Leu Lys Gln Thr
    210                 215                 220

Tyr Gln Glu Lys Val Cys Gly Leu Cys Gly Asn Phe Asp Gly Ile Gln
225                 230                 235                 240

Asn Asn Asp Leu Thr Ser Ser Asn Leu Gln Val Glu Glu Asp Pro Val
                245                 250                 255

Asp Phe Gly Asn Ser Trp Lys Val Ser Ser Gln Cys Ala Asp Thr Arg
            260                 265                 270

Lys Val Pro Leu Asp Ser Ser Pro Ala Thr Cys His Asn Asn Ile Met
        275                 280                 285

Lys Gln Thr Met Val Asp Ser Ser Cys Arg Ile Leu Thr Ser Asp Val
    290                 295                 300

Phe Gln Asp Cys Asn Lys Leu Val Asp Pro Glu Pro Tyr Leu Asp Val
305                 310                 315                 320
```

```
Cys Ile Tyr Asp Thr Cys Ser Cys Glu Ser Ile Gly Asp Cys Ala Ala
                325                 330                 335

Phe Cys Asp Thr Ile Ala Ala Tyr Ala His Val Cys Ala Gln His Gly
            340                 345                 350

Lys Val Val Thr Trp Arg Thr Ala Thr Leu Cys Pro Gln Ser Cys Glu
        355                 360                 365

Glu Arg Asn Leu Arg Glu Asn Gly Tyr Glu Ala Glu Trp Arg Tyr Asn
    370                 375                 380

Ser Cys Ala Pro Ala Cys Gln Val Thr Cys Gln His Pro Glu Pro Leu
385                 390                 395                 400

Ala Cys Pro Val Gln Cys Val Glu Gly Cys His Ala His Cys Pro Pro
                405                 410                 415

Gly Lys Ile Leu Asp Glu Leu Leu Gln Thr Cys Val Asp Pro Glu Asp
            420                 425                 430

Cys Pro Val Cys Glu Val Ala Gly Arg Arg Phe Ala Ser Gly Lys Lys
        435                 440                 445

Val Thr Leu Asn Pro Ser Asp Pro Glu His Cys Gln Ile Cys His Cys
    450                 455                 460

Asp Val Val Asn Leu Thr Cys Glu Ala Cys Gln Glu Pro Gly Thr Ser
465                 470                 475                 480

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
                485                 490                 495

Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
            500                 505                 510

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser
        515                 520                 525

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser
```

```
    530                 535                 540

Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu
545                 550                 555                 560

Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu
                565                 570                 575

Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr
            580                 585                 590

Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu
        595                 600                 605

Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ala Ser
    610                 615                 620

Ser Asp Lys Asn Thr Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile
625                 630                 635                 640

Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe
                645                 650                 655

Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
            660                 665                 670

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
        675                 680                 685

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
    690                 695                 700

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
705                 710                 715                 720

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
                725                 730                 735

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
            740                 745                 750
```

```
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
        755                 760                 765


Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
    770                 775                 780


Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
785                 790                 795                 800


Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
                805                 810                 815


Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
            820                 825                 830


Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
        835                 840                 845


Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
    850                 855                 860


Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
865                 870                 875                 880


