

SEQ
SEQUENCE LISTING

<110> Loxo Oncology, Inc. & The Regents of the University of
Colorado, A Body Corporate

<120> POINT MUTATIONS IN TRK INHIBITOR-RESISTANT CANCER AND METHODS
RELATING TO THE SAME

<130> 40449-0069W01

<150> 62/246,580
<151> 2015-10-26

<150> 62/287,778
<151> 2016-01-27

<150> 62/323,586
<151> 2016-04-15

<160> 9

<170> PatentIn version 3.5

<210> 1
<211> 796
<212> PRT
<213> Homo sapiens

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35 40 45

Arg Cys Thr Arg Asp Gly Ala Leu Asp Ser Leu His His Leu Pro Gly
50 55 60

Ala Glu Asn Leu Thr Glu Leu Tyr Ile Glu Asn Gln Gln His Leu Gln
65 70 75 80

SEQ

His Leu Glu Leu Arg Asp Leu Arg Gly Leu Gly Glu Leu Arg Asn Leu
85 90 95

Thr Ile Val Lys Ser Gly Leu Arg Phe Val Ala Pro Asp Ala Phe His
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Phe Thr Pro Arg Leu Ser Arg Leu Asn Leu Ser Phe Asn Ala Leu Glu
115 120 125

Ser Leu Ser Trp Lys Thr Val Gln Gly Leu Ser Leu Gln Glu Leu Val
130 135 140

Leu Ser Gly Asn Pro Leu His Cys Ser Cys Ala Leu Arg Trp Leu Gln
145 150 155 160

Arg Trp Glu Glu Glu Gly Leu Gly Gly Val Pro Glu Gln Lys Leu Gln
165 170 175

Cys His Gly Gln Gly Pro Leu Ala His Met Pro Asn Ala Ser Cys Gly
180 185 190

Val Pro Thr Leu Lys Val Gln Val Pro Asn Ala Ser Val Asp Val Gly
195 200 205

Asp Asp Val Leu Leu Arg Cys Gln Val Glu Gly Arg Gly Leu Glu Gln
210 215 220

Ala Gly Trp Ile Leu Thr Glu Leu Glu Gln Ser Ala Thr Val Met Lys
225 230 235 240

Ser Gly Gly Leu Pro Ser Leu Gly Leu Thr Leu Ala Asn Val Thr Ser
245 250 255

Asp Leu Asn Arg Lys Asn Val Thr Cys Trp Ala Glu Asn Asp Val Gly
260 265 270

SEQ

Arg Ala Glu Val Ser Val Gln Val Asn Val Ser Phe Pro Ala Ser Val
275 280 285

Gln Leu His Thr Ala Val Glu Met His His Trp Cys Ile Pro Phe Ser
290 295 300

Val Asp Gly Gln Pro Ala Pro Ser Leu Arg Trp Leu Phe Asn Gly Ser
305 310 315 320

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

Ala Asn Glu Thr Val Arg His Gly Cys Leu Arg Leu Asn Gln Pro Thr
340 345 350

His Val Asn Asn Gly Asn Tyr Thr Leu Leu Ala Ala Asn Pro Phe Gly
355 360 365

Gln Ala Ser Ala Ser Ile Met Ala Ala Phe Met Asp Asn Pro Phe Glu
370 375 380

Phe Asn Pro Glu Asp Pro Ile Pro Val Ser Phe Ser Pro Val Asp Thr
385 390 395 400

Asn Ser Thr Ser Gly Asp Pro Val Glu Lys Lys Asp Glu Thr Pro Phe
405 410 415

Gly Val Ser Val Ala Val Gly Leu Ala Val Phe Ala Cys Leu Phe Leu
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Ser Thr Leu Leu Leu Val Leu Asn Lys Cys Gly Arg Arg Asn Lys Phe
435 440 445

Gly Ile Asn Arg Pro Ala Val Leu Ala Pro Glu Asp Gly Leu Ala Met
450 455 460

SEQ

Ser Leu His Phe Met Thr Leu Gly Gly Ser Ser Leu Ser Pro Thr Glu
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Gly Lys Gly Ser Gly Leu Gln Gly His Ile Ile Glu Asn Pro Gln Tyr
485 490 495

