

CLAIMS

1. A fusion protein comprising

a) an antibody moiety that specifically binds to human C5 (anti-human C5 antibody moiety), and a fusion protein partner that inhibits C3 activation,

wherein the anti-human C5 antibody moiety comprises:

i) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 3, a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 4, a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 5, a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 8, a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 9, and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 11;

ii) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 3, a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 4, a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 5, a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 14, a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 9, and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 10;

iii) a VH-CDR1 of a VH comprising the amino acid sequence of SEQ ID NO: 17, a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 4, a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 5, a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 8, a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 9, and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 10;

iv) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 20, a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 4, VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 5, a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 23, a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 9, and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 10;

v) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 3, a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 26, a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 5, a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 8, a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 9, and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 29;

vi) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 3, a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 34, a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 5, a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 8, a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 9, and a VL-CDR3 comprising the amino acid sequence of SEQ

comprising the amino acid sequence of SEQ ID NO: 68, a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 54, a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 23, a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 9, and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 10; or

b) xv) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 3, a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 4, a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 5, a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 8, a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 9, and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 10.

2. The fusion protein of claim 1, wherein the anti-human C5 antibody moiety comprises any of the following:

i) a heavy chain variable region (VH) comprising amino acid residues 20-144 of the amino acid sequence of SEQ ID NO: 2, or a variant thereof comprising at least about 85% sequence identity to amino acid residues 20-144 of the amino acid sequence of SEQ ID NO: 2; and/or a light chain variable region (VL) comprising amino acid residues 21-127 of the amino acid sequence of SEQ ID NO: 13, or a variant thereof comprising at least about 85% sequence identity to amino acid residues 21-127 of the amino acid sequence of SEQ ID NO: 13;

ii) a VH comprising amino acid residues 20-144 of the amino acid sequence of SEQ ID NO: 2, or a variant thereof comprising at least about 85% sequence identity to the amino acid residues 20-144 of the amino acid sequence of SEQ ID NO: 2; and/or a VL comprising amino acid residues 21-127 of the amino acid sequence of SEQ ID NO: 16, or a variant thereof comprising at least about 85% sequence identity to the amino acid residues 21-127 of the amino acid sequence of SEQ ID NO: 16;

iii) a VH comprising amino acid residues 20-144 of the amino acid sequence of SEQ ID NO: 19, or a variant thereof comprising at least about 85% sequence identity to the amino acid residues 20-144 of the amino acid sequence of SEQ ID NO: 19; and/or a VL comprising amino acid residues 21-127 of amino acid sequence of SEQ ID NO: 7, or a variant thereof comprising at least about 85% sequence identity to the amino acid residues 21-127 of the amino acid sequence of SEQ ID NO: 7;

iv) a VH comprising amino acid residues 20-144 of the amino acid sequence of SEQ ID NO: 22, or a variant thereof comprising at least about 85% sequence identity to amino acid residues 20-144 of the amino acid sequence of SEQ ID NO: 22; and/or a VL comprising amino acid residues 21-127 of the amino acid sequence of SEQ ID NO: 25, or a variant thereof comprising at least about 85% sequence identity to amino acid residues 21-127 of the amino acid sequence of SEQ ID NO: 25;

v) a VH comprising amino acid residues 20-144 of the amino acid sequence of SEQ ID NO: 28, or a variant thereof comprising at least about 85% sequence identity to amino acid residues 20-144 of the amino acid sequence of SEQ ID NO: 28; and/or a VL comprising amino acid residues 21-127 of the amino acid sequence of SEQ ID NO: 31, or a variant thereof comprising at least about 85% sequence

identity to amino acid residues 21-127 of the amino acid sequence of SEQ ID NO: 74;

xiii) a VH comprising amino acid residues 20-144 of the amino acid sequence of SEQ ID NO: 78, or a variant thereof comprising at least about 85% sequence identity to amino acid residues 20-144 of the amino acid sequence of SEQ ID NO: 78; and/or a VL comprising amino acid residues 21-127 of the amino acid sequence of the amino acid sequence of SEQ ID NO: 74, or a variant thereof comprising at least about 85% sequence identity to amino acid residues 21-127 of the amino acid sequence of SEQ ID NO: 74;

