1996, 93: 8563-8568), rheumatoid arthritis (Y. Wang et al., *Proc. Natl. Acad. Sci.*, 1995; 92: 8955-8959), cardiopulmonary bypass and hemodialysis (C.S. Rinder, *J. Clin. Invest.*, 1995; 96: 1564-1572), hyperacute rejection in organ transplantation (T.J. Kroshus et al., *Transplantation*, 1995; 60: 1194-1202), myocardial infarction (J. W. Homeister et al., *J. Immunol.*, 1993; 150: 1055-1064; H.F. Weisman et al., *Science*, 1990; 249: 146-151), reperfusion injury (E.A. Amsterdam et al., *Am. J. Physiol.*, 1995; 268: H448-H457), and adult respiratory distress syndrome (R. Rabinovici et al., *J. Immunol.*, 1992; 149: 1744-1750). In addition, other inflammatory conditions and autoimmune/immune complex diseases are also closely associated with complement activation (V.M. Holers, *ibid.*, B.P. Morgan. *Eur. J. Clin. Invest.*, 1994: 24: 219-228), including thermal injury, severe asthma, anaphylactic shock, bowel inflammation, urticaria, angioedema, vasculitis, multiple sclerosis, myasthenia gravis, membranoproliferative glomerulonephritis, and Sjögren's syndrome.

[0006] There is a need for antibody therapeutics in the field of complement-mediated disorders, and humanized anti-Factor D antibodies, and antibody variants thereof, and fragments thereof (e.g. antigen-binding fragments), of the present invention provide high affinity antibodies useful to meet this need.

~~Summary of the Invention~~

[0007] In one ~~aspect~~embodiment, the present disclosure~~invention~~ relates generally to antibodies capable of inhibiting biological activities associated with Factor D.

[0008] In one embodiment~~aspect~~, the present disclosure~~invention~~ relates to humanized anti-Factor D antibodies, having a variety of therapeutically desired characteristics. The disclosure~~invention~~ includes the amino acid sequences of the HVRs of these humanized anti-Factor D antibodies, and their corresponding nucleic acid sequences. The disclosure~~invention~~ includes the amino acid sequences of the variable domains of the heavy and light chain of the humanized anti-Factor D antibodies, and their corresponding nucleic acid sequences. The disclosure~~invention~~ includes the amino acid sequences of the heavy and light chain of the humanized anti-Factor D antibodies, and their corresponding nucleic acid sequences.

[0009] In one embodiment~~aspect~~, specific antibodies within the scope of this disclosure~~invention~~ include, without limitation humanized anti-Factor D antibodies, comprising HVRs of humanized anti-Factor D Fab clones #238, 238-1, 238-2, 238-3, 238-4, 238-5, 238-6, 238-7, 238-8, 238-9, 238-10 or 238-11. In one embodiment, the humanized anti-Factor D antibodies comprise the variable domains of the heavy and/or light chains of humanized anti-Factor D Fab clones #238, 238-1, 238-2, 238-3, 238-4, 238-5, 238-6, 238-7, 238-8, 238-9, 238-10 or 238-11. In one embodiment, the humanized anti-Factor D antibodies comprise the heavy and/or light chains of humanized anti-Factor D Fab clones #238, 238-1, 238-2, 238-3, 238-4, 238-5, 238-6, 238-7, 238-8, 238-9, 238-10 or 238-11. In one embodiment, the disclosure~~invention~~ includes the

humanized anti-factor D Fab clones #238, 238-1, 238-2, 238-3, 238-4, 238-5, 238-6, 238-7, 238-8, 238-9, 238-10 or 238-11. In one embodiment, the disclosure~~invention~~ includes antibody fragments (e.g. antigen-binding fragments) of full-length antibodies of humanized anti-Factor D Fab clones #238, 238-1, 238-2, 238-3, 238-4, 238-5, 238-6, 238-7, 238-8, 238-9, 238-10 or 238-11. In one embodiment, the disclosure~~invention~~ includes full-length antibodies or antigen-binding fragments thereof, comprising the antigen-binding sequences of the heavy chain and/or the light chain of humanized anti-Factor D Fab clones #238, 238-1, 238-2, 238-3, 238-4, 238-5, 238-6, 238-7, 238-8, 238-9, 238-10 or 238-11. In one embodiment, such antigen-binding sequences comprise at least one, two, or three of the HVRs of the heavy chain. In one embodiment, such antigen-binding sequences comprise at least one, two, or three of the HVRs of the light chain. In one embodiment, such antigen-binding sequences comprise at least a portion or all of the heavy chain variable domain. In one embodiment, such antigen-binding sequences comprise at least a portion or all of the light chain variable domain.

[0010] In one embodiment~~aspect~~, the present disclosure~~invention~~ provides antibody fragments (e.g. antigen-binding fragments) or full-length antibodies of humanized anti-Factor D Fab clone #111, comprising at least one modification of the sequence of humanized anti-Factor D Fab clone #111, wherein such full-length antibodies or such antigen-binding fragments comprise the antigen-binding sequences of the heavy chain and/or the light chain of humanized anti-Factor D Fab clone #111. In one embodiment, the antibody fragments (e.g. antigen-binding fragments) or full-length antibodies of humanized anti-Factor D Fab clone #111, comprising at least one modification of the sequence of humanized anti-Factor D Fab clone #111, comprising the antigen-binding sequences of the heavy chain and/or the light chain of humanized anti-Factor D Fab clone #111, further bind essentially to the same epitope as humanized antibody Fab clone #111. In one embodiment, such antigen-binding sequences comprise at least one, two or three of the HVRs of the heavy chain. In one embodiment, such antigen-binding sequences comprise at least one, two or three of the HVRs of the light chain. In one embodiment, such antigen-binding sequences comprise at least a portion or all of the heavy chain variable domain. In one embodiment, such antigen-binding sequences comprise at least a portion or all of the light chain variable domain. In one embodiment, such modification in said antibody fragments or said full-length antibodies, is in the heavy chain. In one embodiment, such modification in said antibody fragments or said full-length antibodies, is in the light chain. In one embodiment, such modification in said antibody fragments or said full-length antibodies, is in the heavy chain variable domain. In one embodiment, such modification in said antibody fragments or said full-length antibodies, is in the light chain variable domain. In one embodiment, such modification in said antibody fragments or said full-length antibodies, is in at least one, two or three of the HVRs of the heavy chain. In one

embodiment, such modification in said antibody fragments or said full-length antibodies, is in at least one, two or three of the HVRs of the light chain.

