

1402-PCT-1_Sequence_Listing
SEQUENCE LISTING

<110> Epizyme, Inc.
Chesworth, Richard
Mitchell, Lorna Helen
Shapiro, Gideon

<120> ARGININE METHYLTRANSFERASE INHIBITORS AND USES THEREOF

<130> E0501.70011W000

<140> PCT/US2014/029710
<141> 2014-03-14

<150> US 61/876,034
<151> 2013-09-10

<150> US 61/781,051
<151> 2013-03-14

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<170> PatentIn version 3.5

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Xaa Arg Leu Ala Arg Arg Gly Gly Val Lys Arg Ile Ser Gly Leu Ile
1 5 10 15

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Asp Tyr Lys Asp Asp Asp Asp Lys
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1402-PCT-1_Sequence_Listing

Met Ser Pro Ile Leu Gly Tyr Trp Lys Ile Lys Gly Leu Val Gln Pro
1 5 10 15

Thr Arg Leu Leu Leu Glu Tyr Leu Glu Glu Lys Tyr Glu Glu His Leu
20 25 30

Tyr Glu Arg Asp Glu Gly Asp Lys Trp Arg Asn Lys Lys Phe Glu Leu
35 40 45

Gly Leu Glu Phe Pro Asn Leu Pro Tyr Tyr Ile Asp Gly Asp Val Lys
50 55 60

Leu Thr Gln Ser Met Ala Ile Ile Arg Tyr Ile Ala Asp Lys His Asn
65 70 75 80

Met Leu Gly Gly Cys Pro Lys Glu Arg Ala Glu Ile Ser Met Leu Glu
85 90 95

Gly Ala Val Leu Asp Ile Arg Tyr Gly Val Ser Arg Ile Ala Tyr Ser
100 105 110

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

Met Leu Lys Met Phe Glu Asp Arg Leu Cys His Lys Thr Tyr Leu Asn
130 135 140

Gly Asp His Val Thr His Pro Asp Phe Met Leu Tyr Asp Ala Leu Asp
145 150 155 160

Val Val Leu Tyr Met Asp Pro Met Cys Leu Asp Ala Phe Pro Lys Leu
165 170 175

Val Cys Phe Lys Lys Arg Ile Glu Ala Ile Pro Gln Ile Asp Lys Tyr
180 185 190

Leu Lys Ser Ser Lys Tyr Ile Ala Trp Pro Leu Gln Gly Trp Gln Ala
195 200 205

Thr Phe Gly Gly Gly Asp His Pro Pro Lys Ser Asp Glu Asn Leu Tyr
210 215 220

Phe Gln Gly Gly Asn Ser
225 230

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1402-PCT-1_Sequence_Listing

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Met Ser Pro Ile Leu Gly Tyr Trp Lys Ile Lys Gly Leu Val Gln Pro
1      5      10
Thr Arg Leu Leu Leu Glu Tyr Leu Glu Glu Lys Tyr Glu Glu His Leu
      20      25      30
Tyr Glu Arg Asp Glu Gly Asp Lys Trp Arg Asn Lys Lys Phe Glu Leu
      35      40      45
Gly Leu Glu Phe Pro Asn Leu Pro Tyr Tyr Ile Asp Gly Asp Val Lys
      50      55      60
Leu Thr Gln Ser Met Ala Ile Ile Arg Tyr Ile Ala Asp Lys His Asn
      65      70      75      80
Met Leu Gly Gly Cys Pro Lys Glu Arg Ala Glu Ile Ser Met Leu Glu
      85      90      95
Gly Ala Val Leu Asp Ile Arg Tyr Gly Val Ser Arg Ile Ala Tyr Ser
      100      105      110
Lys Asp Phe Glu Thr Leu Lys Val Asp Phe Leu Ser Lys Leu Pro Glu
      115      120      125
Met Leu Lys Met Phe Glu Asp Arg Leu Cys His Lys Thr Tyr Leu Asn
      130      135      140
Gly Asp His Val Thr His Pro Asp Phe Met Leu Tyr Asp Ala Leu Asp
      145      150      155      160
Val Val Leu Tyr Met Asp Pro Met Cys Leu Asp Ala Phe Pro Lys Leu
      165      170      175
Val Cys Phe Lys Lys Arg Ile Glu Ala Ile Pro Gln Ile Asp Lys Tyr
      180      185      190
Leu Lys Ser Ser Lys Tyr Ile Ala Trp Pro Leu Gln Gly Trp Gln Ala
      195      200      205
Thr Phe Gly Gly Gly Asp His Pro Pro Lys Ser Asp Glu Asn Leu Tyr
      210      215      220
Phe Gln Gly Gly Asn Ser Asp Tyr Lys Asp Asp Asp Asp Lys Met Ala
      225      230      235      240
Ala Ala Glu Ala Ala Asn Cys Ile Met Glu Asn Phe Val Ala Thr Leu
      245      250      255
Ala Asn Gly Met Ser Leu Gln Pro Pro Leu Glu Glu Val Ser Cys Gly
      260      265      270

