

2016015474.txt  
SEQUENCE LISTING

<110> Merz Pharma GmbH & Co. KGaA  
<120> NOVEL RECOMBINANT CLOSTRIDIAL NEUROTOXINS WITH INCREASED DURATION  
OF EFFECT  
<130> 110806P502PC  
<160> 20  
<170> PatentIn version 3.5  
<210> 1  
<211> 116  
<212> PRT  
<213> human  
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Met Ser Ala Thr Ala Ala Thr Ala Pro Pro Ala Ala Pro Ala Gly Glu  
1 5 10 15

Gly Gly Pro Pro Ala Pro Pro Pro Asn Leu Thr Ser Asn Arg Arg Leu  
20 25 30

Gln Gln Thr Gln Ala Gln Val Asp Glu Val Val Asp Ile Met Arg Val  
35 40 45

Asn Val Asp Lys Val Leu Glu Arg Asp Gln Lys Leu Ser Glu Leu Asp  
50 55 60

Asp Arg Ala Asp Ala Leu Gln Ala Gly Ala Ser Gln Phe Glu Thr Ser  
65 70 75 80

Ala Ala Lys Leu Lys Arg Lys Tyr Trp Trp Lys Asn Leu Lys Met Met  
85 90 95

Ile Ile Leu Gly Val Ile Cys Ala Ile Ile Leu Ile Ile Ile Ile Val  
100 105 110

Tyr Phe Ser Thr  
115

<210> 2  
<211> 288  
<212> PRT  
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<400> 2

Met Lys Asp Arg Thr Gln Glu Leu Arg Thr Ala Lys Asp Ser Asp Asp  
1 5 10 15

Asp Asp Asp Val Ala Val Thr Val Asp Arg Asp Arg Phe Met Asp Glu  
20 25 30

Phe Phe Glu Gln Val Glu Glu Ile Arg Gly Phe Ile Asp Lys Ile Ala  
Seite 1

35

40

45

Glu Asn Val Glu Glu Val Lys Arg Lys His Ser Ala Ile Leu Ala Ser  
 50 55 60

Pro Asn Pro Asp Glu Lys Thr Lys Glu Glu Leu Glu Glu Leu Met Ser  
 65 70 75 80

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

Glu Gln Ser Ile Glu Gln Glu Glu Gly Leu Asn Arg Ser Ser Ala Asp  
 100 105 110

Leu Arg Ile Arg Lys Thr Gln His Ser Thr Leu Ser Arg Lys Phe Val  
 115 120 125

Glu Val Met Ser Glu Tyr Asn Ala Thr Gln Ser Asp Tyr Arg Glu Arg  
 130 135 140

Cys Lys Gly Arg Ile Gln Arg Gln Leu Glu Ile Thr Gly Arg Thr Thr  
 145 150 155 160

Thr Ser Glu Glu Leu Glu Asp Met Leu Glu Ser Gly Asn Pro Ala Ile  
 165 170 175

Phe Ala Ser Gly Ile Ile Met Asp Ser Ser Ile Ser Lys Gln Ala Leu  
 180 185 190

Ser Glu Ile Glu Thr Arg His Ser Glu Ile Ile Lys Leu Glu Asn Ser  
 195 200 205

Ile Arg Glu Leu His Asp Met Phe Met Asp Met Ala Met Leu Val Glu  
 210 215 220

Ser Gln Gly Glu Met Ile Asp Arg Ile Glu Tyr Asn Val Glu His Ala  
 225 230 235 240

Val Asp Tyr Val Glu Arg Ala Val Ser Asp Thr Lys Lys Ala Val Lys  
 245 250 255

Tyr Gln Ser Lys Ala Arg Arg Lys Lys Ile Met Ile Ile Ile Cys Cys  
 260 265 270

Val Ile Leu Gly Ile Val Ile Ala Ser Thr Val Gly Gly Ile Phe Ala  
 275 280 285

<210> 3  
 <211> 134  
 <212> PRT  
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&lt;400&gt; 3

Met Asp Phe Val Met Lys Gln Ala Leu Gly Gly Ala Thr Lys Asp Met  
 1 5 10 15

Gly Lys Met Leu Gly Gly Glu Glu Glu Lys Asp Pro Asp Ala Gln Lys  
 20 25 30

Lys Glu Glu Glu Arg Gln Glu Ala Leu Arg Gln Gln Glu Glu Glu Arg  
 35 40 45

Lys Ala Lys His Ala Arg Met Glu Ala Glu Arg Glu Lys Val Arg Gln  
 50 55 60

Gln Ile Arg Asp Lys Tyr Gly Leu Lys Lys Lys Glu Glu Lys Glu Ala  
 65 70 75 80

Glu Glu Lys Ala Ala Leu Glu Gln Pro Cys Glu Gly Ser Leu Thr Arg  
 85 90 95

Pro Lys Lys Ala Ile Pro Ala Gly Cys Gly Asp Glu Glu Glu Glu Glu  
 100 105 110

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

Gln Asp Met Phe Lys Lys  
 130

&lt;210&gt; 4

&lt;211&gt; 19

&lt;212&gt; PRT

&lt;213&gt; artificial

&lt;220&gt;