Phe Ser Asp Ala Cys Val His His Ile Lys Arg Arg Asp Ile Val Leu
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Lys Trp Glu Leu Gly Glu Gly Ala Phe Gly Lys Val Phe Leu Ala Glu
515 520 525

Cys His Asn Leu Leu Pro Glu Gln Asp Lys Met Leu Val Ala Val Lys
530 535 540

Ala Leu Lys Glu Ala Ser Glu Ser Ala Arg Gln Asp Phe Gln Arg Glu
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Ala Glu Leu Leu Thr Met Leu Gln His Gln His Ile Val Arg Phe Phe
565 570 575

Gly Val Cys Thr Glu Gly Arg Pro Leu Leu Met Val Phe Glu Tyr Met
580 585 590

Arg His Gly Asp Leu Asn Arg Phe Leu Arg Ser His Gly Pro Asp Ala
595 600 605

Lys Leu Leu Ala Gly Gly Glu Asp Val Ala Pro Gly Pro Leu Gly Leu
610 615 620

Gly Gln Leu Leu Ala Val Ala Ser Gln Val Ala Ala Gly Met Val Tyr
625 630 635 640

Leu Ala Gly Leu His Phe Val His Arg Asp Leu Ala Thr Arg Asn Cys
645 650 655

SEQ

Leu Val Gly Gln Gly Leu Val Val Lys Ile Gly Asp Phe Gly Met Ser
660 665 670

Arg Asp Ile Tyr Ser Thr Asp Tyr Tyr Arg Val Gly Gly Arg Thr Met
675 680 685

Leu Pro Ile Arg Trp Met Pro Pro Glu Ser Ile Leu Tyr Arg Lys Phe
690 695 700

Thr Thr Glu Ser Asp Val Trp Ser Phe Gly Val Val Leu Trp Glu Ile
705 710 715 720

Phe Thr Tyr Gly Lys Gln Pro Trp Tyr Gln Leu Ser Asn Thr Glu Ala
725 730 735

Ile Asp Cys Ile Thr Gln Gly Arg Glu Leu Glu Arg Pro Arg Ala Cys
740 745 750

Pro Pro Glu Val Tyr Ala Ile Met Arg Gly Cys Trp Gln Arg Glu Pro
755 760 765

Gln Gln Arg His Ser Ile Lys Asp Val His Ala Arg Leu Gln Ala Leu
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Ala Gln Ala Pro Pro Val Tyr Leu Asp Val Leu Gly
785 790 795

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<212> DNA
<213> Homo sapiens

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<210> 3
 <211> 760
 <212> PRT
 <213> Homo sapiens

<400> 3

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Arg Cys Thr Asn Leu Leu Ala Ala Ser Tyr Ile Glu Asn Gln Gln His
35 40 45

