

CLAIMS

1. An aqueous pharmaceutical formulation comprising:
 - (a) an anti-A β protofibril antibody that binds to human A β protofibrils, at a concentration of 80 mg/mL to 240 mg/mL,
 - (b) 100 mM to less than 300 mM arginine, arginine hydrochloride, or a combination thereof,
 - (c) 0.01% w/v to 0.1% w/v polysorbate 80, and
 - (d) a pharmaceutically acceptable buffer,wherein the pharmaceutical formulation has a pH ranging from 4.5 to 5.5, and wherein the anti-A β protofibril antibody comprises: (i) a heavy chain comprising the amino acid sequence of SEQ ID NO:11, and (ii) a light chain comprising the amino acid sequence of SEQ ID NO:12 .
2. The pharmaceutical formulation according to claim 1, further comprising methionine.
3. The pharmaceutical formulation according to claim 1 and claim 2, wherein the pharmaceutically acceptable buffer is citrate buffer or histidine buffer.
4. The pharmaceutical formulation according to any one of claims 1-3, comprising 10 to 100 mM citrate buffer or 10 to 100 mM histidine buffer.
5. The pharmaceutical formulation according to any one of claims 1-4, comprising 125 to less than 300 mM arginine, arginine hydrochloride, or a combination thereof.
6. The pharmaceutical formulation according to any one of claims 1-5, comprising 200 mM arginine hydrochloride.
7. The pharmaceutical formulation according to any one of claims 1-6, comprising 200 mM arginine hydrochloride and 25 mM histidine buffer.

8. An aqueous pharmaceutical formulation comprising:
 - (a) an anti-A β protofibril antibody that binds to human A β protofibrils, at a concentration of 80 mg/mL to 240 mg/mL, and
 - (b) histidine buffer,wherein the pharmaceutical formulation has a pH ranging from 4.5 to 5.5, and
wherein the anti-A β protofibril antibody comprises: (i) a heavy chain comprising the amino acid sequence of SEQ ID NO:11, and (ii) a light chain comprising the amino acid sequence of SEQ ID NO:12.
9. The pharmaceutical formulation according to claim 8, comprising 15 mM to 35 mM histidine buffer.
10. The pharmaceutical formulation according to claim 8 or claim 9, comprising 25 mM histidine buffer.
11. The pharmaceutical formulation according to any one of claims 8-10, further comprising arginine, arginine hydrochloride, or a combination thereof.
12. The pharmaceutical formulation according to any one of claims 1-11, wherein the anti-A β protofibril antibody is present in a concentration of 100 mg/mL to 200 mg/mL.
13. The pharmaceutical formulation according to any one of claims 1-12, wherein the anti-A β protofibril antibody or fragment thereof is present in a concentration of 100 mg/mL.
14. The pharmaceutical formulation according to any one of claims 1-12, wherein the anti-A β protofibril antibody or fragment thereof is present in a concentration of 200 mg/mL.
15. The pharmaceutical formulation according to any one of claims 1-14, further comprising 0.01% w/v to 0.1% w/v polysorbate 80.

16. An aqueous pharmaceutical formulation comprising:
- (a) 80 mg/mL to 240 mg/mL of an anti-A β protofibril antibody comprising: (i) a heavy chain comprising the amino acid sequence of SEQ ID NO:11, and (ii) a light chain comprising the amino acid sequence of SEQ ID NO:12,
 - (b) 140 mM to 260 mM arginine hydrochloride,
 - (c) 0.02% w/v to 0.08% w/v polysorbate 80, and
 - (d) 15 mM to 35 mM histidine buffer,
- wherein the pharmaceutical formulation has a pH ranging from 4.5 to 5.5.
17. An aqueous pharmaceutical formulation comprising:
- (a) 80 mg/mL to 120 mg/mL of an anti-A β protofibril antibody comprising: (i) a heavy chain comprising the amino acid sequence of SEQ ID NO:11, and (ii) a light chain comprising the amino acid sequence of SEQ ID NO:12,
 - (b) 240 mM to less than 300 mM arginine, arginine hydrochloride, or a combination thereof,
 - (c) 0.02% w/v to 0.08% w/v polysorbate 80, and
 - (d) 30 mM to 50 mM citrate buffer,
- wherein the pharmaceutical formulation has a pH ranging from 4.5 to 5.5.
18. The aqueous pharmaceutical formulation according to claim 1, comprising:
- (a) 100 mg/mL or 200 mg/mL of the anti-A β protofibril antibody,
 - (b) 190 mM to 200 mM arginine hydrochloride,
 - (c) 0.04% w/v to 0.06% w/v polysorbate 80, and
 - (d) 15 mM to 35 mM histidine buffer.

