

What is claimed is:

1. An antibody or antigen-binding fragment thereof that binds specifically to complement factor 5 (C5) protein, wherein the antibody or antigen-binding fragment thereof interacts with one or more amino acids contained within SEQ ID NO: 360 or SEQ ID NO: 361, as determined by hydrogen/deuterium exchange.
2. The antibody or antigen-binding fragment of claim 1, wherein the antibody or antigen-binding fragment thereof interacts with one or more amino acids contained within the alpha chain and/or the beta chain of C5, as determined by hydrogen/deuterium exchange.
3. The antibody or antigen-binding fragment of claim 1 or 2, wherein the antibody or antigen-binding fragment thereof does not interact with an amino acid of the C5a anaphylatoxin region of C5, as determined by hydrogen/deuterium exchange.
4. The antibody or antigen-binding fragment of any one of claims 1 – 3, wherein the antibody or antigen-binding fragment thereof interacts with an amino acid sequence selected from the group consisting of (a) amino acids 591 to 599 of SEQ ID NO: 359; (b) amino acids 593 to 599 of SEQ ID NO: 359; (c) amino acids 775 to 787 of SEQ ID NO: 359; (d) amino acids 775 to 794 of SEQ ID NO: 359; and (e) amino acids 779 to 787 of SEQ ID NO: 359.
5. The antibody or antigen-binding fragment thereof of any one of claims 1 – 4, wherein the antibody or antigen-binding fragment thereof interacts with at least five amino acids contained within an amino acid sequence selected from the group consisting of SEQ ID NOs: 360 and 361.
6. The antibody or antigen-binding fragment of any one of claims 1 – 5, wherein the antibody or antigen-binding fragment thereof interacts with one or more amino acids contained within SEQ ID NO: 360 and SEQ ID NO: 361, as determined by hydrogen/deuterium exchange.
7. The antibody or antigen-binding fragment thereof of any one of claims 1 – 6, wherein the antibody or antigen-binding fragment thereof interacts with the amino acid

sequences of SEQ ID NOs: 360 and 361, as determined by hydrogen/deuterium exchange.

8. The antibody or antigen-binding fragment thereof of any one of claims 1 – 7, wherein the antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and HCDR3) contained within a heavy chain variable region (HCVR) and three light chain CDRs (LCDR1, LCDR2 and LCDR3) contained within a light chain variable region (LCVR), wherein the HCVR comprises:

- (i) the amino acid sequence of SEQ ID NO: 98,
- (ii) an amino acid sequence having at least 90% identity to SEQ ID NO: 98,
- (iii) an amino acid sequence having at least 95% identity to SEQ ID NO: 98; or
- (iv) the amino acid sequence of SEQ ID NO: 98 having no more than 5 amino acid substitutions;

and the LCVR comprises:

- (i) the amino acid sequence of SEQ ID NO: 106,
 - (ii) an amino acid sequence having at least 90% identity to SEQ ID NO: 106,
 - (iii) an amino acid sequence having at least 95% identity to SEQ ID NO: 106;
- or
- (iv) the amino acid sequence of SEQ ID NO: 106 having no more than 5 amino acid substitutions.

9. The antibody or antigen-binding fragment thereof of any one of claims 1 – 8, wherein the antibody has one or more of the following characteristics:

- (a) has serum concentration of more than 10 µg/mL through day 70 upon administration to cynomolgus monkey;
- (b) blocks classical pathway (CP) hemolysis through day 35 upon administration to cynomolgus monkey, as measured in an *ex vivo* hemolysis assay;
- (c) blocks alternate pathway (AP) hemolysis through day 35 upon administration to cynomolgus monkey, as measured in an *ex vivo* hemolysis assay;
- (d) has serum half-life of more than 10 days in cynomolgus monkey;

(e) has serum concentration of more than 10 $\mu\text{g/mL}$ through day 40 upon administration to C5-humanized mice;

(f) blocks CP hemolysis through day 30 upon administration to C5-humanized mice, as measured in an *ex vivo* hemolysis assay; and

(g) has serum half-life of more than 10 days in C5-humanized mice.

