# ANTI-C2 BINDING AGENTS AND CONJUGATES THEREOF

## CROSS-REFERENCE TO RELATED APPLICATION

**[0001]** This application claims the benefit of U.S. Provisional Application No.: 63/547,019, filed November 2, 2023, the content of which is hereby incorporated by reference in its entirety.

## BACKGROUND

**[0002]** The complement system is a critical component of human host defense with a number of biological effects. A properly functioning complement system is required for protection against infection and for maintaining tissue homeostasis. However, the complement system may also cause damage when the complement system is activated improperly or is not properly regulated.

**[0003]** The development of effective therapies to treat complement mediated diseases and conditions is complicated by the pathway's highly diverse and interconnected architecture, making it difficult to identify promising points of therapeutic intervention and to predict clinical study outcomes. Therefore, the art is in need of alternate treatments for complement mediated diseases and conditions that are effective, economical, and decrease patient treatment burden.

## SUMMARY

**[0004]** The present disclosure provides an antibody, or antigen binding fragment thereof, that specifically targets complement component C2, and conjugates thereof.

**[0005]** In a first aspect, the present disclosure provides an anti-complement component (C2) antibody, or antigen- binding fragment thereof, that specifically binds complement component 2 (C2), wherein the antibody or antigen- binding fragment thereof comprises a light chain variable region (VL) and a heavy chain variable region (VH), wherein: (i) the VL comprises a VL complementary determining region (CDR) 1 (CDRL1) having an amino acid sequence as set forth in SEQ ID NO: 7 (RSSQYIVHSNX1NTYLE), a VL CDR 2 (CDRL2) having an amino acid sequence as set forth in SEQ ID NO: 8 (KVSNRFS), and a VL CDR 3 (CDRL3) having an amino acid sequence as set forth in SEQ ID NO: 9 (FQGSHVPLT), and the VH comprises a VH CDR 1 (CDRH1) having an amino acid sequence as set forth in SEQ ID NO: 10 (GYTFTDYSMH), a VH CDR 2 (CDRH2) having an amino acid sequence as set forth in SEQ ID NO: 11 (WINTETGEPT), and a VH CDR 3 (CDRH3) having an amino acid sequence as set forth in SEQ ID NO: 12 (EGHYYAMDY), wherein, solely within alternative (i), X1 is G, K, R, or Q; (ii) the VL comprises a VL complementary determining region (CDR) 1 (CDRL1) having an amino acid sequence as set

forth in SEQ ID NO: 1 (X1ASQDIX2SYLS), a VL CDR 2 (CDRL2) having an amino acid sequence as set forth in SEQ ID NO: 2 (RAX3RLVX4), and a VL CDR 3 (CDRL3) having an amino acid sequence as set forth in SEQ ID NO: 3 (LQYDEFPFT),; and the VH comprises a VH CDR 1 (CDRH1) having an amino acid sequence as set forth in SEQ ID NO: 4 (GYTFTGYX5IE), a VH CDR 2 (CDRH2) having an amino acid sequence as set forth in SEQ ID NO: 5 (EILPRSGSTX6), and a VH CDR 3 (CDRH3) having an amino acid sequence as set forth in SEQ ID NO: 6 (SGGSX7SYYYALGY), wherein, solely within alternative (ii), X1 is K or R; X2 is N, Q, S, or A; X3 is N, Q, S, or A; X4 is D, E, S, or A; X5 is W, H, F, or Y; X6 is N, Q, S, or A; and X7 is N, Q, S, or A; (iii) the VL comprises a CDRL1 having an amino acid sequence as set forth in SEQ ID NO: 13 (RSSQSLENSNGNTYLN), a CDRL2 having an amino acid sequence as set forth in SEQ ID NO: 14 (RVSNRFS), and a CDRL3 having an amino acid sequence as set forth in SEQ ID NO: 15 (LQVTHVPFT),; and the VH comprises a CDRH1 having an amino acid sequence as set forth in SEQ ID NO: 16 (GYTFTNYGMN), a CDRH2 having an amino acid sequence as set forth in SEQ ID NO: 17 (WINTYTGEPT), and a CDRH3 having an amino acid sequence as set forth in SEQ ID NO: 18 (EFWYFDV); (iv) the VL comprises a CDRL1 having an amino acid sequence as set forth in SEQ ID NO: 19 (SASSSVSYMY), a CDRL2 having an amino acid sequence as set forth in SEQ ID NO: 20 (LTSNLAS), and a CDRL3 having an amino acid sequence as set forth in SEQ ID NO: 21 (QQWGNNPYT),; and the VH comprises a CDRH1 having an amino acid sequence as set forth in SEQ ID NO: 22 (GYTFTSYWMH), a CDRH2 having an amino acid sequence as set forth in SEQ ID NO: 23 (VIDPSDNYTN), and a CDRH3 having an amino acid sequence as set forth in SEQ ID NO: 24 (YGGSYGFAY); (v) the VL comprises a CDRL1 having an amino acid sequence as set forth in SEQ ID NO: 25 (KASQSVDYDGDSYMN), a CDRL2 having an amino acid sequence as set forth in SEQ ID NO: 26 (AASNLES), and a CDRL3 having an amino acid sequence as set forth in SEQ ID NO: 27 (QQSNEDPFT),; and the VH comprises a CDRH1 having an amino acid sequence as set forth in SEQ ID NO: 28 (GYTFTTYTMS), a CDRH2 having an amino acid sequence as set forth in SEQ ID NO: 29 (WINTYSGVPT), and a CDRH3 having an amino acid sequence as set forth in SEQ ID NO: 30 (IKTYGYDWYFDV); or (vi) the VL comprises a CDRL1 having an amino acid sequence as set forth in SEQ ID NO: 31 (RSSQSIVHSNGNTYLE), a CDRL2 having an amino acid sequence as set forth in SEQ ID NO: 32 (KVSNRFS), and a CDRL3 having an amino acid sequence as set forth in SEQ ID NO: 33 (FQGSHVPWT).; and the VH comprises a CDRH1 having an amino acid sequence as set forth in SEQ ID NO: 34 (GYSFTDYYMN), a CDRH2 having an amino acid sequence as set forth in SEQ ID NO: 35 (EIDPSTGGTT), and a CDRH3 having an amino acid sequence as set forth in SEQ ID NO: 36 (DYYGSSYFDY); optionally wherein the antibody is a full-length antibody, and/or the antibody or antigen-binding fragment thereof is humanized.

**[0005a]** In another aspect, the present disclosure provides an anti-C2 antibody conjugate comprising: (i) the anti-C2 antibody or antigen- binding fragment thereof of any one of claims 1-605;, and (ii) at least one regulator of complement activation (RCA) polypeptide covalently linked to the antibody or antigen-binding fragment thereof, optionally wherein (a) the at least one RCA polypeptide is selected from FH1-4, FH1-5, FH19-20, DAF1-4, DAF2-4, MCP1-4, C4BP1-3, CR1.1-3, CR1.8-10, CR1.15-17, MCP2-4, MCP3-4, C4BP1-4, and any combination thereof; (b) the at least one RCA polypeptide comprises an amino acid sequence selected from SEQ ID NOs: 114-122, SEQ ID NOs: 240-250, and any combination thereof; and/or (c) the antibody or antigen-binding fragment thereof is covalently linked to the at least one RCA polypeptide via a linker, optionally wherein the linker is a glycine-serine (Gly-Ser) linker, optionally wherein the Gly-Ser linker is a $(Gly_2Ser)n$ or a $(Gly_3Ser)n$ linker, wherein n is 1-10, optionally wherein n is 1-5.

**[0005b]** In another aspect, the present disclosure provides a nucleic acid encoding the anti-C2 antibody or antigen-binding fragment thereof as disclosed herein or the anti-C2 antibody conjugate as disclosed herein.

**[0005c]** In another aspect, the present disclosure provides an expression vector comprising the nucleic acid as disclosed herein.

**[0005d]** In another aspect, the present disclosure provides a host cell comprising the expression vector as disclosed herein.

**[0005e]** In another aspect, the present disclosure provides a method for producing the anti-C2 antibody or antigen-binding fragment thereof as disclosed herein or the anti-C2 antibody conjugate as disclosed herein, the method comprising culturing the host cell as disclosed herein under conditions permitting expression of the antibody or antigen-binding fragment thereof, or the antibody conjugate.

**[0005f]** In another aspect, the present disclosure provides a pharmaceutical composition comprising the anti-C2 antibody or antigen-binding fragment thereof as disclosed herein, or the anti-C2 antibody conjugate as disclosed herein, and a pharmaceutically acceptable carrier.

**[0005g]** In another aspect, the present disclosure provides the anti-C2 antibody or antigen-binding fragment thereof as disclosed herein, the anti-C2 antibody conjugate as disclosed herein, or the pharmaceutical composition as disclosed herein for use in therapy.

**[0005h]** In another aspect, the present disclosure provides a use of the anti-C2 antibody or antigen-binding fragment thereof as disclosed herein, the anti-C2 antibody conjugate as disclosed herein, or the pharmaceutical composition as disclosed herein in the manufacture of a medicament for treating a complement-associated disease or disorder, optionally wherein the complement-associated disease or disorder is selected from amyotrophic lateral sclerosis (ALS), antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, atypical hemolytic uremic syndrome (aHUS), aHUS after kidney transplant, autoimmune encephalitis, bullous pemphigoid, C3 glomerulopathy (C3G), C3 glomerulonephritis (C3GN), C3G relapse after kidney transplant, cold agglutinin disease (CAD), CD59 deficiency, CD59-mediated hemolytic anemia with or without immune-mediated polyneuropathy, CHAPLE syndrome (CD55 deficiency), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), complement Factor I deficiency, diabetic nephropathy, cryoglobulinemia, dense deposit disease, diabetic lumbosacral plexopathy, age-related macular degeneration (AMD), glaucoma, dry AMD, wet AMD, diabetic retinopathy, inherited retinal disease, retinal detachment, familial amyloid polyneuropathy, fibrillary glomerulonephritis, focal segmental glomerulosclerosis (FSGS), geographic atrophy, Goodpasture’s syndrome, Guillain-Barré syndrome, hematopoietic stem cell transplant-associated-thrombotic microangiopathy (HSCT-TMA), hidradenitis suppurativa, Huntington's disease, IgA nephropathy (IgAN), IgAN relapse after kidney transplant antibody mediated rejection post-transplant rejection, immune complex membranoproliferative glomerulonephritis (IC-MPGN), immune-mediated necrotizing myopathy, immunoglobulin A-associated vasculitis (IgAV), immunoglobulin A-associated vasculitis (IgAV) nephritis, immune thrombocytopenia (ITP), immune thrombocytopenic purpura, lupus nephritis, lupus nephritis flares with high urinary Ba or sCb5 -9, multiple sclerosis, multifocal motor neuropathy (MMN), myasthenia gravis, neuromyelitis optica spectrum disorder (NMOSD), paroxysmal nocturnal hemoglobinuria (PNH), post-infectious glomerulonephritis, primary membranous nephropathy (PMN), rhabdomyolysis-induced acute kidney injury (RIAKI), sickle cell disease, Sjogren's syndrome, tauopathy, thrombotic microangiopathy (TMA), systemic lupus erythematosus, thrombotic thrombocytopenic purpura (TTP), warm autoimmune hemolytic anemia (WAHA), acute spinal cord injuries, anti-MAG (myelin-associated glycoprotein) peripheral polyneuropathy (IgM neuropathy), pyoderma gangrenosum, dermatomyositis, hypocomplementemic urticarial vasculitis syndrome (HUVS), auto-immune chronic spontaneous urticaria (aiCUS), Kawasaki disease, Takayasu's arteritis, antiphospholipid therapy - thrombosis prevention (antiphospholipid syndrome), catastrophic antiphospholipid syndrome (CAPS), pre-eclampsia, HELLP syndrome, and autoimmune hepatitis (AIH).

