

CLAIMS

1. —A

1. A monoclonal antibody for use in therapy, wherein the therapy comprises a method of reducing total cerebrospinal fluid p217+tau in a subject in need thereof, the method comprising administering to the subject a composition comprising a pharmaceutically acceptable carrier and about 1 mg/kg to about 60 mg/kg per dose of a monoclonal antibody, the monoclonal antibody,

~~wherein the monoclonal antibody comprises a heavy chain variable complementarity-determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO: 1, a heavy chain variable CDR2 comprising the amino acid sequence of SEQ ID NO: 2, a heavy chain variable CDR3 comprising the amino acid sequence of SEQ ID NO: 3, a light chain variable CDR1 comprising the amino acid sequence of SEQ ID NO: 13, a light chain variable CDR2 comprising the amino acid sequence of SEQ ID NO: 14, and a light chain variable CDR3 comprising the amino acid sequence of SEQ ID NO: 15.~~

2. —A method of reducing free cerebrospinal fluid p217+tau in a subject in need thereof, the method comprising administering to the subject a composition comprising a pharmaceutically acceptable carrier and about 1 mg/kg to about 60 mg/kg per dose of a monoclonal antibody,

wherein the monoclonal antibody comprises a heavy chain variable complementarity-determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO: 1, a heavy chain variable CDR2 comprising the amino acid sequence of SEQ ID NO: 2, a heavy chain variable CDR3 comprising the amino acid sequence of SEQ ID NO: 3, a light chain variable CDR1 comprising the amino acid sequence of SEQ ID NO: 13, a light chain variable CDR2 comprising the amino acid sequence of SEQ ID NO: 14, and a light chain variable CDR3 comprising the amino acid sequence of SEQ ID NO: 15.

2. A monoclonal antibody for use in therapy, wherein the therapy comprises a method of reducing free cerebrospinal fluid p217+tau in a subject in need thereof, the method comprising administering to the subject a composition comprising a pharmaceutically acceptable carrier and about 1 mg/kg to about 60 mg/kg per dose of the monoclonal antibody,

wherein the monoclonal antibody comprises a heavy chain variable complementarity-determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO: 1, a heavy chain variable CDR2 comprising the amino acid sequence of SEQ ID NO: 2, a heavy chain variable CDR3 comprising the amino acid sequence of SEQ ID NO: 3, a light chain variable CDR1 comprising the amino acid sequence of SEQ ID NO: 13, a light chain variable CDR2 comprising the amino acid sequence of SEQ ID NO: 14, and a light chain variable CDR3 comprising the amino acid sequence of SEQ ID NO: 15.

3. — A3. A monoclonal antibody for use in therapy, wherein the therapy comprises a method of reducing total cerebrospinal fluid tau in a subject in need thereof, the method comprising administering to the subject a composition comprising a pharmaceutically acceptable carrier and about 1 mg/kg to about 60 mg/kg per dose of athe monoclonal antibody,

wherein the monoclonal antibody comprises a heavy chain variable complementarity-determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO: 1, a heavy chain variable CDR2 comprising the amino acid sequence of SEQ ID NO: 2, a heavy chain variable CDR3 comprising the amino acid sequence of SEQ ID NO: 3, a light chain variable CDR1 comprising the amino acid sequence of SEQ ID NO: 13, a light chain variable CDR2 comprising the amino acid sequence of SEQ ID NO: 14, and a light chain variable CDR3 comprising the amino acid sequence of SEQ ID NO: 15.

4. — A4. A monoclonal antibody for use in a therapy, wherein the therapy comprises a method of reducing cerebrospinal fluid p181tau in a subject in need thereof, the method comprising administering to the subject a composition comprising a pharmaceutically acceptable carrier and about 1 mg/kg to about 60 mg/kg per dose of athe monoclonal antibody,

wherein the monoclonal antibody comprises a heavy chain variable complementarity-determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO: 1, a heavy chain variable CDR2 comprising the amino acid sequence of SEQ ID NO: 2, a heavy chain variable CDR3 comprising the amino acid sequence of SEQ ID NO: 3, a light chain variable CDR1 comprising the amino acid sequence of SEQ ID NO: 13, a light chain variable CDR2 comprising the amino acid sequence of SEQ ID NO: 14, and a light chain variable CDR3 comprising the amino acid sequence of SEQ ID NO: 15.

