

CLAIMS

1. An isolated monoclonal antibody that binds to human tau
comprising~~competes for binding to human tau with antibody 9F5.~~

three heavy chain CDRs and three light chain CDRs of a mouse antibody
characterized by a heavy chain variable region having an amino acid sequence comprising SEQ
ID NO: 7 and a light chain variable region having an amino acid sequence comprising SEQ ID
NO: 11;

three heavy chain CDRs and three light chain CDRs of a mouse antibody
characterized by a heavy chain variable region having an amino acid sequence comprising SEQ
ID NO: 219 and a light chain variable region having an amino acid sequence comprising SEQ ID
NO: 11;

three heavy chain CDRs and three light chain CDRs of a mouse antibody
characterized by a heavy chain variable region having an amino acid sequence comprising SEQ
ID NO: 225 and a light chain variable region having an amino acid sequence comprising SEQ ID
NO: 228; or

three heavy chain CDRs and three light chain CDRs of a mouse antibody
characterized by a heavy chain variable region having an amino acid sequence comprising SEQ
ID NO: 240 and a light chain variable region having an amino acid sequence comprising SEQ ID
NO: 244.

2. ~~The antibody of claim 1 that binds to the same epitope on human tau as~~
~~9F5.~~

32. The antibody of claim 1, ~~comprising wherein the antibody comprises the~~
~~three heavy chain CDRs and the three light chain CDRs of three light chain CDRs and three~~
~~heavy chain CDRs of monoclonal antibody 9F5, wherein 9F5 is~~ a mouse antibody characterized
by a heavy chain variable region having an amino acid sequence comprising SEQ ID NO: 7 and
a light chain variable region having an amino acid sequence comprising SEQ ID NO: 11.

43. The antibody of claim 42, wherein the three heavy chain [Kabat/Chothia Composite](#) CDRs CDR-H1, CDR-H2, and CDR-H3 are ~~as defined by Kabat/Chothia Composite~~ (SEQ ID NOs: 8, 9, and 10, respectively), except that [Kabat](#) position H28 can be occupied by N or T, [Kabat](#) position H51 can be occupied by I or V, [Kabat](#) position H54 can be occupied by N or D, and [Kabat](#) position H56 can be occupied by D or E, and the three light chain [Kabat/Chothia Composite](#) CDRs CDR-L1, CDR-L2, and CDR-L3 are ~~as defined by Kabat/Chothia Composite~~ (SEQ ID NOs: 12, 13, and 14, respectively), except that [Kabat](#) position L27b is occupied by L, D, T, or Q, [Kabat](#) position L27c is occupied by L, D, G, S, E, T, N, A, P, or I, [Kabat](#) position L30 can be occupied by I, Y, E, K, G, or Q, [Kabat](#) position L31 can be occupied by T, N, or G, [Kabat](#) position L33 is occupied by L, N, T, S, R, or G, [Kabat](#) position L51 can be occupied by M, G, E, D, K, or I, [Kabat](#) position L54 can be occupied by L, R, G, or T, [Kabat](#) position L89 is occupied by A or G, [Kabat](#) position L92 is occupied by L, D, E, G, Q, T, or I, and [Kabat](#) position L93 is occupied by E or G.

54. The antibody of claim 43, wherein CDR-H1 has an amino acid sequence comprising SEQ ID NO: 50, ~~wherein~~ CDR-H2 has an amino acid sequence comprising SEQ ID NO: 51 or SEQ ID NO: 52, ~~wherein~~ CDR-L1 has an amino acid sequence comprising any [one](#) of SEQ ID NO: 53, SEQ ID NO: 54, and SEQ ID NOs: 172 - 193, ~~wherein~~ CDR-L2 has an amino acid sequence comprising any [one](#) of SEQ ID NO: 55 and SEQ ID NOs: 194 - 205, and ~~wherein~~ CDR-L3 has an amino acid sequence comprising any [one](#) of SEQ ID NOs: 206 - 213.

65. The antibody of any one of ~~the preceding claims~~ [claims 2 - 4](#), wherein the antibody is a humanized antibody [comprising a humanized heavy chain variable region and a humanized light chain variable region](#).

76. The ~~humanized~~ antibody of claim ~~65~~, wherein the humanized ~~mature~~ heavy chain variable region comprises the three Kabat heavy chain CDRs of ~~9F5~~ (SEQ ID NO: 40, SEQ ID NO: 9, and SEQ ID NO: 10), and the humanized ~~mature~~ light chain variable region comprises the three Kabat light chain CDRs of ~~9F5~~ (SEQ ID NOs: 12 - 14).

