

SEQUENCE LISTING

<110> Eli Lilly and Company
 <120> Neuregulin-4 Compounds and Methods of Use
 <130> X22153
 <150> US 62/827,386
 <151> 2019-04-01
 <160> 20
 <170> PatentIn version 3.5
 <210> 1
 <211> 47
 <212> PRT
 <213> Homo sapiens

<400> 1

Asp	His	Glu	Glu	Pro	Cys	Gly	Pro	Ser	His	Lys	Ser	Phe	Cys	Leu	Asn
1				5					10					15	

Gly	Gly	Leu	Cys	Tyr	Val	Ile	Pro	Thr	Ile	Pro	Ser	Pro	Phe	Cys	Arg
		20					25						30		

Cys	Val	Glu	Asn	Tyr	Thr	Gly	Ala	Arg	Cys	Glu	Glu	Val	Phe	Leu
	35						40					45		

<210> 2
 <211> 48
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<220>
 <221> VARIANT
 <222> (1)..(1)
 <223> Xaa at position 1 is selected from the group consisting of T, PT, MPT, S, GS, GGS, GGGs, and (GGGGXlambda)n wherein Xlambda is Q, A, E or S and n=1-5 (SEQ ID NO:5), or is absent

<220>
 <221> VARIANT
 <222> (9)..(9)
 <223> Xaa at position 9 is E or P

<220>
<221> VARIANT
<222> (23)..(23)
<223> Xaa at position 23 is Q or V

<220>
<221> VARIANT
<222> (27)..(27)
<223> Xaa at position 27 is F or I

<220>
<221> VARIANT
<222> (36)..(36)
<223> Xaa at position 36 or E or A

<220>
<221> VARIANT
<222> (45)..(45)
<223> Xaa at position 45 is H, K or E

<400> 2

Xaa	Gly	His	Glu	Glu	Pro	Cys	Gly	Xaa	Ser	His	Lys	Ser	Phe	Cys	Leu
1				5					10					15	

Asn	Gly	Gly	Leu	Cys	Tyr	Xaa	Ile	Pro	Thr	Xaa	Pro	Ser	Pro	Phe	Cys
			20					25					30		

Arg	Cys	Val	Xaa	Asn	Tyr	Thr	Gly	Ala	Arg	Cys	Glu	Xaa	Val	Phe	Leu
		35					40					45			

<210> 3
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 3

Met	Pro	Thr	Asp	His	Glu	Glu	Pro	Cys	Gly	Pro	Ser	His	Lys	Ser	Phe
1				5					10					15	

Cys	Leu	Asn	Gly	Gly	Leu	Cys	Tyr	Val	Ile	Pro	Thr	Ile	Pro	Ser	Pro
			20					25					30		

Phe	Cys	Arg	Cys	Val	Glu	Asn	Tyr	Thr	Gly	Ala	Arg	Cys	Glu	Glu	Val
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

35

40

45

Phe Leu Pro Gly Ser Ser Ile Gln Thr Lys Ser Asn Leu Phe Glu Ala
 50 55 60

Phe Val Ala Leu Ala Val Leu Val Thr Leu Ile Ile Gly Ala Phe Tyr
 65 70 75 80

Phe Leu Cys Arg Lys Gly His Phe Gln Arg Ala Ser Ser Val Gln Tyr
 85 90 95

Asp Ile Asn Leu Val Glu Thr Ser Ser Thr Ser Ala His His Ser His
 100 105 110

Glu Gln His
 115

<210> 4
 <211> 47
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 4

Gly His Glu Glu Pro Cys Gly Pro Ser His Lys Ser Phe Cys Leu Asn
 1 5 10 15

Gly Gly Leu Cys Tyr Gln Ile Pro Thr Ile Pro Ser Pro Phe Cys Arg
 20 25 30

Cys Val Glu Asn Tyr Thr Gly Ala Arg Cys Glu Lys Val Phe Leu
 35 40 45

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

<220>
 <223> Synthetic Construct

<220>
<221> VARIANT
<222> (1)..(5)
<223> SEQ ID NO:5 is further represented as (GGGGXlambda)n, wherein:
Xlambda is Q, A, E or S; and n is 1-5.