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1402-PCT-1_Sequence_Listing

Gln Ala Glu Ser Ser Glu Lys Pro Asn Ala Glu Asp Met Thr Ser Lys
 275 280 285
 Asp Tyr Tyr Phe Asp Ser Tyr Ala His Phe Gly Ile His Glu Glu Met
 290 295 300
 Leu Lys Asp Glu Val Arg Thr Leu Thr Tyr Arg Asn Ser Met Phe His
 305 310 315 320
 Asn Arg His Leu Phe Lys Asp Lys Val Val Leu Asp Val Gly Ser Gly
 325 330 335
 Thr Gly Ile Leu Cys Met Phe Ala Ala Lys Ala Gly Ala Arg Lys Val
 340 345 350
 Ile Gly Ile Glu Cys Ser Ser Ile Ser Asp Tyr Ala Val Lys Ile Val
 355 360 365
 Lys Ala Asn Lys Leu Asp His Val Val Thr Ile Ile Lys Gly Lys Val
 370 375 380
 Glu Glu Val Glu Leu Pro Val Glu Lys Val Asp Ile Ile Ile Ser Glu
 385 390 395 400
 Trp Met Gly Tyr Cys Leu Phe Tyr Glu Ser Met Leu Asn Thr Val Leu
 405 410 415
 Tyr Ala Arg Asp Lys Trp Leu Ala Pro Asp Gly Leu Ile Phe Pro Asp
 420 425 430
 Arg Ala Thr Leu Tyr Val Thr Ala Ile Glu Asp Arg Gln Tyr Lys Asp
 435 440 445
 Tyr Lys Ile His Trp Trp Glu Asn Val Tyr Gly Phe Asp Met Ser Cys
 450 455 460
 Ile Lys Asp Val Ala Ile Lys Glu Pro Leu Val Asp Val Val Asp Pro
 465 470 475 480
 Lys Gln Leu Val Thr Asn Ala Cys Leu Ile Lys Glu Val Asp Ile Tyr
 485 490 495
 Thr Val Lys Val Glu Asp Leu Thr Phe Thr Ser Pro Phe Cys Leu Gln
 500 505 510
 Val Lys Arg Asn Asp Tyr Val His Ala Leu Val Ala Tyr Phe Asn Ile
 515 520 525
 Glu Phe Thr Arg Cys His Lys Arg Thr Gly Phe Ser Thr Ser Pro Glu
 530 535 540

1402-PCT-1_Sequence_Listing

Ser Pro Tyr Thr His Trp Lys Gln Thr Val Phe Tyr Met Glu Asp Tyr
545 550 555 560

Leu Thr Val Lys Thr Gly Glu Glu Ile Phe Gly Thr Ile Gly Met Arg
565 570 575

Pro Asn Ala Lys Asn Asn Arg Asp Leu Asp Phe Thr Ile Asp Leu Asp
580 585 590

Phe Lys Gly Gln Leu Cys Glu Leu Ser Cys Ser Thr Asp Tyr Arg Met
595 600 605

Arg

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Xaa Arg Leu Ala Arg Arg Gly Gly Val Lys Arg Ile Ser Gly Leu Ile
1 5 10 15

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Met Asp Tyr Lys Asp Asp Asp Asp Lys
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Met Asp Tyr Lys Asp Asp Asp Asp Lys Ser Gln Pro Lys Lys Arg Lys
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1402-PCT-1_Sequence_Listing