87. The ~~humanized~~ antibody of ~~any one of claims 1-7~~ [claim 5 or 6](#) wherein at least one of the following positions is occupied by the amino acid as specified: [Kabat position](#) H1 is occupied by Q or E, [Kabat position](#) H5 is occupied by Q or V, [Kabat position](#) H11 is

occupied by L or V, [Kabat position](#) H12 is occupied by V or K, [Kabat position](#) H17 is occupied by S or T, [Kabat position](#) H20 is occupied by L or I, [Kabat position](#) H23 is occupied by T or K, [Kabat position](#) H28 is occupied by N or T, [Kabat position](#) H38 is occupied by K, R, or Q, [Kabat position](#) H40 is occupied by R or A, [Kabat position](#) H42 is occupied by E or G, [Kabat position](#) H43 is occupied by Q or K, [Kabat position](#) H48 is occupied by I or M, [Kabat position](#) H51 is occupied by I or V, [Kabat position](#) H54 is occupied by N or D, [Kabat position](#) H56 is occupied by D or E, [Kabat position](#) H66 is occupied by K or R, [Kabat position](#) H69 is occupied by I or M, [Kabat position](#) H75 is occupied by S or T, [Kabat position](#) H76 is occupied by N or D, [Kabat position](#) H79 is occupied by Y, Q, D, N, or G, [Kabat position](#) H80 is occupied by L, M, P, D, G, or E, [Kabat position](#) H81 is occupied by Q or E, [Kabat position](#) H82 is occupied by L, P, K, R, E, or N, [Kabat position](#) H82a is occupied by S or G, [Kabat position](#) H82c is occupied by L, G, D, or S, [Kabat position](#) H83 is occupied by T or R, [Kabat position](#) H93 is occupied by A or T, [Kabat position](#) H94 is occupied by S or T, [Kabat position](#) H108 is occupied by T or L, [Kabat position](#) H109 is occupied by L or V, [Kabat position](#) L3 is V or Q, [Kabat position](#) L7 is A or S, [Kabat position](#) L8 is A or P, [Kabat position](#) L9 is F or L, [Kabat position](#) L11 is N or L, [Kabat position](#) L15 is L or P, [Kabat position](#) L17 is T or E, [Kabat position](#) L18 is S or P, [Kabat position](#) L27b is L, D, T, or Q, [Kabat position](#) L27c is L, D, G, S, E, T, N, A, P, or I, [Kabat position](#) L30 is I, Y, E, K, or G, [Kabat position](#) L31 is T, N, or G, [Kabat position](#) L33 is L, N, T, S, R, or G, [Kabat position](#) L37 is L, Q, G, or I, [Kabat position](#) L39 is R or K, [Kabat position](#) L51 is M, G, E, D, K, or I, [Kabat position](#) L54 is R, G, or T, [Kabat position](#) L60 is N or D, [Kabat position](#) L64 is G or S, [Kabat position](#) L66 is E or G, [Kabat position](#) L73 is L, P, or G, [Kabat position](#) L74 is R or K, [Kabat position](#) L75 is I, D, P, Q, or G, [Kabat position](#) L76 is S, P, or G, [Kabat position](#) L77 is R or D, [Kabat position](#) L78 is V, R, D, E, P, K, G, or Q, [Kabat position](#) L85 is V or G, [Kabat position](#) L86 is Y or T, [Kabat position](#) L89 is A or G, [Kabat position](#) L92 is L, D, E, G, Q, T, or I, [Kabat position](#) L93 is E or G, and [Kabat position](#) L100 is G or Q.

98. The ~~humanized~~ antibody of claim 87, wherein the ~~humanized~~ heavy chain variable region comprises the amino acid sequence of SEQ ID NO:127 or SEQ ID NO:128.

109. The ~~humanized~~ antibody of ~~any one of claims 1-7~~ claim 5 or 6 wherein the ~~mature-humanized~~ heavy chain variable region has an amino acid sequence of any one of SEQ ID NOs: 15-22 and SEQ ID NOs: 109-129, and the ~~mature-humanized~~ light chain variable region

has an amino acid sequence of any one of SEQ ID NO: 23-29, SEQ ID NOs: 61-108, and SEQ ID NOs: 130-171.