xiv) a VH comprising amino acid residues 20-144 of the amino acid sequence of SEQ ID NO: 80, or a variant thereof comprising at least about 85% sequence identity to amino acid residues 20-144 of the amino acid sequence of SEQ ID NO: 80; and/or a VL comprising amino acid residues 21-127 of the amino acid sequence of SEQ ID NO: 74, or a variant thereof comprising at least about 85% sequence identity to amino acid residues 21-127 of the amino acid sequence of SEQ ID NO: 74; and

xv) a VH comprising amino acid residues 20-144 of the amino acid sequence of SEQ ID NO: 2, or a variant thereof comprising at least about 85% sequence identity to the amino acid residues 20-144 of SEQ ID NO: 2; and/or a VL comprising amino acid residues 21-127 of the amino acid sequence of SEQ ID NO: 7, or a variant thereof comprising at least about 85% sequence identity to the amino acid residues 21-127 of SEQ ID NO: 7.

3. The fusion protein of claim 2, wherein the anti-human C5 antibody moiety comprises a VH comprising amino acid residues 20-144 of the amino acid sequence of SEQ ID NO: 2 and a VL comprising amino acid residues 21-127 of the amino acid sequence of SEQ ID NO: 7.

24. The fusion protein of any one of claims 1-3, wherein the binding of the anti-human C5 antibody moiety to human C5 is pH-dependent, and

wherein the anti-human C5 antibody moiety binds more strongly to human C5 at a neutral pH than it does at an acidic pH.

~~3. The fusion protein of claim 1 or 2, wherein the antibody is a bi-functional antibody fusion protein.~~

~~4. The fusion protein of claim 3, wherein the antibody fusion protein inhibits C3 activation.~~

5. The fusion protein of any one of claims 1-4, wherein the fusion protein comprises a complement control protein.

6. The fusion protein of any one of claims 1-5, wherein the fusion protein partner comprises ~~at least one selected from the group consisting one or more of:~~ a complement receptor 1 (CR1) or a fragment thereof, a membrane cofactor protein (MCP) or a factor thereof, a C4b-binding protein (C4BP) or a

fragment thereof, a decay-accelerating factor (DAF) or a fragment thereof, an Apolipoprotein E (ApoE) or a fragment thereof, and a Factor H (FH) ~~protein~~ or a fragment thereof, ~~a human IgG4 or a fragment thereof, a linker, and any combination thereof.~~

7. The fusion protein of any one of claims 1-6, wherein the fragment of fusion protein partner comprises an FH ~~comprises short consensus repeat (SCR) domains 1-5 of the FH protein or a fragment thereof.~~

8. ~~The fusion protein of any one of claims 1-7, wherein the antibody comprises the CDRs: VH-CDR1: SEQ ID NO:3; VH-CDR2: SEQ ID NO:4; VH-CDR3: SEQ ID NO:5; VL-CDR1: SEQ ID NO:8; VL-CDR2: SEQ ID NO:9; and VL-CDR3: SEQ ID NO:11, or a variant or variants thereof.~~

9. ~~The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:2, or a variant thereof.~~

10. ~~The fusion protein of any one of claims 1-7, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO:13, or a variant thereof.~~

11. ~~The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:2 and a light chain comprising the amino acid sequence of SEQ ID NO:13, or a variant or variants thereof.~~

12. ~~The fusion protein of any one of claims 1-7, wherein the antibody comprises the CDRs: VH-CDR1: SEQ ID NO:3; VH-CDR2: SEQ ID NO:4; VH-CDR3: SEQ ID NO:5; VL-CDR1: SEQ ID NO:14; VL-CDR2: SEQ ID NO:9; and VL-CDR3: SEQ ID NO:10, or a variant or variants thereof.~~

13. ~~The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:2, or a variant thereof.~~

14. ~~The fusion protein of any one of claims 1-7, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO:16, or a variant thereof.~~

15. ~~The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:2 and a light chain comprising the amino acid sequence of SEQ ID NO:16, or a variant or variants thereof.~~

16. ~~The fusion protein of any one of claims 1-7, wherein the antibody comprises the CDRs: VH-CDR1: SEQ ID NO:17; VH-CDR2: SEQ ID NO:4; VH-CDR3: SEQ ID NO:5; VL-CDR1: SEQ ID NO:8; VL-CDR2: SEQ ID NO:9; and VL-CDR3: SEQ ID NO:10, or a variant or variants thereof.~~

