



No. 09-071017- -00003-0000

Fecha: 2011-01-21 10:43:59 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 329 CTOINFORMACION Folios: 20

FORMULARIO ÚNICO DE CORRECCIONES Y MODIFICACIONES
2000-10

① **SOLICITUD DE:**

☒ Corrección de Error Material ☐ Modificación a una solicitud

② **SOLICITANTE** Nombre: **ACCELERON PHARMA INC.** IDENTIFICACIÓN
Dirección: **128 Sidney Street,** C.C. NIT
Teléfono: **3132408** Fax: **3161647** C.E. OTRO
E-mail: Número
Domicilio: **Cambridge, Massachusetts 02139, Estados Unidos de America**

③ **REPRESENTANTE** Nombre: **HUMBERTO RUBIO CAMACHO** IDENTIFICACIÓN
Dirección: **Cra. 7 No. 74-64, Of. 506** C.C. X NIT
O APODERADO Teléfono: **3132408** Fax: **3131647** C.E. OTRO
E-mail: No. **17'192.062 TP. 50.007**

④ Número de expediente: **09-071017** Título
"ANTAGONISTAS DE ACTIVINA-ACTRII Y USOS PARA AUMENTAR LOS NIVELES DE GLÓBULOS ROJOS"

⑤ Descripción de la corrección o modificación solicitada

Por un error involuntario la SEQ ID NO:11 es ILGRSTQE. SEQ ID NO:11 fue indicada en la descripción y el listado de Secuencias, debiendo ser leída como ILGRSETQE, por tanto estamos anexando la página número 64 y el listado de secuencias debidamente corregido. Respetuosamente solicitamos que al momento en que se realice el examen de patentabilidad de la presente invención, se tenga en cuenta esta modificación.

Aclaración: SEQ ID NO: 11 se describe como representación de N-secuencia terminal de ActRIIa. Es claro según las otras secuencias de la presente solicitud, por ejemplo SEQ ID NO:7 de la página 54, SEQ ID NO: 13 de la publicación internacional WO 2007/062188, que ILGRSETQE es la secuencia propia de N-terminal de ActRIIa. Adicionalmente, la secuencia de ActRIIa fue conocida en el arte previo antes de la solicitud de la presente solicitud. Verse ejemplo Martzuk y Bradley, Biocimica et Biophysica Acta, 1130: 105-108, 1992. La figura 2 describe cDNA y traduce secuencia de amino acido de humano ActRIIa. Se desprende de esta figura que la secuencia corregida de ActRIIa correspondería a SEQ ID NO:11 y que debe leerse ILGRSETQE. Por tanto consideramos que el error de la SEQ ID NO:11 como se presento es un error obvio y que apoya la modificación de la SEQ ID NO:11 que puede ser encontrada en las especificaciones como se indican y las referencias citadas anteriormente.

⑥ Comprobante de pago No. **11-004802** Fecha: **18 de Enero de 2011**

⑦ Anexos:

☒ Comprobante de pago de la tasa
☒ Poderes, si fuere el caso. *Reposa en el presente expediente*
☒ Certificado de Existencia y Representación legal de las partes, cuando sean personas jurídicas. *Reposa en el presente expediente*

⑧

NOMBRE **HUMBERTO RUBIO CAMACHO**

FIRMA



C.C. **17'192.062** de Bogotá T.P. **50.007**

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800.176.089-2

- / -

Industria y Comercio
SUPERINTENDENCIA

RECIBO DE CAJA

No. 11 - 004802

Bogotá D.C., 18 de 2011 - 13:22:25

RECIBIDO DE : HUMBERTO RUBIO

NI 830.000.228

*** Soporte del Pago ***

TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PAGO	VR PAGO
CONSIGNACION	BANCO DE BOGOTA	062754387	328791750	18/01/2011	2.261.000.00

*** Conceptos Pagados ***

CANT.	RENTISTICO	CONCEPTO	Vr.UNDITARIO	Vr.CONCEPTO
1	50005-01-03	CAMBIO DE MODALIDAD Y MODIFICACIONES EN CREACION CORRECCION A SOLICITUD EN TRAMITE / MODIFICA	118.000.00	118.000.00
				\$118.000.00

