

## SEQUENCE LISTING

<110> BRISTOL-MYERS SQUIBB COMPANY

<120> SUBSTITUTED OXOISOINDOLINE COMPOUNDS

<130> 13397-WO-PCT

<150> US62/993,144

<151> 2020-03-23

<160> 8

<170> PatentIn version 3.5

<210> 1

<211> 526

<212> PRT

<213> Homo sapiens

<400> 1

Met Glu Thr Glu Ala Ile Asp Gly Tyr Ile Thr Cys Asp Asn Glu Leu  
1 5 10 15

Ser Pro Glu Arg Glu His Ser Asn Met Ala Ile Asp Leu Thr Ser Ser  
20 25 30

Thr Pro Asn Gly Gln His Ala Ser Pro Ser His Met Thr Ser Thr Asn  
35 40 45

Ser Val Lys Leu Glu Met Gln Ser Asp Glu Glu Cys Asp Arg Lys Pro  
50 55 60

Leu Ser Arg Glu Asp Glu Ile Arg Gly His Asp Glu Gly Ser Ser Leu  
65 70 75 80

Glu Glu Pro Leu Ile Glu Ser Ser Glu Val Ala Asp Asn Arg Lys Val  
85 90 95

Gln Glu Leu Gln Gly Glu Gly Gly Ile Arg Leu Pro Asn Gly Lys Leu  
100 105 110

Lys Cys Asp Val Cys Gly Met Val Cys Ile Gly Pro Asn Val Leu Met  
115 120 125

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

Met Gln His Pro Pro Ser Thr Ile Ala Glu Val Ala Pro Val Ile Ser  
                   340                  345                  350

Ser Ala Tyr Ser Gln Val Tyr His Pro Asn Arg Ile Glu Arg Pro Ile  
           355                  360                  365

Ser Arg Glu Thr Ala Asp Ser His Glu Asn Asn Met Asp Gly Pro Ile  
       370                  375                  380

Ser Leu Ile Arg Pro Lys Ser Arg Pro Gln Glu Arg Glu Ala Ser Pro  
 385                  390                  395                  400

Ser Asn Ser Cys Leu Asp Ser Thr Asp Ser Glu Ser Ser His Asp Asp  
                   405                  410                  415

His Gln Ser Tyr Gln Gly His Pro Ala Leu Asn Pro Lys Arg Lys Gln  
                   420                  425                  430

Ser Pro Ala Tyr Met Lys Glu Asp Val Lys Ala Leu Asp Thr Thr Lys  
           435                  440                  445

Ala Pro Lys Gly Ser Leu Lys Asp Ile Tyr Lys Val Phe Asn Gly Glu  
       450                  455                  460

Gly Glu Gln Ile Arg Ala Phe Lys Cys Glu His Cys Arg Val Leu Phe  
 465                  470                  475                  480

Leu Asp His Val Met Tyr Thr Ile His Met Gly Cys His Gly Tyr Arg  
                   485                  490                  495

Asp Pro Leu Glu Cys Asn Ile Cys Gly Tyr Arg Ser Gln Asp Arg Tyr  
           500                  505                  510

Glu Phe Ser Ser His Ile Val Arg Gly Glu His Thr Phe His  
           515                  520                  525

