What is claimed is:

1. A combination comprising a first antibody or antigen-binding ~~protein~~fragment thereof that binds specifically to C5~~;~~, and ~~one~~a second antibody or ~~more further~~ antigen-binding ~~proteins~~fragment thereof that

~~(i)~~ binds specifically ~~bind~~ to C5 ~~at an epitope which is different from that of the first antigen-binding protein; and/or~~;

~~(ii) does~~wherein the first antibody or antigen-binding fragment thereof and the second antibody or antigen-binding fragment thereof do not compete ~~with the first antigen-binding protein~~ for binding to C5~~.~~,

wherein the first antibody or antigen-binding fragment thereof comprises a heavy chain variable region (V_H) comprising three heavy chain complementarity determining regions (CDRs) (CDR-H1, CDR-H2, and CDR-H3) of a V_H that comprises the amino acid sequence set forth in SEQ ID NO: 19, and

a light chain variable region (V_L) comprising three light chain CDRs (CDR-L1, CDR-L2, and CDR-L3) of a V_L that comprises the amino acid sequence set forth in SEQ ID NO: 27;

wherein the second antibody or antigen-binding fragment thereof is an IgG4 antibody or IgG4 variant thereof and blocks about 80% or less of alternative pathway-mediated hemolysis of rabbit red blood cells *in vitro* in the presence of normal human serum; and

wherein at a 1:1 molar ratio of antibodies or antigen-binding fragments thereof, the combination completely inhibits alternative pathway-mediated hemolysis of rabbit red blood cells *in vitro* in the presence of normal human serum.

2. The combination of claim ~~1 wherein the first antigen-binding protein is an antibody or antigen-binding fragment that specifically binds to C5; and the further antigen-binding protein is an~~l, wherein the second antibody or antigen-binding fragment ~~or polypeptide~~thereof comprises

a V_H comprising three heavy chain complementarity determining regions (CDRs) (CDR-Hl, CDR-H2, and CDR-H3) of a V_H that ~~specifically binds to C5.~~comprises the amino acid sequence set forth in SEQ ID NO: 3, and

a V_L comprising three light chain CDRs (CDR-Ll, CDR-L2, and CDR-L3) of a V_L that comprises the amino acid sequence set forth in SEQ ID NO: 11.

3. The combination of ~~any one of claims 1-2 comprising a first~~claim 1, wherein the second antibody or antigen~~-~~binding fragment thereof ~~which is H4H12166P; and~~comprises

~~a further antibody or antigen-binding fragment thereof which is one or more selected from the group consisting of:~~

~~H2M11683N; H2M11686N; H4H12159P; H4H12161 P; H4H12164P; H4H12166P2;~~

~~H4H12166P3; H4H12166P4; H4H12166P5; H4H12166P6; H4H12166P7; H4H12166P8; H4H12166P9; H4H12166P10; H4H12168P; H4H12169P; H4H12170P; H4H12171P;~~

~~H4H12175P; H4H12176P2; H4H12177P2; H2M11682N; H2M11684N; H2M11694N and H2M11695N.~~a V_H comprising three heavy chain complementarity determining regions (CDRs) (CDR-Hl, CDR-H2, and CDR-H3) of a V_H that comprises the amino acid sequence set forth in SEO ID NO: 35, and

a V_L comprising three light chain CDRs (CDR-Ll, CDR-L2, and CDR-L3) of a V_L that comprises the amino acid sequence set forth in SEO ID NO: 43.

4. The combination of ~~any one of claims~~claim 1~~-3~~, wherein:

the second antibody or antigen-binding fragment thereof comprises

a V_H comprising three heavy chain CDRs (CDR-H1, CDR-H2, and CDR-H3) of a V_H that comprises the amino acid sequence set forth in SEQ ID NO: 51, and

a V_L comprising three light chain CDRs (CDR-L1, CDR-L2, and CDR-L3) of a V_L that comprises the amino acid sequence set forth in SEQ ID NO: 59.

5. The combination of ~~first~~claim 4, wherein:

the second antibody or antigen-binding ~~protein comprises:~~fragment thereof comprises a V_H comprising three heavy chain CDRs (CDR-H1, CDR-H2, and CDR-H3) of a V_H that comprises the amino acid sequence set forth in SEQ ID NO: 67 and

~~CDR-H1, CDR-H2 and CDR-H3 of~~ a ~~heavy chain variable region of antibody H4H12166P; and~~

~~CDR-L1, CDR-L2 and CDR-L3 of a~~V_L comprising three light chain ~~variable region of antibody H4H12166P; and the further antigen-binding protein comprises:~~

~~(i) CDR-H1, CDR-H2 and CDR-H3 of a heavy chain variable region of antibody H4H12161P; and CDR-L1, CDR-L2 and CDR-L3 of a light chain variable region of antibody H4H12161P;~~