&lt;223&gt; recombinant SNARE complex-binding sequence

&lt;400&gt; 4

Gln Ala Gln Val Asp Glu Val Val Asp Ile Met Arg Val Asn Val Asp  
 1 5 10 15

Lys Val Leu

&lt;210&gt; 5

&lt;211&gt; 59

&lt;212&gt; PRT

&lt;213&gt; artificial

&lt;220&gt;

&lt;223&gt; recombinant SNARE complex-binding sequence

&lt;400&gt; 5

Leu Gln Gln Thr Gln Ala Gln Val Asp Glu Val Val Asp Ile Met Arg  
 1 5 10 15

Val Asn Val Asp Lys Val Leu Glu Arg Asp Gln Lys Leu Ser Glu Leu  
20 25 30

Asp Asp Arg Ala Asp Ala Leu Gln Ala Gly Ala Ser Gln Phe Glu Thr  
35 40 45

Ser Ala Ala Lys Leu Lys Arg Lys Tyr Trp Trp  
50 55

<210> 6  
<211> 26  
<212> PRT  
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<220>  
<223> recombinant SNARE complex-binding sequence

<400> 6

Leu Gln Gln Thr Gln Ala Gln Val Asp Glu Val Val Asp Ile Met Arg  
1 5 10 15

Val Asn Val Asp Lys Val Leu Glu Arg Asp  
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<210> 7  
<211> 26  
<212> PRT  
<213> artificial

<220>  
<223> recombinant SNARE complex-binding sequence

<400> 7

Ser Ile Ser Lys Gln Ala Leu Ser Glu Ile Glu Thr Arg His Ser Glu  
1 5 10 15

Ile Ile Lys Leu Glu Asn Ser Ile Arg Glu  
20 25

<210> 8  
<211> 41  
<212> PRT  
<213> artificial

<220>  
<223> recombinant SNARE complex-binding sequence

<400> 8

Ser Ile Ser Lys Gln Ala Leu Ser Glu Ile Glu Thr Arg His Ser Glu  
1 5 10 15

Ile Ile Lys Leu Glu Asn Ser Ile Arg Glu Leu His Asp Met Phe Met  
20 25 30

Asp Met Ala Met Leu Val Glu Ser Gln  
 35 40

<210> 9  
 <211> 70  
 <212> PRT  
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<220>  
 <223> recombinant SNARE complex-binding sequence

<400> 9

Ser Ile Ser Lys Gln Ala Leu Ser Glu Ile Glu Thr Arg His Ser Glu  
 1 5 10 15

Ile Ile Lys Leu Glu Asn Ser Ile Arg Glu Leu His Asp Met Phe Met  
 20 25 30

Asp Met Ala Met Leu Val Glu Ser Gln Gly Glu Met Ile Asp Arg Ile  
 35 40 45

Glu Tyr Asn Val Glu His Ala Val Asp Tyr Val Glu Arg Ala Val Ser  
 50 55 60

Asp Thr Lys Lys Ala Val  
 65 70

<210> 10  
 <211> 20  
 <212> PRT  
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<220>  
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<400> 10

Ala Lys Met Glu Ala Glu Arg Glu Val Met Arg Gln Gly Ile Arg Asp  
 1 5 10 15

Lys Tyr Gly Ile  
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<210> 11  
 <211> 41  
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<400> 11

Lys Lys Glu Glu Glu Arg Gln Glu Ala Leu Arg Gln Ala Glu Glu Glu  
 1 5 10 15

Arg Lys Ala Lys Tyr Ala Lys Met Glu Ala Glu Arg Glu Val Met Arg  
 20 25 30

Gln Gly Ile Arg Asp Lys Tyr Gly Ile  
35 40

<210> 12  
<211> 53  
<212> PRT  
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<220>  
<223> PAS linker

<400> 12

Ala Ser Pro Ala Ala Pro Ala Pro Ala Ser Pro Ala Ala Pro Ala Pro  
1 5 10 15

Ser Ala Pro Ala Ala Ser Pro Ala Ala Pro Ala Pro Ala Ser Pro Ala  
20 25 30

Ala Pro Ala Pro Ser Ala Pro Ala Ala Ser Pro Ala Ala Pro Ala Pro  
35 40 45

Ala Ser Pro Ala Ala  
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<210> 13  
<211> 33  
<212> PRT  
<213> artificial