Leu Glu Ser Gly Gly Gly Gly Glu Gly Gly Glu Gly Thr Glu Glu Glu
 20 25 30
 Asp Gly Ala Glu Arg Glu Ala Ala Leu Glu Arg Pro Arg Arg Thr Lys
 35 40 45
 Arg Glu Arg Asp Gln Leu Tyr Tyr Glu Cys Tyr Ser Asp Val Ser Val
 50 55 60
 His Glu Glu Met Ile Ala Asp Arg Val Arg Thr Asp Ala Tyr Arg Leu
 65 70 75 80
 Gly Ile Leu Arg Asn Trp Ala Ala Leu Arg Gly Lys Thr Val Leu Asp
 85 90 95
 Val Gly Ala Gly Thr Gly Ile Leu Ser Ile Phe Cys Ala Gln Ala Gly
 100 105 110
 Ala Arg Arg Val Tyr Ala Val Glu Ala Ser Ala Ile Trp Gln Gln Ala
 115 120 125
 Arg Glu Val Val Arg Phe Asn Gly Leu Glu Asp Arg Val His Val Leu
 130 135 140
 Pro Gly Pro Val Glu Thr Val Glu Leu Pro Glu Gln Val Asp Ala Ile
 145 150 155 160
 Val Ser Glu Trp Met Gly Tyr Gly Leu Leu His Glu Ser Met Leu Ser
 165 170 175
 Ser Val Leu His Ala Arg Thr Lys Trp Leu Lys Glu Gly Gly Leu Leu
 180 185 190
 Leu Pro Ala Ser Ala Glu Leu Phe Ile Ala Pro Ile Ser Asp Gln Met
 195 200 205
 Leu Glu Trp Arg Leu Gly Phe Trp Ser Gln Val Lys Gln His Tyr Gly
 210 215 220
 Val Asp Met Ser Cys Leu Glu Gly Phe Ala Thr Arg Cys Leu Met Gly
 225 230 235 240
 His Ser Glu Ile Val Val Gln Gly Leu Ser Gly Glu Asp Val Leu Ala
 245 250 255
 Arg Pro Gln Arg Phe Ala Gln Leu Glu Leu Ser Arg Ala Gly Leu Glu
 260 265 270
 Gln Glu Leu Glu Ala Gly Val Gly Gly Arg Phe Arg Cys Ser Cys Tyr
 275 280 285

1402-PCT-1_Sequence_Listing

Gly Ser Ala Pro Met His Gly Phe Ala Ile Trp Phe Gln Val Thr Phe
290 295 300

Pro Gly Gly Glu Ser Glu Lys Pro Leu Val Leu Ser Thr Ser Pro Phe
305 310 315 320

His Pro Ala Thr His Trp Lys Gln Ala Leu Leu Tyr Leu Asn Glu Pro
325 330 335

Val Gln Val Glu Gln Asp Thr Asp Val Ser Gly Glu Ile Thr Leu Leu
340 345 350

Pro Ser Arg Asp Asn Pro Arg Arg Leu Arg Val Leu Leu Arg Tyr Lys
355 360 365

Val Gly Asp Gln Glu Glu Lys Thr Lys Asp Phe Ala Met Glu Asp His
370 375 380

His His His His His
385

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Xaa Lys Pro Ala Ile Arg Arg Leu Ala Arg Arg Gly Gly Val Lys Arg
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Met Ser Pro Ile Leu Gly Tyr Trp Lys Ile Lys Gly Leu Val Gln Pro
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Thr Arg Leu Leu Leu Glu Tyr Leu Glu Glu Lys Tyr Glu Glu His Leu
20 25 30

