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 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 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. The pharmaceutical composition of claim 8 for use in reducing pathological tau aggregation or spreading of tauopathy in a subject in need thereof.

11. The pharmaceutical composition of claim 9 for use in reducing pathological tau aggregation or spreading of tauopathy in a subject in need thereof.

12. The pharmaceutical composition of claim 8 or claim 9 for use in treating a tauopathy in a subject in need thereof.

13. The pharmaceutical composition of claim 8 or claim 9 for use in treating a tauopathy in a subject in need thereof, 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.