

OPA18601-Sequece Listing

<110> HANMI PHARM. CO., LTD.

<120> Therapeutic enzyme fusion protein having a novel structure and use thereof

<130> OPA18301-PCT

<150> KR 10-2017-0178378

<151> 2017-12-22

<160> 14

<170> KoPatentIn 3.0

<210> 1

<211> 43

<212> DNA

<213> Artificial Sequence

<220>

<223> Fc(S2P)_F

<400> 1

ctggcggtgg cggatcgcca ccatgccag cacctgagtt cct 43

<210> 2

<211> 43

<212> DNA

<213> Artificial Sequence

<220>

<223> Fc(S2P)_R

<400> 2

aggaactcag gtgctgggca tggtggcgat ccgccaccgc cag 43

<210> 3

<211> 43

<212> DNA

<213> Artificial Sequence

<220>

<223> Fc(N71Q)_F

<400> 3

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<210> 4

<211> 43

<212> DNA

<213> Artificial Sequence

<220>

<223> Fc(N71Q)_R

<400> 4

OPA18601-Sequece Listing

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<210> 5
<211> 1287
<212> DNA
<213> Homo sapiens

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accatgggct ggctgcactg ggagcgcttc atgtgcaacc ttgactgcca ggaagagcca 180
gattcctgca tcagtgagaa gctcttcatg gagatggcag agctcatggg ctcagaaggc 240
tggaaggatg caggttatga gtacctctgc attgatgact gttggatggc tcccaaaga 300
gattcagaag gcagacttca ggcagaccct cagcgctttc ctcattggat tcgccagcta 360
gctaattatg ttcacagcaa aggactgaag ctagggattt atgcagatgt tggaaataaa 420
acctgcgcag gcttcccttg gagttttgga tactacgaca ttgatgccca gacctttgct 480
gactggggag tagatctgct aaaatttgat ggttggttact gtgacagttt ggaaaatttg 540
gcagatgggtt ataagcacat gtccttggcc ctgaatagga ctggcagaag cattgtgtac 600
tcctgtgagt ggcctcttta tatgtggccc tttcaaagc ccaattatac agaaatccga 660
cagtactgca atcactggcg aaattttgct gacattgatg attcctggaa aagtataaag 720
agtatcttgg actggacatc ttttaaccag gagagaattg ttgatgttgc tggaccaggg 780
ggttggaatg acccagatat gttagtgatt ggcaactttg gcctcagctg gaatcagcaa 840
gtaactcaga tggccctctg ggctatcatg gctgctcctt tattcatgtc taatgacctc 900
cgacacatca gccctcaagc caaagctctc cttcaggata aggacgtaat tgccatcaat 960
caggaccctt tgggcaagca aggggtaccag cttagacagg gagacaactt tgaagtgtgg 1020
gaacgacctc tctcaggctt agcctgggct gtagctatga taaaccggca ggagattggg 1080
ggacctcgct cttataccat cgcagttgct tccctgggta aaggagtggc ctgtaatcct 1140
gcctgcttca tcacacagct cctccctgtg aaaaggaagc taggggttcta tgaatggact 1200
tcaagggtta gaagtcacat aaatcccaca ggcactgttt tgcttcagct agaaaataca 1260
atgcagatgt cattaaaaga cttactt 1287

<210> 6
<211> 429
<212> PRT
<213> Homo sapiens

<400> 6
Met Gln Leu Arg Asn Pro Glu Leu His Leu Gly Cys Ala Leu Ala Leu
1 5 10 15