5. The ~~method~~monoclonal antibody for use of any one of claims 1-4, wherein the monoclonal antibody comprises a heavy chain variable CDR1 having the amino acid sequence of SEQ ID NO: 1, a heavy chain variable CDR2 having the amino acid sequence of SEQ ID NO: 2, a heavy chain variable CDR3 having the amino acid sequence of SEQ ID NO: 3, a light chain variable CDR1 having the amino acid sequence of SEQ ID NO: 13, a light chain variable CDR2 having the amino acid sequence of SEQ ID NO: 14, and a light chain variable CDR3 having the amino acid sequence of SEQ ID NO: 15.

6. The ~~method~~monoclonal antibody for use of any one of claims 1-5, wherein the monoclonal antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 25, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26.

7. The ~~method~~monoclonal antibody for use of any one of claims 1-6, wherein the monoclonal antibody comprises a heavy chain variable region having the amino acid sequence of SEQ ID NO: 25, and a light chain variable region having the amino acid sequence of SEQ ID NO: 26.

8. The ~~method~~monoclonal antibody for use of any one of claims 1-7, wherein the monoclonal antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 27, and a light chain comprising the amino acid sequence of SEQ ID NO: 28.

9. The ~~method~~monoclonal antibody for use of any one of claims 1-8, wherein the monoclonal antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO: 27, and a light chain having the amino acid sequence of SEQ ID NO: 28.

10. The ~~method~~monoclonal antibody for use of any one of claims 1-9, wherein the composition further comprises histidine, sucrose, polysorbate 20, and ethylenediamine tetra-acetic acid.

11. The ~~method~~monoclonal antibody for use of any one of claims 1-10, wherein the composition has a pH of about 5-6.

12. The ~~method~~monoclonal antibody for use of any one of claims 1-11, ~~comprising~~wherein the method comprises administering to the subject the composition comprising about 10 mg/kg to about 40 mg/kg per dose of the monoclonal antibody.

13. The ~~method~~monoclonal antibody for use of any one of claims 1-11, ~~comprising~~wherein the method comprises administering to the subject the composition comprising about 20 mg/kg to about 60 mg/kg per dose of the monoclonal antibody.

14. The method of any one of claims 1-11, comprising administering to the subject the composition comprising about 40 mg/kg to about 60 mg/kg per dose of the monoclonal antibody.

15. The ~~method~~monoclonal antibody for use of any one of claims 1-11, ~~comprising~~wherein the method comprises administering to the subject the composition comprising about 1 mg/kg, 3 mg/kg, 5 mg/kg, 10 mg/kg, 15 mg/kg, 20 mg/kg, 25 mg/kg, 30 mg/kg, 35 mg/kg, 40 mg/kg, 45 mg/kg, 50 mg/kg, 55 mg/kg, 60 mg/kg, or any value in between, per dose of the monoclonal antibody.

16. The ~~method~~monoclonal antibody for use of any one of claims 1-15, wherein the method comprises administering the composition ~~is administered~~ by intravenous infusion.

17. The ~~method~~monoclonal antibody for use of any one of claims 1-16, wherein the method comprises administering the composition ~~is administered~~ as more than one dose.

18. The ~~method~~monoclonal antibody for use of claim 17, wherein the administration of each dose is separated by a period of about 4 weeks.

19. The ~~method~~monoclonal antibody for use of any one of claims 1-18, wherein the administration of the monoclonal antibody results in a median serum $T_{\max}$ of the monoclonal antibody of about 0.05 days to about 0.25 days after administration.

20. The ~~method~~monoclonal antibody for use of any one of claims 1-19, wherein the administration of the monoclonal antibody results in a median serum $T_{1/2}$ of the monoclonal antibody about 18 days to about 27 days after administration.

21. The ~~method~~monoclonal antibody for use of any one of claims 1-20, wherein the subject in need of a treatment of Alzheimer's Disease.

22. The ~~method~~monoclonal antibody for use of claim 21, wherein the subject is in need of a treatment of early Alzheimer's Disease, mild cognitive impairment (MCI) due to Alzheimer's Disease, or mild to moderate Alzheimer's Disease.