10. The antibody or antigen-binding fragment thereof of any one of claims 1 – 9, wherein the antibody has an additional characteristic selected from the group consisting of:

(a) is a fully human monoclonal antibody;

(b) binds to human C5 with a dissociation constant (K_D) of less than 0.9nM at 25°C, as measured in a surface plasmon resonance assay;

(c) binds to human C5 with a K_D of less than 0.3nM at 37°C, as measured in a surface plasmon resonance assay;

(d) binds to monkey C5 with a K_D of less than 65nM, as measured in a surface plasmon resonance assay;

(e) binds to human C5 variant R885H (SEQ ID NO: 356) with a K_D of less than 0.5nM, as measured in a surface plasmon resonance assay;

(f) binds to human C5 variant R885C (SEQ ID NO: 357) with a K_D of less than 0.5nM, as measured in a surface plasmon resonance assay;

(g) blocks human C5-mediated classical pathway (CP) hemolysis by more than 95% and with IC_{50} less than 6nM, as measured in a CP hemolysis assay;

(h) blocks human C5-mediated alternate pathway (AP) hemolysis by more than 70% and with IC_{50} less than 165nM, as measured in a AP hemolysis assay;

(i) inhibits African green monkey C5-mediated CP hemolysis with IC_{50} less than 185nM, as measured in a CP hemolysis assay;

(j) inhibits African green monkey C5-mediated AP hemolysis with IC_{50} less than 235nM, as measured in a AP hemolysis assay;

(k) inhibits cynomolgus monkey C5-mediated CP hemolysis with IC_{50} less than 145nM, as measured in a CP hemolysis assay; and

(l) inhibits cynomolgus monkey C5-mediated AP hemolysis with IC_{50} less than 30nM, as measured in a AP hemolysis assay.

11. The antibody or antigen-binding fragment thereof of any one of claims 8 – 10, wherein the antibody or antigen-binding fragment thereof comprises a HCVR comprising the amino acid sequence of SEQ ID NO: 98 having no more than 5 amino acid substitutions.

12. The antibody or antigen-binding fragment thereof of any one of claims 8 – 11, wherein the antibody or antigen-binding fragment thereof comprises a LCVR comprising the amino acid sequence of SEQ ID NO: 106 having no more than 5 amino acid substitutions.

13. The antibody or antigen-binding fragment thereof of claim 11 or 12, wherein the antibody or antigen-binding fragment thereof comprises a HCVR comprising the amino acid sequence of SEQ ID NO: 98 having no more than 5 amino acid substitutions and a LCVR comprising the amino acid sequence of SEQ ID NO: 106 having no more than 5 amino acid substitutions.

14. The antibody or antigen-binding fragment thereof of any one of claims 8 – 13 comprising a HCDR1 comprising the amino acid sequence of SEQ ID NO: 100 or an amino acid sequence differing from SEQ ID NO: 100 by 1 amino acid, HCDR2 comprising the amino acid sequence of SEQ ID NO: 102 or an amino acid sequence differing from SEQ ID NO: 102 by 1 amino acid, HCDR3 comprising an amino acid sequence of SEQ ID NO: 104 or an amino acid sequence differing from SEQ ID NO: 104 by 1 amino acid, LCDR1 comprising an amino acid sequence of SEQ ID NO: 108 or an amino acid sequence differing from SEQ ID NO: 108 by 1 amino acid, LCDR2 comprising the amino acid sequence of SEQ ID NO: 110 or an amino acid sequence differing from SEQ ID NO: 110 by 1 amino acid, and LCDR3 comprising the amino acid sequence of SEQ ID NO: 112 or an amino acid sequence differing from SEQ ID NO: 112 by 1 amino acid.

15. The antibody or antigen-binding fragment thereof of any one of claims 8 – 14 comprising a HCVR having the amino acid sequence of SEQ ID NO: 98.

16. The antibody or antigen-binding fragment thereof of any one of claims 8 – 14 comprising a LCVR having the amino acid sequence of SEQ ID NO: 106.

17. The antibody or antigen-binding fragment thereof of claim 14, wherein the antibody or antigen-binding fragment comprises HCDR1-HCDR2-HCDR3-LCDR1-LCDR2-LCDR3 comprising amino acid sequences of SEQ ID NOs: 100-102-104-108-110-112.

18. The antibody or antigen-binding fragment thereof of claim 17, wherein the antibody or antigen-binding fragment thereof comprises a HCVR/LCVR amino acid sequence pair of SEQ ID NOs: 98/106.

19. The antibody or antigen-binding fragment thereof of claim 18 comprising a heavy chain and a light chain, wherein the heavy chain comprises an amino acid sequence of SEQ ID NO: 353.

20. The antibody or antigen-binding fragment thereof of claim 18 comprising a heavy chain and a light chain, wherein the light chain comprises an amino acid sequence of SEQ ID NO: 354.

21. The antibody or antigen-binding fragment of claim 18 comprising a heavy chain/light chain amino acid sequence pair of SEQ ID NOs: 353/354.

22. An antibody or antigen-binding fragment thereof that competes for binding to C5 with an antibody or antigen-binding fragment thereof of claim 8.

