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<110> Regeneron Pharmaceuticals, Inc.
 <120> NON-HUMAN ANIMALS COMPRISING A HUMANIZED COAGULATION FACTOR 12 LOCUS
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 <150> US 62/829,321
 <151> 2019-04-04
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 <213> Mus musculus

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 <223> Signal Peptide

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 <222> (20)..(354)
 <223> Heavy Chain

<220>
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 <222> (355)..(597)
 <223> Light Chain

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 35 40 45

Phe Pro Phe Gln Tyr His Arg Gln Leu His His Lys Cys Ile His Lys
 50 55 60

Arg Arg Pro Gly Ser Arg Pro Trp Cys Ala Thr Thr Pro Asn Phe Asp
65 70 75 80

Glu Asp Gln Gln Trp Gly Tyr Cys Leu Glu Pro Lys Lys Val Lys Asp
85 90 95

His Cys Ser Lys His Asn Pro Cys His Lys Gly Gly Thr Cys Ile Asn
100 105 110

Thr Pro Asn Gly Pro His Cys Leu Cys Pro Glu His Leu Thr Gly Lys
115 120 125

His Cys Gln Lys Glu Lys Cys Phe Glu Pro Gln Leu Leu Lys Phe Phe
130 135 140

His Glu Asn Glu Leu Trp Phe Arg Thr Gly Pro Gly Gly Val Ala Arg
145 150 155 160

Cys Glu Cys Lys Gly Ser Glu Ala His Cys Lys Pro Val Ala Ser Gln
165 170 175

Ala Cys Ser Ile Asn Pro Cys Leu Asn Gly Gly Ser Cys Leu Leu Val
180 185 190

Glu Asp His Pro Leu Cys Arg Cys Pro Thr Gly Tyr Thr Gly Tyr Phe
195 200 205

Cys Asp Leu Asp Leu Trp Ala Thr Cys Tyr Glu Gly Arg Gly Leu Ser
210 215 220

Tyr Arg Gly Gln Ala Gly Thr Thr Gln Ser Gly Ala Pro Cys Gln Arg
225 230 235 240

Trp Thr Val Glu Ala Thr Tyr Arg Asn Met Thr Glu Lys Gln Ala Leu
245 250 255

Ser Trp Gly Leu Gly His His Ala Phe Cys Arg Asn Pro Asp Asn Asp
260 265 270

Thr Arg Pro Trp Cys Phe Val Trp Ser Gly Asp Arg Leu Ser Trp Asp
275 280 285

Tyr Cys Gly Leu Glu Gln Cys Gln Thr Pro Thr Phe Ala Pro Leu Val
290 295 300

Val Pro Glu Ser Gln Glu Glu Ser Pro Ser Gln Ala Pro Ser Leu Ser
305 310 315 320

His Ala Pro Asn Asp Ser Thr Asp His Gln Thr Ser Leu Ser Lys Thr
325 330 335

Asn Thr Met Gly Cys Gly Gln Arg Phe Arg Lys Gly Leu Ser Ser Phe
340 345 350

Met Arg Val Val Gly Gly Leu Val Ala Leu Pro Gly Ser His Pro Tyr
355 360 365

Ile Ala Ala Leu Tyr Trp Gly Asn Asn Phe Cys Ala Gly Ser Leu Ile
370 375 380

Ala Pro Cys Trp Val Leu Thr Ala Ala His Cys Leu Gln Asn Arg Pro
385 390 395 400

Ala Pro Glu Glu Leu Thr Val Val Leu Gly Gln Asp Arg His Asn Gln
405 410 415

Ser Cys Glu Trp Cys Gln Thr Leu Ala Val Arg Ser Tyr Arg Leu His
420 425 430

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

Leu Gln Glu Ser Lys Thr Asn Ser Cys Ala Ile Leu Ser Pro His Val
450 455 460

Gln Pro Val Cys Leu Pro Ser Gly Ala Ala Pro Pro Ser Glu Thr Val
465 470 475 480

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485 490 495

Tyr Ser Thr Phe Leu Gln Glu Ala Gln Val Pro Phe Ile Ala Leu Asp
500 505 510

Arg Cys Ser Asn Ser Asn Val His Gly Asp Ala Ile Leu Pro Gly Met
515 520 525

Leu Cys Ala Gly Phe Leu Glu Gly Gly Thr Asp Ala Cys Gln Gly Asp
530 535 540

Ser Gly Gly Pro Leu Val Cys Glu Glu Gly Thr Ala Glu His Gln Leu
545 550 555 560

Thr Leu Arg Gly Val Ile Ser Trp Gly Ser Gly Cys Gly Asp Arg Asn
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Lys His Ile Ala Ser
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Thr Leu Ser