**[0005i]** In a first example, the present disclosure provides an antibody, or antigen binding fragment thereof, that specifically binds complement component 2 (C2), wherein the antibody or antigen binding fragment comprises a light chain variable region (VL) and a heavy chain variable region (VH), wherein, (i) the VL comprises a VL complementary determining region (CDR) 1 (CDRL1) set forth in SEQ ID NO: 1 ($X_1$ASQDI$X_2$SYLS), a VL CDR 2 (CDRL2) set forth in SEQ ID NO: 2 (RA$X_3$RLV$X_4$), and a VL CDR 3 (CDRL3) set forth in SEQ ID NO: 3 (LQYDEFPFT); and the VH comprises a VH CDR 1 (CDRH1) set forth in SEQ ID NO: 4 (GYTFTGY$X_5$IE), a VH CDR 2 (CDRH2) set forth in SEQ ID NO: 5 (EILPRSGST$X_6$), and a VH CDR 3 (CDRH3) set forth in SEQ ID NO: 6 (SGGS$X_7$SYYYALGY), wherein $X_1$ is K or R; $X_2$ is N, Q, S or A; $X_3$ is N, Q, S or A; $X_4$ is D, E, S or A; $X_5$ is W, H, F or Y; $X_6$ is N, Q, S or A; $X_7$ is N, Q, S or A; (ii) the VL comprises a CDRL1 set forth in SEQ ID NO: 7 (RSSQYIVHSN$X_1$NTYLE), a CDRL2 set forth in

SEQ ID NO: 8 (KVSNRFS), and a CDRL3 set forth in SEQ ID NO: 9 (FQGSHVPLT); and the VH comprises a CDRH1 set forth in SEQ ID NO: 10 (GYTFTDYSMH), a CDRH2 set forth in SEQ ID NO: 11 (WINTETGEPT), and a CDRH3 set forth in SEQ ID NO: 12 (EGHYYAMDY), wherein $X_1$ is G, K, R or Q; (iii) the VL comprises a CDRL1 set forth in SEQ ID NO: 13 (RSSQSLENSNGNTYLN), a CDRL2 set forth in SEQ ID NO: 14 (RVSNRFS), and a CDRL3 set forth in SEQ ID NO: 15 (LQVTHVPFT); and the VH comprises a CDRH1 set forth in SEQ ID NO: 16 (GYTFTNYGMN), a CDRH2 set forth in SEQ ID NO: 17 (WINTYTGEPT), and a CDRH3 set forth in SEQ ID NO: 18 (EFWYFDV); (iv) the VL comprises a CDRL1 set forth in SEQ ID NO: 19 (SASSSVSYMY), a CDRL2 set forth in SEQ ID NO: 20 (LTSNLAS), and a CDRL3 set forth in SEQ ID NO: 21 (QQWGNNPYT); and the VH comprises a CDRH1 set forth in SEQ ID NO: 22 (GYTFTSYWMH), a CDRH2 set forth in SEQ ID NO: 23 (VIDPSDNYTN), and a CDRH3 set forth in SEQ ID NO: 24 (YGGSYGFAY); (v) the VL comprises a CDRL1 set forth in SEQ ID NO: 25 (KASQSVDYDGDSYMN), a CDRL2 set forth in SEQ ID NO: 26 (AASNLES), and a CDRL3 set forth in SEQ ID NO: 27 (QQSNEDPFT); and the VH comprises a CDRH1 set forth in SEQ ID NO: 28 (GYTFTTYTMS), a CDRH2 set forth in SEQ ID NO: 29 (WINTYSGVPT), and a CDRH3 set forth in SEQ ID NO: 30 (IKTYGYDWYFDV); (vi) the VL comprises a CDRL1 set forth in SEQ ID NO: 31 (RSSQSIVHSNGNTYLE), a CDRL2 set forth in SEQ ID NO: 32 (KVSNRFS), and a CDRL3 set forth in SEQ ID NO: 33 (FQGSHVPWT); and a CDRH1 set forth in SEQ ID NO: 34 (GYSFTDYYMN), a CDRH2 set forth in SEQ ID NO: 35 (EIDPSTGGTT), and a CDRH3 set forth in SEQ ID NO: 36 (DYYGSSYFDY); or (vii) the VL comprises a CDRL1 set forth in SEQ ID NO: 50 (ITFTDIDDDMN), a CDRL2 set forth in SEQ ID NO: 38 (EGNTLRP), and a CDRL3 set forth in SEQ ID NO: 39 (LQSDNLPFT); and a CDRH1 set forth in SEQ ID NO: 40 (GYTFTDYNMH), a CDRH2 set forth in SEQ ID NO: 41 (YVYPYIGGTG), and a CDRH3 set forth in SEQ ID NO: 42 (RGYDGIFDY).

**[0006]** In some examples, the CDRL1 is set forth in SEQ ID NO: 43 (RASQDINSYLS), the CDRL2 is set forth in SEQ ID NO: 45 (RANRLVD), the CDRL3 is set forth in SEQ ID NO: 3 (LQYDEFPFT), the CDRH1 is set forth in SEQ ID NO: 46 (GYTFTGYWIE), the CDRH2 is set forth in SEQ ID NO: 47 (EILPRSGSTN), and the CDRH3 is set forth in SEQ ID NO: 48 (SGGSNSYYYALGY).

**[0007]** In some examples, the CDRL1 is set forth in SEQ ID NO: 44 (KASQDINSYLS), the CDRL2 is set forth in SEQ ID NO: 45 (RANRLVD), the CDRL3 is set forth in SEQ ID NO: 3 (LQYDEFPFT), the CDRH1 is set forth in SEQ ID NO: 46

(GYTFTGYWIE), the CDRH2 is set forth in SEQ ID NO: 47 (EILPRSGSTN), and the CDRH3 is set forth in SEQ ID NO: 48 (SGGSNSYYYALGY).

**[0008]** In some examples, the CDRL1 is set forth in SEQ ID NO: 49 (RSSQYIVHSNGNTYLE), the CDRL2 is set forth in SEQ ID NO: 8 (KVSNRFS), the CDRL3 is set forth in SEQ ID NO: 9 (FQGSHVPLT), the CDRH1 is set forth in SEQ ID NO: 10 (GYTFTDYSMH), the CDRH2 is set forth in SEQ ID NO: 11 (WINTETGEPT), and the CDRH3 is set forth in SEQ ID NO: 12 (EGHYYAMDY).

**[0009]** In some examples, the CDRL1 is set forth in SEQ ID NO: 43 (RASQDINSYLS), the CDRL2 is set forth in SEQ ID NO: 45 (RANRLVD), the CDRL3 is set forth in SEQ ID NO: 3 (LQYDEFPFT), the CDRH1 is set forth in SEQ ID NO: 46 (GYTFTGYWIE), the CDRH2 is set forth in SEQ ID NO: 47 (EILPRSGSTN), and the CDRH3 is set forth in SEQ ID NO: 320 (SGGSSSYYYALGY).

**[0010]** In some examples, the CDRL1 is set forth in SEQ ID NO: 327 (RSSQYIVHSNQNTYLE), the CDRL2 is set forth in SEQ ID NO: 8 (KVSNRFS), the CDRL3 is set forth in SEQ ID NO: 9 (FQGSHVPLT), the CDRH1 is set forth in SEQ ID NO: 10 (GYTFTDYSMH), the CDRH2 is set forth in SEQ ID NO: 11 (WINTETGEPT), and the CDRH3 is set forth in SEQ ID NO: 12 (EGHYYAMDY).

**[0011]** In some examples, the CDRL1 is set forth in SEQ ID NO: 50 (ITFTDIDDDMN), the CDRL2 is set forth in SEQ ID NO: 38 (EGNTLRP), the CDRL3 is set forth in SEQ ID NO: 39 (LQSDNLPFT), the CDRH1 is set forth in SEQ ID NO: 40 (GYTFTDYNMH), the CDRH2 is set forth in SEQ ID NO: 41 (YVYPYIGGTG), and the CDRH3 is set forth in SEQ ID NO: 42 (RGYDGIFDY).

**[0012]** In some examples, the VL comprises at least one VL framework region (FR) selected from SEQ ID Nos: 166-169, 174-175, 177, 183-185, 195, 199-201, 205-206, 209-211, 213-214, 312-317, or 428.

**[0013]** In some examples, the VL comprises a FR1 region selected from SEQ ID Nos: 166, 183, 195, 199, 209, 213, 312, and 313, a FR2 region selected from SEQ ID NOs: 167, 174, 177, 184, 200, 205, 206, 210, 314, and 315, a FR3 region selected from SEQ ID NOs: 168, 175, 185, 201, 211, 214, 316, and 317, and a FR4 region selected from SEQ ID Nos: 169, and 428.

**[0014]** In some examples, the VH comprises at least one VH FR selected from SEQ ID Nos: 170-173, 176, 178-182, 186-194, 196-198, 202-204, 207-208, 212, 215-216, 309-311, or 429.

**[0015]** In some examples, the VH comprises a FR1 region selected from SEQ ID Nos: 170, 178, 189, 196, and 309, a FR2 region selected from SEQ ID NOs: 171, 179, 186, 197, 202, 207, and 429 a FR3 region selected from SEQ ID NOs: 172, 176, 180, 181, 182, 187, 188, 190, 191, 192, 193, 194, 198, 203, 208, 212, 215, 216, and 310, and a FR4 region selected from SEQ ID NOs: 173, 204, and 311.

**[0016]** In some examples, the VL comprises the sequence set forth in SEQ ID NO: 58, wherein $X_1$ is N, Q, S or A; $X_2$ is N, Q, S or A; and $X_3$ is D, E, S or A, and the VH comprises the sequence set forth in SEQ ID NO: 52, wherein $X_1$ is W, H, F or Y; $X_2$ is N, Q, S or A; and $X_3$ is N, Q, S or A.

**[0017]** In some examples, the VL comprises the sequence set forth in SEQ ID NO: 68, wherein $X_1$ is Q or E; $X_2$ is I or V; and $X_3$ is G, K, R or Q and the VH comprises the sequence set forth in SEQ ID NO: 62, wherein $X_1$ is I or V; $X_2$ is D or E; $X_3$ is V or S; and $X_4$ is R or G.

**[0018]** In some examples, the VL comprises the sequence set forth in SEQ ID NO: 439, wherein $X_1$ is Q or E; $X_2$ is I or V; $X_3$ is G, K, R or Q; $X_4$ is I or L and the VH comprises the sequence set forth in SEQ ID NO: 62, wherein $X_1$ is I or V; $X_2$ is D or E; $X_3$ is V or S; and $X_4$ is R or G.

**[0019]** In some examples, the VL and the VH comprise amino acid sequences having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to the amino acid sequences selected from:

(a) SEQ ID Nos: 59 and 53, respectively;
(b) SEQ ID Nos: 60 and 53, respectively;
(c) SEQ ID Nos: 61 and 53, respectively;
(d) SEQ ID Nos: 59 and 54, respectively;
(e) SEQ ID Nos: 60 and 54, respectively;
(f) SEQ ID Nos: 61 and 54, respectively;
(g) SEQ ID Nos: 59 and 55, respectively;
(h) SEQ ID Nos: 60 and 55, respectively;
(i) SEQ ID Nos: 61 and 55, respectively;
(j) SEQ ID Nos: 59 and 56, respectively;
(k) SEQ ID Nos: 60 and 56, respectively;
(l) SEQ ID Nos: 61 and 56, respectively;
(m) SEQ ID Nos: 59 and 57, respectively;

(n) SEQ ID Nos: 60 and 57, respectively;

(o) SEQ ID Nos: 61 and 57, respectively; and

(p) SEQ ID Nos: 59 and 440, respectively.

**[0020]** In some examples, the VL and the VH comprise the amino acid sequences selected from:

(a) SEQ ID Nos: 59 and 53, respectively;

(b) SEQ ID Nos: 60 and 53, respectively;

(c) SEQ ID Nos: 61 and 53, respectively;

(d) SEQ ID Nos: 59 and 54, respectively;

(e) SEQ ID Nos: 60 and 54, respectively;

(f) SEQ ID Nos: 61 and 54, respectively;

(g) SEQ ID Nos: 59 and 55, respectively;

(h) SEQ ID Nos: 60 and 55, respectively;

(i) SEQ ID Nos: 61 and 55, respectively;

(j) SEQ ID Nos: 59 and 56, respectively;

(k) SEQ ID Nos: 60 and 56, respectively;

(l) SEQ ID Nos: 61 and 56, respectively;

(m) SEQ ID Nos: 59 and 57, respectively;

(n) SEQ ID Nos: 60 and 57, respectively;

(o) SEQ ID Nos: 61 and 57, respectively; and

(p) SEQ ID Nos: 59 and 440, respectively.

**[0021]** In some examples, the VL and the VH comprise the amino acid sequences of SEQ ID Nos: 59 and 53, respectively.

**[0022]** In some examples, the VL and the VH comprise the amino acid sequences of SEQ ID Nos: 59 and 440, respectively.

**[0023]** In some examples, the VL and the VH comprise amino acid sequences having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to the amino acid sequences selected from:

(a) SEQ ID Nos: 69 and 63, respectively;

(b) SEQ ID Nos: 69 and 64, respectively;

(c) SEQ ID Nos: 69 and 65, respectively;

(d) SEQ ID Nos: 69 and 66, respectively;

(e) SEQ ID Nos: 69 and 67, respectively; and

(f) SEQ ID Nos: 432 and 431, respectively.