Ser Pro Gly
```

<210> 203
<211> 1965
<212> PRT
<213> Artificial Sequence

<220>
<223> Final amino acid sequence of FVIII 312A

<400> 203

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Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
1               5                   10                  15


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


Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg
```

```
        35                  40                  45

Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val
    50                  55                  60

Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile
65                  70                  75                  80

Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln
                85                  90                  95

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

His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser
        115                 120                 125

Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp
    130                 135                 140

Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu
145                 150                 155                 160

Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser
                165                 170                 175

Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile
            180                 185                 190

Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr
        195                 200                 205

Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly
    210                 215                 220

Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp
225                 230                 235                 240

Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr
                245                 250                 255
```

```
Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val
            260                 265                 270

Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile
        275                 280                 285

Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser
    290                 295                 300

Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met
305                 310                 315                 320

Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His
                325                 330                 335

Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro
            340                 345                 350

Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp
        355                 360                 365

Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser
    370                 375                 380

Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
385                 390                 395                 400

Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro
                405                 410                 415

Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
            420                 425                 430

Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met
        435                 440                 445

Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu
    450                 455                 460

Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
465                 470                 475                 480
```

```
Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro
                485                 490                 495

His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys
            500                 505                 510

Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe
        515                 520                 525

Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp
    530                 535                 540

Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg
545                 550                 555                 560

Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu
                565                 570                 575

Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val
            580                 585                 590

Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu
        595                 600                 605

Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp
    610                 615                 620

Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
625                 630                 635                 640

Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp
                645                 650                 655

Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe
            660                 665                 670

Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
        675                 680                 685

Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro
    690                 695                 700
```

```
Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly
705                 710                 715                 720


Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp
                725                 730                 735


Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
            740                 745                 750


Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Gly Thr Ser Glu
        755                 760                 765


Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
    770                 775                 780


Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
785                 790                 795                 800


Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu
                805                 810                 815


Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu
            820                 825                 830


Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
        835                 840                 845


Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
    850                 855                 860


Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
865                 870                 875                 880


Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
                885                 890                 895


Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr
            900                 905                 910


Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
```

```
        915                 920                 925

Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
    930                 935                 940

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
945                 950                 955                 960

Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly
                965                 970                 975

Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
            980                 985                 990

Gly Thr Ser Thr Glu Pro Ser Glu  Gly Ser Ala Pro Gly  Thr Ser Thr
        995                 1000                1005

Glu Pro  Ser Glu Gly Ser Ala  Pro Gly Ser Glu Pro  Ala Thr Ser
    1010                1015                1020

Gly Ser  Glu Thr Pro Gly Thr  Ser Glu Ser Ala Thr  Pro Glu Ser
    1025                1030                1035

Gly Pro  Gly Thr Ser Thr Glu  Pro Ser Glu Gly Ser  Ala Pro Ala
    1040                1045                1050

Ser Ser  Glu Ile Thr Arg Thr  Thr Leu Gln Ser Asp  Gln Glu Glu
    1055                1060                1065

Ile Asp  Tyr Asp Asp Thr Ile  Ser Val Glu Met Lys  Lys Glu Asp
    1070                1075                1080

Phe Asp  Ile Tyr Asp Glu Asp  Glu Asn Gln Ser Pro  Arg Ser Phe
    1085                1090                1095

Gln Lys  Lys Thr Arg His Tyr  Phe Ile Ala Ala Val  Glu Arg Leu
    1100                1105                1110

Trp Asp  Tyr Gly Met Ser Ser  Ser Pro His Val Leu  Arg Asn Arg
    1115                1120                1125
```

```
Ala Gln  Ser Gly Ser Val Pro  Gln Phe Lys Lys Val  Val Phe Gln
    1130                1135                1140

Glu Phe  Thr Asp Gly Ser Phe  Thr Gln Pro Leu Tyr  Arg Gly Glu
    1145                1150                1155

Leu Asn  Glu His Leu Gly Leu  Leu Gly Pro Tyr Ile  Arg Ala Glu
    1160                1165                1170

Val Glu  Asp Asn Ile Met Val  Thr Phe Arg Asn Gln  Ala Ser Arg
    1175                1180                1185

Pro Tyr  Ser Phe Tyr Ser Ser  Leu Ile Ser Tyr Glu  Glu Asp Gln
    1190                1195                1200

Arg Gln  Gly Ala Glu Pro Arg  Lys Asn Phe Val Lys  Pro Asn Glu
    1205                1210                1215

Thr Lys  Thr Tyr Phe Trp Lys  Val Gln His His Met  Ala Pro Thr
    1220                1225                1230

Lys Asp  Glu Phe Asp Cys Lys  Ala Trp Ala Tyr Phe  Ser Asp Val
    1235                1240                1245

Asp Leu  Glu Lys Asp Val His  Ser Gly Leu Ile Gly  Pro Leu Leu
    1250                1255                1260

Val Cys  His Thr Asn Thr Leu  Asn Pro Ala His Gly  Arg Gln Val
    1265                1270                1275

Thr Val  Gln Glu Phe Ala Leu  Phe Phe Thr Ile Phe  Asp Glu Thr
    1280                1285                1290

Lys Ser  Trp Tyr Phe Thr Glu  Asn Met Glu Arg Asn  Cys Arg Ala
    1295                1300                1305

Pro Cys  Asn Ile Gln Met Glu  Asp Pro Thr Phe Lys  Glu Asn Tyr
    1310                1315                1320

Arg Phe  His Ala Ile Asn Gly  Tyr Ile Met Asp Thr  Leu Pro Gly
    1325                1330                1335
```

```
Leu Val  Met Ala Gln Asp Gln  Arg Ile Arg Trp Tyr  Leu Leu Ser
    1340                1345                1350

Met Gly  Ser Asn Glu Asn Ile  His Ser Ile His Phe  Ser Gly His
    1355                1360                1365

Val Phe  Thr Val Arg Lys Lys  Glu Glu Tyr Lys Met  Ala Leu Tyr
    1370                1375                1380

Asn Leu  Tyr Pro Gly Val Phe  Glu Thr Val Glu Met  Leu Pro Ser
    1385                1390                1395

Lys Ala  Gly Ile Trp Arg Val  Glu Cys Leu Ile Gly  Glu His Leu
    1400                1405                1410

His Ala  Gly Met Ser Thr Leu  Phe Leu Val Tyr Ser  Asn Lys Cys
    1415                1420                1425

Gln Thr  Pro Leu Gly Met Ala  Ser Gly His Ile Arg  Asp Phe Gln
    1430                1435                1440

Ile Thr  Ala Ser Gly Gln Tyr  Gly Gln Trp Ala Pro  Lys Leu Ala
    1445                1450                1455

Arg Leu  His Tyr Ser Gly Ser  Ile Asn Ala Trp Ser  Thr Lys Glu
    1460                1465                1470

Pro Phe  Ser Trp Ile Lys Val  Asp Leu Leu Ala Pro  Met Ile Ile
    1475                1480                1485

His Gly  Ile Lys Thr Gln Gly  Ala Arg Gln Lys Phe  Ser Ser Leu
    1490                1495                1500

Tyr Ile  Ser Gln Phe Ile Ile  Met Tyr Ser Leu Asp  Gly Lys Lys
    1505                1510                1515

Trp Gln  Thr Tyr Arg Gly Asn  Ser Thr Gly Thr Leu  Met Val Phe
    1520                1525                1530

Phe Gly  Asn Val Asp Ser Ser  Gly Ile Lys His Asn  Ile Phe Asn
    1535                1540                1545
```

```
Pro Pro  Ile Ile Ala Arg Tyr  Ile Arg Leu His Pro  Thr His Tyr
    1550                1555                1560

Ser Ile  Arg Ser Thr Leu Arg  Met Glu Leu Met Gly  Cys Asp Leu
    1565                1570                1575

Asn Ser  Cys Ser Met Pro Leu  Gly Met Glu Ser Lys  Ala Ile Ser
    1580                1585                1590

Asp Ala  Gln Ile Thr Ala Ser  Ser Tyr Phe Thr Asn  Met Phe Ala
    1595                1600                1605

Thr Trp  Ser Pro Ser Lys Ala  Arg Leu His Leu Gln  Gly Arg Ser
    1610                1615                1620

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

Val Asp  Phe Gln Lys Thr Met  Lys Val Thr Gly Val  Thr Thr Gln
    1640                1645                1650

Gly Val  Lys Ser Leu Leu Thr  Ser Met Tyr Val Lys  Glu Phe Leu
    1655                1660                1665

Ile Ser  Ser Ser Gln Asp Gly  His Gln Trp Thr Leu  Phe Phe Gln