17. ~~The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:19, or a variant thereof.~~

- 18.—The fusion protein of any one of claims 1-7, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO:7, or a variant thereof.
- 19.—The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:19 and a light chain comprising the amino acid sequence of SEQ ID NO:7, or a variant or variants thereof.
- 20.—The fusion protein of any one of claims 1-7, wherein the antibody comprises the CDRs: VH-CDR1: SEQ ID NO:20; VH-CDR2: SEQ ID NO:4; VH-CDR3: SEQ ID NO:5; VL-CDR1: SEQ ID NO:23; VL-CDR2: SEQ ID NO:9; and VL-CDR3: SEQ ID NO:10, or a variant or variants thereof.
- 21.—The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:22, or a variant thereof.
- 22.—The fusion protein of any one of claims 1-7, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO:25, or a variant thereof.
- 23.—The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:22 and a light chain comprising the amino acid sequence of SEQ ID NO:25, or a variant or variants thereof.
- 24.—The fusion protein of any one of claims 1-7, wherein the antibody comprises the CDRs: VH-CDR1: SEQ ID NO:3; VH-CDR2: SEQ ID NO:26; VH-CDR3: SEQ ID NO:5; VL-CDR1: SEQ ID NO:8; VL-CDR2: SEQ ID NO:9; and VL-CDR3: SEQ ID NO:29, or a variant or variants thereof.
- 25.—The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:28, or a variant thereof.
- 26.—The fusion protein of any one of claims 1-7, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO:31, or a variant thereof.
- 27.—The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:28 and a light chain comprising the amino acid sequence of SEQ ID NO:31, or a variant or variants thereof.
- 28.—The fusion protein of any one of claims 1-7, wherein the antibody comprises the CDRs: VH-CDR1: SEQ ID NO:3; VH-CDR2: SEQ ID NO:34; VH-CDR3: SEQ ID NO:5; VL-CDR1: SEQ ID NO:8; VL-CDR2: SEQ ID NO:9; and VL-CDR3: SEQ ID NO:10, or a variant or variants thereof.
- 29.—The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:36, or a variant thereof.

- 30.—The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:36 and a light chain comprising the amino acid sequence of SEQ ID NO:7, or a variant or variants thereof.
- 31.—The fusion protein of any one of claims 1-7, wherein the antibody comprises the CDRs: VH-CDR1: SEQ ID NO:37; VH-CDR2: SEQ ID NO:38; VH-CDR3: SEQ ID NO:39; VL-CDR1: SEQ ID NO:23; VL-CDR2: SEQ ID NO:9; and VL-CDR3: SEQ ID NO:10, or a variant or variants thereof.
- 32.—The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:41, or a variant thereof.
- 33.—The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:41 and a light chain comprising the amino acid sequence of SEQ ID NO:25, or a variant or variants thereof.
- 34.—The fusion protein of any one of claims 1-7, wherein the antibody comprises the CDRs: VH-CDR1: SEQ ID NO:42; VH-CDR2: SEQ ID NO:43; VH-CDR3: SEQ ID NO:44; VL-CDR1: SEQ ID NO:23; VL-CDR2: SEQ ID NO:9; and VL-CDR3: SEQ ID NO:10, or a variant or variants thereof.
- 35.—The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:46, or a variant thereof.
- 36.—The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:46 and a light chain comprising the amino acid sequence of SEQ ID NO:25, or a variant or variants thereof.
- 37.—The fusion protein of any one of claims 1-7, wherein the antibody comprises the CDRs: VH-CDR1: SEQ ID NO:47; VH-CDR2: SEQ ID NO:48; VH-CDR3: SEQ ID NO:49; VL-CDR1: SEQ ID NO:23; VL-CDR2: SEQ ID NO:9; and VL-CDR3: SEQ ID NO:10, or a variant or variants thereof.
- 38.—The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:51, or a variant thereof.
- 39.—The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:51 and a light chain comprising the amino acid sequence of SEQ ID NO:25, or a variant or variants thereof.
- 40.—The fusion protein of any one of claims 1-7, wherein the antibody comprises the CDRs: VH-CDR1: SEQ ID NO:52; VH-CDR2: SEQ ID NO:53; VH-CDR3: SEQ ID NO:54; VL-CDR1: SEQ ID NO:23; VL-CDR2: SEQ ID NO:9; and VL-CDR3: SEQ ID NO:10, or a variant or variants thereof.