OPA18601-Sequece Listing

Arg Phe Leu Ala Leu Val Ser Trp Asp Ile Pro Gly Ala Arg Ala Leu
20 25 30
Asp Asn Gly Leu Ala Arg Thr Pro Thr Met Gly Trp Leu His Trp Glu
35 40 45
Arg Phe Met Cys Asn Leu Asp Cys Gln Glu Glu Pro Asp Ser Cys Ile
50 55 60
Ser Glu Lys Leu Phe Met Glu Met Ala Glu Leu Met Val Ser Glu Gly
65 70 75 80
Trp Lys Asp Ala Gly Tyr Glu Tyr Leu Cys Ile Asp Asp Cys Trp Met
85 90 95
Ala Pro Gln Arg Asp Ser Glu Gly Arg Leu Gln Ala Asp Pro Gln Arg
100 105 110
Phe Pro His Gly Ile Arg Gln Leu Ala Asn Tyr Val His Ser Lys Gly
115 120 125
Leu Lys Leu Gly Ile Tyr Ala Asp Val Gly Asn Lys Thr Cys Ala Gly
130 135 140
Phe Pro Gly Ser Phe Gly Tyr Tyr Asp Ile Asp Ala Gln Thr Phe Ala
145 150 155 160
Asp Trp Gly Val Asp Leu Leu Lys Phe Asp Gly Cys Tyr Cys Asp Ser
165 170 175
Leu Glu Asn Leu Ala Asp Gly Tyr Lys His Met Ser Leu Ala Leu Asn
180 185 190
Arg Thr Gly Arg Ser Ile Val Tyr Ser Cys Glu Trp Pro Leu Tyr Met
195 200 205
Trp Pro Phe Gln Lys Pro Asn Tyr Thr Glu Ile Arg Gln Tyr Cys Asn
210 215 220
His Trp Arg Asn Phe Ala Asp Ile Asp Asp Ser Trp Lys Ser Ile Lys
225 230 235 240
Ser Ile Leu Asp Trp Thr Ser Phe Asn Gln Glu Arg Ile Val Asp Val
245 250 255
Ala Gly Pro Gly Gly Trp Asn Asp Pro Asp Met Leu Val Ile Gly Asn
260 265 270
Phe Gly Leu Ser Trp Asn Gln Gln Val Thr Gln Met Ala Leu Trp Ala
275 280 285
Ile Met Ala Ala Pro Leu Phe Met Ser Asn Asp Leu Arg His Ile Ser
290 295 300
Pro Gln Ala Lys Ala Leu Leu Gln Asp Lys Asp Val Ile Ala Ile Asn
305 310 315 320
Gln Asp Pro Leu Gly Lys Gln Gly Tyr Gln Leu Arg Gln Gly Asp Asn
325 330 335
Phe Glu Val Trp Glu Arg Pro Leu Ser Gly Leu Ala Trp Ala Val Ala
340 345 350

OPA18601-Sequece Listing

Met Ile Asn Arg Gln Glu Ile Gly Gly Pro Arg Ser Tyr Thr Ile Ala
 355 360 365
 Val Ala Ser Leu Gly Lys Gly Val Ala Cys Asn Pro Ala Cys Phe Ile
 370 375 380
 Thr Gln Leu Leu Pro Val Lys Arg Lys Leu Gly Phe Tyr Glu Trp Thr
 385 390 395 400
 Ser Arg Leu Arg Ser His Ile Asn Pro Thr Gly Thr Val Leu Leu Gln
 405 410 415
 Leu Glu Asn Thr Met Gln Met Ser Leu Lys Asp Leu Leu
 420 425

<210> 7
 <211> 666
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Fc varinat

<400> 7
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 agccaggaag accctgaggt ccagttcaac tggtagctgg acggcgtgga ggtgcataat 180
 gccaaagaaa agccgcggga ggagcagttc caaagcacgt accgtgtggt cagcgtcctc 240
 accgtcctgc accaggactg gctgaatggc aaggagtaca agtgcaaggt ctccaacaaa 300
 ggcctcccat cctccatcga gaaaaccatc tccaaagcca aagggcagcc ccgagaacca 360
 caggtgtaca ccctgcccc atcccaggag gagatgacca agaaccaggt cagcctgacc 420
 tgcctggtca aaggcttcta tcccagcgac atcgccgtgg agtgggagag caatgggcag 480
 ccggagaaca actacaagac cagcctccc gtgctggact ccgacggctc cttcttcctc 540
 tacagcaggc taaccgtgga caagagcagg tggcaggagg ggaacgtctt ctcattgctcc 600
 gtgatgcatg aggctctgca caaccactac acgcagaaga gcctctccct gtctctgggt 660
 aaatga 666

