

induced conditions such as boxer's encephalopathy (Tetsuaki Arai, "Shinkei Naika" (Japanese document), Vol.72, special number, (Suppl.6), 2010, pp.46-51).

Tau can be phosphorylated on a large number of amino acid residues, and phosphorylated tau has been believed to be the pathological tau species in tauopathies. While there are many known phosphorylation sites on tau and anti-tau antibodies with different specificities (e.g., targeting total tau, nonphosphorylated tau, or tau that is phosphorylated at various amino acid residues) in the art, it is still uncertain which phosphorylated tau species is the best target for treating tauopathies. Among the known anti-tau antibodies, some do not distinguish between pathological tau species (e.g., tau in the brain of AD patients) and normal tau (e.g., tau in the brain of healthy human beings), and others do not have a sufficiently high affinity and thus have to be administered at very high doses to reach an effective amount in the brain. Thus, there is unmet need to produce high affinity anti-tau antibodies that specifically target pathological tau species (e.g., tau-pS413).

SUMMARY OF THE INVENTION

The present disclosure provides high affinity antibodies or antigen binding fragments thereof that bind to human tau-pS413 (e.g., tau having the amino acid sequence of SEQ ID NO:1 that is phosphorylated at serine 413). Also provided herein are isolated nucleic acids and vectors comprising polynucleotide sequences encoding such high affinity antibodies or antigen binding fragments thereof, cells (e.g., host cells) comprising such isolated nucleic acids or vectors, compositions or kits comprising such high affinity antibodies or antigen binding fragments thereof, and methods or uses involving such high affinity antibodies or antigen binding fragments thereof.

~~In one aspect, p~~Provided herein is an antibody or antigen binding fragment thereof that binds to tau-pS413.

In one aspect, provided herein is an antibody or antigen binding fragment thereof that binds to tau-pS413, comprising:

(a) a heavy chain variable region complementarity determining region 1 (VH-CDR1) comprising the amino acid sequence of SEQ ID NO:41; a heavy chain variable region complementarity determining region 2 (VH-CDR2) comprising the amino acid sequence of SEQ ID NO:42; and a heavy chain variable region complementarity determining region 3 (VH-CDR3) comprising the amino acid sequence of SEQ ID NO:43; and

a light chain variable region complementarity determining region 1 (VL-CDR1) comprising the amino acid sequence of SEQ ID NO:29; a light chain variable region complementarity determining region 2 (VL-CDR2) comprising the amino acid sequence of SEQ ID NO:30; and a light chain variable region complementarity determining region 3 (VL-CDR3) comprising the amino acid sequence of SEQ ID NO:31;

(b) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:41; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:42; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:43; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:33; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:34; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:35;

(c) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:41; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:42; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:43; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:37; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:38; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:39;

(d) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:41; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:42; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:43; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:25; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:26; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:27;

(e) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:41; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:42; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:43; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:17; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:18; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:19;

(f) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:45; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:46; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:47; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:29; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:30; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:31;

5 (g) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:45; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:46; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:47; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:33; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:34; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:35;

10 (h) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:45; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:46; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:47; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:37; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:38; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:39;

15 (i) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:45; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:46; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:47; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:25; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:26; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:27;

20 (j) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:45; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:46; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:47; and

25 a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:17; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:18; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:19;

(k) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:49; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:50; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:51; and

30 a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:29; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:30; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:31;

(l) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:49; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:50; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:51; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:33; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:34; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:35;

(m) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:49; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:50; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:51; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:37; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:38; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:39;

(n) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:49; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:50; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:51; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:25; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:26; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:27;

(o) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:49; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:50; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:51; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:17; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:18; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:19;

(p) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:53; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:54; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:55; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:29; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:30; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:31;

(q) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:53; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:54; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:55; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:33; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:34; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:35;

(r) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:53; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:54; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:55; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:37; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:38; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:39;

(s) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:53; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:54; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:55; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:25; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:26; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:27;

(t) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:53; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:54; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:55; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:17; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:18; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:19;

(u) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:21; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:22; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:23; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:29; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:30; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:31;

(v) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:21; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:22; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:23; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:33; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:34; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:35;

(w) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:21; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:22; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:23; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:37; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:38; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:39;

(x) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:86; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:87; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:88; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:83; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:84; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:85;

(y) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:92; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:93; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:94; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:89; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:90; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:91;

(z) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:98; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:99; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:100; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:95; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:96; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:97;

(aa) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:104; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:105; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:106; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:101; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:102; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:103;

(bb) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO:44; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO:32;

(cc) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:44; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36;

(dd) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:44; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40;

(ee) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:44; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:28;

(ff) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:44; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:20;

(gg) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:32;

(hh) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36;

(ii) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40;

(jj) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:28;

(kk) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:20;

(ll) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:32;

(mm) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36;

(nn) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40;

(oo) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:28;

(pp) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:20;

(qq) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:32;

(rr) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36;

(ss) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40;

(tt) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:28;

(uu) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:20;

(vv) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:24; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:32;

(ww) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:24; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36; or

(xx) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:24; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40.

In one embodimentexample, the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a heavy chain variable region complementarity determining region 1 (VH-CDR1) comprising the amino acid sequence of SEQ ID NO:41; a heavy chain variable region complementarity determining region 2 (VH-CDR2) comprising the amino acid sequence of SEQ ID NO:42; and a heavy chain variable region complementarity determining region 3 (VH-CDR3) comprising the amino acid sequence of SEQ ID NO:43; and a light chain variable region complementarity determining region 1 (VL-CDR1) comprising the amino acid sequence

of SEQ ID NO:29; a light chain variable region complementarity determining region 2 (VL-CDR2)

comprising the amino acid sequence of SEQ ID NO:30; and a light chain variable region complementarity determining region 3 (VL-CDR3) comprising the amino acid sequence of SEQ ID NO:31.

In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:41; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:42; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:43; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:33; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:34; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:35.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:41; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:42; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:43; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:37; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:38; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:39.

In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:41; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:42; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:43; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:25; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:26; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:27.

In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:41; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:42; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:43; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:17; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:18; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:19.

In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:45; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:46; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:47; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:29; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:30; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:31.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:45; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:46; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:47; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:33; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:34; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:35.

In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:45; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:46; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:47; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:37; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:38; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:39.

In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:45; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:46; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:47; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:25; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:26; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:27.

In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:45; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:46; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:47; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:17; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:18; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:19.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:49; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:50; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:51; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:29; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:30; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:31.

In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:49; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:50; and a VH-CDR3 comprising

the amino acid sequence of SEQ ID NO:51; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:33; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:34; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:35.

In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:49; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:50; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:51; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:37; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:38; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:39.

In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:49; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:50; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:51; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:25; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:26; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:27.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:49; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:50; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:51; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:17; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:18; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:19.

In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:53; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:54; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:55; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:29; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:30; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:31.

In ~~one embodiment~~[another aspect](#), [provided herein is an](#) ~~the~~ antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:53; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:54; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:55; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:33; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:34; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:35.

In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:53; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:54; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:55; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:37; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:38; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:39.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:53; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:54; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:55; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:25; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:26; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:27.

In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:53; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:54; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:55; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:17; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:18; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:19.

In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:21; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:22; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:23; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:29; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:30; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:31.

In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:21; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:22; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:23; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:33; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:34; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:35.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:21; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:22; and a VH-CDR3 comprising

the amino acid sequence of SEQ ID NO:23; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:37; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:38; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:39.

In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:86; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:87; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:88; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:83; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:84; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:85.