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 35 40 45

Gly Ser Arg Pro Trp Cys Ala Thr Thr Pro Asn Phe Asp Glu Asp Gln
 50 55 60

Gln Trp Gly Tyr Cys Leu Glu Pro Lys Lys Val Lys Asp His Cys Ser
 65 70 75 80

Lys His Asn Pro Cys His Lys Gly Gly Thr Cys Ile Asn Thr Pro Asn
 85 90 95

Gly Pro His Cys Leu Cys Pro Glu His Leu Thr Gly Lys His Cys Gln
 100 105 110

Lys Glu Lys Cys Phe Glu Pro Gln Leu Leu Lys Phe Phe His Glu Asn
 115 120 125

Glu Leu Trp Phe Arg Thr Gly Pro Gly Gly Val Ala Arg Cys Glu Cys
 130 135 140

Lys Gly Ser Glu Ala His Cys Lys Pro Val Ala Ser Gln Ala Cys Ser
 145 150 155 160

Ile Asn Pro Cys Leu Asn Gly Gly Ser Cys Leu Leu Val Glu Asp His
 165 170 175

Pro Leu Cys Arg Cys Pro Thr Gly Tyr Thr Gly Tyr Phe Cys Asp Leu
 180 185 190

Asp Leu Trp Ala Thr Cys Tyr Glu Gly Arg Gly Leu Ser Tyr Arg Gly
 195 200 205

Gln Ala Gly Thr Thr Gln Ser Gly Ala Pro Cys Gln Arg Trp Thr Val
 210 215 220

Glu Ala Thr Tyr Arg Asn Met Thr Glu Lys Gln Ala Leu Ser Trp Gly
 225 230 235 240

Leu Gly His His Ala Phe Cys Arg Asn Pro Asp Asn Asp Thr Arg Pro
 245 250 255

Trp Cys Phe Val Trp Ser Gly Asp Arg Leu Ser Trp Asp Tyr Cys Gly
260 265 270

Leu Glu Gln Cys Gln Thr Pro Thr Phe Ala Pro Leu Val Val Pro Glu
275 280 285

Ser Gln Glu Glu Ser Pro Ser Gln Ala Pro Ser Leu Ser His Ala Pro
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Cys Trp Val Leu Thr Ala Ala His Cys Leu Gln Asn Arg Pro Ala Pro
35 40 45

Glu Glu Leu Thr Val Val Leu Gly Gln Asp Arg His Asn Gln Ser Cys
50 55 60

Glu Trp Cys Gln Thr Leu Ala Val Arg Ser Tyr Arg Leu His Glu Gly
65 70 75 80

Phe Ser Ser Ile Thr Tyr Gln His Asp Leu Ala Leu Leu Arg Leu Gln
85 90 95

Glu Ser Lys Thr Asn Ser Cys Ala Ile Leu Ser Pro His Val Gln Pro
100 105 110

Val Cys Leu Pro Ser Gly Ala Ala Pro Pro Ser Glu Thr Val Leu Cys
115 120 125

Glu Val Ala Gly Trp Gly His Gln Phe Glu Gly Ala Glu Glu Tyr Ser
130 135 140

Thr Phe Leu Gln Glu Ala Gln Val Pro Phe Ile Ala Leu Asp Arg Cys
145 150 155 160

Ser Asn Ser Asn Val His Gly Asp Ala Ile Leu Pro Gly Met Leu Cys
165 170 175

Ala Gly Phe Leu Glu Gly Gly Thr Asp Ala Cys Gln Gly Asp Ser Gly
180 185 190

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

Arg Gly Val Ile Ser Trp Gly Ser Gly Cys Gly Asp Arg Asn Lys Pro
210 215 220

Gly Val Tyr Thr Asp Val Ala Asn Tyr Leu Ala Trp Ile Gln Lys His
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Ile Ala Ser

<210> 5
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<212> PRT
<213> Homo sapiens

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<223> Heavy Chain

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 <222> (373)..(615)
 <223> Light Chain

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Ala Glu Glu His Thr Val Val Leu Thr Val Thr Gly Glu Pro Cys His
 35 40 45

