

CLAIMS

1. An isolated monoclonal antibody or antigen-binding fragment thereof comprising a heavy complementarity determining region 1 (HCDR1), HCDR2, HCDR3, AND a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3, having the polypeptide sequences of:

- a. SEQ ID NOs: 1, 2, 3, 4, 5, and 6, respectively;
- ~~b. SEQ ID NOs: 1, 7, 3, 4, 5, and 6, respectively;~~
- ~~c. SEQ ID NOs: 1, 7, 3, 8, 5, and 6, respectively;~~
- ~~d. SEQ ID NOs: 1, 2, 3, 8, 5, and 6, respectively;~~
- ~~e. SEQ ID Nos: 56, 57, 3, 8, 5, and 6, respectively; or~~
- ~~f. SEQ ID NOs: 56, 57, 3, 4, 5, and 6, respectively;~~
- ~~g. SEQ ID NOs: 56, 58, 3, 4, 5, and 6, respectively;~~
- ~~h. SEQ ID NOs: 56, 7, 3, 8, 5, and 6, respectively;~~
- ~~i. SEQ ID NOs: 1, 57, 3, 8, 5, and 6, respectively;~~
- ~~j. SEQ ID NOs: 56, 7, 3, 4, 5, and 6, respectively;~~
- ~~k. SEQ ID NOs: 1, 57, 3, 4, 5, and 6, respectively;~~
- ~~l. SEQ ID NOs: 1, 58, 3, 4, 5, and 6, respectively; or~~
- ~~m. SEQ ID NOs: 56, 2, 3, 4, 5, and 6, respectively;~~

wherein the antibody or antigen-binding fragment thereof specifically binds ~~3pE A β~~ amyloid- β peptide having pyroglutamate at the third residue (3pE A β), preferably human 3pE A β .

2. The isolated monoclonal antibody or antigen-binding fragment thereof of claim 1, comprising a heavy chain variable region having a polypeptide sequence at least 95% identical to SEQ ID NO:9, 11, 13, 15, 16, 17, 19, 20, or 21, or a light chain variable region having a polypeptide sequence at least 95% identical to SEQ ID NO:10, 12, 14, 18, or 22, 53, or 55.

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

- a. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:21,
and a light chain variable region having the polypeptide sequence of SEQ ID NO:22;
or
- ~~b. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:9, and
a light chain variable region having the polypeptide sequence of SEQ ID NO:10;~~
- ~~c. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:11,
and a light chain variable region having the polypeptide sequence of SEQ ID NO:12;~~
- ~~d. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:13,
and a light chain variable region having the polypeptide sequence of SEQ ID NO:14;~~
- ~~e. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:15,
and a light chain variable region having the polypeptide sequence of SEQ ID NO:14;~~
- ~~f. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:16,
and a light chain variable region having the polypeptide sequence of SEQ ID NO:14;~~
- ~~g. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:20,
and a light chain variable region having the polypeptide sequence of SEQ ID NO:14;~~
- ~~h. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:17,
and a light chain variable region having the polypeptide sequence of SEQ ID NO:18;~~
- ~~i. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:19,
and a light chain variable region having the polypeptide sequence of SEQ ID NO:18;~~
- ~~j. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:21,
and a light chain variable region having the polypeptide sequence of SEQ ID NO:53;~~
or
- ~~k. b. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:21,
and a light chain variable region having the polypeptide sequence of SEQ ID NO:55.~~

4. The isolated monoclonal antibody or antigen-binding fragment thereof of any one of claims 1-3, wherein the antibody or antigen-binding fragment thereof is chimeric.

5. The isolated monoclonal antibody or antigen-binding fragment thereof of any one of claims 1-4, wherein the antibody or antigen-binding fragment thereof is human or humanized.

6. An isolated monoclonal antibody comprising:
 - a. a heavy chain amino acid sequence comprising SEQ ID NO:37 and a light chain amino acid sequence comprising SEQ ID NO:38; or
 - b. a heavy chain amino acid sequence comprising SEQ ID NO:39 and a light chain amino acid sequence comprising SEQ ID NO:38;
 - ~~c. a heavy chain amino acid sequence comprising SEQ ID NO:37 and a light chain amino acid sequence comprising SEQ ID NO:52; or~~
 - ~~d. a heavy chain amino acid sequence comprising SEQ ID NO:39 and a light chain amino acid sequence comprising SEQ ID NO:54.~~
7. An isolated nucleic acid encoding the monoclonal antibody or antigen-binding fragment thereof of any one of claims 1-6.
8. A vector comprising the isolated nucleic acid of claim 7.
9. A host cell comprising the vector of claim 8.
10. A pharmaceutical composition comprising the monoclonal antibody or antigen binding fragment thereof of any one of claims 1-6 and a pharmaceutically acceptable carrier.
11. An isolated monoclonal antibody or antigen binding fragment thereof of any one of claims 1-6 or the pharmaceutical composition of claim 10 for use in treating a condition associated with the formation of plaques containing beta-amyloid protein in a subject in need thereof.
12. The isolated monoclonal antibody or antigen binding fragment thereof of claim 11, wherein the condition is Alzheimer's disease.
13. The isolated monoclonal antibody or antigen binding fragment thereof of claim 11, wherein the condition is selected from the group consisting of dementia associated with Trisomy 21 (Down's Syndrome), diffuse Lewy body disease, inclusion body myositis, cerebral amyloid

angiopathy and hereditary cerebral hemorrhage with amyloidosis of the Dutch-type (HCHWA-D).

14. An isolated monoclonal antibody or antigen binding fragment thereof of any one of claims 1-6 or the pharmaceutical composition of claim 10 for use in reducing plaques associated with Alzheimer's disease in a subject in need thereof.

15. An isolated monoclonal antibody or antigen binding fragment thereof of any one of claims 1-6 or the pharmaceutical composition of claim 10 for use in preventing seeding activity of 3pE A β associated with Alzheimer's disease in a subject in need thereof.

16. A method of producing the monoclonal antibody or antigen-binding fragment thereof of any one of claims 1-6, comprising culturing a cell comprising a nucleic acid encoding the monoclonal antibody or antigen-binding fragment thereof under conditions to produce the monoclonal antibody or antigen-binding fragment thereof, and recovering the antibody or antigen-binding fragment thereof.

17. A method of producing a pharmaceutical composition comprising the monoclonal antibody or antigen-binding fragment thereof of any one of claim 1-6, the method comprising combining the monoclonal antibody or antigen-binding fragment thereof with a pharmaceutically acceptable carrier to obtain the pharmaceutical composition.