CLAIMS

We claim:

1. An isolated monoclonal antibody or antigen-binding fragment comprising:

(a) immunoglobulin heavy chain complementarity determining regions (HCDRs) HCDR1, HCDR2 and HCDR3 having the polypeptide sequences of SEQ ID NOs: 7, 8 and 9, respectively and immunoglobulin light chain complementarity determining regions (LCDRs) LCDR1, LCDR2 and LCDR3 having the polypeptide sequences of SEQ ID NOs: 19, 20 and 21, respectively;

(b) HCDR1, HCDR2 and HCDR3 having the polypeptide sequences of SEQ ID NOs: 1, 2 and 3, respectively and LCDR1, LCDR2 and LCDR3 having the polypeptide sequences of SEQ ID NOs: 13, 14 and 15, respectively;

(c) HCDR1, HCDR2 and HCDR3 having the polypeptide sequences of SEQ ID NOs: 4, 5 and 6, respectively and LCDR1, LCDR2 and LCDR3 having the polypeptide sequences of SEQ ID NOs: 16, 17 and 18, respectively; or

(d) HCDR1, HCDR2 and HCDR3 having the polypeptide sequences of SEQ ID NOs: 10, 11 and 12, respectively and LCDR1, LCDR2 and LCDR3 having the polypeptide sequences of SEQ ID NOs: 22, 23 and 24, respectively.

wherein the antibody or antigen-binding fragment thereof binds PHF-tau.

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

a heavy chain variable region (VH) having the polypeptide sequence of SEQ ID NO: 27 and a light chain variable region (VL) having the polypeptide sequence of SEQ ID NO: 31.

3. The isolated monoclonal antibody or antigen-binding fragment of claim 2 comprising:

a heavy chain of SEQ ID NO: 45, and a light chain of SEQ ID NO: 46.

4. The isolated monoclonal antibody or antigen-binding fragment of any one of claims 1 to 3 comprising a human heavy chain IgG1 constant region and a human light chain kappa constant region.

5. An isolated nucleic acid encoding the monoclonal antibody or antigen-binding fragment of any one of claims 1 to 4.

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

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

8. A pharmaceutical composition comprising the isolated monoclonal antibody or antigen-binding fragment of any one of claims 1 to 4 and a pharmaceutically acceptable carrier.

9. Use of the pharmaceutical composition of claim 8 in the manufacture of a medicament to reduce pathological tau aggregation or spreading of tauopathy in a subject in need thereof.

10. Use of the pharmaceutical composition of claim 8 in the manufacture of a medicament to treat a tauopathy in a subject in need thereof.

11. The use of claim 10, wherein the tauopathy is selected from the group consisting of familial Alzheimer's disease, 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).

12. A method of producing the monoclonal antibody or antigen-binding fragment of any one of claims 1 to 4, the method 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.

13. A method of detecting the presence of PHF-tau in a biological sample from a subject, the method comprising contacting the biological sample with the antibody or antigen-binding fragment of any one of claims 1 to 4 and detecting binding of the antibody or antigen-binding fragment to PHF-tau in the sample from the subject.

14. The method of claim 13, wherein the biological sample is a blood, serum, plasma, interstitial fluid, or cerebral spinal fluid sample.