[0011] In one embodimentaspect, the disclosureinvention concerns antibodies of the present disclosureinvention, or fragments thereof (e.g. antigen-binding fragments), which bind to Factor D with a binding affinity of at least about 10^{-9} to 10^{-12}M.

[0012] In one embodimentaspect, the disclosureinvention concerns antibodies of the present disclosureinvention, or fragments thereof (e.g. antigen-binding fragments), wherein a Fab fragment of such antibodies inhibits a biological function of Factor D in a Fab fragment to Factor D molar ratio of about 0.05:1 (0.05) to about 10:1 (10), or about 0.09:1 (0.09) to about 8:1 (8), or about 0.1:1 (0.1) to about 6:1 (6), or about 0.15:1 (0.15) to about 5:1 (5), or about 0.19:1 (0.19) to about 4:1 (4), or about 0.2:1 (0.2) to about 3:1 (3), or about 0.3:1 (0.3) to about 2:1 (2), or about 0.4:1 (0.4) to about 1:1 (1), or about 0.5:1 (0.5) to about 1:2 (0.5), or about 0.6:1 (0.6) to about 1:3 (0.33), or about 0.7:1 (0.7) to about 1:4 (0.25), or about 0.8:1 (0.8) to about 1:5 (0.2) or about 0.9:1 (0.9) to about 1:6 (0.17).

[0013] In one embodimentaspect, the antibodies of the present disclosureinvention include human, humanized or chimeric antibodies.

[0014] In another embodimentaspect, the present disclosureinvention includes antibody fragments (e.g. antigen-binding fragments) of humanized anti-Factor D antibodies. The antibody fragments of the present disclosureinvention may, for example, be Fab, Fab', $F(ab')_2$, scFv, $(scFv)_2$, dAb, complementarity determining region (CDR) fragments, linear antibodies, single-chain antibody molecules, minibodies, diabodies, or multispecific antibodies formed from antibody fragments.

[0015] In other aspectsembodiments of the inventiondisclosure, the present disclosureinvention includes compositions comprising an antibody of the disclosureinvention, or fragment thereof (e.g. antigen-binding fragment). In another embodiment, the disclosureinvention provides cell lines and vectors encoding at least a portion of an antibody of the disclosureinvention, or fragment thereof (e.g. antigen-binding fragment). In one embodimentaspect, the disclosureinvention includes method of making, method of producing, and method of using antibodies, or fragments thereof (e.g. antigen-binding fragments) and compositions of the disclosureinvention. In one embodiment, the method of making an antibody of the disclosureinvention, or fragment thereof (e.g. antigen-binding fragment), wherein the method comprises (a) culturing a host cell, for example a eukaryotic or CHO cell, comprising a vector, further comprising a polynucleotide encoding an antibody of the disclosureinvention, or fragment thereof (e.g. antigen-binding fragment), under conditions suitable for expression of the polynucleotide encoding the antibody, or fragment thereof (e.g. antigen-binding fragment) and (b) isolating the antibody, or fragment thereof (e.g. antigen-binding fragment).

[0015a] In one aspect, there is provided a method for determining the efficacy of an anti-Factor D antibody or an antigen-binding fragment thereof comprising: performing an alternative pathway hemolytic assay and detecting inhibition of alternative pathway hemolysis, wherein a half minimal inhibitory concentration (IC50) value of less than 80 nM of the anti-Factor D antibody or the antigen-binding fragment thereof indicates that the anti-Factor D antibody or the antigen-binding fragment thereof is efficacious; wherein the antibody or the antigen-binding fragment thereof comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises light chain hypervariable region (HVR)-1 comprising ITSTDIDDDMN (SEQ ID NO: 30), light chain HVR-2 comprising GGNTLRP (SEQ ID NO: 35), and light chain HVR-3 comprising LQSDSLPYT (SEQ ID NO: 38), wherein the heavy chain variable domain comprises heavy chain HVR-1 comprising GYTFTNYGMN (SEQ ID NO: 39), heavy chain HVR-2 comprising WINTYTGETTYADDFKG (SEQ ID NO: 40), and heavy chain HVR-3 comprising EGGVNN (SEQ ID NO: 41),

wherein the anti-Factor D antibody or antibody fragment thereof further comprises one or more of the following substitutions (a) to (e):

(a) substitution of the amino acid at position 10 of SEQ ID NO: 30 with L or I;

(b) substitution of the amino acid at position 11 of SEQ ID NO: 30 with A or Q;

(c) substitution of the amino acid at position 3 of SEQ ID NO: 35 with S or A;

(d) substitution of the amino acid at position 5 of SEQ ID NO: 41 with A or Q; or

(e) substitution of the amino acid at position 6 of SEQ ID NO: 41 with A or Q,

and/or the heavy chain variable domain comprises an E at position 1.