In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:92; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:93; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:94; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:89; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:90; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:91.

In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:98; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:99; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:100; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:95; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:96; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:97.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:104; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:105; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:106; and a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:101; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:102; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:103.

In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO:44; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO:32.

In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:44; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36.

5 In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:44; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40.

10 In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:44; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:28.

15 In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:44; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:20.

20 In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:32.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36.

25 In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40.

30 In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:28.

In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:20.

5 In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:32.

10 In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36.

15 In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40.

20 In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:28.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:20.

25 In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:32.

30 In ~~one embodiment~~[another aspect](#), [provided herein is an](#) ~~the~~ antibody or antigen binding fragment thereof that binds to tau-pS413 ~~comprises~~[comprising](#) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36.

In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40.

5 In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:28.

10 In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:20.

15 In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:24; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:32.

20 In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:24; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:24; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40.

25 In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:44, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:32.

30 In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:44, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:36.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:44, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:40.

5 In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:44, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:28.

10 In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:44, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:20.

15 In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:48, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:32.

20 In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:48, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:36.

In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:48, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:40.

25 In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:48, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:28.

30 In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:48, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:20.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:52, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:32.

5 In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:52, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:36.

10 In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:52, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:40.

15 In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:52, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:28.

20 In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:52, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:20.

In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:56, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:32.

25 In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:56, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:36.

30 In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:56, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:40.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:56, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:28.

5 In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:56, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:20.

10 In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:24, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:32.

15 In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:24, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:36.

20 In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:24, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:40.

In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:44, and a VL having the amino acid sequence of SEQ ID NO:32.

25 In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:44, and a VL having the amino acid sequence of SEQ ID NO:36.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:44, and a VL having the amino acid sequence of SEQ ID NO:40.

30 In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:44, and a VL having the amino acid sequence of SEQ ID NO:28.

In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:44, and a VL having the amino acid sequence of SEQ ID NO:20.

In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:48, and a VL having the amino acid sequence of SEQ ID NO:32.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:48, and a VL having the amino acid sequence of SEQ ID NO:36.

In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:48, and a VL having the amino acid sequence of SEQ ID NO:40.

In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:48, and a VL having the amino acid sequence of SEQ ID NO:28.

In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:48, and a VL having the amino acid sequence of SEQ ID NO:20.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:52, and a VL having the amino acid sequence of SEQ ID NO:32.

In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:52, and a VL having the amino acid sequence of SEQ ID NO:36.

In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:52, and a VL having the amino acid sequence of SEQ ID NO:40.

In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:52, and a VL having the amino acid sequence of SEQ ID NO:28.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:52, and a VL having the amino acid sequence of SEQ ID NO:20.

In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:56, and a VL having the amino acid sequence of SEQ ID NO:32.

In ~~one embodiment~~[another aspect](#), [provided herein is an](#) ~~the~~ antibody or antigen binding fragment thereof that binds to tau-pS413 ~~comprises~~[comprising](#) a VH having the amino acid sequence of SEQ ID NO:56, and a VL having the amino acid sequence of SEQ ID NO:36.

In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:56, and a VL having the amino acid sequence of SEQ ID NO:40.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:56, and a VL having the amino acid sequence of SEQ ID NO:28.

In still another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:56, and a VL having the amino acid sequence of SEQ ID NO:20.

In one [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:24, and a VL having the amino acid sequence of SEQ ID NO:32.

In another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:24, and a VL having the amino acid sequence of SEQ ID NO:36.

In yet another [embodimentexample](#), the antibody or antigen binding fragment thereof that binds to tau-pS413 comprises a VH having the amino acid sequence of SEQ ID NO:24, and a VL having the amino acid sequence of SEQ ID NO:40.

In various [embodimentexamples](#) of the antibody or antigen-binding fragment thereof that binds to tau-pS413 disclosed herein, the antibody or antigen-binding fragment thereof further comprises a heavy chain constant region having the amino acid sequence of SEQ ID NO:59, 60, 61, 62, 63, 64, 65, 66, 67, or 68. In one [embodimentexample](#), the antibody or antigen-binding fragment thereof further comprises a heavy chain constant region having the amino acid sequence of SEQ ID NO:59. In another [embodimentexample](#), the antibody or antigen-binding fragment thereof further comprises a heavy chain constant region having the amino acid sequence of SEQ ID NO:60. In yet another [embodimentexample](#), the antibody or antigen-binding fragment thereof further comprises a heavy chain constant region having the amino acid sequence of SEQ ID NO:61. In still another

[embodimentexample](#), the antibody or antigen-binding fragment thereof further comprises a heavy chain constant region having the amino acid sequence of SEQ ID NO:62. In one [embodimentexample](#), the antibody or antigen-binding fragment thereof further comprises a heavy chain constant region having the amino acid sequence of SEQ ID NO:63. In another [embodimentexample](#), the antibody or antigen-binding fragment thereof further comprises a heavy chain constant region having the amino acid sequence of SEQ ID NO:64. In yet another [embodimentexample](#), the antibody or antigen-binding fragment thereof further comprises a heavy chain constant region having the amino acid sequence of SEQ ID NO:65. In still another [embodimentexample](#), the antibody or antigen-binding fragment thereof further comprises a heavy chain constant region having the amino acid sequence of SEQ ID NO:66. In one [embodimentexample](#), the antibody or antigen-binding fragment thereof further comprises a heavy chain constant region having the amino acid sequence of SEQ ID NO:67. In another [embodimentexample](#), the antibody or antigen-binding fragment thereof further comprises a heavy chain constant region having the amino acid sequence of SEQ ID NO:68.

In certain [embodimentexamples](#), the antibody or antigen-binding fragment thereof further comprises a light chain constant region having the amino acid sequence of SEQ ID NO:57 or 58. In one [embodimentexample](#), the antibody or antigen-binding fragment thereof further comprises a light chain constant region having the amino acid sequence of SEQ ID NO:57. In one [embodimentexample](#), the antibody or antigen-binding fragment thereof further comprises a light chain constant region having the amino acid sequence of SEQ ID NO:58.

In some [embodimentexamples](#), the antibody or antigen-binding fragment thereof further comprises a heavy chain constant region having the amino acid sequence of SEQ ID NO:59, 60, 61, 62, 63, 64, 65, 66, 67, or 68, and a light chain constant region having the amino acid sequence of SEQ ID NO:57 or 58. In one [embodimentexample](#), the antibody or antigen-binding fragment thereof further comprises a heavy chain constant region having the amino acid sequence of SEQ ID NO:60, and a light chain constant region having the amino acid sequence of SEQ ID NO:58. In another [embodimentexample](#), the antibody or antigen-binding fragment thereof further comprises a heavy chain constant region having the amino acid sequence of SEQ ID NO:63, and a light chain constant region having the amino acid sequence of SEQ ID NO:58. In yet another [embodimentexample](#), the antibody or antigen-binding fragment thereof further comprises a heavy chain constant region having the amino acid sequence of SEQ ID NO:68, and a light chain constant region having the amino acid sequence of SEQ ID NO:58.

In certain [embodimentexamples](#), the antibody or antigen-binding fragment thereof comprises a light chain comprising the amino acid sequence of SEQ ID NO:71 and a heavy chain comprising the amino acid sequence of SEQ ID NO:72.

In some [embodimentexamples](#), the antibody or antigen-binding fragment thereof comprises a light chain comprising the amino acid sequence of SEQ ID NO:73 and a heavy chain comprising the amino acid sequence of SEQ ID NO:74.

