~~**We claim:**~~

CLAIMS

1. An isolated antibody or antigen-binding fragment thereof that binds to paired helical filament-tau (PHF-tau) comprising a heavy chain variable region (V_H) comprising a complementary determining region 1 (HCDR1), an HCDR2, and an HCDR3, and a light chain variable region (V_L) comprising a complementary determining region 1 (LCDR1), an LCDR2, and an LCDR3, wherein:

(a) the antibody or antigen-binding fragment thereof comprises an HCDR1 of SEQ ID NO:1~~;~~, an HCDR2 of SEQ ID NO:2, and an HCDR3 of SEQ ID NO:3; and an LCDR1 of SEQ ID NO:4~~;~~, an LCDR2 of SEQ ID NO:5~~;~~, and an LCDR3 of SEQ ID NO:6;

(b) the antibody or antigen-binding fragment thereof comprises an HCDR1 of SEQ ID NO:7~~;~~, an HCDR2 of SEQ ID NO:8, and an HCDR3 of SEQ ID NO:3; and an LCDR1 of SEQ ID NO:9~~;~~, an LCDR2 of SEQ ID NO:5~~;~~, and an LCDR3 of SEQ ID NO:6;

(c) the antibody or antigen-binding fragment thereof comprises an HCDR1 of SEQ ID NO:7~~;~~, an HCDR2 of SEQ ID NO:10, and an HCDR3 of SEQ ID NO:3; and an LCDR1 of SEQ ID NO:11~~;~~, an LCDR2 of SEQ ID NO:5~~;~~, and an LCDR3 of SEQ ID NO:6;

(d) the antibody or antigen-binding fragment thereof comprises an HCDR1 of SEQ ID NO:7~~;~~, an HCDR2 of SEQ ID NO:12, and an HCDR3 of SEQ ID NO:3; and an LCDR1 of SEQ ID NO:11~~;~~, an LCDR2 of SEQ ID NO:5~~;~~, and an LCDR3 of SEQ ID NO:6;

(e) the antibody or antigen-binding fragment thereof comprises an HCDR1 of SEQ ID NO:7~~;~~, an HCDR2 of SEQ ID NO:13, and an HCDR3 of SEQ ID NO:3; and an LCDR1 of SEQ ID NO:11~~;~~, an LCDR2 of SEQ ID NO:5~~;~~, and an LCDR3 of SEQ ID NO:6; or

(f) the antibody or antigen-binding fragment thereof comprises an HCDR1 of SEQ ID NO:7~~;~~, an HCDR2 of SEQ ID NO:14, and an HCDR3 of SEQ ID NO:3; and an LCDR1 of SEQ ID NO:11~~;~~, an LCDR2 of SEQ ID NO:5~~;~~, and an LCDR3 of SEQ ID NO:6.

2. The isolated antibody or antigen-binding fragment of claim 1, comprising:

(a) a heavy chain variable region comprising a sequence at least 95% identical to SEQ ID NO:15 and a light chain variable region comprising a sequence at least ~~955~~95% identical to SEQ ID NO: 16;

(b) a heavy chain variable region comprising a sequence at least 95% identical to SEQ ID NO:17 and a light chain variable region comprising a sequence at least 95% identical to SEQ ID NO: 18;

(c) a heavy chain variable region comprising a sequence at least 95% identical to SEQ ID NO:19 and a light chain variable region comprising a sequence at least 95% identical to SEQ ID NO: 20;

(d) a heavy chain variable region comprising a sequence at least 95% identical to SEQ ID NO:21 and a light chain variable region comprising a sequence at least 95% identical to SEQ ID NO: 22;

(e) a heavy chain variable region comprising a sequence at least 95% identical to SEQ ID NO:23 and a light chain variable region comprising a sequence at least 95% identical to SEQ ID NO: 20; or

(f) a heavy chain variable region comprising a sequence at least 95% identical to SEQ ID NO:24 and a light chain variable region comprising a sequence at least 95% identical to SEQ ID NO: 25.