<210> 8
 <211> 221
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Fc variant

<400> 8
 Pro Ser Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu
 1 5 10 15

OPA18601-Sequece Listing

Phe Pro Pro Lys₂₀ Pro Lys Asp Thr Leu₂₅ Met Ile Ser Arg Thr₃₀ Pro Glu
 Val Thr Cys₃₅ Val Val Val Asp Val₄₀ Ser Gln Glu Asp Pro₄₅ Glu Val Gln
 Phe Asn₅₀ Trp Tyr Val Asp Gly₅₅ Val Glu Val His Asn₆₀ Ala Lys Thr Lys
 Pro Arg Glu Glu Gln Phe₇₀ Asn Ser Thr Tyr Arg₇₅ Val Val Ser Val Leu₈₀
 Thr Val Leu His Gln₈₅ Asp Trp Leu Asn Gly₉₀ Lys Glu Tyr Lys Cys₉₅ Lys
 Val Ser Asn Lys₁₀₀ Gly Leu Pro Ser Ser₁₀₅ Ile Glu Lys Thr Ile₁₁₀ Ser Lys
 Ala Lys Gly₁₁₅ Gln Pro Arg Glu Pro₁₂₀ Gln Val Tyr Thr Leu₁₂₅ Pro Pro Ser
 Gln Glu Glu Met Thr Lys Asn₁₃₅ Gln Val Ser Leu Thr₁₄₀ Cys Leu Val Lys
 Gly Phe Tyr Pro Ser Asp₁₅₀ Ile Ala Val Glu Trp₁₅₅ Glu Ser Asn Gly₁₆₀
 Pro Glu Asn Asn Tyr₁₆₅ Lys Thr Thr Pro Pro₁₇₀ Val Leu Asp Ser Asp₁₇₅ Gly
 Ser Phe Phe Leu₁₈₀ Tyr Ser Arg Leu Thr₁₈₅ Val Asp Lys Ser Arg₁₉₀ Trp Gln
 Glu Gly Asn Val Phe Ser Cys Ser₂₀₀ Val Met His Glu Ala₂₀₅ Leu His Asn
 His Tyr Thr Gln Lys Ser Leu₂₁₅ Ser Leu Ser Leu Gly₂₂₀ Lys

<210> 9
 <211> 221
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Fc varinat

<400> 9
 Pro Pro Cys Pro Ala₅ Pro Glu Phe Leu Gly₁₀ Gly Pro Ser Val Phe₁₅ Leu
 Phe Pro Pro Lys₂₀ Pro Lys Asp Thr Leu₂₅ Met Ile Ser Arg Thr₃₀ Pro Glu
 Val Thr Cys₃₅ Val Val Val Asp Val₄₀ Ser Gln Glu Asp Pro₄₅ Glu Val Gln
 Phe Asn₅₀ Trp Tyr Val Asp Gly₅₅ Val Glu Val His Asn₆₀ Ala Lys Thr Lys

OPA18601-Sequece Listing

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

<210> 10
<211> 90
<212> DNA
<213> Artificial Sequence

<220>
<223> peptide linker

<400> 10
ggcggcgagg gttcaggtgg tgggtggctct ggcgggtggag ggtcggggggg aggcgggctct 60
ggaggagggg gctccggtgg gggaggtagc 90

<210> 11
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> peptide linker

<400> 11
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1 5 10 15
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
20 25 30

OPA18601-Sequece Listing

<210> 12
 <211> 2043
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> alpha galactosidase-Fc fusion protein