~~(ii) CDR-H1, CDR-H2 and CDR-H3 of a heavy chain variable region of antibody H4H12170P; and CDR-L1, CDR-L2 and CDR-L3 of a light chain variable region of antibody H4H12170P;~~

~~(iii) CDR-H1, CDR-H2 and CDR-H3 of a heavy chain variable region of antibody H4H12171P; and CDR-L1, CDR-L2 and CDR-L3 of a light chain variable region of antibody H4H12171P;~~

~~(iv) CDR-H1, CDR-H2 and CDR-H3 of a heavy chain variable region of antibody H4H12175P; and~~ CDRs (CDR-L1, CDR-L2, and CDR-L3 ~~of a light chain variable region of antibody H4H12175P;~~) of a V_L that comprises the amino acid sequence set forth in SEQ ID NO: 75.

~~(v)~~

6. The combination of claim 4, wherein:

the second antibody or antigen-binding fragment thereof comprises

a V_H comprising three heavy chain CDRs (CDR-H1, CDR-H2, and CDR-H3 ~~of a heavy chain variable region of antibody H4H12176P2; and~~) of a V_H that comprises the amino acid sequence set forth in SEQ ID NO: 87, and

a V_L comprising three light chain CDRs (CDR-L1, CDR-L2, and CDR-L3 ~~of a light chain variable region of antibody H4H12176P2; or~~) of a V_L that comprises the amino acid sequence set forth in SEQ ID NO: 95.

~~(vi) CDR-H1, CDR-H2 and CDR-H3 of a heavy chain variable region of antibody H4H12177P2; and CDR-L1, CDR-L2 and CDR-L3 of a light chain variable region of antibody H4H12177P2.~~

~~5. The combination of~~ any one of claims 1-4 ~~wherein the first antigen-binding protein is antibody H4H12166P or an antibody or antigen-binding fragment thereof comprising the VH and VL thereof; and the further antigen-binding protein is antibody H4H12161P, H4H12170P, H4H12171P, H4H12175P, H4H12176P2 or H4H12177P2; or an antibody or antigen-binding fragment thereof comprising the V_H and V_L thereof.~~

~~6. The combination of any one of claims 1-5 wherein the first antigen-binding protein and the further antigen-binding protein are formulated in a single composition.~~

7. The combination of claim 1 ~~wherein the further antigen-binding protein is a polypeptide which is coversin.~~

~~8. The combination of claim 1 wherein the further antigen-binding protein is an antibody which is eculizumab.~~

~~9. The combination of any one of claims 1-8,~~ which comprises a further therapeutic agent.

~~10~~

8. The combination of ~~any one of claims~~claim 1~~-9~~, which comprises a further therapeutic agent which is an antibody or antigen-binding fragment that specifically binds to C5.

~~11~~

9. The combination of ~~any one of claims~~claim 1~~-10~~, which comprises a further therapeutic agent which is ~~an antibody that specifically binds to C5 which is select from the group consisting of:~~

~~H2M11683N; H2M11686N; H4H12159P; H4H12163P; H4H12164P; H4H12166P2;~~

~~H4H12166P3; H4H12166P4; H4H12166P5; H4H12166P6; H4H12166P7; H4H12166P8;~~
~~H4H12166P9; H4H12166P10; H4H12167P; H4H12168P; H4H12169P; H4H12176P2;~~
~~H4H12177P2; H4H12183P2; H2M11682N; H2M11684N; H2M11694N; and H2M11695N; or an antigen-binding fragment thereof; or which is an antibody that binds to C5,~~ an anti-coagulant, a thrombin inhibitor, an anti-inflammatory drug, an antihypertensive, an immunosuppressive agent, a fibrinolytic agent, a lipid-lowering agent, an inhibitor of hydroxymethylglutaryl CoA reductase, an anti-CD20 agent, an anti-~~TNFα~~TNFα agent, an anti-seizure agent, a C3 inhibitor or an anti-thrombotic agent.

10. A method for making the combination of claim 1, comprising co-packaging:
the first ~~12. The combination of any one of claims 1 -10 which comprises a further therapeutic agent selected from the group consisting of: warfarin, aspirin, heparin, phenindione, fondaparinux, idraparinux, argatroban, lepirudin, bivalirudin, or dabigatran, corticosteroids, and nonsteroidal anti-inflammatory drugs, vincristine, cyclosporine A, methotrexate, ancrod, ε aminocaproic acid, antiplasmin a1 , prostacyclin, defibrotide, rituximab and magnesium sulfate.~~

13. A bispecific or biparatopic antibody or antigen-binding fragment thereof comprising a first ; and

the second antibody or antigen-binding domain that specifically binds to C5 at a first epitope and a second antigen-binding domain that

(i) specifically binds to C5 at a second epitope which is different from that of the first antigen-binding domain and/or

(ii) does not compete with the first antigen-binding domain for binding to C5.