SON: **CIENTO DIECIOCHO MIL PESOS MONEDA CORRIENTE***

Responsable: _____

Recibo de Caja Aplicado al Expediente No. _____

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 09-071017- -00003-0000

Fecha: 2011-01-21 10:43:59 Dep. 2020 DIR.NUEVASCR
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Act. 329 CTOINFORMACION Folios: 20

Sede Centro: Carrera 13 No. 27 - 00 Pisos 3,4,5 y 10 Bogotá, D.C.- Colombia

Web: www.sic.gov.co e-mail: info@sic.gov.co Conmutador: (571) 5870000 Fax: (571) 5870284 Línea: 018000-910165 Call Center: (571) 6513240

Enero 18 de 2011 - 13:22:26

ATGGATGCAATGAAGAGAGGGCTCTGCTGTGTGCTGCTGCTGTGTGGAGCAGTCT
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GGACTGATTGTGTAGAAAAAAAAGACAGCCCTGAAGTATATTTCTGTTGCTGTGA
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CCCATTCAAATCCAGTTACACCTAAGCCACCCACCGGTGGTGGAACCTCACACAT
GCCACCGTGCCCAGCACCTGAACCTCTGGGGGGACCGTCAGTCTTCCTCTTCCC
CCCAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTG
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GGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAG
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ATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCAT
GCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCT
GTCTCCGGGTAAATGAGAATTC (SEC ID N°: 14)

Tanto ActRlla-hFc como ActRlla-mFc fueron marcadamente susceptibles a la expresión recombinante. Como se muestra en la Figura 1, la proteína se purificó como un pico de proteína único bien definido. La secuenciación N-terminal reveló una secuencia única de ILGRSETQE (SEC ID N°: 11). La purificación se pudo conseguir mediante una serie de etapas de cromatografía en columna, que incluyen, por ejemplo, tres o más de las siguientes, en cualquier orden: cromatografía de proteína A, cromatografía de Q sefarosa, cromatografía de fenil sefarosa, cromatografía por exclusión de tamaño y cromatografía de intercambio catiónico. La purificación se pudo completar con filtración viral e intercambio de tampón. La proteína ActRlla-hFc se purificó hasta una pureza de > el 98% como

PHPH-022-W01_Substitute_Sequence_Listing
SEQUENCE LISTING

<110> ACCELERON PHARMA INC.

<120> ACTIVIN-ACTRII ANTAGONISTS AND USES FOR INCREASING RED
BLOOD CELL LEVELS

<130> PHPH-022-W01

<140> PCT/US07/025868

<141> 2007-12-18

<150> 60/875,682

<151> 2006-12-18

<160> 23

<170> PatentIn Ver. 3.3

<210> 1

<211> 513

<212> PRT

<213> Homo sapiens

<400> 1

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

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PHPH-022-W01_Substitute_Sequence_Listing