41. — The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:56, or a variant thereof.
42. — The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:56 and a light chain comprising the amino acid sequence of SEQ ID NO:25, or a variant or variants thereof.
43. — The fusion protein of any one of claims 1-7, wherein the antibody comprises the CDRs: VH-CDR1: SEQ ID NO:47; VH-CDR2: SEQ ID NO:57; VH-CDR3: SEQ ID NO:49; VL-CDR1: SEQ ID NO:23; VL-CDR2: SEQ ID NO:9; and VL-CDR3: SEQ ID NO:10, or a variant or variants thereof.
44. — The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:59, or a variant thereof.
45. — The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:59 and a light chain comprising the amino acid sequence of SEQ ID NO:25, or a variant or variants thereof.
46. — The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:72, or a variant thereof.
47. — The fusion protein of any one of claims 1-7, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO:74, or a variant thereof.
48. — The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:72 and a light chain comprising the amino acid sequence of SEQ ID NO:74, or a variant or variants thereof.
49. — The fusion protein of any one of claims 1-7, wherein the antibody comprises the CDRs: VH-CDR1: SEQ ID NO:37; VH-CDR2: SEQ ID NO:62; VH-CDR3: SEQ ID NO:39; VL-CDR1: SEQ ID NO:23; VL-CDR2: SEQ ID NO:9; and VL-CDR3: SEQ ID NO:10, or a variant or variants thereof.
50. — The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:76, or a variant thereof.
51. — The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:76 and a light chain comprising the amino acid sequence of SEQ ID NO:74, or a variant or variants thereof.
52. — The fusion protein of any one of claims 1-7, wherein the antibody comprises the CDRs: VH-CDR1: SEQ ID NO:42; VH-CDR2: SEQ ID NO:65; VH-CDR3: SEQ ID NO:44; VL-CDR1: SEQ ID NO:23; VL-CDR2: SEQ ID NO:9; and VL-CDR3: SEQ ID NO:10, or a variant or variants thereof.

53. — The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:78, or a variant thereof.
54. — The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:78 and a light chain comprising the amino acid sequence of SEQ ID NO:74, or a variant or variants thereof.
55. — The fusion protein of any one of claims 1-7, wherein the antibody comprises the CDRs: VH-CDR1: SEQ ID NO:52; VH-CDR2: SEQ ID NO:68; VH-CDR3: SEQ ID NO:54; VL-CDR1: SEQ ID NO:23; VL-CDR2: SEQ ID NO:9; and VL-CDR3: SEQ ID NO:10, or a variant or variants thereof.
56. — The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:80, or a variant thereof.
57. — The fusion protein of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:80 and a light chain comprising the amino acid sequence of SEQ ID NO:74, or a variant or variants thereof.
58. — The fusion protein of claims 8, 12, 16, 20, 24, 28, 31, 34, 37, 40, 43, 49, 52, or 55, wherein the antibody comprises a substitution at proline 4 (P4) in VH CDR2, relative to SEQ ID NO:4.
59. — The fusion protein of claim 58, wherein the substitution at proline 4 (P4) is one substitution selected from the group consisting of P4 → F4 (P4F), P4 → L4 (P4L), P4 → M4 (P4M), P4 → W4 (P4W), and P4 → I4 (P4I).
60. — The fusion protein of claim 59, wherein the antibody comprises a substitution at proline 4 (P4) in VH CDR2, relative to SEQ ID NO:4, and a substitution at threonine 9 in VH CDR2, relative to SEQ ID NO:4.
61. — The fusion protein of claim 60, wherein the substitution at proline 4 (P4) is one substitution selected from the group consisting of P4 → F4 (P4F), P4 → L4 (P4L), P4 → M4 (P4M), P4 → W4 (P4W), and P4 → I4 (P4I); and the substitution at threonine 9 (T9) is one substitution selected from the group consisting of T9 → H9 (T9H), T9 → F9 (T9F), T9 → L9 (T9L), T9 → M9 (T9M), T9 → W9 (T9W), and T9 → I9 (T9I).
62. — The fusion protein of claims 8, 12, 16, 20, 24, 28, 31, 34, 37, 40, 43, 49, 52, or 55, wherein the antibody comprises a substitution at valine 16 (V16) in VH CDR3, relative to SEQ ID NO:5.
63. — The fusion protein of claim 62, wherein the substitution at valine 16 (V16) is one substitution selected from the group consisting of V16 → F16 (V16F), V16 → E16 (V16E) and V16 → W16 (V16W).

