CLAIMS

1. An isolated antibody, wherein the antibody binds to one or more tau epitopes and is capable of two or more of the following:

a) displaying a higher affinity for pathological tau than for physiological tau;

b) inhibiting tau-tau aggregation; and

c) mediating uptake and degradation of pathological tau protein by microglia; and wherein each tau epitope comprises an aggregation-promoting region of tau.

2. The isolated antibody according to claim 1, wherein each of the one or more epitopes is independently selected from epitopes within:

i. position 267-273 or residues KHQPGGG (SEQ ID NO: 98), relative to tau_{441};

ii. position 298-304 or residues KHVPGGG (SEQ ID NO: 99), relative to tau_{441}

iii. position 329-335 or residues HHKPGGG (SEQ ID NO: 100), relative to tau_{441}; and

iv. position 361-367 or residues THVPGGG (SEQ ID NO: 101), relative to tau_{441}.

3. The isolated antibody according to claim 2, wherein each of the one or more epitopes is independently selected from epitopes within:

i. position 268-273 or residues HQPGGG (SEQ ID NO: 223), relative to tau_{441};

ii. position 299-304 or residues HVPGGG (SEQ ID NO: 154), relative to tau_{441}

iii. position 330-335 or residues HKPGGG (SEQ ID NO: 224), relative to tau_{441}; and

iv. position 362-367 or residues HVPGGG (SEQ ID NO: 154), relative to tau_{441}.

4. The isolated antibody according to one of claims 1-3, wherein the antibody is capable of binding to one or more forms of pathological tau chosen from misordered tau, misdisordered tau, sarkosyl-insoluble tau, neurofibrillary tangles, neuropil threads, and neuritic plaques in a brain biopsy of a human Alzheimer's disease patient, in a brain sample from an animal model of Alzheimer's disease, or in both.

5. The isolated antibody according to one of claims 1-4, wherein at least one of the epitopes is conformational.

6. An isolated antibody that binds one or more epitopes on tau in a conformationally-specific manner wherein:

a) each of the one or more epitopes is independently selected from epitopes within:
   i. position 267-273 or residues KHQPGGG (SEQ ID NO: 98), relative to tau_{441};
   ii. position 298-304 or residues KHVPGGG (SEQ ID NO: 99), relative to tau_{441}
   iii. position 329-335 or residues HHKPGGG (SEQ ID NO: 100), relative to tau_{441}; and
   iv. position 361-367 or residues THVPGGG (SEQ ID NO: 101), relative to tau_{441};
b) zero, one, two, or three of the epitopes is a linear epitope; and
c) one, two, three, or four of the epitopes is a conformational epitope.

7. An isolated antibody that binds one or more epitopes on tau in a conformationally-specific manner wherein:

a) each of the one or more epitopes is independently selected from epitopes within:
   i. position 268-273 or residues HQPGGG (SEQ ID NO: 223), relative to tau_{441};

ii. position 299-304 or residues HVPGGG (SEQ ID NO: 154), relative to tau_{441}

iii. position 330-335 or residues HKPGGG (SEQ ID NO: 224), relative to tau_{441}; and

iv. position 362-367 or residues HVPGGG (SEQ ID NO: 154), relative to tau_{441}.

b) zero, one, two, or three of the epitopes is a linear epitope; and

c) one, two, three, or four of the epitopes is a conformational epitope.

8. The isolated antibody according to one of claims 1 and 6, wherein the antibody is DC8E8, and wherein DC8E8 is an antibody produced by the hybridoma deposited under American Type Culture Collection Patent Deposit no. PTA-11994.

9. The isolated antibody according to one of claims 1-7, wherein the antibody binds to one or more of the same epitopes on tau as those bound by DC8E8.

10. The isolated antibody according to one of claims 1-7, wherein the antibody competes with monoclonal antibody DC8E8 for binding to tau.

11. An isolated antibody comprising in its epitope binding domain one or more complementarity determining region (CDR) sequences chosen from:

i. QSLLNSRTRKNY (SEQ ID NO: 117)

ii. WAS (SEQ ID NO: 118)

iii. KQSFYLRT (SEQ ID NO: 119)

iv. GYIFTDYVIS (SEQ ID NO: 120)

v. IFPRSGST (SEQ ID NO: 121); and

vi. ARDYYGTSFAMDY (SEQ ID NO: 122).

12. The isolated antibody according to one of claims 1-7, comprising in its epitope binding domain one or more CDR sequences chosen from:

i. QSLLNSRTRKNY (SEQ ID NO: 117)
ii.WAS (SEQ ID NO: 118)
iii.KQSFYLRT (SEQ ID NO: 119)
iv.GYIFTDYVIS (SEQ ID NO: 120)
v.IFPRSGST (SEQ ID NO: 121); and
vi.ARDYYGTSFAMDY (SEQ ID NO: 122).

13. The isolated antibody according to any one of claims 11 and 12, wherein the antibody comprises:

a) an antibody light chain variable region comprising:
    i. QSLLNSRTRKNY (SEQ ID NO: 117) or SEQ ID NO: 247 for CDR1;
    ii. WAS (SEQ ID NO: 118) or SEQ ID NO: 253 for CDR2; and
    iii. KQSFYLRT (SEQ ID NO: 119) or any one of SEQ ID NOs: 255, 257, 258, 259, and 260 for CDR3; and
b) an antibody heavy chain variable region comprising:
    i. GYIFTDYVIS (SEQ ID NO: 120), SEQ ID NO: 261, or SEQ ID NO: 262 for CDR1;
    ii. IFPRSGST (SEQ ID NO: 121), SEQ ID NO: 264, or SEQ ID NO: 265 for CDR2; and
    iii. ARDYYGTSFAMDY (SEQ ID NO: 122), SEQ ID NO: 266, SEQ ID NO: 267, or SEQ ID NO: 269 for CDR3.

14. The isolated antibody according to any one of claims 11 and 12, wherein the antibody comprises:

a) an antibody light chain variable region comprising:
    i. QSLLNSRTRKNY (SEQ ID NO: 117) for CDR1;
    ii. WAS (SEQ ID NO: 118) for CDR2; and
    iii. KQSFYLRT (SEQ ID NO: 119) for CDR3; and
b) an antibody heavy chain variable region comprising:
    iv. GYIFTDYVIS (SEQ ID NO: 120) for CDR1

v. IFPRSGST (SEQ ID NO: 121) for CDR2; and

vi. ARDYYGTSFAMDY (SEQ ID NO: 122) for CDR1.