23. An antibody or antigen-binding fragment thereof that binds to the same epitope as an antibody or antigen-binding fragment thereof of claim 8.

24. An antibody or antigen-binding fragment thereof that binds specifically to complement factor 5 (C5) protein, wherein the antibody or antigen-binding fragment thereof interacts with at least one of the following amino acid residues: N591, M592, A593, T594, G595, M596, D597, S598, W599, W775, E776, V777, H778, L779, V780, P781, R782, R783, K784, Q785, L786, Q787, F788, A789, L790, P791, D792, S793, or L794 of SEQ ID NO: 359.

25. The antibody or an antigen-binding fragment thereof of claim 24 comprising a HCVR and LCVR, wherein the HCVR has at least 90% sequence identity to SEQ ID NO: 98.

26. The antibody or an antigen-binding fragment thereof of claim 24 or 25 comprising a HCVR and LCVR, wherein the LCVR has at least 90% sequence identity to SEQ ID NO: 106.

27. The antibody or antigen-binding fragment thereof of any one of claims 24 – 26 comprising a HCVR/LCVR of SEQ ID Nos: 98/106.

28. A pharmaceutical composition comprising an antibody or antigen-binding fragment thereof that binds to C5 according to any one of claims 1 – 27 and a pharmaceutically acceptable carrier or diluent.

29. An isolated polynucleotide molecule comprising a polynucleotide sequence that encodes a HCVR of an antibody as set forth in any one of claims 1 – 27.

30. An isolated polynucleotide molecule comprising a polynucleotide sequence that encodes a LCVR of an antibody as set forth in any one of claims 1 – 27.

31. A vector comprising the polynucleotide sequence of claim 29 or 30.

32. A cell expressing the vector of claim 31.

33. A method of preventing, treating or ameliorating at least one symptom or indication of a disease or disorder associated with C5, the method comprising administering a pharmaceutical composition comprising a therapeutically effective amount of an antibody or antigen-binding fragment thereof of any one of claims 1 – 27 to a subject in need thereof.

34. The method of claim 33, wherein the disease or disorder is selected from the group consisting of atypical hemolytic uremic syndrome (aHUS), paroxysmal nocturnal hemoglobinuria (PNH), age-related macular degeneration, geographic atrophy, uveitis, neuromyelitis optica, multiple sclerosis, stroke, Guillain Barre Syndrome, traumatic brain injury, Parkinson's disease, disorders of inappropriate or undesirable complement activation, hemodialysis complications, hyperacute allograft

rejection, xenograft rejection, interleukin-2 induced toxicity during IL-2 therapy, inflammatory disorders, inflammation of autoimmune diseases, Crohn's disease, adult respiratory distress syndrome, thermal injury including burns or frostbite, post-ischemic reperfusion conditions, myocardial infarction, capillary leak syndrome, obesity, diabetes, Alzheimer's disease, schizophrenia, stroke, epilepsy, atherosclerosis, vasculitis, bullous pemphigoid, C3 glomerulopathy, membranoproliferative glomerulonephritis, diabetic nephropathy, Alport's syndrome, progressive kidney failure, proteinuric kidney diseases, renal ischemia-reperfusion injury, lupus nephritis, balloon angioplasty, post-pump syndrome in cardiopulmonary bypass or renal bypass, hemodialysis, renal ischemia, mesenteric artery reperfusion after aortic reconstruction, infectious disease or sepsis, immune complex disorders and autoimmune diseases, renal disorders, rheumatoid arthritis, systemic lupus erythematosus (SLE), SLE nephritis, proliferative nephritis, hemolytic anemia, asthma, chronic obstructive pulmonary disease (COPD), emphysema, pulmonary embolisms and infarcts, pneumonia, and myasthenia gravis.

35. The method of claim 33, wherein the disease or disorder is aHUS.

36. The method of claim 33, wherein the disease or disorder is PNH.

37. The method of any one of claims 33 – 36, wherein the pharmaceutical composition is administered prophylactically or therapeutically to the subject in need thereof.

38. The method of any one of claims 33 – 37, wherein the pharmaceutical composition is administered in combination with a second therapeutic agent.

39. The method of claim 38, wherein the second therapeutic agent is selected from the group consisting of an anti-coagulant, an anti-inflammatory drug, an antihypertensive, an immunosuppressive agent, a lipid-lowering agent, an anti-CD20 agent such as rituximab, an anti-TNF agent such as infliximab, an anti-seizure agent, a C3 inhibitor, a second anti-C5 antibody, and an anti-thrombotic agent.

40. The method of any one of claims 33 – 39, wherein the pharmaceutical composition is administered subcutaneously, intravenously, intradermally, intraperitoneally, orally, intramuscularly or intracranially.