<210> 2  
 <211> 500  
 <212> PRT  
 <213> Homo sapiens

&lt;400&gt; 2

Met Glu Thr Glu Ala Ile Asp Gly Tyr Ile Thr Cys Asp Asn Glu Leu  
 1 5 10 15

Ser Pro Glu Arg Glu His Ser Asn Met Ala Ile Asp Leu Thr Ser Ser  
 20 25 30

Thr Pro Asn Gly Gln His Ala Ser Pro Ser His Met Thr Ser Thr Asn  
 35 40 45

Ser Val Lys Leu Glu Met Gln Ser Asp Glu Glu Cys Asp Arg Lys Pro  
 50 55 60

Leu Ser Arg Glu Asp Glu Ile Arg Gly His Asp Glu Gly Ser Ser Leu  
 65 70 75 80

Glu Glu Pro Leu Ile Glu Ser Ser Glu Val Ala Asp Asn Arg Lys Val  
 85 90 95

Gln Glu Leu Gln Gly Glu Gly Gly Ile Arg Leu Pro Asn Gly Glu Arg  
 100 105 110

Pro Phe His Cys Asn Gln Cys Gly Ala Ser Phe Thr Gln Lys Gly Asn  
 115 120 125

Leu Leu Arg His Ile Lys Leu His Ser Gly Glu Lys Pro Phe Lys Cys  
 130 135 140

Pro Phe Cys Ser Tyr Ala Cys Arg Arg Arg Asp Ala Leu Thr Gly His  
 145 150 155 160

Leu Arg Thr His Ser Val Gly Lys Pro His Lys Cys Asn Tyr Cys Gly  
 165 170 175

Arg Ser Tyr Lys Gln Arg Ser Ser Leu Glu Glu His Lys Glu Arg Cys  
 180 185 190

His Asn Tyr Leu Gln Asn Val Ser Met Glu Ala Ala Gly Gln Val Met  
 195 200 205

Ser His His Val Pro Pro Met Glu Asp Cys Lys Glu Gln Glu Pro Ile  
 210 215 220  
 Met Asp Asn Asn Ile Ser Leu Val Pro Phe Glu Arg Pro Ala Val Ile  
 225 230 235 240  
 Glu Lys Leu Thr Gly Asn Met Gly Lys Arg Lys Ser Ser Thr Pro Gln  
 245 250 255  
 Lys Phe Val Gly Glu Lys Leu Met Arg Phe Ser Tyr Pro Asp Ile His  
 260 265 270  
 Phe Asp Met Asn Leu Thr Tyr Glu Lys Glu Ala Glu Leu Met Gln Ser  
 275 280 285  
 His Met Met Asp Gln Ala Ile Asn Asn Ala Ile Thr Tyr Leu Gly Ala  
 290 295 300  
 Glu Ala Leu His Pro Leu Met Gln His Pro Pro Ser Thr Ile Ala Glu  
 305 310 315 320  
 Val Ala Pro Val Ile Ser Ser Ala Tyr Ser Gln Val Tyr His Pro Asn  
 325 330 335  
 Arg Ile Glu Arg Pro Ile Ser Arg Glu Thr Ala Asp Ser His Glu Asn  
 340 345 350  
 Asn Met Asp Gly Pro Ile Ser Leu Ile Arg Pro Lys Ser Arg Pro Gln  
 355 360 365  
 Glu Arg Glu Ala Ser Pro Ser Asn Ser Cys Leu Asp Ser Thr Asp Ser  
 370 375 380  
 Glu Ser Ser His Asp Asp His Gln Ser Tyr Gln Gly His Pro Ala Leu  
 385 390 395 400  
 Asn Pro Lys Arg Lys Gln Ser Pro Ala Tyr Met Lys Glu Asp Val Lys  
 405 410 415

Ala Leu Asp Thr Thr Lys Ala Pro Lys Gly Ser Leu Lys Asp Ile Tyr  
 420 425 430

Lys Val Phe Asn Gly Glu Gly Glu Gln Ile Arg Ala Phe Lys Cys Glu  
 435 440 445

His Cys Arg Val Leu Phe Leu Asp His Val Met Tyr Thr Ile His Met  
 450 455 460

Gly Cys His Gly Tyr Arg Asp Pro Leu Glu Cys Asn Ile Cys Gly Tyr  
 465 470 475 480