15. The isolated antibody according to one of claims 1-7, wherein the antibody comprises:

a) one or more sequences of the light chain CDRs from the monoclonal antibody DC8E8, or one or more sequences having at least 80% identity after optimum alignment with one of these light chain CDRs; and

b) one or more sequences of the heavy chain CDRs from the monoclonal antibody DC8E8, or one or more sequences having at least 80% identity after optimum alignment with one of these heavy chain CDRs;

and wherein:

i. the light chain CDRs comprise a sequence chosen from QSLLNSRTRKNY (SEQ ID NO: 117), WAS (SEQ ID NO: 118), and KQSFYLRT (SEQ ID NO: 119); and

ii. the heavy chain CDRs comprise a sequence chosen from GYIFTDYVIS (SEQ ID NO: 120), IFPRSGST (SEQ ID NO: 121), and ARDYYGTSFAMDY (SEQ ID NO: 122).

16. The isolated antibody according to one of claims 1-7, wherein the antibody comprises:

a) one or more sequences of the light chain CDRs from the monoclonal antibody DC8E8, or one or more sequences having at least 80% identity after optimum alignment with one of these light chain CDRs; and

b) one or more sequences of the heavy chain CDRs from the monoclonal antibody DC8E8, or one or more sequences having at least 80% identity after optimum alignment with one of these heavy chain CDRs;

and wherein:

i. the light chain CDRs comprise a sequence chosen from QSLLNSRTRKNY (SEQ ID NO: 117), WAS (SEQ ID NO: 118), KQSFYLRT (SEQ ID NO: 119), SEQ ID

NO: 247, SEQ ID NO: 253, SEQ ID NO: 255, SEQ ID NO: 257, SEQ ID NO: 258, SEQ ID NO: 259, and SEQ ID NO: 260; and

ii. the heavy chain CDRs comprise a sequence chosen from GYIFTDYVIS (SEQ ID NO: 120), IFPRSGST (SEQ ID NO: 121), ARDYYGTSFAMDY (SEQ ID NO: 122), SEQ ID NO: 261, SEQ ID NO: 262, SEQ ID NO: 264, SEQ ID NO: 265, SEQ ID NO: 266, SEQ ID NO: 267, and SEQ ID NO: 269.

17. An isolated antibody, wherein the antibody is:
an Fab, Fab', $F(ab')_2$, Fabc, Fv fragment, or any other antigen-binding fragment; or
an antigen-binding antibody portion; and
wherein the antibody has one or more of the immunological binding characteristics of the antibody according to one of claims 1-7.

18. An isolated antibody that competitively binds to tau with the isolated antibody according to one of claims 1-17.

19. An isolated antibody that competitively binds to tau with the isolated DC8E8 antibody according to claim 6.

20. The isolated antibody according to one of claims 1-7 and 10-19, wherein the antibody is chosen from :

a) a monoclonal antibody;
b) a polyclonal antibody;
c) a recombinant antibody;
d) a chimeric antibody;
e) a humanized antibody;
f) a human antibody; and
g) an antigen-binding fragment or antigen-binding portion of anyone of (a) through (f).

21. The isolated antibody according to one of claims 1-7 and 9-20, wherein the antibody is raised in a mammal.

22. The isolated antibody according to one of claims 1-7 and 9-20, wherein the antibody is produced by a recombinant animal or by a recombinant host cell.

23. The isolated antibody according to one of claims 1-22, wherein the antibody is detectably labeled with one or more labeling agents.

24. The isolated antibody according to claim 23, wherein at least one labeling agent is chosen from an enzyme, a radioisotope, a fluorophore, a nuclear magnetic resonance marker, and a heavy metal.

25. The antibody according to one of claims 1-24, further comprising at least one drug attached to the antibody.

26. An isolated nucleic acid encoding at least the binding domain or variable region of an immunoglobulin chain of the antibody according to one of claims 1-7 and 9-20.

27. An isolated vector comprising the nucleic acid according to claim 21.

28. An isolated host cell comprising the isolated nucleic acid according to claim 26 and/or a vector according to claim 27.

29. An isolated cell line expressing the isolated antibody according to one of claims 1-7 and 9-20.

30. The isolated cell line according to claim 29, wherein the cell line is a hybridoma.

31. The isolated cell line according to claim 30, wherein the cell line is the hybridoma from which monoclonal antibody DC8E8 is produced.

32. An isolated antibody according to one of claims 1-7 and 9-20 for use as a drug or in the manufacture of a medicament for diagnosis, prevention, or treatment of Alzheimer's disease or related tauopathies.

33. An isolated nucleic acid according to claim 26 for use as a drug or in the manufacture of a medicament for treatment of Alzheimer's disease or related tauopathies.

34. A pharmaceutical composition comprising the antibody according to one of claims 1-25 and a pharmaceutically acceptable carrier and/or diluent.

35. A pharmaceutical composition comprising a combination of antibodies and a pharmaceutically acceptable carrier and/or diluent, wherein the combination comprises at least two different antibodies, and wherein each of the antibodies is independently selected from the antibodies of one of claims 1-25.

36. A composition comprising at least one antibody according to claims 1-25 and a diluent or a carrier.

37. The composition according to claim 36, further comprising at least one compound or agent selected from a detectable label, keyhole limpet hemocyanin, tetanus toxoid or a toxoid derived from other pathogenic bacteria, serum albumins, bovine serum albumin, an immunoglobulin molecule or fragment thereof, thyroglobulin, ovoglobulin, a universal T-cell epitope, a cytokine, a chemokine, IL-1α, IL-1β, IL-2, IL-10, IFN-γ, GM-CSF, MIP1α, MIP1β, and RANTES.

38. An article of manufacture for pharmaceutical or diagnostic use, comprising packaging material and a container comprising a solution of a lyophilized form of the antibody according to one of claims 1-25.

39. The article of manufacture according to claim 39, wherein the container is a component of a device or system for delivery of the antibody to a subject.