In other [embodimentexamples](#), the antibody or antigen-binding fragment thereof comprises a light chain comprising the amino acid sequence of SEQ ID NO:75 and a heavy chain comprising the amino acid sequence of SEQ ID NO:76.

In yet other [embodimentexamples](#), the antibody or antigen-binding fragment thereof consists of two light chains comprising the amino acid sequence of SEQ ID NO:71 and two heavy chains comprising the amino acid sequence of SEQ ID NO:72.

In still other [embodimentexamples](#), the antibody or antigen-binding fragment thereof consists of two light chains comprising the amino acid sequence of SEQ ID NO:73 and two heavy chains comprising the amino acid sequence of SEQ ID NO:74.

In yet still other [embodimentexamples](#), the antibody or antigen-binding fragment thereof consists of two light chains comprising the amino acid sequence of SEQ ID NO:75 and two heavy chains comprising the amino acid sequence of SEQ ID NO:76.

In certain [embodimentexamples](#), the antibody or antigen-binding fragment thereof consists of two light chains consisting of the amino acid sequence of SEQ ID NO:71 and two heavy chains consisting of the amino acid sequence of SEQ ID NO:72.

In some [embodimentexamples](#), the antibody or antigen-binding fragment thereof consists of two light chains consisting of the amino acid sequence of SEQ ID NO:73 and two heavy chains consisting of the amino acid sequence of SEQ ID NO:74.

In other [embodimentexamples](#), the antibody or antigen-binding fragment thereof consists of two light chains consisting of the amino acid sequence of SEQ ID NO:75 and two heavy chains consisting of the amino acid sequence of SEQ ID NO:76.

In various [embodimentexamples](#) of the antibody or antigen binding fragment thereof described herein, the antibody or antigen binding fragment thereof has an equilibrium dissociation constant (KD) of 1×10^{-8} M or less for tau-pS413. In some [embodimentexamples](#), the antibody or antigen binding fragment thereof has an equilibrium dissociation constant (KD) of 9×10^{-9} M or less for tau-pS413. In other [embodimentexamples](#), the antibody or antigen binding fragment thereof has an equilibrium dissociation constant (KD) of 8×10^{-9} M or less for tau-pS413. In yet other

[embodimentexamples](#), the antibody or antigen binding fragment thereof has an equilibrium dissociation constant (KD) of 7×10^{-9} M or less for tau-pS413. In some [embodimentexamples](#), the antibody or antigen binding fragment thereof has an equilibrium dissociation constant (KD) of 6×10^{-9} M or less for tau-pS413. In other [embodimentexamples](#), the antibody or antigen binding fragment thereof has an equilibrium dissociation constant (KD) of 5×10^{-9} M or less for tau-pS413. In yet other [embodimentexamples](#), the antibody or antigen binding fragment thereof has an equilibrium dissociation constant (KD) of 4×10^{-9} M or less for tau-pS413. In still other [embodimentexamples](#), the antibody or antigen binding fragment thereof has an equilibrium dissociation constant (KD) of 3×10^{-9} M or less for tau-pS413. In yet still other [embodimentexamples](#), the antibody or antigen binding fragment thereof has an equilibrium dissociation constant (KD) of 2×10^{-9} M or less for tau-pS413. In some [embodimentexamples](#), the KD is measured by Surface Plasmon Resonance (SPR) assay with the antibody or antigen binding fragment thereof being immobilized. In one [embodimentexample](#), the KD is measured by Biacore. In another [embodimentexample](#), the KD is measured by KinExA.

~~In another aspect, pP~~provided [herein](#) is [also](#) an isolated nucleic acid encoding various polypeptides disclosed herein.

In certain [embodimentexamples](#), the isolated nucleic acid encodes the VH of various antibodies or antigen binding fragments thereof disclosed herein. In some [embodimentexamples](#), the isolated nucleic acid encodes the VL of various antibodies or antigen binding fragments thereof disclosed herein. In other [embodimentexamples](#), the isolated nucleic acid encodes the VH and the VL of various antibodies or antigen binding fragments thereof disclosed herein.

[In another aspect, provided herein is an isolated nucleic acid, encoding: \(a\) a VH of the antibody or antigen binding fragment thereof as disclosed herein; \(b\) a VL of the antibody or antigen binding fragment thereof as disclosed herein; \(c\) a VH and a VL of the antibody or antigen binding fragment thereof as disclosed herein; \(d\) a heavy chain of the antibody as disclosed herein; \(e\) a light chain of the antibody as disclosed herein; or \(f\) a heavy chain and a light chain of the antibody as disclosed herein.](#)

In certain [embodimentexamples](#), the isolated nucleic acid encodes the heavy chain of various antibodies or antigen binding fragments thereof disclosed herein. In some [embodimentexamples](#), the isolated nucleic acid encodes the light chain of various antibodies or antigen binding fragments thereof disclosed herein. In other [embodimentexamples](#), the isolated nucleic acid encodes the heavy chain and the light chain of various antibodies or antigen binding fragments thereof disclosed herein.

In yet another aspect, provided is an expression vector comprising the various isolated nucleic acids disclosed herein.

~~In still another aspect, p~~provided [herein](#) is [also](#) a host cell comprising one or more of the various isolated nucleic acids or one of more of the various expression vectors disclosed herein.

- 5 [In another aspect, provided herein is a host cell comprising the expression vector disclosed herein.](#) In some [embodimentexamples](#), the host cell comprises one of more of the various isolated nucleic acids disclosed herein. In other [embodimentexamples](#), the host cell comprises one of more of the various expression vectors disclosed herein.

~~In yet still another aspect, p~~Provided herein is also a method of producing the antibody or antigen binding fragment thereof disclosed herein. In another aspect, provided herein is a method of producing an antibody or antigen binding fragment thereof, comprising: (a) culturing the host cell as disclosed herein under conditions wherein the antibody or antigen binding fragment thereof is expressed; and (b) harvesting the antibody or antigen binding fragment thereof. In certain embodimentexamples, the method of producing the antibody or antigen binding fragment thereof disclosed herein comprises expressing an isolated nucleic acid described herein under conditions wherein the antibody or antigen binding fragment thereof is expressed. In some embodimentexamples, the method of producing the antibody or antigen binding fragment thereof disclosed herein comprises expressing an expression vector described herein under conditions wherein the antibody or antigen binding fragment thereof is expressed. In other embodimentexamples, the method of producing the antibody or antigen binding fragment thereof disclosed herein comprises culturing the host cell comprising an isolated nucleic acid or an expression vector described herein under conditions wherein the antibody or antigen binding fragment thereof is expressed.

In another aspect, provided is a composition comprising the antibodies or antigen binding fragments thereof described herein and a pharmaceutically acceptable carrier. In another aspect, provided is a composition comprising an antibody as disclosed herein and a pharmaceutically acceptable carrier.

In some embodimentexamples, the composition further comprises an additional agent.