    1670                1675                1680

Asn Gly  Lys Val Lys Val Phe  Gln Gly Asn Gln Asp  Ser Phe Thr
    1685                1690                1695

Pro Val  Val Asn Ser Leu Asp  Pro Pro Leu Leu Thr  Arg Tyr Leu
    1700                1705                1710

Arg Ile  His Pro Gln Ser Trp  Val His Gln Ile Ala  Leu Arg Met
    1715                1720                1725

Glu Val  Leu Gly Cys Glu Ala  Gln Asp Leu Tyr Asp  Lys Thr His
    1730                1735                1740

Thr Cys  Pro Pro Cys Pro Ala  Pro Glu Leu Leu Gly  Gly Pro Ser
```

```
    1745                1750                1755

Val Phe  Leu Phe Pro Pro Lys  Pro Lys Asp Thr Leu  Met Ile Ser
    1760                1765                1770

Arg Thr  Pro Glu Val Thr Cys  Val Val Val Asp Val  Ser His Glu
    1775                1780                1785

Asp Pro  Glu Val Lys Phe Asn  Trp Tyr Val Asp Gly  Val Glu Val
    1790                1795                1800

His Asn  Ala Lys Thr Lys Pro  Arg Glu Glu Gln Tyr  Asn Ser Thr
    1805                1810                1815

Tyr Arg  Val Val Ser Val Leu  Thr Val Leu His Gln  Asp Trp Leu
    1820                1825                1830

Asn Gly  Lys Glu Tyr Lys Cys  Lys Val Ser Asn Lys  Ala Leu Pro
    1835                1840                1845

Ala Pro  Ile Glu Lys Thr Ile  Ser Lys Ala Lys Gly  Gln Pro Arg
    1850                1855                1860

Glu Pro  Gln Val Tyr Thr Leu  Pro Pro Ser Arg Asp  Glu Leu Thr
    1865                1870                1875

Lys Asn  Gln Val Ser Leu Thr  Cys Leu Val Lys Gly  Phe Tyr Pro
    1880                1885                1890

Ser Asp  Ile Ala Val Glu Trp  Glu Ser Asn Gly Gln  Pro Glu Asn
    1895                1900                1905

Asn Tyr  Lys Thr Thr Pro Pro  Val Leu Asp Ser Asp  Gly Ser Phe
    1910                1915                1920

Phe Leu  Tyr Ser Lys Leu Thr  Val Asp Lys Ser Arg  Trp Gln Gln
    1925                1930                1935

Gly Asn  Val Phe Ser Cys Ser  Val Met His Glu Ala  Leu His Asn
    1940                1945                1950
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His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
    1955   1960   1965

<210> 204
<211> 5898
<212> DNA
<213> Artificial Sequence

<220>
<223> Final nucleotide sequence of FVIII 312A (SEQ ID NO: 204)

<400> 204
atgcaaatag agctctccac ctgcttcttt ctgtgccttt tgcgattctg ctttagtgcc 60

accagaagat actacctggg tgcagtggaa ctgtcatggg actatatgca aagtgatctc 120

ggtgagctgc ctgtggacgc aagatttcct cctagagtgc caaaatcttt tccattcaac 180

acctcagtcg tgtacaaaaa gactctgttt gtagaattca cggatcacct tttcaacatc 240

gctaagccaa ggccaccctg gatgggtctg ctaggtccta ccatccaggc tgaggtttat 300

gatacagtgg tcattacact taagaacatg gcttcccatc ctgtcagtct tcatgctgtt 360

ggtgtatcct actggaaagc ttctgaggga gctgaatatg atgatcagac cagtcaaagg 420

gagaaagaag atgataaagt cttccctggt ggaagccata catatgtctg gcaggtcctg 480

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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

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Cys Gln Leu Leu Lys Ser Thr Ser Val Phe Ala Arg Cys His Pro Leu
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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
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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
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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
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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
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Val Tyr Leu Gln Cys Gly Thr Pro Cys Asn Leu Thr Cys Arg Ser Leu
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Ser Tyr Pro Asp Glu Glu Cys Asn Glu Ala Cys Leu Glu Gly Cys Phe
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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
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Leu Lys Tyr Leu Phe Pro Gly Glu Cys Gln Tyr Val Leu Val Gln Asp
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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
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Ser Ser  Asn Leu Gln Val Glu  Glu Asp Pro Val Asp  Phe Gly Asn
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Ser Trp  Lys Val Ser Ser Gln  Cys Ala Asp Thr Arg  Lys Val Pro
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Leu Asp  Ser Ser Pro Ala Thr  Cys His Asn Asn Ile  Met Lys Gln
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Thr Met  Val Asp Ser Ser Cys  Arg Ile Leu Thr Ser  Asp Val Phe
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Gln Asp  Cys Asn Lys Leu Val  Asp Pro Glu Pro Tyr  Leu Asp Val
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Cys Ile  Tyr Asp Thr Cys Ser  Cys Glu Ser Ile Gly  Asp Cys Ala
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Ala Phe  Cys Asp Thr Ile Ala  Ala Tyr Ala His Val  Cys Ala Gln
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His Gly  Lys Val Val Thr Trp  Arg Thr Ala Thr Leu  Cys Pro Gln
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Ser Cys  Glu Glu Arg Asn Leu  Arg Glu Asn Gly Tyr  Glu Ala Glu
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Trp Arg  Tyr Asn Ser Cys Ala  Pro Ala Cys Gln Val  Thr Cys Gln
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His Pro  Glu Pro Leu Ala Cys  Pro Val Gln Cys Val  Glu Gly Cys
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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
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Arg Arg  Phe Ala Ser Gly Lys  Lys Val Thr Leu Asn  Pro Ser Asp
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Pro Glu  His Cys Gln Ile Cys  His Cys Asp Val Val  Asn Leu Thr
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Cys Glu  Ala Cys Gln Glu Pro  Gly Thr Ser Glu Ser  Ala Thr Pro
    1235                1240                1245

Glu Ser  Gly Pro Gly Ser Glu  Pro Ala Thr Ser Gly  Ser Glu Thr
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Pro Gly  Thr Ser Glu Ser Ala  Thr Pro Glu Ser Gly  Pro Gly Ser
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Glu Pro  Ala Thr Ser Gly Ser  Glu Thr Pro Gly Thr  Ser Glu Ser
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Ala Thr  Pro Glu Ser Gly Pro  Gly Thr Ser Thr Glu  Pro Ser Glu
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Gly Ser  Ala Pro Gly Ser Pro  Ala Gly Ser Pro Thr  Ser Thr Glu
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Glu Gly  Thr Ser Glu Ser Ala  Thr Pro Glu Ser Gly  Pro Gly Ser
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Glu Pro  Ala Thr Ser Gly Ser  Glu Thr Pro Gly Thr  Ser Glu Ser
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Glu Gly  Ala Ser Ser Asp Lys  Asn Thr Gly Asp Tyr  Tyr Glu Asp
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Ser Tyr  Glu Asp Ile Ser Ala  Tyr Leu Leu Ser Lys  Asn Asn Ala
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Ile Glu  Pro Arg Ser Phe Ser  Asp Lys Thr His Thr  Cys Pro Pro
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Cys Pro  Ala Pro Glu Leu Leu  Gly Gly Pro Ser Val  Phe Leu Phe
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Pro Pro  Lys Pro Lys Asp Thr  Leu Met Ile Ser Arg  Thr Pro Glu
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Val Thr  Cys Val Val Val Asp  Val Ser His Glu Asp  Pro Glu Val
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Lys Phe  Asn Trp Tyr Val Asp  Gly Val Glu Val His  Asn Ala Lys
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Thr Lys  Pro Arg Glu Glu Gln  Tyr Asn Ser Thr Tyr  Arg Val Val
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Lys Thr  Ile Ser Lys Ala Lys  Gly Gln Pro Arg Glu  Pro Gln Val
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Tyr Thr  Leu Pro Pro Ser Arg  Asp Glu Leu Thr Lys  Asn Gln Val
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Ser Leu  Thr Cys Leu Val Lys  Gly Phe Tyr Pro Ser  Asp Ile Ala
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Val Glu  Trp Glu Ser Asn Gly  Gln Pro Glu Asn Asn  Tyr Lys Thr
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Thr Pro  Pro Val Leu Asp Ser  Asp Gly Ser Phe Phe  Leu Tyr Ser
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Lys Leu  Thr Val Asp Lys Ser  Arg Trp Gln Gln Gly  Asn Val Phe
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tgtgtggccc tggaaaggtg tccctgcttc catcagggca aggagtatgc ccctggagaa 2520

acagtgaaga ttggctgcaa cacttgtgtc tgtcgggacc ggaagtggaa ctgcacagac 2580

catgtgtgtg atgccacgtg ctccacgatc ggcatggccc actacctcac cttcgacggg 2640

ctcaaatacc tgttccccgg ggagtgccag tacgttctgg tgcaggatta ctgcggcagt 2700

aaccctggga cctttcggat cctagtgggg aataagggat gcagccaccc ctcagtgaaa 2760

tgcaagaaac gggtcaccat cctggtggag ggaggagaga ttgagctgtt tgacggggag 2820

gtgaatgtga agaggcccat gaaggatgag actcactttg aggtggtgga gtctggccgg 2880

tacatcattc tgctgctggg caaagccctc tccgtggtct gggaccgcca cctgagcatc 2940

tccgtggtcc tgaagcagac ataccaggag aaagtgtgtg gcctgtgtgg gaattttgat 3000

ggcatccaga acaatgacct caccagcagc aacctccaag tggaggaaga ccctgtggac 3060

tttgggaact cctggaaagt gagctcgcag tgtgctgaca ccagaaaagt gcctctggac 3120

tcatcccctg ccacctgcca taacaacatc atgaagcaga cgatggtgga ttcctcctgt 3180

agaatcctta ccagtgacgt cttccaggac tgcaacaagc tggtggaccc cgagccatat 3240

ctggatgtct gcatttacga cacctgctcc tgtgagtcca ttggggactg cgccgcattc 3300

tgcgacacca ttgctgccta tgcccacgtg tgtgcccagc atggcaaggt ggtgacctgg 3360

aggacggcca cattgtgccc ccagagctgc gaggagagga atctccggga gaacgggtat 3420

gaggctgagt ggcgctataa cagctgtgca cctgcctgtc aagtcacgtg tcagcaccct 3480

gagccactgg cctgccctgt gcagtgtgtg gagggctgcc atgcccactg ccctccaggg 3540

aaaatcctgg atgagctttt gcagacctgc gttgaccctg aagactgtcc agtgtgtgag 3600

gtggctggcc ggcgttttgc ctcaggaaag aaagtcacct tgaatcccag tgaccctgag 3660

cactgccaga tttgccactg tgatgttgtc aacctcacct gtgaagcctg ccaggagccg 3720

ggtacatcag agagcgccac ccctgaaagt ggtcccggga gcgagccagc cacatctggg 3780

tcggaaacgc caggcacatc cgagtctgca actcccgagt ccggacctgg ctccgagcct 3840

gccactagcg gctccgagac tccgggaact tccgagagcg ctacaccaga aagcggaccc 3900

ggaaccagta ccgaacctag cgagggctct gctccgggca gcccagccgg ctctcctaca 3960

tccacggagg agggcacttc cgaatccgcc accccggagt cagggccagg atctgaaccc 4020

gctacctcag gcagtgagac gccaggaacg agcgagtccg ctacaccgga gagtgggcca 4080

gggagccctg ctggatctcc tacgtccact gaggaagggt caccagcggg ctcgcccacc 4140

agcactgaag aaggtgcctc gtctgacaag aacactggtg attattacga ggacagttat 4200

gaagatattt cagcatactt gctgagtaaa aacaatgcca ttgaaccaag aagcttctct 4260

gacaaaactc acacatgccc accgtgccca gctccagaac tcctgggcgg accgtcagtc 4320

ttcctcttcc ccccaaaacc caaggacacc ctcatgatct cccggacccc tgaggtcaca 4380

tgcgtggtgg tggacgtgag ccacgaagac cctgaggtca agttcaactg gtatgtggac 4440

ggcgtggaag tgcataatgc caagacaaag ccgcgggagg agcagtacaa cagcacgtac 4500

cgtgtggtca gcgtcctcac cgtcctgcac caagactggc tgaatggcaa ggagtacaag 4560

tgcaaggtct ccaacaaagc cctcccagcc cccatcgaga aaaccatctc caaagccaaa 4620

gggcagcccc gagaaccaca ggtgtacacc ctgcccccat cccgggatga gctgaccaag 4680

aaccaagtta gcctgacctg cctggtcaaa ggcttctatc ccagcgacat cgccgtggag 4740

tgggagagca atgggcagcc ggagaacaac tacaagacca cgcctcccgt gttggactcc 4800

gacggctcct tcttcctcta ctccaagctc accgtggaca agagcaggtg gcagcagggg 4860

aacgtcttct catgctccgt gatgcatgag gctctgcaca accactacac gcagaagagc 4920

ctctccctgt ctccgggttg a 4941

<210> 207
<211> 1946
<212> PRT

<213> Artificial Sequence

<220>
<223> FVIII(XTEN)-Fc w lead A

<400> 207

Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser Trp Asp Tyr
1 5 10 15

Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro
20 25 30

Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys
35 40 45

Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys Pro
50 55 60

Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val
65 70 75 80

Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val
85 90 95

Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala
100 105 110

Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val
115 120 125

Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn
130 135 140

Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser
145 150 155 160

His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu
165 170 175

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