Ala Gln Leu Leu Asn Glu Tyr Val Ala Val Lys Ile Phe Pro Ile Gln
 210 215 220

Asp Lys Gln Ser Trp Gln Asn Glu Tyr Glu Val Tyr Ser Leu Pro Gly
 225 230 235 240

Met Lys His Glu Asn Ile Leu Gln Phe Ile Gly Ala Glu Lys Arg Gly
 245 250 255

Thr Ser Val Asp Val Asp Leu Trp Leu Ile Thr Ala Phe His Glu Lys
 260 265 270

Gly Ser Leu Ser Asp Phe Leu Lys Ala Asn Val Val Ser Trp Asn Glu
 275 280 285

Leu Cys His Ile Ala Glu Thr Met Ala Arg Gly Leu Ala Tyr Leu His
 290 295 300

Glu Asp Ile Pro Gly Leu Lys Asp Gly His Lys Pro Ala Ile Ser His
 305 310 315 320

Arg Asp Ile Lys Ser Lys Asn Val Leu Leu Lys Asn Asn Leu Thr Ala
 325 330 335

Cys Ile Ala Asp Phe Gly Leu Ala Leu Lys Phe Glu Ala Gly Lys Ser
 340 345 350

Ala Gly Asp Thr His Gly Gln Val Gly Thr Arg Arg Tyr Met Ala Pro
 355 360 365

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

Ile Asp Met Tyr Ala Met Gly Leu Val Leu Trp Glu Leu Ala Ser Arg
 385 390 395 400

Cys Thr Ala Ala Asp Gly Pro Val Asp Glu Tyr Met Leu Pro Phe Glu
 405 410 415

Glu Glu Ile Gly Gln His Pro Ser Leu Glu Asp Met Gln Glu Val Val
 420 425 430

Val His Lys Lys Lys Arg Pro Val Leu Arg Asp Tyr Trp Gln Lys His
 435 440 445

Ala Gly Met Ala Met Leu Cys Glu Thr Ile Glu Glu Cys Trp Asp His
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Asp Ala Glu Ala Arg Leu Ser Ala Gly Cys Val Gly Glu Arg Ile Thr
 465 470 475 480

Gln Met Gln Arg Leu Thr Asn Ile Ile Thr Thr Glu Asp Ile Val Thr
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Val Val Thr Met Val Thr Asn Val Asp Phe Pro Pro Lys Glu Ser Ser
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Leu

PHPH-022-W01_Substitute_Sequence_Listing

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<213> Homo sapiens

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35 40 45
Gly Ser Ile Glu Ile Val Lys Gln Gly Cys Trp Leu Asp Asp Ile Asn
50 55 60
Cys Tyr Asp Arg Thr Asp Cys Val Glu Lys Lys Asp Ser Pro Glu Val
65 70 75 80
Tyr Phe Cys Cys Cys Glu Gly Asn Met Cys Asn Glu Lys Phe Ser Tyr
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Lys Pro Pro
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<223> Description of Artificial Sequence: Synthetic polypeptide

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35 40 45
Gly Ser Ile Glu Ile Val Lys Gln Gly Cys Trp Leu Asp Asp Ile Asn
50 55 60
Cys Tyr Asp Arg Thr Asp Cys Val Glu Lys Lys Asp Ser Pro Glu Val
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Phe Pro Glu Met
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PHPH-022-W01_Substitute_Sequence_Listing

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<213> Homo sapiens

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gatgatatca actgctatga caggactgat tgtgtagaaa aaaaagacag ccctgaagta 300
tatttttgtt gctgtgaggg caatatgtgt aatgaaaagt tttcttattt tccagagatg 360
gaagtcacac agcccacttc aaatccagtt acacctaagc caccctatta caacatcctg 420
ctctattcct tggtgccact tatgttaatt gcggggattg tcatttgtgc attttgggtg 480
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ccccacctt ctccattact aggggttgaac ccactgcagt tattagaagt gaaagcaagg 600
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gcatatttat atgaggatat acctggccta aaagatggcc acaaacctgc catatctcac 960
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tgtttgggac acgacgcaga agccagggtt tcagctggat gtgtaggtga aagaattacc 1440
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<212> DNA
<213> Homo sapiens

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tttgctacct ggaagaatat ttctggttcc attgaaatag tgaaacaagg ttgttggctg 180
gatgatatca actgctatga caggactgat tgtgtagaaa aaaaagacag ccctgaagta 240
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<221> MOD_RES

PHPH-022-W01_Substitute_Sequence_Listing

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<222> (212)
<223> His or Ala

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35 40 45
Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
50 55 60
Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
65 70 75 80
Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
85 90 95
Tyr Lys Cys Xaa Val Ser Asn Lys Ala Leu Pro Val Pro Ile Glu Lys
100 105 110
Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
115 120 125
Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
130 135 140
Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
145 150 155 160
Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
165 170 175
Asp Ser Asp Gly Pro Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
180 185 190
Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
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Lys
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PHPH-022-W01_Substitute_Sequence_Listing