<220>
<221> VARIANT
<222> (5)..(5)
<223> Xaa at position 5 is Xlambda wherein Xlambda is Q, A, E or S

<400> 5

Gly Gly Gly Gly Xaa
1 5

<210> 6
<211> 221
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 6

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

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
20 25 30

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
35 40 45

Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
50 55 60

Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val
65 70 75 80

Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
85 90 95

Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
100 105 110

Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
115 120 125

Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val
130 135 140

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
145 150 155 160

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
165 170 175

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
180 185 190

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

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
210 215 220

<210> 7
<211> 221
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 7

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

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
20 25 30

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
35 40 45

Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
50 55 60

Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val
65 70 75 80

Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
85 90 95

Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
100 105 110

Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
115 120 125

Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Ser Cys Ala Val
130 135 140

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
145 150 155 160

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
165 170 175

Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
180 185 190

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

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
210 215 220

<210> 8

<211> 221

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 8

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

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ala Ser Arg Thr Pro
20 25 30

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
35 40 45

Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
50 55 60

Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val
65 70 75 80

Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
85 90 95

Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
100 105 110

Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
115 120 125

Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val
130 135 140

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
145 150 155 160

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
165 170 175

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
180 185 190

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

Asn Ala Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
210 215 220

<210> 9

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

<220>
<223> Synthetic Construct

<400> 9

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

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ala Ser Arg Thr Pro
20 25 30

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
35 40 45

Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
50 55 60

Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val
65 70 75 80

Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
85 90 95

Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
100 105 110

Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
115 120 125

Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Ser Cys Ala Val
130 135 140

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
145 150 155 160

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
165 170 175

Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp

180

185

190

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

Asn Ala Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 210 215 220

<210> 10

<211> 62

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 10

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 1 5 10 15

His Glu Glu Pro Cys Gly Pro Ser His Lys Ser Phe Cys Leu Asn Gly
 20 25 30

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

Val Glu Asn Tyr Thr Gly Ala Arg Cys Glu Glu Val Phe Leu
 50 55 60

<210> 11

<211> 62

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 11

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 1 5 10 15

His Glu Glu Pro Cys Gly Glu Ser His Lys Ser Phe Cys Leu Asn Gly
 20 25 30

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

Val Glu Asn Tyr Thr Gly Ala Arg Cys Glu Glu Val Phe Leu
50 55 60

<210> 12
<211> 62
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 12

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

His Glu Glu Pro Cys Gly Pro Ser His Lys Ser Phe Cys Leu Asn Gly
20 25 30

Gly Leu Cys Tyr Gln Ile Pro Thr Ile Pro Ser Pro Phe Cys Arg Cys
35 40 45

Val Glu Asn Tyr Thr Gly Ala Arg Cys Glu Glu Val Phe Leu
50 55 60

<210> 13
<211> 62
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 13

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

His Glu Glu Pro Cys Gly Pro Ser His Lys Ser Phe Cys Leu Asn Gly
20 25 30

Gly Leu Cys Tyr Val Ile Pro Thr Phe Pro Ser Pro Phe Cys Arg Cys

35

40

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Val Glu Asn Tyr Thr Gly Ala Arg Cys Glu Glu Val Phe Leu
 50 55 60

<210> 14

<211> 62

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 14

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 1 5 10 15

His Glu Glu Pro Cys Gly Pro Ser His Lys Ser Phe Cys Leu Asn Gly
 20 25 30

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

Val Ala Asn Tyr Thr Gly Ala Arg Cys Glu Glu Val Phe Leu
 50 55 60

<210> 15

<211> 62

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 15

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 1 5 10 15

His Glu Glu Pro Cys Gly Pro Ser His Lys Ser Phe Cys Leu Asn Gly
 20 25 30

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

Val Glu Asn Tyr Thr Gly Ala Arg Cys Glu Lys Val Phe Leu
50 55 60

<210> 16
<211> 62
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 16

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

His Glu Glu Pro Cys Gly Pro Ser His Lys Ser Phe Cys Leu Asn Gly
20 25 30

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

Val Glu Asn Tyr Thr Gly Ala Arg Cys Glu His Val Phe Leu
50 55 60

<210> 17
<211> 62
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 17

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

His Glu Glu Pro Cys Gly Glu Ser His Lys Ser Phe Cys Leu Asn Gly
20 25 30

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

Val Glu Asn Tyr Thr Gly Ala Arg Cys Glu Glu Val Phe Leu

50

55

60

<210> 18
 <211> 52
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 18

Gly Gly Gly Gly Ser Gly His Glu Glu Pro Cys Gly Pro Ser His Lys
 1 5 10 15

Ser Phe Cys Leu Asn Gly Gly Leu Cys Tyr Gln Ile Pro Thr Ile Pro
 20 25 30

Ser Pro Phe Cys Arg Cys Val Glu Asn Tyr Thr Gly Ala Arg Cys Glu
 35 40 45

Lys Val Phe Leu
 50

<210> 19
 <211> 62
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 19

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 1 5 10 15

His Glu Glu Pro Cys Gly Pro Ser His Lys Ser Phe Cys Leu Asn Gly
 20 25 30

Gly Leu Cys Tyr Gln Ile Pro Thr Ile Pro Ser Pro Phe Cys Arg Cys
 35 40 45

Val Glu Asn Tyr Thr Gly Ala Arg Cys Glu Lys Val Phe Leu
 50 55 60

<210> 20
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 20

Gly Gly Gly Ser
1