~~1110.~~ The ~~humanized~~ antibody of claim ~~109~~, wherein: the ~~mature-humanized~~ heavy chain variable region has an amino acid sequence of SEQ ID NO: 127 and the ~~mature~~ ~~humanized~~ light chain variable region has an amino acid sequence of SEQ ID NO: 149; ~~or~~

~~wherein~~ the ~~mature-humanized~~ heavy chain variable region has an amino acid sequence of SEQ ID NO: 127 and the ~~humanized~~ ~~mature~~ light chain variable region has an amino acid sequence of SEQ ID NO: 142; ~~or~~;

~~wherein~~ the ~~humanized~~ ~~mature~~ heavy chain variable region has an amino acid sequence of SEQ ID NO: 127 and the ~~humanized~~ ~~mature~~ light chain variable region has an amino acid sequence of SEQ ID NO: 159; ~~or~~;

~~wherein~~ the ~~humanized~~ ~~mature~~ heavy chain variable region has an amino acid sequence of SEQ ID NO: 127 and the ~~humanized~~ ~~mature~~ light chain variable region has an amino acid sequence of SEQ ID NO: 148; ~~or~~;

~~wherein~~ the ~~humanized~~ ~~mature~~ heavy chain variable region has an amino acid sequence of SEQ ID NO: 127 and the ~~humanized~~ ~~mature~~ light chain variable region has an amino acid sequence of SEQ ID NO: 137; ~~or~~;

~~wherein~~ the ~~humanized~~ ~~mature~~ heavy chain variable region has an amino acid sequence of SEQ ID NO: 127 and the ~~humanized~~ ~~mature~~ light chain variable region has an amino acid sequence of SEQ ID NO: 145; ~~or~~;

~~wherein~~ the ~~humanized~~ ~~mature~~ heavy chain variable region has an amino acid sequence of SEQ ID NO: 127 and the ~~humanized~~ ~~mature~~ light chain variable region has an amino acid sequence of SEQ ID NO: 136; ~~or~~;

~~wherein~~ the ~~humanized~~ ~~mature~~ heavy chain variable region has an amino acid sequence of SEQ ID NO: 127 and the ~~humanized~~ ~~mature~~ light chain variable region has an amino acid sequence of SEQ ID NO: 138; ~~or~~;

~~wherein~~ the ~~humanized mature~~ heavy chain variable region has an amino acid sequence of SEQ ID NO: ~~127~~ and the ~~humanized mature~~ light chain variable region has an amino acid sequence of SEQ ID NO: ~~158~~, ~~or~~;

~~wherein~~ the ~~humanized mature~~ heavy chain variable region has an amino acid sequence of SEQ ID NO: ~~127~~ and the ~~humanized mature~~ light chain variable region has an amino acid sequence of SEQ ID NO: ~~143~~, ~~or~~;

~~wherein~~ the ~~humanized mature~~ heavy chain variable region has an amino acid sequence of SEQ ID NO: ~~127~~ and the ~~humanized mature~~ light chain variable region has an amino acid sequence of SEQ ID NO: ~~144~~, ~~or~~;

~~wherein~~ the ~~humanized mature~~ heavy chain variable region has an amino acid sequence of SEQ ID NO: ~~127~~ and the ~~humanized mature~~ light chain variable region has an amino acid sequence of SEQ ID NO: ~~133~~, ~~or~~;

~~wherein~~ the ~~humanized mature~~ heavy chain variable region has an amino acid sequence of SEQ ID NO: ~~127~~ and the ~~humanized mature~~ light chain variable region has an amino acid sequence of SEQ ID NO: ~~160~~, ~~or~~;

~~wherein~~ the ~~humanized mature~~ heavy chain variable region has an amino acid sequence of SEQ ID NO: ~~127~~ and the ~~humanized mature~~ light chain variable region has an amino acid sequence of SEQ ID NO: ~~161~~, ~~or~~;

~~wherein~~ the ~~humanized mature~~ heavy chain variable region has an amino acid sequence of SEQ ID NO: ~~127~~ and the ~~humanized mature~~ light chain variable region has an amino acid sequence of SEQ ID NO: ~~139~~, ~~or~~

~~wherein~~ the ~~humanized mature~~ heavy chain variable region has an amino acid sequence of SEQ ID NO: ~~128~~ and the ~~humanized mature~~ light chain variable region has an amino acid sequence of SEQ ID NO: ~~168~~.