In particular embodimentexamples, the additional agent is an agent effective to treat the same or different disorder as the anti-tau-pS413 antibodies or antigen-binding fragments thereof disclosed herein are being used to treat. In some embodimentexamples, the additional agent is an agent effective to mitigate one or more side effects of the anti-tau-pS413 antibodies or antigen-binding fragments thereof disclosed herein. Exemplary additional agents include, but are not limited to: cholinesterase inhibitors (such as donepezil, galantamine, rivastigmine, and tacrine), NMDA receptor antagonists (such as memantine), amyloid beta peptide aggregation inhibitors, antioxidants, gamma-secretase modulators, nerve growth factor (NGF) mimics or NGF gene therapy, PPAR γ agonists, HMG-CoA reductase inhibitors (statins), amphotericins, calcium channel blockers, GABA receptor antagonists, glycogen synthase kinase inhibitors, intravenous immunoglobulin, muscarinic receptor agonists, nicotinic receptor modulators, active or passive amyloid beta peptide for immunization, phosphodiesterase inhibitors, serotonin receptor antagonists, anti-amyloid beta peptide antibodies, growth hormone, neurotrophic factor,

brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF), neurotrophin-4/5, fibroblast growth factor (FGF)-2 and other FGFs, neurotrophin (NT)-3, erythropoietin (EPO), hepatocyte growth factor (HGF), epidermal growth factor (EGF), transforming growth factor (TGF)- α , TGF- β , vascular endothelial growth factor (VEGF), interleukin-1 receptor antagonist (IL-1ra), ciliary neurotrophic factor (CNTF), glial-derived neurotrophic factor (GDNF), neurturin, platelet-derived growth factor (PDGF), heregulin, neuregulin, artemin, persephin, interleukins,

glial cell line derived neurotrophic factor (GFR), granulocyte-colony stimulating factor (CSF), granulocyte-macrophage-CSF, netrins, cardiotrophin-1, hedgehogs, leukemia inhibitory factor (LIF), midkine, pleiotrophin, bone morphogenetic proteins (BMPs), netrins, saposins, semaphorins, stem cell factor (SCF), or a different anti-tau antibody.

5 ~~In yet another aspect, p~~Provided [herein](#) is [also](#) a kit comprising the antibodies or antigen binding fragments thereof described herein.

~~In still another aspect, p~~Provided [herein](#) is [also](#) a method of treating tauopathy in a subject, comprising administering to the subject an effective amount of the antibodies or antigen binding fragments thereof described herein.

10 In some [embodimentexamples](#), the method further comprises administering to the subject an additional agent.

In particular [embodimentexamples](#), the additional agent is an agent effective to treat the same or different disorder as the anti-tau-pS413 antibodies or antigen-binding fragments thereof disclosed herein are being used to treat. In some [embodimentexamples](#), the additional agent is

15 an agent effective to mitigate one or more side effects of the anti-tau-pS413 antibodies or antigen-binding fragments thereof disclosed herein. Exemplary additional agents include, but are not limited to: cholinesterase inhibitors (such as donepezil, galantamine, rivastigmine, and tacrine), NMDA receptor antagonists (such as memantine), amyloid beta peptide aggregation inhibitors, antioxidants, gamma-secretase modulators, nerve growth factor (NGF) mimics or
20 NGF gene therapy, PPAR γ agonists, HMG-CoA reductase inhibitors (statins), amphotericins, calcium channel blockers, GABA receptor antagonists, glycogen synthase kinase inhibitors, intravenous immunoglobulin, muscarinic receptor agonists, nicotinic receptor modulators, active or passive amyloid beta peptide for immunization, phosphodiesterase inhibitors, serotonin receptor antagonists, anti-amyloid beta peptide antibodies, growth hormone, neurotrophic factor,
25 brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF), neurotrophin-4/5, fibroblast growth factor (FGF)-2 and other FGFs, neurotrophin (NT)-3, erythropoietin (EPO), hepatocyte growth factor (HGF), epidermal growth factor (EGF), transforming growth factor (TGF)- α , TGF- β , vascular endothelial growth factor (VEGF), interleukin-1 receptor antagonist (IL-1ra), ciliary neurotrophic factor (CNTF), glial-derived neurotrophic factor (GDNF), neurturin,
30 platelet-derived growth factor (PDGF), heregulin, neuregulin, artemin, persephin, interleukins, glial cell line derived neurotrophic factor (GFR), granulocyte-colony stimulating factor (CSF), granulocyte-macrophage-CSF, netrins, cardiotrophin-1, hedgehogs, leukemia inhibitory factor

(LIF), midkine, pleiotrophin, bone morphogenetic proteins (BMPs), netrins, saposins, semaphorins, stem cell factor (SCF), or a different anti-tau antibody.

In some [embodimentexamples](#) of the method, the tauopathy is a neurodegenerative disease, including but not limited to Alzheimer's disease (AD), corticobasal degeneration (CBD) or corticobasal syndrome (CBS), progressive supranuclear palsy, Pick's disease, argyrophilic grain dementia (argyrophilic grain disease), multiple system tauopathy with presenile dementia (MSTD), frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17), dementia with neurofibrillary tangles, diffuse neurofibrillary tangle with calcification (DNTC), white matter tauopathy with globular glial inclusions (WMT-GGI), or frontotemporal lobar degeneration with tau pathology (FTLD-tau). In one [embodimentexample](#), the tauopathy is AD. In another [embodimentexample](#), the tauopathy is CBD. In yet another [embodimentexample](#), the tauopathy is progressive supranuclear palsy. In still another [embodimentexample](#), the tauopathy is Pick's disease. In one [embodimentexample](#), the tauopathy is argyrophilic grain dementia. In another [embodimentexample](#), the tauopathy is MSTD. In yet another [embodimentexample](#), the tauopathy is FTDP-17. In still another [embodimentexample](#), the tauopathy is dementia with neurofibrillary tangles. In one [embodimentexample](#), the tauopathy is DNTC. In another [embodimentexample](#), the tauopathy is WMT-GGI. In yet another [embodimentexample](#), the tauopathy is FTLD-tau.

In other [embodimentexamples](#) of the method, the tauopathy is a non-neurodegenerative disease, including but not limited to infectious diseases, such as Economo's encephalitis sequela and subacute sclerosing panencephalitis, and trauma-induced conditions, such as boxer's encephalopathy. In one [embodimentexample](#), the tauopathy is Economo's encephalitis sequela. In another [embodimentexample](#), the tauopathy is subacute sclerosing panencephalitis. In yet another [embodimentexample](#), the tauopathy is boxer's encephalopathy.

~~In yet still another aspect, p~~Provided [herein](#) is [also](#) a method of decreasing the amount of tau-pS413 in the brain of a subject, comprising administering to the subject in need thereof an effective amount of the antibodies or antigen binding fragments thereof of described herein.

In some [embodimentexamples](#), the method further comprises administering to the subject an additional agent.

In particular [embodimentexamples](#), the additional agent is an agent effective to treat the same or different disorder as the anti-tau-pS413 antibodies or antigen-binding fragments thereof disclosed herein are being used to treat. In some [embodimentexamples](#), the additional agent is an agent effective to mitigate one or more side effects of the anti-tau-pS413 antibodies or antigen-binding fragments thereof disclosed herein. Exemplary additional agents include, but are not limited to:

cholinesterase inhibitors (such as donepezil, galantamine, rivastigmine, and tacrine), NMDA receptor antagonists (such as memantine), amyloid beta peptide aggregation inhibitors, antioxidants, gamma-secretase modulators, nerve growth factor (NGF) mimics or NGF gene therapy, PPAR γ agonists, HMG-CoA reductase inhibitors (statins), ampakines, calcium channel blockers, GABA receptor antagonists, glycogen synthase kinase inhibitors, intravenous immunoglobulin, muscarinic receptor agonists, nicotinic receptor modulators, active or passive amyloid beta peptide for immunization, phosphodiesterase inhibitors, serotonin receptor antagonists, anti-amyloid beta peptide antibodies, growth hormone, neurotrophic factor, brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF), neurotrophin-4/5, fibroblast growth factor (FGF)-2 and other FGFs, neurotrophin (NT)-3, erythropoietin (EPO), hepatocyte growth factor (HGF), epidermal growth factor (EGF), transforming growth factor (TGF)- α , TGF- β , vascular endothelial growth factor (VEGF), interleukin-1 receptor antagonist (IL-1ra), ciliary neurotrophic factor (CNTF), glial-derived neurotrophic factor (GDNF), neurturin, platelet-derived growth factor (PDGF), heregulin, neuregulin, artemin, persephin, interleukins, glial cell line derived neurotrophic factor (GFR), granulocyte-colony stimulating factor (CSF), granulocyte-macrophage-CSF, netrins, cardiotrophin-1, hedgehogs, leukemia inhibitory factor (LIF), midkine, pleiotrophin, bone morphogenetic proteins (BMPs), netrins, saposins, semaphorins, stem cell factor (SCF), or a different anti-tau antibody.