1402-PCT-1_Sequence_Listing

Tyr Glu Arg Asp Glu Gly Asp Lys Trp Arg Asn Lys Lys Phe Glu Leu
35 40 45

Gly Leu Glu Phe Pro Asn Leu Pro Tyr Tyr Ile Asp Gly Asp Val Lys
50 55 60

Leu Thr Gln Ser Met Ala Ile Ile Arg Tyr Ile Ala Asp Lys His Asn
65 70 75 80

Met Leu Gly Gly Cys Pro Lys Glu Arg Ala Glu Ile Ser Met Leu Glu
85 90 95

Gly Ala Val Leu Asp Ile Arg Tyr Gly Val Ser Arg Ile Ala Tyr Ser
100 105 110

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

Met Leu Lys Met Phe Glu Asp Arg Leu Cys His Lys Thr Tyr Leu Asn
130 135 140

Gly Asp His Val Thr His Pro Asp Phe Met Leu Tyr Asp Ala Leu Asp
145 150 155 160

Val Val Leu Tyr Met Asp Pro Met Cys Leu Asp Ala Phe Pro Lys Leu
165 170 175

Val Cys Phe Lys Lys Arg Ile Glu Ala Ile Pro Gln Ile Asp Lys Tyr
180 185 190

Leu Lys Ser Ser Lys Tyr Ile Ala Trp Pro Leu Gln Gly Trp Gln Ala
195 200 205

Thr Phe Gly Gly Gly Asp His Pro Pro Lys Ser Asp Leu Val Pro Arg
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Gly Ser Pro Glu Phe
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Met Ser Pro Ile Leu Gly Tyr Trp Lys Ile Lys Gly Leu Val Gln Pro
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Thr Arg Leu Leu Leu Glu Tyr Leu Glu Glu Lys Tyr Glu Glu His Leu
20 25 30

1402-PCT-1_Sequence_Listing

Tyr Glu Arg Asp Glu Gly Asp Lys Trp Arg Asn Lys Lys Phe Glu Leu
 35 40 45
 Gly Leu Glu Phe Pro Asn Leu Pro Tyr Tyr Ile Asp Gly Asp Val Lys
 50 55 60
 Leu Thr Gln Ser Met Ala Ile Ile Arg Tyr Ile Ala Asp Lys His Asn
 65 70 75 80
 Met Leu Gly Gly Cys Pro Lys Glu Arg Ala Glu Ile Ser Met Leu Glu
 85 90 95
 Gly Ala Val Leu Asp Ile Arg Tyr Gly Val Ser Arg Ile Ala Tyr Ser
 100 105 110
 Lys Asp Phe Glu Thr Leu Lys Val Asp Phe Leu Ser Lys Leu Pro Glu
 115 120 125
 Met Leu Lys Met Phe Glu Asp Arg Leu Cys His Lys Thr Tyr Leu Asn
 130 135 140
 Gly Asp His Val Thr His Pro Asp Phe Met Leu Tyr Asp Ala Leu Asp
 145 150 155 160
 Val Val Leu Tyr Met Asp Pro Met Cys Leu Asp Ala Phe Pro Lys Leu
 165 170 175
 Val Cys Phe Lys Lys Arg Ile Glu Ala Ile Pro Gln Ile Asp Lys Tyr
 180 185 190
 Leu Lys Ser Ser Lys Tyr Ile Ala Trp Pro Leu Gln Gly Trp Gln Ala
 195 200 205
 Thr Phe Gly Gly Gly Asp His Pro Pro Lys Ser Asp Leu Val Pro Arg
 210 215 220
 Gly Ser Pro Glu Phe Met Gly Met Lys His Ser Ser Arg Cys Leu Leu
 225 230 235 240
 Leu Arg Arg Lys Met Ala Glu Asn Ala Ala Glu Ser Thr Glu Val Asn
 245 250 255
 Ser Pro Pro Ser Gln Pro Pro Gln Pro Val Val Pro Ala Lys Pro Val
 260 265 270
 Gln Cys Val His His Val Ser Thr Gln Pro Ser Cys Pro Gly Arg Gly
 275 280 285
 Lys Met Ser Lys Leu Leu Asn Pro Glu Glu Met Thr Ser Arg Asp Tyr
 290 295 300

1402-PCT-1_Sequence_Listing

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Tyr Phe Asp Ser Tyr Ala His Phe Gly Ile His Glu Glu Met Leu Lys
305          310          315

Asp Glu Val Arg Thr Leu Thr Tyr Arg Asn Ser Met Tyr His Asn Lys
          325          330          335

His Val Phe Lys Asp Lys Val Val Leu Asp Val Gly Ser Gly Thr Gly
          340          345          350

Ile Leu Ser Met Phe Ala Ala Lys Ala Gly Ala Lys Lys Val Phe Gly
          355          360          365