64.—The fusion protein of claims 8, 12, 16, 20, 24, 28, 31, 34, 37, 40, 43, 49, 52, or 55, wherein the antibody comprises a substitution at leucine 9 (L9) in VH CDR1, relative to SEQ ID NO:20.

65.—The fusion protein of claim 64, wherein the substitution at leucine 9 (L9) is one substitution selected from the group consisting of L9→W9 (L9W), L9→I9 (L9I), L9→V9 (L9V), L9→Y9 (L9Y), and L9→F9 (L9F).

66.—The fusion protein of claims 8, 12, 16, 20, 24, 28, 31, 34, 37, 40, 43, 49, 52, or 55, wherein the antibody comprises a substitution of two or more substitutions selected from the group consisting of proline 4 (P4) in VH CDR2, relative to SEQ ID NO:4, threonine 9 (T9) in VH CDR2, relative to SEQ ID NO:4, valine 16 (V16) in VH CDR3, relative to SEQ ID NO:5, and leucine 9 (L9) in VH CDR1, relative to SEQ ID NO:20.

67.—The fusion protein of claim 66, wherein the antibody comprises two or more substitutions selected from the group consisting of L9I/P4M, L9I/P4W, L9I/P4F, L9F/P4M, L9F/P4W, L9F/P4F, L9I/P4M/V16W, L9I/P4W/V16W, L9I/P4F/V16W, L9F/P4M/V16W, L9F/P4W/V16W, L9F/P4F/V16W, L9I/P4M/V16E, L9I/P4W/V16E, L9I/P4F/V16E, L9F/P4M/V16E, L9F/P4W/V16E, L9F/P4F/V16E, L9I/P4M/T9H/V16W, L9I/P4W/T9H/V16W, L9I/P4F/T9H/V16W, L9F/P4M/T9H/V16W, L9F/P4W/T9H/V16W, L9F/P4F/T9H/V16W, L9I/P4M/T9H/V16E, L9I/P4W/T9H/V16E, L9I/P4F/T9H/V16E, L9F/P4M/T9H/V16E, L9F/P4W/T9H/V16E, and L9F/P4F/T9H/V16E.

68.—Use of any one of claims 1-67 in the manufacture of a medicament for treating a complement pathway mediated disease or disorder in an individual wherein the disease or disorder is at least selected from the group consisting of: macular degeneration (MD), age related macular degeneration (AMD), ischemia reperfusion injury, arthritis, rheumatoid arthritis, lupus, ulcerative colitis, stroke, post-surgery systemic inflammatory syndrome, asthma, allergic asthma, chronic obstructive pulmonary disease (COPD), paroxysmal nocturnal hemoglobinuria (PNH) syndrome, myasthenia gravis, neuromyelitis optica, (NMO), multiple sclerosis, delayed graft function, antibody mediated rejection, atypical hemolytic uremic (aHUS) syndrome, central retinal vein occlusion (CRVO), central retinal artery occlusion (CRAO), epidermolysis bullosa, sepsis, organ transplantation, inflammation (including, but not limited to, inflammation associated with cardiopulmonary bypass surgery and kidney dialysis), C3 glomerulopathy, membranous nephropathy, IgA nephropathy, glomerulonephritis (including, but not limited to, anti-neutrophil cytoplasmic antibody (ANCA) mediated glomerulonephritis, lupus nephritis, and combinations thereof), ANCA mediated vasculitis, Shiga toxin induced HUS, and antiphospholipid antibody induced pregnancy loss, or any combinations thereof.

69.—Use of an antibody in the form of a fusion protein of any one of claims 1-67 in the manufacture of a medicament for reducing the activity of a complement system of an individual, wherein the

medicament is to be administered to the individual via a route of administration selected from the group consisting of enteral administration, parenteral administration, and a combination thereof.