40. A medical device comprising the antibody according to one of claims 1-25, wherein the device is suitable for contacting or administering the antibody by at least one mode selected from parenteral, subcutaneous, intramuscular, intravenous, intrarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracerebellar, intracerebroventricular, intrathecal, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal, intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, intralesional, bolus, vaginal, rectal, buccal, sublingual, intranasal, and transderrnal.

41. An effective amount of at least one antibody according to one of claims 1-25 for use in the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies

42. The antibody according to claim 41, wherein the antibody is capable of reducing motor impairment, improving motor function, reducing cognitive impairment, improving cognitive function, or a combination thereof.

43. An effective amount of at least one antibody according to one of claims 1-25 for use in ameliorating at least one of the symptoms associated with of Alzheimer's disease or related tauopathies

44. A method of diagnosing or screening a subject for the presence of Alzheimer's disease or a related tauopathy in a subject, or for determining a subject's risk for developing Alzheimer's disease or a related tauopathy, the method comprising:

a) contacting a cell, tissue, organ, fluid, or any other sample of the subject, with an effective amount of at least one antibody according to one of claims 1-25; and

b) determining the presence of a complex comprising pathological tau and the antibody, wherein the presence of the complex is diagnostic of Alzheimer's disease or a related tauopathy associated with the presence of pathological tau.

45. A method of monitoring a subject for the presence, progression, regression, or stabilization of Alzheimer's disease or related tauopathies in a subject, or for determining the stage of Alzheimer's disease or related tauopathies in a subject, the method comprising:

a) contacting a cell, tissue, organ, fluid, or any other sample of the subject, with an effective amount of at least one antibody according to one of claims 1-25; and
b) determining the presence of a complex comprising pathological tau and the antibody, wherein the presence of the complex is diagnostic of Alzheimer's disease or a related tauopathy associated with the presence of pathological tau.

46. The antibody or method according to one of claims 41-45, wherein the effective amount of each antibody is at least 1 mg/kg body weight of the subject, per dose.

47. The antibody or method according to one of claims 41-45, wherein the effective amount of each antibody is at least 10 mg/kg body weight of the subject, per dose.

48. The antibody or method according to one of claims 41-47, wherein at least one of the antibodies is to be administered in multiple dosages over a period of at least six months.

49. The antibody or method according to one of claims 41-48, wherein the antibody is to be administered peripherally to a human subject to exert its beneficial effects.

50. The antibody or method according to claim 49, wherein the antibody, when administered peripherally to a human subject, binds to soluble tau, sarkosyl-insoluble tau, or to both.

51. The antibody or method according to claim 50, wherein the antibody, when administered peripherally to a human subject, binds to both soluble tau and sarkosyl-insoluble tau.

52. The antibody or method according to claim 50 wherein the antibody, when administered peripherally to a human subject, binds to tau, wherein tau is in one or more pathological forms chosen from misordered tau, misdisordered tau, sarkosyl-insoluble tau, neuro-fibrillary tangles, neuropil threads, and neuritic plaques in a brain biopsy of a human Alzheimer's disease patient or in a brain sample from an animal model of Alzheimer's disease.

53. The antibody or method according to one of claims 50-52, wherein the antibody, when administered peripherally to a human subject, exerts one or more effector-function mediated beneficial effects on the subject.

54. An antibody according to any one of claims 1-25, or a nucleic acid according to claim 26, for use in the treatment or diagnosis of a disease chosen from Alzheimer's disease and related tauopathies.

55. A composition comprising an antibody according to any one of claims 1-25 or a nucleic acid according to claim 26, for use in the treatment or diagnosis of a disease chosen from Alzheimer's disease and related tauopathies

56. An isolated peptide, wherein:

a) the isolated peptide is a fragment of tau that is at least 6 amino-acid-residues-long, at least 7 amino-acid-residues-long, at least 9 amino-acid-residues-long, at least 10 amino-acid-residues-long, at least 12 amino-acid-residues-long, or 30 amino-acid-residues-long; and wherein
b) the isolated peptide comprises at least one tau therapeutic epitope.

57. The isolated peptide according to claim 56, wherein the therapeutic epitope comprises a therapeutic epitope selected from those within:

i. position 267-273 or residues KHQPGGG (SEQ ID NO: 98), relative to tau_{441};
ii. position 298-304 or residues KHVPGGG (SEQ ID NO: 99), relative to tau_{441}
iii. position 329-335 or residues HHKPGGG (SEQ ID NO: 100), relative to tau_{441}; and
iv. position 361-367 or residues THVPGGG (SEQ ID NO: 101), relative to tau_{441};

58. The isolated peptide according to claim 56, wherein the therapeutic epitope comprises a therapeutic epitope selected from those within:

i. position 268-273 or residues HQPGGG (SEQ ID NO: 223), relative to tau_{441};
ii. position 299-304 or residues HVPGGG (SEQ ID NO: 154), relative to tau_{441}
iii. position 330-335 or residues HKPGGG (SEQ ID NO: 224), relative to tau_{441}; and
iv. position 362-367 or residues HVPGGG (SEQ ID NO: 154), relative to tau_{441}.

59. The isolated peptide according to one of claims 56-58, wherein the peptide amino acid sequence is a sequence selected from SEQ ID NOs: 1-4, SEQ ID NOs: 9-101, SEQ ID NOs: 108-112, SEQ ID NO:154, SEQ ID NOs: 223-224, NIKAVPGGGS (SEQ ID NO: 200), NIKHVPGGGS (SEQ ID NO: 201), IKHVPGGGS (SEQ ID NO: 202), KHVPGGGSV (SEQ ID NO: 203), HVPGGGSVQ (SEQ ID NO: 204), VPGGGSVQ (SEQ ID NO: 205), GWSIHSPGGGSC (SEQ ID NO: 250), SVFQHLPGGGSC (SEQ ID NO: 251), ANIKHVPGGGS (SEQ ID NO: 144), DAIKHVPGGGS (SEQ ID NO: 146),

DNAKHVPGGGS (SEQ ID NO: 149), DNIAHVPGGGS (SEQ ID NO: 151), DNIKAVPGGGS (SEQ ID NO: 159), DNIKHAPGGGS (SEQ ID NO: 161), and DNIKHVPGGGS (SEQ ID NO: 171).

