CLAIMS

1. Use of an effective amount of a liposome in the manufacture of a medicament for inducing an antibody response against a phosphorylated Tau protein (pTau) in a human subject in need thereof, wherein the liposome comprises:

(1) a Tau phosphopeptide consisting of the amino acid sequence of SEQ ID NO:28 at an amount of 300 μg to 1800 μg per dose;

(2) a toll-like receptor 4 agonist comprising monophosphoryl lipid A;

(3) a helper T-cell epitope having an amino acid sequence selected from the group consisting of SEQ ID NO:13 to SEQ ID NO:17, SEQ ID NO:23 to SEQ ID NO:26, and SEQ ID NO:39 to SEQ ID NO:44; and

(4) a CpG oligonucleotide having a nucleotide sequence selected from the group consisting of SEQ ID NO:18 to SEQ ID NO:22;

wherein:

the Tau phosphopeptide is presented on the surface of the liposome, and

the antibody response lasts at least 20 weeks after the initial administration of the effective amount of the liposome to the human subject.

2. The use of claim 1, wherein the effective amount of the liposome comprises:

(1) the Tau phosphopeptide at the amount of 300 μg to 1800 μg per dose;

(2) the toll-like receptor 4 agonist at an amount of 100 μg to 585 μg per dose;

(3) the helper T-cell epitope at an amount of 75 μg to 550 μg per dose; and

(4) the CpG oligonucleotide at an amount of 150 μg to 900 μg per dose.

3. The use of claim 2, wherein the effective amount of the liposome comprises 300 μg, 900 μg or 1800 μg per dose of the Tau phosphopeptide.

4. The use of claim 1, wherein the effective amount of the liposome is to be administered subcutaneously.

5. The use of claim 1, wherein the effective amount of the liposome is to be administered intramuscularly.

6. The use of claim 1, wherein the CpG oligonucleotide has one or more phosphorothioate internucleotide linkages, and the CpG oligonucleotide is covalently linked to at least one lipophilic group, optionally via a PEG linker.

7. The use of claim 1, wherein the Tau phosphopeptide consists of the amino acid sequence of SEQ ID NO:28, the toll-like receptor 4 agonist comprises monophosphoryl hexa-acyl Lipid A, 3-deacyl, the helper T-cell epitope comprises the amino acid sequence of SEQ ID NO: 39, the CpG oligonucleotide comprises the nucleotide sequence of SEQ ID NO: 18, and the liposome further comprises at least one lipid selected from the group consisting of 1,2-dimyristoyl-sn-glycero- 3-phosphocholine (DMPC), l,2-dimyristoyl-sn-glycero-3-phosphoryl-3'-rac-glycerol (DMPG), and cholesterol.

8. The use of claim 1, wherein the antibody response comprises a specific IgG antibody response directed against the pTau, preferably the specific IgG antibody response has an anti-pTau IgG titer at least 50, 60, 70, 80, 90, 100 or more times higher than that of a placebo control.

9. The use of claim 1, wherein the antibody response induces a class switch of a specific IgM antibody response to a specific IgG antibody response directed against the pTau.

10. The use of claim 1, wherein the antibody response comprises an IgG immune response that preferentially recognizes the pTau over non- phosphorylated Tau protein, preferably the ratio of the anti-pTau IgG titer to the anti-Tau IgG titer is at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65 or 70.

11. The use of claim 1, wherein the antibody response comprises an IgG immune response against an enriched Paired Helical Filament (ePHF).

12. The use of claim 11, wherein the IgG immune response has an anti-ePHF IgG titer at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more times higher than that of a placebo control.

13. The use of claim 12, wherein the anti-ePHF IgG has an increased binding avidity to the pathological ePHF Tau for at least 6 weeks, 8 weeks, 10 weeks, 12 weeks, 14 weeks, 16 weeks, 18 weeks, 20 weeks, 22 weeks, 24 weeks or longer after the initial administration of the effective amount of the liposome, preferably the anti-ePHF IgG has an avidity index of at least 0.3, 0.4, 0.5, 0.6, or 0.7.

14. The use of claim 1, further comprising a second dose of the effective amount of liposome to be administered to the subject 4 to 12 weeks, such as 8 weeks, after the initial administration of the effective amount of liposome.

15. The use of claim 14, wherein the antibody response, preferably the anti-ePHF IgG titer, is boosted after the administration of the second dose of the effective amount of liposome, preferably the antibody response is increased at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100% or more as measured at least 2 weeks after the administration of the second dose of the effective amount of liposome.

16. The use of claim 15, further comprising a third dose of the effective amount of liposome to be administered to the subject 20 to 28 weeks, such as 24 weeks, after the initial administration of the effective amount of liposome.

17. The use of claim 16, wherein the antibody response, preferably the anti-ePHF IgG titer, is boosted after the administration of the third dose of the effective amount of liposome, preferably the antibody response is increased at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100% or more as measured at least 2 weeks after the administration of the third dose of the effective amount of liposome.