3. The isolated antibody or antigen-binding fragment of claim 1, comprising

(a) a heavy chain variable region comprising SEQ ID NO:15 and a light chain variable region comprising SEQ ID NO: 16;

(b) a heavy chain variable region comprising SEQ ID NO:17 and a light chain variable region comprising SEQ ID NO: 18;

(c) a heavy chain variable region comprising SEQ ID NO:19 and a light chain variable region comprising SEQ ID NO: 20;

(d) a heavy chain variable region comprising SEQ ID NO:21 and a light chain variable region comprising SEQ ID NO: 22;

(e) a heavy chain variable region comprising SEQ ID NO:23 and a light chain variable region comprising SEQ ID NO: 20; or

(f) a heavy chain variable region comprising SEQ ID NO:24 and a light chain variable region comprising SEQ ID NO: 25.

4. The isolated antibody or antigen-binding fragment of claim 1 that is humanized.

5. An isolated nucleic acid encoding the antibody or antigen-binding fragment of claim 1.

6. A vector comprising the isolated nucleic acid of claim 5.

7. A host cell comprising the isolated nucleic acid of claim ~~6~~5.

8. A pharmaceutical composition comprising the isolated antibody or antigen-binding fragment of claim 1 and a pharmaceutically acceptable carrier.

9. A pharmaceutical composition comprising the isolated antibody or antigen-binding fragment of claim 4 and a pharmaceutically acceptable carrier.

10. ~~A method of~~The pharmaceutical composition of claim 8 for use in reducing pathological tau aggregation or spreading of tauopathy in a subject in need thereof~~, comprising administering to the subject the pharmaceutical composition of claim 8~~.

11. ~~A method of~~The pharmaceutical composition of claim 9 for use in reducing pathological tau aggregation or spreading of tauopathy in a subject in need thereof~~, comprising administering to the subject the pharmaceutical composition of claim 9~~.

12. ~~A method of~~The pharmaceutical composition of claim 8 or claim 9 for use in treating a tauopathy in a subject in need thereof~~, comprising administering to the subject the pharmaceutical composition of claim 10~~.

13. ~~A method of~~The pharmaceutical composition of claim 8 or claim 9 for use in treating a tauopathy in a subject in need thereof~~, comprising administering to the subject the pharmaceutical composition of claim 11~~, wherein the tauopathy is selected from the group consisting of Alzheimer's disease (including familial Alzheimer's disease and sporadic Alzheimer's disease), frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP-17), progressive supranuclear palsy, corticobasal degeneration, Pick's disease,

progressive subcortical gliosis, tangle only dementia, diffuse neurofibrillary tangles with calcification, argyrophilic grain dementia, amyotrophic lateral sclerosis parkinsonism-dementia complex, Down syndrome, Gerstmann-Sträussler-Scheinker disease, Hallervorden-Spatz disease, inclusion body myositis, Creutzfeld-Jakob disease, multiple system atrophy, Niemann-Pick disease type C, prion protein cerebral amyloid angiopathy, subacute sclerosing panencephalitis, myotonic dystrophy, non-Guamanian motor neuron disease with neurofibrillary tangles, postencephalitic parkinsonism, chronic traumatic encephalopathy, and dementia pugulistica (boxing disease).

14. A method of producing the antibody or antigen-binding fragment of claim 1, comprising culturing a cell comprising a nucleic acid encoding the antibody or antigen-binding fragment under conditions to produce the antibody or antigen-binding fragment, and recovering the antibody or antigen-binding fragment from the cell or cell culture.

15. A method of producing a pharmaceutical composition comprising the humanized antibody or antigen-binding fragment of claim 1, comprising combining the antibody or antigen-binding fragment with a pharmaceutically acceptable carrier to obtain the pharmaceutical composition.

16. A method of detecting the presence of PHF-tau in a biological sample from a subject, comprising contacting the biological sample with the antibody or antigen-binding fragment of claim 1, and detecting binding of the antibody or antigen-binding fragment to PHF-tau in the sample from the subject.

17. The method of claim 16, wherein the biological sample is a blood, urine, or cerebral spinal fluid sample.