60. The isolated peptide according to one of claims 56-59, wherein the peptide is active in at least one assay selected from assays that measure the peptide's:

a) ability to compete with tau for binding to the monoclonal antibody DC8E8;
b) ability to reduce the level of sarkosyl-insoluble tau, *in vivo*;
c) ability to promote tau clearance from the brain, *in vivo*;
d) ability to reduce the level of at least one biochemical marker of AD, *in vivo*;
e) ability to reduce neurofibrillary tangle (NFT) load, *in vivo*;
f) ability to improve at least one neurobehavioral parameter, *in vivo*;
g) ability to beneficially modify the course of AD in a subject;
h) ability to reduce the level of tau in the brain, in the cerebrospinal fluid, or in both;
i) ability to serve as an immunogen in the making of an antibody capable of competing with monoclonal DC8E8 for binding to tau.

61. A compound comprising the isolated peptide according to one of claims 56-60 and a moiety.

62. The compound of claim 61, wherein the moiety is N-terminal, C-terminal, or linked to an internal amino acid of the peptide, and wherein the moiety is selected from one or more of a cysteine residue, phospho group, keyhole limpet hemocyanin, tetanus toxoid or a toxoid derived from other pathogenic bacteria, serum albumins, bovine serum albumin, an immunoglobulin molecule or fragment thereof, thyroglobulin, ovoglobulin, a universal T-cell epitope, a cytokine, a chemokine, IL-1α, IL-1β, IL-2, IL-10, IFN-γ, GM-CSF, MIP1α, MIP1β, and RANTES.

63. A pharmaceutical composition comprising the isolated peptide according to one of claims 56-60 and a pharmaceutically acceptable carrier, and/or a diluent, and/or an adjuvant.

64. A pharmaceutical composition comprising the compound according to one of claims 61-62 and a pharmaceutically acceptable carrier, and/or a diluent, and/or an adjuvant.

65. The pharmaceutical composition according to one of claims 63 and 64, which is adapted to provide a dosage amount of the peptide or of the compound between 1 ng and 10 mg per dose.

66. The pharmaceutical composition according to one of claims 63 and 64, which is adapted to provide a dosage amount of the peptide or of the compound greater than 10 micrograms per dose.

67. An article of manufacture for pharmaceutical or diagnostic use, comprising packaging material and a container comprising a solution of a lyophilized form of the peptide according to one of claims 56-60 or of the compound according to one of claims 61-62.

68. The article of manufacture according to claim 67, wherein the container is a component of a device or system for delivery of the peptide or the compound to a subject.

69. A medical device comprising the peptide according to one of claims 56-60 or the compound according to one of claims 61-62, wherein the device is suitable for contacting or administering the antibody by at least one mode selected from parenteral, subcutaneous, intramuscular, intravenous, intrarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracerebellar, intracerebroventricular, intrathecal, intracolic, intracervical, intragastric, intrahepatic,

intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal, intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, intralesional, bolus, vaginal, rectal, buccal, sublingual, intranasal, and transderrnal.

70. An effective amount of at least one peptide according to one of claims 56-60 and/or at least one compound according to one of claims 61-62 for use in the treatment or preventing the progression of Alzheimer's disease or related tauopathies.

71. The peptide of claim 70, wherein the peptide is capable of reducing motor impairment, improving motor function, reducing cognitive impairment, improving cognitive function, or a combination thereof.

72. An effective amount of at least one peptide according to one of claims 56-60 and/or at least one compound according to one of claims 61-62 for use in the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies.

73. An effective amount of the peptide according to one of claims 70-72, further comprising an adjuvant that augments the immune response, which effects an immune response comprising antibodies against pathological tau, thereby treating, preventing the progression, or ameliorating at least one of the symptoms associated with Alzheimer's disease or related tauopathies in a human.

74. An effective amount of a compound according to one of claims 61-62 which effects an immune response comprising antibodies against pathological tau, for use in the treatment, the prevention of the progression, or the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies in a human.

75. A method of isolating DC8E8, or isolating an antibody that is able to compete with DC8E8 for binding to tau, the method comprising contacting DC8E8 or the antibody with

a peptide according to one of claims 56-60 and/or with a compound according to one of claims 61-62.

76. A method of diagnosing or screening a subject for the presence of Alzheimer's disease or related tauopathies in a subject, or for determining a subject's risk for developing Alzheimer's disease or related tauopathies, the method comprising:

a) contacting a cell, tissue, organ, fluid, or any other sample of the subject, with an an effective amount of at least one antibody; that is able to compete with DC8E8 for binding to tau; and
b) determining the presence of a complex comprising pathological tau and the antibody, wherein the presence of the complex is diagnostic of Alzheimer's disease or a related tauopathy associated with the presence of pathological tau.

77. A method of monitoring a subject for the presence, progression, regression, or stabilization of Alzheimer's disease or a related tauopathy in a subject, or for determining the stage of Alzheimer's disease or a related tauopathy in a subject, for the method comprising:

a) contacting a cell, tissue, organ, fluid, or any other sample of the subject, with an effective amount of at least one antibody, that is able to compete with DC8E8 for binding to tau; and
b) determining the presence of a complex comprising pathological tau and the antibody, wherein the presence of the complex is diagnostic of Alzheimer's disease or a related tauopathy associated with the presence of pathological tau.

78. The method according to one of claims 76-77, wherein the effective amount of each peptide and/or compound is at least 1 µg per dose, at least 10 µg per dose, at least 100 µg per dose.

79. The method according to claim 78, wherein the effective amount of each peptide and/or compound is at least 10 µg per dose in the presence of an adjuvant, and at least at least 100 µg per dose in the absence of an adjuvant.

80. The peptide according to one of claims 70-73 and the method according to one of claims 76-79, wherein at least one peptide or compound is administered in multiple dosages over a period of at least six months.

81. An effective amount of the following components: at least one antibody according to one of claims 1-25, and/or at least one peptide according to one of claims 56-60, and/or at least one compound according to one of claims 61-62, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors for use in the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies.

82. The components of claim 81, wherein the components is/are capable of reducing motor impairment, improving motor function, reducing cognitive impairment, improving cognitive function, or a combination thereof.