In yet additional [embodiment examples](#), provided is the use of an antibody or antigen binding fragment thereof as disclosed herein to treat tauopathy in a subject.

In yet additional [embodiment examples](#), provided is the use of an antibody or antigen binding fragment thereof as disclosed herein for the treatment of tauopathy in a subject.

In yet additional [embodiment examples](#), provided is the use of an antibody or antigen binding fragment thereof as disclosed herein for the preparation of a medicament to treat tauopathy in a subject.

In another aspect, provided herein is use of an antibody or antigen binding fragment thereof as disclosed herein in the manufacture of a medicament for the treatment of tauopathy.

In another aspect, provided herein is use of an antibody as disclosed herein in the manufacture of a medicament for the treatment of tauopathy, wherein the tauopathy is Alzheimer's disease.

In some [embodiment examples](#) of the various uses described herein, the tauopathy is Alzheimer's disease, corticobasal degeneration, progressive supranuclear palsy, Pick's disease, argyrophilic grain dementia (argyrophilic grain disease), multiple system tauopathy with

presenile dementia (MSTD), frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17), dementia with neurofibrillary tangles, diffuse neurofibrillary tangle with calcification (DNTC), white matter tauopathy with globular glial inclusions (WMT-GGI), frontotemporal lobar degeneration with tau pathology (FTLD-tau), Economo's encephalitis sequela, subacute sclerosing panencephalitis, or boxer's encephalopathy. In one [embodimentexample](#), the tauopathy is AD.

In another [embodimentexample](#), the tauopathy is CBD. In yet another [embodimentexample](#), the tauopathy is progressive supranuclear palsy. In still another [embodimentexample](#), the tauopathy is Pick's disease. In one [embodimentexample](#), the tauopathy is argyrophilic grain dementia. In another [embodimentexample](#), the

tauopathy is MSTD. In yet another [embodimentexample](#), the tauopathy is FTDP-17. In still another [embodimentexample](#), the tauopathy is dementia with neurofibrillary tangles. In one [embodimentexample](#), the tauopathy is DNTC. In another [embodimentexample](#), the tauopathy is WMT-GGI. In yet another [embodimentexample](#), the tauopathy is FTLT-tau. In one [embodimentexample](#), the tauopathy is Economo's encephalitis sequela. In another [embodimentexample](#), the tauopathy is subacute sclerosing panencephalitis. In yet another [embodimentexample](#), the tauopathy is boxer's encephalopathy.

In yet a further [embodimentexample](#), provided is an antibody or antigen binding fragment thereof as disclosed herein for use in a method for treating tauopathy in a subject.

In yet additional [embodimentexamples](#), provided is an antibody or antigen binding fragment thereof as disclosed herein for use in a method for diagnosing tauopathy in a subject.

In another aspect, provided herein is an antibody or antigen binding fragment thereof as disclosed herein for use in therapy.

In another aspect, provided herein is an antibody or antigen binding fragment thereof as disclosed herein for use in the treatment of tauopathy.

In another aspect, provided herein is an antibody as disclosed herein for use in treating tauopathy, wherein the tauopathy is Alzheimer's disease.

BRIEF DESCRIPTION OF THE DRAWINGS

FIGS. 1A and 1B show amino acid sequence alignment of VH (**FIG. 1A**) and VL (**FIG. 1B**) of representative antibodies described herein. CDRs shown in these figures are defined by the Kabat numbering system.

FIGS. 2A-2F demonstrate that exemplary high affinity anti-tau-pS413 antibodies V8-AFM and V5-AFM bind specifically to tau-pS413 peptide. V8-AFM (e.g., V8-AFM-hIgG1-LALA-YTE, V8-AFM-hIgG1-LALA, V8-AFM-hIgG4-S228P) and V5-AFM (e.g., V5-AFM-hIgG4-S228P) bind to a peptide that has phosphorylated serine 413 (**FIG. 2A**) but do not bind to the same peptide without serine 413 phosphorylated (**FIG. 2B**) or peptides that are phosphorylated at other positions in the tau protein (**FIGS. 2C-2F**).

FIGS. 3A and 3B show competitive tau-pS413 immunoassay demonstrating binding of various exemplary anti-tau-pS413 antibodies to AD patient brain homogenates. **FIG. 3A** shows representative graph of curve fits with OD 450 nm as readouts and hIgGs as isotype control.

5 **FIG. 3B** shows representative graph of curve fits with % of occupancy as readouts.

FIGS. 4A-4E demonstrate that immuno-depletion of P2 extract of AD brain homogenates with various exemplary anti-tau-pS413 antibodies prevents the induction of tau pathology in hiPSC neurons. **FIG. 4A** illustrates schematic representation of the neutralization protocol. **FIG. 4B** and **4C** represent AlphaLISA[®] data used to confirm successful depletion of
10 tau-pS413 and total tau, respectively. **FIG. 4D** shows representative images demonstrating

WHAT WE CLAIM IS:

1. An antibody or antigen binding fragment thereof that binds to tau-pS413, comprising:

(a) a heavy chain variable region complementarity determining region 1 (VH-CDR1)

comprising the amino acid sequence of SEQ ID NO:41; a heavy chain variable region

5 complementarity determining region 2 (VH-CDR2) comprising the amino acid sequence of SEQ ID NO:42; and a heavy chain variable region complementarity determining region 3 (VH-CDR3) comprising the amino acid sequence of SEQ ID NO:43; and

a light chain variable region complementarity determining region 1 (VL-CDR1)

comprising the amino acid sequence of SEQ ID NO:29; a light chain variable region

10 complementarity determining region 2 (VL-CDR2) comprising the amino acid sequence of SEQ ID NO:30; and a light chain variable region complementarity determining region 3 (VL-CDR3) comprising the amino acid sequence of SEQ ID NO:31;

(b) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:41; a VH-CDR2

comprising the amino acid sequence of SEQ ID NO:42; and a VH-CDR3 comprising the amino

15 acid sequence of SEQ ID NO:43; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:33; a VL-CDR2

comprising the amino acid sequence of SEQ ID NO:34; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:35;

(c) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:41; a VH-CDR2

20 comprising the amino acid sequence of SEQ ID NO:42; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:43; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:37; a VL-CDR2

comprising the amino acid sequence of SEQ ID NO:38; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:39;

25 (d) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:41; a VH-CDR2

comprising the amino acid sequence of SEQ ID NO:42; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:43; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:25; a VL-CDR2

30 comprising the amino acid sequence of SEQ ID NO:26; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:27;

(e) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:41; a VH-CDR2

comprising the amino acid sequence of SEQ ID NO:42; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:43; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:17; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:18; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:19;

(f) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:45; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:46; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:47; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:29; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:30; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:31;

