

X20624SEQLISTINGST25
SEQUENCE LISTING

<110> ELI LILLY AND COMPANY

<120> ANTIBODIES TO TAU AND USES THEREOF

<130> X20624

<150> US 62/121,116

<151> 2015-02-26

<160> 13

<170> PatentIn version 3.5

<210> 1

<211> 219

<212> PRT

<213> Artificial Sequence

<220>

<223> LC of exemplified tau monoclonal antibody of Example 1

<400> 1

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

Glu Arg Ala Thr Leu Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
 20 25 30

Asn Gln Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
 35 40 45

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

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

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

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Thr Leu Val Pro Leu Thr Phe Gly Gly 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

<210> 2
<211> 442
<212> PRT
<213> Artificial Sequence

<220>
<223> HC of exemplified tau monoclonal antibody of Example 1

<400> 2

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Ser Asn Tyr

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20

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

Gly Glu Ile Leu Pro Gly Ser Asp Ser Ile Lys Tyr Glu Lys Asn Phe
 50 55 60

Lys Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
 65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
 85 90 95

Ala Arg Arg Gly Asn Tyr Val Asp Asp Trp Gly Gln Gly Thr Leu Val
 100 105 110

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

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

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

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

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

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

Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro

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210

215

220

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

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

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

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

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

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

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

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

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

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

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

Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly

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405

410

415

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

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

<210> 3
 <211> 16
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> LCDR1 of exemplified tau monoclonal antibody of Example 1
 <400> 3

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

<210> 4
 <211> 8
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> LCDR2 of exemplified tau monoclonal antibody of Example 1
 <400> 4

Tyr Lys Val Asp Asn Arg Phe Ser
 1 5

<210> 5
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> LCDR3 of exemplified tau monoclonal antibody of Example 1
 <400> 5

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Ser Gln Ser Thr Leu Val Pro Leu Thr
1 5

<210> 6
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> HCDR1 of exemplified tau monoclonal antibody of Example 1

<400> 6

Lys Gly Ser Gly Tyr Thr Phe Ser Asn Tyr Trp Ile Glu
1 5 10

<210> 7
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> HCDR2 of exemplified tau monoclonal antibody of Example 1

<400> 7

Glu Ile Leu Pro Gly Ser Asp Ser Ile Lys Tyr Glu Lys Asn Phe Lys
1 5 10 15

Gly

<210> 8
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> HCDR3 of exemplified tau monoclonal antibody of Example 1

<400> 8

Ala Arg Arg Gly Asn Tyr Val Asp Asp

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1 5

<210> 9
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> LCVR of exemplified tau monoclonal antibody of Example 1

<400> 9

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

Glu Arg Ala Thr Leu Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
 20 25 30

Asn Gln Asn Thr Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala
 35 40 45

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

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

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

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

<210> 10
 <211> 116
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> HCVR of exemplified tau monoclonal antibody of Example 1

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<400> 10

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

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

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

Gly Glu Ile Leu Pro Gly Ser Asp Ser Ile Lys Tyr Glu Lys Asn Phe
50 55 60

Lys Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Arg Gly Asn Tyr Val Asp Asp Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 11

<211> 657

<212> DNA

<213> Artificial Sequence

<220>

<223> Nucleotide Sequence Encoding the Exemplified LC (SEQ ID NO:1)

<400> 11

gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60

ctctcctgca gatctagtca gagccttgta cacagtaatc agaacaccta ttacattgg 120

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taccagcaga aacctggcca ggctcccagg ctctcatct ataaagttga caaccgattt	180
tctggcatcc cagacagggt cagtggcagt gggctctggga cagacttcac tctcaccatc	240
agcagactgg agcctgaaga ttttgcagtg tattactgtt ctcaaagtac actggttccg	300
ctcacgttcg gcggaggggac caaggtggag atcaaacgga ccgtggctgc accatctgtc	360
ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg	420
ctgaataact tctatcccag agaggccaaa gtacagtggga aggtggataa cgccctccaa	480
tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc	540
agcagcacc tgacgtgag caaagcagac tacgagaaac acaaagtcta cgcctgcgaa	600
gtcaccatc agggcctgag ctgccccgtc acaaagagct tcaacagggg agagtgc	657

<210> 12
 <211> 1326
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Nucleotide Sequence Encoding the Exemplified HC (SEQ ID NO: 2)

<400> 12	
gaggtgcagc tgggtgcagtc tggagcagag gtgaaaaagc ccggggagtc tctgaagatc	60
tcctgtaagg gttctggcta cacattcagt aactactgga tagagtgggt gcgccagatg	120
cccgggaaag gcctggagtg gatgggggag attttacctg gaagtgatag tattaagtac	180
gaaaagaatt tcaagggccca ggtcaccatc tcagccgaca agtccatcag caccgcctac	240
ctgcagtgga gcagcctgaa ggcctcggac accgccatgt attactgtgc gagaaggggg	300
aactacgtgg acgactgggg ccagggcacc ctggtcaccg tctcctcagc ttctaccaag	360
ggcccatcgg tcttcccgt agcggcctgc tccaggagca cctccgagag cacagccgcc	420
ctgggctgcc tgggtcaagga ctacttcccc gaaccgggtga cgggtgtcgtg gaactcaggc	480
gccctgacca gcggcgtgca caccttcccc gctgtcctac agtcctcagg actctactcc	540
ctcagcagcg tgggtgaccgt gccctccagc agcttgggca cgaagacctc cacctgcaac	600