83. An effective amount of the following components: at least one antibody according to one of claims 1-25, and/or at least one peptide according to one of claims 56-60, and/or at least one compound according to one of claims 61-62, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective

phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid-passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors for use in ameliorating at least one of the symptoms associated with Alzheimer's disease or related tauopathies.

84. The components according to one of claims 82-83, wherein the components further comprise an adjuvant that augments the immune response; in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization, anti-amyloid aggregation inhibitors, and secretase inhibitors; wherein the components effects an immune response comprising antibodies against pathological tau, thereby treating, preventing the progression, or ameliorating at least one of the symptoms associated with AD in a human.

85. A peptide according to one of claims 56-60 in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization, anti-amyloid aggregation inhibitors, and secretase inhibitors; wherein the adjuvant effects an immune response comprising antibodies against pathological tau, for use in the treatment, the prevention of the progression, or the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies in a human.

86. The components according to one of claims 82-84, wherein the combination agent is to be administered prior to, simultaneously with, or after the administration of an antibody according to one of claims 1-25, a peptide according to one of claims 56-60, and/or a compound according to one of claims 61-62.

87. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and/or diluent; and

a) an antibody according to one of claims 1-25; and/or
b) a peptide according to one of claims 56-60; and/or
c) a compound according to one of claims 61-62;

in combination with at least one combinantion agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid-passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors.

88. An isolated peptide, wherein:

a) the isolated peptide is a fragment of tau that is 6 amino-acid-residues-long and wherein
b) the isolated peptide comprises at least one tau therapeutic epitope.

89. The isolated peptide according to claim 88, wherein the therapeutic epitope comprises a therapeutic epitope selected from:

i. position 268-273 or residues HQPGGG (SEQ ID NO: 223), relative to tau_{441};
ii. position 299-304 or residues HVPGGG (SEQ ID NO: 154), relative to tau_{441}
iii. position 330-335 or residues HKPGGG (SEQ ID NO: 224), relative to tau_{441}; and
iv. position 362-367 or residues HVPGGG (SEQ ID NO: 154), relative to tau_{441}.

90. The isolated peptide according to one of claims 88-89, wherein the isolated peptide is selected from HQPGGG (SEQ ID NO: 223), HVPGGG (SEQ ID NO: 154), HKPGGG (SEQ ID NO: 224), and HVPGGG (SEQ ID NO: 154).

91. The isolated peptide according to one of claims 88-90, wherein the peptide is active in at least one assay selected from assays that measure the peptide's:

a) ability to compete with tau for binding to the monoclonal antibody DC8E8;
b) ability to reduce the level of sarkosyl-insoluble tau, *in vivo*;
c) ability to promote tau clearance from the brain, *in vivo*;
d) ability to reduce the level of at least one biochemical marker of AD, *in vivo*;
e) ability to reduce neurofibrillary tangle (NFT) load, *in vivo*;
f) ability to improve at least one neurobehavioral parameter, *in vivo*;
g) ability to beneficially modify the course of AD in a subject;
h) ability to reduce the level of tau in the brain, in the cerebrospinal fluid, or in both;
i) ability to serve as an immunogen in the making of an antibody capable of competing with monoclonal DC8E8 for binding to tau.

92. A compound comprising the isolated peptide according to one of claims 88-91 and a moiety.

93. The compound according to claim 92, wherein the moiety is N-terminal, C-terminal, or linked to an internal amino acid of the peptide, and wherein the moiety is selected from one or more of a cysteine residue, phospho group, keyhole limpet hemocyanin, tetanus toxoid or a toxoid derived from other pathogenic bacteria, serum albumins, bovine serum albumin, an immunoglobulin molecule or fragment thereof, thyroglobulin, ovoglobulin, a universal T-cell epitope, a cytokine, a chemokine, IL-1α, IL-1β, IL-2, IL-10, IFN-γ, GM-CSF, MIP1α, MIP1β, and RANTES.

94. A pharmaceutical composition comprising the isolated peptide according to one of claims 88-91 and a pharmaceutically acceptable carrier, and/or a diluent, and/or an adjuvant.

95. A pharmaceutical composition comprising the compound according to one of claims 92-93 and a pharmaceutically acceptable carrier, and/or a diluent, and/or an adjuvant.

96. The pharmaceutical composition according to one of claims 94 and 95, which is adapted to provide a dosage amount of the peptide or of the compound between 1 ng and 10 mg per dose.

97. The pharmaceutical composition according to one of claims 94 and 95, which is adapted to provide a dosage amount of the peptide or of the compound greater than 10 micrograms per dose.

98. An article of manufacture for pharmaceutical or diagnostic use, comprising packaging material and a container comprising a solution of a lyophilized form of the peptide according to one of claims 88-91 or of the compound according to one of claims 92-93.

99. The article of manufacture according to claim 98, wherein the container is a component of a device or system for delivery of the peptide or the compound to a subject.

100. A medical device comprising the peptide according to one of claims 88-91 or the compound according to one of claims 92-93, wherein the device is suitable for contacting or administering the peptide and/or the compound by at least one mode selected from parenteral, subcutaneous, intramuscular, intravenous, intrarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracerebellar, intracerebroventricular, intrathecal, intracolic, intracervical, intragastric,

intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal, intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, intralesional, bolus, vaginal, rectal, buccal, sublingual, intranasal, and transdermal.

101. An effective amount of the following component or components: at least one peptide according to one of claims 88-91 and/or at least one compound according to one of claims 92-93 for use in the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies.

102. The components according to claim 101, wherein one or more components is capable of reducing motor impairment, improving motor function, reducing cognitive impairment, improving cognitive function, or a combination thereof.

103. An effective amount of the following component or components: at least one peptide according to one of claims 88-91 and/or at least one compound according to one of claims 92-93 for use in the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies in a subject.

104. The components according to one of claims 101-103, wherein one or more components further comprises an adjuvant that augments the immune response, which components and adjuvant effect an immune response comprising antibodies against pathological tau, thereby treating, preventing the progression, or ameliorating at least one of the symptoms associated with Alzheimer's disease or related tauopathies in a human patient.

105. The components according to one of claims 101-103, which effect an immune response comprising antibodies against pathological tau for use in the treatment, the prevention of the progression, or the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies in a human.