```
His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp
        195                 200                 205

His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser
    210                 215                 220

Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg
225                 230                 235                 240

Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His
                245                 250                 255

Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu
            260                 265                 270

Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile
        275                 280                 285

Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly
    290                 295                 300

Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met
305                 310                 315                 320

Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg
                325                 330                 335

Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp
            340                 345                 350

Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro Ser Phe
        355                 360                 365

Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His
    370                 375                 380

Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu
385                 390                 395                 400

Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro
                405                 410                 415
```

```
Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr
            420                 425                 430

Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile
        435                 440                 445

Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile
    450                 455                 460

Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile
465                 470                 475                 480

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

His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys
            500                 505                 510

Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys
        515                 520                 525

Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala
    530                 535                 540

Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp
545                 550                 555                 560

Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe
                565                 570                 575

Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln
            580                 585                 590

Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe
        595                 600                 605

Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser
    610                 615                 620

Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu
625                 630                 635                 640
```

```
Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr
                645                 650                 655

Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro
            660                 665                 670

Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp
        675                 680                 685

Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr Ala
    690                 695                 700

Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu
705                 710                 715                 720

Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala
                725                 730                 735

Ile Glu Pro Arg Ser Phe Ser Gln Asn Gly Thr Ser Glu Ser Ala Thr
            740                 745                 750

Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr
        755                 760                 765

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu
    770                 775                 780

Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr
785                 790                 795                 800

Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
                805                 810                 815

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser
            820                 825                 830

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
        835                 840                 845

Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
```

```
    850                 855                 860

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro
865                 870                 875                 880

Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser
                885                 890                 895

Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
            900                 905                 910

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser
        915                 920                 925

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
    930                 935                 940

Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr
945                 950                 955                 960

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser
                965                 970                 975

Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser
            980                 985                 990

Glu Gly Ser Ala Pro Gly Ser Glu  Pro Ala Thr Ser Gly  Ser Glu Thr
        995                 1000                1005

Pro Gly  Thr Ser Glu Ser Ala  Thr Pro Glu Ser Gly  Pro Gly Thr
    1010                1015                1020

Ser Thr  Glu Pro Ser Glu Gly  Ser Ala Pro Ala Ser  Ser Glu Ile
    1025                1030                1035

Thr Arg  Thr Thr Leu Gln Ser  Asp Gln Glu Glu Ile  Asp Tyr Asp
    1040                1045                1050

Asp Thr  Ile Ser Val Glu Met  Lys Lys Glu Asp Phe  Asp Ile Tyr
    1055                1060                1065
```

```
Asp Glu  Asp Glu Asn Gln Ser  Pro Arg Ser Phe Gln  Lys Lys Thr
    1070                1075                1080

Arg His  Tyr Phe Ile Ala Ala  Val Glu Arg Leu Trp  Asp Tyr Gly
    1085                1090                1095

Met Ser  Ser Ser Pro His Val  Leu Arg Asn Arg Ala  Gln Ser Gly
    1100                1105                1110

Ser Val  Pro Gln Phe Lys Lys  Val Val Phe Gln Glu  Phe Thr Asp
    1115                1120                1125

Gly Ser  Phe Thr Gln Pro Leu  Tyr Arg Gly Glu Leu  Asn Glu His
    1130                1135                1140

Leu Gly  Leu Leu Gly Pro Tyr  Ile Arg Ala Glu Val  Glu Asp Asn
    1145                1150                1155

Ile Met  Val Thr Phe Arg Asn  Gln Ala Ser Arg Pro  Tyr Ser Phe
    1160                1165                1170

Tyr Ser  Ser Leu Ile Ser Tyr  Glu Glu Asp Gln Arg  Gln Gly Ala
    1175                1180                1185

Glu Pro  Arg Lys Asn Phe Val  Lys Pro Asn Glu Thr  Lys Thr Tyr
    1190                1195                1200

Phe Trp  Lys Val Gln His His  Met Ala Pro Thr Lys  Asp Glu Phe
    1205                1210                1215

Asp Cys  Lys Ala Trp Ala Tyr  Phe Ser Asp Val Asp  Leu Glu Lys
    1220                1225                1230

Asp Val  His Ser Gly Leu Ile  Gly Pro Leu Leu Val  Cys His Thr
    1235                1240                1245

Asn Thr  Leu Asn Pro Ala His  Gly Arg Gln Val Thr  Val Gln Glu
    1250                1255                1260

Phe Ala  Leu Phe Phe Thr Ile  Phe Asp Glu Thr Lys  Ser Trp Tyr
    1265                1270                1275
```

```
Phe Thr  Glu Asn Met Glu Arg  Asn Cys Arg Ala Pro  Cys Asn Ile
    1280                1285                1290

Gln Met  Glu Asp Pro Thr Phe  Lys Glu Asn Tyr Arg  Phe His Ala
    1295                1300                1305

Ile Asn  Gly Tyr Ile Met Asp  Thr Leu Pro Gly Leu  Val Met Ala
    1310                1315                1320

Gln Asp  Gln Arg Ile Arg Trp  Tyr Leu Leu Ser Met  Gly Ser Asn
    1325                1330                1335

Glu Asn  Ile His Ser Ile His  Phe Ser Gly His Val  Phe Thr Val
    1340                1345                1350

Arg Lys  Lys Glu Glu Tyr Lys  Met Ala Leu Tyr Asn  Leu Tyr Pro
    1355                1360                1365

Gly Val  Phe Glu Thr Val Glu  Met Leu Pro Ser Lys  Ala Gly Ile
    1370                1375                1380

Trp Arg  Val Glu Cys Leu Ile  Gly Glu His Leu His  Ala Gly Met
    1385                1390                1395

Ser Thr  Leu Phe Leu Val Tyr  Ser Asn Lys Cys Gln  Thr Pro Leu
    1400                1405                1410

Gly Met  Ala Ser Gly His Ile  Arg Asp Phe Gln Ile  Thr Ala Ser
    1415                1420                1425

Gly Gln  Tyr Gly Gln Trp Ala  Pro Lys Leu Ala Arg  Leu His Tyr
    1430                1435                1440

Ser Gly  Ser Ile Asn Ala Trp  Ser Thr Lys Glu Pro  Phe Ser Trp
    1445                1450                1455

Ile Lys  Val Asp Leu Leu Ala  Pro Met Ile Ile His  Gly Ile Lys
    1460                1465                1470

Thr Gln  Gly Ala Arg Gln Lys  Phe Ser Ser Leu Tyr  Ile Ser Gln
    1475                1480                1485
```

```
Phe Ile  Ile Met Tyr Ser Leu  Asp Gly Lys Lys Trp  Gln Thr Tyr
    1490                1495                1500

Arg Gly  Asn Ser Thr Gly Thr  Leu Met Val Phe Phe  Gly Asn Val
    1505                1510                1515

Asp Ser  Ser Gly Ile Lys His  Asn Ile Phe Asn Pro  Pro Ile Ile
    1520                1525                1530

Ala Arg  Tyr Ile Arg Leu His  Pro Thr His Tyr Ser  Ile Arg Ser
    1535                1540                1545

Thr Leu  Arg Met Glu Leu Met  Gly Cys Asp Leu Asn  Ser Cys Ser
    1550                1555                1560

Met Pro  Leu Gly Met Glu Ser  Lys Ala Ile Ser Asp  Ala Gln Ile
    1565                1570                1575

Thr Ala  Ser Ser Tyr Phe Thr  Asn Met Phe Ala Thr  Trp Ser Pro
    1580                1585                1590

Ser Lys  Ala Arg Leu His Leu  Gln Gly Arg Ser Asn  Ala Trp Arg
    1595                1600                1605

Pro Gln  Val Asn Asn Pro Lys  Glu Trp Leu Gln Val  Asp Phe Gln
    1610                1615                1620

Lys Thr  Met Lys Val Thr Gly  Val Thr Thr Gln Gly  Val Lys Ser
    1625                1630                1635

Leu Leu  Thr Ser Met Tyr Val  Lys Glu Phe Leu Ile  Ser Ser Ser
    1640                1645                1650

Gln Asp  Gly His Gln Trp Thr  Leu Phe Phe Gln Asn  Gly Lys Val
    1655                1660                1665

Lys Val  Phe Gln Gly Asn Gln  Asp Ser Phe Thr Pro  Val Val Asn
    1670                1675                1680

Ser Leu  Asp Pro Pro Leu Leu  Thr Arg Tyr Leu Arg  Ile His Pro
```

```
    1685                1690                1695

Gln Ser  Trp Val His Gln Ile  Ala Leu Arg Met Glu  Val Leu Gly
    1700                1705                1710

Cys Glu  Ala Gln Asp Leu Tyr  Asp Lys Thr His Thr  Cys Pro Pro
    1715                1720                1725

Cys Pro  Ala Pro Glu Leu Leu  Gly Gly Pro Ser Val  Phe Leu Phe
    1730                1735                1740

Pro Pro  Lys Pro Lys Asp Thr  Leu Met Ile Ser Arg  Thr Pro Glu
    1745                1750                1755

Val Thr  Cys Val Val Val Asp  Val Ser His Glu Asp  Pro Glu Val
    1760                1765                1770

Lys Phe  Asn Trp Tyr Val Asp  Gly Val Glu Val His  Asn Ala Lys
    1775                1780                1785