**[0024]** In some examples, the VL and the VH comprise the amino acid sequences selected from:

(a) SEQ ID Nos: 69 and 63, respectively;

(b) SEQ ID Nos: 69 and 64, respectively;

(c) SEQ ID Nos: 69 and 65, respectively;

(d) SEQ ID Nos: 69 and 66, respectively;

(e) SEQ ID Nos: 69 and 67, respectively; and

(f) SEQ ID Nos: 432 and 431, respectively.

**[0025]** In some examples, the VL and the VH comprise the amino acid sequences of SEQ ID Nos: 69 and 63, respectively.

**[0026]** In some examples, the VL and the VH comprise the amino acid sequences of SEQ ID Nos: 432 and 431, respectively.

**[0027]** In some examples, the VL and the VH comprise amino acid sequences having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to the amino acid sequences selected from:

(a) SEQ ID Nos: 69 and 63, respectively;

(b) SEQ ID Nos: 69 and 64, respectively;

(c) SEQ ID Nos: 69 and 65, respectively;

(d) SEQ ID Nos: 69 and 66, respectively;

(e) SEQ ID Nos: 69 and 67, respectively;

(f) SEQ ID Nos: 69 and 324, respectively;

(g) SEQ ID Nos: 69 and 63, respectively, wherein the VH comprises a V2I substitution;

(h) SEQ ID Nos: 69 and 63, respectively, wherein the VH comprises a D73E substitution;

(i) SEQ ID Nos: 69 and 63, respectively, wherein the VH comprises a V93S substitution;

(j) SEQ ID Nos: 69 and 63, respectively, wherein the VH comprises a V2I substitution and an R44G substitution;

(k) SEQ ID Nos: 69 and 63, respectively, wherein the VH comprises an R44G substitution and a D73E substitution;

(l) SEQ ID Nos: 69 and 63, respectively, wherein the VH comprises an R44G substitution and a V93S substitution;

(m) SEQ ID Nos: 324 and 63, respectively wherein the VL comprises a Q17E substitution;

(n) SEQ ID Nos: 324 and 63, respectively, wherein the VL comprises an I2V substitution;

(o) SEQ ID Nos: 324 and 63, respectively, wherein the VL comprises an G34K substitution;

(p) SEQ ID Nos: 324 and 63, respectively, wherein the VL comprises an G34R substitution;

(r) SEQ ID Nos: 324 and 63, respectively, wherein the VL comprises an I106L substitution; and

(t) SEQ ID Nos: 432 and 433, respectively.

**[0028]** In some examples, the VL and the VH comprise the amino acid sequences selected from:

(a) SEQ ID Nos: 69 and 63, respectively;

(b) SEQ ID Nos: 69 and 64, respectively;

(c) SEQ ID Nos: 69 and 65, respectively;

(d) SEQ ID Nos: 69 and 66, respectively; and

(e) SEQ ID Nos: 69 and 67, respectively;

(f) SEQ ID Nos: 69 and 324, respectively;

(g ) SEQ ID Nos: 69 and 63, respectively, wherein the VH comprises a V2I substitution;

(h) SEQ ID Nos: 69 and 63, respectively, wherein the VH comprises a D73E substitution;

(i) SEQ ID Nos: 69 and 63, respectively, wherein the VH comprises a V93S substitution;

(j) SEQ ID Nos: 69 and 63, respectively, wherein the VH comprises a V2I substitution and an R44G substitution;

(k) SEQ ID Nos: 69 and 63, respectively, wherein the VH comprises an R44G substitution and a D73E substitution;

(l) SEQ ID Nos: 69 and 63, respectively, wherein the VH comprises an R44G substitution and a V93S substitution;

(m) SEQ ID Nos: 324 and 63, respectively wherein the VL comprises a Q17E substitution;

(n) SEQ ID Nos: 324 and 63, respectively, wherein the VL comprises an I2V substitution;

(o) SEQ ID Nos: 324 and 63, respectively, wherein the VL comprises an G34K substitution;

(p) SEQ ID Nos: 324 and 63, respectively, wherein the VL comprises an G34R substitution;

(r) SEQ ID Nos: 324 and 63, respectively, wherein the VL comprises an I106L substitution; and

(t) SEQ ID Nos: 432 and 433, respectively.

**[0029]** In some examples, the VL and the VH comprise amino acid sequences having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to the amino acid sequences selected from:

(a) SEQ ID Nos: 75 and 70, respectively;

(b) SEQ ID Nos: 75 and 71, respectively;

(c) SEQ ID Nos: 75 and 72, respectively;

(d) SEQ ID Nos: 75 and 73, respectively; and

(e) SEQ ID Nos: 75 and 74, respectively.

**[0030]** In some examples, the VL and the VH comprise the amino acid sequences selected from:

(a) SEQ ID Nos: 75 and 70, respectively;

(b) SEQ ID Nos: 75 and 71, respectively;

(c) SEQ ID Nos: 75 and 72, respectively;

(d) SEQ ID Nos: 75 and 73, respectively; and

(e) SEQ ID Nos: 75 and 74, respectively.

**[0031]** In some examples, the VL and the VH comprise the amino acid sequences of SEQ ID Nos: 75 and 70, respectively.

**[0032]** In some examples, the VL and the VH comprise amino acid sequences having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to the amino acid sequences selected from:

(a) SEQ ID Nos: 79 and 76, respectively;

(b) SEQ ID Nos: 80 and 76, respectively;

(c) SEQ ID Nos: 81 and 76, respectively;

(d) SEQ ID Nos: 82 and 76, respectively;

(e) SEQ ID Nos: 83 and 76, respectively;

(f) SEQ ID Nos: 79 and 77, respectively;

(g) SEQ ID Nos: 80 and 77, respectively;

(h) SEQ ID Nos: 81 and 77, respectively;

(i) SEQ ID Nos: 82 and 77, respectively;

(j) SEQ ID Nos: 83 and 77, respectively;

(k) SEQ ID Nos: 79 and 78, respectively;

(l) SEQ ID Nos: 80 and 78, respectively;

(m) SEQ ID Nos: 81 and 78, respectively;

(n) SEQ ID Nos: 82 and 78, respectively; and

(o) SEQ ID Nos: 83 and 78, respectively.

**[0033]** In some examples, the VL and the VH comprise the amino acid sequences selected from:

(a) SEQ ID Nos: 79 and 76, respectively;

(b) SEQ ID Nos: 80 and 76, respectively;

(c) SEQ ID Nos: 81 and 76, respectively;

(d) SEQ ID Nos: 82 and 76, respectively;

(e) SEQ ID Nos: 83 and 76, respectively;

(f) SEQ ID Nos: 79 and 77, respectively;

(g) SEQ ID Nos: 80 and 77, respectively;

(h) SEQ ID Nos: 81 and 77, respectively;

(i) SEQ ID Nos: 82 and 77, respectively;

(j) SEQ ID Nos: 83 and 77, respectively;

(k) SEQ ID Nos: 79 and 78, respectively;

(l) SEQ ID Nos: 80 and 78, respectively;

(m) SEQ ID Nos: 81 and 78, respectively;

(n) SEQ ID Nos: 82 and 78, respectively; and

(o) SEQ ID Nos: 83 and 78, respectively.

**[0034]** In some examples, the VL and the VH comprise the amino acid sequences of SEQ ID Nos: 79 and 76, respectively.

**[0035]** In some examples, the VL and the VH comprise amino acid sequences having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to the amino acid sequences selected from:

(a) SEQ ID Nos: 88 and 84, respectively;

(b) SEQ ID Nos: 89 and 84, respectively;

(c) SEQ ID Nos: 88 and 85, respectively;

(d) SEQ ID Nos: 89 and 85, respectively;

(e) SEQ ID Nos: 88 and 86, respectively;

(f) SEQ ID Nos: 89 and 86, respectively;

(g) SEQ ID Nos: 88 and 87, respectively; and

(h) SEQ ID Nos: 89 and 87, respectively.

**[0036]** In some examples, the VL and the VH comprise the amino acid sequences selected from:

(a) SEQ ID Nos: 88 and 84, respectively;

(b) SEQ ID Nos: 89 and 84, respectively;

(c) SEQ ID Nos: 88 and 85, respectively;

(d) SEQ ID Nos: 89 and 85, respectively;

(e) SEQ ID Nos: 88 and 86, respectively;

(f) SEQ ID Nos: 89 and 86, respectively;

(g) SEQ ID Nos: 88 and 87, respectively; and

(h) SEQ ID Nos: 89 and 87, respectively.

**[0037]** In some examples, the VL and the VH comprise amino acid sequences having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to the amino acid sequences selected from:

(a) SEQ ID NOS: 305 and 303, respectively;

(b) SEQ ID NOS: 308 and 303, respectively;

(c) SEQ ID Nos: 306 and 303, respectively; and

(d) SEQ ID Nos: 305 and 304, respectively.

**[0038]** In some examples, the VL and the VH comprise amino acid sequences selected from:

(e) SEQ ID NOS: 305 and 303, respectively;

(f) SEQ ID NOS: 308 and 303, respectively;

(g) SEQ ID Nos: 306 and 303, respectively; and

(h) SEQ ID Nos: 305 and 304, respectively.

**[0039]** In some examples, the VL and the VH comprise amino acid sequences having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to the amino acid sequences selected from:

(a) SEQ ID Nos: 435 and 436, respectively; and

(b) SEQ ID Nos: 437 and 438, respectively.

**[0040]** In some examples, the VL and the VH comprise the amino acid sequences selected from:

(a) SEQ ID Nos: 435 and 436, respectively; and

(b) SEQ ID Nos: 437 and 438, respectively.

**[0041]** In some examples, the antibody or antigen binding fragment thereof further comprises a heavy chain constant region. In some examples, the heavy chain constant region is an IgG constant region. In some examples, the IgG constant region is a wild-type IgG constant region. In some examples, the IgG constant region comprises at least one mutation relative to a wild-type IgG constant region. In some examples, the IgG constant region is an IgG1, IgG2, IgG3, or IgG4 constant region. In some examples, the IgG constant region is an IgG1 constant region. In some examples, the IgG1 constant region is a wild-type human IgG1 constant region. In some examples, the IgG1 constant region comprises at least one amino acid substitution relative to a wild-type human IgG1 constant region.

**[0042]** In some examples, the IgG1 constant region comprises at least one amino acid substitution selected from: L234A, L235A, M428L, N434S, and any combination thereof, relative to a wild-type human IgG1 constant region, according to EU numbering.

**[0043]** In some examples, the IgG1 constant region comprises at least one amino acid substitution selected from: L234A, L235A, L235E, H268Q, V309L, A330S, P331S, and any combination thereof, relative to a wild-type human IgG1 constant region, according to EU numbering.

**[0044]** In some examples, the IgG1 constant region comprises at least one amino acid substitution selected from: M252Y, S264T, T256E, M428L, N434S, and any combination thereof, relative to a wild-type human IgG1 constant region, according to EU numbering.

**[0045]** In some examples, the IgG1 constant region comprises an N297A, N297Q or N297G amino acid substitution relative to a wild-type human IgG1 constant region, according to EU numbering.

**[0046]** In some examples, the IgG1 constant region comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to an amino acid sequence selected from SEQ ID Nos: 90-94. In some examples, the IgG1 constant region comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to SEQ ID NO: 93.

**[0047]** In some examples, the IgG2 constant region is a wild-type human IgG2 constant region.

**[0048]** In some examples, the IgG2 constant region comprises at least one amino acid substitution selected from: H268Q, V309L, A330S, P331S, V234A, G237A, P238S, H268A, and any combination thereof, relative to a wild-type human IgG2 constant region, according to EU numbering.

**[0049]** In some examples, the IgG2 constant region comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID No: 95.

**[0050]** In some examples, the IgG3 constant region is a wild-type human IgG3 constant region.

**[0051]** In some examples, the IgG3 constant region comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID No: 96.

**[0052]** In some examples, the IgG4 constant region is a wild-type human IgG4 constant region.

**[0053]** In some examples, the IgG4 constant region comprises an F234A and/or an L235A amino acid substitution relative to a wild-type human IgG4 constant region, according to EU numbering.

**[0054]** In some examples, the IgG4 constant region comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID No: 97.

**[0055]** In some examples, the antibody or antigen binding fragment comprises a light chain constant region. In some examples, the light chain constant region is a kappa light chain or a lambda light chain. In some examples, the kappa light chain comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID No: 98. In some examples, the lambda light chain comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID No: 99.