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35 40 45
Gly Ser Ile Glu Ile Val Lys Gln Gly Cys Trp Leu Asp Asp Ile Asn
50 55 60
Cys Tyr Asp Arg Thr Asp Cys Val Glu Lys Lys Asp Ser Pro Glu Val
65 70 75 80
Tyr Phe Cys Cys Cys Glu Gly Asn Met Cys Asn Glu Lys Phe Ser Tyr
85 90 95
Phe Pro Glu Met Glu Val Thr Gln Pro Thr Ser Asn Pro Val Thr Pro
100 105 110
Lys Pro Pro Thr Gly Gly Gly Thr His Thr Cys Pro Pro Cys Pro Ala
115 120 125
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
130 135 140
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
145 150 155 160
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
165 170 175
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
180 185 190
Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
195 200 205
Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
210 215 220
Leu Pro Val Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
225 230 235 240
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
245 250 255
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
260 265 270
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
275 280 285
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
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<212> PRT

<213> Apis mellifera

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Met Lys Phe Leu Val

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10

15

20

<210> 9

<211> 22

<212> PRT

<213> Unknown Organism

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Plasminogen Activator leader sequence

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5

10

15

20

$\langle 210 \rangle$ 10

<211> 20

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<213> Unknown Organism

<220>

<223> Description of Unknown Organism: Native leader

sequence

<400> 10

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10

15

20

<210> 11

<211> 9

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic

peptide

<400> 11

PHPH-022-W01_Substitute_Sequence_Listing
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<212> PRT
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construct

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

PHPH-022-W01_Substitute_Sequence_Listing

260 265 270

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
275 280 285

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<213> Artificial Sequence

<220>
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Gln Thr Gly Val Glu Pro Cys Tyr Gly Asp Lys Asp Lys Arg Arg His
50 55 60

Cys Phe Ala Thr Trp Lys Asn Ile Ser Gly Ser Ile Glu Ile Val Lys
65 70 75 80

Gln Gly Cys Trp Leu Asp Asp Ile Asn Cys Tyr Asp Arg Thr Asp Cys
85 90 95

Val Glu Lys Lys Asp Ser Pro Glu Val Tyr Phe Cys Cys Cys Glu Gly
100 105 110

Asn Met Cys Asn Glu Lys Phe Ser Tyr Phe Pro Glu Met Glu Val Thr
115 120 125

Gln Pro Thr Ser Asn Pro Val Thr Pro Lys Pro Pro Thr Gly Gly Gly
130 135 140

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
145 150 155 160

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
165 170 175

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
180 185 190

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
195 200 205

PHPH-022-W01_Substitute_Sequence_Listing

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
210 215 220
Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
225 230 235 240
Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Val Pro Ile Glu Lys
245 250 255
Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
260 265 270
Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
275 280 285
Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
290 295 300
Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
305 310 315 320
Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
325 330 335
Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
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Lys

<210> 14
<211> 1114
<212> DNA
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tcgccccgcg ccgctatact tggtagatca gaaactcagg agtgtctttt tttaatgcta 120
attgggaaaa agacagaacc aatcaaactg gtgttgaacc gtgttatggt gacaaagata 180
aacggcgcca ttgttttgct acctggaaga atatttctgg ttccattgaa tagtgaaaca 240
aggttgttgg ctggatgata tcaactgcta tgacaggact gattgtgtag aaaaaaaga 300
cagccctgaa gtatatttct gttgctgtga gggcaatatg tgtaatgaaa agttttctta 360
ttttccggag atggaagtca cacagcccac ttcaaatcca gttacaccta agccaccac 420
cgggtggtgga actcacacat gcccaccgtg cccagcacct gaactcctgg ggggaccgtc 480
agtcttcttc ttcccccaa aacccaagga caccctcatg atctcccga cccctgaggt 540
cacatgcgtg gtggtggacg tgagccacga agaccctgag gtcaagttca actggtacgt 600
ggacggcggtg gaggtgcata atgccaagac aaagccgcgg gaggagcagt acaacagcac 660
gtaccgtgtg gtcagcgtcc tcaccgtcct gcaccaggac tggctgaatg gcaaggagta 720
caagtgaag gtctccaaca aagccctccc agtccccatc gagaaaacca tctccaaagc 780
caaagggcag ccccgagaac cacagggtgta caccctgccc ccatcccggg aggagatgac 840
caagaaccag gtcagcctga cctgcctggg caaaggcttc tatcccagcg acatcgccgt 900
ggagtgggag agcaatgggc agccggagaa caactacaag accacgcctc ccgtgctgga 960
ctccgacggc tccttcttcc tctatagcaa gctcaccgtg gacaagagca ggtggcagca 1020
ggggaacgtc ttctcatgct ccgtgatgca tgaggctctg cacaaccact acacgcagaa 1080