Thr Lys  Pro Arg Glu Glu Gln  Tyr Asn Ser Thr Tyr  Arg Val Val
    1790                1795                1800

Ser Val  Leu Thr Val Leu His  Gln Asp Trp Leu Asn  Gly Lys Glu
    1805                1810                1815

Tyr Lys  Cys Lys Val Ser Asn  Lys Ala Leu Pro Ala  Pro Ile Glu
    1820                1825                1830

Lys Thr  Ile Ser Lys Ala Lys  Gly Gln Pro Arg Glu  Pro Gln Val
    1835                1840                1845

Tyr Thr  Leu Pro Pro Ser Arg  Asp Glu Leu Thr Lys  Asn Gln Val
    1850                1855                1860

Ser Leu  Thr Cys Leu Val Lys  Gly Phe Tyr Pro Ser  Asp Ile Ala
    1865                1870                1875

Val Glu  Trp Glu Ser Asn Gly  Gln Pro Glu Asn Asn  Tyr Lys Thr
    1880                1885                1890
```

```
Thr Pro  Pro Val Leu Asp Ser  Asp Gly Ser Phe Phe  Leu Tyr Ser
    1895                1900                1905


Lys Leu  Thr Val Asp Lys Ser  Arg Trp Gln Gln Gly  Asn Val Phe
    1910                1915                1920


Ser Cys  Ser Val Met His Glu  Ala Leu His Asn His  Tyr Thr Gln
    1925                1930                1935


Lys Ser  Leu Ser Leu Ser Pro  Gly
    1940                1945


<210>  208
<211>  22
<212>  PRT
<213>  Homo sapiens

<400>  208

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
            20


<210>  209
<211>  741
<212>  PRT
<213>  Homo sapiens

<400>  209

Ala Glu Gly Thr Arg Gly Arg Ser Ser Thr Ala Arg Cys Ser Leu Phe
1               5                   10                  15


Gly Ser Asp Phe Val Asn Thr Phe Asp Gly Ser Met Tyr Ser Phe Ala
            20                  25                  30


Gly Tyr Cys Ser Tyr Leu Leu Ala Gly Gly Cys Gln Lys Arg Ser Phe
        35                  40                  45


Ser Ile Ile Gly Asp Phe Gln Asn Gly Lys Arg Val Ser Leu Ser Val
    50                  55                  60


Tyr Leu Gly Glu Phe Phe Asp Ile His Leu Phe Val Asn Gly Thr Val
```

```
65                  70                  75                  80

Thr Gln Gly Asp Gln Arg Val Ser Met Pro Tyr Ala Ser Lys Gly Leu
                85                  90                  95

Tyr Leu Glu Thr Glu Ala Gly Tyr Tyr Lys Leu Ser Gly Glu Ala Tyr
            100                 105                 110

Gly Phe Val Ala Arg Ile Asp Gly Ser Gly Asn Phe Gln Val Leu Leu
        115                 120                 125

Ser Asp Arg Tyr Phe Asn Lys Thr Cys Gly Leu Cys Gly Asn Phe Asn
    130                 135                 140

Ile Phe Ala Glu Asp Asp Phe Met Thr Gln Glu Gly Thr Leu Thr Ser
145                 150                 155                 160

Asp Pro Tyr Asp Phe Ala Asn Ser Trp Ala Leu Ser Ser Gly Glu Gln
                165                 170                 175

Trp Cys Glu Arg Ala Ser Pro Pro Ser Ser Ser Cys Asn Ile Ser Ser
            180                 185                 190

Gly Glu Met Gln Lys Gly Leu Trp Glu Gln Cys Gln Leu Leu Lys Ser
        195                 200                 205

Thr Ser Val Phe Ala Arg Cys His Pro Leu Val Asp Pro Glu Pro Phe
    210                 215                 220

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

Cys Ala Cys Pro Ala Leu Leu Glu Tyr Ala Arg Thr Cys Ala Gln Glu
                245                 250                 255

Gly Met Val Leu Tyr Gly Trp Thr Asp His Ser Ala Cys Ser Pro Val
            260                 265                 270

Cys Pro Ala Gly Met Glu Tyr Arg Gln Cys Val Ser Pro Cys Ala Arg
        275                 280                 285
```

```
Thr Cys Gln Ser Leu His Ile Asn Glu Met Cys Gln Glu Arg Cys Val
    290                 295                 300

Asp Gly Cys Ser Cys Pro Glu Gly Gln Leu Leu Asp Glu Gly Leu Cys
305                 310                 315                 320

Val Glu Ser Thr Glu Cys Pro Cys Val His Ser Gly Lys Arg Tyr Pro
                325                 330                 335

Pro Gly Thr Ser Leu Ser Arg Asp Cys Asn Thr Cys Ile Cys Arg Asn
            340                 345                 350

Ser Gln Trp Ile Cys Ser Asn Glu Glu Cys Pro Gly Glu Cys Leu Val
        355                 360                 365

Thr Gly Gln Ser His Phe Lys Ser Phe Asp Asn Arg Tyr Phe Thr Phe
    370                 375                 380

Ser Gly Ile Cys Gln Tyr Leu Leu Ala Arg Asp Cys Gln Asp His Ser
385                 390                 395                 400

Phe Ser Ile Val Ile Glu Thr Val Gln Cys Ala Asp Asp Arg Asp Ala
                405                 410                 415

Val Cys Thr Arg Ser Val Thr Val Arg Leu Pro Gly Leu His Asn Ser
            420                 425                 430

Leu Val Lys Leu Lys His Gly Ala Gly Val Ala Met Asp Gly Gln Asp
        435                 440                 445

Ile Gln Leu Pro Leu Leu Lys Gly Asp Leu Arg Ile Gln His Thr Val
    450                 455                 460

Thr Ala Ser Val Arg Leu Ser Tyr Gly Glu Asp Leu Gln Met Asp Trp
465                 470                 475                 480

Asp Gly Arg Gly Arg Leu Leu Val Lys Leu Ser Pro Val Tyr Ala Gly
                485                 490                 495

Lys Thr Cys Gly Leu Cys Gly Asn Tyr Asn Gly Asn Gln Gly Asp Asp
            500                 505                 510
```

```
Phe Leu Thr Pro Ser Gly Leu Ala Glu Pro Arg Val Glu Asp Phe Gly
        515                 520                 525

Asn Ala Trp Lys Leu His Gly Asp Cys Gln Asp Leu Gln Lys Gln His
    530                 535                 540

Ser Asp Pro Cys Ala Leu Asn Pro Arg Met Thr Arg Phe Ser Glu Glu
545                 550                 555                 560

Ala Cys Ala Val Leu Thr Ser Pro Thr Phe Glu Ala Cys His Arg Ala
                565                 570                 575

Val Ser Pro Leu Pro Tyr Leu Arg Asn Cys Arg Tyr Asp Val Cys Ser
            580                 585                 590

Cys Ser Asp Gly Arg Glu Cys Leu Cys Gly Ala Leu Ala Ser Tyr Ala
        595                 600                 605

Ala Ala Cys Ala Gly Arg Gly Val Arg Val Ala Trp Arg Glu Pro Gly
    610                 615                 620

Arg Cys Glu Leu Asn Cys Pro Lys Gly Gln Val Tyr Leu Gln Cys Gly
625                 630                 635                 640

Thr Pro Cys Asn Leu Thr Cys Arg Ser Leu Ser Tyr Pro Asp Glu Glu
                645                 650                 655

Cys Asn Glu Ala Cys Leu Glu Gly Cys Phe Cys Pro Pro Gly Leu Tyr
            660                 665                 670

Met Asp Glu Arg Gly Asp Cys Val Pro Lys Ala Gln Cys Pro Cys Tyr
        675                 680                 685

Tyr Asp Gly Glu Ile Phe Gln Pro Glu Asp Ile Phe Ser Asp His His
    690                 695                 700

Thr Met Cys Tyr Cys Glu Asp Gly Phe Met His Cys Thr Met Ser Gly
705                 710                 715                 720

Val Pro Gly Ser Leu Leu Pro Asp Ala Val Leu Ser Ser Pro Leu Ser
                725                 730                 735
```

```
His Arg Ser Lys Arg
            740


<210>  210
<211>  103
<212>  PRT
<213>  Homo sapiens

<400>  210

Ser Leu Ser Cys Arg Pro Pro Met Val Lys Leu Val Cys Pro Ala Asp
1               5                   10                  15


Asn Leu Arg Ala Glu Gly Leu Glu Cys Thr Lys Thr Cys Gln Asn Tyr
            20                  25                  30


Asp Leu Glu Cys Met Ser Met Gly Cys Val Ser Gly Cys Leu Cys Pro
        35                  40                  45