Ile Glu Cys Ser Ser Ile Ser Asp Tyr Ser Glu Lys Ile Ile Lys Ala
370          375          380

Asn His Leu Asp Asn Ile Ile Thr Ile Phe Lys Gly Lys Val Glu Glu
385          390          395

Val Glu Leu Pro Val Glu Lys Val Asp Ile Ile Ile Ser Glu Trp Met
          405          410          415

Gly Tyr Cys Leu Phe Tyr Glu Ser Met Leu Asn Thr Val Ile Phe Ala
          420          425          430

Arg Asp Lys Trp Leu Lys Pro Gly Gly Leu Met Phe Pro Asp Arg Ala
          435          440          445

Ala Leu Tyr Val Val Ala Ile Glu Asp Arg Gln Tyr Lys Asp Phe Lys
450          455          460

Ile His Trp Trp Glu Asn Val Tyr Gly Phe Asp Met Thr Cys Ile Arg
465          470          475

Asp Val Ala Met Lys Glu Pro Leu Val Asp Ile Val Asp Pro Lys Gln
          485          490          495

Val Val Thr Asn Ala Cys Leu Ile Lys Glu Val Asp Ile Tyr Thr Val
          500          505          510

Lys Thr Glu Glu Leu Ser Phe Thr Ser Ala Phe Cys Leu Gln Ile Gln
515          520          525

Arg Asn Asp Tyr Val His Ala Leu Val Thr Tyr Phe Asn Ile Glu Phe
530          535          540

Thr Lys Cys His Lys Lys Met Gly Phe Ser Thr Ala Pro Asp Ala Pro
545          550          555

Tyr Thr His Trp Lys Gln Thr Val Phe Tyr Leu Glu Asp Tyr Leu Thr
          565          570          575

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1402-PCT-1_Sequence_Listing

Val Arg Arg Gly Glu Glu Ile Tyr Gly Thr Ile Ser Met Lys Pro Asn
580 585 590

Ala Lys Asn Val Arg Asp Leu Asp Phe Thr Val Asp Leu Asp Phe Lys
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Gly Gln Leu Cys Glu Thr Ser Val Ser Asn Asp Tyr Lys Met Arg
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Gly Gly Phe Gly
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Met Ser Pro Ile Leu Gly Tyr Trp Lys Ile Lys Gly Leu Val Gln Pro
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Thr Arg Leu Leu Leu Glu Tyr Leu Glu Glu Lys Tyr Glu Glu His Leu
20 25 30

Tyr Glu Arg Asp Glu Gly Asp Lys Trp Arg Asn Lys Lys Phe Glu Leu
35 40 45

Gly Leu Glu Phe Pro Asn Leu Pro Tyr Tyr Ile Asp Gly Asp Val Lys
50 55 60

Leu Thr Gln Ser Met Ala Ile Ile Arg Tyr Ile Ala Asp Lys His Asn
65 70 75 80

1402-PCT-1_Sequence_Listing

Met Leu Gly Gly Cys Pro Lys Glu Arg Ala Glu Ile Ser Met Leu Glu
85 90 95

Gly Ala Val Leu Asp Ile Arg Tyr Gly Val Ser Arg Ile Ala Tyr Ser
100 105 110

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

Met Leu Lys Met Phe Glu Asp Arg Leu Cys His Lys Thr Tyr Leu Asn
130 135 140

Gly Asp His Val Thr His Pro Asp Phe Met Leu Tyr Asp Ala Leu Asp
145 150 155 160

Val Val Leu Tyr Met Asp Pro Met Cys Leu Asp Ala Phe Pro Lys Leu
165 170 175

Val Cys Phe Lys Lys Arg Ile Glu Ala Ile Pro Gln Ile Asp Lys Tyr
180 185 190

Leu Lys Ser Ser Lys Tyr Ile Ala Trp Pro Leu Gln Gly Trp Gln Ala
195 200 205

Thr Phe Gly Gly Gly Asp His Pro Pro Lys Ser Asp Leu Val Pro Arg
210 215 220

Gly Ser
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Met Ser Pro Ile Leu Gly Tyr Trp Lys Ile Lys Gly Leu Val Gln Pro
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Thr Arg Leu Leu Leu Glu Tyr Leu Glu Glu Lys Tyr Glu Glu His Leu
20 25 30

