

SEQUENCE LISTING

<110> OPKO Biologics Ltd

<120> METHODS OF PRODUCING LONG ACTING CTP-MODIFIED GROWTH HORMONE POLYPEPTIDES

<130> SP101130SGA

<150> US 62/090,104

<151> 2014-12-10

<160> 17

<170> PatentIn version 3.5

<210> 1

<211> 33

<212> PRT

<213> Artificial Sequence

<220>

<223> Human origin - amino acid

<400> 1

Asp Pro Arg Phe Gln Asp Ser Ser Ser Ser Lys Ala Pro Pro Pro Ser
1 5 10 15

Leu Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser Asp Thr Pro Ile Leu
20 25 30

Gln

<210> 2

<211> 28

<212> PRT

<213> Artificial Sequence

<220>

<223> Human origin - amino acid

<400> 2

Ser Ser Ser Ser Lys Ala Pro Pro Pro Ser Leu Pro Ser Pro Ser Arg
1 5 10 15

Leu Pro Gly Pro Ser Asp Thr Pro Ile Leu Pro Gln
20 25

<210> 3

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Human origin - amino acid

<400> 3

Ser Ser Ser Ser Lys Ala Pro Pro Pro Ser Leu Pro

1 5 10

<210> 4
 <211> 301
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Human origin - amino acid

<400> 4

Met Ala Thr Gly Ser Arg Thr Ser Leu Leu Leu Ala Phe Gly Leu Leu
 1 5 10 15

Cys Leu Pro Trp Leu Gln Glu Gly Ser Ala Ser Ser Ser Ser Lys Ala
 20 25 30

Pro Pro Pro Ser Leu Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser Asp
 35 40 45

Thr Pro Ile Leu Pro Gln Phe Pro Thr Ile Pro Leu Ser Arg Leu Phe
 50 55 60

Asp Asn Ala Met Leu Arg Ala His Arg Leu His Gln Leu Ala Phe Asp
 65 70 75 80

Thr Tyr Gln Glu Phe Glu Glu Ala Tyr Ile Pro Lys Glu Gln Lys Tyr
 85 90 95

Ser Phe Leu Gln Asn Pro Gln Thr Ser Leu Cys Phe Ser Glu Ser Ile
 100 105 110

Pro Thr Pro Ser Asn Arg Glu Glu Thr Gln Gln Lys Ser Asn Leu Glu
 115 120 125

Leu Leu Arg Ile Ser Leu Leu Leu Ile Gln Ser Trp Leu Glu Pro Val
 130 135 140

Gln Phe Leu Arg Ser Val Phe Ala Asn Ser Leu Val Tyr Gly Ala Ser
 145 150 155 160

Asp Ser Asn Val Tyr Asp Leu Leu Lys Asp Leu Glu Glu Gly Ile Gln
 165 170 175

Thr Leu Met Gly Arg Leu Glu Asp Gly Ser Pro Arg Thr Gly Gln Ile
 180 185 190

Phe Lys Gln Thr Tyr Ser Lys Phe Asp Thr Asn Ser His Asn Asp Asp
 195 200 205

Ala Leu Leu Lys Asn Tyr Gly Leu Leu Tyr Cys Phe Arg Lys Asp Met
 210 215 220

Asp Lys Val Glu Thr Phe Leu Arg Ile Val Gln Cys Arg Ser Val Glu
225 230 235 240

Gly Ser Cys Gly Phe Ser Ser Ser Ser Lys Ala Pro Pro Pro Ser Leu
245 250 255

Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser Asp Thr Pro Ile Leu Pro
260 265 270