Pro Gly Met Val Arg His Glu Asn Arg Cys Val Ala Leu Glu Arg Cys
    50                  55                  60


Pro Cys Phe His Gln Gly Lys Glu Tyr Ala Pro Gly Glu Thr Val Lys
65                  70                  75                  80


Ile Gly Cys Asn Thr Cys Val Cys Arg Asp Arg Lys Trp Asn Cys Thr
                85                  90                  95


Asp His Val Cys Asp Ala Thr
            100


<210>  211
<211>  374
<212>  PRT
<213>  Homo sapiens

<400>  211

Cys Ser Thr Ile Gly Met Ala His Tyr Leu Thr Phe Asp Gly Leu Lys
1               5                   10                  15


Tyr Leu Phe Pro Gly Glu Cys Gln Tyr Val Leu Val Gln Asp Tyr Cys
            20                  25                  30
```

```
Gly Ser Asn Pro Gly Thr Phe Arg Ile Leu Val Gly Asn Lys Gly Cys
        35                  40                  45

Ser His Pro Ser Val Lys Cys Lys Lys Arg Val Thr Ile Leu Val Glu
    50                  55                  60

Gly Gly Glu Ile Glu Leu Phe Asp Gly Glu Val Asn Val Lys Arg Pro
65                  70                  75                  80

Met Lys Asp Glu Thr His Phe Glu Val Val Glu Ser Gly Arg Tyr Ile
                85                  90                  95

Ile Leu Leu Leu Gly Lys Ala Leu Ser Val Val Trp Asp Arg His Leu
            100                 105                 110

Ser Ile Ser Val Val Leu Lys Gln Thr Tyr Gln Glu Lys Val Cys Gly
        115                 120                 125

Leu Cys Gly Asn Phe Asp Gly Ile Gln Asn Asn Asp Leu Thr Ser Ser
    130                 135                 140

Asn Leu Gln Val Glu Glu Asp Pro Val Asp Phe Gly Asn Ser Trp Lys
145                 150                 155                 160

Val Ser Ser Gln Cys Ala Asp Thr Arg Lys Val Pro Leu Asp Ser Ser
                165                 170                 175

Pro Ala Thr Cys His Asn Asn Ile Met Lys Gln Thr Met Val Asp Ser
            180                 185                 190

Ser Cys Arg Ile Leu Thr Ser Asp Val Phe Gln Asp Cys Asn Lys Leu
        195                 200                 205

Val Asp Pro Glu Pro Tyr Leu Asp Val Cys Ile Tyr Asp Thr Cys Ser
    210                 215                 220

Cys Glu Ser Ile Gly Asp Cys Ala Cys Phe Cys Asp Thr Ile Ala Ala
225                 230                 235                 240

Tyr Ala His Val Cys Ala Gln His Gly Lys Val Val Thr Trp Arg Thr
                245                 250                 255
```

```
Ala Thr Leu Cys Pro Gln Ser Cys Glu Glu Arg Asn Leu Arg Glu Asn
            260                 265                 270


Gly Tyr Glu Cys Glu Trp Arg Tyr Asn Ser Cys Ala Pro Ala Cys Gln
        275                 280                 285


Val Thr Cys Gln His Pro Glu Pro Leu Ala Cys Pro Val Gln Cys Val
    290                 295                 300


Glu Gly Cys His Ala His Cys Pro Pro Gly Lys Ile Leu Asp Glu Leu
305                 310                 315                 320


Leu Gln Thr Cys Val Asp Pro Glu Asp Cys Pro Val Cys Glu Val Ala
                325                 330                 335


Gly Arg Arg Phe Ala Ser Gly Lys Lys Val Thr Leu Asn Pro Ser Asp
            340                 345                 350


Pro Glu His Cys Gln Ile Cys His Cys Asp Val Val Asn Leu Thr Cys
        355                 360                 365


Glu Ala Cys Gln Glu Pro
    370


<210>  212
<211>  239
<212>  PRT
<213>  Homo sapiens

<400>  212

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


Leu Tyr Val Glu Asp Ile Ser Glu Pro Pro Leu His Asp Phe Tyr Cys
            20                  25                  30


Ser Arg Leu Leu Asp Leu Val Phe Leu Leu Asp Gly Ser Ser Arg Leu
        35                  40                  45


Ser Glu Ala Glu Phe Glu Val Leu Lys Ala Phe Val Val Asp Met Met
    50                  55                  60
```

```
Glu Arg Leu Arg Ile Ser Gln Lys Trp Val Arg Val Ala Val Val Glu
65                  70                  75                  80

Tyr His Asp Gly Ser His Ala Tyr Ile Gly Leu Lys Asp Arg Lys Arg
                85                  90                  95

Pro Ser Glu Leu Arg Arg Ile Ala Ser Gln Val Lys Tyr Ala Gly Ser
            100                 105                 110

Gln Val Ala Ser Thr Ser Glu Val Leu Lys Tyr Thr Leu Phe Gln Ile
        115                 120                 125

Phe Ser Lys Ile Asp Arg Pro Glu Ala Ser Arg Ile Ala Leu Leu Leu
    130                 135                 140

Met Ala Ser Gln Glu Pro Gln Arg Met Ser Arg Asn Phe Val Arg Tyr
145                 150                 155                 160

Val Gln Gly Leu Lys Lys Lys Lys Val Ile Val Ile Pro Val Gly Ile
                165                 170                 175

Gly Pro His Ala Asn Leu Lys Gln Ile Arg Leu Ile Glu Lys Gln Ala
            180                 185                 190

Pro Glu Asn Lys Ala Phe Val Leu Ser Ser Val Asp Glu Leu Glu Gln
        195                 200                 205

Gln Arg Asp Glu Ile Val Ser Tyr Leu Cys Asp Leu Ala Pro Glu Ala
    210                 215                 220

Pro Pro Pro Thr Leu Pro Pro Asp Met Ala Gln Val Thr Val Gly
225                 230                 235
```

<210> 213
<211> 1334
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<222> (537)..(537)

<223> Xaa can be any naturally occurring amino acid

<400> 213

```
Pro Gly Leu Leu Gly Val Ser Thr Leu Gly Pro Lys Arg Asn Ser Met
1               5                  10                  15


Val Leu Asp Val Ala Phe Val Leu Glu Gly Ser Asp Lys Ile Gly Glu
            20                  25                  30


Ala Asp Phe Asn Arg Ser Lys Glu Phe Met Glu Glu Val Ile Gln Arg
        35                  40                  45


Met Asp Val Gly Gln Asp Ser Ile His Val Thr Val Leu Gln Tyr Ser
    50                  55                  60


Tyr Met Val Thr Val Glu Tyr Pro Phe Ser Glu Ala Gln Ser Lys Gly
65                  70                  75                  80


Asp Ile Leu Gln Arg Val Arg Glu Ile Arg Tyr Gln Gly Gly Asn Arg
                85                  90                  95


Thr Asn Thr Gly Leu Ala Leu Arg Tyr Leu Ser Asp His Ser Phe Leu
            100                 105                 110


Val Ser Gln Gly Asp Arg Glu Gln Ala Pro Asn Leu Val Tyr Met Val
        115                 120                 125


Thr Gly Asn Pro Ala Ser Asp Glu Ile Lys Arg Leu Pro Gly Asp Ile
    130                 135                 140


Gln Val Val Pro Ile Gly Val Gly Pro Asn Ala Asn Val Gln Glu Leu
145                 150                 155                 160


Glu Arg Ile Gly Trp Pro Asn Ala Pro Ile Leu Ile Gln Asp Phe Glu
                165                 170                 175


Thr Leu Pro Arg Glu Ala Pro Asp Leu Val Leu Gln Arg Cys Cys Ser
            180                 185                 190


Gly Glu Gly Leu Gln Ile Pro Thr Leu Ser Pro Ala Pro Asp Cys Ser
        195                 200                 205
```

```
Gln Pro Leu Asp Val Ile Leu Leu Leu Asp Gly Ser Ser Ser Phe Pro
    210                 215                 220

Ala Ser Tyr Phe Asp Glu Met Lys Ser Phe Ala Lys Ala Phe Ile Ser
225                 230                 235                 240

Lys Ala Asn Ile Gly Pro Arg Leu Thr Gln Val Ser Val Leu Gln Tyr
                245                 250                 255

Gly Ser Ile Thr Thr Ile Asp Val Pro Trp Asn Val Val Pro Glu Lys
            260                 265                 270

Ala His Leu Leu Ser Leu Val Asp Val Met Gln Arg Glu Gly Gly Pro
        275                 280                 285

Ser Gln Ile Gly Asp Ala Leu Gly Phe Ala Val Arg Tyr Leu Thr Ser
    290                 295                 300