(g) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:45; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:46; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:47; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:33; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:34; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:35;

(h) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:45; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:46; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:47; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:37; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:38; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:39;

(i) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:45; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:46; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:47; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:25; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:26; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:27;

(j) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:45; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:46; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:47; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:17; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:18; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:19;

(k) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:49; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:50; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:51; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:29; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:30; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:31;

(l) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:49; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:50; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:51; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:33; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:34; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:35;

(m) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:49; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:50; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:51; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:37; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:38; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:39;

(n) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:49; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:50; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:51; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:25; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:26; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:27;

(o) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:49; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:50; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:51; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:17; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:18; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:19;

(p) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:53; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:54; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:55; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:29; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:30; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:31;

(q) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:53; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:54; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:55; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:33; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:34; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:35;

(r) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:53; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:54; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:55; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:37; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:38; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:39;

(s) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:53; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:54; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:55; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:25; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:26; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:27;

(t) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:53; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:54; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:55; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:17; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:18; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:19;

(u) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:21; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:22; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:23; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:29; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:30; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:31;

(v) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:21; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:22; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:23; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:33; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:34; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:35;

(w) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:21; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:22; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:23; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:37; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:38; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:39;

(x) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:86; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:87; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:88; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:83; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:84; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:85;

(y) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:92; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:93; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:94; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:89; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:90; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:91;

(z) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:98; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:99; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:100; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:95; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:96; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:97; ~~or~~

(aa) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:104; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:105; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:106; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:101; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:102; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:103;

(bb) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO:44; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO:32;

(cc) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:44; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36;

(dd) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:44; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40;

(ee) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:44; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:28;

(ff) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:44; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:20;

(gg) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:32;

(hh) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36;

(ii) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40;

(jj) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:28;

(kk) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:20;

(ll) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:32;

(mm) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36;

(nn) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40;

(oo) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:28;

(pp) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:20;

(qq) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:32;

(rr) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36;

(ss) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40;

(tt) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:28;

(uu) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:20;

(vv) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:24; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:32;

(ww) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:24; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36; or

(xx) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:24; and

a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40.

~~2. An antibody or antigen binding fragment thereof that binds to tau-pS413, comprising:~~

~~(a) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO:44; and~~

~~—— a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO:32;~~

5 ~~(b) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:44; and~~

~~—— a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36;~~

10 ~~(c) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:44; and~~

~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40;~~

~~(d) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:44; and~~

15 ~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:28;~~

~~(e) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:44; and~~

20 ~~—— a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:20;~~

~~(f) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and~~

~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:32;~~

25 ~~(g) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and~~

~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36;~~

30 ~~(h) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and~~

~~—— a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40;~~

- (i) ~~a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and~~
~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:28;~~
- 5 (j) ~~a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:48; and~~
~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:20;~~
- 10 (k) ~~a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and~~
~~———— a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:32;~~
- 15 (l) ~~a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and~~
~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36;~~
- 20 (m) ~~a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and~~
~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40;~~
- 25 (n) ~~a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and~~
~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:28;~~
- 30 (o) ~~a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:52; and~~
~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:20;~~
- (p) ~~a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and~~
~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:32;~~

~~(q) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and~~

~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36;~~

5 ~~(r) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and~~

~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40;~~

10 ~~(s) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and~~

~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:28;~~

~~(t) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and~~

15 ~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:20;~~

~~(u) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:24; and~~

20 ~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:32;~~

~~(v) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:24; and~~

~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36; or~~

25 ~~(w) a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:24; and~~

~~a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:40.~~

30 ~~32.~~ The antibody or antigen-binding fragment of claim 1 ~~or 2~~, comprising:

(a) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:44, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:32;

(b) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:44, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:36;

5 (c) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:44, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:40;

(d) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:44, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:28;

10 (e) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:44, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:20;

(f) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:48, and a VL having at least 90% amino acid sequence identity to the amino acid
15 sequence of SEQ ID NO:32;

(g) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:48, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:36;

(h) a VH having at least 90% amino acid sequence identity to the amino acid sequence of
20 SEQ ID NO:48, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:40;

(i) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:48, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:28;

25 (j) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:48, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:20;

(k) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:52, and a VL having at least 90% amino acid sequence identity to the amino acid
30 sequence of SEQ ID NO:32;

(l) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:52, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:36;

(m) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:52, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:40;

5 (n) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:52, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:28;

(o) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:52, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:20;

10 (p) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:56, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:32;

(q) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:56, and a VL having at least 90% amino acid sequence identity to the amino acid
15 sequence of SEQ ID NO:36;

(r) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:56, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:40;

(s) a VH having at least 90% amino acid sequence identity to the amino acid sequence of
20 SEQ ID NO:56, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:28;

(t) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:56, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:20;

25 (u) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:24, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:32;

(v) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:24, and a VL having at least 90% amino acid sequence identity to the amino acid
30 sequence of SEQ ID NO:36; or

(w) a VH having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:24, and a VL having at least 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO:40.

43. ~~An~~The antibody or antigen binding fragment thereof of claim 1~~that binds to tau-pS413,~~
comprising:

(a) a VH having the amino acid sequence of SEQ ID NO:44, and a VL having the amino
5 acid sequence of SEQ ID NO:32;

(b) a VH having the amino acid sequence of SEQ ID NO:44, and a VL having the amino
acid sequence of SEQ ID NO:36;

(c) a VH having the amino acid sequence of SEQ ID NO:44, and a VL having the amino
acid sequence of SEQ ID NO:40;

10 (d) a VH having the amino acid sequence of SEQ ID NO:44, and a VL having the amino
acid sequence of SEQ ID NO:28;

(e) a VH having the amino acid sequence of SEQ ID NO:44, and a VL having the amino
acid sequence of SEQ ID NO:20;

15 (f) a VH having the amino acid sequence of SEQ ID NO:48, and a VL having the amino
acid sequence of SEQ ID NO:32;

(g) a VH having the amino acid sequence of SEQ ID NO:48, and a VL having the amino
acid sequence of SEQ ID NO:36;

(h) a VH having the amino acid sequence of SEQ ID NO:48, and a VL having the amino
acid sequence of SEQ ID NO:40;

20 (i) a VH having the amino acid sequence of SEQ ID NO:48, and a VL having the amino
acid sequence of SEQ ID NO:28;

(j) a VH having the amino acid sequence of SEQ ID NO:48, and a VL having the amino
acid sequence of SEQ ID NO:20;

25 (k) a VH having the amino acid sequence of SEQ ID NO:52, and a VL having the amino
acid sequence of SEQ ID NO:32;

(l) a VH having the amino acid sequence of SEQ ID NO:52, and a VL having the amino
acid sequence of SEQ ID NO:36;

(m) a VH having the amino acid sequence of SEQ ID NO:52, and a VL having the amino
acid sequence of SEQ ID NO:40;

30 (n) a VH having the amino acid sequence of SEQ ID NO:52, and a VL having the amino
acid sequence of SEQ ID NO:28;

(o) a VH having the amino acid sequence of SEQ ID NO:52, and a VL having the amino
acid sequence of SEQ ID NO:20;

(p) a VH having the amino acid sequence of SEQ ID NO:56, and a VL having the amino acid sequence of SEQ ID NO:32;

(q) a VH having the amino acid sequence of SEQ ID NO:56, and a VL having the amino acid sequence of SEQ ID NO:36;

5 (r) a VH having the amino acid sequence of SEQ ID NO:56, and a VL having the amino acid sequence of SEQ ID NO:40;

(s) a VH having the amino acid sequence of SEQ ID NO:56, and a VL having the amino acid sequence of SEQ ID NO:28;

10 (t) a VH having the amino acid sequence of SEQ ID NO:56, and a VL having the amino acid sequence of SEQ ID NO:20;

(u) a VH having the amino acid sequence of SEQ ID NO:24, and a VL having the amino acid sequence of SEQ ID NO:32;

(v) a VH having the amino acid sequence of SEQ ID NO:24, and a VL having the amino acid sequence of SEQ ID NO:36; or

15 (w) a VH having the amino acid sequence of SEQ ID NO:24, and a VL having the amino acid sequence of SEQ ID NO:40.