Tyr Glu Arg Asp Glu Gly Asp Lys Trp Arg Asn Lys Lys Phe Glu Leu
35 40 45

Gly Leu Glu Phe Pro Asn Leu Pro Tyr Tyr Ile Asp Gly Asp Val Lys
50 55 60

Leu Thr Gln Ser Met Ala Ile Ile Arg Tyr Ile Ala Asp Lys His Asn
65 70 75 80

1402-PCT-1_Sequence_Listing

Met	Leu	Gly	Gly	Cys	Pro	Lys	Glu	Arg	Ala	Glu	Ile	Ser	Met	Leu	Glu	85	90	95	
Gly	Ala	Val	Leu	Asp	Ile	Arg	Tyr	Gly	Val	Ser	Arg	Ile	Ala	Tyr	Ser	100	105	110	
Lys	Asp	Phe	Glu	Thr	Leu	Lys	Val	Asp	Phe	Leu	Ser	Lys	Leu	Pro	Glu	115	120	125	
Met	Leu	Lys	Met	Phe	Glu	Asp	Arg	Leu	Cys	His	Lys	Thr	Tyr	Leu	Asn	130	135	140	
Gly	Asp	His	Val	Thr	His	Pro	Asp	Phe	Met	Leu	Tyr	Asp	Ala	Leu	Asp	145	150	155	160
Val	Val	Leu	Tyr	Met	Asp	Pro	Met	Cys	Leu	Asp	Ala	Phe	Pro	Lys	Leu	165	170	175	
Val	Cys	Phe	Lys	Lys	Arg	Ile	Glu	Ala	Ile	Pro	Gln	Ile	Asp	Lys	Tyr	180	185	190	
Leu	Lys	Ser	Ser	Lys	Tyr	Ile	Ala	Trp	Pro	Leu	Gln	Gly	Trp	Gln	Ala	195	200	205	
Thr	Phe	Gly	Gly	Gly	Asp	His	Pro	Pro	Lys	Ser	Asp	Leu	Val	Pro	Arg	210	215	220	
Gly	Ser	Cys	Ser	Leu	Ala	Ser	Gly	Ala	Thr	Gly	Gly	Arg	Gly	Ala	Val	225	230	235	240
Glu	Asn	Glu	Glu	Asp	Leu	Pro	Glu	Leu	Ser	Asp	Ser	Gly	Asp	Glu	Ala	245	250	255	
Ala	Trp	Glu	Asp	Glu	Asp	Asp	Ala	Asp	Leu	Pro	His	Gly	Lys	Gln	Gln	260	265	270	
Thr	Pro	Cys	Leu	Phe	Cys	Asn	Arg	Leu	Phe	Thr	Ser	Ala	Glu	Glu	Thr	275	280	285	
Phe	Ser	His	Cys	Lys	Ser	Glu	His	Gln	Phe	Asn	Ile	Asp	Ser	Met	Val	290	295	300	
His	Lys	His	Gly	Leu	Glu	Phe	Tyr	Gly	Tyr	Ile	Lys	Leu	Ile	Asn	Phe	305	310	315	320
Ile	Arg	Leu	Lys	Asn	Pro	Thr	Val	Glu	Tyr	Met	Asn	Ser	Ile	Tyr	Asn	325	330	335	
Pro	Val	Pro	Trp	Glu	Lys	Glu	Glu	Tyr	Leu	Lys	Pro	Val	Leu	Glu	Asp	340	345	350	