Phe Pro Phe Gln Tyr His Arg Gln Leu Tyr His Lys Cys Thr His Lys
 50 55 60

Gly Arg Pro Gly Pro Gln Pro Trp Cys Ala Thr Thr Pro Asn Phe Asp
 65 70 75 80

Gln Asp Gln Arg Trp Gly Tyr Cys Leu Glu Pro Lys Lys Val Lys Asp
 85 90 95

His Cys Ser Lys His Ser Pro Cys Gln Lys Gly Gly Thr Cys Val Asn
 100 105 110

Met Pro Ser Gly Pro His Cys Leu Cys Pro Gln His Leu Thr Gly Asn
 115 120 125

His Cys Gln Lys Glu Lys Cys Phe Glu Pro Gln Leu Leu Arg Phe Phe
 130 135 140

His Lys Asn Glu Ile Trp Tyr Arg Thr Glu Gln Ala Ala Val Ala Arg
 145 150 155 160

Cys Gln Cys Lys Gly Pro Asp Ala His Cys Gln Arg Leu Ala Ser Gln
 165 170 175

Ala Cys Arg Thr Asn Pro Cys Leu His Gly Gly Arg Cys Leu Glu Val
 180 185 190

Glu Gly His Arg Leu Cys His Cys Pro Val Gly Tyr Thr Gly Pro Phe
 Page 8

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Asn	Trp	Gly	Leu	Gly	Gly	His	Ala	Phe	Cys	Arg	Asn	Pro	Asp	Asn	Asp
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Ile	Arg	Pro	Trp	Cys	Phe	Val	Leu	Asn	Arg	Asp	Arg	Leu	Ser	Trp	Glu
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Tyr	Cys	Asp	Leu	Ala	Gln	Cys	Gln	Thr	Pro	Thr	Gln	Ala	Ala	Pro	Pro
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Ala	Pro	Pro	Lys	Pro	Gln	Pro	Thr	Thr	Arg	Thr	Pro	Pro	Gln	Ser	Gln
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Ser	Met	Thr	Arg	Val	Val	Gly	Gly	Leu	Val	Ala	Leu	Arg	Gly	Ala	His
	370					375					380				
Pro	Tyr	Ile	Ala	Ala	Leu	Tyr	Trp	Gly	His	Ser	Phe	Cys	Ala	Gly	Ser
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Leu	Ile	Ala	Pro	Cys	Trp	Val	Leu	Thr	Ala	Ala	His	Cys	Leu	Gln	Asp
				405					410					415	

Arg Pro Ala Pro Glu Asp Leu Thr Val Val Leu Gly Gln Glu Arg Arg
420 425 430

Asn His Ser Cys Glu Pro Cys Gln Thr Leu Ala Val Arg Ser Tyr Arg
435 440 445

Leu His Glu Ala Phe Ser Pro Val Ser Tyr Gln His Asp Leu Ala Leu
450 455 460

Leu Arg Leu Gln Glu Asp Ala Asp Gly Ser Cys Ala Leu Leu Ser Pro
465 470 475 480

Tyr Val Gln Pro Val Cys Leu Pro Ser Gly Ala Ala Arg Pro Ser Glu
485 490 495

Thr Thr Leu Cys Gln Val Ala Gly Trp Gly His Gln Phe Glu Gly Ala
500 505 510

Glu Glu Tyr Ala Ser Phe Leu Gln Glu Ala Gln Val Pro Phe Leu Ser
515 520 525

Leu Glu Arg Cys Ser Ala Pro Asp Val His Gly Ser Ser Ile Leu Pro
530 535 540

Gly Met Leu Cys Ala Gly Phe Leu Glu Gly Gly Thr Asp Ala Cys Gln
545 550 555 560

Gly Asp Ser Gly Gly Pro Leu Val Cys Glu Asp Gln Ala Ala Glu Arg
565 570 575

Arg Leu Thr Leu Gln Gly Ile Ile Ser Trp Gly Ser Gly Cys Gly Asp
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Arg Asn Lys Pro Gly Val Tyr Thr Asp Val Ala Tyr Tyr Leu Ala Trp
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Ile Arg Glu His Thr Val Ser
610 615

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<213> Homo sapiens

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Thr Leu Ser

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<211> 353

<212> PRT

<213> Homo sapiens

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Gln Tyr His Arg Gln Leu Tyr His Lys Cys Thr His Lys Gly Arg Pro
35 40 45