Glu Met His Gly Ala Arg Pro Gly Ala Ser Lys Ala Val Val Ile Leu
305                 310                 315                 320

Val Thr Asp Val Ser Val Asp Ser Val Asp Ala Ala Ala Asp Ala Ala
                325                 330                 335

Arg Ser Asn Arg Val Thr Val Phe Pro Ile Gly Ile Gly Asp Arg Tyr
            340                 345                 350

Asp Ala Ala Gln Leu Arg Ile Leu Ala Gly Pro Ala Gly Asp Ser Asn
        355                 360                 365

Val Val Lys Leu Gln Arg Ile Glu Asp Leu Pro Thr Met Val Thr Leu
    370                 375                 380

Gly Asn Ser Phe Leu His Lys Leu Cys Ser Gly Phe Val Arg Ile Cys
385                 390                 395                 400

Met Asp Glu Asp Gly Asn Glu Lys Arg Pro Gly Asp Val Trp Thr Leu
                405                 410                 415

Pro Asp Gln Cys His Thr Val Thr Cys Gln Pro Asp Gly Gln Thr Leu
            420                 425                 430
```

```
Leu Lys Ser His Arg Val Asn Cys Asp Arg Gly Leu Arg Pro Ser Cys
        435                 440                 445

Pro Asn Ser Gln Ser Pro Val Lys Val Glu Glu Thr Cys Gly Cys Arg
    450                 455                 460

Trp Thr Cys Pro Cys Val Cys Thr Gly Ser Ser Thr Arg His Ile Val
465                 470                 475                 480

Thr Phe Asp Gly Gln Asn Phe Lys Leu Thr Gly Ser Cys Ser Tyr Val
                485                 490                 495

Leu Phe Gln Asn Lys Glu Gln Asp Leu Glu Val Ile Leu His Asn Gly
            500                 505                 510

Ala Cys Ser Pro Gly Ala Arg Gln Gly Cys Met Lys Ser Ile Glu Val
        515                 520                 525

Lys His Ser Ala Leu Ser Val Glu Xaa His Ser Asp Met Glu Val Thr
    530                 535                 540

Val Asn Gly Arg Leu Val Ser Val Pro Tyr Val Gly Gly Asn Met Glu
545                 550                 555                 560

Val Asn Val Tyr Gly Ala Ile Met His Glu Val Arg Phe Asn His Leu
                565                 570                 575

Gly His Ile Phe Thr Phe Thr Pro Gln Asn Asn Glu Phe Gln Leu Gln
            580                 585                 590

Leu Ser Pro Lys Thr Phe Ala Ser Lys Thr Tyr Gly Leu Cys Gly Ile
        595                 600                 605

Cys Asp Glu Asn Gly Ala Asn Asp Phe Met Leu Arg Asp Gly Thr Val
    610                 615                 620

Thr Thr Asp Trp Lys Thr Leu Val Gln Glu Trp Thr Val Gln Arg Pro
625                 630                 635                 640

Gly Gln Thr Cys Gln Pro Ile Leu Glu Glu Gln Cys Leu Val Pro Asp
```

```
                645                 650                 655

Ser Ser His Cys Gln Val Leu Leu Leu Pro Leu Phe Ala Glu Cys His
            660                 665                 670

Lys Val Leu Ala Pro Ala Thr Phe Tyr Ala Ile Cys Gln Gln Asp Ser
        675                 680                 685

Cys His Gln Glu Gln Val Cys Glu Val Ile Ala Ser Tyr Ala His Leu
    690                 695                 700

Cys Arg Thr Asn Gly Val Cys Val Asp Trp Arg Thr Pro Asp Phe Cys
705                 710                 715                 720

Ala Met Ser Cys Pro Pro Ser Leu Val Tyr Asn His Cys Glu His Gly
                725                 730                 735

Cys Pro Arg His Cys Asp Gly Asn Val Ser Ser Cys Gly Asp His Pro
            740                 745                 750

Ser Glu Gly Cys Phe Cys Pro Pro Asp Lys Val Met Leu Glu Gly Ser
        755                 760                 765

Cys Val Pro Glu Glu Ala Cys Thr Gln Cys Ile Gly Glu Asp Gly Val
    770                 775                 780

Gln His Gln Phe Leu Glu Ala Trp Val Pro Asp His Gln Pro Cys Gln
785                 790                 795                 800

Ile Cys Thr Cys Leu Ser Gly Arg Lys Val Asn Cys Thr Thr Gln Pro
                805                 810                 815

Cys Pro Thr Ala Lys Ala Pro Thr Cys Gly Leu Cys Glu Val Ala Arg
            820                 825                 830

Leu Arg Gln Asn Ala Asp Gln Cys Cys Pro Glu Tyr Glu Cys Val Cys
        835                 840                 845

Asp Pro Val Ser Cys Asp Leu Pro Pro Val Pro His Cys Glu Arg Gly
    850                 855                 860
```

```
Leu Gln Pro Thr Leu Thr Asn Pro Gly Glu Cys Arg Pro Asn Phe Thr
865                 870                 875                 880


Cys Ala Cys Arg Lys Glu Glu Cys Lys Arg Val Ser Pro Pro Ser Cys
                885                 890                 895


Pro Pro His Arg Leu Pro Thr Leu Arg Lys Thr Gln Cys Cys Asp Glu
            900                 905                 910


Tyr Glu Cys Ala Cys Asn Cys Val Asn Ser Thr Val Ser Cys Pro Leu
        915                 920                 925


Gly Tyr Leu Ala Ser Thr Ala Thr Asn Asp Cys Gly Cys Thr Thr Thr
    930                 935                 940


Thr Cys Leu Pro Asp Lys Val Cys Val His Arg Ser Thr Ile Tyr Pro
945                 950                 955                 960


Val Gly Gln Phe Trp Glu Glu Gly Cys Asp Val Cys Thr Cys Thr Asp
                965                 970                 975


Met Glu Asp Ala Val Met Gly Leu Arg Val Ala Gln Cys Ser Gln Lys
            980                 985                 990


Pro Cys Glu Asp Ser Cys Arg Ser  Gly Phe Thr Tyr Val  Leu His Glu
        995                 1000                1005


Gly Glu  Cys Cys Gly Arg Cys  Leu Pro Ser Ala Cys  Glu Val Val
    1010                1015                1020


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


Gly Ser  Gln Trp Ala Ser Pro  Glu Asn Pro Cys Leu  Ile Asn Glu
    1040                1045                1050


Cys Val  Arg Val Lys Glu Glu  Val Phe Ile Gln Gln  Arg Asn Val
    1055                1060                1065


Ser Cys  Pro Gln Leu Glu Val  Pro Val Cys Pro Ser  Gly Phe Gln
    1070                1075                1080
```

```
Leu Ser  Cys Lys Thr Ser Ala  Cys Cys Pro Ser Cys  Arg Cys Glu
    1085                1090                1095

Arg Met  Glu Ala Cys Met Leu  Asn Gly Thr Val Ile  Gly Pro Gly
    1100                1105                1110

Lys Thr  Val Met Ile Asp Val  Cys Thr Thr Cys Arg  Cys Met Val
    1115                1120                1125

Gln Val  Gly Val Ile Ser Gly  Phe Lys Leu Glu Cys  Arg Lys Thr
    1130                1135                1140

Thr Cys  Asn Pro Cys Pro Leu  Gly Tyr Lys Glu Glu  Asn Asn Thr
    1145                1150                1155

Gly Glu  Cys Cys Gly Arg Cys  Leu Pro Thr Ala Cys  Thr Ile Gln
    1160                1165                1170

Leu Arg  Gly Gly Gln Ile Met  Thr Leu Lys Arg Asp  Glu Thr Leu
    1175                1180                1185

Gln Asp  Gly Cys Asp Thr His  Phe Cys Lys Val Asn  Glu Arg Gly
    1190                1195                1200

Glu Tyr  Phe Trp Glu Lys Arg  Val Thr Gly Cys Pro  Pro Phe Asp
    1205                1210                1215

Glu His  Lys Cys Leu Ala Glu  Gly Gly Lys Ile Met  Lys Ile Pro
    1220                1225                1230

Gly Thr  Cys Cys Asp Thr Cys  Glu Glu Pro Glu Cys  Asn Asp Ile
    1235                1240                1245

Thr Ala  Arg Leu Gln Tyr Val  Lys Val Gly Ser Cys  Lys Ser Glu
    1250                1255                1260

Val Glu  Val Asp Ile His Tyr  Cys Gln Gly Lys Cys  Ala Ser Lys
    1265                1270                1275