1402-PCT-1_Sequence_Listing

Asp Leu Leu Leu Gln Phe Asp Val Glu Asp Leu Tyr Glu Pro Val Ser
 355 360 365
 Val Pro Phe Ser Tyr Pro Asn Gly Leu Ser Glu Asn Thr Ser Val Val
 370 375 380
 Glu Lys Leu Lys His Met Glu Ala Arg Ala Leu Ser Ala Glu Ala Ala
 385 390 395 400
 Leu Ala Arg Ala Arg Glu Asp Leu Gln Lys Met Lys Gln Phe Ala Gln
 405 410 415
 Asp Phe Val Met His Thr Asp Val Arg Thr Cys Ser Ser Ser Thr Ser
 420 425 430
 Val Ile Ala Asp Leu Gln Glu Asp Glu Asp Gly Val Tyr Phe Ser Ser
 435 440 445
 Tyr Gly His Tyr Gly Ile His Glu Glu Met Leu Lys Asp Lys Ile Arg
 450 455 460
 Thr Glu Ser Tyr Arg Asp Phe Ile Tyr Gln Asn Pro His Ile Phe Lys
 465 470 475 480
 Asp Lys Val Val Leu Asp Val Gly Cys Gly Thr Gly Ile Leu Ser Met
 485 490 495
 Phe Ala Ala Lys Ala Gly Ala Lys Lys Val Leu Gly Val Asp Gln Ser
 500 505 510
 Glu Ile Leu Tyr Gln Ala Met Asp Ile Ile Arg Leu Asn Lys Leu Glu
 515 520 525
 Asp Thr Ile Thr Leu Ile Lys Gly Lys Ile Glu Glu Val His Leu Pro
 530 535 540
 Val Glu Lys Val Asp Val Ile Ile Ser Glu Trp Met Gly Tyr Phe Leu
 545 550 555 560
 Leu Phe Glu Ser Met Leu Asp Ser Val Leu Tyr Ala Lys Asn Lys Tyr
 565 570 575
 Leu Ala Lys Gly Gly Ser Val Tyr Pro Asp Ile Cys Thr Ile Ser Leu
 580 585 590
 Val Ala Val Ser Asp Val Asn Lys His Ala Asp Arg Ile Ala Phe Trp
 595 600 605
 Asp Asp Val Tyr Gly Phe Lys Met Ser Cys Met Lys Lys Ala Val Ile
 610 615 620

1402-PCT-1_Sequence_Listing

Pro Glu Ala Val Val Glu Val Leu Asp Pro Lys Thr Leu Ile Ser Glu
625 630 635 640

Pro Cys Gly Ile Lys His Ile Asp Cys His Thr Thr Ser Ile Ser Asp
645 650 655

Leu Glu Phe Ser Ser Asp Phe Thr Leu Lys Ile Thr Arg Thr Ser Met
660 665 670

Cys Thr Ala Ile Ala Gly Tyr Phe Asp Ile Tyr Phe Glu Lys Asn Cys
675 680 685

His Asn Arg Val Val Phe Ser Thr Gly Pro Gln Ser Thr Lys Thr His
690 695 700

Trp Lys Gln Thr Val Phe Leu Leu Glu Lys Pro Phe Ser Val Lys Ala
705 710 715 720

Gly Glu Ala Leu Lys Gly Lys Val Thr Val His Lys Asn Lys Lys Asp
725 730 735

Pro Arg Ser Leu Thr Val Thr Leu Thr Leu Asn Asn Ser Thr Gln Thr
740 745 750

Tyr Gly Leu Gln
755

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1402-PCT-1_Sequence_Listing

Glu Gly His His His His His His
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Met Asp Tyr Lys Asp Asp Asp Asp Lys Ala Ala Ala Ala Ala Ala Val
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Gly Pro Gly Ala Gly Gly Ala Gly Ser Ala Val Pro Gly Gly Ala Gly
20 25 30