70. — The use of claim 69, wherein the antibody is an antibody fragment selected from the group consisting of a Fab, Fab', F(ab)2, F(ab')2, scFv, and combinations thereof.

71. — A cell comprising the fusion protein of at least one of claims 1-67.

72. — The cell of claim 71, wherein the cell produces the fusion protein of at least one of claims 1-67.

73. — The cell of claim 72, wherein the cell is a hybridoma.

74. — A genetically modified non human animal that expresses human C5.

75. — The genetically modified non human animal of claim 74, wherein the non human animal is a rodent.

76. — The genetically modified non human animal of claim 75, wherein the non human animal is a mouse.

77. — The genetically modified non human animal of claim 75, wherein the non human animal is a NOD/SCID mouse.

78. — The genetically modified non human animal of claim 75, wherein the non human animal is a FeRn/SCID mouse.

79. — A fusion protein comprising an anti C5 antibody moiety and an FH or a functional fragment thereof.

80. — The protein of claim 79, wherein the anti C5 moiety comprises at least one histidine substitution.

81. — The protein of claim 79, wherein the anti C5 moiety comprises an IgG4 chain.

82. — The protein of claim 81, wherein the IgG4 chain comprises a PLA mutation.

83. — The protein of claim 79, wherein the FH or functional fragment thereof comprises domains 1-5 of the FH protein.

8. — The fusion protein of claim 7, wherein the fragment of FH comprises short consensus repeat (SCR) domains 1-4 or domains 1-5 of the FH.

9. — The fusion protein of claim 7 or 8, wherein the fragment of FH comprises amino acid residues 472-726 of SEQ ID NO: 72.

10. — The fusion protein of any one of claims 1-9, wherein the anti-human C5 antibody moiety is a

full-length antibody, a Fab, a Fab', a F(ab)₂, a F(ab')₂, an scFv, or a combination thereof.

11. The fusion protein of any one of claims 1-10, wherein the fusion protein partner is fused to the C-terminus of the anti-human C5 antibody moiety.

12. The fusion protein of claim 11, wherein the fusion protein partner is fused to the C-terminus of the anti-human C5 antibody moiety via a linker.

13. The fusion protein of claim 10, wherein the anti-human C5 antibody moiety is a full-length antibody (anti-human C5 full-length antibody).

14. The fusion protein of claim 13, wherein the anti-human C5 full-length antibody comprises a heavy chain constant domain derived from human IgG4.

15. The fusion protein of claim 14, wherein the heavy chain constant domain comprises the amino acid sequence of any one of SEQ ID NOs: 32, 33, and 61.

16. The fusion protein of claim 15, wherein the heavy chain constant domain comprises the amino acid sequence of SEQ ID NO: 61.

17. The fusion protein of any one of claims 1-16, wherein the anti-human C5 full-length antibody comprises a heavy chain and the light chain, and wherein:

i) the heavy chain comprises amino acid residues 20-471 of the amino acid sequence of SEQ ID NO: 72, and/or the light chain comprises amino acid residues 21-234 of the amino acid sequence of SEQ ID NO: 74;

ii) the heavy chain comprises amino acid residues 20-471 of the amino acid sequence of SEQ ID NO: 76, and/or the light chain comprises amino acid residues 21-234 of the amino acid sequence of SEQ ID NO: 74;

iii) the heavy chain comprises amino acid residues 20-471 of SEQ ID NO: 78, and/or the light chain comprises amino acid residues 21-234 of the amino acid sequence of SEQ ID NO: 74; or

iv) the heavy chain comprises amino acid residues 20-471 of SEQ ID NO: 80, and/or the light chain comprises amino acid residues 21-234 of the amino acid sequence of SEQ ID NO: 74.

18. The fusion protein of any one of claims 1-17, wherein the fusion protein partner is fused to the C-terminus of one or both heavy chains of the anti-human C5 full-length antibody.

19. The fusion protein of claim 18, wherein the C-terminus of each heavy chain of the anti-human C5 full-length antibody is fused with an FH or fragment thereof.

20. The fusion protein of any one of claims 11-19, wherein the fusion protein comprises a first FH or fragment thereof and a second FH or fragment thereof, wherein the first FH or fragment thereof is fused

to the C-terminus of a first heavy chain of the anti-C5 full-length antibody, and the second FH or fragment thereof is fused to the C-terminus of a second heavy chain of the anti-C5 full-length antibody.