18. The use of claim 17, further comprising a fourth dose of the effective amount of liposome to be administered to the subject 44 to 52 weeks, such as 48 weeks, after the initial administration of the effective amount of liposome.

19. The use of claim 18, wherein the antibody response, preferably the anti-ePHF IgG titer, is boosted after the administration of the fourth dose of the effective amount of liposome,

preferably the antibody response is increased at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100% or more as measured at least 2 weeks by the administration of the fourth dose of the effective amount of liposome.

20. Use of an effective amount of a liposome in the manufacture of a medicament for inducing a sustained immune response against a phosphorylated Tau protein (pTau) in a human subject in need thereof, wherein:

i. the effective amount of a liposome is to be intramuscularly administered to the subject as a primer vaccine ; and

ii. the effective amount of the liposome is to be intramuscularly administered to the subject as a first booster vaccine 6-10 weeks after the administration of the primer vaccine, wherein:

the sustained immune response lasts at least 20 weeks after the administration of the primer vaccine;

the liposome comprises:

(1) a Tau phosphopeptide consisting of the amino acid sequence of SEQ ID NO: 28, and the Tau phosphopeptide is presented on the surface of the liposome;

(2) a toll-like receptor 4 agonist comprising monophosphoryl lipid A;

(3) a helper T-cell epitope having an amino acid sequence selected from the group consisting of SEQ ID NOs:23, 24, 25, and 26; and

(4) a CpG oligonucleotide having a nucleotide sequence selected from the group consisting of SEQ ID NO:18 to SEQ ID NO:22; and

the effective amount of the liposome comprises:

(1) the Tau phosphopeptide at an amount of 300 μg to 1800 μg per dose;

(2) the toll-like receptor 4 agonist at an amount of 100 μg to 585 μg per dose;

(3) the helper T-cell epitope at an amount of 85 μg to 525 μg per dose; and

(4) the CpG oligonucleotide at an amount of 150 μg to 900 μg per dose.

21. The use of claim 20, wherein the helper T-cell epitope has an amino acid sequence selected from the group consisting of SEQ ID NOs:39, 40, 41, 42, and 43.

22. The use of claim 20, wherein the helper T-cell epitope has an amino acid sequence selected from the group consisting of SEQ ID NOs: 13, 14, 15, 16, 17, and 44.

23. The use of claim 20, wherein the lipidated CpG oligonucleotide has the nucleotide sequence of SEQ ID NO:18 and the CpG oligonucleotide is covalently linked to at least one cholesterol via a linker.

24. The use of claim 20, wherein the first booster vaccine is to be administered 8 weeks after the administration of the primer vaccine, and the sustained immune response lasts at least 24 weeks after the administration of the primer vaccine.

25. The use of claim 20, further comprising a second booster vaccine comprising the effective amount of the liposome to be intramuscularly administered to the subject 22-26 weeks after the administration of the primer vaccine, and the sustained immune response lasts at least 36 weeks after the administration of the primer vaccine.

26. The use of claim 25, wherein the second booster vaccine is to be administered 24 weeks after the administration of the primer vaccine, and the sustained immune response lasts at least 48 weeks after the administration of the primer vaccine.

27. The use of claim 26, further comprising a third booster vaccine comprising the effective amount of the liposome to be intramuscularly administered to the subject 45-50 weeks after the administration of the primer vaccine, and the sustained immune response lasts at least 60 weeks after the administration of the primer vaccine.

28. The use of claim 27, wherein the third booster vaccine is to be administered 48 weeks after the administration of the primer vaccine, and the sustained immune response lasts at least 72 weeks after the administration of the primer vaccine.

29. The use of claim 20, wherein the effective amount of the liposome comprises 300 μg per dose of the Tau phosphopeptide.

30. The use of claim 20, wherein the effective amount of the liposome comprises 900 µg per dose of the Tau phosphopeptide.

31. The use of claim 20, wherein the effective amount of the liposome comprises 1800 µg per dose of the Tau phosphopeptide.

32. The use of claim 20, wherein the sustained immune response comprises an IgG immune response that preferentially recognizes the pTau over non- phosphorylated Tau protein, preferably the ratio of the anti-pTau IgG titer to the anti-Tau IgG titer is at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65 or 70.

33. The use of claim 20, wherein the sustained immune response comprises an IgG immune response against enriched Paired Helical Filament (ePHF) having an anti-ePHF IgG titer at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more times higher than that of a placebo control.

34. The use of any one of claims 1-33, wherein the subject is in need of clearance of aggregates of Tau.

35. The use of any one of claims 1-33, wherein the subject is in need of a prevention or treatment of Alzheimer’s Disease, such as preclinical Alzheimer’s Disease, mild to moderate Alzheimer’s Disease or early Alzheimer’s Disease, mild cognitive impairment (MCI) due to Alzheimer’s Disease.