**[0056]** In some examples, the antibody or antigen binding fragment comprises a heavy chain sequence and a light chain sequence comprising amino acid sequences having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequences selected from:

(a) SEQ ID Nos: 106 and 107, respectively;

(b) SEQ ID Nos: 108 and 109, respectively;

(c) SEQ ID Nos; 110 and 111, respectively;

(d) SEQ ID Nos: 112 and 113, respectively;

(e) SEQ ID Nos: 328 and 329, respectively;

(f) SEQ ID Nos: 297 and 332, respectively; and

(g) SEQ ID Nos: 442 and 109, respectively.

**[0057]** In some examples, the antibody or antigen binding fragment comprises a heavy chain sequence and a light chain sequence comprising the amino acid sequences selected from:

(a) SEQ ID Nos: 106 and 107, respectively;

(b) SEQ ID Nos: 108 and 109, respectively;

(c) SEQ ID Nos; 110 and 111, respectively;

(d) SEQ ID Nos: 112 and 113, respectively;

e) SEQ ID Nos: 328 and 329, respectively;

(f) SEQ ID Nos: 297 and 332, respectively; and

(g) SEQ ID Nos: 442 and 109, respectively.

**[0058]** In some examples, the antibody or antigen binding fragment comprises a heavy chain sequence and a light chain sequence comprising amino acid sequences having at least 90%,

91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequences selected from:

(a) SEQ ID Nos: 328 and 329, respectively;

(b) SEQ ID Nos: 297 and 332, respectively; and

(c) SEQ ID Nos: 442 and 109, respectively.

**[0059]** In some examples, the antibody or antigen binding fragment comprises a heavy chain sequence and a light chain sequence comprising the amino acid sequences selected from:

(a) SEQ ID Nos: 328 and 329, respectively;

(b) SEQ ID Nos: 297 and 332, respectively; and

(c) SEQ ID Nos: 442 and 109, respectively.

**[0060]** In some examples, the antibody or antigen binding fragment specifically binds the serine protease domain of C2.

**[0061]** In another example, the disclosure provides an antibody or antigen binding fragment thereof, that specifically binds the serine protease domain of C2.

**[0062]** In another example, the present disclosure provides a conjugate comprising (i) the antibody or antigen binding fragment herein disclosed, and (ii) at least one regulator of complement activation (RCA) polypeptide.

**[0063]** In another example, the present disclosure provides a conjugate comprising (i) an antibody or antigen binding fragment that specifically binds C2, and (ii) at least one RCA polypeptide.

**[0064]** In another example, the present disclosure provides a conjugate comprising (i) a means for binding C2, and (ii) at least one RCA polypeptide.

**[0065]** In some examples, the at least one RCA polypeptide comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence selected from SEQ ID Nos: 114-122, SEQ ID Nos: 240-250, and SEQ ID No. 446.

**[0066]** In some examples, the at least one RCA polypeptide comprises an amino acid sequence selected from SEQ ID Nos: 114-122, SEQ ID Nos: 240-250, and SEQ ID No.446.

**[0067]** In some examples, the antibody or antigen binding fragment, or the means for binding C2, is conjugated to the at least one RCA polypeptide via a linker. In some examples, the at least one RCA polypeptide is selected from SEQ ID Nos: 114, 116, 121, 122, 241, 250, and 446.

**[0068]** In some examples, the linker is a peptide linker. In some examples, the peptide linker is a GlySer linker. In some examples, the GlySer linker is a $(G_4S)_n$ linker, wherein n is 1-10, optionally wherein n is 1-5. In some examples, the GlySer linker comprises an amino acid sequence selected from SEQ ID Nos: 123-125, 252, 256, 258, 259, 261, 263, 265, 266, 269, 271, 272, 274, 276, 278, 279, 280, 282, 284, 285, 286, 287, 288, 289, and 290. In some examples, the peptide linker is a Gly linker. In some examples, the Gly linker comprises an amino acid sequence selected from SEQ ID Nos: 251, 253, 255, 257, 260, 262, 264, 268, 270, 273, 275, 277, 281, 283, and 291-296. In some examples, the conjugate comprises two or more RCA polypeptides. In some examples, the conjugate comprises two RCA polypeptides that are the same. In some examples, the two or more RCA polypeptides are the same. In some examples, the two or more RCA polypeptides are different.

**[0069]** In some examples, the two or more RCA polypeptides are linked to each other via a linker. In some examples, the linker is a peptide linker. In some examples, the peptide linker is a GlySer linker. In some examples, the GlySer linker is a $(G_4S)_n$ linker, wherein n is 1-10, optionally wherein n is 1-5. In some examples, the linker is a GlySer linker comprises an amino acid sequence selected from SEQ ID Nos: 123-125, 252, 256, 258, 259, 261, 263, 265, 266, 269, 271, 272, 274, 276, 278, 279, 280, 282, 284, 285, 286, 287, 288, 289, and 290. In some examples, the peptide linker is a Gly linker. In some examples, the Gly linker comprises an amino acid sequence selected from SEQ ID Nos: 251, 253, 255, 257, 260, 262, 264, 268, 270, 273, 275, 277, 281, 283, and 291-296. In some examples, the two or more RCA polypeptides independently comprise SEQ ID Nos: 121 and 122. In some examples, the two or more RCA polypeptides independently comprise SEQ ID Nos: 114 and 116. In some examples, the two or more RCA polypeptides independently comprise SEQ ID Nos: 121 and 116. In some examples, the two or more RCA polypeptides each comprise SEQ ID Nos: 121. In some examples, the two or more RCA polypeptides independently comprise SEQ ID Nos: 122 and 116. In some examples, the two or more RCA polypeptides independently comprise SEQ ID Nos: 114 and 241. In some examples, the two or more RCA polypeptides independently comprise SEQ ID Nos: 250 and 241. In some examples, the at least one RCA polypeptide is conjugated to a heavy chain of the antibody or the means for binding C2. In some examples, the at least one RCA polypeptide is conjugated to a light chain of the antibody or the means for binding C2.

**[0070]** In some examples, the present disclosure provides a conjugate comprising the formula of: ANTIBODY-$(LINKER1_{X1}$-RCA1$)_n$-$LINKER2_{X2}$-RCA2,

wherein “ANTIBODY” is an antibody or antigen binding fragment described herein, or an antibody or antigen binding fragment thereof that specifically binds C2;
wherein “LINKER1” and “LINKER2” are each independently a peptide linker;
wherein “RCA1” and “RCA2” are each independently an RCA polypeptide; and
wherein "n" is 0-5, X1 is 0 or 1 and X2 is 0 or 1.

**[0071]** In some examples, RCA1 and RCA2 are each independently selected from SEQ ID Nos: 114-122, SEQ ID Nos: 240-250, and SEQ ID No: 446. In some examples, RCA1 and RCA2 are each a complement receptor 1 (CR1) polypeptide, such as CR1.8-10. In some examples, RCA1 and RCA2 each comprises SEQ ID Nos: 121. In some examples, RCA1 or RCA2 comprises SEQ ID NO: 114. In some examples, RCA1 or RCA2 comprises SEQ ID NO: 250. In some examples, RCA1 or RCA2 comprises SEQ ID NO: 241. In some examples, RCA1 comprises SEQ ID NO: 114 and RCA2 comprises SEQ ID NO: 241. In some examples, RCA1 comprises SEQ ID NO: 241 and RCA2 comprises SEQ ID NO: 250. In some examples, RCA1 comprises SEQ ID NO: 250 and RCA2 comprises SEQ ID NO: 241. In some examples, RCA1 comprises SEQ ID NO: 241 and RCA2 is absent. In some examples, RCA1 comprises SEQ ID NO: 434 and RCA2 is absent.

**[0072]** In some examples, LINKER1 and LINKER2 are each a GlySer linker. In some examples, LINKER1 and LINKER2 are each independently a $(G_4S)_n$ linker, wherein n is 1-10, optionally wherein n is 1-5. In some examples, LINKER1 and LINKER2 are each independently selected from SEQ ID Nos: 123-125, 252, 256, 258, 259, 261, 263, 265, 266, 269, 271, 272, 274, 276, 278, 279, 280, 282, 284, 285, 286, 287, 288, 289, and 290.

**[0073]** In some examples, LINKER1 and LINKER2 are each a Gly linker.

**[0074]** In some examples, each Gly linker comprises an amino acid sequence selected from SEQ ID Nos: 251, 253, 255, 257, 260, 262, 264, 268, 270, 273, 275, 277, 281, 283, or 291-296.

**[0075]** In some examples, $(LINKER1_{X1}\text{-}RCA1)_n\text{-}LINKER2_{X2}\text{-}RCA2$ comprises an amino acid sequence as set forth in SEQ ID NO: 441 or as set forth in SEQ ID No: 4345, and wherein n is 1.

**[0076]** In some examples, the “ANTIBODY” specifically binds the serine protease domain of C2. In some examples, the “ANTIBODY” comprises CDRL1 of SEQ ID NO: 43 (RASQDINSYLS), the CDRL2 of SEQ ID NO: 45 (RANRLVD), the CDRL3 of SEQ ID NO: 3 (LQYDEFPFT), the CDRH1 of SEQ ID NO: 46 (GYTFTGYWIE), the CDRH2 of SEQ ID NO: 47

(EILPRSGSTN), and the CDRH3 of SEQ ID NO: 48 (SGGSNSYYYALGY). In some examples, the "ANTIBODY" comprises a VH as set forth in SEQ ID NO: 53 and a VL as set forth in SEQ ID NO: 59. In some examples, the "ANTIBODY" comprises a LC set forth in SEQ ID NO: 108 and a HC as set forth in SEQ ID NO: 109.

**[0077]** In some examples, the "ANTIBODY" specifically binds the serine protease domain of C2. In some examples, the "ANTIBODY" comprises CDRL1 of SEQ ID NO: 43 (RASQDINSYLS), the CDRL2 of SEQ ID NO: 45 (RANRLVD), the CDRL3 of SEQ ID NO: 3 (LQYDEFPFT), the CDRH1 of SEQ ID NO: 46 (GYTFTGYWIE), the CDRH2 of SEQ ID NO: 47 (EILPRSGSTN), and the CDRH3 of SEQ ID NO: 320 (SGGSSSYYYALGY). In some examples, the "ANTIBODY" comprises a VH as set forth in SEQ ID NO: 322 and a VL as set forth in SEQ ID NO: 59. In some examples, the "ANTIBODY" comprises a LC set forth in SEQ ID NO: 109 and a HC as set forth in SEQ ID NO: 321.

**[0078]** In some examples, the "ANTIBODY" specifically binds the serine protease domain of C2. In some examples, the "ANTIBODY" comprises CDRL1 of SEQ ID NO: 327, the CDRL2 of SEQ ID NO: 8, the CDRL3 of SEQ ID NO: 9, the CDRH1 of SEQ ID NO: 10, the CDRH2 of SEQ ID NO: 11, and the CDRH3 of SEQ ID NO: 12. In some examples, the "ANTIBODY" comprises a VH as set forth in SEQ ID NO: 324 and a VL as set forth in SEQ ID NO: 325. In some examples, the "ANTIBODY" comprises a LC set forth in SEQ ID NO: 329 and a HC as set forth in SEQ ID NO: 328.

**[0079]** In some examples, the "ANTIBODY" specifically binds the serine protease domain of C2. In some examples, the "ANTIBODY" comprises CDRL1 of SEQ ID NO: 50, the CDRL2 of SEQ ID NO: 38, the CDRL3 of SEQ ID NO: 39, the CDRH1 of SEQ ID NO: 40, the CDRH2 of SEQ ID NO: 41, and the CDRH3 of SEQ ID NO: 42. In some examples, the "ANTIBODY" comprises a VH as set forth in SEQ ID NO: 330 and a VL as set forth in SEQ ID NO: 331. In some examples, the "ANTIBODY" comprises a LC set forth in SEQ ID NO: 298 and a HC as set forth in SEQ ID NO: 297.

**[0080]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence selected from SEQ ID Nos: 126-136, and a light chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequence of SEQ ID NO: 107.

**[0081]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising an amino acid sequence selected from SEQ ID Nos: 126-136, and a light chain comprising the amino acid sequence of SEQ ID NO: 107.

**[0082]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequence of SEQ ID NO: 106, and a light chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence selected from SEQ ID Nos: 137-138.

**[0083]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 106, and a light chain comprising an amino acid sequence selected from SEQ ID Nos: 137-138.

**[0084]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence selected from SEQ ID Nos: 139-149, 326, 335, 336, 338, 340, 341, 343-346, 348-356, 358-368, 369-370, 372-380, 383, and 441 and a light chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequence of SEQ ID NO: 109.

