

SEQUENCE LISTING

<110> GENENTECH, INC.

<120> METHODS OF TREATING NEURODEGENERATIVE DISEASES

<130> 01146-0069-00PCT

<150> US 62/477,535

<151> 2017-03-28

<150> US 62/532,696

<151> 2017-07-14

<150> US 62/577,559

<151> 2017-10-26

<150> US 62/580,359

<151> 2017-11-01

<160> 28

<170> PatentIn version 3.5

<210> 1

<400> 1

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<210> 2

<211> 23

<212> PRT

<213> Homo sapiens

<400> 2

Ala Glu Pro Arg Gln Glu Phe Glu Val Met Glu Asp His Ala Gly Thr
1 5 10 15

Tyr Gly Leu Gly Asp Arg Lys
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<210> 3

<400> 3

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<210> 4

<211> 23
<212> PRT
<213> Macaca fascicularis

<400> 4

Ala Glu Pro Arg Gln Glu Phe Asp Val Met Glu Asp His Ala Gly Thr
1 5 10 15

Tyr Gly Leu Gly Asp Arg Lys
20

<210> 5

<400> 5
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<210> 6

<400> 6
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<210> 7

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<210> 8

<400> 8
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<210> 9

<400> 9
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<210> 10
<211> 117
<212> PRT
<213> Unknown

<220>

<223> Murine species

<400> 10

Glu Val Gln Leu Val Glu Ser Gly Gly Asp Leu Ala Lys Pro Gly Gly

1	5	10	15
Ser	Leu	Lys	Leu
	20	Ser	Cys
		Thr	Ala
		25	Ser
		Gly	Leu
		Ile	Phe
		30	Arg
		Ser	Tyr
Gly	Met	Ser	Trp
	35	Val	Arg
		Gln	Thr
		40	Pro
		Asp	Lys
		Arg	Leu
		45	Glu
		Trp	Val
Ala	Thr	Ile	Asn
	50	Ser	Gly
		Gly	Thr
		55	Tyr
		Thr	Tyr
		60	Tyr
		Pro	Asp
		Ser	Val
Lys	Gly	Arg	Phe
65		Thr	Ile
		70	Ser
		Arg	Asp
		Asn	Ala
		75	Lys
		Asn	Thr
		Leu	Tyr
Leu	Gln	Met	Ser
		85	Ser
		Leu	Lys
		Ser	Glu
		90	Asp
		Thr	Ala
		Met	Tyr
		95	Tyr
		Cys	
Ala	Asn	Ser	Tyr
		100	Ser
		Gly	Ala
		Met	Asp
		105	Tyr
		Trp	Gly
		Gln	Gly
		110	Thr
		Ser	
Val	Thr	Val	Ser
		115	Ser

<210> 11
 <211> 112
 <212> PRT
 <213> Unknown

<220>
 <223> Murine species

<400> 11

Asp	Asp	Leu	Leu	Thr	Gln	Thr	Pro	Leu	Ser	Leu	Pro	Val	Ser	Leu	Gly
1				5				10						15	

Asp	Pro	Ala	Ser	Ile	Ser	Cys	Arg	Ser	Ser	Gln	Ser	Ile	Val	His	Ser
		20						25					30		

Asn Gly Asn Thr Tyr Phe Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser

35

40

45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
 50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Gly
 85 90 95

Ser Leu Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 12
 <211> 5
 <212> PRT
 <213> Unknown

<220>
 <223> Murine species

<400> 12

Ser Tyr Gly Met Ser
 1 5

<210> 13
 <211> 17
 <212> PRT
 <213> Unknown

<220>
 <223> Murine species

<400> 13

Thr Ile Asn Ser Gly Gly Thr Tyr Thr Tyr Tyr Pro Asp Ser Val Lys
 1 5 10 15

Gly

<210> 14
<211> 8
<212> PRT
<213> Unknown

<220>
<223> Murine species

<400> 14

Ser Tyr Ser Gly Ala Met Asp Tyr
1 5

<210> 15
<211> 16
<212> PRT
<213> Unknown

<220>
<223> Murine species

<400> 15

Arg Ser Ser Gln Ser Ile Val His Ser Asn Gly Asn Thr Tyr Phe Glu
1 5 10 15

<210> 16
<211> 7
<212> PRT
<213> Unknown

<220>
<223> Murine species

<400> 16

Lys Val Ser Asn Arg Phe Ser
1 5

<210> 17
<211> 9
<212> PRT
<213> Unknown

<220>
<223> Murine species

<400> 17

Phe Gln Gly Ser Leu Val Pro Trp Thr
1 5

<210> 18

<211> 117

<212> PRT

<213> Artificial sequence

<220>

<223> hMTAU heavy chain variable region (VH)