Leu Gln His Leu Glu Leu Arg Asp Leu Arg Gly Leu Gly Glu Leu Arg
50 55 60

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

Phe His Phe Thr Pro Arg Leu Ser Arg Leu Asn Leu Ser Phe Asn Ala
85 90 95

Leu Glu Ser Leu Ser Trp Lys Thr Val Gln Gly Leu Ser Leu Gln Glu
100 105 110

Leu Val Leu Ser Gly Asn Pro Leu His Cys Ser Cys Ala Leu Arg Trp
115 120 125

Leu Gln Arg Trp Glu Glu Glu Gly Leu Gly Gly Val Pro Glu Gln Lys
130 135 140

Leu Gln Cys His Gly Gln Gly Pro Leu Ala His Met Pro Asn Ala Ser
145 150 155 160

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

Val Gly Asp Asp Val Leu Leu Arg Cys Gln Val Glu Gly Arg Gly Leu
180 185 190

Glu Gln Ala Gly Trp Ile Leu Thr Glu Leu Glu Gln Ser Ala Thr Val
195 200 205

SEQ

Met Lys Ser Gly Gly Leu Pro Ser Leu Gly Leu Thr Leu Ala Asn Val
210 215 220

Thr Ser Asp Leu Asn Arg Lys Asn Val Thr Cys Trp Ala Glu Asn Asp
225 230 235 240

Val Gly Arg Ala Glu Val Ser Val Gln Val Asn Val Ser Phe Pro Ala
245 250 255

Ser Val Gln Leu His Thr Ala Val Glu Met His His Trp Cys Ile Pro
260 265 270

Phe Ser Val Asp Gly Gln Pro Ala Pro Ser Leu Arg Trp Leu Phe Asn
275 280 285

Gly Ser Val Leu Asn Glu Thr Ser Phe Ile Phe Thr Glu Phe Leu Glu
290 295 300

Pro Ala Ala Asn Glu Thr Val Arg His Gly Cys Leu Arg Leu Asn Gln
305 310 315 320

Pro Thr His Val Asn Asn Gly Asn Tyr Thr Leu Leu Ala Ala Asn Pro
325 330 335

Phe Gly Gln Ala Ser Ala Ser Ile Met Ala Ala Phe Met Asp Asn Pro
340 345 350

Phe Glu Phe Asn Pro Glu Asp Pro Ile Pro Asp Thr Asn Ser Thr Ser
355 360 365

Gly Asp Pro Val Glu Lys Lys Asp Glu Thr Pro Phe Gly Val Ser Val
370 375 380

Ala Val Gly Leu Ala Val Phe Ala Cys Leu Phe Leu Ser Thr Leu Leu
385 390 395 400

SEQ

Leu Val Leu Asn Lys Cys Gly Arg Arg Asn Lys Phe Gly Ile Asn Arg
405 410 415

Pro Ala Val Leu Ala Pro Glu Asp Gly Leu Ala Met Ser Leu His Phe
420 425 430

Met Thr Leu Gly Gly Ser Ser Leu Ser Pro Thr Glu Gly Lys Gly Ser
435 440 445

Gly Leu Gln Gly His Ile Ile Glu Asn Pro Gln Tyr Phe Ser Asp Ala
450 455 460

Cys Val His His Ile Lys Arg Arg Asp Ile Val Leu Lys Trp Glu Leu
465 470 475 480

Gly Glu Gly Ala Phe Gly Lys Val Phe Leu Ala Glu Cys His Asn Leu
485 490 495

Leu Pro Glu Gln Asp Lys Met Leu Val Ala Val Lys Ala Leu Lys Glu
500 505 510

Ala Ser Glu Ser Ala Arg Gln Asp Phe Gln Arg Glu Ala Glu Leu Leu
515 520 525

Thr Met Leu Gln His Gln His Ile Val Arg Phe Phe Gly Val Cys Thr
530 535 540

Glu Gly Arg Pro Leu Leu Met Val Phe Glu Tyr Met Arg His Gly Asp
545 550 555 560

Leu Asn Arg Phe Leu Arg Ser His Gly Pro Asp Ala Lys Leu Leu Ala
565 570 575

Gly Gly Glu Asp Val Ala Pro Gly Pro Leu Gly Leu Gly Gln Leu Leu
580 585 590

SEQ

Ala Val Ala Ser Gln Val Ala Ala Gly Met Val Tyr Leu Ala Gly Leu
595 600 605

His Phe Val His Arg Asp Leu Ala Thr Arg Asn Cys Leu Val Gly Gln
610 615 620

Gly Leu Val Val Lys Ile Gly Asp Phe Gly Met Ser Arg Asp Ile Tyr
625 630 635 640

Ser Thr Asp Tyr Tyr Arg Val Gly Gly Arg Thr Met Leu Pro Ile Arg
645 650 655

Trp Met Pro Pro Glu Ser Ile Leu Tyr Arg Lys Phe Thr Thr Glu Ser
660 665 670

Asp Val Trp Ser Phe Gly Val Val Leu Trp Glu Ile Phe Thr Tyr Gly
675 680 685

Lys Gln Pro Trp Tyr Gln Leu Ser Asn Thr Glu Ala Ile Asp Cys Ile
690 695 700

Thr Gln Gly Arg Glu Leu Glu Arg Pro Arg Ala Cys Pro Pro Glu Val
705 710 715 720

Tyr Ala Ile Met Arg Gly Cys Trp Gln Arg Glu Pro Gln Gln Arg His
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Ser Ile Lys Asp Val His Ala Arg Leu Gln Ala Leu Ala Gln Ala Pro
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Pro Val Tyr Leu Asp Val Leu Gly
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<211> 2581

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<212> DNA

<213> Homo sapiens

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<210> 5
 <211> 822
 <212> PRT