54. The antibody or antigen-binding fragment of ~~any one of claims 1-43~~, further comprising:

20 (a) a heavy chain constant region having the amino acid sequence of SEQ ID NO:59, 60, 61, 62, 63, 64, 65, 66, 67, or 68; and

(b) a light chain constant region having the amino acid sequence of SEQ ID NO:57 or 58.

65. ~~The An~~ antibody or antigen binding fragment thereof ~~that binds to tau-pS413 of claim 1~~, comprising

25 a VH-CDR1 comprising the amino acid sequence of SEQ ID NO:53; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO:54; and a VH-CDR3 comprising the amino acid sequence of SEQ ID NO:55; and

a VL-CDR1 comprising the amino acid sequence of SEQ ID NO:33; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO:34; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:35.

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76. ~~The An~~ antibody or antigen binding fragment thereof ~~that binds to tau-pS413 of claim 2~~, comprising

a VH-CDR1, a VH-CDR2, and a VH-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO:56; and a VL-CDR1, a VL-CDR2, and a VL-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO:36.

5 ~~87.~~ ~~The An~~ antibody or antigen binding fragment thereof ~~that binds to tau-pS413 of claim 4,~~ comprising a VH comprising the amino acid sequence of SEQ ID NO:56 and a VL comprising the amino acid sequence of SEQ ID NO:36.

~~98.~~ ~~An The~~ antibody of claim 5, comprising:

10 (a) a light chain comprising the amino acid sequence of SEQ ID NO:71 and a heavy chain comprising the amino acid sequence of SEQ ID NO:72;

(b) a light chain comprising the amino acid sequence of SEQ ID NO:73 and a heavy chain comprising the amino acid sequence of SEQ ID NO:74; or

15 (c) a light chain comprising the amino acid sequence of SEQ ID NO:75 and a heavy chain comprising the amino acid sequence of SEQ ID NO:76.

~~109.~~ ~~An The~~ antibody ~~consisting of claim 5, comprising:~~

~~(a) two a light chains comprising the amino acid sequence of SEQ ID NO:71 and two heavy chains comprising the amino acid sequence of SEQ ID NO:72;~~

20 ~~(b) two light chains comprising the amino acid sequence of SEQ ID NO:73 and two a heavy chains comprising the amino acid sequence of SEQ ID NO:74; or~~

~~(c) two light chains comprising the amino acid sequence of SEQ ID NO:75 and two heavy chains comprising the amino acid sequence of SEQ ID NO:76.~~

25 ~~11. — An antibody consisting of:~~

~~(a) two light chains consisting of the amino acid sequence of SEQ ID NO:71 and two heavy chains consisting of the amino acid sequence of SEQ ID NO:72;~~

~~(b) two light chains consisting of the amino acid sequence of SEQ ID NO:73 and two heavy chains consisting of the amino acid sequence of SEQ ID NO:74; or~~

30 ~~(c) two light chains consisting of the amino acid sequence of SEQ ID NO:75 and two heavy chains consisting of the amino acid sequence of SEQ ID NO:76.~~

~~12~~10. The antibody or antigen binding fragment thereof of ~~any one of claims 1-8~~claim 1, having an equilibrium dissociation constant (KD) of 1×10^{-8} M or less, ~~9×10^{-9} M or less, 8×10^{-9} M or less, 7×10^{-9} M or less, 6×10^{-9} M or less, 5×10^{-9} M or less, 4×10^{-9} M or less, 3×10^{-9} M or less, or 2×10^{-9} M or less,~~ for tau-pS413.

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~~13~~11. The antibody or antigen binding fragment thereof of claim ~~12~~10, having ~~an a~~a KD of 2×10^{-9} M or less for tau-pS413.

10

~~14~~12. The antibody or antigen binding fragment thereof of claim ~~12 or 13~~11, wherein the KD is measured by Biacore with the antibody or antigen binding fragment thereof being immobilized.

~~15~~13. An isolated nucleic acid, encoding:

(a) ~~the a~~a VH of the antibody or antigen binding fragment thereof of ~~any one of claims 1-14~~claim 3;

15

(b) ~~the a~~a VL of the antibody or antigen binding fragment thereof of ~~claim 3 any one of claims 1-14~~claim 3;

(c) ~~the a~~a VH and ~~the a~~a VL of the antibody or antigen binding fragment thereof of ~~claim 3 any one of claims 1-14~~claim 3;

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(d) ~~the a~~a heavy chain of the antibody ~~or antigen binding fragment thereof of~~ ~~claim 8 any one of claims 1-14~~claim 8;

(e) ~~the a~~a light chain of the antibody ~~or antigen binding fragment thereof of~~ ~~claim 8 any one of claims 1-14~~claim 8; or

(f) ~~the a~~a heavy chain and ~~the a~~a light chain of the antibody ~~or antigen binding fragment thereof of~~ ~~claim 8 any one of claims 1-14~~claim 8.

25

~~16~~14. An expression vector comprising the isolated nucleic acid of claim ~~15~~13.

~~17~~15. A host cell comprising the ~~isolated nucleic acid of claim 15 or the~~ expression vector of claim ~~16~~14.

30

~~18~~16. A method of producing an antibody or antigen binding fragment thereof, comprising:

(a) culturing the host cell of claim 15 under conditions wherein the antibody or antigen binding fragment thereof is expressed; and~~17~~;

(b) ~~expressing~~ harvesting the ~~antibody~~ expression vector of claim 16; or antigen binding fragment thereof.

~~(c) expressing the isolated nucleic acid of claim 15,~~
~~under conditions wherein the antibody or antigen binding fragment thereof is expressed.~~

~~19~~17. A composition comprising the antibody or antigen binding fragment thereof of ~~any one of claims 1-14~~ any of claims 1 to 12, and a pharmaceutically acceptable carrier.

~~20. A kit comprising the antibody or antigen binding fragment thereof of any one of claims 1-14.~~

~~21~~18. Use of an antibody or antigen binding fragment thereof of any of claims 1 to 12 in the manufacture of a medicament for the treatment of ~~A method of treating tauopathy in a subject, comprising administering to the subject an effective amount of the antibody or antigen binding fragment thereof of any one of claims 1-14 or the composition of claim 19.~~

~~22~~19. The ~~method-use~~ of claim ~~21~~18, wherein the tauopathy is Alzheimer's disease, corticobasal degeneration, progressive supranuclear palsy, Pick's disease, argyrophilic grain dementia (argyrophilic grain disease), multiple system tauopathy with presenile dementia (MSTD), frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17), dementia with neurofibrillary tangles, diffuse neurofibrillary tangle with calcification (DNTEC), white matter tauopathy with globular glial inclusions (WMT-GGI), frontotemporal lobar degeneration with tau pathology (FTLD-tau), Economo's encephalitis sequela, subacute sclerosing panencephalitis, or boxer's encephalopathy.