14. The bispecific or biparatopic antibody or fragment of claim 13 which is an IgG.

15. A bispecific or biparatopic antigen-binding protein selected from the group consisting of:

H4H12161PxH4H12177P2;

H4H12166PxH4H12177P2;

H4H12170PxH4H12177P2;

H4H12171PxH4H12177P2;

H4H12175PxH4H12177P2;

H4H12176P2xH4H12177P2;

H4H12176P2xH4H12161P;

H4H12176P2xH4H12166P;

H4H12176P2xH4H12170P;

H4H12176P2xH4H12171P;

H4H12176P2xH4H12175P;

H4H12175PxH4H12161P;

H4H12175PxH4H12166P;

H4H12175PxH4H12170P;

H4H12175PxH4H12171P;

H4H12171PxH4H12161P;

H4H12171PxH4H12166P;

H4H12171PxH4H12170P;

H4H12170PxH4H12161P;

H4H12170PxH4H12166P; and

H4H12166PxH4H12161P.

16. A complex comprising:

one or more C5 polypeptides or antigenic fragments thereof bound to one or more first anti-C5 antigen-binding proteins and one or more further anti-C5 antigen-binding proteins that do not compete for binding to the C5.

17. A complex comprising:

(i) a 1 :1 :2, 2:2:4 or 3:3:6 ratio of first monospecific anti-C5 antigen-binding protein-to-second monospecific anti-C5 antigen-binding protein-to-C5 polypeptide or antigenic fragment thereof;

(ii) a 1 :1, 1 :2, 2:1 or 2:2 ratio of bispecific anti-C5 antigen-binding protein-to-C5 polypeptide or antigenic fragment thereof; or

(iii) a 1 :1 :1; 1 :1 :2 or 1:2:2 ratio of ratio of monospecific anti-C5 antigen-binding protein-to-bispecific anti-C5 antigen-binding protein-to-C5 polypeptide or antigenic fragment thereof.

18. A method for treating or preventing a C5-associated disease or disorder in a subject and/or for inhibiting both the classical complement pathway and the alternative complement pathway in a subject in need of such treatment, prevention and/or inhibition, the method comprising administering, to the subject, a first antigen-binding protein that specifically binds C5 and a second antigen-binding protein that specifically binds C5; wherein the first and second antigen-binding proteins: (a) bind to

distinct, non-overlapping epitopes on C5; and/or (b) do not compete with one another for binding to C5 and/or

a multispecific antigen-binding protein that specifically binds C5; wherein the multispecific antigen-binding protein comprises a first and second antigen-binding domain wherein the domains (a) bind to distinct, non-overlapping epitopes on C5; and/or (b) do not compete with one another for binding to C5.

19. A method for treating or preventing a C5-associated disease or disorder in a subject in need of such treatment or prevention comprising administering an effective amount of combination of any one of claims 1-12 or the bispecific or biparatopic antibody or fragment of any one of claims 13-15 to the subject.

20. The method of any one of claims 18-19 wherein the C5-associated disease or disorder is selected from the group consisting of: Acute respiratory distress syndrome; adult respiratory distress syndrome; age-related macular degeneration; allergy; Alport's syndrome; Alzheimer's disease; asthma; asthma; atherosclerosis; atypical hemolytic uremic syndrome; autoimmune diseases; complement activation caused by balloon angioplasty; bronchoconstriction; bullous pemphigoid; burns; C3 glomerulopathy; capillary leak syndrome; chemical injury; chronic obstructive pulmonary disease; Crohn's disease; diabetes; diabetic macular edema; diabetic nephropathy; diabetic retinopathy; dyspnea; emphysema; epilepsy; fibrogenic dust diseases; frostbite; geographic atrophy; glomerulopathy; Goodpasture's Syndrome; Guillain-Barre Syndrome; complement activation caused by hemodialysis; hemodialysis complications; hemolytic anemia; hemoptysis; hereditary angioedema; hyperacute allograft rejection; hypersensitivity pneumonitis; immune complex disorders; immune complex-associated inflammation; inflammation of autoimmune diseases; inflammatory disorders; inherited CD59 deficiency; injury due to inert dusts and/or minerals; interleukin-2 induced toxicity during IL-2 therapy; lupus nephritis; membraneproliferative glomerulonephritis; membranoproliferative nephritis; mesenteric artery reperfusion after aortic reconstruction; mesenteric artery reperfusion after infectious disease; mesenteric artery reperfusion after sepsis; multiple sclerosis; myasthenia gravis; myocardial infarction; neuromyelitis optica; neuromyelitis optica; obesity; ocular angiogenesis; organic dust diseases; parasitic diseases; Parkinson's disease; paroxysmal nocturnal hemoglobinuria; pneumonia; post-ischemic reperfusion conditions; post-pump syndrome in cardiopulmonary bypass or renal bypass; progressive kidney failure; proteinuric kidney diseases; psoriasis; pulmonary embolisms and infarcts; pulmonary fibrosis; pulmonary vasculitis; renal ischemia; renal ischemia-reperfusion injury; renal transplant; rheumatoid arthritis; schizophrenia; smoke injury; stroke; stroke; systemic lupus erythematosus; systemic lupus