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<213> Homo sapiens

<400> 5

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Pro Thr Ser Cys Lys Cys Ser Ala Ser Arg Ile Trp Cys Ser Asp Pro
 35 40 45

Ser Pro Gly Ile Val Ala Phe Pro Arg Leu Glu Pro Asn Ser Val Asp
 50 55 60

Pro Glu Asn Ile Thr Glu Ile Phe Ile Ala Asn Gln Lys Arg Leu Glu
 65 70 75 80

Ile Ile Asn Glu Asp Asp Val Glu Ala Tyr Val Gly Leu Arg Asn Leu
 85 90 95

Thr Ile Val Asp Ser Gly Leu Lys Phe Val Ala His Lys Ala Phe Leu
 100 105 110

Lys Asn Ser Asn Leu Gln His Ile Asn Phe Thr Arg Asn Lys Leu Thr
 115 120 125

Ser Leu Ser Arg Lys His Phe Arg His Leu Asp Leu Ser Glu Leu Ile
 130 135 140

Leu Val Gly Asn Pro Phe Thr Cys Ser Cys Asp Ile Met Trp Ile Lys
 145 150 155 160

Thr Leu Gln Glu Ala Lys Ser Ser Pro Asp Thr Gln Asp Leu Tyr Cys
 165 170 175

SEQ

Leu Asn Glu Ser Ser Lys Asn Ile Pro Leu Ala Asn Leu Gln Ile Pro
 180 185 190

Asn Cys Gly Leu Pro Ser Ala Asn Leu Ala Ala Pro Asn Leu Thr Val
 195 200 205

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

Val Pro Asn Met Tyr Trp Asp Val Gly Asn Leu Val Ser Lys His Met
 225 230 235 240

Asn Glu Thr Ser His Thr Gln Gly Ser Leu Arg Ile Thr Asn Ile Ser
 245 250 255

Ser Asp Asp Ser Gly Lys Gln Ile Ser Cys Val Ala Glu Asn Leu Val
 260 265 270

Gly Glu Asp Gln Asp Ser Val Asn Leu Thr Val His Phe Ala Pro Thr
 275 280 285

Ile Thr Phe Leu Glu Ser Pro Thr Ser Asp His His Trp Cys Ile Pro
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Phe Thr Val Lys Gly Asn Pro Lys Pro Ala Leu Gln Trp Phe Tyr Asn
 305 310 315 320

Gly Ala Ile Leu Asn Glu Ser Lys Tyr Ile Cys Thr Lys Ile His Val
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Thr Asn His Thr Glu Tyr His Gly Cys Leu Gln Leu Asp Asn Pro Thr
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His Met Asn Asn Gly Asp Tyr Thr Leu Ile Ala Lys Asn Glu Tyr Gly
 355 360 365

Lys Asp Glu Lys Gln Ile Ser Ala His Phe Met Gly Trp Pro Gly Ile
 370 375 380

Asp Asp Gly Ala Asn Pro Asn Tyr Pro Asp Val Ile Tyr Glu Asp Tyr
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Gly Thr Ala Ala Asn Asp Ile Gly Asp Thr Thr Asn Arg Ser Asn Glu
 405 410 415

Ile Pro Ser Thr Asp Val Thr Asp Lys Thr Gly Arg Glu His Leu Ser
 420 425 430

Val Tyr Ala Val Val Val Ile Ala Ser Val Val Gly Phe Cys Leu Leu
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Val Met Leu Phe Leu Leu Lys Leu Ala Arg His Ser Lys Phe Gly Met
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Lys Gly Pro Ala Ser Val Ile Ser Asn Asp Asp Asp Ser Ala Ser Pro
 465 470 475 480

Leu His His Ile Ser Asn Gly Ser Asn Thr Pro Ser Ser Ser Glu Gly
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Gly Pro Asp Ala Val Ile Ile Gly Met Thr Lys Ile Pro Val Ile Glu
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Asn Pro Gln Tyr Phe Gly Ile Thr Asn Ser Gln Leu Lys Pro Asp Thr
 515 520 525

Phe Val Gln His Ile Lys Arg His Asn Ile Val Leu Lys Arg Glu Leu
 530 535 540

Gly Glu Gly Ala Phe Gly Lys Val Phe Leu Ala Glu Cys Tyr Asn Leu
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SEQ