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 accatgggct ggctgcactg ggagcgcttc atgtgcaacc ttgactgcca ggaagagcca 180
 gattcctgca tcagtgagaa gctcttcatg gagatggcag agctcatggt ctcagaaggc 240
 tggaaggatg caggttatga gtacctctgc attgatgact gttggatggc tcccaaaga 300
 gattcagaag gcagacttca ggcagaccct cagcgctttc ctcattggat tcgccagcta 360
 gctaattatg ttcacagcaa aggactgaag ctagggattt atgcagatgt tggaaataaa 420
 acctgcgcag gcttccctgg gagttttgga tactacgaca ttgatgccca gacctttgct 480
 gactggggag tagatctgct aaaatttgat ggttggttact gtgacagttt ggaaaatttg 540
 gcagatgggtt ataagcacat gtccttggcc ctgaatagga ctggcagaag catttgtgtac 600
 tcctgtgagt ggcctcttta tatgtggccc tttaaaaagc ccaattatac agaaatccga 660
 cagtactgca atcactggcg aaattttgct gacattgatg attcctggaa aagtataaag 720
 agtatcttgg actggacatc ttttaaccag gagagaattg ttgatgttgc tggaccaggg 780
 ggttggaatg acccagatat gttagtgatt ggcaactttg gcctcagctg gaatcagcaa 840
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 cgacacatca gccctcaagc caaagctctc cttcaggata aggacgtaat tgccatcaat 960
 caggaccctt tgggcaagca aggggtaccag cttagacagg gagacaactt tgaagtgtgg 1020
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 tcaagggttaa gaagtcacat aaatcccaca ggcactgttt tgcttcagct agaaaataca 1260
 atgcagatgt cattaaaaga cttacttggc ggcggagggt cagggtgggtg tggctctggc 1320
 ggtggaggggt cggggggagg cggctctgga ggagggggct ccggtggggg aggtagccca 1380
 ccatgcccag cacctgagtt cctgggggga ccatcagtct tcctgttccc cccaaaaccc 1440
 aaggacaccc tcatgatctc ccggaccctt gaggtcacat gcgtgggtgg ggacgtgagc 1500
 caggaagacc ctgaggtcca gttcaactgg tacgtggacg gcgtggaggt gcataatgcc 1560
 aagacaaagc cgcgggagga gcagttccaa agcacgtacc gtgtgggtcag cgtcctcacc 1620

OPA18601-Sequece Listing

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gtcctgcacc aggactggct gaatggcaag gagtacaagt gcaaggtctc caacaaaggc      1680
ctcccatcct ccatcgagaa aaccatctcc aaagccaaag ggcagccccg agaaccacag      1740
gtgtacaccc tgcccccatc ccaggaggag atgaccaaga accaggtcag cctgacctgc      1800
ctgggtcaaag gcttctatcc cagcgacatc gccgtggagt gggagagcaa tgggcagccg      1860
gagaacaact acaagaccac gcctcccgtg ctggactccg acggctcctt cttcctctac      1920
agcaggctaa ccgtggacaa gagcagggtg caggagggga acgtcttctc atgctccgtg      1980
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tga                                                                    2043

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<210>      13
<211>      680
<212>      PRT
<213>      Artificial Sequence

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<220>
<223>      alpha galactosidase-Fc fusion protein

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Arg  Phe  Leu  Ala  Leu  Val  Ser  Trp  Asp  Ile  Pro  Gly  Ala  Arg  Ala  Leu
              20              25              30

Asp  Asn  Gly  Leu  Ala  Arg  Thr  Pro  Thr  Met  Gly  Trp  Leu  His  Trp  Glu
      35              40              45

Arg  Phe  Met  Cys  Asn  Leu  Asp  Cys  Gln  Glu  Glu  Pro  Asp  Ser  Cys  Ile
      50              55              60

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

Trp  Lys  Asp  Ala  Gly  Tyr  Glu  Tyr  Leu  Cys  Ile  Asp  Asp  Cys  Trp  Met
              85              90              95

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

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

Leu  Lys  Leu  Gly  Ile  Tyr  Ala  Asp  Val  Gly  Asn  Lys  Thr  Cys  Ala  Gly
      130              135              140

Phe  Pro  Gly  Ser  Phe  Gly  Tyr  Tyr  Asp  Ile  Asp  Ala  Gln  Thr  Phe  Ala
      145              150              155              160