Arg Ser Gln Asp Arg Tyr Glu Phe Ser Ser His Ile Val Arg Gly Glu  
 485 490 495

His Thr Phe His  
 500

<210> 3  
 <211> 452  
 <212> PRT  
 <213> Homo sapiens

<400> 3

Met Glu Thr Glu Ala Ile Asp Gly Tyr Ile Thr Cys Asp Asn Glu Leu  
 1 5 10 15

Ser Pro Glu Arg Glu His Ser Asn Met Ala Ile Asp Leu Thr Ser Ser  
 20 25 30

Thr Pro Asn Gly Gln His Ala Ser Pro Ser His Met Thr Ser Thr Asn  
 35 40 45

Ser Val Lys Leu Glu Met Gln Ser Asp Glu Glu Cys Asp Arg Lys Pro  
 50 55 60

Leu Ser Arg Glu Asp Glu Ile Arg Gly His Asp Glu Gly Ser Ser Leu  
 65 70 75 80

Glu Glu Pro Leu Ile Glu Ser Ser Glu Val Ala Asp Asn Arg Lys Val  
 85 90 95

Gln Glu Leu Gln Gly Glu Gly Gly Ile Arg Leu Pro Asn Gly Glu Arg  
 100 105 110

Pro Phe His Cys Asn Gln Cys Gly Ala Ser Phe Thr Gln Lys Gly Asn  
 115 120 125

Leu Leu Arg His Ile Lys Leu His Ser Gly Glu Lys Pro Phe Lys Cys  
 130 135 140

Pro Phe Cys Ser Tyr Ala Cys Arg Arg Arg Asp Ala Leu Thr Gly His  
 145 150 155 160

Leu Arg Thr His Ser Val Gly Lys Pro His Lys Cys Asn Tyr Cys Gly  
 165 170 175

Arg Ser Tyr Lys Gln Arg Ser Ser Leu Glu Glu His Lys Glu Arg Cys  
 180 185 190

His Asn Tyr Leu Gln Asn Val Ser Met Glu Ala Ala Gly Gln Val Met  
 195 200 205

Ser His His Gly Glu Lys Leu Met Arg Phe Ser Tyr Pro Asp Ile His  
 210 215 220

Phe Asp Met Asn Leu Thr Tyr Glu Lys Glu Ala Glu Leu Met Gln Ser  
 225 230 235 240

His Met Met Asp Gln Ala Ile Asn Asn Ala Ile Thr Tyr Leu Gly Ala  
 245 250 255

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

Val Ala Pro Val Ile Ser Ser Ala Tyr Ser Gln Val Tyr His Pro Asn  
 275 280 285

Arg Ile Glu Arg Pro Ile Ser Arg Glu Thr Ala Asp Ser His Glu Asn  
 290 295 300

Asn Met Asp Gly Pro Ile Ser Leu Ile Arg Pro Lys Ser Arg Pro Gln  
 305 310 315 320

Glu Arg Glu Ala Ser Pro Ser Asn Ser Cys Leu Asp Ser Thr Asp Ser  
 325 330 335

Glu Ser Ser His Asp Asp His Gln Ser Tyr Gln Gly His Pro Ala Leu  
 340 345 350

Asn Pro Lys Arg Lys Gln Ser Pro Ala Tyr Met Lys Glu Asp Val Lys  
 355 360 365

Ala Leu Asp Thr Thr Lys Ala Pro Lys Gly Ser Leu Lys Asp Ile Tyr  
 370 375 380

Lys Val Phe Asn Gly Glu Gly Glu Gln Ile Arg Ala Phe Lys Cys Glu  
 385 390 395 400