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SEQ

Pro Trp Tyr Gln Leu Ser Asn Asn Glu Val Ile Glu Cys Ile Thr Gln
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Gly Arg Val Leu Gln Arg Pro Arg Thr Cys Pro Gln Glu Val Tyr Glu
770 775 780

Leu Met Leu Gly Cys Trp Gln Arg Glu Pro His Met Arg Lys Asn Ile
785 790 795 800

Lys Gly Ile His Thr Leu Leu Gln Asn Leu Ala Lys Ala Ser Pro Val
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Tyr Leu Asp Ile Leu Gly
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acgaagatga tgttgaagct tatgtgggac tgagaaatct gacaattgtg gattctggat 420
taaaatttgt ggctcataaa gcatttctga aaaacagcaa cctgcagcac atcaatttta 480
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<400> 7

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Pro Ala Asn Cys Val Cys Ser Lys Thr Glu Ile Asn Cys Arg Arg Pro
35 40 45

Asp Asp Gly Asn Leu Phe Pro Leu Leu Glu Gly Gln Asp Ser Gly Asn
50 55 60

Ser Asn Gly Asn Ala Asn Ile Asn Ile Thr Asp Ile Ser Arg Asn Ile
65 70 75 80

Thr Ser Ile His Ile Glu Asn Trp Arg Ser Leu His Thr Leu Asn Ala
85 90 95

Val Asp Met Glu Leu Tyr Thr Gly Leu Gln Lys Leu Thr Ile Lys Asn
100 105 110

Ser Gly Leu Arg Ser Ile Gln Pro Arg Ala Phe Ala Lys Asn Pro His
115 120 125

Leu Arg Tyr Ile Asn Leu Ser Ser Asn Arg Leu Thr Thr Leu Ser Trp
130 135 140

Gln Leu Phe Gln Thr Leu Ser Leu Arg Glu Leu Gln Leu Glu Gln Asn
145 150 155 160

Phe Phe Asn Cys Ser Cys Asp Ile Arg Trp Met Gln Leu Trp Gln Glu
165 170 175

Gln Gly Glu Ala Lys Leu Asn Ser Gln Asn Leu Tyr Cys Ile Asn Ala
180 185 190

Asp Gly Ser Gln Leu Pro Leu Phe Arg Met Asn Ile Ser Gln Cys Asp
195 200 205

SEQ

Leu Pro Glu Ile Ser Val Ser His Val Asn Leu Thr Val Arg Glu Gly
210 215 220

Asp Asn Ala Val Ile Thr Cys Asn Gly Ser Gly Ser Pro Leu Pro Asp
225 230 235 240

Val Asp Trp Ile Val Thr Gly Leu Gln Ser Ile Asn Thr His Gln Thr
245 250 255

Asn Leu Asn Trp Thr Asn Val His Ala Ile Asn Leu Thr Leu Val Asn
260 265 270

Val Thr Ser Glu Asp Asn Gly Phe Thr Leu Thr Cys Ile Ala Glu Asn
275 280 285

Val Val Gly Met Ser Asn Ala Ser Val Ala Leu Thr Val Tyr Tyr Pro
290 295 300

Pro Arg Val Val Ser Leu Glu Glu Pro Glu Leu Arg Leu Glu His Cys
305 310 315 320

Ile Glu Phe Val Val Arg Gly Asn Pro Pro Pro Thr Leu His Trp Leu
325 330 335

His Asn Gly Gln Pro Leu Arg Glu Ser Lys Ile Ile His Val Glu Tyr
340 345 350

Tyr Gln Glu Gly Glu Ile Ser Glu Gly Cys Leu Leu Phe Asn Lys Pro
355 360 365

Thr His Tyr Asn Asn Gly Asn Tyr Thr Leu Ile Ala Lys Asn Pro Leu
370 375 380

Gly Thr Ala Asn Gln Thr Ile Asn Gly His Phe Leu Lys Glu Pro Phe