Gly Pro Gln Pro Trp Cys Ala Thr Thr Pro Asn Phe Asp Gln Asp Gln
50 55 60

Arg Trp Gly Tyr Cys Leu Glu Pro Lys Lys Val Lys Asp His Cys Ser
65 70 75 80

Lys His Ser Pro Cys Gln Lys Gly Gly Thr Cys Val Asn Met Pro Ser
85 90 95

Gly Pro His Cys Leu Cys Pro Gln His Leu Thr Gly Asn His Cys Gln
100 105 110

Lys Glu Lys Cys Phe Glu Pro Gln Leu Leu Arg Phe Phe His Lys Asn
115 120 125

Glu Ile Trp Tyr Arg Thr Glu Gln Ala Ala Val Ala Arg Cys Gln Cys
130 135 140

Lys Gly Pro Asp Ala His Cys Gln Arg Leu Ala Ser Gln Ala Cys Arg
145 150 155 160

Thr Asn Pro Cys Leu His Gly Gly Arg Cys Leu Glu Val Glu Gly His
165 170 175

Arg Leu Cys His Cys Pro Val Gly Tyr Thr Gly Pro Phe Cys Asp Val
180 185 190

Asp Thr Lys Ala Ser Cys Tyr Asp Gly Arg Gly Leu Ser Tyr Arg Gly
195 200 205

Leu Ala Arg Thr Thr Leu Ser Gly Ala Pro Cys Gln Pro Trp Ala Ser
210 215 220

Glu Ala Thr Tyr Arg Asn Val Thr Ala Glu Gln Ala Arg Asn Trp Gly
225 230 235 240

Leu Gly Gly His Ala Phe Cys Arg Asn Pro Asp Asn Asp Ile Arg Pro
245 250 255

Trp Cys Phe Val Leu Asn Arg Asp Arg Leu Ser Trp Glu Tyr Cys Asp
260 265 270

Leu Ala Gln Cys Gln Thr Pro Thr Gln Ala Ala Pro Pro Thr Pro Val
275 280 285

Ser Pro Arg Leu His Val Pro Leu Met Pro Ala Gln Pro Ala Pro Pro
290 295 300

Lys Pro Gln Pro Thr Thr Arg Thr Pro Pro Gln Ser Gln Thr Pro Gly
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Ala Leu Pro Ala Lys Arg Glu Gln Pro Pro Ser Leu Thr Arg Asn Gly
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Cys Trp Val Leu Thr Ala Ala His Cys Leu Gln Asp Arg Pro Ala Pro
 35 40 45

Glu Asp Leu Thr Val Val Leu Gly Gln Glu Arg Arg Asn His Ser Cys
 50 55 60

Glu Pro Cys Gln Thr Leu Ala Val Arg Ser Tyr Arg Leu His Glu Ala
 65 70 75 80

Phe Ser Pro Val Ser Tyr Gln His Asp Leu Ala Leu Leu Arg Leu Gln
 85 90 95

Glu Asp Ala Asp Gly Ser Cys Ala Leu Leu Ser Pro Tyr Val Gln Pro
 100 105 110

Val Cys Leu Pro Ser Gly Ala Ala Arg Pro Ser Glu Thr Thr Leu Cys
 115 120 125

Gln Val Ala Gly Trp Gly His Gln Phe Glu Gly Ala Glu Glu Tyr Ala
 130 135 140

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

Ser Ala Pro Asp Val His Gly Ser Ser Ile Leu Pro Gly Met Leu Cys
 165 170 175

Ala Gly Phe Leu Glu Gly Gly Thr Asp Ala Cys Gln Gly Asp Ser Gly
 180 185 190

Gly Pro Leu Val Cys Glu Asp Gln Ala Ala Glu Arg Arg Leu Thr Leu
195 200 205

Gln Gly Ile Ile Ser Trp Gly Ser Gly Cys Gly Asp Arg Asn Lys Pro
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Gly Val Tyr Thr Asp Val Ala Tyr Tyr Leu Ala Trp Ile Arg Glu His
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Thr Val Ser

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Arg Arg Lys Asn	Arg Ile Cys Tyr	Leu Gln Glu Ile	Phe Ser Asn Glu
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Ile Gln Leu Val	Gln Thr Tyr Asn	Gln Leu Phe Glu	Glu Asn Pro Ile
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Pro Asn Phe Lys Ser Asn Phe Asp Leu Ala Glu Asp Ala Lys Leu Gln
 260 265 270

Leu Ser Lys Asp Thr Tyr Asp Asp Asp Leu Asp Asn Leu Leu Ala Gln
 275 280 285

Ile Gly Asp Gln Tyr Ala Asp Leu Phe Leu Ala Ala Lys Asn Leu Ser
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Asp Ala Ile Leu Leu Ser Asp Ile Leu Arg Val Asn Thr Glu Ile Thr
 305 310 315 320

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Tyr Ile Asp Gly Gly Ala Ser Gln Glu Glu Phe Tyr Lys Phe Ile Lys
 370 375 380

Pro Ile Leu Glu Lys Met Asp Gly Thr Glu Glu Leu Leu Val Lys Leu
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Ile Pro His Gln Ile His Leu Gly Glu Leu His Ala Ile Leu Arg Arg
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Ser Pro Ala Ile Lys Lys Gly Ile Leu Gln Thr Val Lys Val Val Asp
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Glu Leu Val Lys Val Met Gly Arg His Lys Pro Glu Asn Ile Val Ile
755 760 765