~~erythematosus nephritis; thermal injury; thermal injury; traumatic brain injury; uveitis; vasculitis; and xenograft rejection.~~

~~21. The method of any one of claims 18-20 wherein the subject is administered one or more further therapeutic agents and/or one or more therapeutic procedures.~~

~~22. The method of claim 21 wherein the subject is administered a further therapeutic agent which is an antibody or antigen-binding fragment that specifically binds to C5.~~

~~23. The method claim of 21 wherein the subject is administered one or more further therapeutic agents which is an antibody that binds to C5 which is select from the group consisting of:~~

~~H2M11683N; H2M11686N; H4H12159P; H4H12163P; H4H12164P; H4H12166P2;~~

~~H4H12166P3; H4H12166P4; H4H12166P5; H4H12166P6; H4H12166P7; H4H12166P8; H4H12166P9; H4H12166P10; H4H12167P; H4H12168P; H4H12169P; H4H12176P2;~~

~~H4H12177P2; H4H12183P2; H2M11682N; H2M11684N; H2M11694N; and H2M11695N; or an antigen-binding fragment thereof;~~

~~or~~

~~which is selected from the group consisting of: an antibody that binds to C5, an anticoagulant, a thrombin inhibitor, an anti-inflammatory drug, an antihypertensive, an immunosuppressive agent, a fibrinolytic agent, a lipid-lowering agent, an inhibitor of hydroxymethylglutaryl-CoA reductase, an anti-CD20 agent, an anti-TNFα agent, an antiseizure agent, a C3 inhibitor and an anti-thrombotic agent;~~

~~and/or~~

~~wherein the subject is administered a therapeutic procedure which is dialysis, a blood or plasma transfusion or exchange and/or a bone marrow/stem cell transplant (BMT/SCT).~~

~~24. The method claim 21 wherein the subject is administered one or more further therapeutic agents selected from the group consisting of: eculizumab, coversin, iron, antithymocyte globulin, a growth factor, warfarin, aspirin, heparin, phenindione, fondaparinux, idraparinux, argatroban, lepirudin, bivalirudin, or dabigatran, corticosteroids, and non-steroidal anti-inflammatory drugs, vincristine, cyclosporine A, methotrexate, ancrod, ε-aminocaproic acid, antiplasmin-a1, prostacyclin, defibrotide, rituximab, magnesium sulfate, avacopan, ravulizumab and avacincaptad pegol.~~

~~25. The method of any one of claims 18-24, wherein one or more of the components of the combination are administered to the subject subcutaneously, intravenously, intradermally, intraperitoneally, orally, intramuscularly or intracranially.~~

~~26. The method of any one of claims 18-25 wherein the subject is human.~~

~~27. A method for making the combination of any one of claims 1-12 comprising~~

~~co-packaging:~~

~~said first antigen-binding protein;~~

~~said one or more of further antigen-binding protein; and,~~

~~optionally, one or more further therapeutic agents,~~ into a kit.

~~28~~

11. A method for making the combination of ~~any one of claims 1-12~~claim 1, comprising co-formulating:

~~said~~the first antibody or antigen-binding ~~protein,~~fragment thereof;

~~said one~~the second antibody or ~~more further~~ antigen-binding ~~proteins~~fragment thereof; and

~~optionally, one or more further therapeutic agents; and~~

~~a~~ a pharmaceutically acceptable carrier,

~~into~~ into a single pharmaceutical formulation.

12. A combination which is the product of the method of claim 10.

13. The method of claim 10, further comprising co-packaging one or more further therapeutic agents into the kit.

14. The method of claim 11, further comprising co-formulating one or more further therapeutic agents into the formulation.

15. ~~and, optionally,~~ The method of claim 11, further comprising incorporating the formulation into a device or vessel.

~~29. A~~

16. The combination ~~which is~~of claim l, wherein the ~~product of~~ second antibody or antigen-binding fragment thereof comprises

a ~~method~~heavy chain variable region (V_H) comprising three heavy chain complementarity determining regions (CDRs) (CDR-Hl, CDR-H2, and CDR-H3) of ~~any one~~a V_H that comprises the amino acid sequence set forth in SEQ ID NO: 103, and

a light chain variable region (V_L) comprising three light chain CDRs (CDR-Ll, CDR-L2, and CDR-L3) of ~~claims 27-28~~a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 95.