19. The aqueous pharmaceutical formulation according to claim 1, comprising:
 - (a) 100 mg/mL of the anti-A β protofibril antibody,
 - (b) 200 mM arginine hydrochloride,
 - (c) 0.05% w/v polysorbate 80, and
 - (d) 25 mM histidine buffer.
20. The aqueous pharmaceutical formulation according to claim 1, comprising:
 - (a) 200 mg/mL of the anti-A β protofibril antibody,
 - (b) 200 mM arginine hydrochloride,
 - (c) 0.05% w/v polysorbate 80, and
 - (d) 25 mM histidine buffer.
21. The pharmaceutical formulation according to any one of claims 3-16 and 18-20, wherein the histidine buffer comprises histidine and histidine hydrochloride.
22. The pharmaceutical formulation according to any one of claims 3-16 and 18-20, wherein the histidine buffer comprises histidine and histidine hydrochloride monohydrate.
23. The pharmaceutical formulation according to any one of claims 1-22, wherein the pharmaceutical formulation has a pH of 5.0.
24. The pharmaceutical formulation according to any one of claims 1-23, wherein the anti-A β protofibril antibody is lecanemab.
25. A method of reducing aggregate formation of an anti-A β protofibril antibody, comprising:
 - providing an aqueous pharmaceutical formulation comprising an anti-A β protofibril antibody comprising: (i) a heavy chain comprising the amino acid sequence of SEQ ID NO:11,

and (ii) a light chain comprising the amino acid sequence of SEQ ID NO:12 at a concentration of 80 mg/mL to 240 mg/mL, and

adding arginine, arginine hydrochloride, or a combination thereof to said aqueous pharmaceutical formulation, wherein the pH of the pharmaceutical formulation ranges from 4.5 to 5.5.

26. The method according to claim 25, wherein the arginine, arginine hydrochloride, or combination thereof is present in a concentration of 150 to 250 mM.

27. The method according to claim 25 or claim 26, wherein the arginine, arginine hydrochloride, or combination thereof is present in a concentration of 200 mM.

28. The method according to any one of claims 25-27, further comprising a pharmaceutically acceptable buffer.

29. The method according to claim 28, wherein the pharmaceutically acceptable buffer is histidine buffer or citrate buffer.

30. The method according to any one of claims 25-29, wherein, after storage at 25°C for 3 months, aggregation of the anti-A β protofibril antibody is less than 3%.

31. The method according to any one of claims 25-29, wherein, after storage at 5°C for 3 months, aggregation of the anti-A β protofibril antibody is less than 2%.

32. A method of reducing fragmentation of an anti-A β protofibril antibody, comprising:
providing an aqueous pharmaceutical formulation comprising an anti-A β protofibril antibody comprising: (i) a heavy chain comprising the amino acid sequence of SEQ ID NO:11, and (ii) a light chain comprising the amino acid sequence of SEQ ID NO:12 at a concentration of 80 mg/mL to 240 mg/mL, and

adding histidine buffer to said aqueous pharmaceutical composition, wherein the pH of the pharmaceutical formulation ranges from 4.5 to 5.5.

33. The method according to claim 32, comprising 15 to 35 mM histidine buffer.
34. The method according to claim 32 or claim 33, comprising about 25 mM histidine buffer.
35. The method according to any one of claims 32-34, further comprising adding arginine, arginine hydrochloride, or a combination thereof.
36. The method according to any one of claims 32-35, wherein, after storage at 25°C for 3 months, fragmentation of the anti-A β protofibril antibody is less than 0.8%.
37. The method according to any one of claims 32-35, wherein, after storage at 5°C for 3 months, fragmentation of the anti-A β protofibril antibody is less than 0.4%.
38. The method according to any one of claims 25-37, wherein the anti-A β protofibril antibody is lecanemab.
39. The method according to any one of claims 29-38, wherein the histidine buffer is a combination of histidine and histidine hydrochloride.
40. The method according to any one of claims 29-38, wherein the histidine buffer is a combination of histidine and histidine hydrochloride monohydrate.
41. The method according to any one of claims 25-40, wherein the pharmaceutical formulation further comprises 0.01% w/v to 0.1% w/v polysorbate 80.