**[0085]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising an amino acid having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence of SEQ ID No: 149, and a light chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence of SEQ ID No: 109.

**[0086]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising an amino acid having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence of SEQ ID No: 326, and a light chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence of SEQ ID No: 109.

**[0087]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising an amino acid having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence of SEQ ID No: 394, and a light chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence of SEQ ID No: 329.

**[0088]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising an amino acid having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence of SEQ ID No: 415 and a light chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence of SEQ ID No: 329.

**[0089]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising an amino acid having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence of SEQ ID No: 319, and a light chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence of SEQ ID No: 332.

**[0090]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising an amino acid having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence of SEQ ID No: 418, and a light chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence of SEQ ID No: 332.

**[0091]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising an amino acid having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence of SEQ ID Nos: 419, and a light chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence of SEQ ID No: 332.

**[0092]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising an amino acid sequence selected from SEQ ID Nos: 139-149 and 326, and a light chain comprising the amino acid sequence of SEQ ID NO: 109.

**[0093]** In another example, the present disclosure provides a conjugate comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequence of SEQ ID NO: 108, and a light chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence selected from SEQ ID Nos: 150-154, 337, 339, 342, 357, 371, 381, 382, 384, and 385.

**[0094]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 108, and a light chain comprising an amino acid sequence selected from SEQ ID Nos: 150-154, 337, 339, 342, 357, 371, 381, 382, 384, and 385.

**[0095]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence selected from SEQ ID Nos: 156-165, and a light chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequence of SEQ ID No: 113.

**[0096]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising an amino acid sequence selected from SEQ ID Nos: 156-165, and a light chain comprising the amino acid sequence of SEQ ID NO: 113.

**[0097]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequence of SEQ ID NO: 155, and a light chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequence of SEQ ID NO: 111.

**[0098]** In another example, the present disclosure provides a conjugate comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 155, and a light chain comprising the amino acid sequence of SEQ ID NO: 111.

**[0099]** In some examples, the present disclosure provides a conjugate comprising a heavy chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to an amino acid sequence selected from SEQ ID Nos: 391-415, and a light chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequence of SEQ ID NO: 329.

**[0100]** In some examples, the present disclosure provides a conjugate comprising an amino acid sequence selected from SEQ ID Nos: 391-415, and a light chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequence of SEQ ID NO: 329.

**[0101]** In another example, the present disclosure provides a conjugate comprising a heavy chain and a light chain comprising amino acid sequences having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequences selected from:

(a) SEQ ID Nos: 126 and 107, respectively;

(b) SEQ ID Nos: 127 and 107, respectively;

(c) SEQ ID Nos: 128 and 107, respectively;

(d) SEQ ID Nos: 129 and 107, respectively;

(e) SEQ ID Nos: 130 and 107, respectively;

(f) SEQ ID Nos: 131 and 107, respectively;

(g) SEQ ID Nos: 132 and 107, respectively;

(h) SEQ ID Nos: 133 and 107, respectively;

(i) SEQ ID Nos: 134 and 107, respectively;

(j) SEQ ID Nos: 135 and 107, respectively;

(k) SEQ ID Nos: 106 and 137, respectively;

(l) SEQ ID Nos: 106 and 138, respectively; and

(m) SEQ ID Nos: 136 and 107, respectively.

**[0102]** In another example, the present disclosure provides a conjugate comprising a heavy chain and a light chain comprising the amino acid sequences selected from:

(a) SEQ ID Nos: 126 and 107, respectively;

(b) SEQ ID Nos: 127 and 107, respectively;

(c) SEQ ID Nos: 128 and 107, respectively;

(d) SEQ ID Nos: 129 and 107, respectively;

(e) SEQ ID Nos: 130 and 107, respectively;

(f) SEQ ID Nos: 131 and 107, respectively;

(g) SEQ ID Nos: 132 and 107, respectively;

(h) SEQ ID Nos: 133 and 107, respectively;

(i) SEQ ID Nos: 134 and 107, respectively;

(j) SEQ ID Nos: 135 and 107, respectively;

(k) SEQ ID Nos: 106 and 137, respectively;

(l) SEQ ID Nos: 106 and 138, respectively; and

(m) SEQ ID Nos: 136 and 107, respectively.

**[0103]** In another example, the present disclosure provides a conjugate comprising a heavy chain and a light chain comprising amino acid sequences having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequences selected from:

(a) SEQ ID Nos: 139 and 109, respectively;

(b) SEQ ID Nos: 140 and 108, respectively;

(c) SEQ ID Nos: 141 and 109, respectively;

(d) SEQ ID Nos: 142 and 109, respectively;

(e) SEQ ID Nos: 143 and 109, respectively;

(f) SEQ ID Nos: 144 and 109, respectively;

(g) SEQ ID Nos: 145 and 109, respectively;

(h) SEQ ID Nos: 146 and 109, respectively;

(i) SEQ ID Nos: 147 and 109, respectively;

(j) SEQ ID Nos: 148 and 109, respectively;

(k) SEQ ID Nos: 108 and 150, respectively;

(l) SEQ ID Nos: 108 and 151, respectively;

(m) SEQ ID Nos: 108 and 152, respectively;

(n) SEQ ID Nos: 108 and 153, respectively;

(o) SEQ ID Nos: 108 and 154, respectively;

(p) SEQ ID Nos: 149 and 109, respectively;

(q) SEQ ID Nos: 335 and 109, respectively;

(r) SEQ ID Nos: 336 and 109, respectively;

(s) SEQ ID Nos: 337 and 109, respectively;

(t) SEQ ID Nos: 338 and 109, respectively;

(u) SEQ ID Nos: 339 and 109, respectively;

(v) SEQ ID Nos: 340 and 109, respectively;

(w) SEQ ID Nos: 341 and 109, respectively;

(x) SEQ ID Nos: 342 and 109, respectively;

(y) SEQ ID Nos: 343 and 109, respectively; and

(z) SEQ ID Nos: 344 and 109, respectively.

**[0104]** In another example, the present disclosure provides a conjugate comprising a heavy chain and a light chain comprising the amino acid sequences selected from:

(a) SEQ ID Nos: 139 and 109, respectively;

(b) SEQ ID Nos: 140 and 109, respectively;

(c) SEQ ID Nos: 141 and 109, respectively;

(d) SEQ ID Nos: 142 and 109, respectively;

(e) SEQ ID Nos: 143 and 109, respectively;

(f) SEQ ID Nos: 144 and 109, respectively;

(g) SEQ ID Nos: 145 and 109, respectively;

(h) SEQ ID Nos: 146 and 109, respectively;

(i) SEQ ID Nos: 147 and 109, respectively;

(j) SEQ ID Nos: 148 and 109, respectively;

(k) SEQ ID Nos: 108 and 150, respectively;

(l) SEQ ID Nos: 108 and 151, respectively;

(m) SEQ ID Nos: 108 and 152, respectively;

(n) SEQ ID Nos: 108 and 153, respectively;

(o) SEQ ID Nos: 108 and 154, respectively;

(p) SEQ ID Nos: 149 and 109, respectively;

(q) SEQ ID Nos: 335 and 109, respectively;

(r) SEQ ID Nos: 336 and 109, respectively;

(s) SEQ ID Nos: 337 and 109, respectively;

(t) SEQ ID Nos: 338 and 109, respectively;

(u) SEQ ID Nos: 339 and 109, respectively;

(v) SEQ ID Nos: 340 and 109, respectively;

(w) SEQ ID Nos: 341 and 109, respectively;

(x) SEQ ID Nos: 342 and 109, respectively;

(y) SEQ ID Nos: 343 and 109, respectively;

(z) SEQ ID Nos: 344 and 109, respectively.

**[0105]** In another example, the present disclosure provides a conjugate comprising a heavy chain and a light chain comprising amino acid sequences having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequences selected from:

(a) SEQ ID Nos: 345 and 109, respectively;

(b) SEQ ID Nos: 346 and 109, respectively;

(c) SEQ ID Nos: 347 and 109, respectively;

(d) SEQ ID Nos: 348 and 109, respectively;

(e) SEQ ID Nos: 349 and 109, respectively;

(f) SEQ ID Nos: 350 and 109, respectively;

(g) SEQ ID Nos: 351 and 109, respectively;

(h) SEQ ID Nos: 352 and 109, respectively;

(i) SEQ ID Nos: 355 and 109, respectively;

(j) SEQ ID Nos: 360 and 109, respectively;

(k) SEQ ID Nos: 361 and 109, respectively;

(l) SEQ ID Nos: 362 and 109, respectively;

(m) SEQ ID Nos: 365 and 109, respectively;

(n) SEQ ID Nos: 363 and 109, respectively;

(o) SEQ ID Nos: 364 and 109, respectively;

(p) SEQ ID Nos: 377 and 109, respectively;

(q) SEQ ID Nos: 372 and 109, respectively;

(r) SEQ ID Nos: 378 and 109, respectively;

(s) SEQ ID Nos: 353 and 109, respectively;

(t) SEQ ID Nos: 354 and 109, respectively;

(u) SEQ ID Nos: 356 and 109, respectively;

(v) SEQ ID Nos: 357 and 109, respectively;

(w) SEQ ID Nos: 358 and 109, respectively;

(x) SEQ ID Nos: 379 and 109, respectively;

(y) SEQ ID Nos: 359 and 109, respectively;

(z) SEQ ID Nos: 381 and 109, respectively;

(aa) SEQ ID Nos: 382 and 109, respectively;

(ab) SEQ ID Nos: 384 and 109, respectively;

(ac) SEQ ID Nos: 380 and 109, respectively;

(ad) SEQ ID Nos: 385 and 109, respectively;

(ae) SEQ ID Nos: 370 and 109, respectively;

(af) SEQ ID Nos: 371 and 109, respectively;

(ag) SEQ ID Nos: 366 and 109, respectively;

(ah) SEQ ID Nos: 367 and 109, respectively;

(ai) SEQ ID Nos: 368 and 109, respectively;

(aj) SEQ ID Nos: 375 and 109, respectively;

(ak) SEQ ID Nos: 376 and 109, respectively;

(al) SEQ ID Nos: 373 and 109, respectively;

(am) SEQ ID Nos: 374 and 109, respectively;

(an) SEQ ID Nos: 369 and 109, respectively;

(ao) SEQ ID Nos: 383 and 109, respectively; and

(ap) SEQ ID Nos: 326 and 109, respectively.

**[0106]** In another example, the present disclosure provides a conjugate comprising a heavy chain and a light chain comprising amino acid sequences selected from:

(a) SEQ ID Nos: 345 and 109, respectively;

(b) SEQ ID Nos: 346 and 109, respectively;

(c) SEQ ID Nos: 347 and 109, respectively;

(d) SEQ ID Nos: 348 and 109, respectively;

(e) SEQ ID Nos: 349 and 109, respectively;

(f) SEQ ID Nos: 350 and 109, respectively;

(g) SEQ ID Nos: 351 and 109, respectively;

(h) SEQ ID Nos: 352 and 109, respectively;

(i) SEQ ID Nos: 355 and 109, respectively;

(j) SEQ ID Nos: 360 and 109, respectively;

(k) SEQ ID Nos: 361 and 109, respectively;

(l) SEQ ID Nos: 362 and 109, respectively;

(m) SEQ ID Nos: 365 and 109, respectively;

(n) SEQ ID Nos: 363 and 109, respectively;

(o) SEQ ID Nos: 364 and 109, respectively;

(p) SEQ ID Nos: 377 and 109, respectively;

(q) SEQ ID Nos: 372 and 109, respectively;

(r) SEQ ID Nos: 378 and 109, respectively;

(s) SEQ ID Nos: 353 and 109, respectively;

(t) SEQ ID Nos: 354 and 109, respectively;

(u) SEQ ID Nos: 356 and 109, respectively;

(v) SEQ ID Nos: 357 and 109, respectively;

(w) SEQ ID Nos: 358 and 109, respectively;

(x) SEQ ID Nos: 379 and 109, respectively;

(y) SEQ ID Nos: 359 and 109, respectively;

(z) SEQ ID Nos: 381 and 109, respectively;

(aa) SEQ ID Nos: 382 and 109, respectively;

(ab) SEQ ID Nos: 384 and 109, respectively;

(ac) SEQ ID Nos: 380 and 109, respectively;

(ad) SEQ ID Nos: 385 and 109, respectively;

(ae) SEQ ID Nos: 370 and 109, respectively;

(af) SEQ ID Nos: 371 and 109, respectively;

(ag) SEQ ID Nos: 366 and 109, respectively;

(ah) SEQ ID Nos: 367 and 109, respectively;

(ai) SEQ ID Nos: 368 and 109, respectively;

(aj) SEQ ID Nos: 375 and 109, respectively;

(ak) SEQ ID Nos: 376 and 109, respectively;

(al) SEQ ID Nos: 373 and 109, respectively;

(am) SEQ ID Nos: 374 and 109, respectively;

(an) SEQ ID Nos: 369 and 109, respectively;

(ao) SEQ ID Nos: 383 and 109, respectively; and

(ap) SEQ ID Nos: 326 and 109, respectively.

