

SEQUENCE LISTING

<110> Merz Pharma GmbH & Co. KGaA

<120> NOVEL USES OF BOTULINUM NEUROTOXIN FOR THE TREATMENT OF TREMOR

<130> 0918-000-PCT

<150> EP19158541.3

<151> 2019-02-21

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<213> Clostridium botulinum

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<212> PRT

<213> Clostridium botulinum

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<211> 1280

<212> PRT

<213> Clostridium botulinum

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<220>
 <223> Xaa can be any naturally occurring amino acid

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

		275					280				285				
Tyr	Asn	Lys	Ala	Leu	Gln	Asn	Phe	Gln	Asp	Ile	Ala	Asn	Arg	Leu	Asn
	290					295					300				
Ile	Val	Ser	Ser	Ala	Gln	Gly	Ser	Gly	Ile	Asp	Ile	Ser	Leu	Tyr	Lys
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Gln	Ile	Tyr	Lys	Asn	Lys	Tyr	Asp	Phe	Val	Glu	Asp	Pro	Asn	Gly	Lys
				325					330					335	
Tyr	Ser	Val	Asp	Lys	Asp	Lys	Phe	Asp	Lys	Leu	Tyr	Lys	Ala	Leu	Met
			340					345					350		
Phe	Gly	Phe	Thr	Glu	Thr	Asn	Leu	Ala	Gly	Glu	Tyr	Gly	Ile	Lys	Thr
		355					360					365			
Arg	Tyr	Ser	Tyr	Phe	Ser	Glu	Tyr	Leu	Pro	Pro	Ile	Lys	Thr	Glu	Lys
	370					375					380				
Leu	Leu	Asp	Asn	Thr	Ile	Tyr	Thr	Gln	Asn	Glu	Gly	Phe	Asn	Ile	Ala
385					390					395					400
Ser	Lys	Asn	Leu	Lys	Thr	Glu	Phe	Asn	Gly	Gln	Asn	Lys	Ala	Val	Asn
				405					410					415	
Lys	Glu	Ala	Tyr	Glu	Glu	Ile	Ser	Leu	Glu	His	Leu	Val	Ile	Tyr	Arg
			420					425					430		
Ile	Ala	Met	Cys	Lys	Pro	Val	Met	Tyr	Lys	Asn	Thr	Gly	Lys	Ser	Glu
		435					440					445			
Gln	Cys	Ile	Ile	Val	Asn	Asn	Glu	Asp	Leu	Phe	Phe	Ile	Ala	Asn	Lys
	450					455					460				
Asp	Ser	Phe	Ser	Lys	Asp	Leu	Ala	Lys	Ala	Glu	Thr	Ile	Ala	Tyr	Asn
465					470					475					480
Thr	Gln	Asn	Asn	Thr	Ile	Glu	Asn	Asn	Phe	Ser	Ile	Asp	Gln	Leu	Ile
				485					490					495	
Leu	Asp	Asn	Asp	Leu	Ser	Ser	Gly	Ile	Asp	Leu	Pro	Asn	Glu	Asn	Thr
			500					505					510		
Glu	Pro	Phe	Thr	Asn	Phe	Asp	Asp	Ile	Asp	Ile	Pro	Val	Tyr	Ile	Lys
		515					520					525			
Gln	Ser	Ala	Leu	Lys	Lys	Ile	Phe	Val	Asp	Gly	Asp	Ser	Leu	Phe	Glu
	530					535					540				
Tyr	Leu	His	Ala	Gln	Thr	Phe	Pro	Ser	Asn	Ile	Glu	Asn	Leu	Gln	Leu
545					550					555					560
Thr	Asn	Ser	Leu	Asn	Asp	Ala	Leu	Arg	Asn	Asn	Asn	Lys	Val	Tyr	Thr
				565					570					575	
Phe	Phe	Ser	Thr	Asn	Leu	Val	Glu	Lys	Ala	Asn	Thr	Val	Val	Gly	Ala
			580					585					590		
Ser	Leu	Phe	Val	Asn	Trp	Val	Lys	Gly	Val	Ile	Asp	Asp	Phe	Thr	Ser
		595					600					605			
Glu	Ser	Thr	Gln	Lys	Ser	Thr	Ile	Asp	Lys	Val	Ser	Asp	Val	Ser	Ile
	610					615					620				
Ile	Ile	Pro	Tyr	Ile	Gly	Pro	Ala	Leu	Asn	Val	Gly	Asn	Glu	Thr	Ala
625															