<400> 18

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Leu Ile Phe Arg Ser Tyr
20 25 30

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

Ala Thr Ile Asn Ser Gly Gly Thr Tyr Thr Tyr Tyr Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Asn Ser Tyr Ser Gly Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 19

<211> 112
<212> PRT
<213> Artificial sequence

<220>
<223> hMTAU light chain variable region (VL)

<400> 19

Asp Asp Val Leu Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Ile Val His Ser
20 25 30

Asn Gly Asn Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95

Ser Leu Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 20
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> hMTAU HVR-H1

<400> 20

Ser Tyr Gly Met Ser
1 5

<210> 21
<211> 17
<212> PRT
<213> Artificial sequence

<220>
<223> hMTAU HVR-H2

<400> 21

Thr	Ile	Asn	Ser	Gly	Gly	Thr	Tyr	Thr	Tyr	Tyr	Pro	Asp	Ser	Val	Lys
1				5					10					15	

Gly

<210> 22
<211> 8
<212> PRT
<213> Artificial sequence

<220>
<223> hMTAU HVR-H3

<400> 22

Ser	Tyr	Ser	Gly	Ala	Met	Asp	Tyr
1				5			

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

<220>
<223> hMTAU HVR-L1

<400> 23

Arg	Ser	Ser	Gln	Ser	Ile	Val	His	Ser	Asn	Gly	Asn	Thr	Tyr	Leu	Glu
1				5					10					15	

<210> 24
<211> 7
<212> PRT

<213> Artificial sequence

<220>

<223> hMTAU HVR-L2

<400> 24

Lys Val Ser Asn Arg Phe Ser
1 5

<210> 25

<211> 9

<212> PRT

<213> Artificial sequence

<220>

<223> hMTAU HVR-L3

<400> 25

Phe Gln Gly Ser Leu Val Pro Trp Thr
1 5

<210> 26

<211> 444

<212> PRT

<213> Artificial sequence

<220>

<223> hMTAU heavy chain version 1

<400> 26

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Leu Ile Phe Arg Ser Tyr
20 25 30

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

Ala Thr Ile Asn Ser Gly Gly Thr Tyr Thr Tyr Tyr Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Asn Ser Tyr Ser Gly Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
115 120 125

Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys
130 135 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145 150 155 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
165 170 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
180 185 190

Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn
195 200 205

Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro
210 215 220

Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe
225 230 235 240

Pro Pro Lys Pro Lys Asp Thr Leu Tyr Ile Thr Arg Glu Pro Glu Val
245 250 255

Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe

260

265

270

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
 275 280 285

Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
 290 295 300

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
 305 310 315 320

Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala
 325 330 335

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln
 340 345 350

Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
 355 360 365

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
 370 375 380

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
 385 390 395 400

Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu
 405 410 415

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
 420 425 430

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
 435 440

<210> 27

<211> 443

<212> PRT

<213> Artificial sequence

<220>

<223> hMTAU heavy chain version 2

<400> 27

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Leu Ile Phe Arg Ser Tyr
20 25 30

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

Ala Thr Ile Asn Ser Gly Gly Thr Tyr Thr Tyr Tyr Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Asn Ser Tyr Ser Gly Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
115 120 125

Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys
130 135 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145 150 155 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
165 170 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
180 185 190

Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn
195 200 205

Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro
210 215 220

Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe
225 230 235 240

Pro Pro Lys Pro Lys Asp Thr Leu Tyr Ile Thr Arg Glu Pro Glu Val
245 250 255

Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe
260 265 270

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
275 280 285

Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
290 295 300

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
305 310 315 320

Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala
325 330 335

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln
340 345 350

Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
355 360 365

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro

370

375

380

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
 385 390 395 400

Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu
 405 410 415

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
 420 425 430

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
 435 440

<210> 28

<211> 219

<212> PRT

<213> Artificial sequence

<220>

<223> hMTAU light chain

<400> 28

Asp Asp Val Leu Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly
 1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Ile Val His Ser
 20 25 30

Asn Gly Asn Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
 50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Phe Gln Gly

85

90

95

Ser Leu Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215