[0015b] In another aspect, there is provided a method for determining the efficacy of an anti-Factor D antibody or an antigen-binding fragment thereof comprising: performing an alternative pathway hemolytic assay and detecting inhibition of alternative pathway hemolysis, wherein a half minimal inhibitory concentration (IC50) value of less than 80 nM of the anti-Factor D antibody or the antigen-binding fragment thereof indicates that the anti-Factor D antibody or the antigen-binding fragment thereof is efficacious; wherein the antibody or the antigen-binding fragment thereof comprises a light chain variable domain comprising light chain hypervariable region (HVR)-1 comprising ITSTDIDDDMN (SEQ ID NO: 30), light chain HVR-2 comprising GGNTLRP (SEQ ID NO: 35), and light chain HVR-3 comprising LQSDSLPYT (SEQ ID NO: 38), and a

heavy chain variable domain comprising HVR-1 comprising GYTFTNYGMN (SEQ ID NO: 39), heavy chain HVR-2 comprising WINTYTGETTYADDFKG (SEQ ID NO: 40), and heavy chain HVR-3 comprising EGGVNN (SEQ ID NO: 41),

wherein the light chain variable domain comprise light chain framework region (FR)-4 comprising FGQGTKVEIK (SEQ ID NO: 51), and wherein the heavy chain variable domain comprises an E at position 1.

[0015c] In another aspect, there is provided a method for determining the efficacy of an anti-Factor D antibody or an antigen-binding fragment thereof comprising: performing an alternative pathway hemolytic assay and detecting inhibition of alternative pathway hemolysis, wherein a half minimal inhibitory concentration (IC50) value of less than 80 nM of the anti-Factor D antibody or the antigen-binding fragment thereof indicates that the anti-Factor D antibody or the antigen-binding fragment thereof is efficacious; wherein the antibody or the antigen-binding fragment comprises a heavy chain variable domain comprising an amino acid sequence of SEQ ID NO: 19 and a light chain variable domain comprising an amino acid sequence of SEQ ID NO: 7.

[0015d] In another aspect, there is provided a method for determining the efficacy of an anti-Factor D antibody or an antigen-binding fragment thereof comprising: performing an alternative pathway hemolytic assay and detecting inhibition of alternative pathway hemolysis, wherein a half minimal inhibitory concentration (IC50) value of less than 80 nM of the anti-Factor D antibody or the antigen-binding fragment thereof indicates that the anti-Factor D antibody or the antigen-binding fragment thereof is efficacious; wherein the antibody or the antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 63 and a light chain comprising an amino acid sequence of SEQ ID NO: 61.

[0016] In a still further embodiment~~aspect~~, the disclosure~~invention~~ concerns a composition of matter comprising an antibody of the disclosure~~invention~~, or fragment thereof (e.g. antigen-binding fragment),

as described herein, in combination with a carrier. Optionally, the carrier is a pharmaceutically acceptable carrier.

[0017] Another embodiment~~aspect~~ of the present disclosure~~invention~~ is the use of these humanized antibodies or antibody fragments thereof (e.g. antigen-binding fragments), for the preparation of a medicament or composition for the prevention and/or treatment of disorders associated with excessive or uncontrolled complement activation. They include complement activation during cardiopulmonary bypass operations; complement activation due to ischemia-reperfusion following acute myocardial infarction, aneurysm, stroke, hemorrhagic shock, crush injury, multiple organ failure, hypobolemic shock, intestinal ischemia or other events causing ischemia. Complement activation has also been shown to be associated with inflammatory conditions such as severe burns, endotoxemia, septic shock, adult respiratory distress syndrome, hemodialysis; anaphylactic shock, severe asthma, angioedema, Crohn's disease, sickle cell anemia, poststreptococcal glomerulonephritis and pancreatitis. The disorder may be the result of an adverse drug reaction, drug allergy, IL-2 induced vascular leakage syndrome or radiographic contrast media allergy. It also includes autoimmune disease such as systemic lupus erythematosus, myasthenia gravis, rheumatoid arthritis, Alzheimer's disease and multiple sclerosis. In another embodiment, complement activation is also associated with transplant rejection. In another embodiment, complement activation is also associated with ocular diseases (all ocular conditions and diseases the pathology of which involve complement, including the classical and the alternative pathway of complement), such as, for example, without limitation, macular degenerative disease, such as all stages of age-related macular degeneration (AMD), including dry and wet (non-exudative and exudative) forms, diabetic retinopathy and other ischemia-related retinopathies, choroidal neovascularization (CNV), uveitis, diabetic macular edema, pathological myopia, von Hippel-Lindau disease, histoplasmosis of the eye, Central Retinal Vein Occlusion (CRVO), corneal neovascularization, and retinal neovascularization. In one example, complement-associated eye conditions include age-related macular degeneration (AMD), including non-exudative (e.g intermediate dry AMD or geographic atrophy (GA)) and exudative (e.g. wet AMD (choroidal neovascularization (CNV)) AMD, diabetic retinopathy (DR), endophthalmitis and uveitis. In a further example, nonexudative AMD may include the presence of hard drusen, soft drusen, geographic atrophy and/or pigment clumping. In another example, complement-associated eye conditions include age-related macular degeneration (AMD), including early AMD (e.g. includes multiple small to one or more non-extensive medium sized drusen), intermediate AMD (e.g. includes extensive medium drusen to one or more large drusen) and advanced AMD (e.g. includes geographic atrophy or advanced wet AMD (CNV). In a further example, intermediate dry AMD may include large confluent drusen. In a further example, geographic atrophy may include photoreceptor and/or Retinal Pigmented Epithelial (RPE) loss. In a

further example, the area of geographic atrophy may be small or large and/or may be in the macula area or in the peripheral retina. In one example, the complement-associated eye condition is intermediate dry AMD. In one example, the complement-associated eye condition is geographic atrophy. In one example, the complement-associated eye condition is wet AMD (choroidal neovascularization (CNV)).