His Cys Arg Val Leu Phe Leu Asp His Val Met Tyr Thr Ile His Met  
 405 410 415

Gly Cys His Gly Tyr Arg Asp Pro Leu Glu Cys Asn Ile Cys Gly Tyr  
 420 425 430

Arg Ser Gln Asp Arg Tyr Glu Phe Ser Ser His Ile Val Arg Gly Glu  
 435 440 445

His Thr Phe His  
 450

<210> 4  
 <211> 239  
 <212> PRT  
 <213> Homo sapiens

<400> 4

Met Glu Thr Glu Ala Ile Asp Gly Tyr Ile Thr Cys Asp Asn Glu Leu  
 1 5 10 15

Ser Pro Glu Arg Glu His Ser Asn Met Ala Ile Asp Leu Thr Ser Ser

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

<210> 5  
 <211> 454  
 <212> PRT  
 <213> Homo sapiens

<400> 5

Met Glu Thr Glu Ala Ile Asp Gly Tyr Ile Thr Cys Asp Asn Glu Leu  
 1 5 10 15

Ser Pro Glu Arg Glu His Ser Asn Met Ala Ile Asp Leu Thr Ser Ser  
 20 25 30

Thr Pro Asn Gly Gln His Ala Ser Pro Ser His Met Thr Ser Thr Asn  
 35 40 45

Ser Val Lys Leu Glu Met Gln Ser Asp Glu Glu Cys Asp Arg Lys Pro  
 50 55 60

Leu Ser Arg Glu Asp Glu Ile Arg Gly His Asp Glu Gly Ser Ser Leu  
 65 70 75 80

Glu Glu Pro Leu Ile Glu Ser Ser Glu Val Ala Asp Asn Arg Lys Val  
 85 90 95

Gln Glu Leu Gln Gly Glu Gly Gly Ile Arg Leu Pro Asn Gly Glu Arg  
 100 105 110

Pro Phe His Cys Asn Gln Cys Gly Ala Ser Phe Thr Gln Lys Gly Asn  
 115 120 125

Leu Leu Arg His Ile Lys Leu His Ser Gly Glu Lys Pro Phe Lys Cys  
 130 135 140

Pro Phe Cys Ser Tyr Ala Cys Arg Arg Arg Asp Ala Leu Thr Gly His  
 145 150 155 160

Leu Arg Thr His Ser Val Pro Pro Met Glu Asp Cys Lys Glu Gln Glu  
 165 170 175

Pro Ile Met Asp Asn Asn Ile Ser Leu Val Pro Phe Glu Arg Pro Ala  
 180 185 190

Val Ile Glu Lys Leu Thr Gly Asn Met Gly Lys Arg Lys Ser Ser Thr  
 195 200 205

Pro Gln Lys Phe Val Gly Glu Lys Leu Met Arg Phe Ser Tyr Pro Asp  
 210 215 220

Ile His Phe Asp Met Asn Leu Thr Tyr Glu Lys Glu Ala Glu Leu Met  
 225 230 235 240

Gln Ser His Met Met Asp Gln Ala Ile Asn Asn Ala Ile Thr Tyr Leu  
 245 250 255

Gly Ala Glu Ala Leu His Pro Leu Met Gln His Pro Pro Ser Thr Ile  
 260 265 270

Ala Glu Val Ala Pro Val Ile Ser Ser Ala Tyr Ser Gln Val Tyr His  
 275 280 285

Pro Asn Arg Ile Glu Arg Pro Ile Ser Arg Glu Thr Ala Asp Ser His  
 290 295 300

Glu Asn Asn Met Asp Gly Pro Ile Ser Leu Ile Arg Pro Lys Ser Arg  
 305 310 315 320

Pro Gln Glu Arg Glu Ala Ser Pro Ser Asn Ser Cys Leu Asp Ser Thr  
 325 330 335

Asp Ser Glu Ser Ser His Asp Asp His Gln Ser Tyr Gln Gly His Pro  
 340 345 350

Ala Leu Asn Pro Lys Arg Lys Gln Ser Pro Ala Tyr Met Lys Glu Asp  
 355 360 365

Val Lys Ala Leu Asp Thr Thr Lys Ala Pro Lys Gly Ser Leu Lys Asp  
 370 375 380

Ile Tyr Lys Val Phe Asn Gly Glu Gly Glu Gln Ile Arg Ala Phe Lys



Ser Asn His Phe Ile Met Glu Ser Leu Phe Cys Glu Ser Ser Gly Asp  
 50 55 60

Ser Ser Leu Glu Lys Glu Phe Leu Gly Ala Pro Val Gly Pro Ser Val  
 65 70 75 80

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

Asn Ser Ile Lys Val Glu Met Tyr Ser Asp Glu Glu Ser Ser Arg Leu  
 100 105 110

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

Glu Asp Ser Leu Ser Glu Pro Leu Gly Tyr Cys Asp Gly Ser Gly Pro  
 130 135 140

Glu Pro His Ser Pro Gly Gly Ile Arg Leu Pro Asn Gly Lys Leu Lys  
 145 150 155 160