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gtagatcaca agcccagcaa caccaagggtg gacaagagag ttgagtccaa atatggtccc	660
ccatgcccac cctgcccagc acctgaggcc gccggggggac catcagtctt cctgttcccc	720
ccaaaaccca aggacactct catgatctcc cggacccctg aggtcacgtg cgtggtggtg	780
gacgtgagcc aggaagaccc cgagggtccag ttcaactggt acgtggatgg cgtggagggtg	840
cataatgcca agacaaaagcc gcgggaggag cagttcaaca gcacgtaccg tgtggtcagc	900
gtcctcaccg tcctgcacca ggactggctg aacggcaagg agtacaagtg caaggctctcc	960
aacaaaggcc tcccgtcctc catcgagaaa accatctcca aagccaaagg gcagccccga	1020
gagccacagg tgtacaccct gccccatcc caggaggaga tgaccaagaa ccaggtcagc	1080
ctgacctgcc tgggtcaaagg cttctacccc agcgacatcg ccgtggagtg ggaaagcaat	1140
gggcagccgg agaacaacta caagaccacg cctcccgtgc tggactccga cggctccttc	1200
ttcctctaca gcaggctaac cgtggacaag agcagggtggc aggaggggaa tgtcttctca	1260
tgctccgtga tgcatgaggc tctgcacaac cactacacac agaagagcct ctccctgtct	1320
ctgggt	1326

<210> 13
 <211> 441
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Amino Acid Sequence of Human, Full-Length Tau

<400> 13

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

Thr	Tyr	Gly	Leu	Gly	Asp	Arg	Lys	Asp	Gln	Gly	Gly	Tyr	Thr	Met	His
		20					25						30		

Gln	Asp	Gln	Glu	Gly	Asp	Thr	Asp	Ala	Gly	Leu	Lys	Glu	Ser	Pro	Leu
	35						40					45			

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Gln Thr Pro Thr Glu Asp Gly Ser Glu Glu Pro Gly Ser Glu Thr Ser
 50 55 60

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

Asp Glu Gly Ala Pro Gly Lys Gln Ala Ala Ala Gln Pro His Thr Glu
 85 90 95

Ile Pro Glu Gly Thr Thr Ala Glu Glu Ala Gly Ile Gly Asp Thr Pro
 100 105 110

Ser Leu Glu Asp Glu Ala Ala Gly His Val Thr Gln Ala Arg Met Val
 115 120 125

Ser Lys Ser Lys Asp Gly Thr Gly Ser Asp Asp Lys Lys Ala Lys Gly
 130 135 140

Ala Asp Gly Lys Thr Lys Ile Ala Thr Pro Arg Gly Ala Ala Pro Pro
 145 150 155 160

Gly Gln Lys Gly Gln Ala Asn Ala Thr Arg Ile Pro Ala Lys Thr Pro
 165 170 175

Pro Ala Pro Lys Thr Pro Pro Ser Ser Gly Glu Pro Pro Lys Ser Gly
 180 185 190

Asp Arg Ser Gly Tyr Ser Ser Pro Gly Ser Pro Gly Thr Pro Gly Ser
 195 200 205

Arg Ser Arg Thr Pro Ser Leu Pro Thr Pro Pro Thr Arg Glu Pro Lys
 210 215 220

Lys Val Ala Val Val Arg Thr Pro Pro Lys Ser Pro Ser Ser Ala Lys
 225 230 235 240

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Ser Arg Leu Gln Thr Ala Pro Val Pro Met Pro Asp Leu Lys Asn Val
 245 250 255

Lys Ser Lys Ile Gly Ser Thr Glu Asn Leu Lys His Gln Pro Gly Gly
 260 265 270

Gly Lys Val Gln Ile Ile Asn Lys Lys Leu Asp Leu Ser Asn Val Gln
 275 280 285

Ser Lys Cys Gly Ser Lys Asp Asn Ile Lys His Val Pro Gly Gly Gly
 290 295 300

Ser Val Gln Ile Val Tyr Lys Pro Val Asp Leu Ser Lys Val Thr Ser
 305 310 315 320

Lys Cys Gly Ser Leu Gly Asn Ile His His Lys Pro Gly Gly Gly Gln
 325 330 335

Val Glu Val Lys Ser Glu Lys Leu Asp Phe Lys Asp Arg Val Gln Ser
 340 345 350

Lys Ile Gly Ser Leu Asp Asn Ile Thr His Val Pro Gly Gly Gly Asn
 355 360 365

Lys Lys Ile Glu Thr His Lys Leu Thr Phe Arg Glu Asn Ala Lys Ala
 370 375 380

Lys Thr Asp His Gly Ala Glu Ile Val Tyr Lys Ser Pro Val Val Ser
 385 390 395 400

Gly Asp Thr Ser Pro Arg His Leu Ser Asn Val Ser Ser Thr Gly Ser
 405 410 415

Ile Asp Met Val Asp Ser Pro Gln Leu Ala Thr Leu Ala Asp Glu Val
 420 425 430

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Ser	Ala	Ser	Leu	Ala	Lys	Gln	Gly	Leu
		435					440	