<210> 15
<211> 512
<212> PRT
<213> Homo sapiens

<400> 15
Met Thr Ala Pro Trp Val Ala Leu Ala Leu Leu Trp Gly Ser Leu Trp
1 5 10 15
Pro Gly Ser Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr
20 25 30
Asn Ala Asn Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg
35 40 45
Cys Glu Gly Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Ala
50 55 60
Asn Ser Ser Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp
65 70 75 80
Asp Phe Asn Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn
85 90 95
Pro Gln Val Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg
100 105 110
Phe Thr His Leu Pro Glu Ala Gly Gly Pro Glu Val Thr Tyr Glu Pro
115 120 125
Pro Pro Thr Ala Pro Thr Leu Leu Thr Val Leu Ala Tyr Ser Leu Leu
130 135 140
Pro Ile Gly Gly Leu Ser Leu Ile Val Leu Leu Ala Phe Trp Met Tyr
145 150 155 160
Arg His Arg Lys Pro Pro Tyr Gly His Val Asp Ile His Glu Asp Pro
165 170 175
Gly Pro Pro Pro Pro Ser Pro Leu Val Gly Leu Lys Pro Leu Gln Leu
180 185 190
Leu Glu Ile Lys Ala Arg Gly Arg Phe Gly Cys Val Trp Lys Ala Gln
195 200 205
Leu Met Asn Asp Phe Val Ala Val Lys Ile Phe Pro Leu Gln Asp Lys
210 215 220
Gln Ser Trp Gln Ser Glu Arg Glu Ile Phe Ser Thr Pro Gly Met Lys
225 230 235 240
His Glu Asn Leu Leu Gln Phe Ile Ala Ala Glu Lys Arg Gly Ser Asn
245 250 255
Leu Glu Val Glu Leu Trp Leu Ile Thr Ala Phe His Asp Lys Gly Ser
260 265 270
Leu Thr Asp Tyr Leu Lys Gly Asn Ile Ile Thr Trp Asn Glu Leu Cys
275 280 285

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

<210> 16
 <211> 116
 <212> PRT
 <213> Homo sapiens

<400> 16
 Ser Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala
 1 5 10 15
 Asn Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu
 20 25 30
 Gly Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Ala Asn Ser
 35 40 45
 Ser Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp Asp Phe
 50 55 60
 Asn Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln
 65 70 75 80

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Val Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr
85 90 95
His Leu Pro Glu Ala Gly Gly Pro Glu Val Thr Tyr Glu Pro Pro Pro
100 105 110
Thr Ala Pro Thr
115

<210> 17
<211> 101
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 17
Ser Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala
1 5 10 15
Asn Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu
20 25 30
Gly Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Ala Asn Ser
35 40 45
Ser Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp Asp Phe
50 55 60
Asn Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln
65 70 75 80
Val Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr
85 90 95
His Leu Pro Glu Ala
100