Glu Met Ala Arg Glu Asn Gln Thr Thr Gln Lys Gly Gln Lys Asn Ser
770 775 780

Arg Glu Arg Met Lys Arg Ile Glu Glu Gly Ile Lys Glu Leu Gly Ser
785 790 795 800

Gln Ile Leu Lys Glu His Pro Val Glu Asn Thr Gln Leu Gln Asn Glu
805 810 815

Lys Leu Tyr Leu Tyr Tyr Leu Gln Asn Gly Arg Asp Met Tyr Val Asp
820 825 830

Gln Glu Leu Asp Ile Asn Arg Leu Ser Asp Tyr Asp Val Asp His Ile
835 840 845

Val Pro Gln Ser Phe Leu Lys Asp Asp Ser Ile Asp Asn Lys Val Leu
850 855 860

Thr Arg Ser Asp Lys Asn Arg Gly Lys Ser Asp Asn Val Pro Ser Glu
865 870 875 880

Glu Val Val Lys Lys Met Lys Asn Tyr Trp Arg Gln Leu Leu Asn Ala
Page 49

885

890

895

Lys Leu Ile Thr Gln Arg Lys Phe Asp Asn Leu Thr Lys Ala Glu Arg
 900 905 910

Gly Gly Leu Ser Glu Leu Asp Lys Ala Gly Phe Ile Lys Arg Gln Leu
 915 920 925

Val Glu Thr Arg Gln Ile Thr Lys His Val Ala Gln Ile Leu Asp Ser
 930 935 940

Arg Met Asn Thr Lys Tyr Asp Glu Asn Asp Lys Leu Ile Arg Glu Val
 945 950 955 960

Lys Val Ile Thr Leu Lys Ser Lys Leu Val Ser Asp Phe Arg Lys Asp
 965 970 975

Phe Gln Phe Tyr Lys Val Arg Glu Ile Asn Asn Tyr His His Ala His
 980 985 990

Asp Ala Tyr Leu Asn Ala Val Val Gly Thr Ala Leu Ile Lys Lys Tyr
 995 1000 1005

Pro Lys Leu Glu Ser Glu Phe Val Tyr Gly Asp Tyr Lys Val Tyr
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Asp Val Arg Lys Met Ile Ala Lys Ser Glu Gln Glu Ile Gly Lys
 1025 1030 1035

Ala Thr Ala Lys Tyr Phe Phe Tyr Ser Asn Ile Met Asn Phe Phe
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Lys Thr Glu Ile Thr Leu Ala Asn Gly Glu Ile Arg Lys Arg Pro
 1055 1060 1065

Leu Ile Glu Thr Asn Gly Glu Thr Gly Glu Ile Val Trp Asp Lys
 1070 1075 1080

Gly Arg Asp Phe Ala Thr Val Arg Lys Val Leu Ser Met Pro Gln
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Arg	Lys	Lys	Asp	Trp	Asp	Pro	Lys	Lys	Tyr	Gly	Gly	Phe	Asp	Ser
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Pro	Thr	Val	Ala	Tyr	Ser	Val	Leu	Val	Val	Ala	Lys	Val	Glu	Lys
1145						1150					1155			
Gly	Lys	Ser	Lys	Lys	Leu	Lys	Ser	Val	Lys	Glu	Leu	Leu	Gly	Ile
1160						1165					1170			
Thr	Ile	Met	Glu	Arg	Ser	Ser	Phe	Glu	Lys	Asn	Pro	Ile	Asp	Phe
1175						1180					1185			
Leu	Glu	Ala	Lys	Gly	Tyr	Lys	Glu	Val	Lys	Lys	Asp	Leu	Ile	Ile
1190						1195					1200			
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1205						1210					1215			
Arg	Met	Leu	Ala	Ser	Ala	Gly	Glu	Leu	Gln	Lys	Gly	Asn	Glu	Leu
1220						1225					1230			
Ala	Leu	Pro	Ser	Lys	Tyr	Val	Asn	Phe	Leu	Tyr	Leu	Ala	Ser	His
1235						1240					1245			
Tyr	Glu	Lys	Leu	Lys	Gly	Ser	Pro	Glu	Asp	Asn	Glu	Gln	Lys	Gln
1250						1255					1260			
Leu	Phe	Val	Glu	Gln	His	Lys	His	Tyr	Leu	Asp	Glu	Ile	Ile	Glu
1265						1270					1275			
Gln	Ile	Ser	Glu	Phe	Ser	Lys	Arg	Val	Ile	Leu	Ala	Asp	Ala	Asn
1280						1285					1290			
Leu	Asp	Lys	Val	Leu	Ser	Ala	Tyr	Asn	Lys	His	Arg	Asp	Lys	Pro
1295						1300					1305			

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Asp Arg Lys Arg Tyr Thr Ser Thr Lys Glu Val Leu Asp Ala Thr
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 ggcaccgagu cggugc 76

