

SEQUENCE LISTING

<110> Crucell Holland B.V.

<120> Stabilized soluble pre-fusion RSV F proteins

<130> 0271 EP P00 PRI

<140> EP16163810

<141> 2016-04-05

<160> 22

<170> PatentIn version 3.5

<210> 1

<211> 544

<212> PRT

<213> Artificial Sequence

<220>

<223> PRPM

<400> 1

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1 5 10 15

Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
20 25 30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
35 40 45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
50 55 60

Lys Glu Ile Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65 70 75 80

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

Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
100 105 110

Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
115 120 125

Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
130 135 140

Gly Ser Ala Ile Ala Ser Gly Val Ala Val Ser Lys Val Leu His Leu
145 150 155 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
165 170 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Ser Lys Val
180 185 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Val Asn
195 200 205

Lys Gln Ser Cys Ser Ile Pro Asn Ile Glu Thr Val Ile Glu Phe Gln
210 215 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225 230 235 240

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

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
260 265 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
275 280 285

Met Ser Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
290 295 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305 310 315 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
325 330 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe

340 345 350

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

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
370 375 380

Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385 390 395 400

Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
405 410 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
420 425 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
435 440 445

Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
450 455 460

Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465 470 475 480

Leu Val Phe Pro Ser Asn Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
485 490 495

Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu
500 505 510

Leu Ser Ala Ile Gly Gly Tyr Ile Pro Glu Ala Pro Arg Asp Gly Gln
515 520 525

Ala Tyr Val Arg Lys Asp Gly Glu Trp Val Leu Leu Ser Thr Phe Leu
530 535 540

<210> 2

<211> 544

<212> PRT

<213> Artificial Sequence

<220>

<223> PRQM

<400> 2

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1 5 10 15

Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
20 25 30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
35 40 45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
50 55 60

Lys Glu Ile Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65 70 75 80

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

Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
100 105 110

Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
115 120 125

Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
130 135 140

Gly Ser Ala Ile Ala Ser Gly Val Ala Val Ser Lys Val Leu His Leu
145 150 155 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
165 170 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Ser Lys Val
180 185 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Val Asn

195 200 205

Lys Gln Ser Cys Ser Ile Pro Asn Ile Glu Thr Val Ile Glu Phe Gln
210 215 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225 230 235 240

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

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
260 265 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
275 280 285

Met Ser Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
290 295 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305 310 315 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
325 330 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
340 345 350

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

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
370 375 380

Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385 390 395 400

Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
405 410 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
420 425 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
435 440 445

Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
450 455 460

Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465 470 475 480

Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
485 490 495

Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu
500 505 510

Leu Ser Ala Ile Gly Gly Tyr Ile Pro Glu Ala Pro Arg Asp Gly Gln
515 520 525

Ala Tyr Val Arg Lys Asp Gly Glu Trp Val Leu Leu Ser Thr Phe Leu
530 535 540

<210> 3
<211> 544
<212> PRT
<213> Artificial Sequence

<220>
<223> PRPM + S46G

<400> 3

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Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
20 25 30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Gly Ala Leu
35 40 45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile

50 55 60

Lys Glu Ile Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65 70 75 80

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

Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
100 105 110

Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
115 120 125

Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
130 135 140

Gly Ser Ala Ile Ala Ser Gly Val Ala Val Ser Lys Val Leu His Leu
145 150 155 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
165 170 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Ser Lys Val
180 185 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Val Asn
195 200 205

Lys Gln Ser Cys Ser Ile Pro Asn Ile Glu Thr Val Ile Glu Phe Gln
210 215 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225 230 235 240

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

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
260 265 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
275 280 285

Met Ser Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
290 295 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305 310 315 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
325 330 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
340 345 350

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

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
370 375 380

Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385 390 395 400

Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
405 410 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
420 425 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
435 440 445

Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
450 455 460

Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465 470 475 480

Leu Val Phe Pro Ser Asn Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
485 490 495

Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu
500 505 510

Leu Ser Ala Ile Gly Gly Tyr Ile Pro Glu Ala Pro Arg Asp Gly Gln
515 520 525

Ala Tyr Val Arg Lys Asp Gly Glu Trp Val Leu Leu Ser Thr Phe Leu
530 535 540

<210> 4
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> CR9501 VHCDR1

<400> 4

Gly Ala Ser Ile Asn Ser Asp Asn Tyr Tyr Trp Thr
1 5 10

<210> 5
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> CR9501 VHCDR2

<400> 5

His Ile Ser Tyr Thr Gly Asn Thr Tyr Tyr Thr Pro Ser Leu Lys Ser
1 5 10 15

<210> 6
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> CR9501 VHCDR3

<400> 6

Cys Gly Ala Tyr Val Leu Ile Ser Asn Cys Gly Trp Phe Asp Ser
1 5 10 15

<210> 7
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> CR9501 VLCDR1

<400> 7

Gln Ala Ser Gln Asp Ile Ser Thr Tyr Leu Asn
1 5 10

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

<220>
<223> CR9501 VLCDR2

<400> 8

Gly Ala Ser Asn Leu Glu Thr
1 5

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

<220>
<223> CR9501 VLCDR3

<400> 9

Gln Gln Tyr Gln Tyr Leu Pro Tyr Thr
1 5

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

<220>
<223> CR9502 VHCDR1

<400> 10

Gly Phe Thr Phe Ser Gly His Thr Ile Ala
1 5 10

<210> 11
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> CR9502 VHCDR2

<400> 11

Trp Val Ser Thr Asn Asn Gly Asn Thr Glu Tyr Ala Gln Lys Ile Gln
1 5 10 15

Gly

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

<220>
<223> CR9502 VHCDR3

<400> 12

Glu Trp Leu Val Met Gly Gly Phe Ala Phe Asp His
1 5 10

<210> 13
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> CR9502 LVCDR1

<400> 13

Gly Ala Asn Asn Ile Gly Ser Gln Asn Val His
1 5 10

<210> 14
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> CR9502 VLCDR2

<400> 14

Asp Asp Arg Asp Arg Pro Ser
1 5

<210> 15

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> CR9502 VLCDR3

<400> 15

Gln Val Trp Asp Ser Ser Arg Asp Gln Ala Val Ile
1 5 10

<210> 16

<211> 228

<212> PRT

<213> Artificial Sequence

<220>

<223> CR9501 heavy chain

<400> 16

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

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

Asn Tyr Tyr Trp Thr Trp Ile Arg Gln Arg Pro Gly Gly Gly Leu Glu
35 40 45

Trp Ile Gly His Ile Ser Tyr Thr Gly Asn Thr Tyr Tyr Thr Pro Ser
50 55 60

Leu Lys Ser Arg Leu Ser Met Ser Leu Glu Thr Ser Gln Ser Gln Phe
65 70 75 80

Ser Leu Arg Leu Thr Ser Val Thr Ala Ala Asp Ser Ala Val Tyr Phe
85 90 95

Cys Ala Ala Cys Gly Ala Tyr Val Leu Ile Ser Asn Cys Gly Trp Phe

100 105 110

Asp Ser Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser Ala Ser Thr
115 120 125

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

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

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

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

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

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

Pro Lys Ser Cys
225

<210> 17

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> CR9501 Light chain

<400> 17

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

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

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

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

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

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

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

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

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

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

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

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

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

Phe Asn Arg Gly Glu Cys
210

<210> 18

<211> 224

<212> PRT

<213> Artificial Sequence

<220>

<223> CR9502 Heavy chain

<400> 18

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

Ser Val Lys Ile Ser Cys Lys Thr Ser Gly Phe Thr Phe Ser Gly His
20 25 30

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

Gly Trp Val Ser Thr Asn Asn Gly Asn Thr Glu Tyr Ala Gln Lys Ile
50 55 60

Gln Gly Arg Val Thr Met Thr Met Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

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

Ala Arg Glu Trp Leu Val Met Gly Gly Phe Ala Phe Asp His Trp Gly
100 105 110

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

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

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

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

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

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

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

<210> 19
<211> 215
<212> PRT
<213> Artificial Sequence

<220>
<223> CR9502 Light chain

<400> 19

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

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

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

Asp Asp Arg Asp Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly
65 70 75 80

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

Ala Val Ile Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln Pro
100 105 110