Gln Ser Ser Ser Ser Lys Ala Pro Pro Pro Ser Leu Pro Ser Pro Ser
275 280 285

Arg Leu Pro Gly Pro Ser Asp Thr Pro Ile Leu Pro Gln
290 295 300

<210> 5
<211> 217
<212> PRT
<213> Homo sapiens

<400> 5

Met Ala Thr Gly Ser Arg Thr Ser Leu Leu Leu Ala Phe Gly Leu Leu
1 5 10 15

Cys Leu Pro Trp Leu Gln Glu Gly Ser Ala Phe Pro Thr Ile Pro Leu
20 25 30

Ser Arg Leu Phe Asp Asn Ala Met Leu Arg Ala His Arg Leu His Gln
35 40 45

Leu Ala Phe Asp Thr Tyr Gln Glu Phe Glu Glu Ala Tyr Ile Pro Lys
50 55 60

Glu Gln Lys Tyr Ser Phe Leu Gln Asn Pro Gln Thr Ser Leu Cys Phe
65 70 75 80

Ser Glu Ser Ile Pro Thr Pro Ser Asn Arg Glu Glu Thr Gln Gln Lys
85 90 95

Ser Asn Leu Glu Leu Leu Arg Ile Ser Leu Leu Leu Ile Gln Ser Trp
100 105 110

Leu Glu Pro Val Gln Phe Leu Arg Ser Val Phe Ala Asn Ser Leu Val
115 120 125

Tyr Gly Ala Ser Asp Ser Asn Val Tyr Asp Leu Leu Lys Asp Leu Glu
130 135 140

Glu Gly Ile Gln Thr Leu Met Gly Arg Leu Glu Asp Gly Ser Pro Arg
145 150 155 160

Thr Gly Gln Ile Phe Lys Gln Thr Tyr Ser Lys Phe Asp Thr Asn Ser
165 170 175

His Asn Asp Asp Ala Leu Leu Lys Asn Tyr Gly Leu Leu Tyr Cys Phe
180 185 190

Arg Lys Asp Met Asp Lys Val Glu Thr Phe Leu Arg Ile Val Gln Cys
195 200 205

Arg Ser Val Glu Gly Ser Cys Gly Phe
210 215

<210> 6
<211> 26
<212> PRT
<213> Artificial Sequence

<220>
<223> Human origin - amino acid

<400> 6

Met Ala Thr Gly Ser Arg Thr Ser Leu Leu Leu Ala Phe Gly Leu Leu
1 5 10 15

Cys Leu Pro Trp Leu Gln Glu Gly Ser Ala
20 25

<210> 7
<211> 275
<212> PRT
<213> Artificial Sequence

<220>
<223> Human origin - amino acid

<400> 7

Ser Ser Ser Ser Lys Ala Pro Pro Pro Ser Leu Pro Ser Pro Ser Arg
1 5 10 15

Leu Pro Gly Pro Ser Asp Thr Pro Ile Leu Pro Gln Phe Pro Thr Ile
20 25 30

Pro Leu Ser Arg Leu Phe Asp Asn Ala Met Leu Arg Ala His Arg Leu
35 40 45

His Gln Leu Ala Phe Asp Thr Tyr Gln Glu Phe Glu Glu Ala Tyr Ile
50 55 60

Pro Lys Glu Gln Lys Tyr Ser Phe Leu Gln Asn Pro Gln Thr Ser Leu
65 70 75 80

Cys Phe Ser Glu Ser Ile Pro Thr Pro Ser Asn Arg Glu Glu Thr Gln
85 90 95

Gln Lys Ser Asn Leu Glu Leu Leu Arg Ile Ser Leu Leu Leu Ile Gln
100 105 110

Ser Trp Leu Glu Pro Val Gln Phe Leu Arg Ser Val Phe Ala Asn Ser
 115 120 125
 Leu Val Tyr Gly Ala Ser Asp Ser Asn Val Tyr Asp Leu Leu Lys Asp
 130 135 140
 Leu Glu Glu Gly Ile Gln Thr Leu Met Gly Arg Leu Glu Asp Gly Ser
 145 150 155 160
 Pro Arg Thr Gly Gln Ile Phe Lys Gln Thr Tyr Ser Lys Phe Asp Thr
 165 170 175
 Asn Ser His Asn Asp Asp Ala Leu Leu Lys Asn Tyr Gly Leu Leu Tyr
 180 185 190
 Cys Phe Arg Lys Asp Met Asp Lys Val Glu Thr Phe Leu Arg Ile Val
 195 200 205
 Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe Ser Ser Ser Ser Lys
 210 215 220
 Ala Pro Pro Pro Ser Leu Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser
 225 230 235 240
 Asp Thr Pro Ile Leu Pro Gln Ser Ser Ser Ser Lys Ala Pro Pro Pro
 245 250 255
 Ser Leu Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser Asp Thr Pro Ile
 260 265 270
 Leu Pro Gln
 275

<210> 8
 <211> 191
 <212> PRT
 <213> Homo sapiens

<400> 8

Phe Pro Thr Ile Pro Leu Ser Arg Leu Phe Asp Asn Ala Met Leu Arg
 1 5 10 15
 Ala His Arg Leu His Gln Leu Ala Phe Asp Thr Tyr Gln Glu Phe Glu
 20 25 30
 Glu Ala Tyr Ile Pro Lys Glu Gln Lys Tyr Ser Phe Leu Gln Asn Pro
 35 40 45
 Gln Thr Ser Leu Cys Phe Ser Glu Ser Ile Pro Thr Pro Ser Asn Arg
 50 55 60
 Glu Glu Thr Gln Gln Lys Ser Asn Leu Glu Leu Leu Arg Ile Ser Leu