Pro Cys Ala Thr Val Ser Val Phe Pro Gly Ala Arg Leu Leu Thr Ile
35 40 45

Gly Asp Ala Asn Gly Glu Ile Gln Arg His Ala Glu Gln Gln Ala Leu
50 55 60

Arg Leu Glu Val Arg Ala Gly Pro Asp Ser Ala Gly Ile Ala Leu Tyr
65 70 75 80

Ser His Glu Asp Val Cys Val Phe Lys Cys Ser Val Ser Arg Glu Thr
85 90 95

Glu Cys Ser Arg Val Gly Lys Gln Ser Phe Ile Ile Thr Leu Gly Cys
100 105 110

Asn Ser Val Leu Ile Gln Phe Ala Thr Pro Asn Asp Phe Cys Ser Phe
115 120 125

Tyr Asn Ile Leu Lys Thr Cys Arg Gly His Thr Leu Glu Arg Ser Val
130 135 140

Phe Ser Glu Arg Thr Glu Glu Ser Ser Ala Val Gln Tyr Phe Gln Phe
145 150 155 160

Tyr Gly Tyr Leu Ser Gln Gln Gln Asn Met Met Gln Asp Tyr Val Arg
165 170 175

Thr Gly Thr Tyr Gln Arg Ala Ile Leu Gln Asn His Thr Asp Phe Lys
180 185 190

Asp Lys Ile Val Leu Asp Val Gly Cys Gly Ser Gly Ile Leu Ser Phe
195 200 205

Phe Ala Ala Gln Ala Gly Ala Arg Lys Ile Tyr Ala Val Glu Ala Ser
210 215 220

1402-PCT-1_Sequence_Listing

Thr 225	Met	Ala	Gln	His	Ala 230	Glu	Val	Leu	Val	Lys 235	Ser	Asn	Asn	Leu	Thr 240
Asp	Arg	Ile	Val	Val 245	Ile	Pro	Gly	Lys	Val 250	Glu	Glu	Val	Ser	Leu 255	Pro
Glu	Gln	Val	Asp 260	Ile	Ile	Ile	Ser	Glu 265	Pro	Met	Gly	Tyr	Met 270	Leu	Phe
Asn	Glu	Arg 275	Met	Leu	Glu	Ser	Tyr 280	Leu	His	Ala	Lys	Lys 285	Tyr	Leu	Lys
Pro	Ser 290	Gly	Asn	Met	Phe	Pro 295	Thr	Ile	Gly	Asp	Val 300	His	Leu	Ala	Pro
Phe 305	Thr	Asp	Glu	Gln	Leu 310	Tyr	Met	Glu	Gln	Phe 315	Thr	Lys	Ala	Asn	Phe 320
Trp	Tyr	Gln	Pro	Ser 325	Phe	His	Gly	Val	Asp 330	Leu	Ser	Ala	Leu	Arg 335	Gly
Ala	Ala	Val	Asp 340	Glu	Tyr	Phe	Arg	Gln 345	Pro	Val	Val	Asp	Thr 350	Phe	Asp
Ile	Arg	Ile 355	Leu	Met	Ala	Lys	Ser 360	Val	Lys	Tyr	Thr	Val 365	Asn	Phe	Leu
Glu 370	Ala	Lys	Glu	Gly	Asp	Leu 375	His	Arg	Ile	Glu	Ile 380	Pro	Phe	Lys	Phe
His 385	Met	Leu	His	Ser	Gly 390	Leu	Val	His	Gly	Leu 395	Ala	Phe	Trp	Phe	Asp 400
Val	Ala	Phe	Ile	Gly 405	Ser	Ile	Met	Thr	Val 410	Trp	Leu	Ser	Thr	Ala 415	Pro
Thr	Glu	Pro	Leu 420	Thr	His	Trp	Tyr	Gln 425	Val	Arg	Cys	Leu	Phe 430	Gln	Ser
Pro	Leu	Phe 435	Ala	Lys	Ala	Gly	Asp 440	Thr	Leu	Ser	Gly	Thr 445	Cys	Leu	Leu
Ile 450	Ala	Asn	Lys	Arg	Gln	Ser 455	Tyr	Asp	Ile	Ser	Ile 460	Val	Ala	Gln	Val
Asp 465	Gln	Thr	Gly	Ser	Lys 470	Ser	Ser	Asn	Leu	Leu 475	Asp	Leu	Lys	Asn	Pro 480
Phe	Phe	Arg	Tyr	Thr 485	Gly	Thr	Thr	Pro	Ser 490	Pro	Pro	Pro	Gly	Ser 495	His

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Tyr Thr Ser Pro Ser Glu Asn Met Trp Asn Thr Gly Ser Thr Tyr Asn
500 505 510

Leu Ser Ser Gly Met Ala Val Ala Gly Met Pro Thr Ala Tyr Asp Leu
515 520 525

Ser Ser Val Ile Ala Ser Gly Ser Ser Val Gly His Asn Asn Leu Ile
530 535 540

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

Ala His Tyr Ala Val Asn Ser Gln Phe Thr Met Gly Gly Pro Ala Ile
565 570 575

Ser Met Ala Ser Pro Met Ser Ile Pro Thr Asn Thr Met His Tyr Gly
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Ser Glu Gly His His His His His His
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<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Polypeptide

<400> 17

His His His His His His
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