[0018] In another embodimentaspect, the disclosureinvention provides a kit, comprising an antibody of the disclosureinvention, or fragment thereof (e.g. antigen-binding fragment). In one embodiment, the disclosureinvention provides a kit, comprising an antibody of the disclosureinvention, or fragment thereof (e.g. antigen-binding fragment) and instructions for use. In one embodiment, the disclosureinvention concerns a kit comprising an antibody of the disclosureinvention, or fragment thereof (e.g. antigen-binding fragment) and instructions for administering said antibody, to treat a complement-associated disorder. In one embodiment, the disclosureinvention provides a kit comprising a first container comprising a composition comprising one or more one or more antibodies of the disclosureinvention, or antibody fragments thereof (e.g. antigen-binding fragments); and a second container comprising a buffer. In one embodiment, the buffer is pharmaceutically acceptable. In one embodiment, a composition comprising an antibody of the disclosureinvention, or fragment thereof (e.g. antigen-binding fragment) further comprises a carrier, which in some embodiments is pharmaceutically acceptable. In one embodiment, a kit further comprises instructions for administering the composition (.e.g the antibody, or antibody fragment thereof (e.g. antigen-binding fragment) to a subject. In one embodiment, a kit further comprises instructions for use of the kit.

[0019] In one embodimentaspect, the disclosureinvention concerns an article of manufacture containing materials useful for the treatment, prevention and/or diagnosis of complement-associated disorders. In one embodiment, the disclosureinvention concerns an article of manufacture, comprising: (a) a container; (b) a label on the container; and (c) a composition of matter comprising an antibody, or variant thereof or fragment thereof (e.g. antigen-binding fragment), of the present disclosureinvention, contained with the container, wherein the label on said container indicates that the composition can be used for treatment, prevention and/or diagnosis of complement-associated disorders.

[0020] In one embodimentaspect, the disclosureinvention provides use of an anti-Factor D antibody of the disclosureinvention, or antibody fragment thereof (e.g. antigen-binding fragment), nucleic acid of the disclosureinvention, expression vector of the disclosureinvention or host cell of the disclosureinvention, in the preparation of a medicament for the therapeutic and/or prophylactic treatment of a disease, such as a complement-associated eye condition. In one embodiment, the complement-associated eye condition is selected from age-related macular degeneration (AMD), including non-exudative (e.g intermediate dry AMD or geographic atrophy (GA)) and exudative (e.g. wet AMD (choroidal neovascularization (CNV)) AMD, diabetic retinopathy (DR), endophthalmitis and

uveitis. In one example, the complement-associated eye condition is intermediate dry AMD. In one example, the complement-associated eye condition is geographic atrophy. In one example, the complement-associated eye condition is wet AMD (choroidal neovascularization (CNV)).

[0021] In one embodiment~~aspect~~, the disclosure~~invention~~ provides use of an article of manufacture of the disclosure~~invention~~ in the preparation of a medicament for the therapeutic and/or prophylactic treatment of a disease, such as a complement-associated eye condition. In one embodiment, the complement-associated eye condition is selected from age-related macular degeneration (AMD), including non-exudative (e.g intermediate dry AMD or geographic atrophy (GA)) and exudative (e.g. wet AMD (choroidal neovascularization (CNV)) AMD, diabetic retinopathy (DR), endophthalmitis and uveitis. In one example, the complement-associated eye condition is intermediate dry AMD. In one example, the complement-associated eye condition is geographic atrophy. In one example, the complement-associated eye condition is wet AMD (choroidal neovascularization (CNV)).

[0022] In one embodiment~~aspect~~, the disclosure~~invention~~ provides use of a kit of the disclosure~~invention~~ in the preparation of a medicament for the therapeutic and/or prophylactic treatment of a disease, such as a complement-associated eye condition. In one embodiment, the complement-associated eye condition is selected from age-related macular degeneration (AMD), including non-exudative (e.g intermediate dry AMD or geographic atrophy (GA)) and exudative (e.g. wet AMD (choroidal neovascularization (CNV)) AMD, diabetic retinopathy (DR), endophthalmitis and uveitis. In one example, the complement-associated eye condition is intermediate dry AMD. In one example, the complement-associated eye condition is geographic atrophy. In one example, the complement-associated eye condition is wet AMD (choroidal neovascularization (CNV)).

Brief Description of the Figures

[0023] Figures 1A-1C shows the alignment of sequences of the variable light chain domains for the following: humanized anti-Factor D Fab clone #111 (SEQ ID NO: 1), humanized anti-Factor D Fabs, 238, 238-1, 238-2, 238-3, 238-4, 238-5, 238-6, 238-7, 238-8, 238-9, 238-10 and 238-11 (SEQ ID NOs: 6-17, respectively) and VL Kappa I consensus sequence (SEQ ID NO: 65). Positions are numbered according to Kabat and hypervariable regions (in accordance with Kabat + Chothia HVR definitions) are boxed (HVRs: (1) HVR-L1 identified as A1-A11 (ITSTDIDDDMN (SEQ ID NO: 30), ITSTDIDDDLN (SEQ ID NO: 31), ITSTDIDDDIN (SEQ ID NO: 32), ITSTDIDDDMA (SEQ ID NO: 33) or ITSTDIDDDMQ (SEQ ID NO: 34)), (2) HVR-L2 identified as B1-B7 (GGNTLRP (SEQ ID NO: 35), GGSTLRP (SEQ ID NO: 36) or GGATLRP (SEQ ID NO: 37)), (3) HVR-L3 identified as C1-C9 (LQSDSLPYT (SEQ

We Claim:

1. An anti-Factor D antibody comprising light chain HVRs of a reference antibody, wherein said anti-Factor D antibody further comprises a substitution at one or more positions of said reference antibody, wherein said reference antibody comprises light chain HVR-1 comprising ITSTDIDDDMN (SEQ ID NO: 30), light chain HVR-2 comprising GGNTLRP (SEQ ID NO: 35), and light chain HVR-3 comprising LQSDSLPYT (SEQ ID NO: 38), and wherein said substitution is one or more of the following:

(a) amino acid at position 33 of the light chain is L or I;

(b) amino acid at position 34 of the light chain is A or Q;

(c) amino acid at position 52 of the light chain is S or A;

(d) amino acid at position 104 of the light chain is V;

(e) amino acid at position 1 of the heavy chain is E;

(f) amino acid at position 99 of the heavy chain is A or Q; or

(g) amino acid at position 100 of the heavy chain is A or Q.