385 390 395 400

SEQ

Pro Glu Ser Thr Asp Asn Phe Ile Leu Phe Asp Glu Val Ser Pro Thr
405 410 415

Pro Pro Ile Thr Val Thr His Lys Pro Glu Glu Asp Thr Phe Gly Val
420 425 430

Ser Ile Ala Val Gly Leu Ala Ala Phe Ala Cys Val Leu Leu Val Val
435 440 445

Leu Phe Val Met Ile Asn Lys Tyr Gly Arg Arg Ser Lys Phe Gly Met
450 455 460

Lys Gly Pro Val Ala Val Ile Ser Gly Glu Glu Asp Ser Ala Ser Pro
465 470 475 480

Leu His His Ile Asn His Gly Ile Thr Thr Pro Ser Ser Leu Asp Ala
485 490 495

Gly Pro Asp Thr Val Val Ile Gly Met Thr Arg Ile Pro Val Ile Glu
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Asn Pro Gln Tyr Phe Arg Gln Gly His Asn Cys His Lys Pro Asp Thr
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Tyr Val Gln His Ile Lys Arg Arg Asp Ile Val Leu Lys Arg Glu Leu
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Gly Glu Gly Ala Phe Gly Lys Val Phe Leu Ala Glu Cys Tyr Asn Leu
545 550 555 560

Ser Pro Thr Lys Asp Lys Met Leu Val Ala Val Lys Ala Leu Lys Asp
565 570 575

Pro Thr Leu Ala Ala Arg Lys Asp Phe Gln Arg Glu Ala Glu Leu Leu
580 585 590

SEQ

Thr Asn Leu Gln His Glu His Ile Val Lys Phe Tyr Gly Val Cys Gly
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Asp Gly Asp Pro Leu Ile Met Val Phe Glu Tyr Met Lys His Gly Asp
610 615 620

Leu Asn Lys Phe Leu Arg Ala His Gly Pro Asp Ala Met Ile Leu Val
625 630 635 640

Asp Gly Gln Pro Arg Gln Ala Lys Gly Glu Leu Gly Leu Ser Gln Met
645 650 655

Leu His Ile Ala Ser Gln Ile Ala Ser Gly Met Val Tyr Leu Ala Ser
660 665 670

Gln His Phe Val His Arg Asp Leu Ala Thr Arg Asn Cys Leu Val Gly
675 680 685

Ala Asn Leu Leu Val Lys Ile Gly Asp Phe Gly Met Ser Arg Asp Val
690 695 700

Tyr Ser Thr Asp Tyr Tyr Arg Leu Phe Asn Pro Ser Gly Asn Asp Phe
705 710 715 720

Cys Ile Trp Cys Glu Val Gly Gly His Thr Met Leu Pro Ile Arg Trp
725 730 735

Met Pro Pro Glu Ser Ile Met Tyr Arg Lys Phe Thr Thr Glu Ser Asp
740 745 750

Val Trp Ser Phe Gly Val Ile Leu Trp Glu Ile Phe Thr Tyr Gly Lys
755 760 765

Gln Pro Trp Phe Gln Leu Ser Asn Thr Glu Val Ile Glu Cys Ile Thr
770 775 780

SEQ

Gln Gly Arg Val Leu Glu Arg Pro Arg Val Cys Pro Lys Glu Val Tyr
785 790 795 800

Asp Val Met Leu Gly Cys Trp Gln Arg Glu Pro Gln Gln Arg Leu Asn
805 810 815

Ile Lys Glu Ile Tyr Lys Ile Leu His Ala Leu Gly Lys Ala Thr Pro
820 825 830

Ile Tyr Leu Asp Ile Leu Gly
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aaaaaaaaaa	accgc					2715

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<212>	PRT
<213>	Artificial Sequence