106. A method of isolating DC8E8, or isolating an antibody that is able to compete with DC8E8 for binding to tau, the method comprising contacting DC8E8 or the antibody with a peptide according to one of claims 88-91 and/or with a compound according to one of claims 92-93.

107. The components according to one of claims 101-104, wherein the peptide and/or compound is to be administered intravenously, intramuscularly, subcutaneously, intraperitoneally, intranasally, intracerebroventricularly, intrathecally, or as an aerosol.

108. The components according to one of claims 101-104 and 107, wherein the effective amount of each peptide and/or compound is at least 1 µg per dose, at least 10 µg per dose, at least 100 µg per dose.

109. The components according to claim 108, wherein the effective amount of each peptide and/or compound is at least 10 µg per dose in the presence of an adjuvant, and at least at least 100 µg per dose in the absence of an adjuvant.

110. The components according to one of claims 101-104 and 107-109, wherein at least one peptide or compound is to be administered in multiple dosages over a period of at least six months.

111. An effective amount of the following components: at least one antibody according to one of claims 1-25, and/or at least one peptide according to one of claims 88-91, and/or at least one compound according to one of claims 92-93, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization, anti-

amyloid aggregation inhibitors, and secretase inhibitors for use in the treatment or prevention of the progression of Alzheimer's disease or related tauopathies .

112. The components of claim 111, wherein the components are capable of reducing motor impairment, improving motor function, reducing cognitive impairment, improving cognitive function, or a combination thereof.

113. An effective amount of the following components: at least one antibody according to one of claims 1-25, and/or at least one peptide according to one of claims 88-91, and/or at least one compound according to one of claims 92-93, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid-passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors for use in the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies

114. The components according to one of claims 111-113, wherein the components further comprise an adjuvant that augments the immune response; in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization, anti-amyloid aggregation inhibitors, and secretase inhibitors; and wherein the components effects an immune response comprising antibodies against pathological tau, thereby treating, preventing the progression, or ameliorating at least one of the symptoms associated with AD in a human.

115. An effective amount of an antibody according to one of claims 1-25 in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization, anti-amyloid aggregation inhibitors, and secretase inhibitors; and wherein the adjuvant effects an immune response comprising antibodies against pathological tau, for use in the treatment, the prevention of the progression, or the ameliorating of at least one of the symptoms associated with AD in a human.

116. The components or antibody according to one of claims 111-115, wherein the combination agent is to be administered prior to, simultaneously with, or after the administration of an antibody according to one of claims 1-25, a peptide according to one of claims 88-91, and/or a compound according to one of claims 92-93.

117. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and/or diluent; and

a) an antibody according to one of claims 1-25; and/or
b) a peptide according to one of claims 88-91; and/or
c) a compound according to one of claims 92-93;

in combination with at least one combinantion agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid-passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors.

118. Use of an effective amount of at least one peptide according to one of claims 56-60 and/or at least one compound according to one of claims 61-62 in the manufacture of a medicament for the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies.

119. The use of claim 118, wherein the medicament is capable of reducing motor impairment, improving motor function, reducing cognitive impairment, improving cognitive function, or a combination thereof.

120. Use of an effective amount of at least one peptide according to one of claims 56-60 and/or at least one compound according to one of claims 61-62 in the manufacture of a medicament for the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies.

121. The use according to one of claims 118-120, wherein the medicament further comprises an adjuvant that augments the immune response, which effects an immune response comprising antibodies against pathological tau, thereby treating, preventing the progression, or ameliorating at least one of the symptoms associated with Alzheimer's disease or related tauopathies in a human.

122. The use of a peptide according to one of claims 56-60 which effects an immune response comprising antibodies against pathological tau, in the manufacture of a medicament for use in the treatment, the prevention of the progression, or the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies in a human.

123. The use according to one of claims 118-121 wherein at least one peptide or compound is administered in multiple dosages over a period of at least six months.

124. Use of an effective amount of the following components: at least one antibody according to one of claims 1-25, and/or at least one peptide according to one of claims 56-60, and/or at least one compound according to one of claims 61-62, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors in the manufacture of a medicament for the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies.

125. The use of claim 124, wherein the medicament is capable of reducing motor impairment, improving motor function, reducing cognitive impairment, improving cognitive function, or a combination thereof.

126. Use of an effective amount of the following components: at least one antibody according to one of claims 1-25, and/or at least one peptide according to one of claims 56-60, and/or at least one compound according to one of claims 61-62, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid-passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors in the manufacture of a medicament for the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies.

127. The use according to one of claims 125-126, wherein the medicament further comprises an adjuvant that augments the immune response; in combination with at

least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization, anti-amyloid aggregation inhibitors, and secretase inhibitors; wherein the medicament effects an immune response comprising antibodies against pathological tau, thereby treating, preventing the progression, or ameliorating at least one of the symptoms associated with AD in a human.

128. Use of a peptide according to one of claims 56-60 together with an adjuvant that augments the immune response; in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization, anti-amyloid aggregation inhibitors, and secretase inhibitors; wherein the adjuvant an immune response comprising antibodies against pathological tau, in the manufacture of a medicament for the treatment, the prevention of the progression, or the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies in a human.

129. The use according to one of claims 125-126, wherein the combination agent is to be administered prior to, simultaneously with, or after the administration of an antibody according to one of claims 1-25, a peptide according to one of claims 56-60, and/or a compound according to one of claims 61-62.

130. Use of an effective amount of the following component or components: at least one peptide according to one of claims 88-91 and/or at least one compound according to

one of claims 92-93 in the manufacture of a medicament for the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies.

131. The use of claim 130, wherein the medicament is capable of reducing motor impairment, improving motor function, reducing cognitive impairment, improving cognitive function, or a combination thereof.

132. Use of an effective amount of the following component or components: at least one peptide according to one of claims 88-91 and/or at least one compound according to one of claims 92-93 in the manufacture of a medicament for the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies in a subject.

133. The use according to one of claims 130-132, wherein the medicament further comprises an adjuvant that augments the immune response, which effects an immune response comprising antibodies against pathological tau, thereby treating, preventing the progression, or ameliorating at least one of the symptoms associated with Alzheimer's disease or related tauopathies in a human.