21. The fusion protein of claim 20, wherein the first FH or fragment thereof is fused to the C-terminus of the first heavy chain of the anti-C5 full-length antibody via a first linker, and the second FH or fragment thereof is fused to the C-terminus of the second heavy chain of the anti-C5 full-length antibody via a second linker.

22. The fusion protein of claim 21, wherein the fusion protein comprises two light chains each comprising the amino acid residues 21-234 of the amino acid sequence of SEQ ID NO: 74, and two FH fragment-fused heavy chains each comprising the amino acid residues 20-777 of any one of the amino acid sequence of SEQ ID NOs: 72, 76, 78, and 80.

23. The fusion protein of claim 21 or 22, wherein the fusion protein comprises two light chains each comprising the amino acid residues 21-234 of SEQ ID NO: 74, and two FH fragment-fused heavy chains each comprising the amino acid residues 20-777 of SEQ ID NO: 72.

24. An isolated nucleic acid encoding the fusion protein of any one of claims 1-23.

25. The isolated nucleic acid of claim 24, wherein the isolated nucleic acid comprises the nucleic acid sequence of any of SEQ ID NOs: 1, 6, 12, 15, 18, 21, 24, 27, 30, 35, 40, 45, 50, 55, 58, 63, 64, 69, 71, 73, 75, 77, and 79.

26. A vector comprising the isolated nucleic acid of claim 24 or 25.

27. The vector of claim 26, wherein the vector is a viral vector.

28. The vector of claim 27, wherein the viral vector is a retrovirus vector, an adenovirus vector, an adeno-associated virus vector, an herpes virus vector, a lentivirus vector, a murine stem cell virus vector, a moloney murine leukemia virus vector, or an human immunodeficiency virus vector

29. A pharmaceutical composition comprising the fusion protein of any one of claims 1-23, the isolated nucleic acid of claim 24 or 25, or the vector of any one of claims 26-28.

30. A host cell expressing the fusion protein of any one of claims 1-23, or comprising the isolated nucleic acid of claim 24 or 25 or the vector of any one of claims 26-28.

31. Use of the fusion protein of any one of claims 1-23 for the manufacture of a medicament for treating a complement pathway-mediated disease or disorder in an individual.

32. The use of claim 31, wherein the disease or disorder is selected from the group consisting of: macular degeneration (MD), ischemia reperfusion injury, stroke, asthma, chronic obstructive pulmonary

disease (COPD), paroxysmal nocturnal hemoglobinuria (PNH) syndrome, myasthenia gravis, multiple sclerosis, delayed graft function, antibody-mediated rejection, atypical hemolytic uremic (aHUS) syndrome, central retinal vein occlusion (CRVO), central retinal artery occlusion (CRAO), epidermolysis bullosa, sepsis, C3 glomerulopathy, membranous nephropathy, IgA nephropathy, Shiga toxin induced HUS, and antiphospholipid antibody-induced pregnancy loss, and any combinations thereof.

33. The use of claim 32, wherein:

i) the inflammation comprises inflammation associated with cardiopulmonary bypass surgery, inflammation associated with kidney dialysis, arthritis, rheumatoid arthritis, neuromyelitis optica (NMO), post-surgery systemic inflammatory syndrome, glomerulonephritis, anti-neutrophil cytoplasmic antibody (ANCA)-mediated vasculitis, lupus, ulcerative colitis, and/or inflammation associated with organ transplantation;

ii) the macular degeneration comprises age-related macular degeneration (AMD); and/or

iii) the glomerulonephritis comprises ANCA- mediated glomerulonephritis, lupus nephritis, and any combinations thereof.

34. Use of the fusion protein of any one of claims 1-23 for the manufacture of a medicament for reducing the activity of a complement system of an individual.

35. The use of any one of claims 31-34, wherein the individual is human.

36. A method of producing a fusion protein, comprising:

a) culturing a host cell comprising the isolated nucleic acid of claim 24 or 25 or vector of any one of claims 26-28, or the host cell of claim 30, under a condition suitable for expression of the fusion protein; and

b) obtaining the expressed fusion protein from said cell.