Asp  Trp  Gly  Val  Asp  Leu  Leu  Lys  Phe  Asp  Gly  Cys  Tyr  Cys  Asp  Ser
      165              170              175

Leu  Glu  Asn  Leu  Ala  Asp  Gly  Tyr  Lys  His  Met  Ser  Leu  Ala  Leu  Asn
      180              185              190

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OPA18601-Sequece Listing

Arg	Thr	Gly	Arg	Ser	Ile	Val	Tyr	Ser	Cys	Glu	Trp	Pro	Leu	Tyr	Met
		195					200					205			
Trp	Pro	Phe	Gln	Lys	Pro	Asn	Tyr	Thr	Glu	Ile	Arg	Gln	Tyr	Cys	Asn
	210					215					220				
His	Trp	Arg	Asn	Phe	Ala	Asp	Ile	Asp	Asp	Ser	Trp	Lys	Ser	Ile	Lys
225					230					235					240
Ser	Ile	Leu	Asp	Trp	Thr	Ser	Phe	Asn	Gln	Glu	Arg	Ile	Val	Asp	Val
				245					250					255	
Ala	Gly	Pro	Gly	Gly	Trp	Asn	Asp	Pro	Asp	Met	Leu	Val	Ile	Gly	Asn
			260					265					270		
Phe	Gly	Leu	Ser	Trp	Asn	Gln	Gln	Val	Thr	Gln	Met	Ala	Leu	Trp	Ala
		275					280					285			
Ile	Met	Ala	Ala	Pro	Leu	Phe	Met	Ser	Asn	Asp	Leu	Arg	His	Ile	Ser
	290					295					300				
Pro	Gln	Ala	Lys	Ala	Leu	Leu	Gln	Asp	Lys	Asp	Val	Ile	Ala	Ile	Asn
305					310					315					320
Gln	Asp	Pro	Leu	Gly	Lys	Gln	Gly	Tyr	Gln	Leu	Arg	Gln	Gly	Asp	Asn
				325					330					335	
Phe	Glu	Val	Trp	Glu	Arg	Pro	Leu	Ser	Gly	Leu	Ala	Trp	Ala	Val	Ala
			340					345					350		
Met	Ile	Asn	Arg	Gln	Glu	Ile	Gly	Gly	Pro	Arg	Ser	Tyr	Thr	Ile	Ala
		355					360					365			
Val	Ala	Ser	Leu	Gly	Lys	Gly	Val	Ala	Cys	Asn	Pro	Ala	Cys	Phe	Ile
	370					375					380				
Thr	Gln	Leu	Leu	Pro	Val	Lys	Arg	Lys	Leu	Gly	Phe	Tyr	Glu	Trp	Thr
385					390					395					400
Ser	Arg	Leu	Arg	Ser	His	Ile	Asn	Pro	Thr	Gly	Thr	Val	Leu	Leu	Gln
				405					410					415	
Leu	Glu	Asn	Thr	Met	Gln	Met	Ser	Leu	Lys	Asp	Leu	Leu	Gly	Gly	Gly
			420					425					430		
Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly
		435					440					445			
Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Pro	Pro	Cys	Pro	Ala
	450					455					460				
Pro	Glu	Phe	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro
465				470						475					480
Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val
				485					490					495	
Val	Asp	Val	Ser	Gln	Glu	Asp	Pro	Glu	Val	Gln	Phe	Asn	Trp	Tyr	Val
			500					505					510		
Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln
		515					520					525			

OPA18601-Sequece Listing

Phe Gln Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
 530 535 540
 Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly
 545 550 555 560
 Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
 565 570 575
 Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr
 580 585 590
 Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
 595 600 605
 Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
 610 615 620
 Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
 625 630 635 640
 Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe
 645 650 655
 Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
 660 665 670
 Ser Leu Ser Leu Ser Leu Gly Lys
 675 680

<210> 14
 <211> 12
 <212> PRT
 <213> Homo sapiens

<400> 14
 Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro
 1 5 10