2. An anti-Factor D antibody comprising heavy chain HVRs of a reference antibody, wherein said anti-Factor D antibody further comprises a substitution at one or more positions of said reference antibody, wherein said reference antibody comprises heavy chain HVR-1 comprising GYTFTNYGMN (SEQ ID NO: 39), heavy chain HVR-2 comprising WINTYTGETTYADDFKG (SEQ ID NO: 40), and heavy chain HVR-3 comprising EGGVNN (SEQ ID NO: 41), and wherein said substitution is one or more of the following:

(a) amino acid at position 33 of the light chain is L or I;

(b) amino acid at position 34 of the light chain is A or Q;

(c) amino acid at position 52 of the light chain is S or A;

(d) amino acid at position 104 of the light chain is V'

(e) amino acid at position 1 of the heavy chain is E;

(f) amino acid at position 99 of the heavy chain is A or Q; or

(g) amino acid at position 100 of the heavy chain is A or Q.

3. An anti-Factor D antibody comprising light chain HVRs and heavy chain HVRs of a reference antibody, wherein said anti-Factor D antibody further comprises a substitution at one or more positions of said reference antibody, wherein said reference antibody comprises light chain HVR-1 comprising ITSTDIDDDMN (SEQ ID NO: 30), light chain HVR-2 comprising GGNTLRP (SEQ ID NO: 35), and light chain HVR-3 comprising LQSDSLPYT (SEQ ID NO: 38), and heavy chain HVR-1 comprising GYTFTNYGMN (SEQ ID NO: 39), heavy chain HVR-2 comprising WINTYTGETTYADDFKG (SEQ ID NO: 40), and heavy chain HVR-3 comprising EGGVNN (SEQ ID NO: 41), and wherein said substitution is one or more of the following:

(a) amino acid at position 33 of the light chain is L or I;

(b) amino acid at position 34 of the light chain is A or Q;

(c) amino acid at position 52 of the light chain is S or A;

(d) amino acid at position 104 of the light chain is V;

(e) amino acid at position 1 of the heavy chain is E;

(f) amino acid at position 99 of the heavy chain is A or Q; or

(g) amino acid at position 100 of the heavy chain is A or Q.

4. An anti-Factor D antibody comprising:

(a) at least one, two, three, four, five or six HVRs selected from the group comprising:

(i) an HVR-H1 comprising the amino acid sequence selected from SEQ ID NO: 39;

(ii) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 40;

(iii) an HVR-H3 comprising the amino acid sequence selected from SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44 and SEQ ID NO: 45;

(iv) an HVR-L1 comprising the amino acid sequence selected from SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33 and SEQ ID NO: 34;

(v) an HVR-L2 comprising the amino acid sequence selected from SEQ ID NO: 35, SEQ ID NO: 36 and SEQ ID NO: 37; and

(vi) an HVR-L3 comprising the amino acid sequence selected from SEQ ID NO: 38; or

(b) at least one variant HVR, wherein the variant HVR comprises modification of at least one residue of the sequence depicted in SEQ ID NO: 39, 40, 41, 42, 43, 44, 45, 30, 31, 32, 33, 34, 35, 36, 37 or 38.

5. The antibody of Claim 4, comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 39

6. The antibody of Claim 4, comprising an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 40.

7. The antibody of Claim 4, comprising an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 41.

8. The antibody of Claim 4, comprising an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 30.

9. The antibody of Claim 4, comprising an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 35.

10. The antibody of Claim 4, comprising an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 38.

11. The antibody of Claim 4, comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 39, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 40, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 41.

12. The antibody of Claim 4, comprising an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 30, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 35, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 38.

13. The antibody of Claim 4, comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 39, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 40, an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 41, an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 30, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 35, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 38.

14. The antibody of Claim 4, wherein the antibody comprises a heavy chain variable domain having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 18.

15. The antibody of Claim 4, wherein the antibody comprises a heavy chain variable domain having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 19.

16. The antibody of Claim 4, wherein the antibody comprises a light chain variable domain having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 6.

17. The antibody of Claim 4, wherein the antibody comprises a light chain variable domain having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 7.

18. The antibody of Claim 4, wherein the antibody comprises a heavy chain variable domain having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 18 and a light chain variable domain having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 6.

19. The antibody of Claim 4, wherein the antibody comprises a heavy chain variable domain having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 19 and a light chain variable domain having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 7.

20. An antibody of Claim 4, wherein the antibody comprises a heavy chain variable domain selected from SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28 and SEQ ID NO: 29.

21. An antibody of Claim 4, wherein the antibody comprises a light chain variable domain selected from SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16 and SEQ ID NO: 17.

22. A polypeptide comprising the following amino acid sequence:

X_1VQLVQSGPELKKPGASVKVSCKASGYTFTNYGMNWVRQAPGQGLEWMGWINTYTGETT YADDFKGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCEREGGVX$_2$X$_3$WGQGTLVTVSS (SEQ ID NO: 74), wherein X_1 is Q or E; X_2 is N, A or Q; and X_3 is N, A or Q.

23. A polypeptide comprising the following amino acid sequence: DIQVTQSPSSLSASVGDRVTITCITSTDIDDDX$_4$X$_5$WYQQKPGKVPKLLISGGX$_6$TLRPGVPSRF SGSGSGTDFTLTISSLQPEDVATYYCLQSDSLPYTFGQGTKX$_7$EIK (SEQ ID NO: 73), wherein X_4 is M, L or I; X_5 is N, A or Q; X_6 is N, S or A; and X_7 is L or V.

24. A polypeptide comprising an amino acid sequence selected from the group comprising SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28 and SEQ ID NO: 29.

25. A polypeptide comprising an amino acid sequence selected from the group comprising SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16 and SEQ ID NO: 17.