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

His Lys Arg Ser His Thr Gly Glu Arg Pro Phe His Cys Asn Gln Cys  
 180 185 190

Gly Ala Ser Phe Thr Gln Lys Gly Asn Leu Leu Arg His Ile Lys Leu  
 195 200 205

His Ser Gly Glu Lys Pro Phe Lys Cys Pro Phe Cys Asn Tyr Ala Cys  
 210 215 220

Arg Arg Arg Asp Ala Leu Thr Gly His Leu Arg Thr His Ser Val Ser  
 225 230 235 240

Ser Pro Thr Val Gly Lys Pro Tyr Lys Cys Asn Tyr Cys Gly Arg Ser  
 245 250 255

Tyr Lys Gln Gln Ser Thr Leu Glu Glu His Lys Glu Arg Cys His Asn

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| 260 |     |     |     |     |     |     | 265 |     |     |     |     | 270 |     |     |     |  |
| Tyr | Leu | Gln | Ser | Leu | Ser | Thr | Glu | Ala | Gln | Ala | Leu | Ala | Gly | Gln | Pro |  |
|     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |  |
| Gly | Asp | Glu | Ile | Arg | Asp | Leu | Glu | Met | Val | Pro | Asp | Ser | Met | Leu | His |  |
|     |     | 290 |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |  |
| Ser | Ser | Ser | Glu | Arg | Pro | Thr | Phe | Ile | Asp | Arg | Leu | Ala | Asn | Ser | Leu |  |
| 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     |     |  |
| Thr | Lys | Arg | Lys | Arg | Ser | Thr | Pro | Gln | Lys | Phe | Val | Gly | Glu | Lys | Gln |  |
|     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     |     |     |  |
| Met | Arg | Phe | Ser | Leu | Ser | Asp | Leu | Pro | Tyr | Asp | Val | Asn | Ser | Gly | Gly |  |
|     |     |     | 340 |     |     |     |     | 345 |     |     |     |     |     |     |     |  |
| Tyr | Glu | Lys | Asp | Val | Glu | Leu | Val | Ala | His | His | Ser | Leu | Glu | Pro | Gly |  |
|     |     | 355 |     |     |     | 360 |     |     |     |     |     | 365 |     |     |     |  |
| Phe | Gly | Ser | Ser | Leu | Ala | Phe | Val | Gly | Ala | Glu | His | Leu | Arg | Pro | Leu |  |
|     |     | 370 |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |  |
| Arg | Leu | Pro | Pro | Thr | Asn | Cys | Ile | Ser | Glu | Leu | Thr | Pro | Val | Ile | Ser |  |
| 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     |     |  |
| Ser | Val | Tyr | Thr | Gln | Met | Gln | Pro | Leu | Pro | Gly | Arg | Leu | Glu | Leu | Pro |  |
|     |     |     |     | 405 |     |     |     |     | 410 |     |     |     |     |     |     |  |
| Gly | Ser | Arg | Glu | Ala | Gly | Glu | Gly | Pro | Glu | Asp | Leu | Ala | Asp | Gly | Gly |  |
|     |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |  |
| Pro | Leu | Leu | Tyr | Arg | Pro | Arg | Gly | Pro | Leu | Thr | Asp | Pro | Gly | Ala | Ser |  |
|     |     | 435 |     |     |     |     | 440 |     |     |     |     | 445 |     |     |     |  |
| Pro | Ser | Asn | Gly | Cys | Gln | Asp | Ser | Thr | Asp | Thr | Glu | Ser | Asn | His | Glu |  |
|     |     | 450 |     |     |     | 455 |     |     |     |     | 460 |     |     |     |     |  |
| Asp | Arg | Val | Ala | Gly | Val | Val | Ser | Leu | Pro | Gln | Gly | Pro | Pro | Pro | Gln |  |
| 465 |     |     |     |     | 470 |     |     |     |     | 475 |     |     |     |     |     |  |