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

Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro
130 135 140

Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys Ala
145 150 155 160

Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala
165 170 175

Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His Arg
180 185 190

Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys Thr
195 200 205

Ile Ala Pro Thr Glu Cys Ser
210 215

<210> 20

<211> 1632

<212> DNA

<213> Artificial Sequence

<220>

<223> Nucleotide sequence encoding PRPM

<400> 20

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tccaagggct acctgagcgc cctgagaacc ggctggtaca ccagcgtgat caccatcgag 180
ctgagcaaca tcaaggaaat caagtgaac ggcaccgacg ccaaggtaa gctgatcaag 240
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aacgccaaaa agaccaacgt gaccctgagc aagaagcgga agcggcgggt cctgggcttc 420
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gaaggcgaag tgaacaagat caagagcgcc ctgctgagca ccaacaaggc cgtggtgtcc 540
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aagcagctgc tgcccatcgt gaacaagcag agctgcagca tcccaacat cgagacagtg 660
atcgagttcc agcagaagaa caaccggctg ctggaaatca cccgcgagtt cagcgtgaac 720
gctggcgtga ccacccccgt gtccacctac atgtgacca acagcgagct gctgagcctg 780
atcaacgaca tgcccatcac caacgaccag aaaaagctga tgagcaacaa cgtgcagatc 840
gtgcggcagc agagctactc catcatgagc atcatcaaag aagaggtgct ggcctacgtg 900
gtgcagctgc ccctgtacgg cgtgatcgac acccctgct ggaagctgca caccagcccc 960
ctgtgcacca ccaacaccaa agagggcagc aacatctgcc tgaccgggac cgaccggggc 1020

tggactgcg ataatgccgg ctccgtgtca ttctttccac aggccgagac atgcaaggtg 1080
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 aagtgcaccg ccagcaacaa gaaccggggc atcatcaaga cttcagcaa cggctgacgac 1320
 tacgtgtcca acaagggggg ggacaccgtg tccgtgggca acaccctgta ctacgtgaac 1380
 aaacaggaag gcaagagcct gtacgtgaag ggcgagccca tcatcaactt ctacgacccc 1440
 ctgggtgtcc ccagcaacga gttcgacgcc agcatcagcc aggtcaacga gaagatcaac 1500
 cagagcctgg cttcatcag aaagagcgac gagctgctgt ccgccatcgg cggctacatc 1560
 cccgagggcc ctagagatgg ccaggcctac gtgcggaagg acggcgagtg ggtgctgctg 1620
 tctaccttcc tg 1632

<210> 21

<211> 1632

<212> DNA

<213> Artificial Sequence

<220>

<223> Nucleotide sequence encoding PRQM

<400> 21

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 tccaagggtt acctgagcgc cctgagaacc ggctggtaca ccagcgtgat caccatcgag 180
 ctgagcaaca tcaaggaaat caagtgaac ggcaccgacg ccaaggtaaa gctgatcaag 240
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 ctgctgggcg tgggctctgc cattgctagc ggcgtggccg tgtctaaggt gctgcacctg 480
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 ctgagcaacg gcgtgtccgt gctgaccagc aaggtgctgg atctgaagaa ctacatcgac 600
 aagcagctgc tgcccatcgt gaacaagcag agctgcagca tcccaacat cgagacagtg 660

atcgagttcc agcagaagaa caaccggctg ctggaaatca cccgcgagtt cagcgtgaac 720
 gctggcgtga ccacccccgt gtccacctac atgtgacca acagcgagct gctgagcctg 780
 atcaacgaca tgcccatcac caacgaccag aaaaagctga tgagcaacaa cgtgcagatc 840
 gtgcggcagc agagctactc catcatgagc atcatcaaag aagaggtgct ggcctacgtg 900
 gtgcagctgc ccctgtacgg cgtgatcgac accccctgct ggaagctgca caccagcccc 960
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 aaacaggaag gcaagagcct gtacgtgaag ggcgagccca tcatcaactt ctacgacccc 1440
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 cagagcctgg cttcatcag aaagagcgac gagctgctgt ccgccatcgg cggctacatc 1560
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 tctaccttcc tg 1632

<210> 22

<211> 1632

<212> DNA

<213> Artificial Sequence

<220>

<223> Nucleotide sequence encoding PRPM + S46G

<400> 22

atggaactgc tgatcctgaa ggccaacgcc atcaccacca tctgaccgc cgtgacctt 60

tgctttgcca gcggccagaa catcaccgag gaattctacc agagcacctg tagcgccgtg 120

tccaagggct atctgggcgc cctgagaacc ggctggtaca ccagcgtgat caccatcgag 180

ctgagcaaca tcaaagaaat caagtgaac ggcaccgacg ccaaagtga gctgatcaag 240

caggaactgg acaagtacaa gaatgccgtg accgaactgc agctgctgat gcagagcacc 300

cccgcacca acaaccgggc cagaagagaa ctgccagat tcatgaacta caccctgaac 360

aacgccaaaa agaccaacgt gaccctgagc aagaagcgga agcggcgggt cctgggcttt 420
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