12. — ~~The antibody of claim 1, comprising three light chain CDRs and three heavy chain CDRs of monoclonal antibody 10C12, wherein 10C12 is a mouse antibody characterized by a heavy chain variable region having an amino acid sequence comprising SEQ~~

~~ID NO:7 and a light chain variable region having an amino acid sequence comprising SEQ ID NO:11.~~

~~13. The antibody of claim 12, wherein the antibody is a humanized antibody.~~

~~1411.~~ The ~~humanized~~ antibody of claim ~~13-5~~ wherein the humanized ~~mature~~ heavy chain variable region comprises the three Kabat heavy chain CDRs of ~~10C12~~ (SEQ ID NO: 40, SEQ ID NO: 9, and SEQ ID NO: 10) and the humanized ~~mature~~ light chain variable region comprises the three Kabat light chain CDRs of ~~10C12~~ (SEQ ID NOs: 12-14).

~~1512.~~ The ~~humanized~~ antibody of ~~any one of claims 12-14~~ claim 11 wherein at least one of the following positions is occupied by the amino acid as specified: Kabat position H1 is occupied by Q or E, Kabat position H24 is occupied by A, Kabat position H48 is occupied by I, Kabat position H67 is occupied by A, Kabat position H69 is occupied by M, Kabat position H93 is occupied by T, Kabat position H94 is occupied by T, Kabat position L64 is S, and Kabat position L104 is V or L.

~~1613.~~ The ~~humanized~~ antibody of ~~any one of claims 12-14~~ claim 11 wherein the ~~mature-humanized~~ heavy chain variable region has an amino acid sequence of ~~any one of~~ SEQ ID NOs: 214- or 215 and the ~~mature-humanized~~ light chain variable region has an amino acid sequence of ~~any one of~~ SEQ ID NO: 216- or 217.

~~1714.~~ The antibody of claim 1, wherein the antibody comprises the comprising three light-heavy chain CDRs and the three heavy-light chain CDRs of ~~monoclonal antibody 12C4, wherein 12C4 is~~ a mouse antibody characterized by a heavy chain variable region having an amino acid sequence comprising SEQ ID NO: 219 and a light chain variable region having an amino acid sequence comprising SEQ ID NO: 11.

~~1815.~~ The antibody of claim ~~1417~~, wherein the antibody is a humanized antibody comprising a humanized heavy chain variable region and a humanized light chain variable region.

~~1916.~~ The ~~humanized~~ antibody of claim ~~18-15~~ wherein the humanized ~~mature~~ heavy chain variable region comprises the three Kabat heavy chain CDRs of ~~12C4~~ (SEQ ID NO:

40, SEQ ID NO: 220, and SEQ ID NO: 10), and the humanized ~~mature~~-light chain variable region comprises the three Kabat light chain CDRs of ~~12C4~~ (SEQ ID NOs: 12-14).

~~2017~~. The ~~humanized~~-antibody of any one of claims ~~17-19~~14-16, wherein at least one of the following positions is occupied by the amino acid as specified: Kabat position H1 is occupied by Q or E, Kabat position H48 is occupied by M or I, Kabat position H93 is occupied by A or T, Kabat position H94 is occupied by R or T, Kabat position L64 is G or S, and Kabat position L104 is V or L.

~~2118~~. The ~~humanized~~-antibody of ~~any one of claims 17-19~~claim 15 or 16, wherein the ~~mature-humanized~~ heavy chain variable region has an amino acid sequence ~~of any one of~~ SEQ ID NOs: ~~221 or~~ 222 and the ~~mature-humanized~~ light chain variable region has an amino acid sequence of ~~any one of~~ SEQ ID NO: ~~223- or~~ 224.

~~2219~~. The antibody of claim 1, wherein the antibody comprises the ~~comprising~~ three light-heavy chain CDRs and the three heavy-light chain CDRs of ~~monoclonal antibody 17C12, wherein 17C12 is~~ a mouse antibody characterized by a heavy chain variable region having an amino acid sequence comprising SEQ ID NO: 225 and a light chain variable region having an amino acid sequence comprising SEQ ID NO: 228.

~~2320~~. The antibody of claim ~~2219~~, wherein the antibody is a humanized antibody comprising a humanized heavy chain variable region and a humanized light chain variable region.

~~2421~~. The ~~humanized~~-antibody of claim ~~23-20~~ wherein the humanized ~~mature~~ heavy chain variable region comprises the three Kabat heavy chain CDRs of ~~17C12~~ (SEQ ID NO: 40, SEQ ID NO: 227, and SEQ ID NO: 10), and the humanized ~~mature~~-light chain variable region comprises the three Kabat light chain CDRs of ~~17C12~~ (SEQ ID NOs: 229-231).