<220>  
<223> recombinant sequence comprising SNARE complex-binding sequence

<400> 13

Gln Ala Gln Val Asp Glu Val Val Asp Ile Met Arg Val Asn Val Asp  
1 5 10 15

Lys Val Leu Ala Gly Ala Gly Leu Val Pro Arg Gly Ser Ala Gly Ala  
20 25 30

Gly

<210> 14  
<211> 71  
<212> PRT  
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<220>  
<223> recombinant sequence comprising SNARE complex-binding sequence

<400> 14

Leu Gln Gln Thr Gln Ala Gln Val Asp Glu Val Val Asp Ile Met Arg  
1 5 10 15

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Val Asn Val Asp Lys Val Leu Glu Arg Asp Gln Lys Leu Ser Glu Leu  
20 25 30

Asp Asp Arg Ala Asp Ala Leu Gln Ala Gly Ala Ser Gln Phe Glu Thr  
35 40 45

Ser Ala Ala Lys Leu Lys Arg Lys Tyr Trp Trp Ala Gly Leu Val Pro  
50 55 60

Arg Gly Ser Ala Gly Ala Gly  
65 70

<210> 15

<211> 38

<212> PRT

<213> artificial

<220>

<223> recombinant sequence comprising SNARE complex-binding sequence

<400> 15

Leu Gln Gln Thr Gln Ala Gln Val Asp Glu Val Val Asp Ile Met Arg  
1 5 10 15

Val Asn Val Asp Lys Val Leu Glu Arg Asp Ala Gly Leu Val Pro Arg  
20 25 30

Gly Ser Ala Gly Ala Gly  
35

<210> 16

<211> 38

<212> PRT

<213> artificial

<220>

<223> recombinant sequence comprising SNARE complex-binding sequence

<400> 16

Ser Ile Ser Lys Gln Ala Leu Ser Glu Ile Glu Thr Arg His Ser Glu  
1 5 10 15

Ile Ile Lys Leu Glu Asn Ser Ile Arg Glu Ala Gly Leu Val Pro Arg  
20 25 30

Gly Ser Ala Gly Ala Gly  
35

<210> 17

<211> 53

<212> PRT

<213> artificial

<220>

<223> recombinant sequence comprising SNARE complex-binding sequence

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<400> 17

Ser Ile Ser Lys Gln Ala Leu Ser Glu Ile Glu Thr Arg His Ser Glu  
1 5 10 15

Ile Ile Lys Leu Glu Asn Ser Ile Arg Glu Leu His Asp Met Phe Met  
20 25 30

Asp Met Ala Met Leu Val Glu Ser Gln Ala Gly Leu Val Pro Arg Gly  
35 40 45

Ser Ala Gly Ala Gly  
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<210> 18

<211> 82

<212> PRT

<213> artificial

<220>

<223> recombinant sequence comprising SNARE complex-binding sequence

<400> 18

Ser Ile Ser Lys Gln Ala Leu Ser Glu Ile Glu Thr Arg His Ser Glu  
1 5 10 15

Ile Ile Lys Leu Glu Asn Ser Ile Arg Glu Leu His Asp Met Phe Met  
20 25 30

Asp Met Ala Met Leu Val Glu Ser Gln Gly Glu Met Ile Asp Arg Ile  
35 40 45

Glu Tyr Asn Val Glu His Ala Val Asp Tyr Val Glu Arg Ala Val Ser  
50 55 60

Asp Thr Lys Lys Ala Val Ala Gly Leu Val Pro Arg Gly Ser Ala Gly  
65 70 75 80

Ala Gly

<210> 19

<211> 32

<212> PRT

<213> artificial

<220>

<223> recombinant sequence comprising SNARE complex-binding sequence

<400> 19

Ala Lys Met Glu Ala Glu Arg Glu Val Met Arg Gln Gly Ile Arg Asp  
1 5 10 15

Lys Tyr Gly Ile Ala Gly Leu Val Pro Arg Gly Ser Ala Gly Ala Gly  
20 25 30



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<210> 20  
<211> .53  
<212> PRT  
<213> artificial

<220>  
<223> recombinant sequence comprising SNARE complex-binding sequence

<400> 20

Lys Lys Glu Glu Glu Arg Gln Glu Ala Leu Arg Gln Ala Glu Glu Glu  
1 5 10 15

Arg Lys Ala Lys Tyr Ala Lys Met Glu Ala Glu Arg Glu Val Met Arg  
20 25 30

Gln Gly Ile Arg Asp Lys Tyr Gly Ile Ala Gly Leu Val Pro Arg Gly  
35 40 45

Ser Ala Gly Ala Gly  
50