		675					680				685				
Asn	Ala	Leu	Lys	Lys	Arg	Asp	Gln	Lys	Trp	Thr	Asp	Met	Tyr	Gly	Leu
	690					695					700				
Ile	Val	Ser	Gln	Trp	Leu	Ser	Thr	Val	Asn	Thr	Gln	Phe	Tyr	Thr	Ile
705					710					715					720
Lys	Glu	Arg	Met	Tyr	Asn	Ala	Leu	Asn	Asn	Gln	Ser	Gln	Ala	Ile	Glu
				725						730					735
Lys	Ile	Ile	Glu	Asp	Gln	Tyr	Asn	Arg	Tyr	Ser	Glu	Glu	Asp	Lys	Met
			740					745					750		
Asn	Ile	Asn	Ile	Asp	Phe	Asn	Asp	Ile	Asp	Phe	Lys	Leu	Asn	Gln	Ser
		755					760					765			
Ile	Asn	Leu	Ala	Ile	Asn	Asn	Ile	Asp	Asp	Phe	Ile	Asn	Gln	Cys	Ser
	770					775					780				
Ile	Ser	Tyr	Leu	Met	Asn	Arg	Met	Ile	Pro	Leu	Ala	Val	Lys	Lys	Leu
785					790					795					800
Lys	Asp	Phe	Asp	Asp	Asn	Leu	Lys	Arg	Asp	Leu	Leu	Glu	Tyr	Ile	Asp
			805						810					815	
Thr	Asn	Glu	Leu	Tyr	Leu	Leu	Asp	Glu	Val	Asn	Ile	Leu	Lys	Ser	Lys
			820					825					830		
Val	Asn	Arg	His	Leu	Lys	Asp	Ser	Ile	Pro	Phe	Asp	Leu	Ser	Leu	Tyr
		835					840					845			
Thr	Lys	Asp	Thr	Ile	Leu	Ile	Gln	Val	Phe	Asn	Asn	Tyr	Ile	Ser	Asn
	850					855					860				
Ile	Ser	Ser	Asn	Ala	Ile	Leu	Ser	Leu	Ser	Tyr	Arg	Gly	Gly	Arg	Leu
865					870					875					880
Ile	Asp	Ser	Ser	Gly	Tyr	Gly	Ala	Thr	Met	Asn	Val	Gly	Ser	Asp	Val
			885						890					895	
Ile	Phe	Asn	Asp	Ile	Gly	Asn	Gly	Gln	Phe	Lys	Leu	Asn	Asn	Ser	Glu
		900						905					910		
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	915						920					925			
Met	Phe	Asp	Asn	Phe	Ser	Ile	Asn	Phe	Trp	Val	Arg	Thr	Pro	Lys	Tyr
	930					935					940				
Asn	Asn	Asn	Asp	Ile	Gln	Thr	Tyr	Leu	Gln	Asn	Glu	Tyr	Thr	Ile	Ile
945					950					955					960
Ser	Cys	Ile	Lys	Asn	Asp	Ser	Gly	Trp	Lys	Val	Ser	Ile	Lys	Gly	Asn
			965						970					975	
Arg	Ile	Ile	Trp	Thr	Leu	Ile	Asp	Val	Asn	Ala	Lys	Ser	Lys	Ser	Ile
		980						985					990		
Phe	Phe	Glu	Tyr	Ser	Ile	Lys	Asp	Asn	Ile	Ser	Asp	Tyr	Ile	Asn	Lys
	995						1000					1005			
Trp	Phe	Ser	Ile	Thr	Ile	Thr	Asn	Asp	Arg	Leu	Gly	Asn	Ala	Asn	Ile
	1010					1015					1020				
Tyr	Ile	Asn	Gly	Ser	Leu	Lys	Lys	Ser	Glu	Lys	Ile	Leu	Asn	Leu	Asp
1025					1030					1035					1040
Arg	Ile	Asn	Ser	Ser	Asn	Asp	Ile	Asp	Phe	Lys	Leu	Ile	Asn	Cys	Thr
			1045						1050					1055	
Asp	Thr	Thr	Lys	Phe	Val	Trp	Ile	Lys	Asp	Phe	Asn	Ile	Phe	Gly	Arg
		1060						1065					1070		
Glu	Leu	Asn	Ala	Thr	Glu	Val	Ser	Ser	Leu	Tyr	Trp	Ile	Gln	Ser	Ser

1075	1080	1085
Thr Asn Thr Leu Lys Asp Phe Trp Gly Asn Pro Leu Arg Tyr Asp Thr		
1090	1095	1100
Gln Tyr Tyr Leu Phe Asn Gln Gly Met Gln Asn Ile Tyr Ile Lys Tyr		
1105	1110	1115
Phe Ser Lys Ala Ser Met Gly Glu Thr Ala Pro Arg Thr Asn Phe Asn		
1125	1130	1135
Asn Ala Ala Ile Asn Tyr Gln Asn Leu Tyr Leu Gly Leu Arg Phe Ile		
1140	1145	1150
Ile Lys Lys Ala Ser Asn Ser Arg Asn Ile Asn Asn Asp Asn Ile Val		
1155	1160	1165
Arg Glu Gly Asp Tyr Ile Tyr Leu Asn Ile Asp Asn Ile Ser Asp Glu		
1170	1175	1180
Ser Tyr Arg Val Tyr Val Leu Val Asn Ser Lys Glu Ile Gln Thr Gln		
1185	1190	1195
Leu Phe Leu Ala Pro Ile Asn Asp Asp Pro Thr Phe Tyr Asp Val Leu		
1205	1210	1215
Gln Ile Lys Lys Tyr Tyr Glu Lys Thr Thr Tyr Asn Cys Gln Ile Leu		
1220	1225	1230
Cys Glu Lys Asp Thr Lys Thr Phe Gly Leu Phe Gly Ile Gly Lys Phe		
1235	1240	1245
Val Lys Asp Tyr Gly Tyr Val Trp Asp Thr Tyr Asp Asn Tyr Phe Cys		
1250	1255	1260
Ile Ser Gln Trp Tyr Leu Arg Arg Ile Ser Glu Asn Ile Asn Lys Leu		
1265	1270	1275
Arg Leu Gly Cys Asn Trp Gln Phe Ile Pro Val Asp Glu Gly Trp Thr		
1285	1290	1295
Glu		