26. An anti-Factor D antibody comprising the polypeptide of Claim 22.

27. An anti-Factor D antibody comprising the polypeptide of Claim 23.

28. An anti-Factor D antibody comprising the polypeptide of Claim 22 and the polypeptide of Claim 23.

29. The antibody of Claim 4, wherein the antibody comprises a heavy chain variable domain sequence of SEQ ID NO: 18.

30. The antibody of Claim 4, wherein the antibody comprises a heavy chain variable domain sequence of SEQ ID NO: 19.

31. The antibody of Claim 4, wherein the antibody comprises a light chain variable domain sequence of SEQ ID NO: 6.

32. The antibody of Claim 4, wherein the antibody comprises a light chain variable domain sequence of SEQ ID NO: 7.

33. The antibody of Claim 4, wherein the antibody comprises a heavy chain variable domain sequence of SEQ ID NO: 18 and a light chain variable domain sequence of SEQ ID NO: 6.

34. The antibody of Claim 4, wherein the antibody comprises a heavy chain variable domain sequence of SEQ ID NO: 19 and a light chain variable domain sequence of SEQ ID NO: 7.

35. The antibody of Claim 4, wherein the antibody comprises a heavy chain variable domain having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 54.

36. The antibody of Claim 4, wherein the antibody comprises a heavy chain variable domain having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 63.

37. The antibody of Claim 4, wherein the antibody comprises a light chain variable domain having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 47.

38. The antibody of Claim 4, wherein the antibody comprises a light chain variable domain having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 61.

39. The antibody of Claim 4, wherein the antibody comprises a heavy chain variable domain having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 54 and a light chain variable domain having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 47.

40. The antibody of Claim 4, wherein the antibody comprises a heavy chain variable domain having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 63 and a light chain variable domain having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 61.

41. The antibody of Claim 4, wherein the antibody comprises a heavy chain variable domain sequence of SEQ ID NO: 54.

42. The antibody of Claim 4, wherein the antibody comprises a heavy chain variable domain sequence of SEQ ID NO: 63.

43. The antibody of Claim 4, wherein the antibody comprises a light chain variable domain sequence of SEQ ID NO: 47.

44. The antibody of Claim 4, wherein the antibody comprises a light chain variable domain sequence of SEQ ID NO: 61.

45. The antibody of Claim 4, wherein the antibody comprises a heavy chain variable domain sequence of SEQ ID NO: 54 and a light chain variable domain sequence of SEQ ID NO: 47.

46. The antibody of Claim 4, wherein the antibody comprises a heavy chain variable domain sequence of SEQ ID NO: 63 and a light chain variable domain sequence of SEQ ID NO: 61.

47. The polypeptide the comprising the amino acid selected from the group comprising SEQ ID NO: 47 and 61.

48. The polypeptide the comprising the amino acid selected from the group comprising SEQ ID NO: 54 and 63.

49. The antibody of claim 4 or 14-19 or 26-28, wherein the antibody is humanized.

50. The antibody of claim 4 or 14-19 or 26-28, wherein the Factor D is mammalian Factor D.

51. The antibody of claim 50, wherein the Factor D is human Factor D.

52. A polynucleotide encoding an antibody of claim 4 or 14-19 or 26-28.

53. A polynucleotide encoding a polypeptide of claim 22-25 or 47-48.

54. A vector comprising the polynucleotide of Claim 52 or 53.

55. A host cell comprising the vector of claim 54.

56. A host cell of claim 55, wherein the host cell is eukaryotic.

57. A host cell of claim 55, wherein the host cell is a CHO cell.

58. A method of making an anti-Factor D antibody, wherein the method comprises (a) culturing the host cell of claim 56 or 57 under conditions suitable for expression of the polynucleotide encoding the antibody, and (b) isolating the antibody.

59. The antibody of claim 4 or 14-19 or 26-28, wherein the antibody is a monoclonal antibody.

60. The antibody of claim 59, wherein the antibody is an antibody fragment selected from a Fab, Fab'-SH, Fv, scFv, or $(Fab')_2$ fragment.

61. The antibody of claim 59, wherein the antibody is humanized.

62. The antibody of claim 59, which is produced in bacteria.

63. The antibody of claim 59, which is produced in CHO cells.

64. A pharmaceutical formulation comprising the anti-Factor D antibody of claim 59, and a pharmaceutically acceptable diluent, carrier or excipient.

65. An article of manufacture comprising:

(a) the pharmaceutical formulation of claim 64;

(b) a container; and

(c) a package insert or label indicating that the compound can be used to treat a complemented-associated disorder.

66. A kit comprising an antibody of claim 4 or 14-19 or 26-28 and instructions for administering said antibody to treat a complement-associated disorder.

67. A kit of claim 66, wherein the complement-associated disorder is selected from the group comprising ocular diseases.

68. A kit of claim 67, wherein the ocular disease is selected from the group comprising age-related macular degeneration, diaetic retinopathy, choroidal neovascularization (CNV), uveitis, diabetic macular edema, pathological myopia, von Hippel-Lindau disease, histoplasmosis of the eye, Central Retinal Vein Occlusion (CRVO), corneal neovascularization, and retinal neovascularization.

69. A kit of claim 68, wherein the age-related macular degeneration is selected from the group comprising intermediate dry AMD, geographic atrophy and geographic atrophy.

70. A method of treating a complement-associated disorder selected from the group comprising inflammatory disorders.

71. A method of claim 70, wherein the inflammatory disorder is an autoimmune disease.

72. A method of claim 71, wherein the autoimmune disease is selected from the group comprising systemic lupus erythematosus, myasthenia gravis, rheumatoid arthritis, Alzheimer's disease and multiple sclerosis.

73. A method of treating a complement-associated disorder selected from the group comprising ocular diseases.

74. A method of claim 73, wherein the ocular disease is selected from the group comprising age-related macular degeneration, diaetic retinopathy, choroidal neovascularization (CNV), uveitis, diabetic macular edema, pathological myopia, von Hippel-Lindau disease, histoplasmosis of the eye, Central Retinal Vein Occlusion (CRVO), corneal neovascularization, and retinal neovascularization.