**[0107]** In another example, the present disclosure provides a conjugate comprising a heavy chain and a light chain comprising amino acid sequences having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequences selected from:

(a) SEQ ID Nos: 155 and 111, respectively;

(b) SEQ ID Nos: 156 and 113, respectively;

(c) SEQ ID Nos: 157 and 113, respectively;

(d) SEQ ID Nos: 158 and 113, respectively;

(e) SEQ ID Nos: 159 and 113, respectively;

(f) SEQ ID Nos: 160 and 113, respectively;

(g) SEQ ID Nos: 161 and 113, respectively;

(h) SEQ ID Nos: 162 and 113, respectively;

(i) SEQ ID Nos: 163 and 113, respectively;

(j) SEQ ID Nos: 164 and 113, respectively;

(k) SEQ ID Nos: 165 and 113, respectively;

**[0108]** In another example, the present disclosure provides a conjugate comprising a heavy chain and a light chain comprising the amino acid sequences selected from:

(a) SEQ ID Nos: 155 and 111, respectively;

(b) SEQ ID Nos: 156 and 113, respectively;

(c) SEQ ID Nos: 157 and 113, respectively;

(d) SEQ ID Nos: 158 and 113, respectively;

(e) SEQ ID Nos: 159 and 113, respectively;

(f) SEQ ID Nos: 160 and 113, respectively;

(g) SEQ ID Nos: 161 and 113, respectively;

(h) SEQ ID Nos: 162 and 113, respectively;

(i) SEQ ID Nos: 163 and 113, respectively;

(j) SEQ ID Nos: 164 and 113, respectively; and

(k) SEQ ID Nos: 165 and 113, respectively;

**[0109]** In another example, the present disclosure provides a conjugate comprising a heavy chain and a light chain comprising amino acid sequences having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequences selected from:

(a) SEQ ID Nos: 391 and 329, respectively;

(b) SEQ ID Nos: 392 and 329, respectively;

(c) SEQ ID Nos: 393 and 329, respectively;

(d) SEQ ID Nos: 394 and 329, respectively;

(e) SEQ ID Nos: 395 and 329, respectively;

(f) SEQ ID Nos: 396 and 329, respectively;

(g) SEQ ID Nos: 397 and 329, respectively;

(h) SEQ ID Nos: 398 and 329, respectively;

(i) SEQ ID Nos: 399 and 329, respectively;

(j) SEQ ID Nos: 400 and 329, respectively;

(k) SEQ ID Nos: 401 and 329, respectively;

(l) SEQ ID Nos: 402 and 329, respectively;

(m) SEQ ID Nos: 403 and 329, respectively;

(n) SEQ ID Nos: 404 and 329, respectively;

(o) SEQ ID Nos: 405 and 329, respectively;

(p) SEQ ID Nos: 406 and 329, respectively;

(q) SEQ ID Nos: 407 and 329, respectively;

(r) SEQ ID Nos: 408 and 329, respectively;

(s) SEQ ID Nos: 409 and 329, respectively;

(t) SEQ ID Nos: 410 and 329, respectively;

(u) SEQ ID Nos: 411 and 329, respectively;

(v) SEQ ID Nos: 412 and 329, respectively;

(w) SEQ ID Nos: 413 and 329, respectively;

(x) SEQ ID Nos: 414 and 329, respectively; and

(y) SEQ ID Nos: 415 and 329, respectively;

**[0110]** In another example, the present disclosure provides a conjugate comprising a heavy chain and a light chain comprising the amino acid sequences selected from:

(a) SEQ ID Nos: 391 and 329, respectively;

(b) SEQ ID Nos: 392 and 329, respectively;

(c) SEQ ID Nos: 393 and 329, respectively;

(d) SEQ ID Nos: 394 and 329, respectively;

(e) SEQ ID Nos: 395 and 329, respectively;

(f) SEQ ID Nos: 396 and 329, respectively;

(g) SEQ ID Nos: 397 and 329, respectively;

(h) SEQ ID Nos: 398 and 329, respectively;

(i) SEQ ID Nos: 399 and 329, respectively;

(j) SEQ ID Nos: 400 and 329, respectively;

(k) SEQ ID Nos: 401 and 329, respectively;

(l) SEQ ID Nos: 402 and 329, respectively;

(m) SEQ ID Nos: 403 and 329, respectively;

(n) SEQ ID Nos: 404 and 329, respectively;

(o) SEQ ID Nos: 405 and 329, respectively;

(p) SEQ ID Nos: 406 and 329, respectively;

(q) SEQ ID Nos: 407 and 329, respectively;

(r) SEQ ID Nos: 408 and 329, respectively;

(s) SEQ ID Nos: 409 and 329, respectively;

(t) SEQ ID Nos: 410 and 329, respectively;

(u) SEQ ID Nos: 411 and 329, respectively;

(v) SEQ ID Nos: 412 and 329, respectively;

(w) SEQ ID Nos: 413 and 329, respectively;

(x) SEQ ID Nos: 414 and 329, respectively; and

(y) SEQ ID Nos: 415 and 329, respectively;

**[0111]** In another example, the present disclosure provides a conjugate comprising a heavy chain and a light chain comprising amino acid sequences having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequences selected from:

(a) SEQ ID Nos: 319 and 298, respectively;

(b) SEQ ID Nos: 418 and 298, respectively;

(c) SEQ ID Nos: 427 and 298, respectively;

(d) SEQ ID Nos: 417 and 298, respectively;

(e) SEQ ID Nos: 419 and 298, respectively;

(f) SEQ ID Nos: 416 and 298, respectively; and

(g) SEQ ID Nos: 318 and 301, respectively.

**[0112]** In another example, the present disclosure provides a conjugate comprising a heavy chain and a light chain comprising amino acid sequences selected from:

(a) SEQ ID Nos: 319 and 298, respectively;

(b) SEQ ID Nos: 418 and 298, respectively;

(c) SEQ ID Nos: 427 and 298, respectively;

(d) SEQ ID Nos: 417 and 298, respectively;

(e) SEQ ID Nos: 419 and 298, respectively;

(f) SEQ ID Nos: 416 and 298, respectively; and

(g) SEQ ID Nos: 318 and 301, respectively.

**[0113]** In another example, the present disclosure provides a composition comprising an antibody or antigen binding fragment herein disclosed.

**[0114]** In another example, the present disclosure provides a composition comprising a conjugate herein disclosed.

**[0115]** In some examples, the composition comprises a pharmaceutically acceptable carrier.

**[0116]** In another example, the present disclosure provides a nucleic acid comprising a nucleotide sequence encoding the VL, the VH, the heavy chain, the light chain, or any combination thereof, of an antibody or antigen binding fragment herein disclosed.

**[0117]** In another example, the present disclosure provides a nucleic acid comprising a nucleotide sequence encoding a conjugate herein disclosed.

**[0118]** In another example, the present disclosure provides an expression vector comprising a nucleic acid herein disclosed.

**[0119]** In another example, the present disclosure provides a cell comprising an expression vector herein disclosed.

**[0120]** In another example, the present disclosure provides a method for producing an antibody or antigen binding fragment or a conjugate described herein, the method comprising

maintaining a cell described herein under conditions permitting expression of the antibody or antigen binding fragment, or the conjugate.

**[0121]** In another example, the present disclosure provides a method for treating a complement-associated disease or disorder in a subject, comprising administering to the subject an antibody or antigen binding fragment, a conjugate, or composition described herein.

**[0122]** In another example, the complement-associated disease or disorder is selected from amyotrophic lateral sclerosis (ALS), antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, atypical hemolytic uremic syndrome (aHUS), aHUS after kidney transplant, autoimmune encephalitis, bullous pemphigoid, C3 glomerulopathy (C3G), C3 glomerulonephritis (C3GN), C3G relapse after kidney transplant, cold agglutinin disease (CAD), CD59 deficiency, CD59-mediated hemolytic anemia with or without immune-mediated polyneuropathy, CHAPLE syndrome (CD55 deficiency), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), complement Factor I deficiency, diabetic nephropathy, cryoglobulinemia, dense deposit disease, diabetic lumbosacral plexopathy, age-related macular degeneration (AMD), glaucoma, dry AMD, wet AMD, diabetic retinopathy, inherited retinal disease, retinal detachment, familial amyloid polyneuropathy, fibrillary glomerulonephritis, focal segmental glomerulosclerosis (FSGS), geographic atrophy, Goodpasture’s syndrome, Guillain-Barré syndrome, hematopoietic stem cell transplant-associated-thrombotic microangiopathy (HSCT-TMA), hidradenitis suppurativa, Huntington's disease, IgA nephropathy (IgAN), IGAN relapse after kidney transplant antibody mediated rejection (i.e., kidney transplant) post-transplant rejection (solid organ antibody mediated rejection), immune complex membranoproliferative glomerulonephritis (IC-MPGN), immune-mediated necrotizing myopathy, immunoglobulin A-associated vasculitis (IgAV), immunoglobulin A-associated vasculitis (IgAV) nephritis, immune thrombocytopenia (ITP), immune thrombocytopenic purpura, lupus nephritis, lupus nephritis flares with high urinary Ba or sCb5 -9, multiple sclerosis, multifocal motor neuropathy (MMN), myasthenia gravis, neuromyelitis optica spectrum disorder (NMOSD), paroxysmal nocturnal hemoglobinuria (PNH), post-infectious glomerulonephritis, primary membranous nephropathy (PMN), rhabdomyolysis-induced acute kidney injury (RIAKI), sickle cell disease, Sjogren's syndrome, tauopathy, thrombotic microangiopathy (TMA), systemic lupus erythematosus, thrombotic thrombocytopenic purpura (TTP), warm autoimmune hemolytic anemia (WAHA), acute spinal cord injuries, anti-MAG (myelin-associated glycoprotein) peripheral polyneuropathy (IgM neuropathy), pyoderma gangrenosum, dermatomyositis, hypocomplementemic urticarial vasculitis syndrome (HUVS),

auto-immune chronic spontaneous urticaria (aiCUS), Kawasaki disease, Takayasu's arteritis, antiphospholipid therapy - thrombosis prevention (antiphospholipid syndrome), catastrophic antiphospholipid syndrome (CAPS), pre-eclampsia, HELLP syndrome, and autoimmune hepatitis (AIH).

**[0123]** In some examples, the complement-associated disease or disorder is selected from cold agglutinin disease (CAD), atypical hemolytic uremic syndrome (aHUS), IgA nephropathy (IgAN), and lupus nephritis (LN).

**[0124]** In another example, the present disclosure provides a kit comprising a container comprising the antibody or antigen binding fragment herein disclosed, or the conjugate herein disclosed, and an optional pharmaceutically acceptable carrier, and a package insert comprising instructions for administration of the antibody or antigen binding fragment, or the conjugate, to a subject in need thereof. In some examples, the subject has a complement-associated disease or disorder.