134. Use of a peptide according to one of claims 56-60 together with an adjuvant that augments the immune response, which effects an immune response comprising antibodies against pathological tau in the manufacture of a medicament for the treatment, the prevention of the progression, or the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies in a human.

135. The use according to one of claims 130-133, wherein the medicament is to be administered intravenously, intramuscularly, subcutaneously, intraperitoneally, intranasally, intracerebroventricularly, intrathecally, or as an aerosol.

136. The use according to one of claims 130-133 and 135, wherein the effective amount of each peptide and/or compound is at least 1 µg per dose, at least 10 µg per dose, at least 100 µg per dose.

137. The use according to claim 136, wherein the effective amount of the medicament is at least 10 µg per dose in the presence of an adjuvant, and at least at least 100 µg per dose in the absence of an adjuvant.

138. The use according to one of claims 130-133 and 135-137, wherein the medicament is to be administered in multiple dosages over a period of at least six months.

139. Use of an effective amount of the following components: at least one antibody according to one of claims 1-25, and/or at least one peptide according to one of claims 88-91, and/or at least one compound according to one of claims 92-93, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization, anti-amyloid aggregation inhibitors, and secretase inhibitors in the manufacture of a medicament for the treatment or prevention of the progression of Alzheimer's disease or related tauopathies .

140. The use of claim 139, wherein the medicament is capable of reducing motor impairment, improving motor function, reducing cognitive impairment, improving cognitive function, or a combination thereof.

141. Use of an effective amount of the following components: at least one antibody according to one of claims 1-25, and/or at least one peptide according to one of claims

88-91, and/or at least one compound according to one of claims 92-93, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid-passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors in the manufacture of a medicament for the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies

142. The use according to one of claims 139-141, wherein the medicament further comprise an adjuvant that augments the immune response; in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization, anti-amyloid aggregation inhibitors, and secretase inhibitors; and wherein the medicament effects an immune response comprising antibodies against pathological tau, thereby treating, preventing the progression, or ameliorating at least one of the symptoms associated with AD in the human.

143. Use of a peptide according to one of claims 56-60 in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization, anti-amyloid aggregation inhibitors, and secretase inhibitors; and wherein the adjuvant effects an immune response comprising antibodies against pathological tau, in the

manufacture of a medicament for the treatment, the prevention of the progression, or the ameliorating of at least one of the symptoms associated with AD in a human.

144. The use according to one of claims 139-143, wherein the combination agent is to be administered prior to, simultaneously with, or after the administration of an antibody according to one of claims 1-25, a peptide according to one of claims 88-91, and/or a compound according to one of claims 92-93.

145. The use of an effective amount of at least one antibody according to one of claims 1-25 in the manufacture of a medicament for the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies

146. The use of claim 145, wherein the medicament is capable of reducing motor impairment, improving motor function, reducing cognitive impairment, improving cognitive function, or a combination thereof.

147. The use of an effective amount of at least one antibody according to one of claims 1-25 in the manufacture of a medicament for ameliorating at least one of the symptoms associated with of Alzheimer's disease or related tauopathies

148. The use according to one of claims 145-147, wherein the effective amount of each antibody is at least 1 mg/kg body weight of the subject, per dose.

149. The use according to one of claims 145-147, wherein the effective amount of each antibody is at least 10 mg/kg body weight of the subject, per dose.

150. The use according to one of claims 145-149, wherein the medicament is to be administered in multiple dosages over a period of at least six months.

151. The use according to one of claims 145-150, wherein the medicament is to be administered peripherally to a human subject to exert its beneficial effects.

152. The use according to claim 151, wherein the antibody, when administered peripherally to a human subject, binds to soluble tau, sarkosyl-insoluble tau, or to both.

153. The use according to claim 151, wherein the antibody, when administered peripherally to a human subject, binds to both soluble tau and sarkosyl-insoluble tau.

154. The use according to claim 151, wherein the antibody, when administered peripherally to a human subject, binds to tau, wherein tau is in one or more pathological forms chosen from misordered tau, misdisordered tau, sarkosyl-insoluble tau, neurofibrillary tangles, neuropil threads, and neuritic plaques in a brain biopsy of a human Alzheimer's disease patient, in a brain sample from an animal model of Alzheimer's disease.

155. The use according to one of claims 151-154, wherein the antibody, when administered peripherally to a human subject, exerts one or more effector-function mediated beneficial effects on the subject.

156. An effective amount of at least one peptide according to one of claims 88-91 for use in the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies.

157. An effective amount of at least one peptide according to one of claims 88-91 for use in ameliorating at least one of the symptoms associated with of Alzheimer's disease or related tauopathies.

158. An effective amount of at least one peptide according to one of claims 88-91, in combination with at least one combination agent chosen from acetylcholinesterase

inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors for use in the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies, for use in ameliorating at least one of the symptoms associated with Alzheimer's disease or related tauopathies.

159. An effective amount of at least one peptide according to one of claims 88-91, in combination with an adjuvant, for use in ameliorating at least one of the symptoms associated with Alzheimer's disease or related tauopathies.

160. Use of an effective amount of at least one peptide according to one of claims 88-91 in the manufacture of a medicament for the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies.

161. The use of claim 160, wherein the medicament is capable of reducing motor impairment, improving motor function, reducing cognitive impairment, improving cognitive function, or a combination thereof.

162. Use of an effective amount of at least one peptide according to one of claims 88-91 in the manufacture of a medicament for the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies.

163. Use of an effective amount of at least one peptide according to one of claims 88-91, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau

aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors in the manufacture of a medicament for the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies

164. Use of an effective amount of at least one peptide according to one of claims 88-91, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors in the manufacture of a medicament for the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies.

165. An isolated peptide wherein the peptide's amino acid sequence is SEQ ID NO. 108.

166. An effective amount of the peptide according to claim 165 for use in the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies

167. An effective amount of the peptide according to claim 165 for use in ameliorating at least one of the symptoms associated with of Alzheimer's disease or related tauopathies.

168. An effective amount of the peptide according to claim 165, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases,

inhibitors of heat shock proteins, anti-amyloid passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors for use in the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies, for use in ameliorating at least one of the symptoms associated with of Alzheimer's disease or related tauopathies.