Ala Met  Tyr Ser Ile Asp Ile  Asn Asp Val Gln Asp  Gln Cys Ser
    1280                1285                1290
```

```
Cys Cys  Ser Pro Thr Arg Thr  Glu Pro Met Gln Val  Ala Leu His
    1295                1300                1305


Cys Thr  Asn Gly Ser Val Val  Tyr His Glu Val Leu  Asn Ala Met
    1310                1315                1320


Glu Cys  Lys Cys Ser Pro Arg  Lys Cys Ser Lys
    1325                1330


<210>  214
<211>  374
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  VWF D3 region EAE

<400>  214

Cys Ser Thr Ile Gly Met Ala His Tyr Leu Thr Phe Asp Gly Leu Lys
1               5                   10                  15


Tyr Leu Phe Pro Gly Glu Cys Gln Tyr Val Leu Val Gln Asp Tyr Cys
            20                  25                  30


Gly Ser Asn Pro Gly Thr Phe Arg Ile Leu Val Gly Asn Lys Gly Cys
        35                  40                  45


Ser His Pro Ser Val Lys Cys Lys Lys Arg Val Thr Ile Leu Val Glu
    50                  55                  60


Gly Gly Glu Ile Glu Leu Phe Asp Gly Glu Val Asn Val Lys Arg Pro
65                  70                  75                  80


Met Lys Asp Glu Thr His Phe Glu Val Val Glu Ser Gly Arg Tyr Ile
                85                  90                  95


Ile Leu Leu Leu Gly Lys Ala Leu Ser Val Val Trp Asp Arg His Leu
            100                 105                 110


Ser Ile Ser Val Val Leu Lys Gln Thr Tyr Gln Glu Lys Val Cys Gly
        115                 120                 125
```

```
Leu Cys Gly Asn Phe Asp Gly Ile Gln Asn Asn Asp Leu Thr Ser Ser
    130                 135                 140

Asn Leu Gln Val Glu Glu Asp Pro Val Asp Phe Gly Asn Ser Trp Lys
145                 150                 155                 160

Val Ser Ser Gln Cys Ala Asp Thr Arg Lys Val Pro Leu Asp Ser Ser
                165                 170                 175

Pro Ala Thr Cys His Asn Asn Ile Met Lys Gln Thr Met Val Asp Ser
            180                 185                 190

Ser Cys Arg Ile Leu Thr Ser Asp Val Phe Gln Asp Cys Asn Lys Leu
        195                 200                 205

Val Asp Pro Glu Pro Tyr Leu Asp Val Cys Ile Tyr Asp Thr Cys Ser
    210                 215                 220

Cys Glu Ser Ile Gly Asp Cys Ala Ala Phe Cys Asp Thr Ile Ala Ala
225                 230                 235                 240

Tyr Ala His Val Cys Ala Gln His Gly Lys Val Val Thr Trp Arg Thr
                245                 250                 255

Ala Thr Leu Cys Pro Gln Ser Cys Glu Glu Arg Asn Leu Arg Glu Asn
            260                 265                 270

Gly Tyr Glu Ala Glu Trp Arg Tyr Asn Ser Cys Ala Pro Ala Cys Gln
        275                 280                 285

Val Thr Cys Gln His Pro Glu Pro Leu Ala Cys Pro Val Gln Cys Val
    290                 295                 300

Glu Gly Cys His Ala His Cys Pro Pro Gly Lys Ile Leu Asp Glu Leu
305                 310                 315                 320

Leu Gln Thr Cys Val Asp Pro Glu Asp Cys Pro Val Cys Glu Val Ala
                325                 330                 335

Gly Arg Arg Phe Ala Ser Gly Lys Lys Val Thr Leu Asn Pro Ser Asp
            340                 345                 350
```

```
Pro Glu His Cys Gln Ile Cys His Cys Asp Val Val Asn Leu Thr Cys
        355                 360                 365


Glu Ala Cys Gln Glu Pro
    370


<210>  215
<211>  745
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  1 to 745 of FVIII

<400>  215

Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser Trp Asp Tyr
1               5                   10                  15


Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro
            20                  25                  30


Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys
        35                  40                  45


Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys Pro
    50                  55                  60


Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val
65                  70                  75                  80


Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val
                85                  90                  95


Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala
            100                 105                 110


Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val
        115                 120                 125


Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn
    130                 135                 140
```

```
Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser
145                 150                 155                 160

His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu
                165                 170                 175

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

His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp
        195                 200                 205

His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser
    210                 215                 220

Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg
225                 230                 235                 240

Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His
                245                 250                 255

Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu
            260                 265                 270

Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile
        275                 280                 285

Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly
    290                 295                 300

Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met
305                 310                 315                 320

Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg
                325                 330                 335

Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp
            340                 345                 350

Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro Ser Phe
        355                 360                 365
```

```
Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His
    370                 375                 380

Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu
385                 390                 395                 400

Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro
                405                 410                 415

Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr
            420                 425                 430

Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile
        435                 440                 445

Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile
    450                 455                 460

Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile
465                 470                 475                 480

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

His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys
            500                 505                 510

Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys
        515                 520                 525

Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala
    530                 535                 540

Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp
545                 550                 555                 560

Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe
                565                 570                 575

Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln
```

580 585 590

Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe
595 600 605

Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser
610 615 620

Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu
625 630 635 640

Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr
645 650 655

Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro
660 665 670

Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp
675 680 685

Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr Ala
690 695 700

Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu
705 710 715 720

Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala
725 730 735

Ile Glu Pro Arg Ser Phe Ser Gln Asn
740 745

<210> 216
<211> 684
<212> PRT
<213> Artificial Sequence

<220>
<223> FVIII 1649-2332

<400> 216

Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr
1 5 10 15

```
Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe Asp Ile Tyr
            20                  25                  30

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

His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr Gly Met Ser
    50                  55                  60

Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser Gly Ser Val Pro
65                  70                  75                  80

Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly Ser Phe Thr
                85                  90                  95

Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly Leu Leu Gly
            100                 105                 110

Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Arg
        115                 120                 125

Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr
    130                 135                 140

Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg Lys Asn Phe Val Lys
145                 150                 155                 160

Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val Gln His His Met Ala
                165                 170                 175

Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp
            180                 185                 190

Val Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu
        195                 200                 205

Val Cys His Thr Asn Thr Leu Asn Pro Ala His Gly Arg Gln Val Thr
    210                 215                 220

Val Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser
```

```
225                 230                 235                 240

Trp Tyr Phe Thr Glu Asn Met Glu Arg Asn Cys Arg Ala Pro Cys Asn
                245                 250                 255

Ile Gln Met Glu Asp Pro Thr Phe Lys Glu Asn Tyr Arg Phe His Ala
            260                 265                 270

Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln
        275                 280                 285

Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn
    290                 295                 300

Ile His Ser Ile His Phe Ser Gly His Val Phe Thr Val Arg Lys Lys
305                 310                 315                 320

Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr Pro Gly Val Phe Glu
                325                 330                 335

Thr Val Glu Met Leu Pro Ser Lys Ala Gly Ile Trp Arg Val Glu Cys
            340                 345                 350

Leu Ile Gly Glu His Leu His Ala Gly Met Ser Thr Leu Phe Leu Val
        355                 360                 365

Tyr Ser Asn Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile
    370                 375                 380

Arg Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro
385                 390                 395                 400

Lys Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr
                405                 410                 415

Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile
            420                 425                 430

Ile His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu
        435                 440                 445
```

```
Tyr Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp
    450                 455                 460

Gln Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly
465                 470                 475                 480

Asn Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile
                485                 490                 495

Ile Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser
            500                 505                 510

Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met
        515                 520                 525

Pro Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala
    530                 535                 540

Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala
545                 550                 555                 560

Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn
                565                 570                 575

Asn Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val
            580                 585                 590

Thr Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr
        595                 600                 605

Val Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr
    610                 615                 620

Leu Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp
625                 630                 635                 640

Ser Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg
                645                 650                 655

Tyr Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg
            660                 665                 670
```

Met Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr
675 680

<210> 217
<211> 226
<212> PRT
<213> Artificial Sequence

<220>
<223> Fc region

<400> 217

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
130 135 140

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

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly
225

<210> 218
<211> 291
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN AE288-3

<400> 218

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
1 5 10 15

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
20 25 30

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
35 40 45

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr
50 55 60

Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr
65 70 75 80

Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
85 90 95

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu

```
            100                 105                 110

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr
        115                 120                 125

Ser Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
    130                 135                 140

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu
145                 150                 155                 160

Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro
                165                 170                 175

Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
            180                 185                 190

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro
        195                 200                 205

Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr
    210                 215                 220

Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
225                 230                 235                 240

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro
                245                 250                 255

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
            260                 265                 270

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
        275                 280                 285

Ala Ser Ser
    290
```