Pro Pro Pro Thr Ile Val Val Gly Arg His Ser Pro Ala Tyr Ala Lys  
485 490 495

Glu Asp Pro Lys Pro Gln Glu Gly Leu Leu Arg Gly Thr Pro Gly Pro  
500 505 510

Ser Lys Glu Val Leu Arg Val Val Gly Glu Ser Gly Glu Pro Val Lys  
515 520 525

Ala Phe Lys Cys Glu His Cys Arg Ile Leu Phe Leu Asp His Val Met  
530 535 540

Phe Thr Ile His Met Gly Cys His Gly Phe Arg Asp Pro Phe Glu Cys  
545 550 555 560

Asn Ile Cys Gly Tyr His Ser Gln Asp Arg Tyr Glu Phe Ser Ser His  
565 570 575

Ile Val Arg Gly Glu His Lys Val Gly  
580 585

|       |              |
|-------|--------------|
| <210> | 8            |
| <211> | 544          |
| <212> | PRT          |
| <213> | Homo sapiens |

$\langle 400 \rangle$  8

Met Asp Ser Arg Tyr Leu Gln Leu Gln Leu Tyr Leu Pro Ser Cys Ser  
1 5 10 15

Leu Leu Gln Gly Ser Gly Asp Ser Ser Leu Glu Lys Glu Phe Leu Gly  
20 25 30

Ala Pro Val Gly Pro Ser Val Ser Thr Pro Asn Ser Gln His Ser Ser  
35 40 45

Pro Ser Arg Ser Leu Ser Ala Asn Ser Ile Lys Val Glu Met Tyr Ser  
50 55 60

Asp Glu Glu Ser Ser Arg Leu Leu Gly Pro Asp Glu Arg Leu Leu Glu  
65 70 75 80

Lys Asp Asp Ser Val Ile Val Glu Asp Ser Leu Ser Glu Pro Leu Gly  
85 90 95

Tyr Cys Asp Gly Ser Gly Pro Glu Pro His Ser Pro Gly Gly Ile Arg  
100 105 110

Leu Pro Asn Gly Lys Leu Lys Cys Asp Val Cys Gly Met Val Cys Ile  
115 120 125

Gly Pro Asn Val Leu Met Val His Lys Arg Ser His Thr Gly Glu Arg  
130 135 140

Pro Phe His Cys Asn Gln Cys Gly Ala Ser Phe Thr Gln Lys Gly Asn  
145 150 155 160

Leu Leu Arg His Ile Lys Leu His Ser Gly Glu Lys Pro Phe Lys Cys  
165 170 175

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

Leu Arg Thr His Ser Val Ser Ser Pro Thr Val Gly Lys Pro Tyr Lys  
195 200 205

Cys Asn Tyr Cys Gly Arg Ser Tyr Lys Gln Gln Ser Thr Leu Glu Glu  
210 215 220

His Lys Glu Arg Cys His Asn Tyr Leu Gln Ser Leu Ser Thr Glu Ala  
225 230 235 240

Gln Ala Leu Ala Gly Gln Pro Gly Asp Glu Ile Arg Asp Leu Glu Met  
245 250 255

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

Asp Arg Leu Ala Asn Ser Leu Thr Lys Arg Lys Arg Ser Thr Pro Gln

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

Leu Phe Leu Asp His Val Met Phe Thr Ile His Met Gly Cys His Gly  
500 505 510

Phe Arg Asp Pro Phe Glu Cys Asn Ile Cys Gly Tyr His Ser Gln Asp  
515 520 525

Arg Tyr Glu Phe Ser Ser His Ile Val Arg Gly Glu His Lys Val Gly  
530 535 540