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uugaaaaagu ggcaccgagu cggugc

86

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23

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Phe Pro Phe Gln Tyr His Arg Gln Leu Tyr His Lys Cys Thr His Lys
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Gly Arg Pro Gly Pro Gln Pro Trp Cys Ala Thr Thr Pro Asn Phe Asp
 65 70 75 80

Gln Asp Gln Arg Trp Gly Tyr Cys Leu Glu Pro Lys Lys Val Lys Asp
 85 90 95

His Cys Ser Lys His Ser Pro Cys Gln Lys Gly Gly Thr Cys Val Asn
 100 105 110

Met Pro Ser Gly Pro His Cys Leu Cys Pro Gln His Leu Thr Gly Asn
 115 120 125

His Cys Gln Lys Glu Lys Cys Phe Glu Pro Gln Leu Leu Arg Phe Phe
130 135 140

His Lys Asn Glu Ile Trp Tyr Arg Thr Glu Gln Ala Ala Val Ala Arg
145 150 155 160

Cys Gln Cys Lys Gly Pro Asp Ala His Cys Gln Arg Leu Ala Ser Gln
165 170 175

Ala Cys Arg Thr Asn Pro Cys Leu His Gly Gly Arg Cys Leu Glu Val
180 185 190

Glu Gly His Arg Leu Cys His Cys Pro Val Gly Tyr Thr Gly Ala Phe
195 200 205

Cys Asp Val Asp Thr Lys Ala Ser Cys Tyr Asp Gly Arg Gly Leu Ser
210 215 220

Tyr Arg Gly Leu Ala Arg Thr Thr Leu Ser Gly Ala Pro Cys Gln Pro
225 230 235 240

Trp Ala Ser Glu Ala Thr Tyr Arg Asn Val Thr Ala Glu Gln Ala Arg
245 250 255

Asn Trp Gly Leu Gly Gly His Ala Phe Cys Arg Asn Pro Asp Asn Asp
260 265 270

Ile Arg Pro Trp Cys Phe Val Leu Asn Arg Asp Arg Leu Ser Trp Glu
275 280 285

Tyr Cys Asp Leu Ala Gln Cys Gln Thr Pro Thr Gln Ala Ala Pro Pro
290 295 300

Thr Pro Val Ser Pro Arg Leu His Val Pro Leu Met Pro Ala Gln Pro
305 310 315 320

Ala Pro Pro Lys Pro Gln Pro Thr Thr Arg Thr Pro Pro Gln Ser Gln
325 330 335

Thr Pro Gly Ala Leu Pro Ala Lys Arg Glu Gln Pro Pro Ser Leu Thr

Gly Asp Ser Gly Gly Pro Leu Val Cys Glu Asp Gln Ala Ala Glu Arg
565 570 575

Arg Leu Thr Leu Gln Gly Ile Ile Ser Trp Gly Ser Gly Cys Gly Asp
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Arg Asn Lys Pro Gly Val Tyr Thr Asp Val Ala Tyr Tyr Leu Ala Trp
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35 40 45

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Arg Trp Gly Tyr Cys Leu Glu Pro Lys Lys Val Lys Asp His Cys Ser
65 70 75 80

Lys His Ser Pro Cys Gln Lys Gly Gly Thr Cys Val Asn Met Pro Ser
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Gly Pro His Cys Leu Cys Pro Gln His Leu Thr Gly Asn His Cys Gln
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115 120 125

Glu Ile Trp Tyr Arg Thr Glu Gln Ala Ala Val Ala Arg Cys Gln Cys
130 135 140

Lys Gly Pro Asp Ala His Cys Gln Arg Leu Ala Ser Gln Ala Cys Arg
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Thr Asn Pro Cys Leu His Gly Gly Arg Cys Leu Glu Val Glu Gly His
165 170 175

Arg Leu Cys His Cys Pro Val Gly Tyr Thr Gly Ala Phe Cys Asp Val
180 185 190

Asp Thr Lys Ala Ser Cys Tyr Asp Gly Arg Gly Leu Ser Tyr Arg Gly
195 200 205

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210 215 220

Glu Ala Thr Tyr Arg Asn Val Thr Ala Glu Gln Ala Arg Asn Trp Gly
225 230 235 240

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Arg

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accaacccgt gcctccatgg gggtcgctgc ctagaggtgg agggccaccg cctgtgccac	540
tgcccgggtgg gctacaccgg agccttctgc gacgtggaca ccaaggcaag ctgctatgat	600
ggccgcgggc tcagctaccg cggcctggcc aggaccacgc tctcgggtgc gccctgtcag	660
ccgtgggcct cggaggccac ctaccggaac gtgactgccg agcaagcgcg gaactgggga	720
ctgggcggcc acgccttctg ccggaaccg gacaacgaca tccgcccgtg gtgcttcgtg	780
ctgaaccgcg accggctgag ctgggagtac tgcgacctgg cacagtgcc a gaccccaacc	840
caggcggcgc ctccgacccc ggtgtcccct aggcttcatg tcccactcat gcccgcgag	900
ccggcaccgc cgaagcctca gcccacgacc cggacccgc ctcagtcca gacccggga	960
gccttgccgg cgaagcggga gcagccgcct tccctgacca ggaacggccc actgagctgc	1020
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<400> 51	
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<210> 53
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<400> 53
accaacccgt gcctccat 18