75. A method of claim 74, wherein the age-related macular degeneration is selected from the group comprising intermediate dry AMD, geographic atrophy and geographic atrophy.

76. The antibody made by the process of:

(a) culturing a cell expressing an antibody comprising a heavy chain variable domain of any of claims 14-15, 29-30, 35-36 or 41-42 and a light chain variable domain of any of claims 16-17, 31-32, 37-38 or 43-44; and

(b) isolating the antibody from said cultured cell.

Claims:

1. A method for determining the efficacy of an anti-Factor D antibody or an antigen-binding fragment thereof comprising: performing an alternative pathway hemolytic assay and detecting inhibition of alternative pathway hemolysis, wherein a half minimal inhibitory concentration (IC50) value of less than 80 nM of the anti-Factor D antibody or the antigen-binding fragment thereof indicates that the anti-Factor D antibody or the antigen-binding fragment thereof is efficacious; wherein the antibody or the antigen-binding fragment thereof comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises light chain hypervariable region (HVR)-1 comprising ITSTDIDDDMN (SEQ ID NO: 30), light chain HVR-2 comprising GGNTLRP (SEQ ID NO: 35), and light chain HVR-3 comprising LQSDSLPYT (SEQ ID NO: 38), wherein the heavy chain variable domain comprises heavy chain HVR-1 comprising GYTFTNYGMN (SEQ ID NO: 39), heavy chain HVR-2 comprising WINTYTGETTYADDFKG (SEQ ID NO: 40), and heavy chain HVR-3 comprising EGGVNN (SEQ ID NO: 41),

wherein the anti-Factor D antibody or antibody fragment thereof further comprises one or more of the following substitutions (a) to (e):

(a) substitution of the amino acid at position 10 of SEQ ID NO: 30 with L or I;

(b) substitution of the amino acid at position 11 of SEQ ID NO: 30 with A or Q;

(c) substitution of the amino acid at position 3 of SEQ ID NO: 35 with S or A;

(d) substitution of the amino acid at position 5 of SEQ ID NO: 41 with A or Q; or

(e) substitution of the amino acid at position 6 of SEQ ID NO: 41 with A or Q,

and/or the heavy chain variable domain comprises an E at position 1.

2. The method of claim 1, wherein the IC50 of the anti-Factor D antibody or the antigen-binding fragment thereof is less than 30 nM.

3. The method of claim 1, wherein the IC50 of the anti-Factor D antibody or the antigen-

4. The method of claim 1, further comprising measuring the binding affinity of the anti-Factor D antibody or the antigen-binding fragment thereof to Factor D, wherein an affinity value of 0.5 pM or higher of the anti-Factor D antibody or the antigen-binding fragment thereof indicates that the anti-Factor D antibody or the antigen-binding fragment thereof is efficacious.

5. The method of claim 4, wherein the binding affinity of the anti-Factor D antibody or the antigen-binding fragment thereof to Factor D is 1.0 pM or higher.

6. The method of claim 4, wherein the binding affinity of the anti-Factor D antibody or the antigen-binding fragment thereof to Factor D is 1.0 nM or higher.

7. The method of any one of claims 1-6, wherein the anti-Factor D antibody or antigen-binding fragment thereof comprises light chain framework region (FR)-4 comprising FGQGTKLEIK (amino acids 98-107 of SEQ ID NO: 1) or FGQGTKVEIK (SEQ ID NO: 51).

8. The method of any one of claims 1-6, wherein the anti-Factor D antibody or antigen-binding fragment thereof comprises light chain framework region (FR)-4 comprising the amino acid sequence of SEQ ID NO: 51, and wherein the heavy chain variable domain comprises an E at position 1.

9. The method of any one of claims 1-6, wherein:

(i) the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 39;

(ii) the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 40;

(iii) the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44 or SEQ ID NO: 45;

(iv) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 30, SEQ ID NO: 31, SE ID NO: 32, SEQ ID NO: 33 or SEQ ID NO: 34;

(v) the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 35, SEQ ID NO: 36 or SEQ ID NO: 37; and

(vi) the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 38.

10. The method of Claim 9, wherein the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 41.

11. The method of Claim 9, wherein the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 30.

12. The method of Claim 9, wherein the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 35.

13. The method of Claim 9, wherein the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 39, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 40, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 41.

14. The method of Claim 9, wherein the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 30, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 35, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 38.

15. The method of Claim 9, wherein the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 39, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 40, the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 41, the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 30, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 35, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 38.

16. The method of any one of claims 1-6, wherein the heavy chain variable domain has at least 90% sequence identity to an amino acid sequence of SEQ ID NO: 19.

17. The method of any one of claims 1-6, wherein the light chain variable domain has at least 90% sequence identity to an amino acid sequence of SEQ ID NO: 7.

18. The method of any one of claims 1-6, wherein the heavy chain variable domain has at least 90% sequence identity to an amino acid sequence of SEQ ID NO: 19 and the light chain variable domain has at least 90% sequence identity to an amino acid sequence of SEQ ID NO: 7.

19. The method of any one of claims 1-6, wherein the heavy chain variable domain comprises an amino acid sequence selected from SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28 and SEQ ID NO: 29.

20. The method of any one of claims 1-6, wherein the light chain variable domain comprises an amino acid sequence selected from SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, and SEQ ID NO: 14.

21. The method of any one of claims 1-6, wherein the heavy chain variable domain comprises the following amino acid sequence:

X1VQLVQSGPELKKPGASVKVSCKASGYTFTNYGMNWVRQAPGQGLEWMGWINTYTGET TYADDFKGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCEREGGVX2X3WGQGTLVTVSS (SEQ ID NO: 74), wherein X1 is Q or E; X2 is N, A or Q; and X3 is N, A or Q.