<210> 18
<211> 1539
<212> DNA
<213> Homo sapiens

<400> 18
atgacggcgc cctgggtggc cctcgccctc ctctggggat cgctgtggcc cggctctggg 60
cgtggggagg ctgagacacg ggagtgcac tactacaacg ccaactggga gctggagcgc 120
accaaccaga gcggcctgga gcgctgcgaa ggcgagcagg acaagcggct gcactgctac 180
gcctcctggg ccaacagctc tggcaccatc gagctcgtga agaagggtg ctggctagat 240
gacttcaact gctacgatag gcaggagtgt gtggccactg aggagaacc ccaggtgtac 300
ttctgctgct gtgaaggcaa cttctgcaac gaggcgttca ctcatttgcc agaggctggg 360
ggcccggaag tcacgtacga gccacccccg acagcccca ccctgctcac ggtgctggcc 420
tactcactgc tgcccatcgg gggcctttcc ctcatcgtcc tgctggcctt ttggatgtac 480
cggcatcgca agcccccta cggatcatgt gacatccatg aggaccctgg gcctccacca 540
ccatccccctc tgggtgggctt gaagccactg cagctgctgg agatcaaggc tcgggggcgc 600
tttgctgtg tctggaaggc ccagctcatg aatgactttg tagctgtcaa gatcttccca 660
ctccaggaca agcagtcgtg gcagagtga cgggagatct tcagcacacc tggcatgaag 720
cacgagaacc tgctacagtt cattgctgcc gagaagcgag gctccaacct cgaagtagag 780
ctgtggctca tcacggcctt ccatgacaag ggctccctca cggattacct caaggggaac 840

PHPH-022-W01_Substitute_Sequence_Listing

atcatcacat ggaacgaact gtgtcatgta gcagagacga tgtcacgagg cctctcatat 900
ctgcatgagg atgtgccctg gtgccgtggc gagggccaca agccgtctat tgcccacagg 960
gactttaaaa gtaagaatgt attgctgaag agcgacctca cagccgtgct ggctgacttt 1020
ggcttggtctg ttcgatttga gccagggaaa cctccagggg acaccacagg acaggtaggc 1080
acgagacggg acatggctcc tgagggtgctc gagggagcca tcaacttcca gagagatgcc 1140
ttcctgcgca ttgacatgta tgccatgggg ttggtgctgt gggagcttgt gtctcgctgc 1200
aaggctgcag acggacccgt ggatgagtac atgctgccct ttgaggaaga gattggccag 1260
cacccttcgt tggaggagct gcaggagggt gtggtgcaca agaagatgag gccaccatt 1320
aaagatcact ggttgaaaca cccgggcctg gccagcttt gtgtgacct cgaggagtgc 1380
tgggaccatg atgcagaggc tcgcttgctc gcgggctgtg tggaggagcg ggtgtccctg 1440
attcggagggt cgggtcaacgg cactacctcg gactgtctcg tttccctggt gacctctgtc 1500
accaatgtgg acctgcccc taaagagtca agcatctaa 1539

<210> 19
<211> 348
<212> DNA
<213> Homo sapiens

<400> 19
tctgggcgtg gggaggctga gacacgggag tgcattact acaacgcaa ctgggagctg 60
gagcgacca accagagcgg cctggagcgc tgcgaaggcg agcaggacaa gcggctgcac 120
tgctacgcct cctgggcca cagctctggc accatcgagc tcgtgaagaa gggctgctgg 180
ctagatgact tcaactgcta cgataggcag gagtgtgtgg ccaactgagga gaacccccag 240
gtgtacttct gctgctgtga aggcaacttc tgcaacgagc gcttactca tttgccagag 300
gctggggggc cggaagtcac gtacgagcca ccccgacag cccccacc 348

<210> 20
<211> 329
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 20
Ser Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala
1 5 10 15
Asn Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu
20 25 30
Gly Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Ala Asn Ser
35 40 45
Ser Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp Asp Phe
50 55 60
Asn Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln
65 70 75 80
Val Tyr Phe Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr
85 90 95
His Leu Pro Glu Ala Gly Gly Gly Thr His Thr Cys Pro Pro Cys Pro
100 105 110
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
115 120 125
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val

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

<210> 21

<211> 344

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 21

Ser Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala
1 5 10 15
Asn Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu
20 25 30
Gly Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Ala Asn Ser
35 40 45
Ser Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp Asp Phe
50 55 60
Asn Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln
65 70 75 80

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

<210> 22
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 22

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Thr Gly Gly Gly Gly
1 5

<210> 23

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 23

Ser Gly Gly Gly Gly
1 5