<210> 54
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<210> 55
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<400> 55
aggatctgac ggtggtgctc 20

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acaccgatgt ggcctactac 20

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gcagaaggct ccggtgtag	19

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<210> 65
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<210> 67
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 accaccggca gctgtaccac aaat 24

<210> 68
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 <400> 68
 tcactggaaa ccactgccag aaagaga 27

<210> 69
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<220>
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 ctgcctagag gtggagggcc acc 23

<210> 70
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 <400> 70
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<220>
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<400> 71
 ccaggaacgc cgtaaccaca gct 23

<210> 72
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 <212> DNA
 <213> Artificial Sequence

<220>
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<400> 72
 ctggatccgg gagcacaccg ttt 23

<210> 73
 <211> 22
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 73
 tcaacagcga caccactcc tc 22

<210> 74
 <211> 300
 <212> PRT
 <213> Homo sapiens

<400> 74

Met	Pro	Ala	Gln	Pro	Ala	Pro	Pro	Lys	Pro	Gln	Pro	Thr	Thr	Arg	Thr
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Pro	Pro	Gln	Ser	Gln	Thr	Pro	Gly	Ala	Leu	Pro	Ala	Lys	Arg	Glu	Gln
			20					25					30		

Pro	Pro	Ser	Leu	Thr	Arg	Asn	Gly	Pro	Leu	Ser	Cys	Gly	Gln	Arg	Leu
		35					40					45			

Arg Lys Ser Leu Ser Ser Met Thr Arg Val Val Gly Gly Leu Val Ala
50 55 60

Leu Arg Gly Ala His Pro Tyr Ile Ala Ala Leu Tyr Trp Gly His Ser
65 70 75 80

Phe Cys Ala Gly Ser Leu Ile Ala Pro Cys Trp Val Leu Thr Ala Ala
85 90 95

His Cys Leu Gln Asp Arg Pro Ala Pro Glu Asp Leu Thr Val Val Leu
100 105 110

Gly Gln Glu Arg Arg Asn His Ser Cys Glu Pro Cys Gln Thr Leu Ala
115 120 125

Val Arg Ser Tyr Arg Leu His Glu Ala Phe Ser Pro Val Ser Tyr Gln
130 135 140

His Asp Leu Ala Leu Leu Arg Leu Gln Glu Asp Ala Asp Gly Ser Cys
145 150 155 160

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

Ala Arg Pro Ser Glu Thr Thr Leu Cys Gln Val Ala Gly Trp Gly His
180 185 190

Gln Phe Glu Gly Ala Glu Glu Tyr Ala Ser Phe Leu Gln Glu Ala Gln
195 200 205

Val Pro Phe Leu Ser Leu Glu Arg Cys Ser Ala Pro Asp Val His Gly
210 215 220

Ser Ser Ile Leu Pro Gly Met Leu Cys Ala Gly Phe Leu Glu Gly Gly
225 230 235 240

Thr Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Glu Asp
245 250 255

Gln Ala Ala Glu Arg Arg Leu Thr Leu Gln Gly Ile Ile Ser Trp Gly
260 265 270

Ser Gly Cys Gly Asp Arg Asn Lys Pro Gly Val Tyr Thr Asp Val Ala
 275 280 285

Tyr Tyr Leu Ala Trp Ile Arg Glu His Thr Val Ser
 290 295 300

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 ccactgagct gcgggcagcg gctccgcaag agtctgtctt cgatgacccg cgtcgttggc 180
 gggctggtgg cgctacgcgg ggcgcacccc tacatcgccg cgctgtactg gggccacagt 240
 ttctgcgccg gcagcctcat cgccccctgc tgggtgctga cggccgctca ctgcctgcag 300
 gaccggcccc caccagagga tctgacggtg gtgctcggcc aggaacgccg taaccacagc 360
 tgtgagccgt gccagacgtt ggccgtgcgc tcctaccgct tgcacgaggc cttctcgccc 420
 gtcagctacc agcacgacct ggctctgttg cgccttcagg aggatgcgga cggcagctgc 480
 gcgctcctgt cgccttacgt tcagccggtg tgcctgcca gggcgccgc gcgaccctcc 540
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 gccagcttcc tgcaggaggc gcaggtaccg ttctctctcc tggagcgctg ctcagccccg 660
 gacgtgcacg gatcctccat cctccccggc atgctctgcg cagggttcct cgagggcggc 720
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 cgccggctca ccctgcaagg catcatcagc tggggatcgg gctgtggtga ccgcaacaag 840
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 tga 903