~~2522~~. The ~~humanized~~-antibody of any one of claims ~~22-24~~19-21, wherein at least one of the following positions is occupied by the amino acid as specified: Kabat position H1 is occupied by Q or E, Kabat position H2 is occupied by I, Kabat position H24 is occupied by A, Kabat position H48 is occupied by I, Kabat position H67 is occupied by A, Kabat position H69 is occupied by M, Kabat position H93 is occupied by T, Kabat position H94 is occupied by

T, [Kabat position](#) H108 is occupied by T or L, [Kabat position](#) H113 is occupied by R or S, [Kabat position](#) L2 is V, [Kabat position](#) L36 is L, and [Kabat position](#) L43 is P or S.

[2623](#). The ~~humanized~~ antibody of [claim 20 or 21](#) ~~any one of claims 22-24~~, wherein the ~~mature-humanized~~ heavy chain variable region has an amino acid sequence of ~~any one of~~ SEQ ID NO: [232](#) ~~or~~ [233](#) and the ~~humanized mature~~ light chain variable region has an amino acid sequence of ~~any one of~~ SEQ ID NO: [234](#) ~~or~~ [235](#).

[2724](#). The antibody of claim 1, [wherein the antibody comprises the comprising](#) three ~~light-heavy~~ chain CDRs and three ~~heavy-light~~ chain CDRs of ~~monoclonal antibody 14H3~~, ~~wherein 14H3 is~~ a mouse antibody characterized by a heavy chain variable region having an amino acid sequence comprising SEQ ID NO: [240](#) and a light chain variable region having an amino acid sequence comprising SEQ ID NO: [244](#).

[2825](#). The antibody of claim [2724](#), wherein the three heavy chain [Kabat/Chothia Composite](#) CDRs CDR-H1, CDR-H2, and CDR-H3 are ~~as defined by Kabat/Chothia Composite~~ (SEQ ID NOs: [241](#), [242](#), and [243](#), respectively), except that [Kabat](#) position H35B can be occupied by G or S, and the three light chain [Kabat/Chothia Composite](#) CDRs CDR-L1, CDR-L2, and CDR-L3 are ~~as defined by Kabat/Chothia Composite~~ (SEQ ID NOs: [245](#), [246](#), and [247](#), respectively).

~~29. The antibody of claim 28, wherein CDR-H1 has an amino acid sequence comprising SEQ ID NO: 277.~~

[3026](#). The antibody of ~~any one of claims 27-29~~ [claim 24 or 25](#), wherein the antibody is a humanized antibody [comprising a humanized heavy chain variable region and a humanized light chain variable region](#).

[3127](#). The ~~humanized~~ antibody of claim ~~30-26~~, wherein the humanized ~~mature~~ heavy chain variable region comprises the three Kabat heavy chain CDRs of ~~14H3~~ (SEQ ID NO: [265](#), SEQ ID NO: [242](#), and SEQ ID NO: [243](#)), and the humanized ~~mature~~ light chain variable region comprises the three Kabat light chain CDRs of ~~14H3~~ (SEQ ID NOs: [245](#)-[247](#)).

3228. The ~~humanized~~ antibody of any one of claims ~~27-31-24-27~~, wherein at least one of the following positions is occupied by the amino acid as specified: Kabat position H35B is occupied by S, Kabat position H108 is occupied by M or L, Kabat position H113 is occupied by L or S, Kabat position L2 is V, L7 is T or S, Kabat position L37 is L or Q, Kabat position L87 is F, Kabat position L100 is G or Q, and Kabat position L104 is V or L.

3329. The ~~humanized~~ antibody of ~~any one of claims 27-31~~ claim 26 or 27, wherein the ~~mature-humanized~~ heavy chain variable region has an amino acid sequence of ~~any one of~~ SEQ ID NOs: ~~248- or~~ 249 and the ~~mature-humanized~~ light chain variable region has an amino acid sequence of ~~any one of~~ SEQ ID NO: ~~250- or~~ 251.

3430. The antibody of any one of claims 1-~~33-29~~ that is an intact antibody.

3531. The antibody of any one of claims 1-~~33-29~~ that is an ~~an~~ -antigen-binding fragment.

3632. The antibody of any one of ~~the preceding claims~~ claims 1-30, wherein the isotype is human IgG1, human IgG2, or human IgG4.

