CLAIMS

1. Use of an inhibitor of the complement pathway in the manufacture of a medicament for preventing, reducing risk of developing, or treating frontotemporal dementia (FTD) or a variant of FTD.

2. The use of claim 1, wherein the variant of FTD is a behavioral variant, a semantic variant, a non-fluent variant, and/or primary progressive aphasia.

3. The use of claim 1, wherein the inhibitor is to be administered to a subject with social symptoms, emotional symptoms, eating and oral symptoms, repetitive or compulsive symptoms, sensory symptoms, motor symptoms, executive symptoms, language symptoms, and/or neuropsychiatric symptoms.

4. The use of any one of claims 1-3, wherein the inhibitor is an antibody.

5. The use of claim 4, wherein the antibody is an anti-C1q antibody.

6. The use of claim 5, wherein the anti-C1q antibody inhibits the interaction between C1q and an autoantibody or between C1q and C1r, or between C1q and C1s.

7. The use of claim 4, wherein the anti-C1q antibody promotes clearance of C1q from circulation or a tissue.

8. The use of any one of claims 5-7, wherein the antibody is an anti-C1q antibody having a dissociation constant (K_D) that ranges from 100 nM to 0.005 nM or less than 0.005 nM.

9. The use of any one of claims 4-8, wherein the antibody comprises a light chain variable domain comprising an HVR-L1 having the amino acid sequence of RASKSINKYLA, an HVR-L2 having the amino acid of SGSTLQS, and an HVR-L3 having the amino acid of QQHNEYPLT.

10. The use of any one of claims 4-9, wherein the antibody comprises a heavy chain variable domain comprising an HVR-H1 having the amino acid sequence of GYHFTSYWMH, an HVR-H2 having the amino acid of VIHPNSGSINYNEKFES, and an HVR-H3 having the amino acid of ERDSTEVLPMDY.

11. The use of any one of claims 4-10, wherein the light chain variable domain comprises an amino acid sequence selected from SEQ ID NO: 35-38.

12. The use of any one of claims 4-11, wherein the heavy chain variable domain comprises an amino acid sequence selected from SEQ ID NO: 31-34.

13. The use of claim 4, wherein the antibody is an anti-C1r antibody.

14. The use of claim 13, wherein the anti-C1r antibody inhibits the interaction between C1r and C1q or between C1r and C1s, or wherein the anti-C1r antibody inhibits the catalytic activity of C1r or inhibits the processing of pro-C1r to an active protease.

15. The use of claim 4, wherein the antibody is an anti-C1s antibody.

16. The use of claim of 15, wherein the anti-C1s antibody inhibits the interaction between C1s and C1q or between C1s and C1r or between C1s and C2 or C4, or wherein the anti-C1s antibody inhibits the catalytic activity of C1s or inhibits the processing of pro-C1s to an active protease.

17. The use of any one of claims 4-16, wherein the antibody specifically binds to and neutralizes a biological activity of C1q.

18. The use of claim 17, wherein the biological activity is (1) C1q binding to an autoantibody, (2) C1q binding to C1r, (3) C1q binding to C1s, (4) C1q binding to phosphatidylserine, (5) C1q binding to pentraxin-3, (6) C1q binding to C-reactive protein (CRP), (7) C1q binding to globular C1q receptor (gC1qR), (8) C1q binding to complement receptor 1 (CR1), (9) C1q binding to beta-amyloid, (10) C1q binding to calreticulin, (11) C1q binding to apoptotic cells, or (12) C1q binding to components of a nerve cell membrane.

19. The use of claim 17 or 18, wherein the biological activity is (1) activation of the classical complement activation pathway, (2) activation of antibody and complement dependent cytotoxicity, (3) CH50 hemolysis, (4) synapse loss, (5) B-cell antibody production, (6) dendritic cell maturation, (7) T-cell proliferation, (8) cytokine production (9) microglia activation, (10) Arthus reaction, (11) phagocytosis of synapses or nerve endings, or (12) activation of complement receptor 3 (CR3/C3) expressing cells.

20. The use of claim 19, wherein CH50 hemolysis comprises human, mouse, rat, dog, rhesus, and/or cynomolgus monkey CH50 hemolysis.

21. The method of claim 19 or claim 20, wherein the antibody is capable of neutralizing from at least about 50%, to at least about 90% of CH50 hemolysis.

22. The method of any one of claims 19-21, wherein the antibody is capable of neutralizing at least 50% of CH50 hemolysis at a dose of less than 150 ng, less than 100 ng, less than 50 ng, or less than 20 ng.

23. The use of any one of claims 4-22, wherein the antibody is a monoclonal antibody, a polyclonal antibody, a recombinant antibody, a humanized antibody, a chimeric antibody, a multispecific antibody, or an antibody fragment thereof.

24. The use of claim 23, wherein the antibody is an antibody fragment and the antibody fragment is a Fab fragment, a Fab' fragment, a F(ab')2 fragment, a Fv fragment, a diabody, or a single chain antibody molecule.

25. The use of claim 4, wherein the antibody is an anti-C1 complex antibody, optionally wherein the anti-C1 complex antibody inhibits C1r or C1s activation or prevents their ability to act on C2 or C4.

26. The use of any one of claims 4-25, wherein the antibody binds mammalian C1q, C1r, or C1s.

27. The use of claim 26, wherein the antibody binds human C1q, C1r, or C1s.

28. The use of any one of claims 4-27, wherein the antibody inhibits the alternative complement activation pathway initiated by C1q binding.

29. The use of any one of claims 4-28, wherein the antibody inhibits complement-dependent cell-mediated cytotoxicity (CDCC).

30. The use of claim 29, wherein the antibody inhibits autoantibody and complement-dependent cell-mediated cytotoxicity (CDCC).

31. The use of any one of claims 4-30, wherein the medicament is to be administered with a second antibody selected from an anti-C1q antibody, an anti-C1r antibody, and an anti-C1s antibody.

32. The use of any one of claims 1-31, wherein the medicament is to be administered with a therapeutically effective amount of an inhibitor of antibody-dependent cellular cytotoxicity (ADCC).

33. The use of any one of claims 1-32, wherein the medicament is to be administered with a therapeutically effective amount of an inhibitor of the classical complement activation pathway.

34. The use of any one of claims 1-33, wherein the medicament is to be administered with a therapeutically effective amount of an inhibitor of the alternative complement activation pathway.

35. The use of any one of claims 1-34, wherein the medicament is to be administered with a therapeutically effective amount of an inhibitor of an interaction between the autoantibody and its corresponding autoantigen.

36. A kit comprising an antibody as defined in any one of claims 4-35, and a package insert comprising instructions for using the antibody to treat or prevent frontotemporal dementia.

37. Use of an antibody as defined in any one of claims 4-36 in the manufacture of a medicament for inhibiting synapse loss in a patient suffering frontotemporal dementia.

38. The use of claim 37, wherein the frontotemporal dementia is associated with loss of synapses or loss nerve connections.

39. The use of claim 37 or claim 38, wherein the frontotemporal dementia is associated with synapse loss that is dependent on the complement receptor 3(CR3)/C3 or complement receptor CR1.

40. The use of any preceding claim, wherein the frontotemporal dementia is associated with pathological activity-dependent synaptic pruning and/or associated with synapse phagocytosis by microglia.