169. An effective amount of the peptide according to claim 165, in combination with an adjuvant, for use in ameliorating at least one of the symptoms associated with of Alzheimer's disease or related tauopathies.

170. Use of an effective amount of the peptide according to claim 165 in the manufacture of a medicament for the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies.

171. The use of claim 170, wherein the medicament is capable of reducing motor impairment, improving motor function, reducing cognitive impairment, improving cognitive function, or a combination thereof.

172. Use of an effective amount of the peptide according to claim 165 in the manufacture of a medicament for the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies.

173. Use of an effective amount of the peptide according to claim 165, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors in the

manufacture of a medicament for the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies.

174. Use of an effective amount of the peptide according to claim 165, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors in the manufacture of a medicament for the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies.

175. A compound comprising the isolated peptide according to claim 165 and a moiety, wherein the moiety is N-terminal and comprises keyhole limpet hemocyanin.

176. An effective amount of the compound according to claim 175 for use in the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies.

177. An effective amount of the compound according to claim 175 for use in ameliorating at least one of the symptoms associated with of Alzheimer's disease or related tauopathies.

178. An effective amount of the compound according to claim 175, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization

reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors for use in the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies, for use in ameliorating at least one of the symptoms associated with Alzheimer's disease or related tauopathies.

179. An effective amount of the compound according to claim 175, in combination with an adjuvant, for use in ameliorating at least one of the symptoms associated with of Alzheimer's disease or related tauopathies.

180. Use of an effective amount of the compound according to claim 175 in the manufacture of a medicament for the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies.

181. The use of claim 180, wherein the medicament is capable of reducing motor impairment, improving motor function, reducing cognitive impairment, improving cognitive function, or a combination thereof.

182. Use of an effective amount of the compound according to claim 175 in the manufacture of a medicament for the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies.

183. Use of an effective amount of the compound according to claim 175, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors in the manufacture of a medicament for the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies.

184. Use of an effective amount of the compound according to claim 175, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors in the manufacture of a medicament for the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies.

185. An isolated antibody that binds tau epitopes HQPGGG, HVPGGG, and HKPGGG in a conformationally-specific manner.

186. An effective amount of the antibody according to claim 185 for use in the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies

187. An effective amount of the antibody according to claim 185 for use in ameliorating at least one of the symptoms associated with Alzheimer's disease or related tauopathies.

188. An effective amount of the antibody according to claim 185, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors for use in the treatment or the prevention of the progression of Alzheimer's disease or related

tauopathies, for use in ameliorating at least one of the symptoms associated with Alzheimer's disease or related tauopathies.

189. Use of an effective amount of the antibody according to claim 185 in the manufacture of a medicament for the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies.

190. The use of claim 189, wherein the medicament is capable of reducing motor impairment, improving motor function, reducing cognitive impairment, improving cognitive function, or a combination thereof.

191. Use of an effective amount of the antibody according to claim 185 in the manufacture of a medicament for the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies.

192. Use of an effective amount of the antibody according to claim 185, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases, inhibitors of heat shock proteins, anti-amyloid passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors in the manufacture of a medicament for the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies

193. Use of an effective amount of the antibody according to claim 185, in combination with at least one combination agent chosen from acetylcholinesterase inhibitors, NMDA receptor antagonists, transition metal chelators, growth factors, hormones, non-steroidal anti-inflammatory drugs (NSAID), antioxidants, lipid lowering agents, selective phosphodiesterase inhibitors, inhibitors of tau aggregation, inhibitors of protein kinases,

inhibitors of heat shock proteins, anti-amyloid passive and active immunization reagents, anti-amyloid aggregation inhibitors, and secretase inhibitors in the manufacture of a medicament for the amelioration of at least one of the symptoms associated with Alzheimer's disease or related tauopathies.

CLAIMS

1. A synthetic peptide whose amino acid sequence consists of CKDNIKHVPGGGS (SEQ ID NO: 218), or a salt thereof.

2. A compound comprising a peptide whose amino acid sequence consists of SEQ ID NO: 218 (CKDNIKHVPGGGS) that is linked to keyhole limpet hemocyanin (KLH) at the N-terminal end of the peptide, or a salt thereof.

3. The compound according to claim 2, wherein the KLH is conjugated to the N-terminal cysteine via a maleimide crosslinker.

4. A pharmaceutical composition comprising the compound according to claim 2 or claim 3, and further comprising a pharmaceutically acceptable carrier, and/or a diluent, and/or an adjuvant.

5. The pharmaceutical composition of claim 4, wherein the adjuvant is aluminum hydroxide.

6. An immunogenic composition comprising the peptide according to claim 1 and a pharmaceutically acceptable excipient.

7. The immunogenic composition of claim 6, further comprising aluminum hydroxide.

8. A pharmaceutical composition comprising a compound according to claim 2 or claim 3 and a pharmaceutically acceptable carrier.

9. A pharmaceutical composition comprising a compound according to claim 2 or claim 3 and a pharmaceutically acceptable diluent.

10. A pharmaceutical composition comprising a compound according to claim 2 or claim 3 and a pharmaceutically acceptable adjuvant.

11. The pharmaceutical composition of claim 10, wherein the adjuvant is aluminum hydroxide.

12. An immunogenic composition comprising the compound according to claim 2 and an adjuvant containing aluminum.

13. An immunogenic composition comprising a synthetic peptide whose amino acid sequence consists of KDNIKHVPGGGS (SEQ ID NO: 108), or a salt thereof, and an adjuvant containing aluminum.

14. The use of the peptide or compound of any one of claims 1-3 in the manufacture of a medicament for the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies in a subject.

15. A peptide or compound of any one of claims 1-3 for use in the treatment or diagnosis of a disease chosen from Alzheimer's disease and related tauopathies.

16. The use of the immunogenic composition of claim 13 in the manufacture of a medicament for the treatment or the prevention of the progression of Alzheimer's disease or related tauopathies in a subject.

17. An immunogenic composition of claim 13 for use in the treatment or diagnosis of a disease chosen from Alzheimer's disease and related tauopathies.