**[0125]** In some examples, the complement-associated disease or disorder is selected from: amyotrophic lateral sclerosis (ALS), antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, atypical hemolytic uremic syndrome (aHUS), aHUS after kidney transplant, autoimmune encephalitis, bullous pemphigoid, C3 glomerulopathy (C3G), C3 glomerulonephritis (C3GN), C3G relapse after kidney transplant, cold agglutinin disease (CAD), CD59 deficiency, CD59-mediated hemolytic anemia with or without immune-mediated polyneuropathy, CHAPLE syndrome (CD55 deficiency), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), complement Factor I deficiency, diabetic nephropathy, cryoglobulinemia, dense deposit disease, diabetic lumbosacral plexopathy, age-related macular degeneration (AMD), glaucoma, dry AMD, wet AMD, diabetic retinopathy, inherited retinal disease, retinal detachment, familial amyloid polyneuropathy, fibrillary glomerulonephritis, focal segmental glomerulosclerosis (FSGS), geographic atrophy, Goodpasture’s syndrome, Guillain-Barré syndrome, hematopoietic stem cell transplant-associated-thrombotic microangiopathy (HSCT-TMA), hidradenitis suppurativa, Huntington's disease, IgA nephropathy (IgAN), IGAN relapse after kidney transplant antibody mediated rejection (i.e., kidney transplant) post-transplant rejection (solid organ antibody mediated rejection), immune complex membranoproliferative glomerulonephritis (IC-MPGN), immune-mediated necrotizing myopathy, immunoglobulin A-associated vasculitis (IgAV), immunoglobulin A-associated vasculitis (IgAV) nephritis, immune thrombocytopenia (ITP), immune thrombocytopenic purpura, lupus nephritis, lupus nephritis flares with high urinary Ba or sCb5 -9,

multiple sclerosis, multifocal motor neuropathy (MMN), myasthenia gravis, neuromyelitis optica spectrum disorder (NMOSD), paroxysmal nocturnal hemoglobinuria (PNH), post-infectious glomerulonephritis, primary membranous nephropathy (PMN), rhabdomyolysis-induced acute kidney injury (RIAKI), sickle cell disease, Sjogren's syndrome, tauopathy, thrombotic microangiopathy (TMA), systemic lupus erythematosus, thrombotic thrombocytopenic purpura (TTP), warm autoimmune hemolytic anemia (WAHA), acute spinal cord injuries, anti-MAG (myelin-associated glycoprotein) peripheral polyneuropathy (IgM neuropathy), pyoderma gangrenosum, dermatomyositis, hypocomplementemic urticarial vasculitis syndrome (HUVS), auto-immune chronic spontaneous urticaria (aiCUS), Kawasaki disease, Takayasu's arteritis, antiphospholipid therapy - thrombosis prevention (antiphospholipid syndrome), catastrophic antiphospholipid syndrome (CAPS), pre-eclampsia, HELLP syndrome, and autoimmune hepatitis (AIH).

**[0126]** In some examples, the complement-associated disease or disorder is selected from cold agglutinin disease (CAD), atypical hemolytic uremic syndrome (aHUS), IgA nephropathy (IgAN), and lupus nephritis (LN).

**[0127]** In another example, the present disclosure provides a use of an anti-C2 antibody or antigen binding fragment herein disclosed, an anti-C2 antibody-conjugate herein disclosed, or the composition herein disclosed, for the manufacture of a medicament for treating a complement-associated disease or disorder as disclosed herein in a subject.

**[0128]** In some examples, the complement-associated disease or disorder is selected from: amyotrophic lateral sclerosis (ALS), antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, atypical hemolytic uremic syndrome (aHUS), aHUS after kidney transplant, autoimmune encephalitis, bullous pemphigoid, C3 glomerulopathy (C3G), C3 glomerulonephritis (C3GN), C3G relapse after kidney transplant, cold agglutinin disease (CAD), CD59 deficiency, CD59-mediated hemolytic anemia with or without immune-mediated polyneuropathy, CHAPLE syndrome (CD55 deficiency), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), complement Factor I deficiency, diabetic nephropathy, cryoglobulinemia, dense deposit disease, diabetic lumbosacral plexopathy, age-related macular degeneration (AMD), glaucoma, dry AMD, wet AMD, diabetic retinopathy, inherited retinal disease, retinal detachment, familial amyloid polyneuropathy, fibrillary glomerulonephritis, focal segmental glomerulosclerosis (FSGS), geographic atrophy, Goodpasture’s syndrome, Guillain-Barré syndrome, hematopoietic stem cell transplant-associated-thrombotic microangiopathy (HSCT-TMA), hidradenitis suppurativa,

Huntington's disease, IgA nephropathy (IgAN), IGAN relapse after kidney transplant antibody mediated rejection (i.e., kidney transplant) post-transplant rejection (solid organ antibody mediated rejection), immune complex membranoproliferative glomerulonephritis (IC-MPGN), immune-mediated necrotizing myopathy, immunoglobulin A-associated vasculitis (IgAV), immunoglobulin A-associated vasculitis (IgAV) nephritis, immune thrombocytopenia (ITP), immune thrombocytopenic purpura, lupus nephritis, lupus nephritis flares with high urinary Ba or sCb5 -9, multiple sclerosis, multifocal motor neuropathy (MMN), myasthenia gravis, neuromyelitis optica spectrum disorder (NMOSD), paroxysmal nocturnal hemoglobinuria (PNH), post-infectious glomerulonephritis, primary membranous nephropathy (PMN), rhabdomyolysis-induced acute kidney injury (RIAKI), sickle cell disease, Sjogren's syndrome, tauopathy, thrombotic microangiopathy (TMA), systemic lupus erythematosus, thrombotic thrombocytopenic purpura (TTP), warm autoimmune hemolytic anemia (WAHA), acute spinal cord injuries, anti-MAG (myelin-associated glycoprotein) peripheral polyneuropathy (IgM neuropathy), pyoderma gangrenosum, dermatomyositis, hypocomplementemic urticarial vasculitis syndrome (HUVS), auto-immune chronic spontaneous urticaria (aiCUS), Kawasaki disease, Takayasu's arteritis, antiphospholipid therapy - thrombosis prevention (antiphospholipid syndrome), catastrophic antiphospholipid syndrome (CAPS), pre-eclampsia, HELLP syndrome, and autoimmune hepatitis (AIH). In some examples, the complement-associated disease or disorder is selected from cold agglutinin disease (CAD), atypical hemolytic uremic syndrome (aHUS), IgA nephropathy (IgAN), and lupus nephritis (LN).

## DETAILED DESCRIPTION

**[0129]** The present disclosure is based, at least in part, on the discovery of antibodies that bind C2, and conjugates of said antibodies with polypeptides of the regulator of complement activation (RCA) family.

**[0130]** Complement activation triggers a proteolytic cascade leading to the production of cleavage products with various biological functions. Diffusible fragments (such as the anaphylatoxins) trigger degranulation of neighboring endothelial and mast cells, increase the permeability of capillaries and recruit immune cells. In addition, complement tags surfaces destined for elimination by covalent attachment of specific fragments to the activating surface. Finally, the complement system is actively involved in the disruption of pathogens owing to the insertion of pore-forming complement proteins into the membrane of the invading microorganism The

**CLAIMS**

1. An anti-complement component (C2) antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a light chain variable region (VL) and a heavy chain variable region (VH), wherein:

(i) the VL comprises a VL complementary determining region (CDR) 1 (CDRL1) having an amino acid sequence as set forth in SEQ ID NO: 7 (RSSQYIVHSNX$_1$NTYLE), a VL CDR 2 (CDRL2) having an amino acid sequence as set forth in SEQ ID NO: 8 (KVSNRFS), and a VL CDR 3 (CDRL3) having an amino acid sequence as set forth in SEQ ID NO: 9 (FQGSHVPLT), and the VH comprises a VH CDR 1 (CDRH1) having an amino acid sequence as set forth in SEQ ID NO: 10 (GYTFTDYSMH), a VH CDR 2 (CDRH2) having an amino acid sequence as set forth in SEQ ID NO: 11 (WINTETGEPT), and a VH CDR 3 (CDRH3) having an amino acid sequence as set forth in SEQ ID NO: 12 (EGHYYAMDY), wherein, solely within alternative (i), $X_1$ is G, K, R, or Q;

(ii) the VL comprises a CDRL1 having an amino acid sequence as set forth in SEQ ID NO: 1 ($X_1$ASQDI$X_2$SYLS), a CDRL2 having an amino acid sequence as set forth in SEQ ID NO: 2 (RA$X_3$RLV$X_4$), and a CDRL3 having an amino acid sequence as set forth in SEQ ID NO: 3 (LQYDEFPFT), and the VH comprises a CDRH1 having an amino acid sequence as set forth in SEQ ID NO: 4 (GYTFTGY$X_5$IE), a CDRH2 having an amino acid sequence as set forth in SEQ ID NO: 5 (EILPRSGST$X_6$), and a CDRH3 having an amino acid sequence as set forth in SEQ ID NO: 6 (SGGS$X_7$SYYYALGY), wherein, solely within alternative (ii), $X_1$ is K or R; $X_2$ is N, Q, S, or A; $X_3$ is N, Q, S, or A; $X_4$ is D, E, S, or A; $X_5$ is W, H, F, or Y; $X_6$ is N, Q, S, or A; and $X_7$ is N, Q, S, or A;

(iii) the VL comprises a CDRL1 having an amino acid sequence as set forth in SEQ ID NO: 13 (RSSQSLENSNGNTYLN), a CDRL2 having an amino acid sequence as set forth in SEQ ID NO: 14 (RVSNRFS), and a CDRL3 having an amino acid sequence as set forth in SEQ ID NO: 15 (LQVTHVPFT), and the VH comprises a CDRH1 having an amino acid sequence as set forth in SEQ ID NO: 16 (GYTFTNYGMN), a CDRH2 having an amino acid sequence as set forth in SEQ ID NO: 17 (WINTYTGEPT), and a CDRH3 having an amino acid sequence as set forth in SEQ ID NO: 18 (EFWYFDV);

(iv) the VL comprises a CDRL1 having an amino acid sequence as set forth in SEQ ID NO: 19 (SASSSVSYMY), a CDRL2 having an amino acid sequence as set forth in SEQ ID NO: 20 (LTSNLAS), and a CDRL3 having an amino acid sequence as set forth in SEQ ID NO: 21

(QQWGNNPYT), and the VH comprises a CDRH1 having an amino acid sequence as set forth in SEQ ID NO: 22 (GYTFTSYWMH), a CDRH2 having an amino acid sequence as set forth in SEQ ID NO: 23 (VIDPSDNYTN), and a CDRH3 having an amino acid sequence as set forth in SEQ ID NO: 24 (YGGSYGFAY);

(v) the VL comprises a CDRL1 having an amino acid sequence as set forth in SEQ ID NO: 25 (KASQSVDYDGDSYMN), a CDRL2 having an amino acid sequence as set forth in SEQ ID NO: 26 (AASNLES), and a CDRL3 having an amino acid sequence as set forth in SEQ ID NO: 27 (QQSNEDPFT), and the VH comprises a CDRH1 having an amino acid sequence as set forth in SEQ ID NO: 28 (GYTFTTYTMS), a CDRH2 having an amino acid sequence as set forth in SEQ ID NO: 29 (WINTYSGVPT), and a CDRH3 having an amino acid sequence as set forth in SEQ ID NO: 30 (IKTYGYDWYFDV); or

(vi) the VL comprises a CDRL1 having an amino acid sequence as set forth in SEQ ID NO: 31 (RSSQSIVHSNGNTYLE), a CDRL2 having an amino acid sequence as set forth in SEQ ID NO: 32 (KVSNRFS), and a CDRL3 having an amino acid sequence as set forth in SEQ ID NO: 33 (FQGSHVPWT). and the VH comprises a CDRH1 having an amino acid sequence as set forth in SEQ ID NO: 34 (GYSFTDYYMN), a CDRH2 having an amino acid sequence as set forth in SEQ ID NO: 35 (EIDPSTGGTT), and a CDRH3 having an amino acid sequence as set forth in SEQ ID NO: 36 (DYYGSSYFDY);

optionally wherein the antibody is a full-length antibody, and/or the antibody or antigen-binding fragment thereof is humanized.