22. The method of any one of claims 1-6, wherein the heavy chain variable domain comprises the following amino acid sequence: DIQVTQSPSSLSASVGDRVTITCITSTDIDDDX4X5WYQQKPGKVPKLLISGGX6TLRPGVPS RFSGSGSGTDFTLTISSLQPEDVATYYCLQSDSLPYTFGQGTKX7EIK (SEQ ID NO: 73), wherein X4 is M, L or I; X5 is N, A or Q; X6 is N, S or A; and X7 is L or V.

23. The method of any one of claims 1-6, wherein the heavy chain variable domain comprises an amino acid sequence of SEQ ID NO: 19.

24. The method of any one of claims 1-6, wherein the light chain variable domain comprises an amino acid sequence of SEQ ID NO: 7.

25. The method of any one of claims 1-6, wherein the heavy chain variable domain comprises an amino acid sequence of SEQ ID NO: 19 and the light chain variable domain comprises an amino acid sequence of SEQ ID NO: 7.

26. The method of any one of claims 1-6, wherein the anti-Factor D antibody or antigen-binding fragment thereof comprises a heavy chain having at least 90% sequence identity to an amino acid sequence of SEQ ID NO: 63.

27. The method of any one of claims 1-6, wherein the anti-Factor D antibody or antigen-binding fragment thereof comprises a light chain having at least 90% sequence identity to an amino acid sequence of SEQ ID NO: 61.

28. The method of any one of claims 1-6, wherein the anti-Factor D antibody comprises a heavy chain having at least 90% sequence identity to an amino acid sequence of SEQ ID NO: 63 and a light chain having at least 90% sequence identity to an amino acid sequence of SEQ ID NO: 61.

29. The method of any one of claims 1-6, wherein the anti-Factor D antibody or antigen-binding fragment thereof comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 63.

30. The method of any one of claims 1-6, wherein the anti-Factor D antibody or antigen-binding fragment thereof comprises a light chain comprising an amino acid sequence of SEQ ID NO: 61.

31. The method of any one of claims 1-6, wherein the anti-Factor D antibody or antigen-binding fragment thereof comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 63 and a light chain comprising an amino acid sequence of SEQ ID NO: 61.

32. A method for determining the efficacy of an anti-Factor D antibody or an antigen-binding fragment thereof comprising: performing an alternative pathway hemolytic assay and detecting inhibition of alternative pathway hemolysis, wherein a half minimal inhibitory concentration (IC50) value of less than 80 nM of the anti-Factor D antibody or the antigen-binding fragment thereof indicates that the anti-Factor D antibody or the antigen-binding fragment thereof is efficacious; wherein the antibody or the antigen-binding fragment thereof comprises a light chain variable domain comprising light chain hypervariable region (HVR)-1 comprising ITSTDIDDDMN (SEQ ID NO: 30), light chain HVR-2 comprising GGNTLRP (SEQ ID NO: 35), and light chain HVR-3 comprising LQSDSLPYT (SEQ ID NO: 38), and a heavy chain variable domain comprising HVR-1 comprising GYTFTNYGMN (SEQ ID NO: 39), heavy chain HVR-2 comprising WINTYTGETTYADDFKG (SEQ ID NO: 40), and heavy chain HVR-3 comprising EGGVNN (SEQ ID NO: 41),

wherein the light chain variable domain comprise light chain framework region (FR)-4 comprising FGQGTKVEIK (SEQ ID NO: 51), and wherein the heavy chain variable domain comprises an E at position 1.

33. A method for determining the efficacy of an anti-Factor D antibody or an antigen-binding fragment thereof comprising: performing an alternative pathway hemolytic assay and detecting inhibition of alternative pathway hemolysis, wherein a half minimal inhibitory concentration (IC50) value of less than 80 nM of the anti-Factor D antibody or the antigen-binding fragment thereof indicates that the anti-Factor D antibody or the antigen-binding fragment thereof is efficacious; wherein the antibody or the antigen-binding fragment comprises a heavy chain variable domain comprising an amino acid sequence of SEQ ID NO: 19 and a light chain variable domain comprising an amino acid sequence of SEQ ID NO: 7.

34. A method for determining the efficacy of an anti-Factor D antibody or an antigen-binding fragment thereof comprising: performing an alternative pathway hemolytic assay and detecting inhibition of alternative pathway hemolysis, wherein a half minimal inhibitory concentration (IC50) value of less than 80 nM of the anti-Factor D antibody or the antigen-binding fragment thereof indicates that the anti-Factor D antibody or the antigen-binding fragment thereof is efficacious; wherein the antibody or the antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 63 and a light chain comprising an amino acid sequence of SEQ ID NO: 61.

35. The method of any one of claims 32-34, wherein the IC50 of the anti-Factor D antibody or the antigen-binding fragment thereof is less than 30 nM.

36. The method of any one of claims 32-34, wherein the IC50 of the anti-Factor D antibody

37. The method of any one of claims 32-34, further comprising measuring the binding affinity of the anti-Factor D antibody or the antigen-binding fragment thereof to Factor D, wherein an affinity value of 0.5 pM or higher of the anti-Factor D antibody or the antigen-binding fragment thereof indicates that the anti-Factor D antibody or the antigen-binding fragment thereof is efficacious.

38. The method of any one of claims 32-34, wherein the binding affinity of the anti-Factor D antibody or the antigen-binding fragment thereof to Factor D is 1.0 pM or higher.

39. The method of any one of claims 32-34, wherein the binding affinity of the anti-Factor D antibody or the antigen-binding fragment thereof to Factor D is 1.0 nM or higher.

40. The method of any one of claims 1-39, wherein the antibody is monoclonal.

41. The method of any one of claims 1-39, wherein the antibody is humanized.

42. The method of any one of claims 1-39, wherein the antibody fragment is a Fab, Fab'-SH, Fv, scFv, or (Fab')2 fragment.

43. The method of any one of claims 1-39, wherein the Factor D is mammalian Factor D.

44. The method of claim 43, wherein the Factor D is human Factor D.