<210> 76
 <211> 246
 <212> PRT
 <213> Homo sapiens

<400> 76

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Tyr Ile Ala Ala Leu Tyr Trp Gly His Ser Phe Cys Ala Gly Ser Leu
20 25 30

Ile Ala Pro Cys Trp Val Leu Thr Ala Ala His Cys Leu Gln Asp Arg
35 40 45

Pro Ala Pro Glu Asp Leu Thr Val Val Leu Gly Gln Glu Arg Arg Asn
50 55 60

His Ser Cys Glu Pro Cys Gln Thr Leu Ala Val Arg Ser Tyr Arg Leu
65 70 75 80

His Glu Ala Phe Ser Pro Val Ser Tyr Gln His Asp Leu Ala Leu Leu
85 90 95

Arg Leu Gln Glu Asp Ala Asp Gly Ser Cys Ala Leu Leu Ser Pro Tyr
100 105 110

Val Gln Pro Val Cys Leu Pro Ser Gly Ala Ala Arg Pro Ser Glu Thr
115 120 125

Thr Leu Cys Gln Val Ala Gly Trp Gly His Gln Phe Glu Gly Ala Glu
130 135 140

Glu Tyr Ala Ser Phe Leu Gln Glu Ala Gln Val Pro Phe Leu Ser Leu
145 150 155 160

Glu Arg Cys Ser Ala Pro Asp Val His Gly Ser Ser Ile Leu Pro Gly
165 170 175

Met Leu Cys Ala Gly Phe Leu Glu Gly Gly Thr Asp Ala Cys Gln Gly
180 185 190

Asp Ser Gly Gly Pro Leu Val Cys Glu Asp Gln Ala Ala Glu Arg Arg
195 200 205

Leu Thr Leu Gln Gly Ile Ile Ser Trp Gly Ser Gly Cys Gly Asp Arg
210 215 220

Asn Lys Pro Gly Val Tyr Thr Asp Val Ala Tyr Tyr Leu Ala Trp Ile
 225 230 235 240

Arg Glu His Thr Val Ser
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 <212> DNA
 <213> Homo sapiens

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 gccgctcact gcctgcagga ccggcccgca cccgaggatc tgacggtggt gctcggccag 180
 gaacgccgta accacagctg tgagccgtgc cagacgttgg ccgtgcgctc ctaccgcttg 240
 cacgaggcct tctcgccgt cagctaccag cacgacctgg ctctgttgcg ccttcaggag 300
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 ggcgccgcgc gaccctccga gaccacgctc tgccaggtgg ccggctgggg ccaccagttc 420
 gagggggcgg aggaatatgc cagcttcctg caggaggcgc aggtaccgtt cctctccctg 480
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 gggttcctcg agggcggcac cgatgcgtgc cagggtgatt ccggaggccc gctggtgtgt 600
 gaggaccaag ctgcagagcg ccggctcacc ctgcaaggca tcatcagctg gggatcgggc 660
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 cgggagcaca ccgtttcctg a 741

<210> 78
 <211> 70
 <212> PRT
 <213> Homo sapiens

<400> 78

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

Leu Thr Leu Gln Gly Ile Ile Ser Trp Gly Ser Gly Cys Gly Asp Arg
 35 40 45

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

Arg Glu His Thr Val Ser
 65 70

<210> 79
 <211> 213
 <212> DNA
 <213> Homo sapiens

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 ccgctggtgt gtgaggacca agctgcagag cgccggctca ccctgcaagg catcatcagc 120
 tggggatcgg gctgtggtga ccgcaacaag ccaggcgtct acaccgatgt ggcctactac 180
 ctggcctgga tccgggagca caccgtttcc tga 213

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 <211> 72
 <212> RNA
 <213> Artificial Sequence

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 <223> Synthetic

<400> 80
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 gucggugcuu uu 72

<210> 81
 <211> 82
 <212> RNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 81
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 aaaaguggca ccgagucggu gc 82

<210> 82
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ggcaccgagu cggugcuuuu uuu 83

<210> 83
<211> 80
<212> RNA
<213> Artificial Sequence

<220>
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<400> 83
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ggcaccgagu cggugcuuuu 80

<210> 84
<211> 92
<212> RNA
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<400> 84
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uugaaaaagu ggcaccgagu cggugcuuuu uu 92