2. The anti-C2 antibody or antigen-binding fragment thereof of claim 1, wherein:

(i) the VL comprises a CDRL1 having an amino acid sequence as set forth in SEQ ID NO: 7 (RSSQYIVHSNX1NTYLE), a CDRL2 having an amino acid sequence as set forth in SEQ ID NO: 8 (KVSNRFS), and a CDRL3 having an amino acid sequence as set forth in SEQ ID NO: 9 (FQGSHVPLT), and the VH comprises a CDRH1 having an amino acid sequence as set forth in SEQ ID NO: 10 (GYTFTDYSMH), a CDRH2 having an amino acid sequence as set forth in SEQ ID NO: 11 (WINTETGEPT), and a CDRH3 having an amino acid sequence as set forth in SEQ ID NO: 12 (EGHYYAMDY); wherein X1 is Q;

(ii) the VL comprises a CDRL1 having an amino acid sequence as set forth in SEQ ID NO: 1 (X1ASQDIX2SYLS), a CDRL2 having an amino acid sequence as set forth in SEQ ID NO: 2 (RAX3RLVX4), and a CDRL3 having an amino acid sequence as set forth in SEQ ID NO: 3 (LQYDEFPFT), and the VH comprises a CDRH1 having an amino acid sequence as set forth in

SEQ ID NO: 4 (GYTFTGYX5IE), a CDRH2 having an amino acid sequence as set forth in SEQ ID NO: 5 (EILPRSGSTX6), and a CDRH3 having an amino acid sequence as set forth in SEQ ID NO: 6 (SGGSX7SYYYALGY); wherein X1 is K or R; X2 is N; X3 is N; X4 is D; X5 is W; X6 is N; and X7 is N;

(iii) the VL comprises a CDRL1 having an amino acid sequence as set forth in SEQ ID NO: 13 (RSSQSLENSNGNTYLN), a CDRL2 having an amino acid sequence as set forth in SEQ ID NO: 14 (RVSNRFS), and a CDRL3 having an amino acid sequence as set forth in SEQ ID NO: 15 (LQVTHVPFT), and the VH comprises a CDRH1 having an amino acid sequence as set forth in SEQ ID NO: 16 (GYTFTNYGMN), a CDRH2 having an amino acid sequence as set forth in SEQ ID NO: 17 (WINTYTGEPT), and a CDRH3 having an amino acid sequence as set forth in SEQ ID NO: 18 (EFWYFDV);

(iv) the VL comprises a CDRL1 having an amino acid sequence as set forth in SEQ ID NO: 19 (SASSSVSYMY), a CDRL2 having an amino acid sequence as set forth in SEQ ID NO: 20 (LTSNLAS), and a CDRL3 having an amino acid sequence as set forth in SEQ ID NO: 21 (QQWGNNPYT), and the VH comprises a CDRH1 having an amino acid sequence as set forth in SEQ ID NO: 22 (GYTFTSYWMH), a CDRH2 having an amino acid sequence as set forth in SEQ ID NO: 23 (VIDPSDNYTN), and a CDRH3 having an amino acid sequence as set forth in SEQ ID NO: 24 (YGGSYGFAY);

(v) the VL comprises a CDRL1 having an amino acid sequence as set forth in SEQ ID NO: 25 (KASQSVDYDGDSYMN), a CDRL2 having an amino acid sequence as set forth in SEQ ID NO: 26 (AASNLES), and a CDRL3 having an amino acid sequence as set forth in SEQ ID NO: 27 (QQSNEDPFT), and the VH comprises a CDRH1 having an amino acid sequence as set forth in SEQ ID NO: 28 (GYTFTTYTMS), a CDRH2 having an amino acid sequence as set forth in SEQ ID NO: 29 (WINTYSGVPT), and a CDRH3 having an amino acid sequence as set forth in SEQ ID NO: 30 (IKTYGYDWYFDV); or

(vi) the VL comprises a CDRL1 having an amino acid sequence as set forth in SEQ ID NO: 31 (RSSQSIVHSNGNTYLE), a CDRL2 having an amino acid sequence as set forth in SEQ ID NO: 32 (KVSNRFS), and a CDRL3 having an amino acid sequence as set forth in SEQ ID NO: 33 (FQGSHVPWT), and the VH comprises a CDRH1 having an amino acid sequence as set forth in SEQ ID NO: 34 (GYSFTDYYMN), a CDRH2 having an amino acid sequence as set forth in SEQ ID NO: 35 (EIDPSTGGTT), and a CDRH3 having an amino acid sequence as set forth in SEQ ID NO: 36 (DYYGSSYFDY).

3. The anti-C2 antibody or antigen-binding fragment thereof of claim 1 or 2, wherein the VH comprises a R44G substitution, wherein the amino acid positions are numbered according to SEQ ID NO: 63; and/or the VL comprises a G34Q substitution, wherein the amino acid positions are numbered according to SEQ ID NO: 69.

4. The anti-C2 antibody or antigen-binding fragment thereof of claim 2, wherein the VH comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 324 and the VL comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 325, or optionally wherein the VH comprises the amino acid sequence as set forth in SEQ ID NO: 324 and the VL comprises the amino acid sequence as set forth in SEQ ID NO: 325.

5. The anti-C2 antibody or antigen-binding fragment thereof of any one of claims 1-4, comprising a heavy chain constant region, optionally wherein the heavy chain constant region is an IgG1 constant region, optionally wherein (i) the IgG1 constant region comprises L234A and L235A substitutions, relative to a wild-type human IgG1 constant region, according to EU numbering; and/or (ii) the IgG1 constant region comprises M428L and N434S substitutions, relative to a wild-type human IgG1 constant region, according to EU numbering, optionally comprising a heavy chain comprising the amino acid sequence as set forth in SEQ ID NO: 328 and a light chain comprising the amino acid sequence as set forth in SEQ ID NO: 329.

6. An anti-C2 antibody conjugate comprising: (i) the anti-C2 antibody or antigen-binding fragment thereof of any one of claims 1-5; and (ii) at least one regulator of complement activation (RCA) polypeptide covalently linked to the antibody or antigen-binding fragment thereof, optionally wherein (a) the at least one RCA polypeptide is selected from FH1-4, FH1-5, FH19-20, DAF1-4, DAF2-4, MCP1-4, C4BP1-3, CR1.1-3, CR1.8-10, CR1.15-17, MCP2-4, MCP3-4, C4BP1-4, and any combination thereof; (b) the at least one RCA polypeptide comprises an amino acid sequence selected from SEQ ID NOs: 114-122, SEQ ID NOs: 240-250, and any combination thereof; and/or (c) the antibody or antigen-binding fragment thereof is covalently linked to the at least one RCA polypeptide via a linker, optionally wherein the linker is a glycine-serine (Gly-Ser) linker, optionally wherein the Gly-Ser linker is a $(Gly_2Ser)n$ or a $(Gly_3Ser)n$ linker, wherein n is 1-10, optionally wherein n is 1-5.

7. The anti-C2 antibody conjugate of claim 6, comprising two or more RCA polypeptides, optionally wherein (i) the two or more RCA polypeptides are the same or the two or more RCA polypeptides are different; and/or (ii) the two or more RCA polypeptides are linked to each other via a linker, optionally wherein the linker is a Gly-Ser linker, optionally wherein the Gly-Ser linker is a $(Gly_2Ser)n$ or a $(Gly_3Ser)n$ linker, wherein n is 1-10, optionally wherein n is 1-5.

8. The anti-C2 antibody conjugate of claim 7, wherein the conjugate comprises:

a) a first protein monomer comprising from N- to C- terminus an antibody heavy chain, a Gly2Ser or a Gly3Ser linker, a DAF domain or a FH domain, a Gly2Ser linker or a Gly3Ser, and a DAF domain or a FH domain; and

b) a second protein monomer comprising an antibody light chain.

9. The anti-C2 antibody conjugate of claim 7, wherein the conjugate comprises:

(i) a) a first protein monomer comprising from N- to C- terminus an antibody heavy chain, a Gly2Ser linker, a DAF domain, a Gly2Ser linker, and a FH domain; and

b) a second protein monomer comprising an antibody light chain;

wherein the antibody heavy chain comprises a VH comprising a CDRH1 having an amino acid sequence as set forth in SEQ ID NO: 10 (GYTFTDYSMH), a CDRH2 having an amino acid sequence as set forth in SEQ ID NO: 11 (WINTETGEPT), and a CDRH3 having an amino acid sequence as set forth in SEQ ID NO: 12 (EGHYYAMDY), and the antibody light chain comprises a VL comprising a CDRL1 having an amino acid sequence as set forth in SEQ ID NO: 327 (RSSQYIVHSNQNTYLE), a CDRL2 having an amino acid sequence as set forth in SEQ ID NO: 8 (KVSNRFS), and a CDRL3 having an amino acid sequence as set forth in SEQ ID NO: 9 (FQGSHVPLT), optionally wherein the first protein monomer comprises the amino acid sequence of SEQ ID NO: 415 and the second protein monomer comprises the amino acid sequence of SEQ ID NO: 329; or

(ii) a) a first protein monomer comprising from N- to C- terminus an antibody heavy chain, a Gly3Ser linker, a FH domain, a Gly3Ser linker, and a DAF domain; and

b) a second protein monomer comprising an antibody light chain;

wherein the heavy chain comprises a VH comprising a CDRH1 having an amino acid sequence as set forth in SEQ ID NO: 10 (GYTFTDYSMH), a CDRH2 having an amino acid sequence as set forth in SEQ ID NO: 11 (WINTETGEPT), and a

CDRH3 having an amino acid sequence as set forth in SEQ ID NO: 12 (EGHYYAMDY), and the light chain comprises a VL comprising a CDRL1 having an amino acid sequence as set forth in SEQ ID NO: 327 (RSSQYIVHSNQNTYLE), a CDRL2 having an amino acid sequence as set forth in SEQ ID NO: 8 (KVSNRFS), and a CDRL3 having an amino acid sequence as set forth in SEQ ID NO: 9 (FQGSHVPLT), optionally wherein the first protein monomer comprises the amino acid sequence of SEQ ID NO: 394 and the second protein monomer comprises the amino acid sequence of SEQ ID NO: 329.

10. A nucleic acid encoding the anti-C2 antibody or antigen-binding fragment thereof of any one of claims 1-5 or the anti-C2 antibody conjugate of any one of claims 6-9.

11. An expression vector comprising the nucleic acid of claim 10.

12. A host cell comprising the expression vector of claim 11.

13. A method for producing the anti-C2 antibody or antigen-binding fragment thereof of any one of claims 1-5 or the anti-C2 antibody conjugate of any one of claims 6-9, the method comprising culturing the host cell of claim 12 under conditions permitting expression of the antibody or antigen-binding fragment thereof, or the antibody conjugate.

14. A pharmaceutical composition comprising the anti-C2 antibody or antigen-binding fragment thereof of any one of claims 1-5, or the anti-C2 antibody conjugate of any one of claims 6-9, and a pharmaceutically acceptable carrier.

15. The anti-C2 antibody or antigen-binding fragment thereof of any one of claims 1-5, the anti-C2 antibody conjugate of any one of claims 6-9, or the pharmaceutical composition of claim 14 for use in therapy.

16. Use of the anti-C2 antibody or antigen-binding fragment thereof of any one of claims 1-5, the anti-C2 antibody conjugate of any one of claims 6-9, or the pharmaceutical composition of claim 14 in the manufacture of a medicament for treating a complement-associated disease or disorder, optionally wherein the complement-associated disease or disorder is selected from

amyotrophic lateral sclerosis (ALS), antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, atypical hemolytic uremic syndrome (aHUS), aHUS after kidney transplant, autoimmune encephalitis, bullous pemphigoid, C3 glomerulopathy (C3G), C3 glomerulonephritis (C3GN), C3G relapse after kidney transplant, cold agglutinin disease (CAD), CD59 deficiency, CD59-mediated hemolytic anemia with or without immune-mediated polyneuropathy, CHAPLE syndrome (CD55 deficiency), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), complement Factor I deficiency, diabetic nephropathy, cryoglobulinemia, dense deposit disease, diabetic lumbosacral plexopathy, age-related macular degeneration (AMD), glaucoma, dry AMD, wet AMD, diabetic retinopathy, inherited retinal disease, retinal detachment, familial amyloid polyneuropathy, fibrillary glomerulonephritis, focal segmental glomerulosclerosis (FSGS), geographic atrophy, Goodpasture’s syndrome, Guillain-Barré syndrome, hematopoietic stem cell transplant-associated-thrombotic microangiopathy (HSCT-TMA), hidradenitis suppurativa, Huntington's disease, IgA nephropathy (IgAN), IgAN relapse after kidney transplant antibody mediated rejection post-transplant rejection, immune complex membranoproliferative glomerulonephritis (IC-MPGN), immune-mediated necrotizing myopathy, immunoglobulin A-associated vasculitis (IgAV), immunoglobulin A-associated vasculitis (IgAV) nephritis, immune thrombocytopenia (ITP), immune thrombocytopenic purpura, lupus nephritis, lupus nephritis flares with high urinary Ba or sCb5 -9, multiple sclerosis, multifocal motor neuropathy (MMN), myasthenia gravis, neuromyelitis optica spectrum disorder (NMOSD), paroxysmal nocturnal hemoglobinuria (PNH), post-infectious glomerulonephritis, primary membranous nephropathy (PMN), rhabdomyolysis-induced acute kidney injury (RIAKI), sickle cell disease, Sjogren's syndrome, tauopathy, thrombotic microangiopathy (TMA), systemic lupus erythematosus, thrombotic thrombocytopenic purpura (TTP), warm autoimmune hemolytic anemia (WAHA), acute spinal cord injuries, anti-MAG (myelin-associated glycoprotein) peripheral polyneuropathy (IgM neuropathy), pyoderma gangrenosum, dermatomyositis, hypocomplementemic urticarial vasculitis syndrome (HUVS), auto-immune chronic spontaneous urticaria (aiCUS), Kawasaki disease, Takayasu's arteritis, antiphospholipid therapy - thrombosis prevention (antiphospholipid syndrome), catastrophic antiphospholipid syndrome (CAPS), pre-eclampsia, HELLP syndrome, and autoimmune hepatitis (AIH).