

CLAIMS

WHAT IS CLAIMED IS:

1. An isolated anti-Tau antibody or antigen-binding moiety thereof comprising:
 - a) a heavy chain variable region comprising i) a complementary determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO: 59; ii) a CDR2 comprising the amino acid sequence of SEQ ID NO: 70; and iii) a CDR3 comprising the amino acid sequence of SEQ ID NO: 81; and
 - b) a light chain variable region comprising iv) a CDR1 comprising the amino acid sequence of SEQ ID NO: 87; v) a CDR2 comprising the amino acid sequence of SEQ ID NO: 93; and vi) a CDR3 comprising the amino acid sequence of SEQ ID NO: 105.
2. The antibody or antigen-binding moiety of claim 1, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 106 or an amino acid sequence having at least 95% sequence identity to SEQ ID NO: 106.
3. The antibody or antigen-binding moiety of claim 1, wherein the light chain variable region comprises the amino acid sequence of SEQ ID NO: 107 or an amino acid sequence having at least 95% sequence identity to SEQ ID NO: 107.
4. The antibody or antigen-binding moiety of claim 1, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 106 or an amino acid sequence having at least 95% sequence identity to SEQ ID NO: 106; and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 107 or an amino acid sequence having at least 95% sequence identity to SEQ ID NO: 107.
5. The antibody or antigen-binding moiety of claim 4, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 106; and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 107.
6. The antibody or antigen-binding moiety of claim 1, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 12 or an amino acid sequence having at least 95% sequence identity to SEQ ID NO: 12; and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 24 or an amino acid sequence having at least 95%

sequence identity to SEQ ID NO: 24.

7. An isolated anti-Tau antibody or antigen-binding moiety thereof comprising:

a) a heavy chain variable region comprising i) a complementary determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO: 50; ii) a CDR2 comprising the amino acid sequence of SEQ ID NO: 61; and iii) a CDR3 comprising the amino acid sequence of SEQ ID NO: 72; and

b) a light chain variable region comprising iv) a CDR1 comprising the amino acid sequence of SEQ ID NO: 83; v) a CDR2 comprising the amino acid sequence of SEQ ID NO: 91; and vi) a CDR3 comprising the amino acid sequence of SEQ ID NO: 97.

8. The antibody or antigen-binding moiety of claim 7, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 3 or an amino acid sequence having at least 95% sequence identity to SEQ ID NO: 3.

9. The antibody or antigen-binding moiety of claim 7, wherein the light chain variable region comprises the amino acid sequence of SEQ ID NO: 15 or an amino acid sequence having at least 95% sequence identity to SEQ ID NO: 15.

10. The antibody or antigen-binding moiety of claim 7, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 3 or an amino acid sequence having at least 95% sequence identity to SEQ ID NO: 3; and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 15 or an amino acid sequence having at least 95% sequence identity to SEQ ID NO: 15.

11. The antibody or antigen-binding moiety of claim 10, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 3; and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 15.

12. The antibody or antigen-binding moiety of claim 7, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 2 or an amino acid sequence having at least 95% sequence identity to SEQ ID NO: 2; and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 14 or an amino acid sequence having at least 95% sequence identity to SEQ ID NO: 14.

13. The antibody or antigen-binding moiety of any one of claims 1-12, wherein the antibody or antigen-binding moiety is a monoclonal antibody.
14. The antibody or antigen-binding moiety of any one of claims 1-12, wherein the antibody or antigen-binding moiety preferentially binds to pathological human Tau species relative to normal human Tau species.
15. The antibody or antigen-binding moiety of claim 14, wherein the pathological human Tau species is:
- from a tauopathy brain;
 - Tau aggregates or an abnormally phosphorylated Tau or both;
 - Tau aggregates or abnormally phosphorylated accumulated at synapses of brain or both; or
 - Tau aggregates or abnormally phosphorylated accumulated at synapses of tauopathy brain or both.
16. The antibody or antigen-binding moiety of any one of claims 1-6, wherein the antibody or antigen-binding moiety binds to amino acid residues R230, T231, S237, T245, K281 and S289 of a human 2N4R Tau isoform.
17. The antibody or antigen-binding moiety of any one of claims 7-12, wherein the antibody or antigen-binding moiety binds to amino acid residues S131, K132, T135, S137 and R155 of a human 2N4R Tau isoform.
18. An isolated anti-Tau antibody or antigen-binding moiety thereof comprising
a heavy chain variable region comprising CDR1, CDR2, and CDR3 comprised in the amino acid sequence of SEQ ID NO: 106; and a light chain variable region comprising CDR1, CDR2, and CDR3 comprised in the amino acid sequence of SEQ ID NO: 107.
19. An isolated anti-Tau antibody or antigen-binding moiety thereof comprising
a heavy chain variable region comprising CDR1, CDR2, and CDR3 comprised in the amino acid sequence of SEQ ID NO: 3; and a light chain variable region comprising CDR1, CDR2, and CDR3 comprised in the amino acid sequence of SEQ ID NO: 15.
20. A labeled antibody comprising the antibody or antigen-binding moiety of any one of claims

1-12 and a detectable label.

21. A pharmaceutical composition comprising the antibody or antigen-binding moiety of any one of claims 1-12 and a pharmaceutically acceptable carrier.