65		70		75		80									
Leu	Leu	Ile	Gln	Ser	Trp	Leu	Glu	Pro	Val	Gln	Phe	Leu	Arg	Ser	Val
				85					90					95	
Phe	Ala	Asn	Ser	Leu	Val	Tyr	Gly	Ala	Ser	Asp	Ser	Asn	Val	Tyr	Asp
		100						105					110		
Leu	Leu	Lys	Asp	Leu	Glu	Glu	Gly	Ile	Gln	Thr	Leu	Met	Gly	Arg	Leu
		115					120					125			
Glu	Asp	Gly	Ser	Pro	Arg	Thr	Gly	Gln	Ile	Phe	Lys	Gln	Thr	Tyr	Ser
	130					135					140				
Lys	Phe	Asp	Thr	Asn	Ser	His	Asn	Asp	Asp	Ala	Leu	Leu	Lys	Asn	Tyr
145					150					155					160
Gly	Leu	Leu	Tyr	Cys	Phe	Arg	Lys	Asp	Met	Asp	Lys	Val	Glu	Thr	Phe
				165					170					175	
Leu	Arg	Ile	Val	Gln	Cys	Arg	Ser	Val	Glu	Gly	Ser	Cys	Gly	Phe	
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<210> 9
 <211> 903
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Human origin - nucleic acid

<400> 9	
atggccaccg gcagcaggac cagcctgctg ctggccttcg gcctgctgtg cctgccatgg	60
ctgcaggagg gcagcgccag ctcttcttct aaggtccac ccccatctct gccagcccc	120
agcagactgc cgggccccag cgacacaccc attctgcccc agttccccac catccccctg	180
agcaggctgt tgcacaacgc catgctgagg gctcacaggc tgcaccagct ggcttttgac	240
acctaccagg agttcgagga agcctacatc cccaaggagc agaagtacag cttcctgcag	300
aacccccaga cctccctgtg cttcagcgag agcatcccca ccccagcaa cagagaggag	360
accagcaga agagcaacct ggagctgctg aggatctccc tgctgctgat ccagagctgg	420
ctggagcccc tgagttcct gagaagcgtg ttcgccaaca gcctggtgta cggcgccagc	480
gacagcaacg tgtacgacct gctgaaggac ctggaggagg gcatccagac cctgatgggc	540
cggctggagg acggcagccc caggaccggc cagatcttca agcagacct cagcaagttc	600
gacaccaaca gccacaacga cgacgccctg ctgaagaact acgggctgct gtactgcttc	660
agaaaggaca tggacaaggt ggagaccttc ctgaggatcg tgcagtgcag aagcgtggag	720
ggcagctgcg gcttcagctc cagcagcaag gccctcccc cgagcctgcc ctccccaaagc	780
aggctgcctg ggccctccga cacaccaatc ctgccacaga gcagctcctc taaggcccct	840
cctccatccc tgccatcccc ctcccggctg cctggcccct ctgacacccc tatcctgcct	900

cag

903

<210> 10
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Human origin - amino acid

<400> 10

Leu Pro Gly Pro Ser Asp Thr Pro Ile Leu Pro Gln Phe Pro Thr Ile
1 5 10 15

Pro Leu Ser Arg
20

<210> 11
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Human origin - amino acid

<400> 11

Ala Pro Pro Pro Ser Leu Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser
1 5 10 15

Asp Thr Pro Ile Leu Pro Gln Phe Pro Thr Ile Pro Leu Ser Arg
20 25 30

<210> 12
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Human origin - amino acid

<400> 12

Leu Pro Gly Pro Ser Asp Thr Pro Ile Leu Pro Gln
1 5 10

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

<220>
<223> Human origin - amino acid

<400> 13

Ser Val Glu Gly Ser Cys Gly Phe Ser Ser Ser Lys
1 5 10

<210> 14

<211> 51
<212> PRT
<213> Artificial Sequence

<220>
<223> Human origin - amino acid

<400> 14

Ala Pro Pro Pro Ser Leu Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser
1 5 10 15

Asp Thr Pro Ile Leu Pro Gln Ser Ser Ser Ser Lys Ala Pro Pro Pro
20 25 30

Ser Leu Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser Asp Thr Pro Ile
35 40 45

Leu Pro Gln
50

<210> 15
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> Human origin - amino acid

<400> 15

Ser Ser Ser Ser Lys Ala Pro Pro Pro Ser Leu Pro Ser Pro Ser Arg
1 5 10 15

Leu Pro Gly Pro Ser Asp Thr Pro Ile Leu Pro Gln Phe Pro Thr Ile
20 25 30

Pro Leu Ser Arg
35

<210> 16
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Human origin - amino acid

<400> 16

Ala Pro Pro Pro Ser Leu Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser
1 5 10 15

Asp Thr Pro Ile Leu Pro Gln
20

<210> 17
<211> 64
<212> PRT
<213> Artificial Sequence

<220>

<223> Human origin - amino acid

<400> 17

Ser Val Glu Gly Ser Cys Gly Phe Ser Ser Ser Ser Lys Ala Pro Pro
1 5 10 15

Pro Ser Leu Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser Asp Thr Pro
20 25 30

Ile Leu Pro Gln Ser Ser Ser Ser Lys Ala Pro Pro Pro Ser Leu Pro
35 40 45

Ser Pro Ser Arg Leu Pro Gly Pro Ser Asp Thr Pro Ile Leu Pro Gln
50 55 60