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

Arg Leu Asn Leu Ser Phe Asn Ala Leu Glu Ser Leu Ser Trp Lys Thr
50 55 60

Val Gln Gly Leu Ser Leu Gln Glu Leu Val SEQ
 65 70 75 80

His Cys Ser Cys Ala Leu Arg Trp Leu Gln Arg Trp Glu Glu Glu Gly
 85 90 95

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

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

Gln Val Pro Asn Ala Ser Val Asp Val Gly Asp Asp Val Leu Leu Arg
 130 135 140

Cys Gln Val Glu Gly Arg Gly Leu Glu Gln Ala Gly Trp Ile Leu Thr
 145 150 155 160

Glu Leu Glu Gln Ser Ala Thr Val Met Lys Ser Gly Gly Leu Pro Ser
 165 170 175

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

Val Thr Cys Trp Ala Glu Asn Asp Val Gly Arg Ala Glu Val Ser Val
 195 200 205

Gln Val Asn Val Ser Phe Pro Ala Ser Val Gln Leu His Thr Ala Val
 210 215 220

Glu Met His His Trp Cys Ile Pro Phe Ser Val Asp Gly Gln Pro Ala
 225 230 235 240

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

SEQ

Phe Ile Phe Thr Glu Phe Leu Glu Pro Ala Ala Asn Glu Thr Val Arg
 260 265 270

His Gly Cys Leu Arg Leu Asn Gln Pro Thr His Val Asn Asn Gly Asn
 275 280 285

Tyr Thr Leu Leu Ala Ala Asn Pro Phe Gly Gln Ala Ser Ala Ser Ile
 290 295 300

Met Ala Ala Phe Met Asp Asn Pro Phe Glu Phe Asn Pro Glu Asp Pro
 305 310 315 320

Ile Pro Asp Thr Asn Ser Thr Ser Gly Asp Pro Val Glu Lys Lys Asp
 325 330 335

Glu Thr Pro Phe Gly Val Ser Val Ala Val Gly Leu Ala Val Phe Ala
 340 345 350

Cys Leu Phe Leu Ser Thr Leu Leu Leu Val Leu Asn Lys Cys Gly Arg
 355 360 365

Arg Asn Lys Phe Gly Ile Asn Arg Pro Ala Val Leu Ala Pro Glu Asp
 370 375 380

Gly Leu Ala Met Ser Leu His Phe Met Thr Leu Gly Gly Ser Ser Leu
 385 390 395 400

Ser Pro Thr Glu Gly Lys Gly Ser Gly Leu Gln Gly His Ile Ile Glu
 405 410 415

Asn Pro Gln Tyr Phe Ser Asp Ala Cys Val His His Ile Lys Arg Arg
 420 425 430

Asp Ile Val Leu Lys Trp Glu Leu Gly Glu Gly Ala Phe Gly Lys Val
 435 440 445

SEQ

Phe Leu Ala Glu Cys His Asn Leu Leu Pro Glu Gln Asp Lys Met Leu
450 455 460

Val Ala Val Lys Ala Leu Lys Glu Ala Ser Glu Ser Ala Arg Gln Asp
465 470 475 480

Phe Gln Arg Glu Ala Glu Leu Leu Thr Met Leu Gln His Gln His Ile
485 490 495

Val Arg Phe Phe Gly Val Cys Thr Glu Gly Arg Pro Leu Leu Met Val
500 505 510

Phe Glu Tyr Met Arg His Gly Asp Leu Asn Arg Phe Leu Arg Ser His
515 520 525

Gly Pro Asp Ala Lys Leu Leu Ala Gly Gly Glu Asp Val Ala Pro Gly
530 535 540

Pro Leu Gly Leu Gly Gln Leu Leu Ala Val Ala Ser Gln Val Ala Ala
545 550 555 560

Gly Met Val Tyr Leu Ala Gly Leu His Phe Val His Arg Asp Leu Ala
565 570 575

Thr Arg Asn Cys Leu Val Gly Gln Gly Leu Val Val Lys Ile Gly Asp
580 585 590

Phe Gly Met Ser Arg Asp Ile Tyr Ser Thr Asp Tyr Tyr Arg Val Gly
595 600 605

Gly Arg Thr Met Leu Pro Ile Arg Trp Met Pro Pro Glu Ser Ile Leu
610 615 620

Tyr Arg Lys Phe Thr Thr Glu Ser Asp Val Trp Ser Phe Gly Val Val
625 630 635 640

SEQ

Leu	Trp	Glu	Ile	Phe	Thr	Tyr	Gly	Lys	Gln	Pro	Trp	Tyr	Gln	Leu	Ser
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Pro	Arg	Ala	Cys	Pro	Pro	Glu	Val	Tyr	Ala	Ile	Met	Arg	Gly	Cys	Trp
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Gln	Arg	Glu	Pro	Gln	Gln	Arg	His	Ser	Ile	Lys	Asp	Val	His	Ala	Arg
								695			700				
Leu	Gln	Ala	Leu	Ala	Gln	Ala	Pro	Pro	Val	Tyr	Leu	Asp	Val	Leu	Gly
705					710					715					720