3733. The ~~humanized~~ antibody of any one of claims ~~5-46-11, 13-16~~ 11-13, 18-21 ~~15-18, 23-26~~ 20-23, and ~~30-36~~ 26-32 wherein the ~~mature~~-light chain variable region is fused to a light chain constant region and the ~~mature~~-heavy chain variable region is fused to a heavy chain constant region.

3834. The ~~humanized~~ antibody of claim 3733, wherein the heavy chain constant region is a mutant form of a natural human heavy chain constant region which has reduced binding to a Fcγ receptor relative to the natural human heavy chain constant region.

3935. A pharmaceutical composition comprising an antibody as defined in any of claims 1-~~38-34~~ and a pharmaceutically-acceptable carrier.

4036. A nucleic acid encoding the heavy chain and/or light chain of an antibody as described in any one of claims 1-~~39~~ 34.

4137. A method of humanizing a mouse antibody, the method comprising:

- (a) selecting one or more acceptor antibody sequences;
- (b) identifying amino acid residues of the mouse antibody to be retained;
- (c) synthesizing a nucleic acid encoding a humanized heavy chain comprising CDRs of the mouse antibody heavy chain and a nucleic acid encoding a humanized light chain comprising CDRs of the mouse antibody light chain; and
- (d) expressing the nucleic acids in a host cell to produce a humanized antibody;

wherein:

the mouse antibody is ~~9F5~~, wherein ~~9F5~~ is characterized by a ~~mature~~ heavy chain variable region of SEQ ID NO:7 and a ~~mature~~ light chain variable region of SEQ ID NO:11;

~~wherein the mouse antibody is 10C12, wherein 10C12 is characterized by a mature heavy chain variable region of SEQ ID NO:7 and a mature light chain variable region of SEQ ID NO:11;~~

~~wherein the mouse antibody is 2D11, wherein 2D11 is characterized by a mature heavy chain variable region of SEQ ID NO:7 and a mature light chain variable region of SEQ ID NO:11;~~

~~wherein the mouse antibody is 12C4, wherein 12C4 is characterized by a mature heavy chain variable region of SEQ ID NO: 219 and a mature light chain variable region of SEQ ID NO: 11;~~

~~wherein the mouse antibody is 17C12, wherein 17C12 is characterized by a mature heavy chain variable region of SEQ ID NO: 225 and a mature light chain variable region of SEQ ID NO: 228; or~~

~~wherein the mouse antibody is 14H3, wherein 14H3 is characterized by a mature heavy chain variable region of SEQ ID NO: 240 and a mature light chain variable region of SEQ ID NO: 244.~~

~~42. — Use of an antibody of any one of claims 1-39 in the manufacture of a medicament for inhibiting or reducing aggregation of tau.~~

~~4338. Use of an antibody as defined by any one of claims 1-39-34 in the manufacture of a medicament for treating or effecting prophylaxis of a tau-related disease.~~

~~44. — The use of claim 43~~ wherein the tau-related disease is Alzheimer's disease, Down's syndrome, mild cognitive impairment, primary age-related tauopathy, postencephalitic parkinsonism, posttraumatic dementia or dementia pugilistica, Pick's disease, type C Niemann-Pick disease, supranuclear palsy, frontotemporal dementia, frontotemporal lobar degeneration, argyrophilic grain disease, globular glial tauopathy, amyotrophic lateral sclerosis/parkinsonism dementia complex of Guam, corticobasal degeneration (CBD), dementia with Lewy bodies, Lewy body variant of Alzheimer disease (LBVAD), chronic traumatic encephalopathy (CTE), globular glial tauopathy (GGT), Parkinson's disease, or progressive supranuclear palsy (PSP).

~~45. — An isolated monoclonal antibody that specifically binds to a peptide consisting of residues (Q/E)IVYK(S/P) (SEQ ID NO:56), or QIVYKP (SEQ ID NO:57), or EIVYKSP (SEQ ID NO:58), or EIVYKS (SEQ ID NO:277).~~

~~46. — Use of an immunogen comprising a tau peptide of up to 20 contiguous amino acids of SEQ ID NO:1 to which antibody 9F5, 10C12, 2D11, 12C4, 17C12, or 14H3 specifically binds, wherein the peptide induces formation of antibodies specifically binding to tau in the manufacture of a medicament for treating or effecting prophylaxis of a tau-related disease.~~