~~20. The use of claim 19, wherein the tauopathy is Alzheimer's disease.~~

~~23. A method of decreasing the amount of tau pS413 in the brain of a subject, comprising administering to the subject in need thereof an effective amount of the antibody or antigen binding fragment thereof of any one of claims 1-14 or the composition of claim 19.~~

~~24~~21. The ~~method-use~~ of claim ~~21 or 23~~19, further comprising ~~administering to the subject~~ an additional agent to be administered.

~~25. The composition of claim 19, further comprising an additional agent.~~

2622. The ~~method-use~~ of claim 24 or the composition of claim 2521, wherein the additional agent is selected from the group consisting of cholinesterase inhibitors, donepezil, galantamine, rovastigmine, tacrine, an NMDA receptor antagonists, memantine, an amyloid beta peptide aggregation inhibitors, an antioxidants, a gamma-secretase modulators, a nerve growth factor (NGF) mimics or NGF gene therapy agent, a PPARy agonists, an HMS-CoA reductase inhibitors, a statins, an ampakines, a calcium channel blockers, a GABA receptor antagonists, a glycogen synthase kinase inhibitors, intravenous immunoglobulin, a muscarinic receptor agonists, a nicotinic receptor modulators, an active or passive amyloid beta peptide for immunization, a phosphodiesterase inhibitors, a serotonin receptor antagonists, an anti-amyloid beta peptide ~~antibodies~~antibody, a growth hormone, a neurotrophic factor, brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF), neurotrophin-4/5, a fibroblast growth factor-~~(FGF)-2 and other FGFs~~, neurotrophin (NT)-3, erythropoietin (EPO), hepatocyte growth factor (HGF), epidermal growth factor (EGF), transforming growth factor (TGF)-~~al~~p-ha, TGF-beta, vascular endothelial growth factor (VEGF), an interleukin-1 receptor antagonist (IL-1ra), ciliary neurotrophic factor (CNTF), glial-derived neurotrophic factor (GDNF), neurturin, platelet-derived growth factor (PDGF), heregulin, neuregulin, artemin, persephin, an interleukins, glial cell line derived neurotrophic factor (GFR), granulocyte-colony stimulating factor (CSF), granulocyte-macrophage-CSF, netrins, cardiotrophin-1, hedgehogs, leukemia inhibitory factor (LIF), midkine, pleiotrophin, bone morphogenetic proteins (BMPs), a netrins, a saposins, a semaphorins, stem cell factor (SCF), ~~or~~and a different anti-tau antibody, or a combination thereof.

23. An antibody or antigen binding fragment thereof of any of claims 1 to 12 for use in therapy.

24. An antibody or antigen binding fragment thereof of any of claims 1 to 12 for use in the treatment of tauopathy.

25. A composition comprising an antibody of claim 7 and a pharmaceutically acceptable carrier.

26. Use of an antibody of claim 7 in the manufacture of a medicament for the treatment of tauopathy, wherein the tauopathy is Alzheimer's disease.

27. An antibody of claim 7 for use in treating tauopathy, wherein the tauopathy is Alzheimer's disease.

28. The antibody of claim 9, wherein the lysine residue at the C-terminus of the heavy chain is absent.

29. A composition comprising the antibody of claim 28, and a pharmaceutically acceptable carrier.

30. The antibody of claim 28 for use in the treatment of tauopathy in a subject, wherein the tauopathy is Alzheimer's disease.

31. Use of the antibody of claim 28 in the manufacture of a medicament for the treatment of tauopathy in a subject, wherein the tauopathy is Alzheimer's disease.

32. The use of claim 31, further comprising using an additional agent.

33. The use of claim 32, wherein the additional agent is selected from the group consisting of a cholinesterase inhibitor, an NMDA receptor antagonist, an amyloid beta peptide aggregation inhibitor, an antioxidant, a gamma-secretase modulator, a nerve growth factor (NGF) mimic or NGF gene therapy agent, a PPAR γ agonist, an HMS-CoA reductase inhibitor, a statin, an ampakine, a calcium channel blocker, a GABA receptor antagonist, a glycogen synthase kinase inhibitor, an intravenous immunoglobulin, a muscarinic receptor agonist, a nicotinic receptor modulator, an active or passive amyloid beta peptide for immunization, a phosphodiesterase inhibitor, a serotonin receptor antagonist, an anti-amyloid beta peptide antibody, a growth hormone, a neurotrophic factor, brain-derived neurotrophic factor (BDNF), a nerve growth factor (NGF), a neurotrophin-4/5, a fibroblast growth factor, neurotrophin (NT)-3, erythropoietin (EPO), hepatocyte growth factor (HGF), epidermal growth factor (EGF), transforming growth factor (TGF)-alpha, TGF- beta, vascular endothelial growth factor (VEGF), an interleukin-1 receptor antagonist (IL-1ra), ciliary neurotrophic factor (CNTF), glial-derived neurotrophic factor

(GDNF), neurturin, platelet-derived growth factor (PDGF), heregulin, neuregulin, artemin, persephin, an interleukin, glial cell line derived neurotrophic factor (GFR), granulocyte-colony stimulating factor (CSF), granulocyte-macrophage-CSF, a netrin, cardiotrophin-1, leukemia inhibitory factor (LIF), midkine, pleiotrophin, a bone morphogenetic protein (BMP), a saposin, a semaphoring, stem cell factor (SCF), and a different anti-tau antibody, or a combination thereof.

34. The use of claim 33, wherein the cholinesterase inhibitor is selected from the group consisting of donepezil, galantamine, rivastigmine, and tacrine.

35. The use of claim 33, wherein the NMDA receptor antagonist is memantine.

~~27. Use of the antibody or antigen binding fragment thereof of any one of claims 1-14 to treat tauopathy in a subject.~~

~~28. Use of the antibody or antigen binding fragment thereof of any one of claims 1-14 for the treatment of tauopathy in a subject.~~

~~29. Use of the antibody or antigen binding fragment thereof of any one of claims 1-14 for the preparation of a medicament to treat tauopathy in a subject.~~

~~30. The use of any one of claims 27-29, wherein the tauopathy is Alzheimer's disease, corticobasal degeneration, progressive supranuclear palsy, Pick's disease, argyrophilic grain dementia (argyrophilic grain disease), multiple system tauopathy with presenile dementia (MSTD), frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17), dementia with neurofibrillary tangles, diffuse neurofibrillary tangle with calcification (DNTE), white matter tauopathy with globular glial inclusions (WMT-GGI), frontotemporal lobar degeneration with tau pathology (FTLD-tau), Economo's encephalitis sequela, subacute sclerosing panencephalitis, or boxer's encephalopathy.~~

~~31. The antibody or antigen binding fragment thereof of any one of claims 1-14 for use in a method for treating tauopathy in a subject.~~

~~32. The antibody or antigen binding fragment thereof of any one of claims 1-14 for use in a method for diagnosing tauopathy in a subject.~~

33. — The antibody or antigen binding fragment thereof of claim 31 or 32, wherein the tauopathy is Alzheimer's disease, corticobasal degeneration, progressive supranuclear palsy, Pick's disease, argyrophilic grain dementia (argyrophilic grain disease), multiple system tauopathy with presenile dementia (MSTD), frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17), dementia with neurofibrillary tangles, diffuse neurofibrillary tangle with calcification (DNTC), white matter tauopathy with globular glial inclusions (WMT-GGI), frontotemporal lobar degeneration with tau pathology (FTLD-tau), Economo's encephalitis sequela, subacute sclerosing panencephalitis, or boxer's encephalopathy.